INTEGRATIVE ONCOLOGY 4.0:
A DIGITAL ECOSYSTEM FOR VALUE-BASED SARCOMA CARE

OVERVIEW

The Swiss Sarcoma Network (SSN), was established in December 2018 with a steadfast commitment to elevating the quality of sarcoma care. Grounded in the principles of the sustainable healthcare triad -clinical metrics, quality & outcome, and costs- SSN operates under the banner of "Integrative Oncology 4.0: A Digital Ecosystem for Value-Based Sarcoma Care," to revolutionize the landscape of oncology through cutting-edge technology and transdisciplinary collaboration.

VISION

SSN envisions a future where sarcoma precision medicine is not just a concept but a lived reality. Leveraging the power of digital twinning, our vision is to create a healthcare paradigm where treatment is as individualized as the patients we serve.

MISSION

Our mission is to cultivate a culture of transdisciplinary and interinstitutional quality care for sarcoma patients. We extend an open invitation to all institutions and physicians who are willing to share data, insights, and expertise in the pursuit of this mission.

MEANS

To achieve our goals, SSN employs a multi-faceted approach grounded in the principles of Value-Based Health Care:

1. ***Integrated Practice Units (IPUs):*** As a cornerstone of our organizational structure, IPUs facilitate transdisciplinary collaboration and streamline patient care pathways.
2. ***Weekly MDT/SB Tumor Conference:*** A platform for experts within the IPU to discuss and strategize patient-specific treatment plans.
3. ***Prospective RWTD/E Data Warehouse/-Lake (Sarconnector):*** Our digital backbone that stores, analyzes, and interprets data, serving as the foundation for our digital twinning and predictive meta-level analytics capabilities.
4. ***Global Webinar Forum***: accessible at www.sarcoma.academy, this educational platform disseminates the best practices and latest research in sarcoma care to a global audience.
5. ***Quality Metrics and Outcome Measures***: Standardized metrics that evaluate not just clinical outcomes but also cost-efficiency and quality of care, thus covering the sustainable healthcare triad and reenforcing our commitment to evidence-based, value-driven healthcare.

By integrating these elements, SSN aims to create a synergistic ecosystem that puts quality and value at the forefront of sarcoma care.

The following summarizes the academic contributions which were made to date:

1. Value-Based Sarcoma Care Metrics (VBSCM)

Papers in this category delve into the development, validation, and application of metrics that are designed to evaluate the quality, effectiveness, and cost-efficiency of sarcoma care. These metrics serve as tools for healthcare providers to measure and improve patient outcomes while optimizing resource allocation.

2. Digital Twinning & Predictive Analytics (DTPA)

This category includes papers that explore the integration of advanced technologies such as Artificial Intelligence, Machine Learning, and digital interoperable platforms, the Sarconnector, in sarcoma care. These technologies are aimed at creating a more personalized and predictive approach to treatment, aligning with the concept of "digital twinning."

3. Transdisciplinary Sarcoma Care (TSC)

Papers under this category emphasize the critical role of interdisciplinary or transdisciplinary teams in sarcoma care. They advocate for the integration of various medical specialties to form a cohesive unit that can address the complex needs of sarcoma patients more effectively.

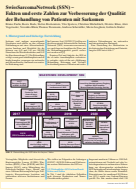
4. Health Service Research & Policy (HSRP)

This category focuses on the discussion of the broader healthcare system, policy implications, or service delivery models. These papers aim to identify gaps, challenges, and opportunities in the existing healthcare infrastructure and propose solutions that can elevate the standard of sarcoma care.

5. Educational Outreach & Global Collaboration (EOGC)

This category highlights educational initiatives and global collaborations, extending beyond academic papers to include interactive webinars. These webinars, available on Sarcoma Academy and its YouTube Channel, feature global experts and come in two types: Multidisciplinary Webinars (MDT) for interdisciplinary discussions, and Focus Webinars for specialized topics. Paper 13, although detailed in Category 2, also fits here due to its focus on digital health and AI's educational potential in sarcoma care.

Nr.	Title	Year/ Journal	Brief Summary of Key Findings	Link
1	**Swiss Sarcoma Network (SSN)**	2019 SwissKnife	The paper focuses on the quality of care for patients with soft tissue sarcomas, emphasizing the importance of interdisciplinary and inter-institutional collaboration. It introduces the Swiss Sarcoma Network's (SSN) telemedicine-based sarcoma board, which aims to enhance expert exposure to sarcoma cases and improve patient management. The paper also discusses the critical role of accurate histopathological diagnosis and critiques existing data registries for their limitations, advocating for better data management through the SSN's Swiss Sarcoma Registry. Overall, the paper aims to improve sarcoma treatment through quality assurance, expert collaboration, and effective data management.	SSN 

2	**Quality assurance in the treatment of sarcoma: an interdisciplinary and interinstitutional challenge**	2019 Schweizer Krebsbulletin	The editorial discusses the challenges of ensuring quality in the treatment of sarcomas, a rare disease requiring interdisciplinary and interinstitutional collaboration. It debates the merits of centralizing treatment in a single, high-volume center versus establishing a network of smaller centers. The editorial advocates for a Quality Management System (QMS) and highlights the Swiss Sarcoma Network (SSN) as an example that aims to centralize expertise and ensure quality and transparency. It also emphasizes the need for real-time data collection and international collaboration to improve treatment quality.	Quality assurance 
3	**SSN – Facts and first figures to improve quality in the treatment of patients with sarcoma**	2021 LAZ	The article discusses the Swiss Sarcoma Network (SSN), a transdisciplinary initiative aimed at improving the quality of care for patients with sarcomas. It provides an overview of the SSN's activities, milestones, and quality indicators. The SSN has established a weekly Sarcoma Board where cases are discussed, and it has also set up a real-world-time data registry. The article emphasizes the importance of accurate diagnosis and timely treatment, highlighting the challenges and pitfalls, such as "Whoops Operations," where a sarcoma is unexpectedly found after unplanned surgery without prior imaging. The SSN aims to standardize care through quality indicators and to foster education and research in the field.	SSN milestones 
4	**Unlocking the Power of Benchmarking: Real-World-Time Data Analysis for Enhanced Sarcoma Patients Outcome**	2023 Cancers	The paper focuses on the utilization of benchmarking and Real-World-Time harmonized data to improve outcomes for sarcoma patients, emphasizing the transition to a value-based care model. It introduces Sarconnector® as a tool for this transition. The paper also discusses the role of chemotherapy and biopsy in sarcoma treatment, highlighting the potential for enhanced, personalized care through real-world-time (meta-) data analysis.	Benchmarking sarcoma care 
5	**Definition of the surgical case complexity in the treatment of soft tissue tumors of the extremities and trunk.**	2022 Cancers	The study introduces a Soft Tissue Tumor Surgery Complexity Score (STS-SCS) aimed at categorizing the complexity of soft tissue tumor surgeries. Applied to a sample of 711 patients, the STS-SCS was effective in stratifying surgeries into four complexity categories. The score aligns with Porter's model of value-based healthcare, potentially enabling better patient allocation to appropriate treatment centers. The study also opens the door for using STS-SCS as a quality indicator in sarcoma surgery.	Surgical complexity STS 
6	**Definition of surgical case complexity in the treatment of bone tumors**	2024 submission	The paper introduces the Bone Tumor Surgery Complexity Score (BT-SCS) and applies it to a cohort of 501 patients undergoing bone tumor surgeries. The BT-SCS aims to quantify surgical complexity based on various factors, enabling efficient healthcare resource allocation and potentially improving treatment quality.	Surgical complexity bone
7	**Enhancing Healthcare for Sarcoma Patients: Lessons from a Diagnostic Pathway Efficiency Analysis**	2023 Cancers	The study fills a significant gap in the literature by examining the total interval for diagnosing mesenchymal tumors, including benign types. It identifies patient interval and secondary care interval as the most significant contributors to the total diagnostic pathway. The study also highlights the role of age, tumor grade, and localization in affecting these intervals. Despite Switzerland's efficient healthcare system, the study suggests that there is room for improvement, particularly in the structure of the	Diagnostic Pathway 

			healthcare system and the multidisciplinary approach required for diagnosing sarcomas.	
8	**Benchmarking Time-to-Treatment Initiation in Sarcoma Care Using Real-World-Time Data**	2023 Cancers	The paper presents a detailed study on the time-to-treatment initiation (TTI) for sarcoma patients. Utilizing data from 266 cases from the Swiss Sarcoma Network, the study reveals a median TTI of 30 days across the cohort. It finds that the length of TTI varies significantly depending on sarcoma type and care institution. The study emphasizes the use of real-world-time data (RWTD) for a more comprehensive capture of patient journeys. It highlights the need for standardized processes across treatment centers and advocates for selective referral to specialized centers. The study identifies significant delays in TTI, particularly in unplanned 'whoops'-resections, underscoring the importance of early specialist referral. The findings are critical for developing healthcare systems that focus on delivering value-based care.	TTI
9	**Exploring Risk Factors for Predicting Clavien-Dindo Complications in Sarcoma Surgery**	2024 Cancers	The paper aims to establish benchmarks for complication rates in sarcoma surgery and identify significant risk factors for postoperative complications. It found that ASA 3 status, bone tumors, presence of metastasis, and the number of erythrocyte concentrates administered were significant predictors of complications. However, the Charlson Comorbidity Index (CCI) was not associated with complications. The study also provides actionable clinical recommendations and acknowledges its limitations, calling for further research.	Risk Factors
10	**SSN – Activities and first results**	2022 LAZ	The article discusses the importance of a multidisciplinary approach in the diagnosis and treatment of sarcomatous diseases. It cites data from international sarcoma networks to show that such an approach significantly improves patient outcomes. The Swiss Sarcoma Network (SSN) is highlighted as a key player in Switzerland for providing comprehensive care for sarcoma patients. The article also updates the key figures and first outcome data based on SSN's documentation over the last four years. Quality indicators for effective sarcoma management are also discussed. The article serves as a comprehensive guide for professionals and offers contact information for further consultations.	SSN activities 
11	**Transdisciplinary Sarcoma Care: a Model for sustainable healthcare transformation**	2024 Swiss Medical Weekly	The paper addresses the urgent challenges facing healthcare organizations, such as labor shortages and financial constraints. It introduces the concept of a sustainable healthcare triad, which aims to align clinical care, quality measures, and cost efficiency. Sarcoma care is presented as a model system that requires a transdisciplinary approach for optimal patient outcomes. The paper also discusses the importance of physician-based metrics and patient-reported outcome measures (PROMs) in assessing and improving healthcare quality. An interoperable digital platform is emphasized for real-time data collection and evidence analytics. The paper concludes by outlining the need for the healthcare industry to evolve and adapt, with a focus on digital transformation.	Sustainable healthcare triad

12	**Pioneering Precision Medicine: Benchmarking RWT-Evidence-Based Insights to Revolutionize Sarcoma Care – The SwissSarcomaNetwork (SSN)**	2023 SwissKnife	The manuscript provides a comprehensive roadmap for revolutionizing sarcoma care through the integration of precision medicine. It emphasizes a multidisciplinary, data-driven approach and discusses the roles of interoperable digital platforms, automated analysis, benchmarking, and value-based healthcare. The paper also introduces innovative concepts like predictive AI/ML modeling and digital twins to further enhance patient outcomes. Overall, it offers a promising vision for the future of sarcoma care, grounded in data-driven methodologies and continuous improvement loops.	Pioneering Precision Medicine
13	**How is sarcoma surgery developing?**	2021 Leading Opinion Ortho&Rhe	The paper from the Swiss Sarcoma Network discusses the complexities and challenges in sarcoma surgery. It emphasizes the critical role of achieving an R0 resection, where the tumor is microscopically completely removed, as no other therapy can compensate for an inadequate resection. The paper also highlights the problem of unplanned resections, known as "Whoops" operations, which account for about 20% of all sarcoma cases and often lead to inadequate treatment and worse prognoses. To address these challenges, the paper advocates for a transdisciplinary approach, forming Sarcoma Competence Teams. It also stresses the importance of comprehensive registers for quality control and outcome measurement, including patient-reported outcome measures (PROM).	sarcoma surgery 
14	**The Next Frontier in Sarcoma Care: Digital Health, AI, and the Quest for Precision Medicine.**	2023 J Personalized Med	This paper discusses the transformative potential of digital health and AI in advancing sarcoma care towards a value-based healthcare model. It introduces the concept of a "Sarcoma Digital Twin," a comprehensive digital avatar of a patient's medical profile, which can be used for predictive modeling and treatment optimization. While acknowledging the challenges in terms of ethics, regulation, and practical implementation, the paper calls for a multidisciplinary approach to seize this transformative opportunity.	Digital Health 
15	**Development of a value-based healthcare delivery model for sarcoma patients**	2021 Swiss Medical Weekly	This article addresses the urgent need to restructure healthcare delivery to control rising costs. It proposes the implementation of a Value-Based Healthcare Delivery (VBHCD) model, particularly focusing on sarcoma, a rare and complex disease. The authors argue for the establishment of Integrated Practice Units (IPUs) that are organized around the medical condition and involve a transdisciplinary team. A key component for the success of VBHC is an integrated information technology platform that allows for real-time data sharing, quality assessment, and ultimately cost-saving. The article also discusses the challenges in implementing this model, such as the current siloed healthcare systems and issues with reimbursement. However, it highlights the opportunities presented by digital platforms to overcome these challenges. In the Swiss context, efforts are already underway to implement this model through the Swiss Sarcoma Network, aiming to make VBHC a reality.	VBHC & sarcoma care 

16	**Quality of sarcoma care: longitudinal real-time assessment and evidence analytics of quality indicators**	2022 Cancers	The paper discusses the development of an interoperable digital platform aimed at enhancing the quality of sarcoma care. It emphasizes the importance of international collaboration and introduces real-time assessment of quality indicators throughout the entire care cycle. The platform is designed to strengthen the collaboration of Integrated Practice Units (IPUs) and aims to pave the way for precision medicine and Value-Based Health Care (VBHC) in treating complex diseases like sarcoma. Overall, the paper advocates for a data-driven, collaborative approach to improve patient outcomes.	quality indicators 
17	**Time and accuracy to establish the diagnosis of soft tissue tumors: a comparative analysis from the SSN**	2022 Sarcoma	The study conducted by the Swiss Sarcoma Network analyzed the time and accuracy of diagnosing soft tissue tumors in two different institutions with varying workflows. The study found that 77.6% of diagnoses were concordant between local and reference pathologists. Institution B, where diagnoses were directly performed by a reference pathologist, had a significantly shorter time to diagnosis (3.3 working days) compared to Institution A (4.7 working days). The study emphasizes the importance of expert review in sarcoma diagnosis and recommends direct analysis by experts for quicker and more accurate results.	time and accuracy of sarcoma diagnosis 
18	**How is the spectrum of sarcoma surgery assessed?**	2023 Cancers	The paper presents a comprehensive study on sarcoma care over a 10-year period, involving 3130 patients and 5930 sarcoma board decisions from one sarcoma surgeon. It introduces an interoperable digital platform for structured surgical data collection and emphasizes the need for a multidisciplinary approach in sarcoma care. The study also critiques the limitations of volume-based metrics for assessing surgical quality and advocates for data harmonization and a nuanced, data-driven approach to meet the challenges of precision medicine.	Spectrum of sarcoma surgery 
19	**Real-time interactive analysis of the treatment quality of sarcoma patients**	2022 Info@onco-suisse	The text emphasizes the complexities of treating sarcomas, a rare but molecularly diverse form of cancer. It highlights the need for a transdisciplinary approach and the challenges posed by the lack of real-time, patient-defined data. The article suggests that digital transformation, particularly in data collection and predictive analytics, could significantly advance sarcoma treatment. It also touches on the potential for these technologies to facilitate a shift towards value-based healthcare. This interoperable platform was awarded the German Medical Award in 2021.	Real-time interactive analysis 
20	**The sarcoma-specific instrument to longitudinally assess health-related outcomes of the routine care cycle**	2023 Diagnostics	This paper emphasizes the urgent need for a sarcoma-specific HRQoL instrument due to the disease's complexity. It proposes a novel approach that utilizes a sum of established generic PROMs, tailored to the patient's longitudinal care cycle. This allows for broader comparison and benchmarking. The paper introduces an interoperable digital platform to manage the large volume of data generated, aiming for real-world-time analytics and predictive modeling. The platform is designed to be an integral part of an institutional electronic health record (EHR) system, paving the way for value-based healthcare. The paper acknowledges the challenges in implementation and emphasizes the need for a new ecosystem of data management, facilitated by digital transformation.	Interoperable platform & HRQoL instrument 

21	**Biopsy ratio of suspected to confirmed sarcoma diagnosis**	2022 Cancers	The paper presents a comprehensive analysis of 950 consecutive biopsies performed for suspected sarcoma over a 3.2-year period. It introduces the concept of the Ratio of Malignancy in Suspicious Tumors (RMST) as a potential quality indicator for sarcoma care. The study emphasizes the need for standardized definitions and categories for better comparison among multidisciplinary teams and suggests that RMST could help in reducing the rate of unplanned resections.	biopsy ratio 

Swiss Sarcoma Network (SSN)

Wie stellen wir die Behandlungsqualität für unsere Sarkompatienten sicher?

Bruno Fuchs, Chefarzt Sarkomchirurgie, Chair SwissSarcomaNetwork, Kantonsspital Winterthur, Kantonsspital Luzern, Universitätsspital und Universitätskinderspital Zürich
fuchs@sarcoma.surgery
Gabriela Studer, Chefärztin Radio-Onkologie, Luzerner Kantonsspital, gabriela.studer@luks.ch
Beata Bode, Leitende Ärztin Institut für Pathologie und Molekularpathologie USZ, beata.bode@patho.ch
Stefan Breitenstein, Direktor Departement Chirurgie, Kantonsspital Winterthur, Präsident Trägerverein SwissSarcomaNetwork, stefan.breitenstein@ksw.ch


Bruno Fuchs


Gabriela Studer


Beata Bode


Stefan Breitenstein

Sarkome sind seltene Tumore, die biologisch durch mehr als 100 verschiedene Entitäten und deren Varianten definiert werden. Sie erfordern eine multidisziplinäre Abklärung und Behandlung. Der Behandlungserfolg wird beeinträchtigt durch ungeplante Resektionen, mangelnde Koordination im Management der Patienten bzw. im weiteren Verlauf durch die Entwicklung von Metastasen.

Eine Hauptursache für die eingeschränkten Erfolgsaussichten liegt in der heutigen Art unserer Medizin, die mit zunehmender Spezialisierung immer mehr Disziplinen-orientiert, weniger Problem-fokussiert agiert. Jede Disziplin oder Fachperson beschränkt sich vornehmlich auf den eigenen Fachbereich, wobei der entsprechende Beitrag ohne interdisziplinäre Vorabsprachen (Tumorkonferenzen) nicht Teil einer komplexen Strategie wird. Dies mag erklären, weshalb wir uns schwertun, interdisziplinäre Daten auch zu erfassen. Hierfür müssten wir eine gemeinsame, Disziplinen-unabhängige Sprache entwickeln und definieren. Ohne ein solches Vorgehen werden wir auch weiterhin keine zuverlässigen Vergleiche anstellen können, weder auf nationaler noch auf internationaler Ebene, weiterhin nicht wissen, wie viele Sarkompatienten wie und wo mit welchem Resultat behandelt werden. In dieser Situation ist nun der HSM-Entscheid anstehend. Die Gefahr diesbezüglich besteht darin, dass durch den Kampf um Fall-Zahlen einzelner Institutionen – statt durch interdisziplinäre Konzepte/Prozesse und Quantifizierung von Resultaten – Konkurrenz, monopolistisches und monodisziplinäres Denken noch mehr gefördert werden.

Ausgangslage

Die Grundlage des Erfolges liegt in der gelebten Interdisziplinarität, sowohl innerhalb einer Institution als auch zwischen den Institutionen, mit einem Austausch auf Augenhöhe, bestimmt durch das Experten-Wissen und nicht durch blosses Zahlen-Denken. Die Organisation nimmt dabei eine kritische Rolle ein. Grundsätzlich stehen alternativ das «Netzwerk of Excellence» oder aber das «Center of Excellence» zur Diskussion, wobei man über die jeweiligen Vor- und Nachteile sicher geteilter Meinung sein kann. Weil im Rahmen der Abklärung das Verhältnis von Sarkomverdacht zu Sarkomdiagnose 5:1 beträgt, und weil ungeplante Resektionen ((20% aller Sarkomdiagnosen werden durch die sogenannten whoops! («unintended resections»)-Operationen gestellt)) weiterhin ein ungelöstes Problem darstellen, wird es illusorisch sein, alle Patienten mit einem Verdacht auf ein Sarkom an einem geografischen Ort zu zentralisieren. Abgesehen von der fehlenden Infrastruktur, die eine solche Patientenmenge z. B. für die Deutschschweiz aufnehmen könnte, und abgesehen davon, dass die wenigsten Patienten gewillt sind, nur schon für eine Biopsie die Stadt zu wechseln. Auch deshalb ist in der Schweiz ein starkes Netzwerk von grosser Bedeutung.

Das Ziel des Swiss Sarcoma Networks (SSN) ist es, Sarkom-Experten aller Disziplinen und aller Institutionen zusammenzubringen, um eine gemeinsame Sprache zu definieren, das diagnostische und therapeutische Vorgehen aller Patienten initial gemeinsam zu besprechen und die Daten nach definierten Qualitätskriterien in einer gemeinsamen Datenbank zu erfassen. Hierbei kann sich jede Institution beteiligen, sofern sie bereit ist, die Patienten mit muskuloskelettalen Tumoren im Rahmen des gemeinsamen Sarkomboardes zu besprechen und die Patientendaten zu registrieren.

Definition interdisziplinärer Qualitätsindikatoren

Das SSN hat in seiner Inaugurationssitzung 2018 diese Qualitätsindikatoren definiert. Sie basieren auf genauen histopathologischen Diagnosen mit Aufschlüsselung, wie viele Tumore gutartig, intermediär oder bösartig sind. Es wird erfasst, wie viele primäre Fälle mit oder ohne Vorbehandlung besprochen werden, bei wie vielen Patienten ungeplante Operationen stattgefunden haben, wie hoch die Lokalrezidiv- und Metastasierungsraten sind, ob die Biopsie durch ein multidisziplinäres Team erfolgte, ob die Gewebe-Analyse durch einen Pathologie-Experten erfolgte und zu welchem Zeitpunkt im Krankheitsverlauf die Vorstellung am Sarkomboard stattfand. Zu jedem Abklärungs- und Behandlungsschritt werden die Disziplin, Art der Ausführung und allfällige Komplikationen erfasst. Selbstverständlich ist diese Liste bei Bedarf beliebig erweiterbar.

Gemeinsames inter-institutionelles telemedizinisches Sarkomboard

Das SSN organisiert jeden Dienstag um 17 Uhr ein interdisziplinäres Sarkomboard, welches telemedizinisch via ActVisual® übertragen wird. Dabei werden alle konsekutiven Patienten aller teilnehmenden Institutionen vorgestellt und diskutiert. Gäste können sich leicht via Computer oder Smartphone selber einloggen und so persönlich teilnehmen. Patienten-Vorstellungen auch anderer, derzeit nicht beteiligter Spitäler sind willkommen. Der grösste Vorteil dieser überregionalen Strategie liegt darin, dass durch dieses telemedizinisch übertragene Sarkomboard die Exposition von Experten zu Sarkomdiagnosen und Herausforderungen des Patienten-Managements maximiert werden kann, wodurch die Expertise jedes einzelnen gesteigert wird, unabhängig von der einzelnen Institution.

Pathologie-Review

Die korrekte histopathologische Diagnose durch die Pathologie ist die Basis, um einem Patienten die optimalen Voraussetzungen für die Behandlung und damit die optimale Überlebensrate zu ermöglichen. Das Pathologie-Expertenwissen ist abhängig vom Fallumfang. Das SSN fördert durch den Austausch unter den Pathologen nicht nur die Exposition, sondern auch die Qualität der Diagnosestellung. Im Rahmen der «Swiss Working Group on Sarcomas» der Schweizerischen Gesellschaft für Pathologie unter der Leitung von Prof. Beata Bode werden die Sarkomdiagnosen in einem consensus-read-out reviewed. Wird keine Einigung erzielt, werden internationale Experten beigezogen. So wird einerseits sichergestellt, dass alle Sarkomdiagnosen einem Expertenreview unterzogen werden, zugleich aber wird auch das Expertenwissen unter den Pathologen gefördert.

Etablierung eines Quality Management Systems (QMS)

Die richtige Diagnose und das korrekte Durchführen einer oft multimodalen Therapie bzw. deren bestmögliche Sequenz für den einzelnen Patienten sind zentrale Pfeiler in jeder Sarkombehandlung. Der zeitlich zielgerichtete Ablauf wird häufig durch infrastrukturelle und logistische Gegebenheiten ungünstig beeinflusst – ein im Alltag oft gesehenes Problem, bislang ohne Quantifizierung/Datenerfassung für die Schweiz. Die zeitlich effiziente Abfolge der Teilschritte ist zentral für den Patienten bzw. seine Prognose. Die zeitlichen Kenndaten gehören genauso wie die vorgenannten Parameter zu den Qualitäts-definierenden Grössen einer Sarkombehandlung.

Register

Wenn die Qualität in Diagnostik und Therapie von Sarkompatienten verbessert werden soll, ist die Datenerfassung die Basis im Sinne einer conditio sine qua non. Register haben häufig den Nachteil, dass sie nicht koordiniert und abgestimmt sind, dass zu viel oder zu wenig Parameter erfasst werden und vor allem, dass systematisch inkorrekte Daten erfasst werden. So erlaubt die ICD-Kodierung keine korrekte Abbildung aller Sarkomdiagnosen, wodurch sich viele Register bereits selber limitieren. Zudem werden die Daten häufig von Datenmanagern eingegeben, die an der Sarkombehandlung unbeteiligt sind und Details nicht verstehen können. Wenn z. B. die Diagnose oder der chirurgische Margin Status nicht sauber definiert werden, kann ein Datenmanager nur inkorrekte Daten eingeben, wodurch ein solches Register die eigentlichen Ansprüche nicht erfüllen wird. Das SSN koppelt deswegen die Informationen des Registers (SwissSarcomaRegistry) mit jenen der Anmeldung für das Sarkomboard, bei welcher alle relevanten Informationen zusammengefasst werden. Eine erste Qualitätskontrolle der Daten kann so bereits am Sarkomboard erfolgen. Das SwissSarcomaRegistry wird von Adjumed bereitgestellt, eine Firma mit 25-jähriger Erfahrung für Qualitätserfassung im Medizinbereich. Das Register ist international abgestimmt mit dem aktuell grössten existierenden Register weltweit. Die französischen Kollegen erstellten ihr Register 2010, haben seither > 60000 Sarkompatienten erfasst. Durch den Abgleich mit diesem französischen Register wird es uns möglich, Daten aus der Schweiz direkt mit jenen aus Frankreich auf internationaler Ebene zu vergleichen.

Internationaler Austausch

Die Rarität der Sarkomdiagnosen in der Schweiz erlaubt es uns nicht, unseren eigenen Weg unabhängig von internationalem Expertenwissen (Internationales Advisory Board) zu gehen, wenn wir optimale Qualität für unsere Patienten anbieten wollen. Zu diesem Zweck baut das SSN auf internationale Kollaborationen, vornehmlich mit den Experten aus Frankreich, Spanien und Italien, welche alle dieselbe Absicht verfolgen: Qualität zu definieren, zu dokumentieren und zu analysieren. Somit wird sichergestellt, dass die Sarkombehandlung in der Schweiz nach internationalem Top-Standard erfolgt und weiter ausgebaut werden kann. Im Rahmen eines solchen International Advisory Boards stehen internationale Experten jederzeit zur Verfügung für Diskussionen anspruchsvoller Situationen in der täglichen Patientenbehandlung, unterstützen mit ihrer Expertise Aufbau und Analyse des Registers und stehen uns für die Aus- und Weiterbildung zur Verfügung.

Weiter- und Fortbildung

Damit sich das SSN mit seinem Hauptziel, Qualität zu fördern, weiter entwickeln kann, sind Lehre, Weiter- und Fortbildung und damit der internationale Austausch unabdingbar. Das SSN organisiert viermal jährlich eine Fortbildungsveranstaltung (jeweils Freitagnachmittag am Ende jedes Quartals, Gliederung in Übersichtsvortrag mit Information zum aktuellen Status der nationalen Register, Fallvorstellungen, und es sollen Themata aus dem Bereich «ungelöste Probleme» (zum Beispiel: Wie wird ein chirurgischer Margin definiert?) adressiert werden, wobei im Anschluss an die Einführung ins Thema ein Consensus erarbeitet wird.

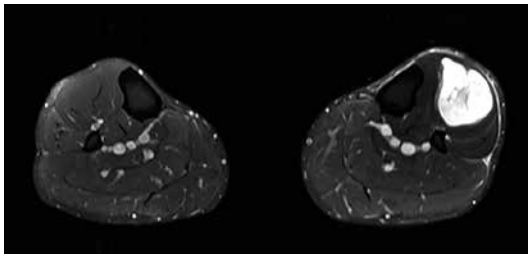
Des Weiteren wird im Mai 2020 das nächste SwissSarcomaSymposium in Luzern stattfinden nebst Exponenten des Internationalen Advisory Board des SSN im Beisein auch von Sarkomexperten aus der Mayo Clinic, USA sowie der IVINS society.

Schlussfolgerungen:

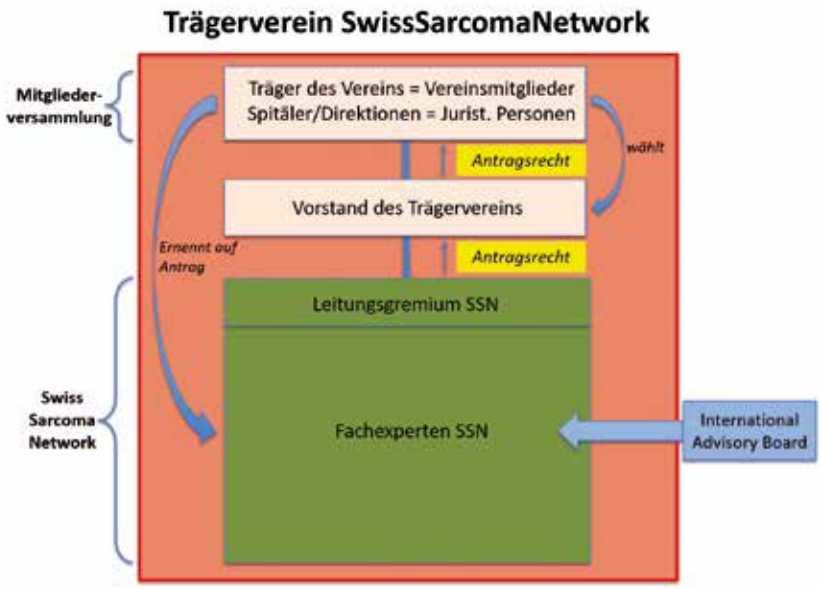
Wir müssen uns lösen von herkömmlichen Fach- und Institutions-zentrierten Dogmen und Verhaltensweisen und alles daransetzen, die interdisziplinäre und interinstitutionelle Zusammenarbeit maximal zu fördern. Die erforderliche Interdisziplinarität wird vor allem durch einen aktiven Austausch zwischen den Experten in verschiedenen Institutionen gefördert, basierend auf gemeinsam definierten inhaltlichen Verbindlichkeiten. Es müssen Strukturen geschaffen werden, die eine interdisziplinäre und interinstitutionelle Gemeinsamkeit fördern, mit gemeinsamen Kriterien. Es muss bewusst(er) werden, dass nicht allein Operations- bzw. Fall-Zahlen Qualität garantieren, da der Schweregrad einer Operation diametral unterschiedlich sein kann und derzeit nicht definiert ist. Die alleinige Orientierung an Operationszahlen kann suboptimale Behandlungen fördern und interdisziplinäre Ansätze verhindern. Die Erfassung interdisziplinär definierter Qualitätsparameter in einem Register mit internationalem Abgleich dürfte wegweisend bzw. zukunftsfähig sein. Es wäre für alle Beteiligten sehr erstrebenswert, wenn das HSM-Fachorgan die Entscheide betreffend Organisation und Management der Sarkome in Zukunft auf sachbasierten, transparenten und einheitlich erfassten Qualitätsindikatoren treffen könnte.

Das SSN stellt eine solche gemeinsame transparente Basis dar, bei der jede Institution und jeder Sarkomexperte in der Schweiz teilnehmen und beitragen kann, sofern die Bereitschaft für die verbindlichen Qualitätsparameter (initiale Sarkomboard-Präsentation aller Primärfälle, Dateneingabe im gemeinsamen Register) besteht.

Weitergehende Informationen unter www.swiss-sarcoma.net



MRI eines Patienten mit Weichteilsarkom im Bereich des Oberschenkels.



Struktur Trägerverein SwissSarcomaNetwork. Die Vereinsmitglieder sind Spitäler/Institutionen, welche Sarkomexperten aus verschiedenen Fachrichtungen ins SwissSarcomaNetwork delegieren.

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Qualitätssicherung in der Behandlung von Sarkomen: Eine interdisziplinäre und interinstitutionelle Herausforderung

Seit jüngerer Zeit rückt die Behandlungsqualität richtigerweise immer mehr in den Fokus des öffentlichen Interesses, obwohl sie für jeden Mediziner spätestens nach der Ausbildung eigentlich die grösste Selbstverständlichkeit darstellt. Eine mögliche Erklärung für diese erhöhte Aufmerksamkeit liegt unter anderem auch darin, dass wir uns der Qualität zwar verpflichtet fühlen, uns aber schwer tun, diese zu definieren und strukturiert zu erfassen. Dies wird besonders offensichtlich bei selteneren Krankheiten wie den Sarkomen, deren Behandlung den Einbezug diverser Disziplinen und Spezialisten oft auch inter-institutionell erfordert, bzw. bei deren Behandlung Expertenwissen und infrastrukturelle Gegebenheiten eine zentrale Rolle spielen.

In den letzten Jahren widmete sich eine Vielzahl von Publikationen den Fragen, welche rund um das Thema Behandlungsqualität und Spezialisierung auftraten (www.sarcoma.surgery → wie finde ich den richtigen Spezialisten?). Insbesondere wird die Definition der Qualität in den Vordergrund gestellt. Basierend auf diversen Studien ist bei Sarkompatienten, die an einem Hochvolumenzentrum/-Netzwerk behandelt wurden, ein besseres Outcome nachgewiesen, auch wenn Letzteres lediglich mit 20 Patienten pro Jahr als Cutoff definiert wird [1-4]. Eine detaillierte Analyse mit grösserem Volumen und demzufolge aussagekräftigen Aussagen existiert in der Sarkomliteratur aber nicht. Zumal das Volumen nur einen von vielen Parametern darstellt. Mindestens so wichtig erscheint die Entwicklung weg vom Disziplinendenken hin zum problemzentrierten Denken. Da die Chirurgie als Hauptpfeiler in der Sarkom-Behandlung für das Outcome zentral ist, steht der Sarkomchirurge im Fokus. In Amerika führen 83% der Sarkomchirurgen 10-30 Operationen für Knochensarkome und 69% 10-50 Operationen für Weichteilsarkome pro Jahr durch [5]. Bezeichnenderweise definieren die Editoren des Annals of Surgical Oncology den Surgical Oncologist nicht über Operationszahlen, sondern über dessen – nebst natürlich technischem – onkologisches Verständnis, dargelegt durch entsprechende Aus- und Weiterbildungen [6]. Es wurde auch gezeigt, dass nicht die Anzahl Operationen für die Qualität entscheidend ist, sondern vielmehr, ob nach den Richtlinien der Sarkomchirurgie operiert wird, was wiederum mit entsprechender Aus- und Weiterbildungen einhergeht [7].

Die Schweiz mit zurzeit zirka 8.4 Millionen Einwohnern würde nach internationalen Massstäben das Volumen für ein einziges, landesweites Sarkomzentrum bieten. Da dies aus diversen Gründen schwierig umzusetzen ist, stehen wir vor der Frage, ob es zielführend ist, mehrere solche Zentren zu unterhalten, die unabhängig voneinander mit entsprechend kleinen Volumina agieren oder ob eine gemeinsame Basis im Sinne eines überregionalen Netzwerkes auf nationaler Ebene angestrebt werden soll, in dem alle relevanten Informationen zentralisiert erfasst werden. Auch diesbezüglich gibt es interessante Hinweise aus der Literatur: traditionellerweise wurde empfohlen, seltene Erkrankungen in dedizierten Referenzzentren zu zentralisieren, um die Multidisziplinarität, Expertise und den Zugang zu Innovation sicherzustellen [8]. Umgekehrt erfordert aber die Zentralisierung sogenannte «*Health Migration*» seitens der Patienten, Ressourcen-Aufbau und potentielle Qualitätseinbussen bei Routine-Arbeiten. Für diese Autoren ist die Netzwerkbildung die logische Antwort [9]. Gerade bei Sarkomen, bei denen ungeplante Resektionen vorgängig nicht histopathologisch diagnostizierter Tumore (sogenannte «Whoops!-Operationen») in der Schweiz 2018 noch immer inakzeptable 20% und mehr beträgt, wird es absolut entscheidend sein, dass Patienten möglichst rasch bei Sarkomverdacht in ein wohnortnah zugängliches Netzwerk eingebunden werden, damit durch die potentielle Health Migration an ein geografisches Zentrum keine Verzögerung auftritt, respektive die ungünstigen Folgen für Qualität und Outcome einer falschen Behandlung minimiert werden können. Deswegen sollte idealerweise ein Netzwerk

mit einem Qualitäts-Management-System (QMS) etabliert werden, das eine zeitnahe Abklärung ermöglicht, das entsprechende Volumen verzeichnet, das die Komplexität von Diagnostik, Therapie und Nachbehandlung berücksichtigt und die Multidisziplinarität gewährleistet [10]. Ein solches QMS sollte zwingend die Transparenz aller Aktivitäten seitens der Behandelnden beinhalten, mit Onlinezugang zu Fallzahlen, Behandlungen und Qualitätsindikatoren.

Das *Swiss Sarcoma Network* (*www.swiss-sarcoma.net*; SSN) entspricht einem solchen überregionalen Netzwerkkonzept wie oben beschrieben. Das SSN wurde 2018 gegründet, wird von einem Trägerverein gebildet und von nationalen Institutionen geführt. Diese Institutionen haben sich vertraglich verpflichtet, die Daten aller konsekutiven Sarkompatienten gemäss festgelegten Qualitätsindikatoren zu erfassen und transparent darzustellen. Der Verein steht grundsätzlich für alle Institutionen offen, die sich diesen Prinzipien ebenfalls verpflichten möchten. Den Hauptpfeiler des SSN bildet das Datenregister der etablierten Firma Adjumed (*www.adjumed.ch*). Adjumed stellt sicher, dass jegliche Daten in Echtzeit analysiert und dargestellt werden. Eine Besonderheit der Datenbank stellt die Kopplung des Registers an das Management des wöchentlich stattfindenden überregionalen Sarkomboardes dar. So müssen zum einen die sowohl für das Register wie für das wöchentliche überregionale Sarkomboard erforderlichen Informationen nicht zusätzlich im Register eingegeben werden, zum andern kann bereits eine Prüfung der Datenqualität am Sarkomboard stattfinden, drittens ist dadurch sichergestellt, dass jegliche Veränderung im Krankheitsverlauf eines Sarkompatienten, die im Rahmen des Tumorboardes diskutiert werden muss, und jede Followup-Information ebenfalls im Register enthalten sind. Am Sarkomboard, das telemedizinisch stattfindet, können sich Experten aus verschiedenen Institutionen direkt miteinander austauschen, so dass eine Diskussion sach- und weniger institutionszentriert oder hierarchiebasiert stattfinden kann. Das SSN definiert SOP's and GCP's nach international gültigen Richtlinien, organisiert Aus- und Weiterbildungs-Curricula inkl. entsprechende Weiterbildungssymposien. Ein weiterer Pfeiler des SSN stellt das «International Advisory Board» dar. Es wird von international anerkannten Sarkom-Experten gebildet, die die Multidisziplinarität abbilden und sich der Qualität und Transparenz verpflichten. Diese internationalen Fachexperten stehen dem SSN für Zweitmeinungen zur Verfügung, was die maximal mögliche Qualität der Therapieentscheidungen für unsere Patienten garantiert. Zusätzlich werden sie für Instructional Course Lectures, der Etablierung eines E-Learning Tools sowie zur Über- und Ausarbeitung der Therapie- und Abklärungsguidelines zur Verfügung stehen. Durch diese Massnahmen wird gewährleistet, dass Qualität nicht nur in Echtzeit erfasst und dargestellt, sondern auch auf internationaler Basis weiterentwickelt wird.

Qualität beinhaltet, unsere Behandlungen und deren Erfolg a) zu definieren, b) zu erfassen und c) auszuwerten, speziell bei seltenen Krankheiten. Unsere aktuelle Realität ist, dass wir noch nicht einmal wissen, wie viele Sarkompatienten in der Schweiz pro Jahr diagnostiziert werden. Dies ist vom medizinisch-ethischen Gesichtspunkt her inakzeptabel. Bezieht man die Tatsache ein, dass Unsummen für die personalisierte Medizin aufgebracht werden, so ist das fast schon skurril. Bislang haben wir kein System, dass es uns erlauben würde, die nach WHO definierten Sarkomentitäten zu erfassen (die ICD10-Codierung erlaubt das nicht) oder deren Behandlungen zu evaluieren und zu vergleichen. Solange wir nicht bereit sind, unsere herkömmlichen Verhaltensweisen zu ändern und einen nächsten Schritt zu tun, wird es konsequenterweise weiterhin nicht möglich sein, die Qualität im wie beschriebenen erforderlichen Sinne zu definieren, und Diskussionen betreffend Sarkommanagement können weiterhin nicht sachbasiert erfolgen. Es wäre selbstverständlich für alle, vor allem aber für unsere Patienten sehr wünschenswert,

vorteilhaft und vor allem einfacher, wenn das HSM-Fachorgan die Entscheide betreffend Organisation und Management der Sarkome in Zukunft auf sachbasierten, transparenten und einheitlich erfassten Qualitätsindikatoren treffen könnte.

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Prof. Bruno Fuchs, MD PhD
Chair, Swiss Sarcoma Network
Chefarzt Sarkomchirurgie
Kantonsspital Winterthur
Kantonsspital Luzern
UniversitätsSpital Zürich USZ
Universitätskinderspital Zürich
fuchs@sarcoma.surgery
www.sarcoma.surgery
www.swiss-sarcoma.net

SwissSarcomaNetwork (SSN) – Fakten und erste Zahlen zur Verbesserung der Qualität der Behandlung von Patienten mit Sarkomen

Bruno Fuchs, Beata Bode, Stefan Breitenstein, Vito Spataro, Christian Michelitsch, Désirée Klass, Alex Vogetseder, Veronika Blum, Thomas Treumann, Andreas Scheiwiller, Mario Scaglioni, Gabriela Studer

1. Hintergrund und bisherige Entwicklung

Sarkome sind maligne mesenchymale Neoplasien und zählen zu den seltenen Erkrankungen mit einer Altersstandardisierten Inzidenz und Mortalität für die Schweiz von 4.43 und 1.42 pro 100 000 Einwohner für Weichteilsarkome, und 0.42 für Knochensarkome [1]. Die Behandlung erfolgt vorwiegend transdisziplinär und ist häufig komplex, weswegen ein nationaler und internationaler Austausch von zentraler Bedeutung sind.

Im Luzerner Arzt 118/2019 [2] stellten wir das überregionale Schweizerische Sarkom-Netzwerk (SSN, www.swiss-sarcoma.net) vor, und dann im Anschluss die Pläne, wie die Behandlungsqualität gezielt verbessert werden soll [3].

Primäres Ziel und Aufgabe des SSN ist die ab initio transdisziplinär orchestrierte, zeitnahe «state-of-the-art»-Abklärung, Behandlung, Betreuung und Verlaufsbeobachtung unserer Patienten mit sarkomatösen Erkrankungen, im nationalen und internationalen Austausch.

Eine Darstellung der Meilensteine in der historischen Entstehung und Entwicklung des SSN bietet Abb. 1.

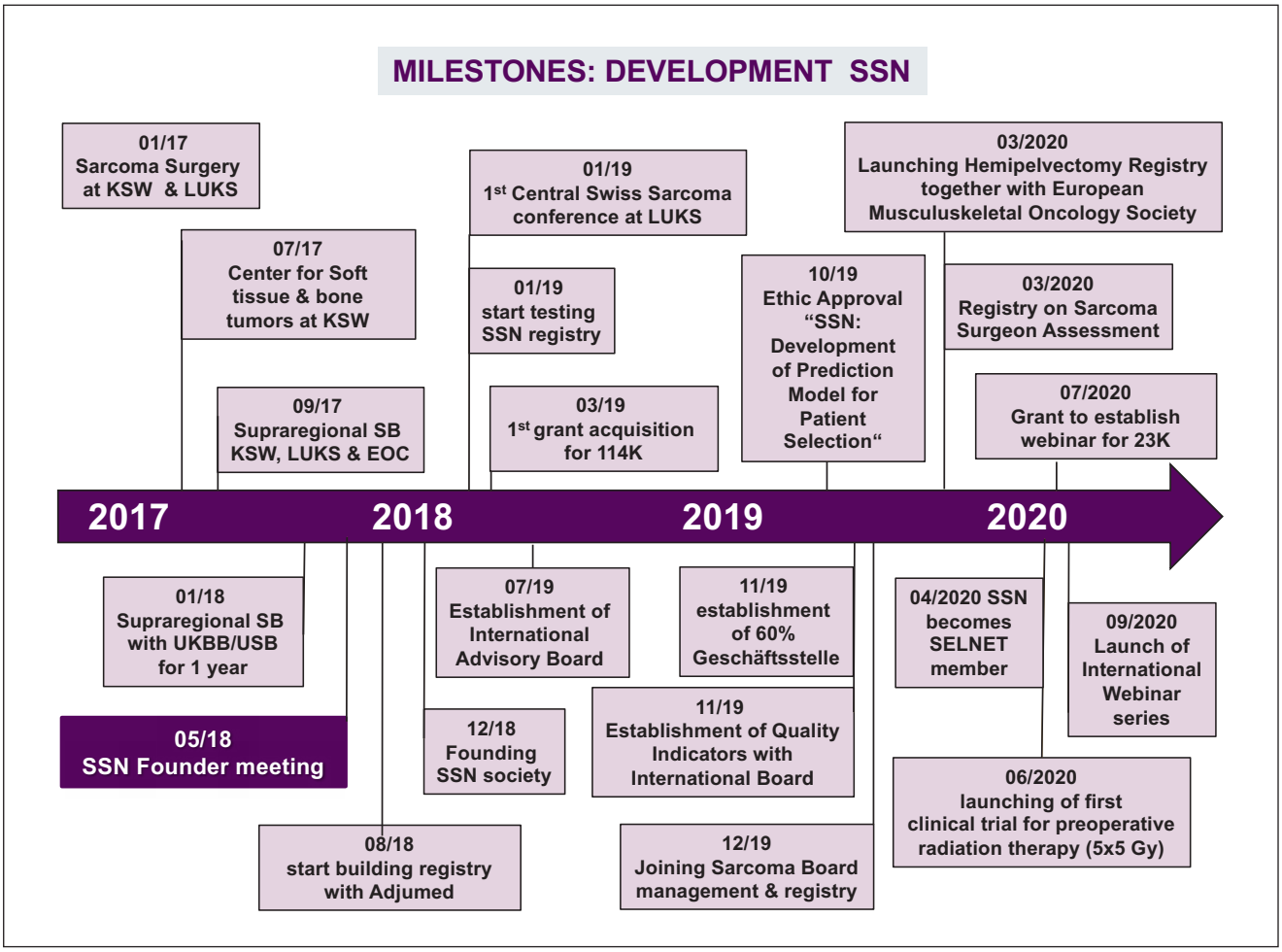

Abb. 1: *Entwicklung des SSN über die letzten 3 Jahre*

Vertragliche Mitglieder sind derzeit die Kantonsspitäler Luzern (LUKS), Winterthur (KSW), Chur (KSGR) und Bellinzona (EOC), unter Mitwirkung des Pathologie-Instituts Enge, Zürich, mit einer Sarkom-Referenzpathologin; Fallbasierte Kooperationen bestehen mit zahlreichen weiteren Institutionen und Praxen.

Wir stellen im Folgenden die bisherigen (09/2017–08/2020) Fakten und Zahlen sowie weitere Meilensteine des SSN vor.

1.2. Wöchentliches SSN Sarkom-Board: Fakten und Zahlen

In Tab. 1 sind die jährlichen Fallzahlen nach diversen Parametern und Tumor-Charakteristika gelistet.

Insgesamt wurden in 3 Jahren ca. 1500 Fallpräsentationen mit Verdacht auf oder bereits diagnostizierter sarkomatöser Erkrankung am überregionalen wöchentlichen SSN-Sarkomboard interdisziplinär besprochen; die Hälfte davon waren Primärfall-Präsentationen, bei annähernd 300 Patienten (43%) wurde eine Sarkom-Diagnose gestellt. Pro Jahr wurden damit über 100

neue Patienten mit einem Sarkom diagnostiziert und behandelt, was im internationalen Vergleich die Definition eines Hochvolumen Zentrum erfüllt. Nebst benignen muskuloskelettalen Entitäten müssen auch Karzinom-Metastasen, Tumor-Simulatoren (also Raumforderungen nicht-maligner Art) oder aber Tumoren aus dem hämatologischen Formenkreis abgeklärt werden, bei denen der initiale Verdacht auf ein Sarkom differentialdiagnostisch im Vordergrund stand, deren weitere histopathologische Abklärungen ein nicht-sarkomatöses Geschehen verifizierte. Diese Zahlen zeigen, dass in lediglich 4 von 10 Patienten, bei denen eine unklare Schwellung und der Verdacht auf ein Sarkom in Betracht gezogen werden muss, ein solches auch bioptisch bestätigt wird. Insgesamt beinhalten 22% aller Vorstellungen Knochentumore, 12% epifasziale, 66% subfasziale Tumore. Diese Zahlen beziehen sich auf alle Vorstellungen inkl. Primärvorstellungen. Pro Jahr wurden 234 Biopsien durchgeführt, wobei die bildgebend geführte Stanzbiopsie in 73% aller Patienten verwendet wurde. Von grösster Bedeutung ist der Umstand, dass 35% aller Biopsien entweder durch eine offene Inzisionsbiopsie oder aber Exzisionsbiopsie ohne Sarkomverdacht durchgeführt wurde, und 20% aller Sarkome durch sogenannte Whoops-Operationen (‹Whoops›: Überraschungsdiagnose, Eingriff entsprechend nicht unter den erforderlichen onkologischen Aspekten durchgeführt, mit erwiesenem prognostischem Nachteil für die betroffenen Patienten) diagnostiziert wurden.

1.3 SwissSarcomaRegister und Qualitätsindikatoren (QI)

Das SwissSarcomaRegistry ist seit Dezember 2019 mit der Anmeldung zum Sarkomboard gekoppelt und erlaubt damit die effiziente real-time-Datenerfassung und -Analyse (keine Mehrfacheingabe derselben Daten). Diese Kopplung erlaubt höchste Datenqualität, da offene Fragen (zB. chirurgischer Margin) bereits im Rahmen der Sartkomboard-Anmeldung eingegeben werden und, falls fehlend, am Sarkomboard geklärt werden können (nicht erst retrospektiv durch einen Datenmanager erfasst werden). Zudem wurden zusammen mit dem Internationalen SSN advisory Board von weltweit bekannten Sarkomexperten 18 Qualitätsindikatoren (QI) betr. der initialen Abklärung und Behandlung von Sarkom Patienten definiert [Tab. 2]. Diese Parameter werden zurzeit im Register programmiert, sodass diese QI's direkt erfasst werden können.

Diese QI's wiedergeben das initiale Patientenmanagement und werden im Sinne eines Quality Management Systems erfasst. Zentralste Schlüssel-Information ist die korrekte histopathologische Sarkom-Diagnose, so ist auch vom French Sarcoma Network die Referenzpathologie zur Etablierung (oder Ausschluss) einer Sarkomdiagnose als von zentraler Bedeutung für

09/2017 - 08/2020	Total	1. Präsentation	FU - Präsentation
Fallpräsentationen (alle)	1494 / 100%		
Primärfallpräsentationen	733 / 49%		
Follow up -Präsentationen	760 / 51%		
Dignität der Diagnosen			
•Benigne	20.7%	14.5%	7.2%
•Intermediär	17.9%	8.6%	1.2%
•Maligne	43.4%	12.4%	30.9%
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•Simulatoren	7.2%	5.4%	1.8%
•Metastasen	3.2%	1.6%	1.6%
•Hämatologische Tumore	1.2%	1.0%	0.2%
•andere	6.4%	5.6%	0.8%
Lokalisationen, alle			
•Knochen (total / primär / follow up)	22.2%	11.6%	16.6%
•Weichteile epifaszial (total / primär / follow up)	11.4%	7.4%	3.8%
•Weichteile subfaszial (total / primär / follow up)	62.4%	29.9%	17.7%
Anteil sarkomatöse 1° Diagnosen (vs alle 1° Diagn.)	43%		
Anteil sarkomatöse 1° Diagnosen (vs alle Vorstellungen)	21%		
Anzahl Biopsien, total	702		
•Feinnadel	5.1%		
•Stanze	73.5%		
•offene Inzision mit Sarkomverdacht	2.6%		
•offene Inzision ohne Sarkomverdacht	3.4%		
•Exzisionsbiopsie mit Sarkomverdacht	4.7%		
•Exzisionsbiopsie ohne Sarkomverdacht	32.1%		

Tabelle 1: *Überblick über die SSN. Sarkomboard Aktivitäten*

QUALITY INDICATORS: Standards of care based on CPG's Quality indicators / Outcome measures	
QI-1	appropriate local imaging before biopsy/treatment initiation (yes/no)
QI-1.1	Diagnosis of malignant tumor considered/noted in the radiological report (yes/no)
QI-2	time from 1st patient contact to biopsy (if performed)
QI-3	type of biopsy: FNA, tru-cut (CT- or US-guided), open incisional, excisional biopsy, enucleation/whoops
QI-4	time from biopsy to establishing diagnosis (1st path review & reference review)
QI-5	time from biopsy until sarcoma board presentation
QI-6	biopsy before initiation of treatment (yes/no)
QI-7	biopsy performed in the center where the patient is operated: (yes/no)
QI-8	extent of disease at diagnosis
QI-9	time from SB to initiation of treatment
QI-10	margin status (R0, R1, R2) at definitive surgery (STS
QI-11	preoperative radiation therapy: (yes/no)
QI-12	postoperative radiation therapy: (yes/no)
QI-13	neo-adjuvant chemotherapy: (yes/no)
QI-14	adjuvant chemotherapy (yes/no)
QI-15	local relapse: yes/no
QI-16	local recurrence: yes/no within 1st year of tumor resection (Bone)
QI-17	metastatic relapse: yes/no
QI-18	Latest follow-up: no evidence of disease (NED); alive with disease (AWD); dead of disease (DOD); dead of other reasons (DOR); no assessment possible; lost to follow-up; other status; unknown

Tabelle 2: *Liste der bislang definierten Qualitäts-Indikatoren betreffend Abklärung / outcome bei Patienten mit muskuloskelettalen Tumoren*

die Qualität der Behandlung nachgewiesen. Eine korrekte Therapie kann nur erfolgen, wenn die richtige Diagnose erstellt wird. Im SSN werden in Konsequenz alle Diagnosen durch die Referenzpathologie begutachtet. Selbstverständlich stellt sich dabei auch hier die Frage nach der Definition des Experten-Levels. Die definierten QI's beinhalten nebst der eigentlichen Diagnose auch die einzelnen Schritte und Durchlaufszeiten bis zur korrekten Diagnosestellung. Da die Abklärung hochkomplex sein kann, und nicht jede Institution die entsprechenden Investitionen tätigen kann oder will, und auch nicht alle Expertise zur Verfügung haben kann, ist es substanziell, bei kleinem Patientenvolumen in der Schweiz im Netzwerk auszutauschen, bzw. Standards zu definieren, innerhalb derer eine fundierte Abklärung in Zukunft erfolgen soll.

1.4 Ausbildung / Forschung

Der Wissenstransfer innerhalb des Netzwerkes mit internationalem Anschluss und Austausch ist für die Weiterentwicklung von zentraler Bedeutung (www.sarcoma.academy). Das SSN hat nun eine Webinar-Serie von acht Veranstaltungen organisiert, wobei alle zwei Monate ein internationaler Sarkomexperte zu einem spezifischen Thema vorträgt (www.swiss-sarcoma.net/pdf/20200910-webinar-invitation.pdf). Die webbasierte Plattform erlaubte zudem, den internationalen Austausch insbesondere während Covid-Zeiten zu forcieren.

Das SSN möchte u.a. auf die Versorgungsforschung fokussieren. Das SSN baut eine Sarcoma Quality Management System auf, um in real-time einen transdisziplinären Qualitätsstandard zu erfassen und womöglich in der Folge zu verbessern. In Arbeit sind derzeit weitere quality and complexity scores der Sarkombehandlung.

1.5 Zusammenfassung und Ausblick

Tab. 3 zeigt im Ueberblick die verschiedenen Aktivitätsfelder des Netzwerks. Das SSN etablierte ein überregionales transdiziplinäres wöchentliches Sarkomboard, wo die sich vertraglich verpflichteten Institutionen alle konsekutiven Patienten mit Sarkom(-Verdacht) vorstellen. Die Anmeldung zum Sarkomboard ist – wie oben erwähnt – gekoppelt mit dem SwissSarcomaRegistry, um eine real-time Datenerfassung zu ermöglichen. Einerseits wird dadurch die Datenqualität maximiert, und andererseits können im Rahmen des Quality Management System die einzelnen Behandlungsschritte erfasst und die Qualität der Ergebnisse ausgewiesen

SwissSarcomaNetwork (www.swiss-sarcoma.net)	
Trägerverein	von nationalen Institutionen geführt, seit 2018 Mitgliedschaft für alle Institutionen mit Bereitschaft, die Daten vorzustellen und zu erfassen
SwissSarcomaRegistry	Firma Adjumed (www.adjumed.ch) als Provider aktuell > 3000 Patienten-Daten erfasst, seit 2019 Kopplung von Sarkomboard und Datenbank zur real-time Datenerfassung
wöchentliches Sarkom-Board (Vidyo® -System)	~ 500 Falldiskussionen/Jahr
SOP / GCP	www.swiss-sarcoma.net
Qualitäts-Management-System (QMS, s.a. unter 1.3.)	Q-Parameter im Daten-Register erfasst
International Advisory Board	international anerkannte Sarkom-Experten der beteiligten Disziplinen stehen dem SSN für Zweitmeinungen zur Verfügung, was bestmögliche Qualität der Therapieentscheide sicherstellt. Zwei-monatliches Webinar (www.sarcoma.academy)
Wissenschaftliche Aktivität	Versorgungsforschung zur Etablierung von Qualitäts- und Komplexität-Scores

Tabelle 3: *Zusammenfassung der SwissSarcomaNetwork-Aktivitäten*

und definiert werden. Dadurch wird ein System geschaffen, welches erlaubt, nicht herkömmliche Aspekte neu zu definieren, um den Fokus auszurichten.

Unsere Zahlen zeigen, dass 35% aller Biopsien (!) durchgeführt wurden, ohne vorgängig ein Sarkom in Betracht zu ziehen. Darüber hinaus wurden 20% aller Sarkomdiagnosen durch sogenannte Whoops-Operationen gefunden. Häufig geschieht dies in der Annahme, dass eine Schwellung/Tumor ‹sowieso› entfernt werden müsste, womit dann gleich die Diagnose gestellt werden könnte. Leider erfolgen solche scheinbar banalen Eingriffe/Gewebeentnahmen häufig ohne Einhaltung der spezifischen Sarkomchirurgischen Prinzipien, was unter Umständen für den Patienten zu unangenehmen Nachresektionen mit weitreichenden unnötigen funktionellen Einbussen führt, wenn nicht sogar mit dem Verlust der Tumorkontrolle einhergehen kann. Zudem zeigen unsere Zahlen aber auch, dass nur gerade 4 von 10 Patienten mit einem möglichen Verdacht auf ein Sarkom auch mit einem solchen diagnostiziert werden. Interessanterweise werden diese Verdachtsfälle, bei denen kein Sarkom diagnostiziert wird, in der Literatur nicht diskutiert (Dunkelziffer; es wird nur vom gesicherten Sarkom-Subkollektiv gesprochen, nicht aber von den Verdachtsfällen). Möglicherweise aber bietet diese skotomisierte Patientengruppe eine Erklärung für die historisch unverändert hohe Whoops-Operationsrate wie oben diskutiert. Die Kapazität einer Abklärungsleistung eines international kompetitiven Sarkom-Zentrums dürfte überfordert werden, wenn auch alle diese Verdachtsfälle zentralisiert abgeklärt werden müssten. Zudem sind Infrastruktur und Kultur derzeit so, dass der Patient erwartet, zumindest diagnostische Abklärungen vor Ort zu erhalten. Konsequenterweise kann es deswegen sinnvoll sein, an regionalen Zentrumsspitälern Sarkom-Abklärungseinheiten einzurichten, die in einem Netzwerk organisiert als Eintrittspforte den Patienten zur bestmöglichen Therapie-Einheit triagieren und weiterweisen können.

Diese Ergebnisse und Ueberlegungen zeigen, wie wichtig es ist, im Sinne der Versorgungsforschung die Zahlen eines Sarkomboards zu erfassen und zu analysieren, um durch neue Ansätze Rückschlüsse für die Patientenversorgung zu gewinnen. Eventuell lässt sich mit diesem neuen Ansatz ein jahrzehntelanges Problem lösen.

Über Behandlungsresultate der SSN Sarkom-Patienten-Kohorte werden wir zu einem späteren Zeitpunkt mit ausreichend langer Verlaufsbeobachtung berichten.

Zur Dunkelziffer (Patienten mit Sarkomerkrankungen ohne prätherapeutische Präsentation und Prozedere-Besprechung im Rahmen eines Boards) kann entsprechend leider keine Aussage gemacht werden (Anzahl? Outcome?).

2. aktualisierte Informationen zum SSN für Ihren praktischen Alltag *(s.a. Luzerner Arzt 118/2019 [2])*

1) Wer kann Mitglied werden?

- jede medizinische Institution

2) Was bedeutet Mitgliedschaft?

- Mitgliedschaft beinhaltet die Bereitschaft, alle konsekutiven Patienten mit einer Sarkom-Erkrankung bzw. Verdacht auf eine sarkomatöse Erkrankung präthera-peutisch gemäss unten abgebildetem Algo-rithmus im gemeinsamen Tumorboard vorzustellen/vorstellen zu lassen (mit vor-gängigem PatientenEinverständnis).
- die Daten dieser Patienten im gemeinsamen Register zu erfassen/erfassen zu las-sen (mit vorgängigem Patienten-Einverständnis)

3) Wie können Sie auch als Nicht-Mitglied Ihre Patienten zur Fallbesprechung einbringen?

- Sie schalten sich via Videokonferenz ans Tumorboard direkt zu (Vidyo®-System; weitere Information: Beatrice.meier@ksw.ch)
- oder: Sie präsentieren selber «live» an einem der Standorte LUKS/KSW/KSGR/ BELLINZONA oder Pathologie Enge (jeden Dienstag, 17–18 Uhr, weitere Infor-mation: beatrice.meier@ksw.ch)
- oder: Sie weisen Ihren Patienten an die Sarkom-Sprechstunde LUKS, mit dann in der Folge Fall-Präsentation durch ein ärztliches Mitglied des Sprechstunde-Teams (Kontakt LUKS: Jehona.vishaj@luks.ch

4) wo/wie findet das SSN-Sarkomboard LUKS statt?

- Ort: Rapportraum 414, EG Hauptgebäu-de, Luzerner Kantonsspital (LUKS)
- Zeit: jeweils dienstags, 17–18 Uhr
- Wie: per Videokonferenz (Vidyo®System; Information: beatri-ce.meier@ksw.ch)

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Korrespondenzadresse

Prof. Dr. Gabriela Studer
Chefärztin Radio-Onkologie LUKS
Luzerner Kantonsspital
Radio-Onkologie
Spitalstrasse
6000 Luzern

Affiliationen

1 Prof. Dr. Bruno Fuchs, Leitender Arzt Orthopädie LUKS, Chefarzt und Leiter Orthopädische Tumorchirurgie Kantonsspital Winterthur KSW, Chair SSN
2 Prof. Dr. Beata Bode-Lesniewska, Stv. Institutsleiterin, Institut Pathologie Enge, Zürich
3 Prof Stefan Breitenstein, Chefarzt Chirurgie KSW, Präsident Trägerverein SSN
4 Dr.med Vito Sptataro, EOC, Medizinische Onkologie, Bellinzona
5 Dr. med. Christian Mitchelitsch, OAmbF Chirurgie, KSGR
6 Dr. med Désirée Klaas, Fachärztin für Radio-Onkologie, KSGR
7 Dr. med. Alexander Vogetseder, LA Histologie LUKS
8 Dr. med. Veronika Blum, OAe Medizinische Onkologie LUKS
9 Dr. med. Thomas Treumann, Co-Chefarzt Radiologie LUKS
10 Dr. med. Andreas Scheiwiller, Chefarzt Viszeralchirurgie LUKS
11 PD Mario Scaglioni, LA Hand-und Plastische Chirurgie LUKS
12 Prof. Dr. Gabriela Studer, Chefärztin Radio-Onkologie LUKS Luzern und Radio-Onkologie am Zuger Kantonsspital; Vize-Präsidentin Trägerverein SSN

cancers

MDPI

Article

Unlocking the Power of Benchmarking: Real-World-Time Data Analysis for Enhanced Sarcoma Patient Outcomes

Bruno Fuchs [1,2,3,*], Georg Schelling [1,3], Maria Elyes [1], Gabriela Studer [1], Beata Bode-Lesniewska [4], Mario F. Scaglioni [1], Pietro Giovanoli [2], Philip Heesen [2] and on behalf of the SwissSarcomaNetwork [†]

[1] Sarcoma Service, University Teaching Hospital LUKS, University of Lucerne, 6000 Lucerne, Switzerland
[2] University Hospital USZ, University of Zurich, 8000 Zurich, Switzerland
[3] Sarcoma Service, Kantonsspital Winterthur, 8400 Winterthur, Switzerland
[4] Patho Enge, SSN Reference Sarcoma Pathology, University of Zurich, 8000 Zurich, Switzerland
* Correspondence: fuchs@sarcoma.surgery
† Additional collaborators of the Swiss Sarcoma Network are indicated in the Acknowledgement.

Simple Summary: Benchmarking is a crucial tool for healthcare providers to improve quality and efficiency, especially for complex conditions like sarcomas. Sarcomas are a type of cancer that require a multidisciplinary approach to treatment. However, despite adherence to international guidelines, differences in the processes used by these boards can affect patient outcomes and treatment costs. This study compared two multidisciplinary teams/sarcoma tumor boards and established an interoperable digital platform, Sarconnector®, for real-world time (RWT) data assessment and automated analysis. Differences were obtained in various areas, such as first-time presentations, follow-up presentations, primary sarcomas, biopsies and chemotherapy indications. By identifying areas of improvement and making data-driven decisions on the meta-level, healthcare providers can optimize resources and improve patient outcomes. Benchmarking with the RWT harmonized data approach provided by the Sarconnector® can help healthcare providers achieve better outcomes for their patients and improve the overall effectiveness of the healthcare system.

Abstract: Benchmarking is crucial for healthcare providers to enhance quality and efficiency, notably for complex conditions like sarcomas. Multidisciplinary teams/sarcoma boards (MDT/SBs) are vital in sarcoma management, but differences in their processes can affect patient outcomes and treatment costs, despite adherence to international guidelines. To address this issue, this study aimed to compare two MDT/SBs and establish an interoperable digital platform, Sarconnector®, for real-time-world data assessment and automated analysis. The study included 983 patients, 46.0% of whom female, with a median age of 58 years, and 4.5% of patients presented with metastasis at diagnosis. Differences were observed in the number of first-time presentations, follow-up presentations, primary sarcomas, biopsies and chemotherapy indications between the two MDT/SB. The results highlight the importance of benchmarking and utilizing a harmonized data approach, such as the RWT approach provided by the Sarconnector®, to standardize and evaluate quality and cost metrics. By identifying areas of improvement and making data-driven decisions on the meta-level, healthcare providers can optimize resources and improve patient outcomes. In conclusion, benchmarking with the RWT harmonized data approach provided by the Sarconnector® can help healthcare providers improve the overall effectiveness of the healthcare system and achieve better outcomes for their patients in terms of both outcomes and costs.

Keywords: IELAS-RWTD/E (interoperable electronic longitudinal absolute structured real-world time data/evidence); MDT/SB (multidisciplinary team/sarcoma board meeting); VBHC (value-based healthcare); AI/ML (artificial intelligence/machine learning); CROMS (clinician-reported outcome measures); PROMS (patient-reported outcome measures); PREMS (patient-experienced outcome measures); IPU (integrated practice unit); SPDT (sarcoma patient digital twin)

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1. Introduction

Surgery is the mainstay treatment in sarcoma care [1,2]. While many standards have been described in sarcoma surgery, such as surgical margins, multidisciplinary approaches, preoperative planning, appropriate surgical techniques with adequate postoperative care and regular follow-ups, and importantly, multidisciplinary team meetings, the overall quality definitions of sarcoma surgery have not been addressed [3–8]. In a pivotal landmark paper and based on an international consensus jury approach, Domenghino et al. proposed a framework to evaluate the quality of surgical interventions and to identify areas for improvement, with the potential to improve the assessment of surgical interventions and facilitate the sharing of best practices [9]. The authors highlight the importance of data management, with data-management systems being designed to capture comprehensive and accurate data on surgical outcomes, including clinical outcomes, patient-reported outcomes and complications of therapy. Data need to be interoperable and allow the integration of data from multiple sources, including electronic health records, registries and administrative databases [10–12]. Specifically, the consensus jury suggests assessing a multilayer outcome to compare results from one's own practices, processes, or outcomes to those of other organizations or practices in the same field, both nationally and internationally, to ultimately allow the establishment of a benchmark as a powerful tool that can be used in many surgical disciplines to improve quality and performance and to establish best practices and standards of care.

Benchmarking in surgery or in healthcare in general is considered difficult for a variety of reasons and has only scarcely been reported up to now [9,13–15]. However, besides the potential of quality improvement through improvement of clinical practices, it allows the establishment of standards of care, identifying best practices and outliers, while also easing resource allocations and regulatory compliances [13,16]. Domenghino et al. suggest building the benchmark based on outcome parameters assessed at different time points, on the routine assessment of PROMS and PREMS in clinical care, and on the record of individual and global morbidity according to the Clavien–Dindo classification and the Comprehensive Complexity Index [9,17–20].

In today's healthcare system, the traditional fee-for-service model creates misaligned incentives where providers incentivize the delivery of a high volume of services rather than focusing on outcome [21,22]. Porter et al. introduced the value-based healthcare (VBHC) principle to better align incentives with outcome, to focus on patient needs, to emphasize outcome over volume, to encourage continuous improvement and to promote transparency and accountability [23–26]. He defined the value of healthcare as the ratio of quality to cost implying that to increase the value of healthcare, the quality of care delivered to patients has to increase, while also reducing the cost of that care. By measuring outcomes, therefore, areas of improvement are not only identified but also drive quality-improvement initiatives to improve patient outcomes. Therefore, to create a sustainable healthcare system and to realize VBHC, every effort has to be taken to define quality of care and to create opportunities to benchmark it and scale it over the geography [27–30].

Obviously, the definition of quality in patient outcomes to establish a benchmark as outlined above involves a shear amount of data, which on top has to address data governance, data integration, enabling analytics and data interoperability to share and to encourage collaboration, as well as ethical and legal considerations [11,31–35]. Modern strategies involving AI and ML approaches will revolutionize current approaches [12,33,36–39]. However, although machine-learning approaches to extract comprehensive data from electronic health records are on the horizon [40], a structured data frame for a given medical condition is necessary, allowing for standardization, interoperability, data analytics, security, transparency, collaboration and further improvements to enable data harmonization over the geography. Above all, real-time follow-up over the entire care cycle, including both clinician and patient perspectives is highly preferable, should be integrated by an interoperable data platform, which ultimately allows federated exchange and learning [41–43].

With respect to sarcoma, our group has recently established the spectrum of sarcoma surgery, the complexity scores for the surgery of soft tissue tumors, as well as the quality indicators of sarcoma care [44–46]. These consists of six groups, namely the MDT/SB-management, therapy-related parameters including surgery, radiation oncology and chemotherapy, the complexity of sarcoma therapy, physician-based clinical metrics (summarized as CROMS; clinician-reported outcome parameters), as well as patient-based outcome and experience measures (PROMS/PREMS). We have also introduced the sarcoma-specific instrument to longitudinally assess health-related outcomes of the routine care cycle from sarcoma patients' perspective [47,48]. To realize VBHC [49], it is our strategy to integrate the outlined data complexity by establishing real-world time data exchange, introducing an interoperable platform to benchmark outcome and to align quality with costs.

Therefore, this article addresses the need to define quality indicators and establish benchmarking in sarcoma surgery and care. Our study fills the gap by proposing a framework implemented through an interoperable digital platform. We present a dataset of parameters for benchmarking sarcoma care, enabling the harmonized comparison of multidisciplinary teams and their (surgical) outcomes on the meta-level. This contribution is significant as it facilitates the assessment and improvement of (surgical) interventions, promotes best practices, and establishes standards of care. Additionally, our study aligns with the principles of value-based healthcare, emphasizing patient outcomes, continuous improvement, and cost reduction. By integrating data complexity on the meta-level and introducing an interoperable digital platform, we pave the way for sustainable healthcare systems and improved patient outcomes in sarcoma care.

Herein, we introduce the Sarconnector® (BF&PH, Zurich, Switzerland) as an interoperable digital platform to pave the way for the benchmarking of sarcoma care through real-world time data assessment of automated analysis. We report the dataset of parameters to define the outcome and quality indicators used for benchmarking and present as the proof of principal of assessing meta-level data (as opposed to the more familiar ground-level data) the comparison of two independent MDT/SBs with its automated data analysis.

2. Materials and Methods

2.1. Study Objectives

The primary objective of this study was to compare the demographics and basic treatment plan of two independent MDT/SBs to set the stage for prospective, large-scale, electronic, structured, longitudinal over the entire care cycle, with consecutive and absolute patient numbers, real-world time data assessment, as well as its automated analysis to create evidence regarding sarcoma care. The second objective was to establish and integrate an interoperable digital platform herein called Sarconnector®, which fulfills all the outlined requirements and allows its use in the daily routine work process.

2.2. Study Population

Data from patients diagnosed with sarcoma and presented at two independent MDT/SB sarcoma centers (MDT/SB-A and MDT/SB-B) were consecutively included and prospectively collected over 15 months. They both included one main tertiary referral University hospital each and its associated hospitals and networks. At both of these MDT/SB, more than 100 newly diagnosed patients with sarcomas each year are being discussed, thereby qualifying as internationally representative sarcoma centers [3]. For both MDT/SB, the same interoperable digital platform was used to assess the information of the patients. For both MDT/SB, it is a prerequisite to have a pathology reference review available to review all relevant imaging studies, and to have all 8 disciplines participating at the respective weekly meetings. All newly diagnosed patients, all patients after completion of each treatment step (for example, if combination therapy is decided on, the patient has to be presented after completion of preoperative radiation therapy and before surgery) or

patients with a change to the treatment plan other than previously decided on are required to be presented at the MDT/SB.

2.3. Sarconnector®

The interoperable digital platform is introduced elsewhere [46,47]. It is now expanded to the Sarconnector®, which presents with a front end as well as a back end (Figure 1). The front end includes both the data entry and the real-time data visualization. The core of the back end bases on the SQL database language with the R program to perform statistical analysis. Data are introduced either through the hospital or cloud server using API data exporter tools and interactive shiny apps. RWTD/E assessment is made possible through the combination of the weekly MDT/SB and the interoperable platform, as well as through PROMS/PREMS assessment by patients during their life-long follow-up [46,47]. Besides PROMS/PREMS, the Sarconnector® also includes clinical metrics (so-called CROMS) and health economics as data dimensions (Figure 2). Because of the RWTD assessment set-up, personalized and automated analytics can also be carried out in real-time.

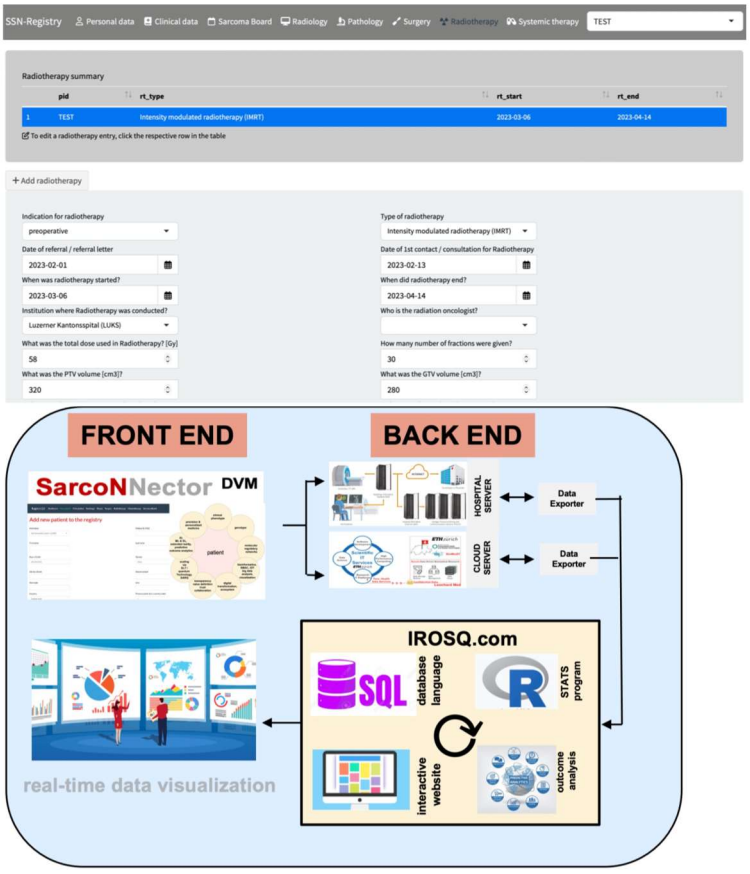


Figure 1. The Sarconnector® as an interoperable digital platform to allow IELAS-RWTD/E. An integrated practice unit (IPU) with an interoperable digital platform is a prerequisite to assessing IELASRWTD/E. A data quality guarantor creates the link between the interoperable digital platform, herein referred to as the Sarconnector®, which combines the assessment of data and simultaneous analysis with descriptive, inferential, non-/parameter and Bayesian statistics, with a great focus on exploratory data analysis and visualization. The front end consists of an easy-to-use data entry site, which simultaneously allows visualization of the data. The core of the back end is based on the SQL database language with the R program to perform statistical analysis.

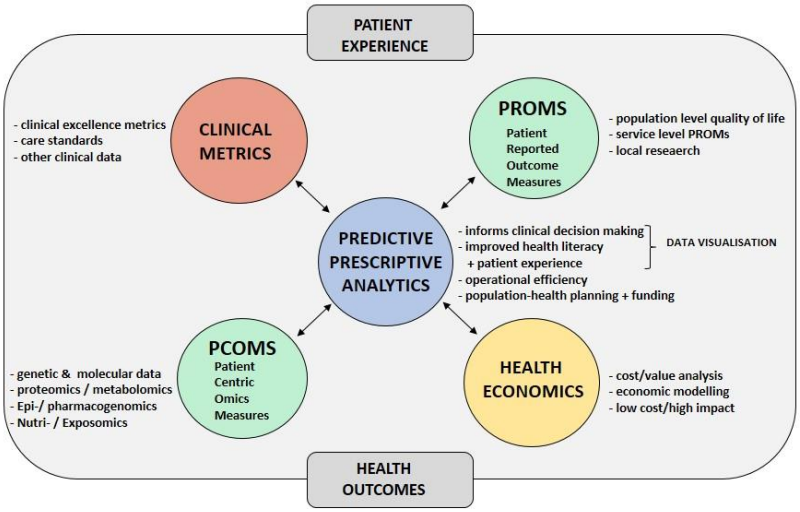


Figure 2. The Sarconnector® includes all data dimensions. This interoperable digital platform (Sarconnector®) includes all relevant physician-based, work-up, therapy and follow-up data, as well as patient-based PROMS and PREMS. To associate costs with outcome, it also includes health economics data. Based on these data, AI/ML approaches can be applied for predictive and prescriptive outcome modelling, ultimately enabling the sarcoma patient digital twin.

The Sarconnector® is designed to synthesize meta-level data to integrate multiple MDT/SB. As such, it provides not only object- or ground-level data, but specifically meta-level data, which yields higher-level analysis that is concerned with the structure, organization or properties of a lower level, related to higher-level thinking. It analyzes the quality indicators for a specific MDT/SB separately but can also integrate the data over several MDT/SB, thereby establishing a benchmark not only for a respective institution with its associated network, but also for a country or continent.

The flowchart of data processing by the Sarconnector® ("Driving precision in sarcoma care: real-world time data, value-based benchmarking, and digital twinning") can be summarized as follows: (A.) Collection of real-world time data over the entire care cycle: data related to sarcoma care, including clinical-reported outcome measures (CROMS), patient-reported outcome measures (PROMS), patient-reported experience measures (PREMS) and quality indicators (QIs), are collected from various sources, such as electronic health records, surveys and patient feedback; (B.) Storage of data on an interoperable digital platform: the collected data are stored securely on a digital platform that allows for interoperability, ensuring compatibility and data exchange between different systems and stakeholders; (C.) Automated analysis on the platform with immediate front end display: the platform employs automated analytical tools and algorithms to process the data and extract relevant insights. This involves statistical analysis, data mining and machine-learning techniques to identify patterns and trends; (D.) Benchmarking and quality indicators: the analyzed data are compared against predefined quality indicators specific to sarcoma care. These indicators include measures such as survival rates, recurrence rates, patient satisfaction scores, adherence to treatment guidelines, etc.; (E.) Assessment of sarcoma care quality: based on the benchmarking results, an assessment can highlight areas of strength and areas that require improvement; (F.) Value-based healthcare assessment: evaluating the value provided by the care process, this assessment takes into account the outcomes achieved relative to the resources used. It considers the effectiveness, efficiency and patient-centeredness of the care provided, aiming to optimize the overall value delivered to patients; (G.) Iterative improvement loop: the assessment findings are used to identify areas for improvement in the sarcoma care process. The healthcare team can take corrective actions, update protocols and implement interventions to enhance the quality of care provided; (H.) Predictive AI/ML modelling: the collected real-world time data are leveraged to develop predictive models using artificial intelligence and machine-learning techniques. These models can

forecast future outcomes, identify high-risk patients and support personalized treatment decisions, enhancing the decision-making process; (I.) Composition of the sarcoma patient digital twin: over time, as more data are collected and analyzed, the information is utilized to create a digital twin of sarcoma care. This digital twin serves as a virtual representation that can stimulate the behavior of the care process, predict outcomes and support decision making.

2.4. Statistical Analysis

Descriptive statistics were used to describe baseline patient characteristics. Categorical variables are presented as N (%), while numerical variables are presented as median (range). Fisher's exact test was performed to test for differences in chemotherapy and biopsy proportions between the two MDT-SBs. Statistical analysis was performed using the R statistical program.

3. Results

3.1. Basic Data and the Sarconnector®

Overall, there were 983 patients included in this study, of which 452 (46.0%) were female, with a median age at diagnosis of 58.0 (range, 1.0 to 59.0) years. Table 1 summarizes the dignity as well as the anatomic location of the lesions. There were 44 (4.5%) patients who presented with metastasis at diagnosis.

Table 1. This table summarizes all relevant basic demographic data of the patients included in this study. The numbers are separately listed for each MDT/SB, as well as overall.

	Overall N = 983	**MDT/SB-A N = 610**	**MDT/SB-B N = 373**	***p*-Value**
Female	452 (46.0%)	283 (46.4%)	169 (45.3%)	0.74
Age at diagnosis	58.0 (1.0, 95.0)	60.0 (8.0, 93.0)	56.0 (1.0, 95.0)	0.001
Bone tumors				<0.001
Chondrogenic	44 (4.5%)	24 (3.9%)	20 (5.4%)	
Osteogenic	19 (1.9%)	6 (1.0%)	13 (3.5%)	
Vascular	18 (1.8%)	14 (2.3%)	4 (1.1%)	
Others/Unknown	81 (8.2%)	60 (9.8%)	21 (5.6%)	
Soft-tissue tumors				
Adipocytic	201 (20.5%)	141 (23.1%)	60 (16.1%)	
(Myo-)fibroblastic	117 (11.9%)	59 (9.7%)	58 (15.6%)	
Fibrohistiocytic	33 (3.4%)	11 (1.8%)	22 (5.9%)	
Muscle tumors	82 (8.3%)	51 (8.4%)	31 (8.3%)	
Undifferentiated/unclassified	87 (8.9%)	50 (8.2%)	37 (9.9%)	
Others	301 (30.6%)	194 (31.8%)	107 (28.6%)	
Primary tumor site				0.37
Appendicular	558 (56.8%)	352 (57.7%)	206 (55.2%)	
Axial	367 (37.3%)	220 (36.1%)	147 (39.4%)	
NA	58 (5.9%)	38 (6.1%)	20 (5.4%)	
Metastasis at diagnosis	44 (4.5%)	26 (4.3%)	18 (4.8%)	0.75

The Sarconnector® presents an intuitive, self-explanatory front end, separated according to the respective disciplines (Figure 1). For each discipline, a minimal dataset of relevant parameters are requested to enter. The case report form is provided in the supplementary data (SUPP). At the top, it provides a summary of what type of, e.g., radiation therapy was performed. Specifically, besides the type of radiation performed, it also includes the use of a flab, the critical tumor volume/gross tumor volume (CTV/GTV) volumes, and the color wash. Because all disciplines assess their respective information regarding work-up and therapy, these parameters can be analyzed in relation to each other.

3.2. Comparison of Two MDT/SB

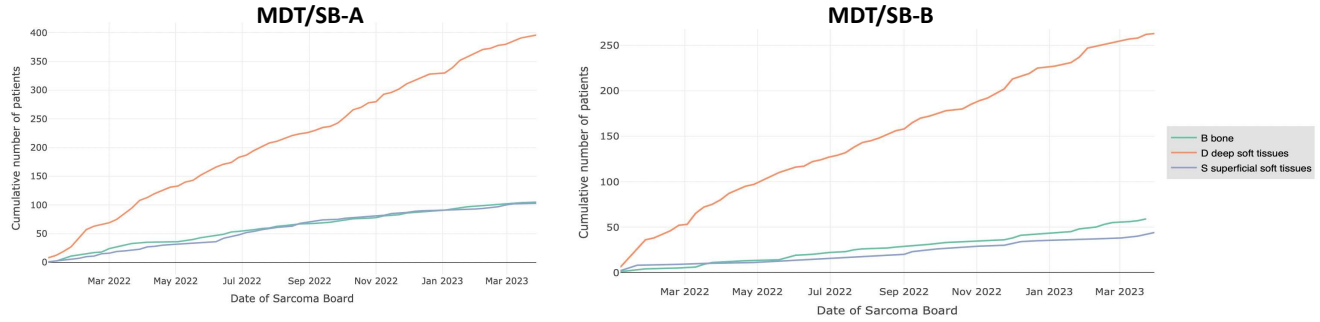
A basic data benchmark framework of consecutive patients over a 15-month period of two MDT/SBs were assessed for comparison (Table 2). While there were twice as many first-time presentations in MDT/SB-A compared with MDT/SB-B, there were equal follow-up presentations for both MDT/SBs. Patients with primary sarcomas were more numerous in MDT/SB-A than in MDT/SB-B, but together, they totaled 321 patients. An important difference relates to the number of biopsies, which are twice as much in MDT/SB-A as opposed to -B. This might be explained partly by the increased number of benign lesions being presented to the MDT/SB-A. While the indications for surgery and radiation therapy are comparable, the indications for chemotherapy differ between the two MDT/SBs. There are important differences pointing towards different strategies with respect to work-up and therapy. For example, there was a statistically significant difference in the proportion of biopsies performed. In the MDT/SB-A, 523/610 (85.7%) patients received a biopsy, but only 259/373 (69.4%) patients did in MDT/SB-B, $p < 0.0001$. Likewise, 23/330 (6.9%) patients with a sarcoma in MDT/SB-A were treated with chemotherapy, while 83/304 (27.3%) of sarcoma patients in MDT/SB-B were treated with chemotherapy, $p < 0.0001$.

Table 2. This table summarizes all relevant oncological data of the patients included in this study. The numbers are separately listed for each MDT/SB as well as overall.

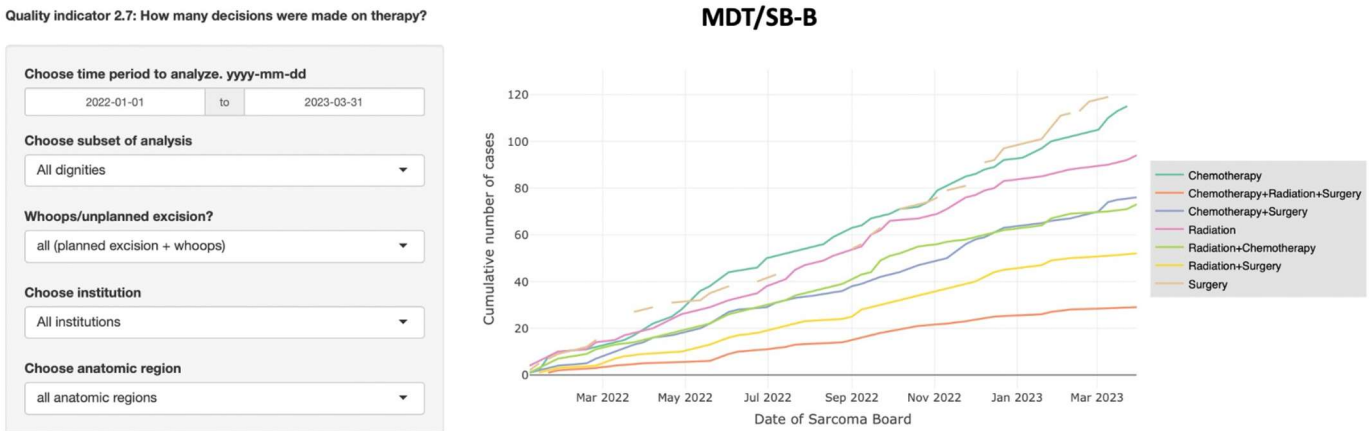
	OVERALL	**MDT-SB/A**	**MDT-SB/B**	***p*-Value**
Total number of patients	983	610	373	<0.001
Total number of presentations	1556	914	642	<0.001
	OVERALL	MDT-SB/A	MDT-SB/B	*p*-value
1st time presentations	650	416	234	<0.001
Follow-up presentations	833	431	402	<0.001
Dignity: 1st time/fup presentation	650/833	416/431	234/402	<0.001/0.17
Benign	120/70	105/54	15/16	<0.001/<0.001
Intermediate	135/50	61/77	74/3	<0.001/<0.93
Malignant	186/548	99/256	97/292	<0.001/<0.001
Simulator	43/20	35/13	8/7	0.01/0.26
Metastasis	10/4	10/4	0/0	0.02/0.13
Blood	53/11	9/1	44/10	<0.01/0.005
Others	103/30	97/26	6/4	<0.01/<0.01
Localization: 1st time/fup presentation	650/833	416/431	234/402	<0.001/0.17
Bone	117/141	77/76	40/65	0.67/0.58
Deep soft tissues	431/579	269/290	162/289	0.26/0.15
Superficial soft tissues	95/103	70/62	28/41	0.11/0.07
NA	7/10	0/3	4/7	0.02/0.21
1st time & intermediate/malignant	321	160	161	0.99
Bone	48	20	28	0.27
Deep soft tissues	224	111	113	0.90
Superficial soft tissues	49	29	20	0.17
Total number of biopsies	782	523	259	<0.001
Bone	133	82	51	0.19
Deep soft tissues	518	348	170	0.81
Superficial soft tissues	131	93	38	0.31
Indications for surgery	393	244	149	0.77
Bone	70	38	32	0.17
Deep soft tissues	259	161	98	0.99
Superficial soft tissues	64	45	19	0.16
Indications for radiotherapy	98	46	52	0.48
Bone	5	2	3	0.99
Deep soft tissues	73	33	40	0.65
Superficial soft tissues	20	11	9	0.46
Indications for chemotherapy	106	23	83	<0.001
Bone	28	9	19	0.18
Deep soft tissues	70	14	56	0.62
Superficial soft tissues	8	0	8	0.20

3.3. Interactive Data Analysis and Visualization

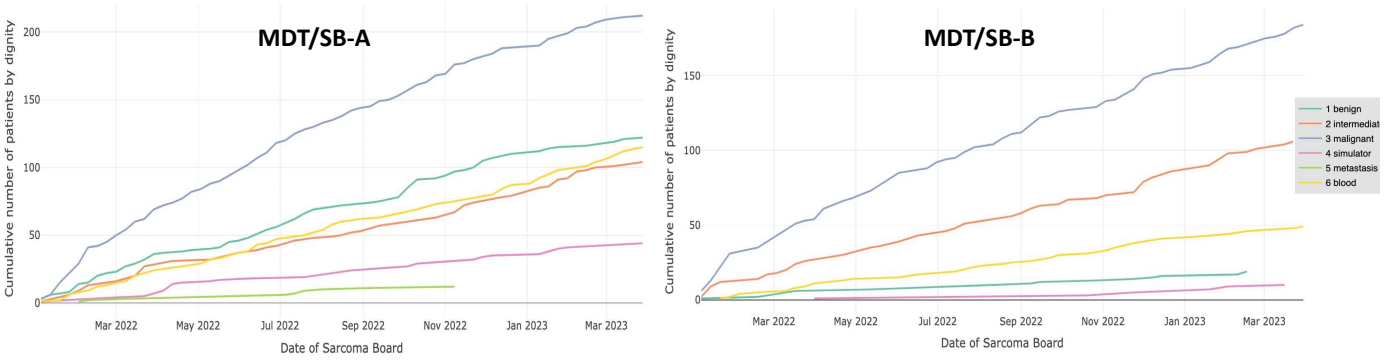
The Sarconnector® allows the interactive comparative visualization of the basic data with respect to a given time period, according to anatomic location, tumor biology or dignity of the tumor, and according to therapy, side by side for the respective MDT/SB (Figure 3a–d). The incidence of diagnosis or type of therapy is visualized over time to easily compare subgroups. Visualization of data is critically important to define subgroups for detailed analysis. Importantly, based on the selection of the subgroups to be defined for analysis, the system links the graphs with the respective raw data such that further detailed analysis can be carried out.



(**a**)

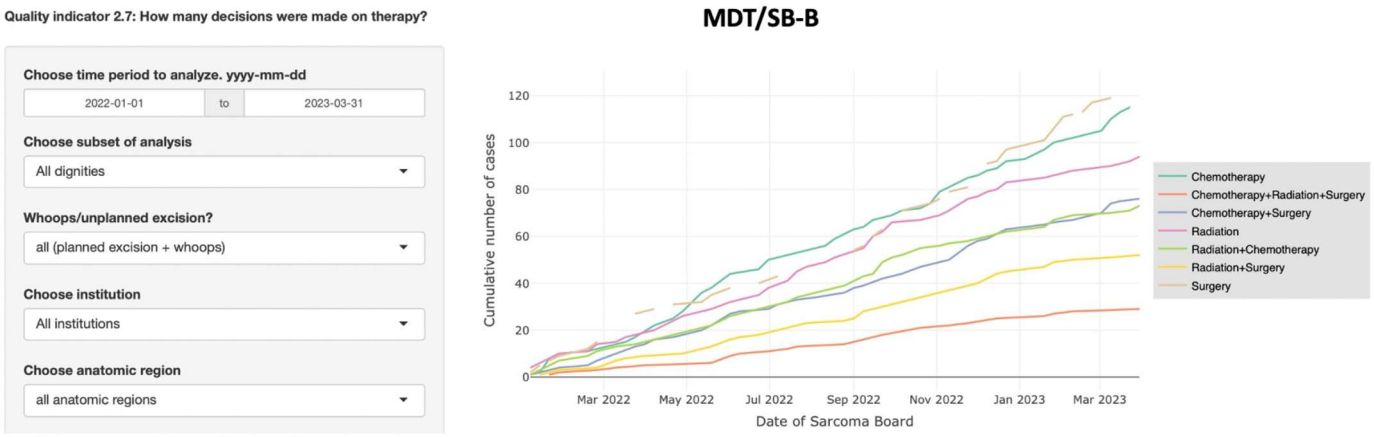


(**b**)



(**c**)

Figure 3. *Cont.*

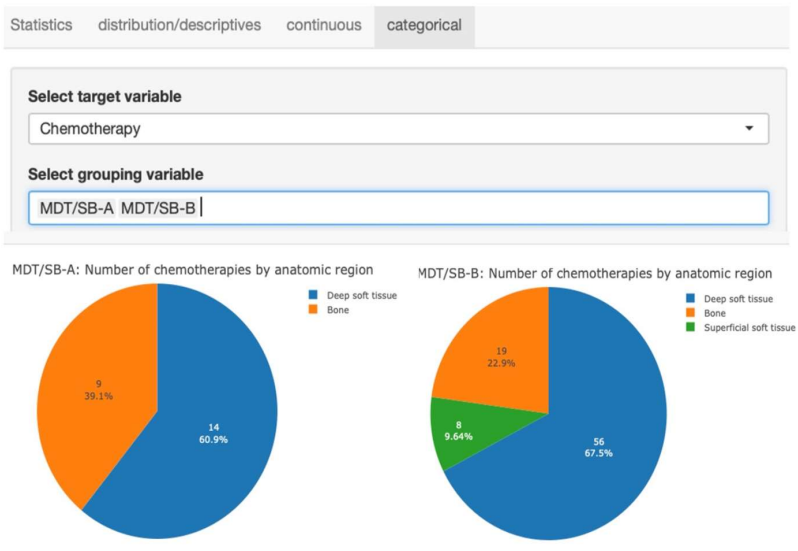


(**d**)

Figure 3. (**a**) These graphs show the cumulative incidence of patients presented at the MDT/SBs over a 15-month period, according to anatomic location of the tumor. (**b**) These graphs show the cumulative incidence of the patients presented at the MDT/SBs over a 15-month period, according to dignity of the tumors. (**c**) This graph shows the cumulative indications of patients presented at the MDT/SB-A over a 15-month period, according to the performed therapy. (**d**) This graph shows the cumulative indications of patients presented at the MDT/SB-Bs over a 15-month period, according to the performed therapy.

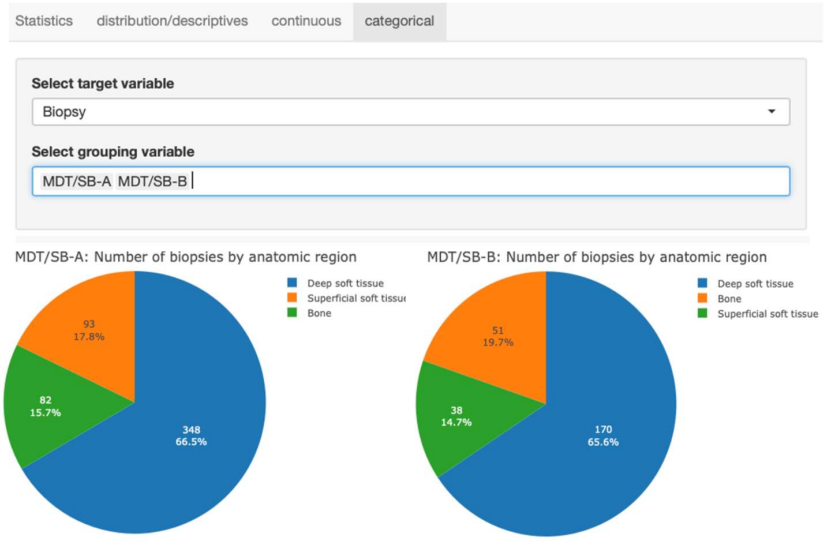
3.4. Automated Statistical Analysis and Visualization

The Sarconnector® allows the analysis of any subgroup parameter, the performance of basic statistical tests, as well as advanced statistical techniques (such as Cox regression, competing risk analysis). As a first step of the workflow, the appropriate statistical measure to analyze the data is chosen. For example, a Shapiro–Wilk normality test and Levene's test for equal variances are performed. Since these tests might suffer from low power [50], the researcher can also visually assess normal distribution by inspecting normal Q-Q plots and histograms. In the next step, the appropriate test is automatically chosen and performed. Furthermore, summary statistics (such as means and standard deviations of the compared samples or Kaplan–Meier estimates) and the corresponding figures are produced, which can be used in scientific publications (such as this one). The Sarconnector® therefore facilitates the conduction of clinical studies (Figure 4).



(**a**)

Figure 4. *Cont.*



(**b**)

Figure 4. (**a**) There was a statistically significant difference in the proportion of biopsies performed. In the MDT/SB-A, 523/610 (85.7%) patients received a biopsy, but only 259/373 (69.4%) patients did in MDT/SB-B, $p < 0.0001$. (**b**) There was a statistically significant difference in the proportion of chemotherapies performed. In the MDT/SB-A, 23/330 (6.3%) patients with a sarcoma were treated with chemotherapy, and 83/304 (27.3%) patients were in MDT/SB-B, $p < 0.0001$.

Figure 4 shows an interactive statistics tool of the Sarconnector®, which allows the performance of statistical tests (such as the *t* test) for continuous and categorical variables and the drawing of figures for publications automatically; (Figure 4a.) biopsy and (Figure 4b.) chemotherapy are shown as representative examples.

4. Discussion

We herein present a novel approach to handling and harmonizing medical data, thereby mirroring sarcoma patient care in real-world time and comparing respective sarcoma centers/IPUs. Large amounts of data are being assessed trans-disciplinarily and trans-institutionally, as well as across centers using the Sarconnector®, which is designed to determine quality indicators of sarcoma care and to provide a quality-management system. It is important to realize that the Sarconnector® does not simply collect data on the object-level but on the meta-level. Herein, we report the comparison of two large sarcoma centers in terms of how patients are being cared for to be subjected for meta-level data analysis. For example, we found important differences regarding the work-up approach of biopsies, as well as of therapeutic approaches, such as the indication to use chemotherapy. This provides unexpected insights about providing sarcoma care of different healthcare ecosystems, with potentially important consequences for both quality and longitudinal cost of care, thereby allowing the establishment of a benchmark. The Sarconnector® with its numerous critical care parameters being harmonized, interoperable and benchmarked over the geography not only allows automated evidence-based insights from the entire care cycle of an individual patient, but also ultimately paves the way for value-based precision care, which may represent the main strength of the novel meta-level approach as presented herein.

Obviously, there are also limitations to consider. The findings reported herein heavily rely on the availability and accuracy of the data collected. Missing or incomplete data could impact the analysis and potentially introduce biases. Also, two large sarcoma centers may not fully represent the diversity of sarcoma care across all healthcare ecosystems. Further, while the Sarconnector® identifies associations between different care approaches, it may not establish causality. Confounding factors that were not accounted for in the

analysis could influence the observed differences. And while we are focusing on sarcoma care herein, benchmarking might not cover all aspects of healthcare delivery or other medical conditions. Last but not least, while this approach presented herein is novel and comprehensive, there might be challenges or complexities in the implementation and widespread adoption of such a system in RWT healthcare settings.

In healthcare, benchmarking targets define the standard approach to improve patient outcomes, including the establishment of the best achievable real-world postoperative outcomes [15]. Ideally, defined parameters are reproducible, objective and universal [51]. The purpose of benchmarking is to stimulate the genuine endeavor for perfection, rather than judge a unit or physician performance [13,15,52,53]. An international jury consensus approach identified benchmarking as one of the key elements to reporting and improving the quality of surgical interventions and medical care [9]. To realize benchmarking, CROMS, PROMS/PREMS and complications of (surgical) treatments as outcome parameters have to be assessed both nationally and internationally. Why do we need benchmarking? By comparing their own performances with peers, best practices can be identified and learning experiences maximized. The best outcome can be defined and be adopted for standard practices. By comparing clinical practices and outcomes, not only can best practices be identified, but so can new and innovative ways to improve patient care. Benchmarking helps recognize outliers performing exceptionally well or poorly, and subsequently then helps investigate the reasons for their performance. By identifying areas where resources can be best utilized, resource allocation is handled more efficiently. As presented herein, biopsies or chemotherapies may be performed too often or not, but having the opportunity to align with outcome will enable the system to optimally allocate resources. In the context of accreditation and certification programs, healthcare providers comply with regulatory requirements and demonstrate the quality of care provided. Benchmarking in medical care and specifically cancer care, however, is not widespread. Furthermore, it has to be distinguished from standard of care, which generally refers to accepted practices, protocols and guidelines for providing medical treatment for a particular condition or disease [1,2]. Such standards are established based on the best available scientific evidence and expert consensus and are often used as a benchmark or reference point for evaluating the quality of care. In contrast, benchmarking involves comparing the performance of healthcare providers or healthcare systems against established standards or against each other. The standard of medical care provides a set of guidelines and expectations for how medical care should be delivered, while benchmarking medical care involves comparing actual performance against those standards to identify areas of improvement and drive quality improvement. In both herein presented MDT/SBs, the provided care is based on guidelines; nevertheless, important differences in practicing do exist, emphasizing the importance of introducing a benchmark tool in addition to the established guidelines. While there are no benchmarks reported for sarcoma care, there are sparse studies in the literature on cancer care and some on surgical disciplines. The international cancer benchmarking partnership (ICBP) is a collaboration of researchers and clinicians from several countries (Australia, Canada, Denmark, Ireland, New Zealand, Norway, Sweden and the United Kingdom) that aims to investigate and explain differences in cancer survival between countries [54,55]. This partnership compares cancer survival rates and stage at diagnosis across different countries using a standardized methodology in order to identify factors that contribute to variations in cancer outcomes [55]. The ICBP's mission statement is to provide policymakers, health professionals and the public with information about international variations in cancer survival and factors that might contribute to it in order to improve outcomes. To achieve this mission, the ICBP conducts research and analysis on cancer survival rates, stage at diagnosis and other related factors across participating countries. While this approach is laudable, it only concentrates on specific aspects of sarcoma care, while the herein presented approach is holistic. Nolte et al., exploring the link between policies and cancer survival, found a positive correlation with improvements in survival over time across various cancer sites analyzed [53]. Perera et al. developed an evidence-based benchmark

rate for cancer surgery used to provide a new template for high-income and emerging economies to rationally plan and assess their cancer surgery provisions [56]. Wind et al. explored the possibilities to benchmark cancer centers by structuring cancer care into pathways, reducing variability in clinical practices and improving patient outcomes [16]. They were successfully establishing and testing a benchmark tool that was pivotal to organizing cancer care in an IPU (integrated practice unit) to yield multiple performance improvements [52]. While benchmarking approaches are sparse for the musculoskeletal system [57], they are fairly common in visceral surgeries [58–62]. While these benchmarks focus on specific one-dimensional diseases, and while it is clear that policies will need to guide the transformation process, there are now efforts being undertaken to establish benchmarks for bottom-up use in more complex diseases [9,13,14]. With respect to sarcomas, there is only little information about benchmarking available [63–65], and they all refer to specific entities or surgeries without a holistic bottom-up approach including all basic parameters, underlining the necessity of our bottom-up approach as presented herein. Conversely, if it is the shared goal to benchmark quality and outcome, then it only makes sense to design a system including basic parameters that is designed to do so, i.e., to allow data harmonization and their scaling [44–48]. As shown herein (considering the discrepancies of performing biopsies or the indication to treat with chemotherapy among MDT/SBs and thereby identifying potential areas of differences in quality and costs), designing a system that allows not only the outcome but also the granular pathway of decisions, such as during an MDT/SB, is of critical importance. The Sarconnector® is designed to assess quality indicators, covering all the respective index and outcome parameters, and analyzes the pathway of decisions during MDT/SB to reproduce why which treatment was initiated. Taking into account the inclusion of long-term follow-up to incorporate outcome discrepancies, such an interoperable digital platform has the potential to ultimately become a sarcoma patient digital twin (SPDT) [40,66].

Data structures with their different types are obtained increased focus, and there is continued debate about its use [39,67]. Electronic health records (EHRs) are routinely used for clinical care and research. Clinical trials databases (CTDs) contain collected data during randomized trials. Administrative claims data representing billing codes and information submitted to insurance companies for reimbursement are usually again stored separately. There are also biobanks that store biological samples and associated data. Each data structure has its strengths and limitations [68]. The choice of data structure depends on the research question and the resources available for data collection and analysis. The advantage of real-world data includes the potential to capture real-world complexity, such as contextual factors and system interactions, which may be difficult to simulate through modelling alone [31,32]. Further, RWTD provides a rich source of information that can be used to calibrate and validate models [69,70]. RCTs are considered the gold standard for medical research as they involve randomization. Because these are typically conducted under highly controlled conditions, they can lead to limitations in terms of generalizability to the broader population and are usually associated with great costs. Conversely, RWTD provides a more comprehensive view of healthcare outcomes as it includes data collected from routine medical practice, electronic health records, administrative claims, and patient-generated data [40,67,69,71]. If incomplete or inaccurate data, confounding factors and selection biases are addressed with respective data structures, RWTD has the potential to complement and enhance the insights gained from RCTs [69,71–73]. An interoperable digital platform helps to overcome the limits by integrating data from various sources and standardizing data formats [74,75]. With an interoperable platform, data can be accessed, shared and analyzed more easily and efficiently. This may facilitate the identification of patterns and associations in the data that may not have been apparent otherwise. It improves the accuracy and completeness of data by reducing errors associated with data entry and enabling real-time capture [67]. If data are collected over time as we reported earlier [47], more accurate and timely information becomes available. Interestingly, an interoperable digital platform enables more extensive data analytics and modelling to

support decision-making processes, such as predictive modelling and machine-learning algorithms [39,74–76]. Integrating all common data sources and dimensions, coupled with the opportunity to analyze it concomitantly, enables the realization of real-world time evidence and prediction [77–79], and ultimately, the sarcoma patient digital twin (SPDT) [40,66].

The definition of outcome benchmarks with specific reference to quality indicators for a given disease, as well as an interoperable digital platform that includes economic data dimensions like the Sarconnector® does, represents the prerequisite for value-based healthcare, which aims to optimize the balance between health outcomes and costs [24,26,30,46]. VBHC incentivizes healthcare providers to deliver high-value care by linking reimbursement to quality indicators and promoting the use of shared decision-making tools that take into account patient preferences and values. In this context, the availability of RWTD/E with its associated analysis as presented herein plays a pivotal role. Because the Sarconnector® enables benchmarking sarcoma care and consequently the creation of a sustainable healthcare system, it is pivotal to support VBHC. Measuring and comparing performances across different healthcare providers or organizations becomes possible, while enabling the identification of best practices and areas for improvement in healthcare delivery is also made possible over time, which may lead to better outcomes and increased efficiency [21,80]. Variations in care delivery and outcomes may allow potential areas for cost savings and improved efficiency to be identified. Such tracking of performance over time allows for the evaluation of the effectiveness of interventions and the identification of trends. Health equity can be promoted by identifying and addressing disparities in healthcare. Benchmarking may also support VBHC by setting goals and targets for improving healthcare outcomes and reductions in costs, which can help to align incentives and motivate providers to improve performance [13,26,51,56]. High-performing providers may be used to inform patient decision making and help drive competition and innovation in the healthcare industry. The development of novel payment models makes it possible to incentivize high-value care, rewarding providers for delivering high quality at lower costs. It not only facilitates collaboration and knowledge sharing among healthcare providers and organizations, but it also supports the development of policies and regulations that promote the delivery of high-value care and encourage sustainability of the healthcare system. As presented herein by comparing two MDT/SBs and assessing consecutive and prospective RWT data, we found important differences regarding the number of biopsies and the number of chemotherapies performed for a comparable patient cohort. Both MDT/SBs treat their patients according to their best knowledge and available evidence. Nevertheless, the reported differences imply that depending on which sarcoma center/IPU a patient is being treated in, a patient may be over- or undertreated, or the set-up to deliver care may be differently organized. Independent of the situation, it is obvious that such differences have a direct impact on the financial burden. It also becomes obvious that the number per se of performed chemotherapies, for example, is merely a measure of volume but is not correlated with quality of care, which conversely can neither be associated with costs. The Sarconnector® is capable of identifying differences in delivering care between MDT/SBs from the same country and of even neighboring counties with partly overlapping patient populations. There are likely obvious differences in delivering care at different outcome qualities, but this is for certain at different costs. This is a somewhat unexpected finding, but it evidences the validity and the necessity of such a tool. Obviously, many more questions arise with these findings that need to be answered. We therefore believe that the Sarconnector® represents a powerful tool to develop a sustainable healthcare system.

5. Conclusions

In conclusion, benchmarking is a crucial tool for improving healthcare quality and efficiency with respective cost containment. The RWT data approach provided by the Sarconnector® offers a valuable method for evaluating quality and cost metrics in a standardized way, allowing for transparent comparisons between different healthcare providers.

This approach enables healthcare providers to identify areas for improvement and make data-driven decisions to optimize their resources and improve outcomes. By utilizing benchmarking and the RWT harmonized data approach, healthcare providers can move towards a value-based care model, where high-quality care is delivered at a reasonable cost. Ultimately, benchmarking with the RWT harmonized data approach provided by the Sarconnector® can help healthcare providers achieve better outcomes for their patients and improve the overall effectiveness of the healthcare system with respect to both outcomes and costs.

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Article

Definition of the Surgical Case Complexity in the Treatment of Soft Tissue Tumors of the Extremities and Trunk

Annika Frei [1,*], Mario F. Scaglioni [2], Pietro Giovanoli [3], Stefan Breitenstein [4], Philip Heesen [5], Bruno Fuchs [3,6,7] and on behalf of the Swiss Sarcoma Network

1 Institut für Pathologie, Kantonsspital Winterthur, 8400 Winterthur, Switzerland
2 Klinik für Hand- und Plastische Chirurgie, Luzerner Kantonsspital, 6000 Lucerne, Switzerland; mario.scaglioni@luks.ch
3 Klinik für Plastische Chirurgie und Handchirurgie, Universitäts Spital Zürich, 8091 Zurich, Switzerland; pietro.giovanoli@usz.ch (P.G.); fuchs@sarcoma.surgery (B.F.)
4 Departement Chirurgie, Kantonsspital Winterthur, 8400 Winterthur, Switzerland; stefan.breitenstein@ksw.ch
5 Medizinische Fakultät, Universität Zürich, 8032 Zurich, Switzerland; philip.heesen@uzh.ch
6 Klinik für Orthopädie und Unfallchirurgie, Luzerner Kantonsspital, 6000 Lucerne, Switzerland
7 Klinik für Orthopädie und Traumatologie, Kantonsspital Winterthur, 8400 Winterthur, Switzerland
* Correspondence: annika.frei@bluewin.ch

Simple Summary: Soft tissue tumors are heterogeneous tumor entities that often require surgical intervention for treatment. While some tumors are easy to resect, others require extremely complex, interdisciplinary surgery depending on the tumor type, localization and biological behavior. Up to now, there has not been an instrument able to objectify the complexity of such a surgery; therefore, we attempted to establish a complexity score for the description of soft tissue tumor surgeries. Furthermore, we aimed to categorize surgeries in such a way that patients can be assigned the best treatment such that a cost-effective approach can be taken.

Abstract: Background: We intend to establish a complexity score for soft tissue tumor surgeries to compare the complexities of different soft tissue tumor surgeries and to ultimately assign affected patients to appropriate treatments. Methods: We developed a soft tissue tumor complexity score (STS-SCS) based on three pillars: in addition to patient-related factors, tumor biology and surgery-associated parameters were taken into account. The STS-SCS was applied to our sampling group of 711 patients. Results: The minimum STS-SCS was 4, the maximum score was 34 and the average score 11.4 ± 5.9. The scores of patients with malignant diagnoses were notably higher and more widely scattered than those of patients with benign or intermediate malignant tumors. To better categorize the complexities of individual surgeries, we established four categories using the collected data as a reference dataset. Each of the categories contained approximately one-quarter of the registered patients. Discussion: The STS-SCS allows soft tissue tumor surgeries to be retrospectively evaluated for their complexity and forms the basis for the creation of a prospective concept to provide patients with the right intervention in the right geographic location, which can lead to better results and provision of the most cost-effective overall treatment.

Keywords: soft tissue tumors; complexity score; sarcoma

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1. Introduction

Soft tissue tumors are rare, and affected patients often initially present to general practitioners or orthopedic surgeons [1]. The clinical differentiation between benign and malignant lesions is often very difficult, and even highly malignant soft tissue tumors are often misdiagnosed as benign tumors [2]. A reliable diagnosis can often only be made by biopsy, which is the only way to determine the histological subtype and grade according to the FNCLCC system [2]. Unfortunately, soft tissue sarcomas are often not primarily

recognized as such, so the term "whoops procedure" describes the situation where a lump is incompletely removed by a surgeon who is not aware of the malignancy of the soft tissue tumor. In this case, extensive subsequent re-excisions are often required as residual tumor tissue is a risk factor for local recurrence [3].

Surgery is the mainstay of therapy for both benign and malignant soft tissue tumors. Sarcomas originate from the entire skeleton and surrounding soft tissues and display various biological behaviors that are dependent on the biologic entity. The goal of surgery is complete en bloc resection with avoidance of positive margins, whenever possible, to reduce the risk of local recurrences, distant metastases and mortality [4]. Surgical techniques of resection are various and often depend on the anatomic site of the lesion. Furthermore, while some resections are followed by complex reconstructions, others require no further surgical interventions. In addition, chemotherapy and radiotherapy are considered important pillars of multimodal and transdisciplinary sarcoma treatment, either preoperatively, postoperatively or in combination. All of these aspects are evidence that surgery for soft tissue sarcomas is a highly complex transdisciplinary action that needs to be personalized for each patient's specific situation.

There is much debate regarding centralization of complex surgery to reduce costs; however, there are no robust data to define surgical complexity, which is obviously a critical determinant because there is a wide spectrum for a given disease. Defining the complexity of surgical resection in terms of center-based medicine is important for several reasons. As early as 1979, Luft et al. postulated a correlation between the surgical volume and mortality. They showed that for various complex interventions, mortality seemed to be inversely proportional to the volume of operations [5], which was also confirmed by others [6]. Despite a wealth of data, recent studies have highlighted various challenges facing centralization efforts [7]. Volume-based morbidity improvements do not seem to be transferrable to all surgeries, with some studies concluding the opposite [8]. A high surgical volume does not guarantee a good outcome for all types of surgeries, and poor processes may become naturalized in centers due to frequent repetition [7].

Modern healthcare concepts, therefore, include integrating the complexity of a procedure and the complexity of a patient (with associated comorbidities) to determine the optimal location for care [9]. With the advent of value-based healthcare delivery, the definitions of quality and outcomes are pivotal to defining the value for the patient, in addition to the cost package over the full care cycle. In most hospitals, costs are still defined by diagnosis/volume-based accounting systems, which by no means reflect the complexity of soft tissue sarcoma surgery. For all these reasons, we aimed to establish a score for the complexity of soft tissue tumor surgery to enable comparison within a diverse surgical spectrum. As sarcomas are rare, occur in all anatomic locations of the body and their treatment is highly multidisciplinary, surgical treatment involves a wide spectrum of complexity, includes both resections and reconstructions and may, therefore, ideally be suited to such an analysis of surgical complexity.

2. Materials and Methods

2.1. Study Population

All surgeries on soft tissue tumors over a 15-year period performed by a single surgeon were registered in the AdjumedCollect "Sarcoma Surgeon's Registry" (Adjumed Services AG, Zurich, Switzerland; www.adjumed.ch (accessed on 22 October 2021)). The AdjumedAnalyze tool (Adjumed Services AG, Zurich, Switzerland) can be used for basic statistics, such as combinations of parameters, and allows the extraction of data. The individual scores were subsequently calculated in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

2.2. Soft Tissue Tumor Surgery Complexity Score (STS-SCS)

Based on the literature and expertise of experienced sarcoma surgeons, we compiled and defined relevant parameters for an STS-SCS. The score is essentially based on three pillars: the patient, tumor biology and surgery-based parameters (Figure 1).

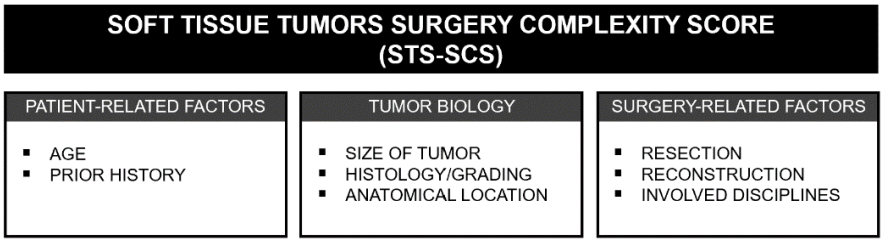

Figure 1. Overview of the three pillars and the individual factors on which the STS-SCS is based.

In the first pillar, patient-related factors such as age and prior history—in particular, previous radio- or chemotherapy—were summarized. It was shown that elderly patients with soft tissue sarcomas of the extremities have lower overall survival compared with younger patients [10]. Neoadjuvant therapies such as radio- or chemotherapy play an increasing role in the treatment of soft tissue tumors and must be included in perioperative management. The number of available neoadjuvant modalities is constantly increasing, and the use of possible therapies must be individually assessed due to the heterogeneity of tumors. Patients with advanced disease, in particular, can often benefit from neoadjuvant therapy modalities, but there are also associated risks. For example, neoadjuvant radiotherapies may lead to wound-healing disorders, while chemotherapies can lead to a delay in surgical treatment or even tumor progression during chemotherapy. In addition, complications during neoadjuvant CHT can significantly delay surgery and prolong the overall treatment time [11]. Previous whoops operations for misjudged soft tissue tumors also complicate perioperative management and often entail excessive re-excisions to reduce the risk of local recurrence [3].

For patients with soft tissue tumors, it has been shown that the smaller the tumor at diagnosis, the better the prognosis [12]. Histological grading seems to be the most important factor for the prognoses of patients with soft tissue tumors and, thus, has an even higher significance than histological typing [13]. In addition to the histological type, the anatomical location of soft tissue tumors also seems to be decisive. For example, it has been shown that metastases occur more frequently in patients with sarcomas of the lower extremities than the upper extremities, and that these tumors are, by far, more frequently larger and deeper [14]. The centralization of soft tissue tumor surgeries in high-volume hospitals can especially improve the survival of patients with non-low-grade and deep-seated tumors [15].

Due to the mesenchymal origin of sarcomas, these tumors often involve multiple anatomical structures and regions [16]. Depending on the location and proximity to surrounding organs, the removal of several structures may be necessary for sarcoma resection. If only soft tissues were removed, a score of 1 was assigned; if other structures such as muscles, nerves, bones, periosteum, tendons or vessels had to be removed, additional points were given. This challenge may require the expertise of different surgical subspecialties, so a multidisciplinary treatment team will include surgical oncologists from several different specialties such as orthopedics, thoracic surgery, general surgery, vascular surgery, neurosurgery, urology and gynecology as well as reconstructive plastic surgery. In addition to the interdisciplinary challenges, the involvement of vascular structures also seems to have an influence on the recurrence rate. It was shown that when the tumor was radiologically surrounded by large vessels, vascular resection and bypass reconstruction provided improved local control [17]. The involvement of vascular structures in a sarcoma significantly complicates surgery but is not, in itself, a contraindication for sarcoma resection [18].

Following sarcoma resection, reconstruction is often not necessary; however, in selected cases, patients may benefit greatly. Reconstructive procedures can be, at times, extremely elaborate, depending on the type and extent. The heterogeneity in tumor reconstruction was thus taken into account with a procedure-specific evaluation system. However, it is obvious that not all possible types of reconstruction can be adequately represented by a score, especially since the possibilities are very extensive and the indication for each patient is individual.

Finally, the previously identified relevant factors were examined for their individual influences on the complexity of surgery and weighted accordingly. This resulted in a total score (Table 1) based on the listed parameters and their corresponding weighting, which was then individually determined for each patient, using the data extracted from Adjumed, by adding the individual factors together.

Table 1. STS-SCS system indicating the weighting of each parameter.

			Points	**Maximum**
Patient's Age	≤17 years		1	
	18–64 years		0	
	≥65 years		1	1
Histology/Grading	Benign		1	
	Simulator		1	
	Intermediate		2	
	Blood-based solid tumor		3	
	Metastasis		5	
	Malignant	G1	5	
	Malignant	G2	6	
	Malignant	G3	7	7
Prior History *	Preoperative radiotherapy		2	
	Preoperative chemotherapy		2	
	Prior whoops		2	6
Size of Lesion	5 cm or less		1	
	more than 5 cm, but no more than 10 cm		2	
	more than 10 cm, but no more than 15 cm		3	
	More than 15 cm		4	4
Anatomical Location	Superficial		1	
	Deep		2	2
Resected Structures (soft tissue, muscles, nerves, bones, periosteum, tendons, vessels) **	1		1	
	2		2	
	3		3	
	4		4	
	5		5	
	6 or more		6	6
Type of Reconstruction ***	Mesh graft		1	
	Tendon/ligament reconstruction		1	
	Bone cementation		1	
	Open reduction internal fixation (ORIF)		1	
	Bone autograft		2	
	Bone allograft chips		2	
	Other bone reconstruction		2	
	Vessel reconstruction		2	
	Nerve reconstruction		2	

Table 1. *Cont.*

		Points	Maximum
	Lymphovenous reconstruction	2	
	Intra-abdominal reconstruction	2	
	Pedicled tissue transfer	3	
	Chest wall reconstruction	3	
	Free tissue transfer	4	16
Number of Involved Disciplines ****	One discipline	0	
	Two disciplines	1	
	Three disciplines	2	
	Four disciplines	3	
	Five and more disciplines	4	4
Total		max.	46

* The points in the section "prior history" can be added together, resulting in a maximum score of 6 in this field. ** For each resected structure (such as muscle, nerve, vessel, etc.) a point is added. *** The four highest scores in the section "type of reconstruction" are summed up. An intervention (for example, various nerve reconstructions) can be listed numerous times. **** If one single surgeon is sarcoma surgeon but has the credentials also for vascular reconstruction, then 2 disciplines are registered.

3. Results

3.1. Characteristics of Soft Tissue Tumor Patients

In this study, we examined the data of 711 patients. The mean age of the analyzed patients was 51.0 ± 18.2 years. Of the operated patients, 70% were between 18 and 64 years old. Males accounted for 383 of the patients, and 328 were females (Figure 2). The male-to-female ratio was 1.17. Of the patients, 263 had benign tumors (37%), 118 patients had tumors with intermediate malignancy (17%) and 270 patients suffered from malignant (38%) soft tissue tumors. The remainder of the patients (8%) had metastases, hematologic solid tumors or tumor simulators (a tumor that may imply a sarcoma on imaging but turns out to be a benign mesenchymal non-tumorous lesion). The most common benign diagnosis was, by far, lipoma (131 patients; 18%). We found that 51 patients (7%) had atypical lipomatous tumors, which are classified as tumors of intermediate malignancy. The most common malignant diagnosis was undifferentiated/unclassified pleomorphic sarcoma (UPS) (76 patients; 11%), followed by myxoid liposarcoma (42 patients; 6%) and myxofibrosarcoma (33 patients; 5%). Other diagnoses were much rarer.

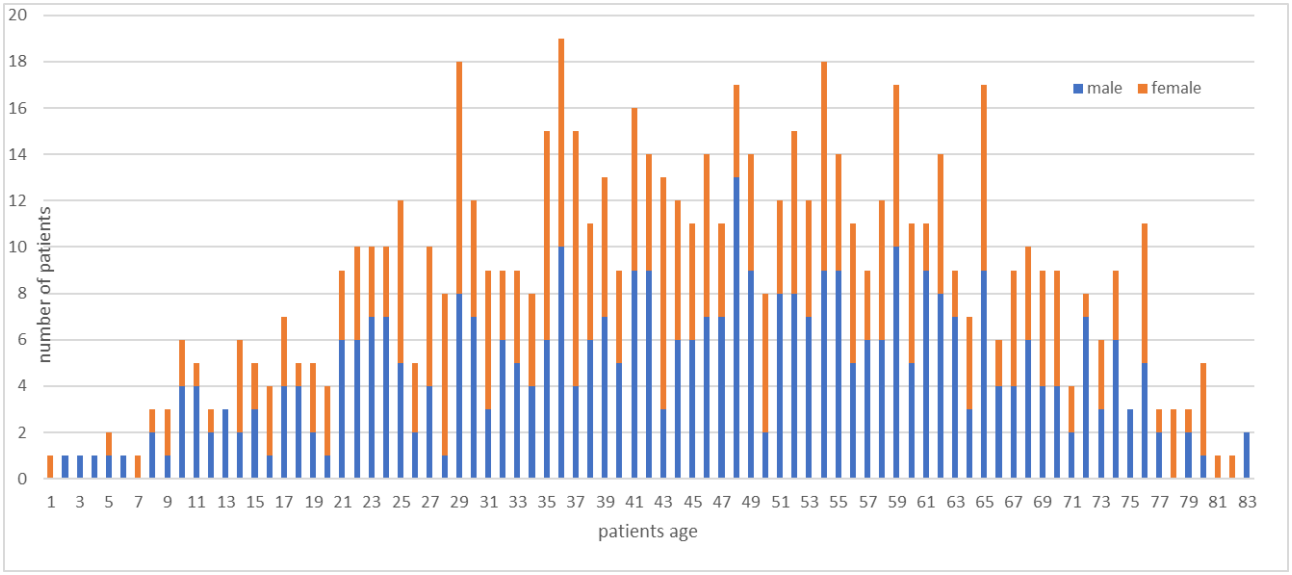

Figure 2. Age and gender distribution in the subject group.

3.2. Application of the STS-SCS

The STS-SCS was applied to our sampling group of 711 patients and the individual scores were calculated for each patient using Microsoft Excel. The minimum score was 4 and the maximum score 34, with an average score of 11.4 ± 5.9. The scores of patients with malignant diagnoses (17.5 ± 4.6) were notably higher and more widely scattered than those of patients with benign (6.8 ± 1.8) or intermediate malignant tumors (10.2 ± 4.1) (Figure 3).

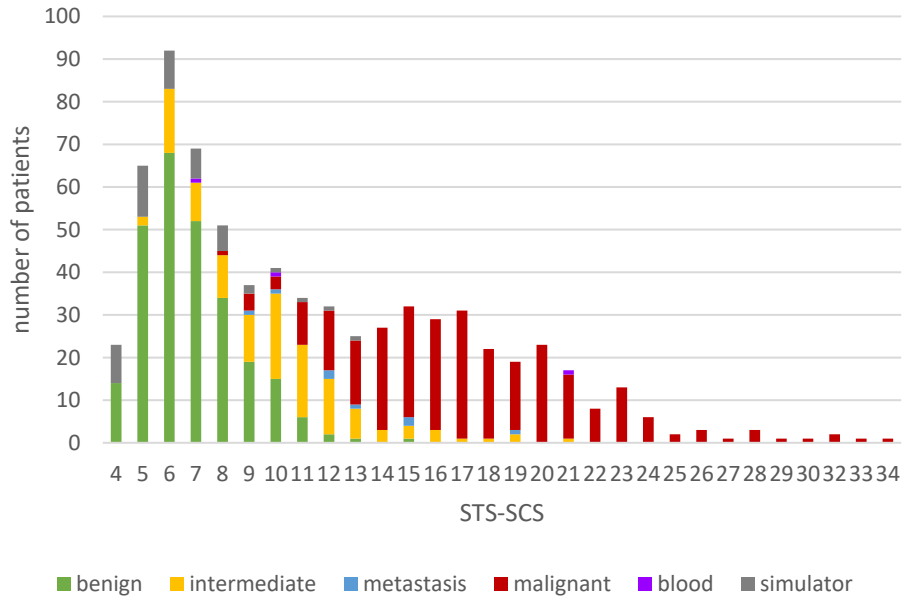

Figure 3. Distribution of the totals of the soft tissue tumor surgery complexity score (STS-SCS) in the sampling group.

3.3. Categorization of Soft Tissue Tumor Surgery Complexity

To better categorize the complexity of individual surgeries, we established four categories using the collected data as a reference dataset. Each of the categories contained approximately one-quarter of the registered patients (Table 2).

Table 2. Division of surgeries into four categories.

Category	Complexity Score	Number of Patients	Percentage (%)
1	≤6	180	25.3
2	7–9	157	22.1
3	10–15	191	26.9
4	≥16	183	25.7

Category 1 included patients with a score lower than 7 points. This covers a relatively wide range of scores and included 180 (25.3%) patients. This category contained patients with benign, intermediate malignant tumors and tumor simulators. Patients with a score of between 7 and 9 points were assigned to category 2, which covered only a very small range of points, but still included 157 patients (22.1%). Most patients in this range had benign or intermediate malignant diagnoses, but there were also a few malignant diagnoses. Category 3 included patients with a score of 10–15 points and comprised 191 patients (26.9%). In the highest category, 4, there were 183 patients (25.7%) with almost exclusively malignant diagnoses, with a few exceptions. The highest category covered the largest range, and the scores were further apart from each other than those in the lower categories (Figure 4).

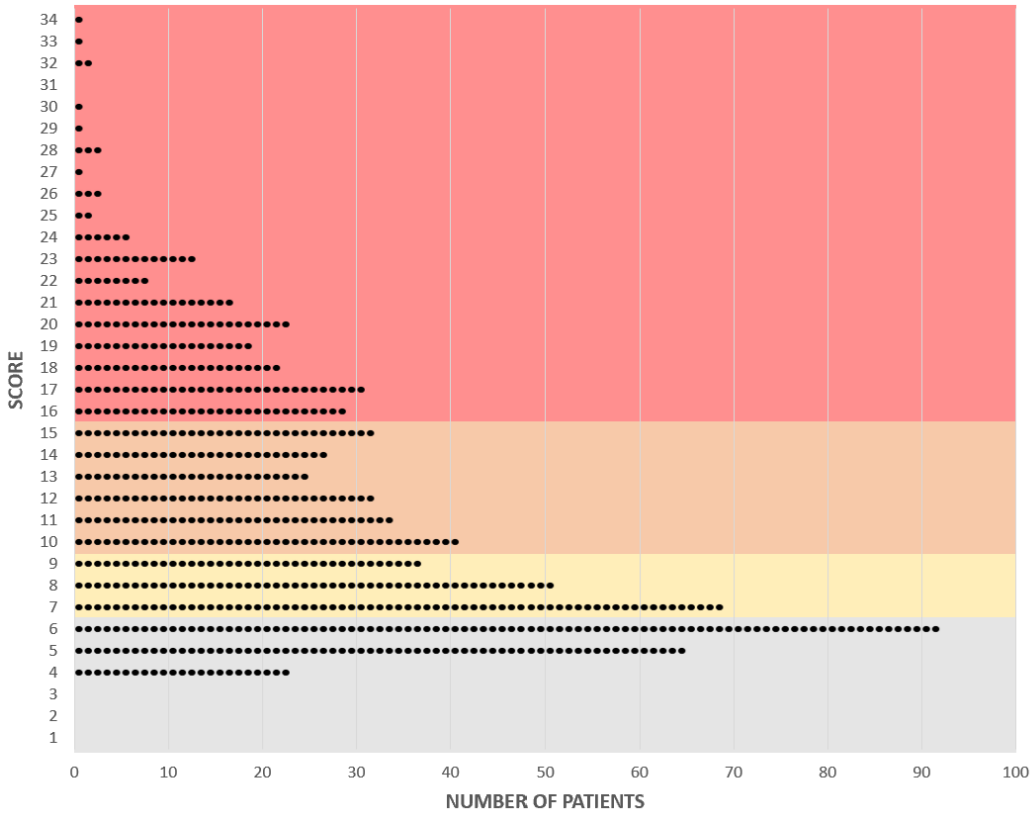

Figure 4. Graphical representation of individual scores and their allocation to the categories of complexity. Each point represents a patient. Category 1: gray, Category 2: yellow, Category 3: orange, Category 4: red.

4. Discussion

In our study, we defined the STS-SCS based on three main pillars: patient-related factors (such as age and prior history), tumor biology (tumor size, histology/grading and anatomical location) and surgery-associated factors, such as the type of resection and reconstruction or the involved disciplines. This score was then applied to a sample group of 711 patients with various soft tissue tumor diagnoses. An individual score was calculated for each of the subjects. Based on these data, four complexity categories were defined that allow the assignment of the individual surgeries to four complexity levels. This strategy allowed the assignment of each soft tissue tumor operation to a complexity level and, thereby, the comparison of the different interventions.

This is the first time such an approach has been attempted; therefore, there were no alternative methods for comparison, which made the selection and weighting of factors challenging. It will never be possible to include all potentially relevant factors to fully describe a patient (e.g., comorbidities), but the current STS-SCS is intended to establish a basis for discussion. Just as particularly complex patients may not be adequately represented, unusually complicated surgeries had to be broken down and, therefore, may not yet be adequately covered by the selected categories.

In the value-based geography of care according to Porter et al. [9], the best possible cost-effective quality care for the patient is defined by the complexities of the procedure and the patient, which in an integrated system, allows the direction of patients requiring complex care to regional or central hubs, while those patients who need less complex care are moved to the most cost-effective local centers (Porter geography model). To realize such a model of geographically-based care, a tool to assess and define the complexity of a surgical procedure is mandatory; we have proposed such a tool, the STS-SCS, which maps the considerations into a complexity score. The integration of patient- and procedure-related factors allows the patient to be matched to the best possible treatment site as well

as the optimal treatment team. Not only does the adequate allocation of patients increase the output, but it also allows the cost of treatment to be reduced for specific diseases or treatments [19]. Assigning the patient to the ideal treatment site seems to be an intuitive matter; however, its implementation, in practice, does not seem to be that easy, and the instruments for decision making are not yet available for sarcoma care. Therefore, the STS-SCS provides a tool to facilitate decisions related to the allocation of soft tissue tumor patients to appropriate treatment sites.

Considering complexity is not only important in terms of the treatment location but also the treatment team. Geography is a powerful tool to optimize value in three dimensions: the right mix of personnel, working together at the right location and with integration across time [9]. Porter et al. defined integrated practice units in which teams over a geographical region communicate and exchange to enhance the quality of care [9]. Patients with benign and malignant soft tissue tumors are often first seen by general practitioners or general and orthopedic surgeons, and making the correct diagnosis is often difficult, which frequently leads to unplanned excisions [20]. In addition, establishing the correct pathological diagnosis of a sarcoma is often difficult, and misdiagnoses often occur due to confusion with benign tumors [20]. Centralized pathological assessment of soft tissue tumors, for example, was shown to save costs while improving the quality of diagnoses [21]. Such an integrated exchange over a geographical region among multidisciplinary and cooperating integrated practice units helps to establish a complex diagnosis and initiate appropriate therapeutic measures [22]. The STS-SCS is an instrument that facilitates and objectifies the allocation of patients to the appropriate care site while considering their comorbidities and possible complications.

The definition of complexity for soft tissue tumor surgery using the STS-SCS also serves as a basis for assessing the quality of soft tissue sarcoma surgery. Up to now, it has been common practice to use the surgical volume as a predictor of the outcome [6], and for some soft tissue tumors, such as large, high-grade and retroperitoneal tumors, it has been shown that a good outcome is associated with a high volume [23,24]; similar results were also obtained for soft tissue tumors of the extremities [25]. Further to this, it has been shown that treatment in a multidisciplinary team improves the surgical margins for deep-seated lesions [26], while the French sarcoma group reported an impact on outcome by the multidisciplinary team approach, but interestingly not by surgical volume [27]. However, the definition of further quality indicators has been lacking until recently, which resulted in our intention to develop an approach to comprehensively assess the quality of sarcoma surgery. Certainly, and foremost, the quality of sarcoma surgery depends on the complexity of the procedure, which must be extensively considered when defining quality. Using the STS-SCS as a basis together with the extended database developed in the framework of this project, we can describe the complexity of a surgery as a common basis and, in a further step, use these tools to make considerations regarding quality.

The outcome for disease control and the quality of surgery not only depends on technical aspects but also on the correct diagnosis and, specifically, on the correct indication to perform the surgery [28]. Indication quality encompasses the appropriateness and necessity of medical interventions but continues to only be given a subordinate role in our current practice [28]. It is, therefore, crucial to establish scientific evidence and guidelines that facilitate the physician's assessment of the appropriateness of an intervention. The STS-SCS greatly facilitates the ability to bundle specific procedures or groups of similar procedures for comparison and analysis and, thereafter, extrapolate to define the indication quality for performing a specific soft tissue tumor resection or reconstruction, thus making the indication quality an entry point for the quality discussion. Once the quality of a surgery is defined, this information can be extrapolated to the choice of the correct indication for the surgery regarding evidence-based principles and standards, which include the results of clinical studies' and guidelines.

5. Conclusions

Currently, we are able to retrospectively assess surgeries according to their complexity using the STS-SCS, which was developed in our study. This score makes it possible, for the first time, to categorize soft tissue tumor surgeries based on their complexity, which allows patients to receive the right intervention or treatment at the right site, which may lead to better outcomes and more cost-effective treatment overall. Based on Porter's principles and the STS-SCS presented in this article, a prospective approach to model soft tissue surgery evaluation was developed to assign patients with soft tissue tumors to the appropriate surgery site based on their individual risk factors and planned surgical intervention.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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Conflicts of Interest: The authors declare no conflict of interest.

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Article

Enhancing Healthcare for Sarcoma Patients: Lessons from a Diagnostic Pathway Efficiency Analysis

Maria Elyes [1], Philip Heesen [2], Georg Schelling [1], Beata Bode-Lesniewska [3], Gabriela Studer [1] and Bruno Fuchs [1,2,4,*,†] on behalf of the Swiss Sarcoma Network

[1] University Teaching Hospital LUKS, Lucerne, Sarcoma Service, University of Lucerne, 6000 Lucerne, Switzerland
[2] University Hospital USZ, Sarcoma Servuce, University of Zurich, 8000 Zurich, Switzerland
[3] Pathologie Institut Enge, University of Zurich, 8000 Zurich, Switzerland
[4] Kantonsspital Winterthur, Sarcoma Service, 8400 Winterthur, Switzerland
* Correspondence: fuchs@sarcoma.surgery
† Additional collaborators of the Swiss Sarcoma Network are indicated in the Acknowledgement.

Simple Summary: The total interval of the diagnostic pathway, which consists of the patient interval and the diagnostic interval, describes the time between the first symptom and the final diagnosis. Thus, it could be used as an efficiency marker of a healthcare system. The efficiency of the most expensive health care system in Europe, Switzerland, for bone and soft tissue sarcomas, as well as their benign representatives, has not yet been described. Sarcomas are rare and have a worse outcome than more common tumors. It is assumed that a short total interval leads to a better outcome. Finding out where to start in the total interval to achieve the greatest potential for optimization and to elicit healthcare efficiency is the goal of this study. We have done this by dividing the total interval into its components and looking at their length, as well as potential influencing factors. This revealed that the patient and secondary care interval represent bottlenecks with age, grade, localization, and size being influencing factors of the length of intervals and probability of sarcoma.

Abstract: Sarcomas, rare and with lower survival rates than common tumors, offer insights into healthcare efficiency via the analysis of the total interval of the diagnostic pathway, combining the patient interval (time between the first symptom and visit with a physician) and diagnostic interval (time between first physician visit and histological diagnosis). Switzerland's healthcare system, Europe's costliest, lacks research on treating rare conditions, like mesenchymal tumors. This study examines the total interval of the diagnostic pathway for optimization strategies. Analyzing a dataset of 1028 patients presented from 2018 to 2021 to the Swiss Sarcoma Board (MDT/SB-SSN), this retrospective analysis delves into bone sarcoma (BS), soft-tissue sarcoma (STS), and their benign counterparts. Demographic and treatment data were extracted from medical records. The patient interval accounted for the largest proportion of the total interval and secondary care interval for the largest proportion of the diagnostic interval. Age, grade, and localization could be elicited as influencing factors of the length of different components of the total interval. An increasing age and tumor size, as well as the axial localization, could be elicited as factors increasing the probability of sarcoma. The patient and secondary care interval (SCI) offer the greatest potential for optimization, with SCI being the bottleneck of the diagnostic interval. New organizational structures for care work-ups are needed, such as integrated practice units (IPU) as integral part of value-based healthcare (VBHC).

Keywords: sarcoma; benign bone tumor; benign soft-tissue tumor; total interval of diagnostic pathway; diagnostic interval; referral patterns; healthcare system; quality management system; MDT/SB-SSN; multidisciplinary Team/Sarcoma Board of the Swiss Sarcoma Network; RWTD/E; real-world-time data evidence

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1. Introduction

Several studies have examined the diagnostic interval of sarcomas, yet none have specifically characterized this interval within Switzerland, the European country with the highest healthcare costs [1]. This research gap underscores a critical need to comprehensively understand the diagnostic pathway for sarcoma patients in a healthcare system characterized by high costs and a unique geographical and cultural landscape.

Sarcomas are among the rare diseases with an incidence of 4.43 per 100,000 person-years for soft-tissue sarcoma (STS) and 0.91 per 100,000 person-years for bone sarcoma (BS) [2,3]. Apart from their mesenchymal origin, sarcomas exhibit remarkable heterogeneity, with more than 80 histological subgroups [4] and diverse ages at disease onset, sites of manifestation, and tumor progression aggressiveness. This complexity combined with the rather limited research on rare cancers leads to an incomplete understanding of sarcoma biology, diagnostic challenges, and less effective therapies and guidelines. Consequently, these factors contribute to the observed lower survival rates compared to more common cancer entities [5].

This situation underscores a relevant concern, as the lack of comprehensive insights presents a significant obstacle for implementing both national and international measures. To comprehend potential variations in the treatment of sarcoma patients within the Swiss healthcare framework, it becomes essential to scrutinize the structure of the healthcare system itself. Switzerland's healthcare system is upheld through a blend of public and private funding. Access to healthcare services necessitates mandatory health insurance for citizens, who are also liable for a significant portion of the healthcare expenses. The Swiss healthcare system is characterized by a high quality of care, great patient satisfaction, extensive patient autonomy in choosing medical service providers, and a wide range of medical service providers [1]. Consequently, patients do not necessarily have to seek a primary care physician first, but can go directly to a secondary care specialist, depending on their insurance model and preferences. The referral patterns of sarcoma patients in Switzerland remain uncharted. Hence, it remains uncertain if the substantial healthcare expenses also lead to a positive outcome in the shape of short diagnostic intervals for uncommon conditions, like mesenchymal tumors. This matter holds significance not just for patients but also for governmental bodies, with potential cost-saving implications.

The diagnostic interval (the time between the first physician visit and a histologically confirmed diagnosis) together with the patient interval (the time between the date of the first symptom and first consultation with a physician) collectively compose the total interval of the diagnostic pathway (the time from the first mesenchymal tumor-related symptom to the histological confirmation of the diagnosis) [6–8]. The diagnostic interval describes the referrals from primary care via secondary care to the tertiary care sector. Tertiary care involves specialized medical facilities, such as sarcoma centers for mesenchymal tumors. To counteract the complex nature of mesenchymal tumors, which leads to diagnostic challenges and suboptimal treatment courses and outcomes, the centralization or regionalization of diagnosis and treatment of sarcoma patients is advocated [9–12]. However, the feasibility of such centralization or regionalization depends on the availability of the necessary logistical capacity, including the presence of sarcoma specialists. Otherwise, there could be a backlog of patients in the tertiary care sector if referrals from the secondary care sector exceed its capacity.

Early diagnosis is essential for the patient outcome in many cancer entities [13]. This is also true for sarcoma patients, for whom early diagnosis has a positive impact on survival [14]. To ensure a timely diagnosis, it is crucial for the total interval of the diagnostic pathway to be minimized.

To optimally shorten the total interval of the diagnostic pathway, it is imperative to gain a comprehensive understanding of how primary, secondary, and tertiary care intervals are interrelated, what the referral structures are, and therefore, what type of physicians (hospital-based vs. practice-based) are involved in the diagnostic pathway for the diagnosis of a mesenchymal tumor. This aspect remains unexplored to date.

To address which components of the total interval of the diagnostic pathway could be improved and to identify the appropriate targets for optimization efforts, aiming to minimize the duration between the initial symptom onset and diagnosis for patients with mesenchymal tumors, as well as to determine which patients are more likely to have a malignant mesenchymal tumor, this study investigates the various components of the total interval of the diagnostic pathway. These include an evaluation of their length, potential factors influencing the length of intervals, as well as the likelihood of a diagnoses, and an analysis of the involvement of different physicians (hospital-based vs. practice-based).

2. Materials and Methods

2.1. Study Design

This study represents a retrospective analysis of a prospectively collected dataset (based on a prospectively collected, real-world-time datawarehouse/-lake; Sarconnector® (PH&BF, Zurich, Switzerland) that included bone sarcoma (BS) and soft-tissue sarcoma (STS) patients, as well as patients diagnosed with a benign bone tumor or benign soft-tissue tumor, at a sarcoma center (MDT/SB-SSN) with its associated network, including seven secondary and tertiary care medical institutions in Switzerland, which constitutes the Swiss Sarcoma Network (SSN).

2.2. Study Objective

The main objective of this study was to analyze the diagnostic pathway from the first symptom to the histologically confirmed diagnosis in terms of physicians involved, length of the total interval, patient interval, and diagnostic interval, consisting of primary, secondary, and tertiary care intervals, as well as possible influencing factors, such as age, gender, grade, and tumor localization, for the four subgroups, BS, STS, benign bone tumors, and benign soft-tissue tumors. The aim was to use these analyses to describe in which part of the total interval of the diagnostic pathway and for which patients the greatest potential for optimization exists.

2.3. Selection Criteria

All consecutive patients presented at the weekly MDT/SB-SSN with a diagnosis of STS, BS, a benign soft-tissue tumor, or a benign bone tumor from 1 January 2018, to 31 December 2021, were included in this study. The diagnoses, which were based on the WHO classification, were divided into benign and malignant, with intermediate tumors categorized as malignant.

Patients were excluded if records were incomplete. Records were considered incomplete if, for example, no conclusion could be drawn from the available medical records as to the date of the primary and secondary care physician visit (see Figure 1). Since in the Swiss healthcare system, a visit to a primary care physician is not obligatory in every case before a visit to a specialist, patients whose data regarding the primary care interval were not complete were included. This was done because it was not possible to distinguish between (1) the absence of physician-directed care and (2) no documentation of a physician visit in the primary care interval. Named patients were listed as not available (NA) in Figures 3 and 4 under the primary care interval. The same reasoning was used for missing data based on the secondary care interval. These patients were also listed as NA in Figures 3 and 4 under secondary care interval. If it was clear from the medical records that a primary or secondary care physician was not involved (e.g., because it was an incidental finding in the context of other examinations in the secondary care interval or because the referral letter from the general practitioner described it as such), the patients were listed in Figures 3 and 4 under the "Absence of physician-directed care".

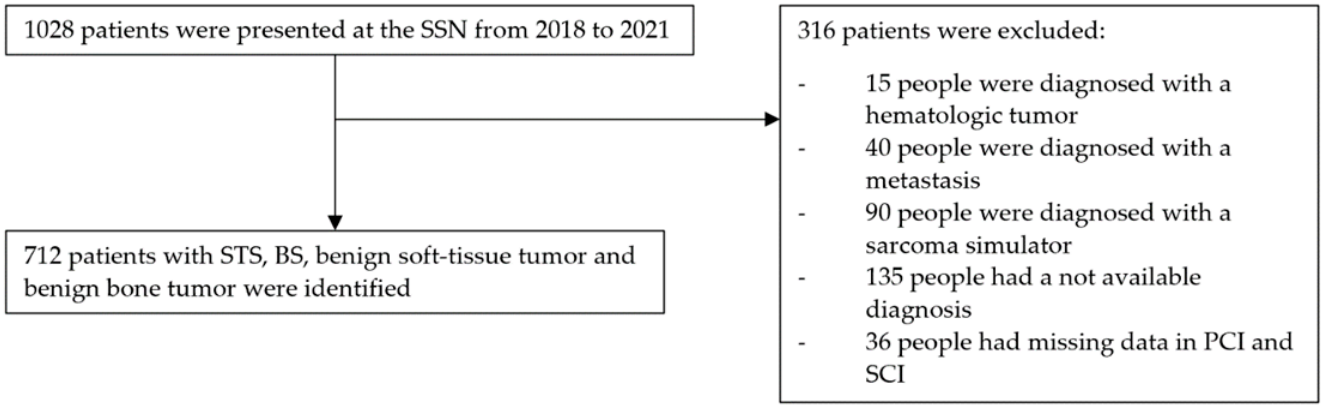

Figure 1. Flow chart of the patient inclusion progress.

2.4. Data Collection

Through a RWTD/E warehouse (Adjumed, Zurich, Switzerland) where the demographic and treatment-specific information of the patients from seven Swiss medical institutions are being collected, 1028 patients were identified. Data on age, sex, the WHO diagnosis, and anatomic region were also obtained from this warehouse. Information on the date of the first symptom that could be attributed to the benign or malignant mesenchymal tumor, the date of the first physician visit, the date of referral from primary to secondary care, the first visit to a secondary care physician, the referral to the sarcoma center in the tertiary care interval, and the date of a histologically confirmed diagnosis were extracted from the medical records. In addition, the medical records were used to determine whether the physician was a practice-based or hospital-based physician in primary and secondary care. Primary care physicians included general practitioners, gynecologists, ophthalmologists, pediatricians, and emergency room physicians. Secondary care physicians included all physicians who were not general practitioners. In PCI and SCI, both practice-based and hospital-based (e.g., physicians in an emergency department) physicians were included. The endpoint in the tertiary care interval was the sarcoma center, which was hospital-based in all cases in the included study population.

2.5. Definition of the Intervals

The definitions of the intervals were adopted from Soomers et al. [6] who adapted the standardized definition proposed by Weller et al. [7] and Olesen et al. [8]. The patient interval (PI) was defined as the time between the first noticed mesenchymal tumor-related symptom and first consultation with a medical doctor. The primary care interval (PCI) was defined as the time between the first physician visit and first secondary referral to a physician of the secondary care. Physicians were divided into practice-based and hospital-based. The secondary care interval (SCI) was defined as the time between the first secondary referral and referral to a specialist sarcoma center. Physicians were divided into practice-based and hospital-based. The timespan from referral to a specialist sarcoma center and the date of the histological diagnosis was defined as the tertiary care interval (TCI). Since the diagnosis of a benign or malignant bone or soft-tissue tumor can also take place outside a sarcoma center, the TCI values were sometimes negative. PCI, SCI, and TCI were summarized as the diagnostic interval (DI). The PI and DI resulted in the total interval of the diagnostic pathway (TIDP) (see Figure 2).

2.6. Statistical Analysis

Continuous variables are presented as the median (1st quartile, 3rd quartile), while categorical variables are presented as a number (percentage). Due to the low number of missing data, no missing data imputation was performed. To study the association between clinical variables (age, gender, histological grade, tumor localization, and size) and

a bone sarcoma versus soft-tissue sarcoma diagnosis or a benign versus sarcoma diagnosis, logistic regression models were created. To assess the association between clinical variables and the described intervals, linear regression was employed. The normal distribution of variables was assessed visually using histograms or QQ-plots. When continuous data were normally distributed, a t-test was performed, while a Mann–Whitney-U test was performed for non-normally distributed data. Differences between categorical variables were tested using a Chi-square test or using Fisher's exact test (if the expected value was below 5). A p-value < 0.05 was considered statistically significant. All analyses were conducted using R (version 4.3.1).

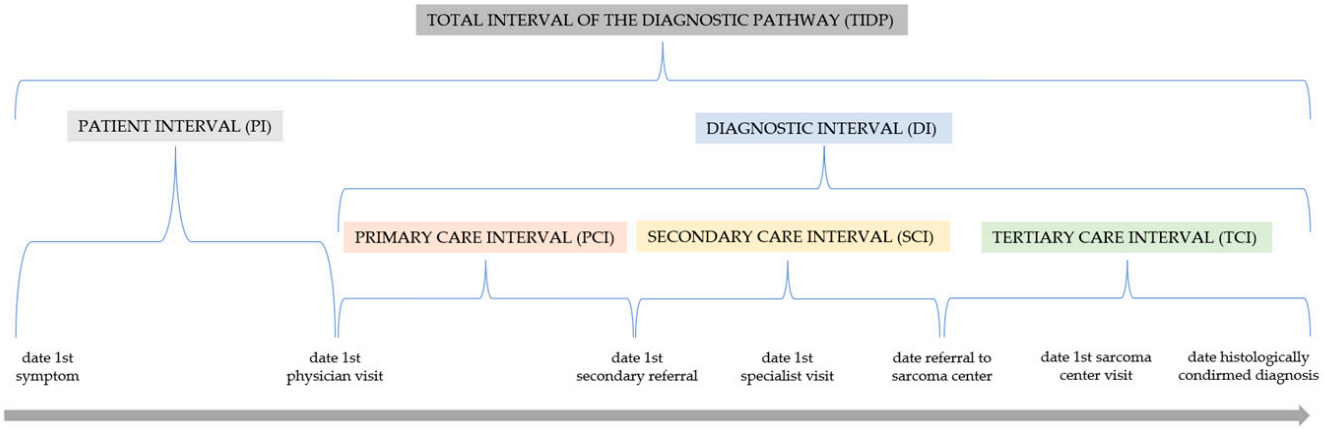

Figure 2. Time intervals from first symptom to the visit to a sarcoma center. Adopted from Soomers et al. 2020 [6]. Patient interval: time between date of first symptom and first visit to a physician. Primary care interval: time between first physician visit and first secondary referral to a specialized physician. Secondary care interval: time between first secondary referral and referral to a specialist sarcoma center. Tertiary care interval: time between referral to a specialist sarcoma center and the date of histological diagnosis. Diagnostic interval: time between first physician visit and histological diagnosis. Total interval of the diagnostic pathway (TIDP): time from first symptom to histological diagnosis.

3. Results

3.1. Diagnosis Probability Based on Patient and Tumor Traits (See Table 1)

Of the factors studied, age, localization, and size influenced the likelihood of bone sarcoma (BS) versus soft-tissue sarcoma (STS) and the likelihood of a benign versus malignant mesenchymal tumor. Most of the included patients (n = 356) were diagnosed with STS, especially deep STS (n = 296). The median age of the studied population was 56.0 years. With a 1-year increase in age, the likelihood of an STS compared with a BS increased by 3%, which was represented by the lower median age of patients with BS (44.0 years) and benign bone tumors (34.0 years). Similarly, the probability of a diagnosis of a malignant compared with a benign bone or soft-tissue tumor increased by 2% with a 1-year increase in age. The overall gender distribution was balanced (48.9% female), with more male patients (63.4%) having BS. However, gender did not affect the likelihood of being diagnosed with BS compared with STS or of being diagnosed with a malignant compared with a benign mesenchymal tumor. Among the sarcomas, grade G3 was the most common. Tumors were more frequently appendicular in location, although the distribution was more balanced in STS. An axial location increased the likelihood of an STS compared with a BS and of a malignant bone or soft-tissue tumor compared with a benign one. Malignant tumors tended to be larger than benign ones. The larger a tumor was, the more likely it was to be diagnosed as STS. The likelihood of a sarcoma compared with a benign tumor also increased with an increasing tumor size. In most subgroups, the number of cases decreased with an increasing tumor size.

Table 1. Diagnosis probability based on patient and tumor traits.

	OVERALL	BONE SARCOMA	LIKELIHOOD OF BONE SARCOMA VS. SOFT-TISSUE SARCOMA [a]			SOFT-TISSUE SARCOMA			LIKELIHOOD OF SARCOMA VS. BENIGN TUMOR [b]			BENIGN BONE TUMOR	BENIGN SOFT-TISSUE TUMOR		
			OR	95% CI	*p*-Value	Deep and Superficial	Deep	Superficial	OR	95% CI	*p*-Value		Deep and Superficial	Deep	Superficial
	n = 712	**n = 82**				**n = 356**	**n = 296**	**n = 60**				**n = 61**	**n = 213**	**n = 172**	**n = 41**
Age, years	56.0 (40.0, 68.0)	44.0 (19.0, 65.0)	1.03	1.02, 1.04	**<0.001**	60.0 (46.0, 72.0)	60.0 (46.0, 72.0)	61.5 (42.3, 74.3)	1.02	1.01, 1.02	**<0.001**	34.0 (23.0, 45.0)	55.0 (44.0, 63.0)	56.0 (44.0, 65.0)	54.0 (44.0, 61.0)
Female, (%)	348 (48.9%)	30 (36.6%)	1.09	0.82, 1.47	0.5	178 (50.0%)	145 (49.0%)	33 (55.0%)	0.87	0.64, 1.17	0.3	30 (49.2%)	110 (51.6%)	90 (52.3%)	20 (48.8%)
Grade												not applicable	not applicable	not applicable	not applicable
G1, (%)	74 (16.9%)	7 (8.5%)				67 (18.8%)	52 (17.6%)	15 (25.0%)							
G2, (%)	54 (12.3%)	5 (6.1%)	1.17	0.37, 4.07	0.8	49 (13.8%)	41 (13.9%)	8 (13.3%)							
G3, (%)	126 (28.8%)	26 (31.7%)	0.46	0.18, 1.03	0.07	100 (28.1%)	85 (28.7%)	15 (25.0%)							
NA	184 (42.0%)	44 (53.7%)				140 (39.3%)	118 (39.8%)	22 (36.7%)							
Region			2.91	2.11, 4.04	**<0.001**				2.34	1.67, 3.30	**<0.001**				
appendicular	469 (65.9%)	65 (79.3%)				193 (54.2%)	165 (55.7%)	28 (46.7%)				50 (82.0%)	161 (75.6%)	131 (76.2%)	30 (73.2%)
axial	243 (34.1%)	17 (20.7%)				163 (45.8%)	131 (44.3%)	32 (53.3%)				11 (18.0%)	52 (24.4%)	41 (23.8%)	11 (26.8%)
Size, mm	60.0 (34.3, 102.0)	60.0 (39.5, 85.0)	1.01	1.00, 1.01	**<0.001**	70.0 (32.0, 124.0)	86.0 (45.0, 130.0)	28.0 (20.0, 44.0)	1.00	1.00, 1.01	**0.001**	31.5 (11.5, 50.5)	60.0 (38.3, 97.3)	61.0 (39.0, 100.5)	54.0 (35.5, 79.5)
0–50 mm, n	247 (34.7%)	25 (30.5%)				106 (29.8%)	70 (23.6%)	36 (60.0%)				33 (54.1%)	83 (39.0%)	65 (37.8%)	18 (43.9%)
51–100 mm, n	179 (25.1%)	30 (36.6%)				67 (18.8%)	59 (19.9%)	8 (13.3%)				10 (16.4%)	72 (33.8%)	55 (32.0%)	17 (41.5%)

Table 1. *Cont.*

	OVERALL	BONE SARCOMA	LIKELIHOOD OF BONE SARCOMA VS. SOFT-TISSUE SARCOMA [a]			SOFT-TISSUE SARCOMA			LIKELIHOOD OF SARCOMA VS. BENIGN TUMOR [b]			BENIGN BONE TUMOR	BENIGN SOFT-TISSUE TUMOR		
			OR	95% CI	*p*-Value	Deep and Superficial	Deep	Superficial	OR	95% CI	*p*-Value		Deep and Superficial	Deep	Superficial
	n = 712	**n = 82**				**n = 356**	**n = 296**	**n = 60**				**n = 61**	**n = 213**	**n = 172**	**n = 41**
101–150 mm, n	91 (12.8%)	11 (13.4%)				50 (14.0%)	50 (16.9%)	0 (0%)				1 (1.6%)	29 (13.6%)	27 (15.7%)	2 (4.9%)
>150 mm, n	57 (8.0%)	1 (1.2%)				42 (11.8%)	41 (13.9%)	1 (1.7%)				0 (0%)	14 (6.6%)	13 (7.5%)	1 (2.4%)
NA	138 (19.4%)	15 (18.3%)				91 (25.6%)	76 (25.7%)	15 (25.0%)				17 (27.9%)	15 (7.0%)	12 (7.0%)	3 (7.3%)

[a]: The likelihood of STS (deep and superficial) vs. BS was determined. STS represented the reference. [b]: The likelihood of sarcoma (STS and BS) vs. benign mesenchymal tumors (benign bone and soft-tissue tumors) was determined. Sarcoma represented the reference.

3.2. Patient Interval (PI)

3.2.1. Length (See Table 2)

The patient interval (median, overall 90.0 weeks) was longer than the diagnostic interval (median, overall 46.0 weeks) in all subgroups. The patient interval was significantly shorter for deep STS (median, 8.3 weeks) than for superficial STS (median, 20.7 weeks) ($p = 0.01$). No such difference was observed between BS and STS. No differences in PI length were detected between benign bone and soft-tissue tumors or between superficial and deep soft-tissue tumors.

3.2.2. Influencing Parameters (See Table 3)

Of the potential influencing parameters investigated, age and localization, each showed a significant effect on the PI length in the benign bone and soft-tissue tumor subgroup, as well as in the overall population. An increasing age correlated significantly with a longer PI in the overall population and in soft-tissue tumors ($p = 0.047$ and $p = 0.04$, respectively). The PI was longer in benign bone tumors for an axial localization rather than for a appendicular localization ($p = 0.002$).

3.3. Diagnostic Interval (DI), Primary Care Interval (PCI)

3.3.1. Length (See Table 2)

The primary care interval was the shortest of the diagnostic intervals in all subgroups (median, overall 4.0 weeks). The subgroups of sarcomas showed comparable lengths of PCI, with BS (median, 0.6 weeks) having the median longest and superficial STS (median, 0.0 weeks) have the shortest, without statistical significance. Benign mesenchymal tumors also showed comparable lengths of the PCI, with bone tumors (median, 0.8 weeks) having the longest median and superficial soft-tissue tumors (median, 0.3 weeks) having the shortest, again without statistical significance. PCIs from benign mesenchymal tumors were slightly longer on average than comparable subsets of malignant mesenchymal tumors.

3.3.2. Influencing Parameters (See Table 3)

Of the potential influencing parameters investigated, only localization in the STS subgroup showed a significant effect on the PCI length. The axial tumor localization showed a significantly shorter PCI for STS compared to an appendicular localization ($p = 0.03$).

3.4. Diagnostic Interval (DI), Secondary Care Interval (SCI)

3.4.1. Length (See Table 2)

The secondary care interval accounted for the largest proportion of the diagnostic interval for sarcomas (median, overall 26.0 weeks). BS (median, 2.2 weeks) had significantly shorter SCIs than STS (median, 4.3 weeks) ($p = 0.005$); again, the SCI of deep STS (median, 3.9 weeks) was significantly shorter than that of superficial STS (median, 8.1 weeks) ($p = 0.01$). Among benign mesenchymal tumors, SCI represented the largest proportion of the DI for the benign soft-tissue tumor group (although this is likely due to deep soft-tissue tumors). For superficial soft-tissue tumors, the lengths of the SCI and TCI were comparable.

3.4.2. Influencing Parameters (See Table 3)

None of the potential influencing parameters investigated had a significant influence on the SCI of any subgroup.

Table 2. Length of patient, diagnostic, primary care, secondary care, tertiary care, and total interval in weeks.

	OVERALL	BONE SARCOMA		SOFT-TISSUE SARCOMA						BENIGN BONE TUMOR	BENIGN SOFT-TISSUE TUMOR				
				Deep and Superficial	Deep		Superficial				Deep and Superficial	Deep		Superficial	
	n = 712	n = 82	*p*-Value [c]	n = 356	n = 296	*p*-Value [d]	n = 60	n = 61	*p*-Value [e]	n = 213	n = 172	*p*-Value [f]	n = 41		
Patient Interval, weeks	90.0 (22.0, 284.0)	7.8 (2.7, 27.5)	0.46	8.8 (2.1, 29.0)	8.3 (2.0, 24.4)	**0.01**	20.7 (4.2, 130.6)	19.1 (4.3, 52.1)	0.17	21.6 (6.4, 109.6)	19.8 (6.3, 75.1)	0.22	29.9 (9.0, 176.4)		
Diagnostic Interval, weeks	46.0 (25.5, 95.5)	7.6 (3.1, 14.2)	0.89	6.7 (3.7, 13.3)	6.9 (3.9, 13.7)	0.22	5.7 (3.6, 9.3)	19.8 (6.8, 79.7)	**0.005**	6.0 (3.6, 13.4)	6.0 (3.6, 14.6)	0.35	5.6 (3.6, 9.5)		
Primary Care Interval, weeks	4.0 (0.0, 18.5)	0.6 (0.1, 6.5)	0.14	0.4 (0.0, 1.4)	0.4 (0.0, 1.3)	0.31	0.0 (0.0, 1.4)	0.8 (0.0, 44.9)	0.30	0.7 (0.0, 3.1)	0.7 (0.0, 4.4)	0.15	0.3 (0.0, 1.0)		
Secondary Care Interval, weeks	26.0 (12.0, 57.0)	2.2 (0.9, 6.6)	**0.005**	4.3 (2.1, 9.1)	3.9 (1.9, 8.1)	**0.01**	8.1 (4.9, 10.2)	2.6 (1.0, 10.7)	0.47	3.5 (1.6, 7.5)	3.9 (1.7, 10.0)	0.14	2.6 (1.5, 3.8)		
Tertiary Care Interval, weeks	14.0 (5.0, 26.3)	2.1 (1.0, 3.7)	**0.006**	1.3 (-0.6, 3.4)	1.6 (-0.2, 3.6)	**0.01**	0.9 (-3.3, 1.9)	3.1 (2.0, 8.1)	0.14	2.6 (1.8, 4.1)	2.6 (1.7, 4.0)	0.36	2.7 (1.9, 5.8)		
Total Interval, weeks	213.0 (84.0, 762.2)	22.8 (11.9, 56.7)	0.82	23.3 (10.4, 59.4)	20.9 (10.4, 55.3)	0.07	34.8 (12.3, 148.0)	100.5 (48.1, 206.6)	0.22	48.2 (17.7, 193.3)	43.0 (14.7, 150.6)	**0.04**	138.1 (29.1, 304.4)		

[c]: The *p*-value was calculated based on a Wilcoxon rank sum test with a continuity correction between STS (deep and superficial) and BS. [d]: The *p*-value was calculated based on a Wilcoxon rank sum test with a continuity correction between deep STS and superficial STS. [e]: The *p*-value was calculated based on a Wilcoxon rank sum test with a continuity correction between benign soft-tissue tumors (deep and superficial) and benign bone tumors. [f]: The *p*-value was calculated based on a Wilcoxon rank sum test with a continuity correction between deep benign soft-tissue tumors and superficial benign soft-tissue tumors.

Table 3. Influence of age, gender, grade, and localization on intervals.

	PI [g]			DI [h]									TI [l]		
				PCI [i]			SCI [j]			TCI [k]					
	Beta	95% CI	*p*-Value	Beta	95% CI	*p*-Value	Beta	95% CI	*p*-Value	Beta	95% CI	*p*-Value	Beta	95% CI	*p*-Value
Overall (n = 712)															
Age	7.07	0.08, 14.05	**0.047**	−0.91	−3.36, 1.54	0.46	0.71	−2.31, 3.73	0.65	−0.28	−1.77, 1.21	0.71	6.79	−1.03, 14.61	0.09
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference

Table 3. *Cont.*

	PI [g]			DI [h]									TI [l]		
				PCI [i]			SCI [j]			TCI [k]					
	Beta	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**
female	86.53	−185.00, 358.05	0.53	−45.41	−142.57, 51.74	0.36	46.20	−68.73, 161.13	0.43	−11.31	−67.84 45.22	0.69	168.90	−132.39, 470.11	0.27
Grade G1	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
G2	−392.10	−1039.97, 255.67	0.24	−17.17	−258.50, 224.15	0.89	17.17	−261.18, 295.52	0.90	−28.42	−149.59, 92.76	0.65	−498.92	−1140.89, 143.05	0.13
G3	−384.70	−911.59, 142.23	0.15	−77.84	−261.66, 105.98	0.41	−18.07	−240.93, 204.78	0.87	116.81	17.25, 216.36	**0.02**	−470.85	−994.55, 52.85	0.08
Localization appendicular	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	−177.51	−463.87, 108.86	0.224	−46.46	−147.89, 54.97	0.37	−21.42	−141.14, 98.29	0.73	−84.47	−143.12, −25.82	0.41	−264.11	−583.97, 55.75	0.11
Bone sarcoma (n = 82)															
Age	5.61	−13.44, 24.66	0.56	−1.48	−10.59, 7.63	0.75	−0.14	−0.95, 0.68	0.74	−0.13	−0.39, 0.13	0.31	7.55	−12.71, 27.80	0.46
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
female	88.12	−830.06, 1006.30	0.85	−53.64	−494.73, 387.45	0.81	2.72	−36.48, 41.93	0.89	−8.45	−21.05, 4.14	0.19	−42.57	−1017.19, 932.04	0.93
Grade G1	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
G2	−37.05	−2366.05, 2291.95	0.98	−107.67	−1167.15, 951.82	0.84	−37.95	−129.28, 53.37	0.41	−12.80	−42.96, 17.36	0.40	−122.40	−2409.75, 2164.95	0.92
G3	48.49	−1679.16, 1776.14	0.96	−90.88	−724.04, 542.28	0.77	−21.64	−82.91, 39.62	0.48	−16.05	−38.39, 6.30	0.16	−15.80	−1815.48, 1783.88	0.99
Localization appendicular	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	−187.90	−1424.36, 1048.56	0.76	472.71	−88.70, 1034.13	0.10	−7.66	−51.97, 36.65	0.73	−2.06	−16.31, 12.19	0.77	−45.29	−1259.59, 1169.00	0.94
Soft-tissue sarcoma (n = 356)															

Table 3. *Cont.*

	PI [g]			DI [h]									TI [l]		
				PCI [i]			SCI [j]			TCI [k]					
	Beta	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**
Age	4.67	−6.17, 15.51	0.40	0.55	−1.51, 2.60	0.60	0.78	−3.91, 5.47	0.74	1.11	−1.71, 3.93	0.44	3.90	−6.60, 14.39	0.47
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
female	−42.41	−427.41, 342.60	0.83	−24.30	−101.26, 52.67	0.53	−22.46	−189.49, 144.57	0.79	−16.93	−115.72, 81.87	0.74	−18.80	−391.39, 353.80	0.92
Grade G1	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
G2	−430.19	−1119.79, 259.41	0.22	−5.59	−157.29, 146.12	0.45	24.29	−291.39, 339.96	0.88	−28.36	−192.80, 136.07	0.74	−525.67	−1148.01, 96.67	0.10
G3	−420.90	−997.45, 155.64	0.15	−73.77	−194.34, 46.79	0.94	−17.01	−277.62, 243.60	0.90	134.37	−3.76, 272.50	0.06	−498.96	−1015.67, 17.75	0.06
Localizationappen	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	−220.20	−604.58, 164.21	0.26	−84.99	−160.21, −9.77	**0.03**	−109.96	−275.68, 55.75	0.19	−112.59	−210.99, −14.18	**0.03**	−297.40	−672.92, 78.11	0.12
Deep soft-tissue sarcoma (n = 296)															
Age	5.03	−6.50, 16.57	0.39	1.43	−0.97, 3.84	0.24	0.72	−4.95, 6.38	0.80	0.63	−2.83, 4.10	0.72	4.06	−7.91, 16.02	0.51
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
female	−77.25	−479.40, 324.89	0.71	−40.20	−128.01, 47.61	0.37	−18.11	−213.53, 177.31	0.86	−40.66	−158.05, 76.72	0.50	−66.69	−481.55, 348.17	0.75
Grade G1	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
G2	−222.90	−966.79, 520.90	0.56	−32.83	−218.91, 153.24	0.73	32.40	−354.26, 419.07	0.87	−54.82	−251.40, 141.76	0.58	−384.41	−1088.57, 319.74	0.28
G3	−302.30	−928.03, 323.33	0.34	−114.18	−260.68, 32.32	0.13	−21.76	−339.89, 296.37	0.89	141.65	−24.05, 307.35	0.09	−477.53	−1060.61, 105.54	0.11
Localization appendicular	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	−292.70	−694.86, 109.40	0.15	−83.18	−169.70, 3.33	0.06	−124.82	−319.22, 69.58	0.21	−128.24	−245.63, −10.84	**0.03**	−314.20	−735.48, 107.05	0.14

Table 3. *Cont.*

	PI [g]			DI [h]									TI [l]		
				PCI [i]			SCI [j]			TCI [k]					
	Beta	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**
Superficial soft-tissue sarcoma (n = 60)															
Age	9.08	−22.59, 40.75	0.56	−3.20	−6.91, 0.52	0.09	0.13	−1.18, 1.43	0.84	2.71	−0.64, 6.06	0.11	3.61	−18.69, 25.91	0.75
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
female	−244.50	−1550.78, 1061.81	0.71	62.06	−98.57, 222.68	0.43	−21.07	−73.30, 31.16	0.41	87.35	−47.66, 222.35	0.20	109.40	−765.23, 984.12	0.80
Grade G1	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
G2	−1031.80	−3045.04, 981.47	0.30	36.96	−205.08, 279.01	0.75	−18.82	−95.17, 57.53	0.61	102.78	−128.78, 334.35	0.38	−1004.50	−2403.36, 394.36	0.16
G3	−414.60	−2092.34, 1263.09	0.62	−9.45	−224.29, 205.39	0.93	−1.07	−68.84, 66.70	0.97	93.13	−100.01, 286.27	0.34	−352.70	−1545.67, 840.24	0.56
Localization appendicular	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	−1.20	−1214.74, 1212.34	0.998	−91.68	−243.05, 59.69	0.22	−11.61	−61.93, 38.71	0.64	−52.58	−187.69, 82.53	0.44	−371.90	−1235.52, 491.64	0.39
Benign bone tumor (n = 61)															
Age	12.03	0.31, 23.75	**0.045**	0.3656	−17.12, 17.85	0.97	−12.059	−32.23, 8.11	0.23	−5.180	−16.54, 6.18	0.35	−11.95	−46.97, 23.06	0.48
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
Female	30.04	−300.40, 360.48	0.86	−367.90	−798.01, 62.17	0.09	337.80	−253.09, 928.69	0.25	271.00	−145.74, 687.74	0.19	314.00	−1011.63, 1639.63	0.63
Grade	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable
Localization appendicular	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	169.01	−229.74, 567.76	**0.002**	−211.10	−797.88, 375.62	0.46	−89.73	−908.39, 728.93	0.82	−119.60	−575.95, 336.65	0.59	−314.90	−1676.93, 1047.06	0.63
Benign soft-tissue tumor (n = 213)															

Table 3. *Cont.*

	PI [g]			DI [h]									TI [l]		
				PCI [i]			SCI [j]			TCI [k]					
	Beta	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**
Age	16.29	0.42, 32.15	0.04	0.756	−6.20, 7.715	0.83	5.24	−2.40, 12.87	0.18	0.2511	−0.84, 1.34	0.65	26.53	8.84, 44.22	0.004
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
female	280.60	−243.33, 804.44	0.29	46.05	−172.08, 264.18	0.68	114.86	−124.11, 353.82	0.34	−23.45	−59.68, 12.79	0.20	515.70	−100.63, 1132.03	0.10
Grade	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable
Localization appendicular	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	21.60	−594.30, 637.50	0.95	−17.69	−268.97, 233.60	0.89	234.58	−42.02, 511.18	0.10	5.99	−37.39, 49.38	0.79	180.70	−569.78, 931.19	0.64
Benign deep soft-tissue tumor (n = 172)															
Age	13.01	−2.12, 28.13	0.09	2.38	−3.62, 8.37	0.43	5.54	−3.47, 14.54	0.23	0.37	−0.94, 1.67	0.58	26.59	8.57, 44.61	0.004
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
female	−1.82	−524.09, 520.46	0.995	144.49	−44.13, 333.12	0.13	127.00	−157.82, 411.82	0.38	−30.23	−75.17, 14.71	0.19	382.50	−285.27, 1050.29	0.26
Grade	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable
Localizationappendicular	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	59.61	−569.86, 689.07	0.85	48.07	−174.99, 271.13	0.67	291.60	−39.66, 622.89	0.08	8.75	−45.72, 63.22	0.75	422.40	−398.51, 1243.35	0.31
Benign superficial soft-tissue tumor (n = 41)															
Age	43.61	−17.13, 104.36	0.15	−5.39	−36.71, 25.93	0.72	−0.16	−0.97, 0.64	0.67	−0.29	−1.11, 0.52	0.47	30.60	−23.82, 85.01	0.26

Table 3. *Cont.*

	PI [g]			DI [h]									TI [l]		
				PCI [i]			SCI [j]			TCI [k]					
	Beta	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**	**Beta**	**95% CI**	***p*-Value**
Gender male	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
female	1364.80	−196.65, 2926.25	0.08	−316.80	−1170.00, 536.33	0.44	6.39	−15.79, 28.57	0.55	6.41	−16.34, 29.15	0.57	1137.60	−350.82, 2625.95	0.13
Grade	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable
Localization appendicular	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference
axial (head, neck, trunk)	−302.60	−2074.28, 1469.01	0.73	−263.20	−1218.54, 692.14	0.56	−9.32	−33.62, 14.99	0.42	−6.88	−32.90, 19.14	0.59	−657.90	−2405.68, 1089.96	0.45

[g]: PI, patient interval. [h]: DI, diagnostic interval. [i]: PCI, primary care interval. [j]: SCI, secondary care interval. [k]: TCI, tertiary care interval. [l]: TI, total interval.

3.5. Diagnostic Interval (DI), Tertiary Care Interval (TCI)

3.5.1. Length (See Table 2)

Sarcomas showed significant differences between BS and STS and between deep and superficial STS in the length of the TCI. BS (median, 2.1 weeks) showed a significantly longer TCI than STS (median, 1.3 weeks) ($p = 0.006$). In STS, in turn, the TCI was significantly shorter for superficial STS (median, 0.9 weeks) than for deep STS (median, 1.6 weeks) ($p < 0.01$). Such differences in TCI were not observed for benign bone and soft-tissue tumors. TCIs of malignant mesenchymal tumors were slightly shorter on average than those of the comparable subset of benign tumors.

3.5.2. Influencing Parameters (See Table 3)

Of the potential influencing parameters investigated, grade and localization had a significant effect on the TCI length in the overall population and the STS subgroup. In the overall population, high-grade tumors had a significantly longer TCI ($p = 0.02$). Axial tumor localization showed a significantly shorter TCI for STS compared to an appendicular localization ($p = 0.03$). This was also reflected in the TCI of deep STS ($p = 0.03$).

3.6. Total Interval (TI)

3.6.1. Length (See Table 2)

Total intervals were shorter for sarcomas than for benign tumors. The shortest TI was observed for both malignant and benign tumors of deep soft-tissue tumors (median, 20.9 and 43.0 weeks, respectively). The same was true for superficial soft-tissue tumors, which had the longest TI of both malignant and benign tumors (median, 34.8 and 138.1 weeks, respectively). However, no significant differences in the length of the TI were observed between the subgroups of benign tumors and between the subgroups of malignant tumors.

3.6.2. Influencing Factors (See Table 3)

Of the potential influencing factors investigated, only age had a significant effect on the length of the TI, but this was only true for benign soft-tissue tumors and benign deep soft-tissue tumors. An increasing age correlated significantly with a longer TI for benign soft-tissue tumors and benign deep soft-tissue tumors ($p = 0.004$ and $p = 0.004$, respectively).

3.7. Involved Physicians in the Primary Care Interval (PCI) (See Figures 3 and 4)

The PCI showed differences between benign and malignant mesenchymal tumors with respect to the involvement of physicians, as well as their localization in hospitals and medical practices. For malignant tumors (87.50% to 95.12%), PCI physicians were involved more frequently on average than for benign tumors (79.65 to 87.80%). In this regard, PCI physicians were visited more often for BS (95.12%) and superficial STS (95.00%) than for deep STS (87.50%). Benign mesenchymal tumors showed a similar pattern. PCI physicians were seen most often for benign superficial soft-tissue tumors (87.80%) and benign bone tumors (86.89%) and slightly less often for benign deep soft-tissue tumors (79.65%). In the PCI, the physicians consulted were more often practice-based. For malignant mesenchymal tumors (9.65 to 26.92%), physicians were more often hospital-based relative to benign mesenchymal tumors (0.00 to 9.43%).

3.8. Involved Physicians in the Secondary Care Interval (SCI) (See Figures 3 and 4)

The SCI showed differences between benign and malignant mesenchymal tumors with respect to the involvement of physicians, as well as their localization in hospitals and medical practices. For malignant tumors (71.28 to 81.67%), SCI physicians were involved more frequently on average than for benign tumors (62.30 to 63.41%). Here, SCI physicians were more frequently involved in superficial STS (81.67%) than in BS (71.95%) or deep STS (71.28%). Benign mesenchymal tumors showed a similar pattern. SCI physicians were most frequently consulted for benign superficial soft-tissue tumors (63.41%), followed by benign deep soft-tissue tumors (62.79%) and benign bone tumors (62.30%). In SCI, physicians

consulted were more often hospital-based than in the PCI. In malignant mesenchymal tumors (73.47 to 83.41%), physicians were more often hospital-based relative to benign mesenchymal tumors (68.42 to 76.92%).

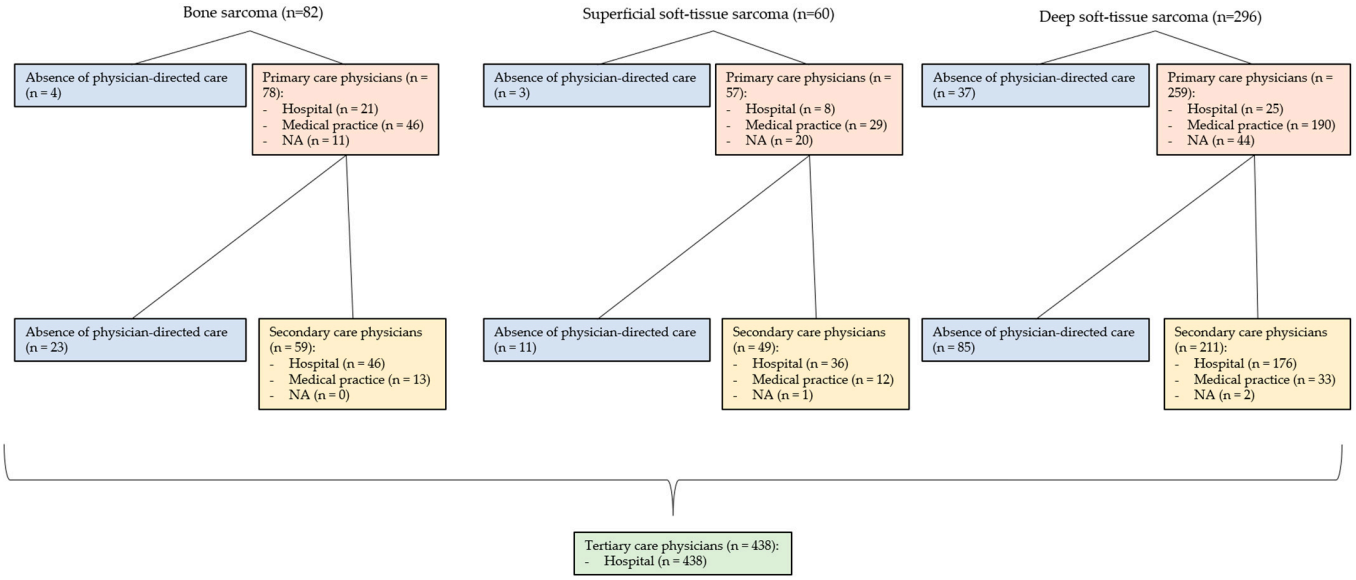

Figure 3. Referral pattern of bone sarcoma, superficial soft-tissue sarcoma, and deep soft-tissue sarcoma.

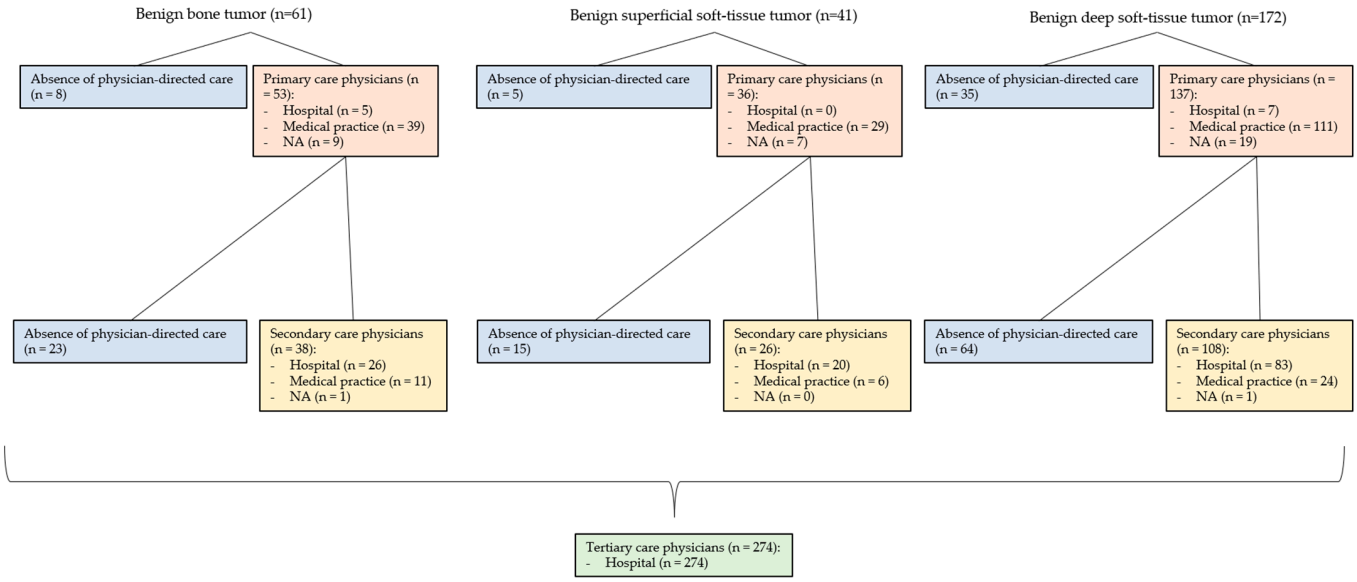

Figure 4. Referral pattern of benign bone tumors, benign superficial soft-tissue tumors, and benign deep soft-tissue tumors.

4. Discussion

This study addresses a significant gap in the literature by comprehensively analyzing the total interval for mesenchymal tumors in patients, particularly focusing on BS and STS, as well as their benign counterparts. The total interval of the diagnostic pathway, a complex measure influenced by diverse tumor-, patient-, and management-specific factors, has been dissected into its components. Notably, this study is the first to explore total intervals for benign mesenchymal tumors.

The patient interval emerges as a key determinant of the total interval of the entire diagnostic pathway, consistently occupying a major share across subgroups. Among malignant tumors, the secondary care interval assumes prominence in the diagnostic interval.

Age, grade, and localization were identified as factors influencing the interval durations of only some intervals, demonstrating the heterogeneity of mesenchymal tumors. A novel finding is the higher involvement of hospital-based practitioners in the diagnosis of sarcomas compared to benign mesenchymal tumors, possibly due to the more severe and urgent symptoms they exhibit that result in more frequent visits to the emergency ward. These insights contribute to a better understanding of the total interval in mesenchymal tumors.

The existing literature shows a wide range in the length of the different intervals of the diagnostic pathway of malignant mesenchymal tumors. The median values (including BS and STS) of the intervals in the present study are in the lower-to-middle range of values in the literature [15–40], indicating a rather efficient healthcare system, which, however, still has potential for optimization. The diagnostic pathway has not been previously analyzed for benign mesenchymal tumors; thus, no comparative values are available. As in the SURVSARC Study [41], the patient interval accounted for the largest proportion of the total interval in this study. This could also be observed in other cancer entities in the literature [42]. In particular, the patient interval accounted for a large proportion of the total interval for benign tumors, which is very important because the greatest potential for optimization lies in shortening the length of the patient interval. Important factors influencing the patient interval were patient age and tumor localization. Higher age has already been seen to be associated with longer intervals in some studies [16,19,27,29,30,43], although there are also studies that found no association [44] or even an opposite association [41]. In our study, there were 38 pediatric tumors (patient age, 2–18 years), 31 bone tumors (20 BSs, 11 benign bone tumors), 7 soft-tissue tumors (2 STSs; one superficial and one deep; 5 benign soft-tissue tumors, all with a deep location). The numbers were too low to compare pediatric with adult tumors.

In the diagnostic interval, the secondary care interval represented the largest proportion in terms of time. Already, Smolle et al. could show that examinations outside a sarcoma center led to a delay [45]. The visit to a GP compared to an emergency ward was associated with a longer primary care interval in the study by Goyal et al. [16]. The present study cannot confirm this; on the contrary, the primary care interval in which practice-based physicians were most frequently visited turned out to be particularly short, reflecting that GPs in Switzerland refer patients for bone and soft-tissue tumors in the shortest possible time. This is a very important finding: in the diagnostic interval, specialists outside a sarcoma center generate the bottleneck rather than primary care physicians. Axial localization leads to shorter patient and diagnostic intervals. Considering that the CNS is also axially located, symptoms are therefore already noticeable with small tumor masses, little room is left for surgery, and assuming that the treating physicians are aware of this, it becomes clear that faster action is required with an axially located tumor.

A longer total interval of the diagnostic pathway has been associated with lower survival by Bandyopadhyay et al. and Ferrari et al. [46,47]. In their study of primary pulmonary artery sarcoma, which had a median total interval of 14.3 weeks, Bandyopadhyay et al. showed a 46% increase in the odds of death when the length of the total interval was doubled [46]. Ferrari et al., in their study on STS in children and adolescents who had a median total interval of 8 weeks, showed a significant negative impact on survival with an increasing length of the total interval ($p = 0.002$) [47]. Translating this for the current examined cohort, where the median length of the total interval was 22.8 weeks for BS and 23.3 weeks for STS, it can be assumed that the survival rate could be increased by shortening the total interval of the diagnostic pathway. However, it is essential to note that a comprehensive investigation of this effect would be necessary. Moreover, aside from its direct impact on survival, a shorter total interval is also desirable due to its influence on patient well-being in cases where the diagnosis remains uncertain [48]. However, it must be taken into account that the patient interval accounts for a larger part of the total interval of the diagnostic pathway than the diagnostic interval.

The patient interval, which had a median duration of 90.0 weeks for this study's overall population, was nearly twice as long as the diagnostic interval, which had a median duration of 46.0 weeks and represented the largest delay in the total interval of the diagnostic pathway. This underscores that the primary issue does not lie with individual physicians, but rather with the referral process and therefore the structure of the healthcare system itself. The high investments in the healthcare system appear to be insufficient in promptly identifying sarcoma patients. The repeatedly mentioned complexity of the work-up and treatment of patients with sarcoma is greatly explained by the fact that sarcomas do not form a conventional medical discipline per se. Addressing the needs of sarcoma patients necessitates a comprehensive approach via a multidisciplinary team (MDT), and a physician head coordinating among disciplines is crucial. Integrated practice units (IPUs) could provide a solution. Here, the focus is on a problem rather than a discipline [49,50]. By bringing together different health professionals in a unified structured organization, challenges, like cumbersome referrals, could be surmounted, potentially leading to shorter intervals. Further, the patient interval could also be shortened by health professionals helping patients to recognize problems as such [51]. Subsequently, the diagnostic interval would also be shortened, as there would be no need for cumbersome referrals. Thus, the secondary care interval, which is the largest part of the diagnostic interval, could be optimized. In terms of value-based healthcare (VBHC), health outcomes, such as quality of life, could account for a larger share of costs by intercepting patients before they are plagued by unpleasant symptoms for a long time [52]. In addition, costs for nontargeted investigations could be saved. Therefore, reorganizing healthcare structures according to the VBHC principles may greatly enhance the work-up of sarcoma patients [51].

This study reflects the contact of patients with a sarcoma center; therefore, the numbers per subgroup are not balanced, which is a limitation of this study. For example, STS is many times more frequent than BS. This could have the consequence that effects of the investigated potential influencing factors did not show up in the smaller subgroups, although they would be present. In addition, a selection bias was found for those patients who presented at a sarcoma center. That is, someone thought of the possibility of a sarcoma diagnosis during the diagnostic interval and involved a sarcoma center. Patients for whom this possibility was not considered may never have been diagnosed with a mesenchymal tumor, thereby remaining within the diagnostic interval indefinitely.

Further investigation is needed to determine the reasons for the delays in the patient and secondary care interval. Regarding the patient interval, the perceived symptoms could be investigated, as well as the reasons that led to the consultation with a physician. Concerning the secondary care interval, a breakdown of the physicians visited in the primary and secondary care interval regarding their specialization, as well as the examinations performed, would be interesting to determine, on the one hand, to whom optimization approaches should be directed and, on the other hand, to determine the correlation of examinations performed with the length of the intervals. In this way, it would be possible to determine which investigations are appropriate and which could be dispensed with, thus saving costs. In addition, the correlation between patient outcome in this study population could be analyzed to confirm or reject the literary data correlating the outcome with the length of the total interval of the diagnostic pathway.

5. Conclusions

In Switzerland's efficient healthcare system, cost does not guarantee an expedited sarcoma diagnosis, possibly due to its multidisciplinary nature. Key factors, such as an older age, larger tumor size, and axial localization are associated with a higher malignancy risk, underscoring the need for shorter diagnostic intervals. Further research is essential for guiding clinicians with sarcoma suspicions. To improve patient outcomes through reduced total and diagnostic intervals, focus must be placed on shortening the patient and secondary care intervals. This necessitates targeted patient education and specialized physician training. In light of our findings, we advocate for the regionalization or centralization

of sarcoma care. While secondary care institutions need not be categorically excluded from sarcoma management, their involvement should be contingent upon active collaborations with a multidisciplinary team or sarcoma board from a tertiary care institution, particularly when complex treatments are required. Given these considerations, the logical next advancement for a sarcoma center is the establishment of Integrated Practice Units (IPUs), in alignment with Value-Based Health Care (VBHC) principles. IPUs offer the added benefits of transparently assessing and sharing treatment metrics and quality indicators within a collaborative network.

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Article

Benchmarking Time-to-Treatment Initiation in Sarcoma Care Using Real-World-Time Data

Markus Schärer [1,2,3], Philip Heesen [4], Beata Bode-Lesniewska [5], Gabriela Studer [2] and Bruno Fuchs [1,2,4,5,*,†] on behalf of the Swiss Sarcoma Network

1 Sarcoma Service, Department of Orthopaedics and Trauma, University Teaching Hospital LUKS, 6000 Lucerne, Switzerland; markus@schaerer-family.ch
2 Health Sciences and Medical Faculty, University of Lucerne, 6001 Lucerne, Switzerland
3 Sarcoma Service, Department of Orthopaedics and Trauma, Kantonsspital Winterthur, 8400 Winterthur, Switzerland
4 Sarcoma Service, University Hospital USZ, University of Zurich, 8000 Zurich, Switzerland; philip.heesen@uzh.ch
5 Pathologie Institut Enge, University of Zurich, 8000 Zurich, Switzerland
* Correspondence: fuchs@sarcoma.surgery
† Additional collaborators of the Swiss Sarcoma Network are indicated in the Acknowledgements.

Simple Summary: Understanding the time it takes for sarcoma patients to start treatment after their diagnosis is essential, as a rapid onset of therapy could mean better survival chances. Sarcomas, which are rare and complex cancers, often require swift and specialized care. Our study delved into this time period, known as time-to-treatment initiation (TTI), across a variety of sarcoma cases using detailed, real-world-time data. We found that the length of TTI can differ significantly depending on the type of sarcoma and where the patients receive care. Notably, our comprehensive data collection process has shown that reported TTI using RWTD reflects a thorough account of the patient's experience from diagnosis to treatment start, which is crucial for developing a healthcare system that focuses on delivering value-based care. The insights from our analysis pinpoint where improvements are needed and how specialized sarcoma centers can better coordinate care to start treatment promptly, especially for those cases where early intervention is critical.

Abstract: Benchmarking is a fundamental tool for enhancing quality within a patient-centered healthcare framework. This study presents an analysis of time-to-treatment initiation (TTI) for sarcoma patients, utilizing a database encompassing 266 cases from the Swiss Sarcoma Network. Our findings indicate a median TTI of 30 days across the cohort, with bone sarcomas and deep soft tissue sarcomas demonstrating a shorter median TTI of 28 days, followed by superficial soft tissue sarcomas at 42 days. The data reveal that the use of real-world-time data (RWTD) may account for a longer TTI observed, as it offers more comprehensive capture of patient journeys, unlike conventional datasets. Notably, variability in TTI was observed between different treatment institutions, which underscores the need for standardized processes across centers. We advocate for a selective referral system to specialized centers to prevent capacity overload and ensure timely treatment initiation. Our analysis also identified significant delays in TTI for unplanned 'whoops'-resections, highlighting the importance of early specialist referral in optimizing treatment timelines. This study emphasizes the potential benefits of a streamlined, data-informed approach to sarcoma care. However, further research is required to establish the direct impact of integrated care models on TTI and patient outcomes in the context of sarcoma treatment.

Keywords: sarcoma; soft-tissue-sarcoma; time-to-treatment initiation (TTI); bone-sarcoma; integrated-practice units (IPUs); value-based healthcare system (VBHCS); multidisciplinary team/sarcoma board (MDT/SB); real-world-time data (RWTD)

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1. Introduction

Benchmarking plays a pivotal role in a patient-centered and quality-driven healthcare system [1–3]. It goes beyond identifying areas that need improvement, providing insights into various aspects like overall performance, treatment timelines, and efficiency [4]. To implement benchmarking in healthcare, the foundation of a value-based healthcare system (VBHCS) is a prerequisite [5–10]. This system is characterized by its emphasis on transparency, trust, and quality, based on real-world-time data (RWTD) assessment. Within the framework of VBHCS, sarcoma care can be assessed and systematically compared across diverse treatment facilities and multidisciplinary treatment teams (MDTs). Healthcare providers can make informed decisions based on data-driven insights, identify areas requiring improvement, and optimize resource allocation. The VBHCS forms the basis for developing strategies aimed at enhancing the overall quality of sarcoma care [11–13].

In sarcoma care, patient treatment has traditionally revolved around MDTs, which have been approved and accepted as an important quality indicator [11,13,14]. MDTs unite professionals from diverse disciplines to collectively elevate the standard of patient care. This is particularly important in sarcomas, a rare and highly heterogeneous group of mesenchymal tumors, where both diagnosis and treatment present significant challenges [15–18]. MDTs were proven to maintain treatment quality through their adherence to established guidelines [11]. This is particularly noteworthy when compared to treatments conducted in non-specialized sarcoma centers. Hence, it is imperative that, prior to the initiation of therapeutic interventions, a referral to an MDT be prioritized [11–13,19].

The Swiss Sarcoma Network (SSN) is dedicated to implementing a RWTD approach aligned with VBHCS principles to enhance benchmarking in sarcoma care [1,20,21]. This initiative includes the development of Sarconnector, a digital platform for RWTD assessment and automated analysis, enabling data-driven decisions to optimize resources and improve patient-centered outcomes [1,5,20,22]. Collaborating with an international consortium, the SSN has identified key quality indicators (QIs) for sarcoma management, with a particular focus on the 'time-to-treatment initiation' (TTI). TTI is pivotal for timing interventions effectively, ensuring optimal treatment processes, and facilitating continuous improvement through benchmarking [23,24]. This metric, measuring the interval from diagnosis to treatment start, is crucial in various tumor diseases and particularly significant in sarcoma care, where its definition is adapted to specific treatment contexts [25–27].

TTI is highly important for patient care and overall survival. Specifically, a delay has consistently been associated with lower overall survival rates [23]. In addition, an unclear or lengthy TTI creates psychological distress for patients, leading to increased anxiety and emotional strain. This emphasizes the importance of prompt care initiation [28–30]. TTI provides insight into treatment processes by revealing waiting times and promoting patient engagement in their care decisions. This involvement not only empowers patients but also enhances the relationship between healthcare teams and their patients. Additionally, TTI is essential for evaluating the efficiency of MDTs, which are responsible for treatment decisions, planning, and overseeing diagnostic and therapeutic processes [11,12,23,24].

Analysis of data from the US National Cancer Database (NCDB) between 2004 and 2013 indicates a median TTI of 22 days for both bone and soft tissue sarcomas, with a non-significant 30% increase over this period due to improvements in diagnostics and treatments [24]. A TTI exceeding 30 days correlates with poorer survival rates in high-grade soft tissue sarcomas, suggesting the importance of initiating treatment within this timeframe [23,28]. Challenges like unplanned resections and a lack of coordinated care, which contribute to prolonged TTI, highlight the need for management in specialized MDTs and emphasize the complex interplay of patient, socioeconomic, and healthcare system factors affecting TTI [31–35]. Notably, longer TTI can sometimes be beneficial, allowing for advanced diagnostics and referrals to specialized centers. This underscores the importance of benchmarking in identifying areas needing improvement and implementing a VBHCS [24,28,31–35].

The focus of this paper is, first, to assess and compare TTI in a real-world-time setting within multidisciplinary sarcoma centers and associated networks, consisting of two tertiary referral centers. Second, we want to compare our TTI to the literature, and third, we want to explore the potential of benchmarking TTI to identify potential areas for improvement.

2. Materials and Methods

2.1. Study Design and SSN

This study uses RWTD from patients registered within the SSN, established in 2018. The register functions as a national data platform connected to the weekly Multidisciplinary-Team/Sarcoma-Board (MDT/SB) meeting, facilitating knowledge exchange among sarcoma experts hailing from various institutions. This fosters transdisciplinary collaboration, promotes transparent practices in sarcoma therapy, and simultaneously yields valuable data for quality assessments. The process of data entry is a collaborative endeavor that engages physicians from diverse disciplines who are integrated into the MDT/SB meetings. These meetings serve as forums for reviewing patient information, treatment adjustments, and outcomes, thereby ensuring the integrity of the data. This study used a retrospective analysis of a prospectively collected dataset (based on a prospectively collected real-world-time data warehouse/lake; Sarconnector® (PH&BF, Zürich, Switzerland). Using predefined quality indicators (QI), as outlined by Heesen et al. [20]. Patients' written informed consent is a prerequisite for registry participation.

2.2. Subjects and Data Extraction

This study included patients affiliated with the SSN who were presented at the SSN MDT/SB between January 2018 and September 2022 and had received a suspected diagnosis of a bone or soft tissue tumor [36]. The diagnosis was established through histological assessment following the guidelines provided by the World Health Organization (WHO). It was distinguished between benign, intermediate, and malignant diseases. To gather more comprehensive data, the Adjumed platform (Adjumed Services AG, Zurich, Switzerland; accessed on 15 July 2023) was utilized subsequently. Patients presented at the SB could be transferred primarily for suspected lesions or secondarily when histological examination revealed sarcoma. Transfers occurred across primary, secondary, and tertiary care centers, ensuring a diverse dataset for analysis.

2.3. Definitions, Outcome Measurements and Clinical Characteristics

In both bone sarcoma and soft tissue sarcoma, TTI was defined as the time span in days between the receipt of the final pathological report and the earliest of the following: the first surgical procedure, the date of the first radiation, or the date of the first systemic therapy. In the context of an unplanned "whoops" resection, TTI was defined as the interval between the non-oncological surgical resection and the initiation of the first planned oncological excision procedure or initiation of either radiation or chemotherapy by the SSN after being presented to the MDT/SSN. To our knowledge, no universally accepted definition of TTI in unplanned resections currently exists.

Through our RWTD warehouse (Adjumed, Zürich, Switzerland), for each patient included, the following demographic and treatment-specific information was extracted and recorded: Age, sex, and treatment institution (A, B, and C, which represent three other institutions that were merged together due to the low number of patients). Furthermore, the tumor's pathological characteristics were documented, including its categorization as benign, intermediate, or malignant. Date of histological report or date of unplanned "whoops" resection, date of first treatment (chemotherapy, radiotherapy, or surgery), and the date of any subsequent treatment.

Sarcomas of the extremities—affecting both the upper and lower extremities—as well as of the abdomen, including retroperitoneal sarcomas, were incorporated into the study. Sarcomas were divided into different compartments (superficial soft tissues, deep soft tissues, or bone). The size was assessed in categories of 0–50 mm, 51–100 mm, 101–150 mm,

and >151 mm [32]. The location according to the fascia was distinguishing between epifascial and subfascial. The type of excision has also been recorded as either "unplanned whoops" or "planned" excision.

2.4. Statistical Analysis

Continuous variables are presented as the median (1st quartile, 3rd quartile), while categorical variables are presented as a number (percentage). The normal distribution of variables was assessed visually using histograms or QQ-plots. When continuous data were normally distributed, a *t*-test was performed, while a Mann–Whitney-U test was performed for non-normally distributed data. Differences between categorical variables were tested using a Chi-square test or Fisher's exact test (if the expected value was below 5). A p-value < 0.05 was considered statistically significant. All analyses were conducted using R (version 4.3.1).

3. Results

3.1. Study Patient Population

During the time period from January 2018 to September 2022, a total of 475 patients with bone or soft tissue tumors were presented to the MDT/SB. For the analysis, benign lesions were excluded since control of time to treatment is less meaningful in view of tumor prognosis and quality measurement, as well as patients with a metastatic disease or without therapy by the SSN, thereby yielding a final cohort of 266 patients with an intermediate or malignant sarcoma diagnosis (Figure 1).

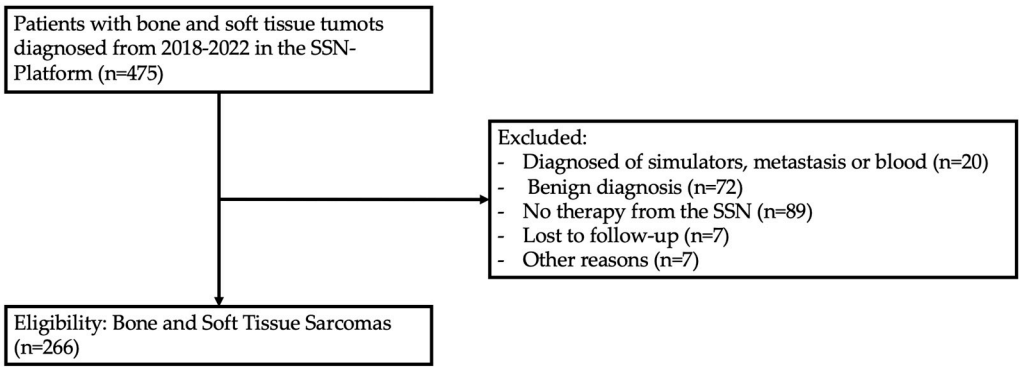

Figure 1. Decision tree on patient inclusion.

Of the 266 patients, 80.1% had a soft tissue sarcoma (STS), whereas bone sarcomas (BS) were seen in 19.9%. Superficial soft tissue sarcoma (S-STS) accounted for 22.5%, whereas deep soft tissue sarcomas (D-STS) were identified in 77.5% (Figure 2). Patients with a BS had a younger median age of 36 years compared to patients with a D-STS and an S-STS, each with a median age of 60 years. Females accounted for 44.7%, and the most common affected anatomical region was the lower extremity with 42.9%. Institution B accounted for the largest proportion with 53.4% (n = 142), followed by institution A with 30.1% (n = 80), and C made up 16.5% (n = 44) of the patients. Further details on baseline characteristics can be found in Table 1.

Table 1. Baseline characteristics of the SSN patients overall according to dignity and and specifically for bone sarcoma, deep and superficial soft tissue sarcoma according to dignity.

	Overall Sarcoma			**Bone Sarcoma**			**Deep Soft Tissue Sarcoma**			**Superficial Soft Tissue Sarcoma**		
	Overall	**Intermediate**	**Malignant**	**Overall**	**Intermediate**	**Malignant**	**Overall**	**Intermediate**	**Malignant**	**Overall**	**Intermediate**	**Malignant**
n, (%)	266 (100)	88 (33.1)	178 (66.9)	53 (19.9)	28 (52.8)	25 (47.2)	165 (62.0)	50 (30.3)	115 (69.7)	48 (18.1)	10 (20.8)	38 (79.2)
TTI, d (IQR)	30 (18–52)	49 (30–70)	25 (15–39)	28 (13–49)	42 (16–58)	20 (11–34)	28 (18–48)	56 (34–70)	22 (14–34)	42 (27–71)	43 (30–71)	42 (26–70)
Age, yrs *n* (IQR)	58 (42–70)	55 (33–66)	59 (47–72)	36 (20–56)	27 (17–46)	51 (22–66)	60 (49–72)	61 (48–71)	59 (49–73)	60 (46–71)	53 (34–65)	62 (53–73)
Female, *n* (%)	119 (44.7)	39 (44.3)	80 (44.9)	21 (39.6)	10 (35.7)	11 (44.0)	71 (43.0)	23 (46.0)	48 (41.7)	27 (56.3)	6 (60.0)	21 (55.3)
Whoops, *n* (%)	41 (15.4)	10 (11.4)	31 (17.4)	0 (0.0)	0 (0.0)	0 (0.0)	15 (9.1)	5 (10.0)	10 (8.7)	26 (54.2)	5 (50.0)	21 (55.3)
Institution, (%)												
A	80 (30.1)	37 (42.0)	43 (24.2)	23 (43.4)	18 (64.3)	5 (20.0)	48 (29.1)	17 (34.0)	31 (27.0)	9 (18.8)	2 (20.0)	7 (18.4)
B	142 (53.4)	40 (45.5)	102 (57.3)	23 (43.4)	8 (28.6)	15 (60.0)	90 (54.5)	25 (50.0)	65 (56.5)	29 (60.4)	7 (70.0)	22 (57.9)
C	44 (16.5)	11 (12.5)	33 (18.5)	7 (13.2)	2 (7.1)	5 (20.0)	27 (16.4)	8 (16.0)	19 (16.5)	10 (20.8)	1 (10.0)	9 (23.7)
Region, (%)												
Abdomen	36 (13.5)	6 (6.8)	30 (16.9)	0 (0.0)	0 (0.0)	0 (0.0)	34 (20.6)	5 (10.0)	29 (25.2)	2 (4.2)	1 (10.0)	1 (2.6)
Upper extremity	37 (13.9)	13 (14.8)	24 (13.5)	12 (22.6)	9 (32.1)	3 (12.0)	17 (10.3)	3 (6.0)	14 (12.2)	8 (16.7)	1 (10.0)	7 (18.4)
Axial	79 (29.7)	28 (31.8)	51 (28.6)	23 (43.4)	11 (39.3)	12 (48.0)	39 (23.6)	12 (24.0)	27 (23.5)	17 (35.4)	5 (50.0)	12 (31.6)
Lower extremity	114 (42.9)	41 (46.6)	73 (41.0)	18 (34.0)	8 (28.6)	10 (40.0)	75 (45.5)	30 (60.0)	45 (39.1)	21 (43.8)	3 (30.0)	18 (47.4)
Size, (%)												
0–50 mm	87 (32.7)	35 (39.8)	52 (29.2)	19 (35.8)	15 (53.6)	4 (16.0)	37 (22.4)	14 (28.0)	23 (20.0)	31 (64.5)	6 (60.0)	25 (65.8)
51–100, mm	91 (34.2)	22 (25.0)	69 (38.8)	25 (47.2)	12 (42.9)	13 (52.0)	51 (30.9)	8 (16.0)	43 (37.4)	15 (31.3)	2 (20.0)	13 (34.2)
101–150, mm	43 (16.2)	12 (13.6)	31 (17.4)	7 (13.2)	1 (3.6)	6 (24.0)	34 (20.6)	9 (18.0)	25 (21.7)	2 (4.2)	2 (20.0)	0 (0)
>150, mm	45 (16.9)	19 (21.6)	26 (14.6)	2 (3.8)	0 (0.0)	2 (8.0)	43 (26.1)	19 (38.0)	24 (20.9)	0 (0.0)	0 (0.0)	0 (0)

If not otherwise specified, data are numbers and percent values in brackets. Data for time-to-treatment initiation are median values with interquartile range in brackets in days. Baseline characteristics presented for patients included from the SSN with a visit between January 2018 and September 2022. Category "overall" includes both malignant and intermediate disease for the specific sarcoma type. "Intermediate" includes patients with an intermediate disease according to the WHO definition as declared in Section 2.2. "Malignant" includes patients with a malignant disease according to the WHO definition as declared in Section 2.2. Colors are used to illustrate the difference between intermediate and malignant dignities. Intermediate diseases are colored in blue; malignant diseases are colored in red. d, days; IQR, interquartile range; *n*, number; na, not applicable; TTI, time-to-treatment initiation; yrs, years.

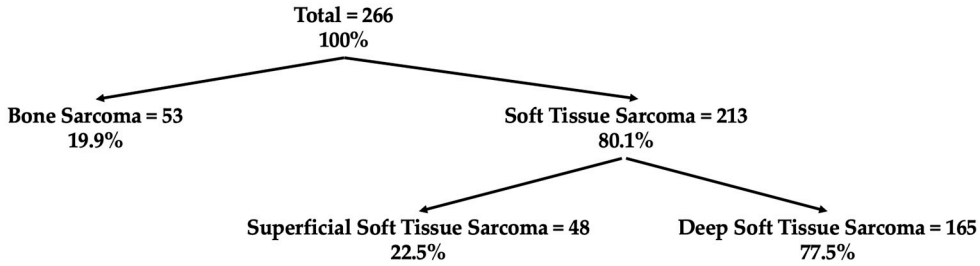

Figure 2. Partitioning of the patient cohort based on sarcoma type. Given in total number and percentage.

3.2. Overall TTI as Quality Assessment in Sarcoma Work-Up

The TTI for the entire cohort of 266 patients was 30 days. When stratified by sarcoma subtype, BS (including both malignant and intermediate) had the shortest TTI at 28 days, followed by D-STS (malignant and intermediate) with a TTI of 28 days, and S-STS (malignant and intermediate) with a TTI of 42 days (Table 1 and Figure 2).

3.2.1. TTI According to Sarcoma Type and Dignity

Significant statistical differences in TTI were identified among sarcoma types according to dignity. The TTI for malignant BS was 20 days, whereas intermediate BS had a TTI of 42 days ($p < 0.05$). TTI in malignant D-STS was 22 days and significantly faster compared to intermediate D-STS with a median TTI of 54 days ($p < 0.001$). No significant difference in TTI between malignant and intermediate sarcomas was seen in S-STS ($p > 0.05$). Malignant S-STS had a median TTI of 42 days, whereas intermediate S-STS had a median TTI of 43 days (Table 2).

Table 2. Time-to-treatment initiation of patients with a bone sarcoma, deep, or superficial soft tissue sarcoma according to dignity and treatment modality.

		Overall		Intermediate		Malignant		*p*-Value [a]
		n **(%)**	**TTI (IQR)**	***n*** **(%)**	**TTI (IQR)**	***n*** **(%)**	**TTI (IQR)**	
Bone sarcoma	Overall	53 (100)	28 (13–49)	28 (52.8)	42 (16–58)	25 (47.2)	20 (11–34)	0.025
	Surgery	37 (69.8)	37 (16–57)	27 (96.4)	41 (16–59)	10 (40.0)	29 (14–53)	0.62
	Chemotherapy	12 (22.6)	13 (8–17)	na	na	12 (48.0)	13 (8–17)	na
	Radiotherapy	4 (7.6)	35 (26–47)	1 (3.6)	51 (51–51)	3 (12.0)	27 (25–43)	0.29
Deep soft tissue Sarcomas	Overall	165 (100)	28 (18–48)	50 (100)	54 (30–70)	115 (100)	22 (14–34)	0.0001
	Surgery	64 (38.8)	41 (29–66)	46 (92.0)	56 (34–70)	18 (15.7)	30 (20–42)	0.007
	Chemotherapy	21 (12.7)	14 (8–18)	1 (2.0)	14 (14–14)	20 (17.4)	14 (8–18)	na
	Radiotherapy	80 (48.5)	25 (18–36)	3 (6.0)	49 (22–117)	77 (67.0)	24 (18–34)	0.11
Superficial soft tissue Sarcomas	Overall	48 (100)	42 (27–71)	10 (100)	43 (30–71)	38 (100)	42 (26–70)	0.63
	Surgery	27 (56.3)	50 (30–75)	10 (100)	43 (30–71)	17 (44.7)	54 (38–75)	0.73
	Chemotherapy	2 (4.2)	11 (10–12)	0 (0.0)	na	2 (5.2)	11 (10–12)	na
	Radiotherapy	19 (39.6)	39 (26–70)	0 (0.0)	na	19 (50.0)	39 (26–70)	na

Data presented in numbers (*n*) of patients for each category, with percent values in brackets. Data for time-to-treatment initiation are median values with interquartile range in brackets in days. Patients are categorized according to sarcoma type and dignity. Category "overall" includes both malignant and intermediate disease for the specific sarcoma type. Category "intermediate" includes patients with an intermediate disease according to the WHO definition as declared in Section 2.2. Category "malignant" includes patients with a malignant disease according to the WHO definition as declared in Section 2.2. Colors are used to illustrate the difference between intermediate and malignant dignities. Intermediate diseases are colored in blue; malignant diseases are colored in red. IQR, interquartile range; *n*, number; na, not applicable; TTI, time-to-treatment initiation; [a] *p*-value was calculated based on a Wilcoxon rank sum test for continuous variables with a continuity correction between intermediate and malignant sarcomas.

3.2.2. TTI According to Treatment Approach and Dignity

When assessing the treatment approaches for malignant sarcomas compared to intermediate sarcomas, the following findings emerged: In malignant BS, surgery and radiotherapy were faster compared to intermediate BS; however, both were statistically not significant ($p > 0.05$). It is important to note that none of the intermediate BS received chemotherapy. In D-STS, radiotherapy and surgery were performed faster in malignant disease; however, surgery was significantly faster in malignant D-STS (TTI of 30 days) compared to intermediate D-STS (TTI of 56 days) ($p < 0.01$). Chemotherapy had the same TTI in intermediate and malignant D-STS. Conversely, for S-STS, surgery was faster in intermediate cases compared to malignant cases, although this difference was not statistically significant ($p > 0.05$). No radiotherapy or chemotherapy was performed in intermediate S-STS. Further details on therapy modalities can be found in Table 2 and Figure 3.

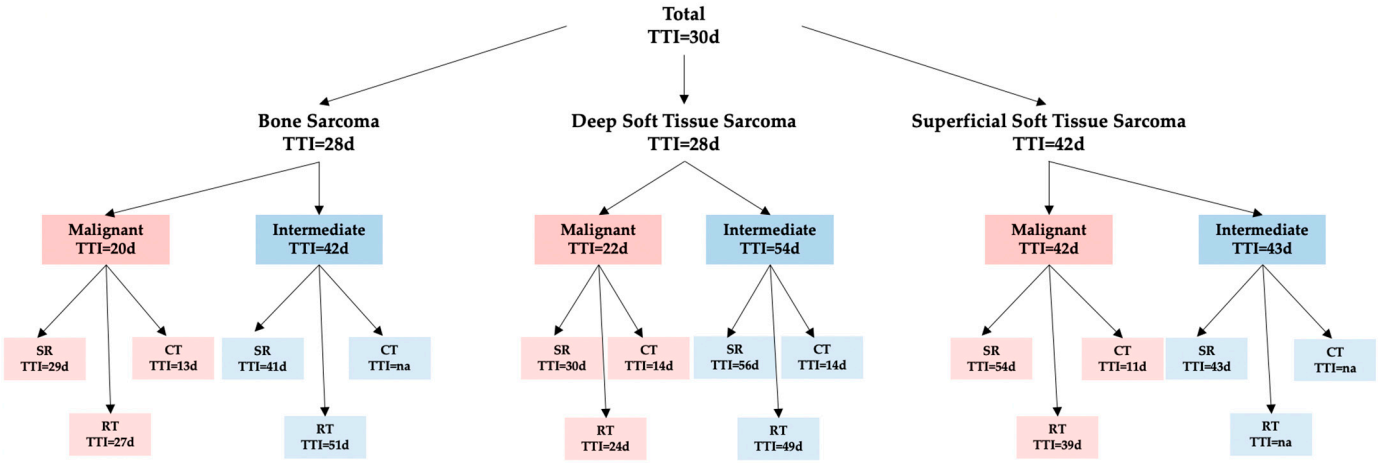

Figure 3. Overview of TTI according to sarcoma sub-type and dignity; SR, Surgery; RT, Radiotherapy; CT, Chemotherapy). Data for TTI are median values.

3.3. TTI in Malignant Sarcomas According to Institution and Therapy Modality

This sub-analysis specifically addresses malignant cases only.

3.3.1. Malignant Bone Sarcoma

In the context of BS, TTI was the shortest in Institution A, with 13 days, followed by Institution C at 14 days, and Institution B at 24 days. However, these differences did not reach statistical significance ($p > 0.05$). Regarding surgical interventions in malignant BS, Institution A had the shortest TTI at 10 days, followed by Institution C at 22 days, and Institution B at 37 days. Also not reaching statistical significance ($p > 0.05$). More details on therapy modalities in malignant BS can be found in Table 3.

Table 3. Analysis of only malignant sarcoma—showing time-to-treatment initiation depending on different institutions.

		Institution A		Institution B		Institution C	
		***n* (%)**	**TTI (IQR)**	***n* (%)**	**TTI (IQR)**	***n* (%)**	**TTI (IQR)**
Bone sarcoma	Overall	5 (100)	13 (10–25)	15 (100)	24 (12–43)	5 (100)	14 (6–30)
	Surgery	1 (20.0)	10 (10–10)	7 (46.7)	37 (24–85)	2 (40.0)	22 (14–30)
	Chemotherapy	3 (60.0)	13 (6–34)	6 (40.0)	13 (11–14)	3 (60.0)	6 (5–38)
	Radiotherapy	1 (20.0)	25 (25–25)	2 (13.3)	35 (27–43)	0 (0.0)	na
Deep soft tissue Sarcomas	Overall	31 (100)	25 (16–34)	65 (100)	21 (15–32)	19 (100)	21 (12–40)
	Surgery	4 (12.9)	13 (12–42)	7 (10.8)	29 (21–42)	7 (36.8)	33 (19–40)
	Chemotherapy	4 (12.9)	15 (12–17)	12 (18.5)	14 (8–21)	4 (21.1)	9 (1–18)
	Radiotherapy	23 (74.2)	29 (23–36)	46 (70.8)	21 (15–34)	8 (42.1)	21 (13–64)
Superficial soft tissue Sarcomas	Overall	7 (100)	38 (15–43)	22 (100)	52 (26–75)	9 (100)	42 (26–62)
	Surgery	2 (28.6)	41 (38–43)	12 (54.6)	55 (26–79)	3 (33.3)	62 (42–78)
	Chemotherapy	1 (14.3)	10 (10–10)	0 (0.0)	na	1 (11.1)	12 (12–12)
	Radiotherapy	4 (57.1)	40 (27–74)	10 (45.5)	44 (26–70)	5 (55.6)	32 (26–45)

Data presented in numbers (*n*) of patients for each categories, with percent values in brackets. Data for time-to-treatment initiation are median values with interquartile range in brackets in days. The analysis includes only patients with a malignant disease. Category "malignant" diseases were defined according to the WHO definition shown in Section 2.2. Data is presented for each different institution according to sarcoma type overall and according to the first treatment modality surgery, chemotherapy, or radiotherapy. IQR, interquartile range; *n*, number; na, not applicable; TTI, time-to-treatment initiation.

3.3.2. Malignant Deep Soft Tissue Sarcoma

In the group of malignant D-STS, Institution B and C had both an overall TTI of 21 days, which was not statistically faster than Institution A with a TTI of 25 days ($p > 0.05$). When considering only surgical interventions, there was a significant difference in time to surgery ($p < 0.01$). Institution A had a significantly shorter time to surgery of 13 days compared to Institutions B and C, which had 30 and 34 days, respectively. In terms of radiotherapy, Institution B had a statistically significant shorter TTI of 21 days compared to Institution A, where the time to radiotherapy was 29 days ($p < 0.01$). However, there were no significant differences in time to chemotherapy among the institutions in malignant D-STS. More details on therapy modalities for malignant D-STS can be found in Table 3.

3.3.3. Malignant Superficial Soft Tissue Sarcoma

In malignant S-STS, the fastest time to surgery was observed in Institution A, with a time of 41 days, compared to 55 days at Institution B and 62 days at Institution C. However, these differences were not significant ($p > 0.05$). Similarly, there were no significant differences in the time to radiotherapy ($p > 0.05$) between the institutions. More detailed information on TTI according to institution and therapy modalities in malignant S-STS can be found in Table 3.

3.4. TTI According to Resection Type

Out of the total of 266 patients (100%), 15.4% had an unplanned so-called whoops resection. The remaining 84.6% underwent planned resections. In whoops resections, 36.6% had a D-STS and 63.4% had a S-STS. In D-STS, 33.3% had an intermediate and 66.7% had a malignant diagnosis. In S-STS, 19.2% had an intermediate and 80.8% had a malignant disease. Notably, there were no occurrences of whoops resections in BS (Figure 4).

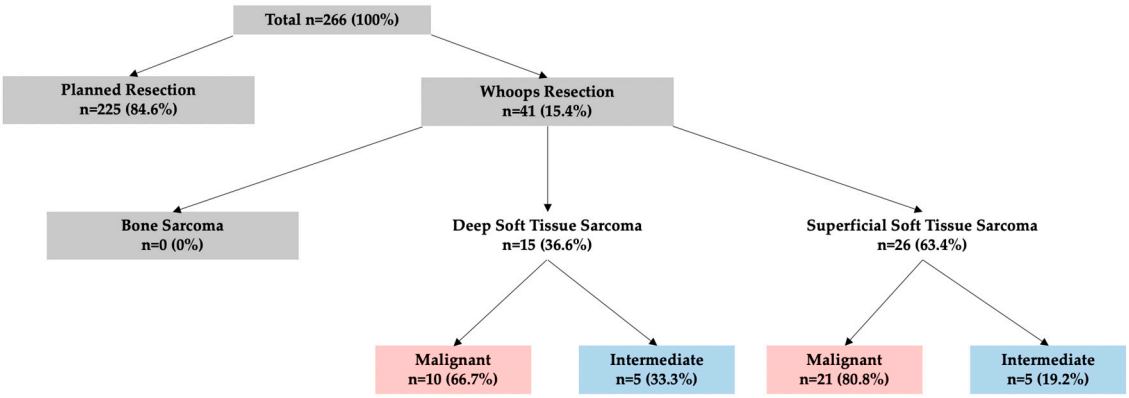

Figure 4. Distribution of whoops resections in total numbers and percentages.

In both malignant S-STS and D-STS, we observed a significant increase in TTI according to resection type. In malignant D-STS, planned resection had a significantly shorter overall TTI of 21 days compared to whoops resections with a TTI of 59 days ($p < 0.001$). The same significance was observed in malignant S-STS, where planned resections had a TTI of 27 days compared to whoops resections with a TTI of 62 days ($p < 0.01$). More detail on resection type in malignant sarcomas can be found in Table 4.

Table 4. Analysis of unplanned surgical resections ("whoops") for time-to-treatment initiation in deep and superficial soft tissue sarcoma compared to planned resections in malignant deep and superficial soft tissue sarcoma.

		Malignant Overall		Unplanned "Whoops"		Planned Malignant		*p*-Value [a]
		n (%)	TTI	*n* (%)	TTI	*n* (%)	TTI	
Deep soft tissue Sarcomas	Overall	115 (100)	22 (14–34)	10 (100)	59 (37–70)	105 (100)	21 (14–31)	0.001
	Surgery	18 (15.7)	30 (20–42)	2 (20.0)	38 (35–40)	16 (15.2)	29 (17–48)	0.44
	Chemotherap	20 (17.4)	14 (8–18)	1 (10.0)	18 (18–18)	19 (18.1)	13 (8–18)	0.49
	Radiotherapy	77 (66.9)	24 (18–34)	7 (70.0)	69 (51–79)	70 (66.9)	23 (15–32)	0.0001
Superficial soft tissue Sarcomas	Overall	38 (100)	43 (26–71)	21 (100)	62 (42–75)	17 (100)	27 (19–42)	0.003
	Surgery	17 (44.7)	54 (38–75)	11 (52.4)	62 (42–78)	6 (35.3)	36 (19–43)	0.09
	Chemotherap	2 (5.3)	11 (10–12)	1 (4.8)	12 (12–12)	1 (5.9)	10 (10–10)	na
	Radiotherapy	19 (50.0)	39 (26–70)	9 (42.9)	64 (45–75)	10 (58.8)	27 (25–39)	0.02

Data presented in numbers (*n*) of patients for each category, with percent values in brackets. Data for time-to-treatment initiation are median values with interquartile range in brackets in days. Analysis of time-to-treatment initiation of unplanned surgical resections ("whoops") compared to planned resections of only malignant sarcoma. Category "malignant overall" includes patients with a malignant disease defined according to the WHO definition shown in Section 2.2. Category "unplanned "whoops"" includes patients who underwent an unplanned surgical resection resulting in a malignant disease, followed by a definitive treatment by SSN. Definition of "whoops" resections is shown in Section 2.3. Category "planned malignant" includes patients diagnosed with a malignant sarcoma by biopsy and receiving a planned first treatment surgery, chemotherapy, or radiotherapy by SSN. IQR, interquartile range; *n*, number; na, not applicable; TTI, time-to-treatment initiation; [a] Comparing time-to-treatment initiation in patients with unplanned and planned resection using a Wilcoxon rank sum test for continuous variables.

Whoops resections are performed on patients not treated by MDT's. In assessing MDT quality, the results indicate that most patients with deep soft tissue sarcomas and all patients with bone sarcomas were aware of their conditions and were referred to an MDT/SB for further work-up and initiation of treatment. However, cases of S-STS were more often treated outside of an MDT/SB before being secondarily referred to it, resulting in whoops resections.

4. Discussion

This study provides RWTD with the aim of improving TTI treatment approaches through meta-level analysis. We conducted an analysis of the time it takes for sarcoma

patients to initiate their first treatment following the histological diagnosis. This approach seeks to optimize patient care, identify areas for improvement, establish standards, and enhance healthcare practices. The objective is to facilitate the attainment of optimal performance, with TTI serving as a quality indicator rather than judging respective units' or physicians' performance. This research contributes to the development of a VBHCS, aiming to shift the healthcare model from a service-driven, competition-based fee-for-service approach to an outcome-driven collaborating system, prioritizing the best possible patient care [37].

The study revealed a median TTI including all sarcoma sub-types with an intermediate or malignant dignity of 30 days. TTI varied based on factors such as the type of tumor, its malignancy, the treatment approach, and the healthcare institution. In a previous study by Curtis et al., conducted from 2004 to 2013, the median TTI for soft tissue sarcomas was 22 days, but it increased to 26 days by 2013 [28]. Similarly, Lawrenz et al. found a TTI of 22 days for primary bone sarcomas in data from the US national cancer database for the period of 2004 to 2013 [23]. However, it is important to note that careful consideration is needed when comparing these findings, as TTI definitions can vary, leading to differences in how diagnosis and treatment start are measured. Lawrenz et al. also studied the accuracy of TTI data from the database compared to manually calculated TTI. They found discrepancies, especially when TTI was recorded as 0 days, indicating potential issues with defining the start of therapy. Manual TTI calculations in one center of the national cancer database showed an average of 34 days with significant variability ($\pm$31.3 days) [38]. This observation underscores the complexity of TTI analysis and emphasizes the importance of standardizing and carefully interpreting data in comparative studies. In interpretation, our study's TTI values appear to be relatively longer when compared to international data. The prolonged TTI could be attributed to our more diverse RWTD dataset. Unlike the previous studies, we included both intermediate and malignant diagnoses and did not differentiate between curative and palliative cases. This approach was driven by our use of RWTD, which reflects the practical complexities of sarcoma care. RWTD offer a precise depiction of clinical practices by collecting observational data within real-life healthcare settings. Its comprehensive and dynamic nature facilitates an in-depth analysis of the medical decision-making process. RWTD provide valuable insights into adherence to clinical guidelines and variation in practices, which can be pivotal in addressing underuse or recommended treatments and standardizing care. By encompassing a broad spectrum of diseases, including rare conditions, RWTD enhance the applicability of research findings to wider patient populations, thereby advancing the quality and relevance of care. In this context, the TTI observed herein may appear somewhat extended when compared to other literature, which can be attributed to the utilization of RWTD. Unlike conventional datasets that might miss the nuances of patient care, RWTD provide a more complete and holistic view. This comprehensive data collection captures a wider range of patient experiences, leading to a more thorough understanding of treatment timelines. Consequently, RWTD's inclusivity and detail-oriented approach can result in a slightly higher TTI, reflecting a realistic scenario that incorporates all aspects of the patient's journey, from diagnosis to treatment initiation. This robust approach ensures a more accurate benchmark for sarcoma care and underscores the necessity for system-wide improvements based on RWTD practices [39–44].

TTI differed according to the therapy modality; we saw an extended time to surgery compared to chemotherapy and radiotherapy. The detailed reasons cannot be extracted from the study results. However, it could be suggested that the delay may be attributed to the complex nature of surgical procedures, which necessitate highly skilled teams from various surgical disciplines [45]. Specialized treatment teams are essential and require meticulous planning to ensure their availability for delivering the necessary care [11,13,14,46]. Despite advancements in diagnostic and therapeutic methods, the fundamental structure of healthcare systems has witnessed limited transformation. Within healthcare systems that emphasize fee-for-service models, patient care tends to remain fragmented and not

adequately centered on the patient's needs. Care is still predominantly confined within departmental boundaries, with some limited interdisciplinary collaboration, such as the introduction of sarcoma boards. However, there is a growing recognition that the existing healthcare model, characterized by departmental silos, may have inherent limitations. Shifting toward a more collaborative model, like a VBHCS with integrated practice units (IPU), could address some of these limitations. Porter et al. were the first to emphasize patient outcomes over sheer volume of services by introducing the VBHC model [6–8,10,37,47–50]. The shift from volume-based to value-based care augments the overall patient experience and satisfaction. The quality of care is gauged by objective indicators and benchmarks, encouraging healthcare providers to continually enhance their services to achieve better patient outcomes [1–3,12,29,51,52]. TTI also differed among the treatment centers, especially in the context of surgical interventions. However, the dataset does not provide clear reasons for these differences. It is worth noting that direct comparisons between the institutions are challenging, and larger patient numbers may help. Additionally, we have not delved into the details of the treatment contracts, which could explain why one center might handle more complex cases, leading to a greater need for diagnostics and complex treatments.

Significant disparities in TTI are evident across varying tumor types, with S-STS consistently exhibiting the lengthiest TTI when compared to BS and D-STS. While our dataset does not provide explicit reasons for the TTI delay associated with S-STS, an intriguing pattern emerges. Patients diagnosed with S-STS often commence their initial treatment outside the specialized environs of dedicated multidisciplinary sarcoma teams. Subsequently, once the diagnosis is definitively established, they are transferred to tertiary care facilities for ongoing management. A noteworthy observation within this context is the number of unplanned surgical excisions, so-called "whoops" resections, outside an MDT. These revelations underscore the immediate necessity for enhanced educational efforts aimed at improving the management of tumor masses and a heightened awareness of the potential repercussions stemming from the misinterpretation of a sarcoma diagnosis, particularly in treatment settings that operate outside sarcoma centers. However, this study serves as a poignant reminder that even superficially located tumor masses can potentially harbor malignancies, warranting greater diligence in the management of S-STS. Nevertheless, redirecting all tumor masses to dedicated sarcoma experts represents a logistical challenge. Striking the balance between timely diagnosis and the initiation of appropriate treatment necessitates a consideration of various factors, including the intricacies of diagnosis, TTI, and therapeutic management. To mitigate the risk of overburdening central sarcoma facilities and prolonging waiting times for patients, not all patients should be centralized; selective referral is essential. Sarcoma centers should facilitate easier access in accordance with the IPU model to prevent overwhelming their capacity. This entails expanding the network to incorporate all secondary surgeons and primary care physicians, allowing them to present their cases with a very low threshold, facilitating efficient and timely referral to a dedicated sarcoma center [22,53–58].

Despite efforts to reduce unplanned surgical excisions, a significant percentage of such incidents still occur. Our study observed a "whoops" resection rate of 15.4%, which is relatively lower compared to findings in existing literature. For example, a study conducted by Melis et al. from 2016 to 2019 reported a higher unplanned "whoops" resection rate of 18.2% in cases of STS. These unplanned "whoops" resections have significant implications for various aspects of sarcoma management, including overall survival, local recurrence rates, financial impacts on both the healthcare system and patients, and disease control. An in-depth examination of these implications is crucial for a comprehensive understanding of how unplanned "whoops" resections affect sarcoma care. This knowledge can guide clinical practices and treatment decisions and ultimately improve the overall management of sarcoma patients [50,59–64].

It is important to note that our dataset does not allow a conclusion about systemic control in patients with prolonged TTI. While our study provides insights into various aspects of sarcoma care, the specifics of systemic control, especially in cases with prolonged

TTI, are not addressed in our data. Factors like metastasis progression, the effectiveness of systemic therapies, and their impact on overall outcomes require more information than our dataset currently provides. These limitations underscore the necessity for more extensive data collection over a longer time period and future studies to explore the relationship between TTI and systemic control. The population of this study encompasses a wide range of sarcoma types, each with its own biology and impact on overall survival. This might as well be a reason for a variation in patient care. This diversity makes it challenging to draw broad conclusions and limits the statistical power of subgroup analyses due to the small sample sizes. TTI was analyzed exclusively for patients presented to the Sarcoma Board (SB), engendering an inherent selection bias as those not presented to the SB. TTI is part of an analysis of further quality metrics, all needed to explore aspects of the healthcare system and be able to improve patient quality care.

5. Conclusions

This study's analysis of time-to-treatment initiation (TTI) using real-world-time data (RWTD) elucidates the current landscape of sarcoma treatment initiation across various centers and sarcoma subtypes. Our findings indicate considerable variability in TTI, with notable delays, especially in cases of superficial soft tissue sarcoma and unplanned 'whoops' resections. The study highlights the imperative for strategic interventions aimed at standardizing care pathways and enhancing the referral process to specialized sarcoma centers. Importantly, while the data reflect a higher TTI relative to other studies, the comprehensive nature of RWTD captures a more accurate depiction of the patient journey, suggesting that previous reports may underrepresent actual TTI. Moving forward, it is crucial to balance the need for specialized care with the risk of central facility overload, advocating for a selective referral system that aligns with integrated practice units. Ultimately, this study serves as a catalyst for ongoing efforts to refine the sarcoma care model, emphasizing the need for a systemic shift towards a value-based healthcare framework that prioritizes patient outcomes and efficient resource utilization.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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Schweizerisches Sarkom-Netzwerk – Aktivitäten und erste Resultate

Autoren: Gabriela Studer [1], Beata Bode [2], Mario Scaglioni [3], Philip Heesen [4], Carlo Theus-Steinmann [5], Christoph Glanzmann [1], Bruno Fuchs [5], für das Swiss Sarcoma Network

Affiliationen:
[1] Radio-Onkologie, Luzerner Kantonsspital
[2] Pathologie Institut Enge, Zürich und Universität Zürich
[3] Hand- und Plastische Chirurgie, Luzerner Kantonsspital
[4] Student, Universität Zürich
[5] Orthopädie und Unfallchirurgie, Luzerner Kantonsspital

1. Einleitung

Die optimale Abklärung und Behandlung von sarkomatösen Erkrankungen ist grundsätzlich multidisziplinär und erfordert eine ab initio prä-festum abgesprochene Abfolge der einzelnen Schritte. Jeder Schritt beeinflusst und/oder bedingt den nächsten – der Folgeschritt kann nur so gut sein wie der vorangegangene (z.B. keine bestmöglich konformierende präoperative Radiatio ohne rezente und sachkundig durchgeführte MRI/-Befundung; keine ideale Chirurgie bei ungünstig durchgeführter Biopsie... usw.). Deshalb erfolgt bei Verdacht auf eine sarkomatöse Erkrankung die weitere Abklärung/Diagnosesicherung optimalerweise in einem multidisziplinären Team (MDT), das vertraut ist mit den Abläufen, Folgeschritten und Entität-bezogenen pitfalls. Ein Beispiel für die Effektivität dieses ab initio multimodalen/multidisziplinären Vorgehens kann u.a. den Daten des Französischen Sarkom-Netzwerks NETSARC+ entnommen werden [1] (2022): Seit 2010 wurden 26 national designierte Sarkom-Referenz-Zentren installiert mit jeweils multidisziplinären Boards. Seither ist es gesetzlich erforderlich (‹mandatory by law›), dass der erstbetraute Pathologe jeden Fall mit Verdacht auf Sarkom oder intermediäre Malignität an die Pathologie eines Referenz-Zentrums überweist. Die Schlüssel-Parameter 1) Fall-Präsentation an einem Multidisziplinären Sarkom-Board VOR Behandlung, 2) Biopsie VOR Behandlung, und 3) Bildgebung VOR Behandlung wurden analysiert. Es fand sich eine deutliche Verbesserung in der Umsetzung der drei Parameter über die letzten 10 Jahre, mit einer dadurch substanziellen nationalen Qualitätsverbesserung des Managements von Sarkom-Patienten. Auch die Spanische Sarkom-Research-Gruppe GEIS konnte den Effizienz-Effekt des Managements von Sarkom-Erkrankungen durch Multidisziplinäre Teams eindrücklich belegen [2] (2019): So zeigte sich ein um annähernd 25% besseres rückfallfreies 5-Jahres-Überleben, wenn die Biopsie an einem Referenz-Zentrum versus an einem Lokalspital durchgeführt wurde, und ein ca. 15% besseres 5-Jahres-Gesamtüberleben von Sarkom-Patienten mit Management an Referenz-Zentren gegenüber Patienten an Lokalspitälern.

Primäres Ziel und Aufgabe des überregionalen Schweizerischen Sarkom-Netzwerks (SSN) ist deshalb die ab initio interdisziplinär orchestrierte, zeitnahe «state-of-the-art»-Abklärung, Behandlung, Betreuung und Verlaufsbeobachtung von Patienten mit sarkomatösen Erkrankungen. Dies erfolgt im nationalen und internationalen Austausch, im Sinne eines überregionalen krankheitsbezogenen Services, der sich nicht auf geographisch-politisch definierte Institutionen/Grenzen beschränkt.

Vertragliche SSN Mitglieder sind derzeit folgende Institutionen: die Kantonsspitäler Winterthur (KSW), Chur (KSGR), Bellinzona (EOC), Luzern (LUKS), Stadt-Spital Triemli/Waid, die Klinik Hirslanden Zürich, sowie das Pathologie-Institut Enge Zürich, mit Affiliation der Sarkom-Referenzpathologin.

Fallbasierte Kooperationen bestehen mit zahlreichen weiteren Institutionen und Praxen.

In früheren Artikeln wurde das SSN vorgestellt ([3,4] 2018), beziehungsweise die Kennzahlen der bis damals erfassten/behandelten PatientInnen gezeigt ([5] 2020).

Mit dem vorliegenden Beitrag sollen die Kennzahlen der letzten 4 Jahre – basierend auf der SSN Sarkomboard-Register-Dokumentation – aktualisiert, und erste Resultate (‹outcome›-Daten) präsentiert werden.

2. SSN-Resultate (Abbildungen 1–14) aus dem Zeitraum vom 01.01.2018 bis 31.12.2021

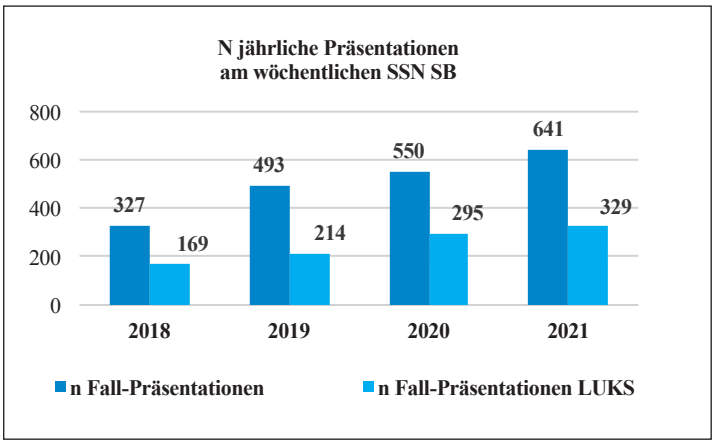

Abb. 1: alle Fallpräsentationen (1.-Präsentationen und Follow-Up-Präsentationen) am wöchentlichen SSN-Sarkomboard (SB) (LUKS-Präsentationen Teilmenge aller Fall-Präsentationen) im Zeitraum 2018–2021

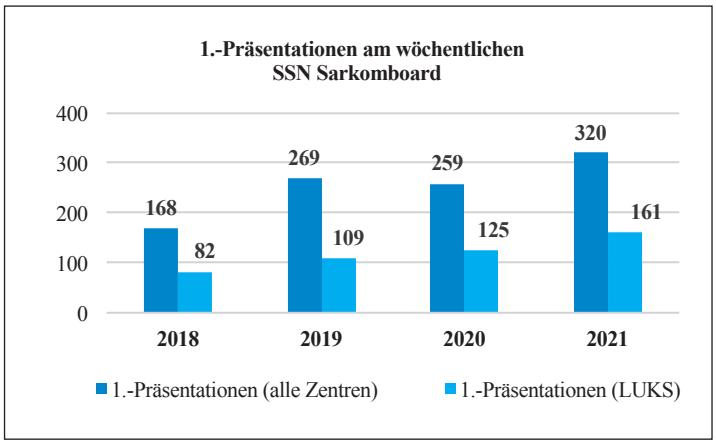

Abb. 2: 1.-Präsentationen am wöchentlichen SSN-Sarkomboard (LUKS-Präsentationen Teilmenge aller Fall-Präsentationen) im Zeitraum 2018–2021

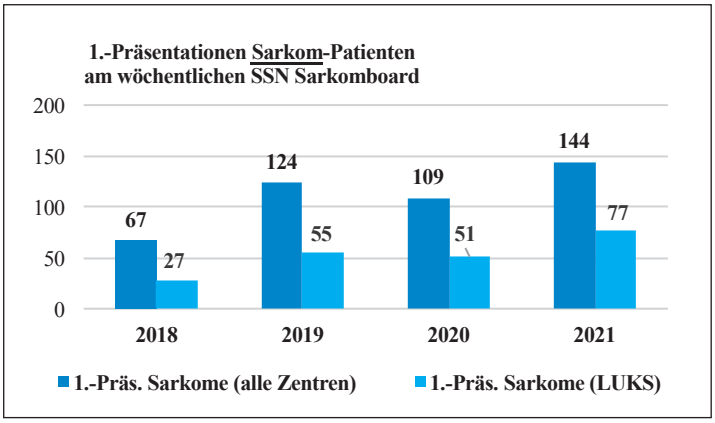

Abb. 3: *1.-Präsentationen von Patienten mit Sarkom-Diagnose (LUKS-Präsentationen Teilmenge aller Fall-Präsentationen) im Zeitraum 2018–2021*

1.-Präsentationen	2018	2019	2020	2021	gesamt
benigne	58	79	75	86	298
SARKOME	67	124	109	144	444
Simulatoren	17	31	23	21	92
Metastasen	5	10	7	13	35
andere	35	28	47	49	159
alle	**182**	**272**	**261**	**313**	**1028**

Abb. 4: *alle SSN-Erstpräsentationen im Zeitraum 2018–2021, gelistet nach Diagnosen*
(Simulator: bildgebend muss der Verdacht eines Sarkoms in Betracht gezogen werden. Eine bioptische Aufarbeitung zeigt aber, dass es sich um eine Läsion handelt, die nicht einem durch die WHO definierten Tumor entspricht, z.B. Infektion, altes organisiertes Hämatom, Metallabrieb bei liegender Prothese usw.)

Indikationen für FU-Präsentation	n	%
im Zusammenhang mit der Initialbehandlung	631	70
1. Lokalrezidiv	47	5
1. systemisches Rezidiv	40	4.5
wichtige FU-Information	24	2.5
andere	162	18
gesamt	**904**	**100**

Abb. 5: *Follow-Up (FU) Präsentationen im Zeitraum 2018–2021, analysiert nach dem Grund der Vorstellung*

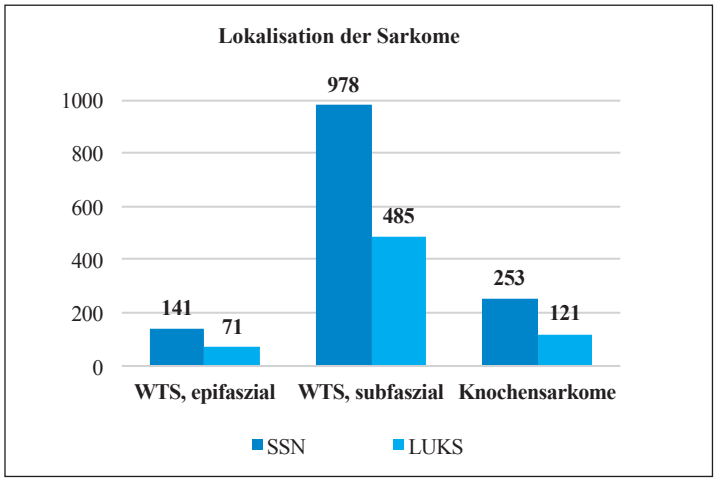

Abb. 6: *Sarkom-Lokalisationen präsentiert im Zeitraum 2018–2021 (LUKS-Präsentationen als Teilmenge aller Fall-Präsentationen)*

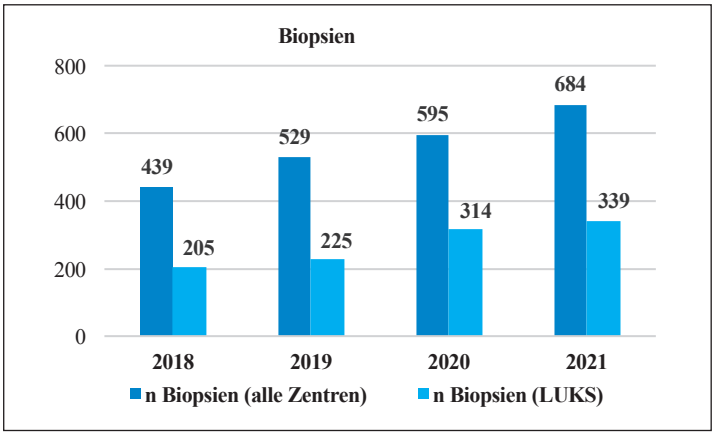

Abb. 7: *Anzahl erfolgter Biopsien zur Diagnosesicherung im Zeitraum 2018–2021 (LUKS-Präsentationen Teilmenge aller Fall-Präsentationen)*

Häufigste Diagnosen	N	%
Lipome	180	9.3
undifferenziertes/unklassifiziertes Sarkom	141	7.3
Dedifferenziertes Liposarkom	125	6.5
nicht-neoplastisch/Tumor-Simulator	118	6.1
Leiomyosarkom	96	5
atypischer lipomatöser Tumor / gut diff. Liposarkom	92	4.8
Myxofibrosarkom	54	2.8
Desmoid-Typ Fibromatosis	53	2.7
Total	**859**	**44.40%**

Abb. 8: *Häufigst gestellte histopathologische Diagnosen aller SSN-Fälle im Zeitraum 2018–2021*

OP-Indikation	N	%
1.-OP	377	83.5
OP nach WHOOPS	31	7
OP Lokalrezidiv	21	4.5
OP pathol. Fraktur	7	1.5
andere	16	3.5
gesamt	**452**	**100**

Abb. 9: *Indikationen für Operationen der SSN-Sarkom-PatientInnen im Zeitraum 2018–2021*

Strahlentherapie	N	%
kurativ präoperativ	122	86
kurativ postoperativ	7	5
definitiv	6	4
palliativ	6	4
gesamt	**141**	**100%**

Abb. 10: *Anzahl erfolgter Radiotherapien der SSN-Sarkom-Patienten im Zeitraum 2018–2021*
(Basierend auf den Daten des prosp. rand. Canadian Trials (2002) soll bei indizierter Kombination der Operation mit einer Strahlentherapie das **präoperative** Vorgehen gewählt werden [6,7].

Systemtherapie	N	%
Kurativ neoadjuvant	34	49
Kurativ adjuvant	13	19
palliativ	23	32
gesamt	**70**	**100%**

Abb. 11: *erfolgte Systemtherapien bei SSN-Sarkom-PatientInnen im Zeitraum 2018–2021, gelistet nach der Intention*

Qualitäts-Indikatoren für die Lokaltherapie	%
1) Radikalität der Operationen	>95% R0 <5% R1 0% R2
2) Wundkomplikationsrate nach kurativer RT&OP	<5%
3) Lokalkontrolle	>95%

Abb. 12: *Qualitäts-Indikatoren zum lokalen Outcome nach Sarkom-Behandlungen im Zeitraum 2018–2021:*

- *Radikalität der Operation*
- *Wundkomplikationsrate nach Kombinationstherapie mit präoperativer Radiatio*
- *Lokalkontrolle*

	2018	2019	2020	2021
n WHOOPS Läsionen/Jahr	19	48	27	28
n 1.-Präsentationen/Jahr	168	269	259	320
% WHOOPS der 1.-Präsentationen	**~11%**	**~28%**	**~10%**	**~9%**
n Sarkom1.-Präsentationen/Jahr	67	124	109	144
% WHOOPS der Sarkom-1.-Präsentationen	**28%**	**39%**	**25%**	**19%**

Abb. 13: *Entwicklung der Anzahl WHOOPS-Eingriffe im SSN-Einzugsgebiet (aktuell wird noch jeder 5. Patient im SSN-Einzugsgebiet initial nicht unter den erforderlichen onkologischen Gesichtspunkten, ausserhalb eines Sarkomboards, anbehandelt).*

‹Whoops lesion› = ungeplante Exzisionen von Weichteilsarkomen ohne vorangehende Diagnostik resp. Bildgebung. Whoops-Läsionen kommen bei 20–50% aller Patienten mit Weichteilsarkomen vor. Whoops-lesions' sind assoziiert mit einer erhöhten Rate an Lokal-Rezidiven und schlechterer Prognose.
Hierzu liegen u.a. Daten des Kanadischen Sarkom-Zentrums in Toronto vor, die den prognostisch ungünstigen Einfluss nach Whoops-Eingriffen deutlich machen [8] (2018): Die 5-Jahres-Lokalkontrollrate nach Operationen mit tumorfreien Rändern betrug 96%, nach geplant positiven Rändern noch immer 90%, bei whoops lesions 82%, nur nach versehentlich positiven Resektions-Rändern noch tiefer mit 72% (p<0.001).

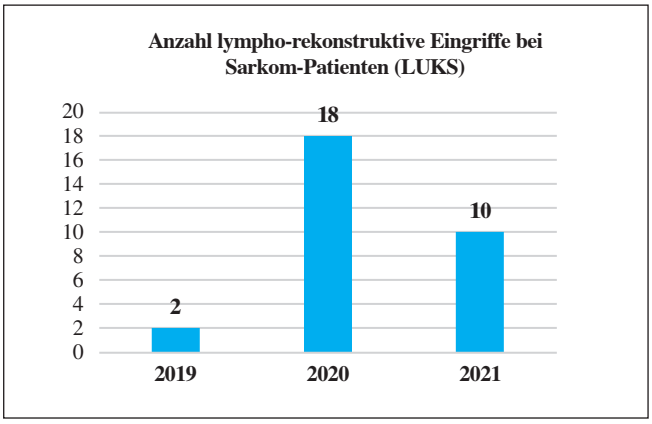

Abb. 14: *durchgeführte lympho-rekonstruktive Chirurgie im Rahmen der Erst-Operation bei Sarkom-PatientInnen (durch Koautor MS, der das Vorgehen bei Sarkom-Operationen eingeführt hat) [9-12] – mit dem Ziel der Verhinderung oder Behandlung eines distalen Oedems bei Sarkom-Therapien v.a. von Extremitäten/Becken*

3. Kontaktaufnahme mit dem SSN

Ich möchte einen Fall präsentieren am SSN Sarkom-Board LUKS:

– Informationen unter:
www. swiss-sarcoma.net

– Anmeldungen für Fallpräsentationen am wöchentlichen Sarkomboard:
office@sarcoma.surgery

Kontaktierung bei Verdacht auf / bei bereits gesicherter Sarkom-Diagnose:

Prof. Dr. Bruno Fuchs
Leitender Arzt
Klinik für Orthopädie
und Unfallchirurgie LUKS
Spitalstrasse, 6000 Luzern 16
Telefon 041 205 66 73
bruno.fuchs@luks.ch

Prof. Dr. Gabriela Studer
Chefärztin
Radio-Onkologie
LUKS und ZGKS
Spitalstrasse, 6000 Luzern 16
Telefon 041 205 58 01
gabriela.studer@luks.ch

Patienten-Kontakt-Adresse:
info@sarkom-schweiz.ch

Websites:
swiss-sarcoma.net | www.sarcoma.surgery | www.sarcoma.academy

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Autoren

Prof. Dr. med.
Gabriela Studer

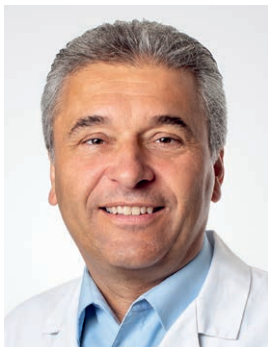
Prof. Dr. med.
Beata Bode-Lesniewska

PD Dr. med.
Mario Scaglioni

Carlo Theus-Steinmann

Philip Heesen

Prof. Dr. med.
Christoph Glanzmann



Prof. Dr. med.
Bruno Fuchs

Korrespondenzadresse

Gabriela Studer
Chefärztin Radio-Onkologie
Luzerner Kantonsspital
6000 Luzerner Kantonsspital
gabriela.studer@luks.ch

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Trägerverein Swiss Medical Weekly
c/o Gyr Gössi Olano Staehelin, Advokatur und Notariat
Malzgasse 15
CH-4052 Basel
office@smw.ch
www.smw.ch

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Transdisciplinary sarcoma care: a model for sustainable healthcare transformation

Bruno Fuchs[a], Beata Bode[b], Philip Heesen[c], Barbara Kopf[d], Christian Michelitsch[e], Manfred Odermatt[f], Pietro Giovanoli[c], Stefan Breitenstein[g], Paul Schneider[h], Guido Schüpfer[a], Stefan Boes[a], Gabriela Studer[a], on behalf of the Swiss Sarcoma Network

[a] LUKS University Teaching Hospital, Medical Faculty, University of Lucerne, Lucerne, Switzerland
[b] Patho Enge, University of Zurich, Zurich, Switzerland
[c] University Hospital Zurich USZ, University of Zurich, Zurich, Switzerland
[d] Ente Ospedaliero Cantonale EOC, Locarno, Switzerland
[e] Kantonsspital Graubünden Chur (KSGR), Chur, Switzerland
[f] Stadtspital Zurich, Triemli, Zurich, Switzerland
[g] Kantonsspital Winterthur KSW, Winterthur, Switzerland
[h] Hirslanden Zurich, Zurich, Switzerland

Introduction

Healthcare organisations worldwide are facing significant challenges, including labour shortages, cost containment and capital contraction, leading to unsustainable workloads, staff shortages and burnout. The projected workforce shortages of both nurses and physicians have prompted the need to rethink healthcare delivery [1]. Hiring workers from other organisations to address staffing gaps ultimately creates a zero-sum game. A global survey highlighted the importance of intrinsic motivators, such as professional development opportunities, that may have been overlooked in the past [1]. There is unanimous agreement that financial expenditure exceeds medical capabilities. In Switzerland, concerns about the sustainability of the healthcare system existed before the COVID-19 pandemic due to sociodemographic changes, such as the retirement of the baby boomer generation and the smaller zoomer generation taking over, resulting in reduced healthcare capital [2–5]. This impending contraction of capital will further challenge the financial situation of hospitals.

Challenges to meet

There is unanimous agreement that a fundamental shift in healthcare delivery is necessary due to dwindling financial resources and staffing. Meyer et al. suggested that the healthcare system should be more integrated, preventive, transparent, outpatient-based and data-driven [6]. Many recognise the importance of digital transformation, although Switzerland is still in the early stages of developing electronic health records and embracing digitisation. Physicians have historically been resistant to defining quality of care due to its complexity, but defining it is crucial. Nearly two decades ago, Porter et al. introduced the concept of value-based healthcare, which involves assessing the quality and outcomes of care based on both patient and physician evaluations and considering the total costs incurred throughout the healthcare cycle [7]. The Swiss Sarcoma Network has proposed ~~a modified~~ an adapted approach for developing a value-based healthcare delivery model specifically for sarcoma patients [8, 9].

The sustainable healthcare triad

The sustainable healthcare triad emphasises the interconnectedness of clinical care, outcomes and quality measures, and cost efficiency. Currently, the fee-for-service system does not consider the quality or cost control of medical procedures, such as surgeries. However, the new ecosystem-based triad necessitates coordinated, multidisciplinary interventions evaluated for their quality, outcome and costs. This approach integrates key parameters from the patient's perspective and identifies key performance indicators for individual physicians. Aligning patient and physician views on cost efficiency, ~~particularly by the objective and transparent determination of variable physician salaries~~, is crucial for establishing a sustainable healthcare system. ~~((Comment language editor: Please confirm that I have not changed the intended meaning here.))~~ including also an objective and transparent definition of variable physician salaries

alternatively you could use this last part

Transdisciplinary sarcoma surgery

Sarcoma surgery and care are highly transdisciplinary, serving as a model for developing a sustainable healthcare system. The complexity of sarcomas necessitates collaboration across multiple disciplines to achieve optimal tumour removal and local control. The Swiss Sarcoma Network (www.swiss-sarcoma.net) exemplifies the integration of disciplines and institutions, fostering a multi-institutional and transdisciplinary approach rather than a mono-institutional silo system.

Requirement 1: Physician-based metrics: Definition of surgical spectrum including complexity and quality of care

Sarcoma surgery is a highly complex procedure influenced by factors such as anatomical location, tumour size and biology. A senior Swiss Sarcoma Network surgeon conducted a 10-year analysis to develop a comprehensive ~~spec-~~

Bruno Fuchs, MD, PhD
LUKS University Teaching Hospital
Spitalstrasse
CH-6000 Luzern 16
fuchs[at]sarcoma.surgery

~~trum~~ that considers all relevant parameters for resections and reconstructions [10]. This spectrum serves as a valuable tool for assessing surgical experience, educating future surgeons and evaluating the complexity and costs of specific interventions. Based on this ~~spectrum,~~ the Swiss Sarcoma Network introduced the soft-tissue surgery complexity score, which incorporates patient-, tumour biology- and surgery-related factors to determine the complexity of each intervention [11]. This score is particularly important for Porter's geography model of care, which strives to deliver the appropriate treatment in the optimal geographic location, leading to improved outcomes and cost-effectiveness. Beyond surgery, sarcoma care entails multiple aspects that demand attention. To address this, the Swiss Sarcoma Network collaborated with an international advisory board of experts to define six categories of quality indicators for sarcoma care [12]. These categories encompass patient work-up, multidisciplinary team management, ~~surgical~~ board management, therapy (including surgery, radiation and systemic therapy), complexity of sarcoma therapy, clinical outcomes and patient-reported outcomes. **((Comment language editor: The first sentence here says there are six categories, but seven categories are listed.))** Evaluating these indicators is vital for sustaining a healthcare ecosystem, as it provides a comprehensive view of patient outcomes and the quality of care, as assessed by physicians.

Requirement 2: Patient-reported outcome measures

In value-based healthcare, patient-reported outcome measures (PROMs) play a crucial role in assessing treatment effectiveness and improving outcomes, providing valuable insights beyond clinical metrics [9]. While numerous patient-reported outcome measures exist, only a few have been created for sarcoma surgery [13]. One widely used patient-reported outcome measure is the EQ-5D, which includes five questions on general health dimensions and has been validated for various diseases, including cancer. The Swiss Sarcoma Network has established a reference score of EQ-5D specifically for sarcoma patients and has revealed that the most significant negative predictor of perceived health is the administration of chemotherapy.

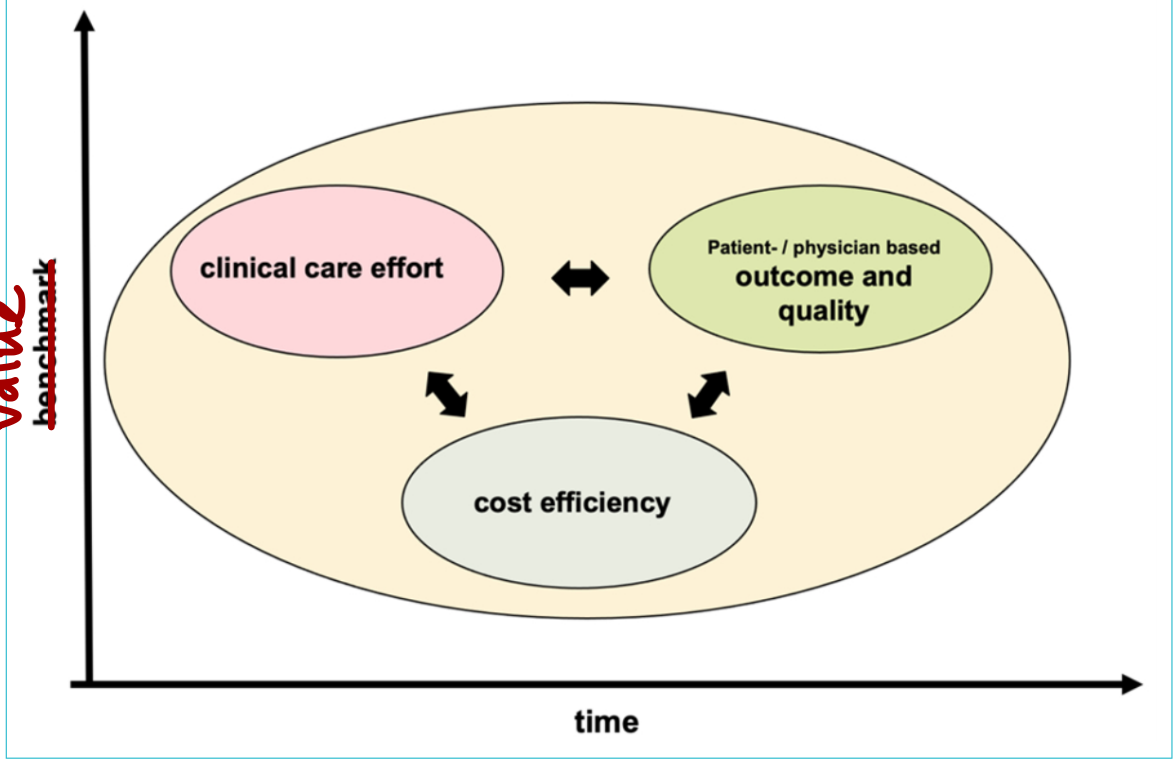
Sarcoma surgery and care present challenges because treatments are individualised and multidimensional. To address these challenges, the Swiss Sarcoma Network has developed a novel health-related quality of life (HRQOL) instrument [13]. This survey instrument utilises over 10 personalised generic patient-reported outcome measure questionnaires, allowing patients to electronically complete questionnaires based on their specific treatments and longitudinal follow-up periods. By incorporating a comprehensive set of patient-reported outcome measures, this approach aims to capture the holistic impact of sarcoma treatment on patients' lives.

Requirement 3: Interoperable digital platform to allow ~~real-time~~ data collection and evidence analytics (RWTD/E)

((Comment language editor: Please confirm that changing "real-world-time" to "real-time" in the title of this section is appropriate.))

Managing healthcare data is a significant challenge in today's world, but the digital transformation of healthcare practices holds great potential for revolutionising current approaches. Instant access to ~~real-time~~ clinical data and automated analyses are crucial, especially in multidisciplinary and multi-institutional settings.

Figure 1: The sustainable healthcare triad aligns the clinical effort with outcome and quality, as well as cost efficiency. The goal is to benchmark these parameters over time.



To integrate complex data into daily practice and generate ~~real-time~~ evidence, a key strategy is combining the management of multidisciplinary team/sarcoma board conferences (MDT/SB) with the patient registry **((Comment language editor: Please confirm that I have not changed the intended meaning here by inserting "patient" before registry))**. By doing so, conflicting issues like surgical margins can be addressed and resolved through a multidisciplinary approach, with data recorded directly in the registry without the need for retrospective data collection.

During MDT/SB, the presenting physician and their team provide patient information, which is associated with the registry. Patients with sarcoma recurrence are automatically presented to the MDT/SB, and their data are stored in the registry. Patients without recurrence undergo regular check-ups and provide electronic patient-reported outcome measures. This system enables ~~real-time~~ follow-up of all patients.

The platform used incorporates over 500 parameters and facilitates calculations of quality indicators and simple statistics for direct visualisation. With ~~real-time~~ data collection and evidence analytics, predictive modelling becomes possible, ultimately leading to the development of a human–sarcoma digital twin and enabling individualised precision care.

Requirement 4: Health services research

Health services research examines the impact of various factors on healthcare access, quality and costs and on patient well-being. Utilising an interoperable digital platform with descriptive and inferential statistics enables ~~real-time~~ research. This interdisciplinary field investigates how social factors, financing systems, organisational structure, health technologies and personal behaviours affect healthcare. A sarcoma study including all patients undergoing biopsy revealed 55% malignancy in suspicious soft tissue and bone neoplasms [14]. This finding has implications for planning and establishing an integrated practice unit (IPU) to streamline diagnostics. Another analysis compared pathology workups from different institutions, emphasising the importance of reference reviews. Incorrect diagnosis impacted treatment in 12.2% of cases [15]. Consulting reference pathologists reduced time to diagnosis. An ongoing project is evaluating the costs of hospitalisations and surgical interventions across three hospitals and is considering the case mix index, complexity score and outcomes.

Embedding health services research within hospitals is crucial. Affiliation with a medical faculty with health-focused research facilitates these analyses. Leveraging digital platforms and data analysis improves healthcare practices and patient outcomes in real time.

Conclusion

Healthcare organisations face numerous challenges, including labour shortages, cost containment and capital contraction. To address these challenges, the development of an integrated, preventive, transparent, outpatient-based and data-driven healthcare system is necessary. The sustainable healthcare triad, comprising clinical care, physician- and patient-based outcomes and quality, and cost efficiency, plays a vital role in this system. Defining the triad enables the establishment of key performance indicators for ~~each physician~~ and aligns patient and physician perspectives on cost efficiency. The transdisciplinary organisation of sarcoma care, involving multiple disciplines and institutions, serves as a model for building a sustainable healthcare system. Defining the surgical spectrum, with its associated complexity, and the quality of care, using physician-based metrics, is crucial to this process. By adopting these strategies, healthcare organisations can deliver improved care while optimising efficiency and sustainability.

Future directions

The healthcare industry must evolve and adapt to overcome challenges like workforce shortages and capital contraction. Digitalisation and electronic health records will play a crucial role. Defining quality of care with physician-based metrics aligns patient and physician views on cost efficiency for a sustainable healthcare system. Embracing and implementing the sustainable healthcare triad is necessary. Further research is needed to explore how the industry can adapt and achieve sustainable healthcare delivery.

Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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The SwissSarcomaNetwork

Pioneering Precision Medicine: Benchmarking RWT-Evidence-Based Insights to Revolutionize Sarcoma Care – the SwissSarcomaNetwork (SSN)

AUTOREN


Prof. Dr. med. Bruno Fuchs
fuchs@sarcoma.surgery


Prof. Dr. med. Stefan Breitenstein
stefan.breitenstein@ksw.ch


Dr. med. Andreas Scheiwiller
andreas.scheiwiller@luks.ch


Jürg Metzger
juerg.metzger@luks.ch


PD Dr. med. Björn Link
bjoern.link@luks.ch

Precision medicine offers personalized and targeted treatment strategies in healthcare. However, the roadmap to realizing precision medicine remains largely unclear. There are multiple challenges in today's healthcare environment, such as optimal collaboration among various disciplines, organizations in networks versus centralization efforts, digital transformation, process efficiency, quality issues and costs.

Implementing precision medicine requires a systematic approach and the integration of various components. By following the roadmap as presented herein, healthcare professionals can enhance care quality, optimize patient outcomes, and provide personalized treatment plans. The integration of data-driven methodologies and the development of the patient digital twin hold great promise for improved patient experiences and better long-term outcomes in medical care.

Surgeons historically played a pivotal role in driving medical innovations, with their advancements subsequently being adopted across the field of medicine. In case of sarcoma surgery, a multidisciplinary and intricate approach is essential to achieve optimal outcomes. The collaboration and coordination of various disciplines are crucial not only for surgical procedures but for all aspects of sarcoma care. This integrated approach holds immense significance in defining precision medicine. By embracing a comprehensive team-based approach, the transdisciplinary sarcoma surgery-based philosophy can pave the way for advancements in the overall care and treatment of sarcoma patients, pushing the boundaries of what is currently possible. The innovations and breakthroughs emerging from sarcoma surgery may set the stage for the next level of development in sarcoma care, benefiting patients by providing more precise and effective interventions and care. The SwissSarcomaNetwork (SSN) focuses on the sustainable health care triad and specifically on the quality of sarcoma care. This article aims to provide a concise roadmap for implementing precision medicine, addressing the main goal of providing personalized treatment. For each step of the roadmap, a brief note is included on the current SSN achievements.

1. Start of the process

The journey to enhance sarcoma care begins by recognizing the importance of data-driven approaches and adopting a systematic methodology. Multidisciplinary teams comprising healthcare professionals, data scientists, and technology experts collaborate to develop a comprehensive framework that encompasses the entire care process, from data collection to personalized treatment planning. This framework integrates data collection, storage, interoperability, analysis, benchmarking, assessment, value-based evaluation, and iterative improvement. It aligns the goals of sarcoma patients and healthcare providers. The framework outlines strategies for collecting real-world-time data, including measures and quality indicators from various sources. Thereby, the roadmap optimizes sarcoma care through data-driven approaches, collaboration, and iterative improvement (Figure 1).

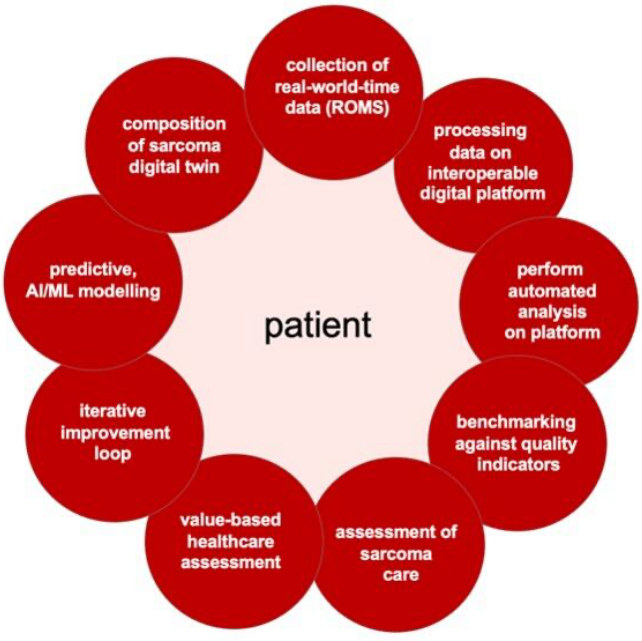


Figure 1: The roadmap to realize precision medicine: Real-world-time data, value-based benchmarking and digital twinning represent the key driver to realize precision medicine in sarcoma care.

2. Collection of Real-World-Time Data

Data collection in sarcoma care involves gathering real-world-time data from multiple sources to gain a comprehensive understanding of the longitudinal care journey. This process encompasses Clinical-Reported Outcome Measures (CROMS), which provide objective clinical indicators recorded by healthcare professionally, such as patients' medical condition, treatment progress, and health outcomes. Patient-Reported Outcome Measures (PROMS) and Patient-Reported Experience (PREMS) capture subjective experiences, including quality of life, symptoms, functional abilities, and satisfaction with care. Holistically, it also involves DROMS (Diagnostic-Reported Outcome Measures), IROMS (Imaging-Reported Outcome Measures), FROMS (Functional-Reported Outcome Measures), SROMS (Safety-Reported Outcome Measures), and EROMS (Economic-Reported Outcome Measures).

Various sources are utilized to collect this diverse data, including electronic health records (EHR), surveys, interviews and focus groups. EHR provide comprehensive information on patients' medical history, treatments, and outcomes. Surveys enable the gathering of additional patient-reported data, focusing on specific aspects of sarcoma care. Interviews and focus groups allow for in-depth qualitative data collection, providing with an opportunity to express their experiences and perspectives. By incorporating data from these different sources, the data collection process ensures a holistic representation of the sarcoma care journey. Such comprehensive evaluation approach allows healthcare professionals to assess both the medical outcomes and the patients' experiences, needs, and satisfaction.

SSN has defined a set of some 500 parameters designed to assess the quality of sarcoma care. These include physician- as well as patient-based information and are collected from daily routine processes. Specifically, SSN published on the Sarcoma-specific instrument to longitudinally assess health-related outcomes of the routine care cycle.

3. Processing Data on an Interoperable Digital Platform (such as Sarconnector)

The use of an interoperable digital platform is crucial for securely storing and managing data in sarcoma care. This platform offers advantages in terms of data integration, accessibility, and analysis. It enables seamless integration of data from various sources, ensuring compatibility across different systems. Healthcare professionals can easily access and retrieve relevant data, promoting collaboration and evidence-based decision-making. The platform also supports effective data management, facilitating the processing of large and complex datasets. It provides tools for efficient data storage, organization, and retrieval, allowing healthcare professionals to navigate and analyze effectively (within a so-called data management ecosystem including data registry, data warehouse and data lake). Additionally, the platform serves as a foundation for subsequent analyses, incorporating advanced analytics techniques to uncover patterns and correlations within the data management ecosystem. Data security is prioritized through encryption, access controls, and adherence to privacy regulations. By leveraging an interoperable digital platform, healthcare professionals can efficiently access, manage, and analyze data, leading to improved decision-making and advancements in sarcoma care.

SSN has introduced the Sarconnector, an interoperable digital platform which allows harmonized data assessment from various sources to include all data dimensions.

4. Performing Automated Analysis on the Interoperable Digital Platform

Once sarcoma care data is securely stored on the interoperable digital platform, automated analysis becomes crucial. It utilizes tools and algorithms for statistical analysis, data mining, and machine learning. Statistical analysis uncovers patterns and trends, summarizing data characteristics and making predictions. Data mining techniques extract valuable insights from large data sets, revealing hidden patterns and anomalies. Machine learning algorithms learn from data to make predictions and optimize treatment decisions. Automated analysis empowers data-driven decisions, improving care strategies and patient outcomes. It uncovers associations between treatments and outcomes, identifies non-adherence factors, and enhances patient experiences. By continuously evaluating and refining practices, healthcare professionals deliver effective and patient-centered care. Therefore, automated analysis reveals insights, supports decision-making, and improves sarcoma care outcomes.

SSN's Sarconnector is designed to synthesize meta-level data to integrate both descriptive, inferential, non-/parametric and Bayesian statistics, with its main focus on exploratory data analysis and its visualization.

5. Benchmarking against quality indicators

Benchmarking against quality indicators is essential for evaluating the effectiveness of sarcoma care. It involves comparing analyzed data against predefined standards specific to sarcoma care. These indicators provide measurable criteria for assessing healthcare performance and identifying areas of improvements.

Survival rates are crucial metrics that reflect treatment effectiveness and patient outcomes, recurrence rates indicate treatment success and the likelihood of cancer returning. Adherence to treatment guidelines evaluates the consistency of care delivery. Patient satisfaction scores capture subjective experiences and preferences, guiding improvements in care. Additional quality indicators include evidence-based practices, safety protocols, multidisciplinary care teams, follow-up care, and patient-centered principles. The choice depends on organizational goals and priorities.

Benchmarking allows healthcare professionals to assess their performance objectively and identify areas for improvement. It provides a quantitative assessment, highlighting specific aspects where standards may not be met. Furthermore, benchmarking facilitates learning from high-performing professionals and organizations. Analyzing their data reveals effective strategies and interventions, enabling others to enhance their care processes and outcomes. Benchmarking therefore is critically important for sarcoma care as it promotes continuous quality improvement. It empowers professionals to evaluate performance, implement interventions, and optimizes care delivery. By striving for excellence, sarcoma patients receive the highest quality care available.

SSN has introduced benchmarking by assessing a multilayer outcome to compare results from one's own practices, processes, or outcomes to those of other organizations or practices in the same field, both nationally and internationally.

6. Assessment of Sarcoma Care

The assessment of sarcoma quality care involves evaluating various dimensions of care, including clinical outcomes, patient experiences, adherence to quality indicators, and relevant parameters. Clinical outcomes, such as survival rates and treatment responses, assess the effectiveness of interventions. Patient experiences, captured through PROMs and PREMs, provide insights into care satisfactions and patient centeredness. Adherence to quality indicators ensures evidence-based practices are followed. Safety measures, coordination of care, and communication are additional considerations. This assessment helps identify areas of improvement and strengths, guiding interventions and resource allocation. It promotes continuous learning and collaboration among healthcare professionals, facilitating knowledge exchange and improvement in sarcoma care. By prioritizing interventions based on assessment findings, healthcare professionals can enhance patient outcomes and experiences. The assessment contributes to overall knowledge and the development of best practices within the field. We expect from the assessment of sarcoma quality care to evaluate clinical outcomes, patient experiences, adherence to quality indicators, and relevant parameters. It guides improvement initiatives, fosters collaboration, and drives continuous enhancement in sarcoma care.

SSN introduced the quality indicators of sarcoma care together with an international advisory board of world-renowned sarcoma experts.

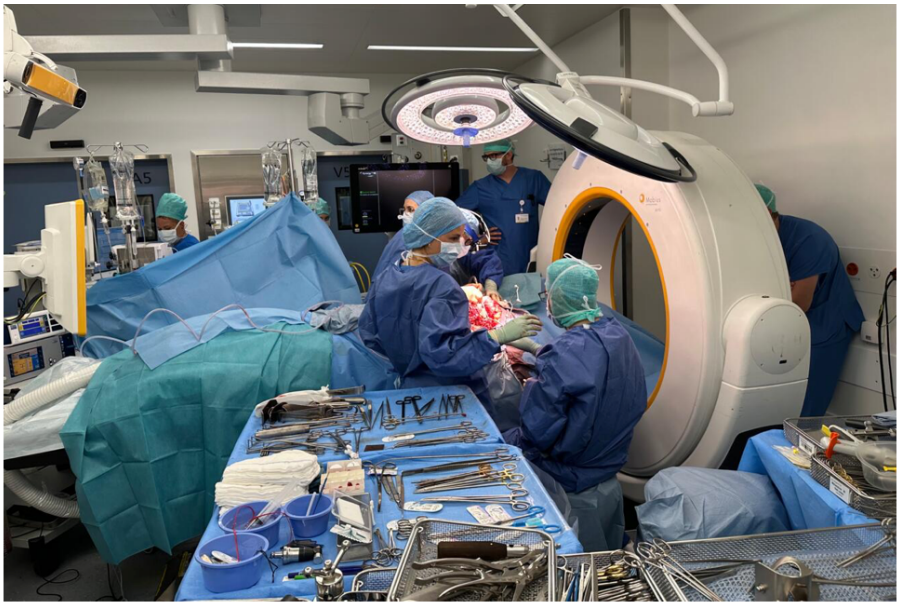


Figure 2: Gelebte Interdisziplinarität: Sarkomchirurge, Thoraxchirurge, Wirbelsäulenchirurge und intraoperative Navigation arbeiten Hand in Hand.

7. Value-based Healthcare Assessment

Value-based healthcare assessment evaluates sarcoma care by considering effectiveness, efficiency, and patient-centeredness. Metrics like cost-effectiveness, patient-reported value, and quality-adjusted life years (QALYs) are used to optimize value. Effectiveness measures outcomes achieved, such as survival rates and patient well-being, to identify best interventions. Efficiency assesses resource utilization in relation to outcomes, using cost-effectiveness analysis to guide resource allocation. Patient centeredness tailors care to individual needs, with patient-reported value capturing satisfaction and quality of life. QALYs measure quantity and quality of life gained through interventions, aiding decision-making. Other metrics like patient-reported outcomes and satisfaction scores provide additional insights. Value-based healthcare assessment aims to optimize value in sarcoma care, ensuring resources are allocated for maximum effectiveness, efficiency, and patient-centeredness. By integrating this assessment, healthcare professionals prioritize interventions that deliver the greatest value, leading to improved patient outcomes and experiences.

SSN has defined a value-based healthcare delivery model for sarcoma patients, and is able to correlate the clinical care efforts with financial expenses by use of the interoperable digital platform, the so-called Sarconnector.

8. Iterative Improvement Loop

The iterative improvements loop is crucial of enhancing sarcoma care based on assessment findings. It involves analyzing assessment results, identifying areas for improvement, and implementing targeted interventions to drive ongoing improvements in clinical outcomes, patient experience, and value delivered. After conducting the assessment, the healthcare team carefully reviews the findings and identifies opportunities for enhancement. Targeted interventions are then developed and implemented within the care process, such as changes to protocols, treatment pathways, patient education, coordination of care, or the adoption of new technologies. Feedback loops are established to monitor the impact of interventions, allowing healthcare professionals to assess effectiveness and make data-driven decisions, adjustments and refinements in sarcoma care, adapting to changing needs and best practices. By continuously refining the care process, healthcare professionals strive to provide the best possible care for sarcoma patients, enhancing outcomes and patient experience while optimizing value delivered.

SSN has established the Sarcoma Academy (www.sarcoma.academy), an international webinar forum for global exchange. This enables an up-to-date input from world-renowned experts of sarcoma care, and the potential to harmonize and share data on the global stage.

9. Predictive AI/ML Modelling

Predictive artificial intelligence (AI) and machine learning (ML) modeling techniques offer valuable insights and decision-making support. These techniques use real-world-time data to develop predictive models that forecast outcomes, identify high-risk patients, and guide treatment decisions.

Predictive AI/ML modeling involves training algorithms on historical data to identify patterns and make predictions or classifications. In sarcoma care, various techniques like decision trees, logistic regression, support vector machines, and deep learning algorithms can be employed.

-*Forecasting future outcomes:* by analyzing collected data, models can identify patterns contributing to disease progression, treatment response, or survival rates. This enables healthcare professionals to anticipate outcomes and plan interventions accordingly. For instance, predicting sarcoma recurrence allows monitoring high-risk patients closely and adjusting treatment plans.

-*identifying high-risk patients:* Models analyze data to pinpoint patients at greater risk of poor outcomes or complications. Healthcare professionals can prioritize resources and intervention for these patients, providing targeted care. Models can predict treatment-related side effects, allowing tailored supportive care.

-*enhancing personalized treatment decisions:* Analyzing patient-specific data like clinical characteristics and genetic profiles enables the identification of suitable treatment options. Tailoring interventions to individual patients improves effectiveness.

-*uncovering hidden patterns:* Insights on risk factors and treatment modalities associated with better outcomes inform care plans and resource allocation, thereby empowering healthcare professionals to optimize care delivery.

SSN's Sarconnector includes currently a 5-year follow-up of patients, which paves the way for outcome studies. A current project for example identifies risk factors to develop Clavien-Dindo complications after sarcoma surgery.

10. Composing sarcoma Digital Twin

Over time, as more data is collected and analyzed, a digital twin of sarcoma care is created. This digital twin is a virtual replica of an individual patient that simulates the behavior of the care process. It incorporates the insights gained from predictive modeling and integrates patient-specific data, enabling the generation of personalized treatment plans. The digital twin serves as a powerful tool to optimize care, providing a platform for experimentation, scenario analysis, and continuous learning. It allows healthcare professionals to simulate the impact of different interventions, refine treatment strategies, and ultimately improve patient outcomes.

The digital twin allows physicians to simulate the impact of interventions, test various treatment options, and refine strategies to achieve optimal patient outcomes. It facilitates evidence-based decision-making and continuous learning, leading to improved care delivery. For patients, the digital twin offers personalized treatment based on individual characteristics and preferences. By incorporating patient-specific data such as treatment response, the digital twin tailors interventions to meet specific needs, enhancing precision and effectiveness of care. Patients thereby actively participate in decision-making, explore different treatment options, and understand potential outcomes. The digital twin empowers patients, improves treatment outcomes, and increases engagement in the care process.

Conclusions

The integration of real-world-time data, interoperable digital platforms, automated analysis, benchmarking, assessment, value-based healthcare evaluation, iterative improvement loops, predictive AI/ML modeling, and the creation of a sarcoma digital twin offer tremendous opportunities to advance sarcoma care. By embracing these steps, healthcare professionals can enhance the quality and effectiveness of care, optimize patient outcomes, and provide personalized treatment plans. Through continuous refinements and the application of data-driven methodologies, the future of sarcoma care holds great promise for improved patient experiences and ultimately better long-term outcomes.

SSN has established the basic requirements to realize precision care for sarcoma patients.

Further reading:

B. Fuchs, Zürich
B. Bode, Zürich

Swiss Sarcoma Network

Wie entwickelt sich die Sarkomchirurgie?

Die Chirurgie erzielt von allen Therapiemodalitäten bei Sarkomen die höchste Lokalkontrollrate. Das primäre Ziel der Sarkomchirurgie besteht darin, den Tumor mikroskopisch komplett zu entfernen. Grundsätzlich kann davon ausgegangen werden, dass, je weiter reseziert wird, desto potenziell besser dieses Ziel erreichbar ist bzw. umso höher die lokale Tumorkontrollrate ist, aber umso potenziell schlechter die resultierende Funktion.

KEYPOINTS

- *Transdisziplinäre Sarkomchirurgie-Kompetenzteams bilden, um die R0-Resektionsrate zu verbessern bzw. die Rate der «Whoops»-Resektionen zu senken*
- *Sarkombehandlung vom in sich abgeschlossenen Disziplinen-Denken zum offenen Netzwerkverhalten entwickeln*
- *«Real world data»-Register führen, welche das Management vom Sarkomboard mit dem Register koppeln*
- *Qualitätsindikatoren definieren und analysieren, die Arzt- und Patienten-basiert sind*

Im Gegensatz zu Karzinomen, die nur im Verbund wachsen, können peritumorale Sarkom-Satellitenzellen als Einzelzelle wieder zu einem Rezidiv heranwachsen. Eine Nachresektion macht deswegen – im Gegensatz zu Karzinomen – nur Sinn, wenn das komplette Tumorbett miteinbezogen wird. Zudem wird eine adäquate Resektion, nebst der Komponente des individuellen Chirurgen, auch durch das biologische Wachstumsmuster der einzelnen Sarkomentität sowie von der lokalen Anatomie beeinflusst («anatomische Grenzen»). Die R0-Resektion ist deswegen in der Sarkomchirurgie ein zentraler, hochkomplexer Parameter – keine andere Therapiemodalität kann für eine inadäquate Resektion kompensieren. «Worst case scenario» chirurgischerseits ist die ungeplante Operation mit Überraschungsresultat «Sarkom» (sog. «whoops lesion»).

Wo liegen die grössten Herausforderungen?

Die wichtigsten Parameter betreffend lokale Tumorkontrolle sind der erzielte chirurgische Resektionsrand bzw. ungeplante Operationen («whoops»); diese sind wichtiger als Grading, Grösse und Lage des Tumors.[1] Obwohl die R0-Resektion einen zentralen Parameter in der Sarkombehandlung darstellt, ist kaum bekannt, wie häufig eine solche erreicht wird. Eine der Erklärungen liegt darin, dass keine einheitliche Definition für «R0» besteht:

- Rein metrisch, oder in Abhängigkeit von biologischen Strukturen und anatomischen Barrieren?
- Mitberücksichtigung neoadjuvanter Therapien?
- Angabe definiert vom Chirurgen, vom Pathologen oder aber aus der Synthese der beiden nach interdisziplinärer Diskussion?
- Zudem undefiniert: Wie wird sichergestellt, dass nicht die postoperative Aufarbeitung des Resektates durch den Pathologen selbst zu einem iatrogenen Resektionsrand führt?

Ungeplante Resektionen («Whoops»-Operationen) nach dem Motto «Schneiden wir den Tumor raus, um zu sehen, was es ist», stellen ein internationales Problem dar und führen häufig zu inadäquaten Resektionen mit potenziellem lokalem Kontrollverlust des Tumors.[2] Rund 20 % aller Sarkome werden auch heute noch auf diese Weise diagnostiziert/operiert, was eine sehr grosse Herausforderung für das allfällig weiterbehandelnde Sarkomteam («best case») darstellt. «Whoops»-Operationen bedeuten für betroffene Patienten eine verzögerte korrekte Behandlung, oft zusätzliche Eingriffe, nicht selten letztlich eine dadurch ab initio schlechtere Prognose. Um diese vielfältigen Herausforderungen meistern zu können, ist ein prätherapeutischer transdisziplinärer Austausch mittels einer gemeinsamen Plattform (Multidisziplinäres Tumorboard, MTB) unabdingbar, zur Definition einerseits des Resektionsrandes und andererseits der weiteren interdisziplinären Abläufe zur

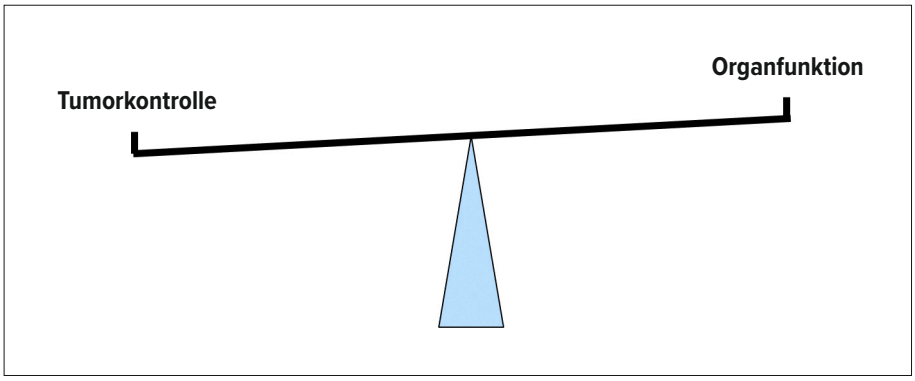
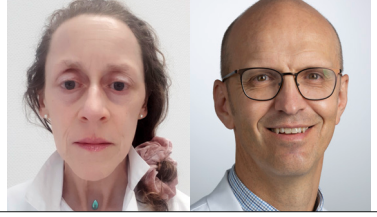


Abb. 1: Das Sarkombehandlungsteam muss zu Beginn mit dem Patienten festlegen, welches Ausmass eine Tumorresektion einnimmt, welche funktionellen Konsequenzen eine solche nach sich zieht und inwieweit dies direkt mit der Tumorkontrolle assoziiert ist



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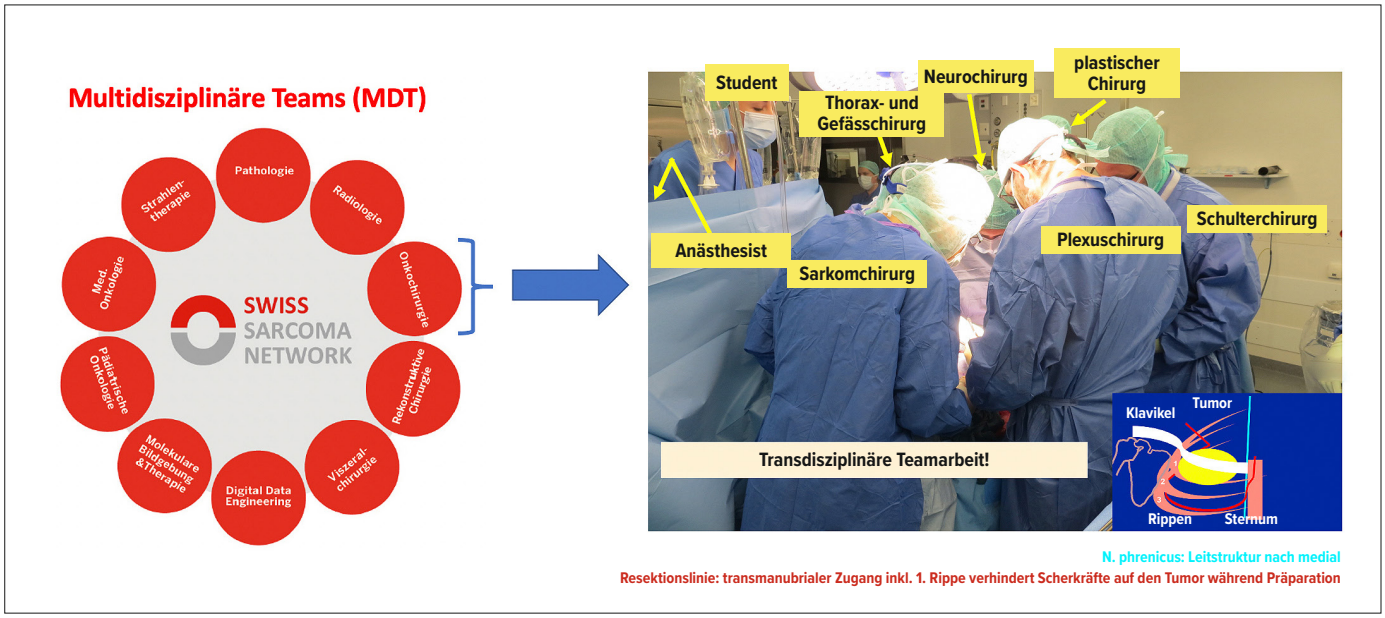

Abb. 2: Die Organisation einer Sarkomeinheit in multidisziplinären Teams – in Analogie zum chirurgischen multidisziplinären Kompetenzteam – ist entscheidend für die optimale Behandlung der Sarkompatienten. Eine solche Einheit verwendet optimalerweise eine gemeinsame digitale Plattform zum nationalen und internationalen Austausch und zur Definition und Erfassung der Qualität

Abklärung bzw. Behandlung von Patienten mit Sarkomverdacht.

Was ist Sarkomchirurgie?

Die Sarkomchirurgie stellt keine eigentliche Disziplin dar, sie setzt sich vielmehr aus verschiedenen Disziplinen zusammen, in Abhängigkeit von der anatomischen Lage des Sarkoms. Sarkomchirurgie ist deshalb nicht Disziplin-fokussiert, sondern vielmehr Problem-orientiert. Da die Chirurgie je nach anatomischer Region technisch hochspezialisiert ist, können prinzipiell nicht alle Operationen von einer Person auf technisch höchstem Niveau durchgeführt werden.

Wie wird ein Sarkomchirurg definiert?[3] Er hat eine entsprechende vertiefte zusätzliche onkologische Ausbildung auszuweisen, eine > 10-jährige Berufserfahrung auf dem Fachgebiet und ist mit den Prinzipien der Sarkomchirurgie vertraut. Darüber hinaus muss er fähig/willig sein, in einer entsprechenden Struktur und Kultur ein Team von technisch versierten Chirurgen-Kollegen einbeziehen zu können, um die anatomischen Erfordernisse ausreichend adressieren zu können (intraprofessionelle Kooperation). Dies gilt sowohl für die Resektion eines Tumors als auch für die anschliessende Rekonstruktion. Dabei geht es immer um die Balance zwischen Tumorkontrolle und resultierender Funktion; diese muss eng abgesprochen werden mit dem Patienten und im Behandlungsteam (Abb. 1). Einen solch engen Austausch hat ein Sarkomchirurg mit dem Pathologen und dem Facharzt für interventionelle Radiologie zu etablieren, um die Abklärung von Patienten mit mesenchymalen Tumoren als Abklärungseinheit möglichst zielgerichtet umzusetzen, damit die Rate der ungeplanten Resektionen gesenkt werden kann; dasselbe gilt für die gemeinsame weitere Therapieplanung im Hinblick auf adjuvante Therapien (interprofessionelle Kooperation).

Diese Überlegungen führen als Konsequenz zur Bildung eines Sarkom-Kompetenzteams, in dem alle erforderlichen Ansprüche transdisziplinär auf den Patienten massgeschneidert unter der Koordination des Sarkomchirurgen orchestriert werden. Es wird dabei inskünftig zentral sein, dass die Leistung eines solchen transdisziplinären Sarkom-Kompetenzteams nicht mehr isoliert wie bisher, sondern Outcome-basiert als Einheitsleistung erfasst und ausgewiesen wird, mittels eines Registers, das die Daten und Qualitätsparameter aller Disziplinen miteinschliesst (Abb. 2).

«The power of data bases»

Wieso ist ein transdisziplinäres Register notwendig? Die «French sarcoma group» bildete 2010 ein Sarkomregister; mittlerweile sind bereits mehr als 55 000 Patienten eingeschlossen, das Register stellt damit die derzeit grösste existierende Sarkom-Informationsquelle dar.[4] Die Franzosen konnten damit zeigen, dass zum Beispiel die Fallbesprechung an einem interdisziplinären Tumorboard assoziiert ist mit besserem rezidivfreiem (sowohl lokal wie systemisch) Überleben, weniger Reoperationen und einem besseren Umsetzen der «clinical practice guidelines».[5] Sie zeigten auch die Wichtigkeit eines Zweit-Reviews der Diagnose durch

einen weiteren Fachpathologen: In einem Kollektiv von 1017 Patienten musste bei 27 % eine Revision der Diagnose vorgenommen werden, die eine relevante Änderung der Therapie nach sich zog.[6] Sie zeigten zudem, dass, wenn die Operation innerhalb des Netzwerks stattfand, die R0-Resektionsrate deutlich höher war (R0-Resektionsrate innerhalb des Netzwerkes bei 52 %, ausserhalb nur gerade 26 %) und dies assoziiert war mit besserem Lokalrezidiv-freiem, ereignisfreiem sowie Gesamtüberleben.[7] Diese Daten erlauben grundlegende Rückschlüsse mit sehr grosser Bedeutung für unseren klinischen Alltag, so wie wir sie bisher nicht kannten.

Was sind die Ansprüche an ein Register?

Ein Register ist ein zentraler Pfeiler, um die Qualität der Patientenbehandlung zu erfassen bzw. die Teamkompetenz zu verbessern. Aufgrund obiger Ausführungen ist evident, dass ein Sarkomregister alle Disziplinen gleichzeitig einzuschliessen hat (Endresultat definiert durch schwächstes Glied in der Kette). Mittlerweile ist die Wichtigkeit von «real world data» erkannt und etabliert. Das Sarkomboard ist der einzige Moment in der Prozesskette, in dem sich alle Disziplinen zur Diskussion der Faktenlage und der weiteren Strategien der Behandlung der Sarkompatienten treffen – dieser Schlüsselmoment muss in einem «Real world data»-Register entsprechend abgebildet werden. Es ist deshalb notwendig, das gesamte Sarkomboard-Management mit dem Register zu koppeln. Ein Sarkomregister muss erlauben, alle aktuellen WHO(«World Health Organization»)-Diagnosen und anatomischen Lokalisationen zu erfassen, idealerweise auch alle Arten von chirurgischen Resektionen und Rekonstruktionen.

Das Register erlaubt die Analyse eines jeden einzelnen Parameters und jegliche Kombination derselben sowie Standard- und spezifische Auswertungen (wie zum Beispiel Qualitätsindikatoren) pro gewählte Zeiteinheit. Da die «patient-reported outcome measures» (PROM) auch in Europa zunehmend wichtiger werden, sollte ein solches System ebenfalls erlauben, entsprechende Rückmeldungen seitens der Patienten im Follow-up zu ergänzen. Ein solches Tool erlaubt nicht nur den erleichterten transdisziplinären Austausch im Alltag, sondern wird auch die Basis darstellen, um die Qualität der Sarkombehandlung zu definieren und zu messen («outcome measurement») – letztlich der einzig rechtfertigende Parameter für die Anerkennung eines solchen MDT bzw. die einzige Möglichkeit für den Vergleich der Analysen mit anderen Zentren.

Definition und Erfassung von Qualitätsindikatoren

In der Schweiz, wie auch in anderen Ländern, wird es ab April 2021 eine gesetzliche Grundlage und damit Verpflichtung zur Qualitätserfassung geben. Der Ausweis von Qualität in der Sarkombehandlung bezieht sich aber nicht nur auf die Sarkomchirurgie, sondern auf die gesamte Organisationseinheit (s. oben). Die Analyse diverser Parameter bei Patienten mit Bindegewebstumoren (z. B.: Wie lange dauert das Erstellen einer Diagnose? Wird eine Biopsie vor Behandlungsbeginn durchgeführt? Wartezeiten auf einzelne Aktionsschritte?) ist ein Qualitätsausweis – bislang kaum beachtet und entsprechend kaum erfasst. Ebenso sollte Sarkomchirurgie hinsichtlich ihrer Komplexität und Qualität analysierbar werden, genauso die Chemotherapie und Radiotherapie. PROM müssen hier ebenfalls als Ergänzung eingebracht werden. Idealerweise soll ein «Real world data»-Register alle diese Herausforderungen abdecken.

Erwartungen und Ausblick

Die Sarkomchirurgie wird sich vom monodisziplinären Denken lösen und sich zunehmend transdisziplinär organisieren müssen. Nur so können wir jeder spezifischen initialen Präsentation eines einzelnen Patienten onkochirurgisch sowie anatomisch-technisch gerecht werden. Durch die Organisation im Sinne eines Sarkom-Kompetenzteams wird erwarteterweise[7] die R0-Resektionsrate verbessert und die Rate ungeplanter Resektionen gesenkt. Dieses transdisziplinäre Denken ist seitens aller beteiligten Disziplinen erforderlich.

Es zeichnet sich damit ab, dass eine solche Kompetenzeinheit nicht an einer einzelnen Institution angesiedelt sein kann, sondern überregional/national in einem Netzwerk organisiert sein muss, um das Wissen der Experten und die Behandlung der Patienten unabhängig von der geografischen Lokalisation zu maximieren. ■

Autoren:
Prof. Dr. med. Dr. sc. nat. **Bruno Fuchs**[1]
Prof. Dr. med. **Beata Bode**[2]
Prof. Dr. med. **Gabriela Studer**[3]
Prof. Dr. med. **Stefan Breitenstein**[4]

[1] Chair SwissSarcomaNetwork, Chefarzt Orthopädische Onkologie/Sarkomzentrum Kantonsspitäler Winterthur und Luzern, Universitätsspital Zürich
E-Mail: fuchs@sarcoma.surgery

[2] Leitende Ärztin Pathologie Pathologiezentrum Enge Universität Zürich

[3] Chefärztin Radio-Onkologie Kantonsspital Luzern

[4] Direktor Departement Chirurgie Chefarzt Viszeral- und Thoraxchirurgie Kantonsspital Winterthur

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Perspective

The Next Frontier in Sarcoma Care: Digital Health, AI, and the Quest for Precision Medicine

Bruno Fuchs [1,2,*], Gabriela Studer [1], Beata Bode-Lesniewska [3], Philip Heesen [4] and on behalf of the Swiss Sarcoma Network [†]

[1] Sarcoma Service, University Teaching Hospital LUKS, University of Lucerne, 6000 Lucerne, Switzerland
[2] Sarcoma Service, Kantonsspital Winterthur, 8400 Winterthur, Switzerland
[3] Patho Enge, SSN Reference Sarcoma Pathology, University of Zurich, 8000 Zurich, Switzerland
[4] University Hospital USZ, University of Zurich, 8000 Zurich, Switzerland
* Correspondence: fuchs@sarcoma.surgery
[†] Additional collaborators of the Swiss Sarcoma Network are indicated in the Acknowledgement.

Abstract: The landscape of sarcoma care is on the cusp of a transformative era, spurred by the convergence of digital health and artificial intelligence (AI). This perspectives article explores the multifaceted opportunities and challenges in leveraging these technologies for value-based, precision sarcoma care. We delineate the current state-of-the-art methodologies and technologies in sarcoma care and outline their practical implications for healthcare providers, administrators, and policymakers. The article also addresses the limitations of AI and digital health platforms, emphasizing the need for high-quality data and ethical considerations. We delineate the promise held by the synergy of digital health platforms and AI algorithms in enhancing data-driven decision-making, outcome analytics, and personalized treatment planning. The concept of a sarcoma digital twin serves as an illustrative paradigm for this integration, offering a comprehensive, patient-centric view of the healthcare journey. The paper concludes with proposals for future research aimed at advancing the field, including the need for randomized controlled trials or target trial emulations and studies focusing on ethical and economic aspects. While the road to this transformative care is laden with ethical, regulatory, and practical challenges, we believe that the potential benefits far outweigh the obstacles. We conclude with a call to action for multidisciplinary collaboration and systemic adoption of these technologies, underscoring the urgency to act now for the future betterment of sarcoma care and healthcare at large.

Keywords: digital health; artificial intelligence; value-based healthcare; sarcoma; precision medicine; benchmarking; interoperable platforms; quality indicators

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1. Introduction

Sarcoma, a rare and heterogenous group of malignant tumors originating from mesenchymal tissues, poses unique challenges for healthcare providers and patients alike. With over 100 subtypes and often complex clinical presentations, treating sarcoma requires a multidisciplinary, data-driven approach—an approach that modern healthcare is progressively leaning towards but has not yet fully realized [1–5]. In terms of the state of the art, recent advancements in genomics, targeted therapies, and immunotherapy have begun to reshape the landscape of sarcoma treatment. However, these advancements are often isolated in their impact, lacking a cohesive, data-driven strategy for implementation across healthcare systems. The integration of artificial intelligence (AI) and digital health platforms represents the next frontier in this context. These technologies have the potential to synthesize large and complex datasets, from genomic information to real-world-time patient outcomes, thereby enabling more precise and personalized care. This is particularly crucial for sarcoma, given its heterogeneity and the consequent need for highly individualized treatment plans. The dawn of precision medicine has ushered in an era

where treatment is personalized, not just to the disease but to the individual [6]. Yet, while the promise of precision medicine is substantial, its full realization is intricately tied to the evolution of healthcare systems towards value-based models, especially for complex conditions like sarcoma [7,8].

The notion of value-based healthcare (VBHC) emphasizes patient-centricity, focusing on metrics that matter most to the patient's well-being. This patient-centricity must be supported by robust, real-world-time data analytics that not only gauge the quality of care but also its cost-effectiveness [9,10]. Recent advancements in digital health technologies and AI have demonstrated unprecedented potential to empower this transition, offering an innovative toolkit for data collection, management, and predictive analytics [11–13].

However, the intersection of digital health and AI remains an underexplored terrain, especially in the context of sarcoma care [14]. This article aims to go beyond a mere review of existing technologies and methodologies. Instead, it seeks to offer a forward-looking perspective on how the confluence of these technologies could redefine the very essence of sarcoma care, contributing to a future where diagnosis is precise, treatment is personalized, and outcomes are continually optimized [15] (Figure 1).

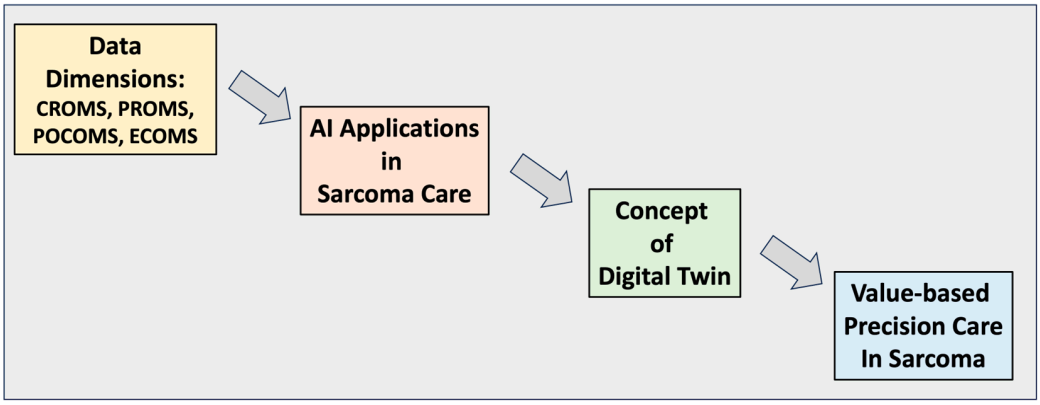

Figure 1. The figure depicts the evolution of sarcoma care, emphasizing patient-centricity and a data-driven approach. Digital health technologies, like Sarconector, form the foundation, streamlining patient data integration. Building on this, AI employs advanced algorithms to precisely characterize sarcoma subtypes and predict treatment outcomes. The pinnacle is the 'digital twin', a virtual patient profile that harnesses AI for predictive modeling and treatment optimization. CROMS = clinician-reported outcome measures; PROMS = patient-reported outcomes measures; POCOMS = patient-omics-centric outcome measures; ECOMS = economic measures.

In doing so, this article embarks on a visionary journey to explore the untapped potential of digital health and AI. It aims to serve as a catalyst for multidisciplinary dialogue and research, encouraging healthcare professionals, policymakers, and technologists to collaborate in transforming the future of sarcoma care—making it more precise, sustainable, and, above all, value-based.

2. The Vision for Value-Based Precision Care in Sarcoma

The pursuit of value-based healthcare is not merely a trend but a paradigm shift—one that brings the patient to the center of the healthcare universe [16]. In the context of sarcoma, a complex and rare malignancy, this transformation is not just aspirational but essential [15]. The heterogeneity of sarcoma, spanning multiple subtypes and clinical complexities, demands an individualized, outcomes-focused approach [17,18]. Traditional healthcare systems, largely built on a volume-based model, often fall short in providing the comprehensive, personalized care that sarcoma patients require. Value-based care in sarcoma envisions a healthcare ecosystem where every stakeholder, from surgeons and oncologists to data scientists and policymakers, collaborates to enhance the patient experience—from diagnosis to treatment and follow-up. It is an approach that goes beyond

the immediate clinical outcomes to consider the patient's quality of life, long-term well-being, and the economic sustainability of the care provided. In this envisioned ecosystem, treatment protocols are not rigid pathways but dynamic algorithms, constantly updated with real-world-time data and adapted to each patient's unique medical history, genomic profile, and even psychosocial needs [19–21].

This vision is not utopian; it is attainable. Emerging technologies in digital health, coupled with advances in artificial intelligence and machine learning, offer the tools needed to actualize this vision. Imagine a future where an interoperable digital platform integrates multi-dimensional data, from medical imaging to genomic sequencing and patient-reported outcomes. These data are then processed by sophisticated AI algorithms to provide actionable insights, ranging from predicting treatment responses to estimating healthcare costs [19,22]. Moreover, the continuous benchmarking against quality indicators ensures that the care provided is not just effective but continually optimized [22].

However, the transition from vision to reality entails overcoming significant barriers—technological, ethical, and institutional. The subsequent sections of this article delve into these challenges, offering a multi-faceted perspective on how the confluence of digital health and AI can serve as the linchpin in materializing the vision for value-based care in sarcoma.

3. Potential of Digital Health

Digital health stands as a cornerstone in the realization of value-based care, especially in the intricate landscape of sarcoma [23,24]. The advent of technologies such as interoperable Electronic Health Records (EHRs), telemedicine, and real-world-time data platforms has enabled healthcare systems to move beyond the siloed structures of the past [19,22]. These technologies permit the seamless integration of multi-dimensional patient data—from diagnostic imaging and laboratory results to patient-reported outcomes and follow-up care metrics [25]. The role of digital health in sarcoma care is not merely auxiliary; it is transformative. For instance, telemedicine has proven to be invaluable in providing specialized sarcoma care to patients in remote locations, breaking down geographical barriers to quality healthcare. This is particularly crucial for a rare and complex disease like sarcoma, where specialized expertise may not be readily available in all regions. Interoperable EHRs, on the other hand, facilitate multi-disciplinary collaboration by allowing seamless data sharing between oncologists, radiologists, pathologists, and even primary care physicians. This is vital in sarcoma care, which often requires a multi-disciplinary approach for optimal outcomes. The EHRs can also be integrated with AI algorithms to flag potential issues or suggest alternative treatment pathways based on historical data and predictive analytics. Moreover, real-world-time data platforms can serve as a tool for continuous quality improvement. By tracking key performance indicators in real-time, healthcare providers can identify areas for improvement almost instantaneously, allowing for rapid intervention and adaptation of care protocols [19].

But the potential of digital health is not just in data collection; it is in data utilization. Advanced digital platforms can streamline the diagnostic journey, enhance treatment personalization, and even predict clinical outcomes, thereby offering a more holistic, patient-centric model of care. For example, digital platforms can automate the pre-diagnostic phase by gathering and analyzing patient history, symptoms, and preliminary test results, thereby aiding clinicians in making more accurate initial assessments. These platforms can also integrate with wearable devices that monitor patient vitals and other health metrics, providing a continuous stream of data that can be invaluable for ongoing care and monitoring. Furthermore, digital health technologies can facilitate patient engagement by providing platforms for virtual consultations, remote monitoring, and even digital therapeutics. These technologies empower patients to take an active role in their healthcare journey, thereby aligning with the principles of value-based care.

In essence, digital health technologies serve as the scaffolding upon which value-based care in sarcoma can be constructed, offering the dual advantages of operational efficiency and clinical efficacy.

4. Future Applications of AI in Sarcoma Care

As we look toward the horizon of sarcoma care, artificial intelligence (AI) emerges as a highly promising tool for advancing the field [26,27]. While current applications have been instrumental in diagnosis and treatment planning, the future holds even greater promise. Advanced machine learning algorithms are poised to delve into multi-omics data, offering unprecedented levels of precision in characterizing sarcoma subtypes and predicting treatment responses. The application of machine learning in sarcoma research extends beyond clinical data and can incorporate environmental, genetic, and lifestyle factors. By creating more comprehensive models that consider these variables, AI has the potential to identify new risk factors and even suggest preventative measures for at-risk populations. Deep learning techniques, a subset of machine learning, could be particularly impactful in image analysis. These algorithms can analyze complex patterns in radiological images that may be too subtle for the human eye, thereby aiding in early diagnosis and more accurate staging of the disease. This is crucial for sarcoma, where early diagnosis can significantly improve prognosis.

These algorithms could also integrate radiomic features with pathological and clinical data, refining prognostic accuracy [28]. Moreover, AI has the potential to support real-time decision making during surgeries through augmented reality interfaces, allowing for more precise surgical interventions. The introduction of natural language processing (NLP) can further enhance patient engagement by automating the analysis of patient-reported outcomes, thereby incorporating the patient's voice directly into the care continuum. NLP's real strength lies in its ability to convert unstructured data, such as patient narratives or free-text clinical notes, into structured data that can be easily analyzed. This is particularly valuable in sarcoma care, where patient experiences and symptoms can be highly variable and complex. By applying NLP algorithms to these unstructured data sources, healthcare providers can gain insights into patient well-being, treatment side effects, and even early indicators of complications that may not be readily apparent through traditional structured data. These structured data can then be integrated into machine learning models to improve predictive accuracy, thereby contributing to more personalized and effective treatment plans.

In a value-based healthcare framework, AI can enable more personalized, efficient, and outcome-oriented care, serving as a catalyst for transforming the ideal of precision sarcoma care into a tangible reality.

5. The Concept of Sarcoma Digital Twin

The notion of a "Digital Twin" in sarcoma care is a groundbreaking concept that aligns closely with the goals of precision medicine and value-based healthcare [29]. Drawing inspiration from the Swiss Sarcoma Network's robust digital platform, the Sarconector, a sarcoma digital twin serves as a virtual replica of an individual patient's medical profile, integrating real-world-time data including Clinical-Reported Outcome Measures (CROMS), Patient-Reported Outcome Measures (PROMS), POCOMS (patient-omics-centric outcome measures), ECOMS (economic measures), and other metrics from multiple sources like Electronic Health Records (EHR), surveys, and interviews [22,30].

The concept of a digital twin goes beyond merely storing or aggregating data; it serves as a dynamic, interactive model that evolves in real-world-time. As new clinical data become available, whether they are from imaging studies, laboratory tests, or patient-reported symptoms, the digital twin updates accordingly. This dynamic nature allows for a more nuanced understanding of the patient's condition, thereby facilitating more informed clinical decisions. Moreover, the digital twin concept is not limited to the individual patient level. When aggregated across a population of sarcoma patients, these digital

twins can serve as a rich data repository for observational studies, clinical trials, and even epidemiological research. This collective data pool can be invaluable for identifying patterns or trends in sarcoma treatment and outcomes, thereby contributing to evidence-based medicine.

By leveraging AI-driven analytical tools, the digital twin can assist in predictive modeling, optimizing treatment plans, and even simulating potential outcomes of various therapeutic strategies. This creates an innovative ecosystem for quality-centric, value-based sarcoma care, enabling iterative improvement based on ongoing assessments and benchmarking. The utility of AI in this context is multifold. For instance, machine learning algorithms can analyze the digital twin data to predict patient responses to different treatment modalities, thereby aiding in personalized treatment planning. Furthermore, natural language processing (NLP) algorithms can sift through clinical notes and patient interviews to extract valuable insights that may not be readily apparent through quantitative data alone. These AI-driven analyses can be integrated into the digital twin, providing a comprehensive, 360-degree view of the patient's health status and treatment options. The concept of a sarcoma digital twin also has implications for healthcare economics. By providing a more accurate and personalized treatment plan, it has the potential to reduce unnecessary tests and treatments, thereby contributing to cost-effectiveness and sustainability in healthcare systems. In doing so, the concept of a sarcoma digital twin pushes the frontier of what is possible in delivering personalized, effective, and efficient care to sarcoma patients.

6. Roadmap to the Future

The Swiss Sarcoma Network's comprehensive roadmap to sarcoma care offers a visionary blueprint for the future, highlighting the synergy between AI and digital health in achieving a sustainable healthcare system. From a practical standpoint, this roadmap serves as a guide for healthcare providers, administrators and policymakers. It outlines actionable steps such as the adoption of interoperable digital platforms, the integration of AI in diagnostic and treatment protocols, and the establishment of quality indicators for continuous improvement. These practical measures aim to facilitate the transition from traditional, volume-based healthcare models to a more dynamic, value-based approach. The roadmap also suggests the use of real-world-time data to validate and refine AI algorithms, thereby ensuring that technological advancements are rooted in tangible clinical benefits. The roadmap outlines a multi-faceted approach that includes real-world-time data collection, interoperable digital platforms for data management, automated analysis employing AI algorithms, and benchmarking against quality indicators specific to sarcoma care [19,26]. These elements come together to assess various dimensions of care, including clinical outcomes and patient experiences. The ultimate aim is to continuously refine sarcoma care through iterative improvements, bringing the healthcare system closer to realizing value-based precision care. Adding another layer of innovation, the roadmap aims to incorporate the concept of a sarcoma digital twin, a virtual replica of an individual patient's medical condition that integrates seamlessly with AI-driven predictive modeling. As the roadmap evolves, there will be an increasing focus on aligning costs with value, thereby contributing to a more sustainable, efficient, and patient-centric healthcare system. Thus, the roadmap represents not just a pathway for sarcoma care but also serves as a model for the broader application of precision medicine and value-based healthcare.

While the Swiss Sarcoma Network provides a innovative model, its potential is not confined to Switzerland alone. By fostering international collaborations and partnerships, this roadmap can be scaled globally, adapted to diverse healthcare infrastructures and socio-cultural contexts. Key to this expansion is the network's emphasis on interoperability and standardization, facilitating seamless data exchange across borders. The establishment of international sarcoma care consortiums, working cohesively within the potential of such platform, can harmonize methodologies, share best practices, and collectively advance the vision of precision medicine. As more regions adopt this model, there is an opportunity for global real-world-time data aggregation, enhancing AI's predictive capabilities and refining

treatment strategies. Thus, the roadmap represents not just a pathway for sarcoma care but also serves as a model for the broader application of precision medicine and value-based healthcare on a global scale.

7. Ethical and Regulatory Forethought

As we advance toward a new paradigm of value-based precision care in sarcoma, underpinned by digital health and AI, ethical and regulatory considerations must be addressed with the same vigor as technological innovations [31,32]. The collection, storage, and analysis of patient data pose questions about data security, privacy, and informed consent. Ensuring equitable access to advanced sarcoma treatments catalyzed by AI and digital tools is paramount to preventing disparities in care. However, it is important to acknowledge the limitations of our approach. While AI and digital health platforms offer transformative potential, they are no without their drawbacks. The quality of AI algorithms is highly dependent on the quality and quantity of the data fed into them. Incomplete or biased data can lead to inaccurate or even harmful clinical decisions. Additionally, the ethical implications of AI decision making in healthcare are still not fully understood and require further study. There is also the risk of over-reliance on technology, which could potentially undermine the role of medical professionals in patient care. Furthermore, the cost of implementing advanced digital solutions may be prohibitive for smaller healthcare facilities, potentially widening the gap in the quality of care. Regulatory bodies and ethical committees must work in concert with healthcare providers, technology developers, and policymakers to standardize protocols, ensuring that they are universally applicable and ethically sound. These protocols must also be flexible enough to adapt to rapid technological advancements without compromising patient safety or data integrity. As real-world data platforms become more integrated into the healthcare system, legal frameworks will play a critical role in shaping the ethical landscape of digital health and AI in sarcoma care. Thus, ethical and regulatory forethought is not a mere afterthought but an integral component of the roadmap to value-based precision care.

8. Challenges and Barriers: A Call to Action

While the horizon is bright with the promise of digital health and AI ushering in a new era of value-based precision care in sarcoma, the path is fraught with challenges that require immediate attention. Practically speaking, the implementation of this roadmap will necessitate substantial investments in technology and human resources. Hospitals and healthcare providers will need to upgrade their existing infrastructures to support data-intensive AI algorithms. Training programs will be essential for clinicians to effectively interpret and act upon AI-generated insights. Moreover, the roadmap calls for a collaborative effort involving not just the medical community but also regulatory bodies and insurance providers. This multi-stakeholder approach is crucial for overcoming the financial, ethical, and logistical barriers to implementing a value-based healthcare model in sarcoma care. Resource constraints, a lack of standardized data protocols, and resistance to change within medical institutions all pose significant barriers. The dearth of expertise in data science within the medical community adds another layer of complexity. Furthermore, data privacy concerns and regulatory hurdles can slow down the pace of innovation. However, these challenges should not deter us; rather, they should serve as a clarion call to action. This involves not only healthcare professionals and technologists but also policymakers, patient advocacy groups, and regulatory bodies. A collective, multidisciplinary effort is crucial to overcome these barriers. Funding must be allocated for research and development, educational initiatives must be put in place, and policy frameworks need to be developed to encourage data sharing and interoperability. By acknowledging and addressing these challenges head-on, we can accelerate the journey toward realizing the full potential of digital health and AI in transforming sarcoma care.

9. Conclusions and Proposals for Future Research

In the evolving landscape of sarcoma care, the convergence of digital health and artificial intelligence offers a beacon of hope for personalized, efficient, and value-based treatment options. We have explored the promise this union holds—from the integration of real-world-time data and interoperable digital platforms to the application of AI for predictive analytics, all the way to the conceptualization of the sarcoma digital twin, thereby enabling predictive and value-based precision sarcoma care. As we look to the future, several avenues for research emerge. First, there is a need for randomized controlled trials (or, alternatively, target trial emulations) to validate the efficacy of AI algorithms in sarcoma diagnosis and treatment planning. Second, research should focus on the ethical implications of AI in healthcare, particularly in the context of data privacy and informed consent. Third, the economic aspects of implementing digital health platforms and AI in sarcoma care warrant in-depth study, including cost–benefit analyses and long-term sustainability assessments. Lastly, future work could explore the integration of other emerging technologies, such as blockchain for secure data sharing or augmented reality for enhanced surgical planning, into the existing digital health ecosystem. These research proposals aim to fill the existing gaps in our understanding and provide a comprehensive framework for the adoption of digital health and AI in sarcoma care. While the challenges are significant, they are not insurmountable. We stand at the cusp of a transformative era in healthcare, one where the systematic adoption of these technologies could revolutionize the way we approach not just sarcoma, but complex diseases at large. However, to realize this vision, a coordinated, multidisciplinary effort is essential. The time for action is now; let us seize this moment to propel sarcoma care into a future replete with the benefits of digital health and AI, ultimately improving outcomes and quality of life for patients around the globe.

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Development of a value-based healthcare delivery model for sarcoma patients

Bruno Fuchs[abcd], Gabriela Studer[ab], Beata Bode[e], Hanna Wellauer[c], Annika Frei[c], Carlo Theus[b], Guido Schüpfer[b], Jan Plock[f], Hubi Windegger[c], Stefan Breitenstein[c], for the SwissSarcomaNetwork

[a] University of Lucerne, Switzerland
[b] Kantonsspital Luzern, Lucerne, Switzerland
[c] Kantonsspital Winterthur, Switzerland
[d] Universitätsspital Zürich, Zurich, Switzerland
[e] Patho Enge, Zurich, Awitzerland
[f] Kantonsspital Aarau, Switzerland

Summary

The urgent need to restructure healthcare delivery to address rising costs has been recognised. Value-based health care aims to deliver high and rising value for the patient by addressing unmet needs and controlling costs. Sarcoma is a rare disease and its care is therefore usually not organised as an institutional discipline. It comprises a set of various diagnostic entities and is highly transdisciplinary. A bottom-up approach to establishing sarcoma integrated practice units (IPUs) faces many challenges, but ultimately allows the scaling up of quality and outcomes of patient care, specific knowledge, experience and education. The key for value-based health care – besides defining the shared value of quality – is an integrated information technology platform that allows transparency by sharing values, brings all stakeholders together in real-time, and offers the opportunity to assess quality of care and outcomes, thereby ultimately saving costs. Sarcoma as a rare disease may serve as a model of how to establish IPUs through a supraregional network by increased connectivity, to advance patient care, to improve science and education, and to control costs in the future, thereby restructuring healthcare delivery. This article describes how the value-based health care delivery principles are being adopted and fine-tuned to the care of sarcoma patients, and already partially integrated in seven major referral hospitals in Switzerland.

Starting point

Cost explosion in health care is a global issue. In 2018, many western countries spent roughly 10% – the USA even 17.7% – of their gross domestic product (GDP) on health care [1]. There is global consensus that the value per spent dollar needs to be optimised [2, 3]. Value-based health care (VBHC) aims to deliver high and rising value for the patient, addressing *unmet needs* and controlling costs. Sarcoma care deals with a rare disease and is therefore usually not organised as an institutional discipline; it comprises a set of various diagnostic entities and is highly transdisciplinary.

Correspondence:
Bruno Fuchs, MD PhD
Chair SwissSarcomaNetwork, University of Lucerne
Brauerstrasse 15
CH-8401 Winterthur
office[at]sarcoma.surgery

Value-based healthcare delivery model

Porter et al. described a healthcare legacy structure, which emerged over decades [4–8]. Such a *siloed system* is organised within disciplines and institutions, provides fee-for-service and measures process compliance, without extramural exchange (fig. 1).

Such systems allow various stakeholders to succeed, but not necessarily the patient. Many support the concept of regionalisation of care based only on patient volume as a key strategy for quality and outcome improvement, specifically for surgical disciplines. However, high volume by itself does not guarantee good outcomes, especially when bad processes are being reinforced by high-volume repetition, without assessing quality indicators [9, 10]. Simply advancing structural changes without process improvements is like pushing on a string [11]. The fundamental purpose and goal of health care is to deliver high and rising value for patients, with value being defined as the *outcomes and quality of care* over the total costs of *delivering these outcomes throughout the entire health cycle* [3, 12]. The key for VBHC – besides defining the shared value of quality – is an integrated information technology platform that allows transparency by sharing values, brings all stakeholders together in real-time, establishes transparency and offers the opportunity to assess quality of care and outcomes, and thereby ultimately saving costs.

Integrated practice units

For the implementation of a VBHCD-based system, the following key steps are required:

(1.) Structuring of an integrated practice unit (IPU) organised around a medical condition by delivering care in a transdisciplinary team whose members devote a significant amount of time to the condition (fig. 2) [13]. An IPU works in dedicated multidisciplinary facilities including all dis-

ciplines under one roof, and takes responsibility for the full cycle of care. Within the IPU, outcomes, costs, care processes and patient experience are routinely measured and shared on a common platform. The team accepts joint accountability for outcomes and costs, and meets regularly, formally and informally, to discuss and improve care plans, results and processes.

(2.) Outcome measurement with value: Outcomes are measured by condition, not for specialties or procedures, and measurement covers the full cycle of care. They are multidimensional and include what matters most to patients, not just to physicians. Initial conditions and risk factors are standardised for each condition and are measured in the line of care.

Figure 1: The legacy system evolved over decades and is based on individual silo solutions of single institutions without exchange. The value-based system builds on shared commitment to defining and assessing quality and outcome using a shared information technology platform. Such an integrated system will prepare our health system to meet the opportunities of the fourth industrial revolution.

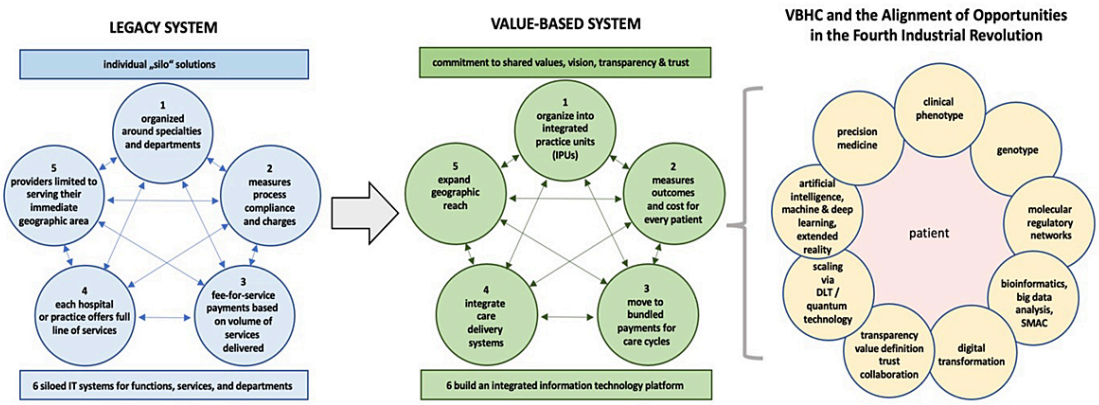
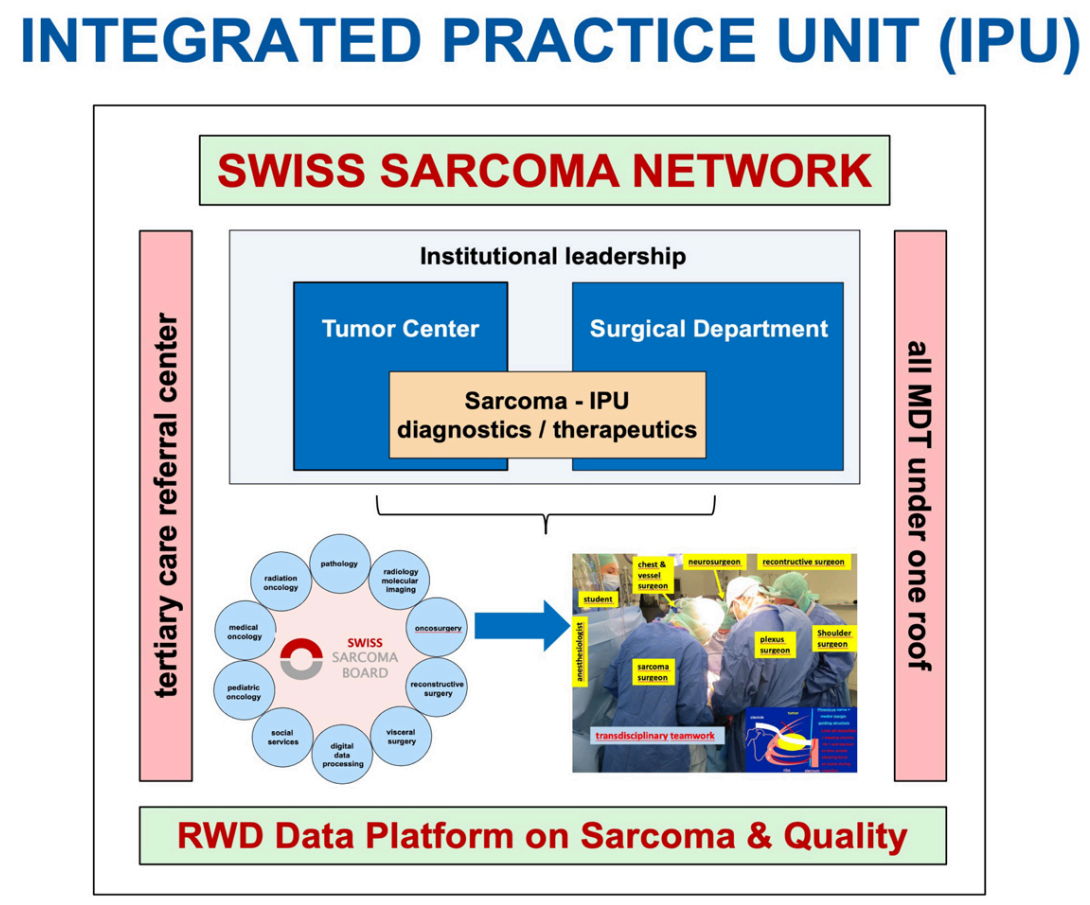


Figure 2: Sarcoma not being a discipline, the sarcoma IPU is built from the surgical transdisciplinary teams and the tumour centre with its associated disciplines. Sharing a common information technology real-world data platform, the sarcoma IPUs can be scaled up across the country.



(3.) Alignment of reimbursement with value:

– *Cost aggregation* must include the total costs of providing the care for the patient's medical condition that matters for value, not the cost of any individual service or intervention.
– *Cost allocation* includes the allocation of shared costs to individual patients on the basis of each patient's actual use of the resources involved, not the average use.

(4.) Systems integration aims to shift the current confederation of stand-alone units/facilities to clinically integrated care-delivery systems.

(5.) Geographic expansion: The strategic principles for the geographic and value model organise care by condition in IPU hubs, where services are allocated across the care cycle to sites based on capabilities, care complexity, patient risk, cost and patient convenience, while incorporating telemedicine, home services and affiliated provider sites [14]. The IPU develops a formal system to direct patients to the most appropriate site.

(6.) Integrated technology platform: Attributes of a value-based information technology platform include all types of data for the full care cycle using standardised definitions and terminology, allowing storage and extraction from a common warehouse, with the capability to aggregate, extract, run analytics and display data in real-time by condition and over time. The warehouse enables the capture and aggregation of outcomes, costing parameters, and billing capacities for bundled payments.

Opportunities

Traditional sarcoma centres function in institutional silos at best, without a common language for exchange between centres or in the referral network, and therefore not specifically referring to a definition of patient value in terms of outcome and quality over the full cycle of care. They also do not provide the opportunity for patient-centred cost alignment. Conversely, the sarcoma IPU importantly highlights the need to focus on the patient as the centre around whom the entire care cycle needs to be organised in order to explicitly define and assess quality and outcome, entailing adoption of the proposed system change.

What does the future of patient care look like? Medicine's most fundamental element remains the relationship between the patient and the physician, which must therefore be at the heart of health care and which has been a constant across cultures and centuries [15]. Team work with a coordinating physician leader is the bedrock principle for success, and is strengthened through the introduction of a sarcoma IPU.

Challenges

Current structures aim to geographically centralise patient volumes independent of quality indicators, and there is continued debate regarding an organisational shift towards networks [16]. Whereas it is undoubtedly correct to centralise care of complex patients, territorial centralisation has the downside of separating the centre from the periphery. The DKG (Deutsche Krebsgesellschaft), for example, has established process-based criteria for the definition of sarcoma centres which ultimately allow at best only two thirds of all sarcoma patients to be treated at such a centre (www.krebsgesellschaft.de). The largest existing dataset from the National Cancer database shows that only 3310 patients were treated in high-volume centers (defined as centres treating >20 soft tissue sarcoma patients only per year!), whereas 22,000 patients were treated in low-volume centres [10]. Various demographic and socio-cultural reasons obviously prevent patients from travelling, and as long as there are no networks – in which surgical complexity allows centralisation – covering the entire country, these numbers will remain unchanged. The inclusion of all sarcoma patients must be the goal, and therefore collaboration in a network is indispensable [17].

Digital opportunities enable unprecedented connectivity and transparency, which above all will advance the knowledge and experience of all network experts without geographic exclusion. Digital connectivity also allows the spread of a common language with aligned definitions on every aspect of disease and therapy. Such a system allows the definition of quality and complexity care indicators based on which centralisation to units with the most experience (and not for territorial reasons) for the patient's needs will become possible, which is the base of personalised medicine.

Today, 21st century medical technology is often delivered with 19th century organisational structures, management practices and pricing models. The consumer cannot fix the dysfunctional structure of the current system. Healthcare workers are caught within the system, and various incentives prevent current structures from changing and improving. A reset is required, and value-based delivery provides the horizon. The driver to alignment of all unmet needs is the digital real-world data platform, providing a common language for all quality indicators and value definitions to enable transparency, operational efficiency and effectiveness, with instant real-time access for all involved stakeholders.

Outlook

Healthcare transformation is well underway. Value-based thinking is restructuring the organisation of care, outcome measurement, personalised payment models and health system strategy. Standardised outcome measure sets and new costing practices ultimately accelerate value improvement. Government and legal bodies will have a critical role in this process. They can require universal measurement and reporting of provider health outcomes, help shift the reimbursement systems to bundled payments for cycles of care instead of payments for discrete treatments or services, remove obstacles to the restructuring of healthcare delivery around the integrated care of medical conditions, open up competition among providers and across the country, and set policies to encourage greater responsibility of individuals for their health and their health care. Physicians have to define quality indicators and start measuring outcome indices for all medical conditions, thereby providing the base for a value-based healthcare system.

Where are we in Switzerland?

The members of the SwissSarcomaNetwork (SSN; www.swiss-sarcoma.net) comprise all institutions that are

willing to consecutively assess and share their transdisciplinary sarcoma data within a prospective real-world data platform (prospective RWD Sarcoma Registry of Quality). Within this national network, transdisciplinary sarcoma care is being organised in IPUs across the country. On the international level, SSN is an official member of SELNET, a Sarcoma European and Latin American network which is supported by a Horizon 2020 framework programme of the European Union, and is thereby embedded in the largest existing sarcoma network of multidisciplinary clinical and translational sarcoma experts aiming to improve diagnosis and clinical care in sarcomas.

Together with an international advisory board of world-renowned sarcoma experts from the world sarcoma network, sarcoma quality indicators of work-up, of the weekly Sarcomaboard/MDT tumour conference, of the complexity of treatment, of the outcome as well as of PROMS/PREMS are being defined, totalling more than 70 parameters. These quality metrics and results of their descriptive analysis are automatically generated from the registry and visualised in real-time on an interactive website for all SSN members, thereby enabling the quality management system which has been required by law in Switzerland since April 2021. With such a set-up, predictive outcome analysis becomes ultimately possible. As a next step in the future, a cost tag will be attributed to each structured data parameter in the registry to assess the costs over the entire healthcare cycle, thereby letting VBHC become a reality. To further extend the quality efforts internationally, the Sarcoma Academy (www.sarcoma.academy) was founded to facilitate exchange between international sarcoma experts through sarcoma webinars and forums.

Conflict of interest

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

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cancers

MDPI

Article

Quality of Sarcoma Care: Longitudinal Real-Time Assessment and Evidence Analytics of Quality Indicators

Philip Heesen [1], Gabriela Studer [2], Beata Bode [1], Hubi Windegger [3], Benjamin Staeheli [3], Paul Aliu [3], Javier Martin-Broto [4], Alessandro Gronchi [5], Jean-Yves Blay [6], Axel LeCesne [7] and Bruno Fuchs [1,2,*]

1 Medical Faculty, University of Zurich, 8091 Zurich, Switzerland
2 Faculty of Medicine, University of Lucerne, 6002 Lucerne, Switzerland
3 Swiss Sarcoma Network, 6000 Luzern, Switzerland
4 Medical Oncology Department, University of Madrid, 28040 Madrid, Spain
5 Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1, 20133 Milano, Italy
6 Department of Medical Oncology, Centre Léon-Bérard Lyon, 69008 Lyon, France
7 Department of Medical Oncology, Gustave Roussy Cancer Campus, 94805 Paris, France
* Correspondence: fuchs@sarcoma.surgery

Simple Summary: This article comprehensively defines, assesses and analyzes quality indicators of sarcoma care. A novel interoperable digital platform is presented that gathers information from physicians (work-up, therapy and MDT information) as well as patients (PROMS/PREMS) consecutively and instantly when a new event occurs, which thereby automatically provides evidence of the quality of care on all aspects. As the platform analyzes annotated real-time world information, predictive modelling and value-based health care may become a reality, thereby giving rise to precision health care in the future.

Abstract: Sarcomas represent a large group of rare to very rare diseases, requiring complex management with a transdisciplinary approach. Overall progress has been hampered because of discipline, institution and network fragmentation, and there is no global data harmonization or quality standards. To report on and improve quality, a common definition of quality indicators (QIs) of sarcoma care as well as the capacity to assess longitudinal real-time data is required. An international advisory board of world-renowned sarcoma experts defined six categories of QIs, totaling more than 80 quality indicators. An interoperable (web-based) digital platform was then created combining the management of the weekly sarcoma board meeting with the sarcoma registry and incorporating patient-reported outcome measures (PROMs) into the routine follow-up care to assess the entire care cycle of the patient. The QIs were then programmed into the digital platform for real-time analysis and visualization. The definition of standardized QIs covering all physician- (diagnostics and therapeutics), patient- (PROMS/PREMS), and cost-based aspects in combination with their real-time assessment over the entire sarcoma care cycle can be realized. Standardized QIs as well as their real-time assessment and data visualization are critical to improving the quality of sarcoma care. By enabling predictive modelling and introducing VBHC, precision health care for a complex disease is on the horizon.

Keywords: interoperable digital platform; quality indicators; real-time assessment; value-based health care; integrated practice unit; sarcoma; data annotation

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1. Introduction

Sarcomas constitute a large group of rare cancers, and their treatment is multidisciplinary and complex. There are a series of evidence- and consensus-based sarcoma guidelines available for the appropriate work-up and treatment of bone and soft tissue sarcomas. Several recent studies examined the compliance of such guidelines, as well as its positive association with clinical outcomes [1–5]. Due to low adherence, sarcoma treatment

is preferentially regionalized to dedicated networks because specialized multidisciplinary sarcoma teams (MDT) provide improved management and care with better adherence to guidelines compared with patients who are treated outside of such networks [6–12]. However, regionalization of care alone does not yet guarantee quality of care, mainly because quality indicators of work-up and treatment have not yet been established at large, and a tool for their large-scale assessment with the possibility of real-life monitoring is lacking [13].

While access to an MDT- or sarcoma-integrated practice unit (IPU) care network plays a pivotal role with respect to quality care, health care costs are constantly rising, despite the fact that the increasing costs may not necessarily match the added quality [14]. Identification of the most effective ways to organize, manage, finance and deliver high-quality care (which is summarized as health services research) to reduce non-compliance to CPG and improve patient safety and outcomes will become increasingly important in the near future. Effective on April 2021, for example, Switzerland introduced a new law regarding the quality and economics of patient care, which commits all care providers to measure quality and to introduce a quality management system, which lays the foundation for value-based health care (VBHC).

VBHC was introduced more than 15 years ago by Porter et al. and is defined by the quality and outcome divided by the total costs over the entire longitudinal health care cycle [15–17]. It transforms a fee-for-service legacy system into a value-based system of shared values, vision, transparency and trust, thereby moving from quantity to quality and from volume to value. Meanwhile, VBHC is a widely accepted instrument to improve quality of care while reducing health care costs [18,19]. There are several important pre-requisites for VBHC. First, an integral information technology platform is required, which allows the preferably real-time interoperable data exchange of IPUs over the entire globe. Second, VBHC requires the definition of quality indicators (QIs) and its assessment. Third, the established quality ultimately then has to be associated with the costs of the entire longitudinal care cycle.

A strategy for evaluating robust information on QIs is the harmonization of data by real-time prospective assessment [20,21]. This requires an interoperable digital platform, ideally between sarcoma networks and their global databases, which represents a digital mirror of prospective patient data in real time and allows the instant visualization of the data. However, it is commonly believed that within current silo hospital structures in many centers (such as data management, "added monodisciplinary" approach and currently available clinical information systems) the digital requirements widely surpass the financial preconditions to achieve such necessary data information.

As far as sarcoma treatment is concerned and to the best of the authors' knowledge, there is no comprehensive definition of quality indicators of shared sarcoma care (beyond local-recurrence-free survival, disease-free survival, metastasis-free survival and overall survival) described in the literature. At this point, their real-time structured assessment, specifically in relation to healthcare costs, has never been realized. Herein, we provide an interoperable digital platform solution focusing on the QIs of sarcoma care.

2. Materials and Methods

2.1. Description of the Interoperable Digital Platform

SSN has established a cloud-based, transparent, harmonized, transdisciplinary, multi-institutional, prospective, real-world-time data sarcoma registry including absolute (not only sarcoma diagnosis but also all patients who undergo a biopsy for suspicion of sarcoma) patient numbers with a focus on the assessment of quality indicators (QI) of sarcoma care, covering the entire longitudinal care cycle. For this purpose, the management of the weekly multidisciplinary team (MDT)/sarcoma board (SB) meeting was coupled with the data registry. To ensure the quality and completeness of all MDT/SB decisions, every new patient and any new event or treatment change is required to be presented to the MDT/SB. Importantly, the patient has to give written consent to the collection and anonymous

use of their data. For each patient presented at the MDT/SB, the treating physician of a given discipline enters the respective information. For example, the surgeon fills in the details of surgery, the radiation oncologist enters the relevant data for radiation therapy, the pathologist and radiologist enter the respective data etc. This may include some 3–5 min for a single treating physician. This is a critically important step because regular clinical information systems most often do not allow for the collection of structured data, which is pivotal for analysis. This shared and structured data collection approach assures minimal time effort and the highest possible data quality. Furthermore, because all data are discussed together at the MDT/SB and because the discussion allows open questions (such as the surgical margin) to be addressed, this meeting that includes all treating physicians is used as a collective data quality check. This setup assures the highest possible data quality in real time, including the decisions on subsequent treatments. Based on the entered data, the interoperable digital platform is programmed to calculate and automatically visualize the QIs in diagrams, tables or figures. In addition, while the MDT/SB assures data inclusion regarding all active treatments, the interoperable digital platform requests PROMS electronically from patients under follow-up and without evidence of disease at predefined intervals. This guarantees longitudinal data coverage over the entire cycle of care for all patients.

2.2. QI and Tools

Using a modified Delphi approach, the Swiss Sarcoma Network (SSN) international advisory board consisting of world-renowned sarcoma experts (A.L., J.B., A.G. and J.M.) defined holistic quality indicators of sarcoma patient care. It encompasses six categories of care aspects (Table 1), totaling more than 80 QIs (Tables 2–7). To guarantee real-time data assessment over time, the patients fill out patient-reported outcome/experience measures (PROMS/PREMS) (Table 7) either at the outpatient visit or online in the case of telemedicine consultations, depending on type of treatment they had and the time point of follow-up. Overall, >385 variables are routinely assessed using the interoperable digital platform (Figure 3). The data are hosted at the Federal Institute of Technology in Switzerland (Leomed, ETH Zurich, Switzerland; https://sis.id.ethz.ch/services/confidentialrese;researchdata; accessed on 20 October 2022) to ensure the highest level of data protection with respect to interinstitutional exchange, political independence, and continuous technology developments. The interoperable digital platform allows the automated extraction of data to be used for calculations of QIs, thereby generating real-world evidence [22,23]. The digital platform allows for instant analysis and visualization, basic statistics and figure creation. The QI analysis of sarcoma care parameters can be customized according to, for example, time period, type of dignity, planned and unplanned (whoops) resections, institution, in real time and interactively. Its modular setup allows the extension and adaptation of the parameters as more data will be collected.

Table 1. Overview of groups of quality indicators.

QI FOR MULTIDISCIPLINARY TEAMS (MDT)
1. Sarcoma work-up of patients
2. MDT/SB management
3. Therapy (incl. surgery, radiation-, chemotherapy)
4. Complexity of sarcoma therapy
5. Clinical metrics outcome (physician based)
6. PROMS/PREMS (patient based)

Table 2. Sarcoma work-up.

QUALITY INDICATORS: SARCOMA WORK-UP
• was imaging performed before biopsy
• time from first patient contact to biopsy
• which type of biopsy was performed
• time from biopsy to MDT/SB presentation
• time from biopsy to SB presentation
• was biopsy performed before initiation of treatment?
separated according to type of treatment
• was there metastasis at presentation
• time from MDT/SB presentation to initiation of treatment
(incl. analysis depending on type of therapy

Table 3. MDT/SB management.

QUALITY INDICATORS: MDT/SB MANAGEMENT
• how many patients were presented per month/per year
• how many presentations took place per month/per year
• how many first presentations
• how many follow-up presentations
• how many bone lesions—superficial/deep soft tissue lesions were presented
• how many malignant—intermediate—benign lesions were discussed
• how many decisions on:
- surgery
- radiation therapy
- combination radiation therapy–surgery
- combination chemotherapy–surgery
- combination surgery–radiation therapy–chemotherapy
• how many decisions were realized/executed?
- Overall
- surgery
- radiation oncology
- chemotherapy
• how many patients were presented over entire cycle of care

Table 4. Therapy.

QUALITY INDICATORS: THERAPY
• % margin status (R0, R1, R2) at definitive surgery
• surgical, pathological, consens
• % amputations
• % preoperative radiation therapy (yes/no)
• % postoperative radiation therapy (yes/no)
• % neoadjuvant chemotherapy (yes/no)
• % adjuvant chemotherapy (yes/no)

Table 5. Complexity of therapy.

QUALITY INDICATORS: COMPLEXITY OF THERAPY	
• surgical complexity STS	Cancers March 2022
• surgical complexity bone sarcoma	Age, grading/type of lesion, prior RT, chemo/whoops, size of lesion, location, resected structures, reconstructed structures, involved disciplines
• surgical complexity visceral sarcoma	Age, grading/type of lesion, prior RT, chemo/whoops, size of lesion, location, resected structures, reconstructed structures, involved disciplines

Table 5. *Cont.*

QUALITY INDICATORS: COMPLEXITY OF THERAPY	
• radiation oncology complexity treatment	Aim of RT (curative, locally curative, palliative, definitive, unknown); RT technique (IMRT, VMAT, SRT, 3DCRT, 2DCRT, unknown; RT type (photons, protons, electrons, brachytherapy (transient, permanent), conventional, other, unknown); total dose/number of fractions; GTV/PTV; Grade III/IV toxicities;
• systemic treatment complexity	Aim of systemic therapy (curative intent pre/postop, additive, maintenance, palliative); number of curative/palliative cycles planned/executed; time to next treatment (TTT); reasons for discontinuation (completed, discontinued (toxicity, PD, planned, patient's wish, death); Grade III/IV toxicities

Table 6. Outcome.

QUALITY INDICATORS: OUTCOME
• local recurrence within 1st year after tumor resection
• local recurrence overall
• systemic recurrence with 1st year of treatment initiation
• systemic recurrence overall
• latest follow-up: NED, AWD, DOD, DOR, no assessment possible; lost to followup, unknown)
• in case of RT: % vascular disorders (lymphedema, ROM, fibrosis); skin disorders (hyper-,hypopigmentation); bone disorders (osteonecrosis)
• in case of chemotherapy: % therapy during last 3 months of life.

NED, no evidence of disease; AWD, alive with evidence of disease; DOD, dead of disease; DOR, death of other reasons.

Table 7. PROMS/PREMS.

SARCOMA QUALITY INDICATORS	PROMS/PREMS
• work-up/regular f-up	-WHO-ECOG -EQ-5D -EQ-VAS -work ability index
• biopsy	-biopsy
• surgery	-MSTS upper/lower extremity -TESS upper/lower extremity
• radiation oncology	-visceral -local effects of RT
• chemotherapy	-EORTC-QLQ-C30 -MDASI
• therapy focused	-cancer therapy satisfaction -satisfaction with RT -control preferences
• Physican related	-CARE
• Institution focused	-satisfaction with institution

2.3. Objectives

In this study, we assessed and described the selection of Qis relating to the sarcoma work-up as well as EQ-5D (a PROM) in a four-year period using the interoperable digital platform.

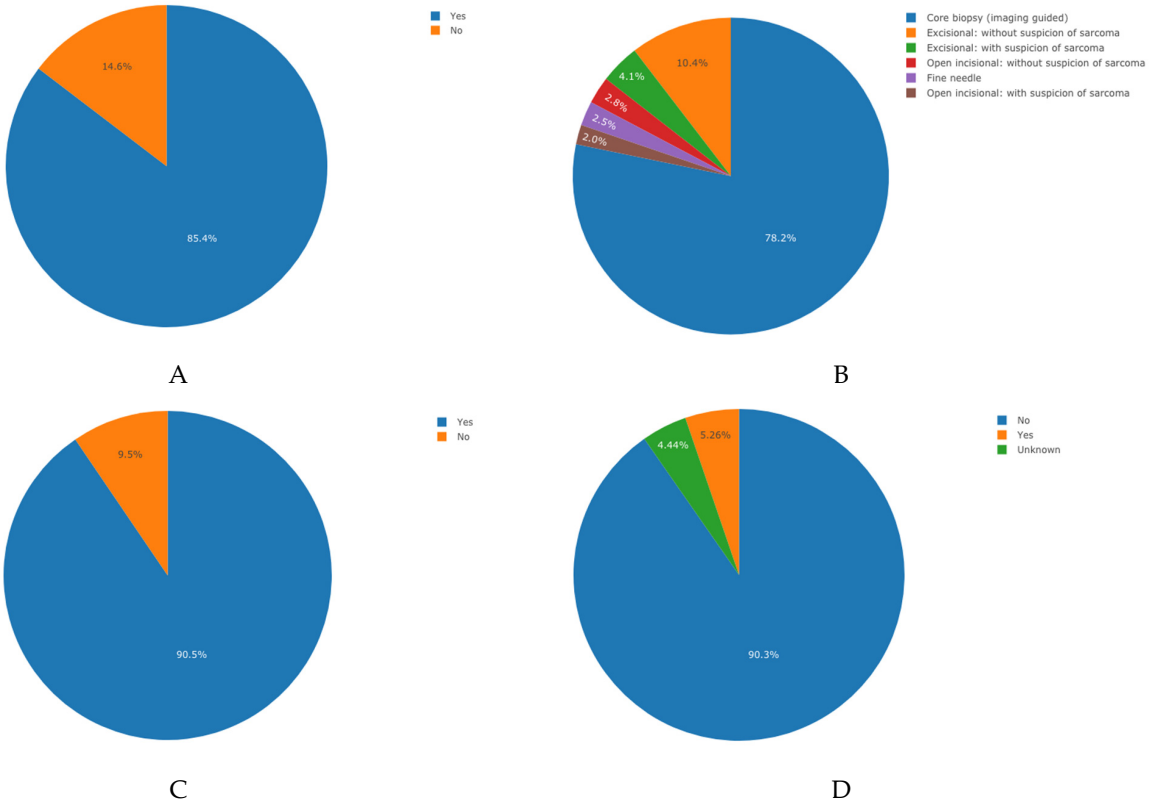
3. Results

3.1. Definition of Quality Indicators of Sarcoma Care

The quality indicators of sarcoma care as defined herein encompass six categories, including the work-up of sarcoma patients, the management of the MDT/SB meeting, type of therapies, the complexity of therapy, outcome measures and PROMS/PREMS (Table 1). Each single category contains a subset of parameters (Tables 2–7) that define the respective category.

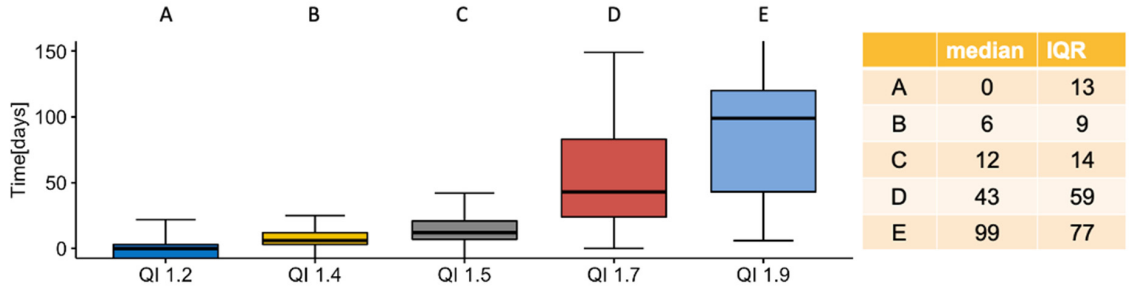
3.2. Quality Indicators of Sarcoma Work-Up

The detailed results of the Qis work-up are summarized in Figures 1 and 2 for 1308 patients with suspected (n = 719, 55%) and (n = 589, 45%) confirmed sarcoma presented within the SSN over a four-year time period (1 January 2018 until 31 March 2022). With respect to the QI sarcoma work-up as an example for all other quality indicators, it was observed that n = 1117 (85.4%) of all patients underwent radiological imaging before performing a biopsy. On the interactive website of the interoperable digital platform, this number can be instantly further analyzed and visualized according to, for example, diagnostic categories, diagnoses, anatomic regions, institution etc. to define how the respective parameter of interest may differ from the mean of the category of interest (Figure 1). This enables the discovery of strengths and weaknesses of each referral network, institution or discipline and may not only specifically define areas of improvement but also provide a benchmark for comparison with other sarcoma networks on an international level (including adjustment to the tumor characteristics and complexity of therapy). Similarly, analyzing the time from the first biopsy to first contact within the sarcoma IPU, we find a median of 0 days and an interquartile range of 13 days, which implies that half of all patients underwent the biopsy performed at the same day as the first contact or present with the biopsy, defining the efficiency of this specific part of the work-up process. With information regarding structured data on the work-up, a cost tag can be attributed to each specific step, thereby generating the effective cost for a given aspect of treatment.



(**a**)

Figure 1. *Cont.*



	median	IQR
A	0	13
B	6	9
C	12	14
D	43	59
E	99	77

(**b**)

Figure 1. (**a**) Pie chart analysis for four of the nine quality indicators of the sarcoma work-up; (**A**), was imaging performed before biopsy? (**B**), which type of biopsy was performed? (**C**), was biopsy conducted before initiation of treatment? (**D**), was metastasis present at diagnosis? (**b**) Box plot analysis for five of the nine quality indicators of the sarcoma work-up; A, time from first patient contact to biopsy, B, time from biopsy until establishment of diagnosis, C, time from biopsy until sarcoma board presentation, D, time from diagnosis to initiation of therapy and E, time from sarcoma board presentation to initiation of treatment.

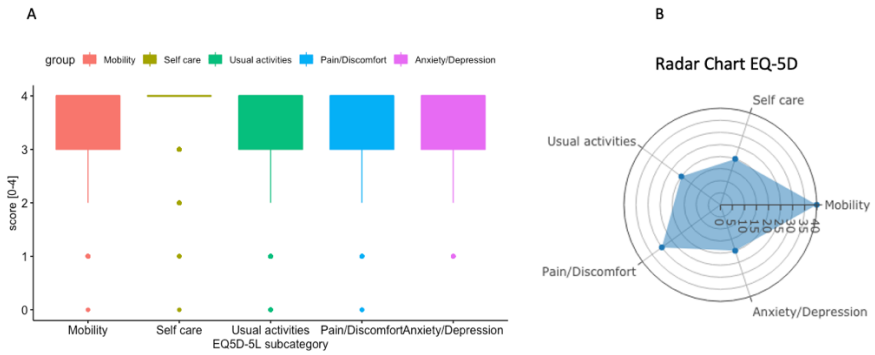


Figure 2. (**A**) Box plot summary of EQ-5D including 511 consecutive patients. (**B**) Radar chart summary of one single patient representing the five dimensions of EQ-5D.

3.3. HRQOL-EQ-5D

In the time period from the 1 October 2021 to the 31 March 2022, 511 EQ-5D questionnaires were routinely assessed in the outpatient clinic, including all patients with suspected and confirmed sarcoma, as summarized in Figure 2 [24]. These results show that the consecutive assessment of health-related quality of life as assessed by EQ-5D scores in the routine outpatient clinic is feasible. Analogous to the QIs, each subcategory can be analyzed longitudinally over time and/or by event of treatment according to clinical metrics using the interactive website. A radar chart (Figure 2B) is provided to assist the interpretation of the results of the discussion with the patient.

4. Discussion

Today's competition in health care is often not aligned with shared value, and financial success of various health care stakeholders may not necessarily equal success for the patient. Because of rising health care costs and the uncontrolled growth of unstructured medical data, the creation of a novel ecosystem with data interoperability focusing on quality care evaluated from practices and patient outcomes is pivotal. The existing misalignment can be overcome with structured data collection, global data harmonization and interactive data assessment with real-time analysis to create evidence-based information.

Existing databases for sarcoma research may often underestimate the true prevalence of sarcoma. This is explained by their dependence on administrative or billing data, insufficient data coding or the use of preexisting documented hospital diagnoses codes, which are reasons why the expansion on real-world evidence-based patient-focused data

sets is mandatory [20]. Furthermore, routine structured assessment and analysis of QIs play an integral role in establishing a novel ecosystem with interoperable and harmonized data exchange to improve the quality of care for sarcoma patients. The six categories of QIs span the entire cycle of care for any given disease of the patient with sarcoma suspicion and are thereby representative for the quality of sarcoma care. To the best of the authors' knowledge, this represents an entirely novel approach that generates absolute numbers including all patients with suspicion of sarcoma (not only with confirmed sarcoma diagnosis).

Herein, we focus on two aspects of QIs to present the feasibility and routine acquisition of the setup: the QI 1 work-up and one of the PROMS (EQ-5D) (Table 1). The QI sarcoma work-up consists of eight questions, which cover the key aspects of preparing a patient for treatment. Detailing the work-up is important, particularly with respect to the historically unchanged and unacceptably high rate of unplanned ("whoops") resections, where more precise data may foster the understanding of why these still occur today. Additionally, the QI 1 work-up includes a second review by an expert sarcoma pathologist, which is a critical and established quality indicator, but it still does not represent common practice mainly because the structure of many current databases simply does not automatically generate such information. Obviously, the definitions always remain debatable but can easily be expanded by further aspects if sarcoma experts deem it necessary. For this purpose, the sarcoma academy (www.sarcoma.academy; accessed 20 October 2022) was founded to enable inter-disciplinarily exchange of cases and to discuss and update the QIs on the global level. The analysis of quality indicators as presented herein summarizes the routine assessment of 1308 patients over a four-year period of one single MDT/SB network and may provide a benchmark for future national and international comparisons.

HRQoL questionnaires are increasingly recognized as a pivotal tool for reporting outcome measures in the medical practice [18,19]. In oncology specifically, the EORTC-QLQ-C30 and the EQ-5D are widely recognized and were introduced for sarcoma patients years ago [25,26]. However, their routine clinical use for sarcoma patients in daily practice has not yet been shown, and there is also not a reference score for all sarcoma entities and respective anatomic locations available. In the current study, our digital platform allows the consecutive assessment of all outpatient visits in daily routine practice. We currently assess the EQ-5D at each single clinical visit, and the EORTC-QLQ-C30 is assessed in addition for all patients who underwent chemotherapy. Overall, the six QI categories cover the entire cycle of patient care, which is further detailed by the single aspects. This setup allows the identification of weak and strong areas, thereby facilitating improvement in sarcoma care within an MDT/SB. It further allows benchmarking and comparison of treatment quality among various MDT/SB in distant geographic areas, which directly benefits the patient. As such, a global definition and comparison of sarcoma shared care becomes possible, which enables us to define areas of improvement based on harmonized data and evidence analysis. Importantly, through global harmonization of data quality, transdisciplinary and structured data can be assessed independent of the location and become interchangeable, and multi-institutional international collaboration on a rare disease is greatly facilitated. It is envisioned that herewith, a sarcoma quality score for a respective MDT/SB network (the center itself and its associated regional network) can be defined and introduced for international benchmark comparisons while importantly respecting the complexities associated with treatment. This may greatly impact the quality of international trials through the generation of more robust data and improved care quality for the patient. Having information regarding structured data on the entire cycle of care including the work-up enables a cost tag to be attributed to each specific step, which thereby generates an effective cost for a given aspect of treatment.

Cost increases in health care is a universal problem. Porter et al. introduced the concept of value-based health care (VBHC) [16,17,27]. Herein, shared value is defined by the quality of patient care and outcome divided by the total cost over the entire cycle of care [28,29]. The prerequisite to introduce VBHC to create a new ecosystem is the definition of quality. Because the digital interoperable platform encompasses the entire cycle of care

and because each structured QI parameter can be attributed a cost tag, it will become possible for the first time to determine the entire costs of the treatment for a given disease and patient (Figure 3). Above all, cost containment will be based uniquely on quality measures with such a setup, which enables the introduction of VBHC through disruption of the current ecosystem. Importantly, this has great potential to achieve cost containment for the benefit of the patient as well as a sustainable health care system [30].

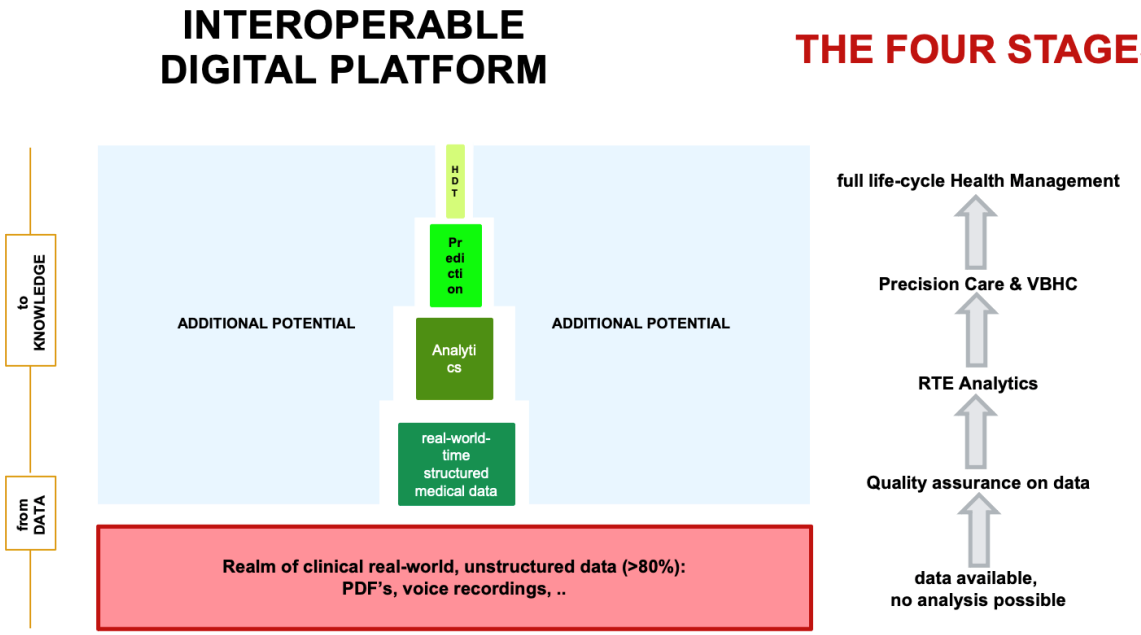


Figure 3. The interoperable digital platform is designed to receive longitudinal, absolute, routine, structured, real-world-time data from daily clinical routine practice. The MDT/SB fulfills the purpose of data quality control. Analytics of these data generate real-time evidence, which is used for precision modelling (through artificial intelligence and machine learning approaches) as well as value-based health care (through attribution of cost tags with structured data). Abbreviations. RTE, real-time evidence; VBHC, value-based health care; HDT, human digital twin.

Data are considered the key driver for the evolution from one-size-fits-all to precision medicine [21,31]. Predicting outcomes has been recognized as a major focus in today's health care, and currently, nomograms are still routinely used in daily sarcoma practice [32,33]. However, these are most often based on retrospective data, sometimes even more than 20 years old, without harmonized data acquisition and definitions and with all institutions independent from each other. Although validation has been performed, calibration curves imply wide ranges of survival predictions and therefore may imperfectly mirror reality. Therefore, because the technical infrastructure is now able to integrate a common, internationally defined and harmonized data language into daily practice, real-time prospective data acquisition may be regarded as today's standard and daily routine. Focusing data acquisition on quality standards, the patient can transparently monitor the quality of the treatment according to international guidelines and quality standards on his own. Having such structured quality data available at a large scale, predictive outcome analytics to individualize treatment decisions based on outcome prediction becomes a reality (Figure 3). As of now, we have integrated clinical data (to represent physician-based data), PROMS & PREMS (to represent patient-based data) as well as data of the costs of the work-up and treatment of patients (to represent health care cost). In the future, we will integrate multi-omic (genomics, epigenomics, proteomics, metabolomics, etc.) functional tumor profiling data for clinical decision support such as realized with the TumorProfiler®or through semantic web technologies [34]. The combination of clinical data and

bioinformatics data allow predictive outcome analytics as a standard of care in the very near future, and digital twin computing (DTC) becomes reality.

Obviously, the exchange and security of patient data remains a constant challenge for global collaboration, as the different laws on data privacy and security issues are usually country specific. However, and because the assessment of quality of sarcoma care—which is in strong contrast to Alphabet, Amazon or Alibaba—focuses not on the individual patient's data but is aggregated, the exchange of anonymized data with the respective patient's consent such as is widely practiced by pharma companies is becoming a reality. Furthermore, one may argue that extrapolating on health care data from a small country with an intricate network of small hospitals in semi-autonomic political areas within close distances and a BIP of close to 12% may not be representative for other countries with different geographies and demographies. However, as previously mentioned, the QIs were determined by sarcoma experts from different countries and from the view of the patient, which is independent of where health care is requested and is therefore considered similar worldwide. Furthermore, the presented QIs may not be considered comprehensive. The system is set up such that any new parameter may be modularly integrated into the interoperable digital platform.

5. Conclusions

It has been recognized for decades that the most pressing questions can only be answered through international collaboration. This has, however, not yet materialized due to the lack of means and technology. The interoperable digital platform takes advantage of current technological opportunities, which defines a common language focused on the quality of sarcoma care, allows real-time assessment over the entire care cycle, strengthens the collaboration of IPUs and transparently integrates and visualizes quality analytics to realize an international exchange. It may ultimately pave the way to realizing precision medicine through predictive modelling and introducing VBHC for a complex disease, which may serve as a role model for other diseases.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: https://www.swiss-sarcoma.net/ (accessed on 22 November 2022).

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Research Article

Time and Accuracy to Establish the Diagnosis of Soft Tissue Tumors: A Comparative Analysis from the Swiss Sarcoma Network

Hanna Wellauer,[1,2] **Gabriela Studer**,[1,3] **Beata Bode-Lesniewska**,[1,4] **and Bruno Fuchs**[1,2,5,6]

[1]*Swiss Sarcoma Network, Luzern 6000, Switzerland*
[2]*Department of Orthopaedics and Traumatology, Cantonal Hospital Winterthur, Winterthur 8401, Switzerland*
[3]*Department of Radiation Oncology, Cantonal Hospital Lucerne, Lucerne 6004, Switzerland*
[4]*Institute of Pathology Enge, Zurich 8005, Switzerland*
[5]*Department of Plastic Surgery and Hand Surgery, University Hospital Zurich, Zurich 8091, Switzerland*
[6]*Department of Orthopaedics and Traumatology, Cantonal Hospital Lucerne, Lucerne 6004, Switzerland*

Correspondence should be addressed to Hanna Wellauer; hanna.wellauer@ksw.ch

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Soft tissue tumors are rare tumors, and their histological examination remains a challenge. The establishment of the correct initial histopathologic diagnosis is critical. However, due to the rarity of soft tissue and bone tumors and the inherent difficulty of their classification and diagnostics, discrepancies may occur in up to one third of cases. For these reasons, several studies recommend the involvement of experienced pathologists frequently performing sarcoma diagnostics. Until now, there is only scarce information about how long it takes to establish a correct sarcoma diagnosis. We thus analyzed all consecutive patients presented to the Swiss Sarcoma Network Tumor Board (SSN-MDT/SB) with a primary diagnosis of a soft tissue tumor over a 2-year period (01/2019 to 12/2020) based on a tumor biopsy. We then compared the final histopathological diagnosis of two comparable institutions with similar case load, but different workflows: (i) institution A, with an initial diagnosis performed by a local pathologist, and reviewed by a reference pathologist, and (ii) institution B, with the final diagnosis performed directly by a reference pathologist. In addition, we analyzed the time from biopsy to establishment of the diagnosis. A total of 347 cases were analyzed, 196 from institution A, and 149 from institution B. In 77.6% of the cases, the diagnosis from the local pathologist was concordant with the expert review. Minor discrepancies were found in 10.2% of the cases without any consecutive changes in treatment strategy. In the remaining 12.2% of the cases, there were major discrepancies which influenced the treatment strategy directly. Establishing the final report took significantly longer in institution A (4.7 working days) than in institution B (3.3 working days; $p < 0.01$). Our results confirm the importance of a pathological second review by a reference pathologist. We recommend direct analysis by experts, as diagnoses can be made more accurately and quickly. Within the SSN, establishing the sarcoma diagnosis is overall accurate and quick but still can be improved.

1. Introduction

Soft tissue tumors are rare tumors and histological examination remains a challenge [1]. The recently published WHO Classification of Soft Tissue and Bone Tumors [2] lists over 100 tumor entities including variants, often characterized by specific genetic aberrations, which can be detected by molecular diagnostic studies. Establishing the precise tissue diagnosis of a soft tissue or bone tumor is of utmost importance with respect to the choice of a correct treatment strategy for the patient. An incorrect histopathological diagnosis may lead to the initiation of an incorrect therapy with potentially severe or even lethal consequences for the patient [3–8].

Yet, due to the rarity of soft tissue and bone tumors and the inherent difficulty for a correct classification and diagnostic, discrepancies may occur in up to one third of cases [3–8]. For these reasons, several studies recommend the involvement of experienced pathologists who are involved in sarcoma diagnostics on a daily basis and who have access to auxiliary studies [3, 4, 9].

Various studies [4, 5, 7, 8] have shown that establishing the correct diagnosis for the treatment of soft tissue tumors is indeed a challenge, with 14% [10] to 43% [4] of all patients receiving an incorrect diagnosis, which could lead to incorrect treatment. Therefore, any multidisciplinary team (MDT) must assess these numbers constantly to compare with the reference benchmark for quality purposes.

Further, there is only scarce information on how long it takes to establish an expert review. Besides the correct diagnosis, the time from biopsy to establishing the diagnosis is an important quality indicator for the work-up of sarcoma patients. To the best of our knowledge, this factor has not yet been considered in published literature.

The patients treated in the Swiss Sarcoma Network (SSN) are either [1] referred directly to the member institutions prior to biopsy or [2] following a diagnosis of a mesenchymal tumor in an earlier outside biopsy. The current study concentrates on the first group in order to study the condition to optimize the diagnostic paths within the network. As the expansion of the network progresses in the future, there is hope that the percentage of the tissue studies outside the network (including "whoops" unintended resections) will diminish. Herein, we report first on the quality of accuracy in establishing the sarcoma diagnosis within the Swiss Sarcoma Network, and second, assess how long it takes to establish the diagnosis including expert review analysis.

2. Materials and Methods

All consecutive patients presented at the Swiss Sarcoma Network Board with a primary diagnosis of a soft tissue tumor from January 1, 2019, to December 31, 2020, were included in this study. Patients with incomplete records were excluded. A record was marked as incomplete when, for example, a case from institution A was missing an expert review, or when a case from institution B was initially diagnosed locally. The diagnoses were classified according to the WHO into benign, intermediate and malignant [11].

The biopsies of the two institutions were analyzed and compared. The samples of institution A were initially analyzed by the local pathology institute. This is a general pathology institute without specific subspecialization. Afterwards, the samples being reviewed and assessed by a reference institute pathologist specialized in soft tissue tumors. Conversely, institution B cases were assessed directly by the reference institute pathologist. These workflows are illustrated in Figure 1.

To determine the time from biopsy to the establishment of the diagnosis, the days between the arrival of the tissue specimen at the pathology institute until the date of the final report were calculated. Weekend days or holidays were not counted, unless the report was issued on one of these days. In the analysis of the current study only cases which can be diagnosed by conventional histopathologic staining, immunohistochemistry, and FISH were included, as these studies have a short turn-around-time of one to two days. The cases requiring PCR or NGS based analyses were excluded as they methodically require several days independently of the performance of the pathologist.

The accuracy of the diagnoses of the local histopathology institute A and the expert analysis was examined in a second step. Here, the diagnoses of institute A were compared with the expert opinion and divided into 3 groups according to the classification of Thway et al. [6]:

(i) Cases without diagnostic discrepancy between local and reference institutions were classified into category A

(ii) Category B includes cases with minor discrepancy in diagnosis but without therapeutic consequences

(iii) Category C contains all cases where the diagnosis from the reference pathologist changed the treatment

In addition, all cases where the final report from institution A did not establish a diagnosis were consequently classified under category C [6].

The data were collected using the Adjumed ® -Database (www.adjumed.ch; Zurich, Switzerland) and analyzed with the statistical package "stats" of the open source software "R" [12].

The cantonal ethic commission has approved the application of the Swiss Sarcoma Network under the agreement number BASEC-NR 2019-01107. The study is also registered on https://climincaltrials.gov with the number NCT04300257 [13].

3. Results

3.1. Patient and Tumor Characteristics. A total of 347 cases were analyzed, 196 from Institution A and 149 from Institution B. 179 patients were female and 168 were male, and the median age was 55 (range 12–90) years. 163 cases were classified as benign (46.9%), 114 cases were malignant (32.8%), 66 cases were intermediate (19%), and 4 cases were unclassifiable (see Table 1).

The most common benign diagnosis was lipoma (69 cases, 42.3% of all benign tumors), followed by Schwannoma (11 cases, 6.7%). Regarding the malignant diagnosis, undifferentiated/unclassified sarcoma was the most common diagnosis (19 cases, 16.6% of all malignant tumors) followed by the dedifferentiated liposarcoma (14 cases, 12.2%, see Table 2).

3.2. Accuracy. Of the 196 tumors specimens from institution A (which underwent initial diagnosis by a local pathologist followed by specimen being reviewed by a reference pathologist, see Figure 1), 152 tumors (77.6%) were diagnostically concordant according to category A. Of the latter 152 tumors, 46.7% were benign, 18.4% were intermediate, 33.5% were malignant, and 1.4% unclassifiable. There were 20 cases (10.2%) with minor discrepancies, according to category B (Table 3). Of these, 70% were malignant, 15% intermediate, and 15% benign diagnoses. There were 24 tumors (12.2%) with major diagnostic discrepancies (Table 3) according to category C. 50% of these were malignant cases. From these major discrepancies, 12 cases were classified in this category because of a missing diagnosis in the

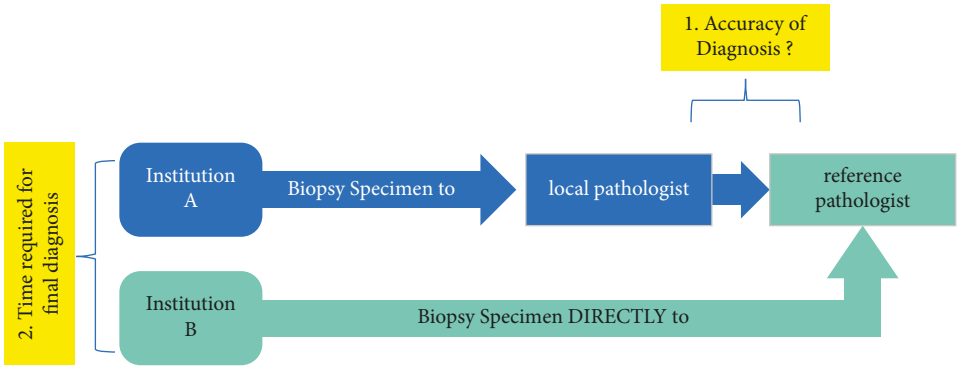

Figure 1: Workflow of the study.

Table 1: Patient and tumor characteristics.

Total	347
Institution A	198 (57%)
Institution B	149 (43%)
Male	168 (48.5%)
Female	179 (51.5%)
Median age	55 (range 12–90) years
Benign diagnosis	163 (46.9%)
Intermediate diagnosis	66 (19%)
Malignant diagnosis	114 (32.8%)
Unclassified diagnosis	4 (1.2%)

Table 2: Most common diagnoses.

Benign	Intermediate	Malignant
Lipoma (69 cases)	Atypical lipomatous tumor/well differentiated liposarcoma (17 cases)	Unclassified/undifferentiated sarcoma (19 cases)
Schwannoma (11 cases)	Aneurysmal bone cyst (11 cases)	Dedifferentiated liposarcoma (14 cases)
Intramuscular myxoma (8 cases)	Desmoid-type fibromatosis (9 cases)	Leiomyosarcoma (11 cases)

final report from institution A. In one case, there was a reclassification from benign to malignant and one case was reclassified from malignant to benign. A summary of all original diagnoses, which were discordant from the expert review is shown in Table 3.

3.3. Analysis of Time to Diagnosis. Establishing the final report took on average 4.7 working days for institution A, which is significantly longer than the 3.3 days required by institution B (Figure 2). 10 cases were excluded from the analysis (7 from institution A and 3 from institution B) due to the necessity of NGS for the final diagnosis. We analyzed the data with a two-sided Wilcoxon t-test and found a p value of $p < 0.01$.

If only malignant diagnoses were considered for analysis, establishing the diagnosis averaged 5.2 days in institution A, and 3.4 days, respectively, for institution B ($p < 0.01$, see Figure 2).

According to the most commonly diagnosed lesion of all, the diagnosis of a lipoma averaged 4.6 days at institution A and 3.2 days, respectively, at institution B ($p < 0.01$). Accordingly, and with respect to undifferentiated/unclassified sarcoma, institution A required 5.2 days, and institution B 3.0 days ($p < 0.01$).

4. Discussion

To the best of our knowledge, this is the first analysis comparing the duration of a histological review to establish a sarcoma diagnosis. Our results confirm the importance of a second pathological review by a reference pathologist. With an overall concordance of 77%, the results are comparable to the already published literature.

In 1986, Presant et al. [7] first reported on a histopathologic peer review of specimens from 216 consecutive patients with soft-tissue or bone sarcomas by a panel of three pathologists. Subtype of sarcoma, degree of confidence in diagnosis, and grade were compared with agreement or disagreement in pathologic opinion from the primary member institution versus the pathology review panel. There was a complete agreement between the primary pathologist

Table 3: Minor/major discrepancies.

	Minor discrepancies	
	Benign	
	Institution A	*Institution B*
L107	Fibroblastic/myofibroblastic proliferates in predominantly tight connective tissue with partly regressive changes.	Collagen-rich myofibroblastic proliferation
L108	Chondrogenic neoplasm, highly differentiated	Enchondroma
L198	Fibrin and blood, intercalated with some lamellar bone tissue and connective tissue	Intraosseous ganglion
	Intermediate	
	Institution A	*Institution B*
L31	Spindle-cell, partly multinucleated giant-cell tumor with osteoid formation	Aneurysmal bone cyst
L34	Giant cell tumor of the soft tissue	Plexiform fibrohistiocytic tumour
L112	Chondroid neoplasia with cancellous bone	Epiphyseal atypic chondrogenic tumor
	Malignant	
	Institution A	*Institution B*
L4	Spindle-cell high-grade sarcoma	Spindle and pleomorphic high-grade malignant unclassified sarcoma G3
L11	Spindle-cell pleomorphic sarcoma, high grade, with evidence of myogenic differentiation	Leiomyosarcoma
L19	Epithelioid sarcoma (proximal type)	Epithelioid angiosarcoma
L29	Lymph node metastasis of a solid tumor (differential diagnosis: clear cell sarcoma or malignant melanoma)	Lymph node metastasis of malignant melanoma
L35	Pleomorphic undifferentiated sarcoma with necrosis zones	Pleomorphic liposarcoma (G3)
L60	Spindle-cell pleomorphic neoplasia with striated muscles	Sclerosing epithelioid fibrosarcoma
L63	Sarcoma, spinel and partly pleomorphic cells	Spindle and pleomorphic cell soft tissue sarcoma at least G2 with FNCLCC score of 4
L64	Highly differentiated liposarcoma	Dedifferentiated liposarcoma with low-grade dedifferentiated portion, malignancy grade at least G2
L84	Myxofibrosarcoma	Undifferentiated spindle cell sarcoma
L110	Myxofibrosarcoma (high grade)	High-grade, unclassifiable spindle cell sarcoma (G2)
L140	Undifferenciated pleomorphic sarcoma	High-grade, unclassifiable spindle cell sarcoma (G2)
L157	Myxofibrosarcoma, high grade	High-grade, unclassifiable spindle cell sarcoma (G2)
L188	Pleomorphic highly proliferative tumor	Giant cell-rich leiomyosarcoma at least G2
L201	Myxofibrosarcoma (high grade)	Spindle cell sarcoma at least G2
	Major discrepancies	
	Benign	
	Institution A	Institution B
L2	Fat necrosis	PHAT (pleomorphic hyalinizing angiectatic tumor of soft parts)
L37	Fibrin-rich connective tissue with low chronic inflammation and regressive changes	Nodular fasciitis
L52	Mature teratoma/dermoid	Spinal dermoid cyst
L57	Spindle-cell mesenchymal myofibroblastic proliferation with low MIB-1 proliferation rate along with skeletal muscles	Intramuscular myxoma
L66	Parts of a spindle-cell myxoid-chondroid impinging neoplasia	Benign portion of a peripheral nerve sheath tumor
L109	Slightly atypical spindle cell tumor with myxoid background and increased proliferation (Ki67) of approx. 30%.	Myofibroblastic proliferation of the nodular fasciitis type
L113	Low-grade fibromyxoid sarcoma	Intramuscular myxoma
L145	Smooth-muscular proliferation with scaly calcifications as well as circumscribed ossification without necrosis or evidence of mitoses	Leiomyoma of the deep somatic soft tissues
L195	Intramuscular lipoma	Intramuscular haemangioma
	Intermediate	
	Institution A	*Institution B*
L100	Spindle cell mast cell-rich proliferation with low proliferation rate and immunohistochemically S-100 positive with negativity for SOX-10	Solitary fibrous tumor (SFT)
L101	Plump spindle-cell tumour with multiple multinucleated giant cells	Periosteal aneurysmal bone cyst (ABC)
L117	Cell-rich neoplasia of oval, plump spindle mononuclear cells intermixed with giant cells and haemorrhage residues in connective tissue.	Tenosynovial giant cell tumor of the diffuse type
	Malignant	
	Institution A	*Institution B*
L1	Epithelioid sarcoma	Angiosarcoma
L6	Osteosarcoma	Chondrosarcoma
L7	Highly differentiated/dedifferentiated or a myxoid liposarcoma	Dedifferentiated liposarcoma (low grade)
L51	Myxoid chondrosarcoma	Myxoid liposarcoma (G1)
L70	Chondroid and focal spindle cell neoplasia	Mesenchymal chondrosarcoma
L76	Slightly hypercellular chondrogenic tissue, connective tissue and skeletal muscle	Conventional chondrosarcoma
L94	Pleomorphic liposarcoma	Round cell liposarcoma G3
L150	Small blue round cell tumor with low proliferation (Ki67) of approx. 10-15%.	Granulosa cell tumor
L164	Atypical lipomatous tumor/well-differentiated liposarcoma	Dedifferentiated liposarcoma, at least G2
L171	Neoplasia, predominantly spindle cell in cancellous bone with focal evidence of irregular osteoid.	Osteosarcoma, high grade
L191	Infiltrates of small, round and blue cell neoplasia	Poorly differentiated neuroendocrine carcinoma (Merkel cell carcinoma)
L204	Spindle and pleomorphic cell neoplasm with myxoid background of partial expression of MDM2	High-grade myxofibrosarcoma (G2-3)

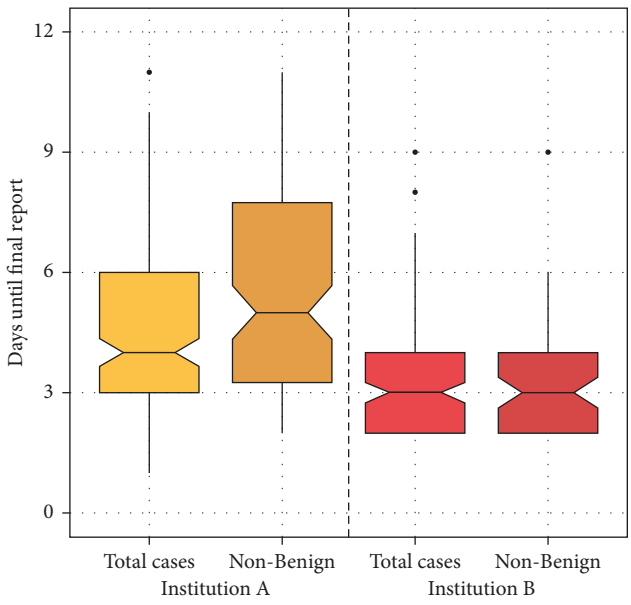

Figure 2: Days until final report.

and reviewer in 66% of cases. However, after the review, 12 cases (6%) were considered not to be sarcoma. In 27% of cases, the subtype of sarcoma was felt to be incorrect by reviewers.

In 2008, Lehnhardt et al. [5] reviewed 603 patients who were operated with the diagnosis of soft tissue sarcoma. They found a concordance in primary diagnostics of 28.3% for pathologists in private clinics, 29.6% for hospital affiliated pathologists, 36.8% for academic medical centers, and 70.5% for the department of pathology at their institution.

In 2010, Lurkin et al. [8] analyzed all histological data of all patients diagnosed with sarcoma in the Rhone-Alpes region between March 2005 and February 2006. Primary diagnoses were systematically compared with second opinions from regional and national experts. They included 366 patients; of these, 199 (54%) had full concordance between primary diagnosis and second opinion, 97 (27%) had partial concordance (identical diagnosis), and 70 (19%) had complete discordance.

Ray-Coquard et al. [4] reviewed the histological data of patients diagnosed with sarcoma in Rhone-Alpes (France), Veneto (Italy) and Aquitaine (France) over a 2-year period. Initial diagnoses were systematically compared with the second opinions from members of the group of pathologists of the GSF-GETO (French Unicancer Sarcoma Group). 1463 cases matched the inclusion criteria and were analyzed. Full concordance between primary and second diagnosis was observed in 824 (56%) cases, partial concordance in 518 (35%) cases and complete discordance in 121 (8%) cases.

A summary of the studies can be found in Table 4.

Interestingly, and specifically contrasting the analysis between benign and malignant lesions, the uncertainty to establish the correct diagnosis was greater in malignant lesions. Considering the analysis of minor discrepancies in the diagnosis comparing first line with expert review, the expert review delivers more diagnostic details or a supplement in the classification without obvious consequences regarding the treatment modality, specifically also for malignant diagnoses.

Our study has several limitations: The number of biopsies analyzed is still relatively small, and many diagnoses are benign, thereby not allowing further subgroup analysis. Also, considering the rarity of the disease and the 68 sarcoma entities included therein, further subtype analysis is not possible. The definition of diagnostic discordances is not always obvious and may skew the results. Arbitrarily, descriptive pathology reports without specification of dignity were classified as major discrepancies because adequate treatment can only be initiated when the final diagnosis is made.

Although there is a significant difference in the time to diagnosis, one may critically question to what extent this value has an influence on the time to diagnosis and further therapy. The time it takes to establish the histological examination is only one step on this path. It would therefore be interesting if a further study examines not only the duration of the biopsy, but the entire process from the suspected diagnosis to the initiation of the correct therapy. But from the point of view of the patient who must wait for a diagnosis, every day that is gained with a faster diagnosis is worth a lot. In addition, a rapid histological diagnosis is essential for a timely discussion at the multidisciplinary sarcoma board.

Any additional examination, especially if not done in the same institution, will lead to delays in the diagnostic process.

Several studies confirmed that a centralized pathological review improved the quality of the diagnosis. Lurkin et al. [8] support the direct analysis by an expert pathologist because of the multitude and complexity of sarcoma tumors. Also, the access to molecular biology analysis can be provided. Compared to the recommendation of the ECCO Essential Requirements for Quality Cancer Care, the pathway of Institution B is to be favored [14].

In a small country like Switzerland, and with sarcoma being a rare disease, establishing the correct pathological diagnosis is very challenging. The main reason is the small amount of cases per individual hospital. Compared with the volume of international sarcoma reference centers, the data of the entire country needs to be pooled and shared to reach high enough numbers for expert experience and teaching purposes. With the recently established Swiss Sarcoma Network, allowing real-world outcome analytics, there is the possibility to improve the precision, timeliness, and accuracy of sarcoma diagnosis in Switzerland in the near future. As of now, 7 central referral institutions joined the Swiss Sarcoma Network so far and benefit from a second opinion by an expert pathologist.

There is no clear definition in the literature on how a sarcoma expert is defined. As for the pathologists, the sarcoma experts within the Swiss Sarcoma Network are defined by their specific training, their specific sarcoma interest, defined by dedication of >30–50% of their duty time spent on treating sarcoma patients, their yearly scientific contributions, their number of cases reviewed and/or treated per year, and their participation of the weekly

Table 4: Overview of literature.

Author (year)	Interval	No. of cases	% concordance	% minor deviations	% major deviations
Peasant (1986)	May 1974 to May 1982	216	66% (137)		
Lehnhardt (2008)	1995 to 2001	603	28.3–70.5%		
Lurkin (2010)	March 2005 to February 2006	366	54%(199)	27% (97)	19% (70)
Ray-Coquard (2012)	March 2005 to February 2007 resp. January 2007 to December 2008	2016	56% (824)	35% (518)	8% (121)
Our study	January 2019 to December 2020	196	77.6% (152)	10.2% (20)	12.2% (24)

multidisciplinary tumor board including the number of discussed cases and strategic decisions.

5. Conclusions

The diagnosis of sarcoma remains challenging. According to our study and the current literature, an expert review by an experienced pathologist within a network such as the Swiss Sarcoma Network proves to be highly useful and beneficial for the patient both regarding accuracy and timeliness to establish the diagnosis. Establishing the sarcoma diagnosis as early as possible after biopsy is a critical quality indicator for a multidisciplinary team. Considering the rapidly rising health care costs, the potential increase in cost efficiency of such a process needs to be determined next.

Data Availability

The data used to support the findings of this study may be released from the Adjumed®-Database upon request to the Swiss Sarcoma Network (office@sarcoma.surgery).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

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cancers

MDPI

Article

How Is the Spectrum of Sarcoma Surgery Assessed?

Carlo Theus-Steinmann [1], Georg Schelling [1], Philip Heesen [1], Stefan Breitenstein [1], Mario F. Scaglioni [1,2] and Bruno Fuchs [1,2,*]

[1] Swiss Sarcoma Network SSN, Luzerner Kantonsspital LUKS, Kantonsspital Winterthur KSW, 6000 Luzern, Switzerland
[2] Faculty of Health Sciences and Medicine, University of Luzern, 6002 Luzern, Switzerland
* Correspondence: fuchs@sarcoma.surgery

Simple Summary: Sarcoma surgery is the cornerstone of sarcoma therapy, which is organized highly multidisciplinarily. The critical determinant of tumor control depends on the experience of the multidisciplinary team (MDT), in which sarcoma surgery plays a pivotal part. In this study, an interoperable digital platform on sarcoma surgery was established to assess its spectrum based on a single sarcoma surgeon over one decade as a pilot. Being used at large scale, this platform may become an indispensable instrument to assess the contributions of sarcoma surgery within an MDT to tailor personalized patient quality care in the future.

Abstract: Purpose: To meet the challenges of the precision medicine era, quality assessment of shared sarcoma care becomes pivotal. The MDT approach is the most important parameter for a successful outcome. Of all MDT disciplines, surgery is the key step to rendering sarcoma patients disease free; therefore, defining its spectrum is critical. To the best of the authors' knowledge, a comprehensive interoperable digital platform to assess the scope of sarcoma surgery in its full complexity is lacking. Methods: An interoperable digital platform on sarcoma surgery has been created to assess the clinical exposure, tumor characteristics, and surgical settings and techniques applied for both resections and reconstructions of sarcomas. Results: The surgical exposure of an individual surgeon over time served as a pilot. Over the study period of 10 years, there were 723 sarcoma board/MDT meetings discussing 3130 patients. A total of 1094 patients underwent 1250 surgical interventions on mesenchymal tumors by one single sarcoma surgeon. These included 615 deep soft tissue tumors (197 benign, 102 intermediate, 281 malignant, 27 simulator, 7 metastasis, 1 blood); 116 superficial soft tissue tumors (45 benign, 12 intermediate, 40 malignant, 18 simulator, 1 blood); and 519 bone tumors (129 benign, 112 intermediate, 182 malignant, 18 simulator, 46 metastasis, 14 blood, and 18 sequelae of first treatment). Detailed types of resections and reconstructions were analyzed. Conclusions: An interoperable digital data platform on sarcoma surgery with transparent real-time descriptive analytics is feasible and enables large-scale definition of the spectrum of sarcoma surgery to meet the challenges of sarcoma precision care in the future.

Keywords: sarcoma; multidisciplinary team/MDT; sarcoma surgery; orthopedic oncology; real-world data; interoperable digital platform; exposure; experience

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1. Introduction

Sarcoma treatment includes various disciplines and is carried out by so-called multidisciplinary teams (MDTs). MDTs represent the cornerstone for the quality of sarcoma care [1–5]. Recently, quality indicators of global sarcoma care were reported [6]. Quality of sarcoma care is greatly dependent on various disciplines collaborating under one roof and its associated infrastructure and processes, as well as an adequate surgery and the surgical margins achieved thereby [7]. The latter, in turn, depends on the experience of the surgeon and his team and the complexity of the procedure. Of all the involved disciplines, surgery is the most important pillar to render a patient disease free and, hence, a surgeon's

experience plays a pivotal role; for this reason, the quality of surgery deserves particular attention [8]. Counting the number of surgeries alone serves at best as a surrogate but does not reflect per se the quality of surgery or the surgeon's experience. For example, the surgical procedure of an Ewing sarcoma of the great toe differs greatly from that on the pelvis, as does the biology of the wide array of sarcoma entities representing different diseases. A sarcoma surgeon, therefore, is not only technically skilled but also understands the biology and various treatment aspects of the disease, including the process of performing longitudinal follow-up of the patients over time [9,10]. Most importantly, the sarcoma surgeon is capable of assembling a multidisciplinary team for sarcoma care, specifically for the wide and complex spectrum of surgical resections and reconstructions [9]. However, before the complexity or indicators of quality for sarcoma surgery are defined specifically, the surgical spectrum needs to be described by outlining the role of a sarcoma surgeon. Sarcomas may arise in any part of the entire body, thereby requiring an entire spectrum of surgical techniques, which one single surgeon in present times is unable to cover. Sarcoma surgery may include not only the resection of the tumor alone, but also subsequent reconstructions, adding another level of surgical complexity. Although sarcoma resection is driven by the biology of the lesion, which is most often independent of the anatomic location, reconstruction is highly site dependent because surgical techniques vary greatly depending on the anatomical locations. For these reasons, sarcoma surgery needs to be organized in a highly transdisciplinary fashion by personalizing each sarcoma surgery specifically to each patient's situation, which does need to be taken into account when defining the complexity or also the quality of sarcoma surgery.

Health care cost explosion and the emerging skills shortage require the development of a novel ecosystem, moving away from a legacy system to a value-based system, in which the patient's value is defined by the quality and outcome divided by the total costs over the full care cycle [4,11–14]. Moreover, from this economic perspective, the definition of quality of sarcoma care is indispensable. Sarcoma surgery shows a great level of complexity, which, in turn, is intimately related to the experience of the respective surgeon [15,16]. Defining the spectrum of sarcoma surgery is paramount to then defining the complexity of a procedure, but also for personalized teaching of the next generation of sarcoma surgeons and for continuous education purposes, as well as ultimately ascertaining the quality in every day practice and patients' safety within an MDT. Defining the spectrum of sarcoma surgery may also assist in addressing the geography model of care by the regionalization of our patients, depending on patient- and disease-based parameters of sarcoma and the establishment of integrated practice units. Above all, it may make it possible to revisit the current reimbursement system in many countries without the capacity to mirror the specific scope of sarcoma surgery adequately using commonly available clinical information systems [4,11–14]. Therefore, challenges include the assessment of the various types and the technical aspects of surgical procedures using structured data on a respective interoperable digital platform [17].

To the best of the authors' knowledge, there are no reports on how to assess and report on the spectrum of sarcoma surgery within an MDT. Because most of the clinical information systems in hospitals are not designed for the detailed search of sarcoma-surgery-specific aspects, we designed a novel web-based interactive real-world-time (RWDT) interoperable digital platform on sarcoma surgery to assess, identify, and analyze the spectrum of sarcoma surgery to meet the challenges of the precision medicine era.

2. Materials and Methods

A set of parameters including all single steps of all types of sarcoma surgeries was assembled [18]. As a prototype, this list was then applied on all surgeries of mesenchymal tumors performed by one single surgeon over a 10-year period. Registration was performed using the AdjumedCollect "Interoperable digital platform on Sarcoma Surgery" (Adjumed Services, AG, Zurich, Switzerland, http://www.adjumed.com/ (accessed on 30 November 2022)). The AdjumedAnalyze tool (Adjumed Services AG, Zurich, Switzerland) can be used

for basic statistics, such as combinations of parameters, and allows for the extraction of data. The individual scores were calculated later in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

The parameters to describe the sarcoma surgery spectrum include four main categories: clinical patient exposure, tumor characteristics, surgical settings, and techniques (Figure 1).

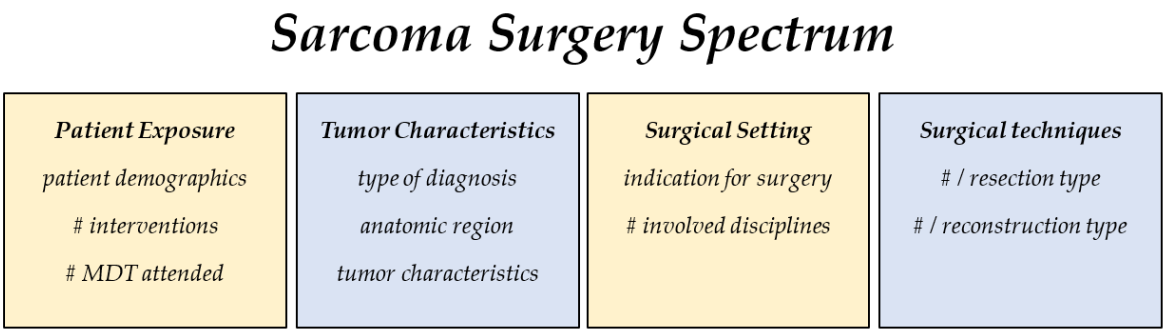

Figure 1. The exposure to sarcoma surgery is assessed in the following 4 categories: patient exposure, tumor characteristics, surgical setting, and surgical techniques applied. # number of.

3. Results

3.1. Patient Exposure

Over a 10-year period of time, there were 723 MDT or sarcoma board meetings, in which 3130 patients were discussed, and 5930 sarcoma board decisions were made (Figure 2). This averages a total of 313 patients and 593 sarcoma board decisions per year.

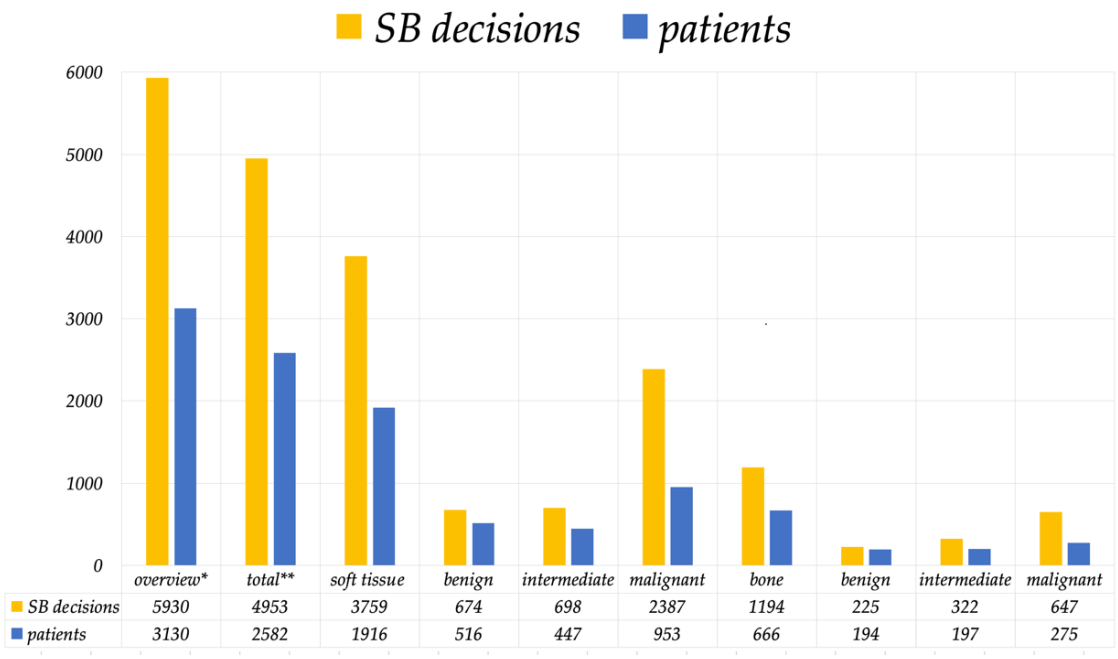

Figure 2. This figure summarizes the number of sarcoma board decisions and patients over a 10-year period. * All evaluations of mesenchymal tumors ** Exclusive metastasis, carcinoma, lymphoma, leukemia, myeloma, and tumor simulator.

During the same 10-year period, one single surgeon performed a total of 1250 surgical interventions on mesenchymal tumors in a total of 1094 patients, who are the subjects of this analysis. There were 484 females and 610 males, with a mean age at surgery of 46.1 years (range: 1 to 91 years) (Figure 3).

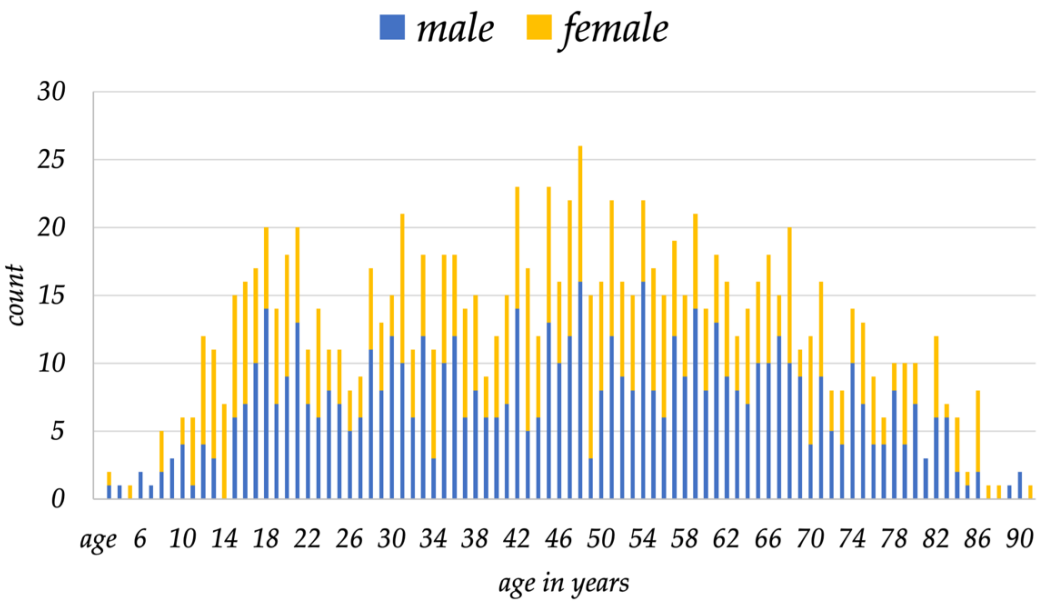

Figure 3. Distribution of gender and age over time of all patients included in this study is shown.

3.2. Tumor Characteristics

In all 1094 patients, there were 628 soft tissue tumors, 339 bone tumors, and 44 metastases treated by surgery. The exact diagnoses are summarized in Table 1.

Table 1. This summary of all tumors included in the analysis over a 10-year period is split according to the diagnoses of the WHO classification.

Soft Tissue	**628**	**Bone**	**339**
Adipocytic	258	Chondrogenic	141
Fibroblastic/myofibroblastic	97	Osteogenic	90
Undifferentiated/unclassified sarcoma	82	Tumors of undefined neoplastic nature	45
Tumors of uncertain differentiation	71	Osteoclastic giant cell rich	24
Nerve sheath tumors	49	Ewing	18
Fibro-histiocytic tumors	21	Notochordal tumors	7
Vascular tumors of soft tumors	14	Undifferentiated high-grade pleomorphic sarcoma	4
Smooth muscle tumors	19	Fibrohistiocytic	3
Chondro-osseous tumors	10	Fibrogenic	2
Pericytic tumors	4	Myogenic, lipogenic, epithelial tumors	2
Skeletal muscle tumors	4	Tumor syndromes	2
		Vascular tumors	1
Non-neoplastic/simulator	62		
Metastasis	44		
Lymphoma myeloma leukemia	12		
Sequelae of prior therapy	8		

Of these tumors, there were 361 benign, 199 intermediate, 409 malignant (34 G1, 85 G2, and 289 G3, respectively), 62 sarcoma simulators, 44 metastases, 12 blood, and 8 sequelae of prior therapy (Figure 4). In total, 266 underwent preoperative radiation therapy, 63 underwent postoperative radiation therapy, and 126 underwent neoadjuvant chemotherapy. The mean size of the tumors averaged 80.3 mm (range: 1 to 550 mm) (Figure 5).

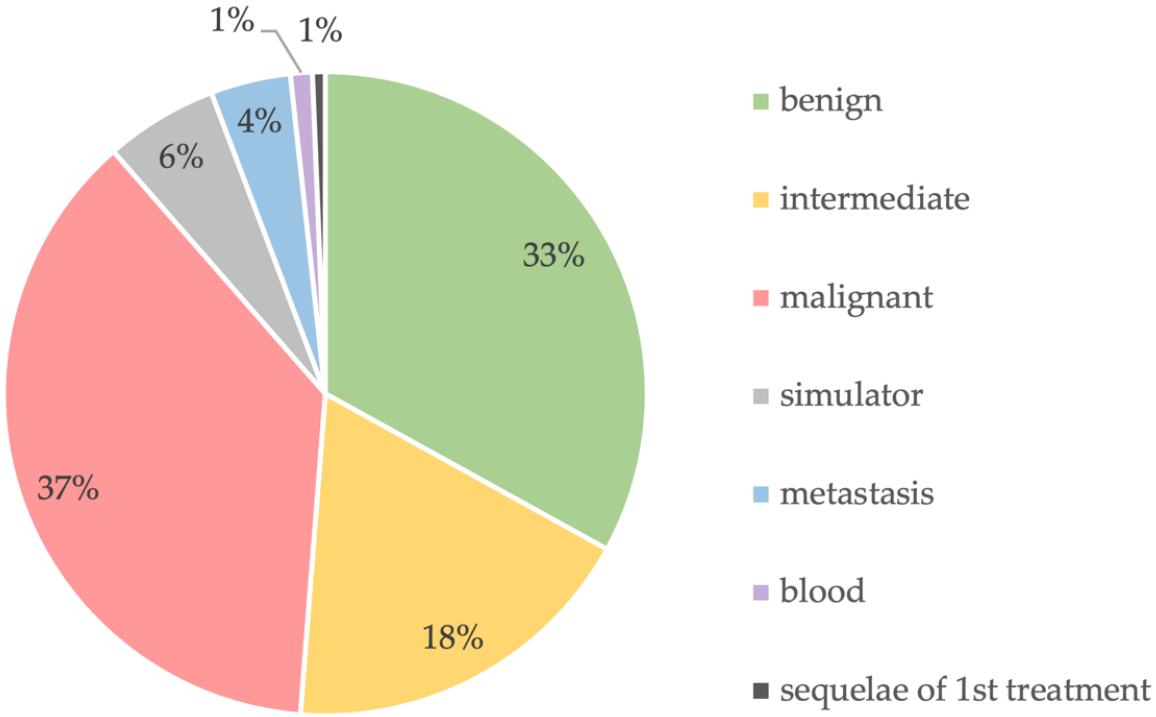

Figure 4. Biological diagnosis of the lesions.

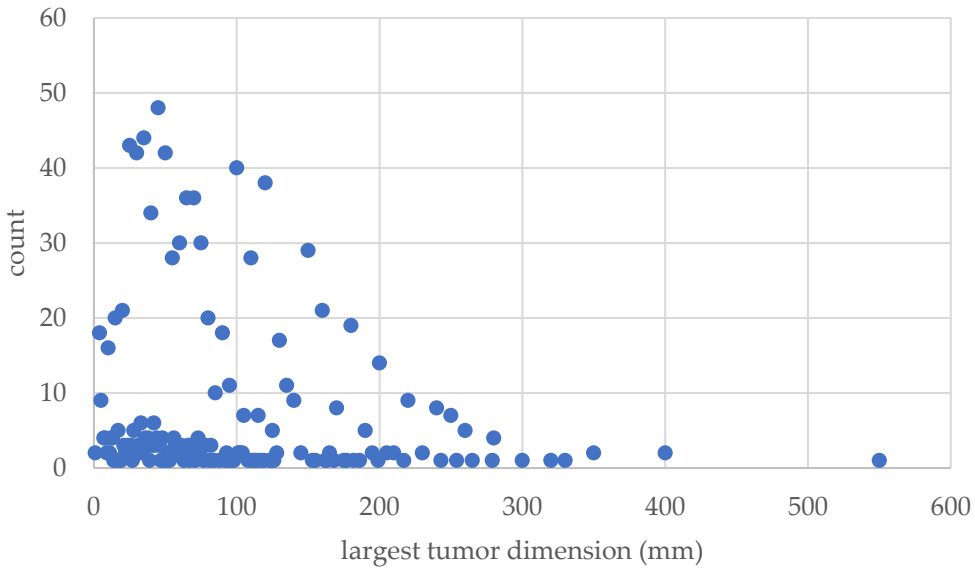

Figure 5. This diagram shows the number and size of the tumors.

Of these interventions, 615 concerned the deep soft tissue (197 benign, 102 intermediate, 281 malignant, 27 simulator, 7 metastasis, 1 blood); 116 cases concerned the superficial soft tissue (45 benign, 12 intermediate, 40 malignant, 18 simulator, 1 blood); and 519 concerned the bone (129 benign, 112 intermediate, 182 malignant, 18 simulator, 46 metastasis, 14 blood, and 18 sequelae of first treatment). From head to toe, 13 of all interventions were located in the head/neck/face region, 301 in the upper extremity, 87 in the torso/chest/abdomen, 159 in the pelvis, and 690 in the lower extremity.

3.3. Surgical Settings

The indication for surgery is an important parameter to describe the complexity of the patient cohort. Of all 1250 surgical interventions, in 996 cases (79.7%), surgery

was indicated for the first time. In total, 56 cases (4.5%) had prior whoops surgery, and 17 cases (1.4%) presented with a pathological fracture. There were 52 first revision surgeries (4.2%) for any cause, and 41 second or more revision surgeries (3.3%). In total, 45 cases (3.6%) underwent surgery for a local recurrence (independent of whether the cases were of primary or referred patients), and 35 surgeries (2.7%) were indicated for more than 2 local recurrences. In total, eight surgeries (0.6%) were performed for other reasons, such as three for regional metastasis, two for systemic recurrence (one intraabdominal and one spine), two for removal of osteosynthesis material after fracture care, and one for a local progression of a multiple myeloma.

The definition of the surgical margin is not uniformly accepted [15], and the surgeon's judgement on the resected margin does not necessarily reflect the pathologist's opinion, nor the shared decision process of the MDT/sarcoma board. In the presented series, the surgeon defined wide/adequate margins in 933 surgeries (95.9%), in 18 marginal (1.8%) surgeries, and 23 intralesional (2.4%) surgeries, and margin status was not applicable in 276 surgeries because there was no sarcoma.

Of all surgeries, 875 were carried out by the sarcoma surgeon alone (70%), whereas 309 surgeries were performed with an expert from another discipline (24.7%), 53 surgeries with 2 additional disciplines (4.2%), and 4 surgeries each with 4 and 5 additional disciplines (0.3% each). In one surgery, namely a forequarter amputation with chest wall resection due to a post-irradiation UPS (undifferentiated pleomorphic sarcoma) infiltrating the brachial plexus, a total of 7 different disciplines were involved (sarcoma, orthopedics, chest, vascular, neuro, plexus, and reconstructive surgery).

3.4. Surgical Techniques

Surgical techniques focus on both resection and reconstruction. Resection techniques depend on the anatomic location and the specific structures that need to be removed. In this series, besides tumor resection itself, additional resection included 1800 surrounding and different types of soft tissues and 489 bone resections, 11 chest/thorax resections, 19 abdominal structures, and 106 sequelae of first treatment (e.g., débridement or prosthesis related resections).

Reconstructions after tumor resection were necessary in a total of 640 cases. They consisted of 319 bony reconstructions, including 94 prostheses, 84 allografts, 79 ORIF (incl. 18 pedicle screws/rods/cages), 24 autografts, 20 cementations (incl. 2 cement spacers), 4 arthrodeses, 2 gore-tex mesh, 1 distraction osteogenesis, and 11 other bone reconstructions (e.g., external fixator or Tikhoff–Linberg hanging bridge reconstruction).

Soft tissue reconstruction consisted of 38 tendon/ligaments, 70 neurovascular structures (56 vessels and 14 nerves), 16 abdominal, and 11 chest wall reconstructions, as well as 159 soft tissue reconstructions for soft tissue coverage (96 pedicle flaps, 22 free tissue transfer, 41 skin-/mesh-graft).

Furthermore, there were 29 sequelae of first treatment (e.g., cementation).

A detailed summary of resected and reconstructured structures is provided in Table 2.

Table 2. This summary provides a detailed overview of performed resections (left) and reconstructions (right).

Resection	Count	Reconstruction	Count
Bone	**489**	**Bone**	**319**
simple curettage	107	cementation	18
rotationplasty (lower extremity)	2	ORIF (incl. bone ankers; removal of OS material)	61
hemi-cortex resection	20	autograft	11
complete bone resection: extra-articular	108	vascularized fibula autograft (based on fibular artery)	10
complete bone resection: transarticular	92	non-vascularized fibula autograft	1
with 3D patient-specific cutting guides	23	allograft chips	45
radiofrequency ablation (RFA); cryotherapy, MR-HIFU	41	bulk allograft	32

Table 2. *Cont.*

Resection	Count	Reconstruction	Count
tendon resection	2	conventional prosthesis	9
ligament resection	1	modular tumor prosthesis	79
forced epiphyseolysis OT (Canadell technique)	1	custom-made prosthesis	2
extra-articular scapulo-humeral resection (Tikhoff–Linberg)	1	growing prosthesis	4
biopsy/gain of diagnostic tissue	12	pedicle screws/rods/cages	18
removal of cement	1	other bone reconstruction	11
resection–replantation (upper extremity)	1	distraction osteogenesis	1
Internal hemipelvectomy	38	artificial bone substitute (Ca-sulfate, etc.)	7
Type I—ilium	15	cement spacer/pseudarthrosis/flail joint	2
Type II—Acetabular	13	arthrodesis	4
Type III—Pubic	4	vascularized epiphyseal transfer (based on tibial anterior artery)	2
Type IV—Sacral	6	Gore-Tex mesh, Trevira, etc.	2
Amputation	39	**Soft Tissues**	**159**
Forequarter	5	skin-/mesh-graft	41
External hemipelvectomy	5	pedicled tissue transfer	96
Upper extremity	5	rectus abdominis	3
Lower extremity	24	rectus abdominis (with skin)	7
Soft Tissues	**1800**	gastrocnemius	10
simple	694	latissimus dorsi	12
tendon resection	23	latissimus dorsi (with skin)	3
ligament resection	5	gracilis	3
resection of funiculus, scrotum, genitals	3	soleus	3
other STS resection	11	ALT	8
muscle resection	419	other muscle flap	47
vessel dissection	225	free tissue transfer	22
nerve dissection	270	latissimus dorsi	8
periosteum resection	41	gracilis	2
bone resection	20	ALT	8
vessel resection	38	other perforator flap	3
nerve resection	50	other free tissue transfer	1
MR-HIFU	1	**Chest wall**	**11**
Chest/Thoracic	**11**	**Abdomen**	**14**
chest wall resection	7	abdominal wall	4
other chest/lung resection	2	colon anastomosis	3
wedge resection	2	bladder	2
Abdomen	**19**	ureter	2
abdominal wall resection	1	other intraabdominal reconstruction	5
kidney	2	**Sequelae of First Treatment**	**29**
suprarenal glands	1	cement spaces implantation	4
ureter	3	partial implantation/replacement	22
bladder	3	complete compartment implantation/replacement	3
colon/rectum	4	**Neurovascular**	**70**
bowel	2	vascular	56
uterus/ovaries	1	artery complete	14
other abdominal resection	2	vein complete	13
Sequelae of 1st treatment	**106**	lympho-venous	21
debridement	27	other vessel reconstruction	8
inlay change	5	neural	14
partial removal of prosthesis	26	nerve reconstruction	8

Table 2. *Cont.*

Resection	Count	Reconstruction	Count
complete removal of prosthesis	3	neurotization/local transfer	2
infection	7	autologous	4
wound healing breakdown	11	**Tendon/Ligament**	**38**
osteosynthesis breakdown	2	autologous tendon transfer	18
fracture	1	allograft tendon reconstruction	2
other	24	local tendon reconstruction	18

4. Discussion

In this article, the authors describe the surgical spectrum of a sarcoma surgeon and provide a web-based means to assess it using a structured interoperable RWDT format. Our group has recently published an article detailing the quality indicators for sarcoma care in a multidisciplinary setting, as well as introducing an interoperable digital platform capable of assessing harmonized, structured data [6]. Achieving global harmonization and scalability of medical data is a crucial step towards achieving precision medicine. Specifically, in this study, our research has focused on the surgical aspects of sarcoma care, which have been integrated into the aforementioned digital platform. The presented parameters include information on patient exposure, tumor characteristics, the surgical setting, and surgical techniques. Such information ultimately allows the definition of the complexity or even the quality of a surgical procedure within an MDT. This will be an important step to establish a new ecosystem to meet the challenges of the precision medicine era [6].

Outcome prediction in medicine with the help of digital transformation and artificial intelligence opportunities will dramatically revolutionize our current treatment approach, but it will largely depend on the availability of structured data sets [17,19]. However, because of the scarcity of sarcomas, and to be able to compare on a large scale at the international level, we need to establish a common language of exchange among experts for data harmonization. It is not enough, for example, to bundle an outcome analysis of all megaprostheses independent of their anatomic localization and (neo-)adjuvant treatments. It is necessary to focus a large-scale analysis on a specific region or clinical circumstances to determine the advantages of subtle differences. The challenge for shared sarcoma care is to, nevertheless, have adequate numbers for an analysis. We therefore need a refined interoperable digital system which allows not only a detailed assessment but also the ability to make comparisons on a large, global scale to compensate for low volume numbers which are inherent with sarcomas. The interoperable digital data platform presented herein may offer a first step in this direction.

Sarcoma surgery meets two great challenges. A sarcoma surgeon has to be technically very skillful and versatile but also needs to have a great understanding of biology. These aspects need to be reflected when the spectrum of sarcoma surgery is assessed. Therefore, we created four main groups. Obviously, from the technical aspects, all specific types of resections and reconstructions matter and are important and need to be reflected in detail in such assessment. Furthermore, the types of tumors, as well as the anatomic regions where the tumors are located, must be reflected as well. We also included indications for surgery and the involved disciplines [18]. The latter is considered important to foster interdisciplinary exchange and to respect increasing technical complexities. Obviously, the current suggestion of surgical exposure presented herein is not comprehensive and may be regularly updated, similarly to how sarcoma pathologists update their WHO classification.

For the resection of sarcomas, the anatomic localization and the biology of the tumor are critically important to define the resection planes. To achieve an oncological and functional outcome in the patient's best interest, it is critically important that sarcoma surgery is carried out with considerations for both biological and technical principles [20,21]. To obtain and improve the biological understanding of these tumors, participation at a weekly MDT's meeting probably represents the minimal requirement because it increases the

exposure to the thinking and approach of other disciplines. Our data, for example, show that interpretations of surgical margins—i.e., how wide is wide?—may continue to vary greatly without universal harmonization of assessment. The surgeons may interpret the margin differently among themselves, but their interpretations may also differ from those of pathologists. This has great consequences for the interpretation of any comparative study and must be addressed. Modern sarcoma surgery [1,9,10,16,22,23], therefore, fosters transdisciplinary collaboration under the direction of surgeons who have a broad biological knowledge and are able to organize a team of surgeons with broad technical skills depending on the anatomic site of the tumor, which is particularly important for reconstruction after tumor resection.

Sarcoma surgery is a critical determinant for a successful treatment and outcome in sarcoma patient care. The German Cancer Society (DKG) defines in their guidelines the minimal surgical interventions per year (n = 15), as well as those in a lifetime experience (n = 50) for the sarcoma surgeon [24]. The Musculoskeletal Tumor Society—MSTS also reported the number of sarcoma surgeries performed per surgeon per year, averaging approximately 35 cases [25]. Although the number of treated patients is important, it is not discriminative enough to determine the entire spectrum of surgical exposures, as sarcoma surgery includes a wide spectrum both anatomically and biologically. The French sarcoma group nicely showed that although the absolute number of performed surgeries is important, the most important discriminator for outcome is the embedding of the surgery within an MDT [2]. This is further confirmed by Baum et al. who questioned the policy of volume-based case thresholds for complex cancer surgeries by reporting risk-standardized mortality rates to be a superior metric of surgical quality compared to volume-based metrics [3,26]. Defining the complexity of surgical procedures will, therefore, be a helpful tool to meet the requirements of the precision medicine era [11,12,18,23,27].

This study has a few limitations. The overall numbers included herein may still be relatively small and concern only one sarcoma surgeon. However, considering the yearly surgical exposure proposed by MSTS or DKG [25,28], the numbers presented herein qualify for a high-volume surgeon as per definition. Furthermore, the data presented herein are considered a starting point which needs to be elaborated on, first to discuss the parameters and then to include data from many sarcoma surgeons globally. Because this RWDT-interoperable digital platform is web-based, any surgeon can store the personal information anonymously within this interoperable digital platform for free, which makes it possible to collect a vast spectrum of information.

5. Conclusions

The spectrum of sarcoma surgery not only is defined by surgical, technical, and biological skills but also critically depends on the integrated understanding of an orchestrated transdisciplinary treatment approach together with non-surgical disciplines. The multidisciplinary team meeting is an integral part of sarcoma surgery. If we aim at improving the quality of sarcoma patient care, it is time to move beyond assessing the raw numbers of surgeries performed. The definition of the quality ultimately assumes the comprehensive assessment of all important transdisciplinary parameters with the help of an interoperable digital platform. If the MDT is accepted as the key component for delivering high-quality care, such a platform has to reflect the interplay of disciplines, which then needs to be expelled as such to meet the precision medicine requirements. In a first step, global harmonization of data assessment on a large scale represents the prerequisite.

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Real-time interaktive Analyse der Behandlungs-Qualität von Sarkom-Patienten

Prof. Dr. med. et Dr sc. nat. Bruno Fuchs
Winterthur, Zürich

Sarkome sind bösartige Tumore des Binde- und Stützgewebes, machen lediglich ca. 1% aller Krebsformen aus, und gehören so zu den seltenen Erkrankungen. Molekular werden fast 200 verschiedene biologische Entitäten unterschieden, und die Behandlung erfolgt ausgesprochen transdisziplinär. Die Weiterentwicklung von neuen Therapieformen für Sarkom Patienten gestaltet sich als sehr schwierig, da es einerseits keine prospektiven, longitudinalen Datenerfassungen -und schon gar nicht in Echtzeit und durch den Patienten definierte Parameter- gibt, und weil diese in der Regel auch nicht transdisziplinär erfasst werden. Zudem müssen immer neue Herausforderungen gemeistert werden.

Abstract: Sarcomas are malignant tumors of the connective and supporting tissues, account for only about 1% of all cancers, and thus belong to the rare diseases. Molecularly, nearly 200 different biological entities are distinguished, and treatment is distinctly transdisciplinary. The further development of new forms of therapy for sarcoma patients is very difficult, because on the one hand there is no prospective, longitudinal data collection – and certainly not in real time and patient-defined parameters – and because these are usually not collected in a transdisciplinary manner. In addition, new challenges must always be mastered.

Key Words: Sarcoma, MDT, real-time/real-world data, predictive outcome analysis

Seit Januar 2020 müssen alle Krebsdiagnosen per Gesetz gemeldet werden, wofür aber keine einheitliche digitalisierte Lösung zur Erfassung von strukturierten Daten besteht. Zudem führte die Schweiz im April 2021 ein Gesetz zur Qualität und Wirtschaftlichkeit in der Medizin ein, obwohl die eigentliche Qualität noch nicht wirklich definiert ist. Darüber hinaus müssen wir uns immer grösseren Herausforderungen in unserem Gesundheitswesen stellen, wo die Kostenexplosion ungebremst zunimmt, und immer neue Sparmassnahmen definiert werden, ohne aber die effektiven Kosten abbilden zu können und dadurch der Spielraum der Akteure an der Front immer weiter eingeengt wird («Silo-Mentalität»).

Swiss Sarcoma Network (SSN)

Das SSN wurde vor 3 Jahren als Verein gegründet. Mitglieder sind die Institutionen, welche sich verpflichten, alle transdisziplinären Patienten prospektiv im wöchentlichen multidisziplinären Sarkom-Tumorboard (MDT-SB) vorzustellen und die Daten im Register zu teilen. Das definierte Ziel beabsichtigt die transparente Erfassung der Qualität der Behandlung von Sarkom Patienten. Grundsätzlich steht das SSN allen Institutionen offen, die zu dieser transparenten Qualitätserfassung bereit sind.

Um dies zu erreichen, werden die Prinzipien der value-based health care (VBHC) verfolgt. Strukturierte, klinisch-metrische Daten werden longitudinal über den gesamten Behandlungsablauf für jeden einzelnen Patienten erfasst.

Zur Beschreibung des Aufbaus sowie der Zielsetzung des SSN können die Qualitätsdimensionen nach Donabedian angewandt werden: Prozessqualität, Strukturqualität und Ergebnisqualität. Prozessqualität erfasst das SSN zum Beispiel dadurch, dass der Zeitpunkt dokumentiert wird, an welchem diagnostische Untersuchungen und therapeutische Schritte durchgeführt werden, um so zeitliche Prozesse abzubilden. Weitere Parameter der Prozessqualität, wie z.B. das Einhalten der Leitlinien während Sarkomboard Entscheiden, werden ebenfalls dokumentiert. Strukturqualität stellt das SSN allein schon durch seinen Aufbau sicher:

Das SSN besteht organisatorisch aus drei Hauptpfeilern: nebst dem wöchentlich stattfindenden MDT-SB ist das SwissSarcoma-Registry zu erwähnen, sowie die Forschung und Fort- und Weiterbildung. Letztere wird unter www.sarcoma.academy zusammengefasst. Hierbei werden monatlich internationale Webinars organisiert, in denen abwechslungsweise ein Hauptthema durch einen weltweit anerkannten Sarkomexperten vorgestellt wird, und Fallbesprechungen stattfinden mit einem internationalen Expertenpanel. Mittlerweile loggen sich jeweils Teilnehmer aus allen fünf Kontinenten ein.

Das SSN ist international eingebettet, einerseits durch das International Advisory Board bestehend aus 4 Exponenten, die das Netzwerk im Aufbau direkt beraten und für konkrete Patientenfragen aus dem MDT-SB direkt zur Verfügung stehen. Andererseits ist das SSN Mitglied von SELNET, einem Horizon2020 geförderten internationalen Sarkom-Netzwerk Programm. Dies integriert das SSN in die international vernetzte Grundlagen- und translationale Forschung. Im SwissSarcomaRegistry sind aktuell die Daten von knapp 4000 Patienten erfasst, was mit dem erwähnten Set-up exzellente Möglichkeiten für die Versorgungsforschung erlaubt.

Ergebnisqualität als letzte Kategorie der Donabedian Kriterien wird durch regelmässige systematische Erhebungen von Patienten berichteten Ergebnissen (PROMs) sowie Patienten berichteten Erfahrungen (PREMs) direkt vom Patienten, sowie durch Bestimmung von «harten» Qualitsindikatoren, wie z.B. Rezidivrate oder Überleben, sichergestellt. Da strukturierte Daten erfasst werden, wird es ebenfalls möglich sein, jedem diagnostischen und thera-

German Medical Award 2021 für das SwissSarcomaNetwork

Der German Medical Award wird seit 2015 jährlich vergeben und steht für die Medizin der Zukunft mit Schwerpunkt auf Qualität, Transparenz von optimalen Versorgungsleistungen sowie Digitalisierung im Gesundheitswesen. Das SwissSarcomaNetwork (www.swiss-sarcoma.net) wurde im Jahr 2021 mit diesem prestigeträchtigen Preis in der Kategorie «Medical Research» ausgezeichnet, in der das Projekt der real-time interaktiven Analyse der Behandlungs-Qualität von Sarkom Patienten vorgestellt wurde.

peutischen Schritt ein entsprechendes «Preisschild« zuzuordnen, wodurch die effektiven Kosten einer Sarkombehandlung ermittelt werden können.

Definition von Qualitätsindikatoren (QI) der Sarkombehandlung

Um die Qualität der Sarkom Behandlung überhaupt erfassen zu können, muss diese zuerst definiert werden. Das Internationale Advisory Board des SSN mit vier weltweit anerkannten Sarkomexperten (Jean-Yves Blay, Lyon; Axel LeCesne, Paris; Javier Martin-Broto, Madrid; Alessandro Gronchi, Milan) definierte zu diesem Zweck Qualitätsindikatoren für die Abklärung und Behandlung von Patienten mit Sarkom. Diese können in 6 Kategorien eingeteilt werden (Tab. 1):

TAB. 1 **Kategorien von Qualitätsindikatoren**

• Abklärung von Patienten mit Sarkomverdacht
• Management des MDT-SB
• Therapie (inkl. Chirurgie, Strahlentherapie, Chemotherapie)
• Komplexität der Sarkomtherapie
• Outcome (definiert durch den Arzt)
• PROMS / PREMS (definiert durch den Patienten)
Jede einzelne dieser Kategorien erhält bis zu 10 Subparameter, welche die Kategorie weiter definieren. Natürlich können diese Kategorien bei Bedarf flexibel erweitert und ergänzt werden.

Real-time and real-world (RTWD) Datenerfassung

Selbstverständlich kann eine solche Fülle von klinischen Parametern und komplexen Daten nicht mit herkömmlichen Methoden abgebildet und erfasst werden. Zudem stellt die «Datenexplosion» in der Medizin ein zunehmend ernstes Problem dar, dem wir uns stellen müssen. Die Herausforderung kann zusammengefasst werden mit den 5V's of big data, nämlich: Geschwindigkeit, Volumen, Variabilität, Korrektheit und Wertigkeit. Die zukünftige Herausforderung besteht darin, Daten nicht nur zu berichten, sondern durch analytische Verfahren neues Wissen zu generieren, welches in Zukunft einen Krankheitsverlauf oder sinnvolle Therapieentscheidungen für jeden einzelnen Patienten voraussagen kann. Dadurch kann eine deskriptive Analyse in eine prädiktive und präskriptive Analyse weiterentwickelt werden. Die Möglichkeiten der digitalen Transformation werden uns dies ermöglichen. Um in einem ersten Schritt RTWD zu generieren, entschloss sich das SSN, das SwissSarcomaRegistry mit dem MDT-SB zu koppeln. Somit kann der Moment, an dem sich alle Vertreter der Fachdisziplinen einmal wöchentlich austauschen und offene Fragen zur Abklärung und Behandlung der Sarkompatienten diskutieren, im Register festgehalten werden. Weiterhin erfolgt die Eingabe von Daten somit zeitgleich zum klinischen Ablauf und interdisziplinär.

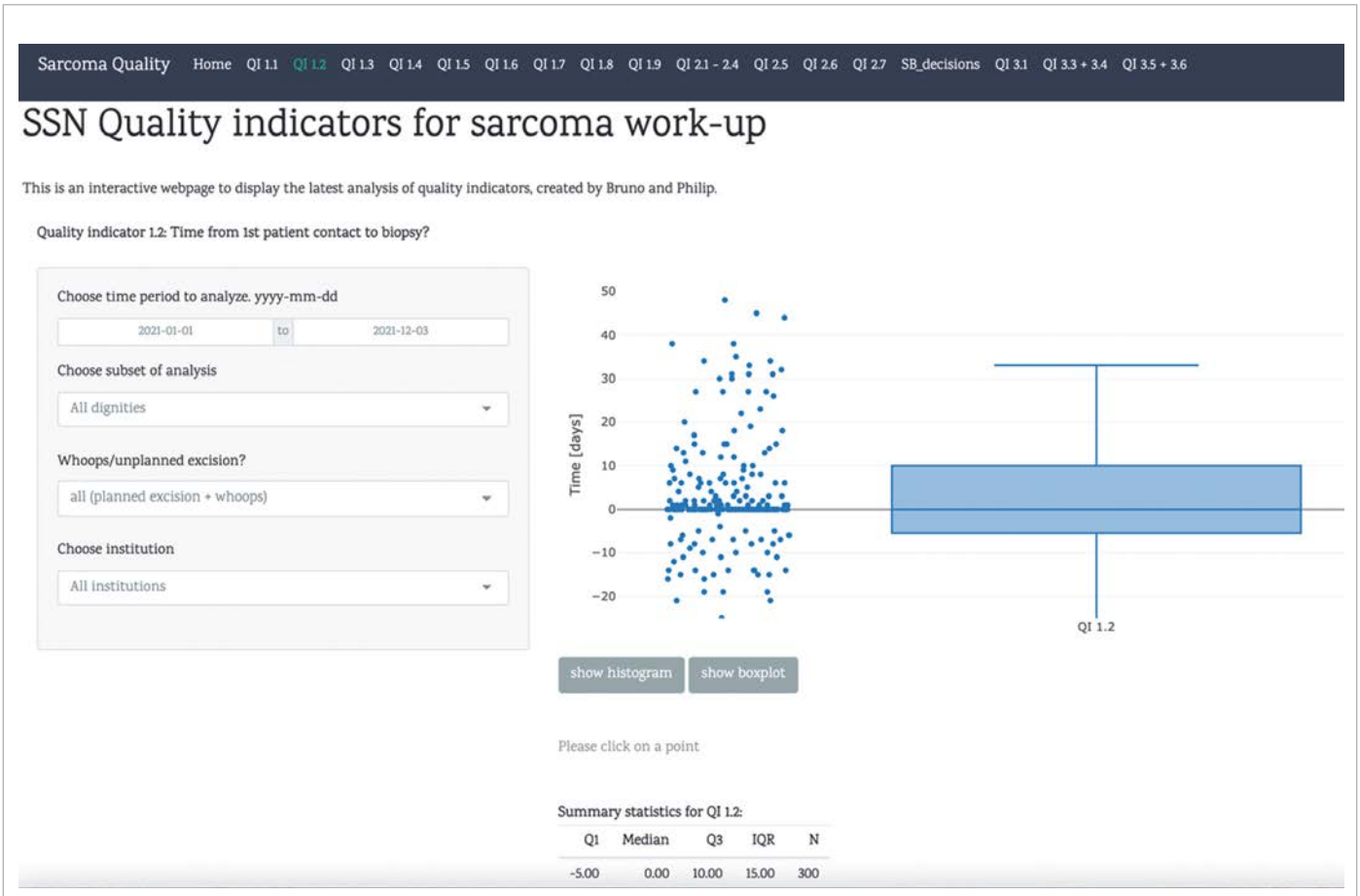

Abb. 1: Ein Auszug der IAW, auf der der QI Work-up «Zeit vom ersten Patienten Kontakt bis zur Biopsie?» dargestellt wird. Im Cockpit links können spezifische Parameter bestimmt werden, woraufhin sich rechts zeitgleich die Diagramm Analyse zeigt.

IT Platform und interaktive Frontside-Website

Eine integrierte IT-Plattform zur Erfassung von strukturierten Daten bildet die Grundvoraussetzung, um RTWD unabhängig von der Geografie und gleichzeitig aus mehreren Institutionen abzubilden. Das SSN kooperiert mit Adjumed Services Zurich, ein digitaler Anbieter mit jahrzehntelanger Erfahrung, der die Standards der Datensicherheit erfüllen und verantworten kann. Das AdjumedCollect bildet die Basis, aufgrund derer die Analysen auf einer interaktiven Website (IAW) abgebildet werden können. Unter einer IAW verstehen wir eine Website, auf der der Sarkom Experte eine Auswahl von definierten Parametern betreffend eines spezifischen Kollektivs frei wählen kann und sich die entsprechende Grafik der korrespondierenden Datenanalyse im Form eines Diagrammes sofort darstellt, mit direktem Zugang zu den Rohdaten zur Kontrolle und Überprüfung (Abb. 1).

Um die Korrektheit der Daten zu überprüfen, wurde eine IAW für fehlende Daten konstruiert. Damit können potentiell fehlende Daten sofort identifiziert und komplettiert werden. Das Herzstück bildet die IAW für die oben aufgeführten Qualitätsindikatoren. Hierbei können auf Knopfdruck deskriptive Analysen von Qualitätsindikatoren eines Kollektivs nach Zeitperiode, nach Dignität, Diagnose, anatomische Lokalisation, Erst- und follow-up Vorstellung, geplante versus ungeplante Resektionen sowie nach Institutionen dargestellt werden. Eine weitere IAW wird für die Kostenerfassung erstellt. Hierbei kann für jede Intervention und z.B. MDT-SB Vorstellung ein «Kostenschild» zugeordnet werden, wodurch die effektiven Kosten für die medizinische Leistung für jeden einzelnen Patienten über den gesamten Behandlungszyklus ermittelt werden können. Zudem wurde eine IAW für PROMS/PREMS erstellt, auf der aktuell insgesamt 9 Fragebogen digital erfasst sind und welche die Patienten z.B. vorgängig zu einer Konsultation auf einem iPad ausfüllen können. Mittlerweile verwenden wir diese routinemässig im Alltag und erfassen alle konsekutiven Patienten. Eine weitere IAW wurde aufgebaut, auf der ein Cockpit erlaubt, eine RTWD Darstellung der PROMS z.B. in Form eines Radar charts direkt zu visualisieren. Selbstverständlich sind alle diese Information mit den Daten des SwissSarcoma-Registry verknüpft, sodass eine holistische Analyse mit allen klinischen metrischen Parametern verknüpft erfolgen kann.

Erwartungen

Die konsekutive, transparente Erfassung eines kompletten Kollektivs von Sarkom Patienten in Form von strukturierten Daten von Qualitätsindikatoren longitudinal über den gesamten Behandlungsverlauf in Echtzeit eröffnet bisher unvorstellbare Möglichkeiten. Diese erlauben, die verschiedenen Abklärungs- und Behandlungsarten in absoluter Zahl zu erfassen, wodurch die Wertigkeit einer Therapie bezogen auf den einzelnen Patienten erstmals definiert und zudem finanziell in Relation zur Behandlungsqualität ausgewiesen werden kann. Dies wird nicht-optimale oder unnötige Behandlungen eliminieren und die Qualität der Behandlung zu definierten Kosten verbessern.

Strukturierte Daten der Behandlung von Sarkompatienten bilden die Grundlage für eine prädiktive Analyse. Mit Hilfe von Machine Learning Algorithmen sowie statistischen Methoden erlauben sie im Kollektiv grundsätzlich eine Aussage betreffend Prognose für einen einzelnen Patienten. Darüber hinaus wird es möglich sein, für jeden Einzelfall Analysen einzelner Therapieschritte zu generieren und aufgrund derer den bestmöglichen Therapieweg für den einzelnen Patienten gezielt auszuwählen. Darauf wird schlussendlich die personalisierte Medizin begründet werden können.

Prof. Dr. med. et Dr. sc. nat. Bruno Fuchs[1]
Philip Heesen[2]
[1]Professor, Orthopedic Oncology,
Sarcoma Service Chair, Swiss Sarcoma Network
Brauerstrasse 15, Postfach 834, 8401 Winterthur
fuchs@sarcoma.surgery
[2]Medizinstudent, Universität Zürich

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Literatur: auf Anfrage beim Verfasser.

Take-Home Message

- Eine RTWD-interaktive Analyse und Monitoring der Qualität der Behandlung von Sarkompatienten ist für alle zugänglich, die bereit sind, Daten zu teilen. Eine solche Datengrundlage bildet die Basis für prognostische und prädiktive Outcome Analysen, welche in naher Zukunft für Sarkompatienten die «precision medicine» Realität werden lässt.

Anmerkung des Chefredaktors

Im auch für seltene Tumorentitäten föderalen Schweizer Gesundheitssystem muss erwähnt werden, dass angestrebte nationale Zusammenschlüsse nicht immer vollständig gelingen. Im hier vorliegenden Fall ist es leider so. Dies erschwert gerade repräsentative Datenerfassungen. Der Vollständigkeit halber seien weitere überregionale Sarkom-Netzwerke für mögliche fachliche Vernetzungen erwähnt:

- Sarcoma Medical Exchange (wöchentlicher Austausch von medizinischen Onkologen und Onkologinnen)
- University Sarcoma Network
- SAKK Sarcoma Working Group

diagnostics

MDPI

Review

The Sarcoma-Specific Instrument to Longitudinally Assess Health-Related Outcomes of the Routine Care Cycle

Nasian Mosku [1], Philip Heesen [2], Salome Christen [3], Mario F. Scaglioni [3,4], Beata Bode [5], Gabriela Studer [3,4] and Bruno Fuchs [3,4,6,7,*,†] on behalf of the Swiss Sarcoma Network

1 Department of Plastic & Reconstructive Surgery, University of Grenoble, 38000 Grenoble, France
2 Department of Plastic & Reconstructive Surgery, University of Zurich, 8091 Zurich, Switzerland
3 Department of Health Sciences and Medicine, University of Lucerne, 6000 Lucerne, Switzerland; mario.scaglioni@luks.ch (M.F.S.)
4 University Teaching Hospital LUKS Lucerne Sarcoma Surgery, University of Lucerne, 6000 Lucerne, Switzerland
5 Patho Enge, University of Zurich, 8000 Zurich, Switzerland
6 Kantonsspital Winterthur (KSW), 8400 Winterthur, Switzerland
7 University Hospital Zurich (USZ), 8000 Zurich, Switzerland
* Correspondence: fuchs@sarcoma.surgery
† Collaborators of the Swiss Sarcoma Network are indicated in the Acknowledgments.

Abstract: Patient-based health related quality of life (HRQoL) measurements are associated with an improvement in quality of care and outcomes. For a complex disease such as sarcoma, there is no disease-specific questionnaire available which covers all clinically relevant dimensions. Herein, we report on the development of an electronically implemented, sarcoma-specific instrument to assess health-related outcomes, which encompasses a combination of generic questionnaires tailored to the respective disease and treatment status covering the entire longitudinal care cycle. An interoperable digital platform was designed to provide a node between patients and physicians and to integrate the sarcoma-specific HRQoL instrument with patient and physician-based quality indicators to allow longitudinal structured real-world-time data evidence analytics. This approach enables the prediction modeling of disease, and by attributing cost tags to quality indicators, treatment effectiveness for a given disease will be directly correlated with financial expenses, which may ultimately lead to a more sustainable healthcare system.

Keywords: sarcoma-specific HRQoL instrument (health-related quality of life); PROMs (patient reported outcome measurements); IELAS-RWTD/E (interoperable electronic longitudinal absolute structured real-world-time data/evidence); VBHC (value-based healthcare)

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1. Why Do We Need Patient Reported Outcome Measures (PROMs)?

Healthcare costs are constantly rising and impose great challenges [1]. Our healthcare system today is largely ignorant of incorporating treatment effectiveness and outcomes, and rising healthcare costs are leading us toward a wasteful and unsustainable trend [2].

Improving value in healthcare is meant to benefit patients, payers, providers and suppliers while increasing the economic sustainability of our healthcare system [3]. Therefore, there is a great need to improve patient-centered care [2] and to possibly redesign a novel healthcare ecosystem with particular focus on shared value [4]. Porter defined shared value as a multidimensional relationship between health outcomes and costs incurred to deliver these outcomes [3,5]. Obviously, there are differences in perceptions of value among patients and between patients and providers [6]. The definition of shared value in healthcare includes the clinical metrics as defined by the physicians as well as by the patients' voice as assessed by the quality of care. Considering the upcoming healthcare transition as projected for the next decade [7], the definition of quality of care becomes

pivotal because our current fee-for-service model will be replaced by a value-based on quality model. In such a model, PROMs are measures used to assess patients' health or quality of life and represent an integral part of patient-defined quality of care. They were introduced to assess treatment effectiveness and improve outcomes, and are meanwhile a pivotal part of value definition [8–14]. There are currently numerous PROMs to assess health-related quality of life (HRQoL). Specifically with regard to cancer, they were shown to be prognostic tools such as for outcome, for example in breast cancer, multiple myeloma, colon and lung cancers [15–18]. PROMs are generally used at the aggregate level for audit and benchmarking, real world evidence generation and as an input or predicted output for clinical tools and AI in health [11]. At an individual level, PROMs facilitate shared decision making, screen or monitor symptoms and provide timely care tailored to individual needs [11,12,19]. Meanwhile, however, it has become obvious that one single (as opposed to a multidimensional) PROM may not cover all aspects of health for a given disease at various timepoints. Further, the definition of which dimensions of disease are to be included is obviously critical. A real challenge to introduce PROMs is that today's healthcare personnel, including clinicians, are not formally trained to consider also the impacts of social determinants of health (SDOH) on health outcomes [17,20] while delivering care [21–23]. According to the County Health Rankings Model, SDOH, such as health behaviors, socioeconomic factors and physical environment, contribute to 80% of the clinical outcomes in a community. In contrast, clinical care contributes to the remaining 20% of clinical outcomes [21,24,25]. Clinicians rely heavily on biomarkers and diagnostic test results to guide their decision-making. Shared-decision making preference elicitation and documentation remain challenges in today's healthcare system, and preferences related to quality of life should be considered in treatment decision making [26]. To cover all healthcare dimensions, Khurana et al. developed a Whole Person Health Score (WPHS) that quantifies a person's health into six domains: physical health, emotional health, resource utilization, socioeconomics, ownerships, and nutrition and lifestyle [21]. The WPHS extends the physical health assessment by five more dimensions to cover all possible parameters impacting the course of a disease. Ideally, these six dimensions are represented when a HRQoL instrument is developed. An instrument covering all health dimensions for a given disease including the incorporation of the patients' view to define the shared value is of great importance to ultimately realize value-based healthcare (VBHC), which will be the base to create a sustainable healthcare system with cost control (Table 1). The question remains, however, how this is being realized specifically for sarcoma patients.

In this review, we first address the challenges of introducing PROMs in routine sarcoma patient care, to then, based on the literature, reason about the selection of which aspects need to be covered. In a further step, we describe a sarcoma-specific instrument which basically is composed of established PROMs. Last, we introduce the interoperable digital sarcoma platform which allows for simultaneous data assessment and its analysis.

Table 1. Summary of main challenges, bibliography included in this introduction and its added value.

Challenge	References	Added Value
Where do we want to go?	[8]	This article describes the transition from the current care to the future state of how our healthcare system will look like in 2030, specifically emphasizing the potential of digital transformation.
What is good health?	[18,21–26]	These articles define the social determinants of health and the delivery of care. Health behaviors, socioeconomic factors and physical environment contribute 80% to health outcomes, whereas clinical care only contributes the remaining 20% to clinical outcomes. For these reasons, the Whole Person Health Score was created.

Table 1. *Cont.*

Challenge	References	Added Value
What is the current problem?	[1,2,6,7,27]	Healthcare costs represent a seemingly unsurmountable problem, and lead us towards an unsustainable trend. While perceptions of value differ among patients and providers, shared decision-making regarding data assessment and documentation remain challenges specifically because most of the healthcare data are unstructured und therefore not ready for analysis.
Potential solutions?	[3–5]	Improving value benefits may lead to a sustainable health system. A novel ecosystem centers on the shared value being the multidimensional relationship between health outcomes and costs incurred to deliver these, as defined by the value-based healthcare principle. For these reasons, quality of care must be defined and assessed using structured data, to which then cost tags can be attributed which allows the definition of the entire costs of a given diagnosis over the entire care cycle.
Why are PROMS important?	[9–19]	These articles summarize how PROMS assess treatment effectiveness and outcome, and show that they can improve survival. PROMS have to be designed such that they cover the entire spectrum of the social determinants of health as suggested by WPHS but are nevertheless disease-specific.

2. Challenges to Introduce PROMs for Sarcoma Patients

Sarcomas represent an extremely heterogenous disease. While being rare or ultra-rare, they are composed of more than 175 distinct diagnostic entities, and occur at all possible anatomic sites of all age groups. Treatment is transdisciplinary, and while surgery is the mainstay of treatment, it is extremely complex because surgical techniques vary greatly from one anatomical site to others, and one surgeon nowadays is unable to cover the entire surgical spectrum of techniques at the required level [27]. Several disciplines together determine the successful outcome of the patients, and weekly multidisciplinary tumor board meetings have proven to be instrumental to achieve this [28–32]. While choosing a sarcoma instrument to define patient-defined quality of care, it cannot only focus on one single diagnostic or therapeutic aspect, but it must incorporate the sum of care provided by all disciplines because its success is determined by the sum of all treatments. As sarcoma patients need life-long follow-up for potential late effects associated with their disease, the assessment has to be designed longitudinally over the entire cycle of care, from the initial work-up of the patient, all types of treatment combinations, until last follow-up or death. If we want to assess the health of sarcoma patients using the WPHS framework, we need to assess a broad range of outcomes. There is already a multitude of PROMs for sarcoma patients available, both for assessing experience and outcomes of treatment [33–40]. Ideally, the information assessed through PROMs in sarcoma could be integrated in some overall sarcoma-specific instrument to define quality of care. The main prerequisites include the possibility of routine collection of data (as opposed to use in clinical trials only) as well as the allocation of PROMs that correspond to patients' clinical metrics such as anatomic location, diagnostic subtypes, type of therapies, age and gender as well as prognosis [36,37]. It currently remains an open question whether generic or cancer-specific questionnaires will push through [41]. Generic questionnaires alone (such as EQ-5D) may not specifically enough address the needs for a given disease at any given timepoint of the care cycle

such as sarcoma, while as opposed to a newly developed sarcoma-specific instrument, an established PRO may allow for cross-comparison among other diseases and benchmark comparisons to the standardized normal population.

3. Which PROMs Are Being Used for Sarcoma Patients?

In a scoping review, Almeida et al. mapped the reported PROMs in sarcoma patients from the available literature and how they were measured, focusing specifically on the nature, extension and reach of research related to PRO and what instruments were being used to assess these [33]. They stressed the importance that PROMs include multidimensional assessments of quality of life, that the evaluation be longitudinal, and that anatomic location should be instrumental to include. Although the assessment of different time points of the care cycle—with respect to different diagnostic procedures or treatments—would provide important information, the complexity of sarcoma as a disease may hinder such introduction and utilization of PROMs with common approaches. Almeida et al. therefore concluded that there must be a new and sarcoma-specific measurement strategy to mirror the quality of sarcoma care [33].

Martins et al. reported on the sarcoma measure (SAM) [34]. They defined 22 items reflecting physical, emotional, financial well-being as well as sexuality and coined the term "sanxiety" of sarcoma patients. The SAM is a patient reported experience measure that can be used in clinical practice for all patients irrespective of age, type of sarcoma or treatment status. Some criticize that it is impossible to have one sarcoma-specific measure that meets the needs of clinical practice, academia and industry [41]. Others put fourth that SAM is only an experience but no outcome measure [36,37].

Within the spectrum of mesenchymal tumors, there are diagnosis specific PROMs for desmoid patients. In the Profiles study, Schut et al. created a disease-specific, desmoid-type fibromatosis questionnaire (DTF-QoL) covering 173 questions (which takes up to one hour for the patient to fill out) and compares it to the well-established and generic EORTC-QLQ and EQ-5D questionnaires, which are currently under investigation. They foresee to use it longitudinally over the entire care cycle depending on their prospective findings upon the conclusion of their study [35,42].

Den Hollander et al. performed an exhaustive systematic literature review unravelling the heterogeneity of disease and sarcoma patients' health related quality of life [37], specifically focusing on the anatomic tumor location. They analyzed fifty-four different questionnaires, most often cancer-generic or generic HRQoL questionnaires. While they found that sarcoma patients in general reported lower HRQoL than the general population, they identified distinctive patterns with respect to symptoms, physical functioning, disability and psychosocial well-being depending on the tumor's location. They also found that other factors such as disease stage should be taken into account to prioritize patients' needs. These authors concluded that a sarcoma-specific strategy should be developed and used covering the heterogeneity of sarcoma, including anatomic location specific issues to improve personalized HRQoL assessment in clinical practice. As a follow-up on this, den Hollander et al. recently published a study protocol to develop a sarcoma specific instrument to develop a comprehensive list of HRQoL issues relevant to sarcoma patients, as well as a measurement strategy indicating which issues should be evaluated in certain subgroups [37]. While such an approach is extremely useful and will hopefully lead to customized measures, it will represent an entirely new instrument which cannot be cross-referenced with existing ones. Therefore, an alternative approach may include the introduction of a set of validated PROMs, which are already being used in many other cancer types and, importantly, for which there is most often information on the normal population available for comparison and benchmarking. These are designed to cover not only different dimensions of health, such as for example physical and mental health, but also the entire care cycle with customized measurements based on type of therapy performed and disease status. A sarcoma-specific instrument to cover the entire longitudinal care cycle using established PROMs would allow cross-referencing with patients with other

cancers as well as with the normal population, thereby greatly enhancing the establishment of quality standards and ultimately sustainable cost accounting in sarcoma care.

4. Sarcoma-Specific HRQoL-Instrument Based on Generic PROMs

The major challenge in defining a sarcoma-specific HRQoL instrument is the complexity of the disease itself and the respective multidisciplinary treatments at various timepoints, with greatly changing expectations from the patients' side over time depending on the disease status. In designing the sarcoma-specific HRQoL instrument, we addressed the following challenges: (1.) use of generic and well-established PROMs to allow benchmarking with other diseases as well as the normal population; (2.) to cover the main WDPS aspects such as physical and emotional health, resource utilization (which is specifically important in sarcoma patients with respect to rehabilitation), socioeconomic aspects, ownership, nutrition and health; (3.) longitudinal assessment from first time presentation until last follow-up or death; (4.) individualized assessment by assigning only PROMs relevant for treatment received as well as follow-up status (Table 2). The herein presented sarcoma-specific instrument includes a variety of PROMs for the baseline visit of the patient. It includes the disease specific physical (EQ-5D-5L) as well as the overall health (PROMIS Global-10; WHO-ECOG) questionnaires. For example, indicated pain level (disease specific) may not necessarily be caused by the soft tissue tumor at the forearm itself but by unrelated back pain (overall health related), which must be distinguished in the assessment. Emotional as well as socioeconomic factors are pivotal and are covered using specifically EQ-VAS, Brief Symptom Inventory (BSI-18) and the work ability index (WAI). As the biopsy is an invasive procedure, it has an important bearing on the patient and therefore must be addressed separately as well. We are currently developing a specific mesenchymal tumor biopsy PROM (MTBP) including 10 questions and this will be reported separately. Toronto Extremity Salvage scores (TESS) as well as Musculoskeletal Tumor Society (MSTS) scores were specifically designed for the extremities and are globally accepted and used. The Transatlantic Australasian Retroperitoneal Sarcoma Working Group (TARPSWG) is in the process of establishing a specific PROM for visceral sarcoma surgeries and will be included here. With respect to radiation therapy, there are two PROMs introduced which evaluate patient-reported symptomatic toxicity (Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) as well as the local effects by the patient (Local effects of radiation therapy). Medical oncologists often use the widely accepted HRQoL measure EORTC-QLQ30 specifically for randomized controlled trials. It provides a holistic overview and includes other well-established PROMs such as MDASI. Obviously, once the patient has completed the therapy and undergoes regular follow-up visits, different needs have to be addressed such as rehabilitation capacities. We are currently working on a synthesis of PROMs which bases on the presented PROMs herein, but with adapted weighting to address specifically emotional health, socio-economic factors, ownership and resource utilization such as rehabilitation capacities and potential.

This herein presented sarcoma-specific HRQoL instrument aims to address the specific needs and challenges of the sarcoma patient depending on disease status as well as type and time-point of therapy, or follow-up. This information will help to compare the different patients for a given time point or treatment type, but also to measure changes over time or effectiveness of new interventions for the individuum. Its design to assess the patient over the entire care cycle allows the personalized longitudinal assessment. Ideally, the patient receives the opportunity to monitor their own disease status and can objectively follow their own progress of disease development, which may enhance the transparent exchange with the physician.

Table 2. Sarcoma-specific HRQOL instrument: summary of established PROMs assigned at the different timepoints and for different treatment status.

Time Point of Assessment & Therapy Status	Type of PROM
Work-up at diagnosis Regular visits during therapy	WHO-ECOGPROMIS [43] EQ-VAS [44] EQ-5D-5L [45] BSI-18 [46] WAI [47]
Biopsy	Mesenchymal Tumor biopsy PROM * (MTBP)
Surgery	TESS (upper/lower extremity) [48] MSTS (upper/lower extremity) [49] Visceral (TARPSWG) *
Radiation Therapy	Local effects of therapy PRO-CTCAE
Chemotherapy	EORTC-QLQ-C30 [50,51]
Follow-up visits after completion of therapy	Combination of above

* in development; ROMS are assessed at each follow-up visit as suggested by Wilson et al. [52], Abbreviations: WHO-ECOG: World Health Organization–Eastern-Cooperative Oncology Group; PROMIS: Patient reported outcome measurement information system; EQ-VAS: EuroQuol Group visual analogue scale; BSI-18: Brief symptom inventory; TESS: Toronto extremity salvage score; MSTS: Musculoskeletal tumor society; TARPSWG: Transatlantic retroperitoneal sarcoma working group; PRO-CTCAE: Patient-reported outcomes Common terminology Criteria for adverse events; EORTC-QLQ-C30: European Organisation for Research and Treatment of Cancer—Core quality of life questionnaire.

5. Interoperable Digital Platform: Data Assessment and Analysis

The large volume of data produced in healthcare overall and also proposed herein to be assessed with the PROMs presents a major obstacle and threat to routine practice [53]. As a consequence, there is a seemingly unsurmountable threshold to introduce a set of PROMs into routine medical practice, being used at best under standardized conditions such as in randomized controlled trials, and to assess these data several times for the same patients over time. Data management is a tremendous challenge, but the advent of digital transformation may lead to the disruption of current practices and will revolutionize healthcare in the decade to come. There is still an ongoing debate on whether PROMs are being assessed on paper versus electronically; although, it has been shown that the latter far exceeds the potential disadvantages, and manual analysis of paper PROMs is not affordable anymore given the current overall labor shortage [9,54–56].

Given the complexity of sarcoma as an extremely heterogenous disease with complex transdisciplinary treatment interactions, there is ideally an interoperable digital platform which integrates all diagnostic and treatment relevant aspects of sarcoma care (Figure 1). As such, the data generated from PROMs assessment can be analyzed in the context of all clinically relevant parameters such as disease status, exact pathological diagnosis, anatomic location as well as treatment decisions at the weekly multidisciplinary tumor board. Further, it also allows automatically tailoring (and therefore decreasing the time spent to fill out a questionnaire) the specific questions of a given PROM to the patient's specific situation. For example, if the patient on the EQ-5D-5L has "no emotional constraints", then it will not be necessary to fill out also the BSI-18 to assess the specifics of emotional constraints. As such, by individualizing the questionnaire to the patient's need, it will be more attractive for the patient to spend more or less time to answer all the questions. Another advantage includes the generation of automatic alerts for the patient by the interoperable digital platform. Having integrated, for example, the date of surgery (or any other treatment aspect), the system can send an alert to the patient at predefined intervals to assess the respective PROM over time. The interoperable digital platform is able, based on the patients' answers, to prepare or generate individualized reports for the regular clinical outpatient or telemedicine visits. We foresee that such an interoperable digital platform is able to integrate all patient

related information (i.e., clinical, molecular, as well as economic parameters) as well as all stakeholders of patient care and to generate IELAS-RWTD/E [57,58]. Therefore, the implementation of PROMs has to be viewed as an integral part of patient care to generate robust data to optimize treatment decisions for the patient, but also to define quality of care, which ultimately is the prerequisite for value-based healthcare, paving the way to establishing a sustainable healthcare system. In a next step, together with all physician-based data of clinical metrics, such an interoperable digital platform allows the holistic analysis of all data dimension parameters, thereby allowing the generation of IELAS-RWTD evidence, which can be instantly analyzed and visualized on a protected interactive website. Ultimately, through machine learning algorithms, such a set-up allows predictive and prescriptive outcome analytics, which is the prerequisite for the upcoming precision medicine era (Figure 1).

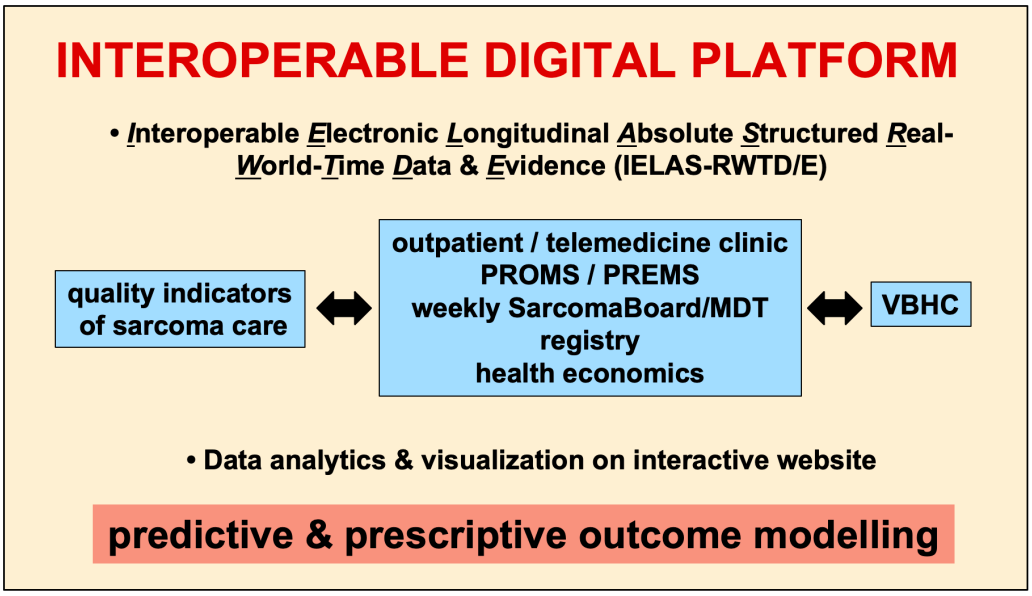

Figure 1. The interoperable digital platform integrates all available data of work-up, therapy and follow-up on the patient, based on quality indicators including the sarcoma-specific HRQOL instrument. It is the node of communication and exchange between patients and care providers of any level. It assesses and integrates routine, structured data in real-time of absolute and prospective patient numbers over time (IELAS-RWTD/E), which ultimately enables VBHC by attributing cost tags. The interoperable digital platform visualizes the descriptive data analytics on an interactive website, and ultimately allows predictive and prescriptive outcome modeling. PREMS: patient reported experience measures; MDT: multidisciplinary tumor board/Sarcoma Board.

6. Discussion

The patient's perception on quality of care and treatment effectiveness are meanwhile established predictors of outcome. The introduction of a sarcoma-specific HRQoL instrument therefore is indispensable, specifically for a complex disease requiring the interplay of multiple disciplines. The literature suggests that novel questionnaires be designed to better reflect the heterogeneity of sarcoma as a disease as well as its treatment because one single PROM does not cover all required needs.

Herein, an alternative approach to define a sarcoma-specific HRQoL instrument is presented using a sum of established generic PROMs which are assessed depending on the respective status of the longitudinal care cycle of the patient [8]. This approach allows comparison and benchmarking with other diseases and, importantly, with the normal population [59]. This is in contrast to the suggestion by Den Hollander et al. who develop an entirely novel sarcoma-specific questionnaire [37]. It will be very interesting to see which parameters this group will ultimately include in their questionnaire, and how it

will compare to the approach presented herein. Obviously, the implementation of this sarcoma-specific HRQoL faces some challenges. Both physicians and patients have to be trained for a novel ecosystem of data handling and assessment by on-site education during their outpatient visit. Similar to an iPhone use, the ease of self-explanatory handling of the program to enter the data does not really present a hurdle. Each patient (or telemedicine visit via a link) receives an iPad to enter the data and, if needed, receives instant support for program handling. Data themselves are stored and protected regarding ethical and legal issues, and only deanonymized data are used for exchange in the context of national and international comparisons, which is very important to scale globally and is also shown by others [60]. To achieve this, we have created the Sarcoma Academy to foster quality in sarcoma care by organizing monthly webinars (www.sarcoma.academy; accessed on 1 March 2023). The patient and their treating physician have access to their own data and represent the main contributors and also the main stakeholders. Once predictive modeling is realized, the results shall benefit the patient and his treatment.

In designing a sarcoma-specific HRQoL instrument, a holistic inclusion of all possible health dimensions is preferred. Ideally, it includes the entire longitudinal care cycle of routine care with the data dimensions as defined by WPHS, structured data which are instantly available for both patients and care providers, to ultimately achieve IELAS-RWTD/E analytics and precision outcome modeling [61]. Obviously, such a comprehensive amount of data cannot be handled with common approaches; a new ecosystem of data management is therefore required in healthcare. With the exciting opportunities created by digital transformation, the definition of different types of data will become increasingly important in the future. The interoperable digital platform is designed as a node for the integration of data generated from both the care providers, as well as the patients, to internationally exchange and scale to create evidence through analytics and, ultimately, knowledge. For this purpose, the interoperable digital platform presented herein allows *E*lectronic capturing of data which are *L*ongitudinal and prospective if they cover the entire care cycle, and *A*bsolute if they are all consecutive and not just a selection of patients is included. The assessment has to be designed so that all data will be *S*tructured instead of unstructured. *R*eal-*W*orld data refers to routine data assessment, and real-*T*ime refers to the instant availability of these *D*ata. The interoperable digital platform allows an automated analysis of these data, thereby creating *E*vidence. As such, it is designed to include all data dimensions as represented by IELAS-RWTD/E. Integrating all data dimensions of quality indicators of care from both the patients' and physicians' view sets the stage for an integral evidence analytics. Additionally, this in turn is the prerequisite for predictive modeling to individualize therapy in the future, thereby realizing precision care. Integrating the sarcoma-specific HRQoL instrument into an interoperable digital platform allows the analysis of each single parameter of the HRQoL instrument with clinical metrics such as specific type of diagnosis, anatomic localization and therapy aspects. It facilitates the coordinated exchange of information between patients and care providers to be transparently shared by both. The interoperable digital platform therefore provides not only information and knowledge for the physician but also for the patient. Such an interoperable digital platform can also be designed to be an integral part of an institutional electronic health record (EHR) system. It is foreseen that an EHR will be composed of many other disease specific interoperable digital platforms, as presented herein for sarcoma. In its entirety, such EHR is then able to not only provide information on the entirety of all medical care provided over the care cycle, but it also assesses the treatment effectiveness both from the physicians' and patients' perspectives with transparent real-time analytics. Further, attributing now a cost tag to each quantifiable structured data unit, the individual costs of treatment for a given disease can be determined longitudinally. This in turn allows the definition of shared value (which equals quality and outcome over costs of the entire longitudinal care cycle), as Porter et al. defined the concept of value-based healthcare [3,5].

In summary, a holistic approach in designing a sarcoma-specific HRQoL instrument includes the sum of multiple generic PROMs tailored to the specific steps of the entire

care cycle. While this, on the one hand, allows for comparison and benchmarking with other diseases as well as the normal population, the large data volume cannot be handled with standard approaches. A novel interoperable digital platform not only integrates both patient- and physician-based quality indicators but also allows IELAS-RWTD/E analytics, paving the way to precision medicine and value-based healthcare [62]. The holistic assessment of the health of sarcoma patients and survivors will contribute to tailoring care to patients' needs and, ultimately, improve health. Further, such an approach will be indispensable to associate treatment effectiveness with healthcare cost control, which is the prerequisite for a sustainable healthcare system.

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Article

Biopsy Ratio of Suspected to Confirmed Sarcoma Diagnosis

Nasian Mosku [1,2], Philip Heesen [2], Gabriela Studer [1,2], Beata Bode [2], Vito Spataro [2], Natalie D. Klass [2], Lars Kern [2], Mario F. Scaglioni [1,2] and Bruno Fuchs [1,2,*]

[1] Faculty of Medicine, University of Lucerne, 6000 Lucerne, Switzerland; nmosku45@gmail.com (N.M.); gabriela.studer@luks.ch (G.S.); mario.scaglioni@luks.ch (M.F.S.)
[2] Swiss Sarcoma Network, 6000 Lucerne, Switzerland; philip.heesen@uzh.ch (P.H.); beata.bode@patho.ch (B.B.); vito.spataro@hin.ch (V.S.); nataliedesiree.klaas@ksgr.ch (N.D.K.); lars.kern@ksw.ch (L.K.)
* Correspondence: fuchs@sarcoma.surgery; Tel.: +41-41-229-50-00

Simple Summary: Determining the biology of mesenchymal tumor, imaging alone is usually not enough, and the final diagnosis is established through tissue analysis If the indication to perform a biopsy is not established frequently enough, an undesired unplanned resection of a sarcoma may result, and conversely, a patient's discomfort as well as costs may increase. In here, using a real-world data registry of quality, we included the absolute number of a consecutive series of patients, to determine the prevalence of biopsies and its related diagnosis, to establish a reference, which may allow for the definition of a quality indicator for the work-up within a multidisciplinary team.

Abstract: The ratio of malignancy in suspicious soft tissue and bone neoplasms (RMST) has not been often addressed in the literature. However, this value is important to understand whether biopsies are performed too often, or not often enough, and may therefore serve as a quality indicator of work-up for a multidisciplinary team (MDT). A prerequisite for the RMST of an MDT is the assessment of absolute real-world data to avoid bias and to allow comparison among other MDTs. Analyzing 950 consecutive biopsies for sarcoma-suspected lesions over a 3.2-year period, 55% sarcomas were confirmed; 28% turned out to be benign mesenchymal tumors, and 17% non-mesenchymal tumors, respectively. Of these, 3.5% were metastases from other solid malignancies, 1.5% hematologic tumors and 13% sarcoma simulators, which most often were degenerative or inflammatory processes. The RMST for biopsied lipomatous lesions was 39%. The ratio of unplanned resections was 10% in this series. Reorganizing sarcoma work-up into integrating practice units (IPU) allows the assessment of real-world data with absolute values over the geography, thereby enabling the definition of quality indicators and addressing cost efficiency aspects of sarcoma care.

Keywords: sarcoma; biopsy; suspicion; confirmation; ratio

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1. Introduction

Sarcomas are malignant tumors of mesenchymal origin [1]. They account for 1% of all human cancers [2]. Sarcomas have an incidence of between 1 and 5 per 1,000,000 people [1], and are therefore considered a rare disease. Their diagnosis usually requires a high level of suspicion from the beginning of the correct and efficient work-up [3–5]. Once the diagnosis is established, not all suspicious lesions turn out to be malignant. According to Rowbotham et al. [6], who assessed all referrals to the sarcoma service in the UK, out of 49 patients who underwent biopsy with the suspicion of sarcoma, only 17 patients (35%) resulted with a malignant diagnosis, of which 13 (27%) were primary soft tissue sarcomas, 4 (8%) were soft tissue metastases (breast cancer, squamous cell carcinoma, colon carcinoma) and 32 (65%) were benign lesions (lipoma n = 19, posttraumatic lesions n = 5, vascular malformations n = 5, fibrous lesions n = 2 and nerve sheath tumor n = 1). In another study, Buvarp-Dyrop et al. [7] assessed the routes to diagnoses for suspected sarcoma in Denmark. Out of 545 patients, 102 (18.7%) were diagnosed as sarcoma and 68 (12.5%) as

other malignancies, of these the most frequent being: metastasis (n = 30), lymphoma (n = 23) and myeloma (n = 6). The remaining 375 (68.8%) were benign lesions, the most frequent being: lipoma (n = 60), reactive tissue changes (n = 46), and schwannoma/neurofibroma (n =23). In another study made in the Rhone-Alpes region in France (Lurkin et al. 2010) [8], to evaluate the concordance between initial diagnosis and central pathology review for sarcoma cases, out of 366 patients diagnosed with sarcoma over a period of 1 year, 199 (54%) had full concordance between primary diagnosis (first pathologist) and second opinion (expert center pathologist), 97 (27%) had partial concordance (identical diagnosis of conjunctive tumor, but different grade or subtype), and 70 (19%) had complete discordance (different histological type or invalidation of the diagnosis of sarcoma). Another study (Gassert, F.G et al.) [9] analyzed retrospectively the histopathologic findings of 1753 patients presenting with a soft tissue lesion $\leq$5 cm. They found that 22.4% of these lesions were malignant.

The information about the relation between clinical suspicion of malignancy and the definitive histopathologic confirmation of sarcoma is important, because not all suspected sarcoma will ultimately be confirmed as such, but nevertheless absorb logistical and manpower capacities within the sarcoma work-up, besides causing inconveniences to the patients [10–12]. As long as the absolute number of biopsies for sarcoma suspicion as well as RMST are not defined, it will be impossible to determine whether too many or too few biopsies within an MDT actually are performed, and what for [13,14]. This may be particularly important in order to possibly understand the often frustratingly high rate of unplanned resections and potentially redefine the process of work-up of patients with mesenchymal tumors.

For these reasons, we are specifically asking the following questions:

(1). How many consecutive biopsies were performed with the suspicion of sarcoma over a 3.2-year period (January 2018–March 2021) in our network?
(2). How often was the suspicion of sarcoma confirmed as sarcoma?
(3). What types of non-sarcoma lesions, so-called sarcoma simulators, were diagnosed?

2. Materials and Methods

Reorganizing the MDT into an integrated practice unit over the geography (IPU) [15], the Swiss Sarcoma Network (www.swiss-sarcoma.net, accessed on 23 February 2022, has established a prospective, real-world shared data sarcoma registry of quality, including the full longitudinal care cycle of patients over time. This registry focuses on the longitudinal assessment of the quality indicators of sarcoma care, with the aim of exchanging transdisciplinary and transparently sarcoma therapy relevant absolute data and of defining quality scores for sarcoma treatment [16].

All prospectively collected data from 1 January 2018 to March 2021 were included in this study for analysis. The data are stored with Adjumed and analyzed with the Adjumed Analyze tool (Adjumed Services AG, Zurich, Switzerland; www.adjumed.ch, accessed on 10 March 2022), which can be used for basic/descriptive statistics (such as combinations of parameters, and the extraction of data), as well as R statistical program (version 4.1.0). In this study, we have used the descriptive summary statistics and the two-sample differences tests.

All consecutive patients who have undergone a biopsy of any type to work up a suspicious mesenchymal mass during the indicated time period, independent of its anatomic location, and presented to the multidisciplinary team meeting/sarcoma board, were included in this study (https://swiss-sarcoma.net/pdf/GCP_1_minimal_workup_requirements.pdf, accessed on 17 January 2022).

Core biopsy is considered standard in this series; ultrasound-guided biopsy was applied for soft tissue tumors, and CT-guided biopsy was usually used with bone tumors. Excisional biopsies were performed when the non-lipomatous lesions were small (>2 cm) and epifascially located. Incisional biopsies were only indicated in exceptions. The diagnostic yield of the biopsies was >93%; for this analysis, only the first diagnostic biopsy per patient was included. In a study done in 2019 [3] to evaluate the diagnostic yield of the

core biopsy in soft tissue lesions of the extremities, Qi, D. et al. [3] found a diagnostic yield of 96%.

All tissue specimens were assessed by a sarcoma reference pathologist according to the World Health Organization (WHO) classification of mesenchymal tumors and defined as benign, intermediate and malignant mesenchymal tumors, hematologic malignancy, metastasis and sarcoma simulators [11].

3. Results

3.1. Biopsies of Mesenchymal Tumors Performed over a 3.2-Year Period

Overall, 950 biopsies with the suspicion of sarcoma were performed during the study period. The biopsy specimens were collected from 950 different patients during the abovementioned time period. The type of biopsy was categorized into ultrasound (musculosceletic and visceral lesions), fluoroscopic (bone lesions) or CT-guided (thoracic, abdominal, pelvic lesions) core biopsy, fine needle aspiration, incisional and excisional biopsies [17,18], each separated into with or without (so-called whoops surgeries) suspicion of sarcoma (Table 1). In our study, sarcoma was confirmed in 62% of excisional biopsies, 57% in core biopsies, 53% in incisional biopsies and 48% in fine needle aspirations. The total amount of unplanned resections, i.e., so-called "whoops" surgeries, was 10% (21 incisional and 75 excisional biopsies without sarcoma suspicion) (Table 2).

Table 1. Classification of mesenchymal biopsies.

Suspicion of Sarcoma	Confirmed Sarcoma	Malignant
		Intermediate
	Benign Mesenchymal Tumors	
	Lesions other than Mesenchymal Tumor	Metastasis
		Hematologic Tumors
		Sarcoma Simulators

Table 2. Types of biopsies performed; n = 950.

	Types of Biopsies	No./% of Cases	No./% of Confirmed Sarcoma
1	Core Biopsy	409/43%	542/57%
2	Fine Needle Aspiration	130/14%	456/48%
3	Incisional Biopsy with suspicion of sarcoma	110/11%	504/53%
4	Excisional Biopsy with suspicion of sarcoma	90/10%	589/62%
5	Incisional Biopsy without suspicion of sarcoma	136/14%	Not Applicable
6	Excisional Biopsy without suspicion of sarcoma	75/8%	Not Applicable

The study found also similar RMST according to anatomic body regions. This ratio was 63% in the head and neck region, 61% in the trunk, 49% in the lower extremity and 47% in the upper extremity (Table 3).

Table 1 describes the 3 groups that resulted from the 950 biopsies and the subgroups for each of them.

Table 2 describes the types of biopsies performed and their respective percentages.

Table 3 describes differences in the RMST according to anatomic body regions.

Table 3. RMST according to anatomic region.

Anatomic Regions Sarcoma Diagnosed	No./RMST
Head and Neck	598/63%
Trunk	579/61%
Upper Extremity	447/47%
Lower Extremity	466/49%

3.2. Types of Tumors Identified through Biopsy

Overall, 55% (n = 522) of tumors were confirmed as sarcomas and, consequently, 45% (n = 428) of all biopsies turned out not to be sarcoma. Of the latter, 28% (n = 259) were benign lesions, and 17% (n = 169) were sarcoma simulators. Hence, the RMST was 0.55. Specifically, the final diagnoses included malignant (358; 38%) and intermediate mesenchymal tumors (164; 17%), benign mesenchymal tumors (259; 28%), metastasis (34; 3.5%), hematologic tumors (14; 1.5%) and sarcoma simulators (121; 13%) (Figures 1–3).

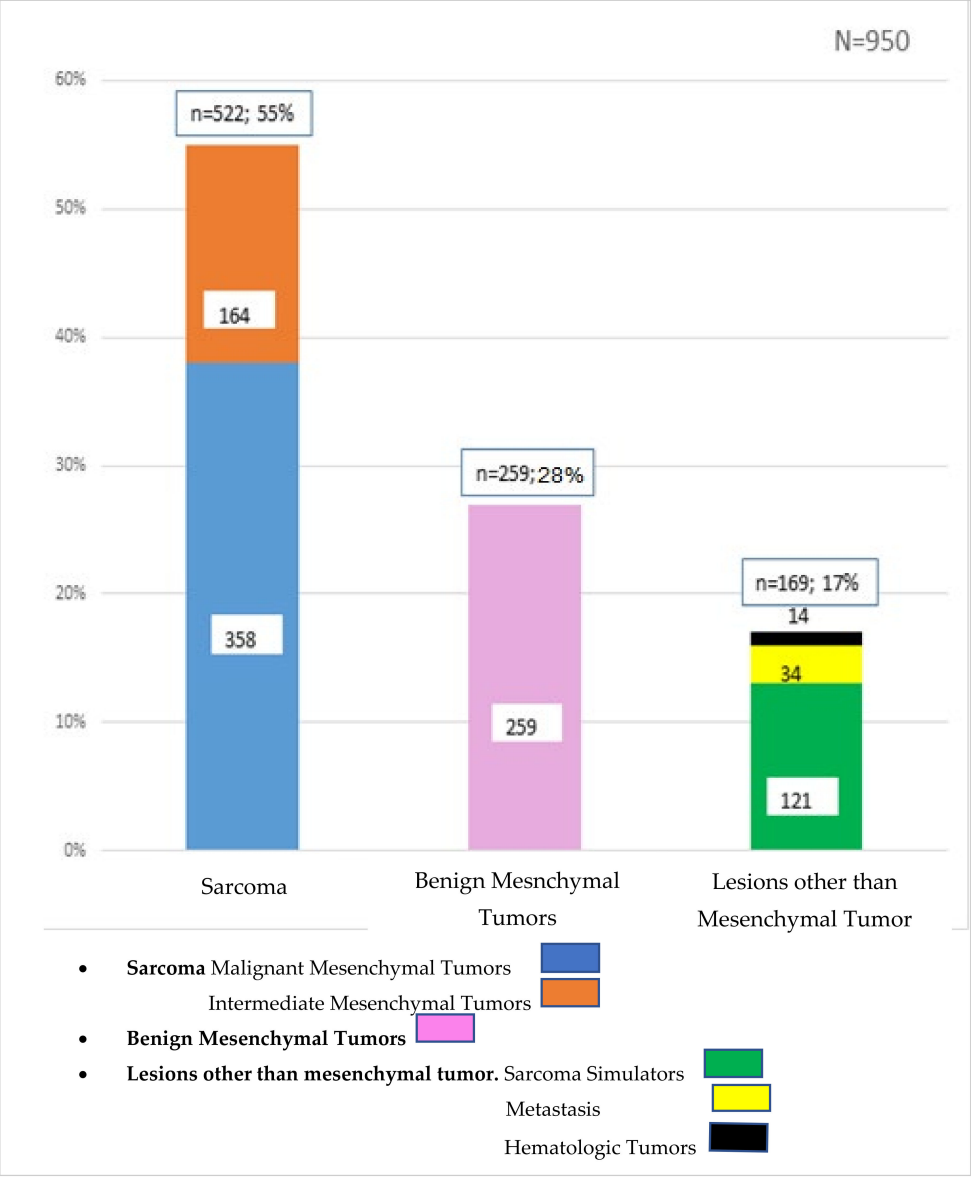

Figure 1. Types of lesions after biopsy.

Figure 2. List of benign mesenchymal tumors.

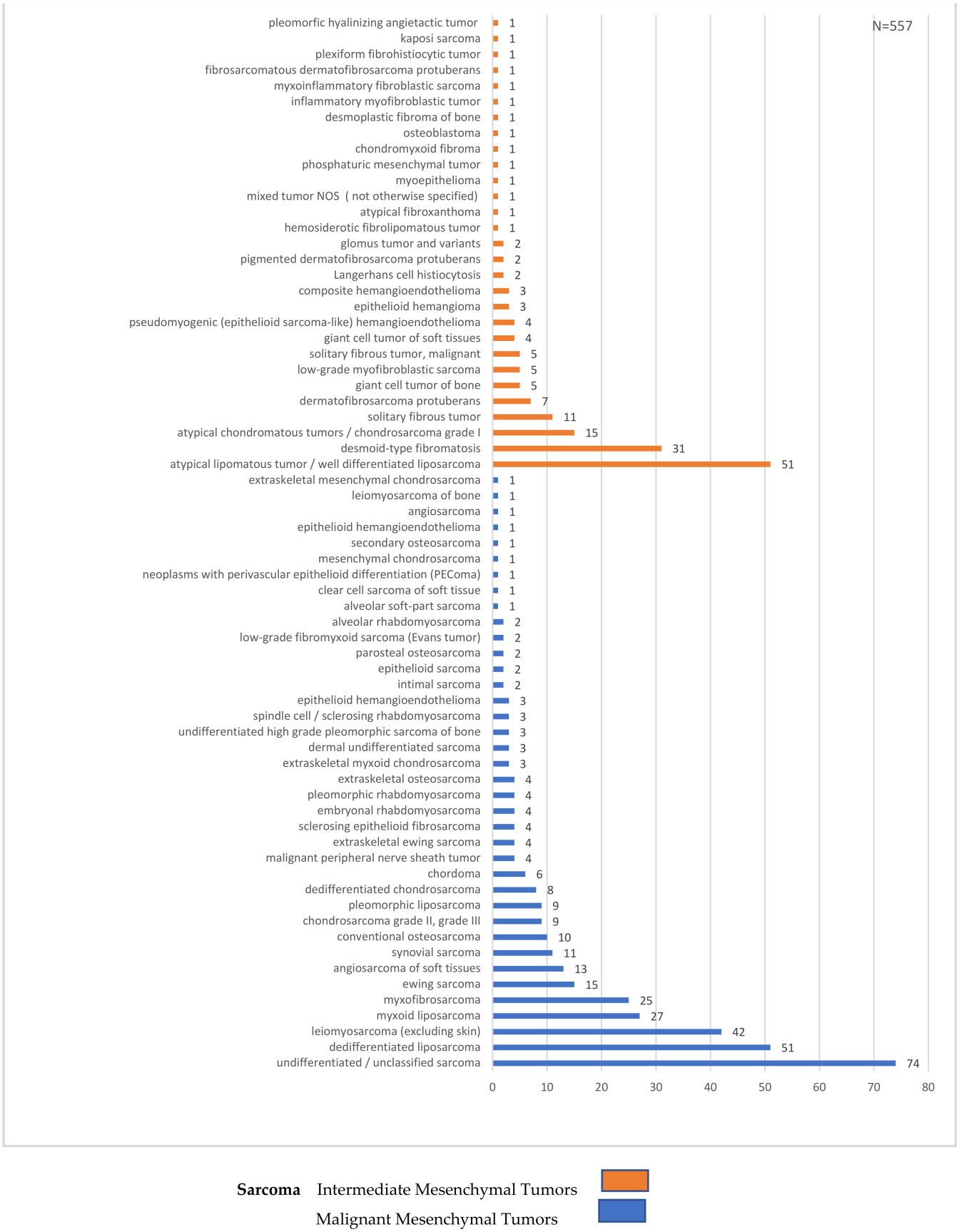

Figure 3. Histological types of sarcoma diagnoses.

3.3. Types of Sarcoma Simulators

Among the diagnoses other than mesenchymal tumors, 20% (n = 34) were metastasis, 8% (n = 14) were hematologic cancers, and 72% (n = 121) were sarcoma simulators.

Sarcoma simulators included 22 different types of lesions, the most common being inflammatory processes of soft tissues (15; 9%), degenerative processes of bones (14; 8%), granulomatous processes of soft tissues (11; 7%), pathologic fractures (9; 5%), hyperplastic granulation tissue (9; 5%), rheumatoid knots (9; 5%), epidermoid cysts (8; 5%), bone infarct (8; 5%) and periprosthetic inflammations (6; 4%) (Figure 4).

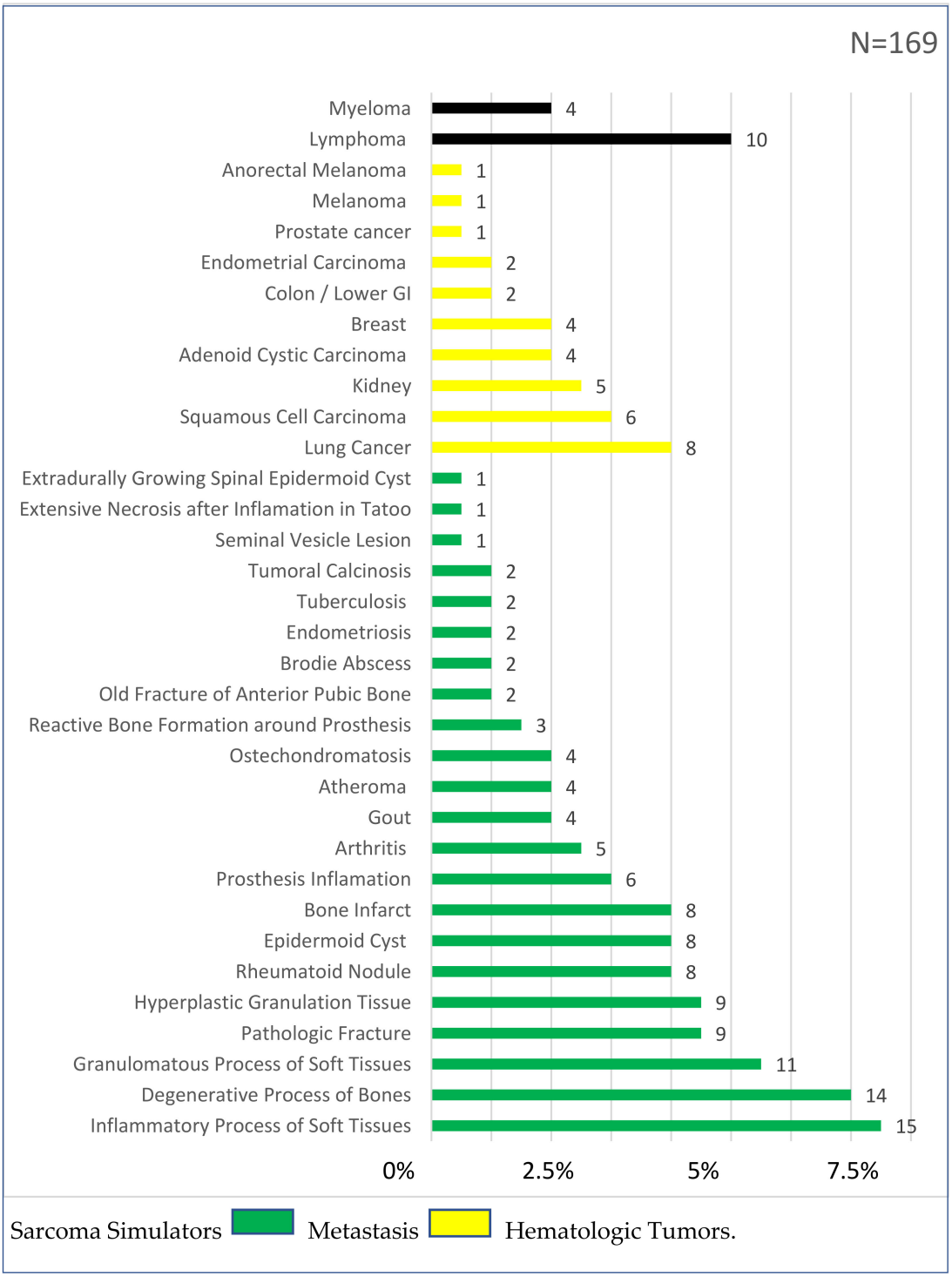

Figure 4. Types of lesions other than mesenchymal tumors.

4. Discussion

This study analyzed 950 consecutive biopsies which were performed for sarcoma suspicion over a 3.2-year period. Of these, 10% were unplanned "whoops" resections. Of all biopsies, 83% were mesenchymal tumors and only 55% ultimately proved to be sarcomas. Of the non-mesenchymal tumors, 4% were other malignancies and 13% were sarcoma simulators with a wide variety of pathologies. Overall, the RMST in this series was 0.55.

There is only sparse information in the literature to include the analysis of a consecutive series of biopsies for mesenchymal tumor suspicions, and there is no analysis of sarcoma simulators specifically reported [19]. The largest study on the analysis of biopsies included 545 patients from Denmark and reported a rate of confirmed sarcoma diagnosis of only 19% (RMST 0.19), which is in contrast to the 55% (RMST 0.55) in this series [7]. The other study made in the Rhone-Alpes region in France, with 366 patients, reported a rate of 54% concordance between primary diagnosis and expert center definitive diagnosis [8]. One reason for this discrepancy may be explained by the lack of accepted defined categories to analyze and compare biopsy results. In addition, RMST depends on a multitude of other parameters. Such discrepancy in establishing the sarcoma diagnosis, however, evidences an unmet need in the work-up of sarcoma patients [9]. It may be helpful to agree on a common definition as to how to analyze biopsies to allow the comparison among multidisciplinary teams (MDTs). We believe that separating mesenchymal tumors (to define intermediate and malignant versus benign lesions) from non-mesenchymal tumors may be helpful [3] (Table 1). The latter category includes hematologic tumors as well as metastases from carcinomas, leaving a group with so-called sarcoma simulators [4]. In our MDT, for example, all subfascially located lipomatous lesions are biopsied, resulting in 114 mdm2-negative tumors and 51 atypical lipomatous tumors in our series, rendering an RMST for lipomatous lesions of 0.39 (39%). A comparison of RMST among various MDTs will be important to define a minimal percentage of conducted biopsies of lipomatous lesions for quality purposes [20]. In this context, it can also be speculated that there may be a minimal amount of sarcoma diagnosis established per diagnostic unit overall. This may reveal, for a respective MDT, whether patients undergo biopsies too frequently, or in contrast, not frequently enough, which conversely is indicated by the number of unplanned ("whoops") resections [5]. Assessing the RMST of an MDT may serve as a quality indicator and ultimately also help to lower the unsatisfactory rate of unplanned resections [21].

The rate of unplanned resections has remained unchanged over decades [16,22], and the introduction of MDT per se may not have influenced this number either. There is currently no obvious strategy to address this issue. According to Abellan, J.F. et al. (2009) [19], in the 1990s, between 19% and 53% of the new patients seen in sarcoma centers were referred after an inadequate initial excision or whoops procedure. Another study (Pretell-Mazzini, J.) [14] pointed out that unplanned excisions of sarcoma occur in up to 50% of all patients with soft-tissue sarcoma. According to Zaidi, M.Y. et al. [16], considering the rarity of soft tissue sarcoma (STS) on the one hand, and the prevalence of benign soft tissue masses on the other hand, up to 50% of patients with STS will undergo a non-oncologic, unplanned excision for a mass initially presumed to be benign.

In this current report, the rate of unplanned resections was 10%, which is lower compared to the reports in the literature, and also lower compared to the rate of our own series before our prospective real-world shared data registry on quality was introduced. Obviously, the lower number in this report is explained by the inclusion of the total number of all biopsies, i.e., including all benign lesions (extrapolated on malignant tumors only, the rate of whoops surgeries was similar to international observations of 20%). On the other hand, based on a value-based geography model (VBGM) of care [23], the MDT herein represents multiple institutions and is therefore responsible for an entire region and not only for a single institution, thereby reaching all frontline care providers over a large geographic area.

When a biopsy for a tumor of the connective tissues is considered, the intention is to either confirm or exclude a sarcoma [24]. To the best of the authors' knowledge, there is no detailed analysis of lesions which turned out to be non-mesenchymal tumors, which in this series totaled 17%. The majority of these were so-called sarcoma simulators, defined as benign lesions mimicking sarcomas clinically or on imaging. They comprise 13% of all biopsies performed and include mainly degenerative and inflammatory diagnoses, as illustrated in Figure 1. Whereas it is important to avoid unnecessary biopsies (to lower costs and potential complications) [25], the risk to not detect all sarcoma diagnoses has to be kept as low as possible. Assessing the sarcoma simulators of other MDTs will be instrumental to define a minimal RMST threshold, as a quality indicator of an MDT. Such information is also valuable to establish integrated practice units (IPU), to include the supra-regional work-up of potential sarcoma patients in the context of VBGM. For example, in dedicating resources, the hospital management must understand that of all lesions being worked up, only half of all patients ultimately need sarcoma care. On the other hand, such supra-regional IPU work-up units are considered the entry gate, allowing the assessment of the absolute number of patients, which is the base for real-world data. The VBGM of care creates new incentives and is associated with a transformation of healthcare delivery, to create a novel ecosystem. A prerequisite for such transformation of healthcare delivery, however, is the assessment of absolute patient numbers and respective interventions [26]. We therefore speculate that such novel ecosystem of care delivery, together with measuring the outcome using RMST, may reduce the rate of unplanned whoops resections.

There are some limitations of this study to be considered. Although the total number of biopsies is sizable, it remains unclear whether a larger cohort of patients may affect the results differently. It has to be taken into account that such analysis may vary from institution to institution, and from one healthcare system to another of respective countries [27]. The numbers for one single MDT presented herein, therefore, cannot be directly compared with other MDTs unless they are consecutive and represent absolute or real-world data (RWD) values. In order to define the ratio of suspected/confirmed sarcoma as a quality indicator, several MDTs would need to assess their own ratio for comparison and define a standard. Based on the absolute numbers, our study revealed some variations in RMST, both with respect for type of biopsy performed and anatomic regions. However, because of the sample bias, a superiority of one method over the other cannot be concluded in order to choose a type of biopsy, and may therefore not alter current practice of using core biopsy as standard of care [28].

To the best of the authors' knowledge, this is the first study which focuses specifically on the ratio between sarcoma suspicion and ultimate sarcoma confirmation, with detailed analysis of sarcoma simulators. Assessing the absolute number of patients as RWD helps to define RMST, which may serve as a potential quality indicator of sarcoma work-up [29]. It may reduce the "scotoma" for unplanned "whoops" resections, which is considered an indicator of underestimation of the true number of sarcoma patients. On the other hand, infrastructure and personnel need to be dedicated to establish supra-regional sarcoma work-up units/IPUs to address and include absolute real-world data, thereby creating a novel ecosystem with a refined work-up approach [30]. This will ultimately allow sharing the experience between sarcoma networks independent of the geography.

5. Conclusions

The ratio of sarcoma suspicion to sarcoma confirmation is an important concept in the management of sarcoma patients. It is a quality indicator of the sarcoma work-up and may be a predictor for the cost efficiency of the care given to these patients. This ratio can be applied to all sarcoma MDTs, to increase the detection of sarcoma without increasing the number of unnecessary biopsies.

6. Patents

The results of this work and the new quality indicators that it has established are possessions of the Swiss Sarcoma Network.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: https://www.swiss-sarcoma.net/ (accessed on 23 February 2022).

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