Prevalence of Soft Tissue Sarcoma (STS) Subtypes in the US and Risk of Metastases at Diagnosis and Survival Outcomes.

Jerome F Sah[1] and Phil Wakefield[2]

[1]Inizio Medical, Yardley, PA, USA; [2]Inizio Medical, London, UK

Executive Summary

Soft tissue sarcomas (STS) are a rare and diverse group of cancers that develop from non-epithelial tissues including muscle, fat, nerves, blood vessels, and other connective tissues and encompass a wide array of subtypes. This White Paper explores the prevalence of various STS subtypes, their associated risk of metastases at first diagnosis, and the impact of metastases at first diagnosis on overall survival outcomes. The data presented are pivotal for healthcare professionals and researchers in strengthening the understanding of the distribution and outcomes of STS subtypes, guiding future research and resource allocation, and improving the efficacy of benchmarking and patient selection in single-arm clinical trials.

I. Introduction

Soft tissue sarcomas are rare malignancies that can occur throughout the body. **Due to their rarity and heterogeneity, data describing STS prevalence and the risk of metastases and survival outcomes across the various subtypes are sparse. Understanding these parameters is necessary to better identify the unmet need and provide meaningful benchmarking of clinical efficacy within this group of cancers.** In the United States, the Surveillance, Epidemiology, and End Results Program (SEER), in collaboration with the National Cancer Institute, maintains curated and anonymized databases on various cancers, including aspects of subject demographics, disease characteristics, treatment, and survival outcomes. We therefore queried the SEER data to evaluate the prevalence of various STS subtypes in the United States, the risk of presenting with metastases at the time of diagnosis, and the impact of metastases on survival.

II. Methods

Data from SEER17 were queried using SEER*Stat (ver 8.4.3). Records were limited to post-2010 (the year SEER began recording metastases at initial diagnosis) and to adults aged 20+ years. Records for which the STS subtype (AYA site recode) was recorded as ‘Kaposi sarcoma’ were excluded because if their distinct etiology. The SEER 17 registry covers approximately 26% of the US population. Record fields included in the analyses were age bands, race, STS subtype, presence of metastases at diagnosis, and survival in months.

Data were summarized descriptively using Excel and Data Analyst (OpenAI).

III. Results

a. Data Overview

After restricting data to adults ages 20+ years, data was available for 29 225 individuals with STS. 'Other' STS types represent the largest category, indicating a diverse array of less common sarcomas not individually listed. **Liposarcoma appears as the most common individual subtype, with 5932 patients accounting for a significant proportion (20.3%) of the cases. The 3 most common STS subtypes were liposarcoma, leiomyosarcoma, and giant cell sarcoma, accounting for >40% of all cases (Figure 1).**

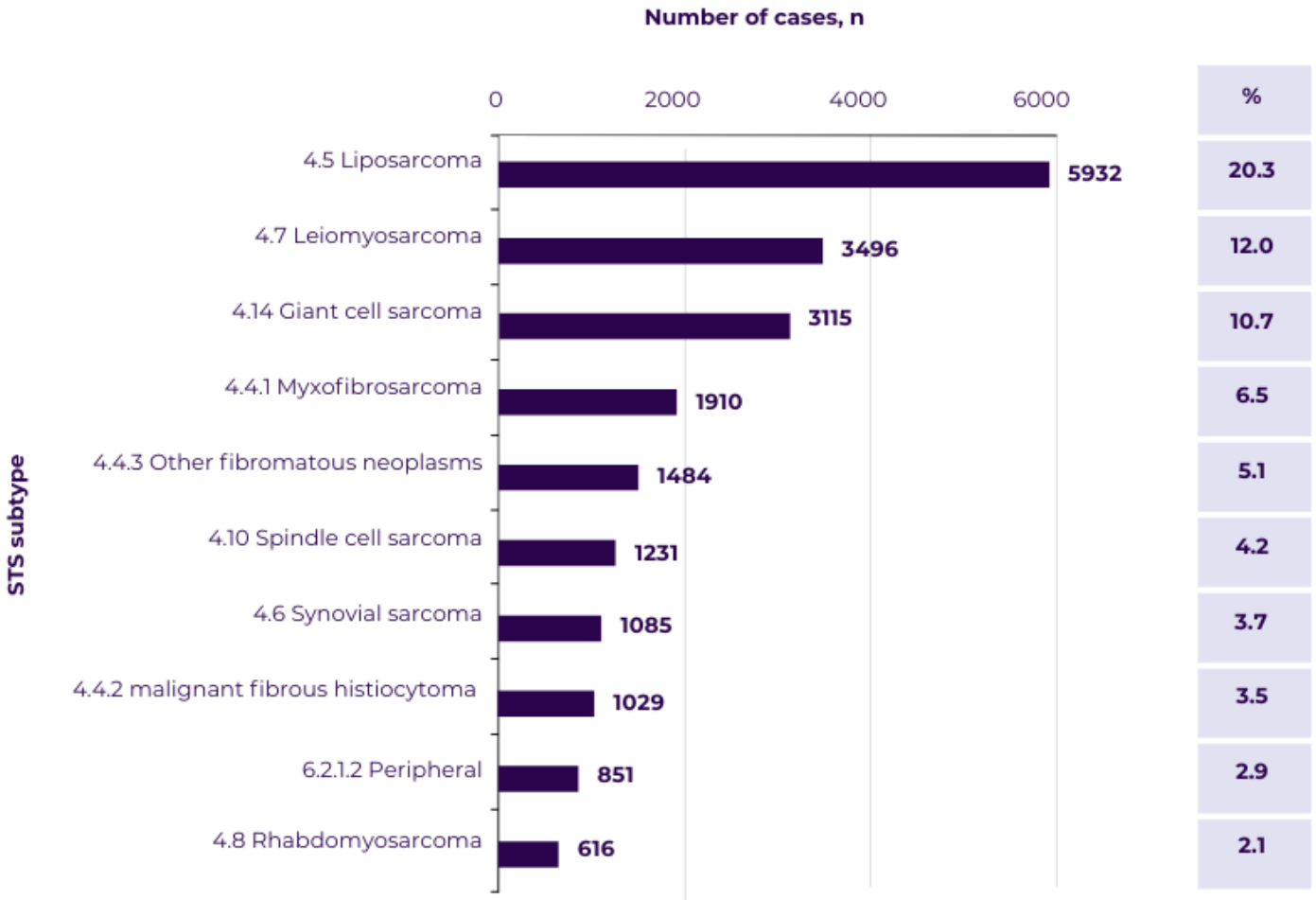


Figure 1. Top 10 STS Subtypes Excluding 'Other' (SEER 17 | 2011–2020)

b. Patient Demographics and Prevalence

Distribution of STS subtype by race did not show any apparent anomalies except in the case of "Other fibromatous neoplasms," which appeared to disproportionately affect Black patients (accounting for 22.6% of all cases, compared with a range of ~7%–10% of cases for all other STS subtypes).

More than 40% of patients received a diagnosis of STS between the ages of 55 and 74 years (**Figure 2**).

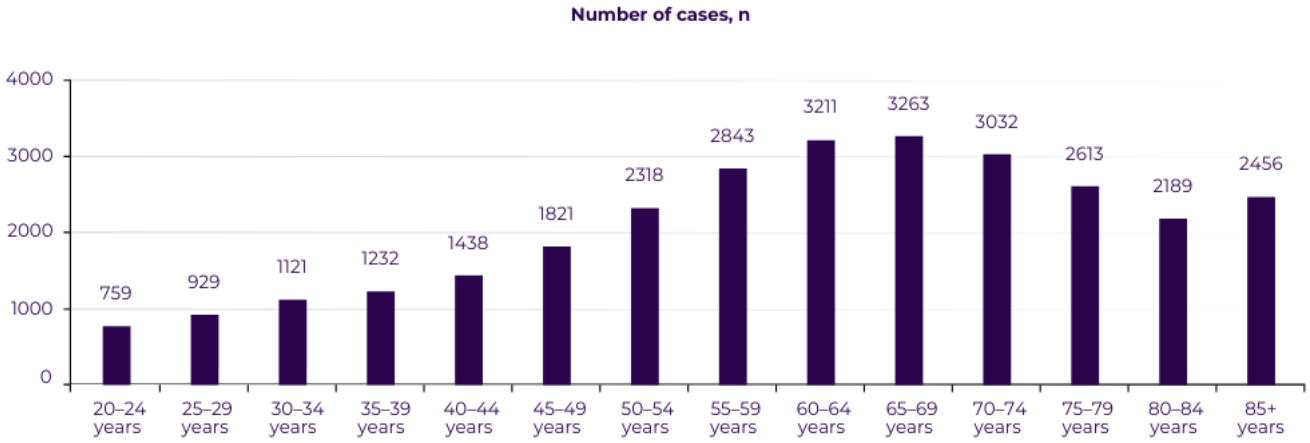


Figure 2. STS Diagnosis By Age Bands (SEER 17 | 2011–2020)

c. Risk of Metastases

The risk of metastases at diagnosis was evaluated as a percentage for each STS subtype. **Rhabdomyosarcoma was associated with the highest risk of metastases, at 29.1%, while leiomyosarcoma accounted for the most cases of metastases at diagnosis (excluding 'Other')**. In contrast, other fibromatous neoplasms have the lowest risk at 2.1% (**Table 1**).

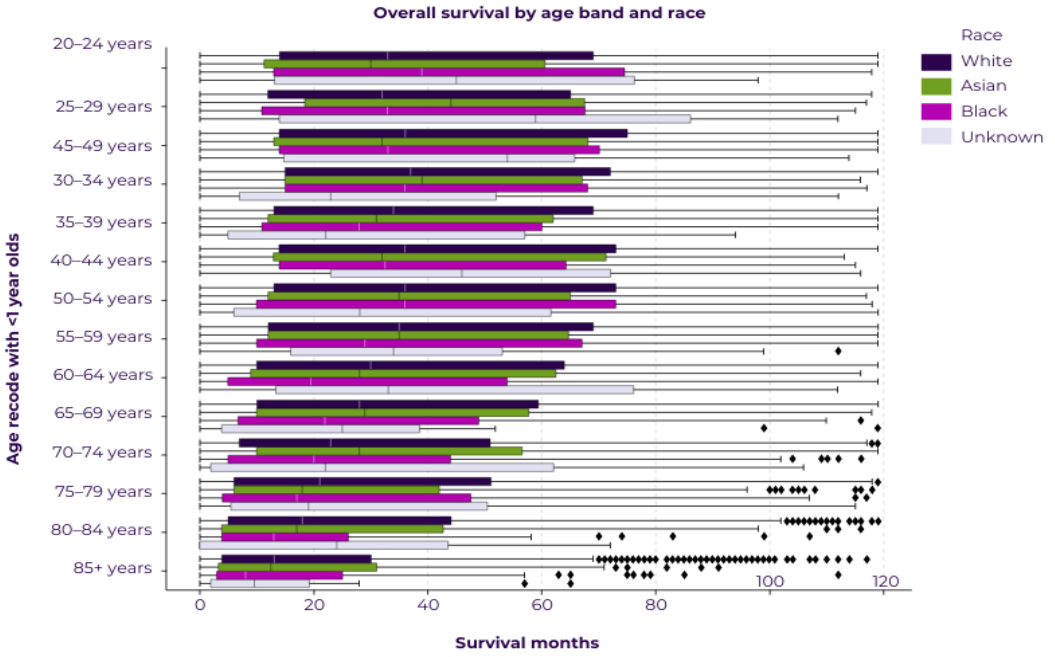
	ALL		Mets		Risk of Metastases
STS type	**Patients, n**	**Proportion of Total %**	**Patients, n**	**Proportion of Total %**	
4.8 Rhabdomyosarcoma	616	2.1	179	5.1	29.1
4.7 Leiomyosarcoma	3496	12.0	633	18.2	18.1
Other	6705	22.9	1200	34.5	17.9
4.10 Spindle cell sarcoma	1231	4.2	219	6.3	17.8
4.6 Synovial sarcoma	1085	3.7	161	4.6	14.8
6.2.1.2 Peripheral	851	2.9	104	3.0	12.2
4.14 Giant cell sarcoma	3115	10.7	290	8.3	9.3
4.4.2 Malignant fibrous histiocytoma	1029	3.5	64	1.8	6.2
4.5 Liposarcoma	5932	20.3	240	6.9	4.0
4.4.1 Myxofibrosarcoma	1910	6.5	51	1.5	2.7
4.4.3 Other fibromatous neoplasms	1484	5.1	31	0.9	2.1

Table 1. Risk of Metastases at First Diagnosis (SEER 17 | 2011–2020)

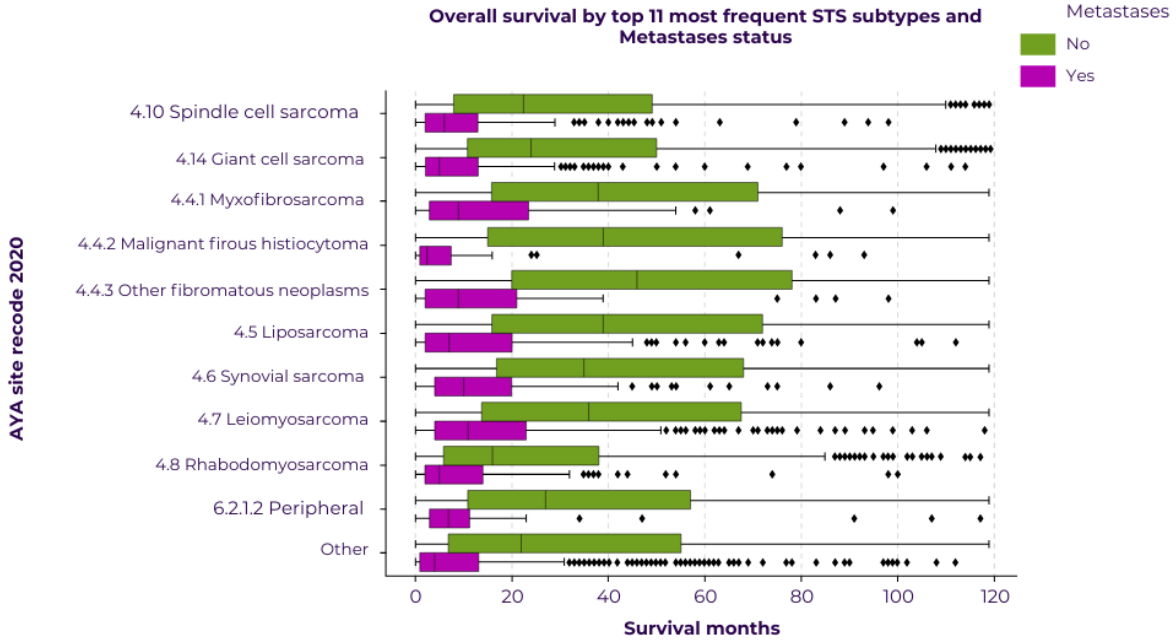
d. Survival outcomes

Survival outcomes were analyzed using demographic variables such as age, race, and STS subtype. Overall, there were no apparent differences in overall survival across the age bands by race.

As expected, there were observable trends in reduced median overall survival with increasing age (**Figure 3A**). **The presence of metastases at diagnosis was a strong negative prognostic for survival, independent of STS subtype. Rhabdomyosarcoma, spindle cell sarcoma, and giant cell sarcoma were the subtypes associated with the least median overall survival outcomes (≤2 years for all | Figure 3B**).



A



B

Figure 3. Overall Survival Outcomes by Age Band and Race (A) and by STS Subtype (no metastases at diagnosis vs metastases at diagnoses | B)

IV. Discussion

This white paper synthesizes available data on STS subtype prevalence and metastasis risk, highlighting the importance of subtype-specific considerations in managing STS. The high prevalence of specific subtypes, such as leiomyosarcoma and liposarcoma, necessitates focused research on these cancers to understand their biology and improve treatment strategies. Moreover, the substantial proportion of 'Other' sarcomas suggests a need for more detailed classification within this group.

The varied risk of metastases across STS subtypes has significant implications for prognosis, treatment, and clinical trial design. For example, subtypes with higher metastatic risk may require more aggressive initial treatment and rigorous follow-up. Taken together, these data/analyses provide a basis for benchmarking survival outcomes in this highly heterogeneous patient population.

V. Recommendations and Future Directions

This white paper is intended as a preliminary analysis and calls for a concerted effort among the medical community to address the challenges presented by STS. The data paints a complex picture requiring collaboration and more detailed analyses to fully understand outcomes and risks in these rare cancers. Some of this may be facilitated by enhancing current approaches to surveillance, for example, by capturing in more detail the natural history and the specifics of treatment intervention(s) in cases. Recognizing the resource utilization involved in these efforts could be burdensome, it may be pragmatic to focus research efforts on the most common STS subtypes and/or those with the highest risk of metastases. Future analyses would seek to include younger patients, particularly for certain STS subtypes such as rhabdomyosarcoma. These types of efforts will help us better understand the impact of treatment approaches on patient outcomes, provide actionable insights to improve clinical practice and define the focus of future clinical research on STS.

VI. Appendices

Data tables for reference by healthcare providers and researchers.

Supplementary Table 1. Prevalence of STS Subtypes in Adult Populations (SEER 17 | 2011–2020)

Row Labels	Patients, n	Proportion of Total
Other	6705	22.94
4.5 Liposarcoma	5932	20.30
4.7 Leiomyosarcoma	3496	11.96
4.14 Giant cell sarcoma	3115	10.66
4.4.1 Myxofibrosarcoma	1910	6.54
4.4.3 Other fibromatous neoplasms	1484	5.08
4.10 Spindle cell sarcoma	1231	4.21
4.6 Synovial sarcoma	1085	3.71
4.4.2 Malignant fibrous histiocytoma	1029	3.52
6.2.1.2 Peripheral	851	2.91
4.8 Rhabdomyosarcoma	616	2.11
4.2 Chondrosarcoma	353	1.21
4.11 Epithelioid sarcoma	312	1.07
4.3.2 Soft tissue	307	1.05
11. Unspecified malignant neoplasms except CNS	279	0.95
4.1 Osteosarcoma	141	0.48
4.12 Desmoplastic small round cell tumor	101	0.35
4.9 Gastrointestinal stromal tumor, malignant	73	0.25
10.2.2 Other specified neoplasms	65	0.22
4.13 Chordoma	42	0.14
10.2.1 Paraganglioma – non-CNS	38	0.13
10.1.3 Other neuronal and embryonal non-CNS tumors	24	0.08
7.4 Germ cell and trophoblastic excluding CNS, ovary, testis	14	0.05
10.1.2 Olfactory and other non-CNS neuroblastomas	13	0.04
Unclassified	6	0.02
4.16 Other bone tumors	2	0.01
3.1.3.2 Ependymoma – invasive	1	0.00
Total	**29 225**	**100.0**

Supplementary Table 2. STS Patients With Metastases at Diagnosis by Subtypes (SEER 17, 2011–2020)

Row Labels	Patients, n	Proportion of Total*
Other	1200	34.47
4.7 Leiomyosarcoma	633	18.18
4.14 Giant cell sarcoma	290	8.33
4.5 Liposarcoma	240	6.89
4.10 Spindle cell sarcoma	219	6.29
4.8 Rhabdomyosarcoma	179	5.14
4.6 Synovial sarcoma	161	4.63
6.2.1.2 Peripheral	104	2.99
4.3.2 Soft tissue	69	1.98
4.4.2 Malignant fibrous histiocytoma	64	1.84
4.11 Epithelioid sarcoma	52	1.49
4.4.1 Myxofibrosarcoma	51	1.47
4.2 Chondrosarcoma	50	1.44
4.12 Desmoplastic small round cell tumor	40	1.15
11. Unspecified malignant neoplasms except CNS	35	1.01
4.4.3 Other fibromatous neoplasms	31	0.89
4.1 Osteosarcoma	24	0.69
10.2.1 Paraganglioma – non-CNS	12	0.34
4.9 Gastrointestinal stromal tumor, malignant	11	0.32
10.2.2 Other specified neoplasms	10	0.29
10.1.3 Other neuronal and embryonal non-CNS tumors	3	0.09
4.13 Chordoma	1	0.03
4.16 Other bone tumors	1	0.03
7.4 Germ cell and trophoblastic excluding CNS, ovary, testis	1	0.03
Total	**3481**	**100.00**

*Risk of metastases diagnosis [(number of patients with metastases by subtype/total number of patients with diagnosis of that STS subtype) *100]