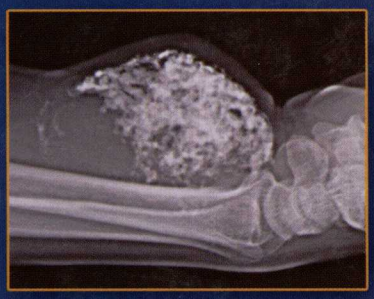
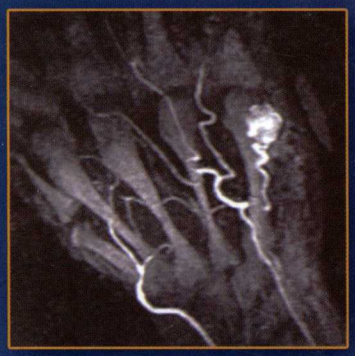
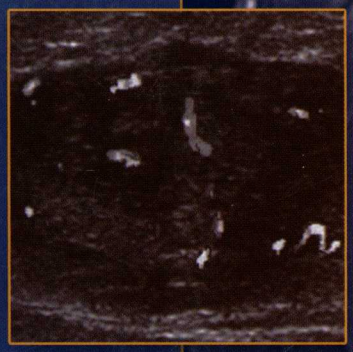
MARK J. KRANSDORF
MARK D. MURPHEY

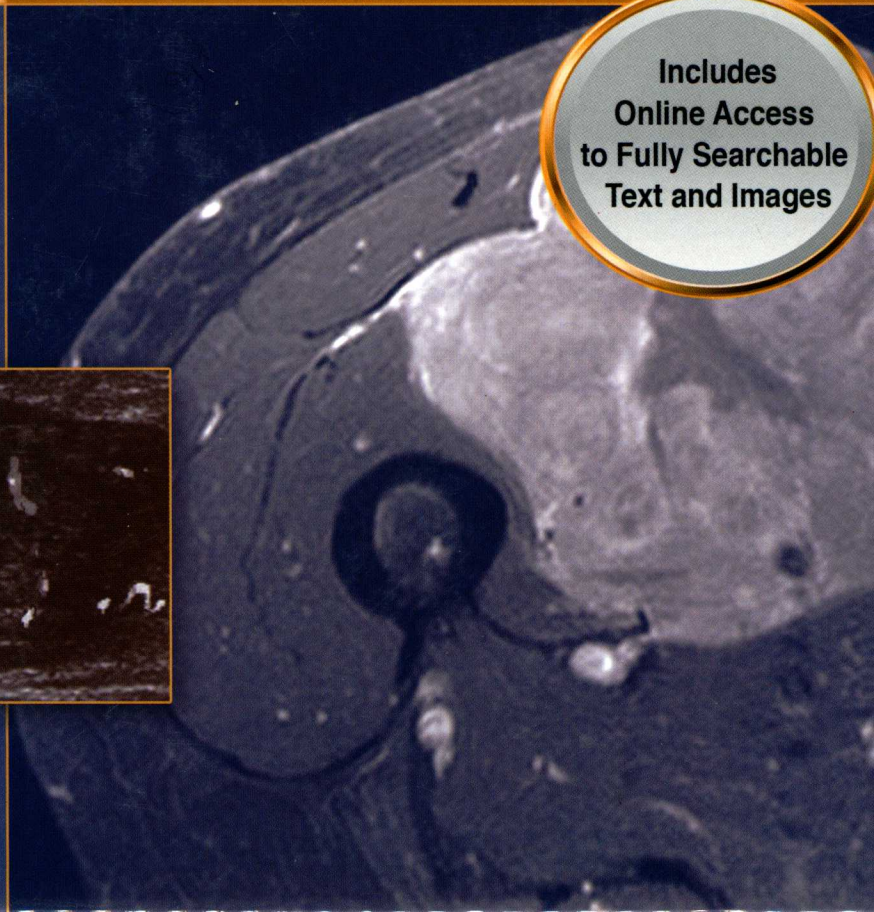
Imaging of Soft Tissue Tumors

THIRD EDITION









Includes Online Access to Fully Searchable Text and Images

Wolters Kluwer Health | Lippincott Williams & Wilkins

Imaging of Soft Tissue Tumors

THIRD EDITION

Mark J. Kransdorf, MD

Consultant, Department of Radiology
Mayo Clinic
Phoenix, Arizona

Mark D. Murphey, MD

Physician-in-Chief
Chief, Musculoskeletal Imaging
American Institute for Radiologic Pathology
Silver Spring, MD

Uniformed Services University of the Health Sciences, Bethesda, MD

Department of Radiology, National Military Medical Center, Bethesda, MD

Wolters Kluwer | Lippincott Williams & Wilkins
Health

Philadelphia • Baltimore • New York • London
Buenos Aires • Hong Kong • Sydney • Tokyo

Senior Executive Editor: Jonathan W. Pine, Jr.
Product Manager: Amy G. Dinkel
Vendor Manager: Alicia Jackson
Senior Manufacturing Coordinator: Beth Welsh
Senior Marketing Manager: Kimberly Schonberger
Designer: Stephen Druding
Production Service: S4Carlisle Publishing Services

Two Commerce Square
2001 Market Street
Philadelphia, PA 19103 USA
LWW.com

Printed in China

Library of Congress Cataloging-in-Publication Data
Kransdorf, Mark J.
Imaging of soft tissue tumors / Mark J. Kransdorf, Mark D. Murphey. — 3rd ed.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-4511-1641-0 (alk. paper) — ISBN 1-4511-1641-1 (alk. paper)
I. Murphey, Mark D. II. Title.
[DNLM: 1. Soft Tissue Neoplasms—diagnosis. 2. Diagnostic Imaging. 3. Soft Tissue Neoplasms—pathology. WD 375]
RC280.S66
616.99'40754—dc23

2013012303

To purchase additional copies of this book, call our customer service department at (800) 638-3030 or fax orders to (301) 223-2320. International customers should call (301) 223-2300.

Visit Lippincott Williams & Wilkins on the Internet: at LWW.com. Lippincott Williams & Wilkins customer service representatives are available from 8:30 am to 6 pm, EST.

10 9 8 7 6 5 4 3 2 1

RRS1306

To our families:

Judy, Pam, and Evan

Jill, Matthew, and Lucas

. . . . . our strength and inspiration

MJK

MDM

PREFACE

This book has been written to provide a systematic approach to the radiologic evaluation and diagnosis of soft tissue tumors and tumor-like masses. We have tried to illustrate the full spectrum of lesions encountered in a clinical practice, emphasizing lesions with a characteristic, or relatively characteristic, radiologic appearance, while not neglecting those with a nonspecific appearance. As our knowledge and experience with the imaging of soft tissue expands, we truly expect the number of those lesions designated as nonspecific to continue to decrease.

Following a brief introductory chapter, we present the results of a retrospective analysis of more than 31,000 soft tissue tumors that were seen in consultation over 10 years by the Department of Soft Tissue Pathology, Armed Forces Institute of Pathology, Washington, DC, to determine the relative prevalence, age at presentation, sex distribution, and skeletal distribution of soft tissue tumors, as well as the relative frequency of those tumors in specific anatomic locations and age groups. These data were collected prior to the nomenclature changes incorporated into the 2013 World Health Organization Classification of Soft Tissue Tumors; therefore, we have chose to present them with the original tumor designations. We have, however, incorporated the current World Health Organization nomenclature throughout the text, emphasizing applicable changes in each chapter.

Tumor population data is followed by an overview of the imaging evaluation of soft tissue tumors, highlighting advantages and limitations of the various modalities available. The imaging evaluation of patients following treatment is also reviewed, as are considerations to be used in the differentiation of benign from malignant soft tissue lesions. The chapter concludes with a review of the criteria required for tumor staging.

The remaining chapters review lipomatous, vascular and lymphatic, fibrous and fibrohistiocytic, muscle, neurogenic, synovial, extraskeletal osseous and cartilaginous tumors, and tumors of uncertain differentiation. A new chapter highlighting superficial masses has been added, underscoring the expanding use of radiologic imaging in evaluating these diverse tumor and tumor-like lesions.

The final chapter addressing tumor imaging is a collection of tumor-like masses of soft tissue arising from a variety of causes. These do not represent a comprehensive review, but rather our experience with lesions that may clinically present as musculoskeletal tumors. Individual discussions highlight magnetic resonance and computed tomography imaging appearances. Radiography, angiography, scintigraphy, ultrasound, and positron emission tomography are covered where appropriate. In addition to imaging appearance, discussions include a summary of general information, clinical presentation, pathology, treatment, and prognosis. The text concludes with a review of compartmental anatomy required for local tumor staging.

MARK J. KRANSDORF
MARK D. MURPHEY

ACKNOWLEDGMENTS

Mark and I greatly appreciate the privilege of serving as members of the Department of Radiologic Pathology at the Armed Forces Institute of Pathology (AFIP) and now, following its transition, the American Institute for Radiologic Pathology (AIRP). Our affiliation with the AFIP and AIRP has allowed us to be both teachers and students.

We are grateful to all of those who have contributed material to the AFIP and AIRP and we would particularly like to thank the radiology residents who attend the Radiologic Pathology Course and our musculoskeletal fellows (past, present, and future), for:

their dedication to knowledge—which inspires us,
their enthusiasm—which gives us the energy to continue, and
their penetrating questions—which keep us humble!

I am particularly indebted to our orthopedic oncology colleagues and would especially like to thank Mary I. O'Connor, H. Thomas Temple, Christopher P. Beauchamp, Adam J. Schwartz, G. Douglas Letson, William C. Foster, and B. Hudson Berrey for allowing me to assist them in the care of their patients.

Special thanks must also be extended to Jeanne M. Meis for her assistance and guidance in the conception of this project, and to Richard P. Moser, for his continued help over the years. Finally, I would like to thank Joseph A. Utz and James S. Jelinek, for their encouragement and council and, more importantly, for teaching and reminding me just how much fun radiology can be.

MJK

I want to acknowledge the importance of the section of Orthopedic Surgery and the Department of Radiology (particularly James R. Neff, Arthur A. DeSmet, and Arch W. Templeton) while I was at the University of Kansas Medical Center for fostering my initial interest in musculoskeletal radiology. I would also like to thank my current colleagues in the musculoskeletal section at the Walter Reed National Military Medical Center Bethesda, Frank Mullens, Steve Chan, and Zachary Fisher, who continue to teach me new ideas and keep me young at heart during my clinical work. I offer a special thank you to Mark J. Kransdorf, for inviting me to participate in this project and for putting up with me during the book's production.

I am also particularly indebted to both musculoskeletal pathology and orthopedic colleagues who have shared their valuable knowledge and allowed me to assist in the care of their patients, including Howard G. Rosenthal, H. Thomas Temple, Fred Gilkey, Francis H. Gannon, Albert J. Aboulafia, Alan M. Levine, Donald Gajewski, Richard Schaefer, John F. Fetsch, Julie C. Fanburg-Smith, Markku Miettinen, Dan Strum, Mary Klassen-Fischer, Kyle Potter and Jonathan Forsberg. Special thanks to my closest musculoskeletal colleagues for their help in teaching me through my academic career: James S. Jelinek, Mark J. Kransdorf, and Donald J. Flemming.

I am grateful to my parents, Douglas K. Murphey and Joyce M. Murphey, for their unwavering support and love and their ability to instill within me a thirst for knowledge without which this book would not be possible. Finally, and most importantly, I want to thank my family, sons Matthew Travis and Lucas Ryan, and Jill (my much better half, a fact with which anybody who knows me will thoroughly agree with). They provide my foundation and strength through their love and support and put up with my often early morning and weekend hours of work.

MDM

SPECIAL ACKNOWLEDGMENT

We would like to acknowledge our personal indebtedness to Donald E. Sweet and Lent C. Johnson for their inspiration in the pursuit of knowledge. They taught us substance over style and concept over doctrine. They may be gone, but their teachings are incorporated into the fundamental fabric of what we know as radiologic pathology.

MJK
MDM

CONTENTS

CHAPTER 1

Origin and Classification of Soft Tissue Tumors

CHAPTER ORGANIZATION

Soft tissue sarcomas, unlike benign soft tissue lesions, are relatively uncommon and are estimated to represent about 1% of all malignant tumors (1–3). Hajdu (1) noted that in the United States, the incidence of soft tissue sarcomas is about the same as that of multiple myeloma or carcinoma of the thyroid. Soft tissue sarcomas are three to four times as common as primary malignant bone tumors (1). An analysis of soft tissue sarcomas by Baldursson et al. (4) in Iceland, between 1955 and 1988, revealed an age-standardized incidence rate of 2.7 per 100,000 of population. Rydholm (5) noted an age-standardized incidence rate of 1.4 per 100,000 of population in Sweden. The incidence of soft tissue sarcoma increases markedly with age; the age-specific annual incidence for patients 80 years and older is 8 per 100,000 (5). It is difficult to estimate the annual incidence of benign soft tissue tumors, because many lipomas, hemangiomas, and other benign lesions do not undergo biopsy; however, the annual clinical incidence of benign soft tissue tumors is estimated at 300 per 100,000 (5).

CLASSIFICATION OF SOFT TISSUE TUMORS

KEY CONCEPTS

- Soft tissue tumors are classified histologically on the basis of the adult tissues that they resemble.
- Poorly differentiated tumors may lack the microscopic features required for histological classification.
- Immunohistochemistry and genetic analysis may aid in further classification.

Fundamental Concepts

The soft tissue is derived primarily from mesenchyme and, by convention, comprises the skeletal muscle, fat, fibrous tissue, peripheral nervous system, and the serving vascular structures (6). Soft tissue tumors are generally classified histologically on the basis of the adult tissues that they resemble (6,7,8). The designations of lipoma and liposarcoma, for example, do not indicate that these lesions arise from fat, but that they "recapitulate to a varying degree normal fatty tissue" (6). Although this concept works well for most lesions, it is important to remember that there are several sarcomas, such as synovial sarcoma or alveolar soft part sarcoma, with no normal cellular counterpart. Many sarcomas are poorly differentiated; consequently, they lack the microscopic features that are required to make a specific diagnosis. In such cases, immunohistochemical staining and genetic analysis have aided pathologists in further classifying tumors. These techniques are well established and are used routinely. Despite the pathologist's best efforts, a small number of soft tissue sarcomas cannot be further classified. This group of sarcomas that cannot be further subclassified previously comprised approximately 5% to 15% of soft tissue sarcomas (4,9), although current immunochemical and genetic techniques will continue to reduce this number.

The histologic classification of soft tissue tumors used in this text reflects the World Health Organization (WHO) classification published in 2013 (10). This updated classification continues the use of a revised categorization of biologic behavior that allows for two designations of intermediate malignancy: locally aggressive and rarely metastasizing (10). The current WHO classification is summarized in Table 1.1 (10,11) and includes peripheral nerve sheath tumors, which were previously addressed by the WHO in a separate publication (12).

Special Stains

Although the diagnosis of soft tissue tumors can frequently be made on the basis of light microscopic features, as many as 20% of cases cannot be definitively classified, even by experienced pathologists (13). Many soft tissue tumors have microscopic features that overlap. This includes various spindle cell tumors as well as other nonsarcomatous lesions such as carcinoma, melanoma, and lymphoma; therefore, additional methods may be required to further classify these lesions (13–15).

In addition to standard hematoxylin–eosin-stained slides, additional staining referred to as histochemical techniques may be used (13–15). For example, trichrome stain may be used to distinguish fibrous tissue from muscle tissue (14). Intracytoplasmic glycogen usually seen

TABLE 1.1 WHO classification of soft tissue tumors[a]

Adipocytic tumors
Benign
- Lipoma
- Lipomatosis
- Lipomatosis of nerve
- Lipoblastoma/lipoblastomatosis
- Angiolipoma
- Myolipoma
- Chondroid lipoma
- Extra-renal angiomyolipoma
- Extra-adrenal myelolipoma
- Spindle cell lipoma/pleomorphic lipoma
- Hibernoma

Intermediate (locally aggressive)
- Atypical lipomatous tumor/well-differentiated liposarcoma

Malignant
- Dedifferentiated liposarcoma
- Myxoid liposarcoma
- Pleomorphic liposarcoma
- Liposarcoma, not otherwise specified

Fibroblastic/myofibroblastic tumors
Benign
- Nodular fasciitis
- Proliferative fasciitis
- Proliferative myositis
- Myositis ossificans
- Fibro-osseous pseudotumor of digits
- Ischemic fasciitis
- Elastofibroma
- Fibrous hamartoma of infancy
- Fibromatosis coli
- Juvenile hyaline fibromatosis
- Inclusion body fibromatosis
- Fibroma of tendon sheath
- Desmoplastic fibroblastoma
- Mammary-type myofibroblastoma
- Calcifying aponeurotic fibroma
- Angiomyofibroblastoma
- Cellular angiofibroma
- Nuchal-type fibroma
- Gardner fibroma
- Calcifying fibrous tumor

Intermediate (locally aggressive)
- Palmar/plantar fibromatosis
- Desmoid-type fibromatosis
- Lipofibromatosis
- Giant cell fibroblastoma

Intermediate (rarely metastasizing)
- Dermatofibrosarcoma protuberans
  - Fibrosarcomatous dermatofibrosarcoma protuberans
  - Pigmented dermatofibrosarcoma protuberans
- Solitary fibrous tumor
- Inflammatory myofibroblastic tumor
- Low-grade myofibroblastic sarcoma
- Myxoinflammatory fibroblastic sarcoma
- Infantile fibrosarcoma

Malignant
- Adult fibrosarcoma
- Myxofibrosarcoma
- Low-grade fibromyxoid sarcoma
- Sclerosing epithelioid fibrosarcoma

So-called fibrohistiocytic tumors
Benign
- Tenosynovial giant cell tumor
  - Localized type
  - Diffuse-type
  - Malignant
- Deep benign fibrous histiocytoma

Intermediate (rarely metastasizing)
- Plexiform fibrohistiocytic tumor
- Giant cell tumor of soft tissue

Smooth muscle tumors
Benign
- Deep leiomyoma

Malignant
- Leiomyosarcoma (excluding skin)

Pericytic (perivascular) tumors
- Glomus tumor (and variants)
  - Glomangiomatosis
  - Malignant glomus tumor
- Myopericytoma
  - Myofibroma
  - Myofibromatosis
- Angioleiomyoma

Skeletal muscle tumors
Benign
- Rhabdomyoma
  - Adult type
  - Fetal type
  - Genital type

Malignant
- Embryonal rhabdomyosarcoma (including botroyoid, anaplastic)
- Alveolar rhabdomyosarcoma
- Pleomorphic rhabdomyosarcoma
- Spindle cell/sclerosing rhabdomyosarcoma

Vascular tumors
Benign
- Hemangiomas
  - Synovial
  - Venous
  - Arteriovenous hemangioma/malformation
  - Intramuscular
- Epithelioid hemangioma
- Angiomatosis
- Lymphangioma

Intermediate (locally aggressive)
- Kaposiform hemangioendothelioma

Intermediate (rarely metastasizing)
- Retiform hemangioendothelioma
- Papillary intralymphatic angioendothelioma
- Composite hemangioendothelioma
- Pseudomyogenic (epithelioid sarcoma-like) hemangioendothelioma
- Kaposi sarcoma

Malignant
- Epithelioid hemangioendothelioma
- Angiosarcoma of soft tissue

Chondro-osseous tumors
- Soft tissue chondroma
- Mesenchymal chondrosarcoma
- Extraskeletal osteosarcoma

Gastrointestinal Stromal Tumors
- Benign gastrointestinal stromal tumor
- Gastrointestinal stromal tumor, uncertain malignant potential
- Benign gastrointestinal stromal tumor, malignant

Nerve Sheath Tumors
Benign
- Schwannoma
- Melanotic schwannoma
- Neurofibroma
  - Plexiform neurofibroma
- Perineurioma
  - Malignant perineurioma
- Granular cell tumor
- Dermal nerve sheath myxoma
- Solitary circumscribed neuroma
- Extopic meningioma
- Benign triton tumor
- Hybrid nerve sheath tumor

Malignant
- Malignant peripheral nerve sheath tumor (MPNST)
- Epithelioid malignant peripheral nerve sheath tumor
- Malignant triton tumor
- Malignant granular cell tumor
- Ectomesenchymoma

Tumors of Uncertain Differentiation
Benign
- Acral fibromyxoma
- Intramuscular myxoma
- Juxta-articular myxoma
- Deep ("aggressive") angiomyxoma
- Pleomorphic hyalinizing angiectatic tumor
- Ectopic hamartomatous thymoma

Intermediate (locally aggressive)
- Hemosiderotic fibrolipomatous tumor

Intermediate (rarely metastasizing)
- Atypical fibroxanthoma
- Angiomatoid fibrous histiocytoma
- Ossifying fibromyxoid tumor
- Mixed tumor
- Myoepithelioma
- Myoepithelial carcinoma
- Phosphaturic mesenchymal tumor

Malignant
- Synovial sarcoma
- Epithelioid sarcoma
- Alveolar soft-part sarcoma
- Clear cell sarcoma of soft tissue
- Extraskeletal myxoid chondrosarcoma
- Extraskeletal Ewing tumor
- Desmoplastic small round cell tumor
- Extra-renal rhabdoid tumor
- Neoplasms with perivascular epithelioid cell differentiation (PEComa)
  - PEComa, benign
  - PEComa, malignant
- Intimal sarcoma

Undifferentiation/Unclassified Sarcomas
- Undifferentiated spindle cell sarcoma
- Undifferentiated pleomorphic sarcoma
- Undifferentiated round cell sarcoma
- Undifferentiated epithelioid sarcoma
- Undifferentiated sarcoma, NOS

* Adapted from Reference 10

in lesions such as Ewing sarcoma may be identified with periodic acid–Schiff (PAS) stain (14). More recently, immunohistochemical techniques have been applied to the diagnosis of soft tissue tumors.

Immunohistochemistry

Immunohistochemistry is the process of detecting the presence of specific proteins in a cell or tissue with the use of antibodies. In soft tissue pathology, the main application of immunohistochemistry is in the detection of differentiation markers specifically related to certain mesenchymal phenotypes (16). Immunohistochemistry is also useful in the detection of various cell proliferation markers, oncoproteins, and tumor suppressor proteins (16). Although immunohistochemistry is not totally specific, it is currently the best way to further characterize soft tissue sarcomas for which light microscopy is not diagnostic (14,17).

For those not directly involved with immunology, the nomenclature is difficult, confusing, and at times overwhelming. Historically, immunohistochemistry was initially developed to distinguish among classes of lymphocytes on the basis of their cell surface antigens by producing antibodies that would selectively recognize different cell subpopulations (18). Surface antigens (markers) were initially named according to the antibodies that reacted with them, and in an attempt to eliminate confusion with their designation, a uniform nomenclature system was adopted. According to this system, surface markers were given a "CD" (cluster of differentiation) designation (18). This system was initially used for human leukocyte antigens and has since been more widely applied to other cells. The most important markers used in the diagnosis of soft tissue tumors and their diagnostic targets are listed in Table 1.2.

Cytogenetics

Advances in molecular biology have added a new dimension to the diagnosis of soft tissue tumors. The ability to detect specific genetic abnormalities, in the form of chromosomal translocations and the resulting translocation fusion products, can be used as a disease-specific marker in diagnosis (19,20). A review of medical genetics is beyond the scope of this text; however, some basic definitions may be useful.

A translocation is the interchange of genetic material between nonhomologous chromosomes—the movement of a DNA fragment from one chromosomal location to another. The result is an abnormal chromosome that contains genetic material from two or more chromosomes (19). A fusion gene is the joining of heterologous gene fragments that occurs as a result of a translocation.

Translocations are generally specific for particular types of tumors and as such are useful diagnostic markers. They are detected by cytogenetics or gene fusion assay. A list of the lesions detectable by specific chromosome translocations and other gene fusions is shown in Table 1.3.

HOW THE TEXT IS ORGANIZED

This text is broadly organized by tissue type. Although many chapters, such as the chapter on lipomatous tumors, will closely follow the classification system used by the WHO, other chapters will not. We have retained the broad tissue-type organization because it is more functional and useful for radiologists in establishing radiologic differential diagnoses.

For example, a radiologist may recognize a mass as originating from a joint or synovial-lined structure and

TABLE 1.2 Immunohistochemical makers used in the diagnosis of soft tissue tumors[a]

Marker	Positive in:
Endothelial markers	
CD31	Angiosarcoma, Kaposi sarcoma
CD34	Kaposi sarcoma, many vascular fibroblastic and other tumors
von Willebrand's factor	Epithelioid hemangioendothelioma, some angiosarcomas
CD141	Variable in angiosarcoma, positive in mesothelioma
Fli-1	Ewing sarcoma, angiosarcoma
Muscle cell markers	
Actin, common muscle	Smooth and skeletal muscle tumors, myofibroblastic tumors
Actin, smooth muscle	Smooth muscle and myofibroblastic tumors
Actin, sarcomeric	Skeletal muscle and rhabdomyosarcoma
Desmin	Smooth and skeletal muscle tumors, some other tumors
Heavy caldesmon	Smooth muscle and its tumors, myoepithelia, GI stromal tumors
Calponin	Smooth muscle, myofibroblasts, synovial sarcoma (often)
MyoD1, myogenin	Rhabdomyosarcoma (regenerative skeletal muscle)
Neural and neuroendocrine-specific markers	
Synaptophysin	Neuroblastoma, paraganglioma, neuroendocrine carcinoma
Chromogranin	Paraganglioma, neuroendocrine carcinoma (especially low-grade)
Neuron-specific enolase	Neuroendocrine tumors, malignant melanoma (low specificity)
Neurofilament proteins	Neuroblastoma, paraganglioma, Merkel cell carcinoma
Alpha-internexin	Neuroblastoma, paraganglioma, Merkel cell carcinoma
S-100 protein and other multispecific neural markers	
S-100 protein	Melanocytic, schwannian, chondroid, Langerhans cell
Nerve growth factor receptor p75	Dermatofibrosarcoma protuberans and other nerve sheath tumors
CD56 (NCAM)	Neuroendocrine carcinoma, rhabdomyosarcoma, other sarcomas
Melanoma markers other than S-100 protein	
HMB45	Melanoma, clear cell sarcoma, angiomyolipoma (PEComas)
Tyrosinase	Nevi, melanoma
Melan A	Nevi, melanoma, angiomyolipoma (variably)
Microphthalmia	Melanoma, osteoclastic giant cells, neurothekeoma
CD63	Melanoma, some carcinomas, alveolar soft parts sarcoma
Histiocytic markers	
Lysozyme	Histiocytes, myelomonocytic cells
Factor XIIIa	Histiocytes, especially dendritic ones
CD68	Histiocytes, melanoma, paraganglioma, schwannoma, granular cell tumor
CD163	Histiocytes, histiocytic sarcoma, juvenile xanthogranuloma
Keratin	
Keratin	Carcinoma, synovial and epithelioid sarcoma, chordoma
Other markers	
EMA	Epithelial tumors, perineural tumors, synovial and epithelioid sarcoma
B72.3	Epithelioid angiosarcoma, many adenocarcinomas
Ber-Ep4	Many adenocarcinomas, biphasic synovial sarcoma
CEA	Many adenocarcinomas, biphasic synovial sarcoma
Desmoplakin	Epithelial tumors in general, meningioma, Ewing sarcoma
HBME-1	Mesothelioma, some adenocarcinoma, synovial sarcoma, chondroma
Wilms tumor protein	Small round cell desmoplastic tumor, mesothelioma
Other important tumor markers	
ALK	Large cell anaplastic lymphoma, inflammatory myofibroblastic tumor (some)
Basement membrane protein	Schwann cell tumors, angiosarcoma

CD10	Endometrial stromal sarcoma, many fibroblastic tumors
CD99	Ewing sarcoma, widespread in different tumors
CD117	GI stromal tumor, angiosarcoma, Ewing sarcoma, and others
GFAP	Glial tumors, schwannomas, myoepithelial tumors
Inhibin	Granular cell tumor, granulosa cell tumor
Osteocalin	Osteosarcoma, osteoid material
Vimentin	Mesenchymal tumors

[a]Adapted from Table 3-1. Miettinen M. Immunohistochemistry of soft tissue tumors. In: Modern Soft Tissue Pathology. Cambridge, England: Cambridge University Press; 2010:44–104, with permission.

TABLE 1.3 Characteristic chromosomal tumor translocations[a]

Tumor	Translocation
Alveolar rhabdomyosarcoma	t(2;13)(q35;q14), t(1;13)(p36;q14), t(X;2)(q13;q35), t(2;2)(q35;p23)
Alveolar soft parts sarcoma	der(17)t(X;17)(p;11;q25)
Aggressive angiomyxoma	12q15 rearrangements
Angiomatoid fibrous histiocytoma	t(12;22)(q13;q12), t(2;22)(q33;q12), t(12;16)(q13;p11)
Chondroid lipoma	t(11;16)(q13;p12-13)
Clear cell sarcoma	t(12;22)(q13;q12), t(2;22)(q33;q12)
Congenital/infantile fibrosarcoma	t(12;15)(p13;q25)
Dermatofibrosarcoma protuberans	t(17;22)(q21;q13)
Epithelioid hemangioendothelioma	t(1;3)(p36;q25)
Ewing sarcoma (PNET)	t(11;22)(q24;q12), t(21;22)(q22;q12), t(7;22)(p22;q12), and others
ES myxoid chondrosarcoma	t(9;22)(q22;q12), t(9;17)(q22;q11), t(9;15)(q22;q21), t(3;9)(q12;q22)
Giant cell tumor tendon sheath	t(1;2),(p13;q37)
Hibernoma	11q13
Inflammatory myofibroblastic tumor	t(1,;2)(q22;p23), t(2;19)(p23;p13), t(2;17)(p23;q23), and others
Lipoblastoma	8q12 rearrangements
Lipoma	12q15 rearrangements
Low-grade fibromyxoid sarcoma	t(7;16)(q33;p11)
Myxoid/round cell liposarcoma	t(12;16)(q13;p11), t(12;22)(q13;q12)
Pericytoma	t(7;12)(p22;q13)
Synovial sarcoma	t(X;18)(p11.2;q11.2), t(X;20)(p11.2;q13.3)

[a]Adapted from Table 4.5 from Bridge JA, Nelson M. Genetics of soft tissue tumors. In: Miettinen M, ed. *Modern Soft Tissue Pathology*. Cambridge, England: Cambridge University Press; 2010:105–126, with permission.

direct the differential accordingly. The WHO classification system does not include a category of synovial lesions. Lesions that typically occur in the juxta-articular region are classified by the WHO on their histogenesis and may be included in the chapters on tumors of uncertain differentiation or on so-called fibrohistiocytic tumors (Table 1.1). The former group includes synovial sarcoma, whereas the latter includes the spectrum of benign proliferative disorders of the synovium (giant cell tumor of tendon sheath and pigmented villonodular synovitis). Although the histiogenic approach is best for the pathologist, the adherence to a broad tissue typing remains more useful for the radiologist. Using the previous example, it gives us greater freedom to include relevant tumor-like lesions and allows us, for example, to include synovial cysts and ganglions in the chapter on synovial lesions.

REFERENCES

1. Hajdu SI. Soft tissue sarcomas: classification and natural history. *CA Cancer J Clin*. 1981;31:271–280.
2. Du Boulay CEH. Immunohistochemistry of soft tissue tumors: a review. *J Pathol*. 1985;146:77–94.
3. Greelee RT, Hill-Harmon MB, Murray T, et al. Cancer statistics 2001. *CA Cancer J Clin*. 2001;51:15–36.
4. Baldursson G, Agnarsson BA, Benediktsdottir KR, et al. Soft tissue sarcomas in Iceland 1955–1988. *Acta Oncol*. 1991;30:563–568.
5. Rydholm A. Management of patients with soft-tissue tumors. Strategy developed at a regional oncology center. *Acta Orthop Scand Suppl*. 1983;203:13–77.
6. Weiss SW, Goldblum JR. General considerations. In: Weiss SW, Goldblum JR, eds. *Enzinger and Weiss's Soft Tissue Tumors*. 5th ed. St. Louis, MO: Mosby; 2008:1–14.
7. Angervall L, Kindblom LG. Principles for pathologic-anatomic diagnosis and classification of soft-tissue sarcomas. *Clin Orthop Relat Res*. 1993;(289):9–18.
8. Miettinen M. Overview of soft tissue tumors. In: Miettinen M, ed. *Modern Soft Tissue Pathology*. Cambridge, England: Cambridge University Press; 2010:1–10.
9. Mettlin C, Priore R, Rao U, et al. Results of the national soft-tissue sarcoma registry. *J Surg Oncol*. 1982;19:224–227.
10. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F, eds. *WHO Classification of Tumours of Soft Tissue and Bone*. Lyon, France: International Agency for Research on Cancer (IARC); 2013.

11. Miettinen M. Nerve sheath tumors. In: Miettinen M, ed. *Modern Soft Tissue Pathology*. Cambridge, England: Cambridge University Press; 2010:660–723.
12. Kleihues P, Cavenee WK. WHO classification of soft tissue tumors. In: *Pathology and Genetics of Tumors of the Nervous System*. Lyon, France: IARC Press; 2000:63–222.
13. Ordóñez NG. Application of immunocytochemistry in the diagnosis of soft tissue sarcomas: a review and update. *Adv Anat Pathol*. 1998;5:67–85.
14. Angervall L, Kindblom LG. Principles for pathologic-anatomic diagnosis and classification of soft-tissue sarcomas. *Clin Orthop*. 1993;289:9–18.
15. Carbone A, Gloghini A, Volpe R. The value of immunohistochemistry in the diagnosis of soft tissue sarcomas. *Ann Oncol*. 1992;3(suppl 2):S51–S54.
16. Zhang P, Brooks JS. Modern pathological evaluation of soft tissue sarcoma specimens and its potential role in soft tissue sarcoma research. *Curr Treat Options Oncol*. 2004;5:441–450.
17. Miettinen M. Immunohistochemistry of soft tissue tumors. In: *Modern Soft Tissue Pathology*. Cambridge, England: Cambridge University Press; 2010:44–104.
18. Abbas AK, Lichtman AH, Pober JS. *Cellular and Molecular Immunology*. Philadelphia, PA: WB Saunders; 1997:15–33.
19. Lasota J. Molecular genetics of soft tissue tumors. In: Miettinen M, ed. *Modern Soft Tissue Pathology*. Cambridge: Cambridge University Press, 2010:127–180.
20. Bridge JA, Nelson M. Genetics of soft tissue tumors. In: Miettinen M, ed. *Modern Soft Tissue Pathology*. Cambridge, England: Cambridge University Press; 2010:105–126.

CHAPTER 2

Soft Tissue Tumors in a Large Referral Population: Prevalence and Distribution of Lesions by Age, Sex, and Location

CHAPTER ORGANIZATION

KEY CONCEPTS

- A correct histologic diagnosis is reached on the basis of MR imaging studies alone in about 50% of cases.
- Imaging can distinguish benign and malignant lesions in most cases.
- Unlike their intraosseous counterparts, nonspecific soft tissue lesions cannot be reliably assessed by evaluation of their growth rate or physical parameters.
- In cases with a nonspecific imaging appearance, knowledge of tumor prevalence, along with the patient's age and the lesion's location allows one to develop a suitably ordered differential diagnosis.

The evaluation of soft tissue tumors has undergone a dramatic change with the advent of computed tomography (CT) and magnetic resonance (MR) imaging. Despite these sophisticated techniques and the increasing number of lesions that may have a characteristic imaging appearance (e.g., lipoma, hemangioma, subacute hematoma, pigmented villonodular synovitis), many lesions remain nonspecific. Initially, investigators noted that the majority of lesions were nonspecific, with a correct histologic diagnosis reached on the basis of imaging studies alone in only approximately 25% to 35% of cases (1–4). More recently, this number has increased to more than 50% of cases with an accuracy of 85% in differentiating between benign and malignant lesions (5).

Despite these positive developments in diagnosis, it is often not possible to establish a meaningful differential diagnosis for nonspecific soft tissue lesions or to reliably determine whether they are benign or malignant. Unlike their intraosseous counterparts, soft tissue lesions cannot be reliably assessed by evaluating their growth rate or physical parameters. In cases with a nonspecific imaging appearance, knowledge of tumor prevalence, along with the patient's age and the lesion's location, allows one to develop a suitably ordered differential diagnosis.

This chapter presents the results of a retrospective analysis of 31,047 soft tissue tumors seen in consultation by the Department of Soft Tissue Pathology, Armed Forces Institute of Pathology, Washington, DC, during the 10-year period starting January 1, 1980 (6,7). The purpose of this analysis was to (a) determine the relative prevalence, age at presentation, sex distribution, and skeletal distribution of soft tissue tumors and (b) ascertain the relative frequency of these tumors in specific anatomic locations and age groups among a population of patients in a large pathologic consultation service.

Only mesenchymal lesions originating in soft tissue were included in the study. Intra-abdominal and retroperitoneal lesions were also included when the lesions were not thought to originate in the bowel or abdominal viscera. Hence, leiomyosarcoma of the vena cava was included, whereas an angiosarcoma of the spleen was not. Lesions arising in the chest and abdominal walls and the paraspinal region were also included, as they are frequently within the purview of the musculoskeletal radiologist.

All soft tissue tumors and tumor-like lesions were placed in one of 121 major diagnostic categories. For purposes of analysis, all lesions were placed in one of 10 locations: hand and wrist, upper extremity, proximal limb girdle (axilla and shoulder), foot and ankle, lower extremity, hip and buttocks region, head and neck, trunk, retroperitoneum, and other lesions. This last category included lesions coded as abdomen, pelvis, mediastinum, or location unknown.

In total, the records of 42,490 lesions occurring in 38,484 patients were reviewed. Multiple lesions were seen in 639 patients (1.7%), including 592 patients with two lesions, 39 patients with three lesions, 7 patients with four lesions, and 1 patient with five lesions. Sequential

biopsy specimens were found in 3,311 cases. A total of 39,179 soft tissue tumors (and tumor-like masses) were available for detailed analysis. From this group, 8,132 nonmesenchymal lesions were excluded.

There were 12,370 malignant mesenchymal lesions. More than 80% were classified into seven pathologic diagnoses: malignant fibrous histiocytoma (24%), liposarcoma (14%), leiomyosarcoma (8%), malignant peripheral nerve sheath tumor (6%), dermatofibrosarcoma protuberans (6%), synovial sarcoma (5%), and fibrosarcoma (5%); 12% could not be further classified. There were 18,677 benign mesenchymal lesions. Approximately 70% of benign lesions were classified into eight pathologic diagnostic categories: lipoma and lipoma variants (16%), fibrous histiocytoma (13%), nodular fasciitis (11%), hemangioma (8%), fibromatosis (7%), neurofibroma (5%), schwannoma (5%), and giant cell tumor of tendon sheath (4%).

A summary of the malignant and benign lesions is presented in Tables 2.1 and 2.2. A summary of the age and sex of the patients as well as the distribution of lesions for all histologic diagnoses is shown in Tables 2.3 to 2.14.

The patient age and lesion location were known in 26,854 patients. For this group, the number and percentage of the seven most common malignant and benign lesions for each age and location are shown in Tables 2.15 to 2.23. All liposarcoma and fibrosarcoma subtypes have been grouped together for this analysis, as have all hemangiomas, lymphangiomas, and superficial and deep fibromatoses. Lipoma, lipomatosis, spindle cell lipoma, pleomorphic lipoma, and intramuscular lipoma have been combined and classified as lipoma. In total, 31 malignant and 52 benign diagnostic categories were used for this analysis.

The referral nature of the cases may introduce a bias for difficult case material and may be responsible for the relatively high percentage of malignancies (approximately 40%). This is greater than the 16% noted by Lattes (8) in citing the records of Columbia University during the 45.5 years from February 1, 1906, to September 1, 1951 (1,349 malignant and 7,337 benign lesions), and considerably greater than the 5% reported by Myhre-Jensen (9) during the 7-year period from April 1970 to April 1977 (72 malignant and 1,331 benign lesions) at the University Institute of Pathology, Aarhus, Denmark. Because of the increased number of malignancies, benign and malignant lesions have been considered separately in order to reflect accurately their relative prevalence.

In 2002, the World Health Organization (WHO) revised its classification of soft tissue tumors, incorporating new cytogenetic and molecular genetic information (10). The WHO updated this again in 2013 (11); however, these updates have had little effect on the tabular data. Accordingly, for this analysis we have retained the original tumor nomenclature and doubt this will cause any difficulty. That is not to say that there have not been changes in nomenclature. For example, the lesion listed in the tables as *MFH (malignant fibrous histiocytoma)* now been designated *undifferentiated pleomorphic sarcoma*. The major diagnostic categories, however, are not significantly changed and variations in nomenclature are explained in the written chapter text.

REFERENCES

1. Crim JR, Seeger LL, Yao L, et al. Diagnosis of soft-tissue masses with MR imaging: can benign masses be differentiated from malignant ones? *Radiology.* 1992;185:581–586.
2. Kransdorf MJ, Jelinek JS, Moser RP Jr, et al. Soft-tissue masses: diagnosis using MR imaging. *AJR Am J Roentgenol.* 1989;153:541–547.
3. Berquist TH, Ehman RL, King BF, et al. Value of MR imaging in differentiating benign from malignant soft-tissue masses: study of 95 lesions. *AJR Am J Roentgenol.* 1990;155:1251–1255.
4. Sundaram M, McLeod RA. MR imaging of tumor and tumorlike lesions of bone and soft tissue. *AJR Am J Roentgenol.* 1990;155:817–824.
5. Gielen JL, De Schepper AM, Vanhoenacker F, et al. Accuracy of MRI in characterization of soft tissue tumors and tumor-like lesions. A prospective study in 548 patients. *Eur Radiol.* 2004;14:2320–2330.
6. Kransdorf MJ. Malignant soft-tissue tumors in a large referral population: distribution of diagnoses by age, sex, and location. *AJR Am J Roentgenol.* 1995;164:129–134.
7. Kransdorf MJ. Benign soft-tissue tumors in a large referral population: distribution of diagnoses by age, sex, and location. *AJR Am J Roentgenol.* 1995;164:395–402.
8. Lattes R. Tumors of the soft tissue. In: *Atlas of Tumor Pathology, Second Series.* Washington, DC: Armed Forces Institute of Pathology; 1982:v.
9. Myhre-Jensen O. A consecutive 7-year series of 1331 benign soft tissue tumors. Clinicopathologic data. Comparison with sarcomas. *Acta Orthop Scand.* 1981;52:287–293.
10. Fletcher CDM, Unni KK, Mertens F, eds. WHO Classification of tumors. In: *Pathology and Genetics: Tumors of Soft Tissue and Bone.* Lyon, France: IARC Press; 2002.
11. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F, eds. *WHO Classification of Tumours of Soft Tissue and Bone.* Lyon, France: International Agency for Research on Cancer (IARC); 2013.

TABLES SUMMARIZING MALIGNANT AND BENIGN SOFT TISSUE TUMORS BY DIAGNOSIS

TABLE 2.1 Malignant soft tissue tumors[a]

Diagnosis	Total no.	%
Malignant fibrous histiocytoma	2,978	24.1
Liposarcoma	1,755	14.2
Sarcoma, not further classified	1,457	11.8
Leiomyosarcoma	1,039	8.4
Malignant schwannoma	775	6.3
Dermatofibrosarcoma protuberans	771	6.2
Synovial sarcoma	672	5.4
Fibrosarcoma, adult	553	4.5
Extraskeletal chondrosarcoma	263	2.1
Angiosarcoma	251	2.0
Rhabdomyosarcoma	239	1.9
Angiomatoid malignant fibrous histiocytoma	199	1.6
Epithelioid sarcoma	170	1.4
Kaposi sarcoma	152	1.2
Malignant hemangiopericytoma	141	1.1
Extraskeletal Ewing sarcoma	131	1.1
Clear cell sarcoma	130	1.1
Atypical fibroxanthoma	121	1.0
Hemangioendothelioma	109	0.9
Infantile fibrosarcoma	97	0.8
Extraskeletal osteosarcoma	79	0.6
Alveolar soft part sarcoma	65	0.5
Malignant mesothelioma	46	0.4
Neuroblastoma	35	0.3
Giant cell fibroblastoma	31	0.3
Malignant mesenchymoma	24	0.2
Malignant granular cell tumor	23	0.2
Peripheral neuroepithelioma	19	0.2
Ganglioneuroblastoma	18	0.2
Malignant giant cell tumor of tendon sheath	10	0.1
Primitive neuroectodermal tumor	9	0.1
Malignant paraganglioma	8	0.1

[a]Based on an analysis of 12,370 cases seen in consultation over 10 years.

TABLE 2.2 Benign soft tissue tumors[a]

Diagnosis	Total no.	%
Lipoma and lipoma variants	2,999	16.1
Fibrous histiocytoma	2,385	12.8
Nodular fasciitis	2,116	11.3
Hemangioma (all)	1,418	7.6
Fibromatosis (all)	1,297	6.9
Neurofibroma	973	5.2
Schwannoma	895	4.8
Giant cell tumor of tendon sheath	731	3.9
Myxoma (all)	597	3.2
Granuloma annulare/necrobiotic nodule	408	2.2
Hemangiopericytoma	384	2.1
Granular cell tumor	348	1.9
Leiomyoma (including angiomyoma)	311	1.7
Chondroma (all)	277	1.5
Fibroma of tendon sheath	272	1.5
Fibroma (all)	217	1.2
Myofibromatosis	178	1.0
Glomus tumor	164	0.9
Pigmented villonodular synovitis	161	0.9
Lymphangioma (all)	160	0.9
Ganglion	159	0.9
Proliferative fasciitis	144	0.8
Myositis ossificans (all)	139	0.7
Papillary endothelial hyperplasia	136	0.7
Infantile fibromatosis	116	0.6
Lipoblastoma	114	0.6
Neurothekeoma	92	0.5
Fibrous hamartoma of infancy	84	0.5
Neuroma	76	0.4
Calcifying aponeuronic fibroma	75	0.4
Mesothelioma	72	0.4
Juvenile xanthogranuloma	71	0.4
Proliferative myositis	57	0.3
Paraganglioma	56	0.3
Tumoral calcinosis	55	0.3
Elastofibroma	51	0.3
(Teno)synovial chondromatosis	46	0.3
Sclerosing retroperitonitis	44	0.2
Hibernoma	41	0.2
Ganglioneuroma	37	0.2
Other	144	0.8
Mesenchymal lesion, not further classified	577	3.1

[a]Based on an analysis of 18,677 cases seen in consultation over 10 years.

TABLE 2.3 Lesions of blood and lymph vessels

A. Age distribution (yr) of lesions of blood and lymph vessels

Diagnosis	<1	1–5	6–10	11–15	16–20	21–25	26–30	31–35	36–40	41–45	46–50	51–55	56–60	61–65	66–70	71–75	76–80	81–85	>85	Unknown age
Benign lesions of blood vessels																				
Capillary hemangioma[a]	32	17	12	20	24	18	23	27	28	21	23	16	13	20	10	10	3	6	2	16
Cavernous hemangioma	21	15	12	10	12	7	7	9	9	5	4	4	5	7	3	3	2			3
Arteriovenous hemangioma	1	13	4	8	4	11	5	5	5	1	3			2	4					
Epithelioid hemangioma			1	1	10	12	16	23	18	11	8	6	4	4	4	1	1		1	10
Intramuscular hemangioma	3	15	23	24	29	46	44	31	20	13	18	8	9	1	8	2	3	1		3
Hemangioma, not further classified	8	26	18	39	35	46	36	29	31	16	18	19	22	8	18	8	1	2	4	12
Angiomatosis	3	6	6	5	6	2		2		3	4	1	1							
Glomus[b]			2	6	9	13	7	7	15	13	13	12	8	12	14	10	6	3	2	12
Hemangiopericytoma	9	1	3	7	11	22	42	34	41	39	40	24	25	21	24	19	9	6	1	6
Papillary endothelial hyperplasia	2		1	5	13	16	9	11	12	16	7	8	9	6	6	7	4		2	2
Benign lesions of lymph vessels																				
Lymphangioma	10	45	11	20	11	12	7	5	3	6	5	2	4	4	1	1	1	2		1
Lymphangiomatosis		3			1	2					1		1				1			
Lymphangiomyoma/ lymphangiomyomatosis					1	1	1	1	1	1	1									
Malignant tumors																				
Hemangioendothelioma			3	5	7	13	12	5	14	7	9	6	8	4	6	3	1	2		4
Angiosarcoma	3	3	8	8	11	16	18	12	14	10	9	23	23	22	21	11	14	9	9	7
Kaposi sarcoma					2		7	10	5	5	3	3	9	18	20	16	29	9	11	5
Malignant hemangiopericytoma	5		2	2	3	12	10	10	10	9	12	18	7	9	8	10	7	2	2	3

[a]Includes juvenile hemangioma.
[b]Includes glomangioma and glomangiomyoma.