The Royal College of Pathologists
Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for the histopathological reporting of soft tissue sarcomas

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Comments	This document supersedes the 2014 document, Dataset for cancer histopathology reports on soft tissue sarcomas. This is an update to accommodate the *TNM Classification of Malignant Tumours (8th edition)* from the International Union against Cancer (UICC). In accordance with the College's pre-publications policy, this dataset was on The Royal College of Pathologists' website for consultation from 10 July to 8 August 2017. **Dr Lorna Williamson** **Director of Publishing and Engagement**

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Foreword

The cancer datasets published by The Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. It may rarely be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be assessed by the relevant multidisciplinary team (MDT); just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not necessarily be deemed negligent.

Each dataset contains **core data items** that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Dataset) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 90% of reports on cancer resections should record a full set of core data items. Other, **non-core data items** are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

As part of the consultation process, this document has been discussed and approved by the British Sarcoma Group and the British Bone and Soft Tissue Tumour Pathology Panel.

The recommendations used in this dataset are based on evidence obtained from the relevant literature on sarcoma diagnosis and management, grading and other predictive factors, and on the National Institute for Health and Clinical Excellence (NICE) guidelines, the World Health Organisation (WHO) classification of 2013,[1] the protocol of the College of American Pathologists[2] and the 8th edition of the staging manual of the Union for International Cancer Control (UICC).[3] Modified SIGN guidance has been used to grade the evidence (see Appendix G). Consensus of evidence in the datasets was achieved by expert review during the consultation process. Gaps in evidence were identified by members via feedback received from consultation.

No major organisational changes or cost implications have been identified that would hinder the implementation of the dataset.

The information used to develop this dataset was collected from electronic searches of the medical literature, previous recommendations from the RCPath, and local guidelines in the United Kingdom.

A formal revision cycle for all cancer datasets takes place on a 3-yearly basis. However, each year, the College will ask the author of the dataset, in conjunction with the relevant subspecialty adviser to the College, to consider whether or not the dataset needs to be updated or revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Histopathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken, whereby a short notice of the proposed changes will be placed on the College website for 2 weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the fully revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Clinical Effectiveness Department, Lay Governance Group and Working Group on Cancer Services. It has been placed on the College website for a consultation with the membership from 10 July to 8 August 2017. All comments received from the Working Group and membership were addressed by the author, to the satisfaction of the Chair of the Working Group and the Director of Publishing and Engagement.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Director of Clinical Effectiveness and are available on request. The author of this document has declared that there are no conflicts of interest.

1 Introduction

Malignant soft tissue tumours are rare, with an incidence of about 25 per million in the general population. They form a large and heterogeneous group of lesions which affect principally skin, subcutaneous tissue and deep soft tissue, as well as viscera, and can present in any anatomical site. Therefore, they are best managed by referral to a specialist multidisciplinary centre with expertise in imaging, histopathology, surgery and oncology. This should include access to cytogenetic and molecular genetic diagnostic services. Decisions about resectability and neoadjuvant therapy in soft tissue sarcomas are made following radiological and pathological assessment. Pathological features that are related to management and clinical outcome include histological type, grade, size, depth, stage and completeness of resection.[4] Vascular invasion has also been suggested as a component of a risk assessment system.[5]

The purpose of these guidelines is to define and assist pathologists in the provision of the core data that should be included in histopathology reports from biopsy and resection specimens of soft tissue sarcomas. Separate guidelines deal with uterine sarcomas, gastrointestinal stromal tumours and bone tumours. Paediatric sarcomas might need to be dealt with differently according to specific guidelines given in trial protocols. Sarcomas arising in the female genital tract can be dealt with either by a sarcoma or gynaecological oncology unit. Cutaneous sarcomas are usually managed by the Specialist Skin Cancer MDT, excluding those infiltrating more deeply, tumours originating in soft tissue and extending into the skin, and histological types requiring specific chemotherapy.

The guidelines are intended to assist pathologists in reporting soft tissue tumours and to gather data for the following reasons:

- to allow accurate histological typing of soft tissue sarcomas and their grading according to a recognised system, as this is essential for planning appropriate treatment
- to provide appropriate information for determining prognosis
- to encourage consistency of reporting, terminology and grading between cancer centres
- to provide information for clinical audit
- to potentially allow selection and appropriate grouping of patients for future clinical trials
- to provide accurate data for cancer registration.

The following changes have been made in this version:

- more detailed specifications have been given for the mitotic index

- the staging has been updated to include recommendations from the 8th edition of the Staging System of the Union for International Cancer Control (UICC). This recommendation includes use of a three-grade system in which grades 2 and 3 are regarded as high grade. The stage groupings have been modified accordingly.
- the references have been updated.

1.1 Who reports soft tissue sarcomas?

The Guidance on Cancer Services issued by NICE[6] indicates that all soft tissue sarcomas should be either first reported or reviewed by a specialist soft tissue sarcoma pathologist. This is defined as a pathologist who regularly reports soft tissue tumours as a significant component of their workload. A specialist pathologist should participate in external quality assessments (EQA), normally through the soft tissue part of the UK National Orthopaedic Pathology EQA scheme, and be a member of a properly constituted sarcoma MDT. All patients with soft tissue tumours assessed in a diagnostic clinic should have their pathology reported by either a specialist soft tissue pathologist or a pathologist nominated by the sarcoma MDT as part of the local diagnostic referral pathway and who has formal links to a specialist soft tissue pathologist.

1.2 Tumour type-specific issues

1.2.1 Types of specimen

Specimen types include needle core biopsies, open biopsies and resection specimens. The latter include local excisions, large specimens such as limb and limb girdle amputations, chest wall resections and intra-abdominal sarcomas with included viscera. Potential for recurrence and, less clearly, for metastasis[7] relates to adequacy of surgical excision. Assessment of clearance at surgical margins is therefore required.

1.2.2 Role of cytogenetics and molecular genetics

Genetic information is increasingly contributory in diagnosing and predicting behaviour of soft tissue sarcomas (Appendix D) and is becoming routinely available in specialist centres. For paediatric small round cell sarcomas, including neuroblastomas, Ewing sarcomas and alveolar rhabdomyosarcomas, genetic data are essential. For spindle cell sarcomas with a wide differential diagnosis, such as monophasic or poorly differentiated synovial sarcomas and low-grade fibromyxoid sarcomas, molecular genetic diagnosis is invaluable. Most investigations can now be performed on fixed tissue. Where a cytogenetic service is available, a portion of fresh tissue can be submitted in a suitable transport medium. The need for this can be anticipated if excision follows core biopsy diagnosis.

1.2.3 Frozen tissue

New antibodies[8] and molecular diagnostic techniques continue to be brought into routine use. While many of these can be applied to formalin-fixed, paraffin-embedded tissue, some approaches, including gene expression profiling, require unfixed material. Where feasible, arrangements should therefore be made for specimens to be submitted to the laboratory in their fresh state and without delay so that a suitable sample of tissue can be frozen in liquid nitrogen and stored at -80 °C in an appropriate facility. Electron microscopy now has a limited role[9] but its use should be considered where specifically indicated, so that a small portion of tissue can be appropriately fixed and saved for referral to a specialist unit if this is subsequently needed.

1.3 Target users and health benefits of this guideline

The target primary users of this dataset are trainee and consultant cellular pathologists and, on their behalf, the suppliers of IT products to laboratories. The secondary users are surgeons,

oncologists, cancer registries and the National Cancer Intelligence Network. Standardised cancer reporting and MDT working reduce the risk of histological misdiagnosis and help to ensure that clinicians have all of the relevant pathological information required for tumour staging, management and prognosis. Collection of standardised cancer specific data also provides information for healthcare providers, epidemiologists, and facilitates international benchmarking and research.

2 Clinical information required on the specimen request form

This must include the patient's name, date of birth, sex, hospital number and NHS/CHI number, and the name of the clinician to whom the report should be sent, as well as the date of the procedure and the specimen type.

In addition, the site of the tumour, its depth from the surface (cutaneous, subcutaneous or subfascial), size and duration are essential clinical data that are required before issuing the report. Details of previous occurrences, surgery, radiation or chemotherapy should also be provided.

3 Preparation of specimens before dissection

Needle core biopsies and open biopsies should be fixed promptly in formalin. If required by local practice, the specimen can be received fresh and a portion can be frozen in liquid nitrogen and stored at -80°C.

If facilities permit, resection specimens should be submitted to the laboratory without formalin, immediately after removal from the patient, to allow orientation and sampling of fresh tissue for genetic studies and storage. Intra-abdominal and retroperitoneal sarcomas can be weighed according to local practice. Specimens are orientated (it is helpful if the surgeon has placed orientating sutures) and measured, and the resection margins identified. This can be done by inking all or part of the specimen, or by cutting the block into a specified shape. The method used should be indicated in the report. Intra-abdominal and retroperitoneal sarcomas do not require surface inking unless locally required by the surgeon. The specimen should then be sliced transversely at 10 mm intervals. After small portions of tumour are removed for freezing, the specimen should be placed in formalin in an adequately sized container and allowed to fix for 24–48 hours. A suitable portion of the specimen should be photographed either before or after fixation; the latter often gives more satisfactory results.

4 Specimen handling and block selection

Needle core biopsies should be counted and measured. If the cores are not fragmented, and resources allow, it is preferable to separate and embed them in more than one cassette to allow maximal use of the available material.

Open biopsies should preferably be divided and placed into more than one cassette if there is sufficient tissue.

Resection specimens should be measured in three dimensions, and the closest distance of each margin from the edge of the tumour noted, including the deep aspect for subcutaneous or intramuscular sarcomas. The tissue plane(s) in which the tumour is located is recorded. Size,

colour, consistency, presence of cysts, haemorrhage and necrosis are noted. The amount of necrosis is assessed as a percentage of the whole tumour.

Blocks are taken to include the nearest resection edge and the deep margin where appropriate. It is not necessary to take a resection margin which is more than 30 mm away from the main tumour with the exceptions of some superficial sarcomas, notably low-grade myxofibrosarcomas[10] and epithelioid sarcomas,[11] which can infiltrate microscopically. Lesions that are smaller than 50 mm in diameter should be processed in their entirety. It is generally recommended that one block be taken per 10 mm of the longest dimension of the tumour, up to a maximum of 12, though cases previously diagnosed on biopsy as of high grade malignancy need fewer blocks.[2]

Areas that appear visibly different require appropriate extra sampling. In large liposarcomas, especially those from the retroperitoneum, any firmer or differently coloured areas should be sampled to detect dedifferentiation.

5 Core data items

5.1 Clinical

- site
- depth from surface.

5.2 Pathological

- size of tumour
- histological type and subtype
- grade
- tissue planes involved
- relationship to margins
- stage
- cytogenetic and molecular genetic findings (for small round cell tumours).

5.2.1 Size

The macroscopic measurements should be given unless different on histology. Measurements should be given for three dimensions, in millimetres.

5.2.2 Histological subtype

Soft tissue sarcomas are currently designated and categorised according to the WHO consensus classification of 2013.[1] This includes malignant neoplasms and those of intermediate malignancy. The latter category comprises locally aggressive neoplasms, e.g. fibromatosis, and those which rarely metastasize, such as plexiform fibrohistiocytic tumours, angiomatoid fibrous histiocytomas and inflammatory myofibroblastic tumours. Tumours in both categories are included in these recommendations.

[Level of evidence: Histological subtype is important for cancer registration and prognosis, and in some subtypes for grading and prediction of response to therapy – level B.]

5.2.3 Grade

The grading system in common use in Europe and elsewhere,[12] and recommended by the European Organization for Research and Treatment of Cancer (EORTC), is that of the French Federation of Cancer Centers Sarcoma Group (FNCLCC).[4,13] This is a three-step scoring system based on summation of independent scores for differentiation (see Appendix C), mitotic index per 10 high power fields, and amount of necrosis. Mitoses should be counted in the most mitotically active areas in ten successive fields using a x40 objective and a standard x10 eyepiece. The mitotic index is expressed as number of mitoses in 10 HPF, using x40 objective in the most proliferative area. 1 HPF (x 400) = 0.1734 square mm.[2,14] The number of high power fields might need to be varied according to the field area of individual microscopes. For low-grade smooth muscle tumours where the mitotic index is critical for assessing malignancy or metastatic potential,[15–17] mitoses should be counted in 50 high power fields. The percentage of necrosis should be assessed macroscopically except in small biopsies.

[Level of evidence B – Histological grade is important for prognostication, as a guide to management, and as a major determinant of stage.]

5.2.4 Tissue planes involved

Specify whether the tumour involves skin/subcutis or deep fascia/subfascial tissue or more than one plane.

[Level of evidence B – Depth of tumour from surface is important for prognostication.]

5.2.5 Relationship to margins

A measurement in millimetres of the clearance at the nearest surgical margin should be given and the type of tissue at the nearest margin stated (e.g. fascia, fat, muscle or skin). A comment should be added on the nature of the invasive margin (infiltrative *versus* pushing) and on vascular invasion if present.[30]

[Level of evidence B – Adequacy of clearance of excision margins is important for predicting local recurrence.]

5.2.6 Stage

Soft tissue sarcomas are staged using the staging system of the UICC (TNM) (see Appendix B) or the American Joint Committee on Cancer (AJCC).[18] Isolated pathologic staging is, however, of limited value and formal tumour staging should be completed after discussion at the MDT. Uterine leiomyosarcomas can be staged by either the modified International Federation of Gynecology and Obstetrics (FIGO) staging system for uterine cancer or the AJCC system for soft tissue sarcomas, though neither is ideal.[19,20]

[Level of evidence B – Staging is important for prognostication, and grading is an important component of staging.]

6 Non-core data items

6.1 Clinical

- duration of lesion
- previous surgery
- previous irradiation or chemotherapy.

6.2 Pathological

6.2.1 Macroscopic

- consistency – presence of cysts, calcification
- colour.

6.2.2 Microscopic

- vascular invasion
- nerve invasion
- bone invasion.

6.2.3 Ancillary investigations

- immunohistochemistry (including Ki-67 index of proliferation)
- cytogenetic and molecular genetic findings (except for small round cell tumours).

7 Diagnostic coding

SNOMED coding is incorporated in the 2013 WHO classification of soft tissue tumours (see Appendix A).

8 Reporting of small biopsy specimens

The report should include histological diagnosis (type and subtype) and grade with the caveat that the excised lesion might be found to have a higher grade of malignancy.[21] Information from immunohistochemical investigations should be included where appropriate. Results from genetic investigations, which might take several days, can be issued in a supplementary report.

9 Reporting of frozen sections

Frozen section diagnosis is rarely required in the United Kingdom because of the widespread use of needle core biopsy. It is occasionally requested for confirmation of the presence of a tumour, but is not indicated for assessment of margins. The report should note the presence or absence of neoplasm.

10 Cytological diagnosis

10.1 Role of fine needle aspiration cytology (FNAC)

Initial diagnosis and grading of soft tissue sarcomas on cytological specimens requires considerable experience, and FNAC therefore has a limited role outside a few specialist centres.[22] It can, however, be of use in confirming recurrence or metastasis in a patient with a previously diagnosed sarcoma.

11 Specific aspects of individual tumours not covered elsewhere

The terms ‘atypical lipomatous tumour’ and ‘well-differentiated liposarcoma’ are used synonymously. However, the latter term is sometimes preferred for deeply located tumours, especially those in the abdomen and retroperitoneum, because of their increased propensity for dedifferentiation.

Extremity pleomorphic sarcomas with myogenic differentiation have a worse prognosis when matched for other variables.[23,24] Since this applies when there is only immunohistochemical evidence of myogenic differentiation, the presence of immunoreactivity for smooth muscle actin, desmin, smooth muscle myosin, h-caldesmon, or MyoD1 or myogenin in nuclei, should be specifically noted, including its amount (diffuse, focal or occasional).

There is evidence that many undifferentiated pleomorphic sarcomas or myxofibrosarcomas arising in retroperitoneum or abdominal cavity represent dedifferentiated liposarcomas.[25,26] The prognosis of a dedifferentiated liposarcoma is better than that of an undifferentiated pleomorphic sarcoma.[27] Therefore, in such cases any apparently innocuous fatty tissue at the periphery should also be sampled to detect a component of a well-differentiated liposarcoma. Immunoreactivity for MDM2 and CDK4 can also facilitate the diagnosis of dedifferentiated liposarcomas.

In most sarcomas, it is not necessary to assess the proliferation index as well as the mitotic count. However, for grade 2 or grade 3 sarcomas, the proliferation index might have a predictive value.[28,29] A semi-quantitative assessment of immunoreactivity for Ki-67 can be reported depending on local clinical practice.

Sarcomas of gynaecological origin can be handled similarly to soft tissue sarcomas where locally requested by clinicians. Uterine sarcomas are the subject of a separate dataset.

Biopsies or excisions of metastatic tumours should be reported in the same way, including grade. Where possible, the pathology should be compared with that of the primary tumour, to confirm that this is indeed metastatic and not a new tumour, to assess grade progression and to evaluate emergence of new or divergent lineages that might influence management.

12 Criteria for audit of the dataset

In keeping with the recommended key performance indicators published by The Royal College of Pathologists (www.rcpath.org/clinical-effectiveness/kpi), reports on soft tissue sarcomas should be audited for the following:

- The inclusion of SNOMED or SNOMED-CT codes:
  - standard: 95% reports should have T, M and P codes.
- The availability of pathology reports and data at MDT meetings:
  - standard: 90% of cases discussed at MDT meetings where biopsies or resections have been taken should have pathology reports/core data available for discussion
  - standard: 90% of cases where pathology has been reviewed for the MDT meeting should have the process of review recorded.
- The use of electronic structured reports or locally agreed proformas (it is assumed that these processes will ensure that 90% of core data items are recorded):

- standard: 80% of resection specimens will include 100% of data items presented in a structured format.

- Turnaround times for biopsies and resection specimens:
  - standard: 80% diagnostic biopsies will be reported within 7 calendar days of the biopsy being taken
  - standard: 80% of all histopathology specimens (excluding those requiring decalcification) will be reported within 10 calendar days of the specimen being taken.

13 References

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Appendix A Histological types of sarcoma with SNOMED and SNOMED-CT coding

Morphological codes	SNOMED code	SNOMED-CT terminology	SNOMED-CT code
Adipocytic tumours			
Intermediate (locally aggressive)			
Atypical lipomatous tumour	M-88501	Atypical lipoma (morphologic abnormality)	116063003
Well-differentiated liposarcoma	M-88503	Well-differentiated liposarcoma	28655007
Malignant			
Dedifferentiated liposarcoma	M-88583	Dedifferentiated liposarcoma (morphologic abnormality)	67280001
Myxoid liposarcoma	M-88523	Myxoid liposarcoma (morphologic abnormality)	27849002
Pleomorphic liposarcoma	M-88543	Pleomorphic liposarcoma (morphologic abnormality)	112683004
Liposarcoma, not otherwise specified	M-88503	Liposarcoma, no ICD-O subtype (morphologic abnormality)	49430005
Fibroblastic/myofibroblastic tumours			
Intermediate (locally aggressive)			
Palmar/plantar type fibromatosis	M-88131	No code	No code
Desmoid-type fibromatosis	M- 88211	Aggressive fibromatosis (morphologic abnormality)	47284001
Lipofibromatosis	M-88511	Lipofibromatosis (morphologic abnormality)	703633001
Giant cell fibroblastoma	M-88341	Giant cell fibroblastoma (morphologic abnormality)	128742004
Intermediate (rarely metastasizing)			
Dermatofibrosarcoma protuberans	M-88321	Dermatofibrosarcoma (morphologic abnormality)	76594008
Fibrosarcomatous dermatofibrosarcoma protuberans	M-88323	No code	No code
Pigmented dermatofibrosarcoma protuberans	M-88331	Pigmented dermatofibrosarcoma protuberans (morphologic abnormality)	62621002
Solitary fibrous tumour	M-88151	Solitary fibrous tumour (morphologic abnormality)	128736003

Morphological codes (continued)	SNOMED code	SNOMED-CT terminology	SNOMED-CT code
Solitary fibrous tumour, malignant	M-88153	Solitary fibrous tumour, malignant (morphologic abnormality)	128737007
Inflammatory myofibroblastic sarcoma	M-88251	Myofibroblastic tumour (morphologic abnormality)	116064009
Low grade myofibroblastic sarcoma	M-88253	Low grade myofibroblastic sarcoma (morphologic abnormality)	703615007
Myxoinflammatory fibroblastic sarcoma	M-88111	Myxoinflammatory fibroblastic sarcoma (morphologic abnormality)	703608004
Infantile fibrosarcoma	M-88143	Infantile fibrosarcoma (morphologic abnormality)	5204006
Malignant			
Adult fibrosarcoma	M-88103	Fibrosarcoma (morphologic abnormality)	53654007
Myxofibrosarcoma	M-88113	Fibromyxosarcoma (morphologic abnormality)	6250003
Low-grade fibromyxoid sarcoma	M-88403	Low grade fibromyxoid sarcoma (morphologic abnormality)	703617004
Sclerosing epithelioid fibrosarcoma	M-88403	Sclerosing epithelioid fibrosarcoma (morphologic abnormality)	703618009
So-called fibrohistiocytic tumours			
Intermediate (rarely metastasizing)			
Plexiform fibrohistiocytic tumour	M-88351	Plexiform fibrohistiocytic tumour (morphologic abnormality)	128743009
Giant cell tumour of soft tissue	M-92511	Giant cell tumour of soft parts (morphologic abnormality)	82125002
Smooth muscle tumours			
Malignant			
Leiomyosarcoma	M-88903	Leiomyosarcoma, no subtype (morphologic abnormality)	51549004
Skeletal muscle tumours			
Malignant			
Embryonal rhabdomyosarcoma (including botryoid, anaplastic)	M-89103	Embryonal rhabdomyosarcoma (morphologic abnormality)	14269005

Morphological codes (continued)	SNOMED code	SNOMED-CT terminology	SNOMED-CT code
Alveolar rhabdomyosarcoma (including solid, anaplastic)	M-89203	Alveolar rhabdomyosarcoma (morphologic abnormality)	63449009
Pleomorphic rhabdomyosarcoma	M-89013	Pleomorphic rhabdomyosarcoma (morphologic abnormality)	77455004
Spindle cell/sclerosing rhabdomyosarcoma	M-89123	Spindle cell rhabdomyosarcoma (morphologic abnormality)	128749008
Vascular tumours			
Intermediate (locally aggressive)			
Kaposiform haemangioendothelioma	M-91301	Hemangioendothelioma (morphologic abnormality)	66229009
Intermediate (rarely metastasizing)			
Retiform haemangioendothelioma	M-91361	Spindle cell hemangioendothelioma (morphologic abnormality)	128769003
Papillary intralymphatic angioendothelioma	M-91351	Endovascular papillary angioendothelioma (morphologic abnormality)	128768006
Composite haemangioendothelioma	M-91361	Spindle cell hemangioendothelioma (morphologic abnormality)	128769003
Pseudomyogenic (epithelioid sarcoma-like) haemangioendothelioma	M-91361	Spindle cell hemangioendothelioma (morphologic abnormality)	128769003
Kaposi sarcoma	M-91403	Kaposi's sarcoma, morphology (morphologic abnormality)	49937004
Malignant			
Epithelioid haemangioendothelioma	M-91333	Epithelioid hemangioendothelioma (morphologic abnormality)	84290008
Angiosarcoma of soft tissue	M-91203	Hemangiosarcoma (morphologic abnormality)	39000009
Nerve sheath tumours			
Malignant			
Malignant peripheral nerve sheath tumour	M-95403	Malignant peripheral nerve sheath tumour (morphologic abnormality)	19897006
Epithelioid malignant peripheral nerve sheath tumour	M-95423	Epithelioid malignant nerve sheath tumour (morphological abnormality)	253033000

Morphological codes (continued)	SNOMED code	SNOMED-CT terminology	SNOMED-CT code
Malignant Triton tumour	M-95613	Malignant peripheral nerve sheath tumour with rhabdomyoblastic differentiation (morphologic abnormality)	354002
Malignant granular cell tumour	M-95803	Granular cell tumour, malignant (morphologic abnormality)	13238004
Ectomesenchymoma	M-89213	Rhabdomyosarcoma with ganglionic differentiation (morphologic abnormality)	128750008
Chondro-osseus tumours			
Mesenchymal chondrosarcoma	M-92403	Mesenchymal chondrosarcoma (morphologic abnormality)	56565002
Extraskeletal osteosarcoma	M-91803	Osteosarcoma, no ICD-O subtype (morphologic abnormality)	21708004
Tumours of uncertain differentiation			
Intermediate (locally aggressive)			
Haemosiderotic fibrolipomatous tumour	M-88111	No code	No code
Intermediate (rarely metastasizing)			
Atypical fibroxanthoma	M-88301	Atypical fibrous histiocytoma (morphologic abnormality)	26496005
Angiomatoid fibrous histiocytoma	M-88361	Angiomatoid fibrous histiocytoma (morphologic abnormality)	128744003
Ossifying fibromyxoid tumour, malignant	M-88423	Ossifying fibromyxoid tumour, malignant (morphologic abnormality)	703631004
Mixed tumour NOS, malignant	M-89403	Mixed tumour, malignant (morphologic abnormality)	8145008
Myoepithelial carcinoma	M-89823	Malignant myoepithelioma (morphologic abnormality)	128884000
Phosphaturic mesenchymal tumour, malignant	M-89903	Mesenchymoma, malignant (morphologic abnormality)	89623007
Malignant			
Synovial sarcoma, NOS	M-90403	Synovial sarcoma (morphologic abnormality)	63211008
Synovial sarcoma, spindle cell	M-90413	Synovial sarcoma, spindle cell (morphologic abnormality)	37206003

Morphological codes (continued)	SNOMED code	SNOMED-CT terminology	SNOMED-CT code
Synovial sarcoma, biphasic	M-90433	Synovial sarcoma, biphasic (morphologic abnormality)	18588008
Epithelioid sarcoma	M-88043	Epithelioid sarcoma (morphologic abnormality)	59238007
Alveolar soft-part sarcoma	M-95813	Alveolar soft part sarcoma (morphologic abnormality)	88195001
Clear cell sarcoma of soft tissue	M-90443	Clear cell sarcoma (except of Kidney M-89643) (morphologic abnormality)	12622007
Extraskeletal myxoid chondrosarcoma	M-92313	Myxoid chondrosarcoma (morphologic abnormality)	75622000
Extraskeletal Ewing sarcoma	M-93643	Peripheral neuroectodermal tumour (morphologic abnormality)	73676002
Desmoplastic small round cell tumour	M-88063	Desmoplastic small round cell tumour (morphologic abnormality)	128735004
Extra-renal rhabdoid tumour	M-89633	Malignant rhabdoid tumour (morphologic abnormality)	83118000
Neoplasms with perivascular epithelioid cell differentiation (PEComa) – PEComa, malignant	M-87143	Perivascular epithelioid tumour, malignant (morphologic abnormality)	703605001
Intimal sarcoma	M-91373	Intimal sarcoma (morphologic abnormality)	703661007

Appendix B Staging system of The Union for International Cancer Control (UICC TNM7 and UICC TNM8)

Please note that UICC TNM7 should be used for all soft tissue sarcomas diagnosed before 1 January 2018. UICC TNM8 should be used for all soft tissue sarcomas diagnosed from 1 January 2018.

UICC TNM7 (until 31 December 2017)

Primary tumour (T)

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

T1 Tumour 50 mm or less in greatest dimension
T1a Superficial tumour*
T1b Deep tumour*

T2 Tumour more than 50 mm in greatest dimension
T1a Superficial tumour*
T1b Deep tumour*

* - Superficial tumour is located exclusively above the superficial fascia without invasion of the fascia; deep tumour is located either exclusively beneath the superficial fascia or superficial to the fascia with invasion of or through the fascia. Retroperitoneal, mediastinal and pelvic sarcomas are classified as deep tumours.

UICC TNM8 (from 1 January 2018)

Primary tumour (T)

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

Extremity and Superficial Trunk

T1 Tumour 50 mm or less in greatest dimension

T2 Tumour more than 50 mm but no more than 100 mm in greatest dimension

T3 Tumour more than 100 mm but no more than 150 mm in greatest dimension

T4 Tumour more than 150 mm in greatest dimension

Retroperitoneum

T1 Tumour 50 mm or less in greatest dimension

T2 Tumour more than 50 mm but no more than 100 mm in greatest dimension

T3 Tumour more than 100 mm but no more than 150 mm in greatest dimension

T4 Tumour more than 150 mm in greatest dimension

Head and Neck

T1 Tumour 20 mm or less in greatest dimension

T2 Tumour more than 20 mm but no more than 40 mm in greatest dimension

T3 Tumour more than 40 mm in greatest dimension

T4a Tumour invades the orbit, skull base or dura, central compartment viscera, facial skeleton and or pterygoid muscles

T4b Tumour invades the brain parenchyma, encases the carotid artery, invades prevertebral muscle or involves the central nervous system by perineural spread

Thoracic and Abdominal Viscera

T1 Tumour confined to a single organ

T2a Tumour invades serosa or visceral peritoneum

T2b Tumour with microscopic extension beyond the serosa

T3 Tumour invades another organ or macroscopic extension beyond the serosa

T4a Multifocal tumour involving no more than two sites in one organ

T4b Multifocal tumour involving more than two sites but not more than 5 sites

T4c Multifocal tumour involving more than 5 sites

Regional lymph nodes (N) [Applies to both UICC TNM 7 and UICC TNM8]

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Regional lymph node metastasis

Distant metastasis (M) [Applies to both UICC TNM 7 and UICC TNM8]

M0 No distant metastasis
M1 Distant metastasis

Stage grouping

Note: In the TNM two-grade system, Grade 1 in the French Federation of Cancer Centers' system is equivalent to low grade, and Grades 2 and 3 are equivalent to high grade.

UICC TNM7 (until 31 December 2017)

Stage	Primary tumour	Regional lymph nodes	Distant metastasis	Grade
IA	T1a, T1b	N0	M0	G1, GX
IB	T2a, T2b	N0	M0	G1, GX
IIA	T1a, T1b	N0	M0	G2,G3
IIB	T2a, T2b	N0	M0	G2
III	T2a, T2b	N0	M0	G3
	Any T	N1	M0	Any G
IV	Any T	Any N	M1	Any G

UICC TNM8 (from 1 January 2018)

Stage	Primary tumour	Regional lymph nodes	Distant metastasis	Grade
IA	T1	N0	M0	G1, GX Low Grade
IB	T2,3,4	N0	M0	G1, GX Low Grade
II	T1	N0	M0	G2,G3 High Grade
IIIA	T2	N0	M0	G2 G3 High Grade
IIIB	T3, T4	N0	M0	G2,G3 High Grade
IIIB	Any T	N1	M1	Any G
IV	Any T	Any N	M1	Any G

Notes

1. The staging system applies to all soft tissue sarcomas except Kaposi sarcoma, dermatofibrosarcoma protuberans, desmoid fibromatosis and angiosarcoma. In addition, sarcomas arising from the dura mater, including the brain, and sarcomas arising in parenchymatous organs (except breast sarcomas) and from hollow viscera are not included.

2. Depth is assessed as follows:

   Superficial: lesion does not involve deep fascia

Deep: (a) lesion involves or is deep to deep fascia

(b) all intraperitoneal, retroperitoneal, visceral, paratesticular, and intrathoracic sarcomas, and non-cutaneous major head and neck sarcomas, are considered to be deep.

Note: deep fascia is considered to be the fascia between subcutaneous fat and muscle.

3. Completeness of resection can be a prognostic factor.[30] Use of the AJCC residual tumour (R) classification of the AJCC/UICC for tumours after treatment is optional:

RX Presence of residual tumour cannot be assessed

R0 No residual tumour

R1 Microscopic residual tumour

R2 Macroscopic residual tumour.

Appendix C French Federation of Cancer Centers' System of Grading[14]

Tumour differentiation

Score 1 Sarcoma histologically very similar to normal adult mesenchymal tissue

2 Sarcoma of defined histological subtype (e.g. myxofibrosarcoma)

3 Sarcoma of uncertain type, embryonal and undifferentiated sarcomas

Mitosis count (see 5.2.3)

Score 1 0–9 / 10 HPF

2 10–19 / 10 HPF

3 >20 / 10 HPF

Microscopic tumour necrosis

Score 0 No necrosis

1 < 50% tumour necrosis

2 > 50% tumour necrosis

Histological grade

Grade 1 Total score 2 or 3

Grade 2 Total score 4 or 5

Grade 3 Total score 6, 7 or 8

Tumour differentiation scores

Well-differentiated liposarcoma	1
Well-differentiated leiomyosarcoma	1
Malignant neurofibroma	1
Well-differentiated fibrosarcoma	1
Myxoid liposarcoma	2
Conventional fibrosarcoma	2
Conventional MPNST	2
Conventional fibrosarcoma	2
Myxofibrosarcoma	2
Myxoid chondrosarcoma	2
Conventional leiomyosarcoma	2
Conventional angiosarcoma*	

High-grade myxoid (round cell) liposarcoma	3
Pleomorphic liposarcoma	3
Dedifferentiated liposarcoma	3
Poorly differentiated/epithelioid angiosarcoma	3
Poorly differentiated MPNST*	3
Malignant Triton tumour*	3
Poorly differentiated/pleomorphic leiomyosarcoma	3
Synovial sarcoma	3
Rhabdomyosarcoma*	3
Mesenchymal chondrosarcoma	3
Poorly differentiated/epithelioid angiosarcoma	3
Extraskeletal osteosarcoma*	3
Extraskeletal Ewing sarcoma*	3
Alveolar soft part sarcoma*	3
Malignant rhabdoid tumour	3
Clear cell sarcoma*	3
Undifferentiated (spindle cell and pleomorphic) sarcoma	3

* Grading of malignant peripheral nerve sheath tumour is of no prognostic value.

Grading of embryonal and alveolar rhabdomyosarcoma, angiosarcoma, extraskeletal myxoid chondrosarcoma, alveolar soft part sarcoma, clear cell sarcoma, and epithelioid sarcoma is not recommended. In practice, the following tumours are graded by definition as below.

Notes

1. Atypical lipomatous tumour/well-differentiated liposarcoma, dermatofibrosarcoma protuberans, infantile fibrosarcoma and angiomatoid fibrous histiocytoma are Grade 1.

2. Ewing sarcoma/PNET, rhabdomyosarcoma (except spindle cell and botryoid variants), angiosarcoma, pleomorphic liposarcoma, soft tissue osteosarcoma, mesenchymal chondrosarcoma, desmoplastic small round cell tumour, and extra-renal malignant rhabdoid tumour are Grade 3.

3. Alveolar soft part sarcoma, clear cell sarcoma, and epithelioid sarcoma are not graded but are usually considered as high grade for management purposes.

Appendix D Translocations and other genetic abnormalities in sarcomas

Histological type	Translocation or rearrangement	Fusion gene or other feature
Alveolar soft part sarcoma	t(X;17)(p11;q25)	*ASPL-TFE3*
Angiomatoid fibrous histiocytoma	t(12;22)(q13;q12) t(12;16)(q13;p11) t (2;22)(q33;q12)	*EWSR1-ATF1* *FUS-ATF1* *EWSR1-CREB1*
Clear cell sarcoma	t(12;22)(q13;q12)	*EWSR1-ATF1*
Clear cell sarcoma (GIT)	t (2;22)(q33;q12)	*EWSR1-CREB1*
Dermatofibrosarcoma protuberans	t(17;22)(q21;q13) Ring form of chromosomes 17 and 22	*COL1A1-PDGFB*
Desmoplastic SRCT	t(11;22)(p13;q12)	*EWSR1-WT1*
Epithelioid haemangioendothelioma	t(1;3)(p36.3;q25)	*WWTR1-CAMTA1*
Epithelioid sarcoma	Abnormalities of 22q	INI1 inactivation
Ewing sarcoma/PNET	t(11;22)(q24;q12) t(21;22)(q12;q12) t(2;22)(q33;q12) t(7;22)(p22;q12) t(17;22)(q12;q12) inv(22)(q12;q12)	*EWSR1-FLI1* *EWSR1-ERG* *EWSR1-FEV* *EWSR1-ETV1* *EWSR1-E1AF* *EWSR1-ZSG*
Extraskeletal myxoid chondrosarcoma	t(9;22)(q22;q12) t(9;17)(q22;q11) t(9;15)(q22;q21)	*EWSR1-NR4A3* *TAF1168-NR4A3* *TCF12-NR4A3*
Fibrosarcoma, infantile	t(12;15)(p13;q26) Trisomies 8, 11, 17, and 20	*ETV6-NTRK3*
Inflammatory myofibroblastic tumour	2p23 rearrangement	*ALK* fusions with various genes
Leiomyosarcoma	Deletion of 1p	
Liposarcoma: Well-differentiated Myxoid/round cell	 Ring form of chromosome 12 t(12;16)(q13;p11) t(12;22)(q13;q12)	 *FUS-DDIT3* *EWSR1-DDIT3*
Pleomorphic	Complex	
Low-grade fibromyxoid sarcoma	t(7;16)(q33;p11)	*FUS-CREB3L2* *FUS-CREB3L1* (rare)
Malignant rhabdoid tumour	Deletion of 22q	INI1 inactivation
Myoepithelial tumour of soft tissue	t(19;22)(q13;q12) t(1;22)(q23;q12) t(6;22)(p21;q12)	*EWSR1-ZNF444* *EWSR1-PBX1* *EWSR1-POU5F1*

Histological type	Translocation or rearrangement	Fusion gene or other feature
MPNST	Complex	
Myxofibrosarcoma	Ring form of chromosome 12	
Primary pulmonary myxoid sarcoma	t (2;22)(q33;q12)	*EWSR1-CREB1*
Rhabdomyosarcoma: Embryonal Alveolar	 Trisomies 2q, 8, and 20 t(1;13)(p36;q14) t(2;13)(q35;q14)	 LOH at 11p15 *PAX7-FKHR* *PAX3-FKHR*
Synovial sarcoma	t(X;18)(p11;q11) t(X;20)(p11;q13)	*SS18-SSX1* *SS18-SSX2* *SS18-SSX4* (rare) *SS18L1-SSX1*

Key

GIT	gastrointestinal tract
SRCT	small round cell tumour
PNET	primitive neuroectodermal tumour
MFH	malignant fibrous histiocytoma
MPNST	malignant peripheral nerve sheath tumour
LOH	loss of heterozygosity

Appendix E Reporting proforma for soft tissue sarcomas

Surname…… Forenames…… Date of birth……..... Sex.....

Hospital…… Hospital no……..... NHS/CHI no……..

Date of receipt……..…… Date of reporting……..…..... Report no……....

Pathologist……..……... Surgeon…….……

Clinical information

Site of tumour† ……

Depth from surface:

Cutaneous ☐ Subcutaneous ☐ Fascial/subfascial ☐ Not known ☐

Pathological information

Maximum tumour dimension†: ……..…. mm

Histological type (and subtype) †: ……

Grade (FNCLCC) †: 1 ☐ 2 ☐ 3 ☐

Tissue planes involved (indicate all planes) †:

Cutaneous ☐ Subcutaneous ☐ Deep fascia ☐ Subfascial ☐ Not known ☐

Status of margins:

Distance to nearest margin† ..... mm Type of tissue at margin .....…….

Margin not assessable ☐

Cytogenetic and molecular genetic data (for small round cell tumours, optional for others) †:

…….

Provisional pathological stage (where known) †

…… (TNM edition: ……)

SNOMED codes: T†…… M†……..

Comments/additional information

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† Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) version 6.

Signature: ……. Date: ……

Notes

Appendix F Reporting proforma for soft tissue sarcomas in list format

Element name	Values	Implementation notes
Site of tumour	Free text	
Depth from surface	Single selection value list: • Cutaneous • Subcutaneous • Fascial/subfascial • Not known	
Maximum tumour dimension	Size in mm x mm x mm	
Histological type (and subtype)	Free text	
Grade (FNCLCC)	Single selection value list: • 1 • 2 • 3	
Tissue planes involved	Multiple selection value list: • Cutaneous • Subcutaneous • Deep fascia • Subfascial • Not known	
Distance to nearest margin	Size in mm	
Type of tissue at margin	Free text	
Margin status	Single selection value list: • Assessable • Not assessable	If distance to margin is not null then assessable
Cytogenetic and molecular genetic data	Free text	
pT stage	Single selection value list: • X • 0 • 1 • 2a • 2b • 3 • 4a • 4b • 4c	

Element name (continued)	Values	Implementation notes
pN stage	Single selection value list: • X • 0 • 1	
pM stage	Single selection value list: • Not applicable • 1	
TNM edition	Single selection value list • 8 • 9 • 10	
SNOMED-T code	May have multiple codes. Look up from SNOMED tables.	
SNOMED-M code	May have multiple codes. Look up from SNOMED tables.	

Appendix G Summary table – explanation of levels of evidence

(modified from Palmer K *et al. BMJ* 2008;337:1832.)

Level of evidence	Nature of evidence
Level A	At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Level B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in A.
Level C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high-quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B.
Level D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix H AGREE monitoring sheet

The cancer datasets of the Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines (www.agreetrust.org). The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated below.

AGREE standard	Section of dataset
SCOPE AND PURPOSE	
1. The overall objective(s) of the guideline is (are) specifically described	Foreword, 1
2. The clinical question(s) covered by the guidelines is (are) specifically described	Foreword, 1
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword, 1
STAKEHOLDER INVOLVEMENT	
4. The guideline development group includes individuals from all the relevant professional groups	Foreword
5. The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6. The target users of the guideline are clearly defined	1
RIGOUR OF DEVELOPMENT	
7. Systematic methods were used to search for evidence	Foreword
8. The criteria for selecting the evidence are clearly described	Foreword
9. The strengths and limitations of the body of evidence are clearly described	Foreword
10. The methods used for formulating the recommendations are clearly described	Foreword
11. The health benefits, side effects and risks have been considered in formulating the recommendations	1
12. There is an explicit link between the recommendations and the supporting evidence	2–11
13. The guideline has been externally reviewed by experts prior to its publication	1
14. A procedure for updating the guideline is provided	Foreword
CLARITY OF PRESENTATION	
15. The recommendations are specific and unambiguous	2–11
16. The different options for management of the condition or health issue are clearly presented	2–11
17. Key recommendations are easily identifiable	2–11
APPLICABILITY	
18. The guideline describes facilitators and barriers to its application	Foreword
19. The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices A–F
20. The potential resource implications of applying the recommendations have been considered	Foreword
21. The guideline presents monitoring and/or auditing criteria	12
EDITORIAL INDEPENDENCE	
22. The views of the funding body have not influenced the content of the guideline	Foreword
23. Competing interest of guideline development group members have been recorded and addressed	Foreword