

SOFT TISSUE TUMOUR
Resection
STRUCTURED REPORTING
PROTOCOL
1st Edition (2011)

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Scope

This protocol contains standards and guidelines for the preparation of structured reports for resections for soft tissue sarcoma and other soft tissue tumours with the potential for aggressive behaviours, such as those classified by the WHO as “intermediate (locally aggressive)” – eg. desmoid type fibromatosis, well differentiated liposarcoma – or “intermediate (rarely metastasising)” – eg. solitary fibrous tumour, angiomatoid fibrous histiocytoma. For convenience, these tumours will henceforth be referred to as sarcoma. Although it may be considered a sarcoma of the gastrointestinal tract, Gastrointestinal Stromal Tumour (GIST) will not be considered in this document as it displays a number of unique features (including different AJCC staging parameters) which warrant its separate consideration. Whilst cutaneous sarcoma may be managed outside the setting of a specialist sarcoma group, the relevant guidelines in this document should be applied to those lesions involving subcutis (eg. a lesion recognised as Atypical Fibroxanthoma when confined to the dermis is likely to behave more aggressively if there is significant subcutaneous extension and/or vascular invasion, and may be more appropriately termed “cutaneous pleomorphic sarcoma”, with a comment as to the possibility of aggressive behaviour, including some risk of distant metastasis). Cutaneous angiosarcoma also tends to behave aggressively and may require referral to a specialist unit.

Structured reporting aims to improve the completeness and usability of pathology reports for clinicians, and improve decision support for cancer treatment. The protocol provides the framework for the reporting of any resection of aggressive soft tissue tumours, whether as a minimum data set or fully comprehensive report. This protocol may be applied to mesenchymal neoplasms arising not only in the extremities but at intracavitary, head and neck, or visceral locations. Some modifications of the standard report may be required to include relevant information for selected sites (eg accurate assessment of margins may be difficult in sarcoma of the retroperitoneum, mediastinum or spermatic cord). The committee recognises that many patients with soft tissue sarcoma (particularly in the paediatric group) will be entered in clinical trials and that adherence to trial protocols may necessitate modifications or additions to the standard report.

This document is based on information contained within multiple international publications and datasets and has been developed in consultation with local practising pathologists, oncologists, surgeons, radiologists and interested national bodies.

Abbreviations

AJCC	American Joint Committee on Cancer
FISH	Fluorescence In-Situ Hybridisation
FNCLCC	Federation Nationale des Centres de Lutte contre le Cancer
ISH	In-Situ Hybridisation
MDT	Multidisciplinary Team
NOS	Not Otherwise Specified
PBS	Pharmaceutical Benefits Scheme
PCR	Polymerase Chain Reaction
PNET	Primitive Neuroectodermal Tumour
POG	Paediatric Oncology Group
RCPA	Royal College of Pathologists of Australasia
STS	Soft Tissue Sarcoma
TNM	Tumour-Node-Metastasis
UICC	International Union Against Cancer
WHO	World Health Organization

Definitions

The table below provides definitions for general or technical terms used in this protocol. Readers should take particular note of the definitions for 'standard', 'guideline' and 'commentary', because these form the basis of the protocol.

Ancillary study	An ancillary study is any pathology investigation that may form part of a cancer pathology report but is not part of routine histological assessment.
Clinical information	Patient information required to inform pathological assessment, usually provided with the specimen request form, also referred to as "pre-test information".
Commentary	<p>Commentary is text, diagrams or photographs that clarify the standards (see below) and guidelines (see below), provide examples and help with interpretation, where necessary (not every standard or guideline has commentary).</p> <p>Commentary is used to:</p> <ul style="list-style-type: none">• define the way an item should be reported, to foster reproducibility• explain why an item is included (e.g. how does the item assist with clinical management or prognosis of the specific cancer).• cite published evidence in support of the standard or guideline• state any exceptions to a standard or guideline. <p>In this document, commentary is prefixed with 'CS' (for commentary on a standard) or 'CG' (for commentary on a guideline), numbered to be consistent with the relevant standard or guideline, and with sequential alphabetic lettering within each set of commentaries (eg CS1.01a, CG2.05b).</p>
General commentary	<p>General commentary is text that is not associated with a specific standard or guideline. It is used:</p> <ul style="list-style-type: none">• to provide a brief introduction to a chapter, if necessary• for items that are not standards or guidelines but are included in the protocol as items of potential importance, for which there is currently insufficient evidence to recommend their inclusion. (Note: in future reviews of protocols, such items may be reclassified as either standards or guidelines, in line with diagnostic and prognostic advances, following evidentiary review).

Guideline	<p>Guidelines are recommendations; they are not mandatory, as indicated by the use of the word 'should'. Guidelines cover items that are not essential for clinical management, staging or prognosis of a cancer, but are considered best practice.</p> <p>Guidelines include key observational and interpretative findings that are fundamental to the diagnosis and conclusion. Such findings are essential from a clinical governance perspective, because they provide a clear, evidentiary decision-making trail.</p> <p>Guidelines are not used for research items.</p> <p>In this document, guidelines are prefixed with 'G' and numbered consecutively within each chapter (eg G1.10).</p>
Macroscopic findings	Measurements, or assessment of a biopsy specimen made by the unaided eye.
Microscopic findings	In this document, the term 'microscopic findings' refers to morphological assessment using a microscope or equivalent.
Predictive factor	A <i>predictive factor</i> is a measurement that is associated with response or lack of response to a particular therapy.
Prognostic factor	A <i>prognostic factor</i> is a measurement that is associated with clinical outcome in the absence of therapy or with the application of a standard therapy. It can be thought of as a measure of the natural history of the disease.
Standard	<p>Standards are mandatory, as indicated by the use of the term 'must'. Their use is reserved for core items essential for the clinical management, staging or prognosis of the cancer.</p> <p>The summation of all standards represents the minimum dataset for the cancer.</p> <p>In this document, standards are prefixed with 'S' and numbered consecutively within each chapter (eg S1.02).</p>
Structured report	A report format which utilises standard headings, definitions and nomenclature with required information.
Synoptic report	A structured report in condensed form (as a synopsis or precis).
Synthesis	Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new. In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more modalities to derive new information

Introduction

SOFT TISSUE SARCOMA

Sarcoma refers to a group of aggressive neoplasms composed primarily of cells arising from or differentiating towards mesenchymally derived tissues including bone, cartilage, fibrous tissue, nerve, muscle, blood and lymphatic vessels, and fat. Tumours arising in bone will be considered in a separate protocol; the remainder may be collectively termed Soft Tissue Sarcoma (STS). This group of tumours, whilst numerically uncommon, are clinically important, occurring at all ages and anatomic locations and resulting in significant morbidity, mortality and years of life lost. Collectively, STS constitute some 1-2% of cancers but comprise more than 50 histotypes, so that individual sarcoma types range from uncommon to very rare. The collective 5-year survival for STS overall is estimated at around 50-60%¹ but within the group there is wide variation in clinical outcome depending on patient age, tumour location and histotype.

Accurate figures for sarcoma incidence and mortality are difficult to obtain because of potential variations in coding: one would expect that soft tissue sarcomata would be coded under categories C47 and C49 but these are in fact likely to reflect mainly extremity tumours, whereas for example there is a separate category (C48) for tumours of the peritoneum and retroperitoneum and it is reasonable to assume that at least some of these registrations (particularly in older males) will represent retroperitoneal sarcoma. Similarly it is unclear whether uterine sarcoma will be classified under C49 or with other gynaecologic cancers (C51-58), and so on. The most recent data (2005) show 536 new registrations in Australia² for (C47 + C49) and a further 167 for C48. In New Zealand the registrations for the same period were 105 and 21, respectively.³

No obvious aetiological agent is apparent in most cases, but a number of conditions (including Li Fraumeni syndrome, hereditary retinoblastoma, neurofibromatosis and Familial Adenomatous Polyposis) predispose some individuals to the development of sarcoma. Longstanding lymphoedema is associated with the development of lymphangiosarcoma and previous irradiation predisposes to angiosarcoma (classically in the breast), or postradiation sarcoma NOS.

Histologically there are a number of benign mimics of sarcoma, including various benign tumours and reactive conditions, and diagnostic errors are not uncommon. Due to their relative rarity, widely varying clinical parameters, pathological complexity and multidisciplinary management needs, STS is best diagnosed and managed in the context of a specialist sarcoma centre, by healthcare professionals with specific interest and expertise in this area. Where a primary diagnosis of soft tissue sarcoma is made outside of this setting, the diagnosis should be reviewed by a pathologist with an interest in soft tissue pathology before definitive treatment is undertaken, and the committee strongly recommend referral of the patient to a specialist unit for further management, even if primary excision has already been attempted. A number of studies have shown that expert review will result in revised diagnoses in a significant number of cases eg Thway & Fisher⁴ found minor diagnostic discrepancies in 15.7% and major discrepancies in 10.9% of 349 specimens reviewed in a 12-month period). Similarly, there is evidence from several countries that patients treated in non-specialist centres, or whose referral to a specialist centre is delayed, have worse outcomes including lower disease-free and overall survival.^{5-6,7} Furthermore, at least in young patients, there is evidence that patients enrolled in clinical trials have consistently better survival than those not in trials⁶. In some cases more

than one multidisciplinary team may need to be involved (eg the sarcoma team may consult with colleagues in gynaecology, urology, cardiothoracic or head and neck teams). All sarcomata "should undergo definitive resection by a sarcoma MDT surgeon or by a surgeon with site-specific or age-appropriate skills, in consultation with the sarcoma MDT".¹

Importance of histopathological reporting

In soft tissue neoplasms, accurate diagnosis and tumour classification is the single most important prognostic indicator, followed by tumour stage and grade. Accurate histotyping not only allows prediction of clinical behaviour but in the more aggressive tumours will guide management including the selection of patients for neoadjuvant or adjuvant chemo- or radiotherapy (eg. the improved likelihood of response to ifosfamide in synovial sarcoma over other types, specific protocols for paediatric rhabdomyosarcoma or PNET, etc) or the administration of targeted therapies such as trabectedin in selected tumours. Prognostic information other than staging and grading may also be provided by careful pathologic assessment (eg. identifying myogenic differentiation in poorly differentiated pleomorphic sarcoma, discussed further in Chapter 4).

Benefits of structured reporting

Structured pathology reports with standardised definitions for each component have been shown to significantly enhance the completeness and quality of data provided to clinicians, and have been recommended both in North America and the United Kingdom.⁸⁻¹¹

The College of American Pathologists and the Royal College of Pathologists (UK) have recently published useful protocols for the reporting of cancer¹²⁻¹³. A protocol endorsed by the Royal College of Pathologists of Australasia and other Australasian organisations involved in the management of soft tissue neoplasms is overdue. By improving consistency in the assessment and reporting of pathologic features and the systematic integration of clinical information and the results of ancillary studies, the structured report will serve as an aid to clinical decision making and ensure consistency of data collection. Furthermore, as the majority of sarcomata diagnosed in non-specialist centres will be referred on for definitive management, a structured report will serve to ensure appropriate information exchange. Secondary benefits include enhanced support for clinical and translation research, which requires accurate classification and prognostic information such as stage, grade and histotype to obtain clinically meaningful data.

Because of the range of tumour types and sites in this group of cancers it is not feasible to develop specific protocols for each different histotype or anatomic location; rather the committee have sought to provide a generic framework which can be adapted to individual cases, highlighting the major points of divergence from general rules (eg. the differing grading systems for paediatric and adult sarcoma and some specific types such as rhabdomyosarcoma).

Design of this protocol

This structured reporting protocol provides a complete framework for the assessment and documentation of all the pathological features of aggressive soft tissue neoplasms.

Mandatory elements (standards) are differentiated from those that are not mandatory but represent best practice (guidelines). Consistency and speed of reporting is improved by the use of discrete data elements recorded from the checklist. However, the pathologist is encouraged to include free text or narrative to document any other relevant issues, to give reasons for coming to a particular opinion and to explain any points of uncertainty.

The structure provided by the following chapters, headings and subheadings describes the elements of information and their groupings, but does not necessarily represent the format of either a pathology report (Chapter 7) or checklist (Chapter 6). These, and the structured pathology request form (Appendix 1) are templates that represent information from this protocol, organised and formatted differently to suit different purposes.

Key documentation

- *Guidelines for Authors of Structured Cancer Pathology Reporting Protocol*¹⁴s
- *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Provider*¹⁵
- *AJCC Cancer Staging Manual, 7th edition*¹⁶
- WHO (World Health Organization) (2002). World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of Soft Tissue and Bone. Fletcher CDM, Unni K and Mertens F (eds). IARC Press, Lyon, France.¹⁷
- Association of Directors of Anatomic and Surgical Pathology (ADASP) Checklists and Guidelines for Surgical Pathology Reports of Malignant Neoplasms.¹⁸

Changes since the last edition

N/A

Authority and development

This section provides details of the committee involved in developing this protocol and the process by which it was developed.

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This protocol was developed by an expert committee, with assistance from relevant stakeholders.

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Stakeholders

Anatomical Pathology Advisory Committee (APAC)

Australian Sarcoma Group/Australasian Sarcoma Study Group

Australian Association of Pathology Practices Inc (AAPP)

Australian Cancer Network

Australian Commission on Safety and Quality in Health Care
Cancer Australia
Cancer Council ACT
Cancer Council NSW
Cancer Council Queensland
Cancer Council SA
Cancer Council Tasmania
Cancer Council Victoria
Cancer Council Western Australia
Cancer Institute NSW
Cancer Services Advisory Committee (CanSAC)
Cancer Voices
Clinical Oncology Society of Australia (COSA)
Department of Health and Ageing
Grampians Integrated Cancer Services (GICS)
Health Informatics Society of Australia (HISA)
Medical Software Industry Association (MSIA)
National Breast and Ovarian Cancer Centre (NBOCC)
National Coalition of Public Pathology (NCOPP)
National E-Health Transition Authority (NEHTA)
National Pathology Accreditation Advisory Council (NPAAC)
National Round Table Working Party for Structured Pathology Reporting of Cancer
New Zealand Guidelines Group (NZGG)
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The Royal Australasian College of Surgeons (RACS)
The Royal Australian and New Zealand College of Radiologists (RANZCR)
The Royal Australian College of General Practitioners (RACGP)
The Royal College of Pathologists of Australasia (RCPA)
Victorian Cooperative Oncology Group (VCOG)
Western Australia Clinical Oncology Group (WACOG)

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Development process

This protocol has been developed following the seven-step process set out in *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols* ¹⁴

Where no reference is provided, the authority is the consensus of the expert group.

1 Clinical information and surgical handling

This chapter relates to information that should be collected before the pathology test, and procedures that are required before handover of specimens to the laboratory.

The standards and guidelines below specify the particular information required for soft tissue sarcoma. Some of this information can be collected on generic pathology request forms; any additional information required specifically for the reporting of soft tissue sarcoma may be recorded on a separate data sheet. Appendix 1 provides a standardised data sheet that may be useful in obtaining all relevant information.

Clinical information

S1.01 Adequate demographic and request information must be provided with the specimen by the requesting clinician.

CS1.01a The Royal College of Pathologists of Australasia (RCPA) *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers* must be adhered to.¹⁵ This document specifies the minimum information to be provided by the requesting clinician for any pathology test. Items relevant to cancer reporting protocols include:

- patient name
- date of birth
- sex
- identification and contact details of requesting doctor
- date of request

Additional information specified in the RCPA *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers* such as the specimen type and clinical information relevant to the investigation is catered for in the following standards and guidelines.

CS1.01b The patient's ethnicity must be recorded, if known.

G1.01 The patient's health identifiers should be recorded where provided.

CG1.01a The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a NHI or the Individual Healthcare Identifier (IHI).

S1.02 The pathology accession number of the specimen must be recorded.

S1.03 The principal clinician involved in the patient's care and responsible for investigating the patient must be identified.

CS1.03a The requesting clinician (identified under S1.01) may be the doctor who performs the surgery or biopsy, and may not be the person with overall responsibility for investigating and managing the patient. Identification of the principal clinician is essential, to ensure that clinical information is communicated effectively.

S1.04 The type of specimen must be recorded.

CS1.04a The type of specimen may include:

- wide local excision
- compartmentectomy
- radical excision
- pelvic exenteration
- amputation (state type)
- other (specify)

S1.05 The anatomical site of the resection must be recorded.

CS1.05a Sufficient information is required to localise the lesion for subsequent therapy. A diagram or photograph can facilitate this. Any muscles and named blood vessels or nerves included in the resection should be clearly indicated, as well as other relevant landmarks (eg "groove at deep surface = dissected off brachial artery")

S1.06 The laterality of the lesion must be recorded.

CS1.06a Laterality information is needed for identification purposes.

G1.02 The clinical diagnosis or differential diagnosis should be recorded.

CG1.02a Providing the provisional clinical diagnosis or differential diagnosis improves clinicopathological correlation and improves diagnostic accuracy.

S1.07 It must be stated if the patient has received neoadjuvant therapy.

CS1.07a After neoadjuvant therapy extensive sampling of the specimen may be necessary to identify any residual tumour cells. Furthermore, the extent of residual viable tumour has prognostic significance.

G1.03 Any relevant imaging findings should be provided.

CG1.03a Imaging findings eg CT, MRI appearances, depth and heterogeneity of lesion, presence of calcification, contrast enhancement, attachment to or involvement of structures such as major nerves or blood vessels, can contribute to the diagnosis and improve accuracy. Ideally the imaging will be reviewed with the pathologist during MDT meetings.

- G1.04 Details of previous relevant biopsy diagnosis and details of the biopsy if performed at another laboratory should be provided.
- G1.05 Details of any known sites of disease including metastases should be provided.
- S1.08 The operative findings must be provided, either on the request form or in direct conversation with the reporting pathologist.**
- CS1.08a Operative findings include tumour extent eg involvement of visceral organs (whether resected or not) and whether all visible tumour was resected.
- G1.06 Any relevant family history or known predisposing factors should be provided.
- CG1.06a Known predisposing factors may include previous radiation exposure or familial syndromes such as Li Fraumeni, Gardner's syndrome or neurofibromatosis.

Surgical handling

- S1.09 The specimen must be oriented in those cases where the status of specific surgical margins is critical in determining the need for, or extent of, further surgery or radiotherapy.**
- CS1.09a Where there are no anatomical landmarks, specimen orientation may be indicated with marking sutures or other techniques. If a specimen is oriented, the orientation should be indicated on the specimen request form (this may be facilitated by the use of a diagram). Close collaboration with surgeon and pathologist enhances accurate identification of relevant landmarks and close margins. This may be facilitated by direct handover of the specimen at the time of surgery (in the operating theatre or laboratory).
- G1.07 Consideration should be given to transporting the specimen to the laboratory unfixed.
- CS1.07a This may be unnecessary if preoperative biopsy has rendered a confident diagnosis, but if it is feasible to transport the specimen rapidly this may enable further ancillary studies (such as cytogenetic analysis) as well as harvesting fresh tissue for tumour banking and allowing optimal fixation of tissue for possible electron microscopy. Wherever possible these decisions are best left to the pathologist in charge of the case.
- G1.08 Labelling of the specimen should include a minimum of 2 of the following: patient name, date of birth, unique identifier, and should also include the date of specimen collection.

2 Specimen handling and macroscopic findings

This chapter relates to the procedures required after the information has been handed over from the requesting clinician and the specimen has been received in the laboratory.

Specimen handling

G2.01 Pathologists may be asked to provide tissue samples from fresh specimens for tissue banking or research purposes. The decision to provide tissue should only be made when the pathologist is sure that the diagnostic process including the assessment of the extent of tumour spread and other important parameters that influence patient prognosis and management will not be compromised.

CG2.01a As a safeguard, tissue taken for research purposes may be “put on hold” until the diagnostic process is complete so that this stored tissue can be retrieved if necessary.

S2.01 Consideration must be given to the differential diagnosis so that appropriate ancillary tests can be requested on fresh tissue (eg microbiology cultures, flow cytometry, cytogenetics, imprints for FISH, electron microscopy).

CS2.01a Where employed, harvesting of tissue for cytogenetics or imprints for FISH should be undertaken immediately on receipt of the specimen.

CS2.01b For more detailed consideration of ancillary tests, refer to Section 4.

S2.02 Specific anatomic landmarks (such as major blood vessels, nerves, fascia or muscle bellies) must be identified prior to inking and incising the specimen.

CS2.02a Identification of landmarks will be easier prior to inking. In the case of skeletal muscle, assessment of margins overlying the tumour will be unreliable once the muscle retracts after being cut and/or exposed to formalin. If there is doubt over the identification of such landmarks or specimen orientation, this should be clarified with the surgeon prior to proceeding further.

G2.02 All relevant margins should be inked prior to incising the specimen.

G2.03 The specimen should be incised at regular intervals to allow penetration of fixative (generally formalin).

CG2.03a Most sarcoma resection specimens will be fairly large and will require a substantial volume of fixative, which may necessitate transferring the specimen to a larger container than that in which the specimen was transported.

Macroscopic findings

S2.03 All measurements are in SI units, unless explicitly stated.

S2.04 Soft tissue resection specimens must be measured and their orientation determined.

CS2.04a Measurements of the specimen and tumour in 3 dimensions should be noted wherever this is practicable.

CS2.04b The dissection and subsequent block selection should demonstrate the relationship of the tumour to the deep fascia, where this is included in the specimen, and other relevant landmarks such as major nerves or blood vessels.

S2.05 The size of the tumour must be recorded.

G2.04 The distance from the tumour to the margins should be measured in 3 dimensions.

G2.05 The nature of the tissue between the tumour and the closest margin should be described (eg fat, muscle or fascia). A comment as to the nature of the tumour interface with normal tissue (eg. infiltrative, well circumscribed or encapsulated) should be offered.

G2.06 The appearance of the cut surface of the tumour should be described, noting areas of necrosis, haemorrhage or any variation in appearance.

CG2.06a Areas of necrosis, haemorrhage or variation in appearance may reflect, for example, dedifferentiation or the presence of heterologous elements.

CG2.06b The presence and extent of necrosis should be noted and expressed as a percentage of the total tumour volume, as this will aid subsequent grading (where FNCLCC grading is used; see later) or provide prognostic information in the event that neoadjuvant therapy has been administered.

CG2.06c Specimen photography is a useful method of recording macroscopic appearances.

G2.07 Adequate sampling of the tumour should be undertaken, with particular attention to areas which may have prognostic value (eg to confirm the presence of necrosis or to identify areas of varying differentiation, such as dedifferentiation in a well differentiated liposarcoma, or round cell component in myxoid liposarcoma,). Where practicable, a full face of the tumour may be appropriate. In general, at least one block per centimetre of the maximum tumour diameter should be sampled. Any previous biopsy tract should be examined and additional tumour nodules sampled.

S2.06 The site and number of any included lymph nodes must be recorded.

- CS2.06a All lymph node tissue should be submitted for histological examination.
- G2.08 A descriptive or narrative field should be provided to record any macroscopic information that is not recorded in the above standards and guidelines, and that would normally form part of the macroscopic description.
- CG2.08a The traditional macroscopic narrative recorded at the time of specimen dissection is often reported separately from the cancer dataset. Although this remains an option, it is recommended that macroscopic information be recorded within the overall structure of this protocol.
- CG2.08b Much of the information recorded in a traditional macroscopic narrative is covered in the standards and guidelines above and in many cases, no further description is required.

3 Microscopic findings

Microscopic findings relates to purely histological (morphological) assessment. Information derived from multiple investigational modalities, or from two or more chapters, are described in Chapter 5.

The types of specimen on which microscopy is performed in the context of soft tissue sarcomas include core biopsy, incisional and excisional biopsies, and larger resection specimens (pre or post adjuvant therapy). Preoperative core biopsy to determine the diagnosis has largely replaced intraoperative frozen section which is now rarely performed. Frozen section is generally not indicated to check surgical margins. The type of specimen submitted for histological examination has an important bearing on interpretation in terms of sampling error and security of the suggested diagnosis. Some of the following aspects for microscopic comment depend on the type of specimen received. This advice is generally applicable for adult tumours and some paediatric tumours treated by primary surgical resection.

Resection will most often be performed following diagnosis by previous biopsy. If neoadjuvant therapy has not been undertaken, formal typing and grading may be performed on the resection specimen. Grading must be performed using an accepted Grading System where applicable. This is dealt with in Chapter 5. Some tumour types are either low or high grade by definition and for some grading is not useful or meaningful (eg epithelioid sarcoma, clear cell sarcoma and alveolar soft part sarcoma). If neoadjuvant therapy has been administered, the alteration in tumour morphology may preclude typing and grading and reference to the previous biopsy material may be necessary.

S3.01 The site and depth of the tumour must be recorded.

CS3.01a Site includes anatomic location (eg limb, muscle group, retroperitoneum, etc) as well as tissue plane (dermis, subcutis, above or below deep fascia, intramuscular, etc.)

G3.01 A general description should be given of the tumour.

CG3.01a Cellularity, growth pattern, cytological characteristics and the nature of the stroma/matrix, and any associated inflammatory infiltrate should be commented on, as well as the interface of the tumour with adjacent tissues (eg. pushing, infiltrative, encapsulated).

CG3.01b Where present, characteristic vascular patterns (eg. arcuate, "chickenwire" or staghorn/"haemangiopericytoma-like") should be described.

G3.02 The mitotic rate should be stated.

CG3.02a The rate should be expressed as the number of mitoses per 10 high-power fields, but counting should be performed in a greater number of fields (perhaps 50) as this may be quite variable throughout the tumour.

- CG3.02b The presence of atypical mitoses should be noted.
- CG3.02c Given the wide variation in field diameter across different microscopes, it is recommended that the field diameter be stated in each case.
- G3.03 The presence and extent of tumour necrosis should be documented.
- CG3.03a True tumour necrosis should be distinguished from stromal hyalinisation or infarction.

S3.02 The histological type and subtype of the tumour must be documented wherever possible.

- CS3.02a Accepting the limitations of sampling and with the use of diagnostic common sense, tumour type should be assigned according to the WHO system ¹⁷, wherever possible. (See Appendix 4 for full list).
- CS3.02b If precise tumour typing is not possible, generic descriptions to describe the tumour may be useful (eg myxoid, pleomorphic, spindle cell, round cell etc), together with the growth pattern (eg fascicular, sheet-like, storiform etc). (See G3.01).
- CS3.02c If the reporting pathologist is unfamiliar or lacks confidence with the myriad possible diagnoses, then at this point a decision to send the case away without delay for an expert opinion would be the most sensible option. Referral to the pathologist at the nearest Regional Sarcoma Service would be appropriate in the first instance. Further International Pathology Review may then be obtained by the treating Regional Sarcoma Multidisciplinary Team if required. Adequate review will require submission of full clinical and imaging information as well as histological sections and paraffin block material.

- G3.04 In the case of nerve sheath tumours, histological evidence of presence or absence of a pre-existing benign lesion should be recorded.

S3.03 The distance of the tumour from close surgical margins must be documented precisely.

- CS3.03a Margins should be measured histologically if under 2cm, and the nature of the tissue constituting that margin (eg fascia/muscle/fat) should be documented as there is an increased risk of local recurrence if surgical margins are less than 1.5 or 2.0 cm, unless that margin is formed by fascia.

S3.04 The presence of vascular invasion must be documented.

S3.05 Where applicable, the presence of lymph node metastases must be noted.

- CS3.05a Where lymph nodes are included with the specimen, their approximate location or group (eg. left paraaortic, right inguinal etc) should be stated where this can be

determined, or their localisation with respect to the tumour or other structures specified (eg "retroperitoneal nodes, superior to left kidney")

CS3.05b The number of lymph nodes per location or group sampled and the number of lymph nodes containing metastatic tumour must be stated.

CS3.05c Although most soft tissue tumours spread haematogenously, with some notable exceptions eg epithelioid sarcoma and synovial sarcoma may spread via lymphatics.

S3.06 The presence or absence of bone invasion must be stated, where applicable.

G3.05 Where neoadjuvant chemo- and/or radiotherapy has been administered, the residual tumour volume and degree of tumour regression/necrosis should be estimated.

CG3.05a The degree of tumour regression following neoadjuvant therapy has independent prognostic value.

G3.06 Diagnostic SNOMED coding (listed in WHO 2002), should be recorded.

G3.07 Any additional relevant microscopic comments should be recorded.

4 Ancillary studies findings

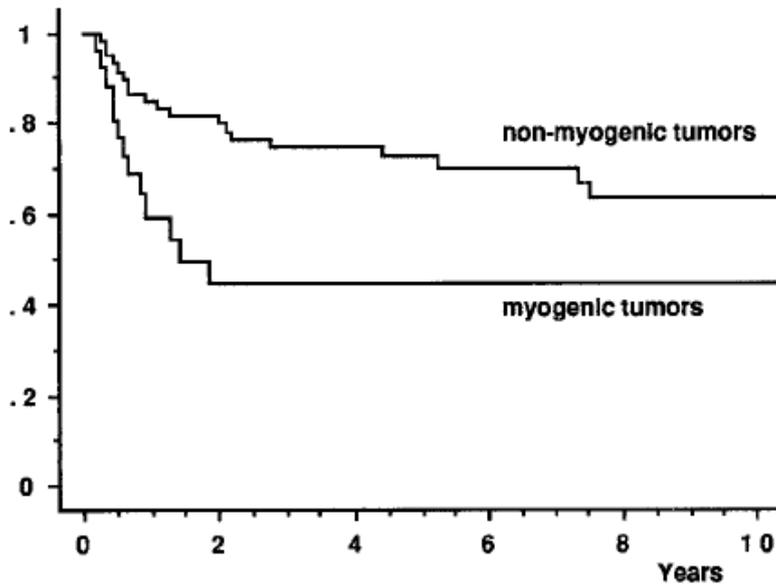
Ancillary studies may be used to determine lineage, clonality or disease classification or subclassification; as prognostic biomarkers; or to indicate the likelihood of patient response to specific biologic therapies.

Immunohistochemistry plays a central role in sarcoma diagnosis; whilst typical examples of some tumour types (such as aggressive fibromatosis, well differentiated liposarcoma or classical examples of biphasic synovial sarcoma) may be identified on the basis of morphology alone, immunohistochemistry will normally be employed to:

- (a) confirm an impression based on morphology;
- (b) distinguish between morphologically similar tumours;
- (c) support the diagnosis of rare tumour types;
- (d) support the diagnosis of a tumour arising in an unusual location or at an unusual age; and in some cases
- (e) provide prognostic information (eg. Ki67 index may enhance the predictive value of grading in some Grade 2 and 3 sarcoma).

Immunohistochemical markers may be employed to elucidate differentiation or lineage (eg SMA, desmin, h-caldesmon, myogenin, S-100 protein, CD31, EMA, various keratins) or to demonstrate protein expression as a surrogate for molecular events (eg. ALK, MDM2, CDK4, TFE3, INI-1, TLE-1). In most instances the pattern of expression of a panel of these markers will serve to clarify the diagnosis (either to accurately classify the type of sarcoma, or to exclude alternative types of poorly differentiated tumour, such as metastatic carcinoma or melanoma). Furthermore, prognostic information may be gained in some cases – eg. the presence of myogenic differentiation in otherwise unclassified pleomorphic sarcoma portends more aggressive behaviour than those which lack myogenic markers, signalling a worse overall prognosis and shorter time to metastasis.^{19,20}

Figure 4. Kaplan-Meier plots of metastasis rates in 88 soft tissue sarcoma of AJCC staging system (5th edition) stage II or III originally diagnosed as MFH; 26 tumours showed myogenic differentiation and 62 did not ($P=.006$).



Reprinted with permission. © 2010 American Society of Clinical Oncology. All rights reserved. Fletcher C et al; J Clin Oncol 19(12), 2001: 3045-3050

Similarly, in rhabdomyosarcoma diffuse expression (defined as >80% of tumour cells) of myogenin (Myf4) appears to correlate with reduced relapse-free and overall survival, independent of translocation status, tumour site or stage.²¹

A subset of soft tissue sarcomata have been found to harbour specific molecular genetic alterations which are characteristic of a particular histotype, and demonstration of these alterations through conventional karyotyping or molecular genetic analysis (such as FISH or PCR-based analysis with amplicon sequencing) may serve to confirm or refute a particular diagnosis, subclassify a tumour type or provide prognostic information (eg demonstration of CDK4 and MDM2 amplification in undifferentiated retroperitoneal sarcoma provides evidence that the tumour is in fact dedifferentiated liposarcoma). In selected cases demonstration of a specific molecular genetic event may guide rational selection of targeted therapy (eg demonstration of the COL1A1/PDGFB fusion transcript in DFSP predicts response to imatinib, and the CHOP-TLS or CHOP-EWS transcripts in myxoid/round cell liposarcoma predict response to trabectedin).

The committee recognises that many of these tests are only available in specialist laboratories and that many are not currently reimbursed; however the committee strongly advocates the application of this technology where there is diagnostic uncertainty. This may necessitate sending material to other laboratories and at present may incur additional cost to the treating institutions or the patient; the committee hopes that this unsatisfactory situation may be resolved in future, where such testing is necessary and appropriate to inform patient management. "Commissioners should fund a formal system of second opinions and review of difficult cases, and molecular pathology and cytogenetics facilities".¹

Although in most instances diagnosis may be achieved through some combination of light microscopy, immunophenotyping, karyotyping and molecular genetic analysis, in a small number of cases ultrastructural examination may also prove helpful in elucidating a line of differentiation, eg. to confirm the presence of endothelial or neural differentiation or to identify alternative lineages such as mesothelial or melanocytic differentiation. Again, this service is not available in all centres, and skilled interpretation of tumour ultrastructure is becoming a rarity amongst pathologists. However in some cases this may provide useful adjunctive information.

Immunohistochemistry

G4.01 Immunohistochemistry should be performed in appropriate cases, and the results incorporated into the pathology report.

CG4.01a Documentation of all relevant ancillary study findings is essential for overarching commentary (see Synthesis and Overview, Chapter 5), in which the significance of each finding is interpreted in the overall context of the case.

CG4.01b Staining of pleomorphic undifferentiated sarcoma for evidence of myogenic differentiation should be performed, as discussed in the preamble above.

Cytogenetic Analysis

G4.02 Cytogenetic analysis should be performed in selected cases, and the results incorporated into the pathology report.

CG4.02a Cytogenetic analysis will normally only be performed at source, as fresh tissue needs to be harvested and processed for cell culture at the time of resection. The committee recognises that this service is not available at every site.

CG4.02b Cytogenetic analysis will not be helpful for every type of soft tissue tumour and may not be necessary if the diagnosis has already been established on biopsy material; however if the diagnosis is uncertain and a cytogenetics service is available, it is prudent to harvest fresh material at the time of resection. This analysis may bring to light an unexpected diagnosis, or confirm the diagnosis in a tumour with non-classical histologic appearances, arising in an unusual site or at an unusual age, or exhibiting an unusual immunophenotype.

Molecular Genetic analysis (In-Situ Hybridisation or PCR-based techniques)

- G4.03 Molecular genetic analysis should be performed in selected cases and the results incorporated into the pathology report.
- CG4.03a Documentation of all relevant ancillary study findings is essential for overarching commentary (see Synthesis and Overview, Chapter 5), in which the significance of each finding is interpreted in the overall context of the case. This is particularly true in the case of molecular genetic testing (eg a FISH breakapart probe for EWSR1 may demonstrate rearrangement of that gene, but this molecular event can occur in several different tumours, so that this information must be interpreted in the context of clinical information, morphology and immunophenotype).
- CG4.03b Ancillary tests performed externally may contain information needed for compliance with NPAAC and RCPA requirements, but that are not relevant to cancer reporting protocols. The specific elements of an ancillary study report needed for cancer reporting include the following:
- laboratory performing the test
 - substrate (e.g. cytology smears, pellets from cell cultures, paraffin block, fresh frozen tissue, etc)
 - method (where relevant)
 - results
 - conclusion (usually a text field)
 - person responsible for reporting the ancillary test.

Electron microscopy

- G4.04 Electron microscopy may be performed in selected cases, and the results incorporated into the pathology report.

5 Synthesis and overview

Information that is synthesised from multiple modalities and therefore cannot reside solely in any one of the preceding chapters is described here. For example, tumour stage is synthesised from multiple classes of information – clinical, macroscopic and microscopic.

By definition, synthetic elements are inferential rather than observational, often representing high-level information that is likely to form part of the report 'Summary' or 'Diagnosis' section in the final formatted report.

Overarching case comment is synthesis in narrative format. Although it may not necessarily be required in any given report, the provision of the facility for overarching commentary in a cancer report is essential.

S5.01 The tumour stage must be recorded according to the AJCC system 7th edition. (Refer to Appendix 6)

CS5.01a The committee recognises that there are limitations in applying a system based on "TNM" parameters when nodal metastases are rare in most types of STS; this tends to dichotomise the staging into those tumours with or without distant metastases, but is less helpful in stratifying localised primary tumours. However the current system still has some prognostic value and does provide a standardised system for consistent data collection.

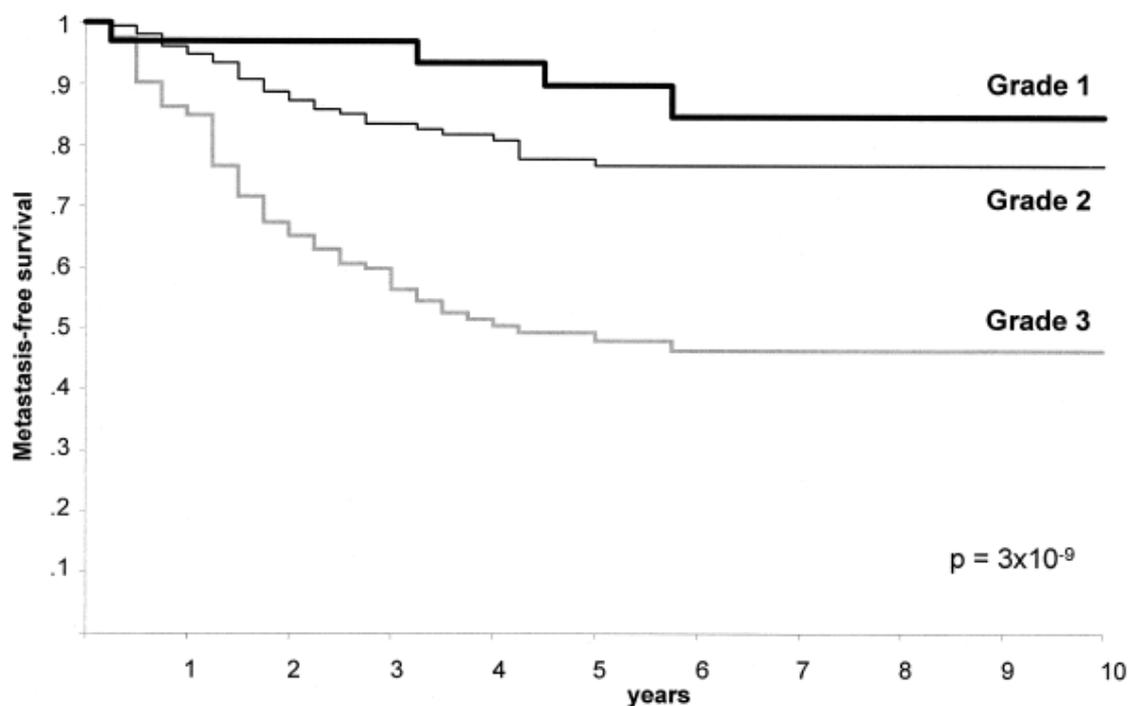
S5.02 The year of publication and edition of the AJCC cancer staging system used in S5.01 must be included in the report.

S5.03 FNCLCC grade must be recorded for adult STS, where this is applicable. (Refer to figure S5.03a and Appendix 5)

CS5.03a Although it is widely recognised that this grading system has its limitations and is not applicable to all sarcoma types, it is relatively easy to learn, is widely employed and has been shown to have better interobserver reproducibility than some other systems. When applied appropriately this system has prognostic value and predicts metastasis-free survival.²² It also forms part of the current AJCC staging parameters and is therefore necessary for allocation of stage.

Histotyping should be performed before any attempt at grading, and grading should not be used on "intermediate malignancy" tumours. Furthermore, some histotypes (eg. PNET, Desmoplastic Small Round Cell Tumour) are definitionally regarded as high grade on the basis of their natural history, regardless of the results of formal grading.²³⁻²⁵ In cases where FNCLCC does not apply, a comment should be offered to this effect (eg. "Desmoplastic Small Round Cell Tumour, definitionally high grade" or "high grade pleomorphic sarcoma, not otherwise classified").

Figure S5.03a MFS curves in MFH (349 patients) according to histologic grade. Grade 1 (33 patients); Grade 2 (160 patients); Grade 3 (156 patients).



Coindre JM, Terrier P, Guillou L, Le DV, Collin F, Ranchere D, Sastre X, Vilain MO, Bonichon F and N'Guyen BB (2001). Predictive value of grade for metastasis development in the main histologic types of adult soft tissue sarcomas: a study of 1240 patients from the French Federation of Cancer Centers Sarcoma Group *Cancer* 91:1914-1926.²² Reproduced with permission from John Wiley and Sons

S5.04 Children's Oncology Group (COG) Grading must be recorded for non-rhabdomyosarcomatous paediatric sarcoma other than Ewing's/PNET. (Refer to Appendix 7)

CS5.04a Numerous studies have verified the prognostic value of this grading system, which is also used to devise treatment strategies.²⁶ Ewing's/PNET is definitionally high grade. These cases will appropriately be managed in a specialist paediatric oncology unit.

S5.05 Intergroup Rhabdomyosarcoma Study grouping must be recorded for paediatric rhabdomyosarcoma.²⁷⁻²⁸ (Refer to Appendix 8)

CS5.05a Tumour site should also be stated, as this also has prognostic significance (eg parameningeal tumours are

definitionally considered to be high risk).

CS5.05b PAX fusion type has prognostic significance and should be recorded.²⁹

G5.01 If a sarcoma has been resected outside a specialist unit or without consultation with a sarcoma MDT, the final diagnosis should be reviewed by a specialist soft tissue pathologist.

CG5.01a As discussed in the preamble (Introduction p1) there is good evidence that diagnostic errors are not uncommon and these discrepancies may have significant implications for clinical management and prognosis.

G5.02 The "Diagnostic summary" section of the final formatted report should include:

- a. Specimen type (S1.04)
- b. Tumour site and laterality (S1.05 and S1.06)
- c. Tumour size (S2.05)
- d. Tumour type (S3.02)
- e. Tumour grade (S5.03, S5.04, S5.05)
- f. Tumour stage (S5.01)
- g. Completeness of excision (S3.04)
- h. Prognostically important results of ancillary studies (such as molecular subclassification or evidence of myogenic differentiation) (G4.01, G4.02, G4.03, G4.04)
- i. Assessment of response to neoadjuvant therapy, where this has been administered (G3.05)

S5.06 The reporting system must provide a field for free text or narrative in which the reporting pathologist can give overarching case comment.

CS5.06a This field may be used, for example, to:

- list any relevant ancillary tests
- document any noteworthy adverse gross and/or histological features
- express any diagnostic subtlety or nuance that is beyond synoptic capture
- elaborate diagnostic uncertainty and document further consultation or results still pending.

CS5.06b Further clinically helpful comments should be included at the end of a definitive report (eg likely prognosis, risk of local recurrence and any associations with hereditary disorders such as neurofibromatosis.)

CS5.06c Use of this field is at the discretion of the reporting pathologist.

6 Structured checklist

The following checklist includes the standards and guidelines for this protocol which must be considered when reporting, in the simplest possible form. The summation of all "Standards" is equivalent to the "Minimum Data Set" for Soft Tissue Sarcoma. For emphasis, standards (mandatory elements) are formatted in bold font.

- S6.01 The structured checklist provided below may be modified as required but with the following restrictions:**
- a. All standards and their respective naming conventions, definitions and value lists must be adhered to.**
 - b. Guidelines are not mandatory but are recommendations and where used, must follow the naming conventions, definitions and value lists given in the protocol.**
- G6.01 The order of information and design of the checklist may be varied according to the laboratory information system (LIS) capabilities.
- CG6.01a Where the LIS allows dissociation between data entry and report format, the structured checklist is usually best formatted to follow pathologist workflow. In this situation, the elements of synthesis or conclusions are necessarily at the end. The report format is then optimised independently by the LIS.
- CG6.01b Where the LIS does not allow dissociation between data entry and report format, (for example where only a single text field is provided for the report), pathologists may elect to create a checklist in the format of the final report. In this situation, communication with the clinician takes precedence and the checklist design is according to principles given in Chapter 7.
- G6.02 Where the checklist is used as a report template (see G6.01), the principles in Chapter 7 and Appendix 2 apply.
- CG6.02a All extraneous information, tick boxes and unused values should be deleted.
- G6.03 Additional comment may be added to an individual response where necessary to describe any uncertainty or nuance in the selection of a prescribed response in the checklist. Additional comment is not required where the prescribed response is adequate.

Clinical information and surgical handling

S1.01 Patient name _____

Date of birth _____

Sex _____

Identification and contact details of requesting doctor _____

Date of request _____

Ethnicity:

Aboriginal or Torres Strait Islander _____

Other ethnicity _____

Unknown _____

G1.01 Patient identifiers (eg MRN, IHI, NHI) _____

S1.02 Pathology accession number _____

S1.03 Principal clinician involved in the patient's care _____

S1.04 Type of specimen:

wide local excision _____

compartmentectomy _____

radical excision _____

pelvic exenteration _____

amputation (state type) _____

other (specify) _____

S1.05 Anatomical site

S1.06 Laterality

Left

Right

N/A

Not stated

G1.02 Clinical or differential diagnosis

S1.07 Details of any neoadjuvant therapy

Not stated

G1.03 Details of any relevant imaging

G1.04 Details of previous biopsy

G1.05 Details of known sites of disease/metastasis

S1.08 Operative findings:

Provided

Not provided _____

If provided record:

Tumour extent _____

All visible tumour resected _____ Yes

_____ No

_____ Not stated

Other relevant information _____

G1.06 Details of relevant family history/pre-disposing factors _____

Macroscopic findings

S2.04 Measurements of specimen _____X_____X_____ mm

S2.05 Measurements of tumour _____x_____x_____ mm

G2.04 Distance from tumour to margins:
Closest margin _____
Distance to closest margin _____ mm
Other margin (specify) _____
Distance to other margin _____ mm

G2.05 Nature of tissue between tumour and closest margin
Fat _____
Muscle _____

Fascia _____

Nature of the tumour interface
with normal tissue (eg
infiltrative, well circumscribed or
encapsulated)

G2.06 Appearance of cut surface of
tumour

Description

Haemorrhage:

absent _____

present _____

Necrosis:

not
identified _____

present _____

_____% tumour volume (estimated)

S2.06 Lymph nodes:

Site 1:

total number of
nodes

Site 2:

total number of
nodes

Site 3:

total number of
nodes

G2.08 Other macroscopic comment

Microscopic findings

S3.01 Tumour site

Tumour depth – tissue plane:

dermis _____

subcutis/superficial to deep fascia _____

subfascial _____

intramuscular _____

other (specify) _____

Tumour depth (if possible) _____mm

_____ Not possible to measure

G3.01 Tumour description (eg cellularity, growth pattern etc)

G3.02 Mitotic rate

_____ per 10hpf

G3.03 Necrosis

not identified _____

present _____

_____ % tumour volume (estimated)

S3.02 Histologic type (WHO):

	Subtype	_____
	Typing not possible	_____
G3.04	Pre-existing benign lesion (nerve sheath tumours)	
	absent	_____
	present	_____
S3.03	Distance from close surgical margins	
	Margin 1 (state type)	_____
	Distance from margin	____mm
	Nature of tissue at margin	_____
	Margin 2 (state type)	_____
	Distance from margin	____mm
	Nature of tissue at margin	_____
S3.04	Vascular invasion	
	not identified	_____
	present	_____
S3.05	Lymph node involvement by tumour:	
	Not applicable	_____
	Location or group 1	_____
	Number of nodes involved by tumour	_____
	Total number of nodes resected	_____
	Location or group 2	_____

Number of nodes involved by tumour _____

Total number of nodes resected _____

Location or group 3 _____

Number of nodes involved by tumour _____

Total number of nodes resected _____

S3.06 Bone invasion

absent _____

present _____

not applicable _____

G3.05 Tumour regression (where neoadjuvant chemo/radiotherapy administered)

absent _____

present _____

____% tumour regression (estimated)

G3.06 Diagnostic SNOMED coding _____

G3.07 Additional microscopic comments

Ancillary test findings

G4.01 Immunohistochemistry:

Antibodies: _____

Positive antibodies _____

Negative antibodies _____

Equivocal antibodies _____

Interpretation _____

G4.02 Cytogenetic analysis:

performing laboratory _____

result _____

conclusion _____

Person responsible for reporting _____

G4.03 Molecular genetic analysis:

performing laboratory _____

substrate _____

method (where relevant) _____

result _____

conclusion _____

Person responsible for reporting _____

G4.04 Electron microscopy:

performing laboratory _____

result _____

conclusion _____

Person responsible for reporting _____

Synthesis and overview

S5.01 AJCC tumour stage:

T _____

N _____

M _____

S5.02 Year of publication and edition of cancer staging system _____

S5.03 Tumour grading (FNCLCC) (adult STS)

Differentiation score (1,2 or 3) _____

Mitotic index score (1,2 or 3) _____

Tumour cell necrosis (0,1 or 2) _____

Total tumour score _____

Grade 1 (total score of 2, 3) _____

Grade 2 (total score of 4, 5) _____

Grade 3 (total score of 6-8) _____

Grading not possible/applicable _____

If grading is not possible include a general statement _____

S5.04 Tumour grading (COG) (non-rhabdomyosarcomatous paediatric sarcoma other than Ewing's/PNET)

Grade 1 _____

Grade 2 _____

Grade 3 _____

Grading not possible/appropriate _____

S5.05 Intergroup Rhabdomyosarcoma Study classification (paediatric rhabdomyosarcoma)

Embryonal, botryoid (favourable prognosis) _____

Embryonal, spindle cell (favourable prognosis) _____

Embryonal, NOS (intermediate prognosis) _____

Alveolar, NOS or solid variant (poor prognosis) _____

Anaplasia, diffuse (poor prognosis) _____

Undifferentiated sarcoma (poor prognosis) _____

Tumour site:

Orbit _____

Head and neck _____

Bladder/prostate _____

Extremity _____

Cranial parameningeal _____

Other (specify) _____

PAX fusion type _____

Grading not possible/appropriate _____

G5.01 Sent for specialist soft tissue review (give details) _____

G5.02 Diagnostic summary _____

S5.06 **Other relevant information and comments** _____

7 Formatting of pathology reports

Good formatting of the pathology report is essential for optimising communication with the clinician, and will be an important contributor to the success of cancer reporting protocols. The report should be formatted to provide information clearly and unambiguously to the treating doctors, and should be organised with their use of the report in mind. In this sense, the report differs from the structured checklist, which is organised with the pathologists' workflow as a priority.

Uniformity in the format as well as in the data items of cancer reports between laboratories makes it easier for treating doctors to understand the reports; it is therefore seen as an important element of the systematic reporting of cancer. For guidance on formatting pathology reports, please refer to Appendix 2.

Appendix 1 Pathology request form for Soft Tissue Sarcoma resection specimens

S1.01 Patient name _____

Date of birth _____

Sex _____

Identification and contact details of requesting doctor _____

Date of request _____

Ethnicity:

Aboriginal or Torres Strait Islander _____

Other ethnicity _____

Unknown _____

G1.01 Patient identifiers (eg MRN, IHI, NHI) _____

S1.03 Principal clinician involved in the patient's care _____

S1.04 Type of specimen:

wide local excision _____

compartmentectomy _____

radical excision _____

pelvic exenteration _____

amputation (state type) _____

other (specify) _____

S1.05 Anatomical site

S1.06 Laterality

Left _____

Right _____

G1.02 Clinical or differential diagnosis

S1.07 Details of any neoadjuvant therapy

G1.03 Details of any relevant imaging

G1.04 Details of previous biopsy

G1.05 Details of known sites of disease/metastasis

S1.08 Operative findings:

Tumour extent

All visible tumour resected **Yes**

No

Other relevant information

G1.06 Details of relevant family history/pre-disposing factors

Appendix 2 Guidelines for formatting of a pathology report

Layout

Headings and spaces should be used to indicate subsections of the report, and heading hierarchies should be used where the LIS allows it. Heading hierarchies may be defined by a combination of case, font size, style and, if necessary, indentation.

- Grouping like data elements under headings and using 'white space' assists in rapid transfer of information.³⁰

Descriptive titles and headings should be consistent across the protocol, checklist and report.

When reporting on different tumour types, similar layout of headings and blocks of data should be used, and this layout should be maintained over time.

- Consistent positioning speeds data transfer and, over time, may reduce the need for field descriptions or headings, thus reducing unnecessary information or 'clutter'.

Within any given subsection, information density should be optimised to assist in data assimilation and recall.

- Configuring reports in such a way that they 'chunk' data elements into a single unit will help to improve recall for the clinician.³⁰
- 'Clutter' should be reduced to a minimum.³⁰ Thus, information that is not part of the protocol (e.g. billing information, Snomed codes, etc) should not appear on the reports or should be minimized.
- Injudicious use of formatting elements (e.g. too much bold, underlining or use of footnotes) constitutes clutter and may distract the reader from the key information.

Where a structured report checklist is used as a template for the actual report, any values provided in the checklist but not applying to the case in question must be deleted from the formatted report.

Reports should be formatted with an understanding of the potential for the information to mutate or be degraded as the report is transferred from the LIS to other health information systems.

As a report is transferred between systems:

- text characteristics such as font type, size, bold, italics and colour are often lost
- tables are likely to be corrupted as vertical alignment of text is lost when fixed font widths of the LIS are rendered as proportional fonts on screen or in print
- spaces, tabs and blank lines may be stripped from the report, disrupting the formatting
- supplementary reports may merge into the initial report.

Appendix 3 Example of a pathology report

Citizen, Georgina W. C/O Paradise Close Wreck Bay Resort Nar Nar Goon East, 3181 Female DOB 1/7/1969 MRN FMC1096785	Lab Ref: 10/P28460 Referred: 30/8/2010	Copy to: Dr N.G.Chapman Rainforest Cancer Centre. 46 Smith Road, Woop Woop, 3478	Referred by: Dr V. Smith Suite 3, AJC Medical Centre, Bunyip Crescent Nar Nar Goon West, 3182
--	--	--	---

SOFT TISSUE TUMOUR STRUCTURED REPORT

Page 1 of 3

Diagnostic Summary

Wide Local Excision, mass left inner thigh measuring 68x65x49mm
Myxoid Liposarcoma, FNCLCC Grade 1

- **AJCC (7th Edition, 2010) stage pT2b, cN0, cM0, G1 = Stage IB**
- **Excision complete at all margins**
- **Cytogenetic analysis pending**

Supporting Information

CLINICAL

Principal clinician:	Dr G Jones
Clinical or differential diagnosis:	Myxoid Liposarcoma on core biopsy, 8cm clinically
Details of any neoadjuvant therapy:	Nil
Relevant imaging:	MRI at Nar Nar Goon Imaging 02/08/10 – homogeneous mass involving gracilis and adductor magnus
Previous biopsy:	Core biopsy 06/08/10, Nar Nar Goon Pathology, ref 10/P 27659 – myxoid liposarcoma
Known sites of disease/metastases:	None
Operative findings	
All visible tumour resected:	Yes
Family history/pre-disposing factors:	None known

MACROSCOPIC

Measurements of specimen:	220x105x70 mm
Measurement of tumour:	68x65x49mm
Distance from tumour to margins	
Longitudinal axis:	40mm distal, 50mm proximal
Circumferential axis:	10mm anterior, 10mm posterior
Other axis:	15mm deep
Nature of tissue between tumour & closest margin:	muscle

Appearance of cut surface of tumour	
Description:	Cut surface shows a well circumscribed, homogeneous, myxoid tumour
Haemorrhage:	Present - probable focal
Necrosis:	Not identified
Lymph nodes:	No lymph nodes were retrieved
Other comment:	The specimen was received directly from theatre and fresh tissue was harvested for cytogenetic analysis. Further tissue was snap frozen for storage at -70 degrees and tissue obtained for tumour banking (patient has consented to tumour banking for research purposes, copy of consent form filed in Pathology).

MICROSCOPIC

Tumour site:	Left inner thigh
Tumour depth/tissue plane:	Tumour into intramuscular (adductor magnus)
Tumour description:	Sections of the tumour show a moderately cellular neoplasm composed of cells with bland bipolar nuclei, arranged singly in an abundant myxoid stroma containing numerous thin-walled blood vessels, having a "crow's-feet" arrangement in places. Scattered uni-, bi- and multivacuolar lipoblasts are noted. Very focally there is increased cellularity and early transition to a more round cell morphology, but no well developed areas of round cell differentiation are seen.
Mitotic rate:	No mitoses are identified (<1 mf/50hpf)
Necrosis:	Not identified
Histologic type (WHO):	Myxoid liposarcoma 8852/3
Distance from close surgical margins	
Posterior margin:	5.5mm, measured histologically
Tissue at this margin:	muscle
All remaining profiled margins are:	>10mm
Vascular invasion	Not identified
Lymph node involvement by tumour:	No lymph nodes were included
Bone invasion:	Absent
Diagnostic SNOMED coding:	T-14530, T- 1A000, M88523

ANCILLARY TESTS

Immunohistochemistry	Not performed
Cytogenetics:	Fresh tissue was harvested for cytogenetic analysis, which will be reported in due course and a supplementary report issued.

SYNTHESIS

Histotype: Myxoid Liposarcoma

Grade (FNCLCC)

Differentiation score:	2
Mitosis score:	1
Necrosis score:	0
TOTAL SCORE:	3 = GRADE 1

Reported by Dr Judith Chan

Authorised 4/9/2010

Appendix 4 WHO classification of soft tissue tumours¹⁷

ADIPOCYTIC TUMOURS

Benign

Lipoma	8850/0*
Lipomatosis	8850/0
Lipomatosis of nerve	8850/0
Lipoblastoma / Lipoblastomatosis	8881/0
Angiolipoma	8861/0
Myolipoma	8890/0
Chondroid lipoma	8862/0
Extrarenal angiomyolipoma	8860/0
Extra-adrenal myelolipoma	8870/0
Spindle cell/ Pleomorphic lipoma	8857/0 8854/0
Hibernoma	8880/0

Intermediate (locally aggressive)

Atypical lipomatous tumour/ Well differentiated liposarcoma	8851/3
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Malignant

Dedifferentiated liposarcoma	8858/3
Myxoid liposarcoma	8852/3
Round cell liposarcoma	8853/3
Pleomorphic liposarcoma	8854/3
Mixed-type liposarcoma	8855/3
Liposarcoma, not otherwise specified	8850/3

FIBROBLASTIC / MYOFIBROBLASTIC TUMOURS

Benign

Nodular fasciitis	
Proliferative fasciitis	
Proliferative myositis	
Myositis ossificans fibro-osseous pseudotumour of digits	
Ischaemic fasciitis	
Elastofibroma	8820/0
Fibrous hamartoma of infancy	
Myofibroma / Myofibromatosis	8824/0
Fibromatosis colli	
Juvenile hyaline fibromatosis	
Inclusion body fibromatosis	
Fibroma of tendon sheath	8810/0
Desmoplastic fibroblastoma	8810/0
Mammary-type myofibroblastoma	8825/0
Calcifying aponeurotic fibroma	8810/0
Angiomyofibroblastoma	8826/0
Cellular angiofibroma	9160/0
Nuchal-type fibroma	8810/0
Gardner fibroma	8810/0
Calcifying fibrous tumour	

Giant cell angiofibroma	9160/0
Intermediate (locally aggressive)	
Superficial fibromatoses (palmar / plantar)	
Desmoid-type fibromatoses	8821/1
Lipofibromatosis	
Intermediate (rarely metastasizing)	
Solitary fibrous tumour	8815/1
and haemangiopericytoma	9150/1
(incl. lipomatous haemangiopericytoma)	
Inflammatory myofibroblastic tumour	8825/1
Low grade myofibroblastic sarcoma	8825/3
Myxoinflammatory	
fibroblastic sarcoma	8811/3
Infantile fibrosarcoma	8814/3
Malignant	
Adult fibrosarcoma	8810/3
Myxofibrosarcoma	8811/3
Low grade fibromyxoid sarcoma	8811/3
hyalinizing spindle cell tumour	
Sclerosing epithelioid fibrosarcoma	8810/3
SO-CALLED FIBROHISTIOCYTIC TUMOURS	
Benign	
Giant cell tumour of tendon sheath	9252/0
Diffuse-type giant cell tumour	9251/0
Deep benign fibrous histiocytoma	8830/0
Intermediate (rarely metastasizing)	
Plexiform fibrohistiocytic tumour	8835/1
Giant cell tumour of soft tissues	9251/1
Malignant	
Pleomorphic 'MFH' / Undifferentiated	
pleomorphic sarcoma	8830/3
Giant cell 'MFH' / Undifferentiated	
pleomorphic sarcoma	
with giant cells	8830/3
Inflammatory 'MFH' / Undifferentiated	
pleomorphic sarcoma with	
prominent inflammation	8830/3
SMOOTH MUSCLE TUMOURS	
Angioleiomyoma	8894/0
Deep leiomyoma	8890/0
Genital leiomyoma	8890/0
Leiomyosarcoma (excluding skin)	8890/3
PERICYTIC (PERIVASCULAR) TUMOURS	
Glomus tumour (and variants)	8711/0
malignant glomus tumour	8711/3
Myopericytoma	8713/1
SKELETAL MUSCLE TUMOURS	

Benign	
Rhabdomyoma	8900/0
adult type	8904/0
fetal type	8903/0
genital type	8905/0

Malignant	
Embryonal rhabdomyosarcoma	8910/3
(incl. spindle cell, botryoid, anaplastic)	8912/3 8910/3
Alveolar rhabdomyosarcoma	
(incl. solid, anaplastic)	8920/3
Pleomorphic rhabdomyosarcoma	8901/3

VASCULAR TUMOURS

Benign	
Haemangiomas of	
subcut/deep soft tissue:	9120/0
capillary	9131/0
cavernous	9121/0
arteriovenous	9123/0
venous	9122/0
intramuscular	9132/0
synovial	9120/0
Epithelioid haemangioma	9125/0
Angiomatosis	
Lymphangioma	9170/0

Intermediate (locally aggressive)	
Kaposiform haemangioendothelioma	9130/1

Intermediate (rarely metastasizing)	
Retiform haemangioendothelioma	9135/1
Papillary intralymphatic angioendothelioma	9135/1
Composite haemangioendothelioma	9130/1
Kaposi sarcoma	9140/3

Malignant	
Epithelioid haemangioendothelioma	9133/3
Angiosarcoma of soft tissue	9120/3

CHONDRO-OSSEOUS TUMOURS	
Soft tissue chondroma	9220/0
Mesenchymal chondrosarcoma	9240/3
Extraskeletal osteosarcoma	9180/3

TUMOURS OF UNCERTAIN DIFFERENTIATION

Benign	
Intramuscular myxoma	8840/0
(incl. cellular variant)	
Juxta-articular myxoma	8840/0
Deep ('aggressive') angiomyxoma	8841/0
Pleomorphic hyalinizing angiectatic tumour	
Ectopic hamartomatous thymoma	8587/0

Intermediate (rarely metastasizing)

Angiomatoid fibrous histiocytoma	8836/1
Ossifying fibromyxoid tumour (incl. atypical / malignant)	8842/0
Mixed tumour/ Myoepithelioma/ Parachordoma	8940/1 8982/1 9373/1

Malignant

Synovial sarcoma	9040/3
Epithelioid sarcoma	8804/3
Alveolar soft part sarcoma	9581/3
Clear cell sarcoma of soft tissue	9044/3
Extraskeletal myxoid chondrosarcoma ("chordoid" type)	9231/3
PNET / Extraskeletal Ewing tumour pPNET	9364/3
extraskeletal Ewing tumour	9260/3
Desmoplastic small round cell tumour	8806/3
Extra-renal rhabdoid tumour	8963/3
Malignant mesenchymoma	8990/3
Neoplasms with perivascular epithelioid cell differentiation (PEComa) clear cell myomelanocytic tumour	
Intimal sarcoma	8800/3

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Appendix 5 FNCLCC grading system

FNCLCC grading system: definition of parameters[#]

Tumour differentiation

Score 1:

sarcomas closely resembling normal adult mesenchymal tissue (e.g., low grade leiomyosarcoma).

Score 2:

sarcomas for which histological typing is certain (e.g., myxoid liposarcoma).

Score 3:

embryonal and undifferentiated sarcomas, sarcomas of doubtful type, synovial sarcomas, osteosarcomas, PNET.

Mitotic Count

Score 1: 0-9 mitoses per 10 HPF*

Score 2: 10-19 mitoses per 10 HPF

Score 3: ≥ 20 mitoses per 10 HPF

Tumour necrosis

Score 0: no necrosis

Score 1: <50% tumour necrosis

Score 2: $\geq 50\%$ tumour necrosis

Histological grade

Grade 1: total score 2, 3

Grade 2: total score 4, 5

Grade 3: total score 6, 7, 8

[#] Modified from Trojani M, Contesso G, Coindre JM, Rouesse J, Bui NB, de Mascarel A, Goussot JF, David M, Bonichon F and Lagarde C (1984). Soft-tissue sarcomas of adults; study of pathological prognostic variables and definition of a histopathological grading system. *Int J Cancer* 33: 37-42.²³ Reproduced with permission from John Wiley and Sons.

PNET: primitive neuroectodermal tumour

*A high power field (HPF) measures 0.1734 mm²

FNCLCC Grading System: Tumour Differentiation Score According to Histologic Type*

Histologic Type	Tumour Differentiation Score
Well-differentiated liposarcoma	1
Myxoid liposarcoma	2
Round cell liposarcoma	3
Pleomorphic liposarcoma	3
Well-differentiated fibrosarcoma	1
Conventional fibrosarcoma	2
Poorly-differentiated fibrosarcoma	3
Myxofibrosarcoma	2
Pleomorphic MFH with storiform pattern	2
Pleomorphic MFH with no storiform pattern	3
Giant cell MFH	3
Well-differentiated leiomyosarcoma	1
Conventional leiomyosarcoma	2
Poorly-differentiated/pleomorphic/epithelioid leiomyosarcoma	3
Embryonal/alveolar/pleomorphic rhabdomyo-sarcoma	3
Mesenchymal chondrosarcoma	3
Osteosarcoma	3
PNET	3
Malignant triton tumour	3
Synovial sarcoma	3
Well-differentiated/conventional angiosarcoma	2
Poorly-differentiated/epithelioid angiosarcoma	3
Epithelioid sarcoma	3
Clear cell sarcoma	3

* Modified from Guillou et al.²⁴ Reprinted with permission. © 2008 American Society of Clinical Oncology. All rights reserved.

FNCLCC indicates Fedration Nationale des Centres de Lutttes Contre le Cancer;

MFH, malignant fibrous histiocyoma;

PNET, primitive neuroectodermal tumour

Appendix 6 AJCC TNM cancer staging system

PRIMARY TUMOUR (T)

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour 5 cm or less in greatest dimension
T1a	Superficial tumour
T1b	Deep tumour
T2	Tumour more than 5 cm in greatest dimension
T2a	Superficial tumour
T2b	Deep tumour

Note: Superficial tumour is located exclusively above the superficial fascia without invasion of the fascia; deep tumour is located either exclusively beneath the superficial fascia, superficial to the fascia with invasion of or through the fascia, or both superficial yet beneath the fascia.

REGIONAL LYMPH NODES (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1*	Regional lymph node metastasis

***Note:** Presence of positive nodes (N1) in M0 tumours is considered Stage III

DISTANT METASTASIS (M)

M0	No distant metastasis
M1	Distant metastasis

ANATOMIC STAGE PROGNOSTIC GROUPS

GROUP	T	N	M	Grade
Stage IA	T1a	N0	M0	G1, GX
	T1b	N0	M0	G1, GX
Stage IB	T2a	N0	M0	G1, GX
	T2b	N0	M0	G1, GX
Stage IIA	T1a	N0	M0	G2, G3
	T1b	N0	M0	G2, G3
Stage IIB	T2a	N0	M0	G2
	T2b	N0	M0	G2
Stage III	T2a	N0	M0	G3
	T2b	N0	M0	G3
	Any T	N1	M0	Any G
Stage IV	Any T	Any N	M1	Any G

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Appendix 7 Non-rhabdomyosarcomatous Soft Tissue Sarcoma Grading System

Children's Oncology Group (COG) NON-RHABDOMYOSARCOMATOUS SOFT TISSUE SARCOMA GRADING SYSTEM

Grade 1

Myxoid and well-differentiated liposarcoma
Deep-seated dermatofibrosarcoma protuberans
Well-differentiated or infantile (less than 4 years old) fibrosarcoma
Well-differentiated or infantile (less than 4 years old) hemangiopericytoma
Well-differentiated malignant peripheral nerve sheath tumour
Extraskeletal myxoid chondrosarcoma

Grade 2

Sarcomas not specifically included in Grades 1 and 3, in which less than 15% of the surface area shows necrosis, and the mitotic count is less than 5/10 hpf using a X40 objective. As secondary criteria, nuclear atypia is not marked, and the tumour is not markedly cellular.

Grade 3

Pleomorphic or round cell liposarcoma
Mesenchymal chondrosarcoma
Extraskeletal osteosarcoma
Malignant triton tumour
Alveolar soft part sarcoma
Sarcomas not included in Grade 1 and with greater than 15% of surface area with necrosis or with greater than 5 mitoses/10 hpf using an X40 objective. Marked atypia or cellularity are less predictive but may assist in placing tumours in this category.

Reproduced with permission: Parham DM, Webber BL, Jenkins JJ, Cantor AB, Maurer HM. Nonrhabdomyosarcomatous soft tissue sarcomas of childhood: formulation of a simplified system for grading. *Mod Pathol.* 1995;8:705-710³¹

Appendix 8 Intergroup Rhabdomyosarcoma Study grading system^a

Diagnosis	Histology	Incidence (%) ^b	Five-year survival (%)	Prognosis
Embryonal, botryoid	Favorable	6	95	Superior
Embryonal, spindle cell	Favorable	3	88	Superior
Embryonal, not otherwise specified (NOS)	Favorable	49	66	Intermediate
Alveolar, NOS or solid variant	Unfavorable	31	53	Poor
Anaplasia, diffuse	Unfavorable	2	45	Poor
Undifferentiated sarcoma	Unfavorable	3	44	Poor

^aWith the addition of IRSC-defined anaplastic variant.

^bTotal incidence is only 94%; some 6% of accepted cases fall into the sarcoma NOS category because of insufficient or inadequate tissue to make a more specific diagnosis.

Reproduced with permission Qualman S, Coffin C and Newton W et al (1998). Intergroup rhabdomyosarcoma study: Update for pathologists. *Ped Developmental Pathol* 1(6):550-561.²⁷

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