Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Services

Soft Tissue Sarcoma Advisory Group

Clinical Guidelines

June 2023

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VERSION CONTROL

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VERSION	DATE ISSUED	SUMMARY OF CHANGE	OWNER'S NAME
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Draft 0.2	26th May 2015	Radiotherapy update	M Beasley
Draft 0.3	1st June 2015	Addition to surgical information	P Wilson
Draft 0.4	27th January 2016	Further addition to surgical information	P Wilson / H Dunderdale
Draft 0.5	20th June 2016	Addition of pathology referral process	F Maggiani, H Dunderdale
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1.1	January 2019	Addition of link to GIST and Fibromatosis Guidelines	G Ayre
1.2	April 2019	Biennial review	G Ayre, H Dunderdale
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Soft Tissue Sarcoma SAG Clinical Guidelines Contents

1. Introduction

The following guidelines pertain to the local management of STS malignancies for the Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Soft Tissue Sarcoma Advisory Group (SAG).

SAG refers to the UK Guidelines for the Management of Soft Tissue Sarcoma, 2016, the National Institute for Health and Care Excellence (NICE) Sarcoma clinical guidelines (January 2015): https://www.nice.org.uk/guidance, the UK clinical practice guidelines for the management of gastrointestinal stromal tumours (2017): https://clinicalsarcomaresearch.biomedcentral.com/track/pdf/10.1186/s13569-017-0072-8, and the European Consensus on Management of Desmoid fibromatosis - Annals Oncology 2017: http://www.swscn.org.uk/wp/wp-content/uploads/2019/01/European-consensus-on-management-of-desmoid-fibromatosis-Annals-Oncology-2017.pdf.

These local guidelines should be reviewed alongside three other key documents for SAG: the Constitution, Annual Report and the Work Programme. The SAG Constitution provides an overview of how SAG operates, outlining the general working processes, the patient referral pathways and the guidelines to which it adheres. The Annual Report reflects the period of activity for SAG from the previous year, and it contains a summary of this activity measured against several key performance indicators that have been outlined in the National Cancer Peer Review Programme. The Work Programme summarises the key areas for growth, development and improvement of SAG over the next financial year (and beyond where appropriate). All four documents should be reviewed together to give a full overview of SAG, its performance and future plans.

Primary care clinicians should refer to the NICE guidelines *Suspected Cancer: recognition and management of suspected cancer in children, young people and adults* (2015) for the signs and symptoms relevant when referring to sarcoma services. Further details on the local process for referral can be found in the SAG constitution.

SAG is committed to offering all eligible patients entry into clinical trials where available. Consent to provide tissue for research purposes will also be sought wherever appropriate.

2. Clinical Guidelines for Soft Tissue Sarcoma (STS)– Limb and Trunk (B12/S/a/g-16-004)

2.1 Diagnostic Pathway

Initial investigations are conducted by the Diagnostic and Local Care Team. If an ultrasound (US) +/- a Magnetic Resonance Imaging (MRI) scan is indicative of a suspected soft tissue sarcoma, the patient is referred to a member of the STS Multi-Disciplinary Team.

All decisions regarding the treatment of patients diagnosed with STS will be made following discussion in the weekly STS supra-regional multidisciplinary team meeting held at North Bristol Trust (NBT).

Following discussion with the surgical team to decide the most desirable approach, a member of the STS MDT will carry out an image guided biopsy of the lesion to confirm the diagnosis. SAG refers all biopsies directly to the members of the specialist sarcoma pathologist (SSP) team, Francesca Maggiani, Zsombor Melegh and Demetris Poyiatzis.

2.2 Staging

Following confirmation of a diagnosis of sarcoma, the stage of disease will be established by performing an MRI of the appropriate area on all patients with extremity soft tissue sarcoma. CT scans will be performed on all patients with retroperitoneal soft tissue sarcomas or truncal lesions. Staging investigations may be undertaken as per the normal practice of a site specialist group, for example gynaecology sarcoma.

Initial chest staging will be performed by spiral computed tomography (CT) of the thorax to determine the presence or absence of metastatic disease.

Sentinel lymph node staging in epithelioid, clear cell, synovial sarcoma, rhabdomyosarcoma and angiosarcoma may also be considered.

A PET scan is not routinely performed, but is considered for high grade lesions.

If the lesion is considered resectable, there will be a discussion at MDT as to whether neoadjuvant radiotherapy, and / or chemotherapy may be appropriate.

2.3 Surgical Guidelines[1]

2.3.1 Surgery for Localised Disease

Surgery is the standard treatment for all patients with adult-type, localised soft tissue sarcomas, and it should be performed by an appropriately trained surgeon. Evaluation of the resectability of a tumour is determined by the surgeon in consultation with the MDT, and depends on the tumour stage and the patient's co-morbidity. The primary aim of surgery is to completely excise the tumour with a margin of normal tissue. What constitutes an acceptable margin of normal tissue is not universally agreed but is commonly accepted as 1 cm soft tissue or equivalent (e.g., a layer of fascia). However, on occasion, anatomical constraints mean that a true wide resection is not possible without the sacrifice of critical anatomical structures (such as major nerves, or blood vessels) and in this situation, it may be acceptable to leave a planned microscopic positive surgical margin, having considered the risks of recurrence and morbidity of more radical surgery and having discussed these fully with the patient.

For patients who have undergone surgery and have an unplanned positive margin, re-excision should be undertaken if adequate margins can be achieved. Macroscopic residual disease imparts a poor prognosis and local control is unlikely to be achieved even with addition of post-operative radiotherapy.

Patients with tumours that, because of size or position, are considered borderline resectable should be considered for down staging treatment (neo-adjuvant) with either chemotherapy or radiotherapy depending on histology of the tumour and the performance status of the patient (see below).

In some situations amputation may be the most appropriate surgical option to obtain local control and offer the best chance of cure. It is recognised that there is a group of low grade tumours which have a low risk of local recurrence and a low risk of metastasis and it is also appropriate to treat these by planned marginal excision. (e.g., atypical lipomatous tumours).

[1] Robert Grimer, Ian Judson, David Peake, and Beatrice Seddon, 'Guidelines for the Management of Soft Tissues Sarcomas,' *Sarcoma,* vol 2010*,* Article ID 506182, 15 pages, 2010, doi:1155/2010/506182.

2.3.2 Surgery in the Presence of Metastatic Disease

Surgical resection of the primary tumour may be considered appropriate as a palliative procedure in patients with metastatic disease, however radiotherapy or chemotherapy may be more appropriate and the decision must take into account factors such as the patient's symptoms (e.g., pain or fungation), co-morbidity, the expected morbidity of surgery, histological sub type and the extent of metastases and, of course, include a full discussion with the patient.

2.3.3. Isolated Limb Perfusion

Isolated limb perfusion (ILP) is a valuable pre-operative technique for reducing the size of difficult but potentially resectable tumours in an extremity, where limb preservation may not otherwise be possible. ILP employs a locally high dose of chemotherapy (melphalan) and tumour necrosis alpha (TNF) with hyperthermia localised to the affected limb using arterial and venous cannulation and a tourniquet. ILP has been shown to shrink peripheral tumours thus rendering them operable and should be considered in selected cases [24, 25]. ILP may also be considered for palliation. (Currently this service is only available for STS at the Royal Marsden Hospital in London and at the Beatson Cancer Centre in Glasgow, but it is more widely available for melanoma).

Key Recommendations:

- Surgery is the standard treatment for all patients with localised STS
- For those patients with resectable disease, a wide excision is the standard surgical procedure
- The definition of "wide" remains unclear but most would accept that an intact fascial layer or 1cm of normal tissue would be considered adequate
- Where a wide excision is not possible due to anatomical constraints, a planned marginal excision plus radiotherapy may be an appropriate means of achieving tumour control while maintaining function
- Occasionally amputation is the only surgical option to achieve adequate margins
- For patients with borderline resectable tumours, pre-operative treatment with chemotherapy or radiotherapy should be considered dependant on individual histology
- Isolated Limb Perfusion may permit limb salvage in some cases where amputation is the only conventional surgical approach.

Local surgical team approach:

High grade STS that are treated with pre-operative radiotherapy are recognised as having an increased risk of wound healing complications. Appropriate plastic surgery reconstruction is offered to all patients. However, for high risk patients, there is a low threshold for offering free flap reconstruction, as this has been shown through a local audit to reduce the possibility of wound complications.

2.4 Pathology Guidelines

The SWAG SAG NSSG pathologists refer to the Royal College of Pathology Guidelines for the reporting of Soft Tissue Sarcomas.

Histopathological/histochemical investigations are carried out and supervised by the Specialist Sarcoma Pathologist, Francesca Maggiani, University Hospitals Bristol NHS Foundation Trust.

All small cell sarcomas are sent for molecular and cytogenetic testing.

The laboratory and histopathological/histochemical investigations and their specific indications are documented within standard operation procedures in accordance with the Royal College of Pathology Dataset.
Pathologists within the region are to refer all suspected sarcoma pathology samples directly to the Sarcoma Unit at North Bristol Trust (NBT). This is to prevent delayed diagnoses occurring when pathology is sent to alternative UK centres. In the event that pathologists wish to send samples to an expert elsewhere, they should prepare a set of slides to send to NBT and your chosen expert at the same time. Details of the expert to which they have been sent should be included with the sample sent to NBT.

2.5 Radical Radiotherapy Treatment of Soft Tissue Sarcomas

Background

Management requires close collaboration with the relevant surgical team to which the patient was referred. Most commonly, this will be the plastic surgical team in North Bristol Trust, or the surgical teams in Oxford, Birmingham or London.

These guidelines do not cover treatment of bone sarcomas, embryonal and alveolar rhabdomyosarcoma, uterine sarcomas or gastrointestinal stromal tumours.

Patient assessment

Selection Criteria

Radiotherapy should be considered for all high grade lesions, and some low-intermediate grade lesions depending on tumour size, depth of lesion and surgical margins. The decision for pre or post-operative radiotherapy will be made at the MDT in conjunction with the surgical team.

Pre-treatment assessment

- Assessment of any co-morbidities which may preclude radiotherapy to the affected area
  Consider baseline blood tests as indicated by tumour site
  Lung function tests if chest wall sarcoma
- Consider evaluation of kidney function (DMSA, EDTA) if retroperitoneal/ abdominal sarcoma
  Histopathology reports and an operation note (if post op RT) are to be available.

Pre-operative radiotherapy is to be utilised where possible, but particularly in cases where the tumour is felt to be borderline operable or inoperable, close to critical structures where surgery would be difficult, or where surgery is likely to be marginal, but amputation is not justified. Surgery should be considered at least 4-6 weeks from the end of radiotherapy. Post-operative radiotherapy can also be considered in those patients who have already had surgical resection prior to referral to the service, or when it is felt that initial surgery is in the patients' best interests.

Localisation

All radical patients should be considered for CT guided planning. A coregistered MRI can also be done if felt to be useful.

CT planning scan should be done within 4 weeks of the commencement of radiotherapy.

Patients will be assessed in CT or mould room when an appropriate treatment position will be determined, in consultation with the CT and physics staff. This position will be maintained with immobilisation aids as needed. A thermoplastic jig is recommended wherever possible. Reproducibility of the positioning of the patients will be maintained using orthogonal laser beams or equivalent methods.

CT scans will be taken at 5 mm intervals (5 mm slice thickness) to include the superior and inferior scanning levels indicated at CT. (A 2mm slice thickness protocol is available if required).

Surgical scars, biopsy sites or the tumour mass if present should be wired and clinical photographs taken of the set up.

Volume Definition

This is at the discretion of the clinician. Patients in clinical trials will be treated according to the relevant protocol. The diagnostic scans must be available and, if post-operative radiotherapy, the operation note and full pathology report should also be available to aid determination of the volume at risk. Try to spare at least 1/3 of the circumference of a limb to reduce the likelihood of lymphoedema. Avoid including joints in the high dose field if possible.

Pre-operative radiation:

- GTV: Tumour and associated oedema (case by case basis as not all oedema must be included in GTV if extensive, but may be included in the CTV)
- CTV: GTV + 5cm superiorly and interiorly, + 2-3cm radially - these margins can be modified taking into account natural barriers such as fascial plane, bones and joints
- PTV: CTV+0.5-1cm margin dependent upon immobilisation and reproducibility
- A tumour boost may be considered post operatively if positive or in close proximity to surgical margins.

Post-operative radiation:

- GTV: Macroscopic tumour present before surgical excision
- CTV: Modified compartment at risk to include the tumour bed, biopsy sites and surgical scar with 5cm superiorly and inferiorly on GTV or 1cm superiorly and inferiorly on surgical scar - (whichever is greater) and 2-3cm radially depending on other boundaries such as fascial planes, bones and joints
- PTV: CTV+5mm-10mm margin
- Post-operative radiation is usually given in a phased manner with at least two and sometimes three phases of shrinking volumes.

Treatment Planning

For each of the above, the field arrangement is planned using 6 and/or 10MV photons and electrons if required.

Normal Tissue Tolerance

Organs at risk to be contoured for dose evaluation by DVHs to be determined on an individual basis e.g. lung, kidney, spinal cord

Dose Prescriptions

Radical radiotherapy limbs / chest wall - pre-operative

50Gy in 25 daily fractions over 5 weeks prescribed to 100%
10-16Gy in 5-8 daily fractions over 1-2 weeks for post-operative boost if needed

Radical radiotherapy limbs / chest wall- post-operative

Phase I - up to 50Gy in 25 daily fractions Phase II - up to 10Gy in 5 daily fractions
Phase III (if surgical margins felt to be close or involved) - up to 6Gy in 3 daily fractions

Radical radiotherapy limbs / chest wall- inoperable Individualised dose after clinical review / Radical

radiotherapy retroperitoneal sarcomas

45Gy in 25 daily fractions
If post op consider further boost of 5.4 in 3 daily fractions to reduced volume if possible

Palliative radiotherapy

A high palliative dose is often required to achieve local control.
45Gy in 15 daily fractions over 3 weeks marked clinically or simulated, delivered using a parallel pair
Alternative regimens:

30Gy in 10 daily fractions, 20Gy in 5 daily fractions, 21Gy in 3 weekly fractions over 3 weeks repeated at 4-6 weeks depending on clinical response

Treatment Verification (for radical treatment)

- Treatment verification images should be taken days 1 to 3 and then weekly on treatment.

Patient Care

- Blood tests should be done as per QAP 8.5B Radiotherapy On-Treatment Review
- Patients are monitored daily by the Radiographers, and are to be reviewed as per QAP 8.5B Radiotherapy On-Treatment Review
- The weekly palliative patients should be seen prior to each weekly fraction.

Follow up

Patients receiving pre-operative radiotherapy will be seen next by the surgical team at NBT and continue follow up in the joint surgical oncology clinic, also at NBT. All patients receiving post op radiotherapy or palliative radiotherapy will be reviewed in clinic 4-6 weeks after the end of the course of radiotherapy at either the BHOC, UH Bristol or NBT.

2.6 Chemotherapy Treatment Algorithms

As per UK Guidelines for the Management of Soft Tissue Sarcoma.

2.7 Follow up Guidelines

The aim is to detect recurrent disease, whether local or distant, while it is still curable and to minimise the morbidity of the recurrent disease where it is not. The risk of recurrence increases with higher grade and greater tumour size. Therefore a more intensive surveillance schedule is adopted for patients with large, high- grade tumours, especially in relation to investigations. The majority of recurrences occur within the first 3 years following primary surgery; hence more frequent visits are required during this period. Follow-up also serves the purpose of identifying any late effects associated with treatment.

Frequency

Intermediate and high grade tumours:

- 1 month after completion of treatment then
- 4 monthly until 1 year
- 4 monthly until 3 years
- 12 monthly until 5 years
- 12 monthly until 10 years then consider discharge.

Low grade tumours:

- 4 monthly until 2 years
- 6 monthly until 5 years
- 12 monthly for at least 10 years.

The frequency for Chest X-ray and other surveillance imaging is detailed below. If the patient has received chemotherapy or radiotherapy, other investigations such as routine blood tests, gonadal function, echocardiography, EDTA GFR, and pulmonary function tests should be considered at intervals as indicated. This

will usually be guided by trial or chemotherapy protocols.

If patients are symptomatic or have metastatic disease, then follow-up should be at the discretion of the physician, however, as a guide every 6 weeks to 3 months is not unreasonable.

Limb and limb girdle

Low grade tumours

Key Points

- Local recurrence is major risk and pulmonary dissemination unlikely
- Ultrasound / MRI / CT if clinical suspicion - to be confirmed by fine needle aspirate or cutting needle biopsy
- Consider annual imaging if site of disease difficult to examine, especially if complicated by radiation-induced fibrosis or oedema
- Annual chest x-rays for small low grade tumours, more regularly if larger tumours
- Need long follow-up, e.g. >10 years.

High grade tumours

Key Points

- The main purpose of follow-up for high grade tumours is to identify patients eligible for potentially curative pulmonary metastectomy
- Surveillance should include history, physical examination, and chest X-ray at each attendance
- Rapid evolution of pulmonary metastatic disease, large tumour size, >10 lesions and short disease-free interval from primary surgery implies poor outcome from metastectomy
- In patients with pulmonary relapse, it is usually recommended to repeat the CT thorax after an interval of 6-8 weeks in order to ensure that new lesions are not developing, rendering surgery fruitless.

Retroperitoneal sarcomas

Visceral tumours

Key Points

- GISTs spread to peritoneal surfaces and liver even when apparently low grade, and patients with high-risk tumours require regular CT in the first few years, the frequency depending on their risk as defined by tumour size, mitotic index, and primary disease site
- Endoscopic ultrasound might be appropriate for detecting local recurrence, but has not been validated.

Other retroperitoneal tumours

Key Points

- Post-operative CT scans act as a useful baseline for future comparison
- History and physical examination are generally adequate for the majority of low or intermediate grade tumours with ultrasound or CT scan performed on clinical suspicion
- Repeat operations are indicated for palliation of symptoms or in the case of imminent threat to organ function
- CXR as in other high grade.

Gynaecological sarcomas

Key Points

- CT scanning or MRI may be required if the anatomy is difficult, or in the obese patient where USS is insufficiently sensitive. Generally a combination of trans-vaginal plus abdominal ultrasound and chest X-ray may be adequate to detect pelvic, liver and lung recurrences.

3. Clinical Guidelines for Bone Sarcoma (B12/S/a/g-16-004)

The SWAG SAG does not undertake diagnosis and treatment of bone sarcoma. All patients with suspected bone sarcoma are referred to Oxford Sarcoma Service.

4. Clinical Guidelines for Soft Tissue Sarcomas Presenting to Site Specialised MDTs (B12/S/a/g-16-004)

4.1 Upper GI

SAG refers to the SWAG Upper GI and Hepato-Pancreato Biliary CAG Clinical Guidelines and team for the treatment of Upper GI STS.

4.2 Gynaecology

SAG refers to the SWAG Gynaecology CAG Clinical Guidelines and team for the treatment of Gynaecology STS.

4.3 Head and Neck

SAG refers to the SWAG Head and Neck CAG Clinical Guidelines and team for the treatment of Head and Neck STS.

4.4 Skin

SAG refers to the SWAG Skin CAG Clinical Guidelines and team for the treatment of Skin STS.

4.5 Breast

SAG refers to the SWAG Breast CAG Clinical Guidelines and team for the treatment of Breast STS.

4.6 Lung

SAG refers to the SWAG Lung CAG Clinical Guidelines and team for the treatment of Lung STS.

4.7 Urology

SAG refers to the SWAG Urology SSG Clinical Guidelines and team for the treatment of Urology STS.

Shared care pathways for the above site specific groups are published on the SWAG website here.

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