Resource Stratified Sarcoma Guidelines 2025

Pacific Islands Orthopaedic Association COSA Global Oncology Group

Principles of Management

1. Histological diagnosis obtained by adequate biopsy is important. The route and method of biopsy can affect the curability of sarcomas. Please consult with surgical mentors if not sure which plane of approach is required to obtain biopsy.
2. Immunohistochemistry may need to complement H&E staining of specimens to determine sarcoma type.
3. Staging of patients with CT scan.
    - If CT is not available then chest Xray and liver ultrasound is required as a minimum.
4. The management of sarcomas is multidisciplinary and ideally cases should be discussed in a multidisciplinary team meeting to determine a treatment plan and whether the aim of therapy is curative.
5. Preoperative or Post operative treatments may include Radiotherapy or Chemotherapy and at times both.
6. Following are the Radiation Therapy and Chemotherapy protocols for Sarcoma

(This is not a comprehensive guideline, but a treatment guide).

Principles of biopsy:

1. **Complete all investigations before biopsy.** This should include plain film XRs, CT of lesion if available, MRI if available. In addition, CT chest, abdomen and pelvis and/or bone scan (if available) looking for metastases. If CT is not available, then chest Xray and liver ultrasound is required as a minimum.
   The biopsy procedure will affect investigations such as an MRI, due to the oedema from the surgical intervention. **That is why investigations should be completed first.**
2. **Discuss with experienced tumour surgeon before doing the biopsy.** We now have a **monthly Pacific Tumour MDT meeting on Zoom** to help with planning. This is held on the **second Saturday each month at 6pm AEST (Brisbane time)**

Zoom link
https://us02web.zoom.us/j/82884690940?pwd=bkpsZTVBZWUyVEYzOHFXWXdYdC9VZz09.

We can help guide biopsy technique and approach, to avoid contaminating the surgical site.

3. **Organise pathologist presence** (if available in your country – can do a frozen section to confirm adequate, representative sample).
4. **Biopsy technique**

a) **Tru cut/core** (tattoo ink around track so it can be excised later with main resection)

Do not do fine needle aspiration. Not suited for musculoskeletal tumours. Fine needle / cytology generally does not provide an adequate sample in musculoskeletal tumours.

b) Open Biopsy technique

Longitudinal incision
Stay in single compartment
Avoid neurovascular structures
Get representative sample
Meticulous haemostasis
If using a drain bring it out in line with wound and close to edge so as not to contaminate wide tissue area
Close in layers with subcuticular suture to avoid dead space and haematoma

General principles:

Bone sarcomas do best with neoadjuvant chemotherapy (Biopsy followed by 2-3 cycles of chemo, followed by excision, followed by further 3+ cycles of chemo). Surgery alone in bone sarcomas provides a very poor outcome with less than 20% survival due to presence of micro-metastases. The pre surgery chemo is designed to "sterilize" and kill the micro-metastases.

Soft tissue sarcomas are generally more responsive to radiation either before or after surgery. If radiation is not available, then surgery alone may be useful.

Treatment regimens suitable for the Pacific Island countries (2025)

Soft tissue sarcomas of Limb and Trunk.

Radiation Therapy

Preoperative or Postoperative Radiation Therapy has shown to be important to reduce local recurrence in large (>5cms) high grade sarcomas. Surgery alone may be an option for patients with small tumours that can be resected with wide surgical margins. In the case of limb sarcomas, it is a vital component of limb salvage surgery. Although surgical margins are the most important to prevent local recurrence, radiation therapy can help even when margins are close or positive.

Volumes – A Gross Tumour Volume (GTV) is created from all available imaging and clinical examination. A 15 millimetre radial and 40 millimetre superior and inferior margin (in limb) is added to create a Clinical Target Volume (CTV). In trunk a uniform 15mm margin maybe used. The CTV may be clipped to structures such as bone.
A 10 mm margin (or more), based on set up variability, is added to create a Planned Target Volume (PTV).

Dose – Common prescription is 50Gy/25 fractions/5 weeks preoperative, and if given post operatively common prescription is 60 to 66 Gy in 30 to 33 fractions/6 weeks.

Palliative Radiation Therapy

Used for pain, compression, skin involvement, ulceration, bleeding. Common dose and fractionations are 30Gy/10 fractions, 20Gy/5 fractions or 8Gy/1 fraction.

Chemotherapy

DOXOrubicin (60 or 75 mg/m^2) every 21 days (maximum of 6 cycles).

<u>NOTE: 75mg/m^2 should only be considered in fit patients.</u>

Sarcomas: in this group would include undifferentiated pleomorphic sarcoma (previously known as malignant fibrous histiosarcoma), myxoid liposarcoma, synovial sarcoma).

Toxicity: cardiac toxicity, emesis, hair loss.

Precautions: Cardiac monitoring – Echo, ECG, LVEF (check baseline, should be >50%).

Cumulative lifetime DOXOrubicin equivalent dose: should not exceed 500mg/m^2 or 450mg/m^2 in elderly or hypertensive cardiomegaly patients.

Osteosarcoma

Radiation Therapy

Inoperable Localised Osteosarcoma – 60Gy30 fractions/6 weeks.
Palliation -30Gy/10 fractions, 20Gy/5 fractions or 8Gy/1 fraction.

Chemotherapy

DOXOrubicin 75mg/m^2 + ciSplatin 80mg/m^2 every 21 days (maximum of 6 cycles).

Toxicity: Emesis, hair loss, myelosuppression, renal impairment, ototoxicity, cardiac toxicity, neurotoxicity.

Precautions: Cardiac monitoring – Echo, ECG, LVEF (check baseline, should be >50%).

Cumulative lifetime DOXOrubicin equivalent dose: should not exceed 500mg/m^2 or 450mg/m^2 in elderly or hypertensive cardiomegaly patients.

Ewing Sarcoma and rhabdomyosarcoma

Radiation Therapy

Inoperable Ewing sarcoma and Rhabdomyosarcomas, or when patient refuses surgery. Radical radiation therapy to doses of 50.4Gy to 54Gy in 28 to 33 fractions over 6 weeks. Radiation usually given with 7th cycle of chemotherapy, but can be given after chemotherapy is completed, if there are concerns about toxicity.

Chemotherapy

VinCRISTine 1.5mg/m^2 (maximum single dose: 2mg) + DOXOrubicin 75mg/m^2 + CYCLOPHOSPHamide 1000mg/m^2 every 21 days (maximum of 6 cycles).

Chemotherapy is generally not effective in chondrosarcomas unless they are mesenchymal. This mesenchymal subgroup could be treated with this protocol. Dedifferentiated chondrosarcoma can be treated with single agent DOXOrubicin however this would usually be with palliative intent.

Pleomorphic rhabdomyosarcoma occur in elderly and should be treated with single agent doxorubicin at 60 mg/m^2.

Toxicity: Emesis, hair loss, myelosuppression, sensory neuropathy, cardiac toxicity, bladder toxicity.

Precautions: Cardiac monitoring – Echo, ECG, LVEF (check baseline, should be >50%).

Cumulative lifetime DOXOrubicin equivalent dose: should not exceed 500mg/m^2 or 450mg/m^2 in elderly or hypertensive cardiomegaly patients.

Patients should be encouraged to hydrate well and empty their bladder regularly including before going to bed to prevent haemorrhagic cystitis.

Leiomyosarcoma

Radiation Therapy

Same Principles as Soft Tissue Sarcoma

Chemotherapy

DOXOrubicin 60mg/m^2 + dacarbazine 750mg/m^2 every 21 days (maximum of 6 cycles).

Toxicity: Emesis, cardiotoxicity, hair loss, myelosuppression.

Single agent DOXOrubicin can be considered in frailer patients or where downstaging for surgery will not be possible.

A higher response rate is associated with the combination of DOXOrubicin and dacarbazine.

Precautions: Cardiac monitoring – Echo, ECG, LVEF (check baseline, should be >50%).

Cumulative lifetime DOXOrubicin equivalent dose: should not exceed 500mg/m^2 or 450mg/m^2 in elderly or hypertensive cardiomegaly patients.

Angiosarcoma

Radiation Therapy
Same Principles as Soft Tissue Sarcoma.

Chemotherapy

PACLitaxel 80 mg/m^2 on day 1, day 8 and day 15 every of each 28 day cycle (continue until disease progression or unacceptable toxicity).

Toxicity: hypersensitivity reaction, mucositis, neuropathy.

Gastrointestinal stromal tumours (GIST)

Radiation Therapy
Mostly for Palliation. 30Gy/10 fractions, 20Gy/5 fractions or 8Gy/1 fraction.

Chemotherapy/Systemic Therapy

These tumours of gut origin do not respond to chemotherapy however do respond well to targeted agents.

Imatinib mesylate 400mg daily (continuously until progression).
NOTE: Increasing dose to 600mg or 800mg daily on progression may regain control of the tumour.

Sunitinib 50 mg daily for 4 weeks out of 6 (continuously until progression) is a second line therapy for advanced GIST if patients progress on or are intolerant to imatinib.

High risk completely resected GISTs also benefit from 3 years of adjuvant imatinib 400 mg daily.

Imatinib and suniitnib are available from the Max Foundation (https://themaxfoundation.org/)

NOTE: DOXOrubicin and vinCRISTine have a risk of extravasation during administration. Anyone administering these agents should know what steps to take if this occurs before commencing therapy.

Metastatic cancer

Consider metastases in bony lesions in patients older than 40 years old.
Common tumour that metastasize to bone include lung, bowel, breast, prostate, thyroid, kidney as well as haematological malignancies. Take a good history and examine and assess for primary source. Renal (kidney) metastases are very vascular and can bleed catastrophically. If available can consider embolization of feeding vessel on day of surgery or day prior to surgery.

Use Mirel's score to calculate risk of fracture and perform pre fracture stabilization.

	1	2	3
Location	Upper limb	Lower limb	Per trochanteric
Size	Less than 1/3 dia	1/3 to 2/3 dia	Greater than 2/3 dia
Type	Blastic	Mixed	Lytic
Pain	Mild	Moderate	Functional

<u>Risk of fracture</u>
If score is 7 or less can observe
All lesions with score of 8 or more should be stabilized before they fracture if patient expected to survive more than 2 months (not in extremis).

IM nails are best as they are load sharing.
If you have a large lytic lesion and have bone cement available can use cement to augment the defect. Still needs plate or IM nail to stabilize it. Best to insert the fixation first before putting in the cement as it is very difficult to drill through the cement.

After stabilizing if radiation is available consider whole bone single dose radiation.

Considerations regarding genetic predisposition

Young age at diagnosis, multiple primary cancers or a family history of young-onset cancers (particularly breast cancer, brain tumour, sarcoma, adrenocortical cancer, leukaemia and rare cancers) in first or second-degree relatives suggest a possible genetic predisposition, most commonly *TP53*-associated with Li Fraumeni Syndrome.

Patients with Li Fraumeni syndrome or a history of childhood retinoblastoma may be at a higher risk of developing another radiation-induced cancer due to increased sensitivity to radiation. However, curative treatment of sarcoma remains the priority. Radiotherapy should not be withheld if no effective alternative exists. Pre-operative radiotherapy is preferred, as it uses a lower total dose and part of the treated tissue is removed during surgery.

Female patients with family and clinical history suggestive Li Fraumeni syndrome should consider annual breast screening, if available.

References:

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These guidelines have been endorsed by the COSA Global Oncology Executive Committee.

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