



How to Treat Melanoma

Professor Rodney Sinclair MBBS, MD, FACD
University of Melbourne and the Epworth Hospital



10 steps to the care of invasive melanoma

1. Complete surgical excision of the primary tumour.
2. Tumour staging including assessment for sentinel lymph node biopsy.
3. Re-excision of surrounding skin with a margin determined principally by the Breslow thickness of the primary tumour.
4. Patient assessment for adjuvant chemotherapy.
5. Patient assessment for adjuvant radiotherapy.
6. Provision of palliative care including surgical resection of metastasis, chemotherapy and radiotherapy.
7. Serial screening examinations for metastasis and also subsequent primary melanoma in both the patient and also first degree relatives.
8. Advice regarding lifestyle modification to reduce risk of subsequent primary melanoma both to patient and also to first degree relatives.
9. Advice regarding appropriate screening for internal malignancy.
10. Access to appropriate patient counselling taking into account the profound social, psychological and financial impact a diagnosis of melanoma has on the affected individual and their family.

Step 1. Surgical excision of the primary tumour

- This remains the single most important step in the treatment of melanoma, and the principal determinant of patient survival.
- Must be completely excised
 - Section should be bread-loafed
 - The pathology synoptic report should document those histologic features important for guiding patient management, including those characteristics on which the diagnosis was based and also prognostic factors.

Step 1. Surgical excision of the primary tumour

- Excisional surgical biopsy with a lateral 2 mm margin of normal surrounding skin and a deep margin that includes the subcutis is recommended for all lesions suspected of being melanoma.
- Where more than one lesion is excised, separate specimen bottles and accurate specimen labelling are essential.
- Shave biopsy is only acceptable when excisional biopsy is not feasible.

Step 1. Surgical excision of the primary tumour

- Referral for specialist assessment is appropriate if the treating doctor is not comfortable performing the biopsy of a suspected melanoma.
- Punch biopsy risks sampling error when a melanoma arises within a benign naevus and is not generally recommended.
- However, punch biopsy does not adversely affect prognosis.

Step 2. Tumour staging including assessment for sentinel lymph node biopsy.

- Clinical staging includes palpation of the regional lymph node basins and examination for hepatomegaly.
- Sentinel node biopsy should be discussed with any patient with the following diagnosis:
 - invasive melanoma greater than 1mm thick;
 - Clark level 4 melanoma;
 - melanoma with more than two mitoses per high-power field;
 - Ulcerated melanoma;
 - melanoma with significant regression;
 - or melanoma of unknown malignant potential.

Step 3 Re-excision Margins

- The scar following removal of an invasive melanoma should be re-excised with a margin of between 1 and 2 cm, with the choice of excision margin determined primarily by the Breslow tumour thickness in mm
- melanoma in situ (restricted to epidermis)—margin 5 mm
 - melanoma <1.0 mm thick—margin 1 cm
 - melanoma <1.0 mm thick—minimum margin 1 cm and maximum 2 cm
 - melanoma >4 mm thick—minimum margin 2 cm

Step 3 Re-excision Margins

- Wider excision has been demonstrated to reduce the risk of local persistence/recurrence of the tumour and local metastasis but there is no evidence that a margin greater than 1 cm offers additional benefit in terms of patient survival.

Step 4 Adjuvant chemotherapy

- Interferon alpha 2b
- Decarbazine
- Ipilimumab
- Vemarafinib
- Debrafinib
- Combination chemotherapy

Step 5 adjuvant radiotherapy

- While primary radiotherapy is occasionally used for unresectable lentigo maligna or invasive melanoma, it is more commonly used as adjuvant radiotherapy for cutaneous melanoma likely to recur locally.
- Indications for adjuvant radiotherapy include a Breslow thickness >4mm, satellite nodules or neurotropic spread.
- Adjuvant radiotherapy is also used to prevent recurrence following regional lymph node resection.
- Common indications include more than three nodes with metastasis, a large tumour mass in a single node or extracapsular spread.

Step 6 Adjuvant surgery

- Therapeutic elective lymph node resection is generally not recommended as adjuvant surgical treatment.
- This is because there is no evidence to suggest a survival advantage and there is significant potential surgical morbidity, including postoperative lymphoedema

Step 6 Adjuvant surgery

- Identification of suspicious lymph nodes on clinical examination should be followed by fine-needle aspiration and ultrasound imaging, MRI or PET.
- If nodal metastasis is confirmed histologically, immediate complete regional lymph node dissection is recommended.
- Cure rates in the order of 30% may be achieved with completion lymphadenectomy for palpable disease.

Step 6 Adjuvant surgery

- Completion lymph node dissection following identification of micrometastasis on sentinel lymph node biopsy is more controversial as the proportion of lymph node micrometastasis that progresses to symptomatic disease is not known
- A prospective randomised multicentre selective lymphadenectomy trial (MSLT-I) comparing completion lymph node dissection with observation showed no difference in overall survival
- Patients with micrometastasis may be enrolled in the multicentre sentinel lymph node treatment trial MSLT-II.1

Step 7. Surgery, chemotherapy and radiotherapy for stage IV disease

- Specialist multi-disciplinary care
- Combination chemotherapy
- Improve survival at 1 year
- No improved survival at 5 years

Step 8. Follow-up examination for metastasis and subsequent primary melanoma

- All patients diagnosed with invasive melanoma require periodic follow-up that includes examination and palpation for local recurrence, in transit metastasis, lymph node metastasis and hepatomegaly.
- Additional examination and investigation should be guided by reported symptoms.

Step 8. Follow-up examination for metastasis and subsequent primary melanoma

- For the 90% of Australians who survive melanoma, the risk of developing a subsequent primary melanoma is in the order of 10%.
- This risk is also influenced by other factors including family history, skin type, hair colour and the presence of significant solar skin damage including non-melanoma skin cancer
- It is recommended that all melanoma patients, including with in situ melanoma, have a complete skin check at least once a year for life following the diagnosis of a melanoma.

Step 8. Follow-up examination for metastasis and subsequent primary melanoma

- As there is a familial tendency to melanoma, all first-degree relatives of a patient diagnosed with melanoma should be encouraged to attend for a full skin examination to identify a previously unsuspected melanoma and to assess risk of future development of melanoma.

Step 9. Lifestyle modifications to reduce risk of metastasis and subsequent primary melanoma

- HRT and oral contraceptives
- Pregnancy
- Sun protection
- Vitamin D
- Screening for other malignancies

Step 10. Counselling

- Patients with invasive melanoma and their families will have complex social, psychological and financial issues.
- Life and income protection insurance may be declined even for people with thin melanomas.
- The nature and intensity of these issues will vary from person to person and with disease severity.
- Psychologists with experience in palliative care should be involved when the patients' needs and those of the family can no longer be met by the treating physician.
