

11 Treatment of primary melanoma

The standard treatment for primary melanoma is wide local excision (WLE) of the skin and subcutaneous tissues around the melanoma. The aim is complete surgical excision of all in situ and invasive melanoma components. This should be confirmed by comprehensive histological examination of the entire excised specimen with special reference to the periphery. The *in-situ* component, where present, often extends beyond the invasive melanoma, and complete excision of both is mandatory.

The recommendations for minimum radial excision margins used for WLE have been based on the maximum Breslow thickness of the primary melanoma. This surgical (clinical) margin is measured clinically from the melanoma edge, using a ruler and marker pen, before the start of the operation. Margins should be measured **before** excision because specimen shrinkage after excision and during formalin fixation reduces the measured margin.

Treatment of the primary melanoma may differ for specific types and locations of melanoma such as desmoplastic, and neurotropic melanomas, mentioned also elsewhere in the guidelines. Acral lentiginous and subungual melanomas are specific types of cutaneous melanoma that arise in the extremities/soles/palms, and nail-beds, respectively.¹ These may require differentiation from haematomas and benign naevi using biopsy where appropriate. Local recurrence (persistence), local metastasis (including in-transit metastasis and satellitosis)²⁻⁴ and distant spread of melanoma may need further assessment and treatment, as discussed elsewhere in the guidelines. (These definitions are listed in the glossary). 'Local recurrence' properly means persistence of residual primary tumour, whereas local metastasis, refers to tumour spread away from the primary site. However, these terms have sometimes previously not been differentiated in the literature.

11.1 Review of the evidence

There are three systematic reviews⁵⁻⁷ and five randomised controlled trials (RCTs)⁸⁻¹³ comparing different clinical excision margins in primary melanoma. The RCTs compare narrow versus wider excision margins and assess overall survival and 'local recurrence', with median follow-up ranging from 5 to 16 years. However, definitions of 'local recurrence' are often inconsistent, unclear, imprecise or not stated, and the impact on patient survival is unclear. Therefore, these 'local recurrence' data must be interpreted with caution.

Evidence from the currently available systematic reviews and RCTs indicate the following:

- ***in-situ* melanoma:** no RCTs are available for assessment
- **melanomas < 1 mm thick:** no RCT specifically assesses melanomas less than 1 mm thick. The French, Swedish and WHO RCTs investigated melanomas less than 2mm thick, which included melanomas < 1 mm thick. No difference in mortality was found for wider excision (5cm in the French study, 5cm in the Swedish study, 3cm in the WHO study) compared with narrower excision (2cm in the French study, 2cm in the Swedish study, 1cm in the WHO study)

- **melanomas 1–2mm thick:** the French, Swedish and WHO RCTs assessed melanomas less than 2mm thick, and 272 patients in the Intergroup study had melanomas between 1mm and 2mm thick. No statistically significant difference in overall survival was demonstrated between the two groups treated with narrow or wide excision
- **melanomas 2–4mm thick:** the Intergroup and the BAPS/MSG RCTs included melanomas between 2mm and 4mm thick. Again, there was no statistically significant difference in overall survival between the two groups treated with narrow or wide excision margins. However, numbers of patients and events were relatively small for statistical comparison
- **melanomas > 4mm thick:** only the BAPS/MSG RCT (~ 207 evaluable patients) had melanomas > 4mm thick, but was insufficient to permit meaningful analysis
- data on acral lentiginous and subungual melanoma are very limited, principally due to the lower incidence compared with other forms of cutaneous melanoma^{14–17}
- acral lentiginous and subungual melanoma may be considered for ‘functional’ amputation, as limited studies show no statistical recurrence or survival differences over more radical amputation.^{14–17} Radiotherapy or isolated limb infusion chemotherapy may be of use where surgery is limited or not possible.^{17,18}

Evidence summary	Level	Reference
There is no convincing RCT evidence that a margin greater than 2cm offers additional benefit for the patient in terms of overall survival or ‘local recurrence’, irrespective of melanoma thickness	I	5–13
Furthermore, two RCTs show no evidence that a margin greater than 1cm offers any survival advantage, although it is not clear whether a wider margin reduces the risk of ‘local recurrence’	I	8, 9, 13
Systematic review indicates that there are inadequate data to confirm a mortality difference between wider and narrower excision for primary invasive melanoma	I	5–7
For acral lentiginous or subungual melanoma there are no RCTs or SRs to define excision margins. Data are from retrospective case studies	IV	14–17

Recommendations	Grade
1. After initial excision biopsy; the radial excision margins, measured clinically from the edge of the melanoma, be: <ol style="list-style-type: none"> 1. (pTis) melanoma <i>in situ</i>: margin 5mm 2. (pT1) melanoma < 1.0mm: margin 1cm 3. (pT2) melanoma 1.0–2.0mm: margin 1–2cm 4. (pT3) melanoma 2.0–4.0mm: margin 1–2cm 5. (pT4) melanoma > 4.0mm: margin 2cm 	<p style="text-align: center;">C</p> <p style="text-align: center;">B</p> <p style="text-align: center;">B</p> <p style="text-align: center;">B</p> <p style="text-align: center;">B</p>
2. Caution be exercised for melanomas 2–4mm thick, because evidence concerning optimal excision margins is unclear. Where possible, it may be desirable to take a wider margin (2cm) for these tumours depending on tumour site and surgeon/patient preference	<p style="text-align: center;">B</p>
3. Acral lentiginous and subungual melanoma are usually treated with a minimum margin as set out above, where practicable, including partial digital amputation usually incorporating the joint immediately proximal to the melanoma	<p style="text-align: center;">D</p>

11.2 Good practice points

- Excisions should have vertical edges to ensure consistent margins
- Caution be exercised for melanomas thicker than 2mm, because evidence concerning optimal excision margins is unclear. Where possible, it may be desirable to take a wider margin (2cm) for thicker tumours depending on tumour site and surgeon/patient preference
- Excision biopsy of the complete lesion with a narrow (2mm) margin is appropriate for definitive diagnosis of primary melanoma. Lesions excised with a margin less than those defined above should be re-excised as soon as practicable to achieve these margins
- Depth of excision in usual clinical practice is excision down to but not including the deep fascia unless it is involved
- Where tissue flexibility is limited, a flap repair or skin graft is sometimes necessary subsequent to an adequate margin of removal
- Treatment of most melanomas can be achieved on an outpatient or day-surgery basis, under local anaesthesia, unless nodal surgery is required
- Melanoma (i) is a risk factor for new primary melanoma(s) and (ii) also has the potential to recur or metastasise. Patients should be appropriately managed and followed-up for these aspects, as discussed elsewhere in these guidelines
- Patients should be informed that surgical excision may be followed by wound infection, haematoma, failure of the skin graft or flap, risk of numbness, a non-cosmetic scar and the possibility of further surgery

- Some tumours may be incompletely excised despite using the above-recommended margins. These include melanomas occurring in severely sun-damaged skin and those with difficult-to-define margins (e.g. amelanotic and desmoplastic melanomas). In these categories, the presence of atypical melanocytes at the margins of excision should be detected by comprehensive histological examination (including immunohistochemical staining)¹ and followed by wider excision. The possible use of staged Mohs excision has been proposed in such situations¹⁹
- Amelanotic melanoma can present significant difficulties for defining a margin with up to one third of subungual and nodular melanomas being non-pigmented. This may dictate choice of a wider margin, or further re-excision, where practicable
- For patients with deeper invasive melanomas (> 1 mm thick), referral to a specialised melanoma centre should be considered to ensure that best practice is implemented and for the collection of national outcome data. This may present logistic difficulties in regional and remote areas, but specialist care is recommended
- The AJCC/UICC (2001) system^{20–23} has been recommended for melanoma staging. Sentinel node biopsy (SNB) is an important prognostic factor for melanoma,²⁴ but there is debate about its use in treatment.^{24–26} SNB should be considered in patients with primary melanomas > 1 mm thick or Clark IV, who want to be as informed as possible about their prognosis. SNB should be performed **before** wider local excision.

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