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Malignant melanoma excision margins: plastic surgery audit in Britain and Ireland, 1991, and a review

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SUMMARY. **In 1991, 146 consultant plastic surgeons in Britain and Ireland were sent a short questionnaire about their policies for excision margins for primary cutaneous malignant melanoma. 106/146 (73%) replied. 39/106 (37%) considered narrow margin (2–3 mm) excision biopsies adequate in certain cases. The minimum tumour thickness for a margin of more than 1 cm was 1 mm or more for 67/106 (63%) on the leg and for 57/106 (54%) on the back. The maximum margin was specified as 4 cm or more on the leg by 37/106 (35%) and on the back by 42/106 (40%). Other sub-groups of results were analysed. A review of the literature is presented.**

Surgeons treating patients with malignant melanoma are confronted by an increasing incidence of malignant melanoma[1,2] while having only a varied, incomplete mixture of evidence on which to base their treatment. In order to find out the policies for the local treatment of primary malignant melanomas in plastic surgery units in Britain and Ireland, a questionnaire was sent to all consultant plastic surgeons in these units in October, 1991.

Questionnaire

1) Do you treat primary malignant melanoma?
2) If yes, considering only two types of patient, first a woman with a malignant melanoma of her calf and second a man with a malignant melanoma of his back, please state:
   For a patient with a malignant melanoma, confirmed by an excision biopsy with a narrow margin (2–3 mm), would you carry out a wider excision of the biopsy site and if so how wide would the excision margin be?
   (A scale of maximum tumour thicknesses was given, as in the histograms below, against which the surgeons wrote their answers.)

Results

Of the 146 consultant plastic surgeons sent the questionnaire, 106 (73%) who treat primary malignant melanoma returned completed forms.

39/106 (37%) considered the excision biopsy adequate in certain cases, mainly thin melanomas less than 0.76 mm thick (see table).

No wider excision if:	*No. of surgeons*
< 0.76 mm on leg	5
< 0.76 mm on leg and back	28
< 1.4 mm on leg, < 0.76 mm on back	1
< 0.9 mm on leg	1
< 0.9 mm on leg and back	4
(plus "maybe" or "probably" for thin tumours:	2)

Having decided on a wider excision for some tumours, most surgeons varied the margin, depending on tumour thickness. 12/106 (11%) did not vary the margin for leg tumours and 14/106 (13%) did not vary the margin for back tumours.

Having decided on a wider margin, 31/106 (29%) would make a wider margin on the back than on the leg for tumours of the same thickness (24 of the 31 only did so for some tumour thicknesses).

The maximum margin on the leg was specified as 3 cm or less by 61/106 (58%) and 4 cm or more by 37/106 (35%) (Fig. 1).

For 81/106 (76%) the maximum margin on the leg was in the range of 3 to 5 cm. Others reported: direct closure (3), margins ten times the tumour thickness (2), twice the diameter of the tumour (1), depending on clinical judgement (1) and not stated (1).

The maximum margin on the back was specified as 3 cm or less by 56/106 (53%) and 4 cm or more by 42/106 (40%) (Fig. 2).

For 77/106 (73%) the maximum margin on the back was in the range of 3 to 5 cm. Others reported: direct closure (3), margins ten times the tumour thickness (2), twice the diameter of the tumour (1), depending on clinical judgement (1) and not stated (1).

The minimum tumour thickness for which a margin of more than 1 cm was specifically excised on the leg was 1 mm or more for 67/106 (63%) (Fig. 3).

27/106 (25%) used margins of more than 1 cm for tumours less than 1 mm thick on the leg.

The minimum tumour thickness for which a margin of more than 1 cm was specifically excised on the back was 1 mm or more for 57/106 (54%) (Fig. 4).

38/106 (36%) used margins of more than 1 cm for tumours less than 1 mm thick on the back.

71/106 (67%) used a margin specified as 3 cm or

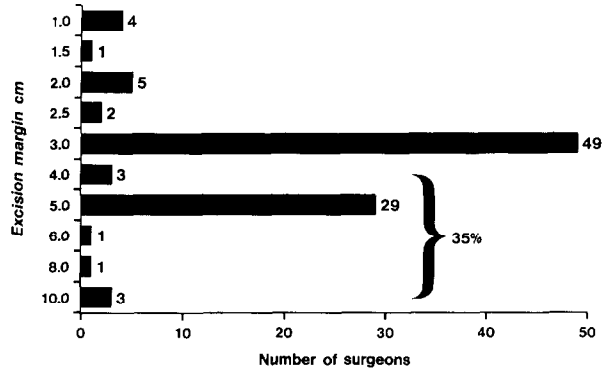

Fig. 1

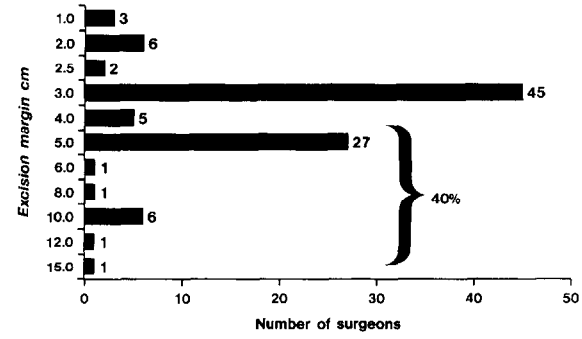

Fig. 2

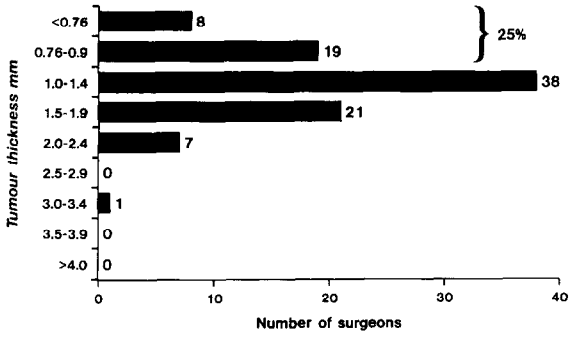

Fig. 3

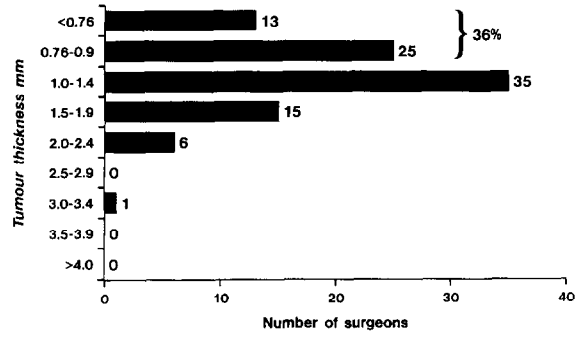

Fig. 4

Figure 1—Maximum excision margin—leg. **Figure 2**—Maximum excision margin—back. **Figure 3**—Minimum tumour thickness for more than 1 cm excision margin—leg. **Figure 4**—Minimum tumour thickness for more than 1 cm excision margin—back.

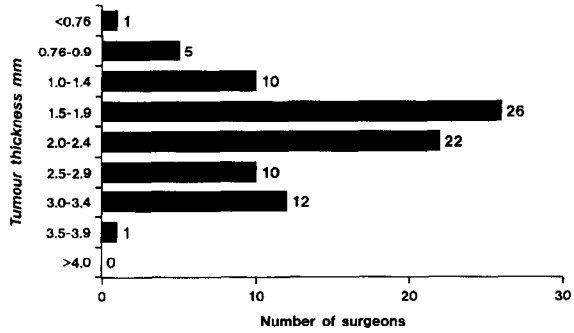

Fig. 5

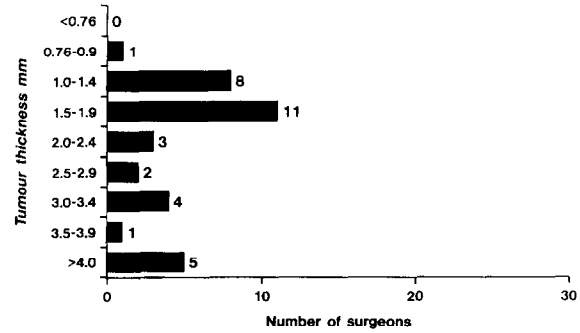

Fig. 6

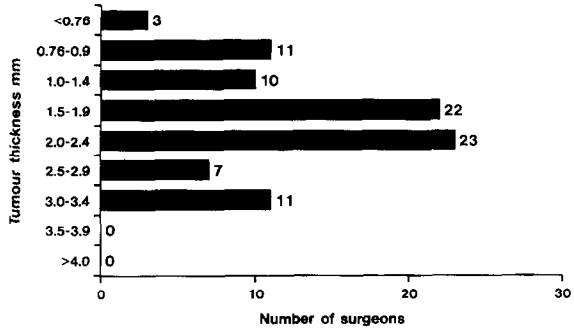

Fig. 7

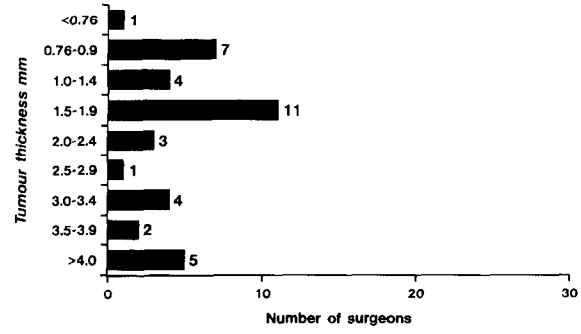

Fig. 8

Figure 5—Minimum tumour thickness for 3 cm or more excision margin—leg. **Figure 6**—Minimum tumour thickness for 5 cm or more excision margin—leg. **Figure 7**—Minimum tumour thickness for 3 cm or more excision margin—back. **Figure 8**—Minimum tumour thickness for 5 cm or more excision margin—back.

more only for tumours 1.5 mm or more thick on the leg (Fig. 5).

Of the 16 using at least 3 cm on thinner lesions, 9 used a margin of 5 cm or more (Fig. 6).

63/106 (59%) used a margin specified as 3 cm or more only for tumours 1.5 mm or more thick on the back (Fig. 7).

Of the 24 using at least 3 cm on thinner lesions, 12 used a margin of 5 cm or more (Fig. 8).

Discussion

83% of the British and Irish plastic surgeons who replied to the questionnaire advocated excision of at least some malignant melanomas of the leg and back with margins specified as 3 cm or more. There were various ideas about "wide excision" and about what types of tumours should be treated by wide excision, and so it seems useful to discuss how these ideas developed and to review recent studies which could modify these ideas.

In the 19th century, malignant melanoma was rare. After early reports by Hunter and Laennec, further detailed studies of the natural history of melanoma were published.[3] Because of the poor prognosis, even surgeons such as Dupuytren advised against surgery.[4] Gradually an international tradition of wide excision in apparently curable cases developed so that, for example, in 1898 Pringle in Glasgow treated a malignant melanoma of a forearm by excision of the tumour and adjacent skin plus a larger zone of the underlying subcutaneous tissue and deep fascia, together with a strip of subcutaneous tissue and fascia over the brachialis with fat and glands up to the apex of the axilla, all in one continuous strip.[5] The patient was alive thirty eight years later.[6]

Similar radical surgery had developed for cancer of the breast. In England, William Sampson Handley followed Watson Cheyne's principle of excision of a breast cancer and surrounding skin with a wider zone of deeper tissue including deep fascia; Handley suggested a skin incision 4 to 5 inches in diameter, centred on the breast cancer and surrounding it at a safe distance, elevation of skin flaps and excision of a 10 inch diameter circle of deep fascia.[7] Following three Hunterian Lectures,[8] he published a book on breast cancer;[7] it included an appendix "On lymphatic permeation as a factor in the dissemination of melanotic sarcoma, with a note on operative treatment" which described the autopsy of a woman with disseminated malignant melanoma. The same single case was described in his Hunterian Lectures on melanotic growths.[9] Initially his principles of surgery for such growths included a skin incision at "a safe and practicable distance".[7] He was later more specific,[9] advising "a circular incision ... through the skin round the tumour ... as a rule about an inch from the edge of the tumour ... just deep enough to expose the subcutaneous fat ... The skin, with a thin attached layer of subcutaneous fat, is now to be separated from the deeper structures for about two inches in all directions round the skin incision." The tumour, with its margin of skin, deep fat and fascia, and part of the underlying muscle, was then to be excised. In 1935 he advised similar margins together with the excision of deep fascia and lymphatics to the nearest lymph glands, all to be excised in continuity.[10]

Excision of the primary tumour in continuity with the regional lymph nodes was advocated by others such as Pack in the USA,[11] although Pack concluded after 1190 cases that it could not be definitely stated what margin of normal skin around a malignant melanoma is necessary.[12] In 1934, margins of at least 3 cm were advocated.[13] Who first thought of 5 cm margins is not clear. Raven (London)[14] advised a skin incision at least 5 cm from the tumour edge, elevation of skin flaps and excision of deep fascia at least 10 cm from the tumour edge. Wright *et al.* (Glasgow)[15] wanted a rational basis for treatment and advised a 5 cm margin of skin down to and including a wider area of deep fascia. Conway (New York, USA)[16] recommended wide excision with, for example, a 9 cm diameter incision around a 1 cm diameter melanoma. In Bodenham's unit in Bristol, 5 cm margins were used from 1947[17] and by 1962 margins up to 15 cm on the trunk were in use.[18]

And so evolved the principle of wide excision for cutaneous malignant melanomas, with the added dogma of 5 cm margins. This principle was supported by dermatologists,[13,19] radiotherapists[13,20] and pathologists[21] as well as surgeons.

Pathology

From the 19th century, attempts have been made to base the extent of surgery on pathology. A "contamination" area[22] or a "field change"[23] of melanocytes around malignant melanomas have been suggested. Increased melanocyte density 5 cm from the edge of 7 of 12 primary malignant melanomas studied by Wong[24] have been used by others to justify 5 cm margins. However, Wong did not consider the increased numbers of melanocytes signified malignant change and postulated similar numbers in the unexcised skin. Three patterns of melanocyte density were found adjacent to 85 tumours by Cochran;[23] a similar incidence to the surrounding skin, a symmetrical increased incidence and an asymmetrical increased incidence. Cases with a similar incidence had more blood borne metastases and a trend to worse survival. Curiously, it was argued that this supported the need for wide excision.

Increased melanocyte numbers and mild atypia around malignant melanomas are now attributed to chronic sun exposure.[25]

More recently, microsatellites of malignant melanoma in the reticular dermis and fat separate from the main tumour have been described.[26] Microsatellites increase in frequency with increasing tumour thickness.[27] They are more common in patients with occult regional node metastases.[28] With melanomas more than 1.5 mm thick, microsatellites are associated with decreased survival.[26] With melanomas 3 mm or more thick, microsatellites are associated with increased local recurrences.[27] Microsatellites found in an excision biopsy of such 3 mm or more thick melanomas might justify wider excision margins, at least to reduce local occurrences, but there is no clinical evidence to support this.

The value of measuring maximum tumour thickness of melanomas is now well known. After early comments on the different prognosis of thin and thick melanomas,[29] several schemes for staging depth of invasion were devised[18,30,31] culminating in that of Clark and colleagues.[32] In 1970, Breslow introduced the concept of maximum tumour thickness[33] and noted in a series of 98 patients that there was no recurrent or metastatic disease after 5 years in those with a lesion less than 5 mm in diameter, less than 0.76 mm thick or less than 6.01 mm^2 in maximal cross-sectional area. Although there are classifications combining tumour thickness with Clark's levels,[34] most studies have used tumour thickness as the criterion for local tumour spread.

Survival

Many retrospective and prospective studies have shown that increasing tumour thickness is related to decreasing survival, for example:

8 year survival (598 patients, prospective study)[35]

< 0.85 mm	99 ± 1%
0.85–1.69 mm	93 ± 2%
1.70–3.6 mm	69 ± 5%
> 3.6 mm	38 ± 6%

5 year survival (1,661 patients, prospective study)[1]

	Female	*Male*
0.1–1.49 mm	95.4%	84.9%
1.5–3.49 mm	77.1%	61.8%
> 3.50 mm	52.9%	38%

Within such arbitrarily selected thickness groups there is also a trend for decreasing survival with increasing thickness, for example 85% (1.51–2.00 mm) to 71% (2.51–3.00 mm).[36] Even so, melanomas less than 0.76 mm thick can be fatal[37] and long term survival is possible after excision of very thick melanomas.[38] Overall, considering the two-dimensional assessment of tumour thickness and possible intra- and inter-observer error[39], it is impressive how well tumour thickness does correlate with survival.

While acknowledging the difficulties of comparing results,[40] what is striking about the results of past radical surgery with wide excision is not how good the results were but how bad they were: for example, 9.7%,[14] 28%,[41] 40% (but 24.8% disease-free)[42] five year survivals. Such figures suggest that thick melanomas were being treated. Pack[43] recorded five year definitive cure rates of 21.4% before 1946 and 37.7% up to January 1951; he suggested that the improvement could be due to earlier diagnosis as well as to "more adequate surgery".

There is no clear correlation between survival and excision margins. In the past, melanomas of the trunk were noted to have a worse prognosis than melanomas of the limbs.[17] This was probably because the trunk melanomas were thicker. One prospective study of stage I, 0.76–1.69 mm thick, Clark level IV melanomas, with a 3–5 year follow up, recorded 11 out of 12 patients who died had tumours in the upper Back, posterior Arm, posterior Neck and posterior Scalp (BANS regions).[44] The poor prognosis of these patients was probably related to the relative depth of invasion of their tumours, not the BANS sites, since some thin but Clark level IV melanomas have a poor prognosis.[45,46] Moreover, other studies have not found that BANS sites have a worse prognosis.[37,45,46,47] However, although tumour thickness is the most important prognostic factor in predicting survival, an analysis of 8500 patients[48] showed that anatomical location also correlates with survival; arm → leg → trunk → head and neck = best → worst prognosis. Nevertheless, there is no evidence to suggest excision margins should be wider on the trunk than on the limbs in order to improve survival of patients with melanoma of the trunk.

As implied by 37% of the plastic surgeons surveyed, for tumours less than 0.76 mm thick wide excision margins are unnecessary[49] and present results suggest that a 2–3 mm margin excision biopsy is sufficient.[50] In the World Health Organization (WHO) Melanoma Group's prospective, randomised study of stage I primary cutaneous malignant melanomas, 2 mm thick or less, disease-free and overall survival (mean follow-up: 90 months) were similar for 1 cm or 3 cm skin margins.[51,52] (It should be noted that beyond the 1 or 3 cm skin margins an additional 1–2 cm margin of subcutaneous fat down to muscle fascia had to be taken but no reason for this was given.) A retrospective WHO review showed no correlation between survival and excision margins of thicker melanomas.[53] A review of melanomas thicker than 2 mm did show survival was worse with margins less than 2 cm, while margins of more than 3 cm did not improve survival;[54] however, this was a small retrospective analysis of only 20 cases. Overall, making excision margins wider does not improve the chances of survival.

For many years it was recommended that excision should be deep to include the deep fascia. There was no clinical evidence to justify this and not much evidence to compare patients with and without excision of deep fascia.[22] One retrospective study, with no tumour thickness figures and with historical controls, showed no significant difference in survival or local recurrence for patients with or without excision of deep fascia.[55] Apart from ensuring adequate excision if a melanoma is close to the deep fascia, excision of deep fascia, once considered mandatory, has quietly ceased to be a routine procedure.

Local recurrences

One reason Halsted developed his radical surgery for breast cancer was to reduce unpleasant local recurrences.[56] Radiotherapy after complete local excision of breast cancer appears more to reduce local recurrences than to improve survival but is still considered worthwhile.[57] Similarly if wider excision can at least reduce local recurrences of melanoma it is reasonable to consider it.

The first problem is to decide what is a "local recurrence". In many studies local recurrence is not

defined. Some distinguish between a local recurrence with an epidermal *in-situ* component and a local metastasis without such an *in-situ* component.[27] For some, local "recurrences" are recurrences within or contiguous with the excision scar or graft.[58] For some, local "metastases" can be in the scar or skin graft, at the edge of the scar/graft, and in transit.[59] Others suggest local "recurrences" are along the scar or in an area of 1 cm or less radius from the scar,[51] while for others local "metastases" are within 5 cm from the perimeter of the primary scar or skin graft.[60]

Local recurrences, variously defined, usually indicate a poor prognosis.[18,61] In one series, median survival time after local recurrence was from 6.1 years (limbs) to 3 years (head and neck) and 2.1 years (trunk).[61] However, local recurrence after complete local excision of either breast cancer or malignant melanoma is probably an indicator not a cause of such a poor prognosis.[57,61] While survival rates decrease, local recurrence rates increase with increasing melanoma thickness; reported local recurrence rates range from about 0–2% for tumours less than 1 mm thick to about 10% for tumours 4 mm or more thick.[58,59,61] Even if they do not improve survival, wide excision margins are reasonable if they reduce local recurrences. How wide is wide excision and does it reduce local recurrence?

62 cases, with melanomas less than 0.76 mm thick and excision margins from 0.1 to 5.5 cm (1 cm or less in 20 cases), were disease free with no local recurrence for five or more years.[49] Similarly no local recurrences have been reported in a series of melanomas less than 0.76 mm, Clark's level II or III, excised with 2–3 mm margins.[50]

In the WHO prospective trial of 1 or 3 cm margins (plus additional fat), it was reported in 1991 that none of 356 patients with melanomas 1 mm or less thick had local recurrences within the 1 cm radius area around the scar or graft.[51] Of the 245 patients with tumours 1.01–2 mm thick, four (1.6%) had local recurrences as the first site of relapse. Their tumour thicknesses, reported in 1988 as 1.0–1.93 mm,[62] were reported in 1991 as 1.1 mm (2 cases) and 1.9 mm (2 cases). All four had 1 cm skin margins (plus additional fat). In 1992 five patients in the narrow margin group and one patient in the wide margin group of this trial were reported to have had a local recurrence as the first relapse.[52] When interpreting these figures it is important to note that the local recurrence rates were low and in contrast 21 patients with 1 cm skin margins and 24 patients with 3 cm skin margins had regional lymph node metastases as the first site of relapse (1991 report[51]).

For melanomas more than 2 mm thick, the WHO retrospective study[53] suggested that local recurrence rates are more related to tumour thickness than to excision margins; a later analysis showed an increased risk of local recurrence with margins 2 cm or less for stage I and stage II melanomas more than 2 cm thick.[63] In another retrospective review, margins 1 cm or less were followed by more local recurrences than 2–3 cm margins for thick tumours (4 mm or more), while 2–3 cm margins were as effective as 4 cm margins.[58] 5 cm margins are no guarantee against local recurrence; in 638 cases with 5 cm margins reviewed retrospectively even tumours less than 0.99 mm thick had 2% "local metastases" and 5–6 mm thick tumours had 14% "local metastases".[59]

Guidelines

The British and Irish plastic surgeons selected a range of excision margins, usually related to tumour thickness. A comparable survey of 614 hospitals in the USA in 1981 also showed a range of excision margins in use; about 61% of surgeons used a margin of 3 cm or more, while about 22% used margins of 1 cm or less.[64] However there was no clear correlation of the margins with either tumour thickness or the level of invasion.

Published guidelines from Europe, Australia and the USA generally give 3 cm as the maximum margin, although some suggest 2 or 2.5 cm.[65,66] While some who used a 5 cm maximum in the past[50,67] now use a 3 cm margin,[67,68] a few still advocate 5 cm margins.[69,70] Most vary excision margins with tumour thickness, generally 1 cm for less than 1 mm thick melanomas and 3 cm for more than 2 mm thick melanomas, with 1.5 to 3 cm for 1–2 mm thick melanomas.[71] Using the tumour thickness groups of Day *et al.*,[35] Fisher advised "no more than" 1 cm margins for melanomas less than 1.69 mm thick; 2 cm for 1.70–3.6 mm; and 3 cm for melanomas more than 3.6 mm thick, or a histologically nodular melanoma, or a melanoma on a BANS site.[72]

Bagley *et al.* followed on from Breslow's observations and linked excision margins to tumour diameter.[73] As Breslow noted, tumour thickness is a more useful measurement than tumour diameter and few (only one of the British and Irish surgeons) use Bagley's system.

Conclusions

Ideas about malignant melanoma surgery are changing. Incisional biopsies, once considered dangerous, have been shown not to affect prognosis if followed by complete tumour excision[74] (although such biopsies obviously do not allow full histological assessment). Excision of deep fascia, once considered essential, is now rarely done. Excision of clinically negative regional lymph nodes, once considered mandatory, is now energetically debated.[71] Taking a skin graft from a limb from which a malignant melanoma has been excised, once considered poor practice, is now acceptable.[75]

Ideas about excision margins are changing. At present each surgeon has to make a choice from the available, often retrospective and limited evidence.[76] Just as breast cancer treatment has been radically changed by scientific trials, so greater understanding of the practical value of excision margins for malignant melanoma will come from the prospective, randomised trials now in progress.

Acknowledgements

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