sciendo
10.2478/AMB-2025-0050

REVIEW

PERSONALIZED NEW (ONE STEP) SURGERY OPTIONS FOR CUTANEOUS MELANOMA PATIENTS: FACTS AND CONTROVERSIES

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Abstract. *The differences in standardized and personalized surgical treatment of cutaneous melanomas lies in the number of surgical interventions performed, each of the mentioned methodologies relying on different basic criteria. The standard model of clinical management is always performed within two surgical sessions, whereas the personalized one-step approach creates the prerequisites for a more sparing single surgical manipulation, providing a number of advantages for patients. The choice of one approach over the other relies both on the patient's characteristics and the professional view of the clinician, tailored largely to the patients' wishes. Because guidelines are recommended but not mandatory, heterogeneous surgical approaches in practice are a good solution, an opportunity for optimization, and a hope for more optimal postoperative outcomes concerning overall survival and the development of recurrences. This article analyzes the positive aspects of personalized single-stage melanoma surgery, comparing it with standard recommendations for surgical treatment of melanomas according to AJCC/EJC and ASCO. Personalized single-stage melanoma surgery achieves the same endpoints as the AJCC/EJC and ASCO criteria for surgical treatment of cutaneous melanomas, but the latter is achievable within two surgical sessions.*

Key words: *melanoma surgery, AJCC, ASCO, EJC, One step melanoma surgery, OSMS*

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Received: *23 September 2024;* ***Accepted:*** *07 October 2024*

CURRENT SURGICAL TREATMENT OF MELANOMA: OPPORTUNITIES FOR FUTURE CHANGES?

The surgical treatment of melanoma has been the subject of considerable debate in recent decades. It could be divided into standard surgical treatment, according to AJCC and EJC recommendations (Table1/Table 2) [1, 2] and personalized surgical treatment based on distinct criteria such as: clinical or dermatoscopic findings and preoperative (clinical, landmark, echographic) determination of tumor thickness (Table 3) [3, 4].

The choice between these two options should always be logically justified and determined mainly by the experience of the dermatologist and the additional diagnostic equipment available in the respective dermatological unit. The patient should fill in a written informed consent concerning the choice of one over the other "mode of clinical management". Guideline

recommendations are generally of an advisory but not mandatory nature. These "recommended regimens" largely protect the clinician from decisions made and tailored to them (guidelines), even in the presence of melanoma progression or lethality [1, 2].

Table 1. Surgical margin recommendations for primary cutaneous melanoma modificated from AJCC, Swetter et al., 2019 [1]

Tumor thickness (Breslow)	Surgical margin*
In situ	0.5-1 cm† always 2 surgical sessions
≤ 1.0 mm	1 cm/always 2 surgical sessions
> 1.0 to 2.0 mm	1-2 cm/always 2 surgical sessions
> 2.0 mm	2 cm/always 2 surgical sessions (if necessary)

*Recommended surgical excision margins are clinically measured from the edge of the lesion or prior biopsy at the time of surgery; they are not histologic margins as measured by the pathologist. Margins may be modified for functional considerations or anatomic location.
†Margins larger than 0.5 cm may be necessary for melanoma in situ, lentigo maligna type.

Table 2. Modificated from EJC recommendations (C. Garbe et al., 2022), [2]

Breslow thickness	Recommended surgical margins/ EJC
Melanoma in situ	0.1-0.3 cm primary excision/ excisional biopsy, followed by secondary excision in order to achieve **total surgical margin of 0.5 cm** in all directions
< 2 mm	0.1-0.3 cm primary excision/ excisional biopsy, followed by secondary excision in order to achieve **total surgical margin of 1 cm** in all directions
> 2 mm	0.1-0.3 cm primary excision/ excisional biopsy, followed by secondary excision in order to achieve **total surgical margin of 2 cm** in all directions

Table 3. Personalized One step Melanoma surgery (OSMS) recommendations (Tchernev et al.) [3-4, 6-7], updated version

Breslow thickness	Recommended surgical margins
Melanoma in situ	1.0 cm (clinical/dermatoscopic evaluation obligate/if possibility for echographical examination – from benefit/ when possible – confocal microscopy additionally)
< 1 mm	1.0 cm (clinical/dermatoscopic evaluation obligate/if possibility for echographical examination – from benefit/ confocal microscopy additionally)
1.01- 2.0 mm / Class A	2.0 cm (with SLNB), (Mandatory: clinical/ dermatoscopic evaluation, echographic tumour thickness measurement preoperatively/when possible – confocal microscopy additionally)
2-4 mm/Class B	2.0 cm (with SLNB), (Mandatory: clinical/ dermatoscopic evaluation, echographic tumour thickness measurement preoperatively/when possible-confocal microscopy additionally)
> 4 mm	2.0 cm complete surgical margin or less with / without SLNB to be discussed on tumour board. Mandatory: clinical/ dermatoscopic evaluation, echographic tumour thickness measurement preoperatively/when possible-confocal microscopy additionally)

However, guidelines do not explain the lack of progression with the application of innovative personalized approaches [3, 4]. And it is here, and in these differences in postoperative outcomes regarding survival or recurrence (achieved or based on the personalized surgical approaches), that the reason for the halting or lack of tumor/melanoma progression should be sought [1-4].

PRIMARY RESECTION MARGINS AND MELANOMA-STANDARD APPROACH

The standard treatment of melanoma requires the initial removal of the primary lesion with a surgical margin of safety of no more than 0.1-0.3 cm [2] or 0.1-0.5 cm [1], with the subsequent second surgical procedure determined by the already established postoperative Breslow tumor thickness [1, 2]. In practice, this treatment is always two-stage and consists of two dermatosurgical procedures: 1) primary excision (Fig. 1a) and 2) re-excision with an additional field of surgical safety, combined or not with the conduct of a so-called draining lymph node [1, 2].

The cumulative resection margins according to the AJCC, achieved within 2 surgical intervention sessions, could be defined according to international recommendations as the following: 1 cm for melanomas with tumor thickness up to 1 mm (Fig. 1a-c); 1-2 cm for melanomas with thickness up to 2 mm; 2 cm for tumors with thickness over 2 mm [1] (Fig. 2a-2b).

Resection margins for melanoma in situ and lentigo maligna vary between 0.5-1 cm, also within 2 surgical sessions [1].

Similar but "slightly stricter" are the EJC recommendations for surgical treatment of melanomas: 5 mm for melanoma in situ, 1 cm for melanomas with tumor thickness less than 2 mm, and 2 cm for melanomas with thickness greater than 2 mm. Wider resection margins should not be recommended [2].

CONTROVERSE OR HOT SPOTS WHEN APPLYING WIDER RESECTION MARGINS

Despite the generally accepted international recommendations for the surgical treatment of cutaneous melanomas, there is also literature evidence in the form of systematic review and meta-analysis that is indicative of the following: that there is evidence that a narrow surgical margin (1-2 cm) may lead to a worse outcome than a wide surgical margin (3, 4 or 5 cm) [5]. The same article is being cited by the EJC guideline [2], pointing at the fact that melanoma-specific survival is worse when narrower surgical margins (1-3 cm) compared to wider surgical margins (3-5 cm for example) are applied [5]. The significance

Fig 1. A: Melanocytic lesion suggestive clinically and dermatoscopically for a thin cutaneous melanoma; **B:** Thin cutaneous melanoma with pretibial localization treated surgically using a near surgical resection margin of 1-2 mm according to AJCC/EJC/ASCO recommendations. Intraoperative finding. First surgical session; **C:** Melanoma with tumor thickness less than 1 mm and no histological evidence of ulceration, treated surgically with a near field of surgical security. Immediate postoperative finding after the first surgical session

Fig. 2a, 2b: Tumor-forming lesion with elastic consistency, hemorrhagic, developed/based on melanocytic nevus, subsequently treated with near field surgical margin of security and with evidence of nodular melanoma with a greater tumor thickness than 10 mm

of the latter statement has yet to be elucidated, as more prospective studies are needed in the future.

FUTURE HORIZONS FOR A NEW FORM OF SURGICAL TREATMENT IN CUTANEOUS MELANOMAS-STARTING POINTS

Future surgical treatment options for melanomas including options that are more sparing (in terms of procedure/number of procedures) and reliable in relation to the melanoma-specific overall survival are to be developed [6, 7]. In practice, the goal should be aimed at a more relaxed current , optimal surgical approach with a view to more reliable future outcomes.

DRAINING LYMPH NODE – WHEN AND WHY?

For primary tumors between 0.8-1.00 mm thick or those less than 0.8 mm with ulceration, draining lymph node is recommended as a surgical procedure [1, 2, 8]. For melanomas with tumor thickness less than 0.8 mm/no ulceration, it should not be recommended [1, 2, 8].

In the absence of ulceration, but other risk criteria such as young patient, high mitotic activity, lymphovascular invasion, and positive resection lines (for tumor cells) are present, sentinel lymph node dissection could be offered as an option [1, 2, 8]. in patients at pT1a stage [1, 8].

Performing a procedure for detection and removal of a draining lymph node could be considered advisable for melanomas with tumor thickness equal to or reciprocal to 1 mm or those with tumor thickness less than 0.8 mm, for which additional histologic aggravating factors are present [2].

With evidence of micrometastases in the draining lymph nodes, performing a complete lymph node dissection is not advisable [2]. In patients with microscopic SLN metastases, two of the largest international studies showed no difference in survival between CLND and observation of patients [9, 10]. In

the DeCOG study, 68% of patients in the observation arm and 65% in the CLND arm were free of distant metastases after five years of follow-up [10].

According to data from the so-called MSLT-II trial (Funded by the National Cancer Institute and others; MSLT-II ClinicalTrials.gov number, NCT00297895), immediate dissection of locoregional lymph nodes increases the rate of regional disease control and provides potentially important prognostic information for treating patients, but does not increase melanoma-specific survival in patients (with melanoma and sentinel node metastases) [11].

As cited in the literature [9-12], the performance of locoregional lymph node dissection in patients with micrometastases in the sentinel lymph node should not be regarded as recommended or strongly indicated [2, 12]. According to the American Society for Surgical Oncology guidelines from 2018, the indications for performing a sentinel lymph node dissection remain very limited [12], namely: a sentinel lymph node dissection could be recommended in 1) cutaneous melanomas that are T1b (0. 8 to 1.0 mm Breslow thickness or < 0.8 mm Breslow thickness with ulceration), but after discussion with the patient about the risks and positives, and in 2) cutaneous melanomas with tumor thickness greater than 4 mm. For cutaneous melanomas between 1 and 4 mm thick, sentinel biopsy remains strongly recommended [12].

A number of single clinical observations in which patients with cutaneous melanomas were treated according to innovative proposals for the treatment of cutaneous melanoma (OSMS/one step melanoma surgery for example) remain controversial, with no subsequent progression afterwards [3, 7, 13]. Interestingly, all of them showed a lack of disease progression [13], and this occurs precisely when AJCC/EJC recommendations for surgical treatment of melanomas are not followed [1, 2].

Wide initial surgical excision with a surgical margin of safety of 2 cm in melanomas about 2 mm thick, for example, without conducting a sentinel lymph node, is also frequently associated with the absence of recurrence in certain patient groups [13, 14]. While in other observed patients strictly following the AJCC/EJC recommendations [1, 2], progression and fatal outcome were observed [14].

It is on the basis of such important clinical observations that the idea of creating innovative guidelines for personalized treatment of melanomas within 1 single surgical session (OSMS/One Step Melanoma Surgery) arose [3, 6, 7]. They could find application in patients with thin melanomas and melanomas in situ, in addition to those with medium and thick melanomas [15, 16].

The idea of a one-step approach of surgical treatment of cutaneous melanomas has been internationally accepted by dermatosurgical schools throughout Europe.

The French school of dermatology remains the undisputed leader in the establishment of this one-step approach to the surgical treatment of melanomas [17], with preoperative measurement of tumor thickness using a 20 MHz resolution head-mounted ultrasonograph proving to be virtually sufficient for accurate assessment of tumor thickness in 82% of patients with cutaneous melanomas [17].

Moreover, reciprocity between preoperatively/sonographically measured tumor thickness (with a 15 MHz probe head) and subsequently histologically established tumor thickness in thin melanomas has been described in the literature by a Spanish author [18].

Again, a Spanish dermatologist [19], similar to other international publications [20], has questioned the therapeutic relevance of sentinel biopsy in patients with cutaneous melanomas. There is a strong (hypo) thesis that sentinel biopsy seems to be useful only in the staging of melanoma patients, i.e. lacking the so-called ″combined diagnostic/therapeutic effect″ [19, 20]. This is probably one of the reasons why ASCO/American Society for Surgical Oncology does not proclaim its mandatory performance in melanomas below 1 mm and above 4 mm, but as subject to debate with the patients themselves [12].

The Spanish team also developed the thesis that the lack of need for lymph node dissection (as a therapeutic option) could be a reason to perform one-step melanoma surgery [19].

Again, according to the same authors, dermatoscopy and preoperative ultrasonographic findings would be able to ″severely tip the scales″ in favor of a one-step model of clinical management in melanoma surgery, especially when patients prefer a less invasive ″diagnostic/therapeutic″ or purely diagnostic option [19, 20].

The Bulgarian contribution to the personalized surgical (one-step) treatment of melanomas is due to the creation of a complex algorithm for the preoperative evaluation of a given pigmented lesion with a view to its one-step removal in the context of OSMS/one step melanoma surgery based on: 1) clinical findings, 2) dermatoscopic findings and 3) ultrasonographic findings/confocal microscopy (if possible) (Table 3) [21].

The choice of surgical field for the treatment of melanomas in OSMS is based on fundamentally different baseline criteria rather than the postoperative

established tumor thickness [21] (Table 3). The final surgical resection field achieved in OSMS/one step melanoma surgery is entirely consistent with the cumulative resection fields that are achieved when following the AJCC/ EJC recommendations [15] but within two surgical sessions [1, 2].

This single surgical session in the context of one-step melanoma surgery (OSMS) takes into account both 1) the AJCC/ EJC recommendations for specific resection margins according to internationally ″known to everyone″ guidelines [1, 2], as well as 2) their recommendations for lymph node conduction plus 3) the individual patient‘s wish (wish concerning a more sparing or more radical one-step surgical intervention) (Table 3) [15, 21].

The recommendations of the generally recognized surgical societies and associations themselves are rather liberal in their recommendations regarding melanoma therapy, and this is what creates the conditions for the promotion of new ideas and approaches such as one-step melanoma surgery. In practice, according to ASCO recommendations, only medium-thick melanomas (1.00-4.00 mm) are subject to the ″strong indication″ for detection and removal of the so-called draining lymph node [12]. And the total resection margin, according to the AJCC/EJC recommendations, ranges between 1 and 2 cm [1, 2].

The following dilemmas remain: 1) Are there any obstacles to the staging of the one-stage model for surgical treatment of thin melanomas: with a total resection field of 1 cm, but also for thick melanomas: with a total resection field of 2 cm (within one surgical session)?

And 2) is there a barrier that would discourage the complex surgical treatment of medium-thick melanomas (tumor thickness 1.00-4.00 mm, morphologically established on the basis of clinical, dermatoscopic and/or ultrasonographic preoperative evaluation) to consist in the simultaneous removal of the primarius and the draining lymph node?

Conflict of Interest Statement: *The authors declare no conflicts of interest related to this work.*

Funding: *The authors did not receive any financial support from any organization for this research work.*

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