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## New Trends in Cutaneous Melanoma Surgery

Jacopo Scala<sup>1</sup>, Aleksandra Vojvodic<sup>2</sup>, Petar Vojvodic<sup>3</sup>, Tatjana Vlasovic-Jovicevic<sup>3</sup>, Zorica Peric-Hajzler<sup>4</sup>, Dusica Matovic<sup>4</sup>, Sanja Dimitrijevic<sup>5</sup>, Jovana Vojvodic<sup>3</sup>, Goran Sijan<sup>6</sup>, Nenad Stepic<sup>7</sup>, Uwe Wollina<sup>8</sup>, Michael Tirant<sup>1</sup>, Nguyen Van Thuong<sup>9</sup>, Massimo Fioranelli<sup>10\*</sup>, Torello Lotti<sup>11</sup>

<sup>1</sup>University G. Marconi, Rome, Italy; <sup>2</sup>Department of Dermatology and Venereology, Military Medical Academy, Belgrade, Serbia; <sup>3</sup>Clinic for Psychiatric Disorders "Dr. Laza Lazarevic", Belgrade, Serbia; <sup>4</sup>Military Medical Academy, Belgrade, Serbia; <sup>5</sup>Department of Gynecology, Military Medical Academy, Belgrade, Serbia; <sup>6</sup>Clinic for Plastic Surgery and Burns, Military Medical Academy, Belgrade, Serbia; <sup>7</sup>Chief of Clinic for Plastic Surgery and Burns, Military Medical Academy, Belgrade, Serbia; <sup>8</sup>Department of Dermatology and Allergology, Städtisches Klinikum Dresden, Dresden, Germany; <sup>9</sup>Vietnam National Hospital of Dermatology and Venereology, Hanoi, Vietnam; <sup>10</sup>Department of Nuclear Physics, Sub-nuclear and Radiation, G. Marconi University, Rome, Italy; <sup>11</sup>Department of Dermatology, University of G. Marconi, Rome, Italy

### Abstract

The main surgical treatment for melanoma consists in wide surgical excision of the primary lesion and the sentinel node but in recent times management of melanoma is rapidly evolving with the introduction of new systemic therapies, like BRAF inhibitors, MEK inhibitors and antibodies anti-PD-1 that show good results in controlling even advanced stages of the disease. This review aims to present data for the optimal surgical management of patients with malignant melanoma.

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**\*Correspondence:** Massimo Fioranelli. Department of Nuclear Physics, Sub-nuclear and Radiation, G. Marconi University, Rome, Italy. E-mail: [massimo.fioranelli@gmail.com](mailto:massimo.fioranelli@gmail.com)

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## Introduction

Surgical removal was the mainstay of therapy in early melanoma, and historically there has been only a marginal role for surgery in managing patients with regional or distant metastases, even if some Authors suggested that metastasectomy could improve survival in stage IV melanoma if compared to non-surgical therapy [1]. In present times management of melanoma is rapidly evolving with the introduction of new systemic therapies, like BRAF inhibitors, MEK inhibitors and antibodies anti-PD-1 that show good results in controlling even advanced

stages of the disease [2], [3]. It's easy to forecast that new treatment algorithms will be developed to utilise all new drugs, but there's still much to debate about the role of surgical treatment in combination with the most recent discoveries in biological therapies.

## Management of primary lesion

The main surgical treatment for invasive malignant melanoma consists of complete surgical

excision and removal and examination of the first draining lymph node possibly affected by metastatic disease. Surgical margins to be removed are based on the maximal melanoma Breslow thickness of the melanoma [4]. Usually, all suspicious pigmented lesions should be removed with a clear clinical margin of least 2mm but not exceeding 5 mm not to damage the lymphatic drainage to be assessed by a later SLNB. Usually, the excision should go through the skin and subcutaneous tissue and stop to the fascia/periosteum/ perichondrium, only for suspected melanoma in situ surgical excision could stop at the superficial subcutaneous tissue [5]. Partial biopsies are to be avoided mainly to not under stage the lesion.

For melanoma in situ, according to a late expert consensus statement, an excision margin of 5 mm is considered sufficient to have a radical treatment. However, more recent data recommends excisions up to 9 mm to obtain clear histological margins [5], [6]. There is no indication to widen surgical margins if histological free margins have already been achieved.

For invasive melanomas with less than 1 mm thickness, a 1 cm surgical margin is considered a sufficient margin according to three randomised control trials (RCTs) [7], [8], [9], [10]. For intermediate and thick melanomas, many RCTs comparing narrow (1 cm) and wide excision (up to 5 cm) have been published. A recent meta-analysis found no difference in overall survival (HR 1.09; 95% CI 0.98 – 1.22;  $p = 0.1$ ) between patients treated with narrow or wide excision, nor in loco-regional recurrence (HR 1.10; 95% CI 0.96 – 1.26;  $p = 0.2$ ). However, in a subgroup analysis including four trials only, reporting on melanoma-specific survival wide excision was favored HR 1.17 (95% CI 1.03 – 1.34;  $p = 0.02$ ) [11], [12], [13].

Surgical excision can in almost every case be performed under local anaesthesia and local flaps should be performed to cover after wide excision only if the surgeon is confident that histologically free margins have been achieved.

## Sentinel lymph node biopsy and Complete lymph node dissection

Sentinel node biopsy (SLNB) is the surgical procedure where the sentinel lymph node is identified and then removed using a radioactive tracer or a biological pigment and could be made even in small hospitals not needing advanced technological resources. SLNB became popular in the 1990s because it was supposed that with lymph node metastases a block dissection of their nodes would have improved survival but the two most important long-term prospective randomised trials of SLNB (MSLT1 and MSLT2) showed that SLNB and

subsequent completion lymphadenectomy does not improve 10-year melanoma-specific survival [14], [15] nevertheless the treatment is still offered because it can detect occult disease and improve staging and prognosis [16]. The complication rate associated with SLNB is approximately 10% [14]. SNB has a false negative rate of approximately 10 – 20% [17] A positive SN has been found in approximately 5% of melanomas  $\leq 1$  mm thickness and in approximately 14 – 20% in intermediate-thickness melanomas [18], [19], [20] thus SLNB may be considered for patients with melanomas with a thickness from 0.8 to 1.0 mm or less than 0.8 mm thickness with ulceration, classified as T1b lesion, or for intermediate-thickness melanomas as reported in AJCC 8th edition [18]. For melanomas  $> 4$  mm thickness, SLNB could be proposed only for staging because for potential disease control its therapeutic benefit is perhaps more limited. In certain cases of very thick melanomas, imaging could archive an appropriate staging, and thus surgery could be avoided [21].

Complete lymph node dissection (CLND) was considered a cornerstone in the management of melanoma patients with a positive SLNB both to prevent the melanoma from spreading and to attain accurate staging [22]. Two RCTs have been published: DeCOG and MSLT-2 comparing the CLND with observation after positive SNB. Even if DeCOG was stopped prematurely and the study finished underpowered, it didn't find any differences in survival. The MSLT-2 meta-analysis compared immediate CLND with observation / delayed CLND and also showed no survival benefit from CLND. However, melanoma-specific survival was higher after immediate CLND compared with delayed CLND in patients with nodal metastasis (HR = 0.63, 95% CI = 0.35 – 0.74,  $p = 0.0004$ ) [15], [23].

Review studies reported a complication rate after CLND variable between 24%-37% and a worse quality of life after CLND compared with SNB only so appears to be important to avoid completion lymphadenectomy to prevent unnecessary complications [15], [24], [25].

## Conclusions

Survival for patients with invasive melanoma still depends mostly on early diagnosis and surgery maintain his undisputed therapeutic role in small and intermediate lesions.

The role of surgery remains to be determined with advanced lesions and lymph nodal metastasis because is unclear if there is a benefit with node dissection compared with observation in combination with adjuvant treatment such as BRAF / MEK inhibition or PD-1 inhibition.

Treatment for invasive melanoma confirms to be a complex and multidisciplinary task that require oncologists and surgeons cooperation to guide treatment decisions.

## References

- Wasif N, Bagaria SP, Ray P, Morton DL. Does metastasectomy improve survival in patients with Stage IV melanoma? A cancer registry analysis of outcomes. *J Surg Oncol*. 2011; 104(2):111-115. <https://doi.org/10.1002/jso.21903> PMID:21381040  
PMCID:PMC3199373
- Tchernev G, Chokoeva AA, Wollina U, Lotti T. De novo congenital malignant melanoma: whats new in diagnosis and treatment? *Dermatol Ther*. 2016; 29(1):13-4. <https://doi.org/10.1111/dth.12279> PMID:26279460
- França K, Lotti T. Stress coping strategies for the optimal treatment of melanoma. *Dermatol Ther*. 2017; 30(1). <https://doi.org/10.1111/dth.12421> PMID:27592687
- Breslow A. Thickness, cross-sectional areas and depth of invasion in the prognosis of cutaneous melanoma. *Ann Surg*. 1970; 172(5): 902-8. <https://doi.org/10.1097/00000658-197011000-00017> PMID:5477666 PMCID:PMC1397358
- Kunishige JH, Brodland DG, Zitelli JA. Margins for standard excision of melanoma in situ. *J Am Acad Dermatol*. 2013; 69(1):164. <https://doi.org/10.1016/j.jaad.2013.01.040> PMID:23768291
- Sober AJ. Diagnosis and management of early melanoma: a con-ensus view. *Semin Surg Oncol*. 1993; 9(3):194-7.
- Managing melanoma. National Institute for Health and Care Excellence, 2018.
- Malignant Melanom. Swedish National Treatment Guidelines. Regional Cancer Centrum, 2017.
- Work G, Swetter SM, Tsao H, Bichakjian CK, Curiel-Lewandrowski C, Elder DE, et al. Guidelines of care for the management of primary cutaneous melanoma. *J Am Acad Dermatol*. 2018.
- Sladden MJ, Balch C, Barzilay DA, Berg DA, Freiman A, Handiside T, et al. Surgical excision margins for primary cutaneous melanoma. *Cochrane Database Syst Rev*. 2009; (4):CD004835. <https://doi.org/10.1002/14651858.CD004835.pub2> PMID:19821334
- Wheatley K, Wilson JS, Gaunt P, Marsden JR. Surgical excision margins in primary cutaneous melanoma: a meta-analysis and Bayesian probability evaluation. *Cancer Treat Rev*. 2016; 42:73- 81. <https://doi.org/10.1016/j.ctrv.2015.10.013> PMID:26563920
- Balch CM, Soong SJ, Smith T, Ross MI, Urist MM, Karakousis CP, et al. Long-term results of a prospective surgical trial comparing 2 cm vs. 4 cm excision margins for 740 patients with 1-4 mm melanomas. *Ann Surg Oncol*. 2001; 8(2):101-8. <https://doi.org/10.1007/s10434-001-0101-x> PMID:11258773
- Hayes AJ, Maynard L, Coombes G, Newton-Bishop J, Timmons M, Cook M, et al. Wide versus narrow excision margins for high- risk, primary cutaneous melanomas: long-term follow-up of surviv- al in a randomized trial. *Lancet Oncol*. 2016; 17(2):184-92. [https://doi.org/10.1016/S1470-2045\(15\)00482-9](https://doi.org/10.1016/S1470-2045(15)00482-9)
- Morton DL, Thompson JF, Cochran AJ, et al. Final trial report of sentinel-node biopsy versus nodal observation in melanoma. *N Engl J Med*. 2014; 370(7):599-609. <https://doi.org/10.1056/NEJMoa1310460> PMID:24521106  
PMCID:PMC4058881
- Faries MB, Thompson JF, Cochran AJ, et al. Completion dissection or observation for sentinel-node metastasis in melanoma. *N Engl J Med*. 2017; 376(23):2211-22. <https://doi.org/10.1056/NEJMoa1613210> PMID:28591523  
PMCID:PMC5548388
- Leiter U, Stadler R, Mauch C, Hohenberger W, Brockmeyer N, Berking C, German Dermatologic Cooperative Oncology Group (DeCOG), et al. Complete lymph node dissection versus no dissection in patients with sentinel lymph node biopsy positive melanoma (DeCOG-SLT): a multi-centre, randomised, phase 3 trial. *Lancet Oncol*. 2016; 17(6):757e67. [https://doi.org/10.1016/S1470-2045\(16\)00141-8](https://doi.org/10.1016/S1470-2045(16)00141-8)
- Lee DY, Huynh KT, Teng A, Lau BJ, Vitug S, Lee JH, et al. Predictors and survival impact of false-negative sentinel nodes in melanoma. *Ann Surg Oncol*. 2016; 23(3):1012-8. <https://doi.org/10.1245/s10434-015-4912-6> PMID:26586498  
PMCID:PMC4984404
- Wong SL, Faries MB, Kennedy EB, Agarwala SS, Akhurst TJ, Ariyan C, et al. Sentinel lymph node biopsy and management of regional lymph nodes in melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2018; 36(4):399-413. <https://doi.org/10.1200/JCO.2017.75.7724> PMID:29232171
- Bartlett EK, Peters MG, Blair A, Etherington MS, Elder DE, Xu XG, et al. Identification of patients with intermediate thickness melanoma at low risk for sentinel lymph node positivity. *Ann Surg Oncol*. 2016; 23(1):250-6. <https://doi.org/10.1245/s10434-015-4766-y> PMID:26215202 PMCID:PMC4697873
- Han D, Zager JS, Shyr Y, Chen H, Berry LD, Iyengar S, et al. Clinicopathologic predictors of sentinel lymph node metastasis in thin melanoma. *J Clin Oncol*. 2013; 31(35):4387-93. <https://doi.org/10.1200/JCO.2013.50.1114> PMID:24190111
- Forschner A, Olthof SC, Guckel B, Martus P, Vach W, la Fougere C, et al. Impact of (18)F-FDG-PET/CT on surgical management in patients with advanced melanoma: an outcome based analysis. *Eur J Nucl Med Mol Imaging*. 2017; 44(8):1312-8. <https://doi.org/10.1007/s00259-017-3674-8> PMID:28315947
- Fioranelli M, Roccia MG, Pastore C, Aracena CJ, Lotti T. Completion dissection or observation for sentinel-node metastasis in melanoma. *Dermatol Ther*. 2017; 30(6). <https://doi.org/10.1111/dth.12544> PMID:28836714
- Delgado AF, Delgado AF. Complete lymph node dissection in melanoma: a systematic review and meta-analysis. *Anticancer Res*. 2017; 37(12):6825-9. <https://doi.org/10.21873/anticancer.12143>
- Moody JA, Botham SJ, Dahill KE, Wallace DL, Hardwicke JT. Complications following completion lymphadenectomy versus therapeutic lymphadenectomy for melanoma - a systematic review of the literature. *Eur J Surg Oncol*. 2017; 43(9):1760-7. <https://doi.org/10.1016/j.ejso.2017.07.003> PMID:28756017
- de Vries M, Hoekstra HJ, Hoekstra-Weebers JE. Quality of life after axillary or groin sentinel lymph node biopsy, with or without completion lymph node dissection, in patients with cutaneous melanoma. *Ann Surg Oncol*. 2009; 16(10):2840-7. <https://doi.org/10.1245/s10434-009-0602-6> PMID:19639366  
PMCID:PMC2749179