***Open Access Maced J Med Sci* electronic publication ahead of print,**
published on June 11, 2017 as https://doi.org/10.3889/oamjms.2017.068

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences.
https://doi.org/10.3889/oamjms.2017.068
eISSN: 1857-9655
Expert Opinion

New Safety Margins for Melanoma Surgery: Nice Possibility for Drinking of "Just That Cup of Coffee"?

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Citation: Tchernev G, Chokoeva AA. New Safety Margins for Melanoma Surgery: Nice Possibility for Drinking of "Just That Cup of Coffee"? Open Access Maced J Med Sci. https://doi.org/10.3889/oamjms.2017.068

Keywords: melanoma; staging; surgical field margins; prognosis; variety.

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Received: 13-Apr-2017; **Revised:** 29-Apr-2017; **Accepted:** 14-May-2017; **Online first:** 11-Jun-2017

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Funding: This research did not receive any financial support.

Competing Interests: The authors have declared that no competing interests exist.

Abstract

BACKGROUND: The American Joint Committee on Cancer (AJCC's) skin melanoma surgical treatment recommendations from 2011 are characterised by a prima facie "freedom of choice" regarding how extensive should be the excisions for melanomas with tumour thickness up to 2 mm and melanoma in situ. It is unclear why the recommended surgical security margins vary between 0.5 and 1 cm for melanoma in situ, whereas for melanomas with a tumour thickness of up to 1.99 mm, the range of variation is also between 1 and 2 cm, without specifying when the surgical field should be broader and, narrower, accordingly. This "uncertainty or lack of intent" of the guilders often leads to the same surgical approach to melanomas at different stages, or to a different approach in cases of melanomas at the same stage, in contrast. Therefore, this should be defined as wrong, logically.

CASE PRESENTATION: We present 3 patients with cutaneous melanomas, treated with similar fields of surgical security. Current issues, generated within the framework of melanoma's surgery guided by the recommendations of the AJCC are also discussed. A new surgical approach in patients with melanoma is recommended, discussed for the first time in world literature. We hypothesize that the introduction of a certain recommendations for a 2 cm surgical field in all directions during the initial excision, combined with the parallel performance of a sentinel lymph node biopsy, will lead in fact to several important advantages: 1) avoiding of the secondary excision in at least 70% - 90% of the patients (depending on the tumor thickness), 2) minimizing the risk of lymphatic effusion change and misinterpretation of the sentinel lymph node biopsy's results in patients with secondary excision; 3) optimization of the surgical team's work; 4) minimizing the possibility of unprepared/uninformed personnel to take part in decisions for treating a specific disease such as skin melanoma, 4) facilitating the appropriate patients' group selection at the appropriate stage when involving them in different studies, leading to equal leveling of the initial positions;

CONCLUSION: Whether the proposed approach will be subjected to a detailed discussion of AJCC's expert's remains currently unclear.

Introduction

Guideline as a term, resulting in choice of treatment regimen (variety of decisions)

A guideline is a statement by which to determine a course of action [1]. A guideline aims to streamline particular processes according to a set routine or sound practice [1]. By definition, following a guideline is never mandatory [1]. Guidelines are not binding and are not enforced [1].

Because of the highlighted possibility of variability in interpretation of the guidelines, as a rule, they generate some problems, which require special attention, regarding the improvement of patients' overall survival rate. Guidelines should be able to specify their recommendations, based on the new proposals if they are well-explained and justified.

Guidelines are either followed or ignored (as they are recommended, not mandatory). In the case of their complete ignorance, however, the explanations of the "sinners" or the non-observers should be at least somehow logically explained. Hence the questions - why should I follow the guidelines, when there are only recommendations? Can no one obligate me? The included possibility for variable interpretation of the recommended parameters raises some problems in determining the appropriate surgical safety margins, in practice. Whether this permissible variety is logically based and widely acceptable remains unclear.

Guidelines' disadvantages

The provided possibility of variations in the

interpretations of the guidelines, weaken the weight of the surgeon's decisions who try to follow them, although they are not obliged, above all protect from the "mistakes" that may follow. Despite that the freedom of the clinician's decisions should be provided, in cases of oncological diseases, it should also be: 1) requiring of more responsibility for the clinician 2) obligating him for strictly following the recommendations for a certain periods of time (at least until the next update of the guidelines) 3) requiring a maximal support and reasonably useful for the patient, by reducing the number of excisions, for example. About these important points, it could be concluded that American Joint Committee on Cancer (AJCC's) proposed melanoma's treating guidelines from 2011 needs a serious rethinking, more frequent renewal, and rigorous follow-up [2].

Critical comments on certain recommendations in the guideline of melanoma's management

The treatment of cutaneous melanoma consists in the initial performance of an excision biopsy or excision with a surgical field of 0.3-0.5 cm in all directions. The further decision for re-excision with additional safety margins should be considered based on the result from histopathological micro-staging and tumour thickness. If the initially measured tumour thickness is between 1 and 2 mm, the surgical field should be extended by 1 cm in all directions, no matter the size of the initially obtained surgical field.

While there is no precise opinion on this issue in the AJCC's recommendations, most of the dermatologic surgeons measure an additional 1 cm field. However, it is unclear why and when AJCC's guideline recommends the size of a surgical field between 1 and 2 cm in the same tumour thickness, namely 1-2 mm (2)? Unlike German guidelines strictly requiring of a certain field of 1 cm in all directions, the American ones allow variations?

On another hand, the performance of a sentinel lymph node biopsy, followed by a re-excision of the primary tumor (with the adequate area of surgical safety that should not exceed 2 cm) is obligatory when there are other two constellations, namely: 1) a tumor thickness above 1 mm; or 2) a tumor thickness below 1 mm with additional risk factors such as: age under 40, vessel or lymphatic invasion, increased number of mitosis, presence of ulceration.

The categorical opinion of some experts in the field, for example, is that the performance of sentinel lymph node biopsy and secondary excision should not exceed 2 weeks after the primary excision, no matter of the applied surgical technique. This is difficult to be performed in practice (at the national level at least), regarding the fact that obtaining of the primitive histology requires at least 10 days up to a month. Furthermore, even after obtaining the result, patients want to consult themselves with other specialists who take additional time. The oncologic committee's decision should be also awaited before the patient is referred to the oncology centre for a further sentinel lymph node biopsy and secondary excision.

If the primary care unit is not oncological, the delay in these procedures is inevitable or very likely (focus on the national level), which makes the reaching of the 2-weeks deadline impossible. Therefore, the loss of this precious time should be optimised and precise on a national level at least.

Another significant problem is the histological evaluation, which is unsatisfactory and needs optimisation in the majority of cases (national level). The following points should be improved; 1) Better control of the tumor thickness measurement after the primary excision, and 2) Refinement of the histopathological reports, obtaining accurate data on the number of mitosis, the presence of ulceration, the absence or presence of vessels or lymphatic invasion, the satellites, state of the resection lines, etc., which is of a great importance for melanomas with tumor thickness less than 1 mm and 0.8 mm, as these are considered to be additional important criteria for performance of a sentinel lymph nodes biopsy.

The lack of this data does not assist the clinician in selecting patients for further sentinel lymph node removal, neither assist in improving the survival rate.

The question why according to AJCC's 2011 recommendations, the melanoma in situ is removed with a field of surgical safety equivalent to the former, applied to aggressive thin melanomas below 1 mm, which also requires additional removal of the sentinel lymph node, remains open? The lack of logic or data on the issue should not bind the experts' hands for adequate solutions at clearly defined micro-staging.

After thorough interpretation of the AJCC's melanoma guidelines from 2011 [2], it should be concluded that the surgical treatment of this type of tumour is unclear explained and supported and requires serious criticism. The following controversial claims are defined in the guideline [2]:

"The primary treatment modality for cutaneous melanoma is surgical excision [2]. After the diagnosis ***of melanoma has been histologically confirmed and the primary lesion has been adequately micro stage,*** *a wider and frequently deeper excision is needed to ensure complete removal [2]. It is recognized that melanoma cells may extend subclinically several millimeters to several centimetres beyond the clinically visible lesion [1].* ***Recommended surgical margins are based partly on prospective randomised controlled trials and partly on consensus opinion when no prospective data exist [2]."***

"It is essential to recognise that surgical margin recommendations are based on studies in which margins were clinically measured around the primary tumour and ***may not correlate*** *with histologically measured tumor-free margins. "*

It turns out that regardless of clinically measured distances of 2 cm from the tumour tissue, in practice, the histological distances would be significantly smaller? Doesn't it require: 1) an aggressive initial approach? Doesn't this comment in practice include the very decision for significant change of the recommendations? What should we do if the fields of the clinically measured and histologically proven fields of safety surgical distance differ significantly? And 2) the logic requires immediate re-exercises, whether primary or secondary excision. This is the only way that patients could be identified and treated according to the guidelines, and then their data could also be used in future studies. Going further, why are we always accurate in completing and enrolling melanoma patients into a variety of expensive surveys instead of focusing on clearing out the starting positions that are likely to generate future problems?

The question why the clinically measured distances in healthy tissue or the so-called resection margins should not be equivalent to histologically measured remains also open [2]:

*"Treatment of choice for primary cutaneous melanoma of any thickness is surgical excision with histologically negative margins. Surgical margins for invasive melanoma should be a****t least 1 cm and no more than 2 cm clinically measured around primary tumour;*** *clinically measured surgical margins do not need to correlate with histologically negative margins.* ***For melanoma in situ, wide excision with 0.5- to 1.0-cm margins is recommended;*** *lentigo malignant histologic subtype may require [0.5-cm margins to achieve histologically negative margins, because of characteristically broad subclinical extension."*

Even "more unstable" are the following experts' recommendations [2]:

"Based on available evidence and consensus opinion, the expert work group recommends that primary melanomas 1.01 to 2.0 mm in thickness are widely excised with ***1- to 2-cm*** *margins [1]. However, clear evidence* ***is not available,*** *and final surgical margins* ***may vary based on tumour location and functional or cosmetic considerations*** *[3-7]."*

Unfortunately, in the AJCC's „variable surgical margins" recommendations, there is no indication of who defines the concepts as "unpleasant or unacceptable for a tumour location surgery," and who makes the final decision whether the "reduced" surgical safety fields are aesthetically pleasing? Does the patient or therapist decide this? In practice, the recommendations leave an absolute freedom in the dermatologist's decisions regarding the choice of the resection field [2], while he still has the right to be influenced by the patient's opinion and desire. What surgical safety field should be applied in cases of tumours over 1 mm thickness- 1 or 2cm? Why should we operate melanomas with a thickness of 1, 01 mm and those with 4 mm and more mm in the same way then (2 cm in all directions) [2]? The same situation is obtained with tumours with 1.9 mm thickness and melanoma in situ (1 cm in all directions)? Even the histopathological type of the melanoma is not included into consideration [2]? Therefore, this histological "substaging" could be at least a "gateway" for the guideline formating. The question remains open: Are the decisions of the US experts' group always the right ones?

The psychological and physical pressure of the patients during these interventions is also significant, and furthermore some of them could not be follow up for one or another reason (loss of trust for example due to 1) reading the recommendations on the internet and/or 2) lack of clear explanation for one or another field of surgical safety, 3) progression of the disease in cases of patients with the same tumor thickness, but different field of surgical safety). So would it be advisable or at least logically determined wider resection fields, firmly stated according to guidelines? Don't we need guidelines that provide more accurate recommendations instead of a variation of choice [2]? 10 years ago, experts considered that the initial tumours should be excited with a small field of surgical safety, without plastic reconstruction, as it could alternate the lymph flow. It is now considered that whether or not plastic reconstruction for initial defect closure is performed, the performance of sentinel lymph node biopsy followed by re-excision is necessary for 2 weeks of the period. Perceptions of melanoma's surgery are quite dynamic. The question remains: isn't it better to perform: 1) ultrasound of the tumour thickness providing the decision for a single surgical intervention, namely: simultaneous removal of the sentinel lymph node and a primary tumour? Therefore the lymph flow would be at least modified and patients would get the maximum profits. The experts' response in these cases would probably be: "We should be humans, we can not apply invasive methodologies and approaches in the uncertainty of what are the tumour thickness?" Our answer would be: "What were you up to now?"

It would be logical to ask the following: Is the prognosis of patients with melanoma in situ and those with a tumour thickness of 1.99 mm uniform? AJCC's guidelines indirectly support the absurd thesis of inadequate melanoma treatment at different stages [2]. Isn't that also the clue, regarding the controversial results of the various studies around the world concerning the survival and recurrence rate in general?

The freedom of the surgeon's interpretation of

the AJCC's recommended resection fields [2] is embarrassing and at the very least needs rethinking! The critical insight into internationally established criteria should not be inevitably crossed out, but should give rise to a more in-depth analysis of the actual criteria and their rethinking and pre-definition, instead! "Variability" is unlikely to lead to progress and success in oncology. We should remember that scientific results are unthinkable without strict initial data or, in other words, without unification of the starting positions of the cases. The experts' comments themselves show that radicality in the surgical approach is the key point to overall melanoma survival [2]. Billions could not be invested in future projects on targeted therapy, for example, including patients in different stages who treated with equal approaches or patients in the same stage but treated with different approaches in contrast.

Referring to the AJCC's recommendations, the following statements are also interesting although not considered in creating their recommendations, even supported by serious studies [2]:

"In melanomas thicker than 2.0 mm, one study found that narrow excision with 1-cm margin was associated with a somewhat higher combined local, regional, and nodal recurrence rate than wider excision with 3-cm margin [4, 8]."

Why the following is also not taken into consideration?

"Several other studies have found slightly higher local recurrence rates for melanomas thicker than 1 mm treated with narrow excision with a 1-cm margin versus a wider excision with a 3-cm margin [9]."

Why are wider surgical fields not recommended then? Why does the classification give scope for flexibility and variability? Who is interested in data not being standardised, resulting in full chaos?

And then the experts wonder how within the different double-blind, multicentric, randomised etc. studies, expectations and results do not match or there is no explanation for them? Or perhaps the "era of melanoma surgical therapy variability" occurred? Freedom of treatment with different resection fields, although data supporting both of the theories are available? The term "clear positioning" should be more seriously implicated in the AJCC's guidelines.

It is unclear how data are presented in AJCC from 2011 to nowadays which are not taken into account, despite the categorical need for wider excision fields?

Resection margins - a need for revolutionary thinking

In addition to the needed standardisation of the material and methods for scientific studies, reconsideration of the resection fields should also be done for another purpose: reducing the number of secondary excisions. Secondary excisions are generally at least as severe as the initially performed and more burdensome for the patients themselves. Often, dermatologists face unpleasant patient's question:

"Doctor, why the initial surgical field was not safety and wide enough?

Another interesting case, reported by patient:

"I saw on the web that the melanomas should be removed with a surgical excision margins ranging between 1 and 2 cm, recommended by the experts. My tumour is 1.5 mm in thickness, the patient's next to me is also 1.5 mm, but he had a bigger scar and had been operated with a 2 cm security field, while I had been operated with a 1 cm surgical security margin…Why? And furthermore, why is he alive and healthy second year after the surgery, while I'm full of metastases? "

Are these questions answered in the AJCC'S guidelines?

These dilemmas provoke not only the patients to think about the humanity of the established guidelines and the choice of a therapeutic approach. Isn't it better to operate with a larger initial field of surgical safety, namely one of a minimum of 2 cm, with parallel performances of a sentinel lymph node removal? Which, in turn, would be beneficial to patients' physical and psychical relieve, not only in early-stage melanomas but also in more advanced stages. Clearing of these "inaccuracies" would certainly result in profiling of all of the involved patients and physicians. There will be no future if we do not understand the past. And when it is unclear, the best thing would be to try to clear it out by clearing the mistakes. Our past will always reflect on our present and future.

This way will inevitably optimise the work of the qualified staff with the lack of secondary excision. In practice, in tumours with a tumour thickness of more than 1 mm and above 2 mm, the optimal choice would always be a solid field of surgical safety of 2 cm while the draining lymph node is removed during the same session!

On the other hand, we should also think about the fact that the patients themselves do not always agree with a secondary excision and do not appear regularly for second excisions and sentinel lymph node evaluation. Logically, the more aggressive initial pattern of behaviour in these patients should also yield better long-term outcomes, regarding the overall survival. Even for a limited number of patients, this approach would be beneficial.

From the philosophically point of view, we would ask the question: "Isn't it better to drink your coffee on the square, even with more severe scars or

even lymphedema (?), instead of the lack of this opportunity at all?"

Unfortunately, the guidelines and the possibility of their variability determine at the current moment the possibility for NOT drinking of "just that cup of coffee"!

Another serious question is whether pre-operative measurement of tumour thickness ultrasonographically should be mandatory implicated? Why ultrasound measurement of tumour thickness is recommended, but does not belong to the "gold standard" or mandatory recommendations for clinical behaviour in the AJCC guidelines? These are the issues that should impose important solutions and narrower limits of variability within the AJCC recommendations.

Presentation of Cases

We present 3 interesting cases of patients with cutaneous melanoma, where the tumor thickness was not measured by ultrasound prior the initial excisions, but the diagnosis was made clinically and dermoscopic ally, while the choice of a surgical field is based on multiple factors, not at least, considered with patient’s opinions (Fig. 1-3). The clinically suggested tumour thickness was confirmed histologically in both of the cases, post surgically.

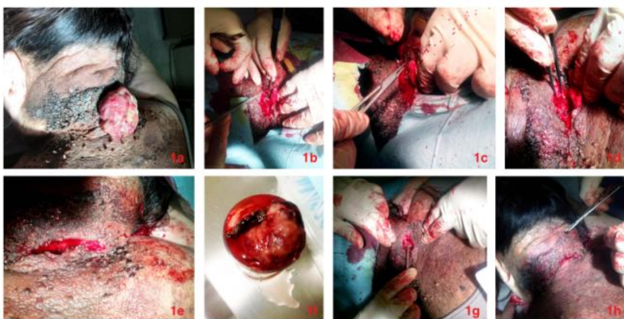

Figure 1: 1a) Female patient with achromatic melanoma in the neck area occurred on a giant congenital melanocytic nevus. A local excision has been done and the histopathology confirmed the diagnosis of malignant melanoma with a maximum thickness of16 mm. Additional re-excision with 1.5 cm safety margins has been planned. Immunohistopathological stainings with HMB-45 (diffusely positive) and S-100 have shown a strong positive reaction. The patient denied sentinel lymph node biopsy. Tumour was staged as IIB (T4aN0M0). 1b, 1c, 1d, 1e, 1g, 1h) Surgical removal of the tumour, coagulation with single subcutaneous stitches and electrocoagulation. Adaptation of the wound’s edges. 1f) Achromatic melanoma, measuring approximately the size of a fist. Postoperative finding

If the newly recommended by us surgical approach were performed initially, the second excisions would have been avoided, and the performance of the sentinel lymph node removal has to be applied in one and the same session.

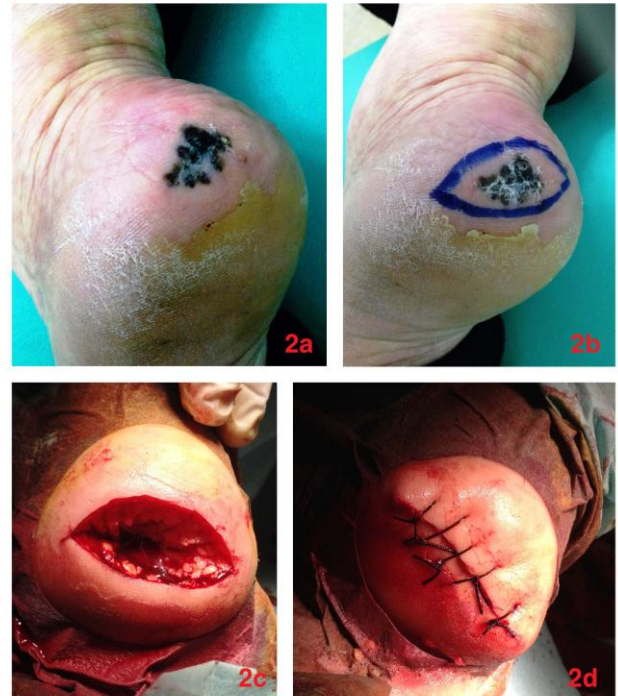

Figure 2: 2a) Patient with heel melanoma and delayed re-excision, developing distant metastasis. 2b) Determination of the surgical field. 2c) Intraoperative findings. 2d) Postoperative findings.

Disadvantages: The patient comes 2 months later for excision with sentinel lymph node evaluation performance.

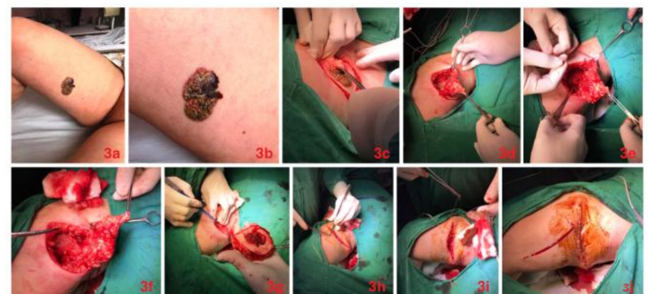

Figure 3: 3a, 3b) A patient with a verrucous keratotic form of melanoma located on the inside of the upper limb. 3c, 3e, 3f, 3g) Gradual detoxification of the tumour tissue in depth, accompanied by ligation of vena safe manga. 3d) Postoperative findings; 3x, 3i, 3j) Staging suture and drainage placement

The disadvantages of the AJCC standards methodology lies in two main facts: 1) Need for re-excision after tumour thicknesses measurement; 2) Conducting of the drainage lymph node removal, as well as the possibility of it being falsely negative due to the extensive excision. 3) After an ultrasound examination of the loco regional lymph nodes and the exclusion of the possible metastases spread, the patient did not appear for re-examination and sentinel lymph node removal.

Disadvantages of the applied approach: The

patient did not appear either for re-excision or the evaluation of the sentinel lymph node. The question whether a wider initial excision combined with sentinel lymph node removal would be more benefit in this type of patients remains open. Certainly, these criteria, namely the AJCC's, create prerequisites for generating different problems.

Recommendations and advantages of the proposed by us method or clinical approach: Mandatory ultrasonographically measurement of tumour thickness and removal of the draining lymph node simultaneously with the single primary excision with at least 2 cm surgical safety field would be a wonderful solution for the benefit of the patients. Thus, neither the patient nor the therapist could act improperly.

Discussion

We present 3 patients with melanomas with a tumour thickness of 2 mm or more. The terms “variability” and “positioning” are discussed, concepts that need rethinking and strict follow-up, at least when it comes to patients with skin melanoma.

We highlight the essential need for stricter guidelines for surgical treatment of melanoma as a whole and in particular for AJCC's guideline refurbishment in future periods as the variability of current recommendations does not create optimal conditions for an initial surgical approach and could lead to poor prognosis in some patients. The surgical approach should be more radical about melanoma patients. The approach should be combined and may be shortened as some procedures when the draining lymph node is removed within one surgical session in parallel with the initial excision adjusted to the measured ultrasound tumour thickness.

The "freedom of action" in the surgical treatment of cutaneous melanoma, which is provided as a type of recommendation in the AJCC postulates, should be rethought and re-formulated for a more aggressive initial approach or choice of clinical behaviour (larger fields of surgical safety margins to be clearly defined). This freedom about the determination of the surgical margins is at least or somewhat confusing and misleading and does not answer the question:

Why do we treat melanomas in different stages, with significant differences in tumour thickness in the same way?

But this gives a very good, though rather probable or hypothetical answer to the question: *Why do patients at different stages have the same prognosis or why do patients with the same stages have different prognosis?*

Creating problems that we can solve is a well-known method of antiquity for governing the masses in obedience. Interesting, but also the tragic thing about creating these guidelines in medicine is that it creates unnecessary problems and dividing lines, questions with many unknowns, which at a later stage could not be solved, or at least resolved with a favourable outcome.

We would appeal to the AJCC 2011 melanoma's experts and creators of the guideline with a few key questions (as we will be very happy and flattered if the experts' group answers or comments on each point):

1) Why ultrasound measurement of tumour thickness is not a standard procedure in patients with melanoma suspicion? Wouldn't this optimise the subsequent therapeutic approach?

2) Why is the primary excision not combined with the parallel removal of the sentinel lymph node? Moreover, sentinel lymph node removal is already recommended for tumours with a thickness less than 1 mm or even less than 0,75mm, according to some literary data?

3) Why aggressive melanomas with a thickness less than 1 mm should be removed with a surgical field of 1 cm- namely, the resection zone equivalent to melanoma in situ (a choice of 0.5 to 1 cm)? And for tumours less than 1 mm in thickness, with additional aggressive criteria, a sentinel lymph node is removed? Is the prognosis for these two conditions identical? And why is the approach, let's say, at least identical?

4) Don't you think that all these facts impose a "recent promulgation", "calling an experts' council / or an expert group” to optimise the melanoma's surgical approach?

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