



Melanoma and Sentinel Node: Which Course should be Taken?

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Article History

Received: 03.05.2024

Accepted: 11.06.2024

Published: 14.06.2024

Abstract: The sentinel lymph node is the first lymph node to drain the tumour territory. Sentinel lymph node biopsy was first introduced in the management of melanoma patients in 1992 by Morton *et al.*, Since then, its use has expanded to and become the standard of care in other cancer types. Lymphoscintigraphy is the standard technique for locating this node, and the surgical technique for removing it requires training. Anatomopathology uses standard histology and immunohistochemistry techniques. The aim of this examination is to look for micrometastases, which indicate lymph node invasion. If the sentinel lymph node is healthy, lymph node dissection is unnecessary.

Keywords: Sentinel lymph node, lymphoscintigraphy, melanoma.

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I. INTRODUCTION

Melanoma is the most serious skin tumor. The incidence has been increasing in the last two decades. Currently, its incidence in Morocco is estimated at 700 new cases per year with a sex ratio of 1.85 [1], this incidence is low despite the high solar exposure. The prognosis is correlated with the Breslow index (the maximum thickness of the tumor). However, melanoma has a lymphophilic potential responsible for lymph node metastases [2]. The first site invaded is generally the locoregional lymphatic drainage area. Dissemination can also be hematogenous, hence the development of distant metastases [3-5].

Surgical treatment is essential and must be early, appropriate and carcinological. This tumor is curable at the primary tumor stage but its prognosis is poor at the metastatic stage, despite the introduction of new medical treatments [6].

The sentinel lymph node technique is a surgical technique which allows the first relay of a lymph node chain to be sampled and analyzed as part of the spread assessment of certain cancers. The

absence of metastatic cells seems to be a reliable sign of the absence of invasion of other lymph nodes and allows the patient to avoid the morbidity of lymph node dissection. Lymph node dissection is therefore reserved for patients with one or more invaded lymph nodes [7].

II. HISTORY OF THE SENTINEL NODE CONCEPT

The sentinel lymph node was first described by Gould *et al.*, In 1960 in a patient suffering from parotid gland cancer and was clinically implemented on a large scale by Cabanas in penile cancer [8]. The sentinel lymph node radio localization technique was co-founded by James C. Alex, MD, FACS and David N. Krag MD (University of Vermont Medical Center) considered being the pioneers of this method for the use of cutaneous melanoma, breast cancer, head and neck cancer and Merkel cell carcinoma. Confirmatory trials followed shortly thereafter [9].

In 1992, Morton established the sentinel lymph node theory by injecting patent blue into the dermis surrounding cutaneous melanoma and observing lymphatic drainage during the procedure. The sentinel lymph node is identified

Citation: S. Charboub, H. El Kamch, A. Balkoula, A. Mesbahi, J. Hafidi, N. Gharib, A. Abbassi, S. El Mazouz (2024). Melanoma and Sentinel Node: Which Course should be Taken? *Glob Acad J Med Sci*; Vol-6, Iss-3 pp- 133-139.

intraoperatively by its blue color (Fig 1). In his pilot study, he systematically combined lymph node dissection. The absence of metastasis during histological examination, at the level of the first node

staining blue, virtually excluded the risk of metastasis to other nodes. Morton introduced the notion of prognostic staging for patients with stages I and II melanoma [3].

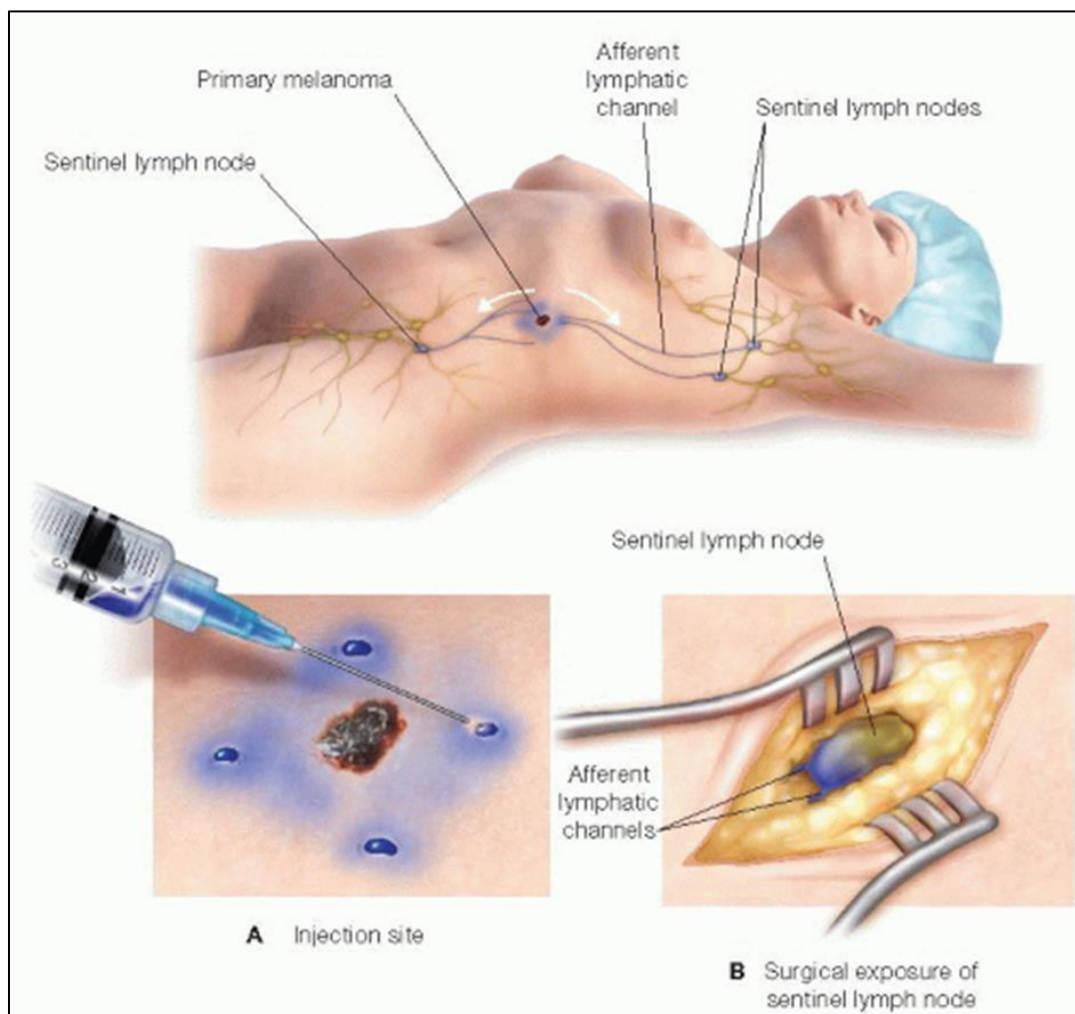


Fig 1: Injection of ^{99m}Tc for identification of sentinel node with identification by gamma probe and subsequent removal of lymph nodes from nodal basin

The detection technique was later improved by Alex *et al.*, in 1993 by the use of lymphoscintigraphy with colloidal rhenium sulfide labeled with metastable technetium-99 (^{99m}Tc), associated with intraoperative detection using a gamma detection probe. The success rate of this procedure was 97%. It is now the reference technique [9]

The reliability of the technique was also studied by Carcoforo in 2002, who published a prospective series of 110 patients where the sentinel lymph node was removed in 98% of cases using a combined scintigraphy and methylene blue. Furthermore, he noted that the sentinel lymph node was only colored blue in 81% of cases [10].

These studies provide arguments in favor of the reliability and interest of lymphoscintigraphy. In 2003, Trost *et al.*, published a retrospective study describing the habits of French dermatology services, concerning the practice of sentinel lymph node testing in patients classified as stages I and II. 64% percent of the teams surveyed practiced the sentinel lymph node technique, while 36% of them offered surveillance. There were no geographical groupings [11]

III. INDICATION

The sentinel lymph node search and excision technique is performed during surgical revision of melanoma. Indeed, most often the diagnosis of melanoma is made following excision without margin of a suspicious skin lesion. A surgical revision must therefore be carried out, removing the excision scar,

with safety margins whose size depends on the thickness of the melanoma [12].

The primary objective of the technique being to know the lymph node status of an a priori localized disease, it will therefore not be indicated in the event of already known lymph node or extra-nodal metastatic invasion. As enlarged excision modifies regional lymphatic drainage, the sentinel lymph node technique must be performed during surgical revision [13] and not afterward. In addition to a poor general condition preventing any surgical treatment, relative contraindications are common to all imaging techniques using radioactive isotopes: pregnancy and breastfeeding.

The risk of lymph node invasion increases with the thickness of the melanoma, varying from 1% for lesions less than 0.75 mm to 35.5% for melanomas greater than 4 mm [14].

For “thin” melanomas, the procedure for searching for the sentinel lymph node is optional for both the American [15] and European [16] recommendations, included in the French guide [17]. In the event of lesions < 0.75 mm, the risk of lymph node invasion being 1%, the search for GS is not indicated.

For the intermediate situation (0.76 - 1 mm), the risk of lymph node dissemination is approximately 5%. Research and excision of the GS may then be proposed, despite the absence of undeniable scientific proof to support this practice. The presence of poor prognostic factors, such as tumor ulceration or a high mitotic index (stage T1b),

must on the other hand motivate recourse to the GS technique.

For melanomas of “intermediate” thickness (1 - 4 mm), the risk of lymph node invasion varies between 8 and 30%. International recommendations agree to indicate the carrying out of the procedure of search and excision of the GS in this situation. Note, however, that the French “Standard Option and Recommendations” of 2005 [11], prior to the international recommendations, only recommend carrying out the GS research procedure as an option in this indication. For “thick” melanomas (> 4 mm), the risk of lymph node metastasis is high, greater than 35%. Despite the lack of scientific data, here again international recommendations agree to indicate the GS technique, of course in the absence of clinical lymph node invasion or identified on imaging.

IV. STEPS IN EXERCISE OF THE SENTINEL NODE

• Preoperative lymphoscintigraphy

Its principle on the physiological transport towards the vessels and lymph nodes of small radioactive colloid particles injected into the interstitial tissue [18, 19]. The scintigraphy technique was standardized thanks to the collaboration of the EORTC (European Organization of Research and Treatment of Cancer) and the EANM (European Association of Nuclear Medicine). This must be carried out 4 to 24 hours before the surgical procedure [20]. Two hours before the start of the scintigraphic protocol, an analgesic ointment is applied to the injection site. Colloidal rhenium sulfide labeled with technetium 99m is injected intradermally at the four cardinal points of the melanoma or excision scar (Fig 2).



Fig 2: Intradermal injection of radioactive marker at the four cardinal points of excision site

The total injected activity is of the order of 60 MBq. The dose of irradiation delivered to the body during this examination is much lower than during a standard X-ray. The patient is then placed on the gamma camera examination table. The detectors are focused on the theoretical lymphatic drainage areas of melanoma.

The scintigraphic images are obtained with a double-headed wide-field rectangular gamma camera, equipped with a high-resolution low-energy parallel collimator.

Dynamic then static acquisitions are carried out immediately after intradermal injection of the nanocolloid, because the migration of the radio-colloids is very rapid and the sentinel lymph node is revealed almost immediately [21, 22].

- **Surgical Excision**

After placing the fields, using the gamma detection probe covered with sterile protection, the surgeon verifies that the maximum signal is in line with the preoperative marking (percutaneous reference count) and makes his skin incision. This must be oriented in such a way that it is compatible with the approach for a possible subsequent cure. The dissection is progressive and guided by the detection probe.

The most radioactive lymph node (in vivo count) is identified and then removed. The ex vivo radioactive count (number of counts per second) of the ganglion is recorded (Fig 3).

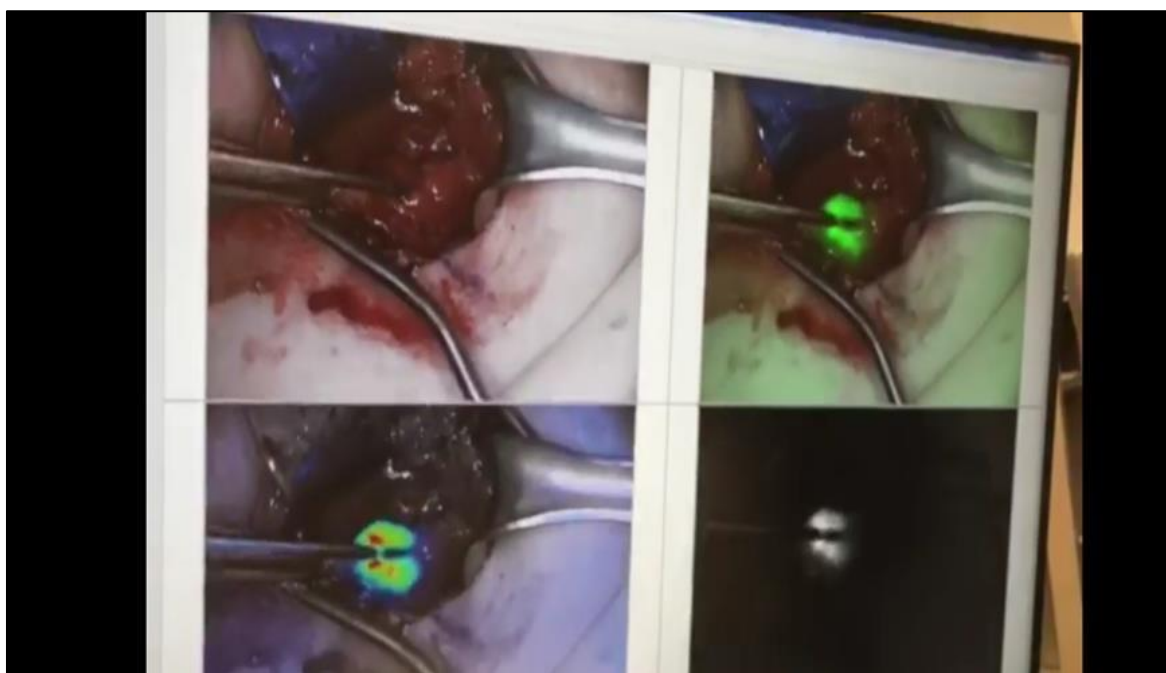


Fig 3: Visualization of lymph node with indocyanine green during dissection

The absence of significant radioactivity in the adenectomy site is verified. The residual activity should not exceed 10% of the activity of the sentinel lymph node [18]. The wound is then closed after careful hemostasis. Analysis of the data in the literature reveals that the surgeon must strive to collect a small number of lymph nodes to limit postoperative complications, without this strategy altering the diagnostic reliability of this technique. The combination of lymphoscintigraphy and the intraoperative use of the gamma detection probe

makes it possible to detect the sentinel lymph node in 96% (Figure 4).

It is not always easy to distinguish the sentinel lymph node from a satellite lymph node. The sentinel node is defined scintigraphically as the first hyperfixing focus detected at the level of the theoretical drainage area of the tumor. Other hyperfixing points can be detected downstream on the same drainage route. These are satellite nodes of the sentinel lymph node, considered hot nodes [8].



Figure 4: The combination of lymphoscintigraphy and the intraoperative use of the gamma detection

- **Histological study**

The operating documents are sent for anatomopathological analysis in order to obtain the result of the analysis of the sentinel lymph node(s) as quickly as possible. The analysis of the removed node is not carried out extemporaneously given the risk of loss of material and the lack of sensitivity of this technique [24, 25]. The aim of the pathological analysis is to identify micrometastases which indicate lymph node invasion.

V. DISCUSSION

The sentinel lymph node search technique is currently validated by isotopic method. Morbidity is low and there are very few false negatives during dissection checks [26-30]. The point is made on the existence of a learning curve [31, 32].

The detection rate of the sentinel lymph node is greater than 93%, although there are topographical difficulties in the cervico-facial region and more particularly the parotid region.

The search for the sentinel lymph node has challenged classical anatomy by highlighting atypical drainage pathways, particularly in cervico-facial and truncal locations [33, 34].

Sentinel lymph node involvement in melanoma is a major factor both in terms of recurrence-free survival and overall survival, independently of the thickness and ulceration of the primary tumor [35].

The risk of the sentinel node being positive reaches 50% for a Breslow index between 3.0 and 3.9 mm with pejorative factors (ulceration, high mitotic index, vascular invasion) [36].

The discovery of a positive sentinel node is followed by a dissection, the rate of additional positive nodes being less than 20%. Proof of the therapeutic benefit of such a strategy has not been demonstrated [37, 38]. Gershenwald was interested in the recurrences of patients (10%) with negative sentinel lymph nodes and in the interest of a new histological analysis a posteriori. Rereading the slides using standard histology and immunohistochemistry found that 80% of the nodes were positive, which highlights the need for good anatomopathological technique [39].

VI. CONCLUSION

The sentinel node technique allows lymph node staging of patients with melanoma, at the cost of low morbidity. The presence of lymph node invasion being a major prognostic element, European and American learned societies have introduced the practice of this technique, as standard or as an option, in the management of patients with stage T1b, T2, T3 melanoma or T4.

The procedure reduces morbidity and increases recurrence-free survival. The benefit in terms of specific survival is more uncertain, as is the benefit of complete lymph node dissection in cases of GS invasion.

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