Can SPET/CT Technique Improve the Sentinel Lymph Node Radio-Guided Research in Cutaneous Malignant Melanoma?

Artor Niccoli Asabella*, Valentina Lavelli, Cristina Ferrari, Nunzio Merenda, Francesca Iuele, Emilio Paolo Mossa, Valentina Loseto and Giuseppe Rubini

Nuclear Medicine Unit, University of Bari "Aldo Moro", Bari, Italy

Abstract: *Background:* the aim of the study is to define the role of SPET/CT in radio-guided sentinel lymph node surgery identification in cutaneous Malignant Melanoma (MM) and to assess if SPET/CT data can modify surgery time.

Materials and Methods: 96 patients with MM (58 men and 38 women, mean age of 44 years, range 14-71 years) were divided into two groups. 66 patients (group I) were submitted to sentinel node (SN) research by planar lymphoscintigraphy; 30 patients (group II) performed both planar and SPET/CT lymphoscintigraphy. SN surgery identification percentage, SN anatomical site identification and surgery times were evaluated in each group.

Results: Group II presented a percentage of SN surgery identification, both globally (96.5%) and in specific sites (axilla lymph nodes 94.5%; upon clavicle lymph nodes 100%), better than group I. Furthermore surgery time was shorter in the group II (10'-20').

Conclusions: SPET/CT allows a more accurate SN identification than planar lymphoscintigraphy, especially in axillar and upon-clavicular nodes and contributes to a correct staging of cutaneous MM. It can improve surgery success percentage and shortens surgery time, reducing also surgery team irradiation.

Keywords: Malignant melanoma, Sentinel node, Lymphoscintigraphy, Planar scintigraphy, SPECT/CT.

INTRODUCTION

Malignant Melanoma (MM) is the most frequent malignant cutaneous tumor. The incidence of melanoma varies from 3–5/100,000/year in Mediterranean countries to 12–25/100,000 in Nordic countries. Increased ultraviolet light exposure of a genetically predisposed population seems to be, at least in part, responsible for an ongoing increase in incidence with signs of stabilization of mortality over recent decades, except in elderly males [1, 2].

In the last years, incidence rates are rising worldwide with an important increase in many European countries, including the Southern and Eastern ones [3]. In 2008 the incidence of invasive cutaneous MM was globally of almost 200,000 new cases with estimated 46,000 deaths for this pathology [3].

Patients with a histopathologic diagnosis of MM are staged by the TNM system that is important to correctly assess treatment and prognosis [4, 5].

Preoperative lymphoscintigraphy and the subsequent radio-guided surgery is the most reliable methods for the SN detection, contributing to nodal staging by revealing lymphatic drainage patterns and the locations of single or multiple SN. The histological status of SN is considered to be the most important prognostic factor after biopsy of MM.

In this study we compared planar and SPET/CT lymphoscintigraphy in patients with cutaneous MM in radio-guided sentinel lymph node surgery identification, answering to the following questions: Can SPET/CT play a role in the SN research? Furthermore, can SPET/CT data modify surgery time?

MATERIALS AND METHODS

Patients' Population

Our study included 96 patients (58 men and 38 women) with mean age of 44 years (range 14 - 71 years) affected by MM. Patients' characteristics are reported in Figure **1**.

The most frequent MM sites in our population were trunk (47 patients) and legs (30 patients); head and neck were involved in 12 patients and arms in 7 patients.

Patients were divided into 2 groups. The group I, of 66 patients, was submitted to SN research only by planar lymphoscintigraphy; the group II, of 30 patients, was submitted to SN research by both planar lymphoscintigraphy and SPET/CT hybrid technique.

*Address correspondence to this author at the Piazza G. Cesare 11, 70124 Bari, Italy; Tel: +39 080 5592913; Fax: +39 080 5593250;
E-mail: artor.niccoliasabella@uniba.it

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In each group we evaluated surgery SN identification percentage, the SN anatomical site identification and the surgery time.

NR. TOTAL PATIENTS	96
male/female	58/38
AGE	
mean (SD)	44 (± 11.55)
range	14-71
AJCC STAGE	
I stage	56/96 (58%)
II stage	40/96 (42%)
CLARK INVASION	
I level	41/96 (43%)
II level	29/96 (30%)
III level	26/96 (27%)
IV and V level	0/96 (0%)
BRESLOW INVASION (mm)	
Range	0.4-3.1
ANATOMIC MM SITE	
Head and neck	12/96 (12.5%)
Trunk	47/96 (49%)
Arms	7/96 (7.25%)
Legs	30/96 (31.25%)

Figure 1: Patients' characteristics.

Fisher exact test for percentage comparison was used to calculate surgery SN identification percentage; T-student test for unpaired samples was performed to evaluate the surgery time. A p value <0.05 was considered statistically significant. The analyses were performed using MedCalc software version 14.12.0 (MedCalc Software bvba, Ostend, Belgium).

Technique

Planar lymphoscintigraphy (all patients): 80 MBq of 99mTc-Nanocolloid (Nanocoll©, GE Healthcare) were injected at the borders of the primary tumor site or around the scar. Scintigraphic images were acquired with Infinia Hawkeye (GE Healthcare Technologies, Milwaukee, WI). Soon after intradermal tracer injection a dynamic acquisition was made with 90 frames in 20", matrix 128 x 128, LEHR collimators, followed by a static acquisition of 300", matrix 256 x 256, LEHR collimators. A cutaneous marker was then applied at first hot spot of every draining path.

SPET/CT (only group II patients): SPET exam was performed with the following parameters: 360°, 60 frames x 30", 128 x 128 matrix, LEHR collimators. We used a low dose CT protocol (20mAs, 130Kv, 1.5 pitch, Slices 5mm) without contrast media.

Radio-guided intraoperatory SN research (all patients): a 15mm-LVR Gamma-Probe (Scinti-Probe MR100 Pol.Hi.Tech.) was passed slowly over the drainage path and cutaneous markers.

Surgery time was calculated from the beginning of the incision till the moment of the SN excision.

The radiation counts were measured on the excised SN and on the surgical field to ensure the complete removal of the radioactive lymph node.

RESULTS

The percentage of SN surgery identification was 92% in the group I and 96.5% in the group II respectively. The SN anatomical site identification percentage was 92% for neck lymph nodes and 100% for inguinal ones in both groups, while 90% for axilla lymph nodes in the group I versus 94.5% in the group II and 50% for upon-clavicle lymph nodes in the group I versus 100% in the group II. By using Fisher exact test for percentage comparison, the difference between the two groups was not statistically significant, neither for SN surgery identification in overall sites or in specific anatomical sites (Figure **2**).

The measured range of the SN surgery time was 10-38 minutes in the group I and 10-20 minutes in the group II (Figure **2**). By using T-student test for unpaired samples, the difference between the two groups was statistically significant (t= -2.485; p=0.015).

	GROUP I	**GROUP II**	***p* (<0.05)**
SN SURGERY IDENTIFICATION			
Overall sites	92%	96.5%	0.662
ANATOMICAL SITE SN IDENTIFICATION PERCENTAGES			
Inguinal lymph nodes	100%	100%	1
Neck lymph nodes	92%	92%	1
Axillar lymph nodes	90%	94.5%	1
Upon-clavicle lymph nodes	50%	100%	0.464
SURGERY TIME	10'-38'	10'-20'	**0.015**

Figure 2: Results in the two groups.

DISCUSSION

Regional lymph nodes are the most common initial localization of metastasis in cutaneous MM. SN is the

first lymph node involved by the direct lymphatic drainage of the tumor. The absence of metastatic involvement of this lymph node can almost definitively exclude the involvement of the remainder of the lymphatic chain, making radical lymphadenectomy unnecessary [6].

For this reason, the evaluation of lymph nodes involvement is essential in patients with MM and, in particular, selective SN biopsy results crucial [7].

Lymphoscintigraphy shows where lymph from the primary tumor site travels and is, therefore, an essential element of lymphatic mapping [4]. It can contribute to nodal staging by revealing lymphatic drainage patterns and the locations of single or multiple sentinel lymph nodes in one or more sites [8]. Selective SN biopsy allows also the identification of microscopic metastasis, providing more precise staging and more adequate treatment [9].

Moreover, the histological status of SN is the most important prognostic factor after biopsy of MM [4]. Multicenter studies demonstrated that recurrences and global survival are related to the state of the SN [6].

Lymphoscintigraphy is of particularly usefulness in regions like trunk or head and neck, in which SN drainage of melanoma can be variable [10].

While preoperative planar lymphoscintigraphy in melanoma patients has become a gold standard, the role of SPET/CT as part of the standard sentinel scintigraphy protocol has yet to be determined [11]. Our study focused on comparing planar lymphoscintigraphy and SPET/CT technique in patients with cutaneous MM, to define if there is a role for SPET/CT in radio-guided SN surgery identification and if it can modify surgery time.

SPET/CT was introduced in lymphatic mapping with the goal to show more SNs and to show them more clearly than conventional lymphoscintigraphy: the number and size of the nodes, but also the relationship between the SN and its surrounding structures [12].

SPET/CT is a multimodal imaging technique that fuses the radioactivity distribution detected by SPET with the anatomic information gathered by CT. SPET/CT has some important advantages over conventional lymphoscintigraphy. The tomographic acquisition, together with the CT correction for tissue attenuation and scatter of the gamma ray signals, imply a better SN visualization. The identification of the node in relation to anatomic structures facilitates interpretation and optimally prepares the surgeon for the operation [13].

Different studies showed that SPET/CT can provide supplementary, clinically relevant information in 50% of patients as well as visualize additional SN in patients with multiple lymphatic drain basins in approximately 23% of cases. This results in a change of surgical approach in up to 35%, with a different incision, an incision at another site or an extra incision, demonstrating the great advantage of the use of SPET/CT [14, 15].

Our results showed that the percentage of SN surgery identification in the group II was greater than the group I (96.5% vs. 92%), without a statistically significant difference. According to the literature, we highlighted the use of SPET/CT increases the possibility of SN detection. A more accurate localization was evident especially in some SN anatomical sites such as: the axilla, with an identification percentage of 94.5% in the group II versus 90% in the group I; the upon-clavicle lymph nodes, with an identification percentage of 100% in the group II versus 50% in the group I. On the contrary, the SN anatomical site identification percentage was perfectly the same in the two groups for inguinal (100%) or neck (92%) lymph nodes. Then, it seems the use of SPET/CT didn't give additional information or advantages in these cases. In Figure **3** and **4** we reported two exemplar cases of group II in which the SNs drainage is showed by both planar and SPECT/CT lymphoscintigraphy.

The combination of SPET/CT and planar imaging allows the identification of SN with precise anatomical localization, resulting in increased surgeon confidence, especially in difficult surgical cases, as well as improved preoperative planning and possibly staging [16].

Also in our experience the surgeon was quite confident with the SPET/CT images: he asked for the vision of the images and discussed it with the nuclear physician before every operation to plan and to improve the surgical approach.

All the above-mentioned advantages of SPET/CT lead to a surgery time reduction. Covarelli *et al*. compared conventional imaging to only SPET/CT imaging and found that the latter shortened the mean biopsy time from 31 to 21 minutes [17].

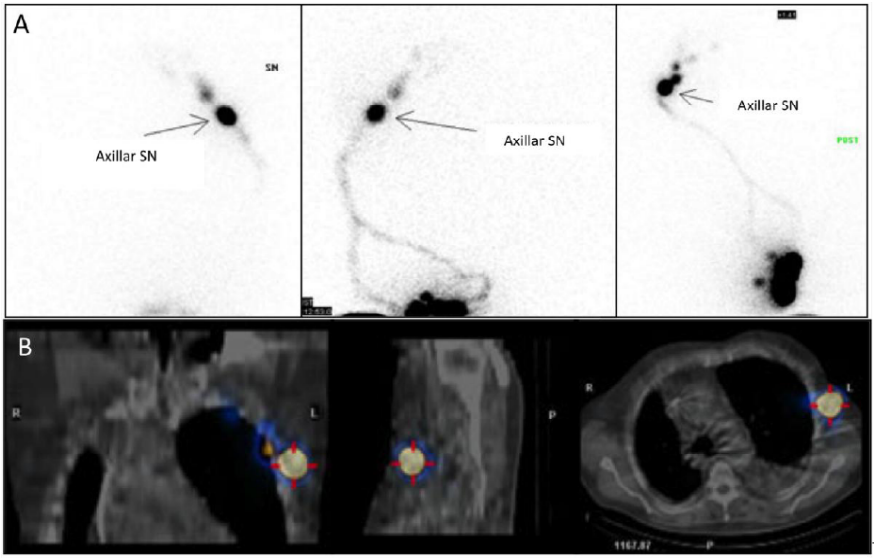

Figure 3: Cutaneous malignant melanoma of the back. Detection of left axillar lymph node at (**A**) planar (anterior, posterior and lateral views) and (**B**) SPET/CT (coronal, sagittal and axial) lymphoscintigraphy.

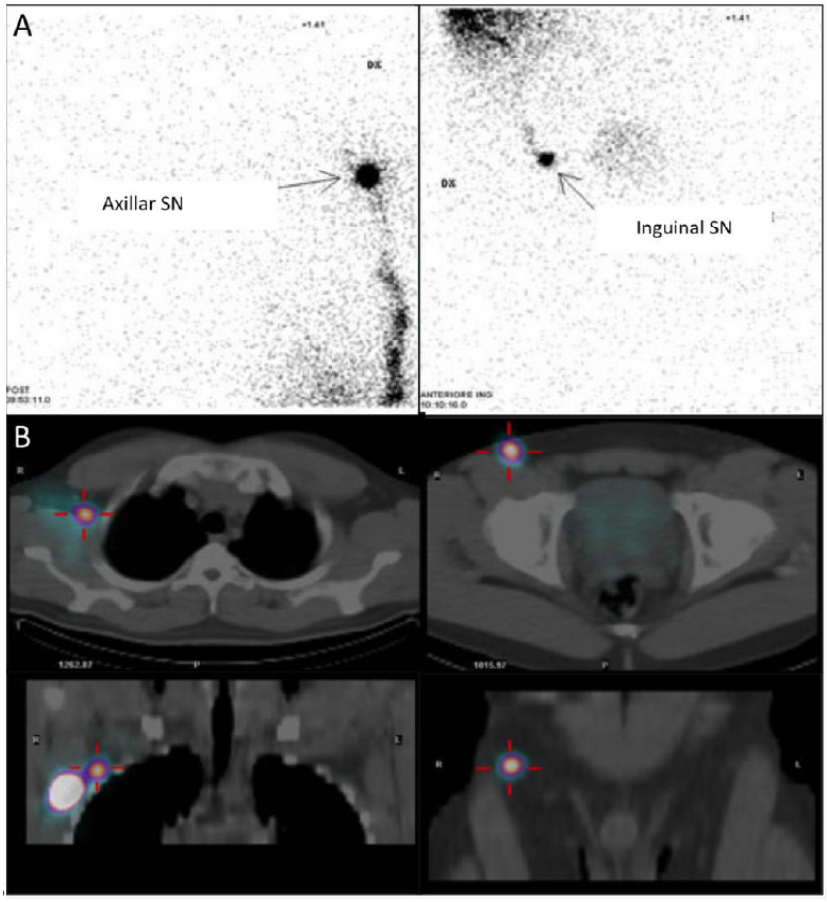

Figure 4: Cutaneous malignant melanoma of the back. Detection of right axillar and inguinal lymph nodes at (**A**) planar (posterior and anterior views) and (**B**) SPET/CT (axial and coronal) lymphoscintigraphy.

Our results concerning the SN surgery time highlighted a shorter one in the group II (10-20 minutes) compared with the group I (10-38 minutes) with a statistically significant difference between the two groups (t= -2.485; *p*=0.015). So, for the patients submitted to SPET/CT, it is possible to define a reduction of SN surgery mean time of about 40%.

Moreover, the use of SPET/CT in pre-surgery phases has positive effects on the surgical team exposition to radiations that is already normally limited, with a further global reduction of irradiation.

Skin contamination, nodes close to the injection site and overweight patients are three noted planar images limitations that can also be overcome with the SPET/CT technique [4].

One limitation of the SPET/CT technique can be the greater irradiation for patients even if the use of low dose CT protocol minimizes this effect.

CONCLUSIONS

Our results demonstrated that SPET/CT can play a role in patients with MM, allowing a more accurate SN identification than planar lymphoscintigraphy, especially in axillar and upon-clavicular nodes and contributes to a correct staging.

It facilitates surgical exploration, in particular in difficult cases, and improves surgery success percentage. Using the hybrid technique, surgery times are shorter, reducing also surgery team irradiation.

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