Available online at www.sciencedirect.com

ScienceDirect

EJSO 40 (2014) 55–60

EJSO the Journal of Cancer Surgery

www.ejso.com

Lymphoscintigraphy in clinical routine practice: Reproducibility and accuracy in melanoma patients with a long-term follow-up

G.C. Vitali [a,*], G. Trifirò [b], M. Zonta [c], E. Pennacchioli [a], L. Santoro [d], L.L. Travaini [e], M. Barberis [f], A. Testori [a]

[a] *Division of Melanoma and Soft Tissue Sarcoma, European Institute of Oncology, Via Ripamonti 435, Milan, Italy*
[b] *Nuclear Medicine Unit, Fondazione Salvatore Maugeri, Via S. Maugeri 4, Pavia, Italy*
[c] *Surgical Division, Mater Medical Centre, 21-37 Fulham Road, Townsville, Australia*
[d] *Division of Epidemiology and Biostatistics, European Institute of Oncology, Via Ripamonti 435, Milan, Italy*
[e] *Division of Nuclear Medicine, European Institute of Oncology, Via Ripamonti 435, Milan, Italy*
[f] *Division of Pathology and Laboratory Medicine, European Institute of Oncology, Via Ripamonti 435, Milan, Italy*

Accepted 1 September 2013
Available online 12 September 2013

Abstract

Introduction: The sentinel node status is the most important single factor determining overall survival for patients with localized melanoma. Preoperative lymphoscintigraphy (LS) is essential in locating the correct sentinel lymph node (SN) and the reproducibility of the method determines the accuracy of the sentinel node biopsy (SNB). This study aims at determining the reproducibility and accuracy of LS in routine clinical practice after long-term follow-up.

Patients and methods: One hundred and eight melanoma patients with clinically unpredictable lymphatic drainage were prospectively enrolled to undergo two LS. The first LS was performed to determine the site and number of the lymphatic basins to plan SNB anesthesia and the second preoperative LS was to allow SN localization intra-operatively.

Results: Lymphatic drainage was demonstrated in all patients. In 84 of 108 cases, both LSs were concordant in terms of site and number of nodal basins visualized. After a median follow-up of 80 months, no nodal recurrence was observed in the five patients with a decreased number of lymph node basins. In the group with increased number of lymph node basins, one patient developed nodal metastases in the same regional lymph node basin visualized by both LS studies.

Conclusion: LS is an accurate and reproducible method to determine the localization of the sentinel node in the day-to-day routine to clinical practice when primary melanoma is also located in body sites with variable lymphatic drainage.

Keywords: Sentinel lymph node; Lymphoscintigraphy; Melanoma; Reproducibility; Clinical routine practice

Introduction

Sentinel lymph node (SN) status represents the most important single factor determining overall survival for cutaneous melanoma patients at clinical stage I–II. Sentinel node biopsy (SNB) technique is widely accepted as a standard staging tool for patients with primary melanoma and no clinically palpable nodes.[1] About 20% of melanoma patients who undergo SNB are positive for metastatic disease and may benefit from subsequent completion lymph node dissection (CLND). Thus, the remaining 80% of patients can avoid the morbidity associated with CLND.[2]

The accuracy of harvesting the SN, by combining intradermal blue dye injection and radioactive lymphatic mapping, is approximately 98% with a low false-negative rate.[3]

Lymphatic pathways described by Sappey were highly predictable with the assumption that lymphatic drainage from the skin of the trunk and limbs was always to nodes in the nearest groin or axilla.[4] Early lymphoscintigraphic studies have shown that lymphatic drainage, from different sites of primary melanoma, is highly variable and clinically

* Corresponding author. Tel.: +39 025749459; fax: +39 0294379230.
E-mail addresses: giulio.vitali@ieo.it, giuliocesare.vitali@gmail.com (G.C. Vitali).

0748-7983/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejso.2013.09.003

unpredictable especially for truncal melanomas arising on the midline and near Sappey's lines.[5]

Therefore, the role of preoperative LS has become essential in locating and radiolabelling the correct SN(s) and the reproducibility of the method determines the accuracy of SNB.[6]

Multiple studies have reported variability in the lymphatic drainage patterns of cutaneous melanomas from different body regions with a reproducibility rate of approximately 85%. The majority of studies were not performed in clinical routine practice to avoid variables that could adversely affect the reproducibility of the method.[7–9] Only one recent study published by Vidal et al. has shown higher reproducibility (95%) of the procedure in clinical routine practice.[10]

This study aims to determine the reproducibility of lymphoscintigraphy in routine clinical practice in selected melanoma patients with highest variability, evaluating the accuracy of the procedure after long-term follow-up.

Materials and methods

At the European Institute of Oncology (IEO) in Milan, wide local excision (WLE) and SNB are usually performed simultaneously under local anesthesia (LA) if the SNs are located in one regional lymph node basin or if the SNs are in two basins and WLE is not required. When LS identifies multiple basins or SNs in the head–neck or popliteal fossa, WLE and SNB are performed under general anesthesia (GA) according to our divisional protocol.

Before the opening of IEO Day Hospital Center (2010), patients were re-scheduled to undergo WLE and SNB under GA when the LS showed two or more basins, and repeating LS was then necessary.

Patients

From January 2001 to December 2007, 108 selected patients with primary cutaneous melanoma were prospectively enrolled to undergo two LSs; the first in order to evaluate the lymphatic basins involved and the second one before performing WLE and SNB. The study was approved by the Ethic Committee of IEO and informed consent was obtained from each patient.

The inclusion criteria were the site of primary lesion and its pathological characteristics.

Three groups of patients were defined on the basis of the site of the primary lesion: one group with truncal melanoma, a second group with melanomas located below the knee (lower limbs) and a third group with melanomas on the forearm or hand (upper limbs).

Patients with a melanoma between popliteal fossa and trunk and between cubital fossa and trunk were not included in the study because their lymphatic drainage mapped unambiguously to the local anatomical lymph node basin. Patients with head and neck cutaneous melanoma were excluded because SNB is not feasible in LA for complex lymphatic drainage pattern to multiple nodal basins.

All melanoma patients with a Breslow thickness of $\geq$1.0 mm or $<$1.0 mm with at least one adverse pathological feature (i.e. mitoses $\geq$1/mm^2, ulceration) according to the Final Version of 2009 AJCC Melanoma Staging and Classification and patients who preferred to be submitted to lymphatic mapping and SNB, were considered.

Patients with clinical evidence of metastases detected by physical examination and ultrasound study or previously treated with cutaneous WLE were excluded. The first LS was performed to determine the site and the number of lymphatic draining basins to plan SNB anesthesia, whilst the preoperative LS was performed to enable intraoperative localization of the SNs.

Lymphoscintigraphy and SNB

Based on IEO standard protocol, in all patients both lymphoscintigraphies were performed by injecting a total amount of 0.5 mL of 30–50 MBq of 99 mTc-labeled human serum albumin nanocolloids (Nanocoll, GEHC) intradermally as double aliquots in two sites adjacent to the scar of the excisional biopsy (within 1 cm).

Whole-body, early and delayed static images in multiple projections were acquired 30 min and 2 h after injection.

All SNs were marked on the skin using a dermographic pen. Early and delayed images were attached to the LS report to assist surgical excision. Different and experienced physicians and technologists of the nuclear medicine team were involved for all procedures.

Intra-operatively, the SN was identified by using a handheld γ-probe (Neoprobe 1000, Neoprobe Corporation, Dublin, Ohio, USA) and the blue dye-based lymphatic technique. After the induction of local or general anesthesia, 0.5–1 mL of Patent blue dye was intradermally injected (2–4 injections) around the excision biopsy site at a distance of up to 5 mm from the scar and subsequently the area was massaged to promote lymphatic flow.

All radiolabeled and/or stained nodes were removed until the maximal residual background count was less than 10% of the count of the hottest node. Pelvic SNs were not removed.

Definitive WLE of the primary cutaneous melanoma was performed at the same time as the SNB procedure.

Pathologic evaluation

The pathological status of the SN was evaluated according to the IEO melanoma protocol. All the SNs were formalin-fixed and paraffin-embedded. Frozen sections were not performed. SNs larger than 5 mm were bivalved along their longitudinal axis and sectioned at 50-μm intervals to give 5 levels. From each level, five consecutive sections were obtained; two were stained with H&E and S-100 protein marker and the remaining three sections