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# Patterns of node mapping differ for axial and extremity primary cutaneous melanoma: A case for a more *selective use of* pre-operative imaging

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ABSTRACT

*Purpose:* Preoperative lymphoscintigraphy for sentinel lymph node mapping in melanoma improves the ability to locate nodes. However, it still remains unclear whether this step is required for all patients.

*Methods:* Patients diagnosed with cutaneous melanoma from 1996 to 2012 were identified. Exclusion criteria were in situ disease, metastatic disease, or no SLN biopsy.

*Results:* 214 patients were evaluated. Median age was 57 years, the majority were male (59.8%), white (97.2%), and stage I (60.7%). SLN revealed metastatic disease in 14.5% of patients. The most common primary site was the trunk (43.4%) followed by head and neck (21%), upper extremity (19.2%), and lower extremity (16.4%). Multiple lymphatic basins were most common for head and neck lesions (66.7%) followed by those on the trunk (28.8%), with fewer identified when lower (11.4%), and upper extremities were involved (4.2%). When comparison was restricted to extremity vs. axial, a single basin was noted in 94.5% vs. 59.9% of patients, $p < 0.0001$. For all extremity lesions the SLN was located in the primary basin. Additional sites included in-transit (popliteal) and second tier basins. The only melanomas with bilateral or contralateral SLN were axial melanomas.

*Conclusions:* Patients with axial melanomas benefit most from lymphoscintigraphy. This step may not be required for extremity melanoma.



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## Introduction

*Sentinel lymph node (SLN) biopsy defines prognosis and directs therapy for patients with melanoma.*[1] Preliminary animal model studies reported lymphatic mapping with vital blue dye alone.[2] The initial clinical trial reported by Morton presented a technique of preoperative lymphoscintigraphy and intra-operative mapping with vital blue dye alone.[3] The addition of intra-operative lymphatic mapping with a hand held gamma probe has improved the accuracy and ease of this procedure.[4] Most of the reported series use the combined techniques of preoperative lymphoscintigraphy and intraoperative mapping with vital blue dye and hand held gamma probe.[5,6]

*The pattern of lymphatic drainage is reported as variable.* Secondary to this variability many authors have advocated for routine lymphoscintigraphy to accurately identify the SLN.[7] Prior to the routine use of lymphoscintigraphy, it was hypothesized that lymphatic drainage was fairly uniform. Sappey's original descriptions of lymphatic channels reported a predictable pattern based upon topographic location.[8] However, data from radiotracer lymphoscintigraphy in the 1960s and 1970s and routine Technetium-99 (Tc-99) lymph node mapping for cutaneous neoplasia demonstrated a more complex pattern.[8] Multiple authors have described unpredicted lymphatic drainage patterns for patients with melanoma; these include bilateral, non-contiguous, and in-transit locations.[7,9–11] Unusual drainage sites include intramuscular space, para-aortic, retroperitoneal, and costal margin.[12] Others have reported aberrant/multi-basin lymphatic mapping in 0.4–15% of melanoma patients.[9,10,13–17] These sites of aberrant drainage are clinically relevant because 6.3–21% contain microscopic disease and when metastasis is present this will be the only site in more than 50% of the cases.[9,11,14–16] In summary the aberrant drainage sites, when present, are just as likely to contain metastatic disease as those found in the primary basin.[15]

Understanding the factors associated with the complexity of drainage may guide the choice of pre-operative imaging. Potential imaging strategies include static planar imaging, SPECT-CT imaging or omission of imaging when a predictable location can be anticipated. The incidence of unexpected findings on lymphatic mapping varies with anatomic location of the primary melanoma. Literature suggests a fairly unpredictable pattern of drainage for melanoma on the trunk and head and neck. In these melanomas there is a higher incidence of bilateral disease and unusual or difficult to identify sites for SLNs.[10,12,18,19] It is possible that variability in lymphatic drainage maybe lower when the primary melanoma is located on the extremity. Although some authors have described a fairly rich and variable lymphatic drainage from extremity melanomas, others have described a more predictable pattern.[9,14,18] Clinical practices have not evolved to account for these mapping patterns, many centers including our own continue to use static planar imaging as the standard.

This study was undertaken to review the experiences of lymphoscintigraphy and SLN biopsy at a rural academic medical center for better understanding of the patterns of lymphatic drainage and location of SLN observed in axial vs. extremity melanomas. We hypothesize that a clear understanding of drainage patterns associated with patient factors may enable surgeons to individualize preoperative imaging.

## Material and methods

### *Study population*

This study was conducted at East Carolina University and Vidant Medical Center, a rural academic medical center in Eastern North Carolina. Study design and execution were approved by the East Carolina University institutional review board. Index cases of cutaneous melanoma from July 1996 to July 2012 were identified from our tumor registry. Patients were excluded if they had in situ disease, no preoperative lymphoscintigraphy, no SLN biopsy, stage IV disease or incomplete clinical data. We expanded our definition of regional nodal basins from the standard description of inguinal, axillary, and cervical to better reflect the complexities of lymph node drainage reported on lymphoscintigraphy. Lymph node basins were defined as submental, submandibular, anterior cervical, postauricular, supraclavicular fossa, popliteal, epitrochlear, inguinal, iliac, axillary, and parotid.

### *Technique*

Sentinel lymph node biopsy was performed in a standard manner for all patients. TC-99 was injected in four quadrants around the tumor on the day of surgery followed by full body lymphoscintigraphy to identify first draining basin(s) and all subsequent basins. The radiologist marked sentinel lymph nodes cutaneously using an indelible marker. Thereafter, vital blue dye was injected intraoperatively in four quadrants in the dermis around the tumor. All lymph nodes that sequestered blue dye and/or radiotracer were removed until background count was less than 10% of the hottest lymph (sentinel) node. Lymph nodes were subsequently evaluated with serial step sectioning. Immunohistochemistry was utilized at the discretion of the pathologist.

### *Data analysis*

We analyzed the collected data using the SAS platform JMP version 9.0 (SAS Institute Cary, NC). Univariate analysis was performed with $\chi^2$ or students *t*-test as indicated. Multivariate analysis was performed using bivariate logistic regression. Statistical significance was defined as $p < 0.05$.

## Results

### *Patient demographics*

Initially a total of 525 patients were identified. More than half of the patients were excluded for in situ disease (105), no SLN (201), and incomplete clinical data (8). The final study population consists of 214 patients. Table 1 depicts overall patient demographics. The median age was 57 years, the majority were male (59.8%, $p < 0.001$), white (97.2%, $p < 0.001$), and stage

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