Hot or not? The 10% rule in sentinel lymph node biopsy for malignant melanoma revisited

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Received 24 May 2013; accepted 12 November 2013

Summary

Background: The surgeon needs a practical rule to follow when deciding whether to excise a lymph node during sentinel node biopsy (SLNB). The “10% rule” dictates that all nodes with a radiation count of greater than 10% of the hottest node and all blue nodes should be removed, and this study observes the effects of following this rule in SLNB in melanoma.

Methods: We reviewed the records of 665 patients with primary melanoma who underwent sentinel lymph node over a 5-year period (2007–2011).

Results: 2064 nodes were identified in 898 nodal basins in 665 patients. 141 (21%) patients had at least one positive sentinel node. 105 positive nodal basins were identified in which more than one sentinel node was removed. In 18 of these, a less radioactive node was positive for tumour when the most radioactive node was negative. Of 175 positive nodes 157 (90%) contained blue dye staining. For cases in which the positive sentinel node was not the hottest node, the positive node had apparent blue dye staining in all 18 cases (100%), and was the second hottest node in the basin.

Conclusion: In this series removing just the hottest node and all blue nodes would not have missed a single positive basin and would have resulted in a 38% reduction in the number of nodes removed compared to those taken following the 10% rule, without changing the staging in any patient.

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Introduction

Introduced by Morton et al. in 1992, sentinel lymph node biopsy (SLNB) has become standard of care in lymph node basin staging in malignant melanoma. A sentinel lymph node is the first draining node on a direct lymphatic channel from the primary tumour site. The sentinel lymph nodes are identified by intradermal injection of a vital blue dye, a radioactive tracer, or both around the site of the primary tumour. Pre-operative lymphoscintigraphy as well as intra-operative gamma probe localization and visualization of the blue dye increase the diagnostic accuracy of the sentinel node procedure.2

The radiocolloids are only partially filtered in the sentinel nodes, so secondary nodes are seen to have some degree of radioactivity, which would have not been detected with blue dye alone. Some of these were found to be positive for tumour presence.3-5 A number of early studies sought to define the sentinel node in terms of absolute radiation count, in vivo or ex vivo radiation count relative to the background radioactivity, or relative to the most radioactive node in the basin.5-9

Since McMasters’ paper analysing the results of the Sunbelt Melanoma Trial in 2001 the “10% rule” has been widely followed. That is that all blue nodes and all nodes containing 10% or more of the radioactive count of the ex vivo count of the hottest node should be removed and considered a sentinel node, along with any macroscopically abnormal nodes. While this approach reduces the risk of missing a positive node with a low radiation count compared to hotter negative nodes in the lymphatic basin, it may result in a large number of nodes being removed during the sentinel lymph node biopsy procedure. This study aims to re-evaluate the 10% rule by retrospectively examining the outcomes of 665 patients undergoing SLNB over a 5-year period for malignant melanoma.

Materials & methods

A retrospective review was performed of 665 consecutive patients undergoing sentinel lymph node biopsy for malignant melanoma between January 2006 and December 2011. All patients with American Joint Committee on Cancer10 stage IB or greater melanoma, who had no clinically detectable nodal, regional or distant metastases, and were medically fit to undergo a completion lymphadenectomy should the result of SLNB be positive were offered sentinel lymph node biopsy.

After informed consent was obtained patients underwent sentinel node localization using triple method identification; dynamic lymphoscintigraphy, intra-operative gamma probe localization and intra-dermal Patent Blue V injection. All patients underwent lymphoscintigraphy with 99mTc-human serum albumin colloid (nanocoll GE Health-care). Four depots of 0.2 mL of radiocolloid was injected intradermally around the primary melanoma biopsy site on the morning of surgery or the evening prior. Dynamic scanning was carried out with a planar dual-head gamma camera (Siemens). Images were taken every 10 s for 10 min post-injection followed by multiple static images up to 90 min post-injection. A mark was made on the skin overlying the node(s) and the depth estimated.

The pre-operative lymphoscintogram was used as a guide to the location, and number of nodes, to be removed. Radioactivity in the nodes was measured intraoperatively using a hand-held gamma probe (Neoprobe®. Neoprobe Corp., Ohio, USA). Pre-operatively 0.5–1 mL of Patent Blue V dye (Guerbet Laboratories Ltd., Solihull, UK) was injected in the dermis around the excision site. Ex-vivo counts of the removed sentinel nodes were obtained and blue dye staining was recorded. All nodes containing blue dye staining and/or 10% or more of the radioactive count of the hottest node were removed.

Sentinel nodes underwent hematoxylin& eosin staining at multiple levels followed by immunohistochemical staining for S100 protein. The pathology of each sentinel node was correlated with the node count/hottest node count and blue dye status.

Statistical analysis was performed with Student’s t-test. Significance was determined at \( p \leq 0.05 \).

Results

The demographics of the study group are represented in Table 1. There were 665 patients in total; 318 male and 347 female. The mean age was 54 years. A total of 2064 nodes were sampled (median, 3/patient). The mean and median tumour thicknesses were 2.36 mm and 1.70 mm respectively. The mean Breslow thickness in the node positive group was 2.7 mm, significantly greater than the node negative group, which was 2.1 mm (\( p < 0.05 \)).

141 patients had at least one positive sentinel node (21.5%). These 141 patients had nodes sampled from 190 lymph node basins. 115 patients had only one basin sampled whereas18 patients had nodes taken from 2 basins, another6 patients had 3 lymphatic basins sampled, and 2 patients had nodes taken from 4 basins. Nodal metastases were found in 143 basins in these 141 patients.

In 105 basins more than one sentinel node was removed – the cohort of interest in this study. In 18 of these 105 basins a less radioactive node was positive for disease when another, more radioactive, node was negative for disease. Overall, in

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Study demographics.</th>
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<tbody>
<tr>
<td>Number of cases (%)</td>
<td>665</td>
</tr>
<tr>
<td>Sex (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>318 (48)</td>
</tr>
<tr>
<td>Female</td>
<td>347 (52)</td>
</tr>
<tr>
<td>Mean age</td>
<td>54.42</td>
</tr>
<tr>
<td>Breslow thickness (mm)</td>
<td>Number (%)</td>
</tr>
<tr>
<td>0–1.0 (T1)</td>
<td>69 (10.5)</td>
</tr>
<tr>
<td>1.01–2.0 (T2)</td>
<td>320 (48)</td>
</tr>
<tr>
<td>2.01–4.0 (T3)</td>
<td>192 (29)</td>
</tr>
<tr>
<td>&gt;4 (T4)</td>
<td>84 (12.5)</td>
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<tr>
<td>Mean number of nodes sampled</td>
<td>3.1</td>
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<tr>
<td>Median number of nodes sampled</td>
<td>3</td>
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</tbody>
</table>
of 190 basins (9.5%), the hottest node was negative when a colder node was positive. The mean radiation read relative to the hottest node was 56% with a range of 14–86%. In all cases the positive node was the second hottest node in the basin. In the 175 positive sentinel lymph nodes blue dye staining was seen in 157 (90%). In the 232 negative nodes blue dye was seen in only 133 (57%). In the 18 basins where the positive node was not the hottest node all positive nodes had blue dye staining present.

Discussion

SLNB allows the surgeon to determine the presence or absence of nodal spread from a primary melanoma through the lymphatic channels. It has been shown to be the most accurate predictor of disease progression and outcome.\(^1\)\(^2\)

Since the original description of the sentinel node concept in lymphatic basin staging by Morton et al., in 1992\(^3\) there have been various rules to guide the surgeon in deciding when to stop removing nodes. The original paper described using between 0.5 and 1 mL of patent blue-V or isosulfan blue dye that was tracked to the regional lymph node basin(s) and all blue lymph nodes removed. The authors described successfully finding at least one sentinel node in 82% of cases.

The addition of radiolabelled colloid to the blue dye technique increased the identification of at least one sentinel node to over 96%.\(^4\) Several different definitions of the sentinel lymph node were proposed after the introduction of this technique. McMasters et al. showed that sampling just the hottest node, that is the node with the highest radiation count, would result in 13% of basins having a negative sentinel node result when another less radioactive node was positive for tumour.\(^5\) In 99% of basins the positive node was either the hottest or second hottest node present. This study led to the establishment of the 10%-rule, which has become standard of care since.

In our study we show that removing just the hottest node would have resulted in a miss rate of 12.5% (18 of 143 basins). However, in all of these cases the second hottest node was positive for tumour presence. In no basin did the third or subsequent node change the staging of that basin.

These results are in keeping with the findings or Porter et al. who showed that the hottest two nodes defined the basin staging in 633 patients with malignant melanoma.\(^6\) Recent works advocating in favour of continued use of the 10%-rule have not looked at the order of the nodes removed, merely the percentage radiation read compared to the hottest node.\(^7\)\(^8\)

Liu et al. dismiss the role of blue dye in SLNB and suggest using only radiation count as a means to select which nodes to sample. 90% of positive nodes in our series had macroscopic evidence of blue dye staining, whereas only 57% of negative nodes did. Since the presence of blue dye implies a direct lymphatic channel from the primary tumour site, it is prudent to harvest these nodes regardless of radiation levels. While it may appear that removing only the hottest node plus any blue nodes would result in the same results as removing the hottest two plus all blue nodes (308 vs. 309) we would caution against this approach as we have shown that 10% of positive nodes did not contain blue dye. Using radiation count and blue dye presence independently to determine which nodes to sample potentially reduces the risk of a false negative result.

Following the 10%-rule in our cohort resulted in the removal of a mean of 3.1 lymph nodes per patient, 2064 nodes in total. In those who had at least one positive node following the 10%-rule resulted in removal of 470 lymph nodes. Were we to have only removed the hottest two nodes we could have reduced this number to 293, a 38% reduction, with no compromise of accuracy of SLNB (Table 2). Taking the two hottest as well as all blue nodes adds only an extra 18 nodes to this number (309).

Replacing the 10%-rule with a "Hottest Two + Blue" has the potential to reduce the operative time and cost associated with sentinel lymph node biopsy without increasing the false negative rate of this procedure. In our 5-year series we would have removed 1357 lymph nodes in total rather than 2064 which has a significant cost-saving potential.

Conflict of interest/funding

None.

Acknowledgements

The work of the staff of the Nuclear Medicine Department St George’s Hospital in carrying out the Lymphoscintigraphy is acknowledged.

References


