



## EDITORIALS

# Sentinel lymph node biopsy in melanoma

Useful only to a small minority of patients who have the procedure

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There are two diametrically opposed positions on the role of sentinel lymph node biopsy in the management of patients with melanoma. Either sentinel node biopsy affords patients with the best prognostic information and biopsy followed by complete lymph node dissection provides a survival advantage for patients with intermediate thickness melanomas, or the procedures are expensive and invasive, add little or no prognostic information, and have no survival advantage. The lack of consensus is reflected in the ambiguity of guidelines internationally.<sup>1-5</sup>

What additional prognostic information is provided by sentinel lymph node biopsy? Many studies indicate that compared with thickness, ulceration, inflammation, or mitotic rate, sentinel lymph node status is a stronger predictor of disease-free, disease specific, or overall survival,<sup>6</sup> but we don't know whether sentinel lymph node status alone is a better predictor of overall survival than a combination of known prognostic indicators.<sup>7</sup> An important confounder is that knowledge of sentinel lymph node status affects patients' subsequent treatment. People with negative results are followed less vigorously and those with positive results usually have complete node dissection, more extensive evaluation, more frequent surveillance, and may be offered adjuvant therapy.

### Survival

Does sentinel lymph node biopsy improve survival? Data from the Multicenter Selective Lymphadenectomy Trial (MSLT-1) show no survival advantage of sentinel node biopsy followed by complete lymph node dissection compared with wide excision and observation.<sup>7,8</sup> The study also proved no survival advantage for patients with intermediated thickness melanomas in the biopsy group compared with the observation group in intent to treat analyses.<sup>7,8</sup> Any apparent benefit in disease-free survival is clearly a result of trial design and mislabelling of patients with positive biopsy results who had complete dissection as disease-free and those who had complete dissection after detection of clinical nodes as diseased.<sup>7,8</sup> The claims of survival benefit by the advocates of sentinel node biopsy are based on misinterpretation of the data or are disingenuous and should stop. As McGregor and Sasieni point out, adoption of the terms

“biopsy based management” and “local disease control” is unhelpful and serves only to cloud the negative results of a well designed and difficult study.<sup>9</sup>

Sentinel lymph node biopsy is not useful to the majority of patients (roughly 80%) who have negative results,<sup>8,10</sup> and it is not likely to be useful to those with positive results (again roughly 80%) who do not have metastatic disease in their resected nodes.<sup>11</sup> Thus, roughly 96% of patients having biopsy are unlikely to benefit from the procedure. If it is useful for the small, remaining minority of patients, advocates should prove it.

It is argued that a negative result is reassuring to patients. This assumption may not take into account the lack of consensus on what constitutes a positive result (in MSLT-1 it was one cell detected by immunohistochemistry); whether patients are informed that the false negative rate varies (5% in MSLT-1<sup>8</sup> and between 0% and 34%, mean 13% (95% confidence interval 11% to 14%) in other published data<sup>10</sup>); or that patients who develop metastatic disease after a negative result have a worse prognosis than those who are followed clinically after wide local excision.<sup>8</sup>

### What patients need to know

What should patients with intermediate thickness melanomas be told about the risks and benefits of sentinel lymph node biopsy followed by complete dissection? Some patients with negative results (about 5% based on MSLT-1 data) are falsely reassured because the result is a false negative.<sup>8</sup> The predictive value of a negative result is limited. For example, of patients with intermediate or thick melanomas who have a negative result, 15% and 35% respectively will die of melanoma within 10 years.<sup>12</sup> Some patients with positive results (maybe 14%<sup>9</sup>) would not have gone on to develop clinically relevant nodal disease because the test was either false positive (melanoma was not in the node) or biologically false positive (melanoma in the node would not produce clinically meaningful progression). The predictive value of a positive result is similarly limited. For example, 62% and 48% of patients with

intermediate or thick melanomas who have positive results will be alive at 10 years.<sup>12</sup> Complications after sentinel node biopsy are about 10% and those after complete node dissection are much higher (about 37%) and more severe.<sup>13</sup> The procedure might be useful only if you belong to the small minority of patients (roughly 4%) with early lymph node disease removed by complete lymph node dissection. Patients who have complete node dissection after a positive biopsy result have less extensive surgery and less morbidity than patients who have complete dissection after clinical detection of diseased nodes.<sup>8</sup>

Physicians caring for patients with melanoma should not be made to feel guilty or to fear litigation for either advocating that their patients have sentinel node biopsy or advising them not to. Patients who are sent for biopsy should be adequately informed of the risks and benefits. They should also be encouraged to participate in ongoing and future studies, especially studies that examine whether the procedure has survival advantage for the small minority of patients who have early lymph node disease removed by complete dissection.

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