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Nodal Observation *vs.* Immediate Lymphadenectomy in the Management of Melanoma

Brooks NA*
Skin Cancer Medical Center, Encino, California, USA

***Corresponding author:** Norman A. Brooks, 16311 Ventura Blvd. Ste. 690 Encino, California, USA

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Description

The final report of the Multicenter Selective Lymphadenectomy Trial revealed no overall 10-year melanoma survival advantage for sentinel node biopsy and immediate lymphadenectomy over observation [1]. Although, retrospectively, a survival advantage was reported (56.0% sentinel node biopsy *vs.* 41.5% observation; P=0.04) for the intermediate-thickness melanomas (1.2-3.50mm), multiple commentaries have questioned the interpretation of the data and concluded no increase in survival based on the data presented [2]. Three basic reasons have been given: (1) false positives (2) false negatives and (3) there is no significant difference in survival between the study groups from the time of randomization. With regard to the false negatives, there was a high incidence of false negative sentinel node biopsies in the trial. 20% of the patients had a negative biopsy, and later developed positive nodes with poorer survival (34.4% survival) than node positive observation patients (41.5% survival). Please see footnote for discussion of false positives.

Sentinel node biopsy can be of value as a staging tool especially in young patients, despite that no overall survival advantage was reported for immediate lymphadenectomy. However, many patients would prefer to avoid lymph node surgery. The high incidence of false negative biopsies (20% incidence) reported in the trial attests to the fact that sentinel node biopsy is not always accurate. The procedure can be complicated by centrally located lesions potentially draining into multiple different lymph node basins. There is also a potential for surgical morbidity and chronic lymphedema following lymphadenectomy.

For patients who would prefer to forego sentinel node biopsy, observation procedures include palpation, ultrasonography of the draining lymph node basins, and, in selected patients, whole body PET CT scan. Blood testing including lactate dehydrogenase, serum S100, clinical examination, and chest radiography at first can be performed every 3 months. Patients can be informed to gently palpate and check their lymph node basins on a monthly basis.

In the previously referenced lymphadenectomy trial, the frequency of nodal metastases across all Breslow-thickness groups was 20.8%. In the observation group with intermediate-thickness melanomas 17.4% of patients developed nodal metastases at a median of 19.2 months. For thick melanomas (>3.50mm) nodal relapse occurred at a median of 9.2 months. Many patients incorrectly believe that if no positive node is found at the time of initial melanoma surgery, then they are cured. Patients must be informed of the potential for delay in the development of nodal metastases, and the importance of careful follow-up over time to maximize the benefits of observation management.

Footnote: There was a 12% higher incidence rate of nodal metastases reported in the biopsy group over the observation group. Any false positive nodal biopsies would nullify statistical benefits reported for the intermediate-thickness melanomas, and account for the equal overall survival in both groups. Strong evidence suggesting possible false positive sentinel node biopsies is the reported interpretation of single immunopositive cells in nodal parenchyma or in an afferent lymphatic vessels as nodal tumors. There are reports in the literature that micrometastases less than 0.1mm in size may have no biologic significance and may be destroyed by host immunity [3]. Isolated melanoma cells have frequently been found, using molecular testing (reverse transcriptase-polymerase chain reaction) capable of detecting 1 malignant cell within 1 million normal cells, in otherwise negative sentinel nodes examined by conventional pathology and immunostaining [4,5].

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