

Sentinel node in management of malignant melanoma

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ABSTRACT

Objectives: One of the most important prognostic features of malignant melanoma is the involvement of regional lymph nodes. The aim of this study is to identify the sentinel lymph node which is the first node to be involved by metastases from malignant melanoma and then decide which patients can benefit from lymph node dissection and which will only need clinical follow-up.

Methods: Forty-four patients were included in this study from October 2000 to November 2001. The study was carried out at the St. Bartholomew's and Royal Hospital, London, United Kingdom. We undertook a pilot study of patients with malignant melanoma involving the outline technique. A consent form for all patients was taken. The only criteria for inclusion in this study was the Breslow thickness of the tumor which had to be over 2 mm. There were 18 females and 26 males, mean age of 57 years. The primary tumor site varied: upper limbs 14, lower limbs 10, trunk 18, and head and neck 2.

Results: Excision of one to 3 sentinel nodes (mean 1.4) was performed. The number of sentinel nodes was removed: one in 24 patients, 2 in 12, 3 in 6, and 4 in 2 patients. In 8/44 patients metastatic disease was detected in the sentinel node. Three patients had therapeutic lymph node dissection. There was no major complication. Four patients with one positive node each (evidence of micrometastases) have gone for lymph node dissection; one of them had one further positive node.

Conclusion: Sentinel lymph node biopsy is increasingly used to stage melanoma in order to avoid lymph node dissection in patients who clinically have no lymph node involvement. Sentinel lymph node biopsy is a valuable technique for melanoma staging; however, impact on overall survival requires longer follow-up.

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Malignant melanoma is a malignant tumor of melanocytes, the pigment cells in skin.¹ The majority of patients present with no evidence of metastatic spread nodes; however, studies report that 20% with micro-metastases to regional lymph nodes.² Prognosis relates to the vertical depth of the tumor through skin (the Breslow depth) and evidence of spread to regional lymph nodes. If depth is less than 4 mm then there is a 30% risk of relapse. If the depth is more than 4 mm or there is spread to lymph nodes then the risk of relapse is 70%.³ Current treatment methods involve wide local excision, with some centers proceeding to elective lymph nodes dissection (of regional draining nodes). Other centers

offer clinical follow up alone. Systemic chemotherapy is of limited use; however, in some studies high dose interferon may be beneficial in the presence of micro metastases. Elective lymph nodes dissection confers advantages over clinical follow up in that it leads to accurate staging with early removal of residual disease. It does however, has disadvantages: it is an excessive treatment in 80% of patients (who at presentation have no metastatic disease); it is also associated with post-operative morbidity and mortality; and it is technically difficult (studies have shown that lymphatic drainage may be difficult to predict).^{4,5} Clinical follow-up encompasses a lot more uncertainty and has

The study was carried out at St. Bartholomew's and Royal Hospital, London, United Kingdom and the present posts with the Department of Radiology, King Hussein Medical Center, Amman, Jordan.

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implications, and there is no proven evidence of increase in a long time survival with elective lymph nodes dissection. An ideal follow up to wide local excision should: 1) Be a minimally invasive procedure. 2) Have a low complication rate. 3) Lead to accurate staging. 4) Lead to early diagnosis of patients with metastatic disease. 5) Select a group of patients suitable for elective lymph nodes dissection.

Methods. Forty-four patients were included in this study, from October 2000 to November 2001. The study was carried out in the St. Bartholomew's and Royal Hospitals, London, United Kingdom. We undertook a pilot study of patients with malignant melanoma involving the outlined technique. A consent form for all patients were taken. The only criteria for inclusion is the Berslow thickness of the tumor had to be over 2 mm (shown to have increase incidence of micrometastases). There were 18 females and 26 males, mean age of 57 years. The primary tumor site varied: upper limbs 14, lower limbs 10, trunk 18, and head and neck 2.

Results. There was an average of 1.2 sentinel nodes in the axillary and groin regions for truck injection. While for lower limb injections there are 3.5 sentinel nodes in the groin. One sentinel lymph node was removed in 24 patients, 2 in 12, 3 in 6 and 4 in 2 patients. Four patients with one positive node each (evidence of micrometastases) have gone to lymph node dissection; one of them had one further positive node. Eight patients had more than one sentinel node, which were found closer together at surgery but only one node was identified during imaging. This was due to limited resolution of the gamma camera (10 mm). Two patients had 2 nodes identified by imaging but only one identified at surgery. None of the identified nodes were positive and the patients subsequently had negative lymph node dissection. There were 8 patients with complication: 2 seroma at the injection site; 4 retained blue dye at the injection site; 2 methemoglobinemia due to methylene blue.

Discussion. *Malignant melanoma.* Malignant melanoma is a malignant tumor of melanocytes, the pigment cells in skin (Figure 1). Its incidence is currently increasing with a worldwide risk of 1:90 of developing melanoma during a person's lifetime. Ultraviolet light has been shown to be of importance in the etiology with lighter skinned races more susceptible.^{2,3}

Lymphatic drainage pattern. It should be emphasized that lymphatic drainage is unpredictable from any point of the skin; however, common patterns of drainage are present from various regions. In all areas drainage tend to be in the ipsilateral nodes groups, though contralateral drainage can

occur. The tumor within 10 cm of the midline often drain to nodes bilaterally and had multiple sentinel nodes. The common pattern of drainage includes:^{5,6} head and neck to deep cervical and preauricular nodes; truck to axillary, groin and supraclavicular nodes; upper limbs to axilla and lower limb to groin nodes. The possibility of unusual drainage patterns must always be kept in mind so sentinel nodes are not missed.

The sentinel lymph node concept. The problem for any external scanning method for staging melanoma patients is that it must be sufficiently sensitive to detect microscopic deposit in the draining lymph nodes. The presence of such nodal micro-metastases is critically important in predicting the clinical outcome for each patient. Whether any external scanning method will ever achieve this goal is doubtful. As new systemic therapies are developed for patients with metastatic melanoma, it will become increasingly desirable to have a screening method to select which patient has micro metastases and which will thus benefit from such systemic therapies. One hundred years ago Halstead postulated that a primary tumor would initially drain to a single lymph node in the regional lymphatic chain. More recently Morton has belt upon this work with the concept of "sentinel lymph node (SLN)" (Figure 2). The sentinel node is defined as the first node among any particular lymphatic drainage channel. Identification and biopsy of this node or nodes (where there is more than one channel) is useful that the statues of the sentinel node reflect the status of the lymphatic basin as a whole (particularly when it is clean of metastatic disease). Melanoma metastases appear to pass in an orderly fashion first to the SLN then to the 2nd and 3rd tier nodes entering the general circulation, at which time systemic metastases occur. Thus the SLN biopsy technique may provide the accurate screening method required in most patients with melanoma.

A different approach. Identification of the SLN was achieved by a dual technique following biopsy of the primary tumor but before wide local excision (as the lymphatic drainage is likely to be different). The patients were admitted for the day case unit and initially attended the Nuclear Medicine Department. There were positioned in an IGE Star cam gamma camera with the field of view centred over the tumor. Twenty Mbq of technetium ^{99m} labelled nanocolloid in a volume of less than one mm injected intradermally all the way around the tumor site in several dividing doses (Figure 3). Nanocolloid is a macromolecule which, if introduced intradermally is taken up by the draining lymphatic ducts and accumulates in the draining nodes.^{7,9} The Technetium ^{99m} allow us to visualize these lymphatic channels as it undergoes radioactive decay with emission of gamma rays, which are detected with the gamma camera.¹⁰ Imaging was commencing immediately



Figure 1 - Malignant melanoma.

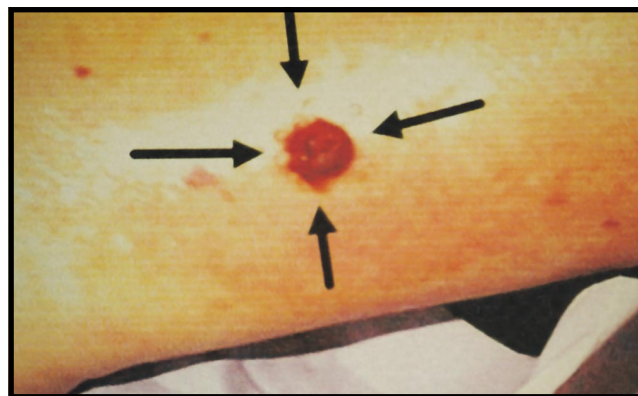


Figure 3 - Intradermal injection of 20 Mbq technetium nanocolloid. Mbq - megabecquerel.

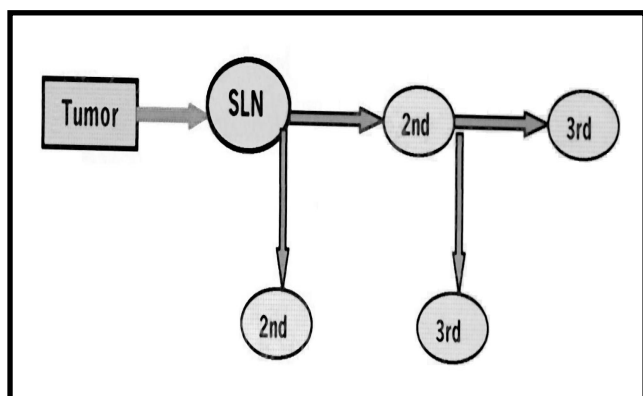


Figure 2 - Morton's model of tumor spread. SLN - sentinel lymph node.



Figure 4 - Dynamic acquisition.

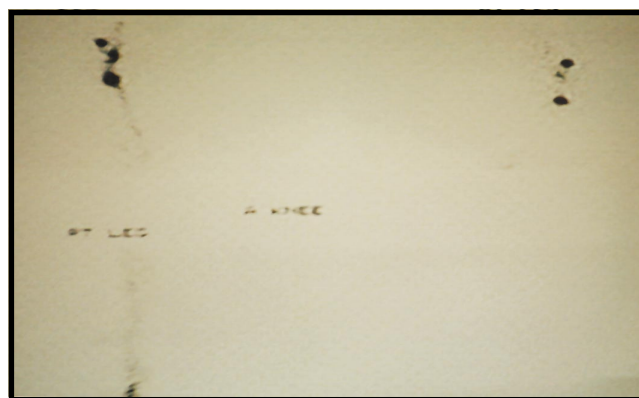


Figure 5 - Static acquisition. Sentinel lymph node is demonstrated in the right groin with two 2nd nodes seen superior to it.

following injection with acquisition (20 frames of 60 seconds, 128 x 128 matrix). The time of injection should be noted and imaging commences immediately, so that the major draining lymphatic channels can be followed to the sentinel nodes and the rate of lymphatic drainage in cm/min can be recorded. Static images with a 5 minutes acquisition were obtained immediately after the dynamic study and at 2 hours. Frontal, lateral and oblique images may be necessary depending on the anatomical location of the node (Figures 4 and 5). The sentinel nodes were identified in accordance with Morton's identification. A cobalt pen was used to identify the site of the sentinel node (the pen activity being detected by the camera) in several plans. The skin overlaying the node then marked. The patient then transferred to the theater. The surgeon injects one mm of methylene blue dye intradermally around the tumor site. Under general anesthesia the surgeon performed excision biopsy of the sentinel node guided by the intra operative gamma probe (which detect the accumulated technetium labeled nanocolloid) and methylene blue dye (also taken up by the lymphatic tissue) which allowed easier identification of the lymphatic channels. Following surgery the excised tissue was sent to histology for hematoxylin and eosin stain and immunohistology. If micro metastases were demonstrated patients then offered lymph node dissection (with subsequent histology).

In conclusion, the steadily increasing incidence of melanoma in the western countries offers opportunities and challenges to the nuclear medicine radiologists, who have the opportunity and techniques to locate sentinel nodes before excision, a procedure that has a direct impact on the surgical management of individual patients. We have outlined a useful staging procedure, which is a minimally

invasive and select patient who may benefit from lymph node dissection (or high dose interferon). This technique demands close liaison between radiologist, surgeon and histopathologist. Results to date are encouraging but larger numbers may be required. If further studies are concordant then this technique offers significant advantages over current practice and could be incorporated into the management plan. Successful future treatment strategies could well include the therapeutic administration of radionuclide.

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