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EDITORIAL – MELANOMA

Evaluating and Embracing Modern Imaging Technology to Guide Sentinel Node Biopsy for Melanoma

Marc D. Moncrieff, MD, FRCS(Plast.)[1], and John F. Thompson, MD, FRACS, FACS[2]

[1]Department of Plastic and Reconstructive Surgery, Norfolk and Norwich University Hospital, Norwich, UK; [2]Melanoma Institute Australia and The University of Sydney, Sydney, NSW, Australia

It is well documented that surgeons are often hesitant to change the procedures that they were taught during their training, and the reluctance to embrace new procedures and technologies has been exhibited by surgeons for a very long time. For instance, in the management of melanoma, the concept of lymphatic mapping and sentinel node biopsy (SNB), rather than routine elective regional lymph node dissection or nodal basin observation, was similarly resisted for a considerable period, even when its value had been established by a large-scale randomised clinical trial, namely MSLT-1.[1] Today, SNB for all but very thin melanomas is recommended in most national melanoma management guidelines,[2] and it is required for staging according to the internationally accepted staging system published by the American Joint Committee on Cancer.[3] However, techniques for improving the accuracy of SN identification have been progressively introduced, so that the originally proposed use of blue dye injection alone for lymphatic mapping has been augmented by preoperative lymphoscintigraphy (LSG), with intraoperative use of a handheld gamma-detection probe to increase the reliability of SN identification.[4,5]

In a recent publication in Annals of Surgical Oncology, the ability of SPECT-CT to further improve the reliability of SN identification was reported by Moncrieff et al.[6] In this study, undertaken at a high-volume British academic centre, the outcome of SNB with SN localisation using planar LSG alone was found to be inferior to the outcome following the introduction of routine preoperative SN localisation with co-registered SPECT-CT and planar LSG combined. However, in an accompanying editorial, Dr Delman and colleagues suggested that the use of SPECT-CT was mostly unnecessary.[7] They likened its use to assess SNs in patients with melanoma to using a very expensive, high-performance sports car for everyday transportation, rather than a basic, inexpensive, "no frills" family truck.

Moncrieff et al.[6] reported that the SPECT-CT protocol identified significantly more SNs and more node fields receiving lymph directly from the primary melanoma site compared with the planar LSG protocol. The increased anatomic detail, in turn, increased diagnostic accuracy of the technique, as evidenced by an increased SN-positivity rate. These findings were consistent with the conclusions of a large meta-analysis undertaken by Quartuccio et al.[8] The SPECT-CT protocol was associated with an improved prognosis in the short term [HR = 0.60 (95% CI 0.37–0.96); $p = 0.031$], presumably as a result of the removal of additional metastatic melanoma deposits. However, there was a significant caveat with the newer technology in that the provision of greater anatomic detail resulted in an increased proportion of patients choosing not to proceed with SNB after preoperative localisation with the SPECT-CT imaging protocol (9.3% vs. 2.5%; $p < 0.0001$). The underlying reason for this in the SPECT-CT cohort was the concern raised by identification of a greater number of nodes (median of 6 in the group who chose not to proceed, versus median of 1 in the group who did proceed; $p < 0.0001$). In contrast, the predominant reason for not proceeding with SNB in the LSG cohort was the occasional failure of migration of the tracer agent, though the rate of this event was identical to that in the SPECT-CT cohort.

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M. D. Moncrieff, MD, FRCS(Plast.)
e-mail: marc.moncrieff@nnuh.nhs.uk

The importance of the prognostic staging information that is afforded by SNB is today well established, and it is the foundation of the AJCC system for staging locoregionally confined melanoma (AJCC stage I to III).[3] With the advent of routine adjuvant systemic therapy for patients with SNB metastases, the accurate identification of positive SNs has taken on an increased level of importance.[2] Concern regarding the possibility of false-negative SNBs has been expressed for decades[9–11] and is the underlying reason why a dual localisation protocol is the current standard of care.[5] A study by Karim et al. indicated that false-negative SNs were equally attributable to technical failures of the preoperative SN localisation process, of intraoperative surgical technique and of postoperative pathological analysis.[12] We suggest that these principal sources of SN false-negativity do not occur in isolation and that suboptimal preoperative imaging protocols may lead to problems in intraoperative localisation, particularly in anatomically challenging areas such the pelvis or head and neck. Delman et al. state that "outside the head and neck, the reliability of standard lymphoscintigraphy is hard to improve upon" and cite a series in which the in-basin recurrence rate was only 2.5% after a negative SN biopsy for non-head and neck primary melanomas.[11] However, considerably higher failure rates have been reported in other series,[13,14] and the quality of the information provided by lymphoscintigraphy varies greatly not only from country to country, depending primarily on the colloid tracer that is available for lymphatic mapping, but also from centre to centre, where differing imaging protocols and equipment are employed.[15]

A second important matter that arises from the issues discussed by Delman et al. in their editorial[7] is when appropriately informed consent for SNB should be obtained. The authors advocate that if the decision has been made that a patient merits a SNB and lymph nodes are identified during lymphoscintigraphy, then the procedure should always be performed. We must disagree with such an inflexible approach, and clearly so do some patients. It is our practice in the UK and Australia to warn patients that, on occasion, multiple lymph nodes or multiple node fields may be identified on their preoperative LSG and that this may necessitate further discussion in the short time window between imaging and surgery. This ensures adherence to the core principle of informed consent by recognising that not all relevant information is available to the patient (and their treating surgeon) until immediately prior to the SNB procedure. Only then can there be a fully informed discussion about consent. Results from the study by Moncrieff et al. suggest that the ultimate decision to proceed with SNB entails a complex decision-making process, but the data point to some patients deciding against proceeding based on the perceived risk of increased postoperative morbidity and long-term quality of life exceeding the potential benefits of determining SN status.[6] The data indicate that the concerns regarding postoperative quality of life are a significant consideration in younger patients with lower risk primary melanomas (pT1b-pT2a), particularly those located on a lower extremity or in the head and neck region.

The concluding emotional statement by Delman et al. that "it would be heartbreaking to decide not to pursue a potentially curative intervention for an otherwise good surgical candidate" is probably overstated. They appropriately emphasize the therapeutic benefit of SN biopsy and its potential value by surgically removing regional disease, as well as its utility in identifying patients suitable for adjuvant systemic therapy. Patients should be appropriately counselled on this issue, although it must be borne in mind that the outcomes of the MSLT-1 study[1] were reported in a period where no effective systemic therapy for resectable stage III disease existed. This is no longer the case.[2] Available evidence suggests that if SNB is not performed for whatever reason, focused ultrasound follow-up is a reasonable fall-back strategy, facilitating early detection of SN metastases before they become clinically apparent, and this may not greatly disadvantage the patient.[16,17]

Overall, currently available data are highly suggestive that the accuracy of preoperative sentinel node localisation is increased by SPECT-CT. Accordingly, we would shift the paradigm of the statement by Delman et al. by suggesting that it would be disappointing to submit our patients to an SNB only to fail to detect a metastatic focus through a lack of accurate preoperative localisation, thereby depriving them of the opportunity to access systemic therapy that the diagnosis affords. The available data have also shown that this increased anatomical detail comes at a potential cost, in that more patients are deciding not to proceed with their surgery and, as a result, some of those patients are presenting with nodal metastases that are much more likely to have been identified if they had proceeded with the SNB. Ultimately, however, the choice to proceed is the prerogative of the well-informed patient. Therefore, in conclusion, we would much prefer to liken SPECT-CT to an in-car GPS navigation system, which very accurately informs the users where they are and what lies ahead, and which is now routinely fitted as standard to most modern automobiles, including the average family truck.

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