An update of sentinel node biopsy in breast cancer

Robert Mansel

Department of Surgery, Cardiff University, Cardiff, UK

Sentinel node biopsy (SNB) is now the standard of care in many countries, and is used in most women with operable breast cancer and clinically negative axillas. Developed from the pioneering work of Donald Morton in melanoma, the technique began to be used in breast cancer in the early 1990s in the US. In 1994, Krag reported the first series of isotopic sentinel node biopsies after blue dye had been used in the very early series. Since this time the technique has become very popular with the combined isotope/blue dye technique being used by the majority of clinicians. The extension of SNB was based on perceived advantages for the patient in lower morbidity based on case series, some of which were quite small. Concerns were expressed about variable methodologies and safety as the true false negative rates were not accurately assessed in most studies as surgeons rapidly moved on to using SNB as a routine after brief training and audit.

However, the place of SNB has been assured by recently published large randomised studies showing clear advantages in quality of life and morbidity for patients who undergo the procedure [1–4].

Particular advantages shown in the ALMANAC trial are the reductions in sensory disturbance and lymphoedema compared with patients who undergo axillary node dissection. The trials also show better arm mobility and return to work for SNB patients. As a result of these trials and large institutional case series, the value of SNB has been accepted, and this is reflected in the adoption of the technique in national guidelines such as the NICE (National Institute of Clinical Excellence) guidance in the UK which recommended SNB as the preferred axillary staging technique in breast cancer patients with clinically negative axillas. The Association of Breast Surgeons in the UK have also recommended SNB as the standard of care and have recommended that surgeons should have audited training in the procedure. The large multicentre trials such as the UK ALMANAC, the Australian/NZ SNAC and the US NSABP-32 trials are important because they all set quality assurance standards for the performance of SNB and therefore reduce the variability between surgeons inherent in the performance of any surgical technique. The overall results are remarkably similar showing success rates for locating sentinel nodes of around 99% and false negative rates of around 5–9%. These trials have all used isotopes or isotopes combined with blue dye (lymphazurin in the US and mostly Patent Blue I in Europe). Thus, there is now general acceptance that SNB will replace axillary node dissection in staging of the axilla. Increasingly, preliminary ultrasound is being used to identify obviously abnormal nodes, which can be sampled by needle biopsy, and if found pathologically positive are treated by upfront axillary clearance.

As with all new techniques many new issues have been raised by SNB, such as the pathological examination of the sentinel node and the biological meaning of micrometastases. The fact that the pathologist receives only one to two nodes means that these nodes are examined more carefully than in the past, and the use of extensive examination will reveal more metastases, as well described by Viale [5]. Although the American College of Pathology guidelines do not recommend routine immunohistochemistry, many groups are using it and consequently many more micrometastases are being discovered. Another problem is the variability of the histological techniques that are in use and these have well described in Europe by Cserni [6] who found wide variations between laboratories in the description of micrometastases. Currently, the prognostic meaning of micrometastases remains unclear, as some retrospective institutional studies suggest a worse prognosis, but the detailed pathological ongoing studies are more likely to clarify the position in due course.

A further development is the use of intraoperative molecular assays for examination of the sentinel node. These have been developed in response to the variability in frozen section sensitivity and the lack of pathology manpower in many countries that precludes the availability of a pathologist at every breast operation. Two systems have been developed, a polymerase chain reaction system measuring mammaglobin and

cytokeratin (Gene Search™)), and a chemical amplification system (OSNA™) measuring cytokeratin alone [7–9]. Recent results of these systems have shown an assay time of around 30–35 min and sensitivities compared with routine histology of around 90–95%. An added advantage is that these systems can be operated by a technician and do not require the pathologist to examine frozen sections intraoperatively. Economic studies suggest that these assays may also save money compared with conventional routine post operation histopathology.

When the sentinel node is found to be positive a further question of axillary treatment arises, although currently most surgeons are opting to perform an immediate or delayed axillary clearance. The issue that arises is that radiotherapy may be a reasonable alternative. Although little randomised data exists on the role of radiotherapy in this setting, this question is currently being examined in the EORTC AMAROS trial, which is randomising positive sentinel node patients between surgery or radiotherapy to the axilla. The trial has enrolled over 4000 patients and will answer important questions on the treatment of the axilla in the sentinel node era.

Conflict of interest statement

None declared.

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