

Sentinel node biopsy gets an excellent report

→ Janet Fricker

The latest study on use of the sentinel node biopsy has prompted calls for the procedure to be universally adopted. But can inexperienced teams be trusted to get it right?

A new study has shown that the sentinel node biopsy can be a highly reliable way of checking whether breast cancer has metastasised to lymph nodes. The procedure avoids routine removal of axillary lymph nodes in breast cancer patients by looking only at the first node that lymph from the cancerous tissue drains to – the ‘sentinel node’.

The study, which was published in January in the *European Journal of Cancer* (vol 41, pp231-237), followed 953 women operated for breast cancer who did not undergo dissection of the axillary lymph nodes, after a biopsy revealed no metastases in the sentinel node. Patients were initially examined at four-monthly intervals for three years and then at six-monthly intervals, with axilla palpation and ultrasound when deemed necessary.

The results after a median follow-up of 38 months, showed a much lower rate of overt ipsilateral axillary metastasis than had been anticipated.

An earlier validation study published in the *Journal of the National Cancer Institute* in 1999 (vol 91, pp368-373), had found metastases in the dissected lymph nodes of 6% of women with negative sentinel node biopsy results. Based on these results, and assuming

all positive nodes become clinically evident at a constant rate over 15 years, the investigators in the current study were expecting around 13 patients to develop ipsilateral metastases.

The results showed only three cases of overt ipsilateral axillary metastasis (0.3%) – much lower than the expected 13. In all three cases, the women received total axillary dissection and are presently alive and well. In addition, results show the five-year overall survival rate of the whole series was 98% and that 55 unfavourable events occurred, 37 of which related to the primary breast carcinoma.

“These patients are surviving well – their curability is very high and they have an excellent quality of life,” says Umberto Veronesi, from the European Institute of Oncology, Milan, Italy, who was a pioneer of the technique and was the principal investigator of the study. He adds that local morbidity following the sentinel node biopsy was low, with three cases of local haematoma, five cases of seroma, seven of local infection and six of limited anaesthesia of the arm.

It is also noteworthy that only 20 women developed distant metastases – the trial team believe such low rates may be attributable to the beneficial

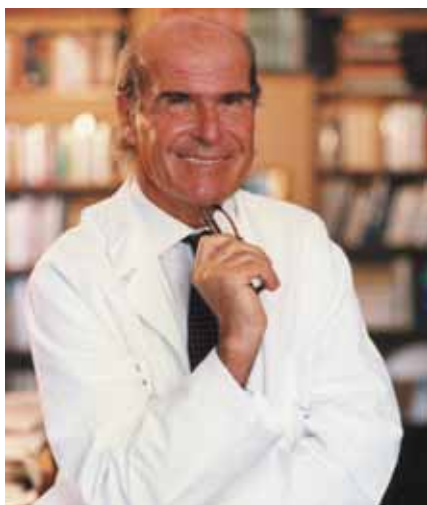
effects of maintaining healthy immunological tissue.

The authors of the study believe their research confirms the safety of sentinel node biopsy and makes a strong case for its universal introduction. “After the results of this study I think all centres in the world should be undertaking sentinel node biopsy,” says Veronesi.

This was the largest series yet following women with negative sentinel nodes, and it adds weight to earlier research by the same group, published two years ago in the *New England Journal of Medicine* (vol 349, pp546-553). That study showed the number of sentinel nodes identified with malignancies was the same for women who had undergone sentinel node biopsy followed by automatic axillary dissection as for those who only underwent axillary dissection if the sentinel node contained metastases. In the group randomised to receive automatic axillary dissection regardless of result, investigators found the overall accuracy of sentinel node biopsy compared to pathology of the other nodes was 96.9%.

ADVANTAGES

Veronesi’s 2003 study had shown considerable advantages for sentinel node



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biopsy, with the women undergoing sentinel node biopsy experiencing less pain and better arm mobility than those who also underwent surgery. “Such low rates of false-negatives are widely accepted, since the advantage of avoiding axillary side effects is thought to outweigh any negative aspects,” says Veronesi. He adds that removing normal lymph nodes in patients with cancer is now viewed as a biological mistake since it reduces their defence mechanisms.

Sentinel node biopsy is a simple procedure involving injecting 5–10 MBq of technetium-99-labelled human colloid particles in the sub dermis above the tumour or in the tissue immediately surrounding it. The sentinel node can be visualised 30 minutes to three hours later, with mammary and axillary planar scintigraphic scans, as it has the highest concentration of radioactive material. Possible explanations for the lower than expected rate of ipsilateral axillary metastasis, say the investigators, include post-operative radiotherapy to



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the breast reaching the lymph nodes, and adjuvant treatment (mainly tamoxifen) delaying the clinical appearance of metastasis. But the most likely explanation, they suggest, is that a number of occult metastases will never become clinically evident, and will remain silent in a dormant state or may even disappear.

“Such thinking is in line with the new concept that in a population of cancer cells only a minority are stem cells with the ability to produce new cancer cells,” explained Veronesi. “And if stem cells aren't present in the lymph glands the metastasis will disappear.” Exploring his theory further, Veronesi is conducting a new trial where women with positive sentinel nodes are being randomised to receive either axillary section or no treatment, with periodic PET (positron emission tomography) examination and ultrasound every six months. In the event of a metastasis appearing, the women would undergo immediate surgery. “We confidently expect the great majority of these women will not

develop metastasis,” he says, adding that ultimately they hope to identify a marker for stem cells that could be used to aid decision-making in sentinel node biopsy.

Emiel Rutgers, from the Netherlands Cancer Institute, comments that the results represent good news for sentinel node biopsy, but urges caution. “These results are from a single institution with extremely experienced surgeons, nuclear medicine doctors and pathologists. It's a best case scenario which can't be expected to translate to all centres,” he says.

Indeed, a recent phase III trial involving about 140 centres, presented at the San Antonio meeting in December, produced a false-negative rate of 9.7%. In other words, in about one in ten patients lymph node metastases in the axilla were missed¹. “To me this is difficult to accept. It's only fair that when women have this procedure they're informed of the risks they're taking for that institution,” says Rutgers, adding that increasing the number of these procedures undertaken by individual surgeons has been shown to decrease their failure rate of identifying the sentinel node. “To be considered competent, breast surgeons need to undertake at least six sentinel node procedures a month, but ideally it should be 10 or 20.” Furthermore, he says, surgeons who offer this procedure to their patients need to work within an experienced ‘SN-team’, comprising an experienced breast surgeon, nuclear medicine specialist and pathologist.

1. Preliminary technical results of NSABP B-32, a randomised phase III clinical trial to compare sentinel node resection to conventional axillary dissection in clinically node-negative breast cancer patients.