Sentinel lymph node biopsy in breast cancer – a modified audit for surgeons in private practice

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Background. Sentinel lymph node biopsy (SLNB) is a technique that is widely used in the management of early breast cancer. Surgeons are encouraged to validate their initial SLNB results by performing an audit in which both a SLNB and an axillary lymph node dissection (ALND) are performed. For surgeons in solo private practice this is not financially viable as the SLNB would not be paid for by the medical insurance companies.

Methods. Forty consenting patients were enrolled in the audit. The initial 5 patients (group A) were entered into a traditional audit – an ALND and a SLNB. The next 35 patients (group B) formed part of a modified audit – an axillary sample was performed if the sentinel node was negative (group B1) and an ALND if the node was positive (group B2).

Results. Ninety-two per cent of patients with an ipsilateral sentinel axillary node on preoperative scintigraphy had their node identified at the time of surgery. Eight patients had evidence of lymphatic spread. Two patients had parasternal sentinel nodes which were not removed. Group A had a mean of 10.8 nodes removed, group B1 5.8 nodes, and group B2 13.2 nodes. Twenty-three of 35 patients (66%) in group B were spared an axillary dissection.

Conclusion. The modified audit of group B allowed patients to benefit from the procedure (and thus the medical aids charged) and yet permitted our team to ascertain the accuracy of the technique in our hands. We feel this is an approach that may be used by other surgeons working alone.

S Afr Med J 2007; 97: 451-455.

In the 1960s sentinel lymph node biopsy (SLNB) was described[1] as a technique for detecting spread from parotid cancer. More recently it has been accepted as standard management in early breast cancer, but with some reservations.[2,3] Axillary lymph node dissection (ALND) has been used as the gold standard for staging the axilla in patients with breast cancer. When compared with ALND, SLNB may not always reflect the true status of the axilla. In large series, false-negative rates of 11% have been noted.[4,5] This decreases with the experience of the team. Morrow *et al*.[6] found that when a team had performed SLNB in less than 10 patients, the success rate was 70%. This increased to 91% if the team had performed more than 30 SLNBs. A questionnaire sent to a random 1 000 surgeons in the USA showed that 30% of surgeons performed only 10 audited cases before relying solely on a SLNB, and 3% of surgeons performed no audit presuming that a SLNB performed by them reflected the true axillary status.[7] As a result, it has been recommended that each surgeon (and the team involved) perform both a SLNB and an ALND on a number of cases before relying solely on a SLNB. For example, the New Start programme in the UK[8] trains teams around the country; after training the teams submit their first 30 cases as an audit.

Surgeons working alone in private practice have financial constraints, making a traditional audit of patients impractical. We do not have the infrastructure associated with a large centre and are limited by the constraints of medical insurance companies. If both an ALND and SNLB were performed, the medical insurance companies would not cover the extra expense of an additional procedure.

We performed a modified audit of our first 40 cases based on the UK experience from the Axillary Lymphatic Mapping Against Nodal Axillary Clearance (ALMANAC) Trial.[9] We modified the audit, along the lines of the current New Start programme, to suit our needs in private practice. This allowed our patients to benefit from the SLNB technique, yet enabled us to validate our results.

Methods

Study population

Women with clinically node-negative breast cancer presenting to a single surgeon in private practice in Cape Town (JE) were invited to participate. They were all asked to sign informed consent. The target number of patients for the audit was 40. The inclusion criteria were patients with proven invasive breast cancer and clinically node-negative axillary examination. Breast cancer was diagnosed histologically with a core biopsy if the patient was to have a mastectomy; a triple test (cytology,

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radiology and clinical) in which all the results suggested a malignancy was considered to be diagnostic for a wide local excision. In cases of an impalpable tumour or if there was diagnostic ambiguity, a preoperative excision biopsy was performed. Exclusion criteria included evidence of axillary spread, pregnancy, neoadjuvant chemotherapy or tumours larger than 35 mm.

The mean (± standard deviation (SD)) age was 52 ± 13 years. The mean tumour size was 14.4 ± 6 mm. Fourteen of the tumours (35%) were 10 mm or less. Thirty-one tumours (77.5%) were classified as ductal carcinoma, and 9 (22.5%) as lobular carcinoma.

Method of sentinel node biopsy

A preoperative radionuclide scan was performed to ascertain the number of nodes and their position. The scan was performed a day before the scheduled surgery. All patients were injected with 50 - 80 MBq of 99m Technetium nanocolloid using small volume injections of 0.3 - 0.4 ml. Injections were given intratumourally in patients with a palpable lump. In patients who had undergone excision biopsy before the scan, 2 injections were given in subcutaneous tissue around the tumour site about 2 cm away from the surgical scar, on either side.

A dynamic/flow study was performed after completion of injection of the radiotracer to demonstrate the migration of the radiotracer from the injection site/s as cine images. The study was done from the lateral view at 20 seconds per frame for 20 minutes, with the patient in a supine position with the ipsilateral arm raised above the shoulder. A set of the same images was done at about 2 hours post injection to confirm the site of the sentinel node. After completion of delayed images, positions of all visible lymph nodes were marked on the skin in both the anterior and lateral planes.

At the time of surgery, the pre-marked nodes were scanned using a portable gamma probe. After induction of general anaesthesia, a volume of 0.5 - 1 ml of methylene blue or Patent Blue V (subject to availability) was injected in the sites as described above. During surgery, if a blue lymphatic channel was identified, it was traced and the blue sentinel node identified. The gamma probe was used to confirm that the node was radioactive, both *in vivo* and *ex vivo*. If a blue node was not seen, the gamma probe alone was used to identify the radioactive lymph node. In case of more than 1 node, 10 second counts for node-to-background were done. The axilla was considered to be clear of all the potentially involved nodes when all the nodes with 10% or more of the *ex vivo* count of the sentinel node had been removed.

The nodes removed were tested for metastatic spread using a frozen section and cytological imprint technique. Any node smaller than ±8 mm (longitudinal axis) was bisected and imprinted on both sides; one half was frozen and sectioned. Larger nodes were sectioned with a microtome blade at 3 mm intervals, all slices were imprinted on both sides, and 1 slice was frozen for histological section. All intraoperative diagnoses were confirmed by paraffin imbedding and serial sectioning of all the lymph node tissue. The haematoxylin and eosin stain was used for both histological and cytological samples. Immunohistochemical cytokeratin stains (AE1/AE3) were not used routinely, but were performed in suspicious cases only. This technique represented a cost-effective and reproducible methodology.[10]

The audit was performed in two parts. The first 5 patients (group A) were all subjected to an ALND after identification of the sentinel node. Their nodes were tested postoperatively and they were not charged for the procedure. The next 35 patients (group B) were subjected to axillary sampling if the node was negative (group B1) and an ALND if the node was positive for metastatic spread (group B2). Sentinel node sampling involved removing nodes from around the sentinel node. The aim was to remove a total of 4 nodes. In the case of the sentinel nodes being pararsternal or when the surgeon was not adequately convinced that the sentinel node had been found, the patient had an ALND.

Statistical analysis

Analysis of the data was performed using StatXact 4. For comparison of the number of nodes removed, the Wilcoxon rank-sum test was used. The chi-square goodness-of-fit test was performed to evaluate the actual rates versus the expected results.

Results

Forty-one women were asked to participate. One woman opted for an ALND. Forty women took part in the audit.

The primary breast surgery performed was mastectomy in 14 patients (35%) and wide local excision in 26 (65%). Eight patients (20%) had had a diagnostic excision biopsy preoperatively.

All patients had nodes visible on the preoperative scan, although 1 was very faint. Scinigraphy showed 2 patients to have parasternal sentinel nodes and 38 patients to have a sentinel node in the ipsilateral axilla. The mean time between preoperative injection and surgery was 23.3 ± 0.34 hours.

Thirty-five patients (92%) with an ipsilateral axillary sentinel node had their node successfully located intraoperatively (Table I). The 2 patients with parasternal sentinel nodes had an ALND. Three patients did not have any 'hot' nodes intraoperatively. One had her node totally replaced by tumour, another had her node obscured by the biopsy cavity in the tail of the breast, and the third patient (with a faint preoperative scan) had complete fatty replacement of her nodes histologically. All 3 patients had an ALND (Table II).

Table I. Size of tumour and SLNB results

Tumour size (mm)	Type of cancer	No. of patients	Failed	Sentinel node-positive
≤ 5	Ductal	3	1	0/2
	Lobular	0		
5 - 10	Ductal	7	2	0/5
	Lobular	4	0	1/4
10 - 20	Ductal	18	2	4/16
	Lobular	5	0	1/5
20 - 30	Ductal	2	0	0/2
	Lobular	0		
> 30	Ductal	1	0	1/1
	Lobular	0		
Total		40	5	7/35

SLNB = sentinel lymph node biopsy.

Of the 35 patients who had their nodes located intraoperatively, 28 were found to contain no evidence of metastases. A total of 7 patients had evidence of metastatic spread to their sentinel node. They were all from group B and underwent an ALND (group B2). A mean of 13.2 ± 5 nodes were removed. No patients in group A had metastatic spread and a mean number of 11 ± 5 nodes were removed. In group B1, a mean of 6 ± 3 nodes were removed (Table III). The mean stay in hospital was 3.4 ± 3 days for the group that had axillary sampling and 6.5 ± 1 days for the group that had an ALND.

The positive predictive value of SLNB was 100%. When the node was successfully identified, the negative predictive value was 100%. There were no significant complications related to the axillary surgery in either group.

Discussion

The primary role of axillary surgery in early breast cancer is to stage the patient's disease status accurately. This should be done with minimal morbidity. SLNB is a technique associated with less complications than a standard ALND;[11,12] however, before implementing any new technique a surgeon must be certain of the accuracy of the procedure in his or her hands.

Table II. Reasons for unsuccessful SLNB

Reason for failed identification	No. of patients
Parasternal nodes	2
Node replaced by tumour	1
Obscured by biopsy cavity	1
No significant uptake	1
Total	5

SLNB = sentinel lymph node biopsy.

In the UK, as a result of the ALMANAC trial, the New Start programme[8] has been set up to facilitate the training of breast surgeons in the technique of SLNB. The programme consists of a training day followed by supervision in the trainee surgeon's hospital for the first 5 patients undergoing SLNB. The surgeon then has to complete an audit of a further 25 cases in which both a SLNB and either an ALND or axillary sampling are performed. This allows standardisation of the procedure.

For surgeons working alone, it can be difficult to accrue the number of patients to take part in an audit where both an ALND and a SLNB are performed. Private insurance companies cannot be expected to fund an 'extra' procedure. We performed 5 SLNB with ALND without passing the cost on to the patient while we standardised our approach, and then did a further 35 patients who had a SLNB and then had either axillary sampling or an ALND depending on the status of the sentinel node. In doing this we have modified the New Start training programme, which was not accessible to us in South Africa, in a way that allows any surgeon working alone to be able to demonstrate the accuracy of SLNB in their hands.

In our practice, although a SLNB adds approximately R4 000 ($651 based on a rand/dollar exchange rate of R6.41/$ in February 2006) to the cost of the procedure, we have shown it to be cost effective. A SLNB decreases the overall cost

Table III. Number of nodes removed from patients with successful intraoperative SLNB

	Surgery	Number of patients	No. of nodes removed (±SD)
Group A	ALND	5	10.8 (±5)
Group B (pos)	ALND	7	13.2 (±5.5) } **
Group B (neg)	Axillary sampling	23	5.8 (±3) } **

**Significant difference $p < 0.04$.
SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection; SD = standard deviation.

of hospital admission by reducing the average number of days as an inpatient. In our series those who were spared an ALND stayed for 3 days less than those who had an ALND. This represented a saving of approximately R3 000 ($488) per patient. Patients who did not have an ALND did not have a suction drain, saving a further R750 ($122). (The cost of a modified radical mastectomy is approximately R20 - 25 000 ($3 257 - 4 071), and a wide local excision and axillary dissection R15 - 20 000 ($2 443 - 3 257)).

Axillary sampling is a technique that has been shown to accurately reflect the status of the axilla. A consistent finding has been that accuracy increases if 4 or more nodes are removed and there is less morbidity than with an ALND.[13,14] We removed an average of 5.8 nodes (Table III) and used the location of the sentinel node to guide us to our area of sampling. We believe it provided a reasonable assessment of the axillary status for audit purposes. The patients who had an ALND (groups A and B2) had significantly more nodes removed than those with axillary sampling (group B1).

Only 8 patients had evidence of spread to the axilla. Silverstein evaluated the number of patients who would be expected to have axillary involvement and found it to be dependent on tumour size and whether the tumour was palpable at the time of presentation.[14,15] Table IV looks at the expected and actual results. There was no significant difference in our results.

Ideally, a preoperative diagnosis of breast cancer is made without a formal excision biopsy. However, Wong *et al*. have shown that SLNB may be successfully carried out even if an excision biopsy has been performed.[16] Eight patients had a prior breast biopsy. In 1 case the cavity did obscure the sentinel node. The tumour was in the axillary tail.

The approach to patients whose sentinel node is in the internal mammary chain is controversial. Surgically identifying the node is justified if the status of the node would change the staging of the cancer and thus the adjuvant treatment. Fabry *et al*. suggest that that is not the case.[17] However, the classification of breast cancer has been changed during the time of the audit to take account of the parasternal node status.[18] We now aim to remove a parasternal sentinel node.

Fourteen patients had a mastectomy – 8 had multicentric tumours and 3 widespread ductal carcinoma *in situ* (DCIS). Three patients requested mastectomy as they did not wish to have radiotherapy. SLNB has been shown to be accurate in patients with multicentric disease.[19]

The pathological technique adopted, which included both intraoperative imprint cytology and frozen section of thin (2 - 3 mm) slices of the sentinel node(s), has been shown to increase the sensitivity of intraoperative assessment.[20] The major weakness of intraoperative assessment of sentinel nodes is a described low sensitivity for micrometastases (< 2.0 mm) and metastatic lobular carcinoma.[21] The frozen section histological evaluation, in addition to the cytological evaluation assists in the assessment of lobular carcinoma. There were no false-negative cases of metastatic lobular carcinoma in this group. Immunohistochemical cytokeratin staining was not routinely performed in this study, and although no false-negative cases of micrometastases were found, routine cytokeratin staining may have increased the pick-up rate, on paraffin-fixed tissue, for micrometastases.[22] However the prognostic, predictive and clinical significance of occult micrometastases (< 2. 0 mm) is controversial.[20]

We have audited our first 40 SLNB patients and have done so while allowing the patient to benefit from the procedure. No patients had any complications from SLNB, and in our hands there were no false-positive results. We have shown that a formal training programme, such as New Start, can be modified and applied to surgeons working in isolation around the world. We feel it is a useful, safe and cost-effective approach that could be followed by other surgeons working alone in private practice thus allowing them to demonstrate the accuracy of SLNB in their hands.

With thanks to Dr E Panieri, Groote Schuur Hospital, Cape Town, South Africa.

Table IV. Comparison of expected and observed number of patients with axillary involvement

Tumour stage	Palpable/non-palpable	Predicted axillary involvement	No. of patients	Expected in sample (*N*)**	Observed in sample (*N*)**
T1a	Non-palpable	4%	1	0.04	0
	Palpable	6%	2	0.12	0
T1b	Non-palpable	7%	1	0.07	0
	Palpable	23%	10	2.30	1
T1c	Non-palpable	16%	2	0.32	1
	Palpable	31%	21	6.51	5
T2	Non-palpable				
	Palpable	48%	3	1.44	1
		40		10.8	8

**No significant difference between these two groups (*p*-value = 0.8).

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Accepted 11 April 2007.