Sentinel lymph node biopsy: An audit of intraoperative assessment after introduction of a cytotechnology service

J Edge,[1] MB BChB, BSc, FRCS, MMed (Surg); **N Lloyd**,[2] MB BChB, MSc, DTM&H, MRCS; **C van der Velde**,[3] MT; **J Whittaker**,[3] MB ChB, MMed (Anat Path), FIAC

[1] *Christiaan Barnard Memorial Hospital, Cape Town, South Africa*
[2] *Plastic Surgery Registrar, John Radcliffe Hospital, Oxford, UK*
[3] *Well Woman Diagnostics, Cape Town, South Africa*

Corresponding author: *J Edge (jmedge@mweb.co.za)*

Objective. To audit results from intraoperative assessment of sentinel lymph node biopsy (SLNB) after the introduction of a cytotechnologist.
Study design. Since 2010, a cytotechnologist has been involved in the intraoperative assessment of SLNB in our breast cancer patients. The data from patients over the period 2006 - 2013 were used to compare outcomes before and after the introduction of a cytotechnology service. The database was divided into the periods 2006 - 2008 and 2010 - 2013 (2009 was the training period).
Results. A total of 335 intraoperative SLNB assessments were performed: 165 between 2006 and 2008 (group 1) and 170 between 2010 and 2013 (group 2). In the study period (2010 - 2013), 2 (1%) metastatic deposits >2 mm were missed in patients with lobular carcinoma and 1 in a patient with ductal carcinoma. There was one (0.6%) false positive in a patient with a lobular carcinoma in each group. For patients with metastases >2 mm, group 1 had a sensitivity of 87% and a specificity of 99%. Group 2 had a sensitivity of 92% and a specificity of 99%.
Conclusion. A trained cytotechnologist performing imprint cytology on SLNB to determine metastatic breast cancer can deliver results comparable with those of a group of pathologists.

S Afr J Surg 2015;53(2):47-49. DOI:10.7196/sajsnew.7850

Sentinel lymph node biopsy (SLNB) has become routine for the management of node negative melanoma and breast cancer since its introduction in 1990. SLNB use in other malignancies including colorectal, oesophageal, non-small cell lung and thyroid cancers is being researched but is not yet standard practice.[1]

The use of SLNB in breast cancer management has evolved and landmark trials have shaped the use and understanding of its role.[2-4] In 1999 the College of American Pathologists released

a consensus statement on pathological factors in breast cancer.[5] Among the recommendations, the college proposed that the sentinel lymph node (SLN) could be examined intraoperatively with macroscopic examination plus imprint cytology rather than with frozen section. This minimises tissue sample loss (required for cryostat studies), leaving greater tissue volumes for subsequent analysis. Imprint cytology permits more thorough sampling of large or multiple specimens and carries a 90.9% sensitivity, 98.5% specificity and 96% overall accuracy.[5] Postoperatively, all sentinel node tissue should be evaluated using standard paraffin blocks and immunohistochemistry for micrometastases. Although technicians are utilised for the preparation of the intraoperative slides, we are not aware of any studies utilising technicians rather than pathologists for the intraoperative assessment of the node. The aim of this study was to assess whether the intraoperative assessment of SLNB by imprint cytology for carcinoma of the breast can be adequately and safely performed by a trained cytotechnologist. Sensitivity and specificity was compared with the results produced by a group of cytopathologists.

Methods

The study cohort was taken from breast cancer patients presenting to a single surgeon. All patients who were clinically and radiologically node negative with an invasive cancer less than 5 cm in diameter and had not had neoadjuvant treatment had a SLNB. Some patients with ductal carcinoma *in situ* (DCIS) were included: those who were known to have high-grade disease, those who had areas of disease greater than 4 cm radiologically or those having a mastectomy.

Since 2011, as a result of the findings from the American College of Surgeons Oncology Group,[6] the authors no longer perform intraoperative assessment for those patients undergoing radiotherapy postoperatively, as lymph node clearance yields no survival benefit in these patients. This change does not affect the comparison criteria of the two groups.

Data were collected retrospectively from 2010 to 2013 analysing the intraoperative cytological findings using imprint cytology by the trained cytotechnologist. The true negatives and positives and false negatives and positives were compared with the post-operative histological report produced by the pathologists. Sensitivity and specificity were compared with a historical control group from 2006 to 2008 over which period both intraoperative and postoperative assessments were performed by a group of cytopathologists. All data from 2009 were excluded since this was the period of training of the cytotechnologist and both technologist and the pathologist were in attendance for the intraoperative assessments. Three pathologists were involved in the initial assessments prior to 2009 (Group 1). There was one trainee cytotechnologist (who had 30 years' experience) and two pathologists involved in the training period. The single cyto-technologist assessed all the nodes in Group 2.

Each lymph node submitted intra-operatively was serially sectioned at 2 - 3 mm intervals. The cut surface of the node was imprinted onto a glass slide and then stained with a rapid standard Papanicolaou staining technique. The slides were methodically examined under the microscope to assess the presence or absence of metastatic tumour cells. A verbal result was given to the surgeon: positive, negative or inconclusive. All the lymph nodes were then placed in buffered formalin and taken to the laboratory for formal processing: paraffin embedding, staining with haematoxylin and eosin, microscopic assessment and immunohistochemical analysis utilising a pan-epithelial marker (AE1/AE3) for micrometastatic disease.

The methodology of each of the

Table 1. Types of cancer in either group

	Total number (*N*)	DCIS, *n* (%)	Ductal cancer, *n* (%)	Lobular cancer, *n* (%)	Other, *n* (%)
Group 1 2006 - 2008	165	18 (11)	123 (75)	21 (12)	3 (2)
Group 2 2010 - 2013	170	19 (11)	135 (80)	14 (8)	2 (1)

DCIS = ductal carcinoma in situ.

Table 2. Intraoperative assessment of SLNB in the periods 2006 - 2008 compared with 2010 - 2013

	Total (*N*)	True negative, *n* (%)	True positive, *n* (%)	False negative mets*, *n* (%)	False negative micromets†, *n* (%)	False positive, *n* (%)
Group 1	165	121 (73) CI 66 - 80	34 (21) CI 15 - 28	5 (3) CI 1 - 7	4 (2.5) CI 1 - 6	1 (0.5) CI 0 - 3
Group 2	170	118 (69) CI 62 - 76	39 (23) CI 17 - 30	3 (2) CI 0.5 - 6	9 (5) CI 2 - 10	1 (0.6) CI 0 - 3

CI = confidence interval.

*mets: metastatic deposits >2 mm.

†micromets: metastatic deposit <2 mm.

Table 3. Patient with nodal involvement

	Metstases >2 mm (*N*)	True positive, *n* (%)	Micrometastases <2 mm (*N*)	True positive, *n* (%)
Group 1	39	34 (87) CI 72 - 96	4	0 (0)
Group 2	42	39 (92) CI 80 - 98	10	1 (10)

pathologists may have differed slightly initially, but the method was standardised when the cytotechnologist was trained. During the training period, the technologist would be given a bank of previously prepared slides with results, to study. She was then taken into the theatre laboratory where every sentinel node was submitted and assessed. The slides were analysed by the trainee under supervision and rescreened by the training pathologist before the result was conveyed to the surgeon. Once the technologist was assessed as competent, i.e. no discrepant results for at least a 2 month period, she became the primary intraoperative cytology assessor. All her slides were subsequently taken to the laboratory for rescreening and comparison with the ultimate definitive histology results.

Results

There were a total of 335 intraoperative assessments of SLNB performed: 165 between 2006 and 2008 (group 1) and 170 between 2010 and 2013 (group 2). The case-mix of cancers in both groups was comparable (Table 1).

In group 1, 39 patients had a positive node with a metastatic deposit of >2 mm and 4 patients had micrometastases (<2 mm). In group 2, 42 patients had metastases >2 mm and 10 had micro-metastases.

Overall, in the study period, the true negative rate was 69% and the true positive rate was 23%. This compares favourably with 73% and 21% in the control group. In the study period (2010 - 2013), 2 (1%) metastatic deposits >2 mm were missed in patients with lobular carcinoma and one in a patient with ductal carcinoma. There was one false positive (0.6%) in a patient with a lobular carcinoma in each group (Table 2).

For patients with metastases >2 mm, group 1 had a sensitivity of 87% and a specificity of 99%. Group 2 had a sensitivity of 92% and a specificity of 99%. In group 2, there were more patients with micrometastatic disease (10 compared with 4 in group 1). In the study group, one patient had their disease identified (Table 3).

Discussion

Since 2003, imprint cytology has been used for intraoperative assessment of the SLN. Initially, this was done by a cytopathologist. A cytotechnologist has been used since 2010 after 1 year of training. Our study demonstrates that a suitably trained cytotechnologist is able to produce reliable intraoperative assessment of a sentinel node in a selected group of breast cancer patients.

In the early days of clinical pathology the medical pathologist would often have an assistant as an apprentice. As cytopathology developed, largely as a result of the widespread use of the cervical smear or 'Pap' test, this apprentice position was formalised. In 1957, the post of cytotechnologist was registered and subject to entry by examinations set by the American Society of Clinical Pathology. The position was further formalised in 1962, when essential standards were qualified and adopted by the American Medical Association.[6] The traditional role of the cytotechnologist is to prepare specimens, examine slides, note any cellular changes providing an initial interpretation and submit to a pathologist for a final evaluation.[7] Cytotechnologists now perform a greater array of specialised investigations such as immunohistochemistry, cytogenetics, *in situ* hybridisation, flow cytometry and polymerase chain reaction.[8]

Two recent studies using cytotechnologists to provide immediate on-site adequacy assessments for pancreatic and thyroid tissue, yielded accuracy of results comparable with those of a cytopathologist.[9,10] Affording cytotechnologists the opportunity to assess tissues creates a new role for these allied health professionals. Furthermore, cost savings are realised for patients and the healthcare system.[11]

The role of the cytotechnologist looks set to grow in light of these increasingly evident advantages.[12] It is important, however, to bear in mind the suggestions of Clary *et al*.[13] that the results of the cytotechnologist must be monitored for discrepancies with the pathologist to ensure standards are maintained. Central to this is establishing communication and feedback between the two disciplines of cytotechnology and cytopathology, which will ensure continued development of both.[14]

REFERENCES

1. Chen SL, Iddings DM, Scheri RP, Bilchik AJ. Lymphatic mapping and sentinel node analysis: current concepts and applications. CA Cancer J Clin 2006;56(5):292-309.
2. Black DM, Mittendorf EA. Landmark trials affecting the surgical management of invasive breast cancer. Surg Clin North Am 2013;93(2):501-518. [http://dx.doi.org/10.1016/j.suc.2012.12.007]
3. Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer: A multicenter validation study. N Engl J Med 1998;339(14):941-946. [http://dx.doi.org/10.1056/NEJM199810013391401]
4. Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: A randomized clinical trial. JAMA 2011;305(6):569-575. [http://dx.doi.org/10.1001/jama.2011.90]
5. Fitzgibbons PL, Page DL, Weaver D, et al. Prognostic factors in breast cancer: College of American Pathologists Consensus Statement 1999. Arch Pathol Lab Med 2000;124(7):966-978.
6. Naik K, Zaleski S. Cytotechnology: A profession on the move – then and now. Lab Med 2008;39(4):201-206.
7. Russell WO. Technologist-pathologist relationships and role of American Society of Clinical Pathologists. Tech Bull Regist Med Technol 1966;36(9):217-220.
8. Kane LE, Root RR, Voss JS, et al. Molecular diagnostics, personalized medicine, and the evolving role of the cytotechnologist: An institutional experience. Acta Cytol 2012;56(6):678-685. [http://dx.doi.org/10.1159/000341169]
9. Olson MT, Tatsas AD, Ali SZ. Cytotechnologist-attended on-site adequacy evaluation of thyroid fine-needle aspiration: Comparison with cytopathologists and correlation with the final interpretation. Am J Clin Pathol 2012;138(1):90-95. [http://dx.doi.org/10.1309/AJCP84AXSRABZCTZ]
10. Olson MT, Ali SZ. Cytotechnologist on-site evaluation of pancreas fine needle aspiration adequacy: Comparison with cytopathologists and correlation with the final interpretation. Acta Cytol 2012;56(4):340-346. [http://dx.doi.org/10.1159/000338646]
11. Wotruba AL, Stewart J 3rd, Scheberl T, Selvaggi SM. Added value, decreased cost: The evolving role of the cytotechnologist for preliminary screening and triage of thyroid aspirates. Diagn Cytopathol 2011;39(12):896-899. [http://dx.doi.org/10.1002/dc.21487]
12. Keebler CM. The future role of the cytotechnologist. Acta Cytol 1977;21(5):655-657.
13. Clary KM, Davey DD, Naryshkin S, et al. The role of monitoring interpretive rates, concordance between cytotechnologist and pathologist interpretations before sign-out, and turnaround time in gynecologic cytology quality assurance: Findings from the College of American Pathologists Gynecologic Cytopathology Quality Consensus Conference working group 1. Arch Pathol Lab Med 2013;137(2):164-174. [http://dx.doi.org/10.5858/arpa.2012-0120-CC]
14. Whigham P, Ilario MJM, Flanagan MB, Mauser N, Raab SS, Ohori NP. Discrepancy analysis, communication, and feedback for cytotechnologist quality improvement of nongynecologic cytopathology. Diagn Cytopathol 2006;34(4):265-269. [http://dx.doi.org/10.1002/dc.20456]