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A comparison of large block macrosectioning and conventional techniques in breast pathology

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Abstract Two techniques for the histological handling of breast specimens, namely conventional sampling using small blocks (SB) and a large block (LB) macrosectioning technique have been compared, with special emphasis on tumour size and in situ carcinoma, in an attempt to objectively demonstrate the advantages of the latter method. This is considered to be of particular importance in guiding the clinicians in their use of the many treatment modalities available for breast carcinoma. All cases were from the routine surgical caseload; 100 examined by the LB technique and 111 using conventional SB. The LB technique gave a reliable measurement of invasive carcinoma in 100% of cases compared to only 63% of SB cases. Ductal carcinoma in situ (DCIS), was found more frequently (80% versus 64%) and its extent was more easily and reliably measured in the large blocks. The extent of DCIS was significantly greater in all cases using large block techniques. Concurrent carcinomas were found more frequently in the LB series and these tumours were smaller than those in the SB series. Similar differences were noted with radial scars, and other proliferative lesions also had a higher incidence in the LB series. We conclude that the LB technique has sufficient advantages to recommend it as a standard technique in breast pathology.

Key words Breast carcinoma
Conventional block · Large block
Ductal carcinoma in situ · Prognostic factors

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Introduction

The implementation of a national breast screening programme in the UK has resulted in an increased number of early or impalpable breast lesions being removed. This has coincided with a tendency towards less radical surgery and increasing refinement of treatment depending on factors which are largely derived from histological assessment. These include the grade, size and type of the tumour and the presence, type and extent of any in situ component. Information on the completeness of excision by assessment of margins is also becoming essential. As a result, methods of eliciting this information using conventional histological techniques have been evolved and are being adopted. However they are time consuming and, in order to be accurate require very laborious application.

The alternative method of examining large sections of the whole extent of the breast has been recommended and adopted by few. The authors have all been involved with large block (LB) macrosectioning and feel that it provides far superior information regarding invasive carcinoma, in situ disease and the interrelationship of these changes in the breast. A macrosection is also a powerful and convincing tool when demonstrating pathology to clinicians and students. However before recommending the LB technique for breast pathology it is first necessary to demonstrate an advantage of this technique objectively, when applied to routine specimens.

We have assessed the validity of macrosectioning techniques by comparing the data derived from three centres. One is associated with a long established screening centre (Guildford) and uses macrosectioning methods. The other two use conventional techniques and comprise a London teaching hospital (St. George's) and a district general hospital (St. Helier's).

Methods

The cases examined were derived from the sequential routine surgical caseload from all three centres both screened and un-

screened, although the proportion of screened cases was higher at Guildford. Specimens less than 100 mm in maximum diameter were excluded so that cases would be of comparable complexity and so that a standardised routine could be applied to each case. In practice most cases were described as either segmental/wide local excisions or mastectomies. Specimens were included only if they contained a malignant tumour.

One hundred cases were examined from Guildford and compared with 50 cases from St. Helier and 61 cases from St. George's, a combined total of 111.

The procedure at Guildford is to examine specimens using large blocks. The other two centres examine specimens by recommended standard procedures and produce comparable material.

The authors are all familiar with, and have used, the procedures which are outlined below.

Macroscopical methods (LB)

The major difference with this method is that the breast tissue is sliced radially from the nipple (or the identified nipple aspect) through the main lesion. Radial slicing follows the radial anatomy of the breast (Fig. 1).

Mastectomies

These are sliced before fixation in a radial fashion, namely a section is taken through the nipple, skin, underlying breast tissue and deep margin radiating out to the tumour and peripheral breast. This section is fixed flat before processing, the maximum dimensions possible being 150×100 mm. Further slices are made through the rest of the breast tissue, firstly from the nipple at right angles to the original section, and additional LB are taken if the original tumour is poorly defined or if any other pathology is identifiable in the other segments. Small blocks (SB) are also taken of the tumour, unless it is so small that it is entirely within the LB, and also of the nearest resection margin if not included in the plane of the macrosection.

Segmental/wide local excision

The approach to these specimens is similar. The specimens are received fresh with sutures to aid orientation. A macrosection is made radially from the nipple end of the specimen through the tumour to the periphery. A SB is taken of the lesion. The proximity of the margin is measured, and SB taken as needed.

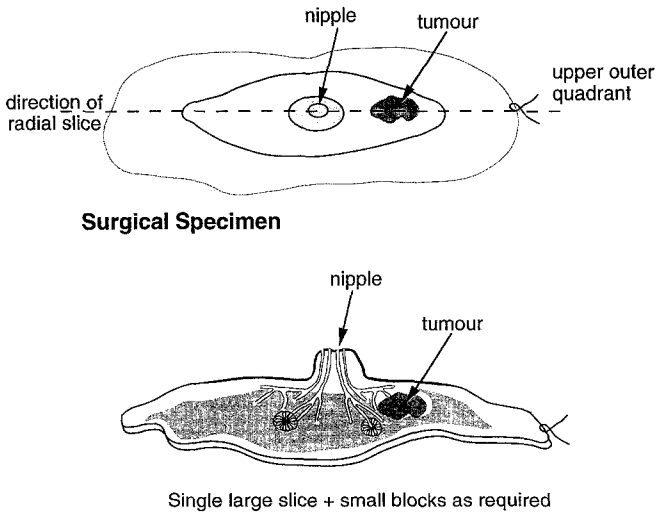

Fig. 1 Surgical specimen with orientation suture and corresponding large slice

Localisation biopsies of impalpable tumours

These are received unfixed with marking sutures and a specimen X-ray. A radial slice is made from the nipple end of the specimen through the area containing the abnormality. If the lesion is apparent on the cut surface only the relevant slice is processed. If the identification of the lesion is still in doubt both halves of the specimen are taken for processing. Whenever the tumour or area of calcification, which is being sought surgically, is not apparent microscopically, the blocks and any residual tissue are X-rayed and the radiographs compared with the mammogram and specimen films.

The large slices are fixed for 24 h and then processed in a standard histokinette using a 48 h processing time. They are part cleared in chloroform and impregnated with a polymer paraffin wax. The blocks are then cut on a Jung tetrander sledge microtome at 4–5 μm. The total time for production of the stained slides is 3 days. SB are processed and cut with the routine work. Examples are shown in Fig. 2 and Fig. 3.

Macroscopical methods (conventional SB)

[Standard methods as recommended in the Association of Clinical Pathologists (ACP) broadsheet Bogomoletz and Davies [4] are used at both centres]

Mastectomies The specimen is examined fresh or fixed by multiple sagittal slices. Three or more SB are taken from the tumour or lesion and then blocks from the nearest margin and nipple. Random blocks are taken from uninvolved quadrants.

Wide local/segmental excisions Multiple sagittal slices are made and SB are taken of tumour and margins as recommended in the ACP broadsheet [4].

Localisation biopsies Multiple sagittal slices are made and, if necessary, X-rayed. The relevant blocks are selected, and a detailed block key recorded, as outlined by Armstrong and Davies [3] and Anderson [1].

The SB produced are then processed with the routine work.

Microscopical methods

The haematoxylin and eosin sections for each tumour were evaluated and reviewed independently by at least two pathologists. Observations included details of the tumour, the in situ component and other proliferative lesions and margins of excision. In areas of disagreement the sections were re-examined and results obtained by discussion, thereby reducing the effects of inter- and intra-observer error. On the first review there was greater than 80% agreement and where there was a difference it was usually less than a 5% variance.

The tumours were classified in accordance with the booklet produced by the Royal College of Pathologists' working group [14]. The extent of any ductal carcinoma in situ (DCIS) component beyond the infiltrating margin of the tumour was measured. The surface area of tissue examined in each case was also measured. In addition, the time taken from the receipt of the tissue to issue of the report was noted.

The features given particular emphasis in this comparability study were: tumour size, DCIS and its extent and margins of clearance.

Results

The types, and sampling characteristics of specimens received at each centre are shown in Table 1. The samples received at the Royal Surrey County Hospital and

Table 1 Specimen and sampling characteristics (*LB* large block, *SB* small block, *RSCH* Royal Surrey County Hospital, *SGH* St. George's Hospital, *SHH* St. Helier Hospital, *Comb* Combined, *WLE* wide local excision, *na* not available)

	LB RSCH	SB SGH	SB SHH	SB Comb
Number of specimens	100	61	50	111
Mastectomy	37	54	32	86
WLE	63	7	18	25
Area examined (cm^2)	45	26	28	27
Number of blocks	1(+1)	8.4	6.6	7.6
Time of report (days)	9	5	na	5

Table 2 Types of tumour (*IDC* invasive ductal carcinoma, *ILC* invasive lobular carcinoma, *DCIS* ductal carcinoma in situ)

	LB RSCH	SB SGH	SB SHH	SB Comb
IDC (total number)	75	52	47	99
ILC (total number)	10	3	2	5
DCIS (total number)	9	5	1	6
Special types (total number)	6	1	0	1

Table 3 Dimensions of invasive tumours

	LB RSCH	SB SGH	SB SHH	SB Comb
Macroscopic size (mm)	17.8	37.8	27.5	31.6
Microscopic size (mm)	19.3	17.0	20.7	18.6
Number of cases assessable	100%			63%
Difference in macroscopic/microscopic	23%			25%

Table 4 DCIS and other lesions

	LB RSCH	SB SGH	SB SHH	SB Comb
IDC+DCIS-number (%)	60 (80%)	33 (64%)	30 (64%)	63 (64%)
Extent of DCIS (mm)	19.1	6.25	4.45	5.0
Concurrent tumours and average size (mm)	20 (20%) 5.42	9 (14.75%)	6 (12%)	15 (13.5%) 11.8
Ductal hyperplasia	24 (24%)	10 (16.4%)	5 (10%)	15 (14%)
Radial scars	6	0	1	1

St. Helier were somewhat smaller than those at St. George's, as St. George's had a higher proportion of complete mastectomy specimens. The distribution of tumour types is shown in Table 2. As is to be expected, the bulk of the lesions were invasive ductal carcinoma (IDC), but at Guildford there was a higher percentage of invasive carcinomas of special type. Results in the two groups were used to compare a number of parameters.

Tumour size

Firstly, the average macroscopic size of IDCs in the 75 LB cases was 17.8 mm (range 6–60 mm) and in the 99 SB cases 31.6 mm (range 5–190 mm). The microscopical dimension was readily assessable in all LB cases with an average of 19.3 mm (range 4–80 mm). The SB series yielded a measurable microscopic size in 72 of the 99 cases, but the retrospective assessment was judged as reliable in only 62 cases. Tumours greater than 35 mm were deemed unassessable on reviewing the histology due to the fact that a single block would not be able to accommodate such tumours. (In practice this would be overcome by taking blocks across the full width of tumour and indicating the orientation.) Overall the difference between macroscopic and microscopic tumour size (when available) showed a difference of 23% for the LB series (all larger) and 25% for the SB series (not reproducibly larger or smaller; Table 3).

DCIS

In relation to the DCIS component associated with the IDC a number of points are emphasised (Table 4). DCIS was observed in association with IDC in 60 of the 75 LB cases (80%) and in 63 of the 99 SB cases (64%). Using the χ^2 test this difference is not significant ($\chi^2=0.55$, $P>0.1$), however the extent of the DCIS was assessable in all LB cases and it extended beyond the main invasive tumour in 39 (52%) cases by an average of 19.1 mm (range 1–80 mm). In the SB series DCIS extended beyond the IDC in 36 cases (36.4%) but the extent was measurable in only 14 of these cases (39%), with an average of 5 mm (range 1–15 mm). The measured extent of DCIS in this group was significantly less than DCIS in the LB group ($t=2.3973$, $P<0.05$).

Additional lesions

Concurrent carcinomas were present in 20% of the LB specimens and in 13.5% of SB cases. It was noted that the size of these synchronous tumours in the LB series was markedly smaller (5.4 mm versus 11.8 mm, Table 4). In addition, the incidence of other proliferative changes was significantly different. Twenty-four out of 100 LB cases (24%) and 15 out of 111 SB cases (14%) showed epithelial hyperplasia ($\chi^2=3.84$, $P\geq0.05$). Radial scars were noted in 6 LB cases and only one was found in the SB cases ($\chi^2=4.26$, $P<0.05$).

The surface area examined by the LB method was much larger, even though the specimens in the LB series were, on average, smaller and so proportionately a much larger surface area for a given volume of breast tissue was examined. The time taken from receipt of the specimen to issue of a report was longer with the LB technique (Table 1).

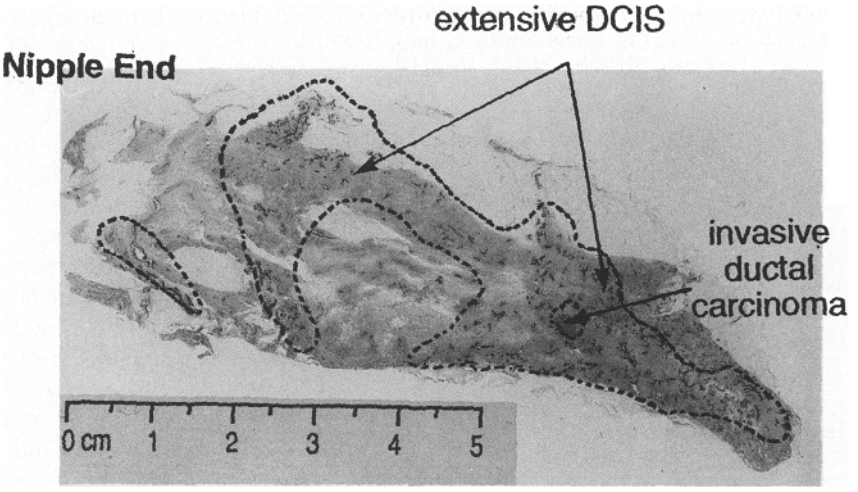

Fig. 2 Large section showing extensive ductal carcioma in situ; (DCIS 83 mm) and containing a small invasive carcinoma (4 mm)

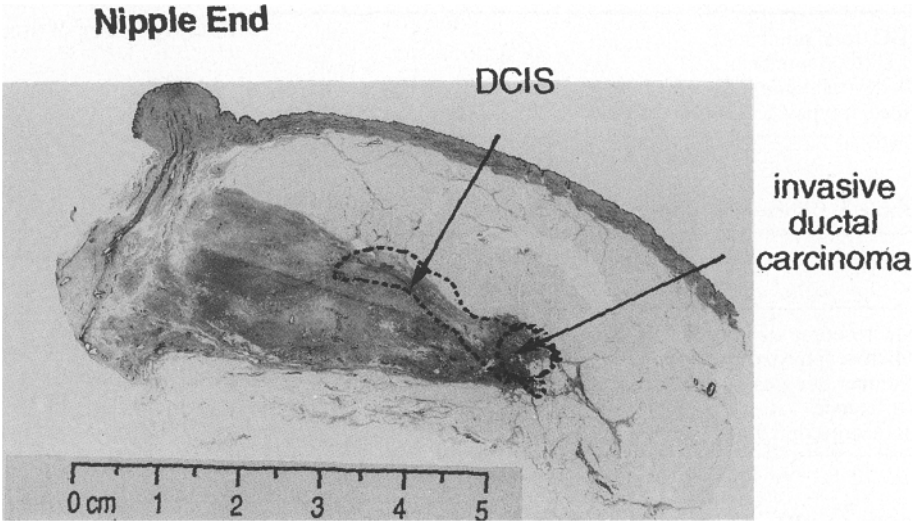

Fig. 3 Large section showing an invasive carcinoma (8 mm) and DCIS extending beyond the invasive carcinoma by 21 mm

Discussion

Many of the prognostic factors used in assessing breast carcinomas rely on detailed histopathological examination of specimens. The assessment is of considerable importance in view of the number of treatment modalities now available and the way they can be combined depends on pathological data.

In performing this work we acknowledge that the patient populations are not directly matched nor could they be because the study involved three centres, each with its own accepted working practice, both surgical and pathological. However the comparisons made are between the methods used in day to day practical reporting of routine surgical cases from three geographically close areas and those at St. George's and St. Helier are probably typical of procedures in most departments. The pathologists at these centres have either worked together or trained together and use similar methods for examination and reporting. The authors have all used the LB technique and have worked in at least two of the three centres. For these reasons we feel that the overall conclusions based on the comparisons are valid.

Many studies have shown that the size of an invasive tumour is an important prognostic factor [5, 9, 11, 12]. Our study shows that the gross assessment of size is inaccurate, in all three centres, by up to 25%. In the SB series the difference in measured size was not predictable suggesting that the error was in the macroscopic measurement rather than due to differences in processing. In the LB series the macroscopic size was on average an underestimate of the final measurement made on the stained large section, suggesting that a large block provides a better representation of the disease state. In the SB series, however, up to 37% of cases had microscopic measurements that were unreliable in the absence of complex labelling techniques since the tumour was too large to fit in one cassette. The overall smaller size of tumours in the LB series is probably related to their derivation from a screened population. Tumours in screened populations have been shown to be smaller [1, 8].

Ductal carcinoma in situ, the likely source of many recurrences, was found with a higher frequency and greater measured extent in the LB series. Furthermore the extent of DCIS was not assessable in 61% of SB cases. The true dimension of DCIS is unlikely to be demonstrated by a SB approach that cuts across the duct system at right angles unlike the LB system that samples the breast radially, and in which DCIS can be easily measured and more importantly related to any invasive component and the margins of the specimen. Extensive DCIS has been shown to be an important factor linked with local recurrence and greater incidence of multicentric tumours [6, 8]. Lagios et al. [10] demonstrated that DCIS over 26 mm diameter is associated with a threefold increase in multicentric tumours, and Schmitt et al. [13] indicates that the majority of recurrent carcinomas following excisional biopsy represent failure to control the primary disease rather than new tumours.

Our LB series demonstrated a higher frequency of concurrent invasive carcinomas, despite there being fewer mastectomy specimens. Furthermore the LB technique appears to be a more sensitive means of detecting concurrent carcinomas as is indicated by the smaller microscopic size of many of the tumours compared to those at the other centres which were usually obvious macroscopically. A similar finding was noted for radial scars and ductal hyperplasias.

Assessment of completeness of excision is a pathological detail of prime importance particularly as limited resection is becoming an increasingly popular mode of treatment. The LB technique provides a simple, easy to understand record of the relationship of invasive and in situ carcinoma to the margins of the specimen. It is worth noting that the LB, with their larger surface area, display a greater proportion of the excision margin and that the radial nature of the examination delineates the relevant duct system involved by DCIS. A margin at right angles to the duct system is only of importance in relation to an expansile tumour. In our SB series we were often not able to identify the blocks representing margins; however surgical reports prepared contemporaneously did state completeness of excision. The SB procedure relies on accurate macroscopic recording of the location of each block and must be kept as a permanent record. It is not easy to piece together the spatial relationships of tumour and magins and, as we have shown, the extent of DCIS is not accurately assessed in 61% of cases, making reliable assessment of clearance magins low or impossible. Frazier et al. [7] have shown in patients undergoing re-excision following a previous segmental excision, that of those cases originally described as completely excised on histology, residual tumour was found in 26.3%.

In addition to the above advantages of the LB system we found additional information which could not be demonstrated by the SB system. This included the exact site of lesions within the breast specimen and the spatial relationship between central core, invasive tumour, in situ component and other proliferative changes. The LB is a useful educational tool in discussions with surgeons and radiologists and can be superimposed on mammograms and specimen X-rays providing a dramatic demonstration of the pathology.

Arguments against the LB technique include increased cost, more equipment, technical complexity and time delay. We have estimated the overall running costs at the Royal Surrey County Hospital to be double that for conventional SB and the overall time from receiving the specimen to issuing a final report is also double. However we, and the clinicians find this time delay acceptable in view of the extra information provided. We find the quality of the macrosections very good and in general there are no problems in assessment of tumours at both low and high magnification. In doubtful cases the presence of a standard SB is helpful since it can be used for special stains and immunohistochemistry.

During this study histological-mammographic comparisons were not made as this is a matter for clinical management and not all patients had mammograms prior to surgery. From our own clinical experience however, we have found that LB are ideal for comparison to mammograms and specimen X-rays. The demonstrated lesions can be directly superimposed and compared to the X-ray films thereby negating the need for complex slicing, repeat X-raying and complicated orientation and block identification necessary when using conventional techniques. LB eliminate the need for three dimensional rebuilding of a biopsy in order to assess the complete lesion.

In summary, LB provide more data and it is presented in a form which is easy to interpret and review. Radial slicing of the breast is an attempt to display the duct system which is known to have a radial arrangement [2]. The technique picks up more proliferative changes and allows the extent of carcinoma and associated in situ component to be accurately mapped.

We consider that the LB method of examination of breast specimens reveals much more useful information than can be easily derived from conventional SB techniques. In order for comparable data to be gained from the SB techniques there would need to be a much greater use of time and materials with end results more difficult to interpret and a rise in cost to that of the LB technique. The usefulness of macrosections is highlighted in the study of DCIS and invasive lobular carcinoma where macroscopic examination can be misleading. For these reasons we advocate the LB method as a standard procedure in histopathology of the breast.

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