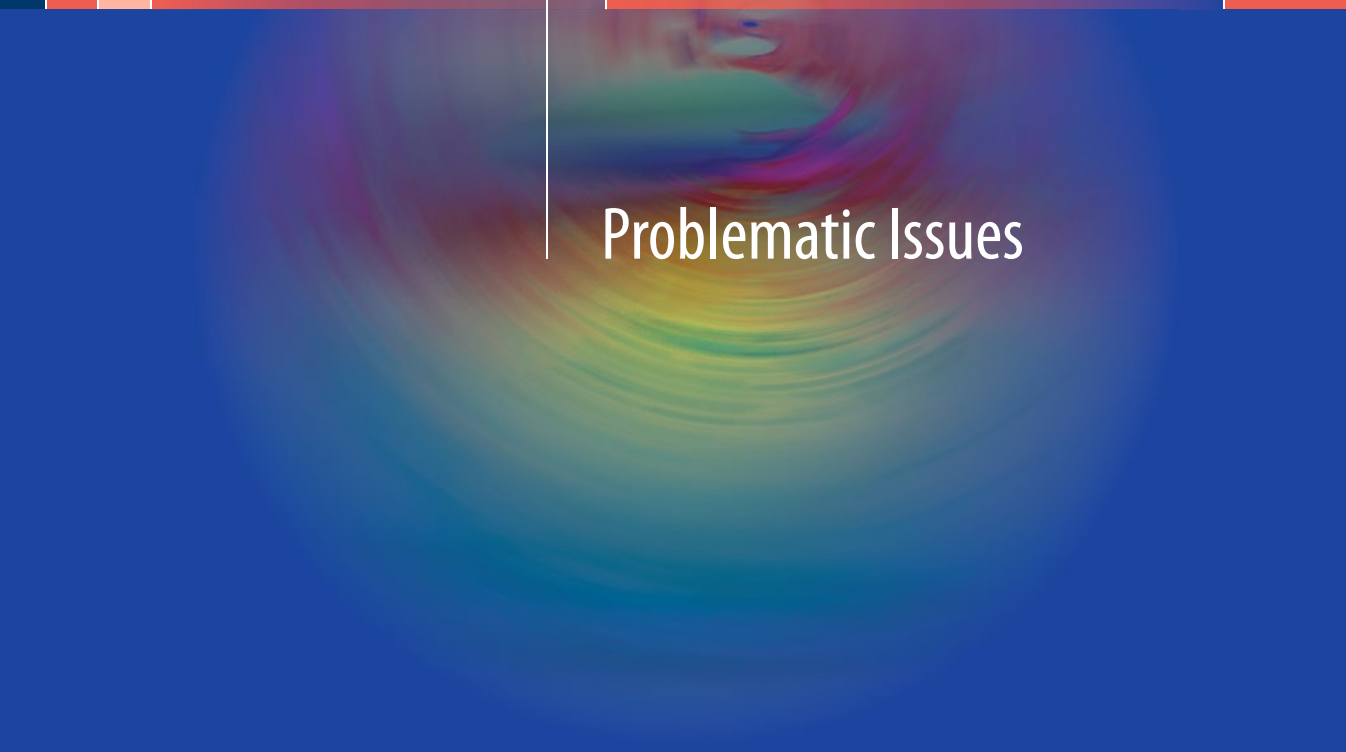
Sami Shousha
Editor

Breast Pathology

Problematic Issues



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To Seham, Sarah, and Susan

Introduction

This is not a textbook of breast pathology. It is rather a modern version of the late John Azzopardi's classic book, *Problems in Breast Pathology*, which was published in 1979. In fact, this book is mainly based on the annual "Hammersmith Diagnostic Histopathology of Breast Disease Course" of which Azzopardi was the main instigator and lecturer for a very long time during the 1980s. Although the course has grown enormously since, Azzopardi's spirit is still there guiding us to concentrate on tackling the problems that face us in our daily working life as diagnostic breast pathologists.

Some of the problems that faced Azzopardi's generation of pathologists are still there, and his classic book still provides needed help, but time has passed and new developments and attitudes in the diagnosis and treatment of breast diseases have arisen calling for a book that deals with added new problems. That is the aim of this book, and I hope that aim is fulfilled. All the book's authors teach in the Hammersmith course, and all are eminent practicing breast pathologists with a wide experience in that field. But as with any multiauthor book, each author has his own way of writing and of expressing his approach in solving problems. This also sometimes creates a degree of repetition, but this may be useful in confirming ideas that all agree on or providing different approaches to solving specific problems.

I hope you will find the book useful and enjoyable at the same time.

Sami Shousha
London, May 2016

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Dealing with the Gross Specimen

1

Sami Shousha

Abstract

The main thrust of this chapter concerns dealing with the tissue removed from patients with breast carcinoma treated with conservative surgery. Dealing with other specimens is also briefly discussed as dealing with core biopsies, specimens from patients with DCIS, specimens from patients who had neoadjuvant chemotherapy, and axillary lymph node specimens are dealt with in other Chaps. (4, 5, 2, and 14, respectively). The accounts in this chapter are mainly based on the practice at Charing Cross Hospital, London.

Keywords

Core biopsies • Excision biopsies • Microcalcification • Lumpectomy • Mastectomy • Excision margins

Introduction

Good fixation is essential for proper diagnosis. In our department we prefer to receive all breast specimens, except core biopsies, fresh in a plastic bag, immediately after surgical excision whenever this is feasible and in the absence of any suspected infections. The specimen is registered, given a laboratory number, and the pathologist in charge is called to deal with it. For biopsies coming from other hospitals, we ask the surgeons to immerse it in an adequate amount of formalin and send it to us as soon as possible where it is dealt with immediately. If there is going to be a delay, we advise slicing mastectomy specimens before immersing it in formalin. Core biopsies are put in formalin straight after being removed from the patient or, in case of stereotactic biopsies, after x-raying the specimen by the radiologist to ensure the presence of calcification in the cores. The specimen container must be clearly labeled with the patient identity and side and type of specimen. It should be accompanied by a request form detailing the patient's name, date of birth, hospital number, the responsible clinician, location, date of request, and relevant clinical history. The information written on the specimen container is checked with that on the request

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form, particularly as regards the patient's name and type and side of the biopsy. Any tissue left after sampling a specimen is retained for 4–5 weeks after authorization of the report.

Core Biopsies

These are thoroughly dealt with in Chap. 4 but will mention here a few points which we apply in our institution. In our hospital, hard copies of the x-rays of stereotactic core biopsies are not available anymore. Instead, the x-rays are sent to us as e-mail messages from the Radiology Department. They are also available via the hospital net, but we find receiving them as e-mails to be more convenient and easier to access, although the quality of the pictures can be sometimes not as good. Viewing the x-rays when reporting these core biopsies is essential to ensure the presence of the biopsied calcification in the stained sections. If no microcalcification is seen in the three stained sections, or if only fine microcalcification is present in spite of the presence of coarser calcification in the submitted x-ray, further sections have to be cut and examined.

If more than one case is received at the same time, they are not accessioned into the laboratory consecutively but separated by another type of specimen to avoid possible mix-up. The number of cores received from each case is recorded, together with their length and color. In addition to the case number, we usually write the patient's name by pencil on the side of the cassette. The specimen is entirely submitted for histological examination, preferably not more than four cores in each cassette. Three shallow levels are cut and stained with hematoxylin and eosin (H&E). Three intervening sections are kept unstained in case they are needed later for the immunohistochemical assessment of hormone receptors and HER2 status if the case proved to be an invasive carcinoma. Additional sections can be requested if more immunohistochemical or special stains are needed. For vacuum biopsies, six levels are cut and stained with H&E if the procedure was carried out for microcalcification. Otherwise, only three levels are cut with intervening spares on coated slides for immunohistochemistry if required.

Dealing with Specimens from Conservative Surgery

Many cases of breast carcinoma, invasive and in situ, are now treated by limited (conservative) surgery rather than mastectomy. These are usually relatively small mono-focal tumors that are detected by palpation or by screening mammography. If the tumor is palpable, it can be removed by a wide local excision or a quadrantectomy depending on the size of the tumor and the size of the breast. If the lesion is impalpable, it is removed by a wire-guided wide local excision. The lesion is localized by inserting a wire radiologically, either by stereotactic or ultrasound technique. The wire guides the surgeon to the site of the tumor, and the area around the tip of the wire is removed.

The size of the excised biopsy depends on the size of the tumor as determined radiologically. The surgeon orientates the specimen by attaching sutures of different lengths to the margins of the specimen. At least two margins have to be marked, and these are usually the lateral, indicated by a long suture, and the superior indicated by a short suture (Fig. 1.1). An additional looped suture maybe attached to the anterior surface for confirming the orientation. Metal clips are usually attached to the sutures to help identifying the margins when the specimen is x-rayed (see below).

If the lesion was originally detected because of the presence of microcalcification, the excised specimen is usually x-rayed by the surgeon in the operating theater, using a Faxitron, to ensure the removal of all microcalcifications, with a

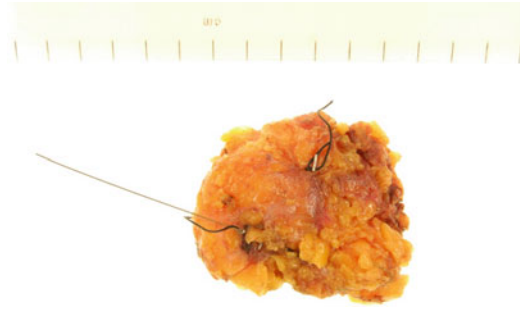

Fig. 1.1 Specimen with marking sutures

reasonable distance (around 10 mm) between the microcalcification and the margins of the specimen [1]. If this is not the case, the surgeon may have to remove more breast tissue from the biopsy cavity. A copy of the specimen x-ray is sent with the specimen or is made available for the pathologist to examine via the hospital computer system (Fig. 1.2). To be on the safe side, some surgeons take additional "bed biopsies" from different parts of the post-biopsy cavity, particularly that part of the cavity where the tumor was felt to be nearest [2]. These bed biopsies are sent to the pathologist in separate containers labeled with the side from which the biopsy was taken, lateral, medial, etc. and with a stitch attached to one, usually the outer, surface.

The role of the pathologist in these cases is not only to make a diagnosis but also to decide whether or not the lesion has been completely excised. If it has not, a re-excision biopsy, or biopsies, will be needed, to ensure the complete removal of the lesion and to minimize the possibility of recurrence.

The specimens received are described, weighed, and measured. To assess completeness of excision, ink has to be applied to the margins of the specimens. For the main specimen, different colored inks are applied to different margins. There are different ways of slicing specimens, and coloring will depend on how the specimen is going to be sliced. As we usually "bread slice" our specimens, we use four colors, for example, black anterior, blue posterior, red superior, and yellow inferior (Fig. 1.3). A few drops of 1% acetic acid and absolute alcohol are added to the inked areas to help the adherence of the ink to the specimen surface. A couple of minutes are allowed for the ink to dry, and excess ink is removed by blotting paper. The specimen is then sliced from one margin to the other, say from medial to lateral, into 3–4 mm thick slices. In this case, the first slice will indicate the medial margin and the last slice the lateral margin; hence there is no need to ink the medial and lateral margins with different colors. This sequence of coloring may vary according to the shape of the specimen. In the above example, if the tumor is felt to be close to the medial or lateral margin, that margin is cut into cruciate sections in order to be able to assess accurately the distance between tumor and margin.

Once the specimen is sliced, the slices are sampled and processed for microscopic examination. Fat is not trimmed off the slices, as ink usually seeps through the fat down to the surface of the more firm tissue underneath, which would give a false impression of the actual surgical resection margin if the fat is removed. The slices are laid flat on the dissecting board and inspected (Fig. 1.4). Most invasive tumors can be easily visualized by inspecting and palpating the slices, because of their grayish color and harder consistency. DCIS is more difficult to visualize but may appear as granular area(s). The gross appearance of any abnormality is described. If the specimen is small, weighing around 25 g or less, all slices are processed. For larger specimens, all slices with obvious tumor or abnormal appearance, including the site of any previous recent needle

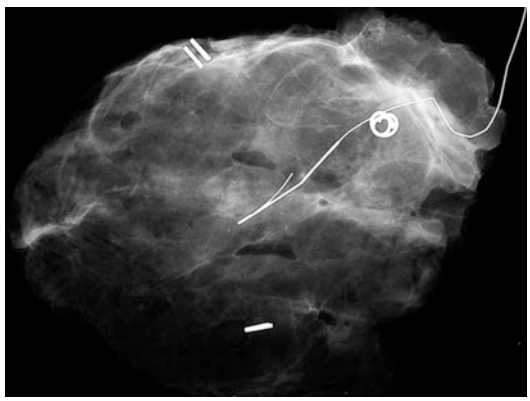

Fig. 1.2 Specimen x-ray with attached wire and orientating clips

Fig. 1.3 Painted specimen

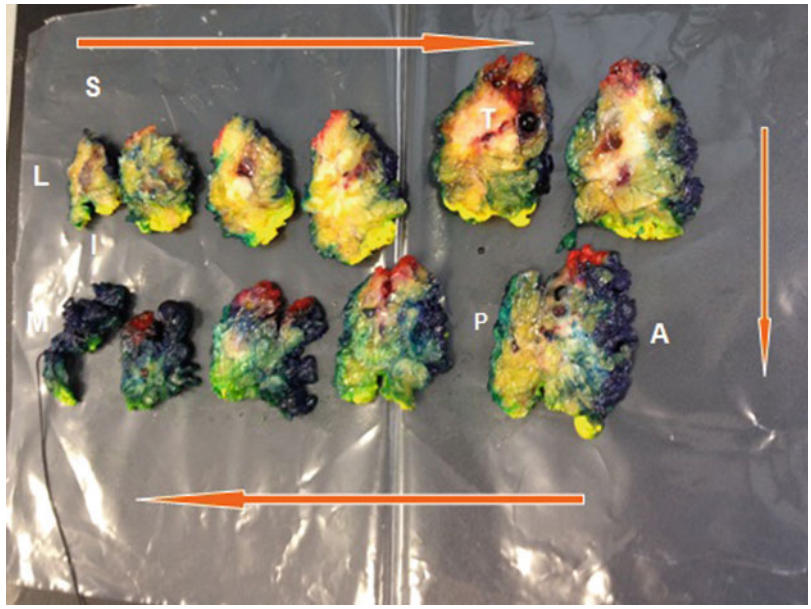

Fig. 1.4 Sliced specimen

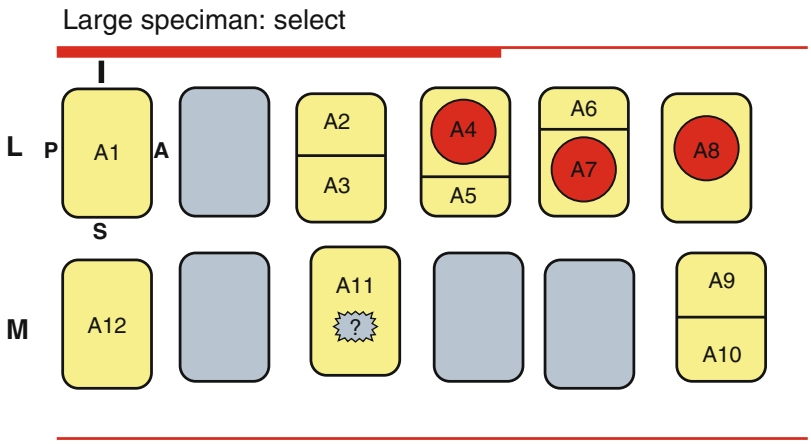

Fig. 1.5 A diagram showing slice selection for processing. The tumor is in *red. Yellow*-colored slices are processed. Slice 11 has an additional abnormal-looking area. *A1-A12* refer to cassette numbers. *L*: *lateral*, *M*: *medial*, *I*: *inferior*, *S*: *superior*, *A*: *anterior*, *P*: *posterior*

aspiration or core biopsies which is usually indicated by an area of hemorrhage or discoloration, have to be processed together with the preceding and following slices, as well as the first and last slice (Fig. 1.5). Many cases of invasive lobular carcinoma present in the form of a diffuse thickening, rather than a well-defined mass, and satellite lesions adjacent to the main tumor may be present, some being impalpable. Thorough sampling is especially required in these cases, particularly from the excision margins, to assess complete removal.

If a slice is too big to fit in a small cassette, it is divided into two or more pieces. We usually process the slice containing the main part of the tumor, with four margins, in one cassette, which in many cases is a mega-cassette (double the size of a normal cassette, Fig. 1.6). The cassettes are given consecutive numbers. A map is kept to identify where each section has come from. For

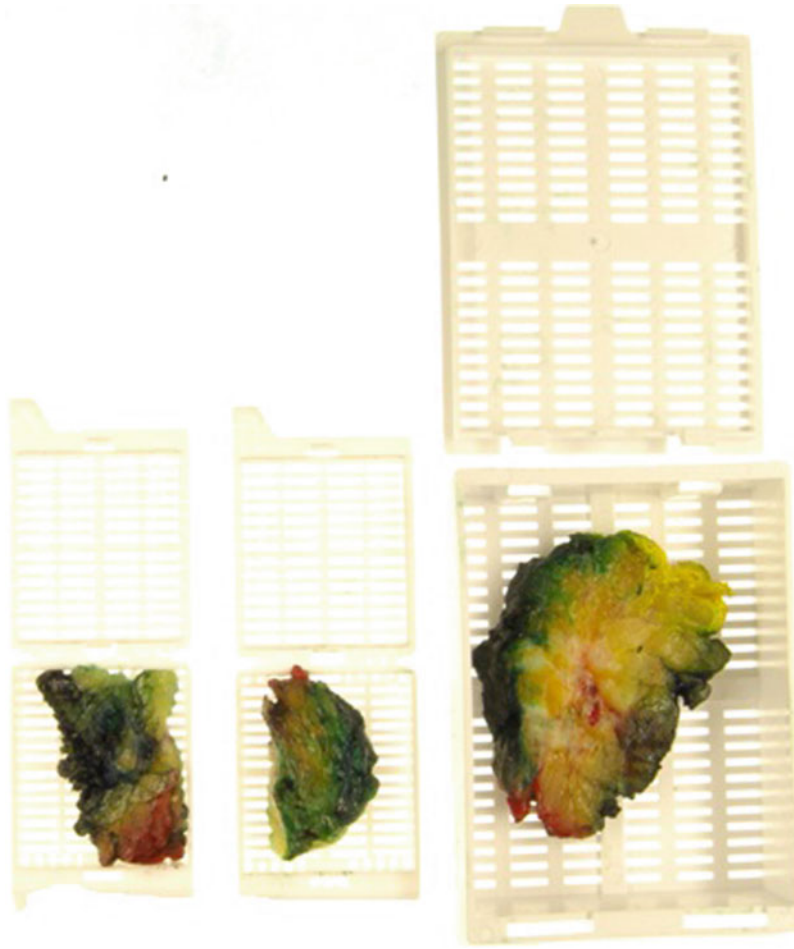

Fig. 1.6 A large cassette used to include the tumor with all margins

this purpose we use a pro forma diagram (Fig. 1.7). Alternatively, the slices can be x-rayed in a departmental Faxitron [3] or in the Radiology Department, and the x-ray image is used to identify where the sections were taken from (Fig. 1.8). We also have an additional form to list all the cassettes used with their given number, the number of samples in each and where the tissue in each has come from (Fig. 1.9).

For re-excision and bed biopsies, only one color is applied to the outer surface of the specimen and then cut into vertical slices with each slice having an outer inked surface and inner uninked surface.

In some centers, frozen sections of the biopsy margins or cytology imprints of its surface are carried out to ensure completeness of excision. This is not the practice in our hospital as we believe that these time-consuming intraoperative procedures use less than optimal microscopic methods for diagnosis and are done under pressure while the patient is still anesthetized and the surgeon waiting for the result to proceed with the operation.

Reporting Excision Margin Status

It is recommended that the histopathology report should state the distances between the tumor and all margins: medial, lateral, anterior, posterior, superior, and inferior. The actual distance in

Specimen No: _____ Patient Name: _____

Date: / / Pathologist: _____ BMS / MLA: _____

Type of Specimen: WLE ☐ Mastectomy ☐ NLB ☐

Weight: _____ No. of Slices: _____ Sliced from ___ to ___

Colour of Margins	
Medial (M)	
Lateral (L)	
Superior (S)	
Inferior (I)	
Anterior (A)	
Posterior (P)	

Measurments:	
M – L :	mm
S – I :	mm
A – P :	mm
EOS :	
Nipple :	

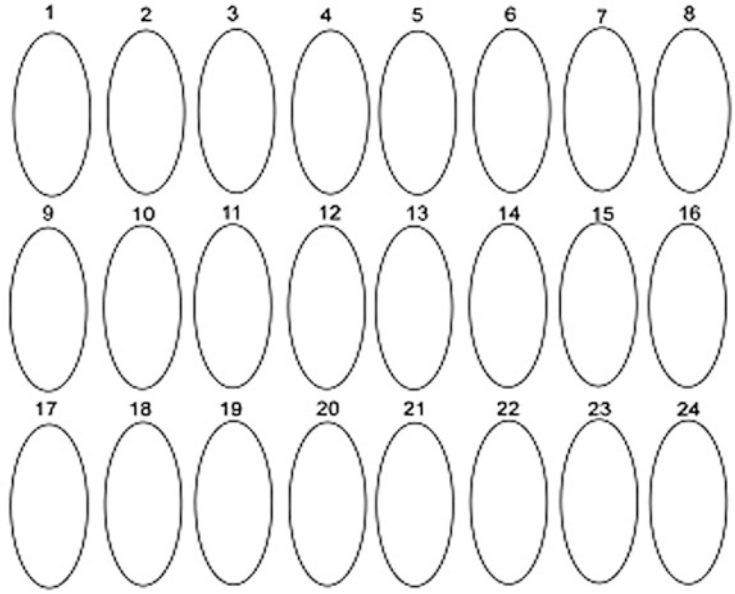

Fig. 1.7 A pro forma map used to indicate where the samples are taken from

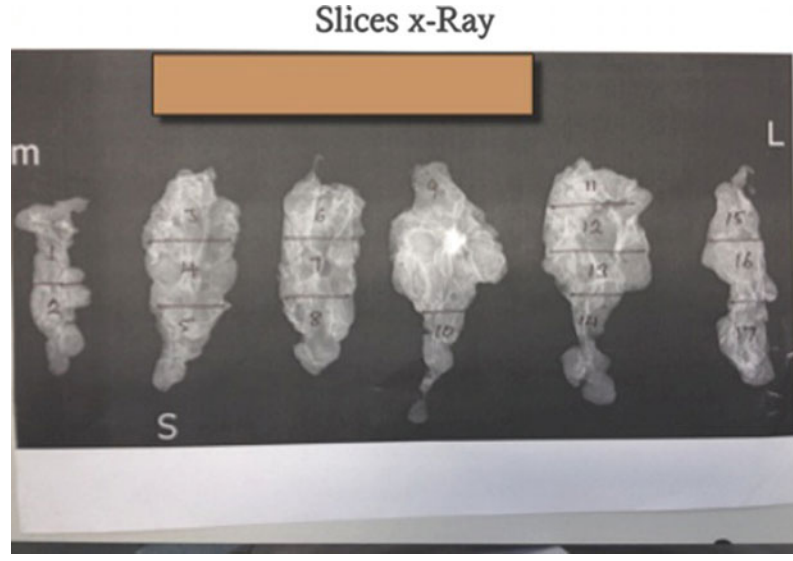

Fig. 1.8 Slices x-ray can be used instead of the map shown in Fig. 1.7