10th BDIAP seminar for trainees in histopathology

Approach to Cut-Up; Macroscopic Examination as the Precursor to Accurate Microscopic Interpretation – Breast

Sarah E Pinder
King's College London
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Tuesday 14th March 2017

The Royal College of Pathologists

Pathology: the science behind the cure

Pathology reporting of breast disease in surgical excision specimens incorporating the dataset for histological reporting of breast cancer

June 2016

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https://www.rcpath.org/resourceLibrary/g148-breastdataset-hires-jun16-pdf.html

Breast Specimen Handling
Principles - Breast Unit Protocols

Request form with appropriate clinical information including:

- Name, date of birth
- Surgical procedure
- Side & site of lesion in the breast
- Nature of lesion - microcalcification, mass, deformity
- Single or multiple foci, neo-adjuvant therapy etc

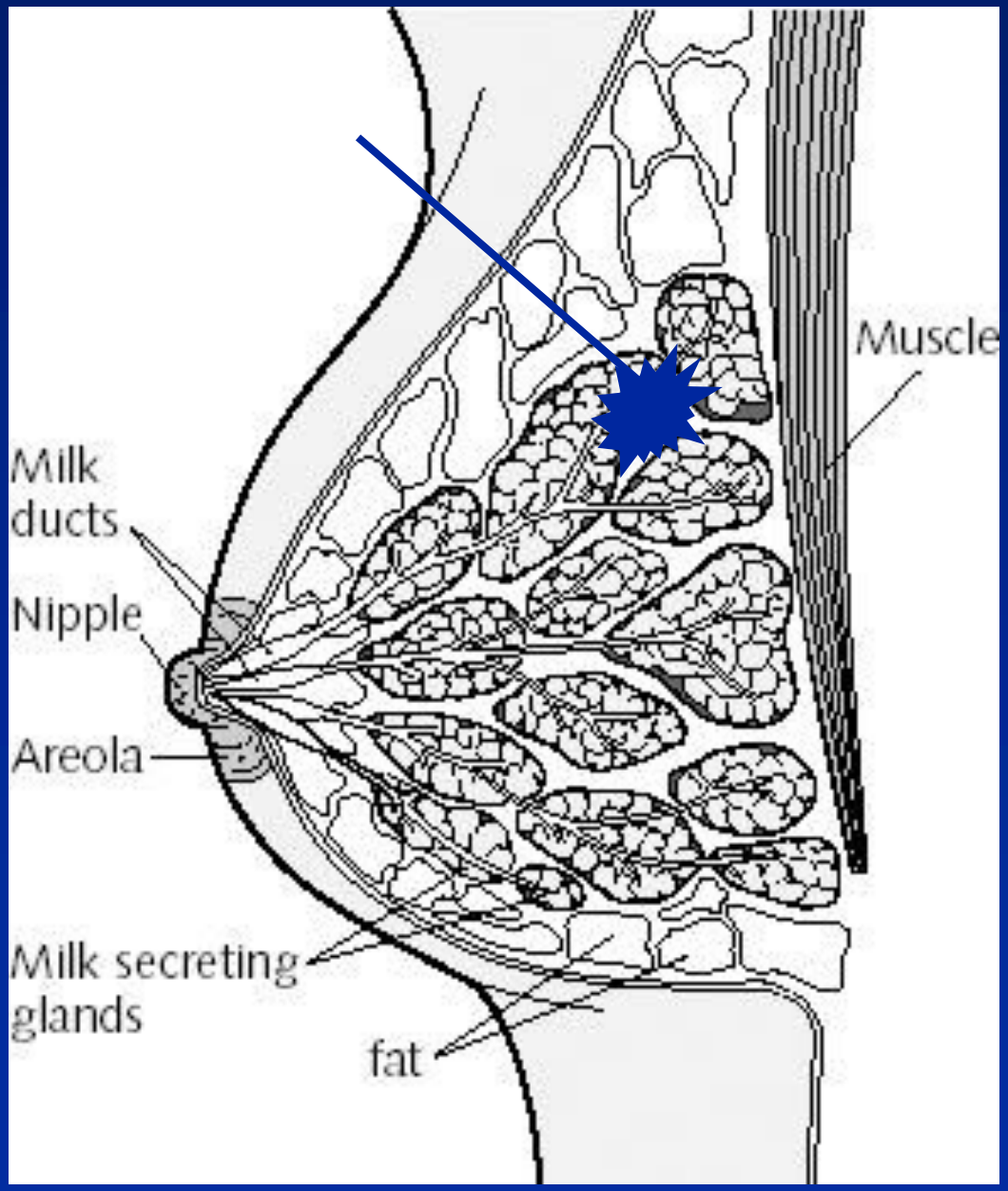
Specimen:

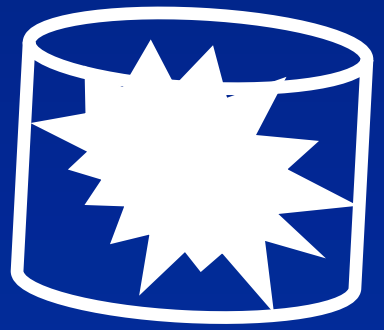
- Appropriate orientation sutures and/or clips
- X-ray

Breast Specimen Handling
Principles - Breast Unit Protocols

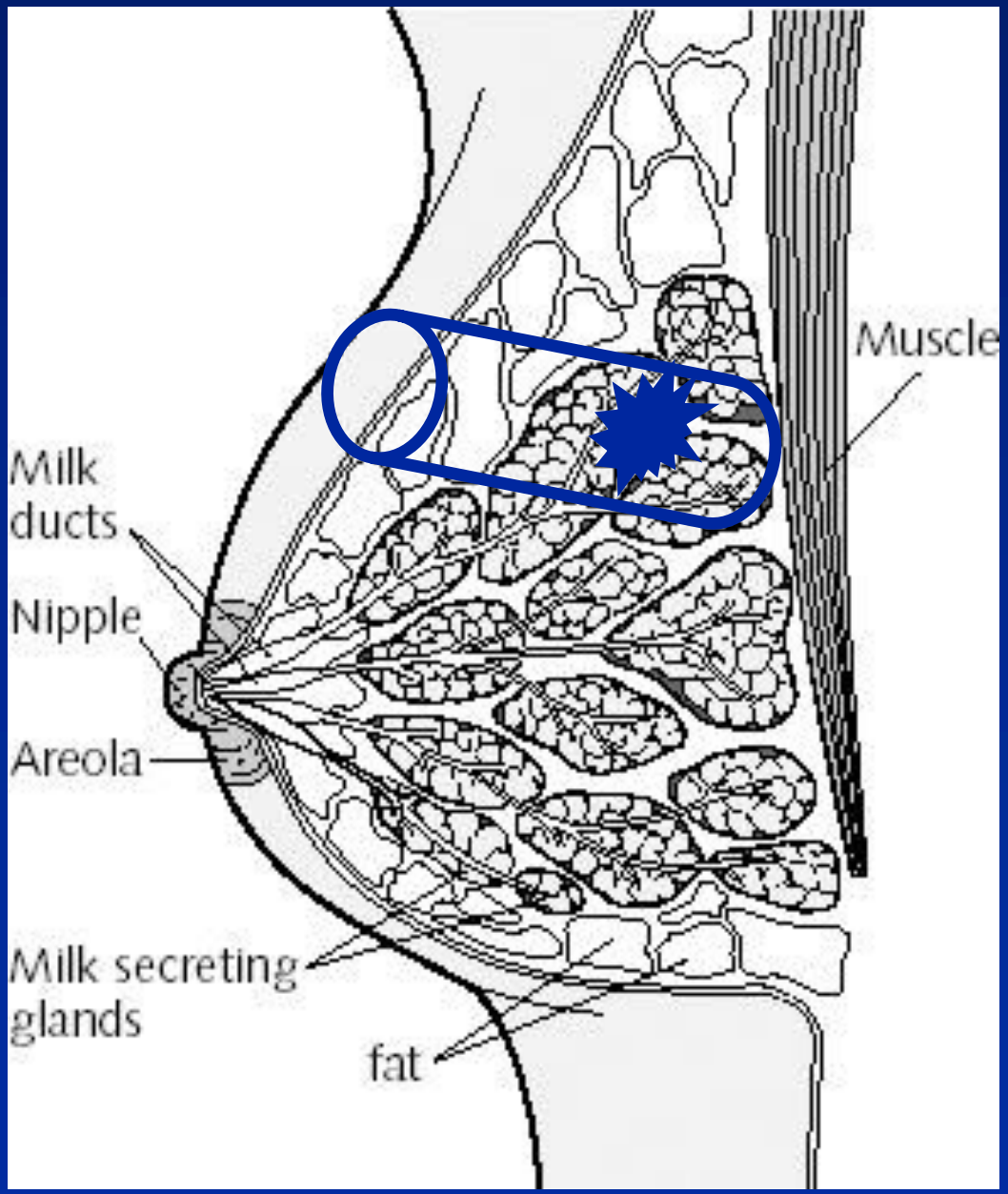
- Lesions should be surgically resected and orientated according to a defined (ABS) protocol
- If the surgical resection differs, this should be discussed

Diagnostic Surgery

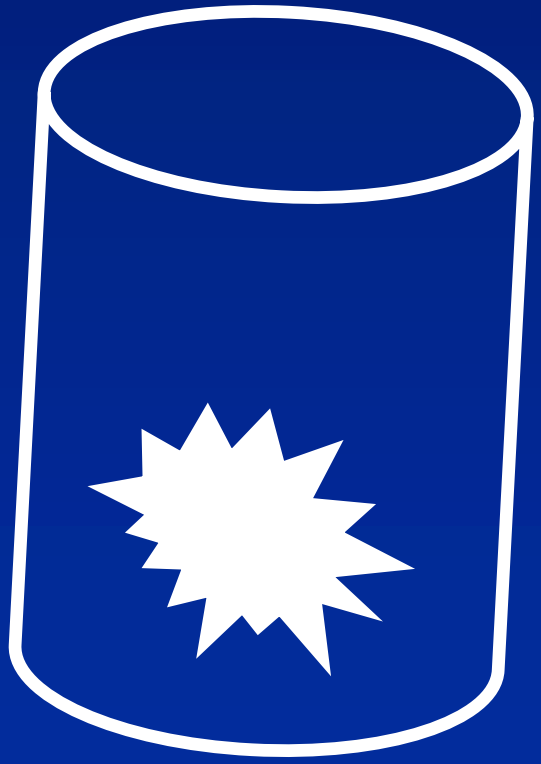




Therapeutic Breast Surgery (1)

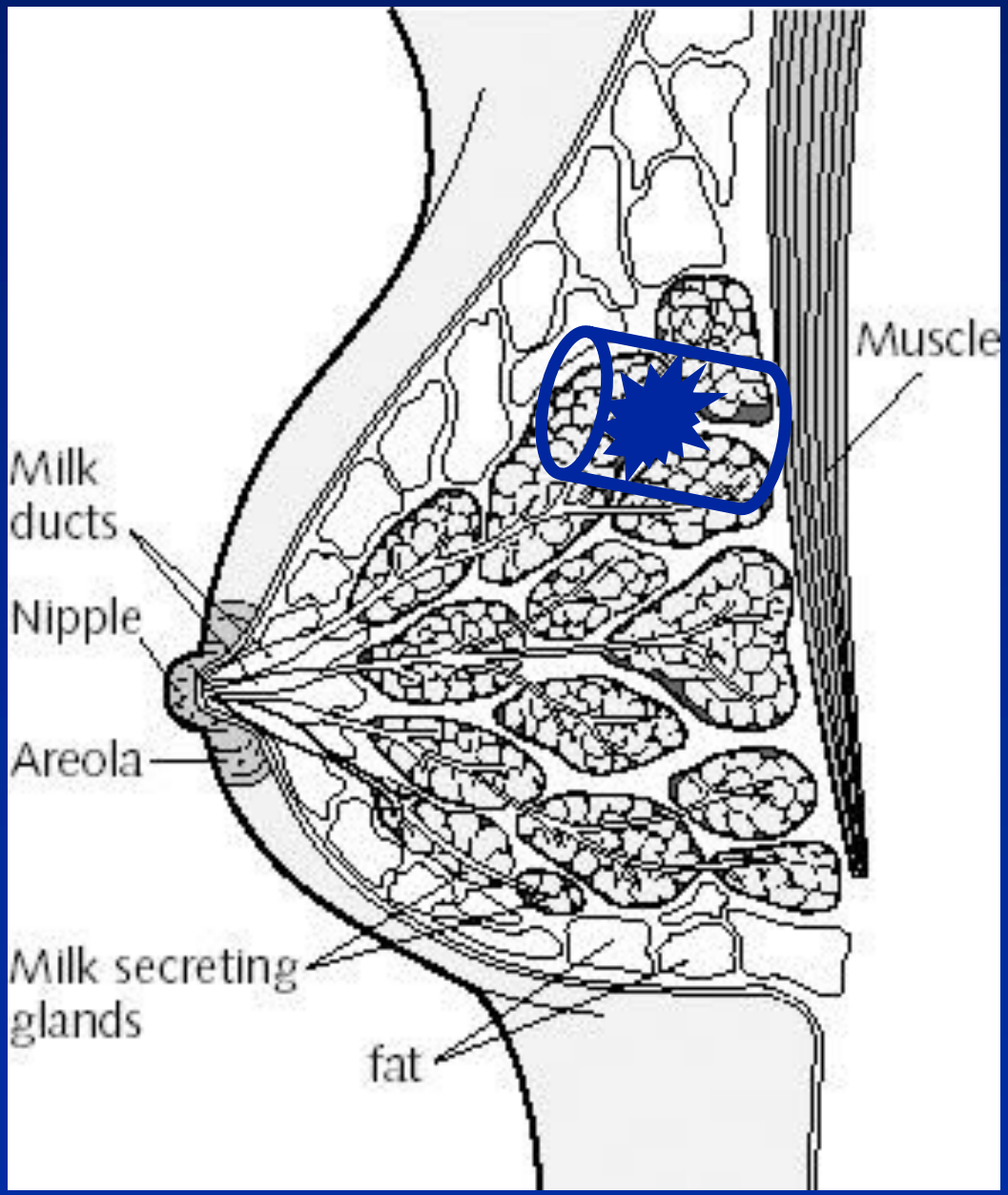


Anterior = skin

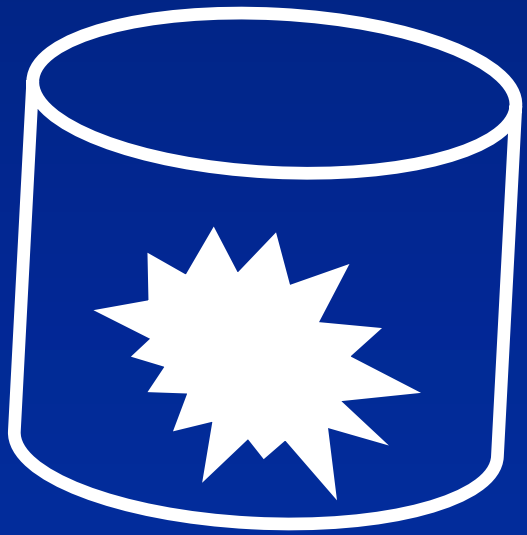


Posterior = fascia

Therapeutic Breast Surgery (2)



Anterior = breast



Posterior = fascia

Specimen orientation
Sutures or clips

According to local protocol

e.g.

Long – Lateral

Short – Superior

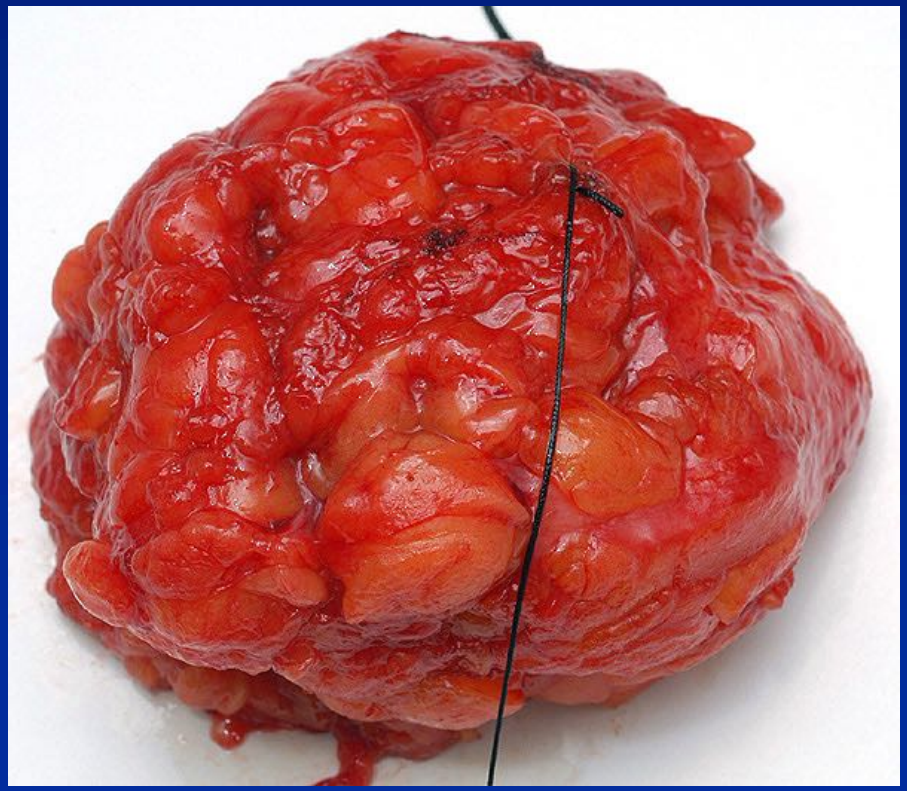
(Medium – Medial)

or

1 = Anterior

2 = Superior

3 = Nipple margin

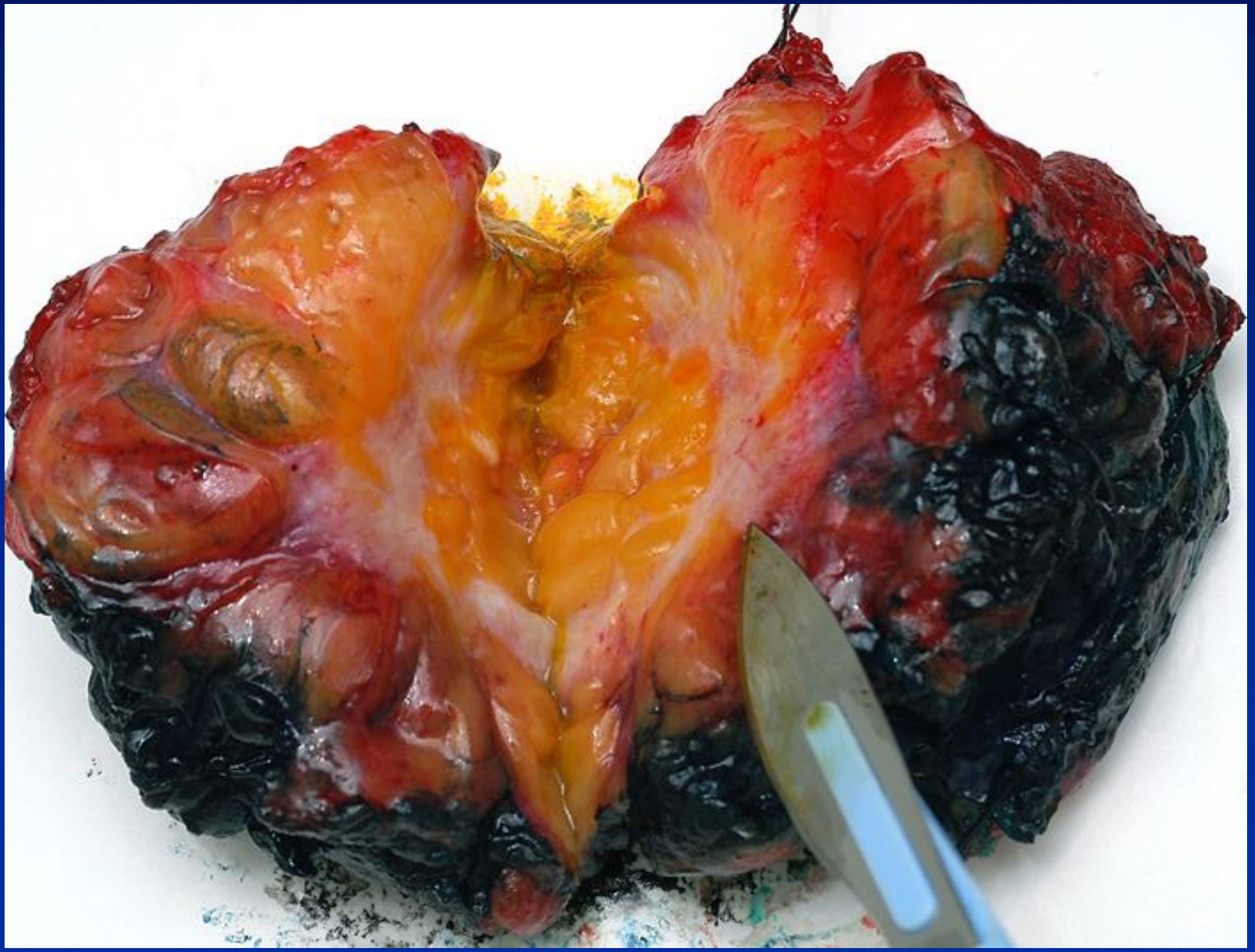


Specimen Handling
Practice

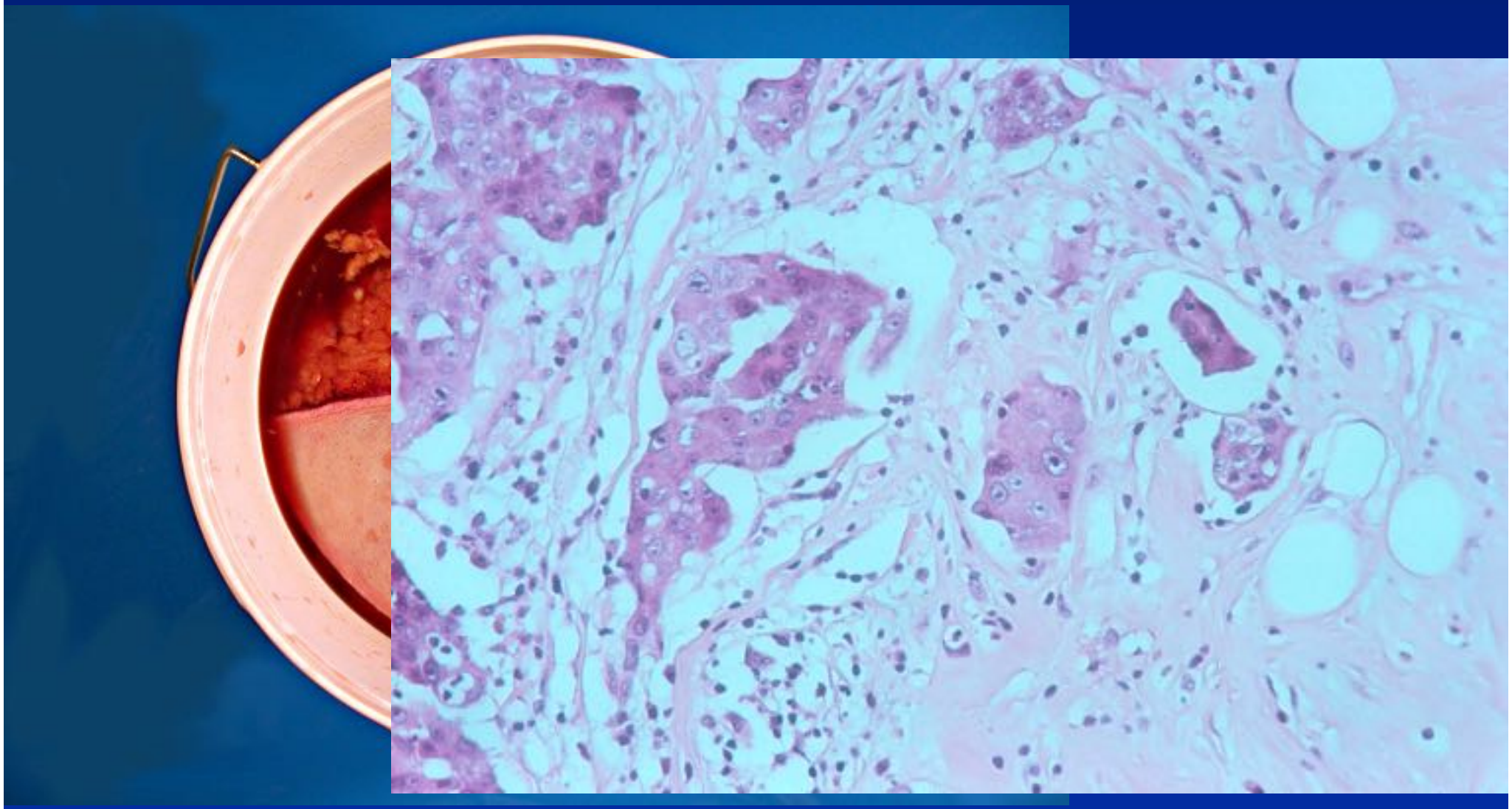
- Measure
- Weigh
- Ink – standard protocol

e.g.

- Anterior, red
- Lateral, orange
- Deep, black
- Medial, green
- Superior, blue
- Inferior, black



- Incise fresh for optimal fixation (& bank tissue)
- Paper towels along incision(s) to act as “wicks”
- Wrap in paper towels to maintain shape
- Fix overnight



Macro image courtesy of Dr James Going

Minimum Dataset

Invasive Breast Carcinoma

- Tumour type and histological grade
- Lympho-vascular invasion
- Oestrogen receptor status

} Fixation

- Size
- Axillary nodes
- Excision margins

} Operator

How to Slice?

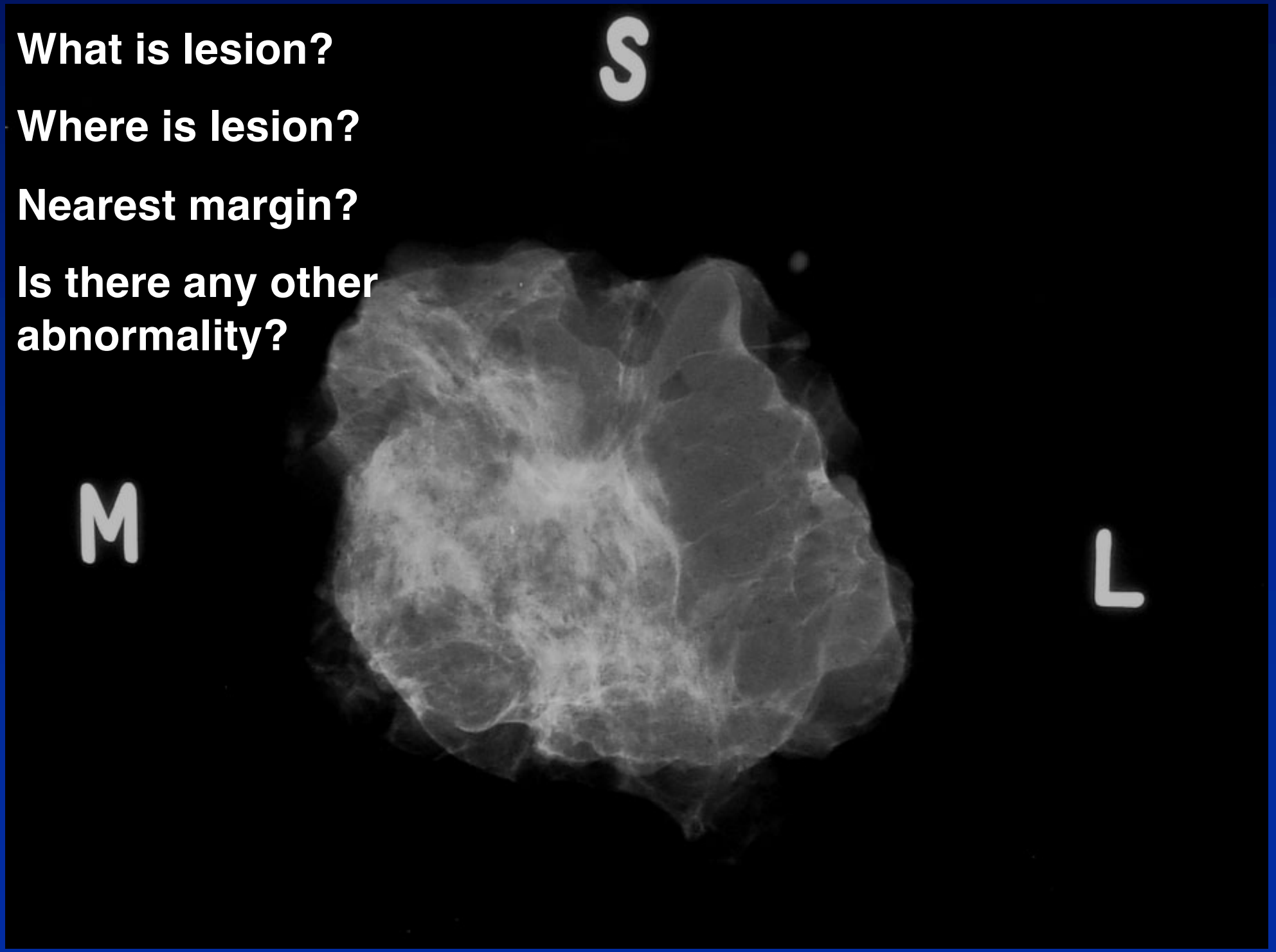
- 3 main approaches
- Depends on size & shape of specimen, lesion type & personal preference:
  1. Bread-slice - medial to lateral or superior to inferior
  2. Bread-slice - anterior to posterior
  3. Cruciate

What is lesion?

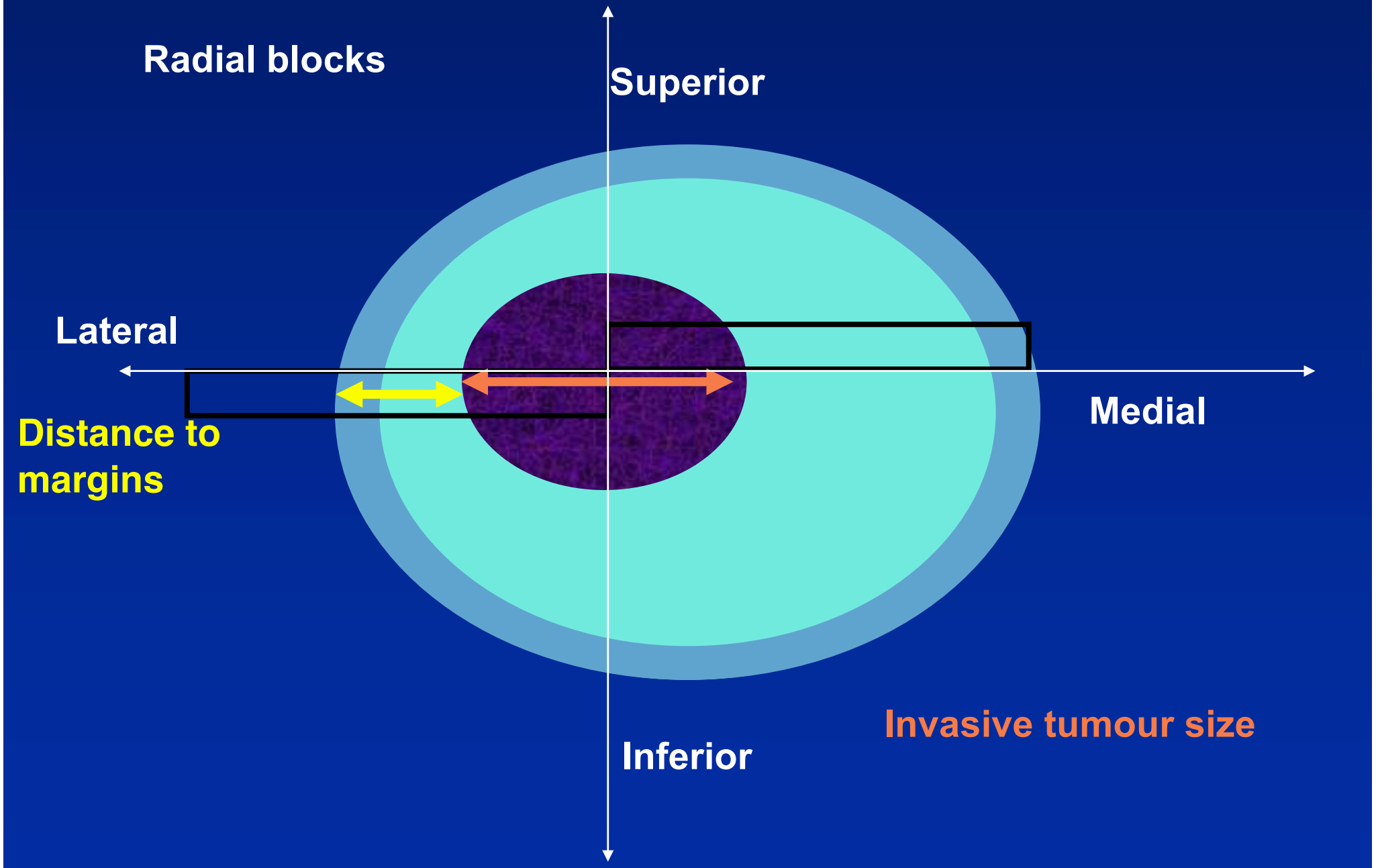
Where is lesion?

Nearest margin?

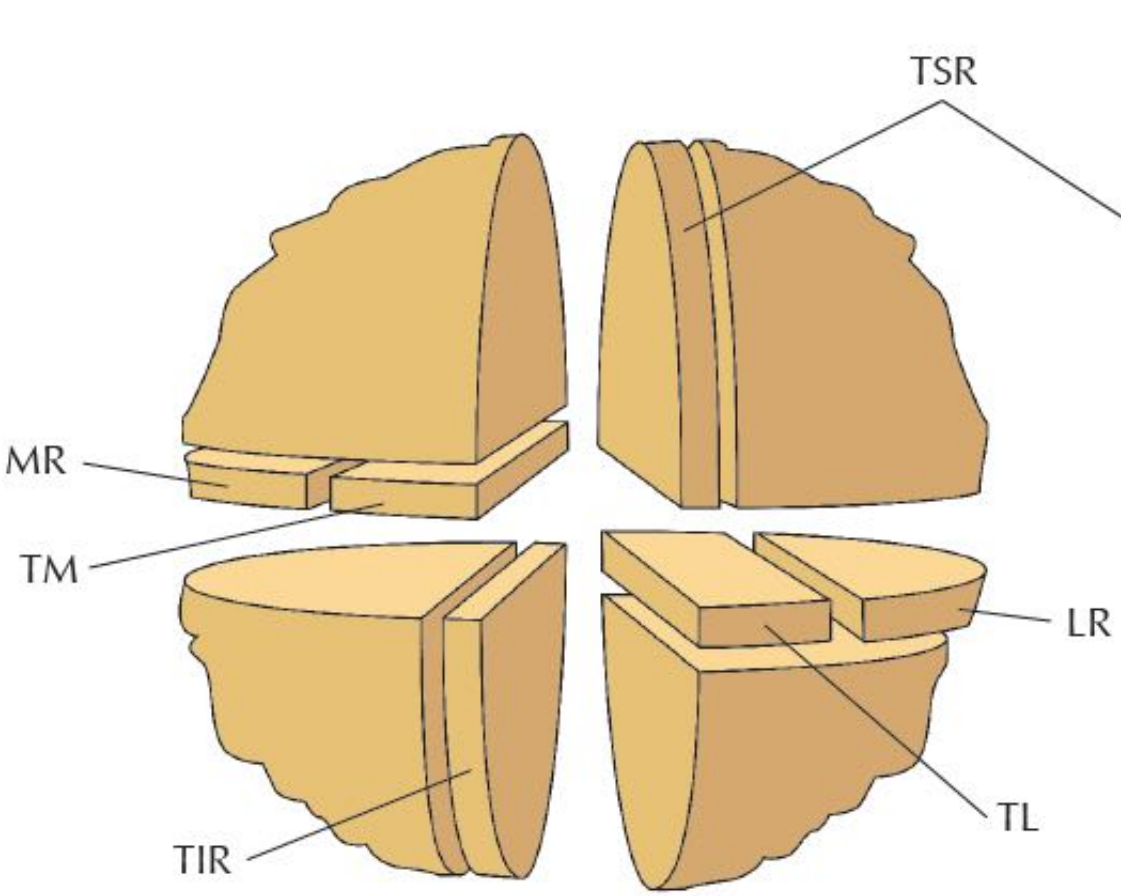
Is there any other abnormality?

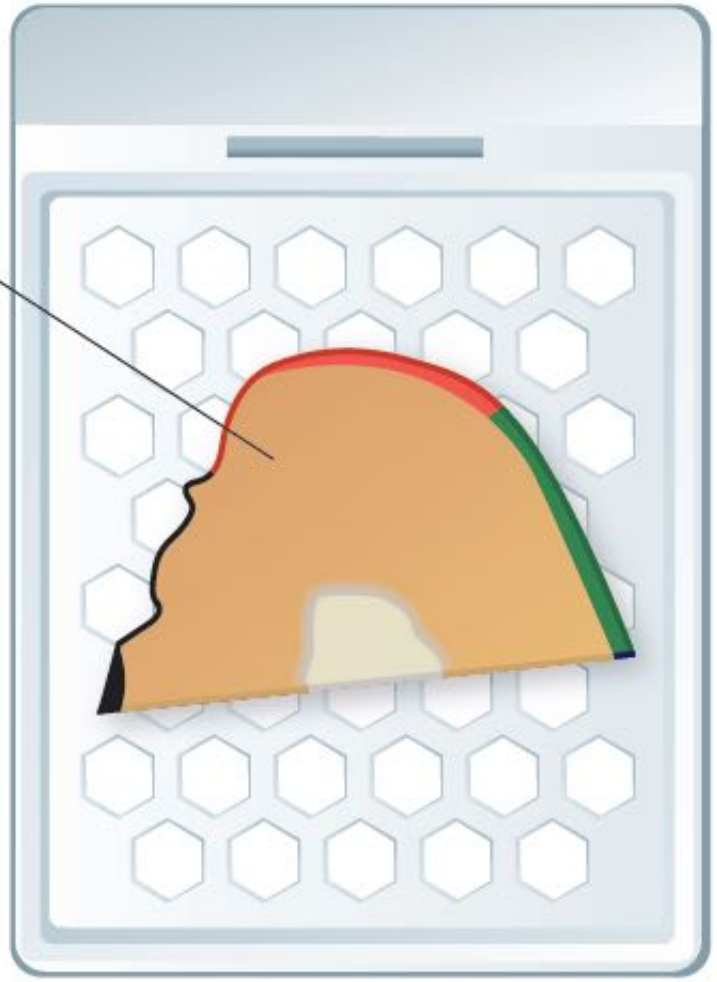


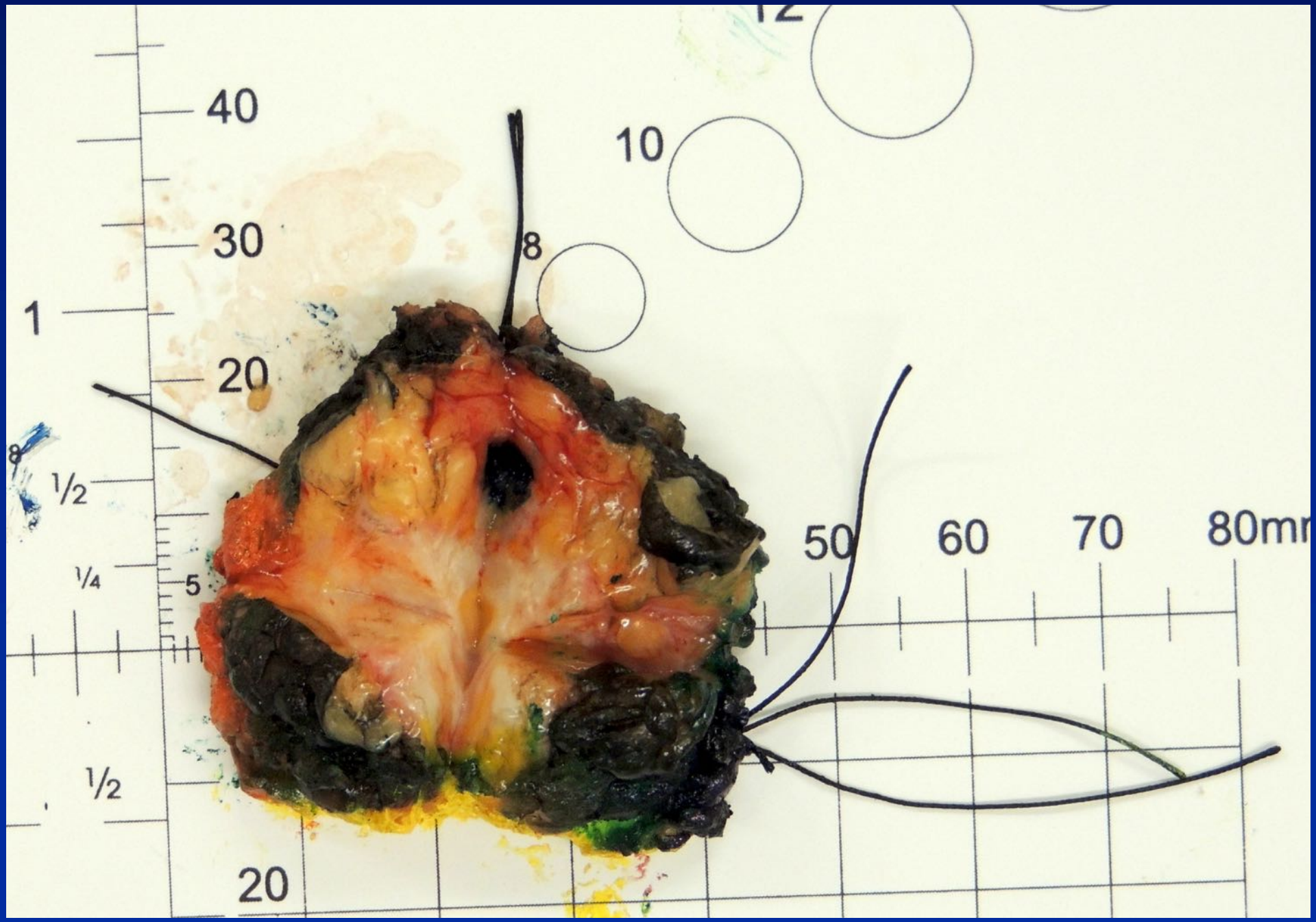
Cruciate - mass lesion

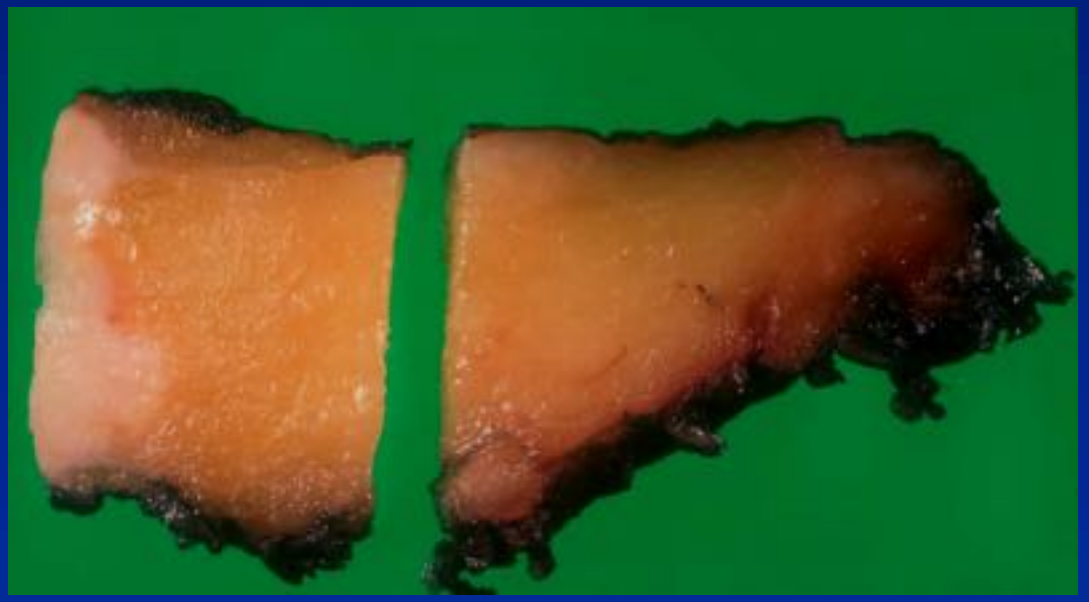


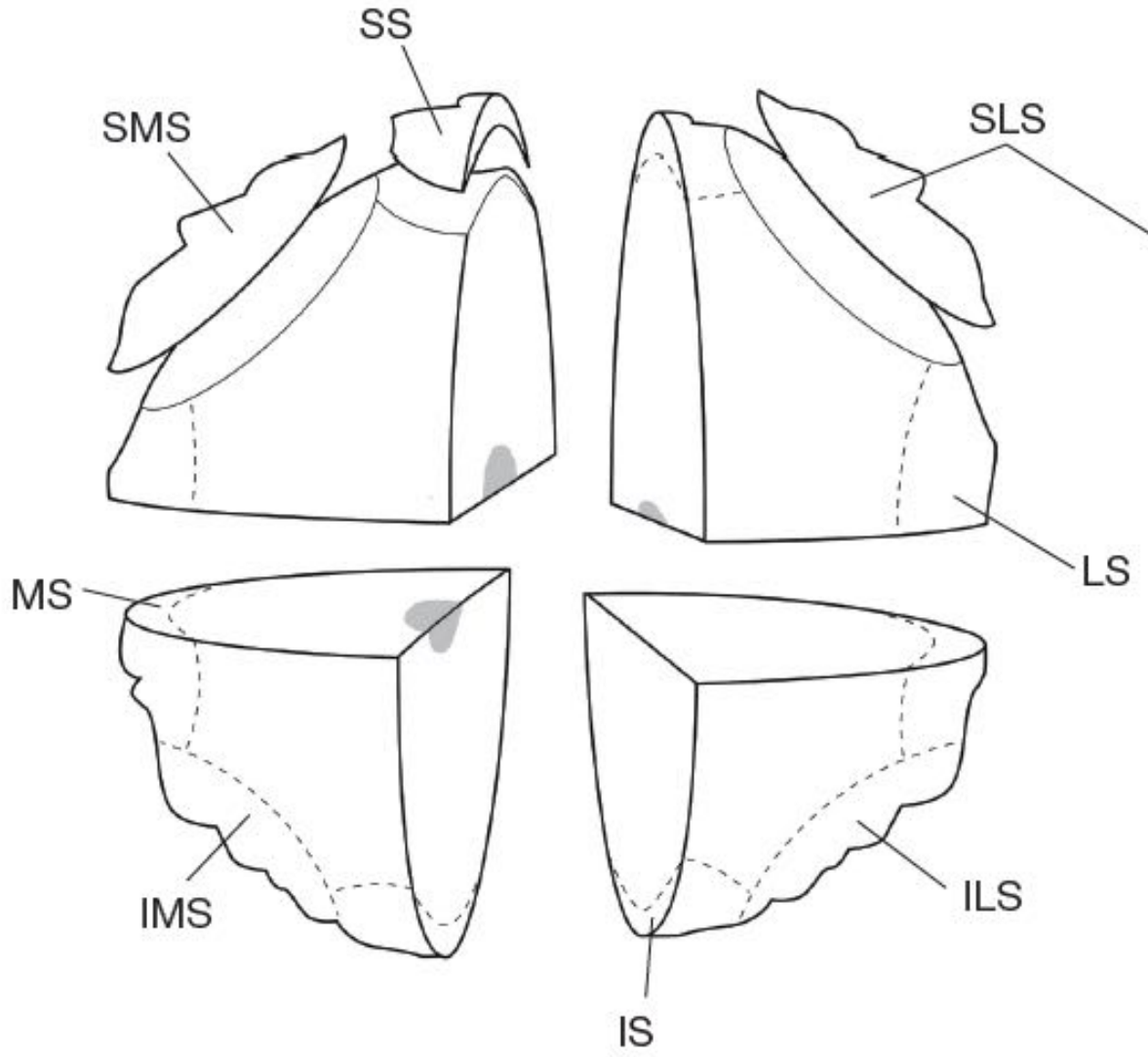
Cruciate - mass lesion






40
30
1
20
1/2
1/4
5
1/2
20
10
8
50
60
70
80mm




SS
SMS
SLS
LS
MS
IMS
ILS
IS

Shaves & Radial Margins

- 179 of 471 (38%) WLEs for carcinoma had positive margins
- 76 radial margins only (<5mm from margin) (42%)
- 45 shaves only (25%)
- 58 both types of margin blocks (32%)

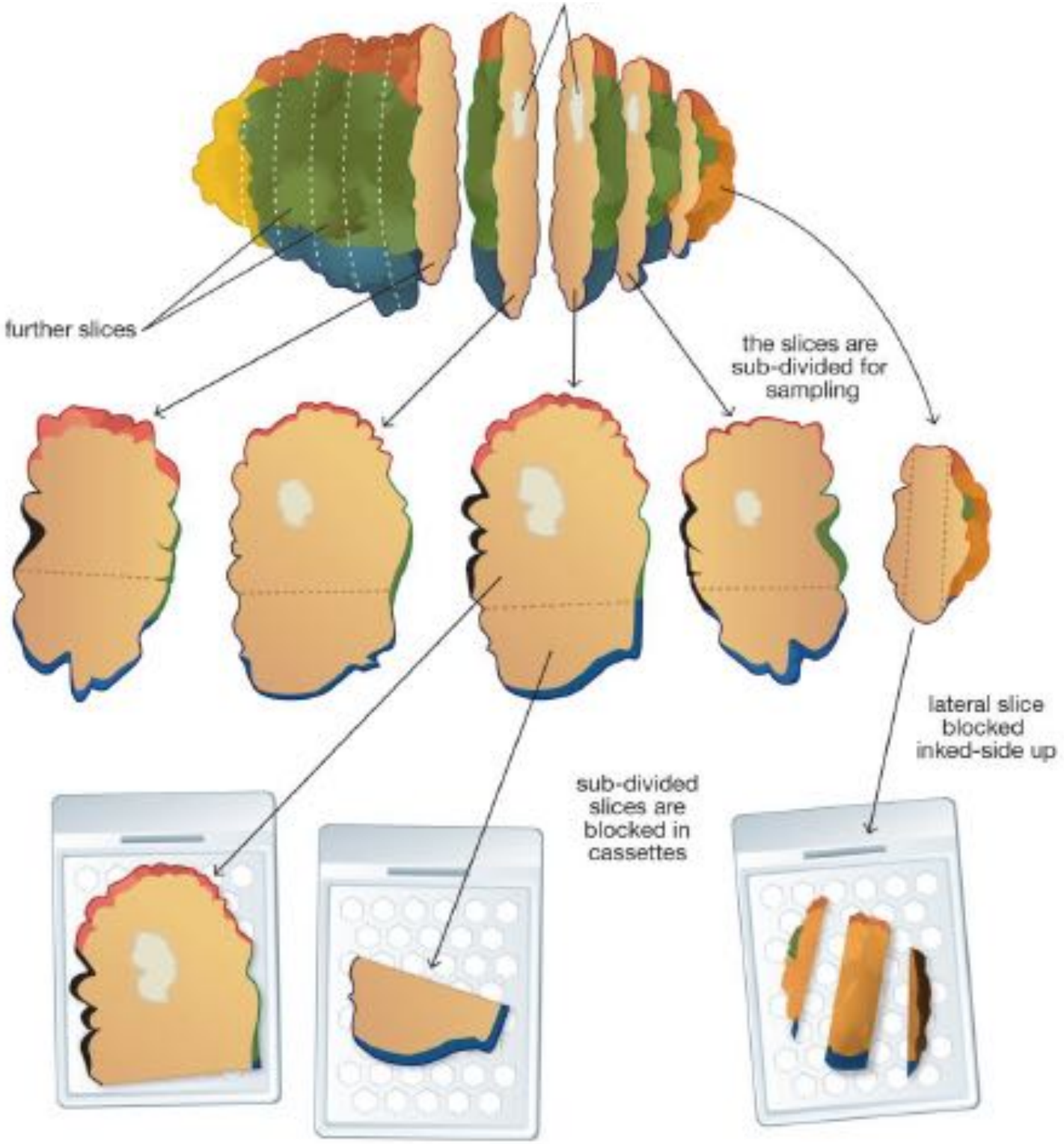
- Extra information to that from ‘radial’ sections, obtained from ‘shave’ sections in 67 specimens (37%)
  - 45 only shave margin was involved
  - 22 shave margins different aspect to radial margins

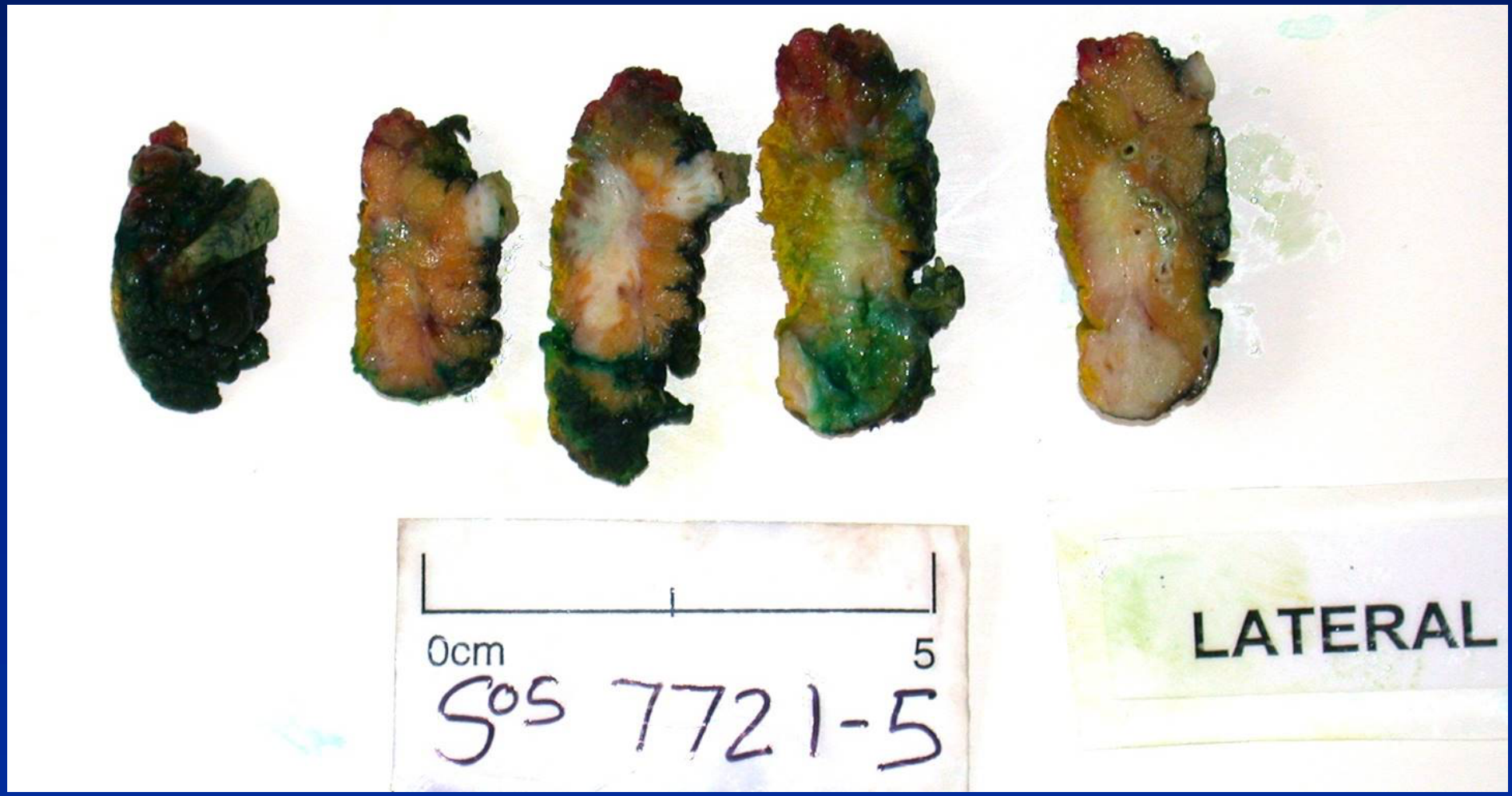
Hodi Z et al. Histopathol 2010 Apr;56(5):573-80.

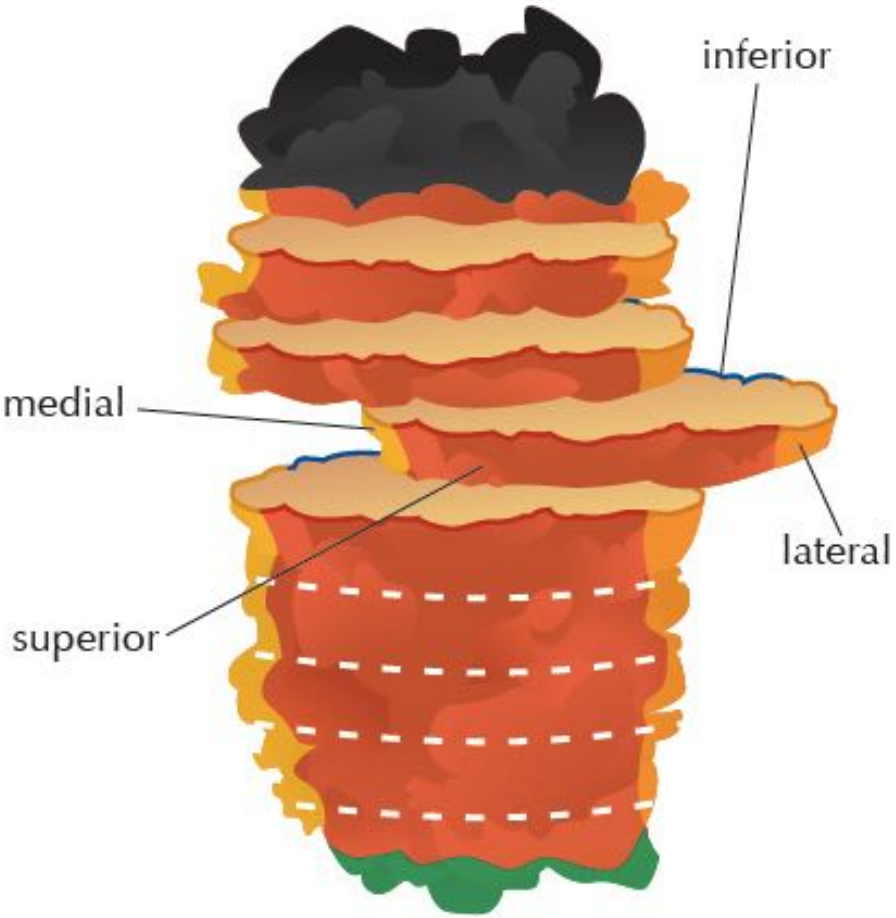
Shaves & Radial Margins

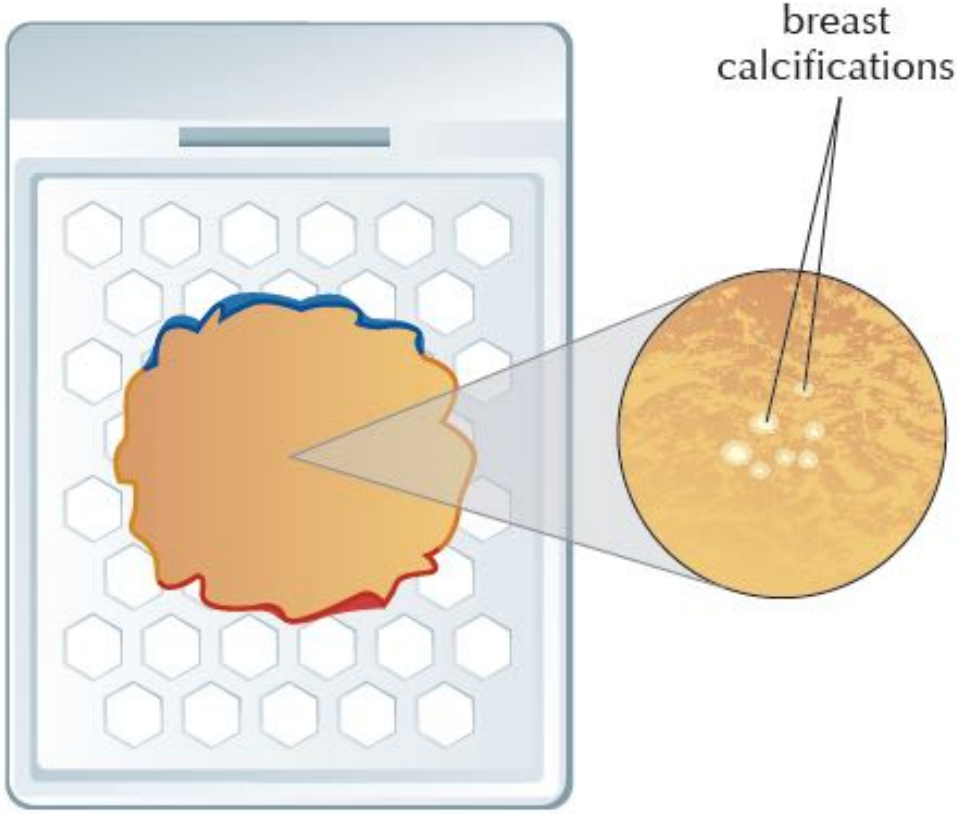
Macroscopic distance to margin	Total no. margins	Carcinoma within 5mm of radial	Shave margin involved
		DCIS or invasive ca	DCIS or invasive ca
0-1mm	13	12 (92%)	4 (31%)
2-4mm	46	24 (52%)	9 (20%)
5-9mm	199	42 (21%)	15 (8%)
10-20mm	1044	67 (6%)	60 (6%)
21-30	439	20 (5%)	19 (4%)
31mm+	143	3 (2%)	5 (3%)
Total	1884	168 (9%)	112 (6%)

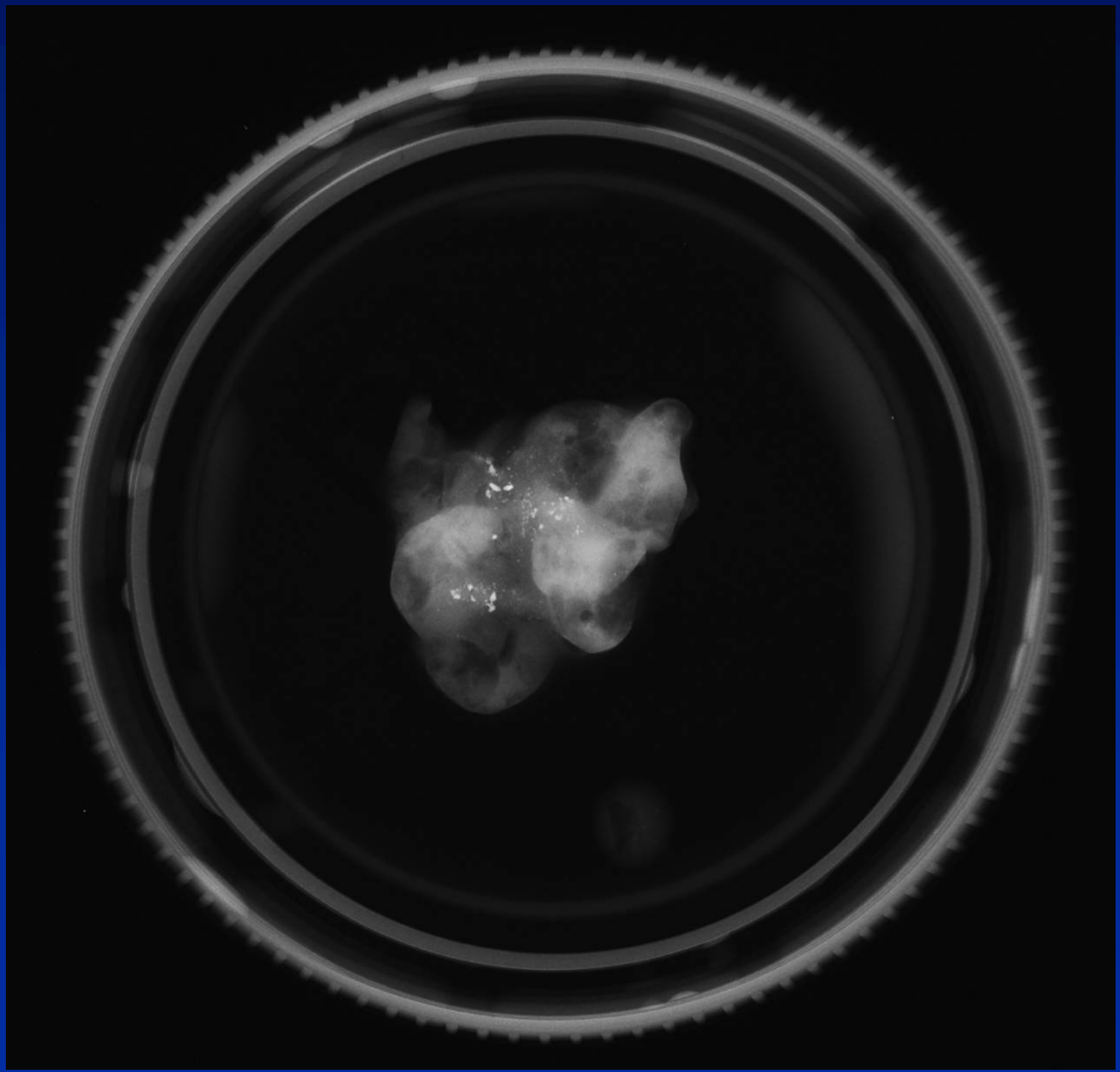
Hodi Z et al. Histopathol 2010 Apr;56(5):573-80.


further slices
the slices are sub-divided for sampling
lateral slice blocked inked-side up
sub-divided slices are blocked in cassettes


0cm
5
SOS 7721-5
LATERAL


inferior
medial
lateral
superior

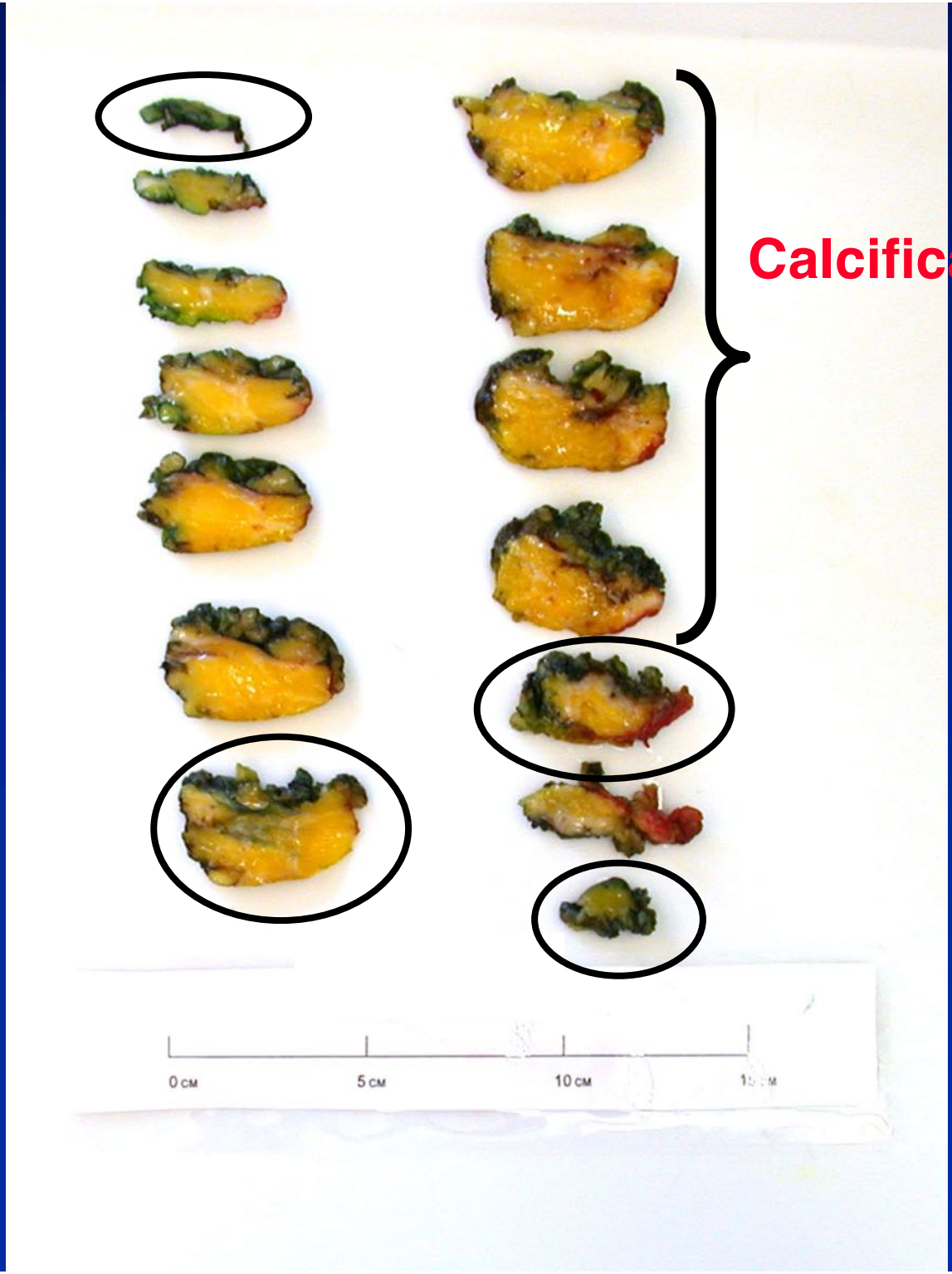

breast
calcifications



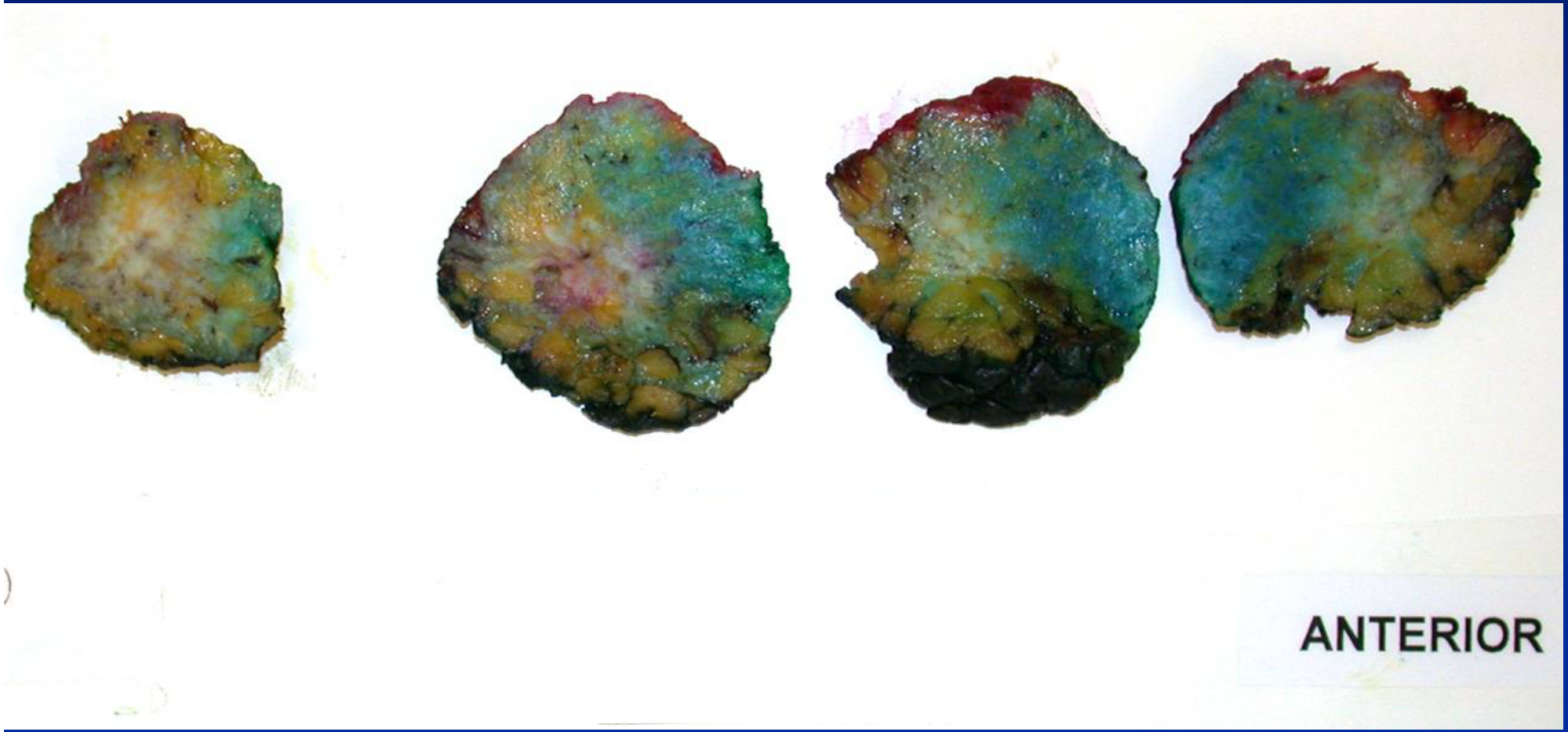
Excision of DCIS

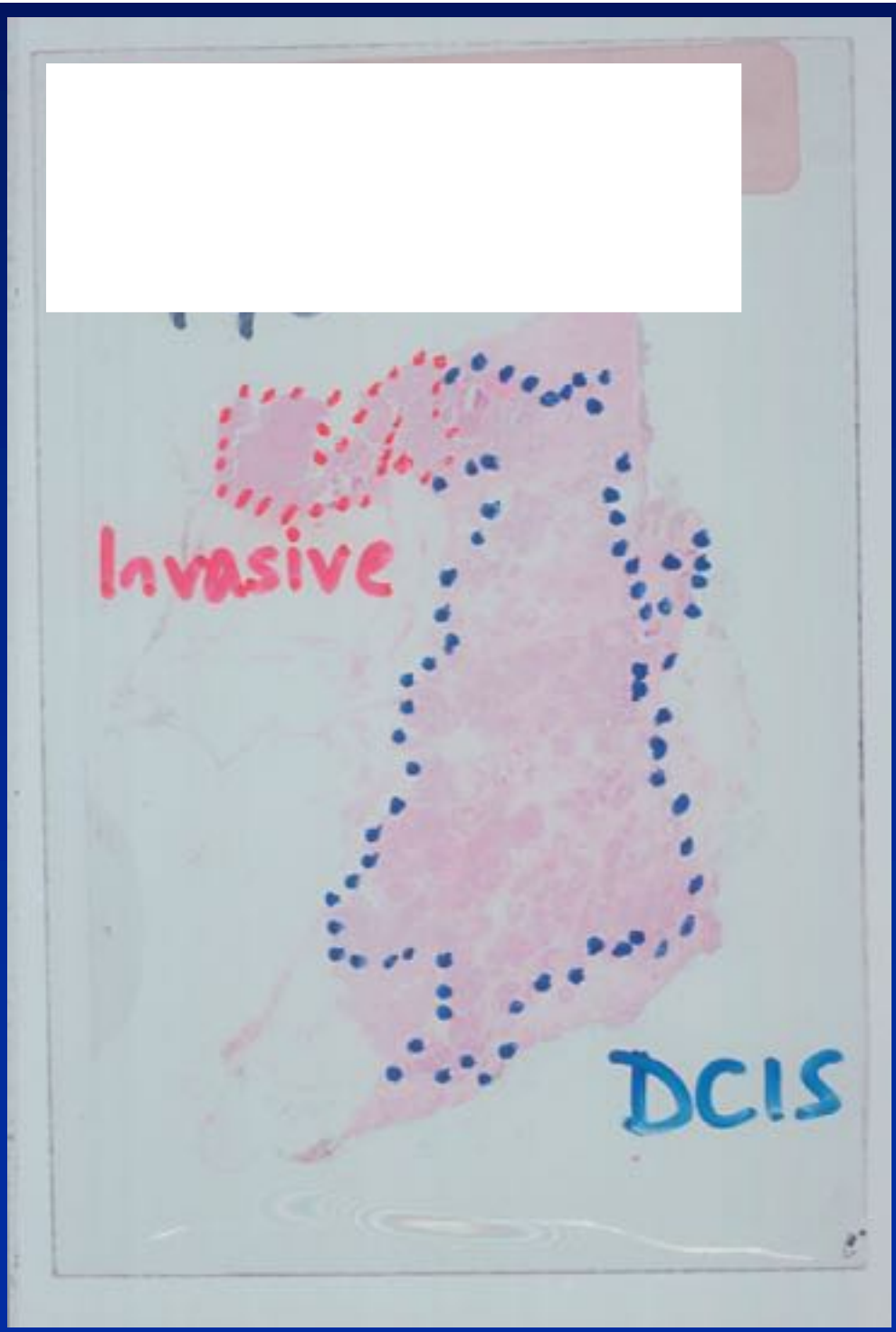
Prediction of Disease Extent by Radiology

Comedo / Solid	85% of area visible mammographically
Micropapillary / Cribriform	50% of area visible mammographically


Calcification
0 см
5 см
10 см

Slicing from anterior to posterior




Invasive
DCIS

Audit

- 101 cases invasive breast cancer at STH
- 63 (62%) examined macroscopically by bread-slicing method
- 38 cases (38%) by cruciates
- In bread-slicing, medial to lateral measurement was largest plane in 44% of cases in contrast to 58% of cases when using cruciate method
- Combining the two approaches: in 50% of cases medial to lateral measurement was largest (average 18mm) cf superior to inferior (average 14mm) & anterior to posterior (average 15mm)

Max Whibley, unpublished

Specimen Handling
Practice - Mastectomy

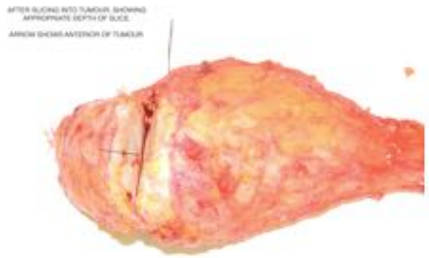
- Specimen arrives fresh
- Orientated
- *(Ink)*
- Slice
- Fix
- *(X-ray)*

PICTORAL GUIDE FOR SURGEONS FOR INCISING TUMOURS IN MASTECTOMY SPECIMENS FOR SATURDAY LISTS.

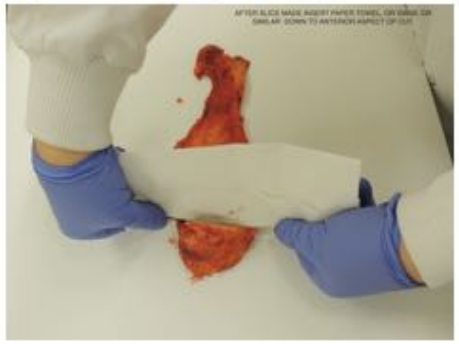
Step one – back of specimen

Step two – Single continuous slice from posterior of specimen through the middle of tumour. This should extend through the full thickness of the tumour up to its anterior border

J Owen & SE Pinder 21/11/12



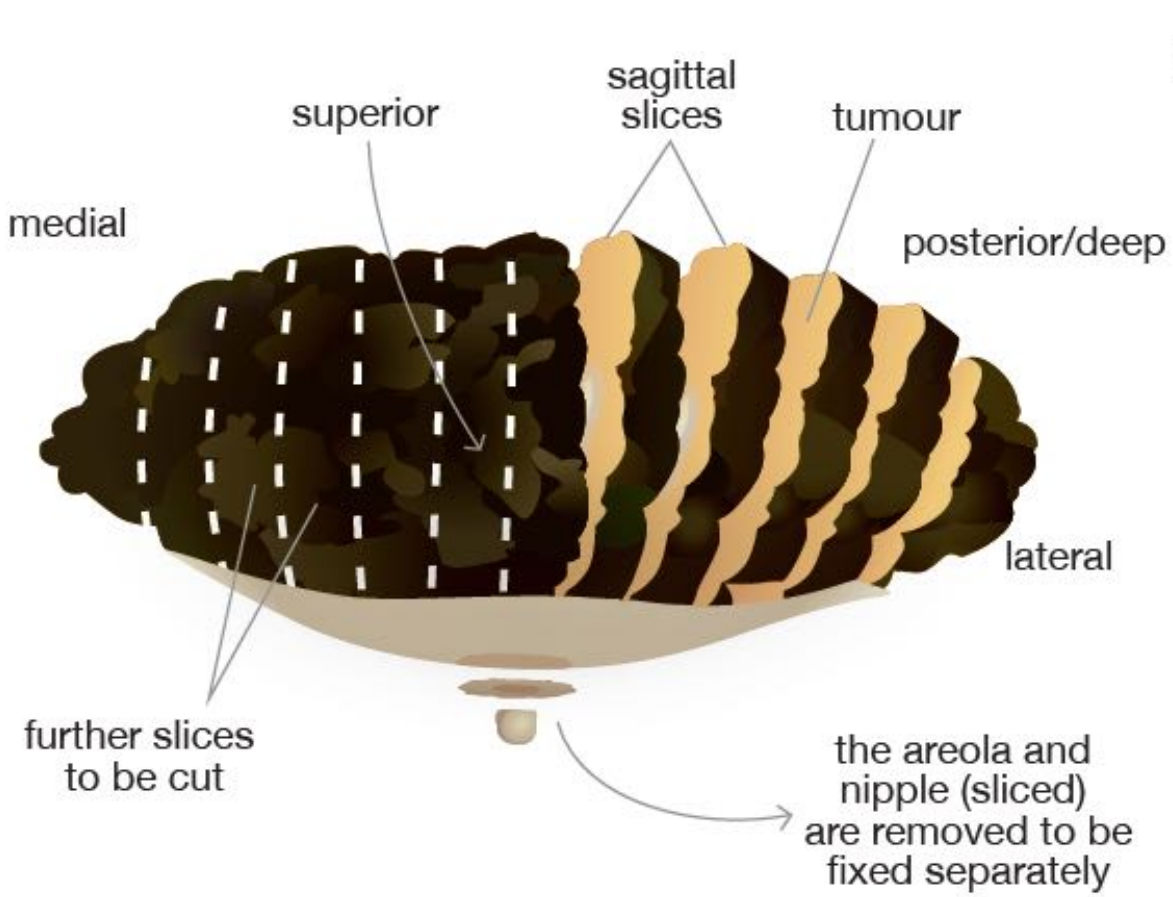
Step three – Insert tissue through full tickness of your cut

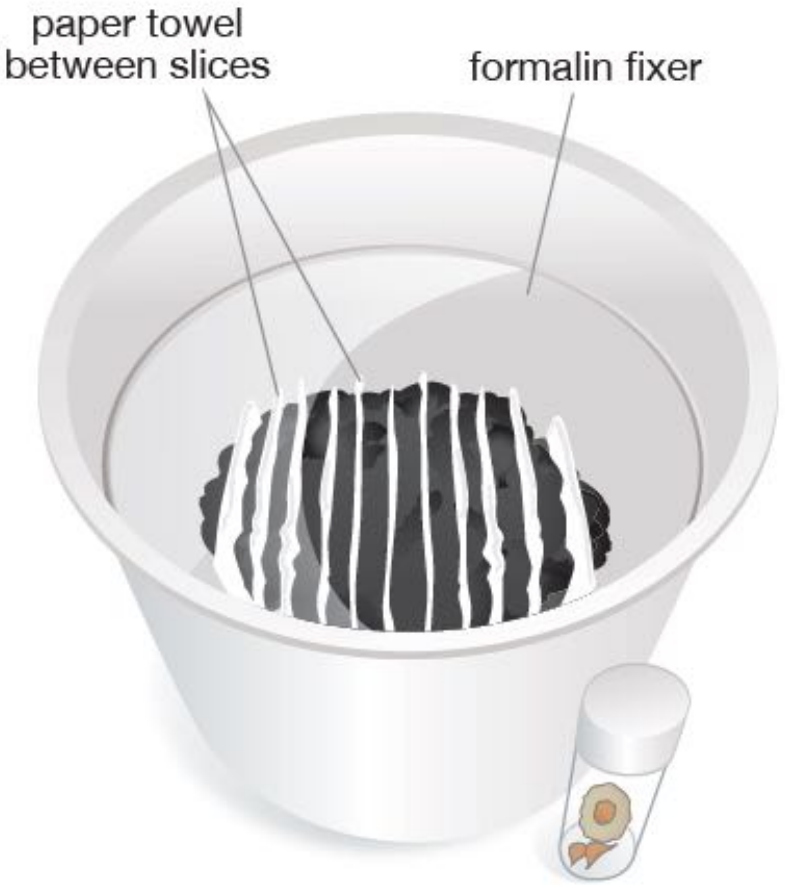


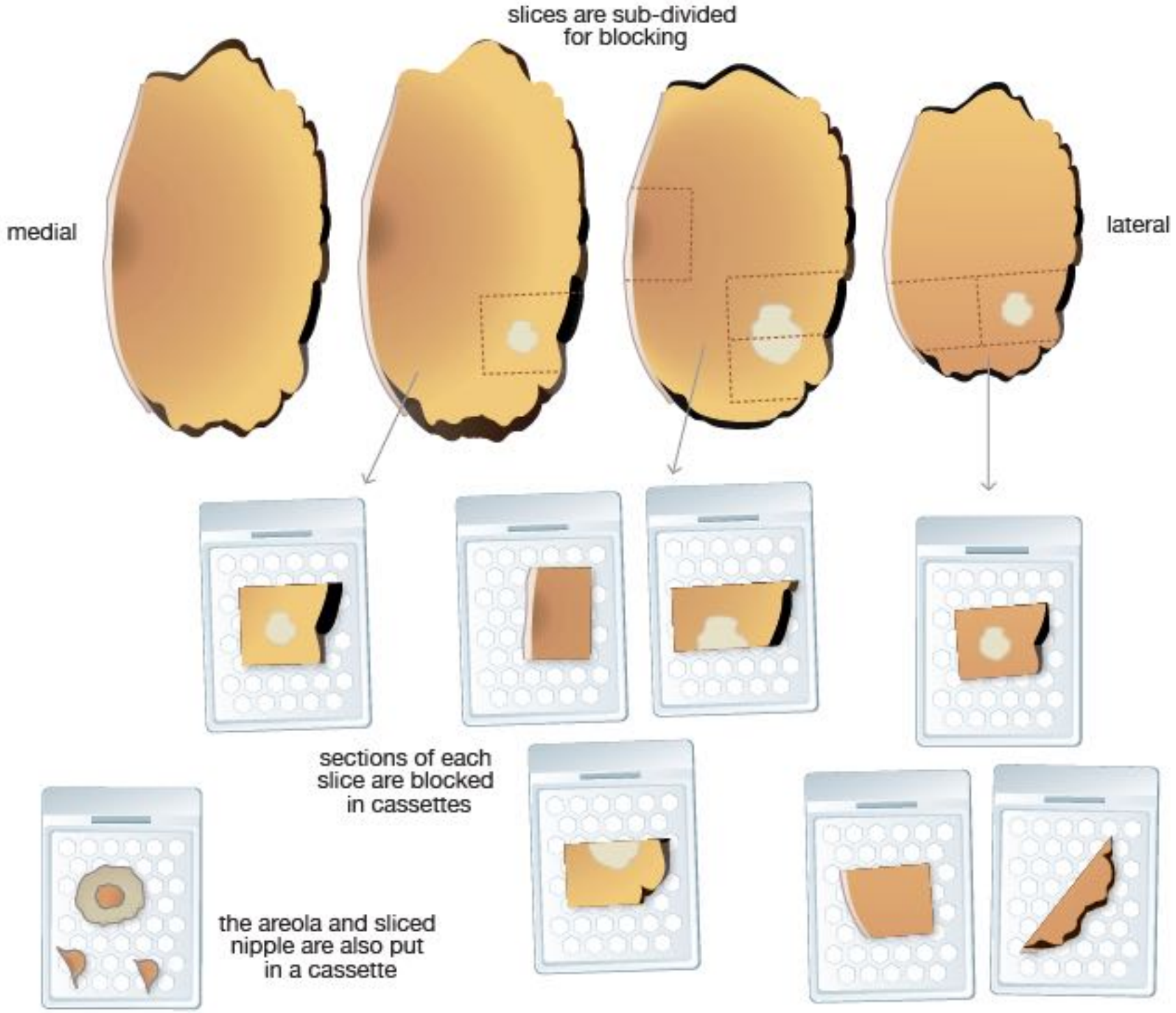
J Owen & SE Pinder 21/11/12

Step four – Put in sufficient formalin with tissue in place (you can insert suture, although not essential, to hold the two posterior edges together as long as there is tissue or swab between). Ideally also place tissue over the whole specimen, as shown, to submerge.

Mastectomy (left): sagittal slicing






slices are sub-divided
for blocking
medial
lateral
sections of each
slice are blocked
in cassettes
the areola and sliced
nipple are also put
in a cassette


LATERAL
0cm
5
805
7767
INFERIOR

Sections of the nipple & quadrants in mastectomy specimens

- 259 consecutive mastectomies
- New diagnosis of Paget's disease in 3 (1%)
- All 4 quadrants sampled in 230
- Unsuspected multifocality microscopically in quadrant sections in 14, in nipple in 3, in both in 1 (total = 8%)
- Such findings do not affect patient management

Sikand et al. J Clin Pathol. 2005;58:543-5


MEDIAL
SLICE
8
0cm
5

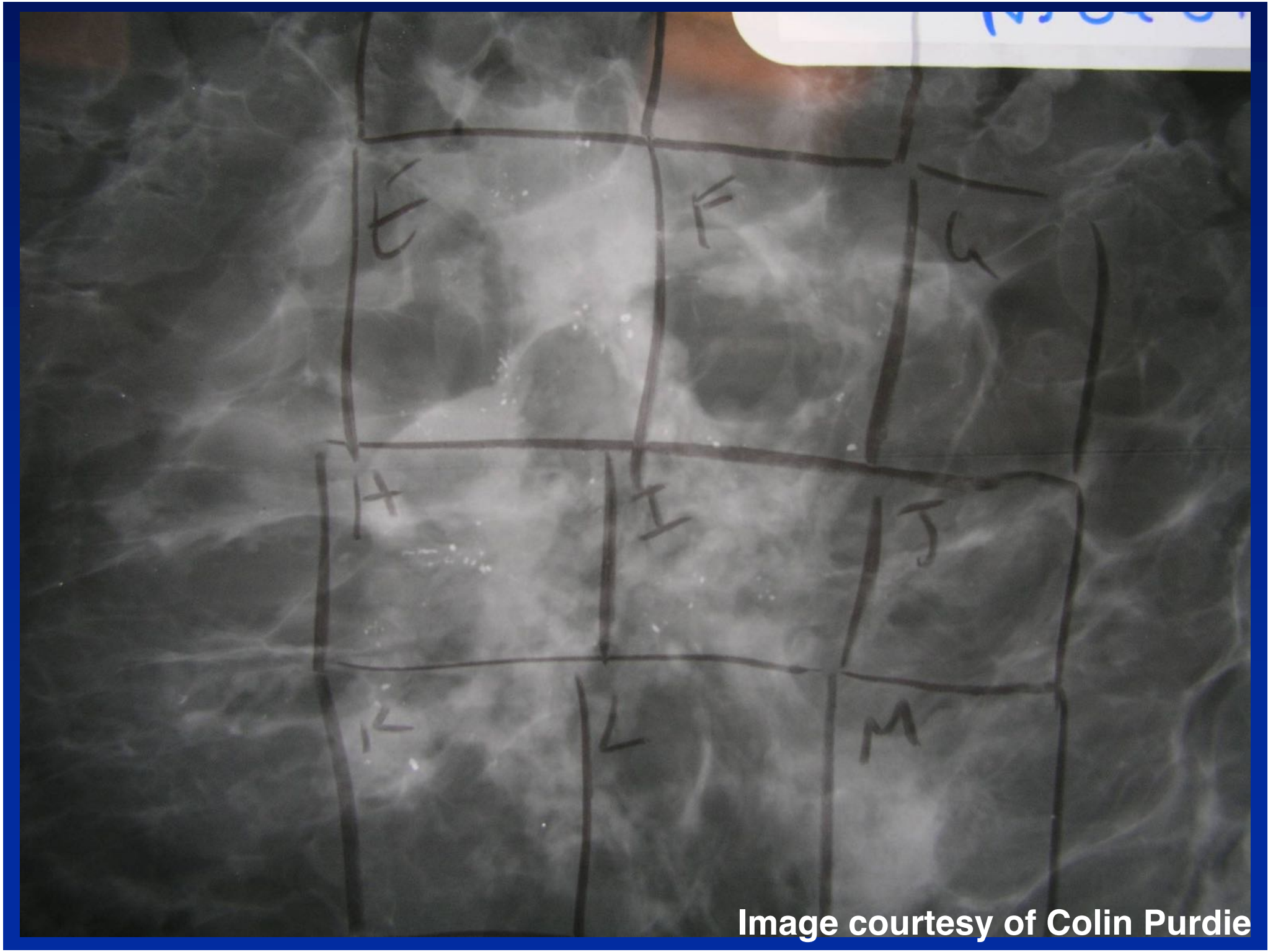


Image courtesy of Colin Purdie

Neoadjuvant Therapy Specimens

If, on slicing, there is no obvious tumour check if marker coil inserted, site on pre-operative core/FNAC report, search for area of stellate fibrous scarring & thoroughly sample, including margins

Histopathology 2007, **50**, 409–417. DOI: 10.1111/j.1365-2559.2006.02419.x

REVIEW

Laboratory handling and histology reporting of breast specimens from patients who have received neoadjuvant chemotherapy

S E Pinder, E Provenzano, H Earl[1] & I O Ellis[2]
Departments of Histopathology and [1]Oncology, Cambridge University Hospitals NHS Foundation Trust, Cambridge and [2]Department of Histopathology, Nottingham City Hospital, Nottingham, UK

Histopathology

Histopathology 2015, **67**, 279–293. DOI: 10.1111/his.12649

REVIEW

Macroscopic handling and reporting of breast cancer specimens pre- and post-neoadjuvant chemotherapy treatment: review of pathological issues and suggested approaches

Sarah E Pinder, Emad A Rakha,[1] Colin A Purdie,[2] John M S Bartlett,[3] Adele Francis,[4] Robert C Stein,[5] Alastair M Thompson,[6] & Abeer M Shaaban[7] on behalf of the Translational Subgroup of the NCRI Breast Clinical Studies Group

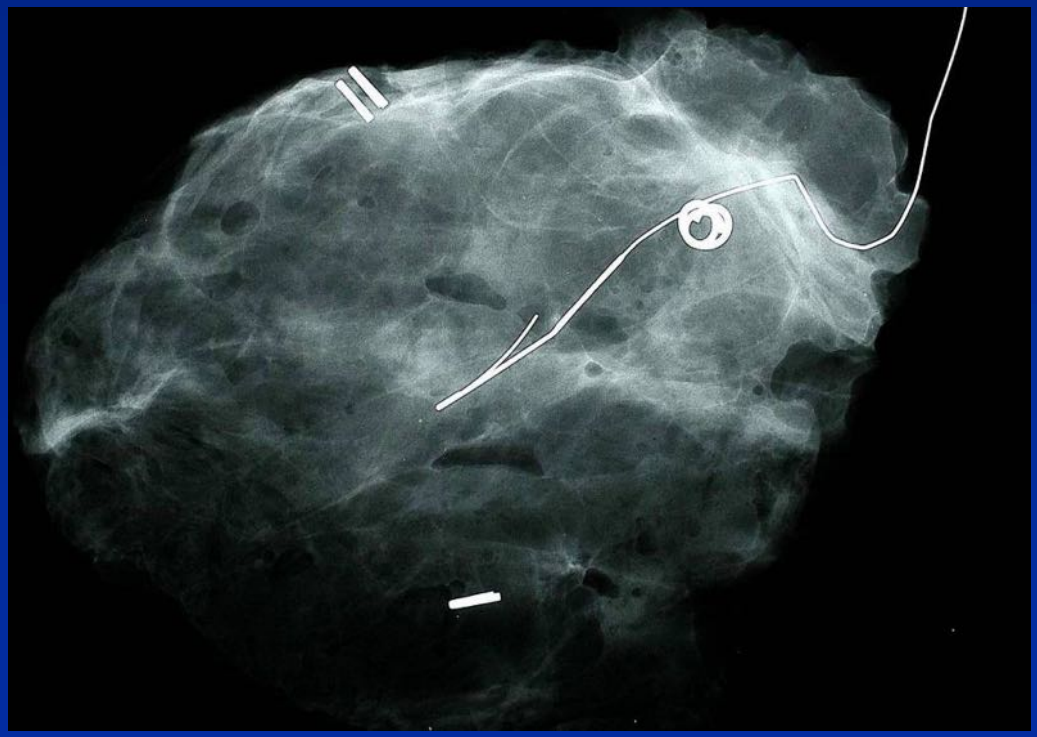
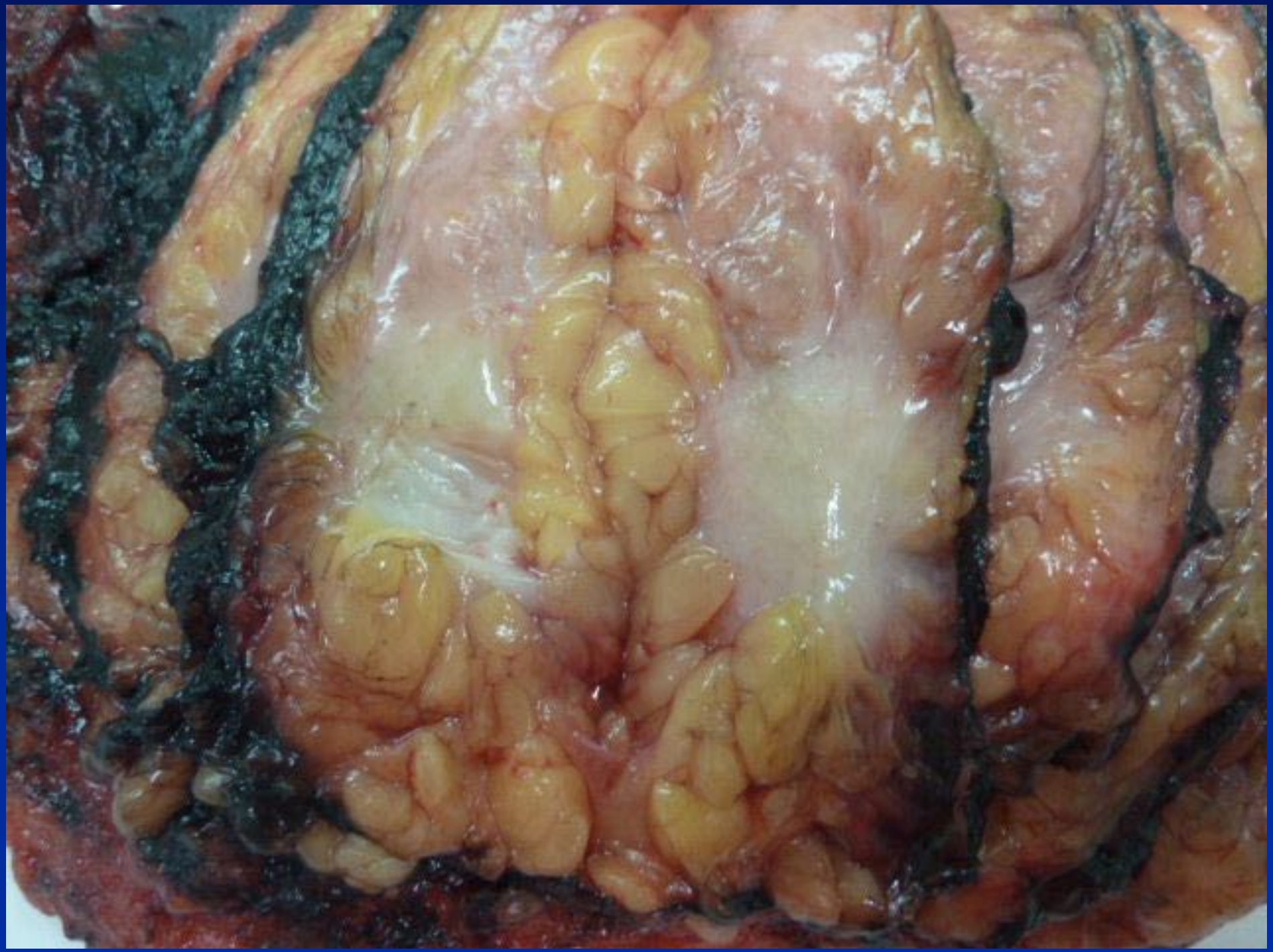


Image courtesy of Sami Shousha



Axillary Clearances

Minimum standard

- Every lymph node examined histologically
- Total number of nodes assessable - at least 1 slice per node
- Allows multiple nodes per block

Ideal method

One node per cassette - multiple slices

Do not:

- Bread-slice and put in consecutive slices
- Bisect some nodes & include in a cassette with intact nodes

Sentinel Lymph Nodes

- UK guidelines - methodology should provide highest chance of finding metastases on routine H&E
- Each node sliced thinly (2mm or less) perpendicular to long axis, blocked separately and all embedded
- Lymph nodes 4mm or less should be bisected

- Levels not routine
- IHC if suspicious cells identified (AE1/AE3)

Axillary Metastasis Reporting

(Macro)metastasis	> or = 2mm	LN Positive
Micrometastasis	<2mm >0.2mm	
Isolated Tumour Cell Clusters (ITCs)	<0.2mm	LN Negative

2009 (7th) edition of TNM classification of Malignant Tumours & Cancer Staging Manual

- Added word “cluster” to name of staging category to make it “isolated tumour cell clusters”
- Micrometastasis: >0.2mm but not >2mm &/or >200 cells
- ITCs = clusters of cells not >0.2mm or single metastatic cells or clusters with <200 cells in a single section
- 0.2mm size limit is for clusters, & 200 cell upper limit is for discohesive cells or nearly cohesive clusters

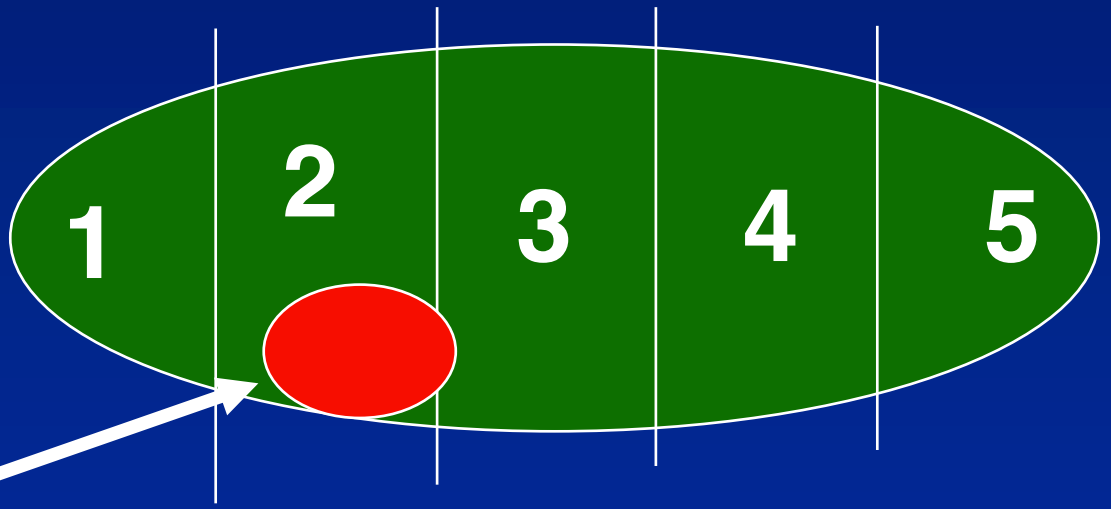
Edge SB, Byrd DR, Compton CC, et al., ed. *AJCC Cancer Staging Handbook: From the AJCC Cancer Staging Manual, 7th edition.* New York: Springer; 2009.

SLN Histopathological Handling

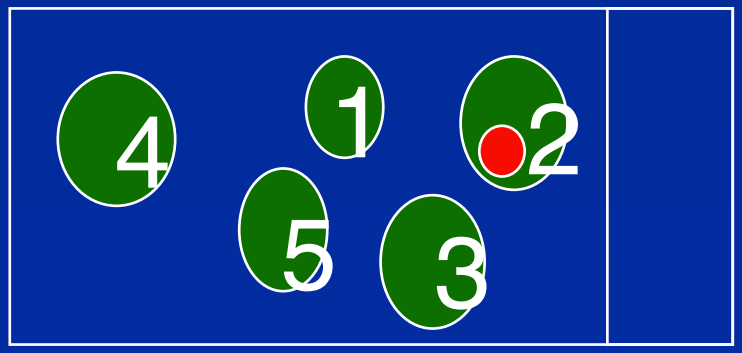
Slicing

Lymph node

Thin slices



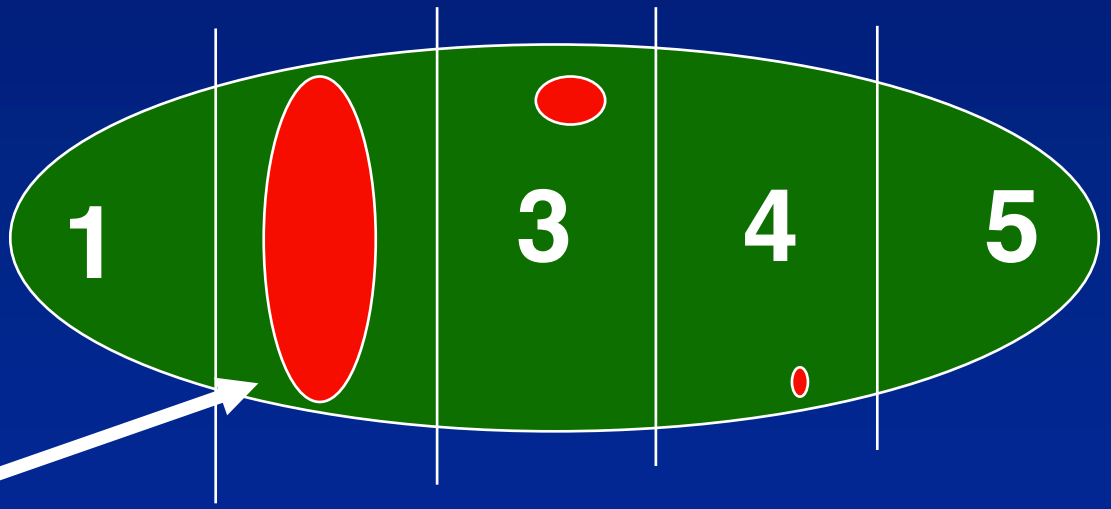
Metastasis



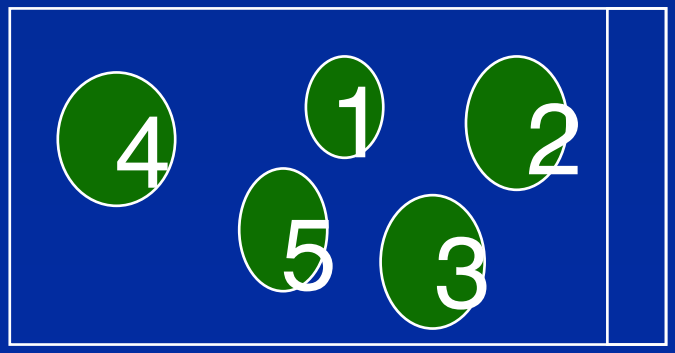
SLN Histopathological Handling

Lymph node

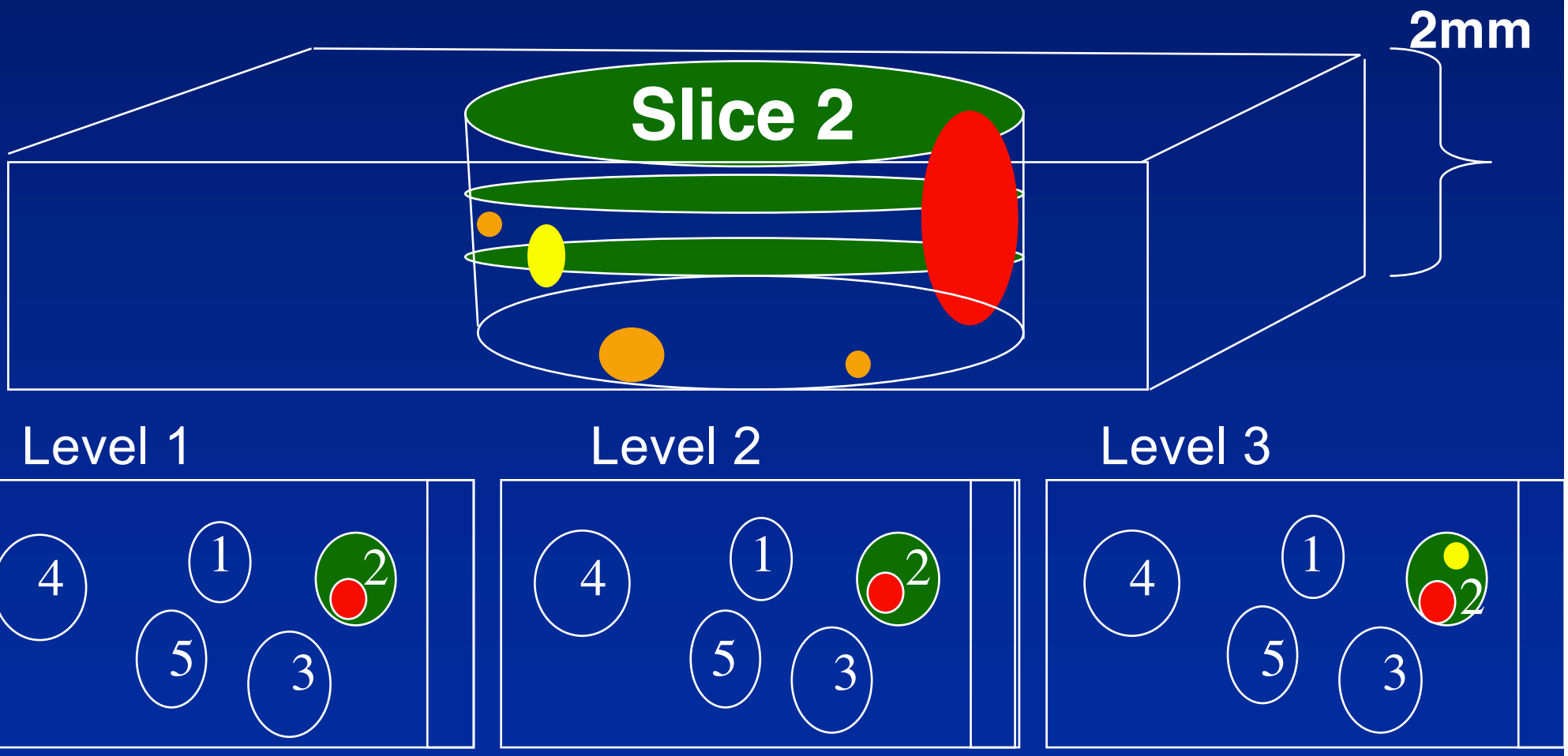
Thin slices



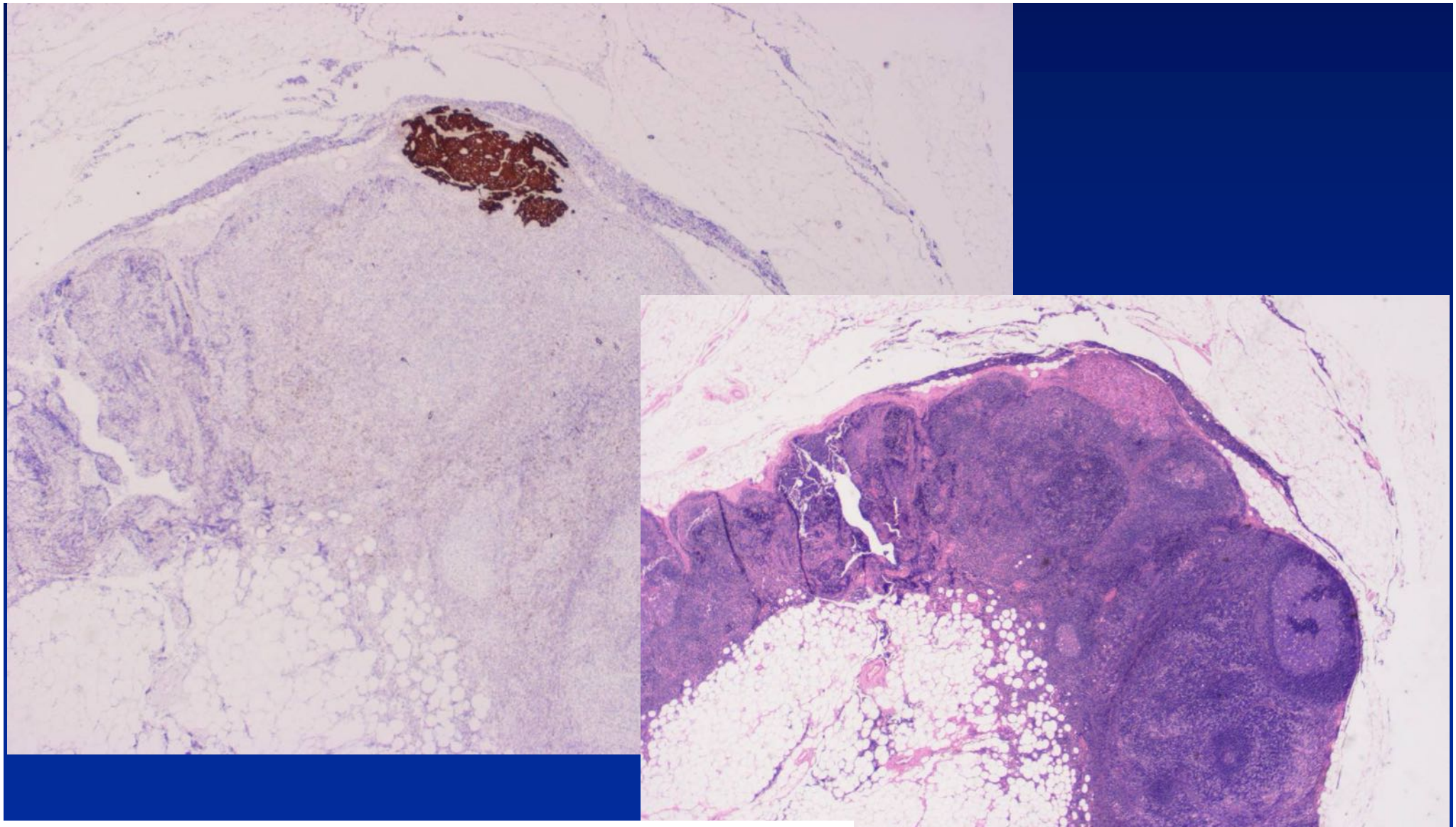
Metastatic cells



Handling SLNs - Levels/Step Sections



Identification of an isolated tumour cell would require 312 sections of a 1cm LN



Full Paper

The value of immunohistochemistry in sentinel lymph node histopathology in breast cancer

MB Klevesath[1], LG Bobrow[2], SE Pinder[*,2] and AD Purushotham[1]

[1]Cambridge Breast Unit, Department of Surgery, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, England, UK; [2]Department of Pathology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, England, UK

Summary / Take-home messages

- Good clinical liaison and knowledge of local protocols (e.g. margin widths)
- Think before slicing, each case
- If bread-slicing consider slicing ‘horizontally’
- Sample all radial margins
- Sample beyond extent of lesion, particularly for calcifications
- Concentrate on the tumour rather than random quadrants and nipple
- Slice SLNs as thinly as possible
- Report to minimum dataset/proforma