INVASIVE BREAST CANCER STRUCTURED REPORTING PROTOCOL

(2nd Edition 2012)

Core Document versions:

- AJCC Cancer Staging Manual 7th edition (including errata corrected with 5th reprint 10th Aug 2010).
- World Health Organization Classification of Tumours of the Breast 4th edition (2012).

ISBN: 978-1-74187-805-9
Publications number (SHPN): (CI) 120396

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First published: November 2012, 2nd Edition (Version 2.0)

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Contents

Scope

This protocol contains standards and guidelines for the structured reporting of invasive breast cancer and DCIS from a range of specimens, including: diagnostic open biopsy, wide local excision (partial mastectomy, quadrantectomy or segmentectomy), re-excision, mastectomy, breast surgery post neoadjuvant therapy, lymph node biopsy (sentinel or non-sentinel), axillary sample, axillary clearance.

Structured reporting aims to improve the completeness and usability of pathology reports for clinicians, and improve decision support for cancer treatment. The protocol provides the framework for the reporting of any breast cancer, whether as a minimum data set or fully comprehensive report.

This protocol is intended for use by pathologists, surgeons, radiologists and oncologists.

Abbreviations

ACN	Australian Cancer Network
ADH	Atypical ductal hyperplasia
AJCC	American Joint Committee on Cancer
ALH	Atypical lobular hyperplasia
CAP	College of American Pathologists
CTCs	Circulating tumour cells
DCIS	Ductal carcinoma in situ
DTCs	Disseminated tumour cells
ER	Oestrogen receptor
FISH	Fluorescence in situ hybridisation
H&E	Haematoxylin and eosin
HPF	High-power fields
IHC	Immunohistochemistry
ISH	In situ hybridisation
ITC	Isolated tumour cells
LCIS	Lobular carcinoma in situ
NBOCC	National Breast and Ovarian Cancer Centre
PBS	Pharmaceutical Benefits Scheme
PR	Progesterone receptor
RCPA	Royal College of Pathologists of Australasia
SNOMED	Systematized Nomenclature of Medicine
TNM	Tumour–node–metastasis
UICC	Union Internationale Contre le Cancer (International Union Against Cancer)
VNPI	Van Nuys Prognostic Index
WHO	World Health Organization

Definitions

The table below provides definitions for general or technical terms used in this protocol. Readers should take particular note of the definitions for 'standard', 'guideline' and 'commentary', because these form the basis of the protocol.

Ancillary study	An ancillary study is any pathology investigation that may form part of a cancer pathology report but is not part of routine histological assessment.
Clinical information	Patient information required to inform pathological assessment, usually provided with the specimen request form, also referred to as "pre-test information".
Commentary	Commentary is text, diagrams or photographs that clarify the standards (see below) and guidelines (see below), provide examples and help with interpretation, where necessary (not every standard or guideline has commentary). Commentary is used to: • define the way an item should be reported, to foster reproducibility • explain why an item is included (eg how does the item assist with clinical management or prognosis of the specific cancer). • cite published evidence in support of the standard or guideline • state any exceptions to a standard or guideline. In this document, commentary is prefixed with 'CS' (for commentary on a standard) or 'CG' (for commentary on a guideline), numbered to be consistent with the relevant standard or guideline, and with sequential alphabetic lettering within each set of commentaries (eg CS1.01a, CG2.05b).
General commentary	General commentary is text that is not associated with a specific standard or guideline. It is used: • to provide a brief introduction to a chapter, if necessary • for items that are not standards or guidelines but are included in the protocol as items of potential importance, for which there is currently insufficient evidence to recommend their inclusion. (Note: in future reviews of protocols, such items may be reclassified as either standards or guidelines, in line with diagnostic and prognostic advances, following evidentiary review).

Guideline	Guidelines are recommendations; they are not mandatory, as indicated by the use of the word 'should'. Guidelines cover items that are not essential for clinical management, staging or prognosis of a cancer, but are recommended. Guidelines include key observational and interpretative findings that are fundamental to the diagnosis and conclusion. Such findings are essential from a clinical governance perspective, because they provide a clear, evidentiary decision-making trail. Guidelines are not used for research items. In this document, guidelines are prefixed with 'G' and numbered consecutively within each chapter (eg G1.10).
Macroscopic findings	Measurements, or assessment of a biopsy specimen made by the unaided eye.
Microscopic findings	In this document, the term 'microscopic findings' refers to histo-morphological assessment.
Predictive factor	A *predictive factor* is a measurement that is associated with response or lack of response to a particular therapy.
Prognostic factor	A *prognostic factor* is a measurement that is associated with clinical outcome in the absence of therapy or with the application of a standard therapy. It can be thought of as a measure of the natural history of the disease.
Standard	Standards are mandatory, as indicated by the use of the term 'must'. Their use is reserved for core items essential for the clinical management, staging or prognosis of the cancer and key information (including observations and interpretation) which is fundamental to the diagnosis and conclusion. These elements must be recorded and at the discretion of the pathologist included in the pathology report according to the needs of the recipient of the report. The summation of all standards represents the minimum dataset for the cancer. In this document, standards are prefixed with 'S' and numbered consecutively within each chapter (eg **S1.02**).
Structured report	A report format which utilises standard headings, definitions and nomenclature with required information.
Synoptic report	A structured report in condensed form (as a synopsis or precis).

Synthesis

Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new.

The Oxford dictionary defines synthesis as “the combination of components or elements to form a connected whole”.

In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more modalities to derive new information.

Introduction

Breast cancer

Breast cancer is the most common invasive cancer among Australian women. The age-standardised incidence rate for Australian women has increased from 80.6 in 1983 to 112.4 in 2006.[1] Breast cancer is the most common cancer among Aboriginal and Torres Strait Islander women, but the incidence rate is lower than for the non-Indigenous population.

Breast cancer in males is rare. The number of new cases of breast cancer in males per year increased from 45 in 1983 to 102 in 2006.[1]

Breast cancer is one of the leading causes of cancer-related death in Australian women. However, owing to earlier detection by screening mammography and improved treatment, survival from breast cancer has been improving.[1] Australia's death rate from breast cancer is similar to those of Canada and the United States of America, and lower than those of New Zealand and Western Europe.[1]

Importance of histopathological reporting

The pathology findings are pivotal to any consideration of treatment options. As the biology of breast cancer is becoming better understood, and as new treatments emerge, the management of breast cancer is increasingly being tailored according to the patient's clinical profile and tumour characteristics.

Providing an accurate understanding of the distinct pathological features enables treatment protocols to be tailored to tumour characteristics based on the latest evidence. Correlation of the pre-operative clinical findings with those of imaging, percutaneous biopsy and surgical histopathology is a vital part of the multidisciplinary assessment process and is fundamental to the effective management of breast cancer and quality care of the patient.

Clinical oncologic practice relies on accurate histopathologic and immunopathologic data to provide both predictive and prognostic information that is used in planning pre-operative or post-operative local and/or systemic treatment. For example, the presence of involved regional nodes is the strongest prognostic factor for regional and systemic relapse and overall survival. This information determines the type of systemic adjuvant therapy chosen. Accurate measurement of predictive markers such as hormone receptors and HER2 similarly determines the choice of systemic therapies, both in the adjuvant setting and for advanced or metastatic breast cancer.

Benefits of structured reporting

Structured reports that follow a standardised, agreed format offer a systematic method of ensuring that all relevant information is included in a way that is easily interpreted by the clinical team, and minimise the chance of misinterpretation. This reporting format also simplifies the processes of auditing and entering data to cancer registries.

Structured pathology reports with standardised definitions for each component have been shown to significantly enhance the completeness and quality of data provided to clinicians, and have been recommended both in North America and the United Kingdom.[2-5] The College of American Pathologists and the Royal College of Pathologists (UK) have recently published useful protocols for the reporting of cancer.[6-7] In Australia, structured reporting of breast cancer pathology is recommended in current guidelines endorsed by National Breast and Ovarian Cancer Centre, Australian Cancer Network, Cancer Council, The Royal College of Pathologists of Australia, The Royal Australian College of Surgeons and The Royal Australian and New Zealand College of Radiologists.[8]

Design of this protocol

This structured reporting protocol provides a complete framework for the assessment and documentation of all the pathological features of invasive breast cancer. Mandatory elements (standards) are differentiated from those that are not mandatory but represent best practice (guidelines). Consistency and speed of reporting is improved by the use of discrete data elements recorded from the checklist. However, not all pathology information can be expressed in discrete variables or on a numerical scale. A prose description may be required to supplement the synoptic report in the case of complex findings or to express biological variation. Therefore, the pathologist is encouraged to include free text or narrative to document any other relevant issues, to give reasons for coming to a particular opinion and to explain any points of uncertainty.

The structure provided by the following chapters, headings and subheadings describes the elements of information and their groupings, but does not necessarily represent the format of either a pathology report (Chapter 7) or checklist (Chapter 6). These and the structured pathology request form (Appendix 1) are templates that represent information from this protocol, organised and formatted differently to suit different purposes.

Key documents

This protocol draws on the following key documents:

- National Breast and Ovarian Cancer Centre and Australian Cancer Network. *The pathology reporting of breast cancer. A guide for pathologists, surgeons, radiologists and oncologists (3rd edition).* Surry Hills, NSW; National Breast and Ovarian Cancer Centre, 2008.[8]

- The Royal College of Pathologists of Australasia (2004). *Chain of information custody for the pathology request-test-report cycle in Australia (guidelines for pathology requesters and pathology providers)*. RCPA, Surry Hills.[9]

- Guidelines Working Group of the National Coordinating Committee for Breast Pathology of the National Health Service Breast Screening Programme (2005). *Pathology reporting of breast disease. A joint document incorporating the third edition of the NHS Breast Screening Programme's guidelines for pathology reporting in breast cancer screening and the second edition of The Royal College of Pathologists' minimum dataset for breast cancer histopathology. NHSBSP Publication No 58*. NHS Cancer Screening Programmes and The Royal College of Pathologists, Sheffield.[10]

- Edge S, Byrd D, Carducci M, Compton C, editors.(2009) AJCC cancer staging manual. 7th edition: Springer, New York.[11]

- *Guidelines for authors of structured cancer pathology reporting protocols.* Sydney; Royal College of Pathologists of Australasia, 2009.[12]

Changes since last version

This document has been revised significantly from the 1st edition and as such a comprehensive list of changes is not useful.

Authority and development

This section provides details about the process undertaken in developing this protocol.

This edition of the protocol is the product of the work of two groups:

a) The first edition of the Breast protocol was published in Feb 2010. It was developed by an expert committee, adapted from National Breast and Ovarian Cancer Centre and Australian Cancer Network. *The pathology reporting of breast cancer. A guide for pathologists, surgeons, radiologists and oncologists (3rd edition).* Surry Hills, NSW; National Breast and Ovarian Cancer Centre, 2008. This document was developed by an expert working group representing relevant stakeholders (NBOCC and ACN guidelines 2008).

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b) This second edition was modified and updated from the original version by the following expert committee:

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Acknowledgements

The authors wish to thank all the pathologists and clinicians who contributed to the discussion around this document.

Stakeholders

Australian Cancer Network (ACN)
Breast Cancer Network Australia
Cancer Council Australia
Independent Review Group of Pathologists
National Breast and Ovarian Cancer Centre (NBOCC)
Medical Oncology Group of Australia
Royal Australasian College of Surgeons
The Royal Australian and New Zealand College of Radiologists
The Royal College of Pathologists of Australasia

Secretariat

Meagan Judge, Royal College of Pathologists of Australasia.

Development process

This protocol has been developed following the seven-step process set out in *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols.*[12]

Where no reference is provided, the authority is the consensus of the expert group.

1 Pre-analytical

This chapter relates to information that should be recorded on receipt of the specimen in the laboratory.

The pathologist is reliant on the quality of information received from the clinicians or requestor. Some of this information may be received in generic pathology request forms, however, the additional information required by the pathologist specifically for the reporting of invasive breast cancer is outlined in Appendix 1. Appendix 1 also includes a standardised request information sheet that may be useful in obtaining all relevant information from the requestor**.**

Surgical handling procedures affect the quality of the specimen and recommendations for appropriate surgical handling are included in Appendix 1.

S1.01 All demographic information provided on the request form and with the specimen must be recorded.

CS1.01a The Royal College of Pathologists of Australasia (RCPA) *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers* must be adhered to.[9] This document specifies the minimum information to be provided by the requesting clinician for any pathology test.

CS1.01b The patient's ethnicity must be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.

CS1.01c The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a patient's Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

S1.02 All clinical information as documented on the request form must be recorded verbatim.

CS1.02a The request information may be recorded as a single text (narrative) field or it may be recorded atomically.

S1.03 The pathology accession number of the specimen must be recorded.

S1.04 The principal clinician involved in the patient's care and responsible for investigating the patient must be recorded.

CS1.04a Knowledge of the clinical presentation is an essential part of the overall patient workup, particularly the triple assessment, yet it may not be available for a number of reasons:

- The clinical assessment and staging may be

incomplete at the time of biopsy.

- The pathology request is often authored by the clinician performing the biopsy rather than the clinician who is investigating and managing the patient.

- The identity of this clinician is often not indicated on the pathology request form

In practice therefore, it is important in such cases that the reporting pathologist should be able to communicate with the managing clinician for clarification.

G1.01 Any clinical information received in other communications from the requestor or other clinician should be recorded together with the source of that information.

2 Specimen handling and macroscopic findings

Specimen handling

- **Tissue for biomarker assays must be fixed in formalin as soon as possible after the specimen is taken.**

  - Receptor antigens may not be preserved if there is a delay in fixation. Fixation may be enhanced by placing a separate thin slice of the tumour in fixative or, where a delay in transport to the pathology laboratory is anticipated for a large excision, by placing a partial slice through the tumour to allow the fixative to permeate that part of the tumour.

- Hormone receptor assays can be performed on paraffin-embedded biopsy material (including excised tissue), cytological smears or cell-block preparations.

  - Current published evidence is inconsistent as to which type of specimen yields the most accurate results for hormone receptor assays. Some studies favour excision biopsies,[13-14] while others suggest that core biopsies might provide more reliable hormone receptor estimations than excision biopsies or mastectomies.[15] Institutions that have established protocols for carrying out receptor staining on core biopsy specimens may do so, ensuring that there is representative tumour present with optimal fixation. In acknowledgement of the central importance of hormone receptor status on patient management, when the excision specimen is hormone receptor (ER and PR) negative, laboratories may wish to repeat the hormone receptor assessment on the specimen and also to check the hormone receptors on the core biopsy sample in order to confirm the original findings. In the same vein, if hormone receptor assessment has been undertaken on core biopsies and has been found to be negative, this assessment should be repeated on the resection specimen to avoid a false negative result. Core biopsies must be assessed for biomarkers when the patient is a candidate for neoadjuvant chemotherapy or there are severe fixation and processing issues with the excised specimen.

  - Hormone receptor assays can be performed on cytologic specimens.[16]

    HER2 assessment is ideally performed on excision specimens, as there may be amplified foci within tumour that can be missed on core biopsy.

  - Optimal specimen handling is probably a key factor in ensuring accurate assays, regardless of specimen type.

- **The resection specimen must be fixed in 10% neutral buffered**

formalin for 8-24 hours.

- Fixation for 24 hours will achieve optimal results for both small samples (eg core biopsies) and larger samples (eg excision biopsy), because formalin fixation is a time-dependent chemical reaction which proceeds at a similar rate in both cases. Short fixation times (eg < 6–8 hours) are likely to compromise hormone receptor assay results.[14]

- Hormone receptor staining may be compromised by fixation in hot formalin or fixatives other than 10% neutral buffered formalin.

- Immunoreactivity may also be impaired by prolonged formalin fixation (possibly only extreme fixation times),[14,17] but this risk is rarely relevant, given clinical imperatives for rapid reporting.

➢ Antigen retrieval methods such as microwaving or heating tissue should be performed.

- These are usually necessary to optimise results.[18-19]

➢ When selecting test blocks, non-neoplastic glandular tissue should be included to provide an internal positive control that has undergone similar fixation to the carcinoma.

➢ Some researchers recommend selecting positive controls with both low and high hormone receptor levels, in order to avoid false negative results.[20]

Macroscopic findings

S2.01 The number of specimens submitted must be recorded.

S2.02 The laterality of each specimen must be recorded.

S2.03 The nature of the specimen must be recorded.

CS2.03a The pathologist should record the type of specimen as diagnostic open biopsy, wide local excision (partial mastectomy, quadrantectomy or segmentectomy), re-excision, mastectomy, mastectomy post neoadjuvant therapy, lymph node biopsy (sentinel or non-sentinel), axillary sample, axillary clearance.

CS2.03b The pathologist should record whether intraoperative consultation was required (eg frozen section, imprint cytology or gross examination for margin assessment).

S2.04 Record whether orientation markers have been used and if so the location of orientating markers (sutures or clips).

S2.05 The method of localisation must be recorded (eg hook wire or carbon track).

S2.06 The specimen size must be recorded in 3 dimensions.

CS2.06a For oriented excisions, measurements along medial-lateral, anterior-posterior (superficial-deep) and superior-inferior lengths should be provided.

S2.07 The weight of the specimen must be recorded.

S2.08 The presence of macroscopically visible tumours, and if present, the number of foci must be recorded.

S2.09 The gross description of each tumour must be recorded.

CS2.09a The nature of each tumour should be recorded.

CS2.09b The macroscopic size of each tumour must be recorded in 3 dimensions.

CS2.09c If multifocal, record the distance to nearest separate tumour foci.

CS2.09d Recording the minimum macroscopic clearance from margins may be valuable for radiology pathology correlation as well as for management purposes.

S2.10 The presence of skin in the specimen must be recorded.

CS2.10a If present, the dimensions of the skin must be recorded.

CS2.10b The presence of any skin abnormalities must be recorded. This will include:

- Ulceration
- Paget disease
- Satellite nodules
- Other (specify)

S2.11 The presence of muscle in the specimen must be recorded.

S2.12 Details of lymph node (sentinel or non-sentinel) biopsy must be recorded, if performed.

CS2.12a For each sentinel node sampled, the radioactive count should be recorded, if available.

CS2.12b For each sentinel node, an indication of whether it has taken up the dye should be recorded (eg blue: yes/no).

CS2.12c For each sentinel node the size in 3 dimensions should be recorded.

CS2.12d For non-sentinel nodes, specify the total number of nodes harvested, the size range and a description which should include the location of nodes according to standard code eg axilla level I, axilla level II, axilla level III, internal mammary chain (specify interspace if given).

S2.13 The site of origin within the specimen of each block taken (block key) must be recorded.

CS2.13a The use of specimen photographs or diagrams to illustrate the block key is strongly encouraged.

G2.01 A descriptive or narrative field should be provided to record any macroscopic information that is not recorded in the above standards and guidelines, and that would normally form part of the macroscopic description.

CG2.01a The traditional macroscopic narrative recorded at the time of specimen dissection is often reported separately from the cancer dataset. Although this remains an option, it is recommended that macroscopic information be recorded within the overall structure of this protocol.

CG2.01b Much of the information recorded in a traditional macroscopic narrative is covered in the standards and guidelines above and in many cases, no further description is required.

3 Microscopic findings

Invasive carcinoma

S3.01 The presence of multiple tumours and number of foci must be recorded.

CS3.01a The pathology report must indicate if there are multiple tumours present. Multifocality refers to the presence of two or more tumour foci within the same quadrant. By contrast multicentricity is the presence of two or more tumours in different quadrants of the same breast. For multifocal and multicentric tumours, the size, grade, subtype and biomarker status of each tumour must be stated, if they are distinctly different.

CS3.01b If multifocal, the maximum size of the tumour bed (the distance over which invasive carcinoma is present, including fibrotic areas between tumours) must be recorded.

S3.02 The maximum size of the invasive tumour and whole tumour size must be recorded.

CS3.02a When multiple tumours are present, each should be measured separately. T stage is based on the maximum dimension of the largest invasive tumour.

CS3.02b The maximum dimension of the invasive component must be recorded for each tumour. Foci of pure DCIS are measured elsewhere (refer to S3.11).

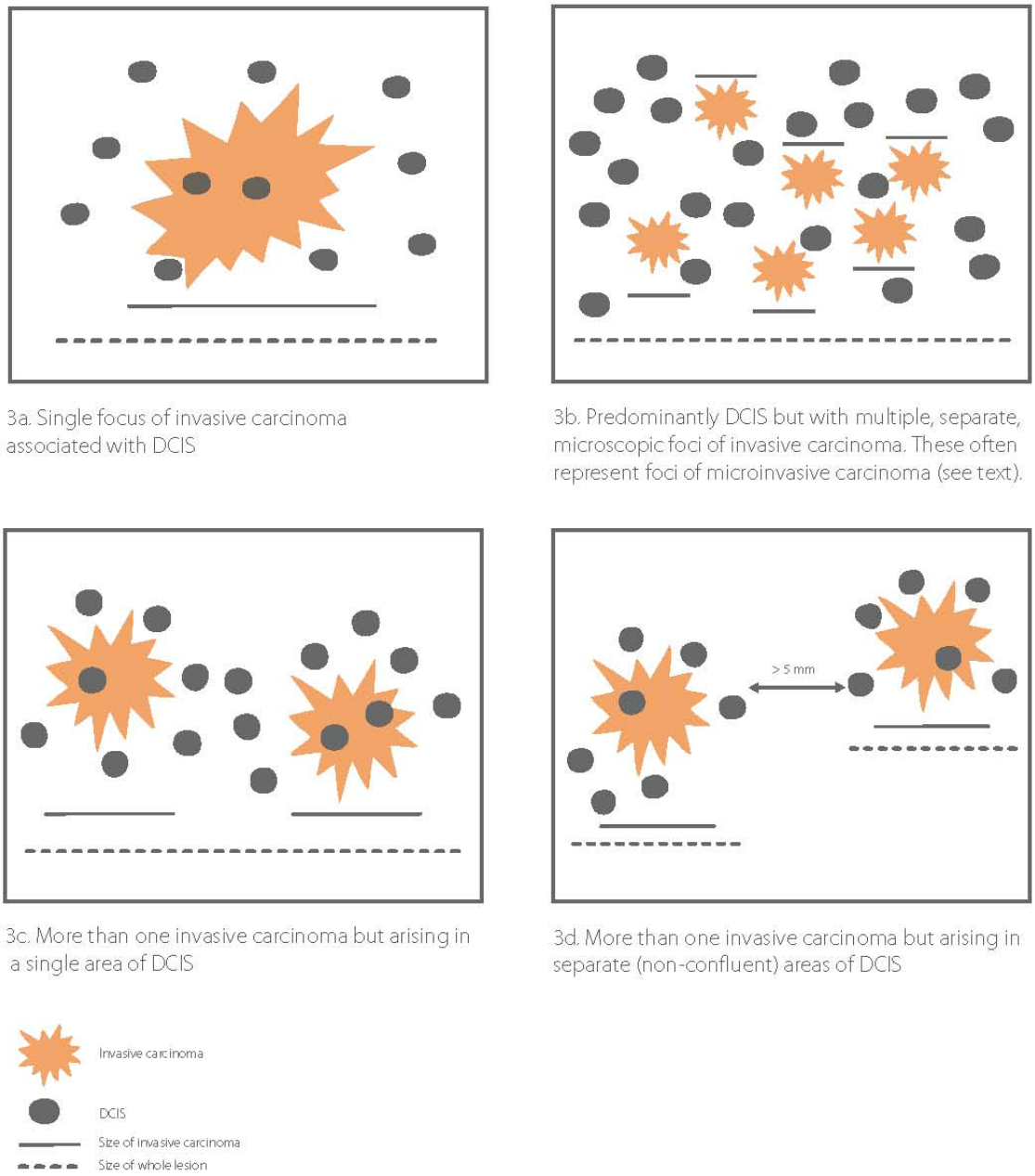
CS3.02c For tumours with an admixture of both in situ and invasive disease, only the size of invasive tumour is used for T staging.

CS3.02d Whole tumour size is a different measurement than maximum tumour size. Whole tumour size refers to the size of the entire tumour inclusive of both DCIS and invasive disease, when the DCIS component extends beyond the confines of the invasive elements. This item assists with imaging correlation for cases with extensive in situ carcinoma. Refer to Figure S3.02 below. The extent of LCIS is not included in the assessment of whole tumour size.

CS3.02e Invasive tumour size and whole tumour size differ only when ductal carcinoma in situ extends beyond the edges of the invasive tumour, where the whole tumour size will exceed the invasive tumour size. Staging is based on the maximum size of the invasive tumour.

CS3.02f Invasive tumours measuring 1 mm or less are classified as microinvasive (pT1mic). They are usually found in the setting of extensive DCIS.

Figure S3.02 Assessing the size of invasive carcinoma and whole lesion



3a. Single focus of invasive carcinoma associated with DCIS

3b. Predominantly DCIS but with multiple, separate, microscopic foci of invasive carcinoma. These often represent foci of microinvasive carcinoma (see text).

3c. More than one invasive carcinoma but arising in a single area of DCIS

3d. More than one invasive carcinoma but arising in separate (non-confluent) areas of DCIS

G3.01 Additional macroscopic dimensions of the tumour may be provided by gross and microscopic examination and included in the report.

CG3.01a In cases of invasive carcinoma, the largest dimension is measured and recorded in S3.02. Other measurements from the macroscopic or microscopic examination of the

specimen may be provided.

S3.03 The histological grade of the invasive carcinoma must be recorded.

CS3.03a Histologic grade is a powerful prognostic factor. Regardless of subtype, all invasive carcinomas should be graded. If the carcinoma is too small to be graded then the term "not assessable" should be used and the reason should be stated.

In cases with intratumoural heterogeneity the overall grade should be based on the degree of tubule formation determined from an overall assessment of the tumour, the nuclear grade and mitoses from the least differentiated areas and/or the periphery of the tumour.

CS3.03b The Elston and Ellis modification of the Bloom and Richardson grading system[21] must be used. The histological grade is derived from the sum of mitotic score, nuclear pleomorphism score and tubular differentiation score.

It is essential to know the field diameter of the microscope, so that the mitotic score (scale of 1–3) can be calculated from both the field diameter and mitosis count using Figure S3.03 and Table S3.03.[10]

CS3.03c The mitotic score is calculated from the number of mitoses per 10 high-power fields using a 40x objective, based on a representative area at the periphery of the tumour. In cases of intra-tumoural variation, the least differentiated or most proliferative area should be selected based on a low power assessment.

For mitotic rates in the borderline range between two scores, a further set of 10 HPF should be counted and the higher figure used.

CS3.03d Nuclear grade/pleomorphism is assessed by reference to normal duct epithelial nuclei as follows:

Score 1: Size equivalent to normal breast epithelial cells, regular outlines, uniform chromatin; inconspicuous nucleoli, little size variation.

Score 2: Larger nuclei, open vesicular chromatin; visible nucleoli, moderate variability in size and shape

Score 3: Vesicular nuclei; often with prominent nucleoli; exhibiting marked variation in size and shape, occasionally very large and bizarre forms.

CS3.03e Tubular differentiation is assessed from the overall appearance of the invasive carcinoma scanned at low power and taking into account any acinar, ductal or tubular structures. It is scored according to the percentage of tubular differentiation seen in the carcinoma as follows:

Score 1: >75% of invasive carcinoma forming tubular or glandular structures

Score 2: 10–75% of invasive carcinoma forming tubular or glandular structures

Score 3: <10% of invasive carcinoma forming tubular or glandular structures.

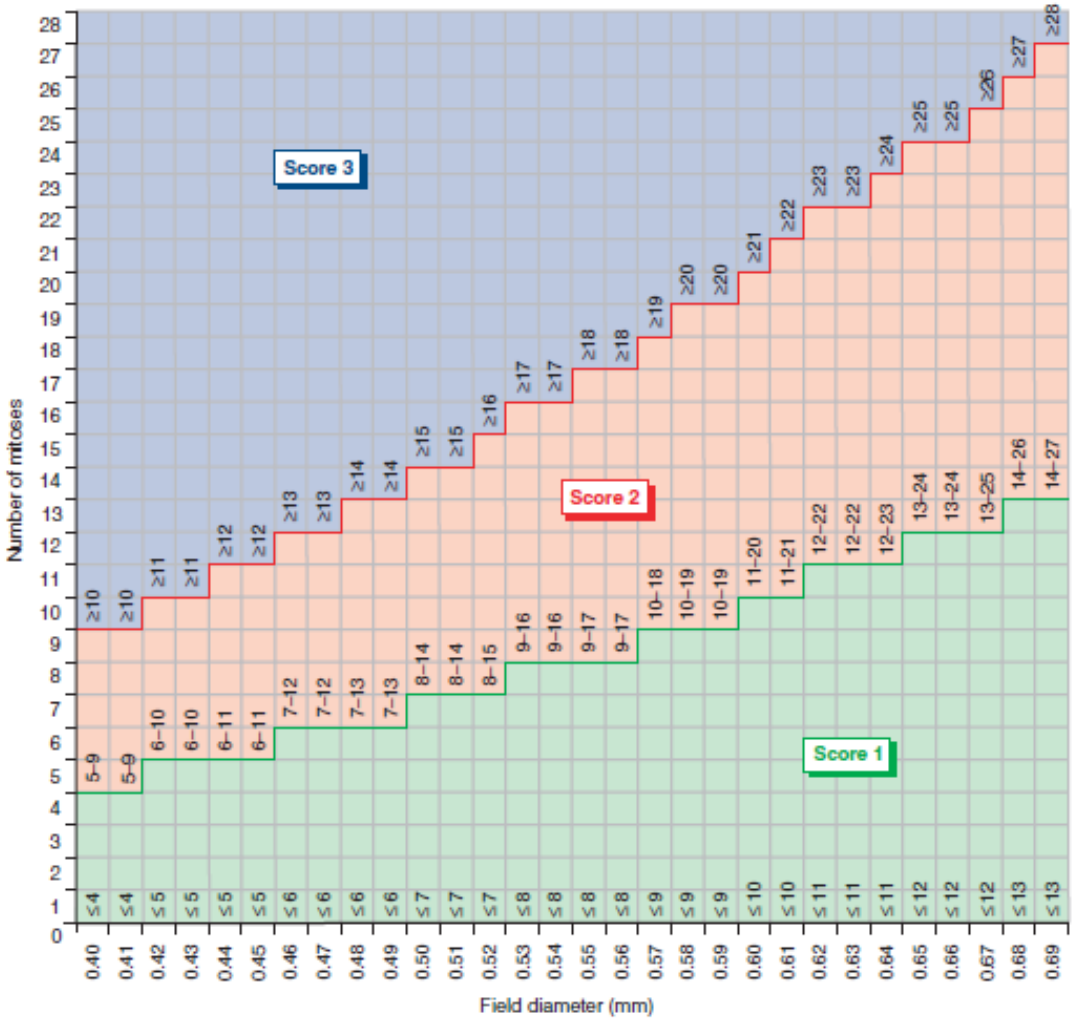
CS3.03f The mitotic score, nuclear /pleomorphism score and tubular differentiation score are added together and the histological grade is derived from their sum as follows:

Grade 1 Total score of 3–5

Grade 2 Total score of 6 or 7

Grade 3 Total score of 8 or 9.

Figure S3.03 Calibration of microscopic field diameter against mitotic frequency[10]



The above chart is an aide-memoire to assist calibration of microscope field diameter with mitotic frequency count grading cut off point.

Table S3.03 Mitotic counts by field diameter[10]

Field diameter (mm)	Mitotic frequency score 1	2	3	Field diameter (mm)	Mitotic frequency score 1	2	3	Field diameter (mm)	Mitotic frequency score 1	2	3
0.40	≤4	5–9	≥10	0.50	≤7	8–14	≥15	0.60	≤10	11–20	≥21
0.41	≤4	5–9	≥10	0.51	≤7	8–14	≥15	0.61	≤10	11–21	≥22
0.42	≤5	6–10	≥11	0.52	≤7	8–15	≥16	0.62	≤11	12–22	≥23
0.43	≤5	6–10	≥11	0.53	≤8	9–16	≥17	0.63	≤11	12–22	≥23
0.44	≤5	6–11	≥12	0.54	≤8	9–16	≥17	0.64	≤11	12–23	≥24
0.45	≤5	6–11	≥12	0.55	≤8	9–17	≥18	0.65	≤12	13–24	≥25
0.46	≤6	7–12	≥13	0.56	≤8	9–17	≥18	0.66	≤12	13–24	≥25
0.47	≤6	7–12	≥13	0.57	≤9	10–18	≥19	0.67	≤12	13–25	≥26
0.48	≤6	7–13	≥14	0.58	≤9	10–19	≥20	0.68	≤13	14–26	≥27
0.49	≤6	7–13	≥14	0.59	≤9	10–19	≥20	0.69	≤13	14–27	≥28

S3.04 The invasive carcinoma subtype must be recorded.

CS3.04a The following list is based on the World Health Organization Classification of Tumours of the Breast[22]:

- Invasive carcinoma of No Special Type (Ductal)
  - Pleomorphic carcinoma
  - Carcinoma with osteoclast like stromal giant cells
  - Carcinoma with choriocarcinomatous features
  - Carcinoma with melanotic features
- Invasive lobular carcinoma
  - Classical
  - Tubulolobular
  - Alveolar
  - Solid
  - Pleomorphic
  - Mixed
  - Others – signet ring, histiocytoid, etc
- Tubular carcinoma
- Cribriform carcinoma
- Mucinous carcinoma
- Carcinoma with medullary features
  - Medullary
  - Atypical medullary
  - Invasive carcinoma NST (ductal) with medullary features
- Carcinoma with apocrine differentiation
- Carcinoma with signet ring cell differentiation

- Invasive micropapillary carcinoma

- Metaplastic carcinoma
    - Low grade adenosquamous carcinoma
    - Fibromatosis-like metaplastic carcinoma
    - Squamous cell carcinoma
    - Spindle cell carcinoma
    - Metaplastic carcinoma with mesenchymal differentiation
        - Chondroid differentiation
        - Osseous differentiation
        - Other types of mesenchymal differentiation
    - Mixed metaplastic carcinoma
    - Myoepithelial carcinoma

<u>Rare Types of Invasive Cancer:</u>

- Carcinomas with Neuroendocrine features
    - Neuroendocrine tumour, well differentiated
    - Neuroendocrine tumour, poorly differentiated (small cell carcinoma)
    - Carcinoma with neuroendocrine differentiation
- Secretory carcinoma
- Invasive papillary carcinoma
- Acinic cell carcinoma
- Mucoepidermoid carcinoma
- Polymorphous carcinoma
- Oncocytic carcinoma
- Lipid rich carcinoma
- Glycogen rich/Clear cell carcinoma
- Sebaceous carcinoma
- Salivary gland/skin adnexal type tumours
- Adenoid cystic carcinoma
- Adenomyoepithelioma with carcinoma

S3.05 The presence or absence of peritumoural lymphovascular invasion must be reported.

CS3.05a The distinction between lymphatic versus vascular invasion is unreliable and not prognostically significant. Therefore the term lymphovascular invasion (LVI) should be used.

LVI is relevant if it is found outside of the perimeter of the invasive carcinoma. The space should have an endothelial lining. Lymphatics are often found adjacent to blood vessels.

In distinguishing LVI from retraction artefact, it is useful to remember that unlike retraction artefact, tumour emboli may not conform to the outlines of the affected vessel completely.

The most reliable method of assessing whether lymphovascular invasion is present is by examining

peritumoural tissue. However, immunostaining may on occasion be helpful in individual cases to distinguish true lymphovascular invasion from an artefactual cleft or fat space.

CS3.05b While it is acknowledged that on occasion the findings are not conclusive, the categories of suspicious or probable LVI do not assist with clinical decision making. These terms should be reserved for the rare cases where despite careful examination, consultation and possible immunohistochemical evaluation (D2-40) this distinction cannot be made.

S3.06 The presence or absence of skin involvement including the presence or absence of dermal lymphatic invasion must be recorded.

CS3.06a If there is invasion of the dermis it must be recorded whether this is:

- Paget disease of the nipple (DCIS extending to skin contiguous with lactiferous sinuses)
- Invasive carcinoma involving dermis or epidermis without ulceration
- Invasive carcinoma involving dermis or epidermis with ulceration
- Ipsilateral satellite skin nodules, ie dermal deposits of invasive carcinoma, separate from the main tumour

CS3.06b Paget disease of the nipple (DCIS extending to skin contiguous with lactiferous sinuses) can be correlated with clinical findings of skin tethering. However, it has no effect on stage.

CS3.06c Invasive carcinoma involving dermis or epidermis with ulceration is assigned stage T4b.

CS3.06d Ipsilateral satellite skin nodules are assigned stage T4b.

CS3.06e Tumour emboli in dermal lymphatics have a particular association with the clinical finding of inflammatory breast cancer. This feature should be reported (refer to S3.05) but the diagnosis of inflammatory carcinoma is a clinical diagnosis. Further, dermal lymphatic emboli alone do not qualify the tumour for the T4d stage.

CS3.06f Dermal lymphatic invasion is also associated with local recurrence.

S3.07 The presence or absence of muscle involvement must be recorded.

CS3.07a If pectoral muscle is included in the specimen, documenting the presence of invasive carcinoma into skeletal muscle may assist in decisions regarding radiation

therapy post mastectomy.

CS3.07b Invasion into skeletal muscle does not alter the stage independently. Invasion through the pectoralis major into the chest wall is required for classification as T4a.

S3.08 If administered, any neoadjuvant treatment effect in the breast must be recorded.

CS3.08a Treatment effect can be recorded as:

- **No definite response** to pre-surgical therapy in the invasive carcinoma
- **Partial** response to pre-surgical therapy in the invasive carcinoma, residual carcinoma identified. (See Figure CS3.08c (i) Residual Cancer Burden Assessment tool below)
- **Complete** pathologic response in breast and lymph nodes: No residual invasive carcinoma is present in the breast or lymph nodes after pre-surgical therapy

CS3.08b The estimate of the percentage of cellularity of each tumour post therapy, ie the proportion of area of tumour involved with invasive carcinoma must be recorded. This may be compared with the percentage of cellularity of tumour pre therapy, if information from the previous biopsy is available.

There are several published systems for assessing pathologic response to neoadjuvant therapy. There are variations between these systems. If neoadjuvant therapy is offered in the context of a clinical trial, the pathologic response assessment system specified in the design of the particular clinical trial should be utilised.

CS3.08c There are a number of response classification systems available to assess the pathologic response of breast cancer to neoadjuvant therapy.[23] If neoadjuvant therapy is employed in the setting of a clinical trial and a specific system has been recommended for use in the particular trial, then the pathologist should apply the specified system.

If a system is not specified by the clinical trial or treatment is outside a clinical trial, the pathologist should specify the response classification system they choose and provide the data items used in the determinations of that system. Pathologic Complete Response (pCR) should be specified, noting that various systems differ as to whether they permit the finding of residual DCIS or nodal disease in the definition of pCR. Near-pCR and residual disease are other final categories of response specified by the response classification systems, with specific reference to the system used.

For cases with residual disease, assessment of tumour size

and the reduction in cellularity of the invasive carcinoma compared to the pre-treatment biopsy are common data elements. The response in lymph nodes is prognostically significant and should be specified, as indicated in section S3.23.

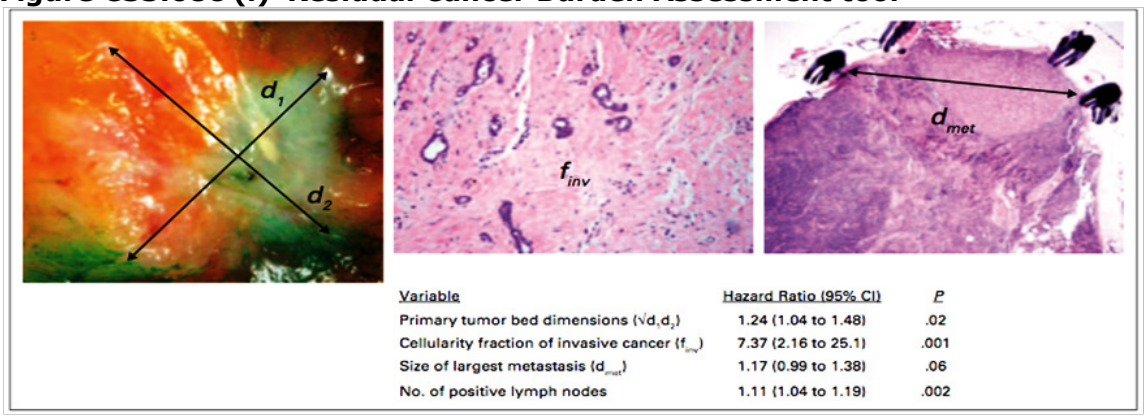
The Residual Cancer Burden system proposed by Symmans et al has been validated clinically.[24] This system is based on an assessment of the bidirectional diameter of the tumour bed, the percentage cellularity of the invasive carcinoma, the size of the largest nodal deposit and the number of positive lymph nodes. The finding of residual DCIS does not preclude a diagnosis of pCR in this system. On line tools and a web calculator are available to assist with this assessment at www.mdanderson.org. Refer to Figure CS3.08c (i) and (ii) below.

The assessment of the tumour size may be problematic in cases where there has been a substantial response since the tumour usually "fragments" into multiple foci of disease. Reference to the original imaging may assist in distinguishing truly multifocal cancers, from those that appear to be so after therapy. If the original tumour was unifocal then the largest extent of diseased area is to be used for assessment of response to Neoadjuvant chemotherapy (NAC).

Assessment of tumour margins is also more problematic after neoadjuvant therapy. Because the residual disease may have a patchy distribution, the absence of disease at surgical margins may not constitute a guarantee that there is no further tumour in the remaining breast tissue. Nevertheless, the pathology report should state the status of resection margins.

Tumour grade should be based on the original biopsy since treatment effects may introduce greater nuclear atypia. Few and somewhat conflicting data are available on the changes in biomarkers after NAC, such that definitive statements regarding mandatory repeating of biomarkers after NAC cannot be substantiated. Such assessments can be accommodated upon request.

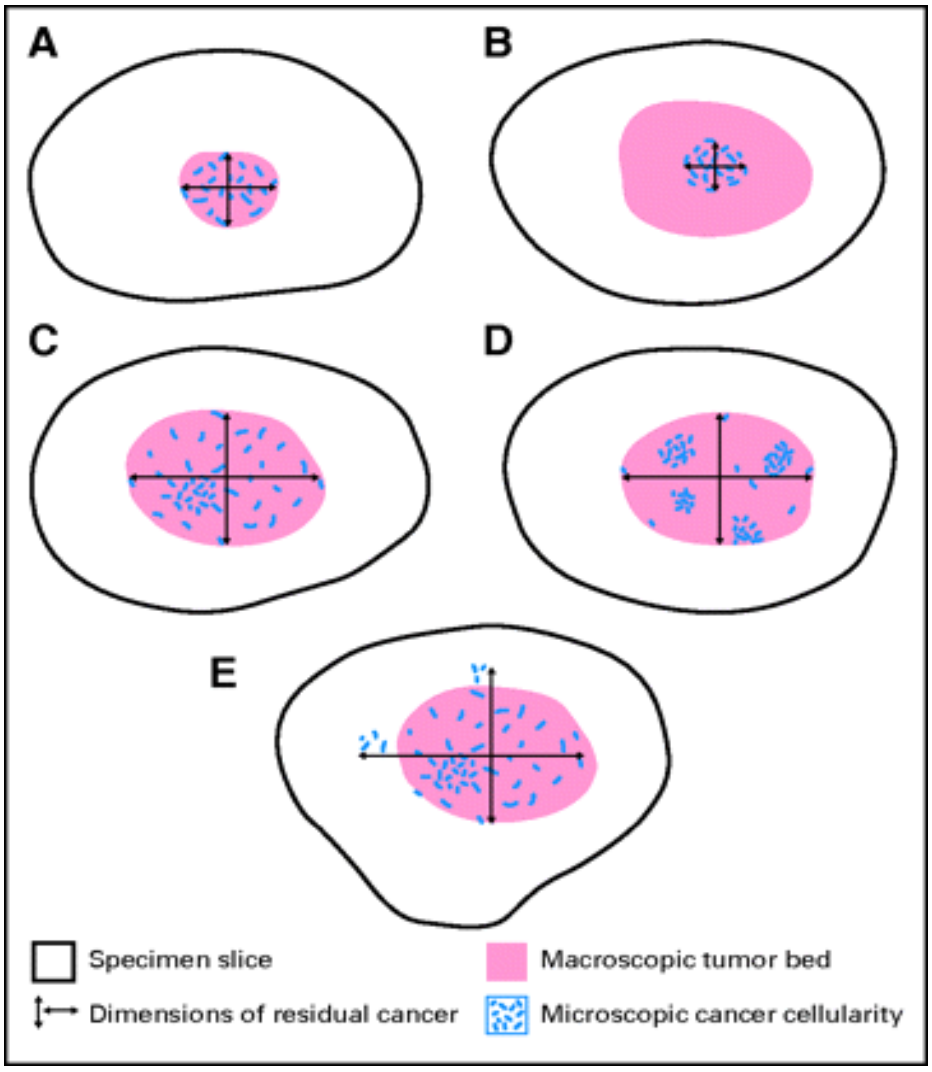
Figure CS3.08c (i) Residual Cancer Burden Assessment tool



Variable	Hazard Ratio (95% CI)	P
Primary tumor bed dimensions ($\sqrt{d_1 d_2}$)	1.24 (1.04 to 1.48)	.02
Cellularity fraction of invasive cancer (f_{inv})	7.37 (2.16 to 25.1)	.001
Size of largest metastasis (d_{met})	1.17 (0.99 to 1.38)	.06
No. of positive lymph nodes	1.11 (1.04 to 1.19)	.002

$$RCB = 1.4\ (f_{inv}\, d_{prim})^{0.17} + [4(1 - 0.75^{LN})\, d_{met}]^{0.17}$$

Figure CS3.08c (ii) Residual Cancer Burden Assessment



DCIS

S3.09 The presence of DCIS must be recorded.

CS3.09a If DCIS is present, then it must be noted whether the DCIS is present only in conjunction with the invasive carcinoma or whether there are foci of pure DCIS.

CS3.09b Foci of pure DCIS are those which are >5mm from the invasive tumour.

S3.10 If DCIS is present, then the estimated maximum extent of involved breast must be recorded.

S3.11 For each case of pure DCIS, the maximal size must be reported.

CS3.11a The maximum dimension of the DCIS must be measured, using measurement on the slide and reference to the gross specimen and/or imaging findings as necessary.

S3.12 If DCIS is present, the highest nuclear grade of the DCIS must be recorded.

CS3.12a Nuclear grade must be reported as low, intermediate or high, a recognised grading system for DCIS. The Van Nuys system, used in the AJCC/UICC CAP or the NHSBSP systems are well known. (See Table S3.12 below).

CS3.12b If heterogeneity is observed, then the grade should be reported as the highest grade to which the features correspond. The 'next most prevalent' grade may be reported at G3.02. The use of combined grades, for eg intermediate to high or low to intermediate, is discouraged.

CS3.12c Various studies have established nuclear grade as a predictive factor in breast-conserving management of DCIS, although the grading schemes utilised were diverse. In addition, there is significant correlation between DCIS grade and the grade of any corresponding invasive component, if present, regardless of the grading system used.[25-27]. These grades have also been associated with a range of biological characteristics. High-nuclear-grade lesions may show a more aggressive biological profile with absence of oestrogen and progesterone receptor expression, aneuploidy, a high proliferative index, membrane reactivity for HER2, p53 nuclear expression and absent bcl2 expression. Low-nuclear-grade lesions show the converse, and intermediate-grade DCIS exhibits mixed patterns of biological marker expression.

Table S3.12 The Van Nuys and NHS BSP 2005 nuclear grading systems

Van Nuys	**Non-high grade without necrosis:** Low grade nuclei (1-1.5X RBC), inconspicuous nucleoli, diffuse chromatin. Or, intermediate grade nuclei (1-2X RBC), occasional nucleoli, coarse chromatin. No comedo type necrosis	**Non-high grade with necrosis:** Low grade nuclei (1-1.5X RBC), inconspicuous nucleoli, diffuse chromatin. Or, intermediate grade nuclei (1-2X RBC), occasional nucleoli, coarse chromatin. Comedo type necrosis present (disregard individual cell necrosis)	**High grade:** High grade nuclei (>2 X RBC), 1 or more nucleoli. Comedo necrosis is surrounded by pleomorphic cells or by cribriform and micropapillary patterns. Necrosis not mandatory if nuclei are high grade.
NHS BSP 2005	**Low grade DCIS:** Monomorphic, evenly spaced cells with rounded, centrally placed nuclei, inconspicuous nucleoli. Nuclei typically small (1-2 x RBC). Few mitoses. There is rarely individual cell necrosis. Growth pattern mostly cribriform or micropapillary. Nuclear polarity retained. Less commonly solid.	**Intermediate grade** DCIS: Cannot be assigned to high or low grade categories. Moderate pleomorphism but lacking monotony of low grade DCIS. Mildly enlarged nuclei (2-3xRBC). Raised N:C ratio. One or two nucleoli may be identified. Growth pattern may be solid, cribriform or micropapillary. Some degree of polarity retained. Clear cell or apocrine types often fall into this category.	**High grade DCIS**: Pleomorphic, irregularly spaced, large nuclei (3xRBC), marked pleomorphism, irregular nuclear contours, coarse chromatin, prominent nucleoli. Frequent and abnormal mitoses. Frequently solid and associated with comedo type necrosis. May see other patterns. May be solid without necrosis. Loss of nuclear polarity.

G3.02 Where heterogeneity of nuclear grade is present, then in addition to the highest grade, the next most prevalent grade should also be recorded.

CG3.02a In approximately 30% of cases more than one nuclear grade is noted.

CG3.02b The presence of another distinct nuclear grade of DCIS may be recorded, however as noted in CS3.12b, 'combined' grades eg low to intermediate, are discouraged.

S3.13 The presence or absence of necrosis in DCIS must be recorded.

CS3.13a Necrosis is defined as the presence of ghost cells and eosinophilic, granular karyorrhectic debris mostly in the centre of the affected ducts.[28]

CS3.13b Classification schemes that use the term comedo necrosis, regard it as a confluent central zone, as defined above. Single apoptotic cells do not qualify for necrosis for this purpose. If only isolated apoptotic cells are seen, necrosis should be reported as absent.

There has been discussion regarding disbanding the use of the term 'comedo' due to lack of a common definition. The

AJCC/CAP retain the comedo terminology. The UK NHSBSP refer to comedo type necrosis. The Van Nuys system, used widely for clinical trials uses comedo necrosis. Pathology QA data suggest high kappa values for recognition of comedo necrosis. There is no consensus on this issue, for the time being the writing committee have therefore agreed to retain the term comedo pending consensus.

S3.14 If DCIS is present, a description of the DCIS architecture must be recorded.

CS3.14a Many tumours show more than one architectural pattern. Most DCIS falls within the categories of comedo, solid, cribriform, micropapillary, apocrine or papillary.

CS3.14b It is the overall grade of the DCIS that has prognostic significance. Architecture is correlated with grade. Comedo and solid architectures are frequently seen in high grade DCIS and cribriform and micropapillary architectures are often associated with low grade DCIS.

S3.15 The presence or absence of microcalcifications in breast tissue must be recorded.

CS3.15a Microcalcifications must be recorded as present (specify whether associated with necrosis), or absent.

CS3.15b If present, the report must specify which type of lesion is associated with microcalcifications, so as to enable accurate correlation with the pre-operative imaging findings.

CS3.15c An accurate description of calcification helps in correlating pathological findings with radiological findings. In some cases, detailed descriptions of the size and extent of microcalcifications may be needed to assist in confirming excision of the lesion. This may require close consultation with the radiologist and careful histological study, in conjunction with specimen radiography.

CS3.15d Careful documentation of microcalcifications is particularly important when the surgery was performed to sample or remove the microcalcifications.

CS3.15e Note that calcium oxalate may be subtle on H&E stained sections, but it is refractile.

S3.16 The presence or absence of Paget disease of the nipple must be recorded.

CS3.16a Paget disease of the nipple may have implications for clinical management and prognosis.

Margins

S3.17 The presence or absence of invasive carcinoma and/ or DCIS at the resection margin must be recorded.

CS3.17a If margins are clear, this must be recorded and the distance from each margin must be stated in millimetres, when less than 10 mm, and otherwise stated as "> 10 mm".

If DCIS is closer to the margin than invasive carcinoma, the distances from both should be included. If invasive carcinoma is closer to the margin than DCIS, it is acceptable to mention the distance from the invasive component only.

CS3.17b A specimen must be reported as having an "involved margin" if there is ink on malignant cells (DCIS or invasive). The involved margin(s) must be specified.

CS3.17c If margins are involved, an assessment of the extent of the margin front involved must be recorded, eg focal, or measured in millimetres. The extent of margin involvement has both prognostic and management implications.

CS3.17d The orientation of involved margins must be recorded.

Other findings in breast tissue

S3.18 The presence or absence of lobular neoplasia (atypical lobular hyperplasia or lobular carcinoma in situ) must be recorded.

CS3.18a If LCIS is present, the type must be stated as classical or variant type (eg pleomorphic, signet ring) and the extent should be recorded subjectively as focal or extensive.

CS3.18b The current World Health Organization Classification of Tumours of the Breast (4th Edition)[22] uses the term lobular neoplasia to incorporate the traditional ALH/LCIS terminology. In recognition of the higher risk of subsequent invasive carcinoma, the pathologists may choose to distinguish LCIS from ALH.

G3.03 The presence or absence of the following specific subtypes of LCIS at margin should be recorded: i) classic LCIS with comedo necrosis, ii) classic LCIS which is extensive and 'bulky/mass forming', and iii) pleomorphic LCIS.

CG3.03a Although the morphology and biology would suggest a more aggressive biologic potential, the significance of these subtypes for recurrence and prognosis remains unclear at present; the international consensus (WHO 4th Edition[22]) is that these features should be recorded to allow a multidisciplinary discussion with case-by-case

recommendation for further management.

CG3.03b The presence or absence of classic LCIS at margins should not be recorded.

CG3.03c Classic LCIS is not visible macroscopically. Since LCIS is multifocal and multicentric, the absence or presence at margins, which will be in tissue blocks selected randomly, does not provide meaningful information, hence the international recommendation, including the WHO publication, is not to record this feature.

S3.19 A description of any associated breast changes observed must be recorded, including a reference to calcification if present.

CS3.19a Associated breast changes include atypical proliferative lesions such as atypical ductal hyperplasia, flat epithelial atypia and lobular neoplasia (ALH/ LCIS), and non-neoplastic lesions, for example radial scars, sclerosing adenosis and fibrocystic change.

CS3.19b The presence of microcalcifications within any associated lesions may explain a discrepancy between DCIS size and mammographic lesion size if the latter is based on extent of microcalcifications.

Lymph nodes

S3.20 The sentinel lymph node status must be recorded.

CS3.20a The total number of sentinel nodes examined must be recorded.

CS3.20b The number of sentinel nodes with:

i) macrometastases (>2mm)

ii) micrometastases (>0.2mm to 2mm or >200 cells in a single section)

iii) isolated tumour cells (≤0.2mm OR ≤ 200 cells in a single section)

must be recorded.

S3.21 The non-sentinel lymph node status must be recorded.

CS3.21a The total number of non-sentinel lymph nodes examined and the number of non-sentinel lymph nodes with metastases must be recorded.

S3.22 The presence or absence of extranodal spread must be recorded.

S3.23 In the neoadjuvant setting, any treatment effect in the lymph nodes must be recorded.

CS3.23a Treatment effect is defined as areas of scarring, hyalinisation, necrosis, extensive myxoid change in the lymph node.

CS3.23b Nodal response should be classified as:

- nodes negative, no treatment effect
- nodes negative, with treatment effect
- nodes positive, with treatment effect
- nodes positive, no treatment effect

G3.04 Any additional relevant information should be recorded.

CG3.04a There must be a free text field so that the pathologist can add any essential information that is not addressed by the above points.

4 Ancillary studies findings

Hormone receptor assays

S4.01 Immunohistochemical assays of oestrogen receptor (ER) and progesterone receptor (PR) must be reported for all cases of invasive breast carcinoma.

CS4.01a These tests provide independent prognostic information and predict response to hormonal therapy.[18,29-30] These are now routinely performed on all invasive breast carcinoma specimens. A number of commercially available antibodies are in routine use.[18]

CS4.01b ER or PR assays must be interpreted and reported based on nuclear staining only (cytoplasmic staining does not correlate with tumour response to endocrine therapy or biochemical assay results). The result must include an estimate of the percentage of nuclei stained and the predominant intensity of staining must be recorded as low (1+), intermediate (2+) or high (3+). The result for ER or PR must be reported as positive or negative.

CS4.01c An ER or PR assay should be reported as positive if ≥1% of nuclei are stained, irrespective of the intensity of staining. This cut-point represents the current recommendation of ASCO.[31]

G4.01 ER and PR assays should be performed for DCIS if requested and incorporated into the report.

CG4.01a Hormone receptor status may be a predictor of response to hormonal therapy and prevent recurrence in DCIS. Clinical trials are in progress to clarify this issue.[32] (www.ibis-trials.org)

CG4.01b When performing ER or PR assay in a DCIS specimen, the same standards and guidelines apply as for invasive carcinoma.

G4.02 If the results of hormone receptor assays are not available at the time the pathology report is made, a statement should be inserted in the pathology report to indicate that hormone receptor status is being assessed.

CG4.02a Hormone receptor assay results are generally available concurrent with the histopathology report, or within 1–2 days.

S4.02 A copy of hormone receptor assay results must be sent to the surgeon and other managing clinicians.

CS4.02a When hormone receptor assays are performed by an external pathology service, a copy must also be sent to the originating pathology department.

HER2 assays for early breast cancer

S4.03 Testing for HER2 (c-ERBB2, HER2/neu) via in situ hybridisation (ISH) to detect gene amplification must be performed for all newly diagnosed early invasive breast cancers.

CS4.03a HER2 assay is also likely to be requested in recurrent or metastatic disease or after neoadjuvant chemotherapy.[33] HER2 status predicts the potential response to specific anti-HER2 therapies, and other systemic therapies, as well as being a general prognostic marker.[33]

Under the Australian Pharmaceutical Benefits Scheme (PBS), patients with early breast cancer are eligible for treatment with trastuzumab (Herceptin, Roche) only if HER2 gene amplification has been demonstrated by ISH regardless of the HER2 immunohistochemical (IHC) status.

CS4.03b HER2 IHC testing may supplement ISH assessment in early breast cancer to correlate with the ISH result and to help detect any intratumoural heterogeneity, which may guide the ISH analysis. IHC testing is not mandatory.

CS4.04c Cases with a Her2/CEP17 ratio exceeding 2.2 or Her2 copy number > 6.0 are considered amplified.

CS4.03d In all cases of early breast cancer where ISH testing is not available, or if bright field ISH does not provide a definitive result, a sample must be provided for HER2 fluorescence ISH (FISH) testing in an accredited laboratory

Metastatic breast cancer

G4.03 The current government regulations regarding the listing of trastuzumab (Herceptin, Roche) in the metastatic setting are such that for metastatic breast cancer specimens, HER2 testing can be performed using either ISH for detecting gene amplification or an IHC technique for detecting protein overexpression. However, for patients who have progressed on trastuzumab, HER 2 testing by ISH is required for PBS supply of lapatinib.

Thus, it is strongly recommended that testing for metastatic specimens is either with ISH alone, or all specimens with IHC 3+ or 2+ result should proceed to ISH testing. This will facilitate patient management and will reduce the need for double handling of samples.

CG4.03a Patients with metastatic disease are eligible for trastuzumab therapy under the PBS if either (i) a 3+

positive result has been demonstrated by IHC or (ii) HER2 gene amplification has been demonstrated by ISH.

CG4.03b Confirmation by ISH testing is recommended if there is any doubt about the validity of a 3+ result on IHC.

CG4.03c Patients with HER2-positive metastatic disease who have progressed on trastuzumab therapy require the HER2 status to be determined by ISH in order to qualify for PBS-funded lapatinib therapy.

CG4.03d All metastatic breast cancer specimens that show an initial IHC result of 2+ (equivocal) must be retested using ISH. If subsequent ISH testing does not demonstrate amplification of HER2 gene signals, the result should be reported as negative. If ISH demonstrates amplification of HER2 gene signals, the result should be reported as positive.

5 Synthesis and overview

Information that is synthesized from multiple modalities and therefore cannot reside solely in any one of the preceding chapters is described here. For example, tumour stage is synthesized from multiple classes of information – clinical, macroscopic and microscopic. Overarching case comment is synthesis in narrative form. Although it may not necessarily be required in any given report, the provision of the facility for overarching commentary in a cancer report is essential.

By definition, synthetic elements are inferential rather than observational, often representing high-level information that is likely to form part of the 'Diagnostic summary' section in the final formatted report.

S5.01 The tumour stage and stage grouping must be recorded to the extent possible, based on the *AJCC Cancer Staging Manual* (7th Edition).[11] (See Tables S5.01a and S5.01b below.)

Table S5.01a **AJCC breast cancer TNM classification.** Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springerlink.com.

Descriptor	Definition	Author's notes
TNM descriptors Required only if applicable; select all that apply		
m	multiple foci of invasive carcinoma	Add after primary tumour descriptor, eg pT(m)NM
r	recurrent	Applies when tumour is staged after a documented disease-free interval
y	post treatment	Applies to staging following initial multimodality therapy Add as prefix to pTNM descriptor (eg ypTNM)

Primary Tumour (Invasive Carcinoma) (pT)		
Classification	**Definition**	**Authors notes:**
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	Applies only in case of neoadjuvant therapy in which a previously diagnosed invasive

		carcinoma is no longer present after treatment
Tis (DCIS)	Ductal carcinoma in situ	As above
Tis (LCIS)	Lobular carcinoma in situ	As above Cases with both DCIS & LCIS are designated pTis (DCIS)
Tis (Paget's)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget's disease are categorized based on size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted.	
T1	Tumour ≤ 20 mm in greatest dimension	
T1mi	Tumour ≤1 mm in greatest dimension	When multiple foci of microinvasion present, measure the largest focus (do not add together).
T1a	Tumour >1 mm but ≤ 5 mm in greatest dimension	
T1b	Tumour >5 mm but ≤10 mm in greatest dimension	
T1c	Tumour >10 mm but ≤20 mm in greatest dimension	
T2	Tumour >20 mm but ≤50 mm in greatest dimension	
T3	Tumour >50 mm in greatest dimension	
T4	Tumour of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules) Note: Invasion of the dermis alone does not qualify as pT4	
T4a	Extension to the chest wall, not including only pectoralis muscle adherence/invasion	
T4b	Ulceration and/or ipsilateral satellite nodules and/or oedema (including peau d'orange) of the skin, which do not meet criteria for inflammatory	

	carcinoma	
T4c	Both T4a and T4b	
T4d	Inflammatory carcinoma	

Regional Lymph Nodes (pN)*

***Note:** Classification is based on axillary lymph node dissection with or without sentinel lymph node biopsy. Classification based solely on sentinel lymph node biopsy without subsequent axillary lymph node dissection is designated (sn) for "sentinel node" for example, pN0(sn)

Classification	Definition
pNX	Regional lymph nodes cannot be assessed (eg previously removed, or not removed for pathologic study)
pN0	No regional lymph node metastasis identified histologically Note: isolated tumour cell clusters (ITC) are defined as small clusters of cells not greater than 0.2mm, or single tumour cells, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by immunohistochemical (IHC) methods. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.
pN0 (i-)	No regional lymph node metastases histologically, negative IHC
pN0 (i+)	Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by H&E or IHC including ITC)
pN0 (mol-)	No regional lymph node metastases histologically, negative molecular findings (RT-PCR)
pN0 (mol+)	Positive molecular findings (RT-PCR)**, but no regional lymph node metastases detected by histology or IHC
pN1	Micrometastases; or metastases in 1-3 axillary lymph nodes; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected.***
pN1mi	Micrometastases (greater than 0.2 mm and/or more than 200 cells, but none greater than 2.0 mm)
pN1a	Metastases in 1-3 axillary lymph nodes, at least 1 metastasis greater than 2.0 mm
pN1b	Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected.***
pN1c	Metastases in 1-3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected.
pN2	Metastases in 4-9 axillary lymph nodes; or clinically detected**** internal mammary lymph nodes in the *absence* of axillary lymph node metastases
pN2a	Metastases in 4-9 axillary lymph nodes (at least one tumour deposit greater than 2.0 mm)

pN2b	Metastases in clinically detected**** internal mammary lymph nodes in the *absence* of axillary lymph node metastases
pN3	Metastases in ten or more axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or in clinically detected**** ipsilateral internal mammary lymph nodes in the *presence* of one or more positive level I, II axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected***; or in ipsilateral supraclavicular lymph nodes
pN3a	Metastases in 10 or more axillary lymph nodes (at least one tumour deposit greater than 2.0 mm); or metastases to the infraclavicular (level III axillary lymph) nodes
pN3b	Metastases in clinically detected**** ipsilateral internal mammary lymph nodes in the *presence* of one or more positive axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected****
pN3c	Metastases in ipsilateral supraclavicular lymph nodes
Notes: **RT-PCR: reverse transcriptase/polymerase chain reaction ***'Not clinically detected' is defined as not detected by imaging studies (excluding lymphoscintigraphy) or not detected by clinical examination ****'Clinically detected' is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologic examination.	

Distant Metastasis (M)	
M0	No clinical or radiographic evidence of distant metastases
cM0(i+)	No clinical or radiographic evidence of distant metastasis, but deposits of molecularly or microscopically detected tumour cells in circulating blood, bone marrow, or other nonregional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastasis
M1	Distant detectable metastasis as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

Table S5.01b AJCC/UICC pathological stage grouping for breast cancer.[11] Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springerlink.com.

Stage	T	N	M
0	Tis	N0	M0
IA	T1*	N0	M0
IB	T0	N1mi	M0
	T1*	N1mi	M0
IIA	T0	N1†	M0
	T1*	N1†	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

*T1 includes T1mi

† T0 and T1 tumours with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.

Notes:

- M0 includes M0(i+)
- The designation pM0 is not valid; any M0 should be clinical.
- If a patient presents with M1 prior to neoadjuvant systemic therapy, the stage is considered stage IV and remains stage IV regardless of response to neoadjuvant therapy.

- Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.

- Postneoadjuvant therapy is designated with "yc" or "yp" prefix. Of note, no stage group is assigned if there is a complete pathologic response (CR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

S5.02 The year of publication and edition of the cancer staging system used in S5.01 must be included in the report.

G5.01 When assigning pT descriptors, the following guidance applies:[11,34]

CG5.01a The pathologic assessment of the primary tumour (pT) is generally based on resection of the primary tumour from a single specimen. If the tumour is resected in pieces or a previous biopsy has been performed, overall size should be estimated and may involve assessment of imaging, macroscopic and microscopic findings.

CG5.01b Postneoadjuvant therapy T should be based on clinical or imaging (ycT) or pathologic findings (ypT).

G5.02 When assigning pN descriptors, the following guidance applies:[11,34]

CG5.02a At least one node with the presence or absence of cancer documented by pathologic examination is required for pathologic staging N.

CG5.02b When size is the criterion for N category, stage by size of metastasis, not size of node when reported (unless specified in disease-specific rules).

CG5.02c Intramammary lymph nodes reside within breast tissue and are coded as axillary lymph nodes for staging purposes.

CG5.02d Cancerous nodules in the axillary fat adjacent to the breast, without histologic evidence of residual lymph node tissue, are classified as regional lymph node metastases (≥N1).

CG5.02e Direct extension of primary tumour into regional node classified as node positive.

CG5.02f Small clusters of cells not greater than 0.2 mm, or nonconfluent or nearly confluent clusters of cells not exceeding 200 cells in a single histologic lymph node cross section are classified as isolated tumour cells.

ITCs may be detected by routine histology or by immunohistochemical (IHC) methods.

Cases with ITC only in lymph nodes or distant sites are classified as pN0 or cM0. This rule also generally applies to cases with findings of tumour cells or their components by nonmorphologic techniques such as flow cytometry or DNA analysis.

Approximately 1000 tumour cells are contained in a three-dimensional 0.2-mm cluster. Thus, if more than 200 individual tumour cells are identified as single dispersed tumour cells or as a nearly confluent elliptical or spherical focus in a single histologic section of a lymph node there is a high probability that more than 1000 cells are present in the lymph node. In these situations, the node should be classified as containing a micrometastasis (pN1mi). Cells in different lymph node cross or longitudinal sections or levels of the block are not added together; the 200 cells must be in a single node profile even if the node has been thinly sectioned into multiple slices.

It is recognised that there is substantial overlap between the upper limit of the ITC and the lower limit of the micrometastasis categories because of inherent limitations in pathologic nodal evaluation and detection of minimal tumour burden in lymph nodes. Thus, the threshold of 200 cells in a single cross-section is a guideline to help pathologists distinguish between these 2 categories. The pathologist should use judgment regarding whether it is likely that the cluster of cells represents a true micrometastasis or is simply a small group of isolated tumour cells.

Nodes containing only tumour deposits ≤0.2mm (ITCs) are excluded from the positive node count for purposes of N classification but should be recorded as additional ITC involved nodes and should be included in the total nodes evaluated.

CG5.02g For post-therapy or post-neoadjuvant therapy classification (yTNM), N is classified by using the same categories as for clinical or pathologic staging for the disease type, and the findings are recorded by using the prefix designator "y" (eg ycN, ypN).

G5.03 When assigning pM descriptors, the following guidance applies:[11,34]

CG5.03a The pathologic assignment of the presence of metastases (pM1) requires a biopsy positive for cancer at the metastatic site.

CG5.03b Pathologic M0 is an undefined concept and the category "pM0" may not be used. Pathologic classification of the absence of distant metastases can only be made at autopsy. However, the assessment of metastases to group a patient by pathologic TNM groupings may be either clinical (cM0 or cM1) or pathologic (pM1) (eg, pTNM = pT; pN; cM or pM).

CG5.03c Cases with a biopsy of a possible metastatic site that shows ITC such as circulating tumour cells (CTCs) or disseminated tumour cells (DTCs), or bone marrow micrometastases detected by IHC or molecular techniques are classified as cM0(i+) to denote the uncertain prognostic significance of these findings, and to classify the stage group according to the T and N and M0.

CG5.03d For post-therapy or post-neoadjuvant therapy cases, (yTNM), the M component should be classified by the M status defined clinically or pathologically prior to therapy.

G5.04 When assigning additional TNM prefixes and suffixes, the following guidance applies:[11,34]

CG5.04a **Post-therapy or post-neoadjuvant therapy classification (yTNM):** Cases where systemic and/or radiation therapy are given before surgery ("neoadjuvant"), or where no surgery is performed, may have the extent of disease assessed at the conclusion of the therapy by clinical or pathologic means (if resection performed). This classification is useful to clinicians because the extent of response to therapy may provide important prognostic information to patients and help direct the extent of surgery or subsequent systemic and/or radiation therapy.

T and N are classified by using the same categories as for clinical or pathologic staging for the disease type, and the findings are recorded by using the prefix designator "y" (eg, ycT; ycN; ypT; ypN). The "yc" prefix is used for the clinical stage after therapy, and the "yp" prefix is used for the pathologic stage for those cases that have surgical resection after neoadjuvant therapy.

The M component should be classified by the M status defined clinically or pathologically prior to therapy.

CG5.04b **Retreatment classification (rTNM):** The retreatment classification (rTNM) is assigned when further treatment is planned for a cancer that recurs after a disease-free interval. The original stage assigned at the time of initial diagnosis and treatment does not change when the cancer recurs or progresses. The use of this staging for retreatment or recurrence is denoted with the "r" prefix (rTNM). All information available at the time of retreatment should be used in determining the rTNM stage.

CG5.04c **Multiple tumours:** When there are multiple simultaneous tumours of the same histology in one organ, the tumour with the highest T category is the one selected for classification and staging, and the multiplicity or the number of tumours is indicated in parentheses: for example, T2(m) or T2(5). For simultaneous bilateral cancers in paired organs, the tumours are classified separately as independent tumours in different organs.

CG5.04d **Metachronous primaries:** Second or subsequent primary cancers occurring in the same organ or in different organs are staged as a new cancer using the TNM system. Second cancers are not staged using the "y" prefix unless the treatment of the second cancer warrants this use.

CG5.04e **Residual tumour and surgical margins:** The absence or presence of residual tumour after treatment is described by the symbol "R." cTNM and pTNM describe the extent of cancer in general without consideration of treatment. cTNM and pTNM can be supplemented by the R classification, which deals with the tumour status after treatment. In some cases treated with surgery and/or with neoadjuvant therapy there will be residual tumour at the primary site after treatment because of incomplete resection or local and regional disease that extends beyond the limit or ability of resection. The presence of residual tumour may indicate the effect of therapy, influence further therapy, and be a strong predictor of prognosis. In addition, the presence or absence of disease at the margin of resection may be a predictor of the risk of recurrent cancer. The presence of residual disease or positive margins may be more likely with more advanced T or N category tumours. The R category is not incorporated into TNM staging itself. However, the absence or presence of residual tumour and status of the margins may be recorded in the medical record and cancer registry.

The R categories for the primary tumour site are as follows:

- R0 No residual tumour
- R1 Microscopic residual tumour
- R2 Macroscopic residual tumour
- RX Presence of residual tumour cannot be assessed.

G5.01 The 'diagnostic summary' section of the final formatted report should include:

- Specimen type and laterality (S2.02, S2.03)
- Histological grade (S3.03)
- Maximum tumour size (S3.02)
- Margin status (S3.17)
- Lymph node status (S3.20, S3.21)
- Lymphovascular invasion (S3.05)

S5.03 The reporting system must provide a field for free text or narrative in which the reporting pathologist can give overarching case comment.

CS5.03a This field may be used, for example, to:

- explain the decision-making pathway, or any

elements of clinicopathological ambiguity, or factors affecting diagnostic certainty, thereby allowing communication of diagnostic subtlety or nuance that is beyond synoptic capture

- give recommendations for further action or investigation

- document further consultation or results still pending.

CS5.03b Use of this field is at the discretion of the reporting pathologist.

6 Structured checklist

The following checklist includes the standards and guidelines for this protocol which must be considered when reporting, in the simplest possible form. The summation of all 'standards' is equivalent to the 'minimum dataset' for breast cancer. For emphasis, standards (mandatory elements) are formatted in bold font.

S6.01 The structured checklist provided may be modified as required but with the following restrictions:

a. All standards and their respective naming conventions, definitions and value lists must be adhered to.

b. Guidelines are not mandatory but are recommendations and where used, must follow the naming conventions, definitions and value lists given in the protocol.

G6.01 The order of information and design of the checklist may be varied according to the laboratory information system (LIS) capabilities and as described in *Functional Requirements for Structured Pathology Reporting of Cancer* Protocols.[35]

CG6.01a Where the LIS allows dissociation between data entry and report format, the structured checklist is usually best formatted to follow pathologist workflow. In this situation, the elements of synthesis or conclusions are necessarily at the end. The report format is then optimised independently by the LIS.

CG6.01b Where the LIS does not allow dissociation between data entry and report format, (for example where only a single text field is provided for the report), pathologists may elect to create a checklist in the format of the final report. In this situation, communication with the clinician takes precedence and the checklist design is according to principles given in Chapter 7.

G6.02 Where the checklist is used as a report template (see G6.01), the principles in Chapter 7 and Appendix 2 apply.

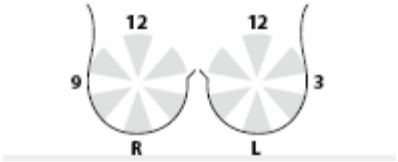
CG6.02a All extraneous information, tick boxes and unused values should be deleted.

G6.03 Additional comment may be added to an individual response where necessary to describe any uncertainty or nuance in the selection of a prescribed response in the checklist. Additional comment is not required where the prescribed response is adequate.

Values in italics are conditional on previous responses.

Values in all caps are headings with sub values.

S/G	Item description	Response type	Conditional
Pre-analytical			
S1.01	**Demographic information provided**		
S1.02	**Clinical information provided on request form**	**Text** OR **Structured entry as below:**	
	Specimen type	**Multi select value list (select all that apply):** • diagnostic open biopsy • wide local excision (partial mastectomy, quadrantectomy or segmentectomy) • re-excision • mastectomy • mastectomy post neoadjuvant therapy • lymph node biopsy - sentinel • lymph node biopsy - non-sentinel • axillary sample • axillary clearance	**If sentinel lymph nodes are submitted complete the section below.**
	SENTINEL NODES		**Conditional on the selection of Lymph node biopsy – sentinel**

			above
	Sentinel nodes location (eg Axillary, Internal mammary)	Text	
	Sentinel nodes number	**Numeric: _____** Note: Record for each type eg axillary recorded above	
	Sentinel nodes colour	**Text** Note: Record for each type eg axillary recorded above	
	Sentinel nodes radioactive count	**Numeric: _____** Note: Record for each type eg axillary recorded above	
	Tumour site and laterality	**Text (use clock-face analogy)**  	
	Method of localisation	**Single selection value list:** • Carbon track	

		• Hook wire	
	New primary cancer or recurrence	**Single selection value list:** • New primary • Regional (local) recurrence • Distant metastases	
S1.03	**Pathology accession number**	**Alpha-numeric**	
S1.04	**Principal clinician caring for the patient**	**Text**	
G1.01	Any other relevant information	**Text**	
Macroscopic findings			
S2.01	**Number of specimens submitted**	**Numeric: _____**	
S2.02	**Specimen laterality**	**Single selection value list:** • Left • Right <u>Notes:</u> Specimen laterality should be recorded for *each* specimen submitted (S2.01)	
S2.03	**Specimen type**	**Single select value list:** • Diagnostic open biopsy • Wide local excision (partial mastectomy, quadrantectomy or segmentectomy)	**If other, record the other type of tissue submitted**

		• Re-excision • Mastectomy • Mastectomy post neoadjuvant therapy • Other	
	Other tissue submitted	***Text***	
	Lymph tissue	**Multi select value list (select all that apply):** • Not submitted • Lymph node biopsy - sentinel • Lymph node biopsy - non-sentinel • Axillary sample • Axillary clearance	**If Lymph node tissue submitted record S2.12 and S3.20/S3.21 as applicable.**
	Intraoperative consultation	**Single selection value list:** • Not performed • Performed	**If performed record type**
	Type	***Multi select value list (select all that apply):*** • *frozen section* • *imprint cytology* • *gross examination for margin assessment* • *other*	**If other, provide details**
	Details	***Text***	

S2.04	**Specimen orientation**	**Single selection value list:** • Not oriented • Oriented	**If used, describe the markers and locations**
	Markers and locations	***Text***	
S2.05	**Method of localisation**	**Single select value list:** • Carbon track • Hook wire • N/A	
S2.06	**Specimen size**	**Numeric: __x__x__mm**	**Conditional on specimen not being oriented. If the specimen is oriented the following 3 measures should be used.**
	Medial-lateral length	***Numeric: __mm***	**Conditional on specimen being oriented.**
	Superficial-deep length	***Numeric: __mm***	**Conditional on specimen being oriented.**
	Superior-inferior length	***Numeric: __mm***	**Conditional on specimen being oriented.**
S2.07	**Specimen weight**	**Numeric: __g**	
S2.08	**Macroscopically visible tumours?**	**Single select value list:** • Absent • Present	**If present, record the number of foci**

	Number of foci	***Numeric: __***	
S2.09	**GROSS DESCRIPTION OF TUMOUR(S)**	**NOTE: Complete for each tumour identified.**	
	Nature of tumour	**Text**	
	Tumour size	**Numeric: __x__x__mm**	
	Distance to nearest separate tumour foci	***Numeric: __mm***	**Conditional on tumour multifocality being present**
	Minimum macroscopic margin clearance from any tumour deposit	**Numeric: __mm from _____Margin: text**	
S2.10	**Skin**	**Single select value list:** • Absent • Present	**If present, record the dimensions and any skin abnormalities.** **If present, S3.06 is required.**
	Skin dimensions	***Numeric: __x__mm***	
	Skin abnormalities	***Absent*** ***OR*** ***Multi select value list (select all that apply):*** • *Ulceration* • *Paget disease*	**If other provide other skin abnormality**

		• *Satellite nodules* • *Other*	
	Other skin abnormality	***Text***	
S2.11	**Muscle**	**Single select value list:** • Absent • Present	**If present, S3.07 is required.**
S2.12	***SENTINEL LYMPH NODES***		**Conditional on Sentinel Lymph nodes being submitted in S2.03**
	Node 1		**Repeat for each node received.**
	Site	***Single select value list:*** • *Axilla* • *Internal mammary chain*	
	Radioactive count	***Numeric: ___***	
	Uptake of dye	***Single select value list:*** • *No* • *Yes - Blue*	
	Size	***Numeric: __x__x__mm***	
	NON-SENTINEL LYMPH NODES/TISSUE		**Conditional on Non-Sentinel Lymph nodes/tissue being submitted in S2.03**
	Total number of nodes	***Numeric: __***	

	Size range	***Numeric: ___mm to ___mm***	
	Description	***Text***	
S2.13	**Block identification key**	**Text**	
G2.01	Other macroscopic comment	**Text**	
Microscopic findings			
S3.01	**Multiple tumours?**	**Single select value list:** • Absent • Present	**If present, record the quadrants involved and the total number of tumour deposits**
	Quadrants involved	***Text***	
	Total number of tumour deposits	***Numeric: __***	**If >2 record the max size of multifocal tumour bed involved.**
	Max. span of multifocal tumour bed involved	***Numeric:___x___mm***	
S3.02	**MAXIMUM INVASIVE TUMOUR SIZE**	Notes: Whole tumour size and invasive tumour size must be repeated for each tumour identified.	
	Whole tumour size	**Numeric: ___mm**	
	Maximum size of invasive tumour	**Numeric : ___mm**	
G3.01	Other invasive tumour dimensions	**Numeric:___x___mm** Notes:	

		May be recorded for each tumour for which a maximum invasive tumour size is recorded (S3.02)	
S3.03	**HISTOLOGIC GRADE INVASIVE CARCINOMA**	Notes: Record for each tumour identified (S3.01) that has a different grade	
	Score for nuclear grade	**Single selection value list:** • Score 1: Size equivalent to normal breast epithelial cells, regular outlines, uniform chromatin; inconspicuous nucleoli, little size variation • Score 2: Larger nuclei, open vesicular chromatin; visible nucleoli, moderate variability in size and shape • Score 3: Vesicular nuclei; often with prominent nucleoli; exhibiting marked variation in size and shape, occasionally very large and bizarre forms.	
	Score for tubule differentiation	**Single selection value list:** • Score 1: >75% of invasive carcinoma forming tubular or glandular structures • Score 2: 10–75% of invasive carcinoma forming tubular or glandular structures • Score 3: <10% of invasive carcinoma forming tubular or glandular structures • Not assessable*	

		Notes: * microinvasion only (each focus ≤ 1mm)	
	Score for mitotic rate	**Numeric:** _____ per10HPF* which is a score of ___ (using the tables provided in the text) OR **Not assessable**** Notes: *number of mitoses per 10 high-power fields ** microinvasion only (each focus ≤ 1mm)	
	Total Score	**Single selection value list:** • Grade 1 Total score of 3–5 • Grade 2 Total score of 6 or 7 • Grade 3 Total score of 8 or 9 • Not assessable* Notes: *microinvasion only (each focus ≤ 1mm)	
S3.04	**Invasive carcinoma subtype**	**Single selection value list:** • Invasive carcinoma of No Special Type (Ductal) ○ Pleomorphic carcinoma	

		○ Carcinoma with osteoclast like stromal giant cells ○ Carcinoma with choriocarcinomatous features ○ Carcinoma with melanotic features • Invasive lobular carcinoma ○ Classical ○ Tubulolobular ○ Alveolar ○ Solid ○ Pleomorphic ○ Mixed ○ Others – signet ring, histiocytoid, etc • Tubular carcinoma • Cribriform carcinoma • Mucinous carcinoma • Carcinoma with medullary features ○ Medullary ○ Atypical medullary ○ Invasive carcinoma NST (ductal) with medullary features • Carcinoma with apocrine differentiation • Carcinoma with signet ring cell differentiation • Invasive micropapillary carcinoma • Metaplastic carcinoma	

		○ Low grade adenosquamous carcinoma ○ Fibromatosis-like metaplastic carcinoma ○ Squamous cell carcinoma ○ Spindle cell carcinoma ○ Metaplastic carcinoma with mesenchymal differentiation ▪ Chondroid differentiation ▪ Osseous differentiation ▪ Other types of mesenchymal differentiation ○ Mixed metaplastic carcinoma ○ Myoepithelial carcinoma <u>Rare Types of Invasive Cancer:</u> • Carcinomas with Neuroendocrine features ○ Neuroendocrine tumour, well differentiated ○ Neuroendocrine tumour, poorly differentiated (small cell carcinoma) ○ Carcinoma with neuroendocrine differentiation • Secretory carcinoma • Invasive papillary carcinoma • Acinic cell carcinoma • Mucoepidermoid carcinoma • Polymorphous carcinoma • Oncocytic carcinoma • Lipid rich carcinoma • Glycogen rich/Clear cell carcinoma • Sebaceous carcinoma	

		• Salivary gland/skin adnexal type tumours • Adenoid cystic carcinoma • Adenomyoepithelioma with carcinoma <u>Notes:</u> Record for each invasive carcinoma tumour subtype identified.	
S3.05	**Peritumoural lymphovascular invasion**	**Single selection value list:** • Not identified • Present • Suspicious	**If suspicious record the block**
	Block	***Text***	
S3.06	***Skin***	***Single selection value list:*** • *Not involved* • *Paget disease of the nipple (DCIS extending to skin contiguous with lactiferous sinuses)* • *Invasive carcinoma involving dermis or epidermis without ulceration* • *Invasive carcinoma involving dermis or epidermis with ulceration* • *Ipsilateral satellite skin nodules, ie dermal deposits of invasive carcinoma, separate from the main tumour*	**Conditional on skin being included in the specimen S2.10**
S3.07	***Muscle***	***Single selection value list:*** • *Not involved*	**Conditional on muscle being included in the specimen S2.11**

		• *Involved*	
S3.08	**Treatment effect (after neoadjuvant hormonal or chemotherapy)**	**Single selection value list:** • **No definite response** to pre-surgical therapy in the invasive carcinoma • **Partial** response to pre-surgical therapy in the invasive carcinoma, residual carcinoma identified. (See residual cancer burden assessment tool page 30) • **Complete** pathologic response in breast and lymph nodes: No residual invasive carcinoma is present in the breast or lymph nodes after pre-surgical therapy • **Not applicable**	**If no definite or partial response, record the estimate of overall level of cellularity for invasive cancer** **If any response other than not applicable, then specify neoadjuvant response classification system used and the result of treatment.**
	Estimate of overall level of cellularity for invasive cancer	***Numeric: ___%***	
	Specify neoadjuvant response classification system used	**Text**	
	Result of treatment	**Text** <u>*Notes:*</u> *No/Minimal response and complete pathologic response will be common to all systems. For cases with incomplete response, the reporting of the extent of residual disease depends on the specific response classification system used.*	

S3.09	**DCIS**	**Single selection value list:** • Absent • Present only in conjunction with invasive carcinoma • Present only as pure DCIS • Present as both pure DCIS and in conjunction with invasive carcinoma	**If Present only in conjunction with invasive carcinoma then record S3.10, S3.12, S3.13, S3.14 and consider recording G3.02.** **If Present only as pure DCIS, or Present as both pure DCIS and in conjunction with invasive carcinoma then record S3.11.**
S3.10	***Max extent of breast involved by DCIS***	***Numeric: ___mm***	**Conditional on the presence of DCIS in S3.09**
S3.11	***Maximum dimension pure DCIS***	***Numeric: ____mm***	**Conditional on pure DCIS being present in the specimen (S3.09)**
S3.12	***Highest nuclear grade of DCIS***	***Single selection value list:*** • *Low* • *Intermediate* • *High*	**Conditional on DCIS being present in the specimen (S3.09)**
G3.02	*Nuclear grade heterogeneity of DCIS*	***Single selection value list:*** • *Absent* • *Present*	**Conditional on DCIS being present in the specimen (S3.09)** **If present, record the next most prevalent grade**
	Next most prevalent grade	***Single selection value list:*** • *Low* • *Intermediate* • *High*	

S3.13	***Necrosis in DCIS***	***Single selection value list:*** • *Absent* • *Present*	**Conditional on DCIS being present in the specimen (S3.09)**
S3.14	***Architecture of DCIS***	***Multi select value list (select all that apply):*** • *comedo* • *solid* • *cribriform* • *micropapillary* • *apocrine* • *papillary* • *other*	**Conditional on DCIS being present in the specimen (S3.09)** **If other, record the other architecture**
	Other architecture	***Text***	
S3.15	**Microcalcification**	**Multi select value list (select all that apply):** • Absent • Present in DCIS • Present in benign tissue • Present in invasive cancer	**If present, specify the lesion(s) with microcalcification, record if associated with necrosis, and record the size and extent (if required).**
	Lesion(s) with microcalcification	***Text***	
	Associated with necrosis?	***Single selection value list:*** • *No* • *Yes*	

	Size and extent of microcalcification *(if required)*	***Text*** *<u>Note:</u>* *Repeat for each lesion with microcalcification if required*	
S3.16	**Paget disease**	**Single selection value list:** • Absent • Present	
S3.17	**Margin involvement by invasive carcinoma or DCIS**	**Single selection value list:** • Margins not involved • Margins involved	**If involved, record details of involved margin** **If not involved, record the distance of invasive carcinoma from closest margins**
	Involved margin	***Margin: Text*** ***AND*** ***Type of involvement:*** ***Single selection value list:*** • *DCIS* • *Invasive carcinoma* • *DCIS and invasive carcinoma* ***AND***	

		Orientation of margin: Text ***AND*** ***Extent of involvement: ___mm OR Focal*** <u>Note:</u> *Information on Involved margins should be repeated for each involved margin identified.*	
	Distance of invasive carcinoma to closest margins	***Margin: Text*** ***AND*** ***Clearance:*** ***___mm OR >10mm*** ***OR*** *(if DCIS is closer to the margin record)* ***___mm OR >10mm and ___mm to DCIS*** <u>Note:</u> *Distance from margin should be repeated for each clear margin.*	
S3.18	**Lobular neoplasia**	**Single selection value list:** • Absent • Present	**If present, record type and extent.** **If present consider recording G3.03.**

	Type	***Single selection value list:*** • *Classical* • *Variant (pleomorphic, signet ring)*	
	Extent	***Single selection value list:*** • *Focal* • *Extensive*	
G3.03	*LCIS at the margin*	***Single selection value list:*** • *LCIS with comedo necrosis present* • *Pleomorphic LCIS present*	**Conditional on LCIS being present in S3.18**
S3.19	**Associated breast changes**	**Multi select value list (select all that apply):** • atypical ductal hyperplasia • flat epithelial atypia • lobular neoplasia (ALH/ LCIS) • radial scars • sclerosing adenosis • fibrocystic change • other	**If other, record other breast changes**
	Other breast changes (eg calcification)	***Text***	
	LYMPH NODES		**Required only if Lymph tissue submitted in S2.03**
S3.20	SENTINEL NODES		

	Total number of sentinel nodes	**Numeric: _____**	
	Number of sentinel nodes with macrometastases	**Numeric: _____**	
	Number of sentinel nodes with micrometastases	**Numeric: _____**	
	Number of sentinel nodes with isolated tumour cells	**Numeric: _____**	
S3.21	NON-SENTINEL NODES		
	Total number of non-sentinel nodes	**Numeric: _____**	
	Number of non-sentinel nodes with metastases	**Numeric: _____**	
S3.22	**Extranodal spread**	**Single selection value list:** • Absent • Present	
S3.23	**Treatment effect in LN**	**Single selection value list:** • nodes negative, no treatment effect • nodes negative, with treatment effect • nodes positive, with treatment effect • nodes positive, no treatment effect • Not applicable	
G3.04	Other microscopic comment	**Text**	

Ancillary test findings			
S4.01	**Oestrogen receptors**	**Single selection value list:** • Not performed • Performed • Pending	**If performed, record the percentage of nuclei staining, predominant staining intensity, and the result**
	Percentage of nuclei staining	***Numeric range: ___to___%***	
	Predominant staining intensity	***Single selection value list:*** • *1+ Low* • *2+ Intermediate* • *3+ High*	
	ER result	***Single selection value list:*** • *Negative* • *Positive*	
	Progesterone receptors	**Single selection value list:** • Not performed • Performed • Pending	**If performed, record the percentage of nuclei staining, predominant staining intensity, and the result**
	Percentage of nuclei staining	***Numeric range: ___to___%***	
	Predominant staining intensity	***Single selection value list:*** • *1+ Low*	

		• *2+ Intermediate* • *3+ High*	
	PR result	***Single selection value list:*** • *Negative* • *Positive*	
S4.03	**HER2 (ISH)**	**Single selection value list:** • Not performed • Performed • Pending	**If performed, record the number of copies of HER2 the number of copies of CEP17 (of assessed) and the HER2 result.**
	Number of copies of HER2	***Numeric: _____***	
	Number of copies of CEP17	***Not assessed*** ***OR*** ***Numeric: _____***	
	HER2 Result	***Single selection value list:*** • *Amplified* • *Non-amplified diploid* • *Non-amplified polysomic* • *Indeterminate*	
	HER2 IHC *(if performed)*	***Single selection value list:*** • ***0*** • ***1+***	

		• ***2+*** • ***3+*** • ***Not performed***	
Synthesis and overview			
S5.01	**Tumour stage and stage grouping**		

Descriptor	**Definition**	**Notes**
TNM descriptors Required only if applicable; select all that apply		
m	multiple foci of invasive carcinoma	Add after primary tumour descriptor, eg pT(m)NM
r	recurrent	Applies when tumour is staged after a documented disease-free interval
y	post treatment	Applies to staging following initial multimodality therapy Add as prefix to pTNM descriptor (eg ypTNM)
Primary Tumour (Invasive Carcinoma) (pT)		
Classification	Definition	Notes:
TX	Primary tumour cannot be assessed	

		T0	No evidence of primary tumour	Applies only in case of neoadjuvant therapy in which a previously diagnosed invasive carcinoma is no longer present after treatment
		Tis (DCIS)	Ductal carcinoma in situ	As above
		Tis (LCIS)	Lobular carcinoma in situ	As above Cases with both DCIS & LCIS are designated pTis (DCIS)
		Tis (Paget's)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinoma in the breast parenchyma associated with Paget's disease are categorized based on size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted.	
		T1	Tumour ≤ 20 mm in greatest dimension	
		T1mi	Tumour ≤1 mm in greatest dimension	When multiple foci of microinvasion present, measure the largest focus (do not add together).

		T1a	Tumour >1 mm but ≤ 5 mm in greatest dimension	
		T1b	Tumour >5 mm but ≤10 mm in greatest dimension	
		T1c	Tumour >10 mm but ≤20 mm in greatest dimension	
		T2	Tumour >20 mm but ≤50 mm in greatest dimension	
		T3	Tumour >50 mm in greatest dimension	
		T4	Tumour of any size with direct extension to the chest wall and/or to the skin (gross ulceration or skin nodules) Note: Invasion of the dermis alone does not qualify as pT4	
		T4a	Extension to chest wall, not including only pectoralis muscle adherence/invasion	
		T4b	Ulceration and/or ipsilateral satellite nodules and/or oedema (including peau d'orange) of the skin, which do not meet criteria for inflammatory carcinoma	
		T4c	Both T4a and T4b	
		T4d	Inflammatory carcinoma	
		Regional Lymph Nodes (pN)		

		(sn)	Only sentinel node(s) evaluated	Modifier required only if applicable Do not use if 6 or more sentinel nodes and/or nonsentinel nodes are submitted

Classification	Definition
pNX	Regional lymph nodes cannot be assessed eg previously removed, or not removed for pathologic study
pN0	No regional lymph node metastasis identified histologically
pN0 (i-)	No regional lymph node metastases identified histologically, negative IHC
pN0 (i+)	Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by H&E or IHC including ITC)
pN0 (mol-)	No regional lymph node metastases histologically, negative molecular findings (RT-PCR)
pN0 (mol+)	Positive molecular findings (RT-PCR), but no regional lymph node metastases detected by histology or IHC
pN1	Micrometastases; or metastases in 1-3 axillary lymph node; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected.
pN1mi	Micrometastases (greater than 0.2 mm and/or more than 200 cells, but none greater than 2.0 mm)
pN1a	Metastases in 1 - 3 axillary lymph nodes, at least 1 metastasis greater than 2.0 mm
pN1b	Micrometastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph

	node biopsy but not clinically detected.
pN1c	Metastases in 1 - 3 axillary lymph nodes and in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected.
pN2	Metastases in 4 - 9 axillary lymph nodes; or clinically detected internal mammary lymph node in the absence of axillary lymph node metastases
pN2a	Metastases in 4 - 9 axillary lymph nodes (at least 1 tumour deposit greater than 2.0 mm)
pN2b	Metastases in clinically detected internal mammary lymph nodes in the absence of axillary lymph node metastases
pN3	Metastases in ten or more axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or in clinically detected ipsilateral internal mammary lymph nodes in the presence of one or more positive level I, II axillary lymph nodes; or in more than three axillary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected or in ipsilateral supraclavicular lymph nodes
pN3a	Metastases in 10 or more axillary lymph nodes (at least one tumour deposit greater than 2.0 mm); or metastases to the infraclavicular (level III axillary lymph) nodes
pN3b	Metastases in clinically detected ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected
pN3c	Metastases in ipsilateral supraclavicular lymph nodes

Distant Metastasis (M)	
M0	No clinical or radiographic evidence of distant metastases
cM0(i+)	No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumour cells in circulating blood, bone marrow, or other nonregional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastasis
M1	Distant detectable metastasis as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

Stage	**T**	**N**	**M**
0	Tis	N0	M0
IA	T1*	N0	M0
IB	T0	N1mi	M0
	T1*	N1mi	M0
IIA	T0	N1[†]	M0
	T1*	N1[†]	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0

		IIIB	T4	N0, N1, N2	M0
		IIIC	Any T	N3	M0
		IV	Any T	Any N	M1

*T1 includes T1mic

† T0 and T1 tumours with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.

Notes:

- M0 includes M0(i+)
- The designation pM0 is not valid; any M0 should be clinical.
- If a patient presents with M1 prior to neoadjuvant systemic therapy, the stage is considered stage IV and remains stage IV regardless of response to neoadjuvant therapy.
- Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.
- Post-neoadjuvant therapy is designated with "yc" or "yp" prefi x. No stage group is assigned if there is a complete pathologic response (CR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

S5.02	**Year and edition of staging system**	**Numeric:** year **AND** **Text**: Edition eg 1st, 2nd etc	
G5.01	Diagnostic summary. Include:	**Text**	

	• Specimen type and laterality (S2.02, S2.03) • Histological grade (S3.03) • Maximum tumour size (S3.02) • Margin status (S3.17) • Lymph node status (S3.20, S3.21) • Lymphovascular invasion (S3.05)		
S5.03	**Overarching comment**	**Text**	

7 Formatting of pathology reports

Good formatting of the pathology report is essential for optimising communication with the clinician, and will be an important contributor to the success of cancer reporting protocols. The report should be formatted to provide information clearly and unambiguously to the treating doctors, and should be organised with their use of the report in mind. In this sense, the report differs from the structured checklist, which is organised with the pathologists' workflow as a priority.

Uniformity in the format as well as in the data items of cancer reports between laboratories makes it easier for treating doctors to understand the reports; it is therefore seen as an important element of the systematic reporting of cancer. For guidance on formatting pathology reports, please refer to Appendix 2.

Appendix 1 Pathology request information and surgical handling procedures

This appendix describes the information that should be collected before the pathology test. Some of this information can be provided on generic pathology request forms; any additional information required specifically for the reporting of breast cancer may be provided by the clinician on a separate request information sheet. An example request information sheet is included below. The elements in bold text are those which pathologists consider to be required information. Those in non-bold text are recommended.

Also included in this appendix are the procedures that are recommended before handover of specimens to the laboratory.

Patient information

- **Adequate demographic and request information should be provided with the specimen.**
  - Items relevant to cancer reporting protocols include:
    - i patient name
    - ii date of birth
    - iii sex
    - iv identification and contact details of requesting doctor
    - v date of request
  - The patient's ethnicity should be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.
- The patient's health identifiers should be provided.
  - The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a patient's Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

Clinical & Imaging Information

- **The specimen type should be recorded.**
  - Record the type of specimen as diagnostic open biopsy, wide local excision (partial mastectomy, quadrantectomy or segmentectomy), re-excision, mastectomy, mastectomy post neoadjuvant therapy, lymph node biopsy (sentinel or non-sentinel), axillary sample, axillary clearance.
  - If sentinel lymph nodes are submitted, record the number, radioactivity count and colour and whether they are axillary or internal mammary nodes.
- **The site and laterality of the lesion should be recorded.**

- Laterality information is needed for identification purposes. A clock face analogy should be used to describe the position of lesions.

- The method of localisation should be recorded (eg hook wire or carbon track).

- **Record if this is a new primary cancer or a recurrence of a previous cancer, if known.**

  - The term recurrence defines the return, reappearance or metastasis of cancer (of the same histology) after a disease free period.

    Recurrence should be classified as distant metastases or regional (local) recurrence.

    Regional (local) recurrence refers to the recurrence of cancer cells at the same site as the original (primary) tumour or the regional lymph nodes.

    Distant metastasis refers to the spread of cancer of the same histologic type as the original (primary) tumour to distant organs or distant lymph nodes.

  - This information will provide an opportunity for previous reports to be reviewed during the reporting process, which may provide valuable information to the pathologist. This information also has implications for recording cancer incidence and evidence based research.

- Any other relevant information should be included in a free text field provided on the request form including:

  - The history and clinical findings must be recorded.

  - The clinical diagnosis or differential diagnosis. Providing the provisional clinical diagnosis or differential diagnosis improves clinicopathological correlation and improves diagnostic accuracy.

  - Any neoadjuvant therapy, such as the use of pre-surgical XRT, hormonal therapy or chemotherapy should be recorded.

    Prior to neoadjuvant therapy the lesion should be localised to assist identification in cases of substantial pathologic response.

    In cases of neoadjuvant therapy a radiologic assessment of current lesion extent and location should be provided.

  - The results of specimen imaging. The imaging grade, morphology (eg discrete mass or microcalcifications), location and number of lesions should be specified.

  - Any previous relevant laboratory results.

Surgical handling

- The specimen should be capable of orientation if the status of specific surgical margins is critical in determining the need for, or extent of, further surgery.

  - Where there are no anatomical landmarks, specimen orientation

may be indicated with marking sutures or other techniques. If a specimen is orientated, the orientation should be indicated on the specimen request form (this may be facilitated by the use of a diagram).

- Identification of research sections should preferably be done in consultation with the pathologist in order to avoid compromising the diagnosis.

Example Request Information Sheet

Invasive Breast Cancer Histopathology Request Information

Family name

Given name(s)

Date of birth DD – MM – YYYY

Date of request DD – MM – YYYY

Sex
- ☐ Male
- ☐ Female
- ☐ Intersex/indeterminate

Ethnicity
- ☐ Unknown
- ☐ Aboriginal/Torres Strait Islander
- ☐ Other ethnicity:

Patient identifiers
e.g. MRN, IHI or NHI (please indicate which)

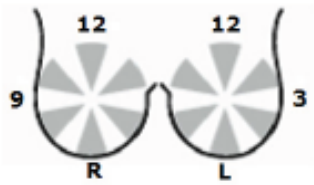
Requesting doctor - name and contact details

Copy to doctor name and contact details

Tests Requested

Specimen type (select all that apply)
- ☐ diagnostic open biopsy
- ☐ wide local excision (partial mastectomy, quadrantectomy or segmentectomy)
- ☐ re-excision
- ☐ mastectomy
- ☐ mastectomy post neoadjuvant therapy
- ☐ lymph node biopsy - non-sentinel
- ☐ axillary sample
- ☐ axillary clearance
- ☐ lymph node biopsy - sentinel

Tumour site and laterality



Method of localisation
- ☐ Carbon track
- ☐ Hook wire

New primary cancer or recurrence
- ☐ New primary
- ☐ Regional (local) recurrence
- ☐ Distant metastases

Sentinel nodes

Location:

Number: Colour:

Radioactive count:

Location:

Number: Colour:

Radioactive count:

Principal clinician

Record other relevant information below/overleaf
(eg imaging, neoadjuvant therapy; laboratory results, history and clinical information etc.

Vers. 2.0 Request Information from Invasive Breast Cancer Structured Reporting Protocol 2nd Edition

The above Request Information Sheet is published to the RCPA website.

Appendix 2 Guidelines for formatting of a pathology report

Layout

Headings and spaces should be used to indicate subsections of the report, and heading hierarchies should be used where the LIS allows it. Heading hierarchies may be defined by a combination of case, font size, style and, if necessary, indentation.

Grouping like data elements under headings and using 'white space' assists in rapid transfer of information.[36]

Descriptive titles and headings should be consistent across the protocol, checklist and report.

When reporting on different tumour types, similar layout of headings and blocks of data should be used, and this layout should be maintained over time.

Consistent positioning speeds data transfer and, over time, may reduce the need for field descriptions or headings, thus reducing unnecessary information or 'clutter'.

Within any given subsection, information density should be optimised to assist in data assimilation and recall. The following strategies should be used:

- Configure reports in such a way that data elements are 'chunked' into a single unit to help improve recall for the clinician.[36]
- Reduce 'clutter' to a minimum.[36] Thus, information that is not part of the protocol (eg billing information or SNOMED codes) should not appear on the reports or should be minimised.
- Reduce the use of formatting elements (eg bold, underlining or use of footnotes) because these increase clutter and may distract the reader from the key information.

Where a structured report checklist is used as a template for the actual report, any values provided in the checklist but not applying to the case in question must be deleted from the formatted report.

Reports should be formatted with an understanding of the potential for the information to 'mutate' or be degraded as the report is transferred from the LIS to other health information systems.

As a report is transferred between systems:

- text characteristics such as font type, size, bold, italics and colour are often lost
- tables are likely to be corrupted as vertical alignment of text is lost when fixed font widths of the LIS are rendered as proportional fonts on screen or in print
- spaces, tabs and blank lines may be stripped from the report, disrupting the formatting
- supplementary reports may merge into the initial report.

Appendix 3 Example of a pathology report

Citizen, Georgina
C/O Paradise Close
Wreck Bay Resort
Nar Nar Goon East, 3181

Female

DOB 1/7/1962
MRN 1296885

Lab Ref: **12/P28460**
Referred: 30/8/2012

Copy to: Dr N.G.Chappie
Rainforest Cancer Centre.
46 Smith Road,
Woop Woop, 3478

Referred by: Dr V. Brown
Suite 3, AJC Medical Centre,
Bunyip Crescent
Nar Nar Goon West, 3182

INVASIVE BREAST CANCER STRUCTURED REPORT

Diagnostic Summary

Mastectomy; left; Grade 1; Infiltrating ductal carcinoma; 14mm (maximum invasive size); Margins not involved; Lymph node biopsy – sentinel;1, Not involved; Peritumoural lymphovascular invasion not identified; Pathological Stage T1cN0 Stage IA (AJCC 7th edition, 2010)

Supporting Information

CLINICAL

History and clinical findings:	Previous (L) WLE and SNBx 2006. 7mm impalpable lesion; mastectomy and intramammary SNBx. ER/PR/HER2 Receptors

MACROSCOPIC

Number of specimens submitted:	3
Intraoperative consultation:	Not performed
Method of localisation:	Carbon track. Identified in the superior part of the mastectomy specimen

Specimen 1:

Specimen type and laterality:	Mastectomy left
Specimen orientation:	Oriented. Stitch - short superior, long lateral. The specimen is inked: blue superior, black inferior and green deep
Specimen size	
Medial-lateral length:	190mm
Anterior-posterior length:	210mm
Superior-inferior length:	20mm
Specimen weight:	693.2g
Multiple macroscopically visible tumours?:	No
Nature of tumour:	A small stellate firm nodule located in upper outer quadrant, 90mm from the lateral edge of the mastectomy, close to the carbon tract
Tumour size	
Medial-lateral length:	15mm. Extent in this aspect is least well defined.
Anterior-posterior length:	5mm
Superior-inferior length:	11mm

Minimum macroscopic margin clearance:	13mm from superior edge. Inferior 95mm at least, deep 25 mm, superficial 35mm
Skin:	Present. The skin surface shows periareolar blue staining. The nipple is normal.
Skin dimensions:	200 x 93mm
Skin abnormalities:	Absent
Muscle:	Absent
Block identification key:	1A x 5 TS nipple; 1B - 1E medial to lateral sequential slices of tumour bearing tissue; 1F - 1I breast disc representative section; 1J-1M prominent breast markings adjacent to tumour; 1N random upper inner quadrant;1O random lower inner quadrant; 1P random upper outer; 1Q random lower outer

Specimen 2:

Specimen type and laterality:	Lymph node biopsy – sentinel. Left
Site:	Internal mammary chain
Radioactive count:	89
Uptake of dye:	Blue
Size:	7 x 5 x 3mm
Block identification key:	2A x 2 AE, sentinel node protocol grossly not suspicious

Specimen 3:

Specimen type and laterality:	Axillary sample. Left
Description:	Fat from left axilla. A firm fibrofatty tissue showing a fibrotic firm irregular central lesion when trisected.
Size:	21 x 11 x 5mm
Block identification key:	3A x 3 AE

Other microscopic comment:

There is a possible prior healed surgical scar in the lower outer quadrant. No areas suspicious for comedo DCIS are seen but prominent breast marking extend along a longitudinal ridge towards the deep aspect of the specimen and merging with an area of firm parenchyma (breast disc). The remainder of the breast is extensively fatty.

MICROSCOPIC

Multiple tumours?:	No
MAXIMUM INVASIVE TUMOUR SIZE	
Whole tumour size:	14mm
Maximum size of invasive tumour:	14mm
Other invasive tumour dimensions:	11 x 5mm

HISTOLOGIC GRADE INVASIVE CARCINOMA

Nuclear grade:	Score 1
Tubule differentiation:	Score 3
Mitotic rate:	<7 per10HPF which is a score of 1
Total score:	Grade 1
Invasive carcinoma subtype:	Invasive carcinoma of No Special Type (Ductal)
Peritumoural lymphovascular invasion:	Not identified
Skin:	Not involved
Treatment effect:	Not applicable
DCIS:	Absent
Microcalcification:	Absent
Paget disease:	Absent
Margin involvement by invasive ca or DCIS:	Margins not involved
Distance of invasive ca from closest margins:	Superior edge clearance 13mm to invasive front. Inferior 95mm at least Deep 25 mm. Superficial 35mm
Lobular neoplasia:	Absent
Associated breast changes:	Atypical ductal hyperplasia. Noted in sections taken from various regions which show some of the ducts and lobules colonised by atypical cells.

SENTINEL LYMPH NODES

Total number:	1
Number with macrometastases:	0
Number with micrometastases:	0
Number with isolated tumour cells:	0
Extranodal spread:	Absent
Treatment effect in LN:	Not applicable

Other microscopic comment:

Prior diagnosis of left breast cancer is noted (06-6454). By report, this was a mucinous carcinoma Grade II, 12 mm maximum diameter, with close but clear margins. Current sections confirm malignancy. The tumour arises in an area of scarring with a few ducts. Retraction artefact is prominent. Some large calibre vessels are seen in this region, but convincing features of vascular invasion are not found. Occasional ducts are incorporated in the lesion, but a well developed component of DCIA is not observed in this region and the surrounding breast tissue is markedly atrophic. The prominent ridge described grossly consists of a linear scar.

The axillary sample (specimen 3) consists of fat with bindles of nerves showing a proliferation of neuritis and fibrosis. These could be related to prior surgical site. No tumour found.

ANCILLARY TESTS

Hormone receptors: Pending

Reported by Dr Sarah Choudhary Authorised 4/9/2012

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