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Ductal Carcinoma In Situ, Variants of Lobular Carcinoma In Situ and Low Grade Lesions Histopathology Reporting Guide

ICCR

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.

☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (Note 1)

◯ Information not provided

Presentation mode

◯ Information not provided ◯ Screening

◯ Symptomatic

Current clinical findings for which this surgery is performed (select all that apply)

◯ Information not provided ☐ Paget disease of the nipple

☐ Nipple discharge ☐ Palpable mass

☐ Other, *specify*

Prior history of breast cancer

◯ Information not provided ◯ No

◯ Yes, *specify laterality, site(s), diagnosis, and prior treatment(s)*

Imaging modality (select all that apply)

◯ Information not provided ◯ None

☐ Mammography ☐ Ultrasound

☐ Magnetic resonance imaging (MRI)

☐ Other, *specify*

Radiological findings (select all that apply)

◯ Information not provided ◯ None

☐ Single lesion ☐ Multiple lesions

☐ Calcifications ☐ Architectural distortion

☐ Mass

☐ Other, *specify*

Extent by imaging, if available mm

Clip inserted ◯ Yes ◯ No ◯ Not known

Specimen x-ray available

◯ Information not provided ◯ Yes ◯ No

Known genetic predisposition

◯ Information not provided ◯ None

◯ Gene predisposition, *specify*

Other clinical information, *specify*

OPERATIVE PROCEDURE[a] (Note 2)

◯ Not specified

◯ Excision (less than total mastectomy)

- ◯ Diagnostic excision/excision biopsy/localisation biopsy
- ◯ Therapeutic wide local excision
- ◯ Duct excision/microdochectomy
- ◯ Re-excision

◯ Total mastectomy

- ◯ Simple mastectomy
- ◯ Nipple-sparing mastectomy
- ◯ Skin-sparing mastectomy
- ◯ Modified radical mastectomy
- ◯ Radical mastectomy

◯ Additional specimens, *specify*

[a] *If a lymph node staging specimen is submitted, then a separate dataset is used to record the information.*

SPECIMEN LATERALITY (Note 3)

◯ Left ◯ Right ◯ Not specified

SPECIMEN DIMENSIONS

mm x mm x mm

SPECIMEN WEIGHT

g

TUMOUR SITE (select all that apply) (Note 4)

◯ Not specified

Distance from nipple mm

AND

Position, *specify* o'clock

OR

☐ Upper outer quadrant

☐ Lower outer quadrant

☐ Upper inner quadrant

☐ Lower inner quadrant

☐ Central

☐ Other, *specify*

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TUMOUR DIMENSIONS (Note 5)

◯ No residual ductal carcinoma in situ (DCIS) or lesion *(dimension from previous core biopsy)*

Maximum dimension of DCIS *(specify exact measurement rounded to nearest mm)*[b] ____ mm

Additional dimensions ____ mm x ____ mm

Number of microinvasive foci ____

◯ Cannot be assessed, *specify*

[b] *Based on a combination of macroscopic and microscopic assessment.*

DIAGNOSTIC CLASSIFICATION (select all that apply) (Note 6)

(Value list based on the World Health Organization Classification of Breast Tumours (2019))

- ☐ DCIS
- ☐ Paget disease of the nipple
- ☐ Encapsulated papillary carcinoma
- ☐ Solid papillary carcinoma in situ
- ☐ Pleomorphic lobular carcinoma in situ (LCIS)
- ☐ Florid LCIS
- ☐ Mixed, *specify subtypes present*[c]
- ☐ Other, *specify*

[c] *Tumour exhibiting more than one tumour type should be designated mixed and the types present stated.*

HISTOLOGICAL NUCLEAR GRADE (Note 7)

(Applicable to DCIS, encapsulated papillary carcinoma and solid papillary carcinoma in situ)

- ◯ Grade 1 (Low)
- ◯ Grade 2 (Intermediate)
- ◯ Grade 3 (High)

HISTOLOGICAL ARCHITECTURAL PATTERN (select all that apply) (Note 8)

(Applicable to DCIS only)

- ☐ Cribriform
- ☐ Micropapillary
- ☐ Papillary
- ☐ Solid
- ☐ Other (e.g., clinging/flat[d]), *specify*

[d] *Applies to high nuclear grade DCIS only.*

NECROSIS (Note 9)

- ◯ Not identified
- ◯ Present
  - ◯ Central (Comedo) necrosis
  - ◯ Focal (Punctate) necrosis (<10% duct diameter)

MARGIN STATUS[e] (Note 10)

◯ Cannot be assessed

Anterior margin

◯ Involvement cannot be determined, *specify*

◯ Involved
Extent of margin involvement ____ mm

◯ Not involved
Distance of tumour from closest margin (if <5 mm) ____ mm
- ◯ ≥5 mm
- ◯ Cannot be determined, *specify*

Posterior margin

◯ Involvement cannot be determined, *specify*

◯ Involved
Extent of margin involvement ____ mm

◯ Not involved
Distance of tumour from closest margin (if <5 mm) ____ mm
- ◯ ≥5 mm
- ◯ Cannot be determined, *specify*

Superior margin

◯ Involvement cannot be determined, *specify*

◯ Involved
Extent of margin involvement ____ mm

◯ Not involved
Distance of tumour from closest margin (if <5 mm) ____ mm
- ◯ ≥5 mm
- ◯ Cannot be determined, *specify*

Inferior margin

◯ Involvement cannot be determined, *specify*

◯ Involved
Extent of margin involvement ____ mm

◯ Not involved
Distance of tumour from closest margin (if <5 mm) ____ mm
- ◯ ≥5 mm
- ◯ Cannot be determined, *specify*

[e] *Core for all wide local excision specimens, similar non-complete mastectomy and some (refer to Note) complete mastectomy specimens.*

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Medial margin

- ○ Involvement cannot be determined, *specify*
- ○ Involved
  - Extent of margin involvement ____ mm
- ○ Not involved
  - Distance of tumour from closest margin (if <5 mm) ____ mm
  - ○ ≥5 mm
  - ○ Cannot be determined, *specify*

Lateral margin

- ○ Involvement cannot be determined, *specify*
- ○ Involved
  - Extent of margin involvement ____ mm
- ○ Not involved
  - Distance of tumour from closest margin (if <5 mm) ____ mm
  - ○ ≥5 mm
  - ○ Cannot be determined, *specify*

Other margin, *specify*

- ○ Involvement cannot be determined, *specify*
- ○ Involved
  - Extent of margin involvement ____ mm
- ○ Not involved
  - Distance of tumour from closest margin (if <5 mm) ____ mm
  - ○ ≥5 mm
  - ○ Cannot be determined, *specify*

BIOPSY SITE (select all that apply) (Note 11)

- ○ Information not provided
- ☐ Evidence of marker clip reaction
- ☐ Evidence of previous core biopsy

COEXISTENT PATHOLOGY (Note 11)

- ○ None identified
- ○ Present, *specify*

MICROCALCIFICATIONS (select all that apply) (Note 12)

- ○ Not applicable
- ○ Not identified
- ☐ Lesional calcification present
- ☐ Present in non-neoplastic tissue

ANCILLARY STUDIES (Note 13)

- ○ Not performed
- ○ Performed (select all that apply)
  - ☐ Estrogen receptor (ER), *record results*
  - ☐ Progesterone receptor (PR), *record results*
  - ☐ Other, *specify test(s) and result(s)*

Representative blocks for ancillary studies, *specify those blocks best representing tumour and/or normal tissue for further study*

PATHOLOGICAL STAGING (UICC TNM 8th edition)[f] (Note 14)

TNM Descriptors (only if applicable) (select all that apply)

- ☐ m - multiple foci of DCIS
- ☐ r - recurrent

Primary tumour (pT)[g]

- ○ TX Primary tumour cannot be assessed
- ○ T0 No evidence of primary tumour
- ○ Tis (LCIS) Lobular carcinoma in situ[h]
- ○ Tis (DCIS) Ductal carcinoma in situ
- ○ Tis (Paget) Paget disease of the nipple not associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma[i]
- ○ T1mi Microinvasion 0.1 cm or less in greatest dimension[j]

[f] *Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 8th Edition, eds by James D. Brierley, Mary K. Gospodarowicz, Christian Wittekind. 2016, Publisher Wiley (incorporating any errata published up until 6th October 2020).*

[g] *Note that the results of surgically removed lymph nodes are derived from a separate dataset.*

[h] *The AJCC exclude Tis (LCIS).*

[i] *Carcinomas in the breast parenchyma associated with Paget disease are categorised based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.*

[j] *Microinvasion is the extension of cancer cells beyond the basement membrane into the adjacent tissues with no focus more than 0.1 cm in greatest dimension. When there are multiple foci of microinvasion, the size of only the largest focus is used to classify the microinvasion. (Do not use the sum of all individual foci.) The presence of multiple foci of microinvasion should be noted, as it is with multiple larger invasive carcinomas.*

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Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the expert committee. An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the Dataset Authoring Committee.

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Scope

The dataset has been developed for the reporting of resection specimens for ductal carcinoma in situ (DCIS) of the breast. The protocol applies to cases of DCIS and for where microinvasion (≤1 millimetres (mm)) is present. It also covers other in situ lesions including pleomorphic and florid variants of lobular carcinoma in situ (LCIS), as well as encapsulated papillary carcinoma and solid papillary carcinoma in situ. This dataset may also be used in those rare cases of DCIS removed at core biopsy but without evidence of residual DCIS in a subsequent excision specimen[a]. This protocol should only be used for re-excisions when they contain the largest extent of DCIS.

A separate dataset should be completed for bilateral DCIS and for each excision specimen in unilateral disease.

[a] If no residual disease is identified, a biopsy scar should be sought and reported if present. If after surgical/ radiological/pathological consultation, it is concluded that the entire lesion was removed with the biopsy, features of the biopsy should be reported as the final pathology.

Ductal carcinoma in situ (DCIS) (with or without microinvasion) diagnosed on needle core biopsies only, and residual DCIS post neoadjuvant therapy are outside the scope. Separate International Collaboration on Cancer Reporting (ICCR) datasets cover DCIS associated with invasive breast carcinomas[2] and breast resections in the neoadjuvant setting. Surgically removed lymph nodes are covered in a separate ICCR dataset which may be used, as appropriate, in conjunction with this dataset.[3]

The authors of this dataset can be accessed here.

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Note 1 – Clinical information (Core)

The provision of accurate clinical information is considered important to provide context to the specimen. This includes the nature of the abnormality, its method of detection, and the patient's medical history, including past history of breast disease or other cancer, prior treatments, and inherited genetic mutations, such as *BRCA1* or *BRCA2*.

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Note 2 – Operative procedure (Core)

The nature of the operation or procedure(s) performed is important to ensure appropriate pathological examination protocols are followed, and to inform clinical correlation and post-operative management. The nature, extent, focality of the abnormality and patient choice can influence the type of operation. Multiple procedures may be performed and sent as separate specimens, which require cross correlation. Many different surgical procedures are used to manage breast disease and, as appropriate, more details can be included as free text.

Partial mastectomy, lumpectomy and quadrantectomy/segmental excision are considered synonymous with wide local excision.

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Note 3 – Specimen laterality (Core)

Specification of the side and site in the breast is important for clinical correlation and accuracy of the patient medical record.

A separate dataset should be completed for each tumour in the instance of bilateral DCIS and for each excision in unilateral disease.

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Note 4 – Tumour site (Core)

A measure of distance from the nipple is required. Clock face delineation of location is a more commonly used determination of site than quadrant alone, but either is acceptable.

Specification of the side and site in the breast is important for clinical correlation, post-operative management discussion and accuracy of the patient medical record especially when there are multiple lesions for correlation with radiology/prior biopsies.

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Note 5 – Tumour dimensions (Core and Non-core)

Although not required for pT classification or stage assignment, the size (extent) of DCIS is an important factor in patient management[4,5] as it is correlated with close or positive margins,[6,7] the likelihood of residual disease after re-excision,[6-9] local recurrence,[4,10,11] and the possibility of missed areas of invasion.[12,13] There may be challenges to size determination of DCIS, in which case multiple parameters including radiological input, will be helpful. Large sections (whole-mount) are useful for size evaluation.

Size should also be given for pleomorphic and florid LCIS lesions (but not classic LCIS which is considered a 'benign' lesion in the American Joint Committee on Cancer (AJCC) Staging Manual 8th edition[14] (unlike the Union for International Cancer Control (UICC) TNM 8th edition[15]) where no invasive disease is seen; pleomorphic and florid LCIS behave more like DCIS being less likely to be multifocal/bilateral and having a higher incidence of associated ipsilateral invasive carcinoma than classic LCIS.

If no residual disease is identified, a biopsy scar should be sought and reported if present. If after surgical/radiological/pathological consultation, it is concluded that the entire lesion was removed with the biopsy, features of the biopsy should be reported as the final pathology.

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Note 6 – Diagnostic classification (Core)

To ensure consensus and consistency of reporting, it is recommended to use the nomenclature and definitions for diagnosis and classification provided by the most recent edition of the World Health Organization (WHO) Classification of Breast Tumours, 5th edition, 2019.[16] The ICCR dataset includes 5th edition Corrigenda, September 2020.[17]

Ductal carcinoma in situ (DCIS) varies in cell appearance, growth pattern and extent of disease and is now considered to represent a heterogeneous group of in situ neoplastic processes. When DCIS involves the epidermis of the nipple only, without underlying invasive carcinoma or DCIS, the classification is Paget disease of the nipple, the majority of which are high nuclear grade and strongly positive for HER2.

Pleomorphic LCIS has overlapping features with DCIS and may be treated similarly, but at present there is insufficient evidence to establish definitive recommendations for treatment. The current understanding of the natural history of pleomorphic LCIS and florid LCIS is limited, and the optimal treatment is unknown with regard to pursuing negative margins and consideration of additional adjuvant therapies. Nevertheless, although pleomorphic and florid LCIS are not currently included in the AJCC pTis classification[14] they remain as a category in the UICC TNM 8th edition[15] and there is emerging evidence suggesting that these forms of LCIS might be better treated as DCIS,[16,18] in particular the practice of excision to negative margins.

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Note 7 – Histological nuclear grade (Core)

Nuclear grading of entities within the scope of this dataset includes DCIS, encapsulated papillary carcinoma and solid papillary carcinoma in situ. For high nuclear grade encapsulated papillary carcinoma, the ICCR Invasive carcinoma of the breast dataset should be used.[2]

High nuclear grade is considered a high risk factor for recurrence[19-22] and breast cancer specific mortality,[23] although some studies do not show such an effect,[24,25] which may be due to interobserver variability in grading or use of different classification schemes.[26]

Nuclear grade of DCIS is largely determined by nuclear size and pleomorphism although other morphologic features (see Table 1) are also useful.[27]

Table 1: Nuclear grade of ductal carcinoma in situ.

Feature	Grade I (Low)	Grade II (Intermediate)	Grade III (High)
Pleomorphism	Monotonous (monomorphic)	Intermediate	Markedly pleomorphic
Size	1.5 to 2 x the size of a normal RBC or a normal duct epithelial cell nucleus	Intermediate	>2.5 x the size of a normal RBC or a normal duct epithelial cell nucleus
Chromatin	Usually diffuse, finely dispersed chromatin	Intermediate	Usually vesicular with irregular chromatin distribution
Nucleoli	Only occasional		Prominent, often multiple
Mitoses	Only occasional	Intermediate	May be frequent
Orientation	Polarised toward luminal spaces	Intermediate	Usually not polarised toward the luminal space

Definition: RBC, red blood cell.

Reproduced with permission from College of American Pathologists (CAP). *Protocol for the Examination of Resection Specimens From Patients With Ductal Carcinoma In Situ (DCIS) of the Breast*. Breast DCIS Resection 4.3.0.2. College of American Pathologists, February 2020.[28]

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Note 8 – Histological architectural pattern (Non-core)

Historically DCIS has been classified according to architectural pattern with some systems also including 'comedo DCIS' as an architectural type. Other classification systems have used nuclear grade and the presence or absence of comedo necrosis for categorisation. It should be noted that comedo necrosis can be seen in association with a range of architectural patterns and nuclear grades.[27,29]

However, there is significant variability of architectural pattern within an individual case of DCIS, and the perceived lack of reproducibility makes its application problematic. Therefore, cytonuclear morphology is now recommended for histological grading of DCIS[28] as although true grade variation does occur, in general, there is greater homogeneity of nuclear grade than of architectural pattern in DCIS within a lesion.[30]

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Note 9 – Necrosis (Core)

Although there is significant inter-observer variation, two broad types of necrosis have been identified: 1) Central (comedo) necrosis, most often associated with high nuclear grade and worse breast cancer specific survival[23] but only inconsistently with recurrence; and 2) Focal (punctate) necrosis, the clinical significance of which is unclear. Therefore, a pragmatic approach for classification of necrosis is proposed: central (comedo), focal (punctate) and 'not identified' as follows:

- **Central ("comedo"):** The central portion of an involved ductal space is replaced by an area of expansive necrosis that is easily detected at low magnification. Ghost cells and karyorrhectic debris are generally present. Although central (comedo) necrosis is generally associated with high grade nuclei, it can also occur with DCIS of intermediate (or occasionally low) nuclear grade and in pleomorphic LCIS and florid LCIS.
- **Focal ("punctate"):** Small foci, or single cell necrosis (≤10%) that are indistinct at low magnification, which are not considered central (comedo).
- **Necrosis not identified.**

Although there is inconsistency in the thresholds and criteria used to assign presence or absence of central (comedo) necrosis, a cut off of at least 10% of duct diameter which captures most central (comedo) necrosis[31] is to be used, with focal (punctate) necrosis as <10%.

The presence of necrosis is associated with mammographic calcifications, with central (comedo) necrosis often correlating with a linear and/or branching pattern on radiology. There is also frequent calcification in patients with recurrent DCIS that originally presented with mammographic calcifications.[22,25]

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Note 10 – Margin status (Core and Non-core)

Assessment of the adequacy of excision requires close correlation between the surgical excision procedure and pathological examination and in some circumstances such as the presence of calcification, as well as radiological correlation. In particular it is essential that the pathologist is made aware of the depth of tissue excised and whether the surgeon has excised all the tissue from the subcutis to the pectoral fascia.

There remains some controversy regarding the minimum width of uninvolved tissue that defines 'complete' excision in breast conserving surgery, although narrower margins are now more widely accepted as adequate than previously. For this reason it is recommended that the pathologist reports the measurement of the distance between the inked margins and DCIS (and invasive carcinoma).

Some centres find it helpful to report the approximate extent of margin involvement and the following system is recommended:

- Unifocal: one focus of carcinoma at the margin (single duct involvement)
- Multifocal: two or more foci of carcinoma at the margin
- Extensive: carcinoma present at the margin over a broad front (>5 mm).

If additional margins are taken, it is important to incorporate that into the margin measurements.

Note: There is an assumption that all breast tissue will be resected in patients undergoing a complete mastectomy and that pathological examination of margins is of limited value. However, there is evidence that margin involvement can increase the risk of local recurrence after mastectomy[32,33] and a statement of the distance to the closest margin(s) and site(s) of margin (including nipple if nipple sparing mastectomy) for such mastectomy specimens should be included.

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Note 11 – Biopsy site (Core) and Coexistent pathology (Non-core)

In some cases, other pathologic findings are important for the clinical management of patients.

If the biopsy was performed for a benign lesion and the DCIS is an incidental finding, this should be documented e.g., DCIS in an excision for a palpable fibroadenoma.

Peritumoural lymphovascular invasion is a very rare finding in association with DCIS alone. Additional sampling should be pursued to attempt to identify an area of invasion. If there has been prior surgery or needle biopsy, the possibility of artifactual displacement of epithelial cells into lymphatics should be considered. Lymph node biopsy may be performed in patients with DCIS and lymphovascular invasion.

If there has been a prior core needle biopsy or incisional biopsy, the biopsy site should be sampled and documented in the report. If the intention was to completely re-excise a prior surgical site, the report should document biopsy changes at the margin that could indicate an incomplete excision.

In some situations, inclusion of coexisting conditions can be also considered beneficial if this supports clinicopathological correlation or patient management. Examples include: microcalcification detected mammographically and extension into or involvement of a benign lesion such as a sclerosing lesion, papillary lesion, or fibroepithelial lesion.

An exhaustive description of all coexisting conditions is not required.

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Note 12 – Microcalcifications (Core)

Ductal carcinoma in situ (DCIS) found in biopsies performed for microcalcifications will almost always be at the site of the calcifications or in close proximity.[29,34] Some of these lesions may also include an invasive component.

The pathologist must be satisfied that the specimen has been sampled in such a way that the lesion responsible for the calcifications has been examined microscopically. The presence of the targeted calcifications in the specimen can be confirmed by specimen radiography. The relationship of the radiologic calcifications to the DCIS should be indicated.

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Note 13 – Ancillary studies (Core and Non-core)

The results of any additional ancillary studies such as multigene test results are recommended to be included or added subsequently to the pathology report to ensure a record of all assays performed on the case are recorded in a single comprehensive report. Testing of DCIS for estrogen receptor (ER) is recommended to determine potential benefit of endocrine therapy as adjuvant chemo-prevention (depending on surgery undertaken), while testing DCIS for progesterone receptor (PR) is considered optional, and testing for other biomarkers is currently not relevant.[35]

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Note 14 – Pathological staging (Core)

The Tumour Node Metastasis (TNM) system of the UICC 8th edition Staging Manual is recommended.[15]

Pathologic Classification

Additional descriptors can be used:

The suffix ‘m’ indicates the presence of multiple primary tumours in a single site and is recorded in parentheses, e.g., pT(m) NM.

The ‘r’ prefix indicates a recurrent tumour when staging is carried out after a documented disease-free interval.

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