Renal Biopsy for Tumour Histopathology Reporting Guide

Family/Last name | Date of birth DD – MM – YYYY

Given name(s)

Patient identifiers | Date of request DD – MM – YYYY | Accession/Laboratory number

Elements in **black text** are REQUIRED. Elements in **grey text** are RECOMMENDED.

SPECIMEN LATERALITY (Note 1)

- ○ Not specified
- ○ Left
  - ○ Unifocal
  - ○ Multifocal
- ○ Right
  - ○ Unifocal
  - ○ Multifocal
- ○ Bilateral
  - ○ Unifocal in both kidneys
  - ○ Multifocal in one kidney
  - ○ Multifocal in both kidneys
- ○ Other eg horseshoe kidney
  - ○ Unifocal
  - ○ Multifocal

OPERATIVE PROCEDURE

- ○ Core/needle biopsy
  - Number of cores
  - OR ○ Number cannot be determined

Core id.	Length (in mm)

- ○ Wedge biopsy
  - Number of wedges

Wedge id.	Max. Dimension (in mm)

- ○ Other, *specify*

TUMOUR SITE(S) (Note 2)

- ☐ Upper pole
- ☐ Mid zone
- ☐ Lower pole
- ☐ Cortex
- ☐ Medulla
- ☐ Other, *specify*
- ○ Not provided
- ○ Cannot be assessed

HISTOLOGICAL TUMOUR TYPE** (Note 3)

(Value list from the World Health Organization Classification of Tumours of the Urinary System and Male Genital Organs, Fourth edition (2016) classification of renal cell tumours and the International Society of Urological Pathology Vancouver classification of renal neoplasia)
***Occasionally more than one histologic type of carcinoma occurs within the same kidney specimen. Each tumour type should be separately recorded.*

- ○ Non diagnostic, *specify why*
- ☐ Clear cell renal cell carcinoma
- ☐ Multilocular clear cell renal cell neoplasm of low malignant potential
- ☐ Papillary renal cell carcinoma
  - ☐ Type 1
  - ☐ Type 2
  - ☐ Oncocytic
  - ☐ NOS
- ☐ Chromophobe renal cell carcinoma
  - ☐ Hybrid oncocytic chromophobe tumour
- ☐ Oncocytic tumour
- ☐ Collecting duct carcinoma
- ☐ Renal medullary carcinoma
- ☐ MiT family translocation renal cell carcinoma
  - ☐ Xp11 translocation renal cell carcinoma
  - ☐ t(6;11) renal cell carcinoma
  - ☐ Other, *specify*
- ☐ Mucinous tubular and spindle cell carcinoma
- ☐ Tubulocystic renal cell carcinoma
- ☐ Acquired cystic disease associated renal cell carcinoma
- ☐ Clear cell papillary/tubulopapillary renal cell carcinoma
- ☐ Hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma
- ☐ Succinate dehydrogenase (SDH) deficient renal carcinoma
- ☐ Renal cell carcinoma, unclassified
- ☐ Other, *specify*

HISTOLOGICAL TUMOUR GRADE - WHO/ISUP (Note 4)

- ◯ Not applicable
- ◯ Grade X - Cannot be assessed
- ◯ Grade 1 - Nucleoli absent or inconspicuous and basophilic at 400x magnification
- ◯ Grade 2 - Nucleoli conspicuous and eosinophilic at 400x magnification, visible but not prominent at 100x magnification
- ◯ Grade 3 - Nucleoli conspicuous and eosinophilic at 100x magnification
- ◯ Grade 4 - Extreme nuclear pleomorphism and/or multi nuclear giant cells and/or rhabdoid and/or sarcomatoid differentiation

SARCOMATOID MORPHOLOGY (Note 5)

- ◯ Not identified
- ◯ Present

RHABDOID MORPHOLOGY (Note 6)

- ◯ Not identified
- ◯ Present

NECROSIS (Note 7)

- ◯ Not identified
- ◯ Present

LYMPHOVASCULAR INVASION (Note 8)

- ◯ Not identified
- ◯ Present

CO-EXISTING PATHOLOGY IN NON-NEOPLASTIC KIDNEY (Note 9)

- ◯ None identified
- ◯ Insufficient tissue for evaluation
- ☐ Glomerular disease

Specify type

- ☐ Tubulointerstitial disease

Specify type

- ☐ Vascular disease

Specify type

- ☐ Cyst(s)

Specify type

- ☐ Tubular (papillary) adenoma(s)
- ☐ Other

Specify

ANCILLARY STUDIES (Note 10)

- ◯ Not performed
- ◯ Performed

Specify test and results

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Scope

This dataset has been developed for core or wedge biopsy specimens for neoplasms of renal tubular origin. Non-epithelial tumours should be reported according to established guidelines.[1] Excision specimens are not included – a separate dataset is available and should be used for these cases.

Note 1 – Specimen laterality (Required)

Reason/Evidentiary Support

Specimen laterality information is needed for identification and patient safety purposes.

Core biopsy from two different tumours is fairly uncommon. This may occur in presumed von Hippel Lindau syndrome patients. If, for example, more than 1 tumour is being monitored for growth rate, both may be sampled as part of the same procedure.

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Note 2 – Tumour site(s) (Recommended)

Reason/Evidentiary Support

The position of the tumour in relation to the renal cortex or medulla may also have diagnostic importance. This is especially important for small tumours where a site of origin within the medulla would support a diagnosis of collecting duct carcinoma or medullary carcinoma.[1]

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Note 3 - Histological tumour type (Required)

Reason/Evidentiary Support

Many of the various sub-types of renal epithelial neoplasia exhibit differing clinical behaviour and prognosis.[1,2,9-14] This has been confirmed in large single and multicentre studies for the main tumour sub-types. Several series have also clearly demonstrated that many of the newly described entities of renal malignancy have a prognosis that differs from that of clear cell renal cell carcinoma.[14] In addition to this protocols for the various types of adjuvant anti-angiogenic therapy relate to specific tumour sub-types.[15]

The 2013 International Society of Urological Pathology (ISUP) Vancouver Classification of adult renal tumours identified an emerging/provisional category of renal cell carcinoma (RCC).[8] While appearing distinctive, these rare tumours had not been fully characterized by morphology, immunohistochemistry and molecular studies. This category was also included in the fourth edition of the World Health Organisation (WHO) classification of renal neoplasia. In the WHO classification oncocytoid RCC post-neuroblastoma, thyroid-like follicular RCC, anaplastic lymphoma kinase (ALK) rearrangement-associated RCC and RCC with (angio) leiomyomatous stroma are included in this category. These entities should be classified under 'other' with the name specified.

Papillary RCC has traditionally been subdivided into Type 1 and Type 2.[16] Recent studies have shown these tumours to be clinically and biologically distinct. Type 1 tumours are associated with alterations in the MET pathway while type 2 tumours are associated with activation of the NRF2-ARE pathway. On the basis of molecular features type 2 tumours may be sub-divided into at least 3 subtypes.[17] Type 1 and type 2 tumours show differing immunohistochemical staining with type 1 tumours more frequently expressing cytokeratin 7 in comparison to type 2.[1,8,16,17]

Oncocytic papillary renal cell carcinoma is a category included in the fourth edition of the WHO renal tumour classification.[1] While not fully characterized, this tumour is best included in the broader papillary category.

Papillary RCC is associated with a more favourable outcome than clear cell renal cell carcinoma (ccRCC), collecting duct carcinoma and hereditary leiomyomatosis and renal cell carcinoma (HLRCC)[1,14] Papillary subtyping is also of prognostic significance with type 1 tumours having a more favourable prognosis then those with type 2 morphology.[14,16,17]

On occasion it may be difficult to accurately classify tumours with deeply eosinophilic cytoplasm on renal biopsy. Here the differential diagnosis includes oncocytoma, chromophobe renal cell carcinoma, oncocytic papillary renal cell carcinoma and post-neuroblastoma renal cell carcinoma. Immunohistochemical assessment may be helpful but due to the limited tissue available in a needle biopsy this may be inconclusive. In such instances the term oncocytic neoplasm may be used with a note emphasising that this is not a diagnostic category but a descriptor that includes both benign and malignant entities.[18,19]

The benign entities of renal neoplasia commonly encountered in renal biopsies such as oncocytoma, angiomyolipoma, papillary adenoma, metanephric adenoma and other forms of adenoma should be classified under 'other' with the diagnosis specified.

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Note 4 – Histological tumour grade – WHO/ISUP (Required)

Reason/Evidentiary Support

Grade should be assigned based on the single high power field showing the greatest degree of nuclear pleomorphism.

This grading system is the World Health Organization/ International Society of Urological Pathology (WHO/ISUP) grading system for renal cell carcinoma which is recommended in the 2016 WHO.[1,14] This system has been validated as a prognostic parameter for clear cell and papillary renal cell carcinoma.[14,20,21] It has not been validated for other types of renal cell carcinoma but may be used for descriptive purposes.[22] The current recommendation is that chromophobe renal cell carcinoma is not graded.[1,23]

There is debate regarding the validity of grading renal cell neoplasms in needle biopsies because of the likelihood that the tissue sampled may not be representative. This is of particular concern in large renal neoplasms where there can be considerable morphologic variability. In some series it is recommended that tumours in renal core biopsies not be graded. If a grade is given it should be qualified with a note stating that the provided grade may underestimate the true grade of the tumour.[18,19]

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Note 5 - Sarcomatoid morphology (Required)

Reason/Evidentiary Support

The presence of sarcomatoid morphology is seen in approximately 5% of renal cell carcinomas and is associated with a poor prognosis.[14,24-27] Numerous studies have confirmed that sarcomatoid morphology may occur within any of the main subtypes of renal cell carcinoma and represents high grade disease.[1,8] The five year survival for patients with sarcomatoid morphology is of the order of 15 to 22%.[1,8,24-27] The outcome associated with sarcomatoid morphology is stage dependent.[28] The presence of sarcomatoid morphology is incorporated into the WHO/ISUP grading system (Grade 4).[14]

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Note 6 - Rhabdoid morphology (Required)

Reason/Evidentiary Support

Similar to the sarcomatoid morphology, rhabdoid morphology is a feature of high grade disease.[14,29] Tumours showing this phenotype resemble rhabdoid cells having bulky eosinophilic cytoplasm and an eccentric nucleus, often with a prominent nucleolus.[1,8] Rhabdoid change is associated with a poor prognosis. It has been shown that 71% of patients with rhabdoid morphology developed metastases with a mean follow-up of 4.5 months. Within 2 years it was also noted that 43% of patients in this series had died, with a median survival rate of 8-31months.[14,29-31] In approximately 25% of tumours with rhabdoid morphology, there is co-existing sarcomatoid carcinoma.[1] The presence of rhabdoid morphology is incorporated into the WHO/ISUP grading system (Grade 4).[14]

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Note 7 - Necrosis (Required)

Reason/Evidentiary Support

The presence of tumour necrosis has been shown to be a prognostic indicator for clear cell renal cell carcinoma and chromophobe renal cell carcinoma independent of tumour stage.[14,37] Papillary renal cell carcinoma typically contains foci of necrosis, however the prognostic significance of this is, at best debated. At present it is recommended that the presence of macroscopic (confluent) and microscopic (coagulative) necrosis be recorded.[14]

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Note 8 – Lymphovascular invasion (Required)

Reason/Evidentiary Support

Microvascular invasion has been shown to correlate with the development of metastases and with survival, independent of tumour size, primary tumour category, and grade.[42]

In both clear cell and papillary RCC, tumour spread is predominantly haematogenously via the sinus veins, renal vein and vena cava to the lung. Infiltration of the perirenal fat can result in retroperitoneal spread. Lymphatic spread to the nodes of the renal hilum may also occur and is more common in papillary RCC than with ccRCC.[2]

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Note 9 – Co-existing pathology in non-neoplastic kidney (Required)

Reason/Evidentiary Support

It is important to recognize that medical kidney diseases may be present in nonneoplastic renal tissue in nephrectomy and nephroureterectomy specimens.[1,2] Arterionephrosclerosis (or hypertensive nephropathy) and diabetic nephropathy are seen in approximately 30% and 20% of cases, respectively. Other medical renal diseases that have been identified include thrombotic microangiopathy, focal segmental glomerulosclerosis, and IgA nephropathy. The findings of greater than 20% global glomerulosclerosis or advanced diffuse diabetic glomerulosclerosis are predictive of significant decline in renal function 6 months after radical nephrectomy.[2] Evaluation for medical renal disease should be performed in each case; PAS and/or Jones methenamine silver stains should applied if necessary. Consultation with a nephropathologist should be pursued as needed.

For the assessment of co-existing pathology in renal tissue adjacent to tumour the local effects of an expansile and/or infiltrative neoplasm should be considered. This may be associated with an appreciable degree of inflammation and scarring, and it is not uncommon to see localized secondary interstitial nephritis, glomerulosclerosis and tubular atrophy.

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Note 10 – Ancillary studies (Recommended)

Reason/Evidentiary Support

Ancillary studies are being increasingly utilized for subtyping of renal cell neoplasms. Fluorescent in-situ hybridization (FISH) can be used to confirm a diagnosis of translocation carcinoma (MiT family tumour) and has been shown to be of utility in distinguishing oncocytoma from chromophobe renal cell carcinoma.[1] Cytogenetics may be undertaken in some instances; however, this is not usually performed as part of the routine assessment of a renal tumour. It is now recognized that Immunohistochemical assessment of tumours can be diagnostically helpful. There are currently no ancillary tests that are accepted as having prognostic significance for renal cell neoplasms.[43,44]

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