The Royal College of Pathologists
Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for renal tumours in childhood

November 2015

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Comments	This document replaces the 1st edition of *Dataset for renal tumours in childhood*, published in 2007. In accordance with the College's pre-publication policy, this document was on the College website for consultation from 17 June to 15 July 2015. Twelve items of feedback were received and the dataset was amendments as necessary. Please email publications@rcpath.org if you wish to see the responses. **Dr Lorna Williamson** **Director of Publishing and Engagement**

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Contents

Foreword

The cancer datasets published by The Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. It may rarely be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be assessed by the relevant multidisciplinary team (MDT); just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not necessarily be deemed negligent.

Each dataset contains core data items that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 90% of reports on cancer resections should record a full set of core data items. Other, non-core, data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The dataset has been approved by special interest groups, including the Children's Cancer and Leukaemia Group.

The information used to develop this document was derived from the Renal Tumours of Childhood Trials protocols followed in the UK. All evidence included in this guideline has been graded using modified SIGN guidance (see Appendix H).

No major organisational changes or cost implications have been identified that would hinder the implementation of the dataset.

A formal revision cycle for all guidelines takes place on a three-year cycle. The College will ask the authors of the guideline to consider whether or not the guideline needs to be revised. A full consultation process will be undertaken if major revisions are required. If minor revisions or changes are required, a short note of the proposed changes will be placed on the College website for two weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the guideline and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Working Group on Cancer Services (WGCS) and was placed on the College website for consultation with the membership from 17 June to 15 July 2015. All comments received from the membership were addressed by the author to the satisfaction of the WGCS Chair and the Director of Publishing and Engagement.

This dataset was developed without external funding to the writing group. The College requires the authors of guidelines to provide a list of potential conflicts of interest; these are monitored by the Clinical Effectiveness Department and are available on request. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

Renal tumours comprise 7–8% of all tumours in children under 15 years of age. The most common paediatric renal tumours include nephroblastoma (Wilms tumour), clear cell sarcoma of the kidney, rhabdoid tumour of the kidney and mesoblastic nephroma.[1] Wilms tumour is the most common (85%), followed by mesoblastic nephroma (5%), clear cell sarcoma of the kidney (4%), rhabdoid tumour of the kidney (2%), and miscellaneous rare tumours (4%). Their treatment and prognosis are very different and depend on accurate histological diagnosis and their stage.

Renal tumours in children in the UK are treated according to the protocols of the International Society of Paediatric Oncology (SIOP).[2] These entail biopsy to establish tumour type to determine pre-operative chemotherapy regime. Chemotherapy is followed by surgery and further chemotherapy and/or radiotherapy, if necessary, depending on their histological subtype and stage.[3]

The pathologist has an essential role in:

- diagnosis
- identifying the histological subtype and risk group
- making a precise evaluation of the abdominal stage of the tumour as even in children with stage IV disease, local staging is critical to determine the utilisation of radiotherapy. Based on the correlation between the histological features and survival, three prognostic groups of typical renal tumours of childhood were discerned in the SIOP trials and studies (Appendix C).

The criteria for subclassifying the tumours are detailed elsewhere.[2,14] Since the tumours are treated with pre-operative chemotherapy, it is important to assess the percentage of non-viable and viable tumour, and then the percentage of different histological components of the viable tumour.[14]

1.1 Target users of this guideline

The target primary users of the dataset are trainee and consultant (paediatric) pathologists who are dealing with and reporting these tumours and, on their behalf, the suppliers of IT products to laboratories. The secondary users are surgeons and oncologists, cancer registries and the National Cancer Intelligence Network. Standardised cancer reporting and multidisciplinary team (MDT) working reduce the risk of histological misdiagnosis and help to ensure that clinicians have all of the relevant pathological information required for tumour staging, management and prognosis. Collection of standardised cancer specific data also provides information for healthcare providers, epidemiologists, and facilitates international benchmarking and research.

These are rare tumours and it is recommended that they are handled by pathologists with a special interest in paediatric oncology or renal pathology. There should be ready access to an expert opinion. Consultation of patient groups was not considered necessary. However, the document emphasises the need for meaningful communication between pathologists and clinicians.

2 Clinical information required on the specimen request form

Clinical information provided must include details of pre-operative chemotherapy and information regarding distant metastases. Per-operative details should include information regarding pre- or intra-operative tumour rupture. Ideally the site of per-operative rupture should be marked by the surgeon.

3 Preparation of specimens before dissection

The intact surgical specimen should be presented to the pathologist without being opened by the surgeon. The specimen should be received fresh and unfixed in the laboratory. Specimens must be transferred promptly to the laboratory to enable snap freezing of fresh tissue, which should be done within 60 minutes of excision.

4 Specimen handling and block selection

In order to obtain accurate information about the stage of the tumour, the nephrectomy specimen should be dealt with as follows.

4.1 Description

a) The whole specimen should be weighed, measured and photographed (photography allows discussion with the multidisciplinary team in cases of difficulty and also facilitates central pathological review with regard to sample site interpretation). Any areas of ruptures or fissuring should be identified and any suspicious areas should be inked in different colours from the rest of the specimen. The specimen should not be decapsulated, as this makes determination of growth beyond the capsule impossible.

[Level of evidence D – tumour volume, with other parameters, may be a significant prognostic factor.]

b) Any peri-renal and perihilar lymph nodes (which are rare) should be blocked separately and the site recorded.

[Level of evidence A – Lymph node involvement affects SIOP staging.]

c) The renal vein, artery and ureter should be identified and a transverse section block of each taken near the resection margin.

[Level of evidence A – Margin involvement affects SIOP staging.]

d) The surface of the whole specimen (or at least areas in which excision margins are dubious) and renal sinus should be inked and allowed to dry before opening the specimen. This is a critical step as without inking it might be impossible to stage the tumour correctly and give adequate therapy, in particular, assessment of resection margins for local stage III.

e) The specimen should be opened with a longitudinal incision to bivalve and reveal the tumour and its relation to the kidney, capsule and renal sinus.

f) The cut surface should be photographed to demonstrate the tumour, the extent of tumour necrosis and multicystic cut surface (if present).

g) The report must include the size of the tumour in three dimensions, and the percentage of non-viable tumour. The latter is of critical importance in classification of tumours treated with pre-operative chemotherapy.[14]

[Level of evidence A – Percentage of necrotic tumour affects SIOP risk group classification.]

h) Samples required for biology studies (these are prospective studies done in order to try to identify biological markers of prognosis):

- tumour: at least two pieces (0.5–1 cm^3 each) of morphologically different parts of the tumour should be sampled and snap frozen in liquid nitrogen or at –70°C (freeze more aliquots if available). If a biopsy is performed prior to commencing pre-operative chemotherapy, then a sample of this should also be frozen, if adequate tissue is available
- a 'mirror' sample of tumour adjacent to the frozen sample should be fixed in formalin and studied for histology. This wax block should accompany the frozen tissue, when requested for additional studies
- adjacent normal kidney: two pieces (0.5–1 cm^3) snap frozen in liquid nitrogen or at –70°C
- if present, nephrogenic rests should be sampled as above
- 10 ml peripheral blood in EDTA (if national procedure for storage available)
- samples should be stored at –70°C or under liquid nitrogen until transported to the appropriate national research laboratory on dry ice for cases consenting to research studies.

The time interval between removal of the tumour and the freezing of the samples should be as short as possible and certainly not exceed a period of 30–60 minutes.

[Level of evidence GPP – For preservation of samples the time interval should not exceed 30–60 minutes.]

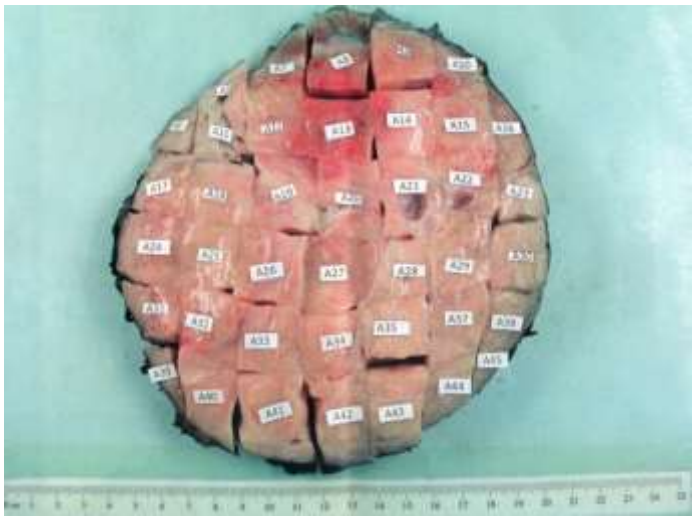
i) The specimen should be fixed in 10% buffered formalin for 24–48 hours according to the usual procedure of the laboratory. Several additional cuts can be made parallel to the initial cut to divide the specimen into 'slabs' for better fixation. (Alternatively, instead of parallel longitudinal sections, horizontal sections and sampling the tumour may give a better view of the renal sinus and a tumour-sinus relationship.)

4.2 Blocks selection

A photograph or a pre-prepared diagram in the SIOP Institutional Pathology Form should preferably be used (Appendix A). The samples for histological examination should include:

a) at least one longitudinal slice of tumour and kidney surface, completely sampled (see Figure 1) (mega-blocks make histological assessment much easier, and they are less time consuming for both pathologists and their labs)

Figure 1: Recommended sampling of renal tumours



In addition, please sample the following:

b) the macroscopically different areas of the tumour (it is advised to take at least one block per cm of the largest diameter of the tumour, not forgetting to take blocks from grossly necrotic areas too); mostly from the periphery rather than from the central areas of the tumour

c) areas suspected to be possible incompletely resected or surgically adherent should be marked by the surgeon for the special attention of the pathologist (they should be marked with appropriate ink or dye)

d) sinus lymph nodes when present

e) other lymph nodes

f) renal pelvis and pelvic fat, ureter and sinus vessels. The renal vein should especially be inspected for evidence of tumour thrombus; if present, it is critical to assess whether it is completely resected

g) each nodule away from the main mass (in multifocal tumours)

h) tumour-kidney interface

i) tumour-kidney capsule

j) areas of the capsule that are suspected of being invaded by the tumour

k) areas of perirenal fat suspected for tumour infiltration (important for assessment whether the tumour is completely resected)

l) areas of adhesions of the tumour to surrounding tissues

m) at least two blocks of the normal kidney and blocks from abnormal looking areas in the remaining renal tissue.

Please make sure to have a 'block guide' (as in Figure 1), i.e. all the samples should be numbered and their sites recorded as well as all other samples taken at the time of operation, i.e. adrenals, lymph nodes and various biopsies.

In the histopathology report, all relevant findings should refer to the block/slide number (e.g. "There is renal sinus invasion in block A7"), as this assists central pathology review.

5 Core data items

a) Total weight of kidney with tumour

b) Size of specimen

c) Size of the tumour (in all three dimensions)

d) Location of tumour

e) Is the tumour multifocal?

[Level of evidence D – tumour volume, with other parameters, may be a significant prognostic factor.]

f) Is the specimen received intact from the operating theatre?

g) Is the renal capsule grossly intact?

[Level of evidence A – Renal capsule status is important prognostic information used in SIOP staging.]

h) Has the surface been inked?

[Level of evidence GPP – Inking of resection margins affects certainty of margin status and therefore staging.]

i) What is the percentage of necrosis/regressive changes on gross examination?

j) What is the percentage of necrosis/regressive changes on microscopic examination?

[Level of evidence A – Percentage of necrosis/regressive change provides prognostic information.]

k) What is the percentage of blastemal?

[Level of evidence A – Relative percentage of tumour components provides prognostic information.]

l) Is anaplastic nephroblastoma present and if so is it focal or diffuse?

[Level of evidence A – The presence of anaplastic nephroblastoma affects risk group stratification.]

m) Is perirenal fat invasion present?

[Level of evidence A – Perirenal fat invasion is important prognostic information used in SIOP staging.]

n) Is renal sinus invasion present?

[Level of evidence A – Renal sinus invasion is important prognostic information used in SIOP staging.]

o) Is renal vein tumour present?

[Level of evidence A – Renal vein invasion by tumour is important prognostic information used in SIOP staging.]

p) Is the resection margin involved and if yes, is this by viable or non-viable tumour?

[Level of evidence A – Resection margin status is important prognostic information used in SIOP staging.]

q) Have lymph nodes been examined? For each lymph node group state the number of nodes identified, the number of nodes positive, negative or uncertain and whether the tumour involvement is viable or non-viable for each node.

[Level of evidence A – Lymph node involvement is important prognostic information used in SIOP staging.]

r) Histological diagnosis and subtype

[Level of evidence A – Histological type determines SIOP tumour risk group.]

s) Tumour risk group – this is the risk grouping based on the SIOP classification (see Appendix C)

[Level of evidence A – Tumour risk group is important prognostic information.]

t) Local tumour stage using SIOP staging system

[Level of evidence A – SIOP stage predicts prognosis.]

u) Reason for staging – the reason for the stated SIOP stage

v) SNOMED T and M codes or SNOMED CT codes (Appendix B).

6 Non-core data items

a) Microscopic assessment of the percentage of other viable components (from 100% viable tumour).

b) The presence/absence of nephrogenic rests.

c) Background renal parenchyma

7 Diagnostic coding and staging

The tumours are staged according to the SIOP staging system (see Appendix D).

Stage is one of the most important therapeutic and prognostic criteria for renal tumours. It has been shown in all multicentre trials that accuracy of staging still represents a major problem. This is partly because of the fact that renal tumours are usually very large at nephrectomy and often it is very difficult to assess their relationship with normal renal anatomical structures such as the renal capsule and the renal sinus. The renal sinus is best recognised by the presence of blood and lymphatic vessels, and especially nerves which are never present within the tumour.

The local (abdominal) staging of primary tumour is done following pre-nephrectomy chemotherapy and is very important even in stage IV cases. The presence/absence of metastases is evaluated at presentation, on the basis of imaging studies.

Separate proformas should be completed for bilateral tumours and the local stage stated for each.

The tumour should be coded according to the SNOMED system, applying appropriate T (topographic) and M (morphologic) codes or using SNOMED CT (see Appendix B).

SNOMED P (procedure) codes should be recorded for the procedure. P codes vary according to the SNOMED system in use in different organisations, therefore local P codes should be recorded and used for audit purposes.

8 Reporting of biopsy specimens

The main purpose of biopsy is to establish whether the tumour is a Wilms tumour or another renal tumour which may require different preoperative treatment.

9 Reporting of frozen sections

Frozen section diagnosis is not appropriate for paediatric tumours since many entities share a common morphological phenotype ('small round blue cell') and cannot be distinguished on morphological grounds alone. Frozen section is not recommended for renal tumours of childhood.

10 Criteria for audit

All paediatric pathologists should participate in the national external quality assessment (EQA) scheme.

Other audits are also recommended by the RCPath as key performance indicators (KPIs) (see *Key Performance Indicators – Proposals for implementation* (July 2013) on www.rcpath.org/clinical-effectiveness/kpi/KPI), as follows.

- Cancer resections must be reported using a template or proforma, including items listed in the English COSD which are, by definition, core data items in RCPath cancer datasets. English Trusts are required to implement the structured recording of core pathology data in the COSD by January 2014.

  Standard: 95% of reports must contain structured data

- Histopathology cases that are reported, confirmed and authorised within seven and ten calendar days of the procedure.

  Standard: 80% of cases must be reported within seven calendar days and 90% within ten calendar days.

11 References

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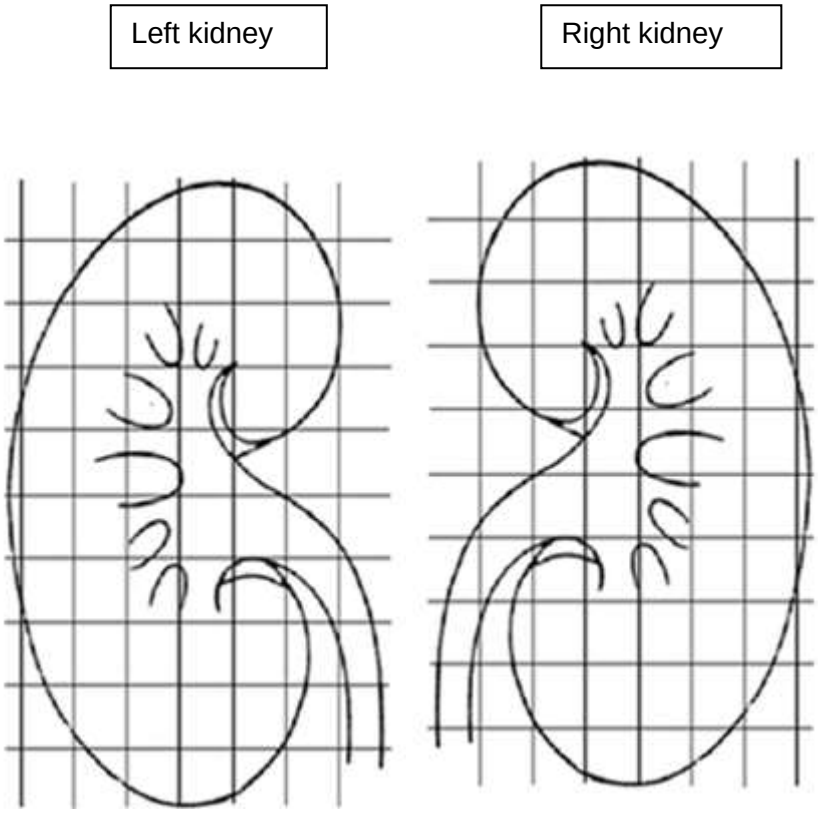
Appendix A SIOP diagram for renal tumours



Please draw or photograph the tumour and document the exact site (by using numbers or letters) of each section taken.

Appendix B SNOMED T and M codes and SNOMED CT codes for paediatric renal tumours

SNOMED T codes

Topographical codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Kidney	T71000	Kidney structure (body structure)	64033007

M codes

Morphological codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Cystic nephroma	M89590	Benign cystic nephroma (morphologic abnormality)	128757006
Cystic partially differentiated nephroblastoma	M89591	Cystic partially differentiated nephroblastoma (morphologic abnormality)	128758001
Mesoblastic nephroma	M89601	Mesoblastic nephroma (morphologic abnormality)	11793003
Nephroblastoma (Wilms' tumour)	M89603	Nephroblastoma (morphologic abnormality)	25081006
Rhabdoid tumour of the kidney	M89633	Malignant rhabdoid tumor (morphologic abnormality)	83118000
Clear cell sarcoma of the kidney	M89643	Clear cell sarcoma of kidney (morphologic abnormality)	24007003

Appendix C The revised SIOP working classification of renal tumours of childhood (2001)[3]

A. For pre-treated cases

I Low risk tumours

- mesoblastic nephroma[4,5]
- cystic partially differentiated nephroblastoma
- completely necrotic nephroblastoma.[6]

II Intermediate risk tumours

- nephroblastoma – epithelial type[7]
- nephroblastoma – stromal type[7]
- nephroblastoma – mixed type
- nephroblastoma – regressive type
- nephroblastoma – focal anaplasia.[8,9]

III High risk tumours

- Nephroblastoma – blastemal type[3]
- Nephroblastoma – diffuse anaplasia[8,9]
- Clear cell sarcoma of the kidney[10,11]
- Rhabdoid tumour of the kidney.[12-13]

B. For primary nephrectomy cases

I Low-risk tumours

- Mesoblastic nephroma
- Cystic partially differentiated nephroblastoma.

II Intermediate-risk tumours

- Non-anaplastic nephroblastoma and its variants
- Nephroblastoma – focal anaplasia.

III High-risk tumours

- Nephroblastoma – diffuse anaplasia
- Clear cell sarcoma of the kidney
- Rhabdoid tumour of the kidney.

Appendix D SIOP staging criteria for paediatric renal tumours

Stage I

a) The tumour is limited to kidney or surrounded with a fibrous (pseudo)capsule if outside of the normal contours of the kidney. The renal capsule or pseudocapsule may be infiltrated by the tumour but it does not reach the outer surface.

b) The tumour may be protruding ('bulging') into the pelvic system and 'dipping' into the ureter but it is not infiltrating their walls.

c) The vessels or the soft tissues of the renal sinus are not involved.

d) Intrarenal vessel involvement may be present.

Notes:

- *Fine needle aspiration or percutaneous core needle ('tru-cut') biopsy does not upstage the tumour but the size of the needle gauge should be mentioned to the pathologist.*
- *The presence of necrotic tumour or chemotherapy-induced change in the renal sinus and/or within the perirenal fat should not be regarded as a reason for upstaging a tumour providing it is completely excised and does not reach the resection margins.*
- *Infiltration of the adrenal gland does not upstage tumour if the external capsule of the adrenal gland is intact.*
- *Liver: tumour might be attached to the liver capsule and this should not be regarded as infiltration of the adjacent organ; only if clear infiltration of the liver parenchyma is present, tumour should be regarded as stage III.*

Stage II

a) Viable tumour penetrates through the renal capsule and/or fibrous pseudocapsule into perirenal fat but is completely resected (resection margins 'clear').

b) Viable tumour infiltrates the soft tissues of the renal sinus.

c) Viable tumour infiltrates blood and lymphatic vessels of the renal sinus or in the perirenal tissue but it is completely resected.

d) Viable tumour infiltrates the renal pelvic or ureter's wall.

e) Viable tumour infiltrates adjacent organs or vena cava but is completely resected.

Stage III

a) Viable or non-viable tumour extends beyond resection margins.

b) Any abdominal lymph nodes are involved.

c) Tumour rupture before or intra-operatively (irrespective of other criteria for staging).

d) The tumour has penetrated through the peritoneal surface.

e) Tumour implants are found on the peritoneal surface.

f) The tumour thrombi present at resection margins of vessels or ureter, trans-sected or removed piecemeal by surgeon.

g) The tumour has been surgically biopsied (wedge biopsy) prior to pre-operative chemotherapy or surgery.

Note: The presence of necrotic tumour or chemotherapy-induced changes in a lymph node or at the resection margins is regarded as proof of previous tumour with microscopic residue and therefore the tumour is assigned stage III (because of the possibility that some viable tumour is left behind in the adjacent lymph node or beyond resection margins).

Stage IV

Haematogenous metastases (lung, liver, bone, brain, etc.) or lymph node metastases outside the abdomino-pelvic region.

Stage V

Bilateral renal tumours at diagnosis. Each side should be sub-staged according to the above criteria.

Appendix E Reporting proforma for paediatric renal tumours

Surname: …… Forenames: …… Date of birth: …… Sex: ……

Hospital……..…….. Hospital no: ……..…… NHS no: …….

Date of surgery: ……..…. Date of report authorisation: …… Report no: ……

Date of receipt:…… Pathologist: ……..…….. Surgeon: ……....

Clinical data and specimen type

Pre-operative chemotherapy Yes □ No □ Not stated □

Pre- or intra-operative tumour rupture Yes □ No □ Not stated □

Tumour site Left □ Right □

Bilateral Yes □ No □ (if bilateral, complete separate forms for left and right)

Nephrectomy Unilateral □ Total □ Partial □

Bilateral □ Left: Total □ Partial □

Right: Total □ Partial □

Macroscopic features

Total weight of kidney with tumour ……g Size …….. x …….. x ……. mm

Tumour size …….. x …….. x ……. mm

Location of tumour: Lower pole □ Upper pole □ Whole kidney □ Multifocal□

Tumour multifocal? Yes □ No. foci…… No □ Uncertain □

Specimen received intact from operating theatre? Yes □ No □ Uncertain □

Renal capsule grossly intact? *(before opening specimen)* Yes □ No □ Uncertain □

Surface inked? No □ Yes □ Before opening specimen □ After opening specimen □

Percentage of necrosis/regressive changes on gross examination ……. *(please state)*

Histology

Percentage of necrosis/regressive changes on histological examination

<65% *(please state)* …… 65–99% *(please state)* …… 100% ……..…

Percentage of: Blastema…….. Epithelium …… Stroma ……..

Anaplastic nephroblastoma Yes □ No □ Uncertain □

If yes, subclassify: Focal □ Diffuse □ Uncertain □

Perirenal fat invasion Yes □ No □ Uncertain □

Renal sinus invasion Yes □ No □ Uncertain □

Renal vein tumour Yes □ No □ Uncertain □

Resection margins involved Yes □ No □ Uncertain □

If yes, is tumour Viable □ Non-viable □

Lymph nodes examined Yes □ No □

Site of node	No. nodes identified	Lymph node status			Node involved by viable or non-viable tumour or both
		No of negative nodes	No of positive nodes	No of uncertain nodes	
Hilar					Viable □ Non-viable □ Both □
Para-aortic					Viable □ Non-viable □ Both □
Other					Viable □ Non-viable □ Both □

Total number of positive lymph nodes: ……

Conclusion

Tumour diagnosis and risk group:

Risk group	Diagnosis, for pre-treated cases	Diagnosis, for primary nephrectomy cases
Low risk □	Mesoblastic nephroma □ Cystic partially differentiated nephroblastoma □ Completely necrotic nephroblastoma □	Mesoblastic nephroma □ Cystic partially differentiated nephroblastoma □
Intermediate risk □	Nephroblastoma – epithelial type □ Nephroblastoma – stromal type □ Nephroblastoma – mixed type □ Nephroblastoma – regressive type □ Nephroblastoma – focal anaplasia v	Non-anaplastic nephroblastoma and its variants □
High risk □	Nephroblastoma – blastemal type □ Nephroblastoma – diffuse anaplasia □ Clear cell sarcoma of the kidney □ Rhabdoid tumour of the kidney □	Nephroblastoma – focal anaplasia □ Nephroblastoma – diffuse anaplasia □ Clear cell sarcoma of the kidney □ Rhabdoid tumour of the kidney □

Tumour local SIOP stage: I □ II □ III □

Reason for stage …..……..

SNOMED CODES: T …….. M ……..

Pathologist

Name ……..…….. Signature …… Date ……..

Appendix F Reporting proformas for paediatric renal tumours in list format

Element name	Values	Implementation notes
Pre-operative chemotherapy	Single-selection value list: • Yes • No • Not stated	
Pre- or intra-operative tumour rupture	Single-selection value list: • Yes • No • Not stated	
Tumour site	Single-selection value list: • Left • Right	
Tumour bilateral	Single-selection value list: • Yes • No	
Nephrectomy unilateral or bilateral	Single-selection value list: • Unilateral • Bilateral	
Unilateral nephrectomy total or partial	Single-selection value list: • Total • Partial	Only applicable if 'Unilateral' is selected for 'Nephrectomy unilateral or bilateral'
Left nephrectomy total or partial	Single-selection value list: • Total • Partial	Only applicable if 'Bilateral' is selected for 'Nephrectomy unilateral or bilateral'
Right nephrectomy total or partial	Single-selection value list: • Total • Partial	Only applicable if 'Bilateral' is selected for 'Nephrectomy unilateral or bilateral'
Total weight of kidney	Weight in grams	
Size of kidney	Size in mm in 3 dimensions	
Location of tumour	Single-selection value list: • Lower pole • Upper pole • Whole kidney • Multifocal	
Tumour multifocal	Single-selection value list: • Yes • No • Uncertain	
Number of tumour foci	Integer	Only applicable if 'Tumour multifocal' is selected.

Specimen receive intact from operating theatre	Single-selection value list: • Yes • No • Uncertain	
Renal capsule grossly intact	Single-selection value list: • Yes • No • Uncertain	
Surface inked	Single-selection value list: • Yes • No	
Surface inked timing	Single-selection value list: • Before opening specimen • After opening specimen • Not applicable	Not applicable if 'Surface inked' is no.
Percentage of necrosis/regressive changes on gross examination	Single-selection value list: • <65% • 65–99% • 100%	
Percentage of necrosis/regressive changes on gross examination, specify	Number between 0 and 99	Not to be completed if 'Percentage of necrosis/ regressive changes on gross examination' is 100%
Percentage of necrosis/regressive changes on histological examination	Single-selection value list: • <65% • 65–99% • 100%	
Percentage of necrosis/regressive changes on histological examination, specify	Number between 0 and 99.99	Not to be completed if 'Percentage of necrosis/ regressive changes on histological examination' is 100%
Percentage of blastema	Number between 0 and 100	
Percentage of epithelium	Number between 0 and 100	
Percentage of stroma	Number between 0 and 100	
Anaplastic nephroblastoma	Single-selection value list: • Yes • No • Uncertain	
Anaplastic nephroblastoma, subclassify	Single-selection value list: • Focal • Diffuse • Uncertain • Not applicable	Not applicable if 'Anaplastic nephroblastoma' is no
Perirenal fat invasion	Single-selection value list: • Yes • No • Uncertain	

Renal sinus invasion	Single-selection value list: • Yes • No • Uncertain	
Renal vein tumour	Single-selection value list: • Yes • No • Uncertain	
Resection margins involved	Single-selection value list: • Yes • No • Uncertain	
Resection margin tumour viable	Single-selection value list: • Viable • Non-viable • Not applicable	Not 'Applicable if resection margin' is 'No' or 'Uncertain'.
Lymph nodes examined	Single-selection value list: • Yes • No	
Hilar, number of nodes identified	Integer	
Hilar, number of negative nodes	Integer	
Hilar, number of positive nodes	Integer	
Hilar, number of uncertain nodes	Integer	
Hilar, type of nodal involvement	Single-selection value list: • Viable • Non-viable • Both • Not applicable	Not applicable if 'Hilar, number of positive nodes' is 0.
Para-aortic, number of nodes identified	Integer	
Para-aortic, number of negative nodes	Integer	
Para-aortic, number of positive nodes	Integer	
Para-aortic, number of uncertain nodes	Integer	
Para-aortic, type of nodal involvement	Single-selection value list: • Viable • Non-viable • Both • Not applicable	Not applicable if 'Para-aortic, number of positive nodes' is 0.
Other, number of nodes identified	Integer	

Other, number of negative nodes	Integer	
Other, number of positive nodes	Integer	
Other, number of uncertain nodes	Integer	
Other, type of nodal involvement	Single-selection value list: • Viable • Non-viable • Both • Not applicable	Not applicable if 'Other, number of positive nodes' is 0.
Total number of positive lymph nodes	Integer	
Risk group	Single-selection value list: • Low risk • Intermediate risk • High risk	
Low-risk type	Single-selection value list: • Pre-treated case: Mesoblastic nephroma • Pre-treated case: Cystic partially differentiated nephroblastoma • Pre-treated case: Completely necrotic nephroblastoma Primary nephrectomy case: Mesoblastic nephroma • Primary nephrectomy case: Cystic partially differentiated nephroblastoma	Only completed if 'Risk group is low risk'
Intermediate-risk type	Single-selection value list: • Pre-treated case:Nephroblastoma - epithelial type • Pre-treated case: Nephroblastoma - stromal type • Pre-treated case: Nephroblastoma - mixed type • Pre-treated case: Nephroblastoma - regressive type • Pre-treated case: Nephroblastoma - focal anaplasia • Primary nephrectomy case: Non-anaplastic nephroblastoma and its variants	Only completed if 'Risk group' is 'Intermediate risk'

High-risk type	Single-selection value list: • Pre-treated case: Nephroblastoma - blastemal type • Pre-treated case: Nephroblastoma - diffuse anaplasia • Pre-treated case: Clear cell sarcoma of the kidney • Pre-treated case: Rhabdoid tumour of the kidney • Primary nephrectomy case: Nephroblastoma – focal anaplasia • Primary nephrectomy case: Nephroblastoma – diffuse anaplasia • Primary nephrectomy case: Clear cell sarcoma of the kidney • Primary nephrectomy case: Rhabdoid tumour of the kidney	Only completed if 'Risk group' is 'High risk'
Tumour local SIOP stage	Single-selection value list: • 1 • 2 • 3	
Reason for stage	Free text	
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables.	
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables.	

Appendix G Summary table – Explanation of grades of evidence

(modified from Palmer K *et al. BMJ* 2008; 337:1832)

Grade (level) of evidence	Nature of evidence
Grade A	At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Grade B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in A.
Grade C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high-quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B.
Grade D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group

Appendix H AGREE compliance monitoring sheet

The tissue pathways of The Royal College of Pathologists comply with the AGREE standards for good quality clinical guidelines. The sections of this tissue pathway that indicate compliance with each of the AGREE standards are indicated in the table below.

AGREE standard	Section of guideline
SCOPE AND PURPOSE	
1. The overall objective(s) of the guideline is (are) specifically described.	1
2. The clinical question(s) covered by the guidelines is (are) specifically described.	1
3. The patients to whom the guideline is meant to apply are specifically described.	Foreword, 1
STAKEHOLDER INVOLVEMENT	
4. The guideline development group includes individuals from all the relevant professional groups.	Introduction
5. The patients' views and preferences have been sought.	n/a*
6. The target users of the guideline are clearly defined.	Introduction
7. The guideline has been piloted among target users.	Foreword, 1
RIGOUR OF DEVELOPMENT	
8. Systematic methods were used to search for evidence.	Foreword
9. The criteria for selecting the evidence are clearly described.	Foreword
10. The methods used for formulating the recommendations are clearly described.	Foreword
11. The health benefits, side effects and risks have been considered in formulating the recommendations.	Foreword
12. There is an explicit link between the recommendations and the supporting evidence.	Throughout
13. The guideline has been externally reviewed by experts prior to its publication.	Foreword
14. A procedure for updating the guideline is provided.	Foreword
CLARITY OF PRESENTATION	
15. The recommendations are specific and unambiguous.	Throughout
16. The different options for management of the condition are clearly presented.	Throughout
17. Key recommendations are easily identifiable.	Throughout
18. The guideline is supported with tools for application.	Appendices E and F
APPLICABILITY	
19. The potential organisational barriers in applying the recommendations have been discussed.	Foreword
20. The potential cost implications of applying the recommendations have been considered.	Foreword
21. The guideline presents key review criteria for monitoring and/audit purposes.	10
EDITORIAL INDEPENDENCE	
22. The guideline is editorially independent from the funding body.	Foreword
23. Conflicts of interest of guideline development members have been recorded.	Foreword