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REVIEW

Data set for reporting paediatric renal tumours: recommendations from the international collaboration on cancer reporting (ICCR)

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Tumours arising within the developing kidney of children vary widely in their histological appearance and outcome; optimal therapy requires accurate classification and staging. The two major paediatric cooperative groups provide different therapeutic protocols based on different staging and classification, initially developed to serve patients in North America and Europe, but also used in many other parts/regions of the world. The International Collaboration on Cancer Reporting (ICCR) has developed a structure whereby such complex information may be harmonised, and able to be applied to patients globally. An international expert panel consisting of paediatric pathologists and oncologists produced a set of items critical to cancer reporting and subjected these to review and discussion using the structured processes provided by

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Abbreviations: COG, Children's Oncology Group; DAC, Dataset Authoring Committee; ICCR, International Colaboration on Cancer Reporting; LOH, loss of heterozygosity; NWTS, National Wilms Tumor Study; RTSG, Renal Tumour Study Group; SIOP, International Society of Paediatric Oncology; SNP, single nucleotide polymorphism; WAGR, Wilms, Aniridia, Genitourinary, Range; WHO, World Health Organization; WT, Wilms tumour.

the ICCR. A formal ICCR structure was assembled, and consensus surrounding elements and their application to different therapeutic protocols was developed. The data set underwent open international consultation. This resulted in the first international data set for Wilms tumour (WT) and other paediatric renal tumours, provided herein. The use of ICCR methods enables a full understanding of highly complex and often overlapping reporting elements by international experts, and the potential of developing a set of commonly applied data elements that are fully defined. This sets the groundwork for future consolidation of definitions and harmonisation of therapies for WT and other paediatric renal tumour patients. It also allows institutions outside the major paediatric cooperative groups to provide therapy based on known elements.

Keywords: checklist, data set, ICCR guidelines, paediatric renal tumours, protocol, structured report, synoptic report, Wilms tumours

Introduction

Tumours of the developing kidney account for approximately 5% childhood cancers; Wilms tumours (WT), or nephroblastoma, constitute 85% of paediatric renal tumours. Improvement in the outcome of patients with paediatric renal tumours has largely been due to two different therapeutic approaches applied by the major paediatric cooperative groups: the Renal Tumour Study Group (RTSG)/International Society of Paediatric Oncology (SIOP) and the National WT Study Group (NWTS)/Children's Oncology Group (COG).[1] In SIOP, an initial radiographic diagnosis is usually followed by pre-operative chemotherapy, then by surgery. Further chemotherapy and/or radiotherapy is then given depending on post-therapy histology and stage. In contrast, COG patients most commonly undergo primary surgery followed by chemotherapy and radiotherapy that is determined by the pretherapy tumour histology and stage. The two strategies utilise different histological classification and staging approaches, determined at different time-points with respect to therapy. This has made direct comparison of outcome data for many prognostic factors difficult although, overall, the outcome for both approaches is the same.[2] Due to the close working relationship between COG and SIOP, the lack of harmonisation of key histology and staging factors is being addressed with good progress.

In our quest for optimisation of outcomes for children with paediatric renal tumours within cooperative groups, of equal importance is the fact that most children with cancer are treated in countries lacking the availability of expertise and the treatment strategies applied by COG and SIOP. The utility of a resource describing the features that drive therapeutic decisions is therefore needed. The current efforts seek to address the similarities and differences between pre- and post-therapy histological assessment of WT used by the different classification systems and, in so doing, harmonising their definitions so that they may be useful more broadly. To meet these aims, The International Collaboration on Cancer Reporting (ICCR) was utilised. ICCR is a global alliance of the major international pathology and cancer organisations. The ICCR coordinates the production of freely available evidence-based reporting data sets that have a consistent style and contain the parameters needed to guide patient management (https://www.iccr-cancer.org/datasets/published-datasets/).

Methods

The current effort utilises the ICCR standardised operating procedures for selecting an ICCR Series Champion, an ICCR project manager, an expert and diverse panel constituting a Dataset Authoring Committee (DAC) and a DAC chair, each with carefully defined responsibilities. Care was taken to select an international expert panel consisting of pathologists and medical oncologists from the major cooperative groups. To create a data set, data from the relevant medical literature were assessed, including the 5th edition of the World Health Organisation (WHO) classification, as well as other existing published data sets (http://www.iccr-cancer.org/datasets/dataset-development). The DAC chair and ICCR project manager produced initial draft documents that were circulated to the DAC. All data set items were discussed at a coordinated series of teleconferences until consensus was obtained. An agreed version of the revised data set was posted for international consultation for 2 months. All resulting comments were discussed by

the DAC and when consensus agreement was obtained, the appropriate changes were made. The final version of the data set was ratified by the ICCR Dataset Steering Committee prior to publication.

Results

SCOPE

This data set has been developed for the reporting of the pathology of resection specimens from paediatric patients with nephroblastoma, also known as WT, and all other primary renal tumours of childhood, excluding renal cell carcinomas, for which the ICCR invasive carcinoma of renal tubular origin data set should be used.[3] Rarely, other primitive tumours of childhood (including neuroblastoma, Ewing sarcoma/peripheral neuroectodermal tumour, synovial sarcoma, desmoplastic small round cell tumour, among others) arise within the kidney, but these tumours are not specific to nephrogenic precursor cells. This data set does not apply to these tumours, which should be staged and treated according to recommendations specific for their diagnosis, and does not apply to procedures involving only biopsy of renal tumours. This is due to the highly individualised and variable nature that characterises the extent and the timing of biopsies with respect to the different therapies provided. The ICCR may be able to contribute a biopsy-only data set in the future.

Core (required) and non-core (optional) elements are listed in Table 1. Core elements are described in detail below.

CORE ELEMENTS DESCRIBING THE PATIENT AND PROCEDURE

Protocol followed

There are two treatment protocols commonly followed by institutions (developed by either the NWTS/COG or SIOP/RTSG), even if the institution is not affiliated with a cooperative group. If known, the protocol by which the child will be treated is indicated. This aids in the clarification of other core elements discussed below.

Previous therapy

The treatment of WT may include the use of chemotherapy prior to resection or biopsy.[1,4,5] The staging systems used for these different approaches, although similar, have significant differences. Further, the histological appearance differs following chemotherapy, as does the assessment of risk stratification.[6,7] Thus, it is critical that the status of pre-operative therapy is known so that the relevant staging and classification systems can be applied. When completing this element, only therapy used to treat the current renal tumour is considered as 'prior treatment'.

Operative procedure

There are three overall approaches to the initial diagnosis of WT: (i) upfront neoadjuvant chemotherapy (with no biopsy) for presumed WT (within specified clinical parameters) followed by post-therapy resection; (ii) initial biopsy followed by chemotherapy and then resection; and (iii) primary resection prior to chemotherapy. The type and extent of the surgical procedure chosen depends upon the approach as well as other factors, including the site, size and extent of the tumour. Total or radical nephrectomy includes resection of an intact kidney and any associated lymph nodes or tissue/organs adherent to the tumour. This data set does not distinguish between total and radical nephrectomy. Partial nephrectomy seeks to completely excise a tumour with a margin of non-tumour renal tissue while sparing the remaining kidney. Enucleation seeks to remove the entire tumour, minimising the margin of non-tumoral tissue.

The choice of performing a biopsy has different implications depending upon which staging system is used. In the COG staging system, biopsy of any type, including percutaneous core or needle biopsy, increases the tumour to at least a stage III.[8,9] In the SIOP/RTSG staging system, only open biopsy increases the tumour to at least stage III;[6] needle or core biopsy using a posterior retroperitoneal approach does not upstage the tumour.[10]

It is important to note that in COG, all procedures are newly staged based on features for the tumour at the time of that procedure in order to best guide the subsequent therapy. For example, a biopsy taken prior to therapy in a COG patient supports a local stage of III at the time of that biopsy. The same pretherapy biopsy is not itself a criterion for stage III following a subsequent post-therapy resection. In contrast, in SIOP/RTSG an open/wedge biopsy mandates a stage III designation, even for subsequent procedures.

Other rare operative procedures merit annotation. WT rarely originates outside the kidney. Extrarenal WT may be associated with other congenital anomalies and the operative approach should be provided.[11]

Presence of pre-operative rupture or intra-operative spillage

WT, particularly prior to therapy, may rupture spontaneously or following pre-operative or operative

Table 1. Core and non-core elements for the pathology reporting of the paediatric renal tumours data set

Core	Non-core
Protocol followed	
Previous therapy	• Clinical information guiding previous therapy, specify if available
Operative procedure	
Pre-operative rupture or intra-operative Spillage	
Accompanying/attached structures	
Specimen laterality	
Specimen weight	
Tumour focality	
Tumour dimensions • Largest dimension of two nodules determining stage and histology	• Additional dimension of the two nodules determining stage and histology
Renal sinus involvement	
Renal capsule penetration	
Primary tumour excised in one piece	
Nephrogenic rests	
Histological tumour type	
Post-therapy histological classification of Wilms tumour	
Margin status	• Distance of viable tumour from mm closest margin • Specify closest margin(s), if possible
Lymph node status	• Location of involved lymph nodes
Ancillary studies	• Representative blocks for ancillary studies, specify those blocks best representing tumour and/or normal tissue for further study
Histologically confirmed distant metastasis	
Pathological staging	
	Coexistent pathology
	Block identification key

trauma.[12] In SIOP/RTSG and COG protocols, tumours that rupture either prior to surgery or at the time of surgery (the latter is an event more recently termed 'spillage' by COG) are considered to have local stage III disease and to require additional therapy.[1,13] The pathological appearance of rupture/spillage changes with the passage of time. Spillage at the time of resection and rupture near the time of resection both result in disruption of the Gerota fascia and the underlying tumour. However, at times the pathological evidence of the spillage/rupture may be limited and may only be evident to the surgeon. Furthermore, the same gross appearance may be seen following trauma to the specimen after operative removal of the tumour, requiring correlation with intra-operative findings. Rupture prior to surgery results in the same disruptive process, but with the increasing passage of time several changes occur to varying degrees, including tumour devitalisation, resolving haemorrhage, fibrosis and inflammation within the perirenal soft tissue. With even further passage of time, the site of rupture may heal and may become inapparent pathologically. The determination of whether rupture/spillage has occurred is

therefore often difficult based on pathological findings alone, and may require multidisciplinary input, particularly by the surgeon. Pathologists should seek the opinion of the surgeon prior to establishing the presence of rupture or spillage and should be aware that the surgeon may independently establish the presence and extent of rupture/spillage for treatment purposes.

It is important to note that the following situations do not constitute rupture: (1) growth of the tumour through the renal capsule (or the peritumoral pseudocapsule) and extension of the tumour into the perirenal soft tissue; and (2) appearance of rupture/spillage confined to the renal capsule (not involving the Gerota fascia). Further, in these situations, if the tumour then extends to the surgical margin, this is defined as a positive margin and not rupture. This distinction may impact upon the type and amount of radiation therapy given.

Sufficient data are not currently available to utilise the presence of tumour cells detected within abdominal or pleural fluid in staging of WT.

Presence of accompanying/attached structures

Depending upon the size and relationship of the tumour with the adrenal gland, the surgeon may choose to remove the adjacent adrenal gland with the goal of completely resecting the tumour. Whether or not the patient has one or two adrenal glands may be important in their care in the future. Similarly, to achieve total removal of the tumour, the surgeon may remove pieces of other organs adherent to the tumour (such as spleen, liver, bowel or diaphragm). In addition, this information may be useful in the management of the patient in the future. When these accompanying structures are resected intact with the kidney, the presence of tumour within the accompanying structure does not support a local stage of III unless the surgical margin of the resection of the specimen is positive for tumour.

Specimen laterality

The anatomical location of the tumour being evaluated is an elemental part of the accurate description of the tumour under consideration.

Specimen weight

Nephrectomy specimens should be weighed prior to sectioning or processing. Nephrectomy weight may be an eligibility factor for some clinical trial protocols,[9] and in certain circumstances may influence therapy decisions.[14] While the amount of perinephric soft tissue and/or additional tissues resected in one piece with the kidney may vary, the pathologist should not attempt to remove these prior to weighing.

CORE ELEMENTS DESCRIBING FEATURES OF THE TUMOUR

Tumour focality

Most WT are solitary, but multifocal unilateral and/or bilateral disease may occur in more than 10% of cases.[14,15] Multifocal tumours are associated with an increased risk of WT developing in the contralateral kidney, usually in association with nephrogenic rests.[16] The presence of multifocality often determines the treatment approach.[17] In case of multiple synchronous tumours in a specimen, a single data set should be completed providing the number of tumours and their size. Within each kidney, each tumour should be individually staged and classified, and the stage and classification should then be determined for the entire kidney. For example, a kidney with a 4-cm tumour showing diffuse anaplasia, local stage I and a 10-cm local stage III tumour with favourable histology would receive a classification of diffuse anaplasia, local stage III. This example illustrates that there will be unusual combinations that need to be carefully discussed among a multidisciplinary team in order to determine the final treatment strategy. When bilateral tumours are sampled, a data set should be recorded for each kidney.

Tumour dimensions

The macroscopic size of the tumour determines the pathological handling, whereby at least one microscopic section is taken per centimetre of maximal tumour diameter.[2,9,18] The SIOP/RTSG recommends mapping out at least one longitudinal slice of tumour to evaluate percentages of different elements (chemotherapy-induced changes, blastema, stroma and epithelium) to establish the diagnosis. The pathological and radiological tumour dimensions may also be used to calculate the volume of the tumour or the volume of the different histological counterparts at the time of central review.[13] These are currently important questions being addressed within SIOP/RTSG studies. For kidneys with more than two tumours, the two tumours impacting upon the stage and histology should be provided in the data set.

At least the greatest tumour dimension should be reported (core); preferably, all three dimensions should be evaluated, particularly if tumour volume is desired.

Renal sinus involvement

The renal sinus is composed predominantly of adipose tissue and harbours nerves and vessels supplying and draining the kidney and the extrarenal collecting system. The renal sinus also extends deeply into the contours of the kidney. The most important renal sinus sections are those taken from regions adjacent to the tumour. SIOP/RTSG and COG protocols separately evaluate the invasion of renal sinus soft tissue and the involvement of renal sinus vessels to provide tumour staging which dictates subsequent treatment. For both SIOP/RTSG and COG, only viable tumour within the renal sinus results in upgrading to local stage II, provided that the margins are negative for viable and non-viable tumour.[13,18]

Sinus soft tissue. Unlike the majority of the kidney, the renal sinus lacks a fibrous capsule separating the kidney from the adjacent adipose tissue. Therefore, tumour that is confined to the kidney may directly abut the renal sinus fat, without truly invading the renal sinus soft tissue. Similarly, nephrogenic rests located deep in the kidney may also involve the renal sinus soft tissue and mimic involvement by WT. COG protocols include an additional refinement that identifies patients with only minimal renal sinus soft tissue invasion that is distant from the soft tissue margin. Unless there are other features upstaging these patients, they are treated as local stage I tumours. In practice, 'minimal invasion' includes tumours that show tumour extension into the sinus that is less than 5 mm in greatest dimension, and is located greater than 5 mm from a surgical margin.

Sinus vessels. Evaluating renal sinus vascular involvement may be similarly challenging. During processing, small fragments of tumour may be displaced into vascular structures and mimic true vascular involvement. Artefactually displaced tumour fragments are commonly highly irregularly ragged, and may contain ink that is displaced by the knife or blade. True vascular involvement has a smooth surface and is often (but not always) adherent to the vessel. Any degree or size of true sinus vascular involvement is a criterion for local stage II. This is distinct from staging based upon invasion of sinus soft tissue, as above.

Renal capsule penetration

Invasion of tumour beyond the renal capsule dictates subsequent treatment for both COG and SIOP/RTSG.[1,13] The renal capsule is a layer of collagen covering the entire kidney, except for the renal sinus. The renal capsule may be quite thin, particularly if compressed by an expanding tumour. The fibrous pseudocapsule formed by the tumour itself may merge with the renal capsule, making the distinction between the tumour pseudocapsule and the renal capsule difficult. The presence of the tumour beyond the renal capsule is best seen by taking sections of the triangular region where the normal kidney and renal capsule meets the confluence of the tumour with its pseudocapsule.

Beyond the renal capsule is a layer of adipose tissue, often containing dilated vessels, which is covered by the Gerota fascia. Viable tumour that penetrates the renal capsule and invades or is otherwise present within this soft tissue or vessels without invasion beyond, or rupture of, the Gerota fascia meet the criteria for stage II. Non-viable tumour in this region, in the absence of other criteria, does not upstage to stage II. For institutions that treat patients according to SIOP/RTSG protocols, additional refinements have been made that identify a small number of patients with viable tumour within the perirenal fat or within the adrenal gland that is surrounded by a fibrous pseudocapsule, which is allowed within local stage I for SIOP/RTSG (but not for COG).

Primary tumour excised in one piece

In the COG and National Wilms Tumour Study Group protocols, removal of tumour in more than one piece is a criterion for local stage III.[1] Some examples include: (1) primary tumour excised in more than one piece; (2) tumour identified in a separately excised adrenal gland; (3) a tumour thrombus within the renal vein that is removed separately from the nephrectomy specimen; and (4) tumour nodules within the perirenal fat (resembling lymph nodes) that are separately excised. The separately excised specimens may or may not represent contiguous tumour.

Presence of nephrogenic rests

Nephrogenic rests are foci of persistent embryonic tissue, and may be single, multiple or diffusely distributed. More than 30% of Wilms nephrectomy specimens contain nephrogenic rests. Rests often appear paler than surrounding non-neoplastic kidney parenchyma, and these areas should be sampled. The two fundamental categories of nephrogenic rests are based on the topography and histology; perilobar nephrogenic rests are located at the periphery of the lobule, are usually subcapsular and comprised predominantly of blastema or epithelial differentiation. Intralobar nephrogenic rests are usually located deep

within the lobule. They have indistinct margins and contain blastemal, tubular and prominent stromal elements interspersed among normal glomerular and tubular elements.[19,20] Diffuse hyperplastic perilobar nephroblastomatosis is a rare form of perilobar nephrogenic rests that forms a rind of nephroblastomatosis involving one or both kidneys, in whole or in part.[21,22] Nephrogenic rests are often difficult to distinguish from Wilms tumours, particularly following therapy; they also have important implications concerning the risk of contralateral WT development and association with certain syndromes.[16,23]

Histological tumour type

Histological diagnosis is based on the 2022 WHO Classification of Paediatric Tumours, 5th edition (Table 2).[24] Accurate histological diagnosis of paediatric renal tumours is critical in order to provide the optimal therapy and outcome. Because they are rare, they often present a diagnostic challenge. More than 85% of renal malignancies in children will be WT (favourable and anaplastic subtypes), which are malignancies arising in the primitive metanephric precursor cells. While the vast majority are of favourable histology (see Figure 1), those with enlarged, polyploid atypical mitotic figures, marked nuclear enlargement and hyperchromasia are classified as anaplastic (see Figure 2).[24] Wilms tumours may arise

Table 2. World Health Organisation classification of paediatric renal tumours[24]

Descriptor	ICD-O codes[a]
Wilms tumour (nephroblastoma)	8360/3
Nephrogenic rest	
Congenital mesoblastic nephroma	8960/1
Paediatric cystic nephroma	8959/0
Cystic partially differentiated nephroblastoma	8959/1
Metanephric stromal tumour	8935/1
Metanephric adenoma	8325/0
Metanephric adenofibroma	8965/0
Ossifying renal tumour of infancy	8967/0
Clear cell sarcoma of kidney	8964/3
Rhabdoid tumour	8963/3
Anaplastic sarcoma of kidney (DICER-1 associate)	8800/3

[a]These morphology codes are from the International Classification of Diseases for Oncology, 3rd edition, second revision (ICD-O-3.2). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline or uncertain behaviour; /2 for carcinoma *in-situ* and grade III intra-epithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site.

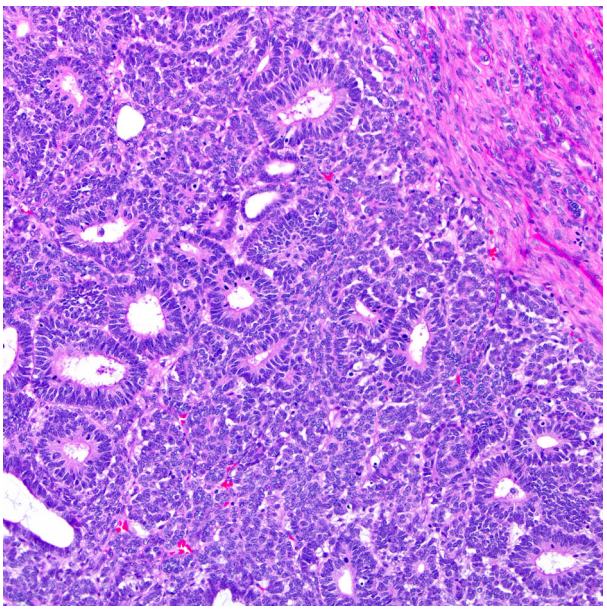

Figure 1. Favourable histology Wilms tumour. By far the most common paediatric renal tumour, Wilms tumour may show a variety of histological patterns, including blastema (undifferentiated), epithelial and stromal. Further, the epithelial and stromal components may also show heterologous differentiation, including mucinous, muscle and adipose differentiation, among others. The tumour in this figure illustrates epithelial and blastemal components.

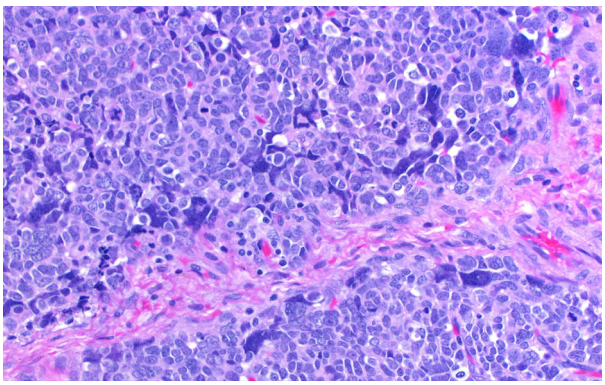

Figure 2. Anaplastic Wilms tumour: demonstrated are the enlarged, polyploid mitotic figures and marked nuclear enlargement with hyperchromasia that define anaplastic Wilms tumours. These are often subcategorised as focal or diffuse, depending upon the extent of anaplasia.

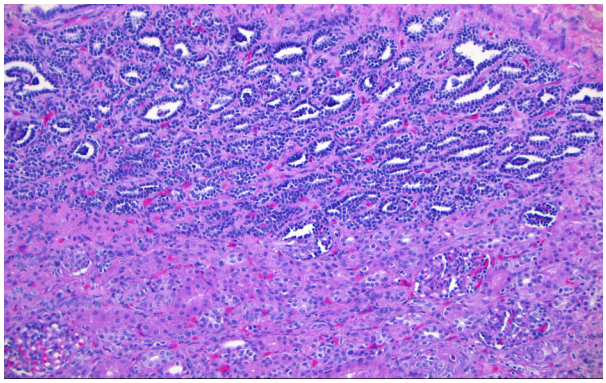

Figure 3. Nephrogenic rest: many Wilms tumours arise within precursor lesions known as nephrogenic rests. Like Wilms tumours, nephrogenic rests may vary from proliferative to regressing. Experts have distinguished between intralobar and perilobar nephrogenic rests based on the position in the renal lobe, the presence or absence of sharp demarcation and the cellular composition. Illustrated is a sharply demarcated perilobar nephrogenic rest composed of epithelial tubules.[59]

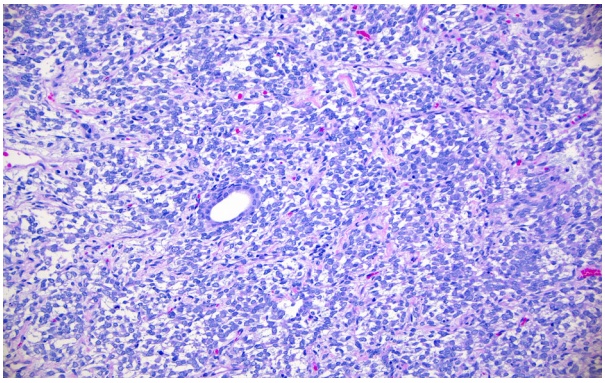

Figure 5. Clear cell sarcoma of kidney: these mesenchymal neoplasms show a wide spectrum of histological appearances, and often mimic Wilms tumours as well as other childhood neoplasms. Features distinguishing CCSK from Wilms tumour include a fine, open chromatin pattern, low mitotic rate and a subtly infiltrative border, with entrapment of native renal elements, as seen in the centre of this figure.

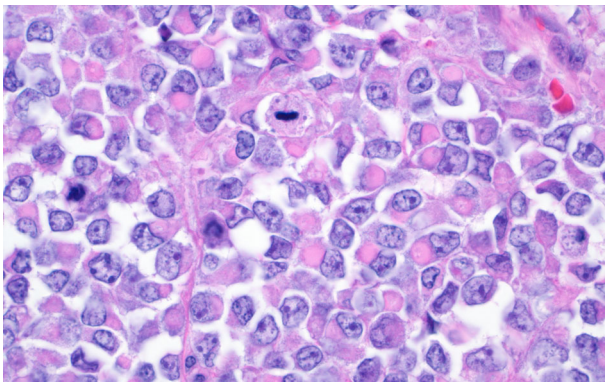

Figure 4. Rhabdoid tumour of kidney: this highly malignant tumour, most commonly occurring in infancy, is composed of a monomorphic population of large cells with vesicular nuclei, often with prominent and large nucleoli, and a large cytoplasmic inclusion composed of intermediate filaments.

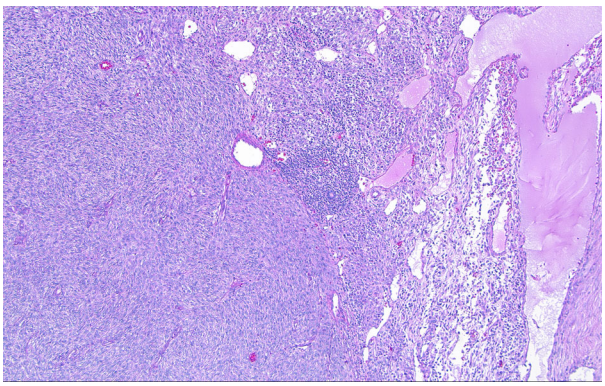

Figure 6. Congenital mesoblastic nephroma: these stromal neoplasms present most commonly in infancy and may be composed of plump, variably spindled cells (classified as the cellular subtype, illustrated in this figure), or may be composed of markedly elongated, interdigitating cells (classified as the classic subtype).

in the setting of precursor lesions known as nephrogenic rests (see Figure 3). Other paediatric renal tumours appear to arise within the soft tissue elements of the primitive kidney, and may have a similar appearance to WT. These include rhabdoid tumour of the kidney (Figure 4), clear cell sarcoma of the kidney (see Figure 5) and mesoblastic nephroma (see Figure 6). The addition of immunohistochemical and molecular analyses aid in differentiating these various tumour types, as discussed further below. It is beyond the scope of this document to provide detailed descriptions of the subtypes of paediatric renal tumours (refer to WHO 5th edition[24]).

Post-therapy histological classification of WT

The histological response to prior therapy is taken into consideration by both SIOP and COG in order to guide future therapy of patients with post-therapy WT.[2,25] Tumours are stratified into three risk groups based on the histology following pre-operative chemotherapy and on the assessment of percentages of chemotherapy-induced changes and all viable components, as follows:

1. *Low-risk*: Completely necrotic tumours showing no viable tumour are classified as low-risk. Small foci of tubules, stroma and/or blastema representing residual nephrogenic rests may be present.

2. *Intermediate-risk*: All favourable histology WTs falling outside low- and high-risk as defined above are classified as intermediate-risk. In addition, SIOP WT tumours with focal anaplasia are included in the intermediate risk category. COG WT tumours with focal and diffuse anaplasia are separately classified and treated. SIOP also separately classifies intermediate-risk tumours by histological subtype due to their potential prognostic implications.[26,27]

3. *High-risk*: WT with diffuse anaplasia are classified as high-risk by SIOP, and are separately classified and treated by COG. Favourable histology WT that are ≥ 33% viable with > 66% of the viable tumour composed of blastema are classified by both SIOP and COG as high-risk.

Margin status

Margin status is critical for the staging of paediatric renal tumours. Margins positive for viable tumour upstage the tumour to stage III in all staging systems. The evaluation of non-viable tumour at the margin differs depending upon margin location and on the staging system used. In SIOP, non-viable tumour at the ureteral or renal vein margin or within abdominal or peritoneal implants is considered local stage III, whereas non-viable tumour at the soft tissue margin is not considered local stage III. COG considers non-viable tumour at all margins to represent local stage III.

The status of the renal parenchymal margin for partial nephrectomy is important, as positive margins are associated with consideration of the need for radiotherapy. After radiotherapy, however, the local recurrence rate was not greater in such patients.[28] The presence of nephrogenic rest at the parenchymal margin of partial nephrectomy specimen represents a challenge in interpretation, but is not considered to be positive.

Assessment of the renal vein margin may be challenging, particularly if there is bulging thrombus. If the thrombus is intact (by gross assessment and discussion with the surgeon), and if the renal vein wall is not attached to the thrombus at its most distal aspect, the margin can be assumed to be negative.[29]

Lymph node status

Lymph node involvement is a critical factor in determining stage, and lymph node involvement by either viable or non-viable tumour requires a designation of stage III in both the COG and SIOP/RTSG staging systems.[13,30] Positive lymph node status in any site is associated with a worse prognosis,[31] particularly for those patients with anaplastic WT.[30]

In certain circumstances the recognition of lymph node metastasis can be challenging. Small aggregates of tumour cells in the subcapsular sinuses may be overlooked, and these sites should be examined carefully for metastatic disease. In post-treatment tumours, lymph nodes may contain totally necrotic tumour, which still increases the tumour to local stage III.[2,32] Such necrotic tumour foci should replace part of the nodal architecture; prominent sinus histiocytes should not be considered evidence for stage III tumour. Lastly, when tumour causes obstruction of the kidney, Tamm-Horsfall protein may accumulate within the kidney and be displaced into the regional lymph node. This may be accompanied by displaced non-neoplastic renal tubular epithelial cells and such foci may mimic lymph node metastasis.[33] Such foci are cytologically consistent with reactive epithelial cells and do not resemble WT.[29]

Involvement of abdominal or pelvic lymph nodes is a criterion for local stage III; lymph node involvement in the thorax or other extra-abdominal sites is a criterion for stage IV.

Histologically confirmed distant metastases

Documentation of known metastatic disease correlates with outcome and is an important part of the pathology report.[34] Such information, if available, should be recorded with as much detail as is available, including the site, specimen type, size and histological pattern.

If distant sites are sampled and pathologically shown to be negative, metastatic disease is 'not identified', whereas if sampling is not performed, this section is 'not applicable'.

Pathological staging

Two main systems for staging of paediatric renal tumours are in use: the SIOP/RTSG staging system is predominantly used for pretreated tumours and the COG staging system is used for tumours undergoing primary resection as well as following therapy.[2,13] The evaluation of tumour viability is only taken into consideration following therapy. The local staging criteria for COG are provided below.

COG local stage I: Tumour (viable) is limited to the kidney with negative margins and lymph nodes. All criteria listed below are met.

a Renal capsule is not penetrated by viable tumour.
b Tumour may protrude (botryoid) into the renal pelvis or ureter but does not infiltrate their walls.
c The vessels of the renal sinus are not involved by viable tumour.

d The soft tissue of the renal sinus is not more than minimally involved by viable tumour.
e The tumour was not ruptured or biopsied prior to removal.
f There is no evidence of tumour at or beyond the margin of resection.
g Necrotic tumour may be present within the renal sinus or beyond the renal capsule and remain as local stage I provided the margins are negative for viable and non-viable tumour.
h Extrarenal primary tumours are not eligible for stage I.

COG local stage II: The tumour is resected in one piece; there is no evidence of tumour at or beyond the margins and the lymph nodes are negative for tumour (viable or non-viable); at least one of the following is present.

a Viable tumour is present in the perirenal fat or adrenal gland.
b Viable tumour infiltrates the blood or lymphatic vessels outside the renal parenchyma, including the renal sinus.
c Viable tumour more than minimally infiltrates the soft tissue of the renal sinus.
d Viable tumour infiltrates the wall of the renal pelvis or the ureter.
e Viable tumour may infiltrate the adrenal gland or be adherent to adjacent structures but remain stage II if surgical margins are negative for tumour.

COG local stage III: Residual non-haematogenous tumour present after surgery and confined to the abdomen. At least one of the following is present.

a Tumour (viable or non-viable) involves abdominal/pelvic lymph nodes.
b Tumour (viable or non-viable) is present at a surgical margin of resection (documented by microscopic examination).
c Pre- or intra-operative tumour rupture/spillage has occurred (documented histologically or confirmed by the surgeon).
d The tumour is resected in more than one piece (piecemeal).
e The tumour is biopsied before surgery regardless of biopsy type: tru-cut, open or fine-needle aspiration. (Only applies to staging at time of biopsy, should not be used as a criterion for assigning the stage III in a post-therapy resection specimen.)
f Tumour (viable or non-viable) has penetrated through the peritoneal surface.
g Tumour implants (viable or non-viable) are found anywhere in the abdomen.

The local staging criteria for SIOP are provided below:

SIOP local stage I: Viable tumour is limited to the kidney with negative margins and lymph nodes. All criteria listed below are met.

a Renal capsule intact, not penetrated by viable tumour.
b Tumour might protrude (botryoid) into the renal pelvis or ureter but does not infiltrate their walls.
c The vessels of the renal sinus are not involved by viable tumour.
d The soft tissue of the renal sinus is not involved by viable tumour.
e Non-viable tumour may be present within the renal sinus or beyond the renal capsule and remain stage I.
f Viable tumour may remain Stage I if present in the perirenal fat or within the adrenal gland but surrounded by a fibrous pseudocapsule.

SIOP local stage II: The margins are negative for viable tumour and the lymph nodes are negative for viable or non-viable tumour; at least one of the following is present.

a Viable tumour is present in the perirenal fat or adrenal gland and is not covered by a pseudocapsule.
b Viable tumour infiltrates the blood or lymphatic vessels outside the renal parenchyma.
c Viable tumour infiltrates the soft tissue of the renal sinus.
d Tumour may be adherent to adjacent structures but remain stage II if the surgical margin is negative.
e Viable tumour infiltrates the vena cava or adjacent organs (except the adrenal gland), but is completely resected.
f Viable tumour infiltrates the wall of the renal pelvis or the ureter.

SIOP local stage III: Residual non-haematogenous tumour present after surgery and confined to abdomen. Any one of the following may occur.

a Tumour (viable or non-viable) involving abdominal–pelvic lymph nodes.
b Tumour (viable only) present at a soft tissue surgical margin of resection.
c Tumour (viable or non-viable) present at resection margins of ureter, renal vein or inferior vena cava.
d Pre- or intra-operative tumour rupture/spillage, if confirmed by microscopic examination (positive margin in area of the rupture).
e Tumour thrombus (viable or non-viable) attached to the inferior vena cava wall removed piecemeal.

f Wedge/open tumour biopsy prior to pre-operative chemotherapy or surgery.
g Tumour implants (viable or non-viable) are found anywhere in the abdomen.
h Tumour (viable or non-viable) has penetrated through the peritoneal surface.

Reporting of pathological staging categories is based upon the evidence available to the pathologist at the time of reporting. The final stage grouping of a patient's tumour is based upon a combination of pathological staging and other clinical and imaging information.

ANCILLARY STUDIES

Non-morphological testing, e.g. molecular or immunohistochemical testing, is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, ICCR includes the most relevant ancillary testing in their data sets, recognising that the technical capability may not yet exist. Representative blocks recommended for ancillary studies may be provided.

The following summarises clinically relevant ancillary studies.

Wilms tumour

Ancillary studies are usually not necessary for the diagnosis of WT in resection specimens. However, immunohistochemical staining for WT1 and/or PAX8 may be useful for problematic cases when differentiating blastemal-predominant WT from other embryonal soft tissue tumours presenting within the kidney. Similarly, no dominant recurrent genetic abnormality has been found in WT, although molecular genetic tests may be performed for diagnostically difficult cases. Several studies suggest that the common underlying marker of anaplasia is mutation of the *TP53* gene.[35–37] Mutation of *TP53* often (but not always) results in abnormal p53 protein accumulation and strong nuclear positivity for p53 by immunohistochemistry. However, the diagnostic utility of immunohistochemistry for p53 protein is limited by difficulties in performing and interpreting the test. Furthermore, some *TP53* mutations do not cause abnormal protein accumulation. However, strong nuclear p53 protein accumulation identified in a tumour that is suspicious for anaplasia may contribute to the diagnosis.[38]

Molecular tests such as loss of heterozygosity (LOH) at chromosomes 1p and 16q, gain of 1q and 11p15 loss have prognostic significance in certain patient populations. Augmentation of therapy has been shown to be effective for WT with combined LOH at 1p and 16q; therefore, analysis of these loci, most commonly by targeted or genome-wide microarray that includes evaluation of zygosity (SNP array), has become routine practice in North America.[39,40] While 1q gain is associated with adverse prognosis, the benefit of increased therapy is an area of active investigation.[41] LOH and imprinting abnormalities of 11p15 have been associated with increased risk of relapse in young patients with stage I favourable histology WT treated with nephrectomy alone without adjuvant therapy.[42,43] On occasion, ancillary germline genetic testing may be useful after the diagnosis has been made. For example, there is an association between perilobar nephrogenic rests, LOH for *IGF2* and overgrowth syndromes; and between intralobar nephrogenic rests, mutations of the *WT1* gene and the WAGR and Denys–Drash syndromes (reviewed in Beckwith 1998[23]).

Clear cell sarcomas of the kidney

Clear cell sarcomas of the kidney often show expression of BCOR, cyclin D1, NGFR and TLE1 by immunohistochemistry; however, none of these are either fully sensitive or specific.[44-47] Clear cell sarcoma of the kidney frequently contain *BCOR*–ITD mutations or other *BCOR* alterations[48]; a minority have *YWHAE*::*NUTM2B* fusion.[49,50]

Rhabdoid tumours of the kidney

Rhabdoid tumours of the kidney are most often characterised by alterations in *SMARCB1* gene, causing loss of INI1 expression by immunohistochemistry.[51]

Paediatric cystic nephromas

Paediatric cystic nephromas (but not cystic partially differentiated nephroblastomas) are often associated with germline or somatic mutations in the *DICER1* gene and are associated with pleuropulmonary blastoma familial cancer syndrome.[53–55] Rarely, sarcomas with varying degrees of anaplasia histologically similar to pleuropulmonary blastoma may also be identified within the kidney, and these have been classified as anaplastic sarcoma of the kidney[24,56] which, at times, may arise within a cystic nephroma.[57,58]

Metanephric tumours

Metanephric tumours (adenomas, adenofibromas, and stromal tumours) often carry somatic *BRAF* mutations.[52]

Congenital mesoblastic nephromas

Congenital mesoblastic nephromas containing a cellular component often demonstrate *ETV6*::*NTRK3* fusions (as well as other variant fusions); alterations of *EGFR*, *BRAF* and other genes have also been reported in *ETV6*::*NTRK3*-negative cases.[52]

Discussion

In light of the increasing amount of data collected following the surgical excision of tumours, structured reporting of the results has become increasingly important to ensure that all meaningful elements are included in the therapeutic decision-making process. Structured reporting is also required for creating robust data to support changes in future therapeutic recommendations by clinical investigators. The ICCR has been particularly important for this effort, largely because of their ability to navigate the differences in practices of diverse organisations due to structured neutrality and inclusiveness and reliance upon data. This was certainly true of the current efforts to create an ICCR data set for the excision of paediatric renal tumours. As described in the Introduction, most of the data that have been collected over the years for paediatric renal tumours has been performed through the efforts of the NWTS/COG (treating the majority of children with cancer in predominately North America) and SIOP/RTSG (treating children in predominately Europe). These two different sources of data are remarkable for their different approaches. COG has long advocated for resection followed by therapy, whereas SIOP has advocated for therapy prior to surgery. Indeed, most of the complexity of the resulting data set is due to whether or not the tumour being examined and reported has received prior therapy. Despite these differences, COG and SIOP work closely together and recognise the advantages of understanding this complexity, particularly as this may allow future simplification, as well as increased power of data collection, given the increased numbers of patients when both groups are included in studies. Given the historical reliance upon these different approaches, it appears unlikely that significant reduction of this largest source of complexity will be achieved in the near term. Greater promise of simplification is evident in the many smaller ways in which the different groups have implemented differences in definitions of stages. Increasing our full understanding of all the criteria will help to move towards more consistency and continue to improve outcomes.

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Conflicts of interest

The authors report no relevant conflicts of interest.

Data availability statement

No data were directly utilised in this paper. All references cited in the text are listed in the reference list.

References

1. Dome JS, Perlman EJ, Graf N. Risk stratification for wilms tumor: current approach and future directions. *American Society of Clinical Oncology Educational Book* 2014; 215–223. https://doi.org/10.14694/EdBook_AM.2014.34.215
2. Vujanić GM, Parsons LN, D'Hooghe E, Treece AL, Collini P, Perlman EJ. Pathology of Wilms' tumour in International Society of Paediatric Oncology (SIOP) and Children's oncology group (COG) renal tumour studies: similarities and differences. *Histopathology* 2022; **80**; 1026–1037.
3. International Collaboration on Cancer Reporting. *Invasive Carcinoma of Renal Tubular Origin, Histopathology Reporting* Guide. 2017 1st edition. Available at: https://www.iccr-cancer.org/datasets/published-datasets/urinary-male-genital/renal-tubular/ (Accessed 15th December 2024).
4. Sonn G, Shortliffe LM. Management of Wilms tumor: current standard of care. *Nat. Clin. Pract. Urol.* 2008; **5**; 551–560.
5. Vujanić GM, D'Hooghe E, Graf N *et al.* Prognostic significance of histopathological response to preoperative chemotherapy in unilateral Wilms' tumor: an analysis of 899 patients treated on the SIOP WT 2001 protocol in the UK-CCLG and GPOH studies. *Int. J. Cancer* 2021; **149**; 1332–1340.
6. Vujanić GM, D'Hooghe E, Popov SD, Sebire NJ, Kelsey A. The effect of preoperative chemotherapy on histological subtyping and staging of Wilms tumors: the United Kingdom Children's cancer study group (UKCCSG) Wilms tumor trial 3 (UKW3) experience. *Pediatr. Blood Cancer* 2019; **66**; e27549.
7. Perlman EJ. Pediatric renal tumors: practical updates for the pathologist. *Pediatr. Dev. Pathol.* 2005; **8**; 320–338.
8. Dome JS, Graf N, Geller JI *et al.* Advances in Wilms tumor treatment and biology: progress through international collaboration. *J. Clin. Oncol.* 2015; **33**; 2999–3007.
9. College of American Pathologists. *Protocol for the Examination of Resection Specimens From Patients With Wilms and Other Pediatric Renal Tumors.* 2023 Available at: https://documents.cap.org/protocols/Kidney.Wilms_4.3.0.1.REL_CAPCP.pdf (Accessed 25th September 2024).

10. Jackson TJ, Brisse HJ, Pritchard-Jones K *et al*. How we approach paediatric renal tumour core needle biopsy in the setting of preoperative chemotherapy: a review from the SIOP renal tumour study group. *Pediatr. Blood Cancer* 2022; **69**; e29702.
11. Liang H, He Y, Fu L *et al*. Extrarenal Wilms tumor in children: a retrospective observational case series. *J. Pediatr. Urol.* 2020; **16**; 664.e661–664.e667.
12. Zhang Y, Song HC, Yang YF, Sun N, Zhang WP, Huang CR. Preoperative Wilms tumor rupture in children. *Int. Urol. Nephrol.* 2021; **53**; 619–625.
13. Vujanić GM, Gessler M, Ooms A *et al*. The UMBRELLA SIOP-RTSG 2016 Wilms tumour pathology and molecular biology protocol. *Nat. Rev. Urol.* 2018; **15**; 693–701.
14. Wiener JS, Coppes MJ, Ritchey ML. Current concepts in the biology and management of Wilms tumor. *J. Urol.* 1998; **159**; 1316–1325.
15. Shearer P, Parham DM, Fontanesi J *et al*. Bilateral Wilms tumor. Review of outcome, associated abnormalities, and late effects in 36 pediatric patients treated at a single institution. *Cancer* 1993; **72**; 1422–1426.
16. Coppes MJ, Arnold M, Beckwith JB *et al*. Factors affecting the risk of contralateral Wilms tumor development: a report from the National Wilms Tumor Study Group. *Cancer* 1999; **85**; 1616–1625.
17. Ehrlich PF, Chi YY, Chintagumpala MM *et al*. Results of treatment for patients with multicentric or bilaterally predisposed unilateral Wilms tumor (AREN0534): a report from the Children's Oncology Group. *Cancer* 2020; **126**; 3516–3525.
18. Zuppan CW. Handling and evaluation of pediatric renal tumors. *Am. J. Clin. Pathol.* 1998; **109**(4 Suppl 1); S31–S37.
19. Beckwith JB. Precursor lesions of Wilms tumor: clinical and biological implications. *Med. Pediatr. Oncol.* 1993; **21**; 158–168.
20. Beckwith JB, Kiviat NB, Bonadio JF. Nephrogenic rests, nephroblastomatosis, and the pathogenesis of Wilms' tumor. *Pediatr. Pathol.* 1990; **10**; 1–36.
21. Ehrlich PF, Tornwall B, Chintagumpala MM *et al*. Kidney preservation and Wilms tumor development in children with diffuse hyperplastic perilobar Nephroblastomatosis: a report from the Children's Oncology Group Study AREN0534. *Ann. Surg. Oncol.* 2022; **29**; 3252–3261.
22. Perlman EJ, Faria P, Soares A *et al*. Hyperplastic perilobar nephroblastomatosis: long-term survival of 52 patients. *Pediatr. Blood Cancer* 2006; **46**; 203–221.
23. Beckwith JB. Nephrogenic rests and the pathogenesis of Wilms tumor: developmental and clinical considerations. *Am. J. Med. Genet.* 1998; **79**; 268–273.
24. WHO Classification of Tumours Editorial Board ed. *Pediatric Tumours, WHO Classification of Tumours, Volume 7*. 5th ed. Lyon: IARC Publications, 2022.
25. Zuppan CW, Beckwith JB, Weeks DA, Luckey DW, Pringle KC. The effect of preoperative therapy on the histologic features of Wilms' tumor. An analysis of cases from the third National Wilms' tumor study. *Cancer* 1991; **68**; 385–394.
26. Verschuur AC, Vujanic GM, Van Tinteren H, Jones KP, de Kraker J, Sandstedt B. Stromal and epithelial predominant Wilms tumours have an excellent outcome: the SIOP 93 01 experience. *Pediatr. Blood Cancer* 2010; **55**; 233–238.
27. Weirich A, Leuschner I, Harms D *et al*. Clinical impact of histologic subtypes in localized non-anaplastic nephroblastoma treated according to the trial and study SIOP-9/GPOH. *Ann. Oncol.* 2001; **12**; 311–319.
28. Kieran K, Williams MA, Dome JS, McGregor LM, Krasin MJ, Davidoff AM. Margin status and tumor recurrence after nephron-sparing surgery for bilateral Wilms tumor. *J. Pediatr. Surg.* 2013; **48**; 1481–1485.
29. Murphy WM, Grignon DJ, Perlman EJ. *Tumors of the Kidney, Bladder, and Related Urinary Structures*. AFIP atlas of tumor pathology, series 4. Washington, D.C., USA: American Registry of Pathology, 2004.
30. Kieran K, Anderson JR, Dome JS *et al*. Lymph node involvement in Wilms tumor: results from National Wilms tumor studies 4 and 5. *J. Pediatr. Surg.* 2012; **47**; 700–706.
31. Honeyman JN, Rich BS, McEvoy MP *et al*. Factors associated with relapse and survival in Wilms tumor: a multivariate analysis. *J. Pediatr. Surg.* 2012; **47**; 1228–1233.
32. Vujanić GM, Sandstedt B, Harms D, Kelsey A, Leuschner I, de Kraker J. Revised International Society of Paediatric Oncology (SIOP) working classification of renal tumors of childhood. *Med. Pediatr. Oncol.* 2002; **38**; 79–82.
33. Weeks DA, Beckwith JB, Mierau GW. Benign nodal lesions mimicking metastases from pediatric renal neoplasms: a report of the National Wilms' tumor study pathology center. *Hum. Pathol.* 1990; **21**; 1239–1244.
34. Berger M, Fernandez-Pineda I, Cabello R *et al*. The relationship between the site of metastases and outcome in children with stage IV Wilms tumor: data from 3 European pediatric cancer institutions. *J. Pediatr. Hematol. Oncol.* 2013; **35**; 518–524.
35. Bardeesy N, Falkoff D, Petruzzi MJ *et al*. Anaplastic Wilms' tumour, a subtype displaying poor prognosis, harbours p53 gene mutations. *Nat. Genet.* 1994; **7**; 91–97.
36. Lahoti C, Thorner P, Malkin D, Yeger H. Immunohistochemical detection of p53 in Wilms' tumors correlates with unfavorable outcome. *Am. J. Pathol.* 1996; **148**; 1577–1589.
37. Ooms AH, Gadd S, Gerhard DS *et al*. Significance of TP53 mutation in Wilms tumors with diffuse anaplasia: a report from the Children's Oncology Group. *Clin. Cancer Res.* 2016; **22**; 5582–5591.
38. Franken J, Lerut E, Van Poppel H, Bogaert G. p53 immunohistochemistry expression in Wilms tumor: a prognostic tool in the detection of tumor aggressiveness. *J. Urol.* 2013; **189**; 664–670.
39. Dix DB, Fernandez CV, Chi YY *et al*. Augmentation of therapy for combined loss of heterozygosity 1p and 16q in favorable histology Wilms tumor: a Children's Oncology Group AREN0532 and AREN0533 study report. *J. Clin. Oncol.* 2019; **37**; 2769–2777.
40. Dome JS, Mullen EA, Dix DB *et al*. Impact of the first generation of Children's Oncology Group Clinical Trials on clinical practice for Wilms tumor. *J. Natl. Compr. Cancer Netw.* 2021; **19**; 978–985.
41. Gratias EJ, Dome JS, Jennings LJ *et al*. Association of chromosome 1q gain with inferior survival in favorable-histology Wilms tumor: a report from the Children's Oncology Group. *J. Clin. Oncol.* 2016; **34**; 3189–3194.
42. Fernandez CV, Perlman EJ, Mullen EA *et al*. Clinical outcome and biological predictors of relapse after nephrectomy only for very low-risk Wilms tumor: a report from Children's Oncology Group AREN0532. *Ann. Surg.* 2017; **265**; 835–840.
43. Perlman EJ, Grundy PE, Anderson JR *et al*. WT1 mutation and 11P15 loss of heterozygosity predict relapse in very low-risk wilms tumors treated with surgery alone: a Children's Oncology Group Study. *J. Clin. Oncol.* 2011; **29**; 698–703.
44. Argani P, Pawel B, Szabo S, Reyes-Múgica M, Timmons C, Antonescu CR. Diffuse strong BCOR immunoreactivity is a

sensitive and specific marker for clear cell sarcoma of the kidney (CCSK) in pediatric renal neoplasia. *Am. J. Surg. Pathol.* 2018; **42**; 1128–1131.
45. Arva NC, Bonadio J, Perlman EJ, Cajaiba MM. Diagnostic utility of Pax8, Pax2, and NGFR immunohistochemical expression in pediatric renal tumors. *Appl. Immunohistochem. Mol. Morphol.* 2018; **26**; 721–726.
46. Creytens D, Ferdinande L, Van Dorpe J. Diagnostic utility of cyclin D1 in the diagnosis of small round blue cell tumors in children and adolescents: beware of cyclin D1 expression in clear cell sarcoma of the kidney and CIC-DUX4 fusion-positive sarcomas. Comment on Magro et al (2016). *Hum. Pathol.* 2017; **67**; 225–226.
47. Kenny C, Grehan D, Ulas M *et al*. Immunophenotype-genotype correlations in clear cell sarcoma of kidney-an evaluation of diagnostic ancillary studies. *Pediatr. Dev. Pathol.* 2020; **23**; 345–351.
48. Ueno-Yokohata H, Okita H, Nakasato K *et al*. Consistent in-frame internal tandem duplications of BCOR characterize clear cell sarcoma of the kidney. *Nat. Genet.* 2015; **47**; 861–863.
49. Rakheja D, Weinberg AG, Tomlinson GE, Partridge K, Schneider NR. Translocation (10;17)(q22;p13): a recurring translocation in clear cell sarcoma of kidney. *Cancer Genet. Cytogenet.* 2004; **154**; 175–179.
50. O'Meara E, Stack D, Lee CH *et al*. Characterization of the chromosomal translocation t(10;17)(q22;p13) in clear cell sarcoma of kidney. *J. Pathol.* 2012; **227**; 72–80.
51. Hoot AC, Russo P, Judkins AR, Perlman EJ, Biegel JA. Immunohistochemical analysis of hSNF5/INI1 distinguishes renal and extra-renal malignant rhabdoid tumors from other pediatric soft tissue tumors. *Am. J. Surg. Pathol.* 2004; **28**; 1485–1491.
52. Treece AL. Pediatric renal tumors: updates in the molecular era. *Surg. Pathol. Clin.* 2020; **13**; 695–718.
53. Cajaiba MM, Khanna G, Smith EA *et al*. Pediatric cystic nephromas: Distinctive features and frequent *DICER1* mutations. *Hum. Pathol.* 2016; **48**; 81–87.
54. Doros LA, Rossi CT, Yang J *et al*. DICER1 mutations in childhood cystic nephroma and its relationship to DICER1-renal sarcoma. *Mod. Pathol.* 2014; **27**; 1267–1280.
55. González IA, Stewart DR, Schultz KAP, Field AP, Hill DA, Dehner LP. DICER1 tumor predisposition syndrome: an evolving story initiated with the pleuropulmonary blastoma. *Mod. Pathol.* 2022; **35**; 4–22.
56. Vujanić GM, Kelsey A, Perlman EJ, Sandstedt B, Beckwith JB. Anaplastic sarcoma of the kidney: a clinicopathologic study of 20 cases of a new entity with polyphenotypic features. *Am. J. Surg. Pathol.* 2007; **31**; 1459–1468.
57. Wu MK, Vujanic GM, Fahiminiya S *et al*. Anaplastic sarcomas of the kidney are characterized by DICER1 mutations. *Mod. Pathol.* 2018; **31**; 169–178.
58. Wu MK, Cotter MB, Pears J *et al*. Tumor progression in DICER1-mutated cystic nephroma–witnessing the genesis of anaplastic sarcoma of the kidney. *Hum. Pathol.* 2016; **53**; 114–120.
59. Molina LM, Rao A, Meade J *et al*. Hiding in plain sight: radiologic and pathologic findings can identify Beckwith-Wiedemann syndrome in patients with wilms tumor. *J. Pediatr. Hematol. Oncol.* 2024; **46**; 424–428.