



# Handling and reporting of nephrectomy specimens for adult renal tumours: a survey by the European Network of Uro-pathology

Ferran Algaba,<sup>1</sup> Brett Delahunt,<sup>2</sup> Daniel M Berney,<sup>3</sup> Philippe Camparo,<sup>4</sup> Eva Compérat,<sup>5</sup> David Griffiths,<sup>6</sup> Glen Kristiansen,<sup>7</sup> Antonio Lopez-Beltran,<sup>8</sup> Guido Martignoni,<sup>9</sup> Holger Moch,<sup>10</sup> Rodolfo Montironi,<sup>11</sup> Murali Varma,<sup>6</sup> Lars Egevad<sup>12</sup>

<sup>1</sup>Department of Pathology, Fundacion Puigvert-University Autonomous, Barcelona, Spain  
<sup>2</sup>Department of Pathology and Molecular Medicine, Wellington School of Medicine and Health Sciences, University of Otago, Wellington, New Zealand  
<sup>3</sup>Department of Molecular Oncology, Barts Cancer Institute, London, UK  
<sup>4</sup>Service d'anatomie et cytologie pathologiques, Hôpital Foch, Paris, France  
<sup>5</sup>Department of Pathology, Hôpital Pitié-Salpêtrière, Paris, France  
<sup>6</sup>Department of Pathology, University Hospital of Wales, Cardiff, UK  
<sup>7</sup>Institute of Pathology, University Hospital Bonn, Germany  
<sup>8</sup>Unit of Anatomic Pathology, Cordoba University Medical School, Cordoba, Spain  
<sup>9</sup>Anatomia Patologica, Department of Pathology and Diagnostics, University of Verona, Italy  
<sup>10</sup>Institute for Surgical Pathology, University Hospital, Zurich, Switzerland  
<sup>11</sup>Institute of Pathological Anatomy and Histopathology, School of Medicine, Polytechnic University of the Marche Region, Ancona, Italy  
<sup>12</sup>Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden

## Correspondence to

Professor Lars Egevad, Department of Pathology, Radiumhemmet P1:02, Karolinska University Hospital, Stockholm 17176, Sweden; lars.egevad@ki.se

The first two authors contributed equally to the study.

Accepted 27 August 2011  
 Published Online First  
 30 September 2011

## ABSTRACT

**Aim** To collect information on current practices of European pathologists for the handling and reporting of nephrectomy specimens with renal tumours.

**Methods and Results** A questionnaire was circulated to the members of the European Network of Uro-pathology, which consists of 343 pathologists in 15 European countries. Replies were received from 48% of members. These replies indicated that nephrectomy specimens are most often received in formalin. Lymph nodes are found in less than 5% of nephrectomy specimens. All respondents give an objective measure of tumour size, most commonly in three diameters. The most common method to search for capsule penetration is to slice tissue outside the tumour perpendicularly into the tumour. The most common sampling algorithm from tumours greater than 2 cm is one section for every centimetre of maximum tumour diameter. Most respondents use the 2004 WHO renal tumour classification although only slightly over half consider small papillary tumours malignant if the diameter is greater than 5 mm. The Fuhrman grading system is widely used. Almost all use immunohistochemistry for histological typing in some cases, while only 7% always use it. The most utilised special stains are CK7 (95%), CD10 (93%), vimentin (86%), HMB45 (68%), c-kit (61%) and Hale's colloidal iron (52%). Only 18% use other ancillary techniques for diagnosis in difficult cases.

**Conclusions** While most pathologists appear to follow published guidelines for reporting renal carcinoma, there is still a need for the development of consensus and further standardisation of practice for contentious areas of specimen handling and reporting.

The second edition of the WHO classification of renal tumours, published in 1981, divided carcinomas of the renal parenchyma into two categories—renal cell carcinoma and other.<sup>1</sup> At that time, there were limited treatment options for these tumours and as there were few validated prognostic factors, histological reports were somewhat basic. In recent years there has been an enormous expansion in our understanding of the histogenesis, morphology and molecular biology of these tumours, and it is now recognised that renal cell carcinoma is not a single entity but a diverse group of tumours with differing morphology, genetics and clinical course.<sup>2</sup>

The introduction of targeted therapies for renal epithelial malignancies has provided an impetus for pathologists and oncologists to investigate molecular pathways associated with the development of each tumour morphotype.<sup>3</sup> Coupled with these developments considerable advances have been made in the identification and validation of prognostic factors for these tumours.<sup>4</sup> As a consequence of these advances the pathologist is now expected to provide a detailed report containing not only the diagnosis, but also a detailed description of prognostic features relevant to each specific morphotype, in order to facilitate management decisions and outcome prediction.

The handling of surgical specimens remains central to the evaluation of all forms of renal cell carcinoma, and in recent years several guidelines have been published relating to the handling and reporting of kidney specimens containing either benign or malignant tumours.<sup>5–10</sup> These protocols are frequently detailed, demanding extensive specimen examination and careful documentation. Clearly, the implementation of the recommendations contained within these protocols has led to a considerable increase in laboratory workload and may conflict with the diminishing availability of resources, which is a feature of contemporary medical practice. In view of these constraints it remains uncertain as to how these protocols are implemented and their recommendations are followed in the clinical setting. In order to investigate current practices we have undertaken this survey, which we anticipate will inform a refinement of reporting recommendations.

## MATERIALS AND METHODS

The participants in the survey are members of the European Network of Uro-pathology (ENUP), which was established in 2006 and has, as one of its aims, the development of evidenced-based reporting guidelines.<sup>11</sup> For the purpose of this study a web-based questionnaire was developed containing 51 questions specifically related to the handling and reporting of nephrectomy specimens from adult patients with renal parenchymal malignancies. The questions were framed by a multinational committee consisting of 13 senior specialist urological pathologists. All of these had previous experience in formulating questionnaires of this nature.

Questions were proposed by individual members of the committee and then circulated for comment and amendment. The process of revision passed through several cycles and at the completion there was unanimous agreement that all questions were of relevance to the study. In their final form all questions were of the multiple choice type but in some of these there was an opportunity for the respondent to provide alternative answers or record comments.

The web tool used for the publication of questionnaires and the collection of data was that employed in previous surveys conducted by the ENUP (<http://www.surveymonkey.com>).<sup>12</sup>

An invitation to participate in the survey was circulated to all members of the network by email during December 2009 and a reminder was sent to all those who had failed to return the survey just before the close off date of January 2010.

## RESULTS

The overall response to the survey was 175 replies from a total of 343 ENUP members circulated (47.5%). The geographical distribution of the respondents is shown in table 1.

Not all respondents answered all the questions in the survey. Of the pathologists who replied, 54.9% (89/162) worked at a university (academic) hospital, 41.4% (67/162) in a community (public healthcare) hospital, 1.9% (3/162) in private healthcare and 1.9% (3/162) in another type of institution. Among replying ENUP members, 42% (68/162) were also members of the International Society of Urological Pathology.

The workload in relation to renal malignancies was quite variable among participants in the survey. The number of total nephrectomy specimens processed per year in the laboratory of the respondents was 20 or less in 13.1% (21/160), 21–40 in 29.4% (47/160), 41–60 in 26.3% (42/160), 61–100 in 20.6% (33/160), 101–150 in 8.8% (14/160) and more than 150 in 1.9% (3/160).

### Gross examination and handling

These results are detailed in tables 2–4.

It was reported that the specimens were most frequently handled by a fully qualified medical pathologist. In slightly more than half the cases the renal specimen is always placed in formalin before submission to the laboratory. Separate lymphadenectomy specimens were rarely received and in less than 5% of the cases was a lymph node found within the

**Table 1** Countries participating in the ENUP and in the RCC survey study

Country	No of ENUP members	% of ENUP members	No of respondents	% of respondents
Austria	7	2.0	5	3.1
Belgium	19	5.5	7	4.5
Denmark	14	4.1	4	2.5
Finland	9	2.6	6	3.7
France	42	12.2	16	9.8
Germany	45	13.1	15	9.2
Ireland	5	1.5	2	1.2
Italy	45	13.1	30	18.4
The Netherlands	25	7.3	7	4.3
Norway	16	4.7	8	4.9
Portugal	14	4.1	8	6.1
Spain	19	5.5	10	7.4
Sweden	27	7.9	12	7.4
Switzerland	13	3.8	8	4.9
United Kingdom	43	12.5	24	14.7
Total	343	100	162	100

ENUP, European Network of Urology; RCC, renal cell carcinoma.

**Table 2** Initial handling of nephrectomy specimens (submission, type of tissue included, harvesting for research)

Question	%	Number
Who usually grossly examines the specimens		
Qualified medical pathologist	67.5	108/160
A resident (trainee) pathologist	32.5	52/160
Method of submission of specimens		
Fresh	45.4	74/163
In formalin	54.6	89/163
Submission of separate lymphadenectomy specimens together with nephrectomy specimen		
<10%	82.0	132/161
10–15%	12.4	20/161
26–50%	3.1	5/161
51–75%	1.2	2/161
76–100%	1.2	2/161
Lymph nodes found in the nephrectomy specimen		
Never	3.7	6/162
Very rarely (<5%)	77.8	126/162
5–10%	12.3	20/162
11–25%	4.3	7/162
26–50%	0.6	1/162
51–75%	0.6	1/162
76–100%	0.6	1/162
Harvesting of fresh tissue for research		
Always	21.0	34/162
In some case	41.4	67/162
Never	37.7	61/162

nephrectomy specimen itself. More than 60% of respondents noted that in some instances, or always, fresh tissue was harvested for research purposes.

There was some variation in the methods used for determining capsule penetration by tumour, although the majority of respondents reported that they preferred to slice the extra-tumoural tissue, as well as the tumour, perpendicular to the capsular surface.

Reported sampling methods varied, with the majority of respondents noting that they sliced the tumours at 10 mm intervals and took one section for each centimetre of the maximum tumour diameter. In the case of multifocal tumours the majority of respondents noted that they sampled each tumour present.

All respondents reported that they take sections of normal renal parenchyma, while 80% of these sampled tissues far from the tumour, as well as normal tissues immediately adjacent to the tumour edge. Sections of renal pelvis tissue as well as grossly normal hilar vessels were almost always sampled. Although sections were taken from sinus fat that was grossly suspicious for tumour invasion in almost 100% of instances, there was variation in sampling protocols with the majority taking two to three sections from this area (figure 1A). The majority of respondents also reported that they sectioned sinus fat that appeared grossly normal and that they undertook complete sampling of the renal sinus margin. Almost all respondents noted that they sampled any macroscopically normal adrenal gland if this was with the renal specimen.

Fewer than 20% of respondents regularly inked renal surgical margins of radical nephrectomy specimens. The majority noted, however, that they would ink margins if they were grossly suspicious of tumour invasion, although 15% of respondents noted that they would never do so. The situation differed for partial nephrectomy specimens in which 81% of respondents reported that they always ink the renal surgical margin.

**Table 3** Cutting of nephrectomy specimens (capsule penetration, sections taken)

Question	%	Number
Method for searching for capsule penetration		
Fibrous capsule stripped to adherent area	24.1	39/162
Blunt dissection of adipose capsule	4.9	8/162
Perpendicular slicing into tumour	69.1	112/162
Other	1.9	3/162
No of slices cut through tumour		
1	0.6	1/163
2–4	16.0	26/163
>4	24.5	40/163
Every 10 mm	49.1	80/163
Other	9.8	16/163
No of tumour blocks taken from tumours >2 cm in diameter (combinations allowed)		
Only 1	0.0	0/163
Arbitrary but more than 1	21.5	35/163
Complete inclusion if <3	38.0	62/163
1 per cm of maximum diameter	61.3	100/163
Other	14.7	24/163
Sections from all tumours in cases of multifocal tumour		
Yes	96.9	158/163
No	1.8	3/163
Other	1.2	2/163
Sections of normal renal parenchyma taken		
Always. Usually far from tumour + edge of tumour	79.8	130/163
Always. Usually only far from tumour	14.7	24/163
Always. Usually only edge of tumour	5.5	9/163
Sometimes	0.0	0/163
Never	0.0	0/163
Sections of renal pelvis taken		
Yes	98.1	159/162
No	1.9	3/162
Sections of grossly normal hilar vessels		
Yes	96.3	156/162
No	3.7	6/162
Sections of grossly suspicious sinus fat?		
Yes, 1 section	27.5	44/160
Yes, 2–3 sections	55.6	89/160
Yes, >3 sections	16.3	26/160
No	0.6	1/160
Sections of grossly normal sinus fat?		
Yes	71.8	117/163
No	28.2	46/163
Systematic sections of renal sinus margin?		
Yes, usually complete sampling	68.7	112/163
Yes, a fixed proportion of margin	22.7	37/163
No	8.6	14/163
Sections of grossly normal adrenal when present?		
Yes	98.8	161/163
No	1.2	2/163

### Specimen reporting

The detailed results regarding specimen reporting are shown in tables 5–10.

All respondents noted that they measured the size of the tumour and in the majority of instances three separate dimensions were recorded. The majority of the respondents also measured the size of individual tumours in the case of multifocal neoplasia. Almost all respondents employed the WHO classification for assigning tumour type, although most of these would also utilise more recently described diagnostic tumour terminology.

The majority of respondents required more than the presence of epithelial cell elongation before rendering a diagnosis of

**Table 4** Cutting of nephrectomy specimens (margins, frozen sections)

Question	%	Number
Do you ink margins of radical nephrectomy specimens?		
Never	14.9	24/161
Only when suspicious	66.5	107/161
Always	18.6	30/161
Do you ink renal parenchyma margins of partial nephrectomy specimens?		
Always	81.1	129/159
Depends of gross distance to margin	17.0	27/159
Never	1.9	3/159
In what percentage do you receive frozen sections from partial nephrectomy specimens?		
Never	22.4	36/161
Very rarely (<5%)	37.9	61/161
5–10%	9.9	16/161
11–25%	4.3	7/161
26–50%	3.7	6/161
51–75%	3.7	6/161
76–100%	18.0	29/161
How do you handle intraoperative consultation regarding surgical margins from partial nephrectomy specimens?		
Macroscopic inspection sufficient	5.8	9/155
Microscopic section always done	56.1	87/155
Microscopic section done only if gross examination not convincing	16.1	25/155
Not applicable, intraoperative consultations not done	21.9	34/155

sarcomatoid carcinoma. For small papillary tumours most respondents followed the recommendations of the 2004 WHO classification, considering tumours less than 5 mm in diameter as benign. While few placed any significance on the degree of nuclear pleomorphism, almost all respondents subtyped papillary renal cell carcinoma as type 1 or type 2 (figure 1B,C), and a similarly high proportion noted that they report any papillary microadenomas found incidentally in nephrectomy specimens.

There was almost universal use of the Fuhrman grading system and most recognised necrosis in clear cell carcinoma to be of prognostic significance (figure 1D), although only a minority reported the percentage of necrosis in these tumours. Routine immunohistochemistry was used as an adjunct to histological typing only in some instances (figure 1E,F), while fluorescence in-situ hybridisation (FISH) and other ancillary studies were only rarely used for diagnostic purposes in difficult cases.

The majority of respondents utilised the current Union for International Cancer Control tumour–node–metastasis (TNM) staging criteria to assign a pT category to the tumour, although only one-third specified the edition of the TNM classification utilised in the report. Only a small number of the respondents noted that they stage oncocytoma.

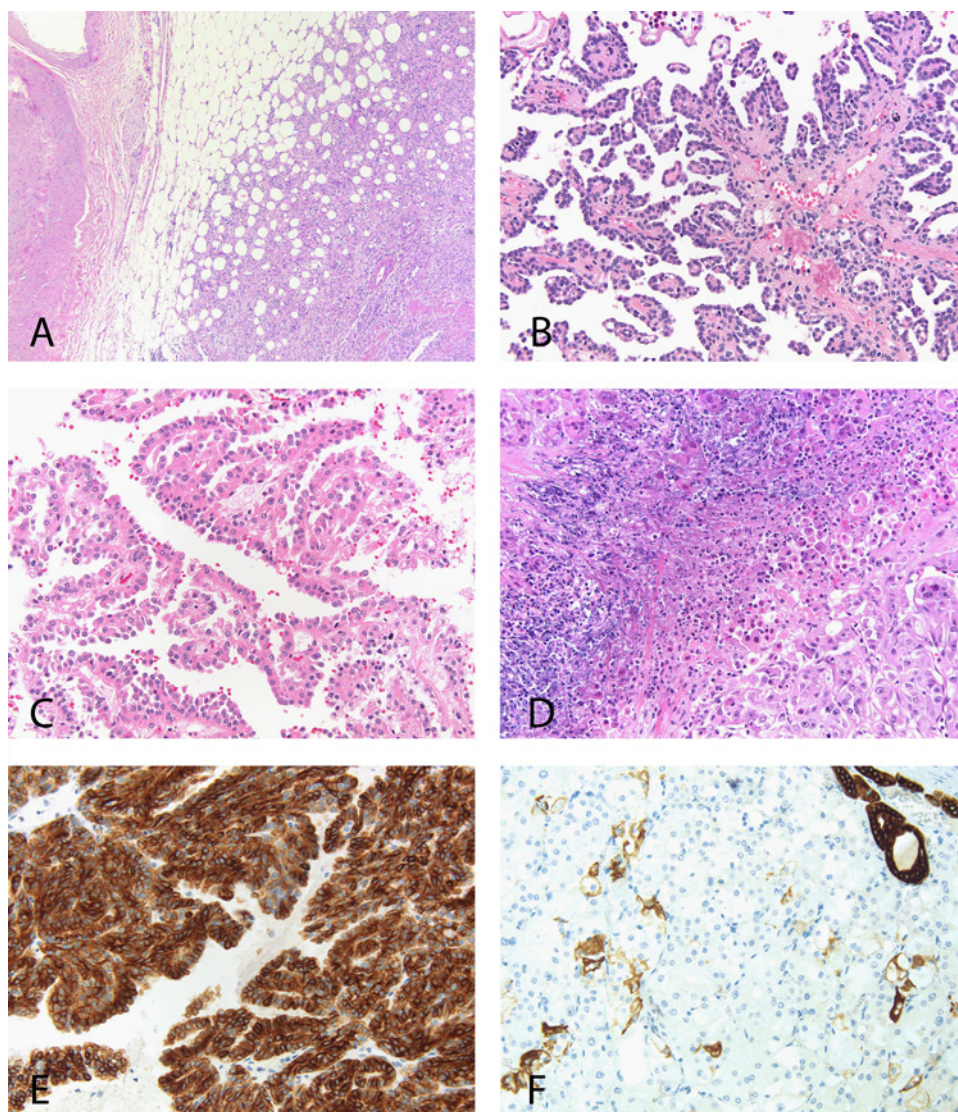
The definition of infiltration of perinephric or hilar fat varied, although the majority of the respondents preferred to consider this to be present only when tumour was in direct contact with adipose tissue. Most respondents noted that they reported the status of surgical margins. This latter parameter was considered more important in partial nephrectomy specimens in which almost 100% of respondents reported that they described the surgical margin status. Surprisingly, over a quarter of the respondents did not specifically look for disease in the adjacent non-tumoral kidney and only 50% stated they searched for premalignant lesions in apparently normal renal parenchyma.

### DISCUSSION

In this study we have investigated the habits of European specialist uropathologists for the reporting of neoplastic



**Figure 1** (A) Clear cell carcinoma with renal sinus invasion. Lens magnification 5×. (B) Papillary carcinoma type 1. Lens magnification 20×. (C) Papillary carcinoma type 2. Lens magnification 20×. (D) Clear cell carcinoma grade 4 with necrosis. Lens magnification 20×. (E) Papillary carcinoma with positive immunostaining for cytokeratin 7. Lens magnification 20×. (F) Oncocytoma with patchy cytokeratin 7 positivity. Lens magnification 20×.



nephrectomy specimens. As we have noted previously, studies of this nature often suffer from selection bias due to the over-representation of academic pathologists in the study cohort.<sup>12</sup> For this study; however, almost half of the respondents noted that their main practice was in a public general hospital, rather than in an academic institution. Furthermore, consensus recommendations should preferably be based on evidence rather than on the current practice of the majority of pathologists. Yet, it is useful to know which routines are already common so realistic recommendations can be issued in consensus documents. If the gap between guidelines and current practice becomes too wide, the credibility of the guidelines will decrease.

Interestingly, almost half of the respondents reported that they receive kidney specimens in the fresh state. Despite this, only 20% of tumours were routinely harvested of fresh tissue for research purposes. Lymphadenectomy specimens were rarely received and lymph nodes were detected in nephrectomy specimens only on rare occasions. This practice reflects that reported in the USA, where lymph nodes are rarely sampled and where lymphadenectomy is not generally performed.<sup>10 13</sup> It has been estimated that only 5% of radical nephrectomy specimens have lymph nodes detectable in adipose tissue, these being most frequently seen in hilar tissue surrounding major vessels.<sup>8 10 13</sup>

Most respondents did not routinely ink surgical margins of radical nephrectomy specimens, although this is recommended in some tumour protocols. This practice is not surprising as the completeness of excision is usually detectable on gross examination. For partial nephrectomy specimens over 80% reported that they did ink surgical margins, while a majority never or very rarely received intraoperative frozen sections in accordance with evidence-based recommended practice.<sup>14</sup>

Few guidelines exist regarding the extent of sampling of tumours and the respondents in the survey appear to sample widely, with a majority using the algorithm of one section per centimetre diameter of tumour.<sup>7</sup> Almost all respondents took sections from all tumours in cases of multifocal neoplasia. Recent evidence has shown that, especially in the setting of renal scarring, several different tumour morphotypes may coexist.<sup>15 16</sup> As the type of renal neoplasia is an important prognostic parameter it would seem prudent that all tumour foci be sampled.

Staging of renal cell carcinoma is recognised as the singularly most powerful prognostic indicator for these tumours and assessment of this necessitates careful examination by the reporting pathologist.<sup>17</sup> Tumour size and evidence of local invasion are integral to the assignment of a TNM staging category.

**Table 5** Reporting of tumour size

Question	%	Number
If you measure diameter(s) of tumour, do you measure?		
Largest diameter only on cut surface	28.2	46/163
2 Perpendicular diameters	20.2	33/163
3 Diameters (by adding thickness of slices)	49.7	81/163
Other	1.8	3/163
In multifocal tumours do you report tumour size of all foci?		
Yes	76.7	125/163
No, average or range given	1.2	2/163
Only for the biggest and average or range given for the others	20.2	33/163
Other	1.8	3/163

All respondents noted that they reported the greatest tumour diameter, while just under 50% of respondents reported that they measured the tumour in three dimensions. It has been noted that there is a discrepancy between the radiological size and diameter of tumours as reported from the gross specimen, which may show up to a 10% variance.<sup>18 19</sup> The reason for this discrepancy remains uncertain and highlights the need for consensus regarding the measurement of tumours in gross specimens. This may necessitate the development of a consistent measurement of tumour volume rather than the assessment of a single diameter.

Evidence of infiltration of tumour beyond the renal capsule or into the renal sinus is indicative of regional extension of tumour.<sup>20</sup> In a number of published protocols it is recommended that where tumour approaches close to the renal capsule, sections should include tumour, renal capsule and adjacent perirenal fat, so as to facilitate the identification of perirenal fat infiltration. Almost 70% of participants noted that, when searching for capsule penetration they took perpendicular slices into the tumour, although 30% of the respondents preferred to separate fat and underlying renal capsule/tumour, despite the fact that this may obliterate evidence of early extension into pericapsular adipose tissue.

**Table 6** Grading and staging of renal cell tumours

Question	%	Number
Do you use the WHO 2004 classification for tumour type?		
Yes	99.4	161/162
No	0.6	1/162
Which grading system do you use?		
Fuhrman	95.7	155/162
Mayo	0.0	0/162
Arbitrary system	0.6	1/162
Other	3.7	6/162
Do you report the UICC T category of TNM staging?		
Yes, using the current edition	76.7	122/159
Yes, using earlier editions	1.9	3/159
Yes, other TNM	11.9	19/159
No, using another staging system	1.3	2/159
Stage not included in report	8.2	13/159
Do you specify edition of the TNM classification?		
Yes	34.4	56/163
No	60.1	98/163
Not applicable, stage not included in report	5.5	9/163
Do you stage oncocytoma?		
Yes	6.3	10/160
No	93.8	150/160

TNM, tumour—node—metastasis; UIPP, Union for International Cancer Control.

**Table 7** Reporting of other features of renal tumours

Question	%	Number
Do you report necrosis in clear cell RCC?		
Yes	90.2	147/163
No	9.8	16/163
Do you report percentage of necrosis in the tumour?		
Yes	23.6	35/148
No	60.8	90/148
Other assessment of amount of necrosis	15.5	23/148
Do you describe status of benign renal parenchyma		
Yes	81.0	132/163
No	19.0	31/163
Do you describe status surgical margin status in total nephrectomy specimens?		
Always	70.4	114/162
Only if tumour close to margin	22.8	37/162
Rarely	6.8	11/162
Do you describe status surgical margin status in partial nephrectomy specimens?		
Always	97.5	155/159
Only if tumour close to margin	0.6	1/159
Other	1.9	3/159

RCC, renal cell carcinoma.

There was some variability in the definitions employed by respondents to define extrarenal extension of tumour. One-third accepted spread of tumour beyond the renal surface as evidence of invasion, while two-thirds required tumour to be in direct contact with perirenal fat. In published reporting protocols the infiltration of adipose disease is considered diagnostic of extrarenal spread,<sup>8 10</sup> while the TNM classification simply requires direct invasion of perirenal tissues for staging category pT3a.<sup>20</sup> In view of this dichotomy there is clearly a need for the development of an evidenced-based consensus on the defining features of extrarenal spread.

It is well recognised that infiltration of the renal sinus is underrecognised, especially in tumour series collected before 2004, when the importance of renal sinus infiltration was first reported.<sup>21</sup> Renal sinus infiltration is an important prognostic factor, with incorporation of this feature into the TNM

**Table 8** Ancillary techniques use for reporting of renal tumours

Question	%	Number
Is immunohistochemistry used for histological typing?		
Always	6.7	11/163
Only in some cases	92.0	150/163
Never	1.2	2/163
Do you use any of these stains for typing of renal tumours?		
CD10	92.6	150/162
RCC-Ma (RCC)	30.9	50/162
CK7	95.1	154/162
HMW cytokeratin	52.5	85/162
Vimentin	85.8	139/162
AMACR	57.4	93/162
c-kit (CD117)	61.1	99/162
TFE3	17.3	28/162
HMB45	67.9	110/162
Hale's colloidal iron	52.5	85/162
Other	25.3	41/162
Do you use FISH or other ancillary techniques than immunohistochemistry for diagnosis in difficult cases?		
Yes	17.8	29/163
No	82.2	134/163

FISH, fluorescence in-situ hybridisation; RCC, renal cell carcinoma.



**Table 9** Classification of renal tumours

Question	%	Number
If you would find new entities not included in the WHO 2004 classification, would you report them by their proposed names?		
Yes	80.7	130/161
No, would report as unclassified	19.3	31/161
Do you consider a tumour sarcomatoid if:		
It has a spindle cell pattern	50.9	81/159
It is very atypical and looks like any type of sarcoma	49.1	78/159
Do you recognise early sarcomatoid change (elongation of epithelial cells) as sarcomatoid carcinoma?		
Yes	28.8	45/156
No	71.2	111/156
How are sarcomatoid carcinomas reported?		
Unclassified carcinoma	0.0	0/160
Unclassified carcinoma but mention sarcomatoid component	10.0	16/160
If evidence of another histological type, this type is diagnosed with sarcomatoid transformation	90.0	144/160
Are small papillary tumours		
Considered malignant if diameter >2 mm	3.8	6/159
Considered malignant if diameter >5 mm	55.3	88/159
Considered malignant if diameter >10 mm	5.7	9/159
Only if nuclear grade sufficiently high	9.4	15/159
Called papillary tumour with size reported	25.8	41/159
Do you report papillary microadenomas incidentally found in nephrectomy specimens?		
Yes	96.3	157/163
No	3.7	6/163
Do you subtype papillary RCC as type I or II?		
Yes	86.5	141/163
No	13.5	22/163

RCC, renal cell carcinoma.

classification as category pT3a. Despite this, only two-thirds of respondents reported that they undertook complete sampling of the renal sinus margin, while slightly over 70% took sections from grossly normal renal sinus adipose tissue. Almost all respondents reported that they took sections from apparently abnormal renal sinus fat, although in 20% of cases this was limited to one tissue slice and in more than 80% of cases this was limited to a maximum of three sections. There is good evidence to suggest that there is an association between tumour size and the presence of renal sinus invasion,<sup>22–24</sup> especially for clear cell renal cell carcinomas and as such it would seem more

**Table 10** Reporting of other features of nephrectomy specimens

Question	%	Number
When do you consider renal perinephric or hilar fat tissue invasion present?		
Only when direct contact with adipose tissue	66.0	107/162
If cancer extends sufficiently beyond renal surface	34.0	55/162
Do you study invasion into renal sinus fat/vessels?		
Yes	98.8	160/162
No	1.2	2/162
Do you look for microscopic lymphovascular involvement?		
Yes	96.9	157/162
No	3.1	5/162
Do you look for premalignant lesions in the renal parenchyma?		
Yes	58.6	95/162
No	41.4	67/162
Do you look for glomerular/tubular (nephrology) lesions in the non-tumoral kidney?		
Yes	74.5	120/161
No	25.5	41/161

logical that pT2 tumours defined according to the current TNM classification be re-assigned as pT3a. For the present it would seem reasonable to suggest that extensive sampling of the renal sinus be recommended and that a standardised approach to this be adopted, especially for those tumours that are either situated in the central portion of the kidney or are greater than 5 cm in maximum extent.

Over 90% of genitourinary pathologists circulated in the survey reported that they included a comment regarding the stage of the tumour in their report. Well over three-quarters of respondents did so utilising the latest edition of the TNM classification. Somewhat surprisingly, only one-third of respondents; however, reported that they specified which edition of the classification was used. This is of some significance as small but important changes have been made to the defining features of renal tumour staging in the various editions of the UICC TNM classification.<sup>17–20</sup> As a consequence, the prognostic significance of tumour staging is somewhat negated if the clinician is unaware of the criteria the pathologist has employed in assigning a pT category to the specimen. Of interest, 6.3% reported that they staged oncocytomas, despite the fact that these are universally recognised as benign tumours.

Most respondents reported that they employed the 2004 WHO renal tumour classification. They also appeared to be willing to embrace newly identified entities, preferring to abandon the recommendation in the WHO classification that novel tumours be classified as renal cell carcinoma.<sup>25</sup> Although the classification of the tumours in the WHO classification is based upon morphological criteria, virtually all participants utilised immunohistochemical staining, at least occasionally. Despite the evidence that FISH is an important diagnostic adjunct for some renal tumours,<sup>26–27</sup> this was rarely employed.

There was considerable divergence noted in the survey in the reporting of small papillary tumours, with only slightly over half of respondents following the 2004 WHO recommendations.<sup>25</sup> A quarter of respondents preferred to use the term 'papillary tumour' for small papillary neoplasms, which has the potential to create uncertainty with respect to subsequent patient management. There is considerable evidence to indicate that papillary adenomas, as defined in the 2004 WHO classification, follow a benign clinical course, and in view of the frequency that these lesions are detected in routine practice,<sup>28–29</sup> it would seem alarmist that they were classified as anything but benign. There was strong support for dividing papillary renal cell carcinomas according to morphotype.<sup>30</sup>

Numerous prognostic parameters have been proposed for the main types of renal cell carcinoma, however, few of these are applied in routine clinical practice.

Most respondents recognised tumour grade, sarcomatoid differentiation, the presence of tumour necrosis and lymphovascular infiltration to be prognostic markers worthy of reporting. Despite the problems associated with the validity and application of the Fuhrman grading classification,<sup>17–31–35</sup> it is clear from the survey that it remains in almost universal usage. Almost all participants in the survey recognised the prognostic importance of sarcomatoid differentiation, with 90% following the recommendations of the 2004 WHO classification and diagnosing this in the context of the parent tumour type. Although almost 30% of respondents considered early sarcomatoid change (elongation of epithelial cells) as diagnostic of sarcomatoid carcinoma, this is specifically excluded in studies on sarcomatoid carcinoma.<sup>34</sup> Furthermore, it has been shown that cells showing early sarcomatoid change express collagen

## Take-home messages

A survey among urological pathologists in 15 European countries on handling and reporting of renal tumour specimens shows that there is a general compliance with current guidelines and classifications, but in some areas there is considerable variation in practice. There is an awareness that for correct staging, there is a need to sample the renal sinus fat, but there is a variation in how this is done and the interpretation of microscopic evidence of perinephric or hilar fat infiltration. Similarly, the diameter of the tumour must be reported but methods for measurement vary widely which may affect stage assignment. The Fuhrman system is almost universally used for grading of renal cancer. The 2004 WHO Classification is generally used for assignment of tumour type, but most pathologists would also report more recently described tumour entities.

types that differ from those of typical sarcomatoid carcinoma cells.<sup>35</sup>

The presence of coagulative necrosis of tumour cells has been shown to be of prognostic significance, especially for clear cell and chromophobe renal cell carcinoma.<sup>36–38</sup> Not surprisingly, relatively few pathologists reported that they quantified the amount of necrosis, presumably due to difficulties in assessing this, but also because the amount of necrosis present does not appear to have prognostic significance.<sup>39</sup>

In a series of T1 and T2 tumours intrarenal microvascular invasion has been shown to be of prognostic significance independent of pT category, grade and perineural fat invasion.<sup>40</sup> Despite this, lymphovascular invasion is not a feature of UICC TNM staging, although it was widely recognised to be an important prognostic parameter by participants in the survey.

Over half of the respondents noted that they searched for premalignant lesions within the non-neoplastic kidney. While small papillary tumours are frequently seen, other potentially premalignant lesions are less common in the setting of sporadic rather than familial neoplasia.<sup>41</sup> Several morphotypes of renal cell carcinoma have been associated with acquired cystic renal disease and all solid areas in these kidneys should be sampled.<sup>42</sup>

Finally three-quarters of respondents reported that they excluded non-neoplastic pathology within the kidney. It has been noted that coincidental non-neoplastic pathology is present in over 16% of kidneys, with diabetic nephropathy predominating.<sup>43</sup> Hypertensive nephropathy, IgA nephropathy, focal segmental glomerulosclerosis, thrombotic microangiopathy and amyloidosis are less frequently encountered.<sup>44</sup> This may have significant prognostic consequences and as such it is recommended that all kidneys should be appropriately sampled and examined to exclude coexisting pathology.

In summary, this study has shown that European pathologists closely follow international guidelines for the sampling and reporting of renal tumours and that the majority of discrepancies arise in areas where guidelines are unclear. In view of this it would appear that it is now timely to update and expand consensus on the evaluation and reporting of adult renal carcinomas.

**Acknowledgements** The authors would like to thank those ENUP members who participated in the survey for their support.

**Competing interests** None.

**Provenance and peer review** Not commissioned; externally peer reviewed.

## REFERENCES

1. **Mostofi FK**, Sesterhenn IH, Sobin LH, *et al*. *Histological Typing of Kidney Tumours. International Histological Classification of Tumours No. 25*. Geneva: World Health Organization, 1981;26.
2. **Srigley JR**, Delahunt B. Uncommon and recently described renal carcinomas. *Mod Pathol* 2009;**22**:S2–23.
3. **Allory Y**, Culine S, de la Taille A. Kidney cancer pathology in the new context of targeted therapy. *Pathobiology* 2011;**78**:90–8.
4. **Delahunt B**, Bethwaite PB, Nacey JN. Outcome prediction for renal cell carcinoma: evaluation of prognostic factors for tumours divided according to histological subtype. *Pathology* 2007;**39**:4549–65. Suppl 2:S2–S23.
5. **Eble JN**. Recommendations for examining and reporting tumor-bearing kidney specimens from adults. *Semin Diagn Pathol* 1998;**15**:77–82. Suppl 2:S24–36.
6. **Algaba F**, Trias I, Scarpelli M, *et al*. Handling and pathology reporting of renal tumor specimens. *Eur Urol* 2004;**45**:437–43.
7. **Che M**, Grignon DJ. Handling and reporting of tumor-containing kidney specimens. *Clin Lab Med* 2005;**25**:417–32.
8. **Higgins JP**, McKenney JK, Brooks JD, *et al*. Recommendations for the reporting of surgically resected specimens of renal cell carcinoma. The Association of Directors of Anatomic and Surgical Pathology. *Hum Pathol* 2009;**40**:456–63.
9. **Delahunt B**, Charles A, Clouston D, *et al*. *Renal Parenchymal Malignancy (renal cell carcinoma). Structured Reporting Protocol*. Sydney: Royal College of Pathologists of Australasia, 2010;51.
10. **Srigley JR**, Amin MB, Delahunt B, *et al*. Protocol for the examination of specimens from patients with invasive carcinoma of renal tubular origin. *Arch Pathol Lab Med* 2010;**134**:e25–30.
11. **Egevad L**, Algaba F, Berney DM, *et al*; The European Network of Uropathology. A novel mechanism for communication between pathologists. *Anal Quant Cytol Histol* 2009;**31**:90–5.
12. **Egevad L**, Algaba F, Berney DM, *et al*. Handling and reporting of radical prostatectomy specimens in Europe: a web-based survey by the European Network of Uropathology (ENUP). *Histopathology* 2008;**53**:333–9.
13. **Dimashkieh HH**, Lohse CM, Blute ML, *et al*. Extranodal extension in regional lymph nodes is associated with outcome in patients with renal cell carcinoma. *J Urol* 2006;**176**:1978–82.
14. **Algaba F**, Arce Y, López-Beltrán A, *et al*; European Society of Uropathology; Uropathology Working Group. Intraoperative frozen section diagnosis in urological oncology. *Eur Urol* 2005;**47**:129–36.
15. **Boorjian SA**, Crispen PL, Lohse CM, *et al*. The impact of temporal presentation on clinical and pathological outcomes for patients with sporadic bilateral renal masses. *Eur Urol* 2008;**54**:855–63.
16. **Brennan C**, Srigley JR, Wheelan C, *et al*. Type 2 and clear cell papillary renal cell carcinoma, and tubulocystic carcinoma. A unifying concept. *Anticancer Res* 2010;**30**:641–4.
17. **Delahunt B**. Advances and controversies in the grading and staging of renal cell carcinoma. *Mod Pathol* 2009;**22**:S24–36.
18. **Jeffery NN**, Douek N, Guo DY, *et al*. Discrepancy between radiological and pathological size of renal masses. *BMC Urol* 2011;**11**:2.
19. **Kanofsky J**, Phillips C, Stifelman M, *et al*. Impact of discordant radiologic and pathologic tumour size on renal cancer staging. *Urology* 2006;**68**:728–31.
20. **Sobin LH**, Gospodarowicz M, Wittekind Ch, eds. *International Union Against Cancer. TNM Classification of Malignant Tumours*, 7th edn. New York, NY: Wiley-Liss, 2009.
21. **Bonsib SM**. The renal sinus is the principal invasive pathway: a prospective study of 100 renal cell carcinomas. *Am J Surg Pathol* 2004;**28**:1594–600.
22. **Bonsib SM**. T2 clear cell renal cell carcinoma is a rare entity: a study of 120 clear cell renal cell carcinoma. *J Urol* 2005;**174**:1199–202.
23. **Bonsib SM**. Renal lymphatic and lymphatic involvement in sinus vein invasive (pT3b) clear cell renal cell carcinoma. A study of 40 cases. *Mod Pathol* 2006;**19**:746–53.
24. **Bonsib SM**. Renal vein and venous extension in clear cell renal cell carcinoma. *Mod Pathol* 2007;**20**:944–53.
25. **Eble JN**, Sauter G, Epstein JI, *et al*, eds. *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs*. Lyon: IARC Press, 2004.
26. **Brunelli M**, Delahunt B, Gobbo S, *et al*. Diagnostic usefulness of fluorescent cytogenetics in differentiating chromophobe renal cell carcinoma from renal oncocytoma. A validation study combining metaphase and interphase analyses. *Am J Clin Pathol* 2010;**133**:116–26.
27. **Brunelli M**, Fiorentino M, Gobbo S, *et al*. Many facets of chromosome 3p cytogenetic findings in clear cell renal carcinoma: the need for agreement in assessment FISH analysis to avoid diagnostic errors. *Histol Histopathol* 2011;**26**:1207–13.
28. **Delahunt B**, Eble JN. Papillary adenoma of the kidney an evolving concept. *J Urol Pathol* 1997;**7**:99–112.
29. **Algaba F**. Renal adenomas: pathological differential diagnosis with malignant tumours. *Adv Urol* 2008;**97**:4848.
30. **Delahunt B**, Eble JN. Papillary renal cell carcinoma: a clinicopathologic and immunohistochemical study of 105 tumors. *Mod Pathol* 1997;**10**:537–44.
31. **Sika-Paotonu D**, Bethwaite PB, McCredie MR, *et al*. Nucleolar grade but not Fuhrman grade is applicable to papillary renal cell carcinoma. *Am J Surg Pathol* 2006;**30**:1091–6.
32. **Delahunt B**, Sika-Paotonu D, Bethwaite PB, *et al*. Fuhrman grading is not appropriate for chromophobe renal cell carcinoma. *Am J Surg Pathol* 2007;**31**:957–60.

33. **Delahunt B**, Sika-Paotonu D, Bethwaite PB, *et al.* Grading of clear cell renal cell carcinoma should be based on nucleolar prominence. *Am J Surg Pathol* 2011;**35**:1134–9.
34. **de Peralta-Venturina M**, Moch H, Amin M, *et al.* Sarcomatoid differentiation in renal cell carcinoma. A study of 101 cases. *Am J Surg Pathol* 2001;**25**:275–84.
35. **Delahunt B**, Bethwaite PB, McCredie MR, *et al.* The evolution of collagen expression in sarcomatoid renal cell carcinoma. *Hum Pathol* 2007;**38**:1372–7.
36. **Cheville JC**, Lohse CM, Zinke BS, *et al.* Comparison of outcome and prognostic features among histologic subtypes of renal cell carcinoma. *Am J Surg Pathol* 2003;**27**:612–24.
37. **Kim H**, Cho NH, Kim D, *et al.* Renal cell carcinoma in South Korea: a multicenter study. *Hum Pathol* 2004;**35**:1556–63.
38. **Moch T**, Gasser T, Amin MB, *et al.* Prognostic utility of the recently recommended histologic classification and revised TNM staging system of renal cell carcinoma. A Swiss experience with 588 tumors. *Cancer* 2000;**89**:604–14.
39. **Algaba F**. Is tumor necrosis a predictor of survival in patients with renal cell carcinoma? *Nat Clin Pract Urol* 2006;**3**:196–7.
40. **Madbouly K**, Al-Qahtani SM, Ghazwani Y, *et al.* Microvascular tumour invasion: prognostic significance in low stage renal cell carcinoma. *Urology* 2007;**69**:670–4.
41. **Van Poppel H**, Nilsson S, Algaba F, *et al.* Precancerous lesions in the kidney. *Scand J Urol Nephrol Suppl.* 2000;**205**:136–65.
42. **Fleming S**. Renal cell carcinoma in acquired cystic kidney disease. *Histopathology* 2010;**56**:395–400.
43. **Henriksen KJ**, Meehan SM, Chang A. Non-neoplastic renal diseases are often unrecognized in adult tumor nephrectomy specimens: a review of 246 cases. *Am J Surg Pathol* 2007;**31**:1703–8.
44. **Henriksen KJ**, Meehan SM, Chang A. Nonneoplastic kidney diseases in adult tumor nephrectomy and nephroureterectomy specimens: common, harmful, yet underappreciated. *Arch Pathol Lab Med* 2009;**133**:1012–25.

Journal of  
**CLINICAL  
PATHOLOGY**

# SAVE TIME AND KEEP INFORMED SCAN. SIGN UP. eTOC.



## WHY SIGN UP?

A quick and simple way to keep updated with developments in your speciality

Utilise our Quick Response code (QR) to sign up for our electronic table of contents (eTOC) alert.

To make this simple you can sign up now via your Smartphone.

### FOLLOW THESE THREE EASY STEPS:

1. Download a free QR reader from your handset's app store
  2. Hold your Smartphone over the QR code
  3. You will then be forwarded to the eTOC sign up page
- To find out more about QR codes visit [group.bmj.com/products/journals/qr-codes](http://group.bmj.com/products/journals/qr-codes)



[jcp.bmj.com](http://jcp.bmj.com)

BMJ Journals