Challenges in Pathologic Staging of Renal Cell Carcinoma

A Study of Interobserver Variability Among Urologic Pathologists

汇 报 人： 魏 洁
指导教授： 张 静

Sean R. Williamson, MD. Am J Surg Pathol . Volume 42, Number 9, September 2018

原发性肾癌的AJCCpTNM分期

原发肿瘤（T）

Tx：原发肿瘤无法评估

T0：无原发肿瘤

T1：肿瘤仅限于肾内，最大直径≤7cm

T1a：肿瘤直径≤4cm

T1b：肿瘤直径4~7cm

T2：肿瘤仅限于肾内，最大直径＞7cm

T2a：肿瘤局限在肾内，最大直径＞7cm，但≤10cm

T2b：局限在肾内，最大直径＞10cm

T3：肿瘤侵及主要静脉，或肾周组织，但未侵及同侧肾上腺且未超越肾筋膜（Gerota’s筋膜）

T3a：肿瘤侵及肾静脉或其分支，或肾盂肾盏系统，或肾周和/或肾窦脂肪，但未突破肾筋膜

T3b：肿瘤侵及横膈以下下腔静脉

Am J Surg Pathol. 2013 Oct;37(10):1505-17. doi: 10.1097/PAS.0b013e31829a85d0.

Handling and staging of renal cell carcinoma: the International Society of Urological Pathology Consensus (ISUP) conference recommendations.

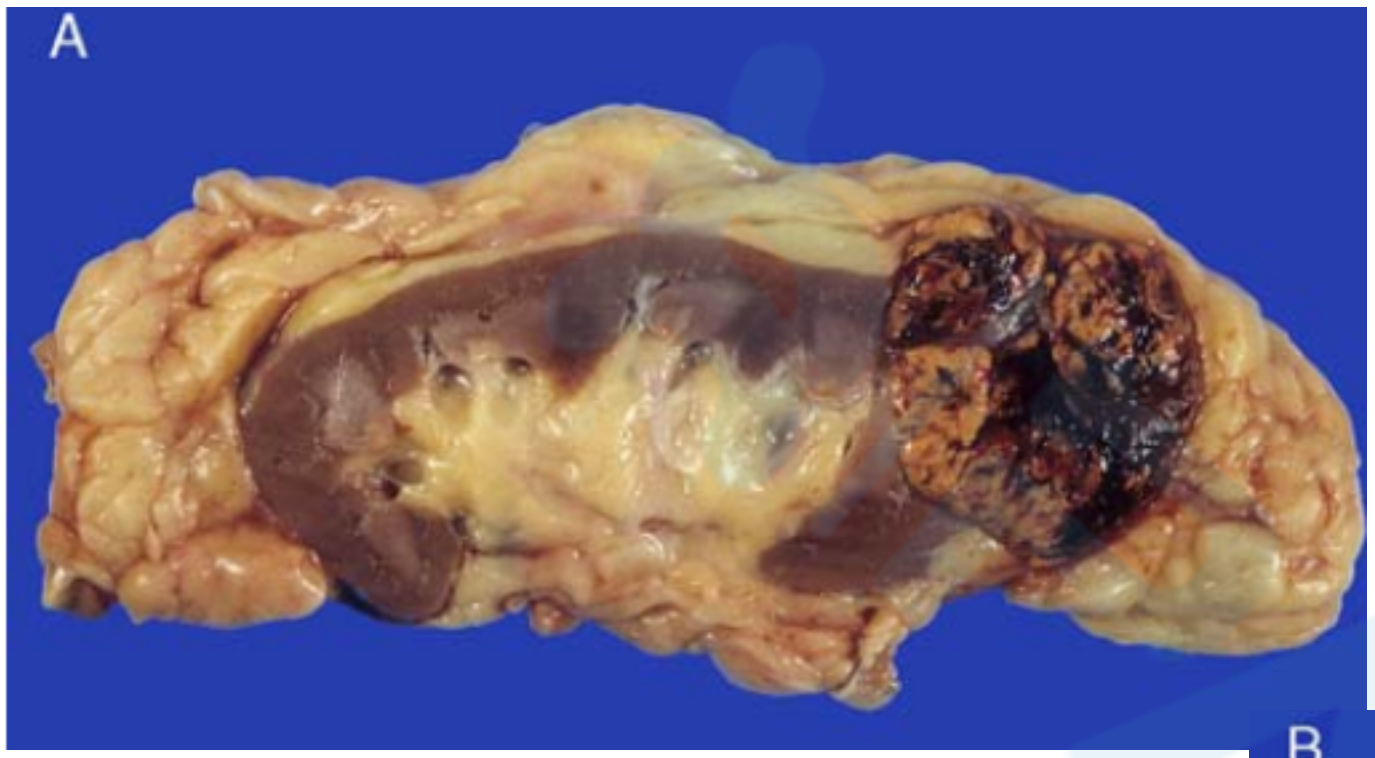
Trpkov K[1], Grignon DJ, Bonsib SM, Amin MB, Billis A, Lopez-Beltran A, Samaratunga H, Tamboli P, Delahunt B, Egevad L, Montironi R, Srigley JR; members of the ISUP Renal Tumor Panel.

Mx：远处转移无法评估

M0：无远处转移

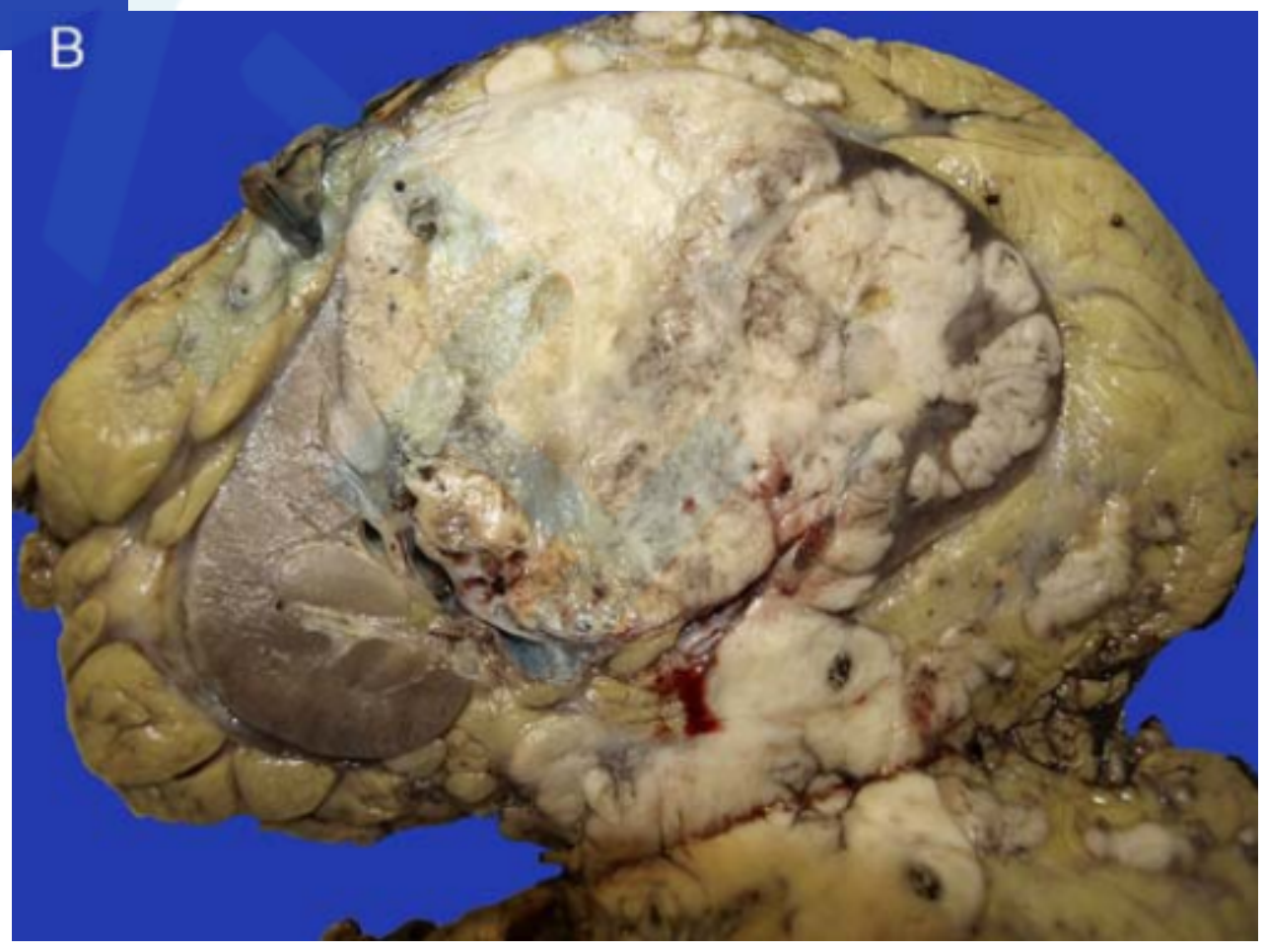
M1：远处转移

FAT INVASION

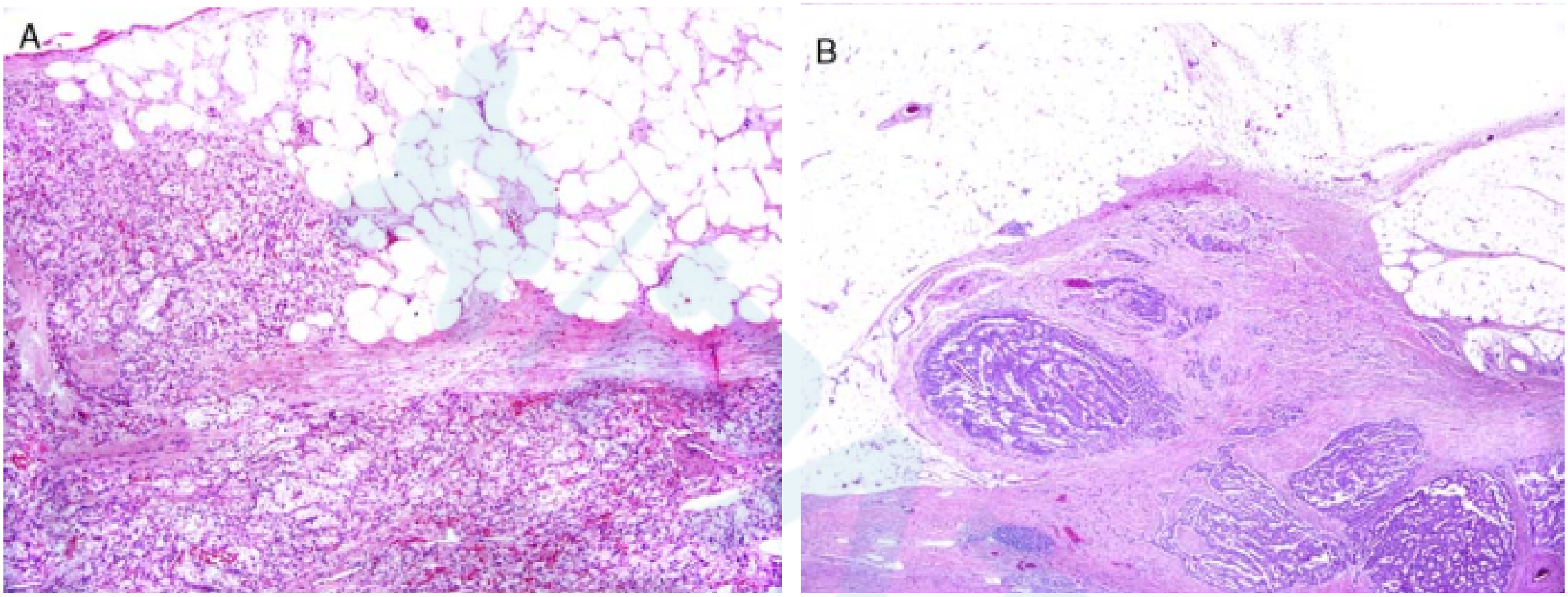


A, Presence of a circumscribed, pushing tumor border, even if extending well beyond the normal outline of the renal cortex, is not diagnostic of perinephric fat invasion.

B, Penetration of the renal capsule and infiltration into the perinephric fat can sometimes be established grossly when the tumor loses its rounded and smooth interface with the capsule and the perinephric fat or when visible as nodules or irregular tumor masses protruding within the perinephric fat.

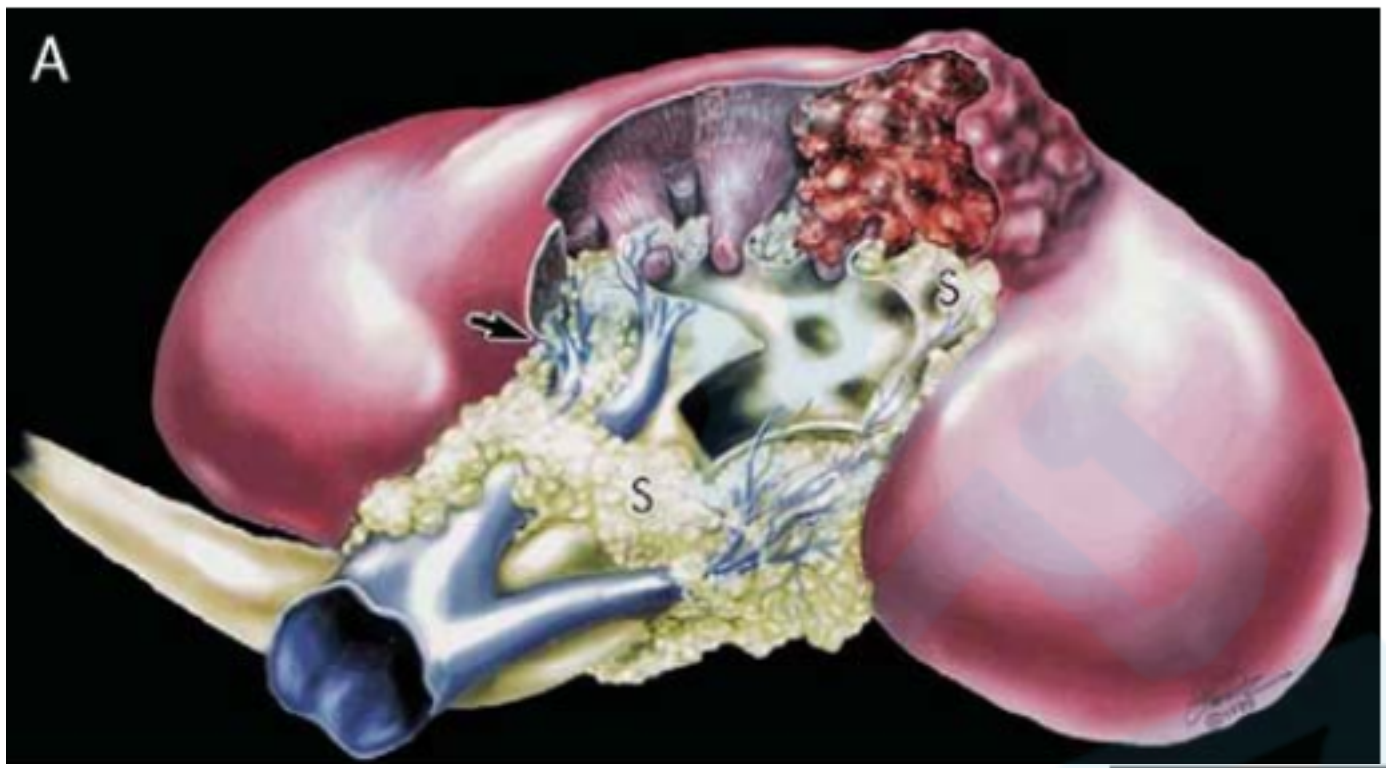


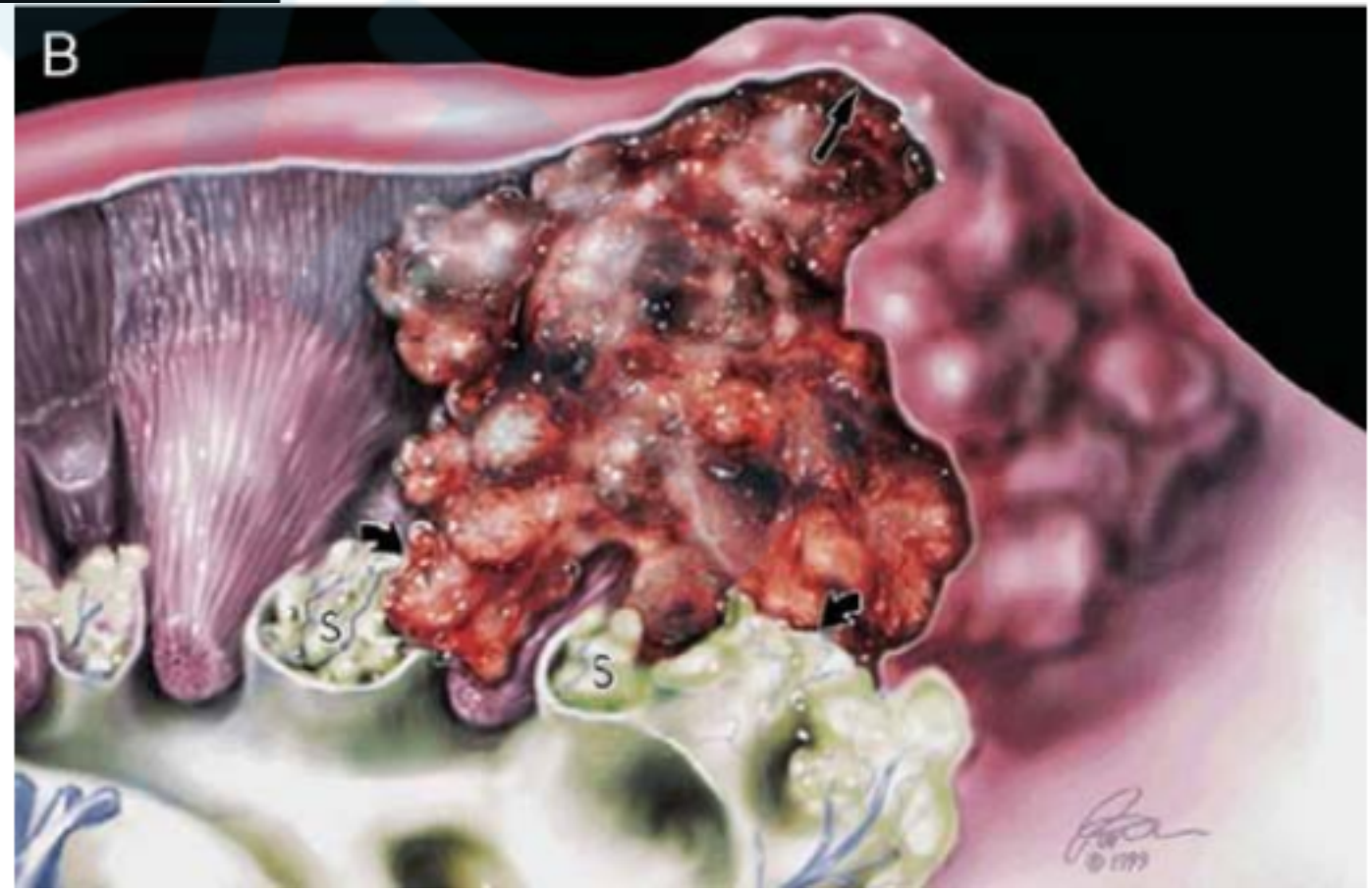
FAT INVASION



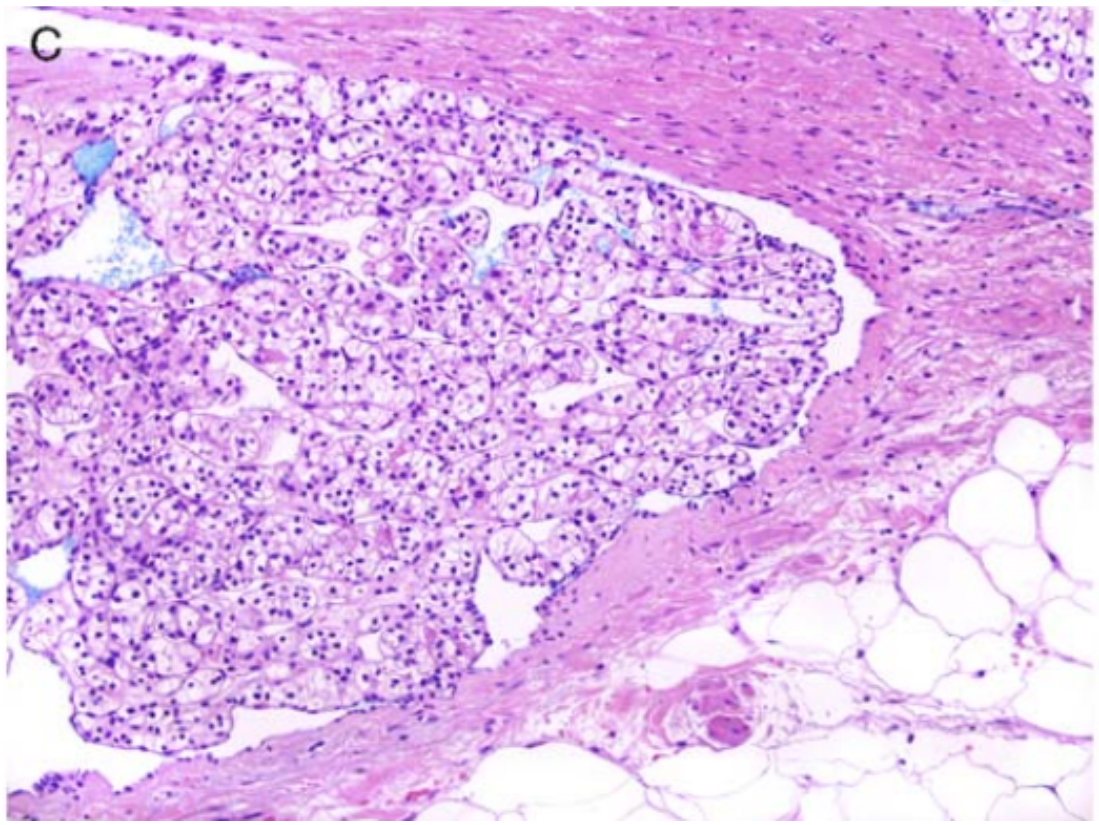
The most significant histologic findings required to establish perinephric fat invasion are the tumor either touching the fat (A) or extending as irregular tongues into the perinephric tissue (with or without desmoplasia) (B).

SINUS INVASION



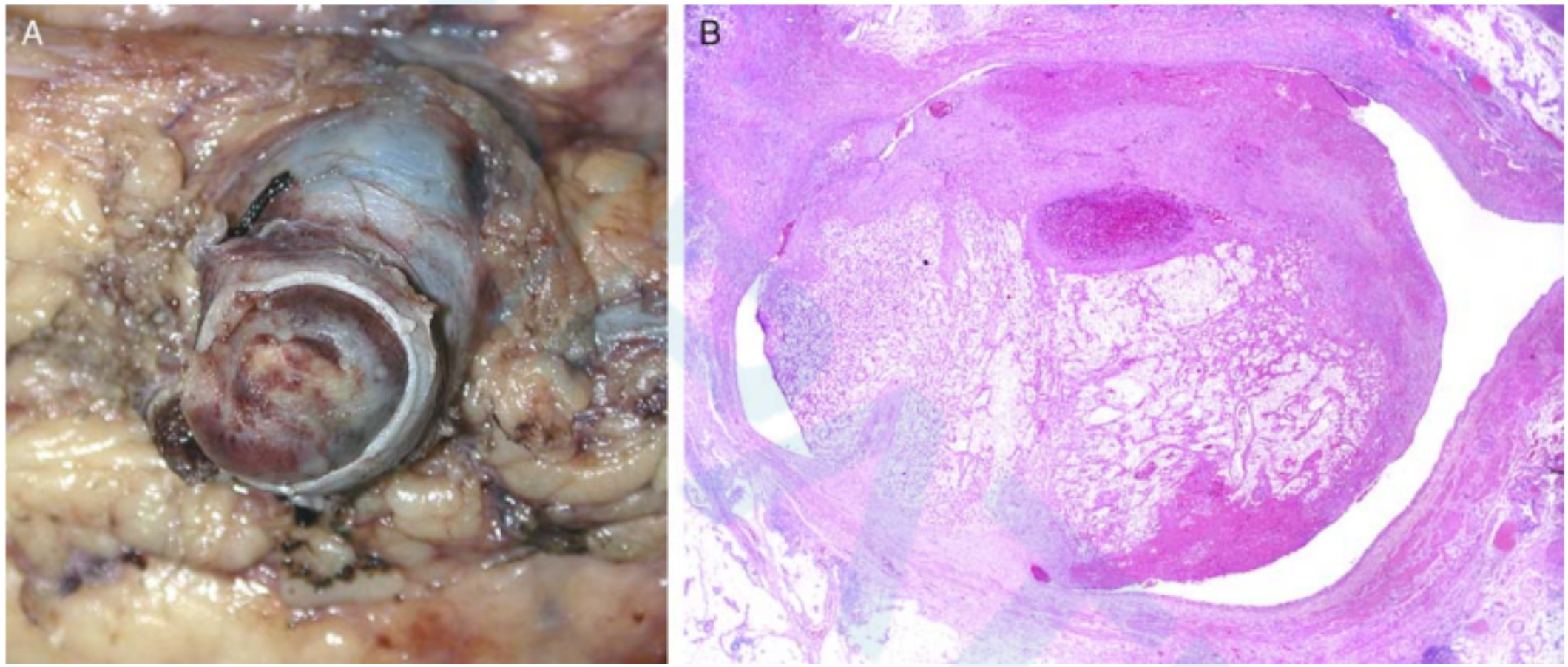


SINUS INVASION



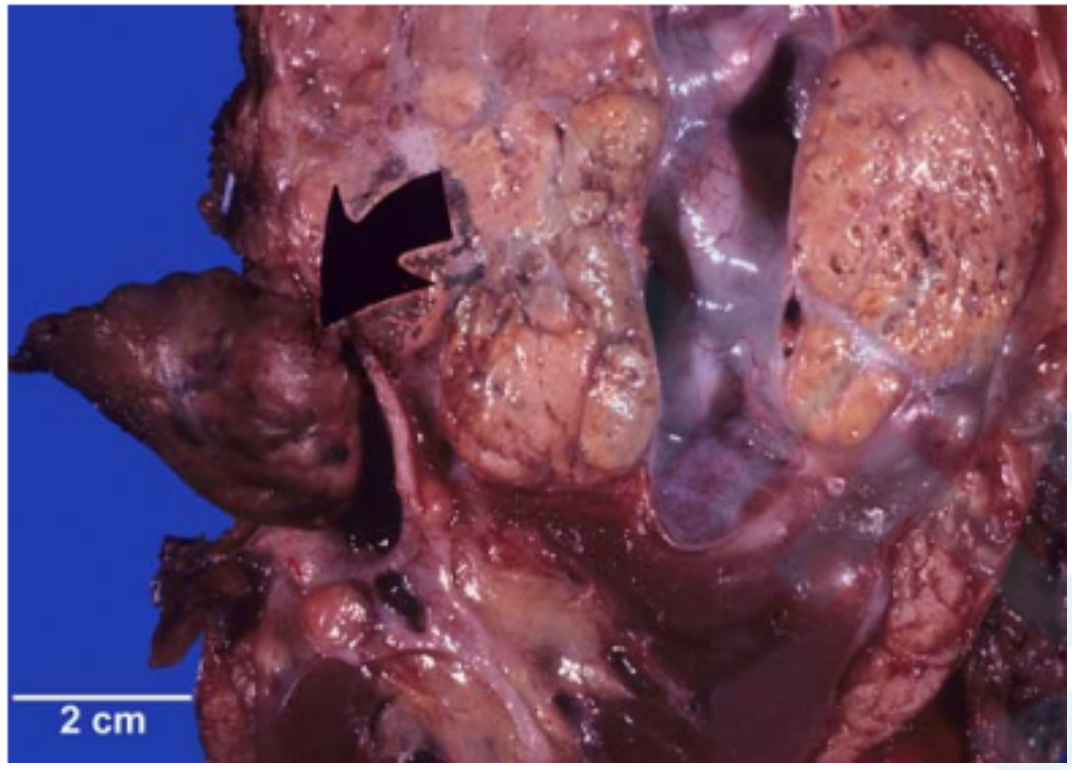
Renal sinus invasion can be established when the tumor is in direct contact with the sinus fat (A) or in the loose connective tissue clearly beyond the renal parenchyma (B). C, In addition, it was agreed upon that involvement of any endothelium-lined spaces within the renal sinus, regardless of the size, should also be considered renal sinus invasion (pT3a).

RENAL VEIN INVASION

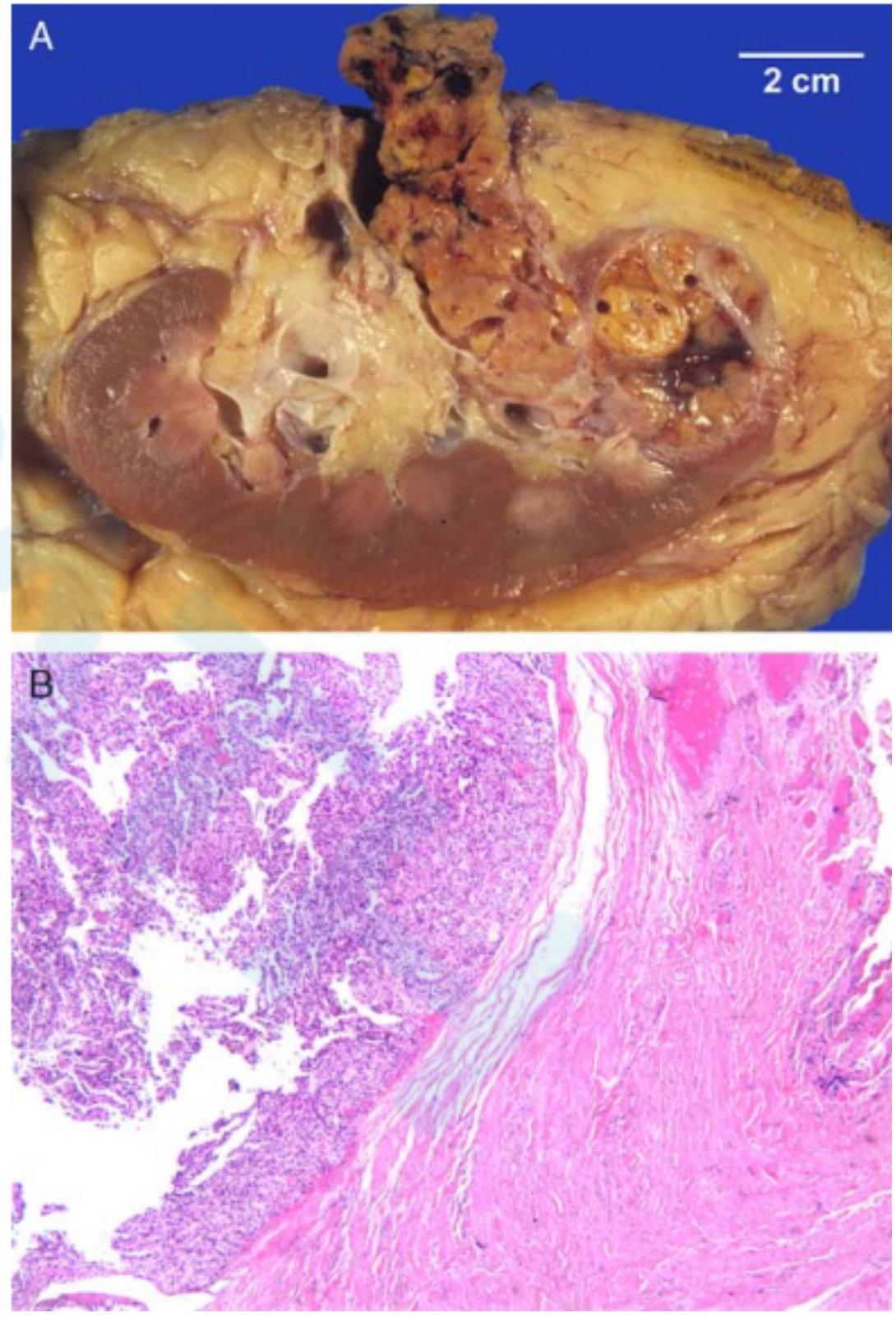


A, Renal vein invasion (pT3a) is when the tumor grossly extends into the renal vein or its segmental (musclecontaining) branches. B, In sections taken from the renal sinus, it is not uncommon to identify the tumor within musclecontaining branches of the renal vein that was not documented on gross examination.

RENAL VEIN MARGIN POSITIVITY



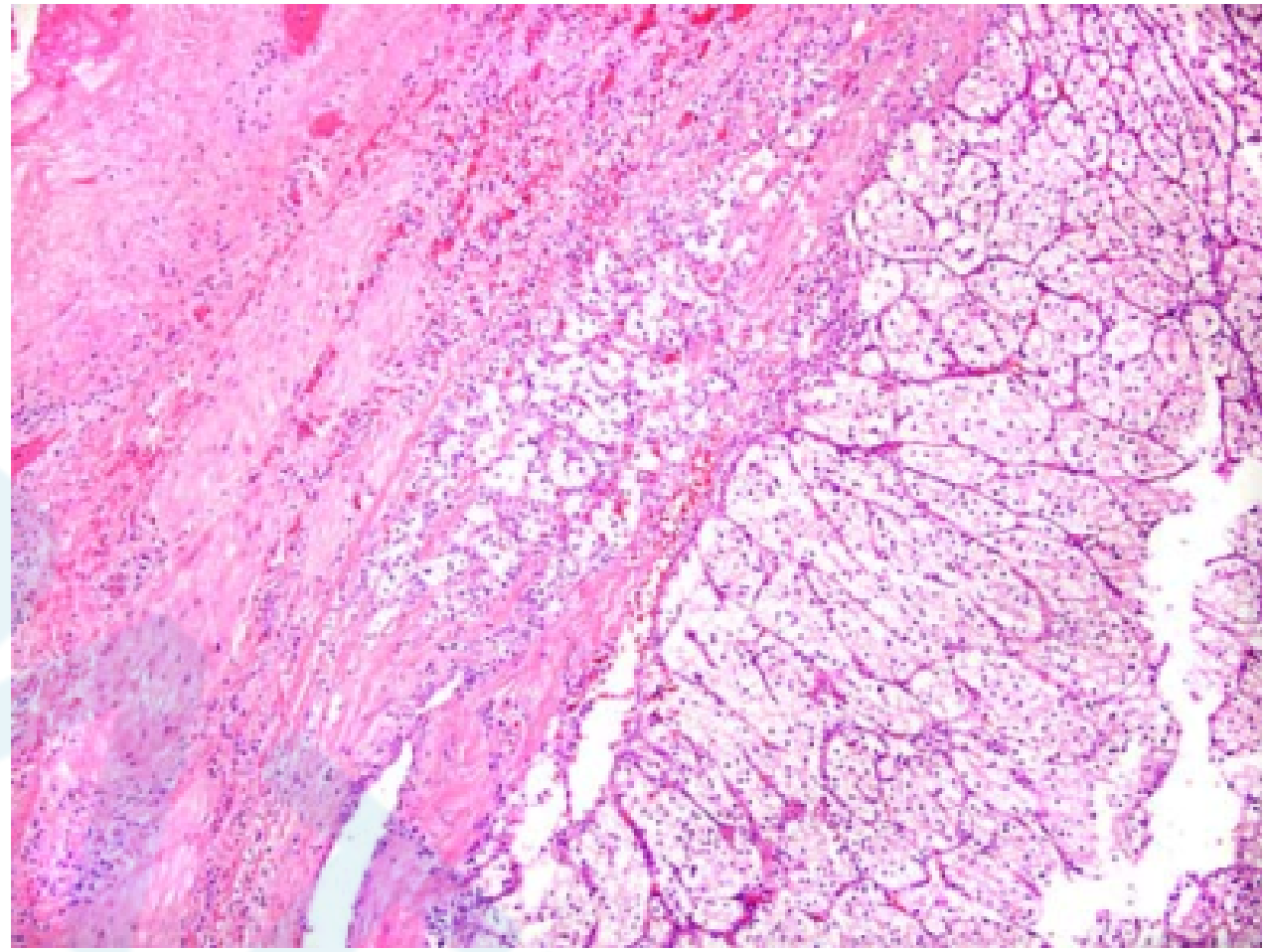
The assessment of the renal vein margin can also be problematic, particularly because the vessel wall tends to retract beyond the bulging thrombus after surgical resection and fixation (arrow).



The renal vein margin is considered positive only if there is a grossly adherent tumor at the actual margin (A),which is confirmed microscopically (B).

VENA CAVA INVASION

Renal tumor thrombus extends from the tumor in the left kidney into the vena cava above the diaphragm.



When a specimen is submitted separately as "caval thrombus," the pathologist's role is to confirm that the thrombus consists of tumor and to establish whether there is
adherent caval wall tissue, in order to examine the caval wall invasion.

BACKGROUND

- Renal cell carcinoma tumors are largely rounded or spherical, with stage categories defined based on extension into the renal sinus, perinephric fat, and renal veins.
- Pathologic staging may have substantial importance for determining clinical follow-up schedules, patient counseling, and enrollment in clinical trials for patients harboring higher-risk renal cancers.
- In this study, we sought to assess the extent of interobserver variability in assigning pathologic stage variables in renal cell carcinoma, with emphasis on testing the earliest and borderline thresholds for higher stage categories.

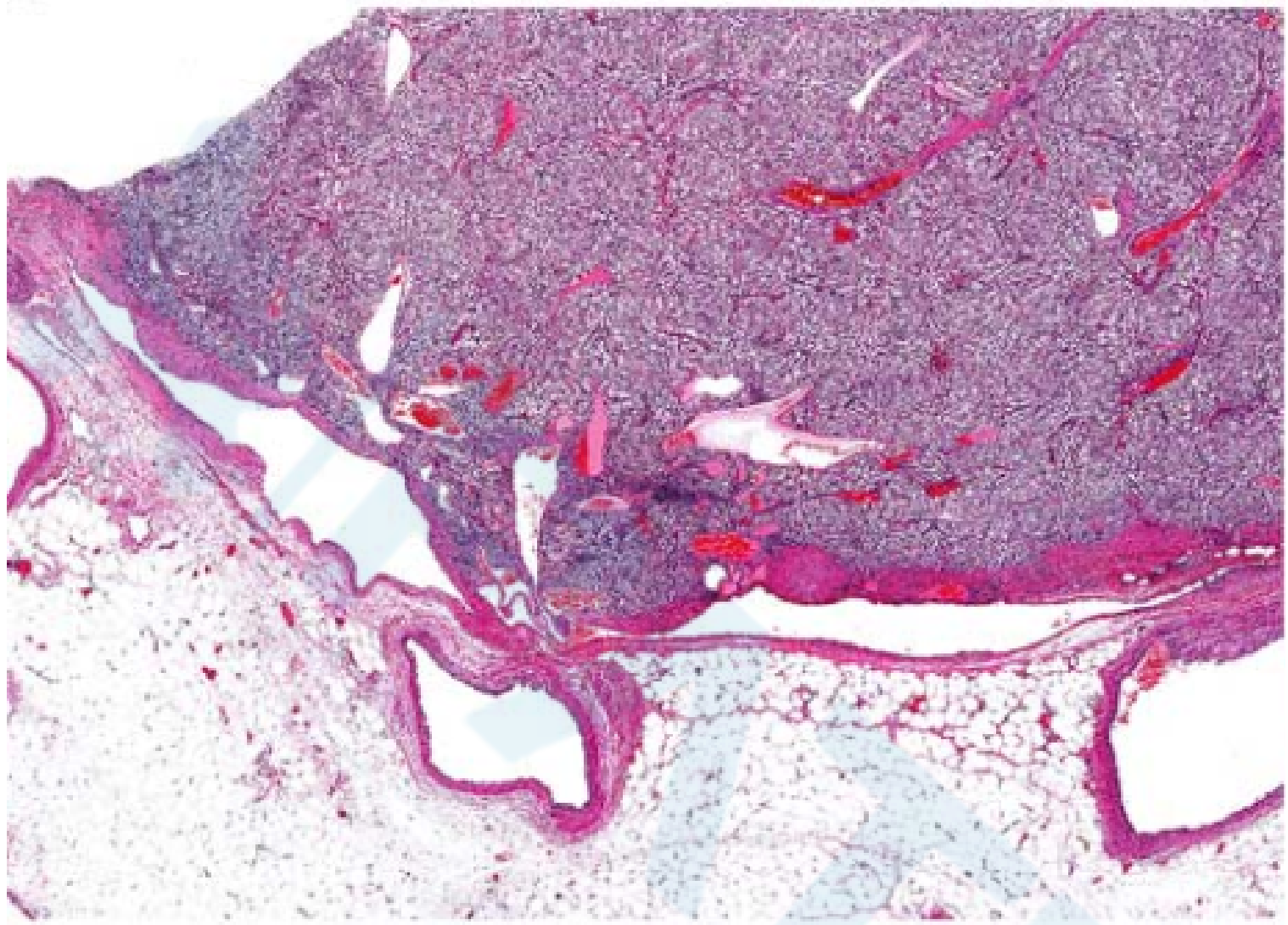
METHODS

- An online survey
- Thirty-one pathologists
- Questions: vascular and renal sinus invasion (n = 24),
  perinephric invasion (n = 9)
  gross pathology/specimen handling (n = 17)
- Consensus: 2/3 (67%) agreement
- Strong consensus: ⩾ 80% agreement
- Interpretations: Positive, negative, equivocal

RESULTS

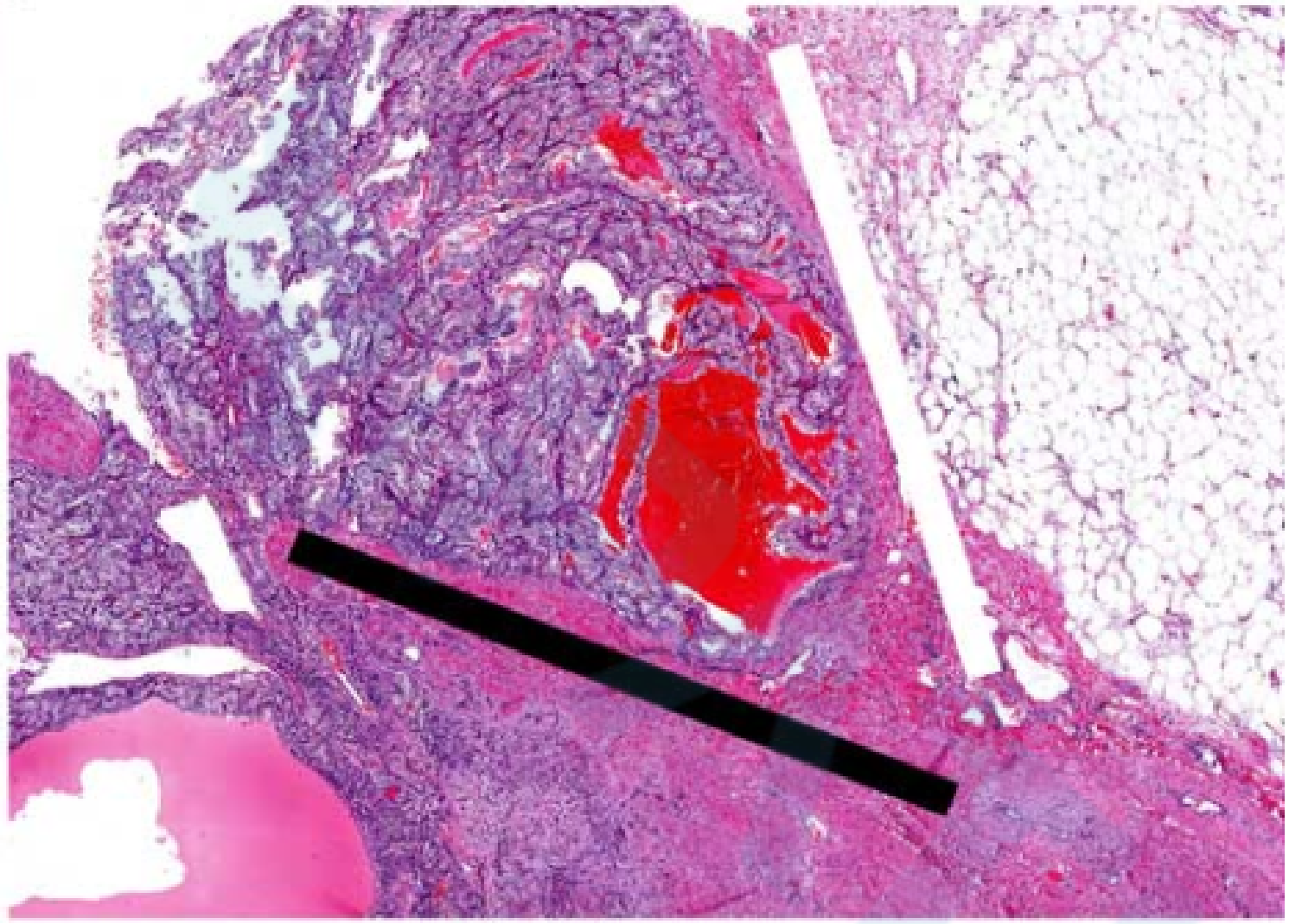
Consensus of 67% (2/3) was reached in 20/33 (61%) evaluable scenarios regarding renal sinus, perinephric, or vein invasion,of which 13/33 (39%) had >80% consensus.

Challenging cases for potential early vein branch invasion are shown in Figure 1.

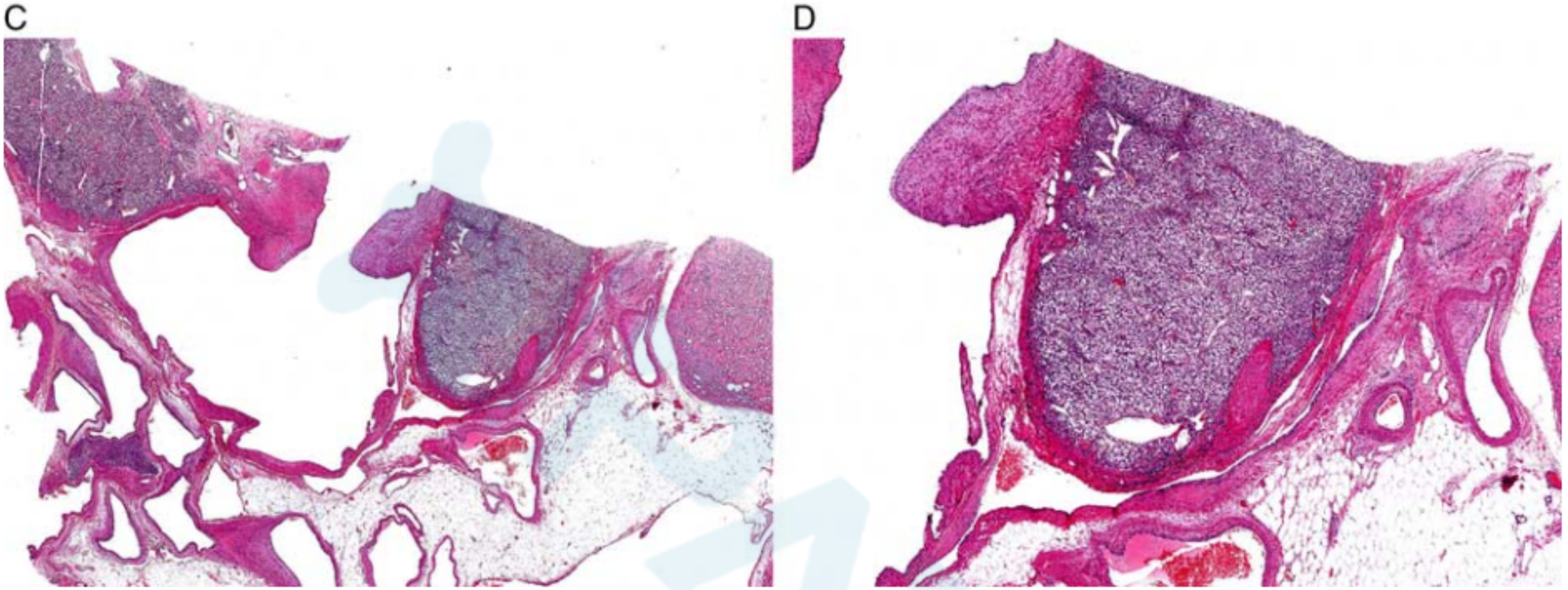


A selected image from question 3 demonstrates a clear cell renal cell carcinoma tumor that abuts and indents a large vein at the hilum. This example had no consensus for pT3a (52% yes, 48% no/equivocal).

B



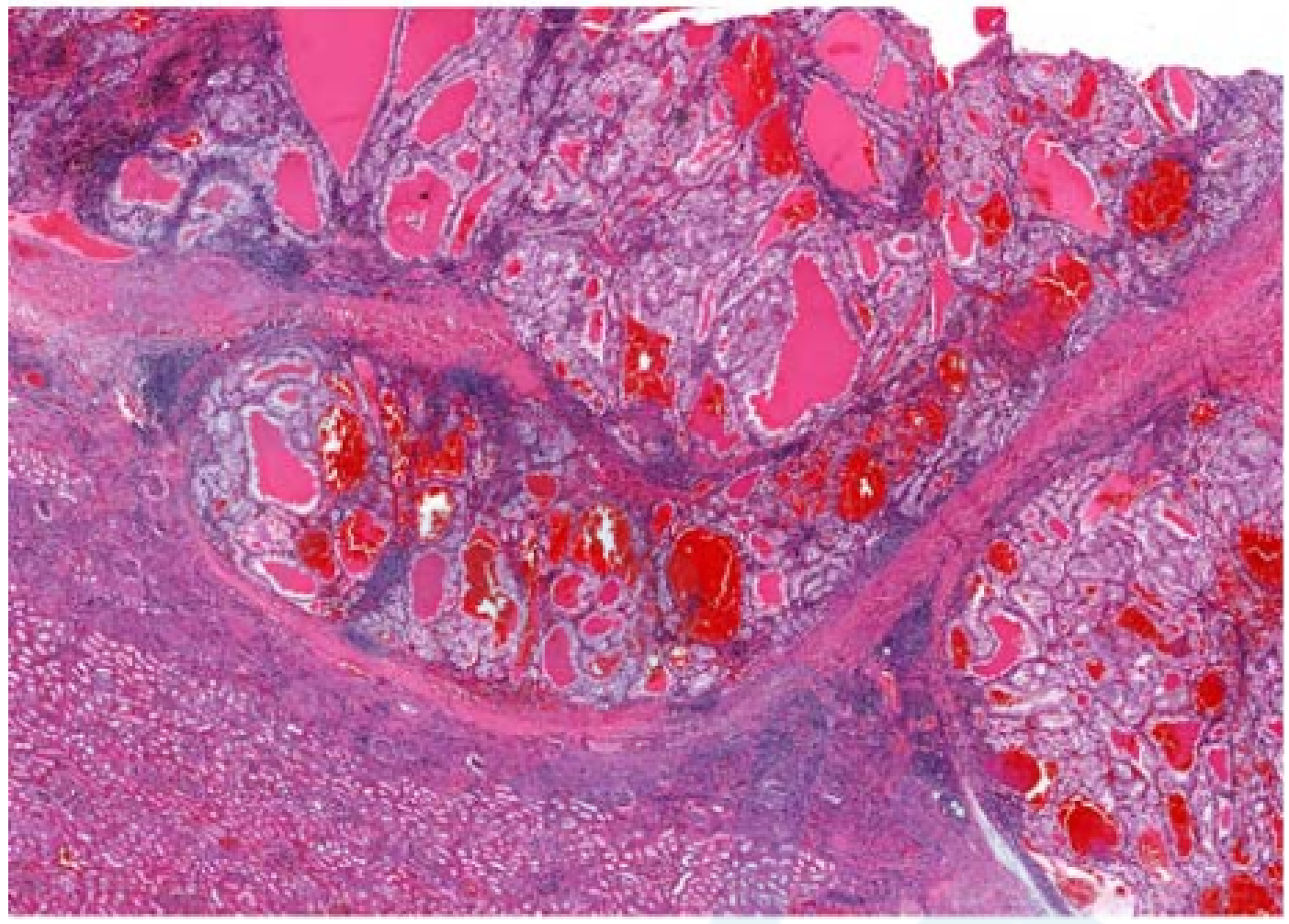
A selected image from question 5 demonstrates a clear cell renal cell carcinoma tumor that extends beyond 1 fibromuscular plane (black line) but is separated from the hilar fat by a second fibromuscular plane (white line).This example had no consensus for pT3a (42% yes, 58% no/equivocal).



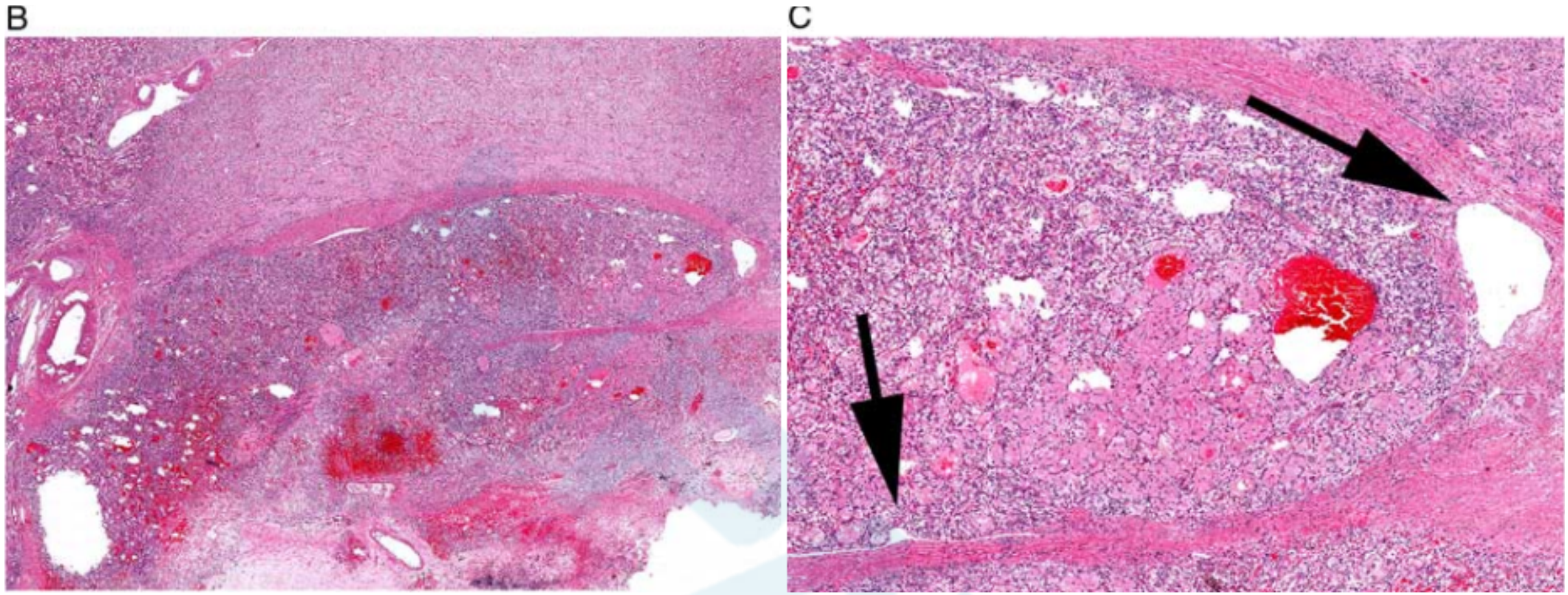
Two images from question 4 demonstrate a clear cell renal cell carcinoma tumor with tumor nodules that extend into hilar vascular tissue with rounded to elongated finger-like extension. This example had no definite consensus for pT3a (61% yes, 39% no/equivocal).

In the context of a tumor outpouching or finger-like protrusion possibly corresponding to a vein, interpretation as pT3a increased when the possible venous structure demonstrated a more robust lumen and when it was juxtaposed to renal sinus fat (Fig. 2) or within renal sinus (Fig. 3).

A

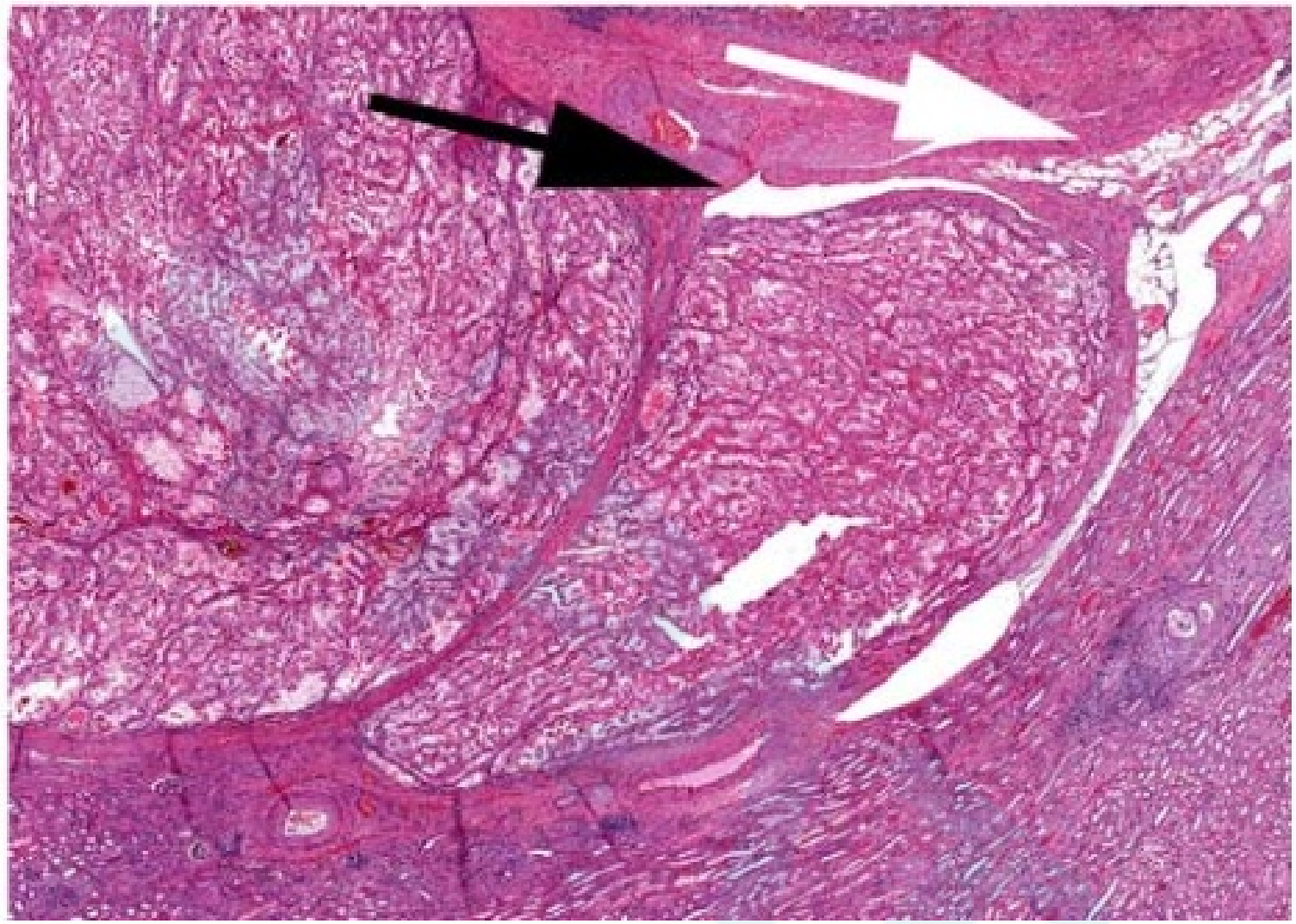


A selected image from question 7 demonstrates a clear cell renal cell carcinoma tumor with a finger-like extension that herniates beyond the fibromuscular pseudocapsule of the tumor. This example had consensus against pT3a (6% yes, 94% no/equivocal).

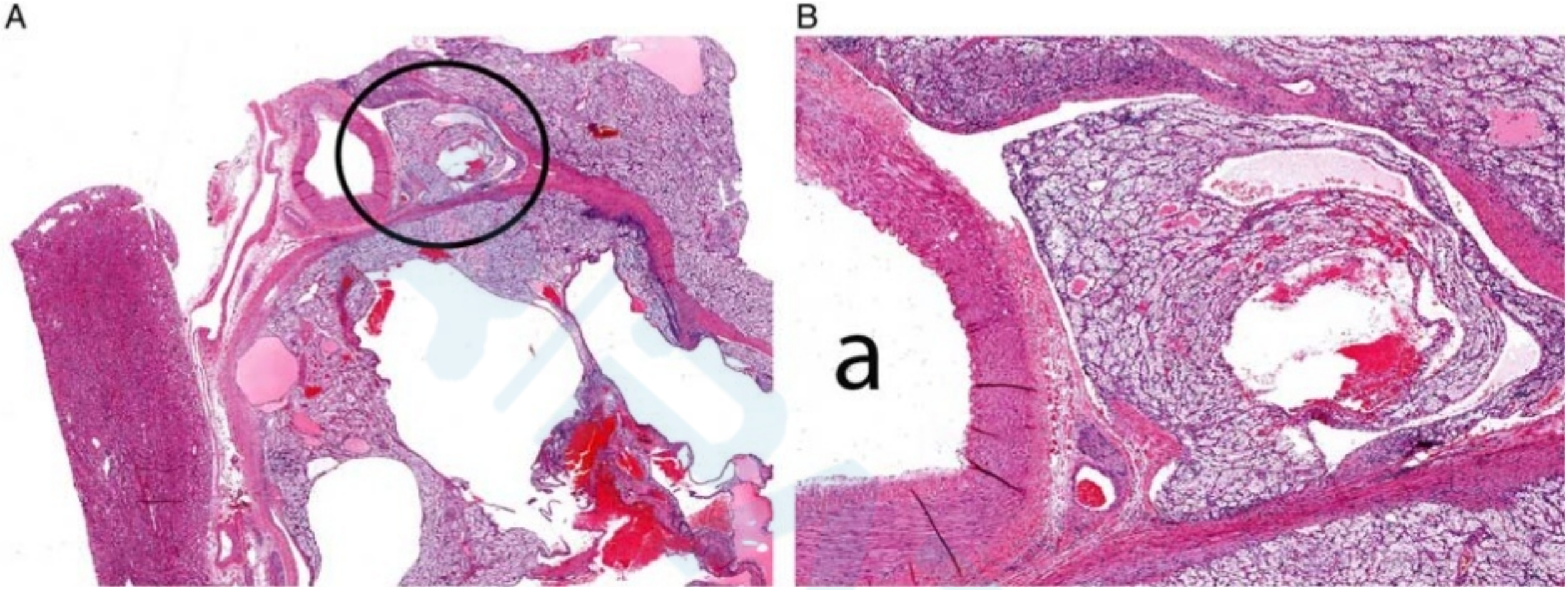


Selected images from question 10 demonstrate another finger-like extension away from the mass, but still within the kidney. In contrast to question 7, there is a focal possible vascular lumen (C, arrows). This example had consensus against pT3a, but with a higher fraction of participants interpreting as vein invasion (29% yes, 71% no/equivocal).

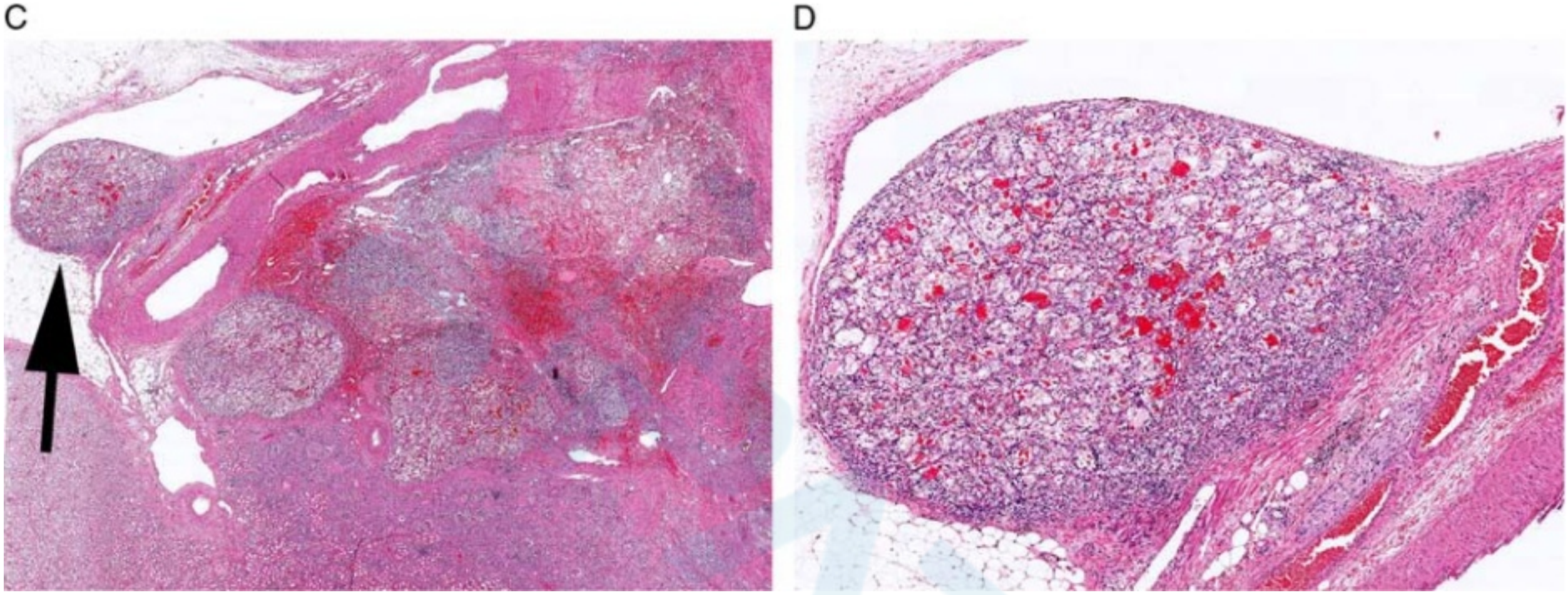
D



A selected image from question 12 demonstrates a clear cell renal cell carcinoma tumor with a finger-like extension. This example includes a possible vein lumen (black arrow) and focal renal sinus fat (white arrow). Interpretation shifted in favor of pT3a for this case but did not reach consensus (58% yes, 42% no/equivocal).

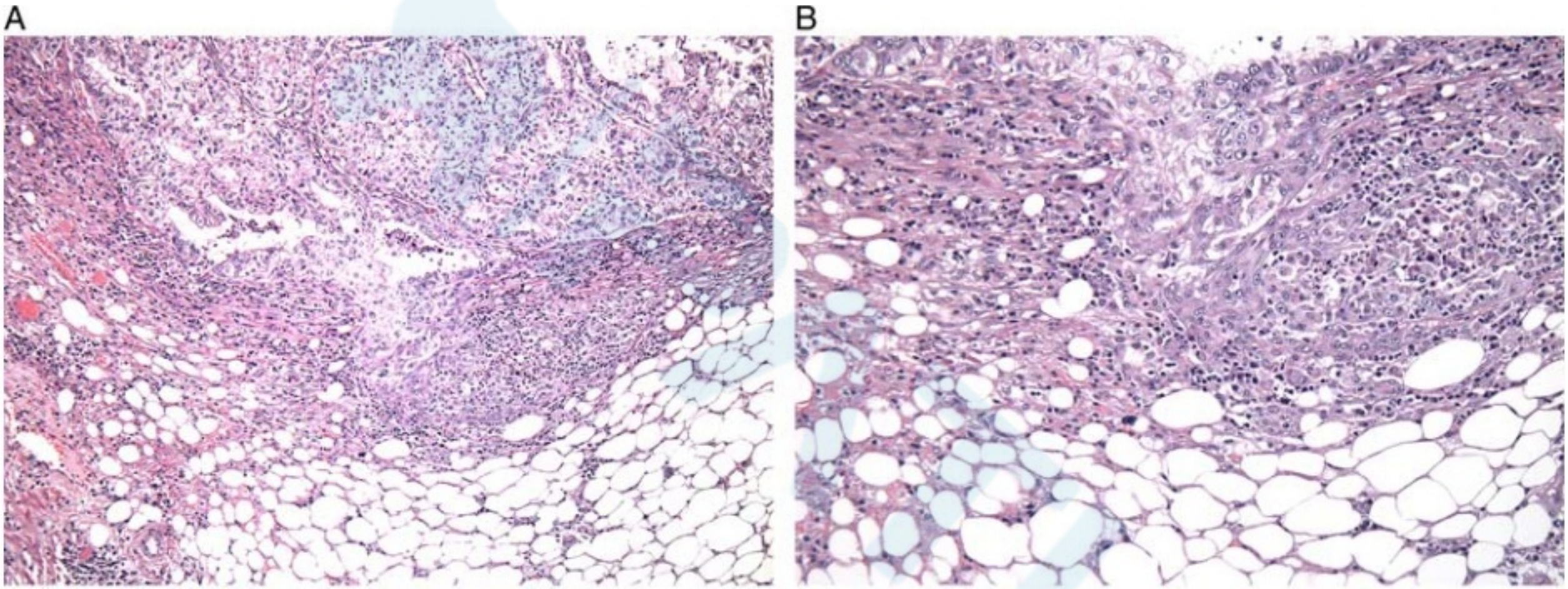


Selected images from question 16 demonstrate a clear cell renal cell carcinoma tumor with a polypoid nodule loosely connected within a vascular space (A, circled). Higher magnification reveals the paired artery (a) and tumor nodule within accompanying vein. This example reached consensus in favor of pT3a (84% yes, 16% no/equivocal).



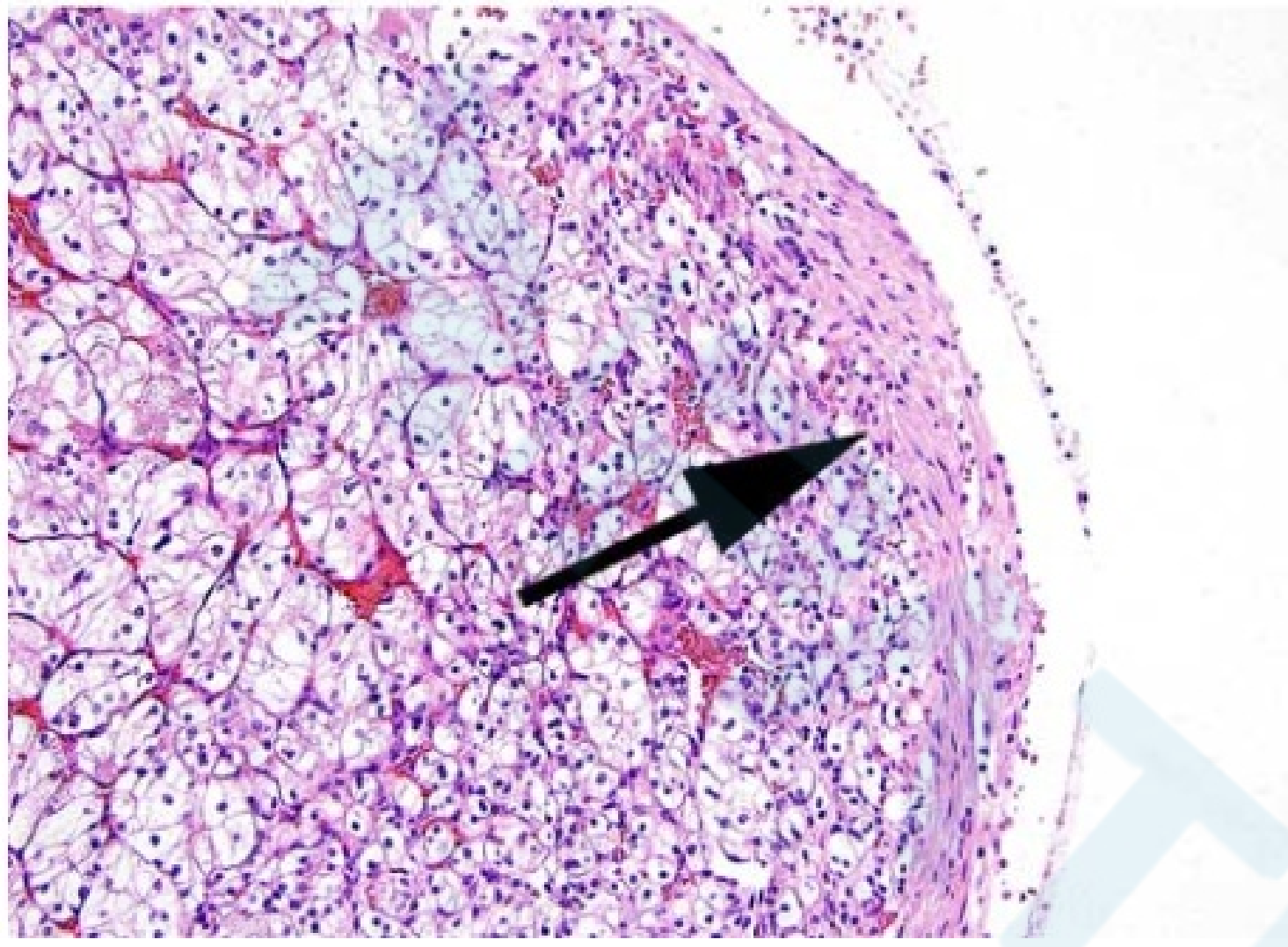
Selected images from question 11 demonstrate a clear cell renal cell carcinoma tumor with a polypoid nodule protruding into a renal sinus vein (A, arrow and B). This example reached consensus in favor of pT3a (94% yes, 6% no/equivocal).

Scenarios demonstrating direct soft tissue extension into the renal sinus all reached consensus for renal sinus invasion.



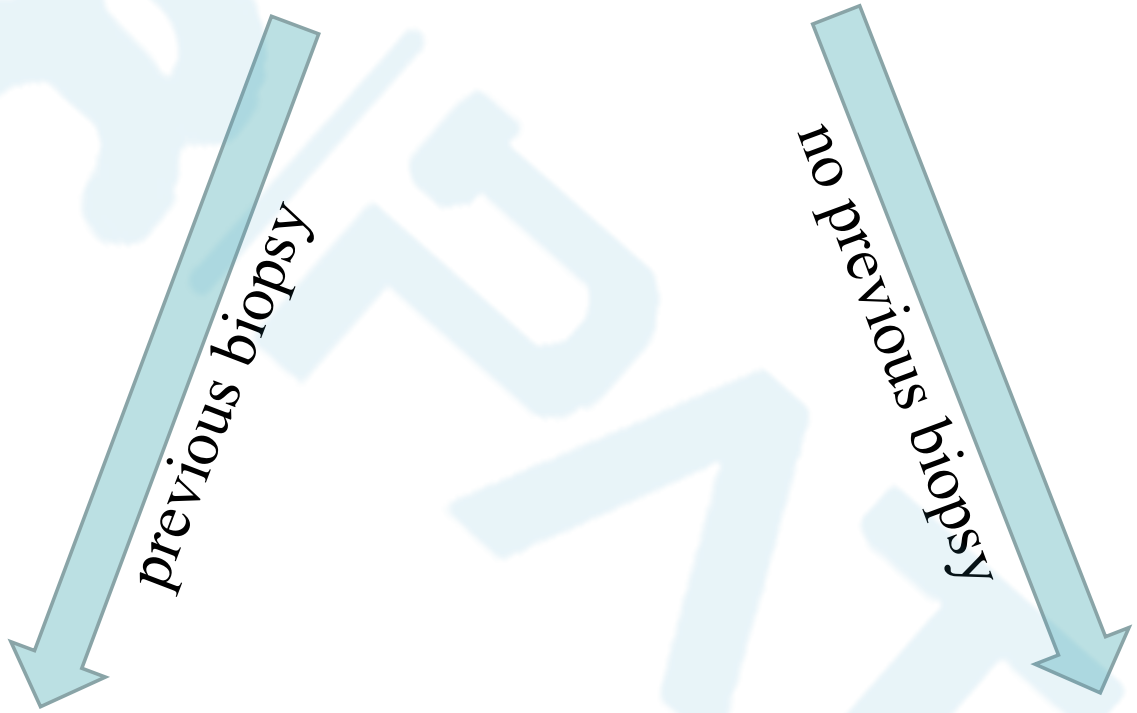
The 2 images provided to participants from question 22 show tumor cells from a clear cell renal cell carcinoma extending into renal sinus fat. This example reached consensus for pT3a (97% yes, 3% no/equivocal).

C



A representative image from question 26 shows a possible intravascular tumor with a layer of smooth muscle tissue at the edge (arrow). This question approached but did not reach consensus as to whether this type of smooth muscle argues against vascular invasion (35%) or does not affect the interpretation (tumor can bring vein wall with it and still represent vein invasion, 65%).

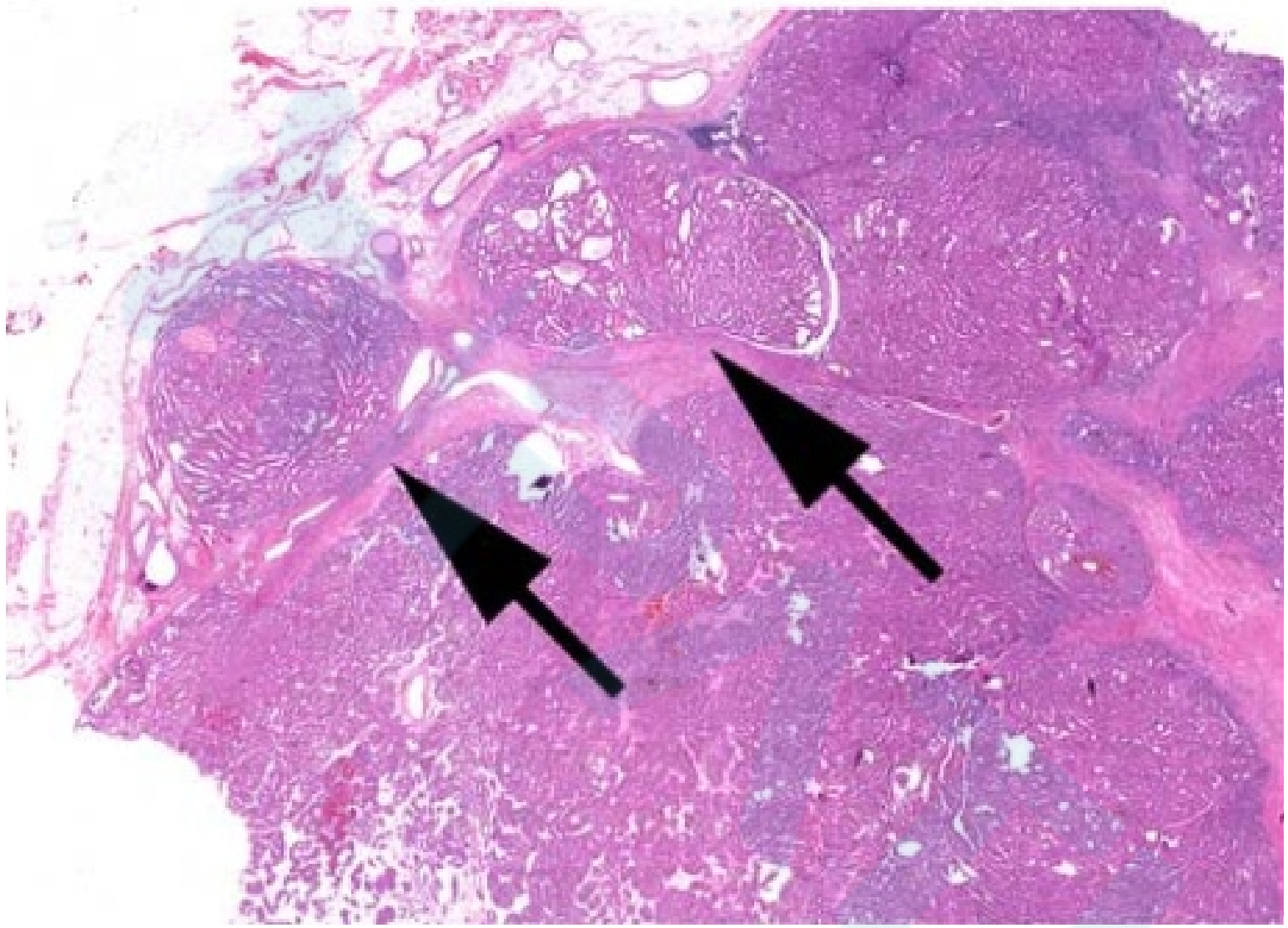
papillary renal cell carcinoma with a few tubules extending into loose tissue at the perinephric interface



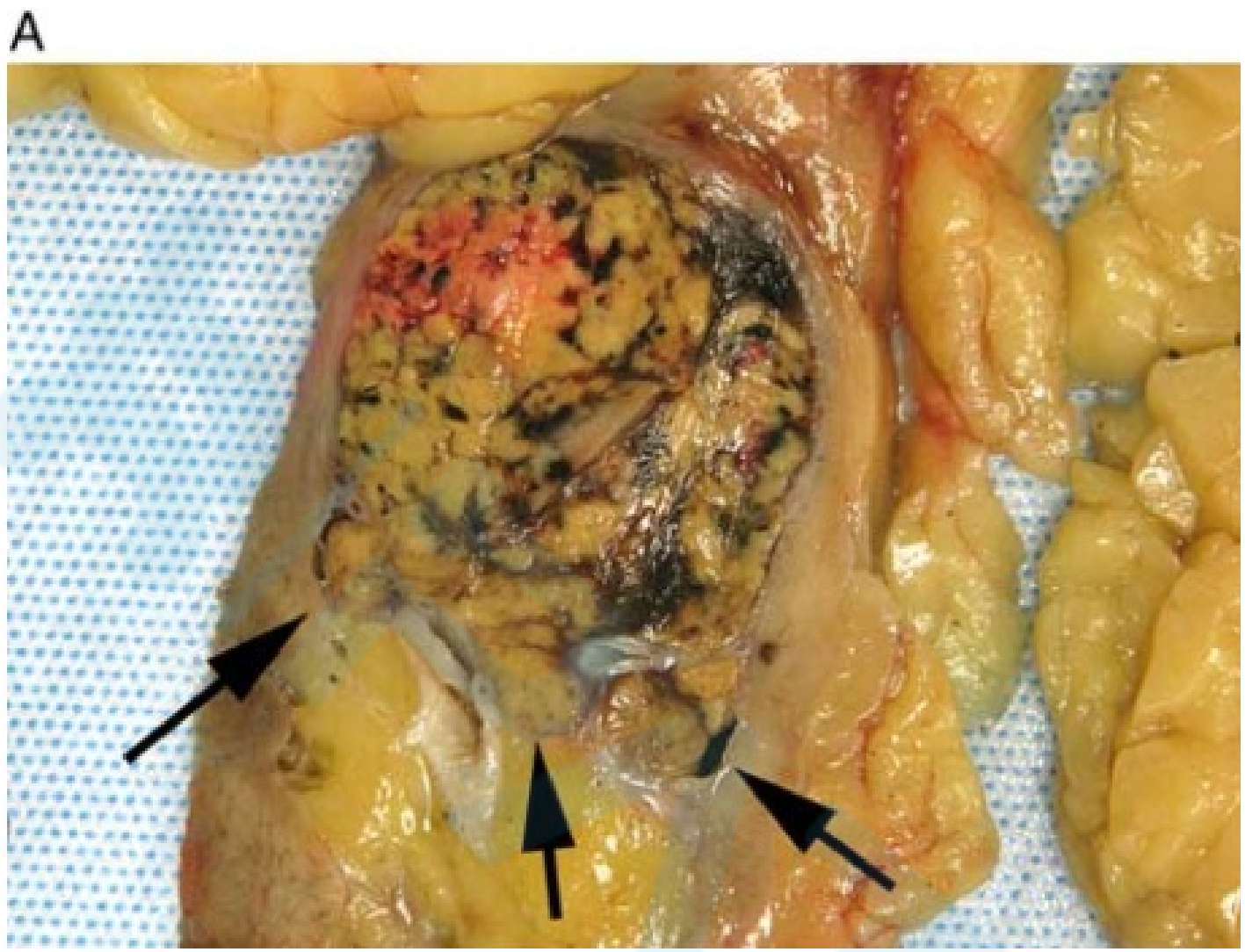
not definitive for invasion (68%)

Consensus agreement (74%) regarding pT3a stage

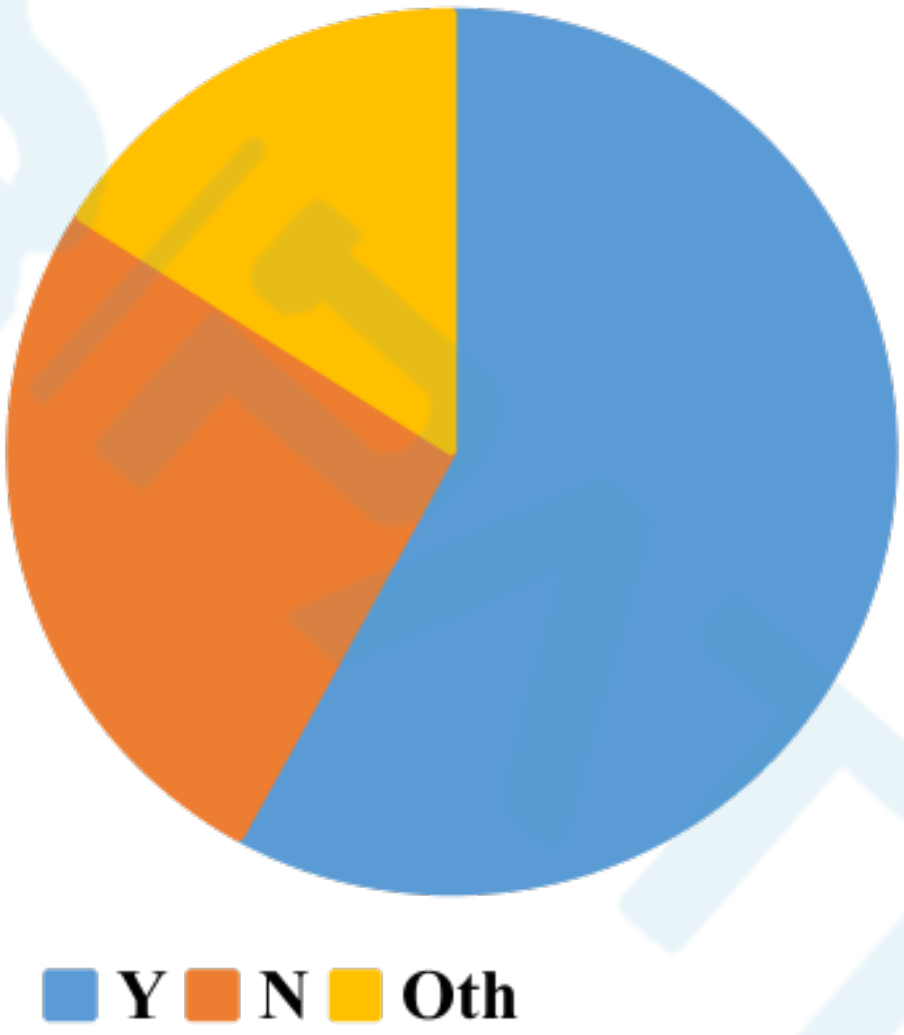
D



This selected image from question 28 shows eosinophilic chromophobe renal cell carcinoma with multinodular growth bulging into perinephric fat (arrows). This question did not reach consensus for pT3a (61% yes, 39% no/equivocal).



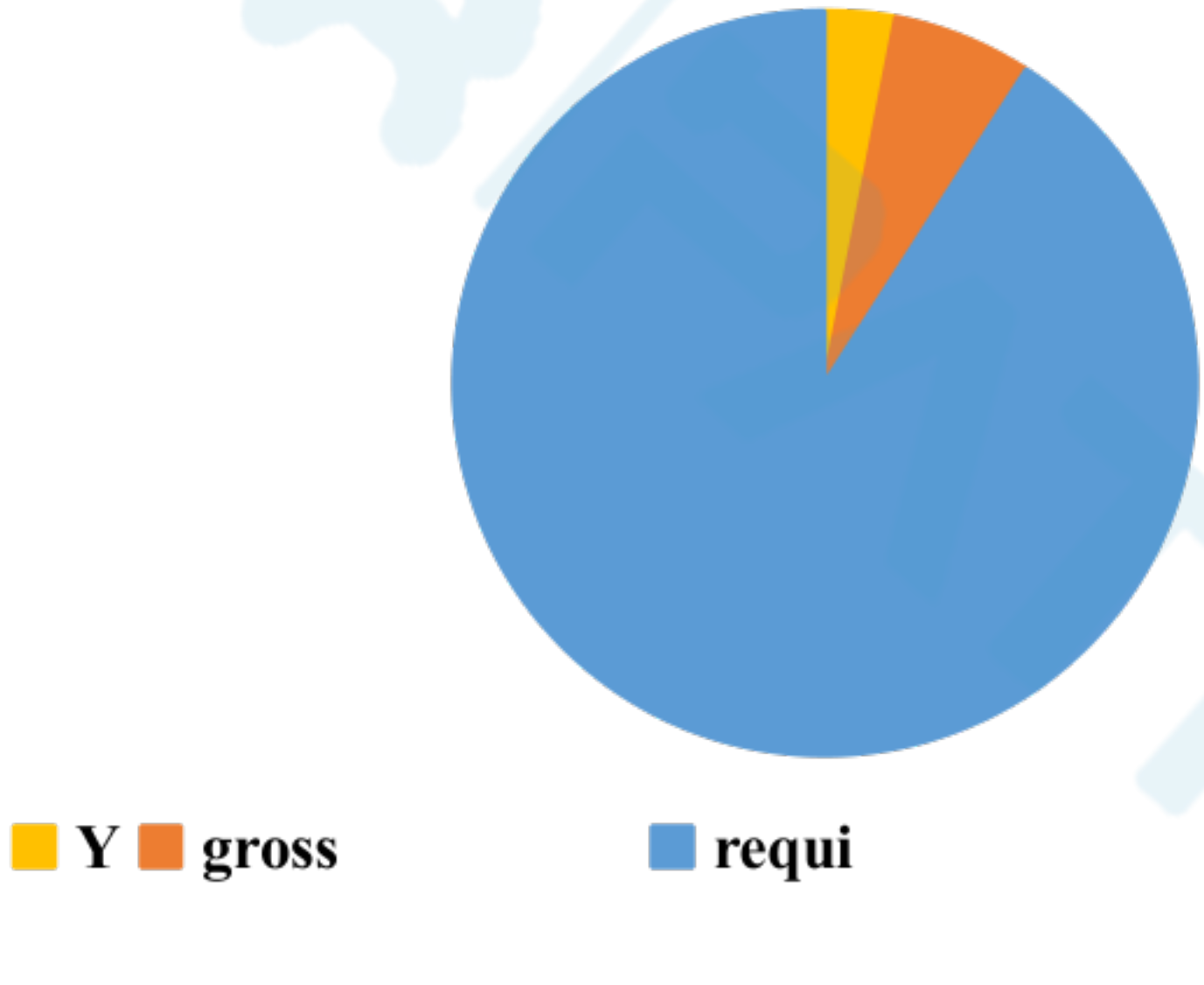
A gross image from question 38 demonstrates outpouchings of clear cell renal cell carcinoma into renal sinus and vascular tissue (arrows). Most participants responded that this was suspicious for vascular invasion (68%) but that histologic confirmation is required. A minority (19%) reported that this was unequivocal for vein invasion based on the gross features alone.

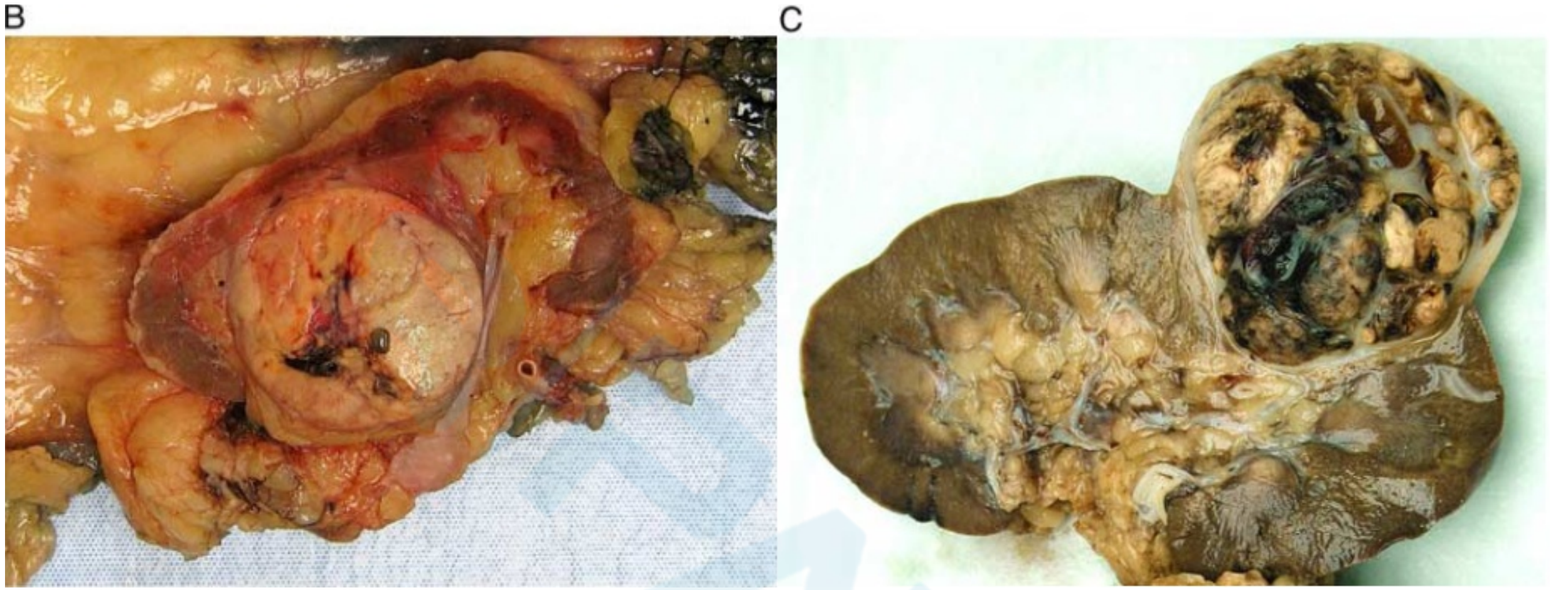


other response:
submitting additional sections
preparing additional section levels
using additional stains to confirm the vascular lumen

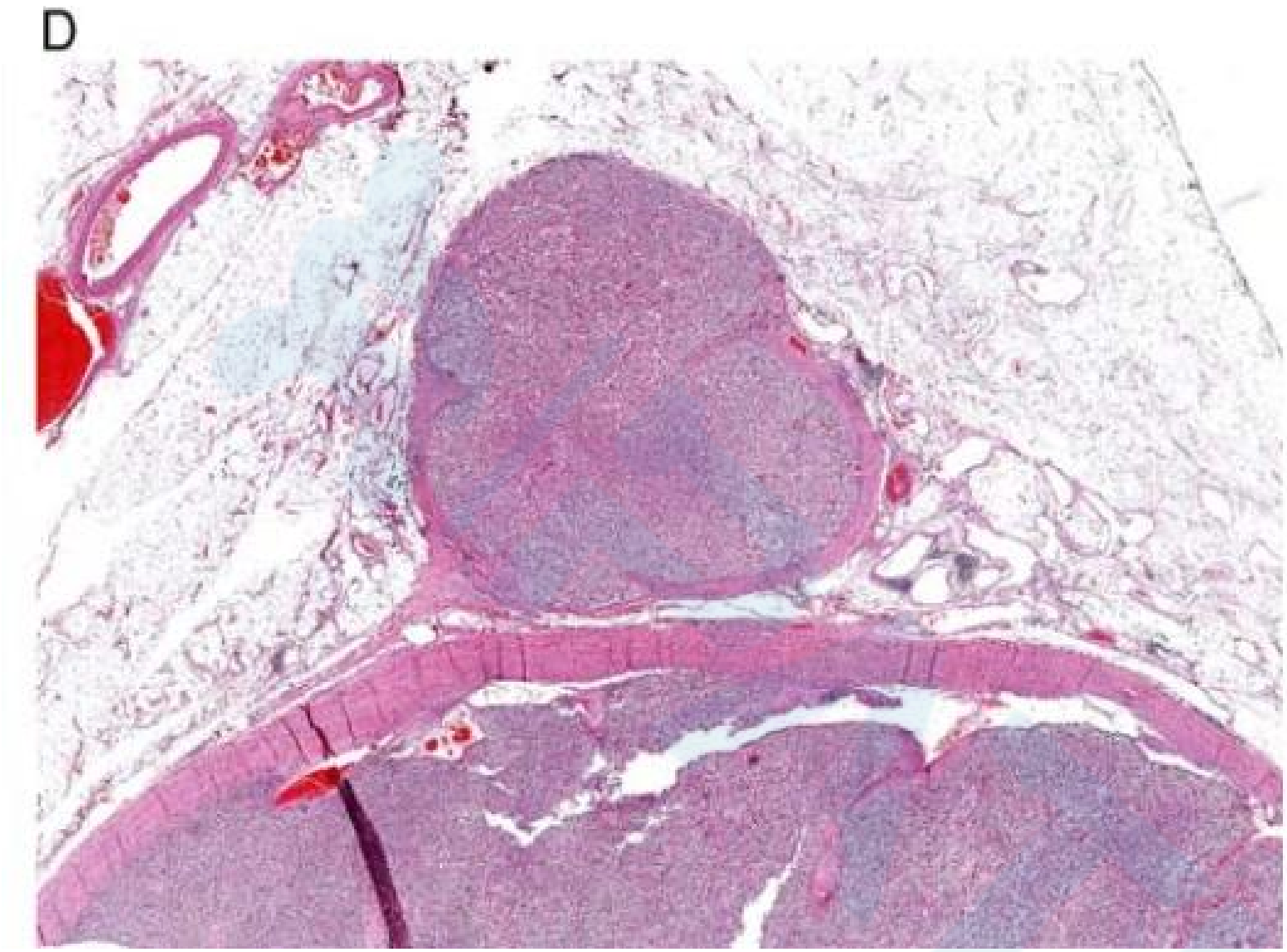
vein margin

if i



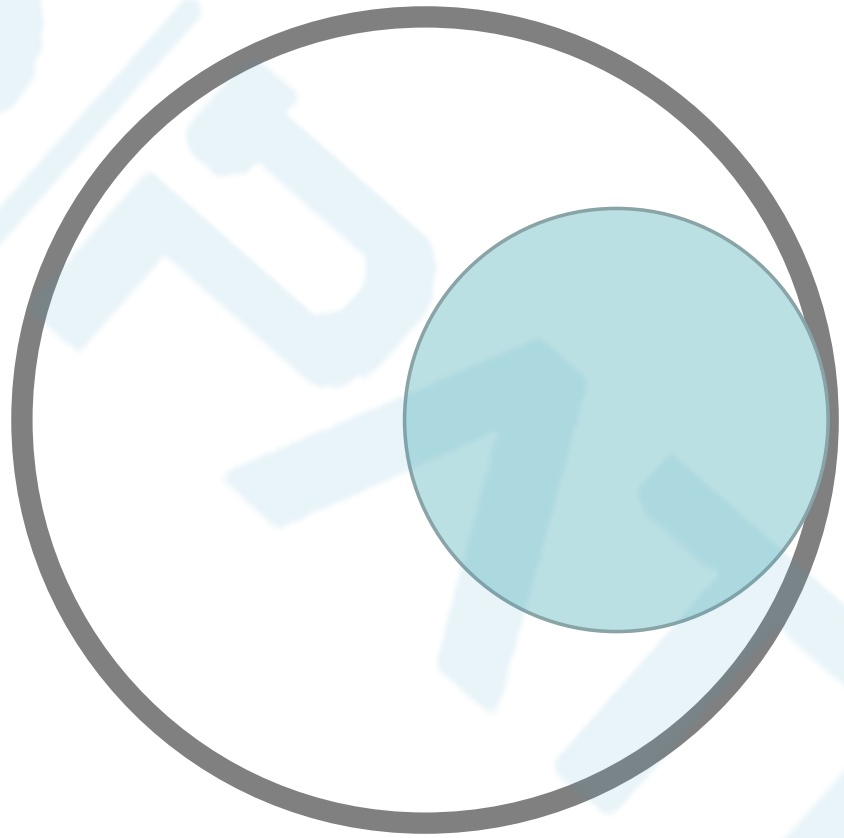


B, For a round tumor bulging into the renal sinus, 71% of participants indicated that this was not sufficient to assign pT3a.C, For a round tumor bulging into the perinephric fat, 90% of participants indicated that this was not sufficient to assign pT3a.



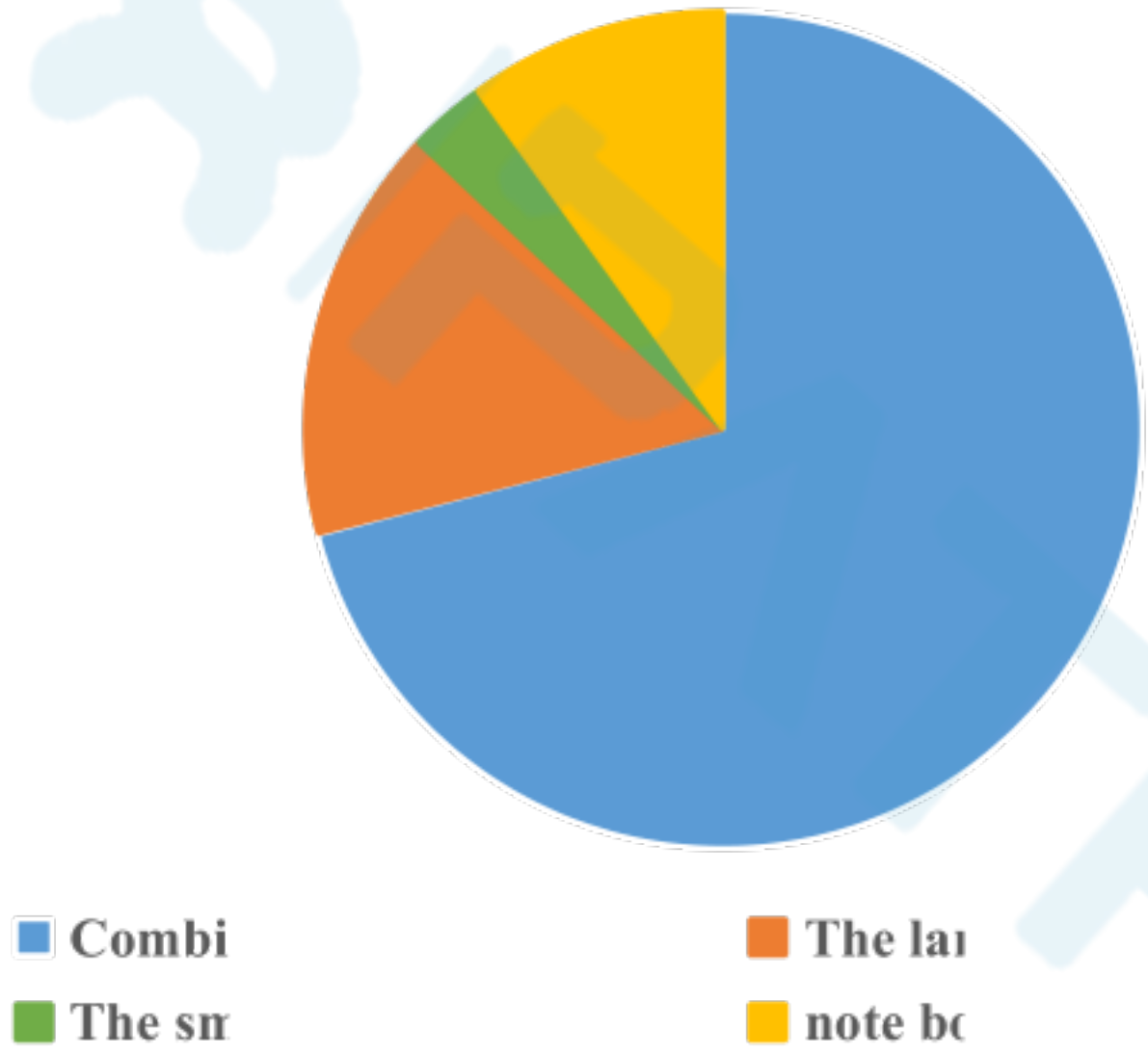
D. Histologically, a rounded nodule beyond the apparent renal capsule did not reach consensus for pT3a (55% yes, 45% no/equivocal).

A renal tumor composed of a large unilocular cyst with a single nodule of solid tumor in 1 wall of the cyst.

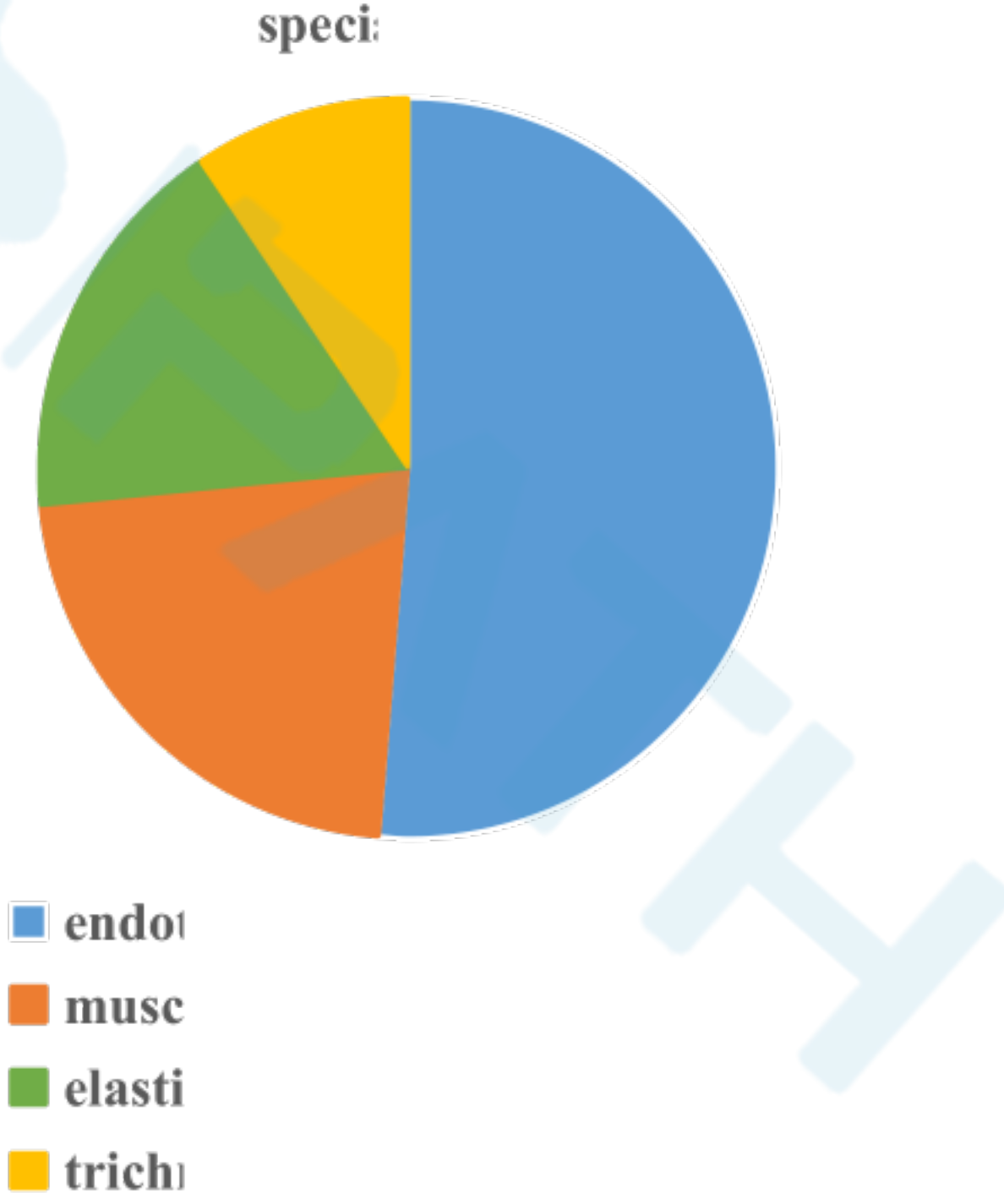


solid tumor **cyst**

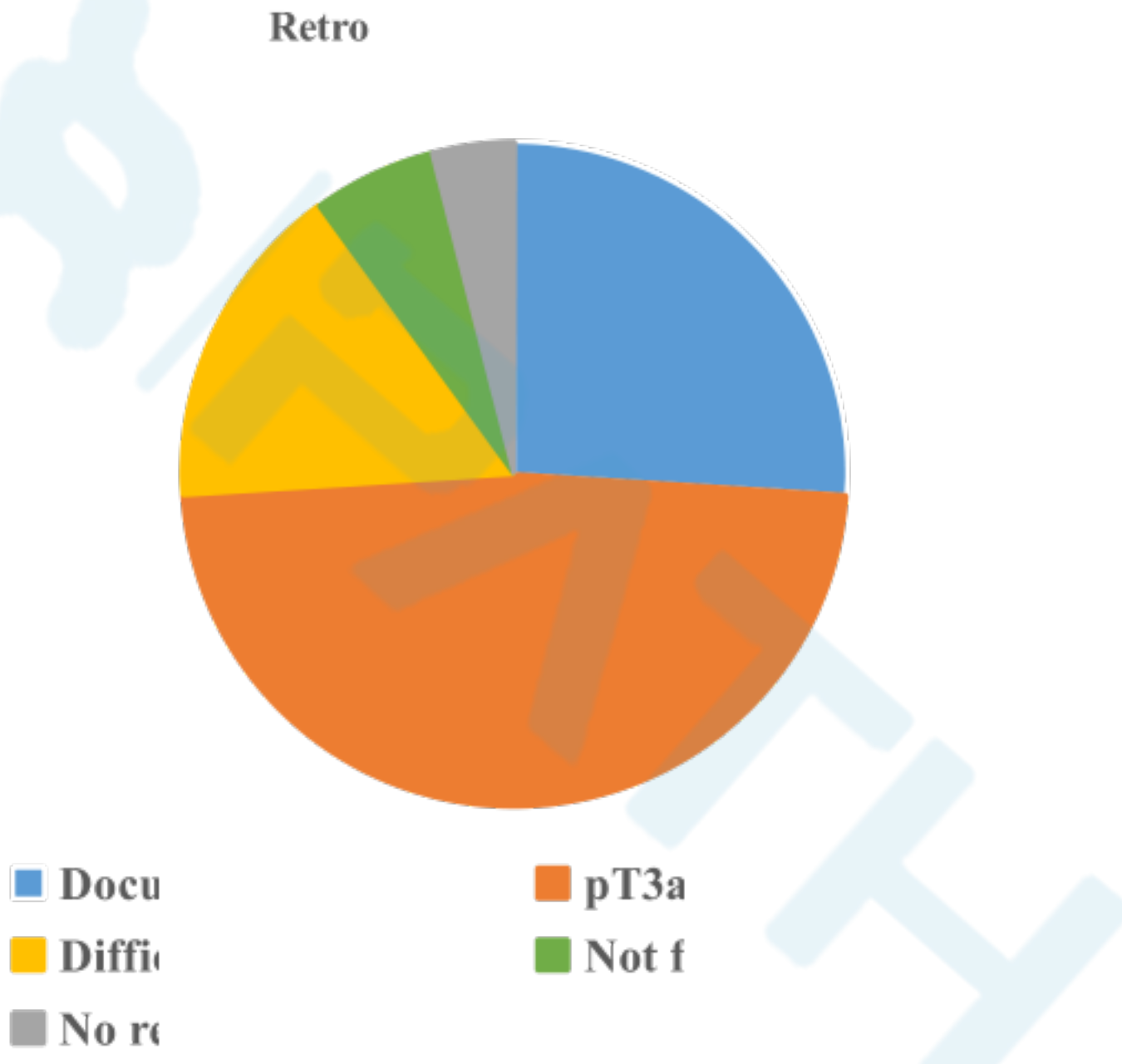
A re



Diagnosis of vascular invasion



Retrograde venous invasion



The AJCC/TNM staging system defines renal vein invasion (pT3a) as a tumor that “grossly extends into the renal vein or its segmental (muscle-containing) branches”

pathologists in the United States VS those of other countries

	US	**non-US**
Q6	N	Y
Q1	Y	N
Another (Renal sinus or vein invasion).	N	Equivocal
The new AJCC criteria	95%	60%

DISCUSSION

Innovation:

The first major attempt to evaluate the application of specific staging criteria in scenarios which have not been previously covered by specific guidelines.

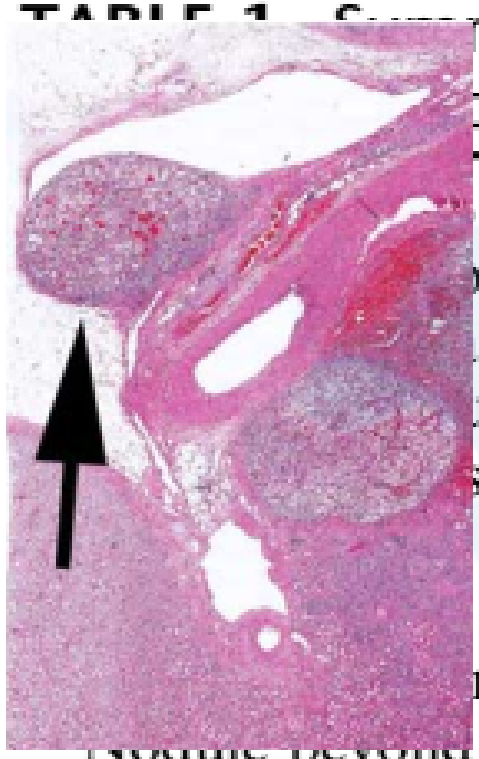
This study provides some potential guidance (based on subspecialty opinion) for a few areas of uncertainty.

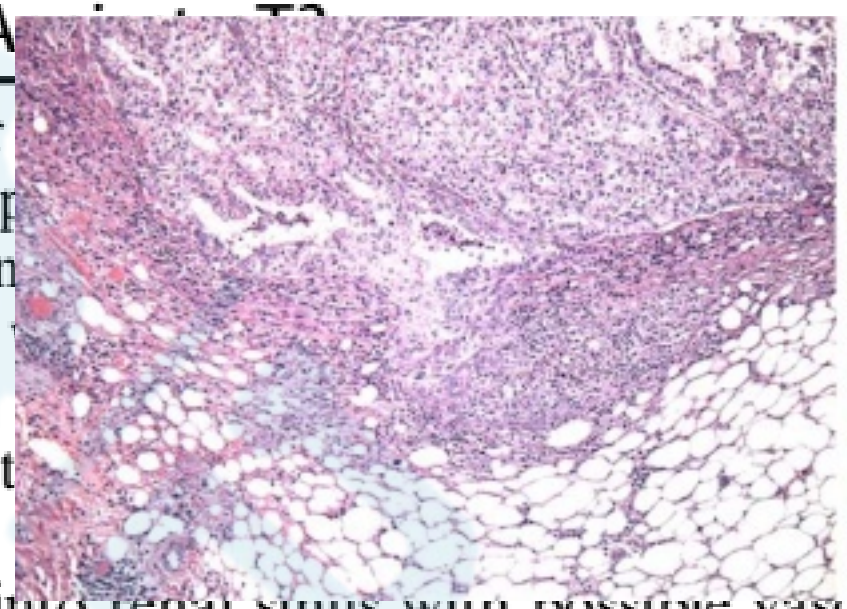
Aim:

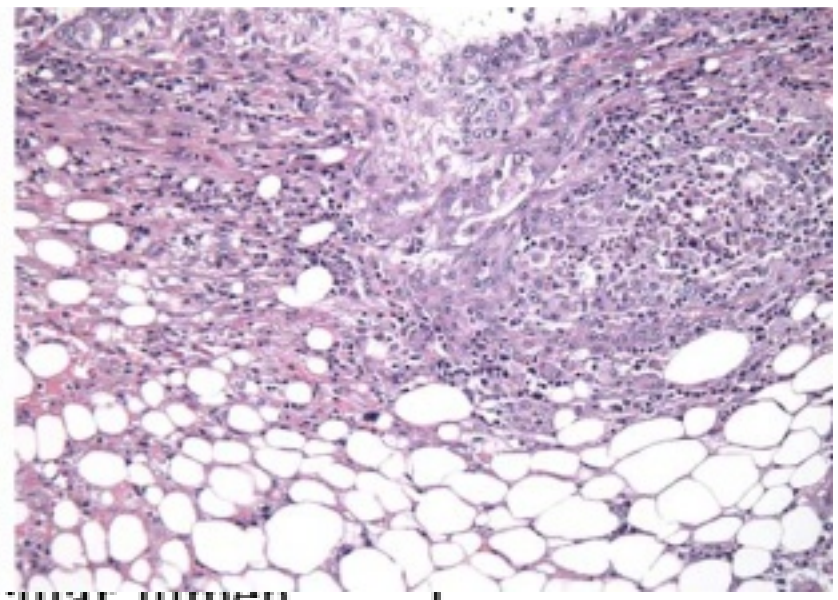
Evaluate whether urologic pathologists use similar thresholds .

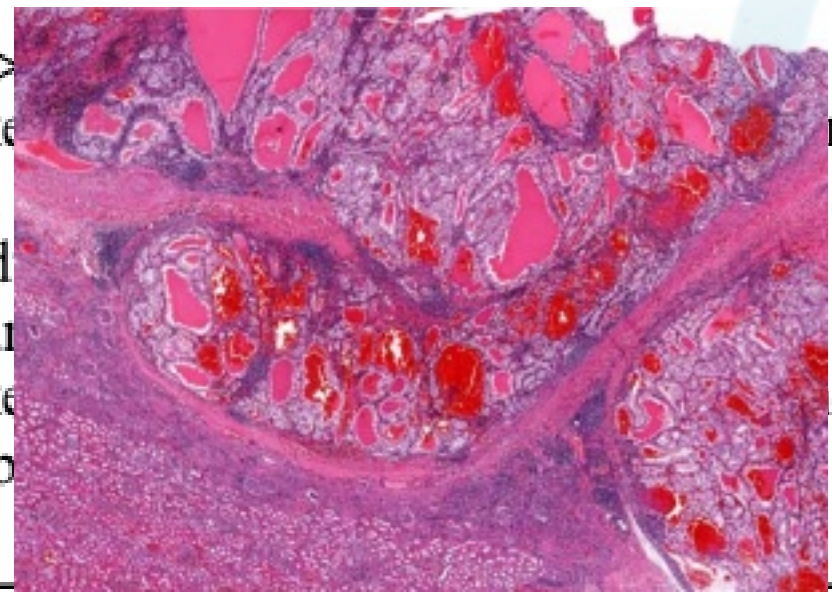
TABLE 1. Summarized Features of Cases Reaching Strong Consensus for Angiomyolipoma With Minimal Fat

Finger-like projections of fat into renal sinus with possible vascular lumen	1
Nodule beyond tumor pseudocapsule in the plane of fat in renal sinus	1
Total	9
Consensus >	
Finger-like men, within the kidney, 2A)	1
Small nod with no definite vascular	1
Finger-like d) renal capsule	1
Nodular b	1
Total	4









Limitation: It does not assess the true biological behavior of the depicted cases.

Hope : Highlighting these interpretations, combined with the study illustrations, may aid practicing pathologists in evaluating challenging cases.

THANK YOU