Management of High Risk Cystic Lesions of the Kidney

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TEACHING HOSPITAL

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Financial Disclosures

None

Background

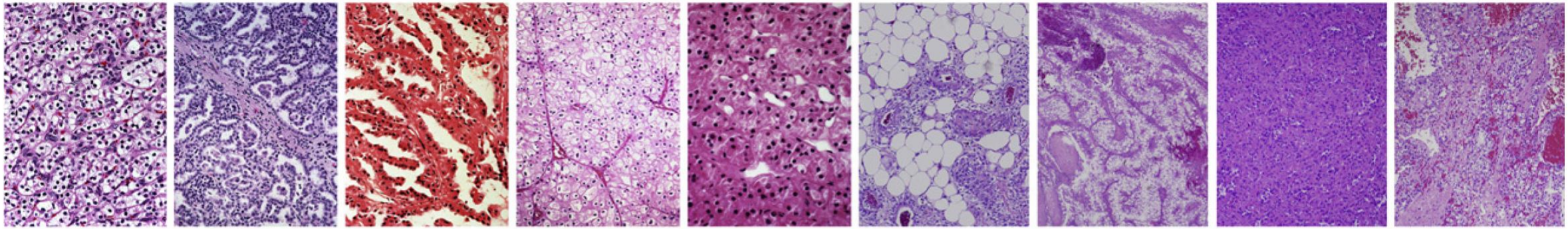
- greater than 50% of adults greater than 50 years old have renal cysts, the vast majority being benign simple cysts.
- cystic renal lesions are increasingly being detected with utilization of cross-sectional imaging
- the Bosniak Criteria for determining surgical cysts versus benign has been used for greater than 20 years in categorizing renal mass lesions
- 4-7% of renal cell carcinoma have cystic component

Background: Renal cell carcinoma

Epidemiology

- 3.8% of all new cancers
- Affects more males than females (3:2)

Human Renal Epithelial Neoplasms

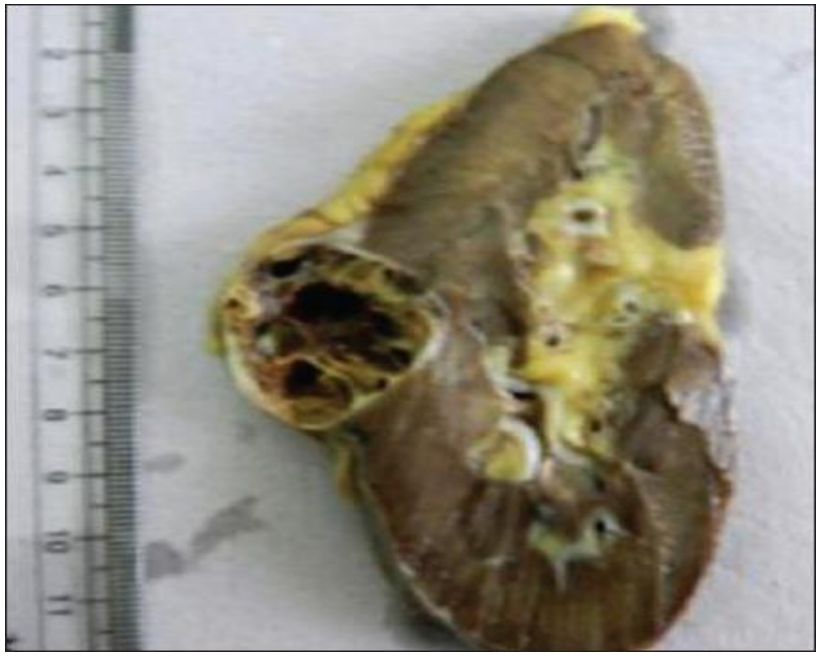


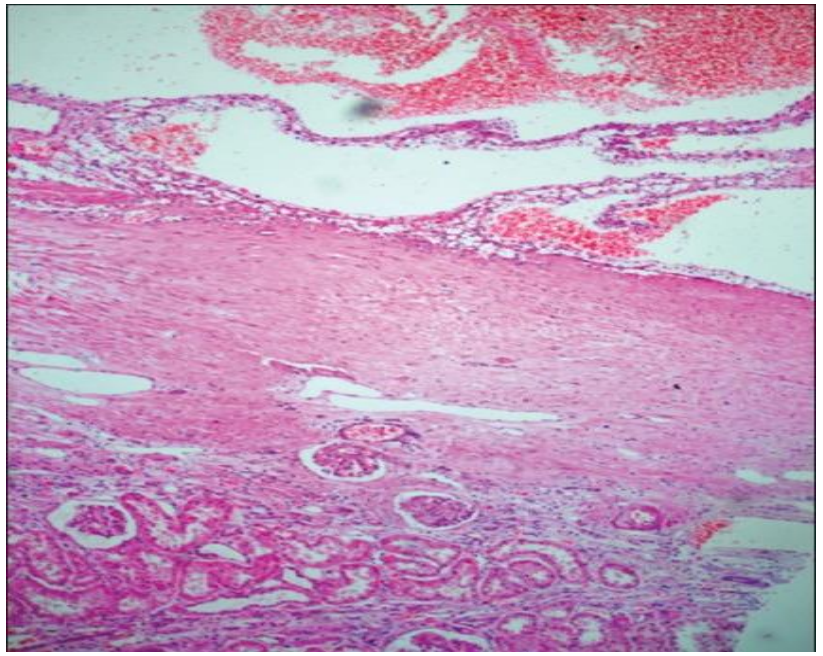
Clear Cell	Papillary Type 1	Papillary Type 2	Chromophobe	Oncocytoma	Angiomyolipoma	TFE3	Oncocytic	Clear/Chromophobe
VHL	*Met*	*FH*	*FLCN*		*TSC1, TSC2*	*MITF*	*SDHB, SDHD*	*PTEN*
VHL (89%)	*Met* (13%)	TBD*	TBD*		*TSC1, TSC2*	*TFE3, TFEB*	TBD*	TBD*

Linehan *et al. Seminars in Cancer Biology* 23 (2013) 46– 55
NCCN Guidelines (2019)

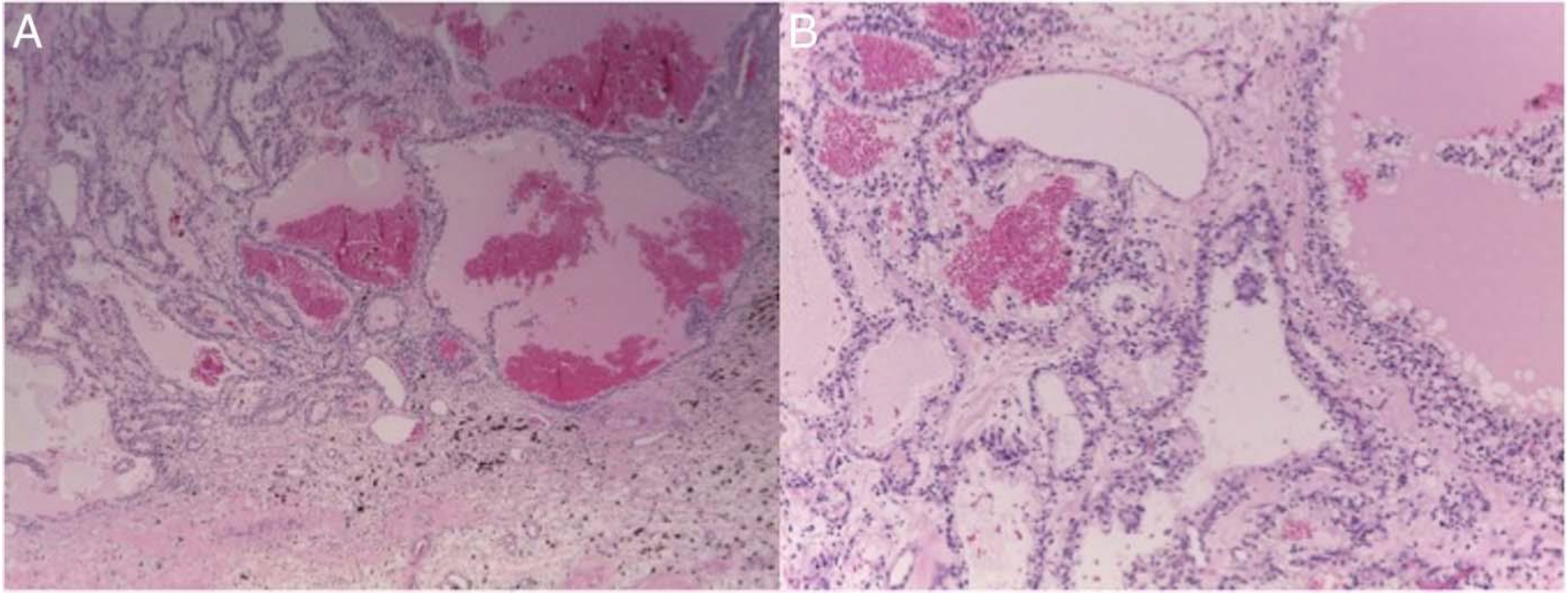
Multilocular Cystic Clear Cell Neoplasm of Low Malignant Potential

- A histologic variant of clear cell RCC (<5% of clear cell RCC)
- Formerly known as “multi-locular cystic RCC”
- Well-circumscribed, entirely cystic
- Cysts lined with single layer of clear cells (grade 1 nuclei)
- No recurrence or metastasis reported after resection

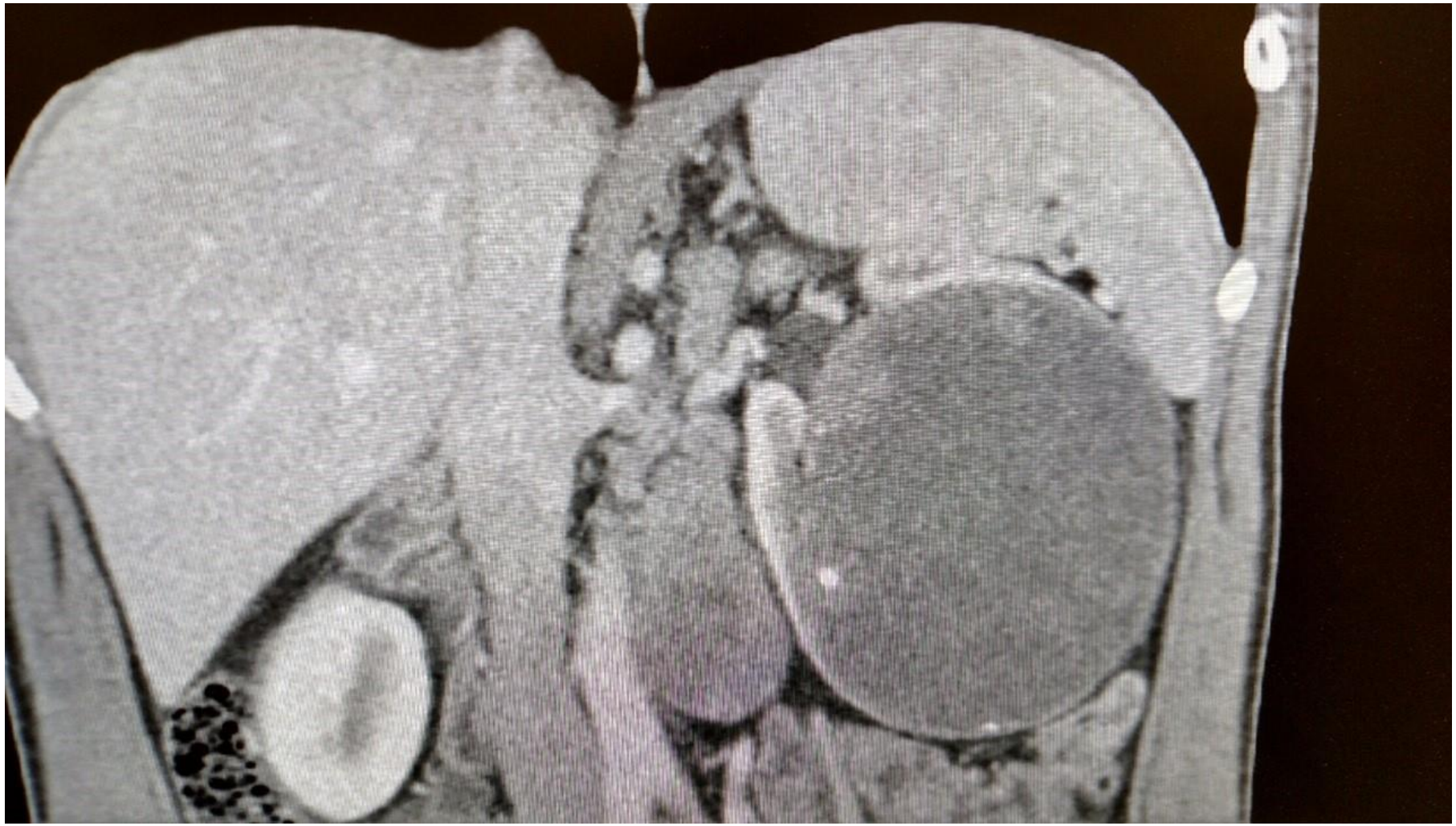




Cystic Renal Cell Cancer



30 yo male with gross hematuria cystic ccRCC. note para aortic lymphadenopathy



Bosniak Classification of Renal Cysts

BOSNIAK CLASSIFICATION	IMAGING CHARACTERISTICS	INCIDENCE OF MALIGNANCY	THERAPY
I	Simple cyst with a hairline thin wall that does not contain septa, calcifications, or solid components. It measures water density in Hounsfield units and does not enhance with intravenous administration of a contrast agent.	1.7%	No therapy or follow-up required
II	Cyst may contain a few hairline thin septa and fine calcifications, or a short segment of slightly thickened calcification may be present in the wall or septa. Uniformly high-attenuation lesions <3 cm (so-called high-density cysts) are well marginated and do not enhance with intravenous administration of a contrast agent.	18.5%	No therapy or follow-up required
IIF	Cysts may contain multiple hairline thin septa or minimal smooth thickening of their wall or septa. Their wall or septa may contain calcifications that may be thick and nodular, but no measurable contrast enhancement is present. These lesions are typically well marginated. Totally intrarenal nonenhancing high-attenuation renal lesions ≥3 cm are also included in this category.	18.5%	Repeat imaging to assess stability of size and radiographic characteristics
III	"Indeterminate" cystic masses have thickened irregular or smooth walls or septa in which measurable contrast enhancement is present.	33%	Excision or ablation
IV	Clearly malignant cystic masses can have all the criteria of category III but also contain enhancing soft-tissue components.	92.5%	Excision or ablation

Bosniak III & IV

- 67-100% are malignant
- the risk of malignancy is not clear-cut for Bosniak III and unnecessary surgery is a potential in up to 60% of lesions

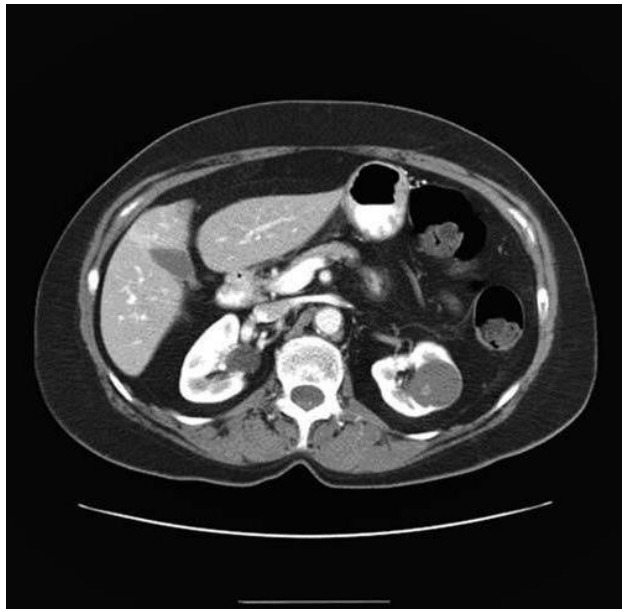
Bosniak Category

III IV IV

Which one is malignant?

1

2



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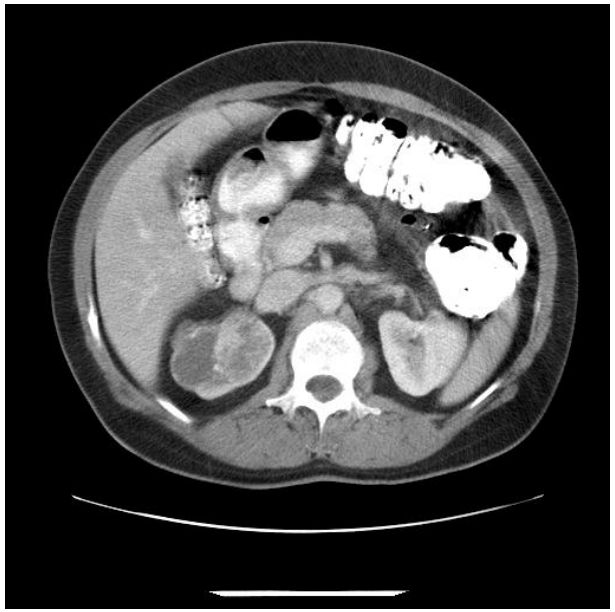

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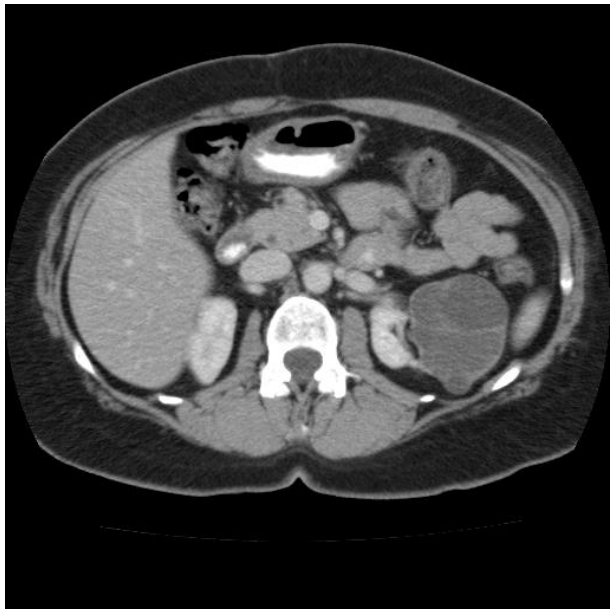
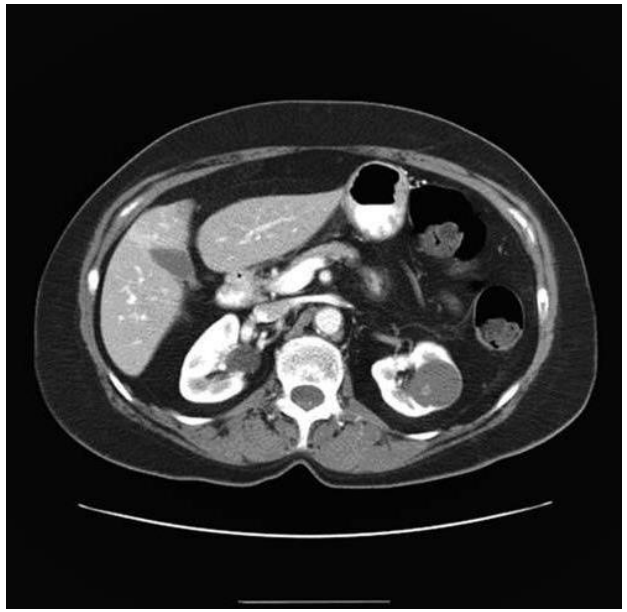


1

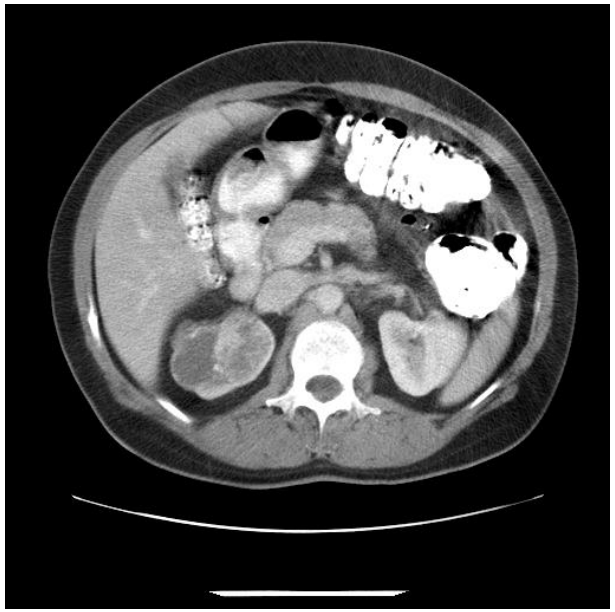
MEST

2



ccRCC

3



Benign Cystic

4

Epithelioid AML

Malignancy Rate, Histologic Grade, and Progression of Bosniak Category III and IV Complex Renal Cystic Lesions

Mousessian; et al.. *American Journal Of Roentgenology*, 2017 Dec; Vol. 209 (6), pp. 1285-1290

100 Cystic Renal Lesions

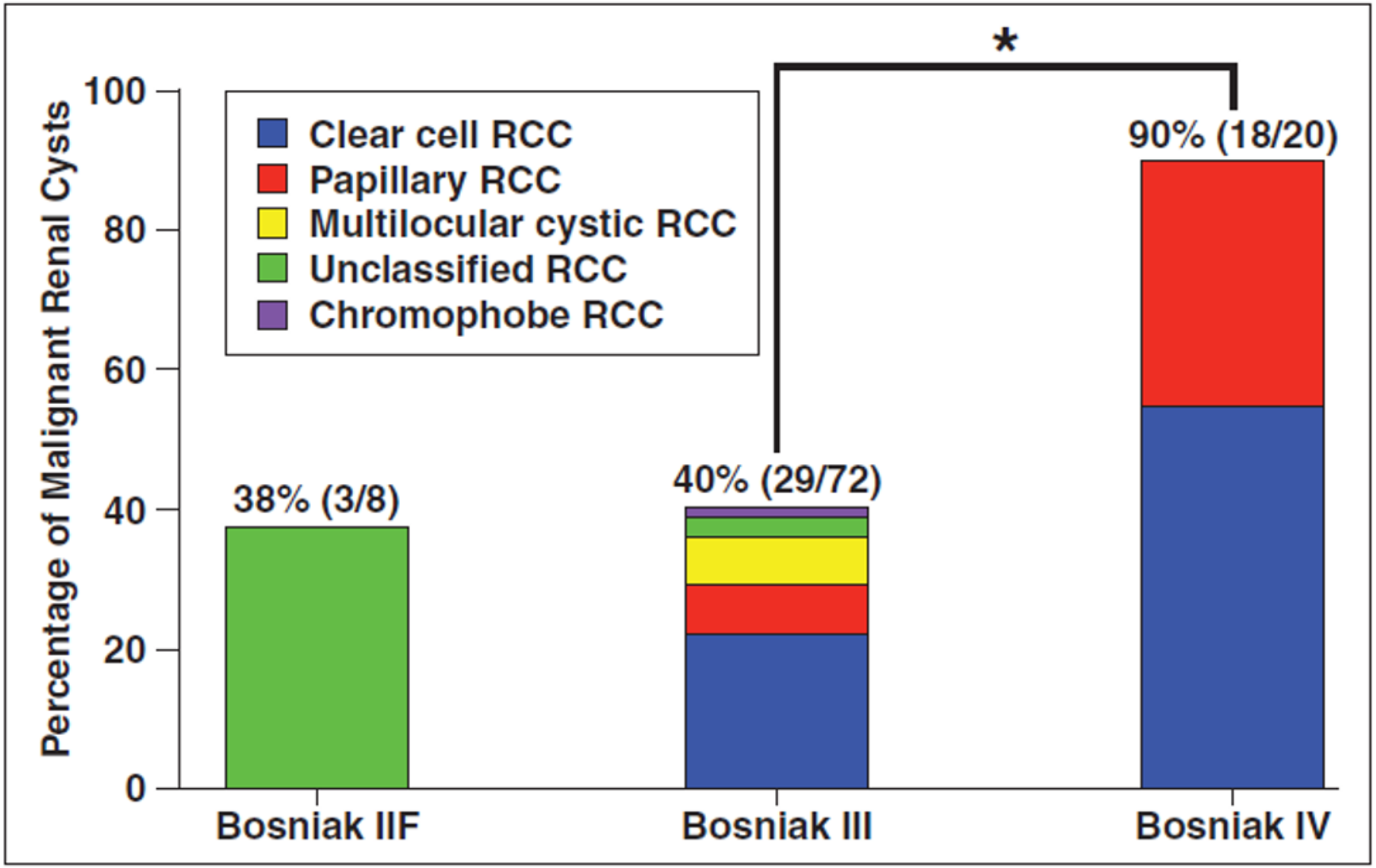


TABLE 2: Association Between Nuclear Grade and Bosniak Category

Fuhrman Nuclear Grade	Bosniak Category III	Bosniak Category IV	Total
1	36 (10/28)	11 (2/18)	26 (12/46)
2	61 (17/28)	72 (13/18)	65 (30/46)
3	4 (1/28)	17 (3/18)	9 (4/46)
4	0	0	0

Note—Data are percentage of lesions (no. of lesions/total lesions). Percentages do not total 100% because of rounding.

TABLE 3: Association Between TNM Staging and Bosniak Category

TNM Stage	Bosniak Category III	Bosniak Category IV	Total
pT1a	86 (24/28)	78 (14/18)	83 (38/46)
pT1b	7 (2/28)	6 (1/18)	7 (3/46)
pT2	7 (2/28)	17 (3/18)	11 (5/46)
pT3	0	0	0
pT4	0	0	0

Note—Data are percentage of lesions (no. of lesions/total lesions). Percentages do not total 100% because of rounding.

Management of High Risk Cystic Lesions of the Kidney

Outline

- Renal Mass Biopsy
- Management Strategy
  - Active Surveillance
  - Thermal Ablation
  - Surgery

MGH Experience with Image Guided Biopsies of High Risk Cystic Renal Lesions

Harisinghani et al AJR 2003;180

MGH Experience

CT guided small renal mass biopsies (n=392)

28 biopsies for Bosniak III lesions (1991-2000)

18 men 10 women

Results: 17 (60.7%) positive for malignancy

16 renal cell cancer, 1 lymphoma

11 (39.3%) Benign (hemorrhagic cysts, adenoma, oncocytoma)

- 16 were surgically excised all correlated with the biopsy
- 1 lymphoma responded appropriately to chemotherapy
- none of the benign lesions progressed on follow up (negative predictive value was 100%)
- recommend elderly with comorbidity small renal mass biopsy is indicated for Bosniak III lesions
- up to 40% of patients can avoid surgery or treatment, negative biopsy of lesions under surveillance have not progressed (negative predictive value 100%)

Active Surveillance for High Risk(Bosniak III / IV) Lesions

Assumption 1:

- lesion growth or change in character (complexity) increases likelihood of malignancy

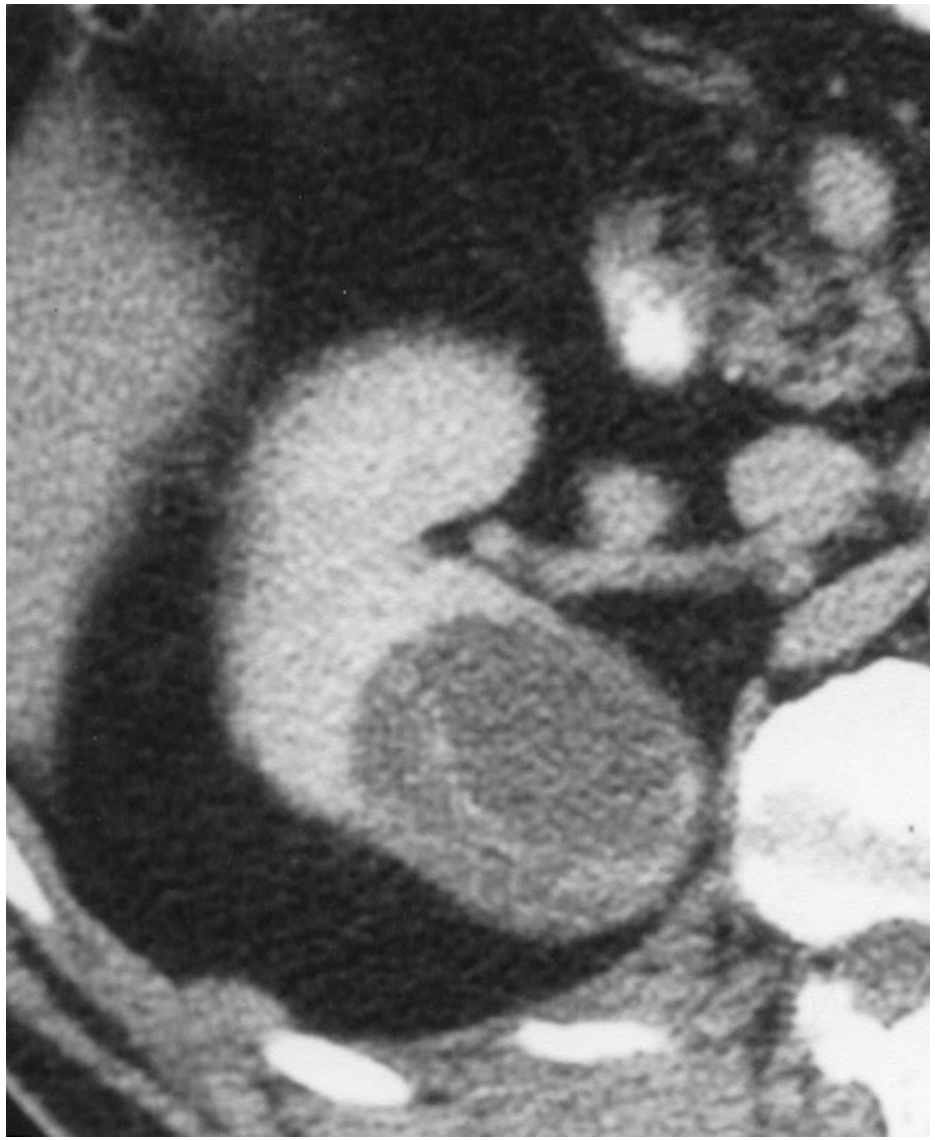
Assumption 2:

- Lesions are indolent and surveillance will not compromise outcome

Assumption 3:

- no change (stability) over 3-5 years then very low risk, (?) cease follow up

Progression = ↑ size and/or ↑ enhancement



Radiographic surveillance of minimally and moderately complex renal cysts

Gabr; et al.. *BJU International*, 2009 Apr; Vol. 103 (8), pp. 1116-9

- n=43 mean F/U 3 yrs
- 7 revealed progression, 39 no change
- lesion growth with no change in character 2

  1 malignancy

  1 benign
- lesion increase in character (hyperdense wall) enhancing nodule

  n=5 All were malignant
- 36 no change
- radiographic surveillance was effective, malignant lesions treated were still low grade

- active surveillance as per small renal mass protocol
- cross-sectional imaging CT/MRI every six months for three years, then yearly
- ensure stability reached; yearly for beyond midterm i.e. 5 years

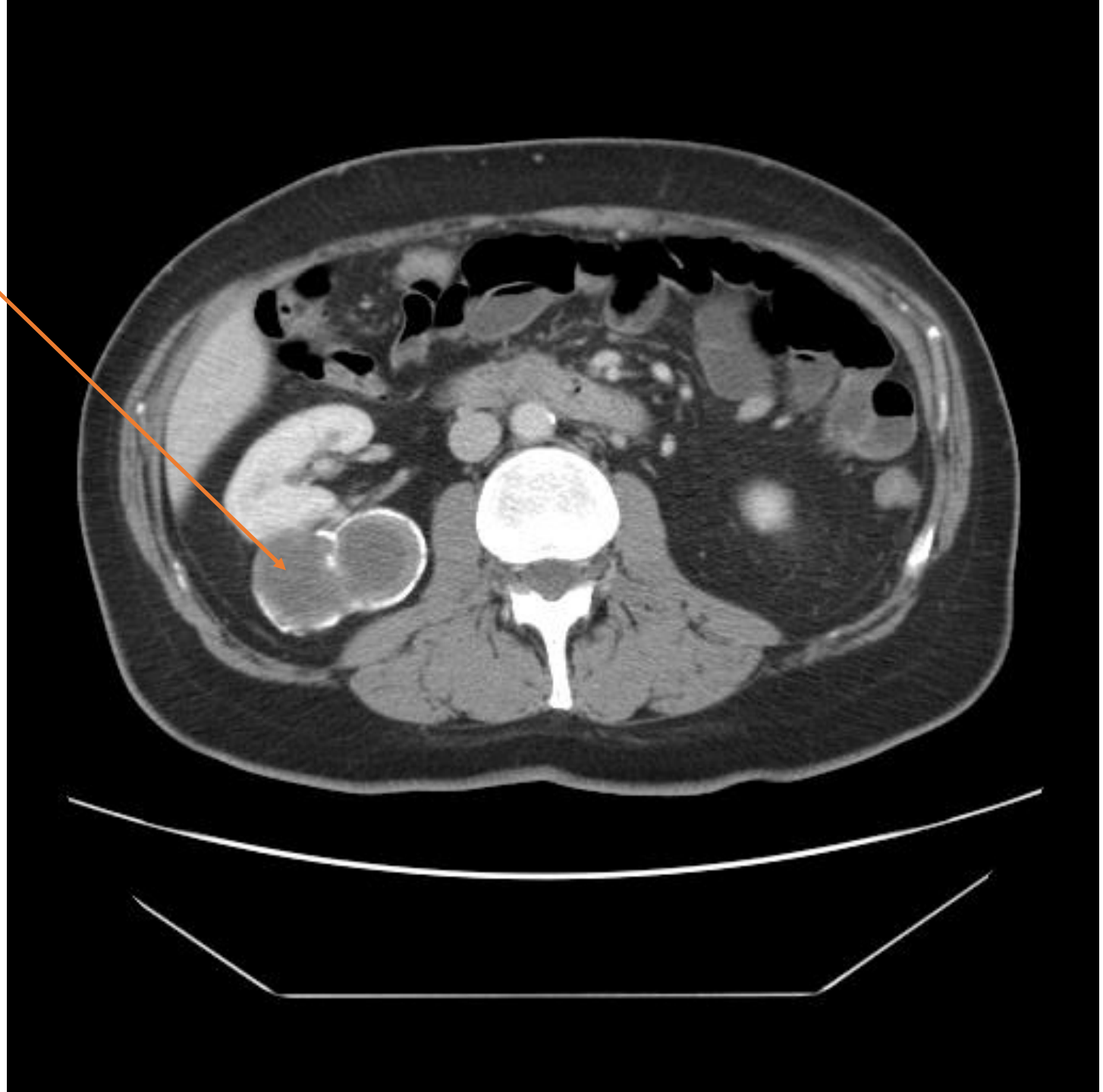
59 year old male

Calcified cystic mass

Right kidney

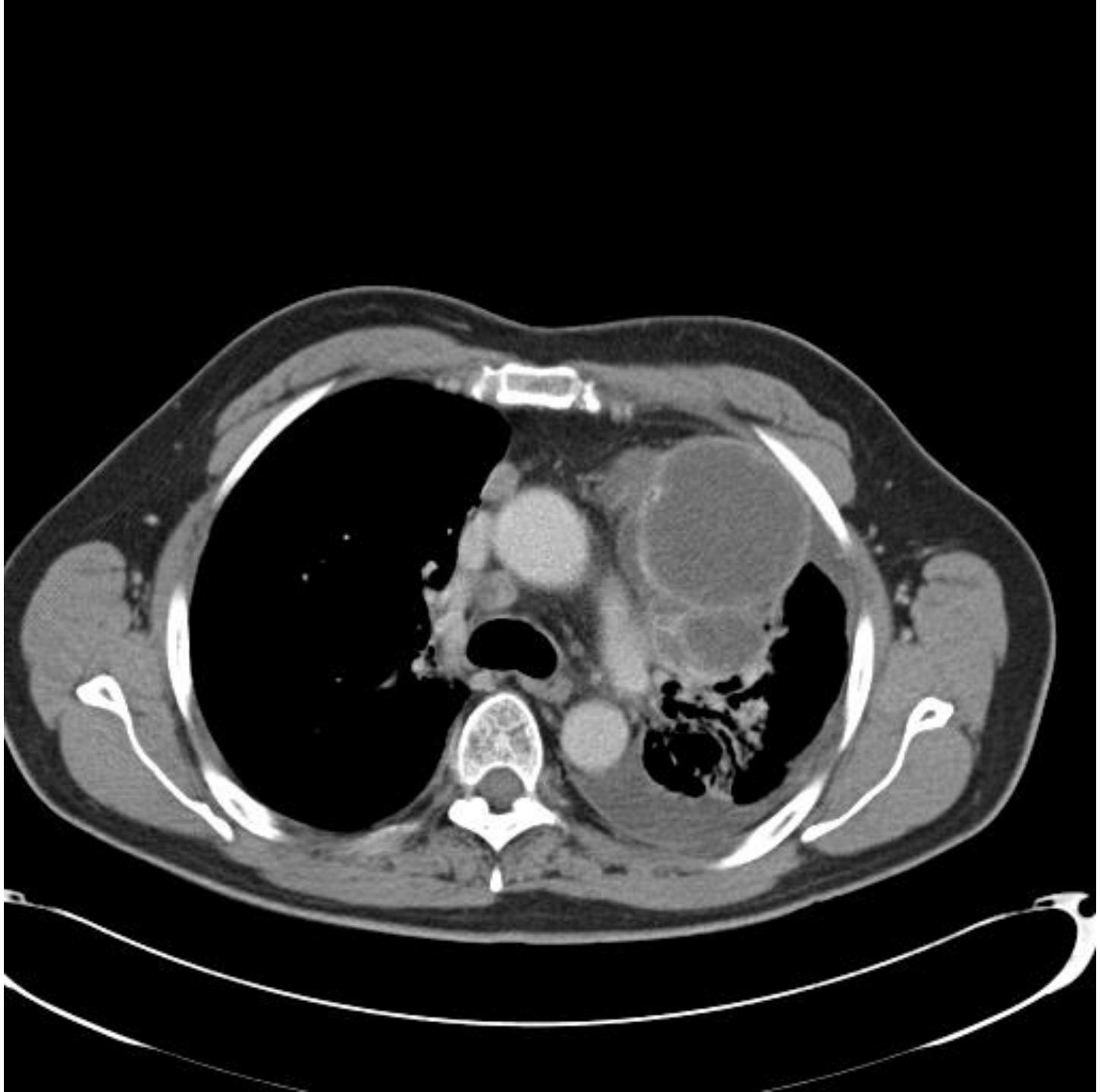
Surveillance 5 yrs

Stable D/C from clinic

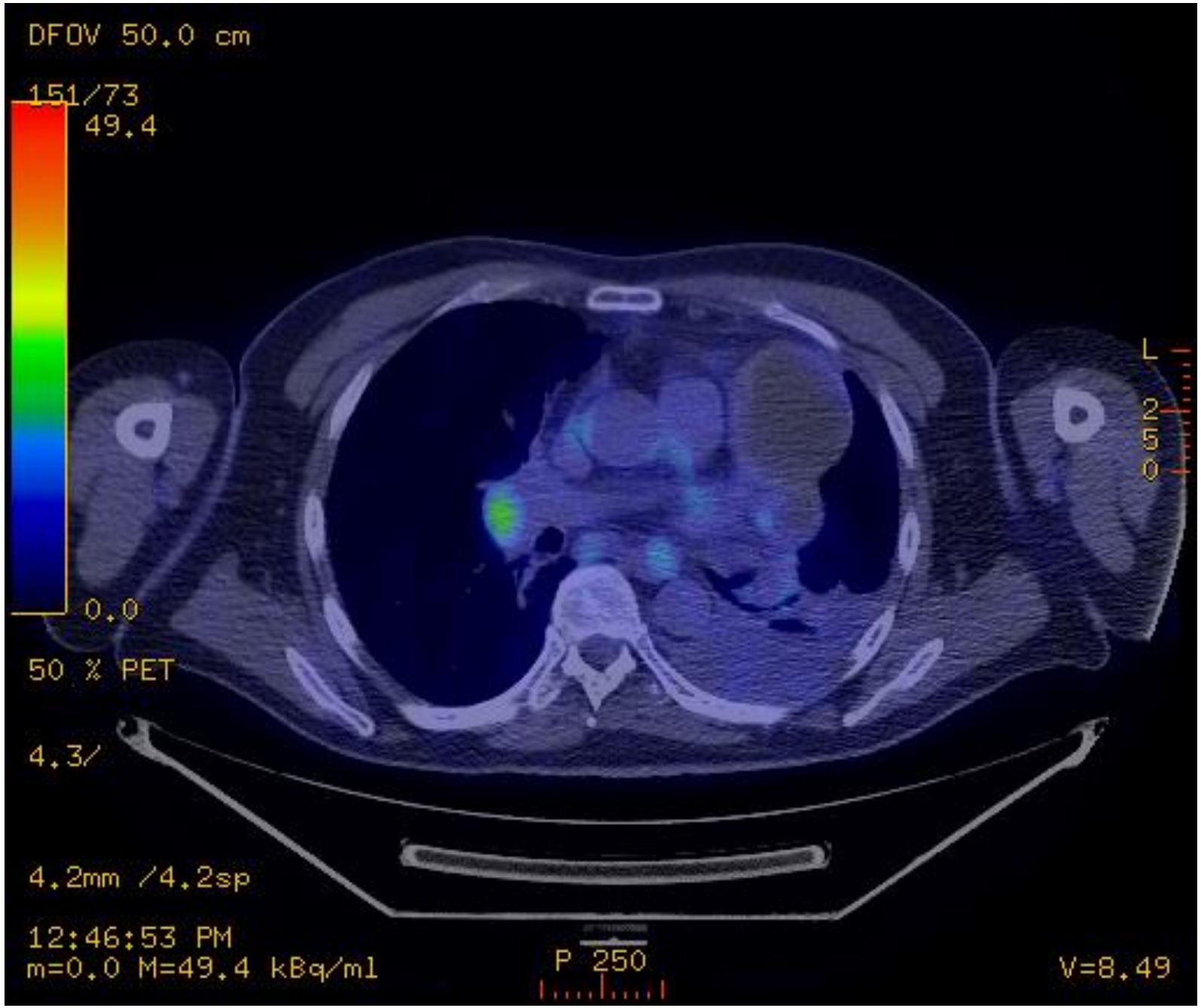


Managed by surveillance
11 years

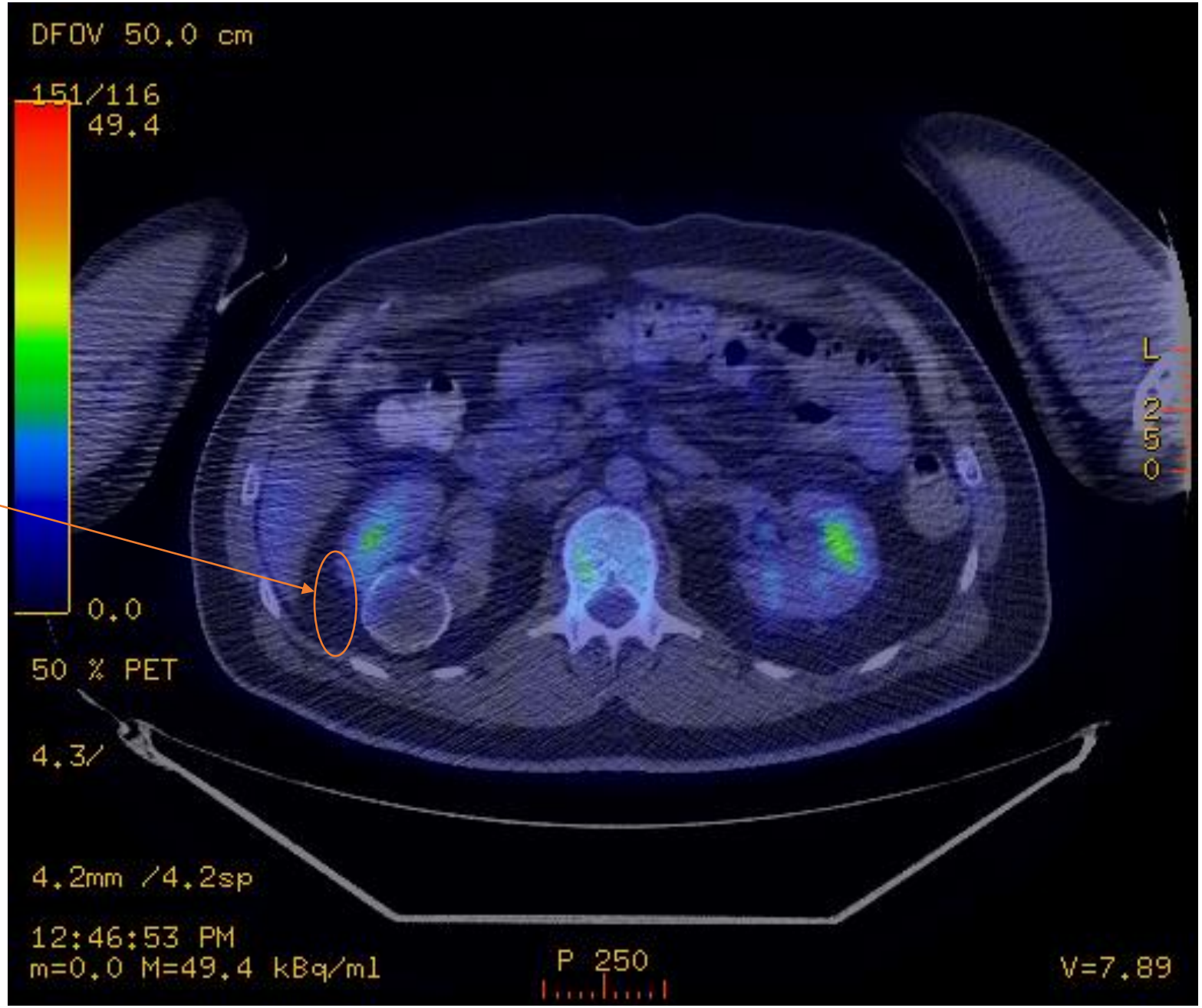
Presents with thoracic inlet mass



Mediastinum mets



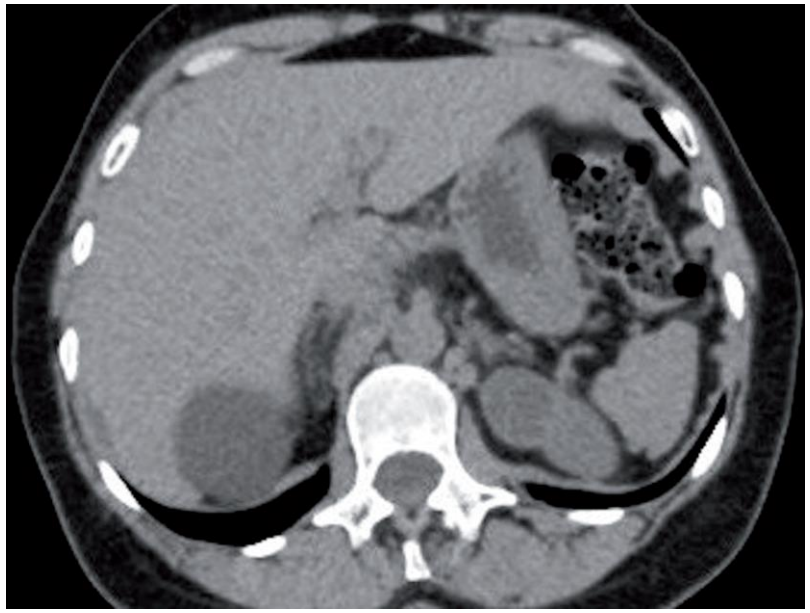
Isodense mass

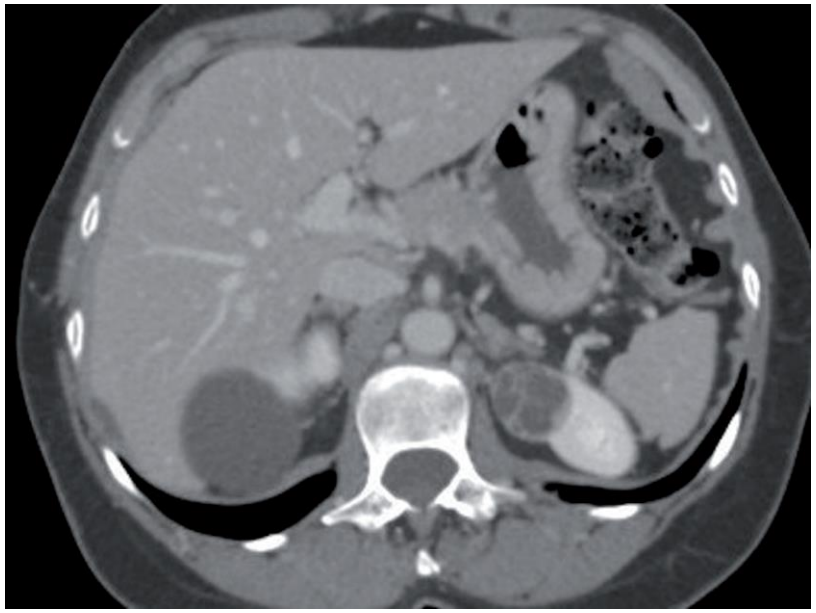


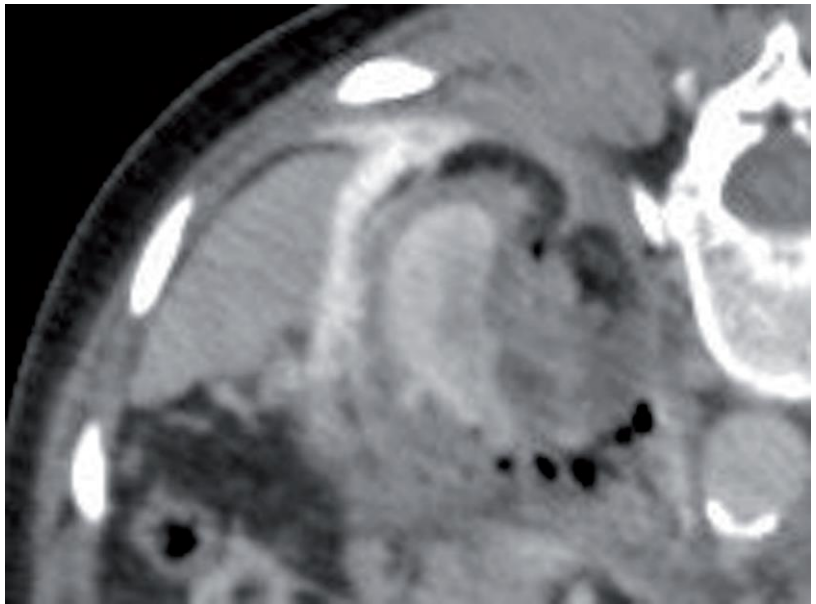
Thermal Ablation in Cystic Renal Lesions III and IV (Consider Percutaneous Biopsy)

- RFA
- Cryo ablation
- Microwave

Thermal Ablation Left Upper Pole Renal Mass







Complete Response = No Enhancement

Imaging-guided radiofrequency ablation of cystic renal neoplasms

Allen; et al.. *American Journal of Roentgenology*, 2013 Jun; 200(6): 1365-1369. 5p

Image Guided RFA Cystic Renal Mass

- n=38 mean F/U 2.8 yrs no progression
- non-surgical candidates (age, comorbidity)
- 61% malignancy by biopsy
- complications 5.3% one major CHF
- effective and safe treatment for cystic lesions

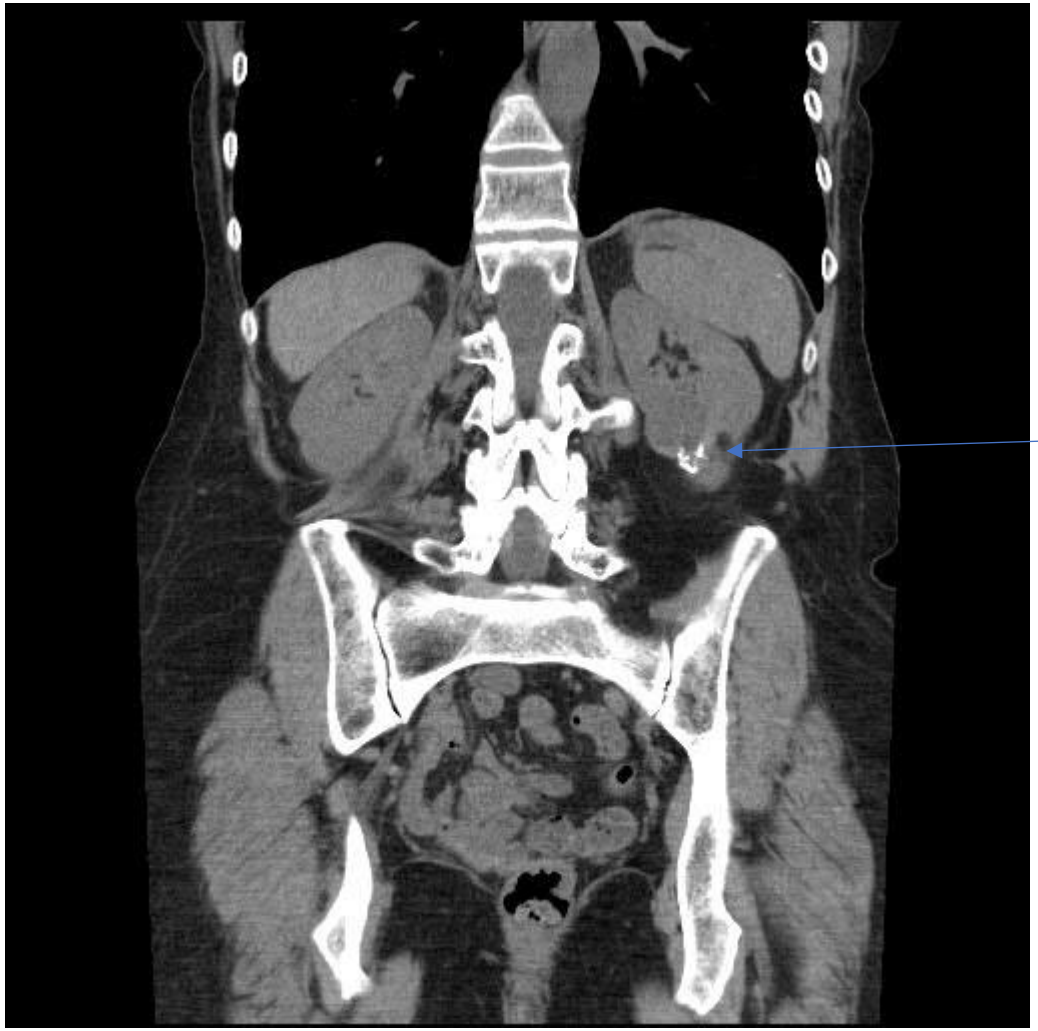
Surgical options for high risk cystic renal lesions

Principals of small renal mass management*

- Radical Nephrectomy
- Partial Nephrectomy (nephron sparing surgery)
- Open
- Laproscopic or Robotic

*caveat: consider nephrons sparing surgery for large (≥1b) cystic lesions as long-term response is excellent

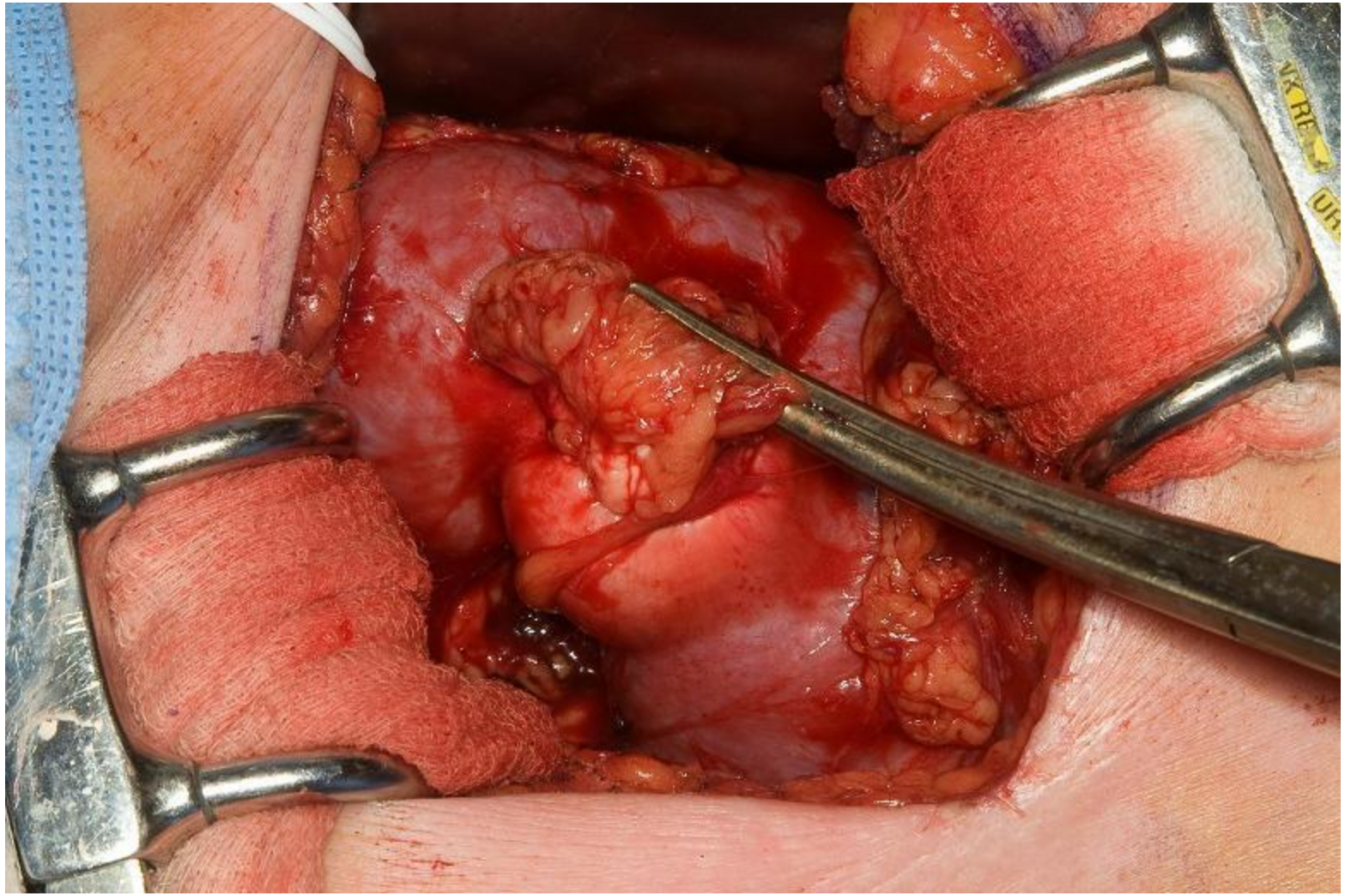
52 YO Male with Left Flank Pain/ Hematuria



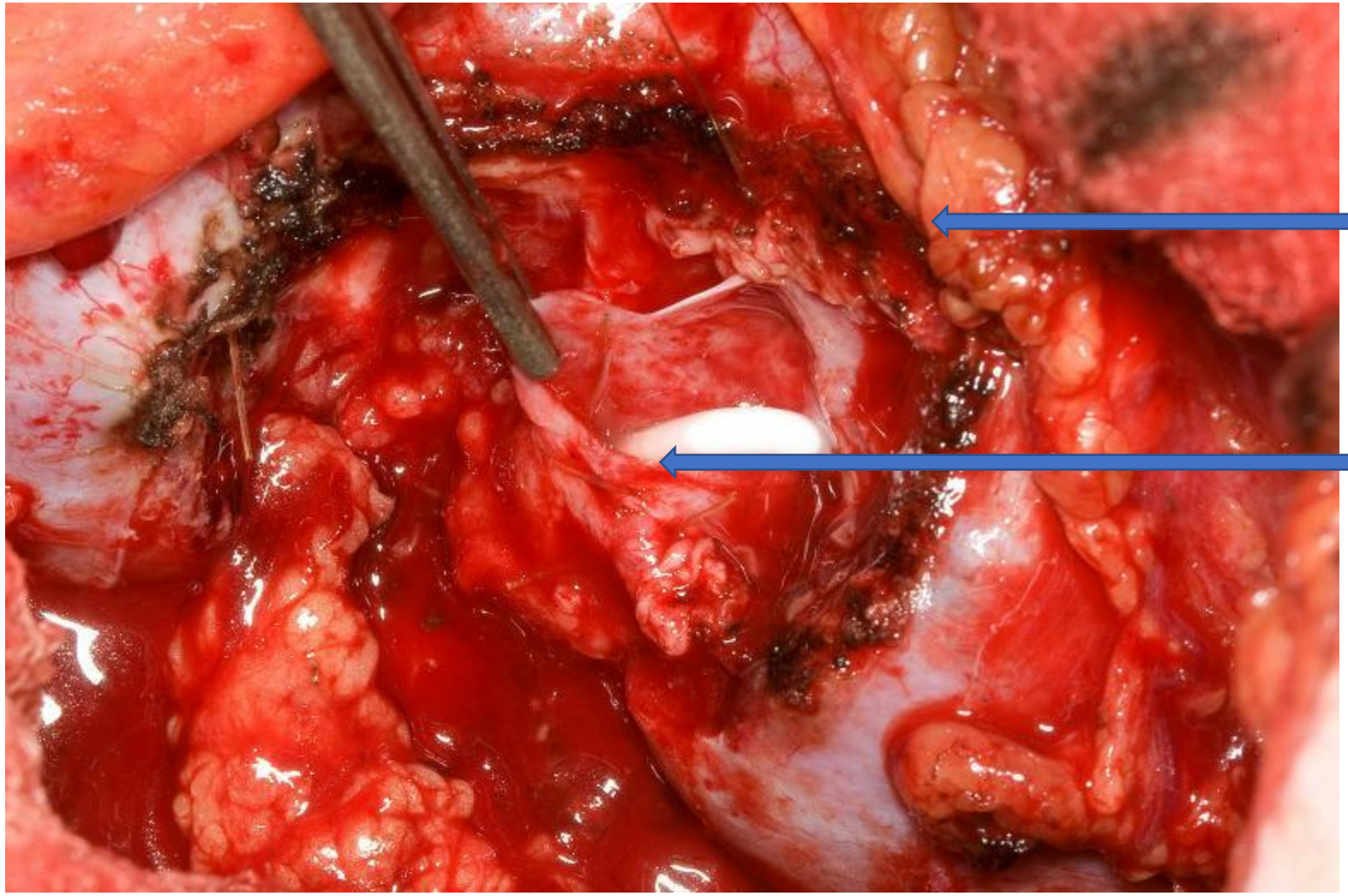
Calcified Mid Pole Lesion

Filling Defect Left Renal Pelvic Cystic Lesion

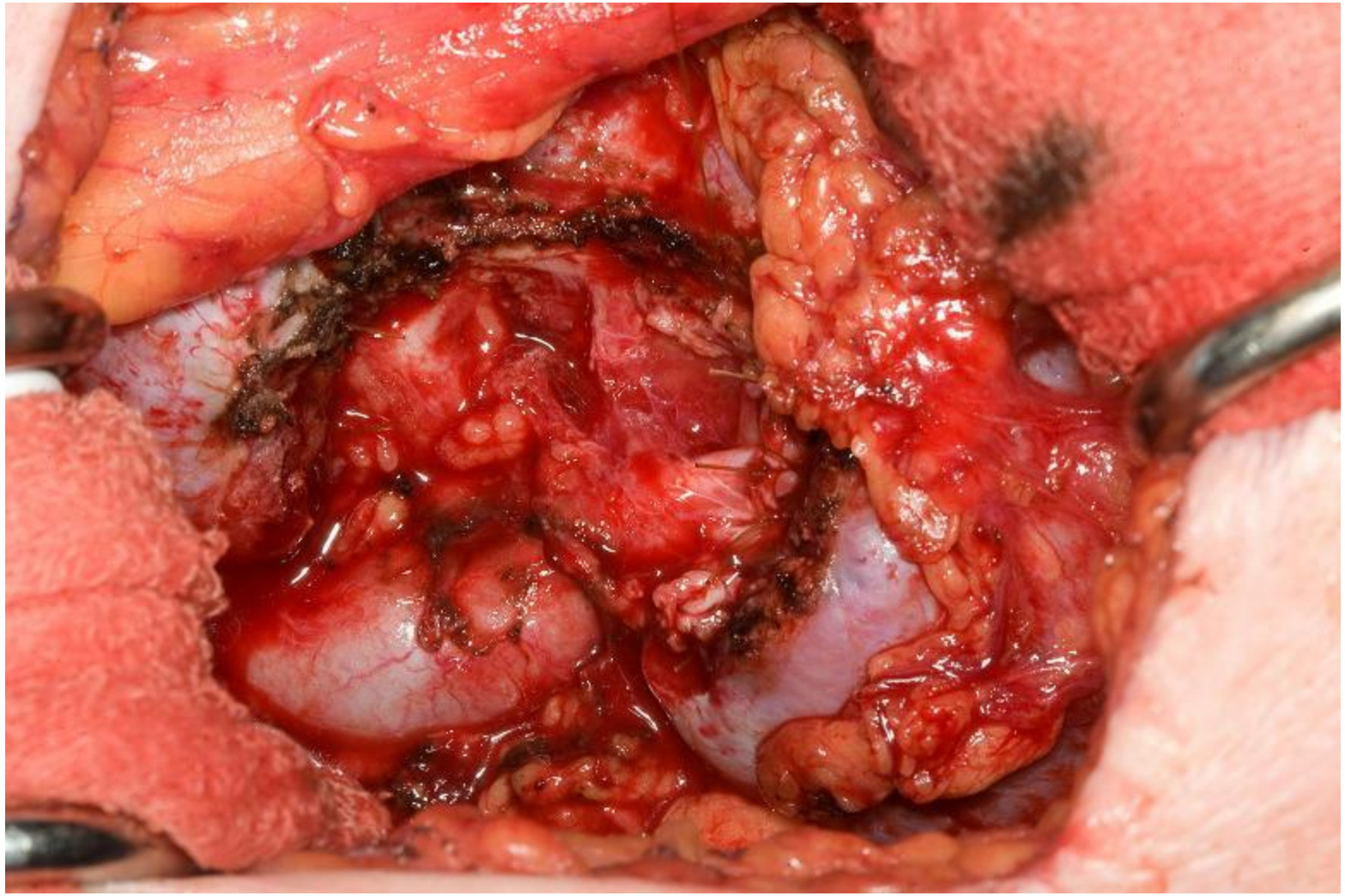
Lesion Exposed through Mini Flank Incision



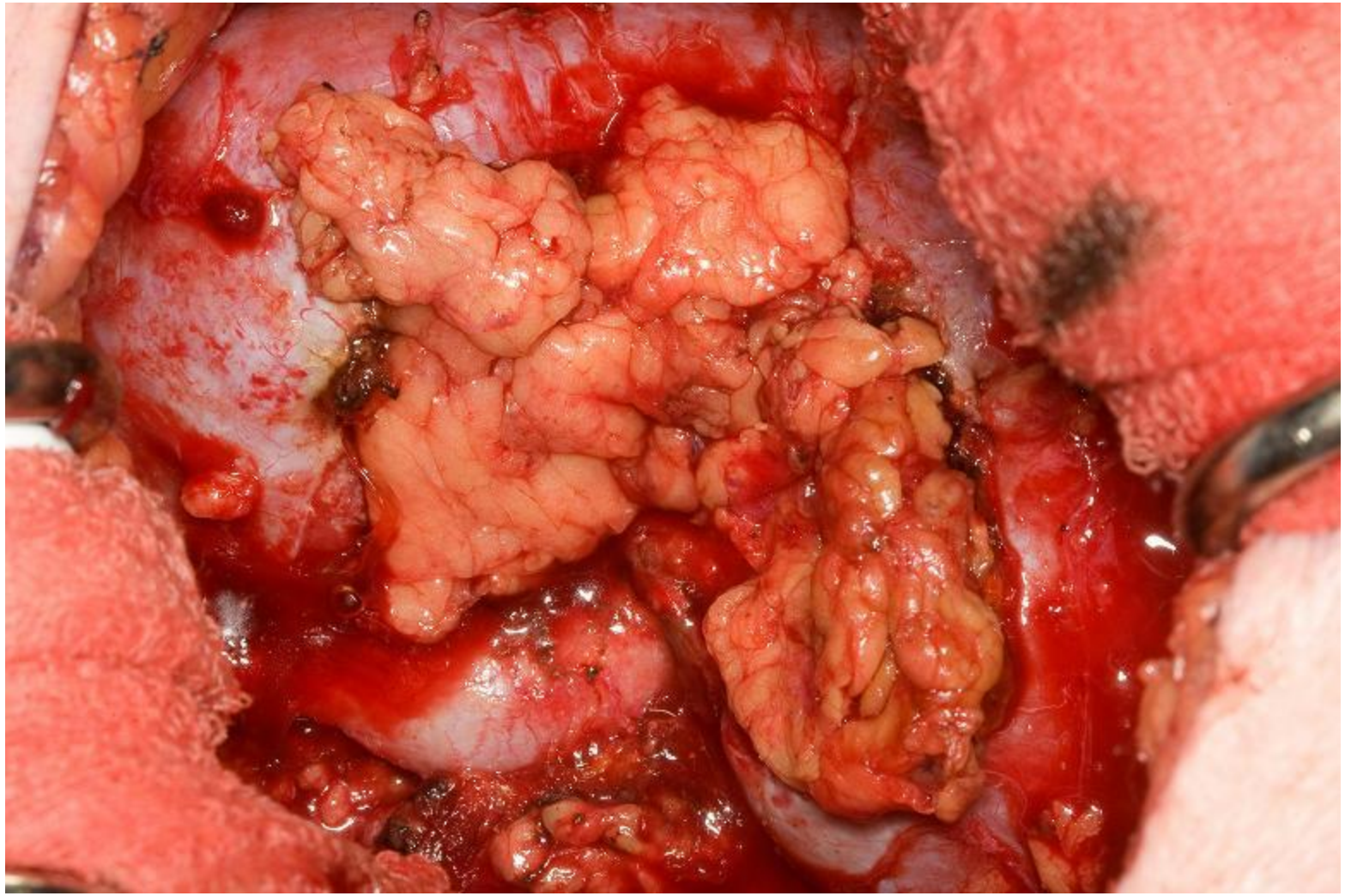
Frozen Section Negative



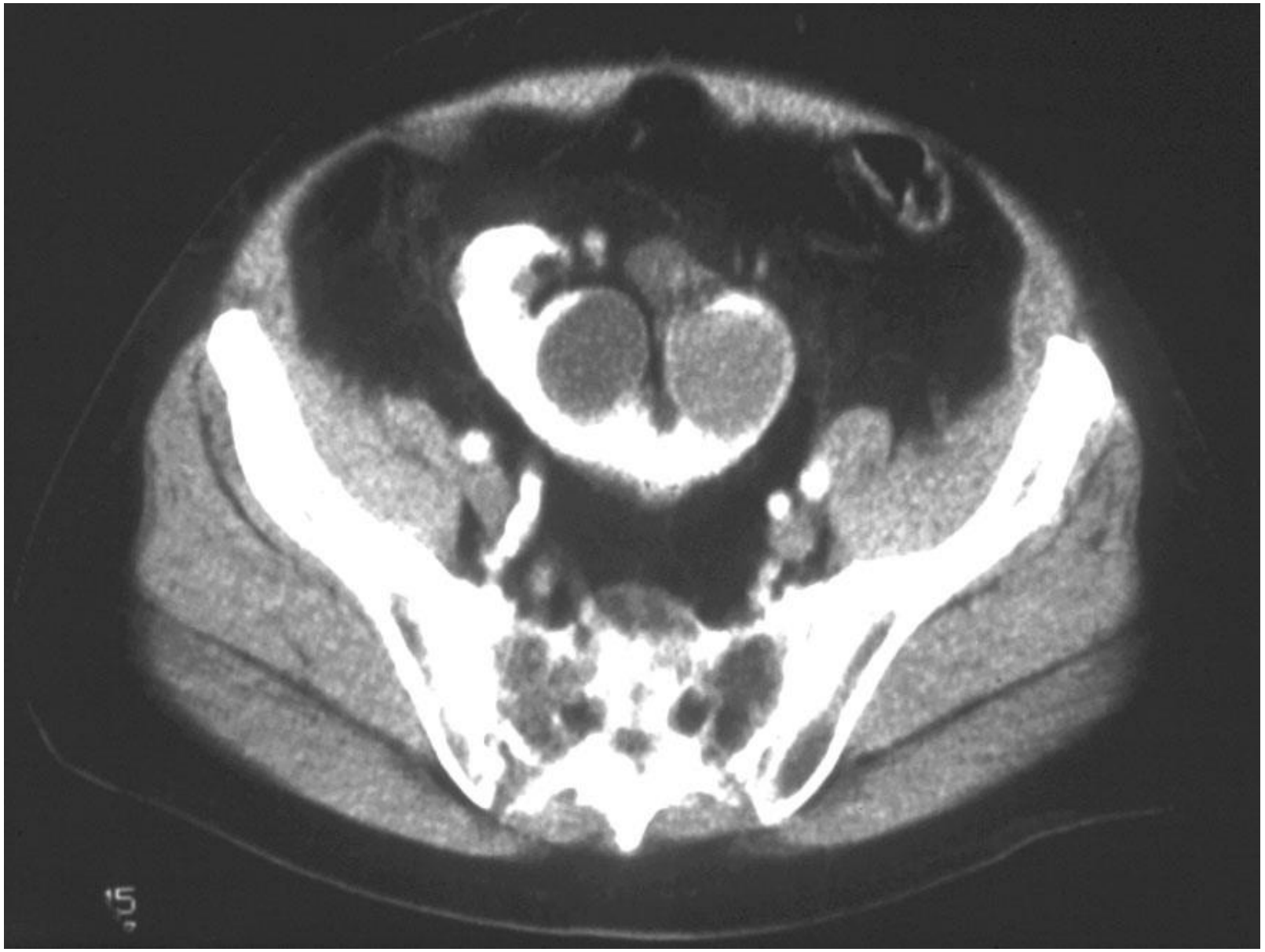
Stent and Renal Pelvis Reconstruction



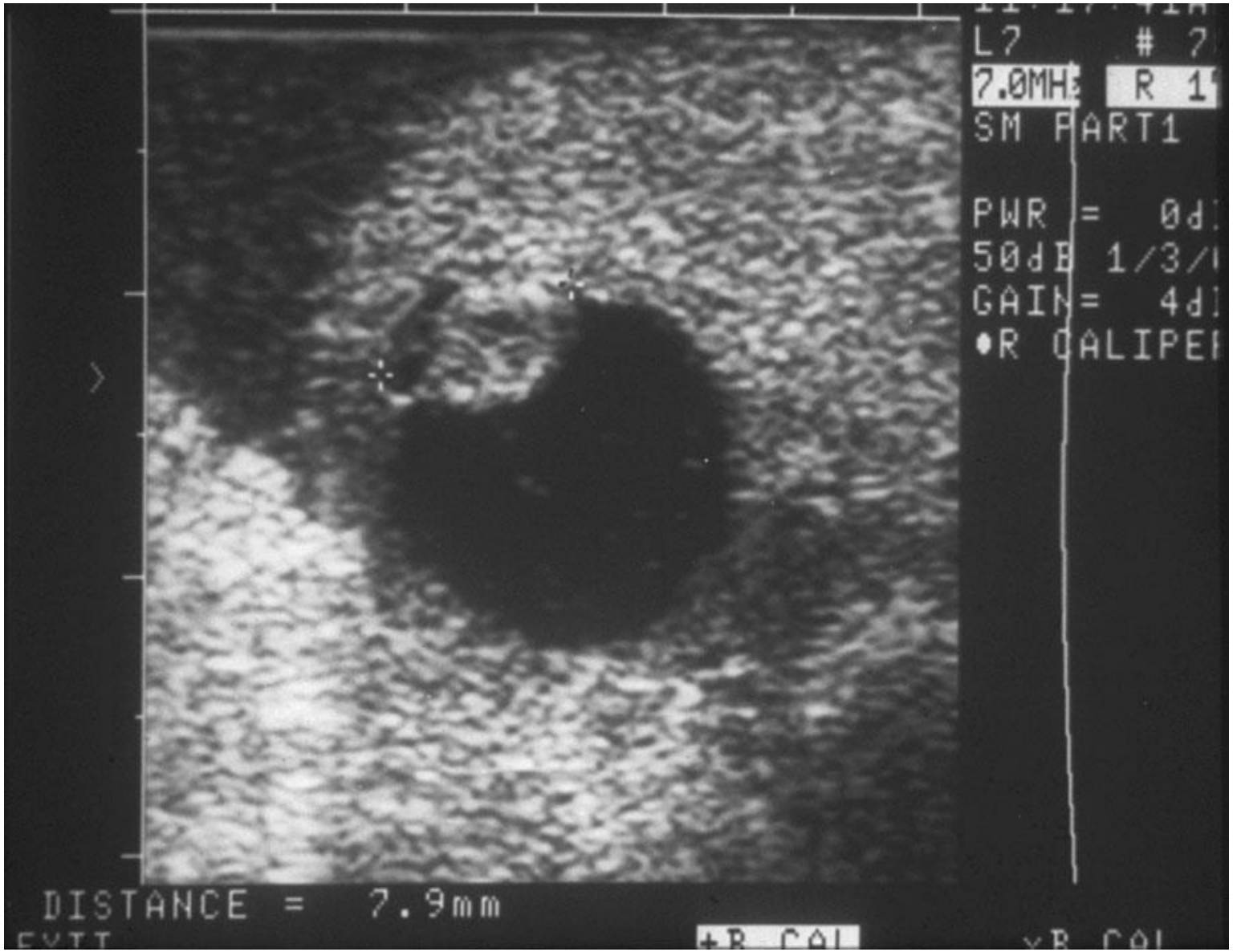
Renal Pelvis Perinephric Fat Patch

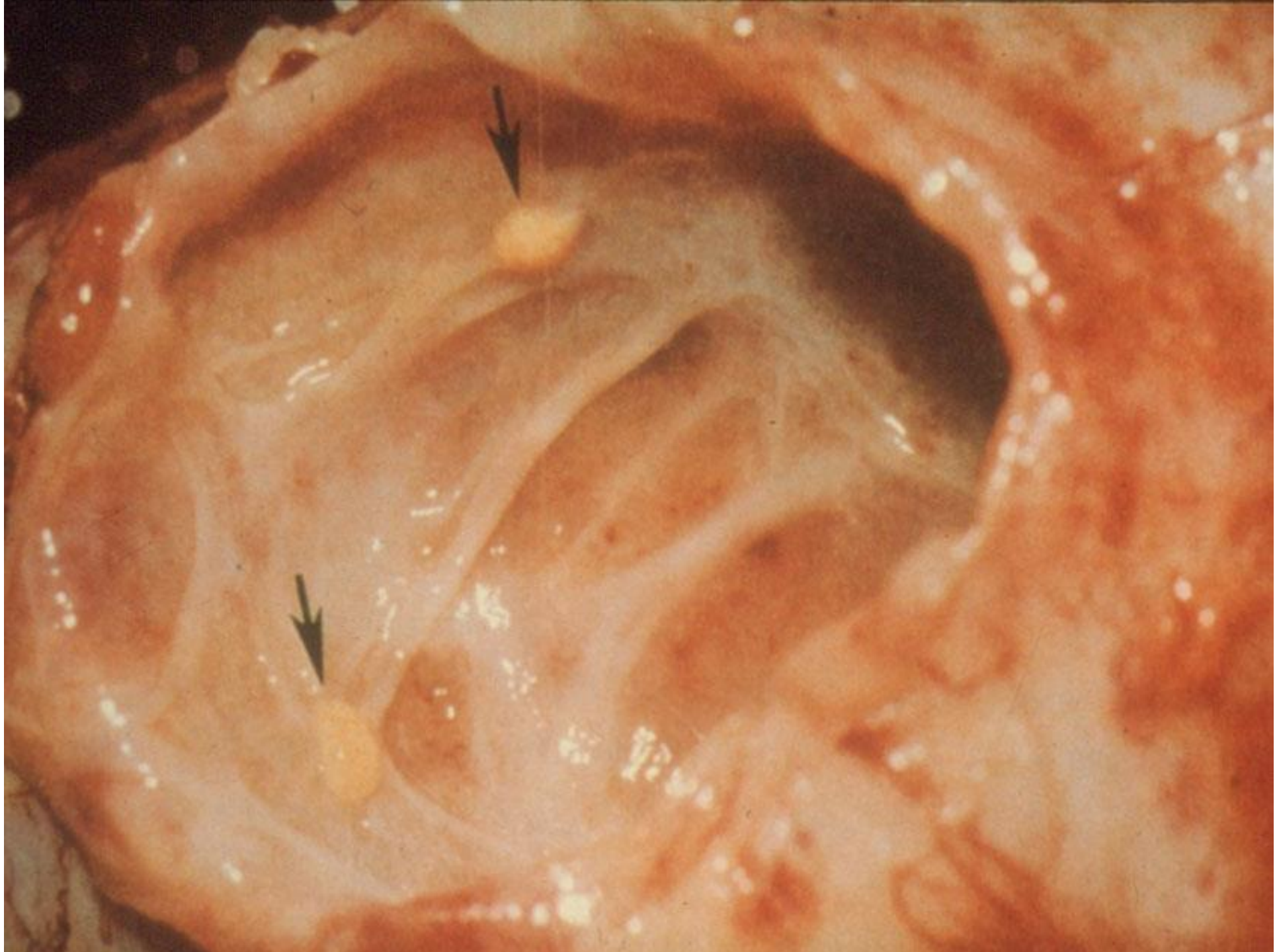


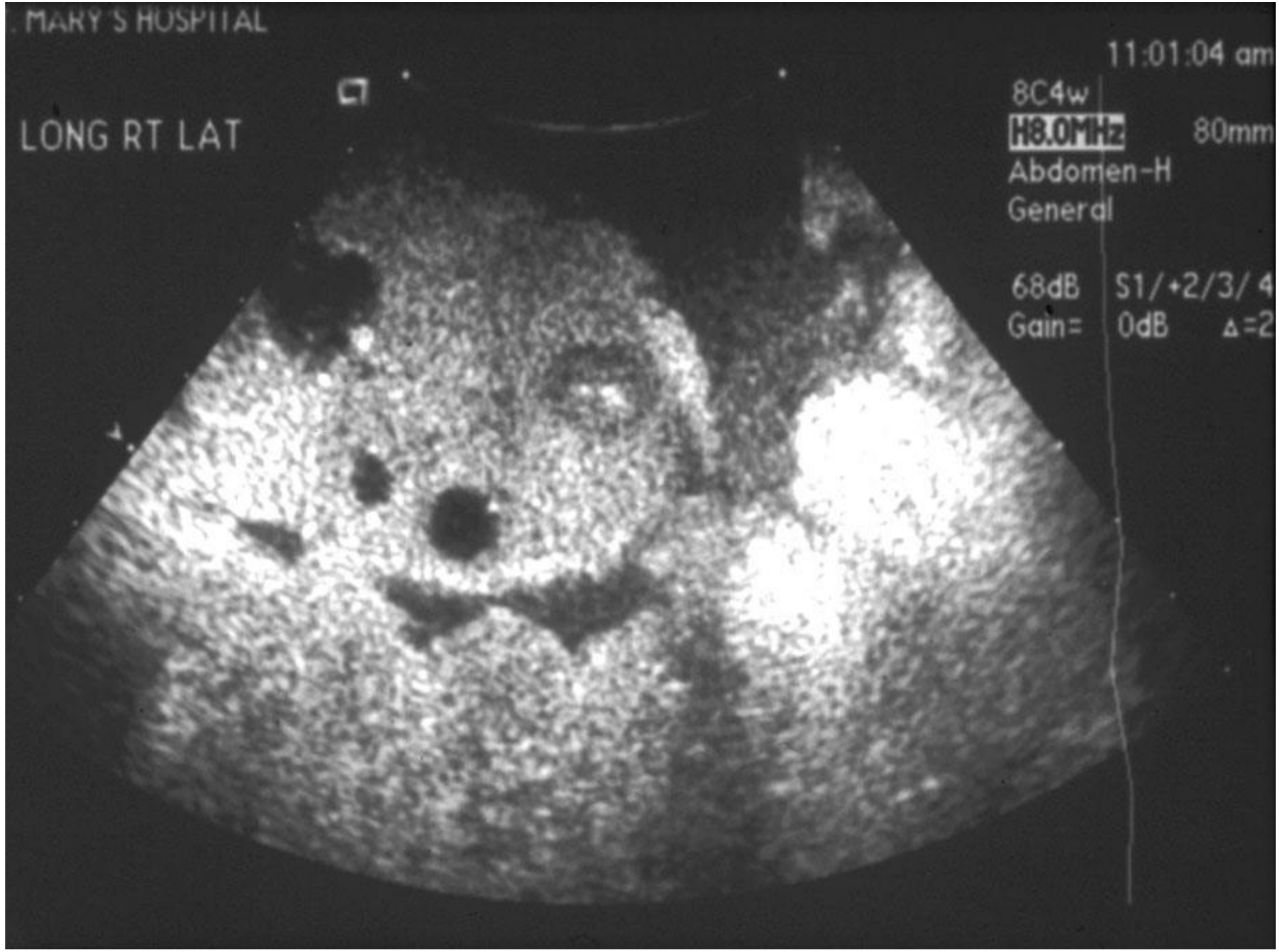
Ectopic Solitary Pelvic Kidney with Solid/Cystic Mass



Intraoperative Ultrasound



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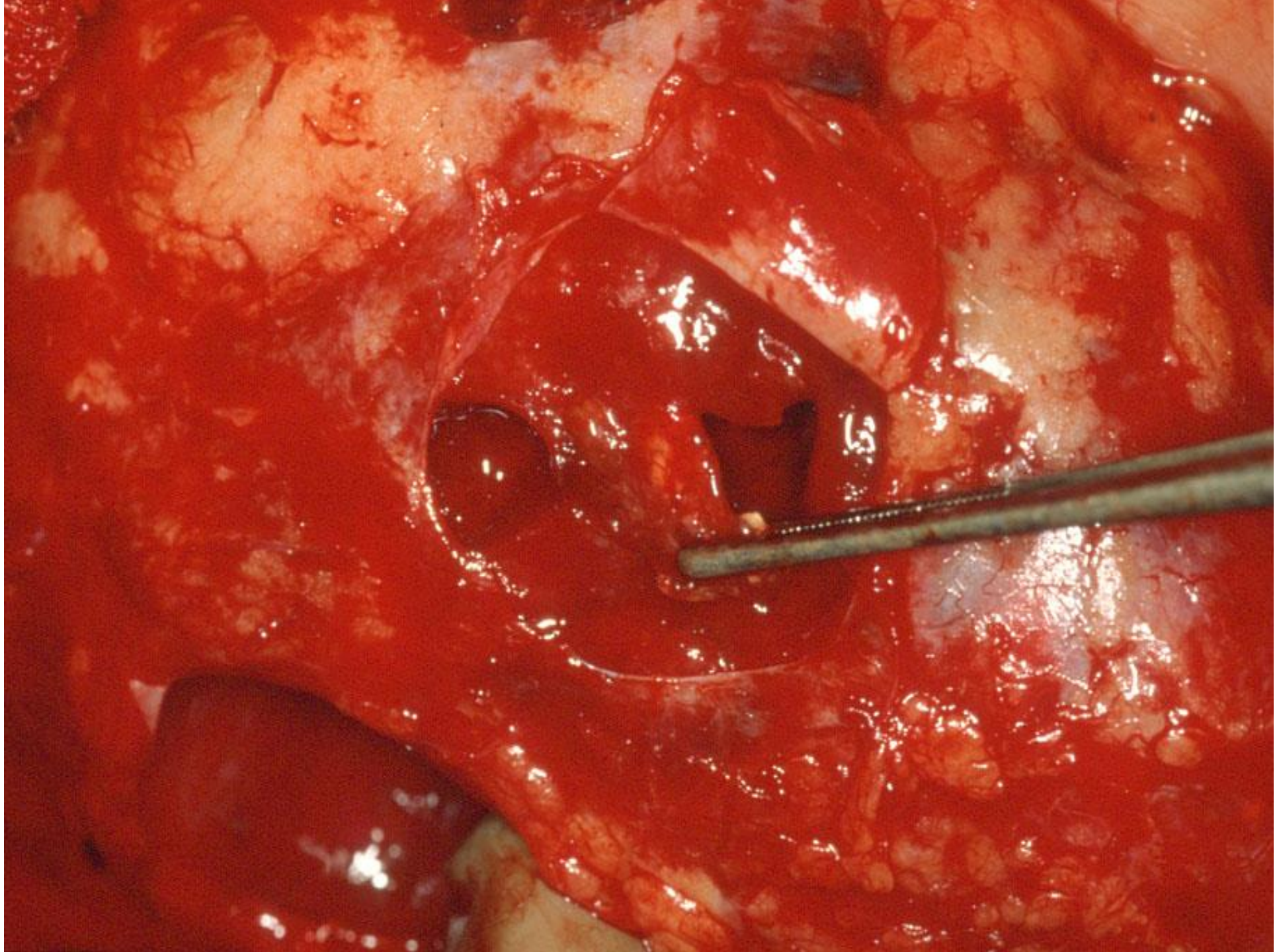
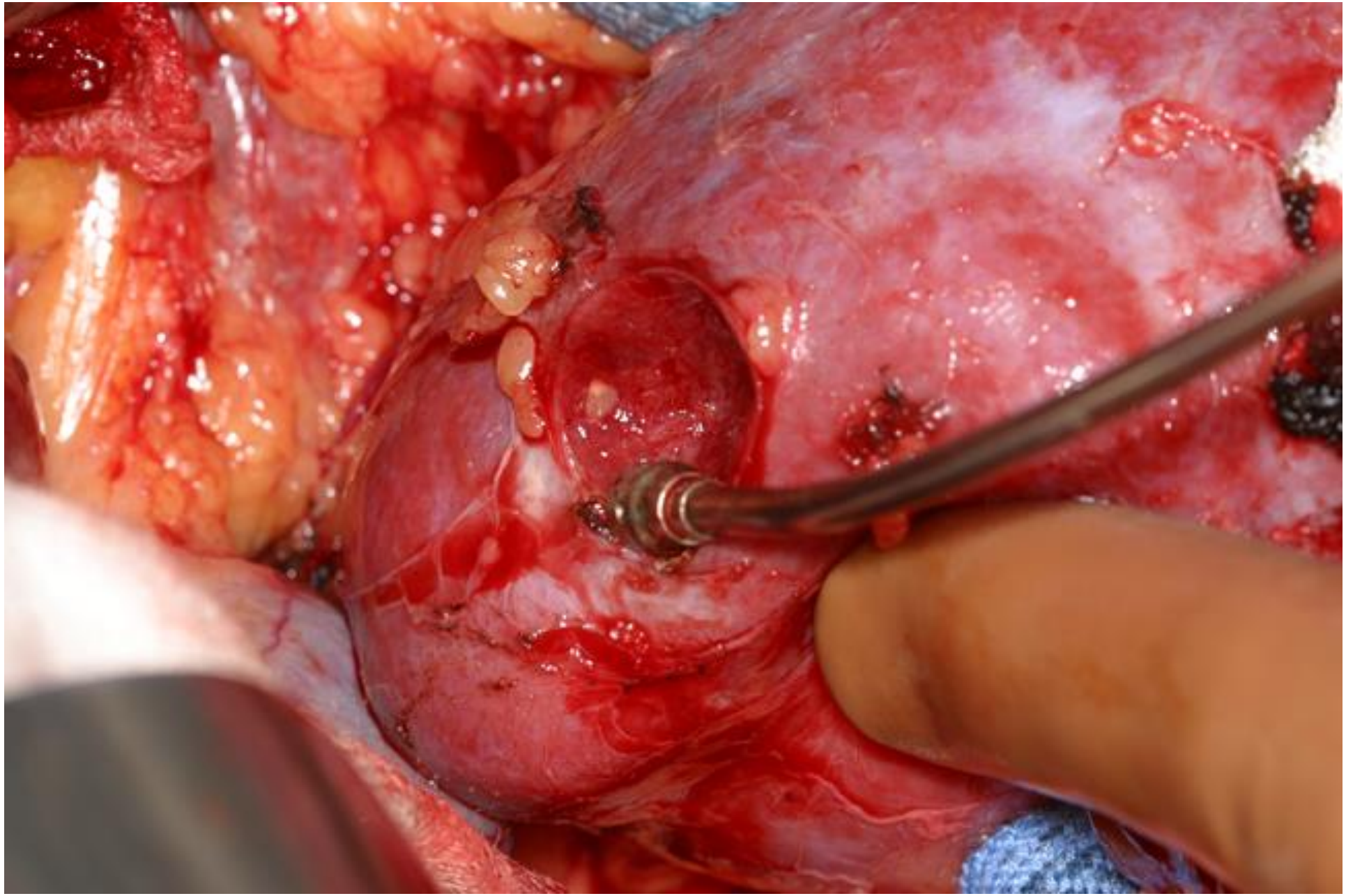
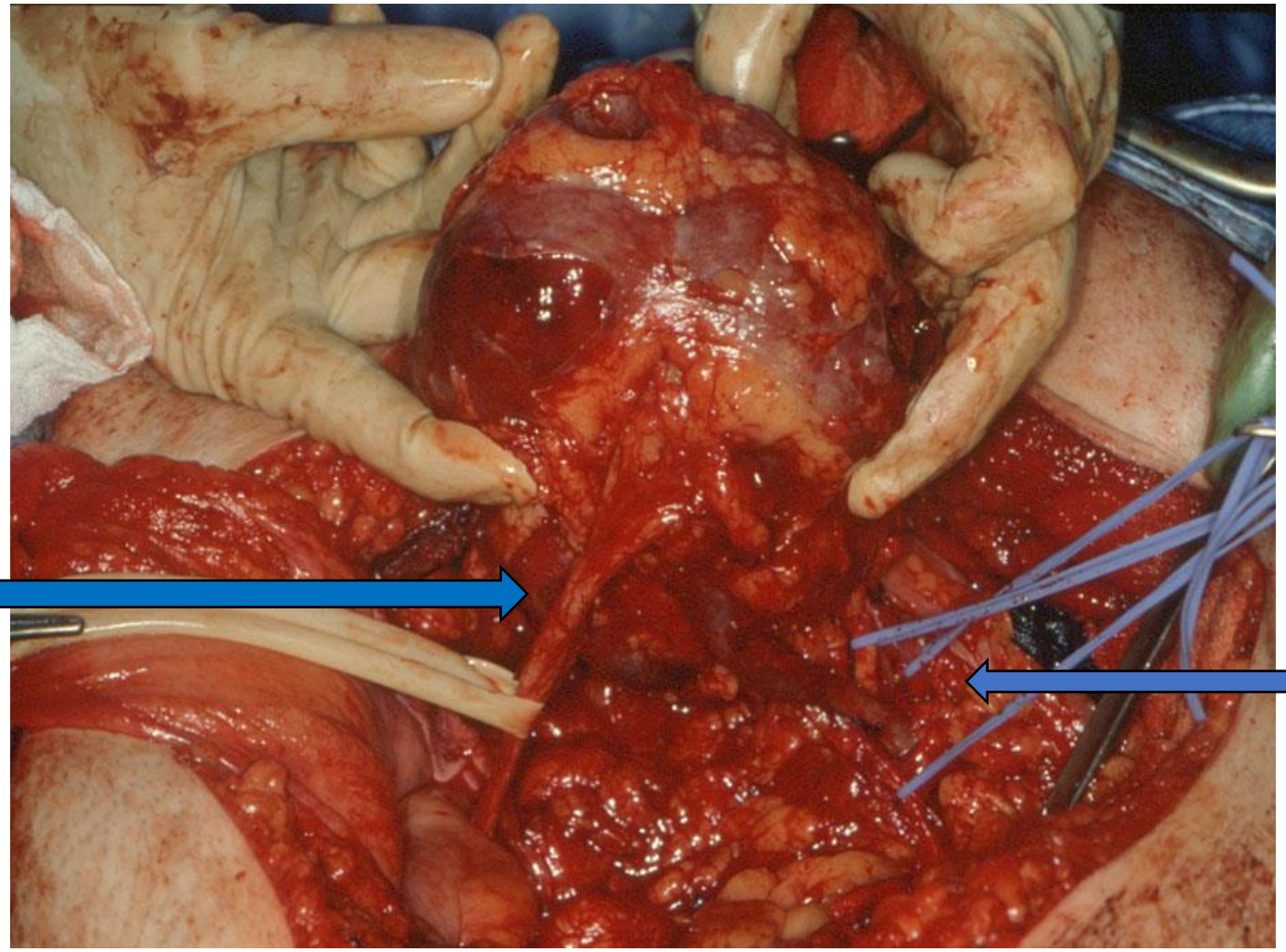


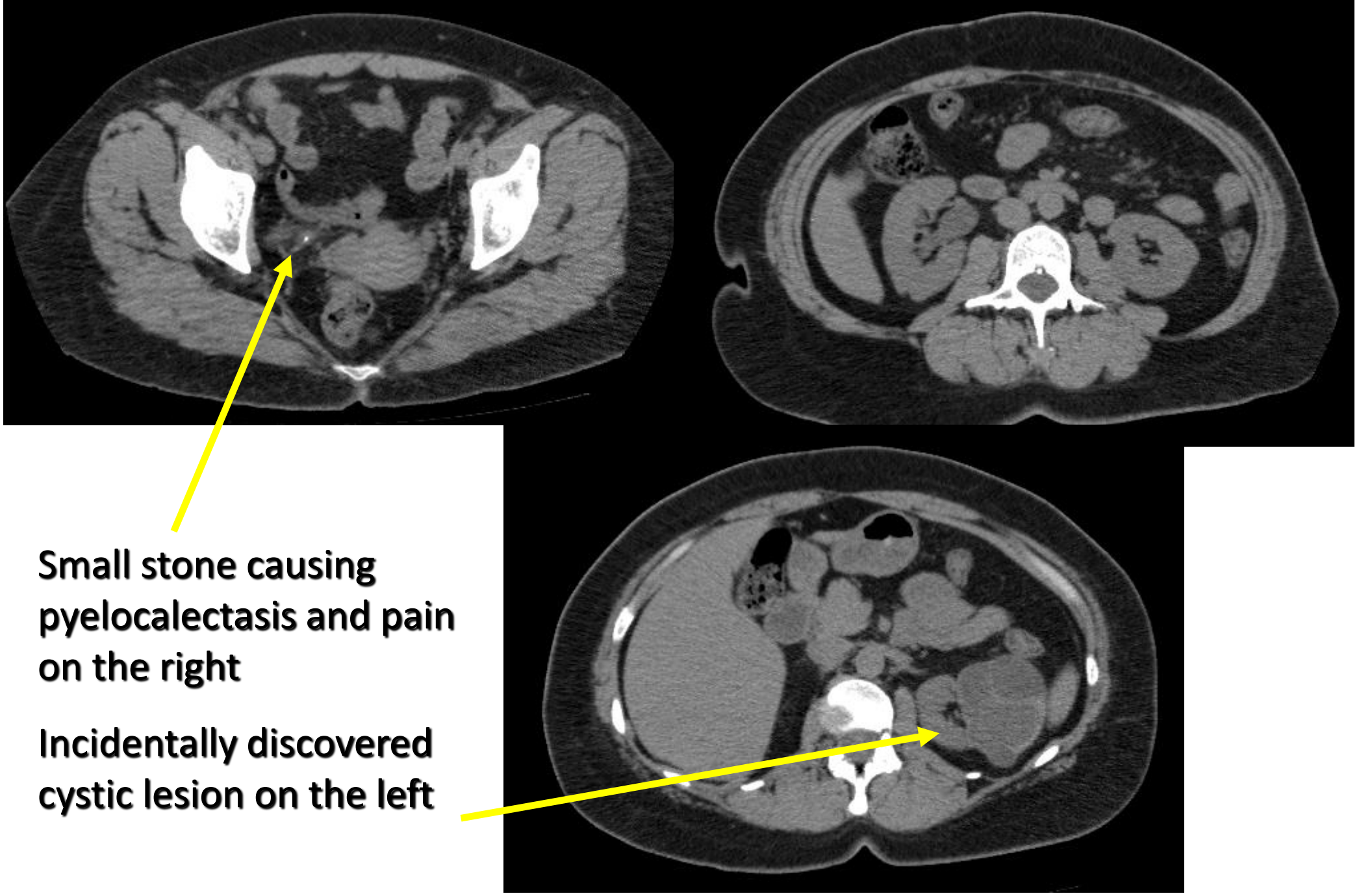


Ectopic Pelvic Kidney



History of present illness

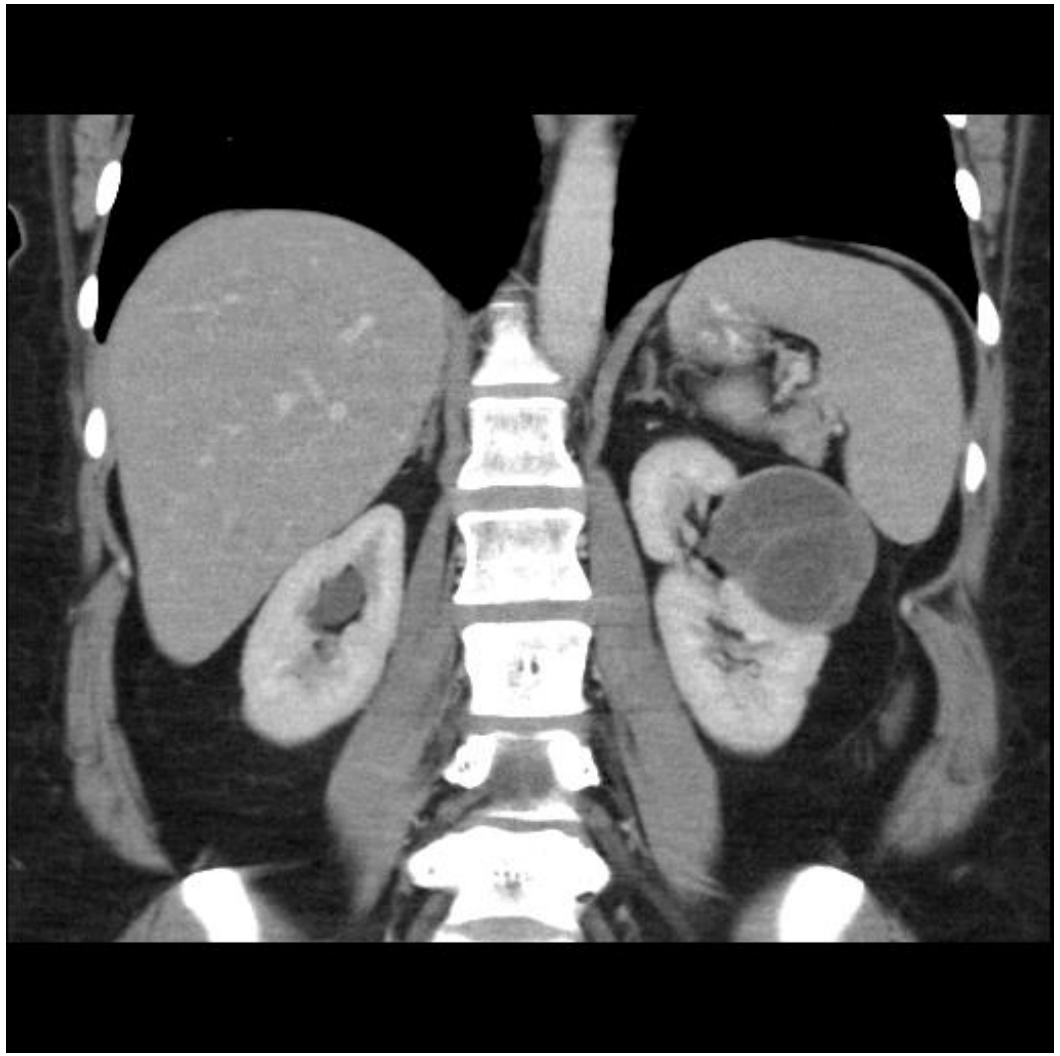
- Healthy 57 year old female
- Acute onset of right flank pain
- CT scan obtained



Small stone causing pyelocalectasis and pain on the right

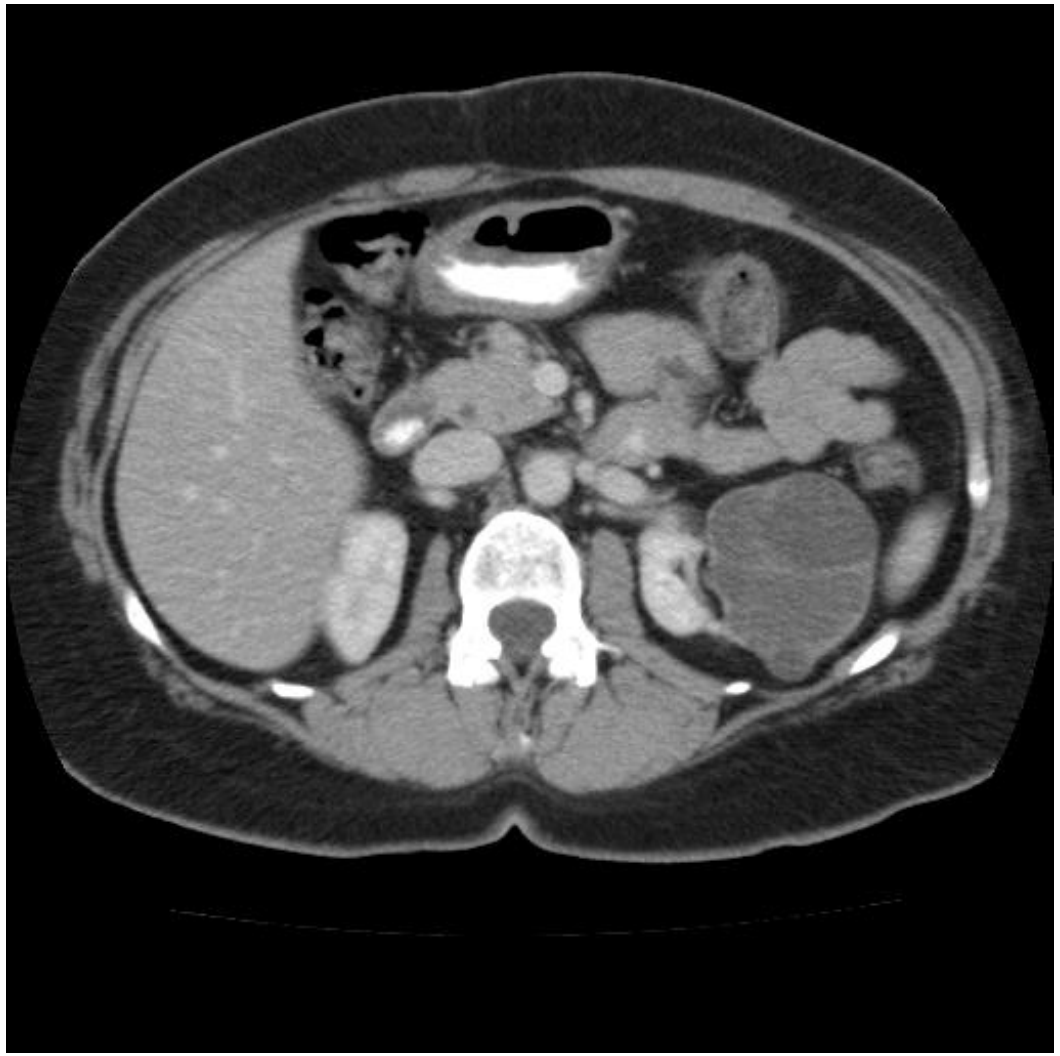
Incidentally discovered cystic lesion on the left

Cystic renal lesion

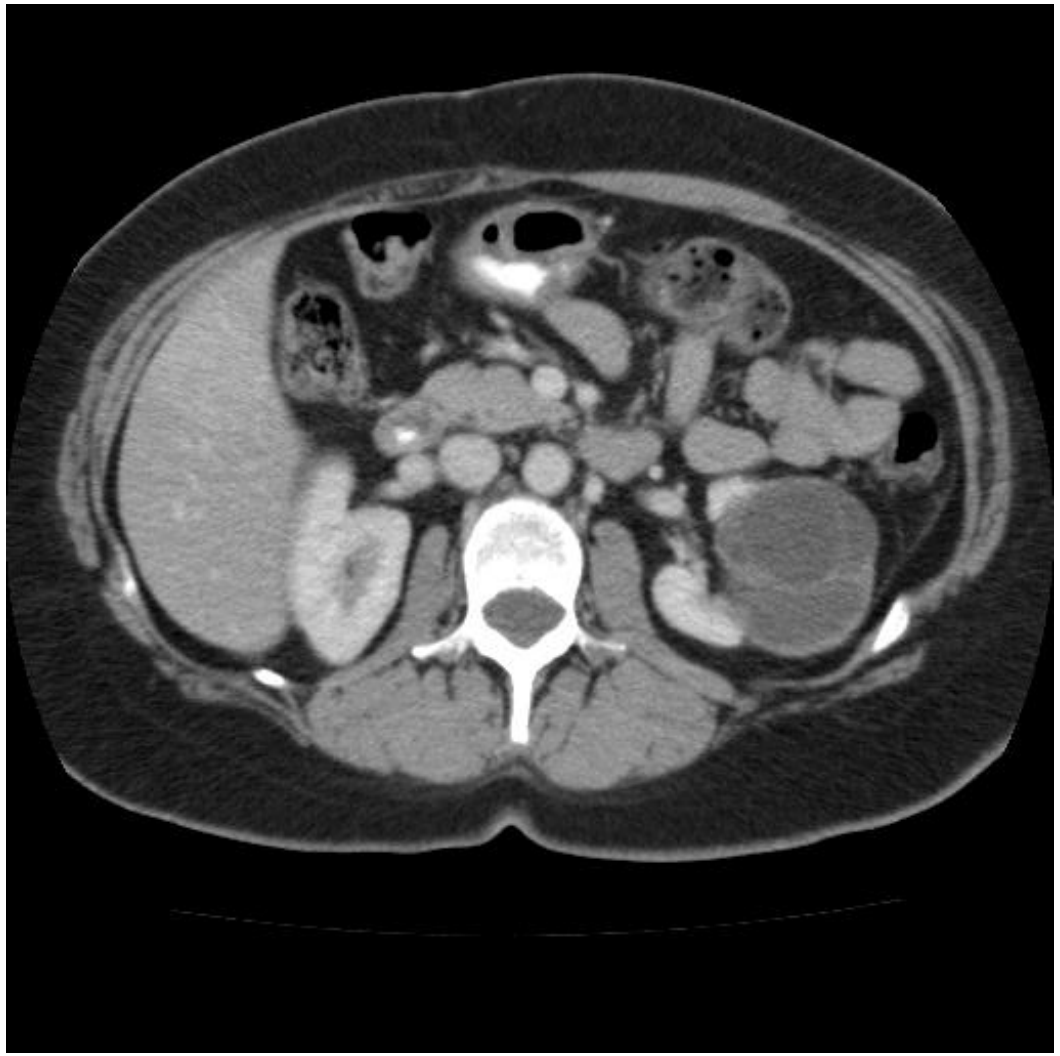


Cystic renal lesion

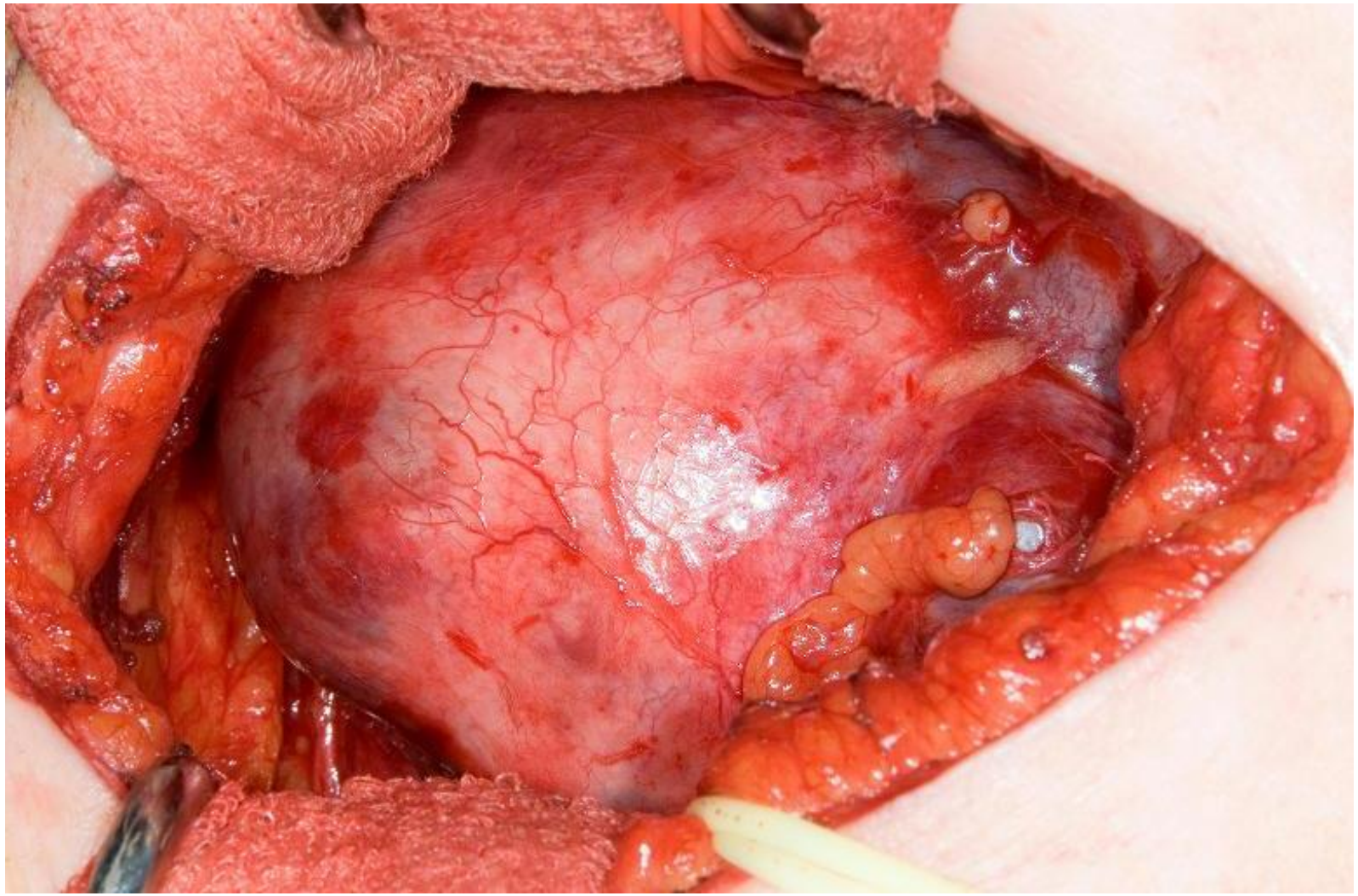
Cystic renal lesion



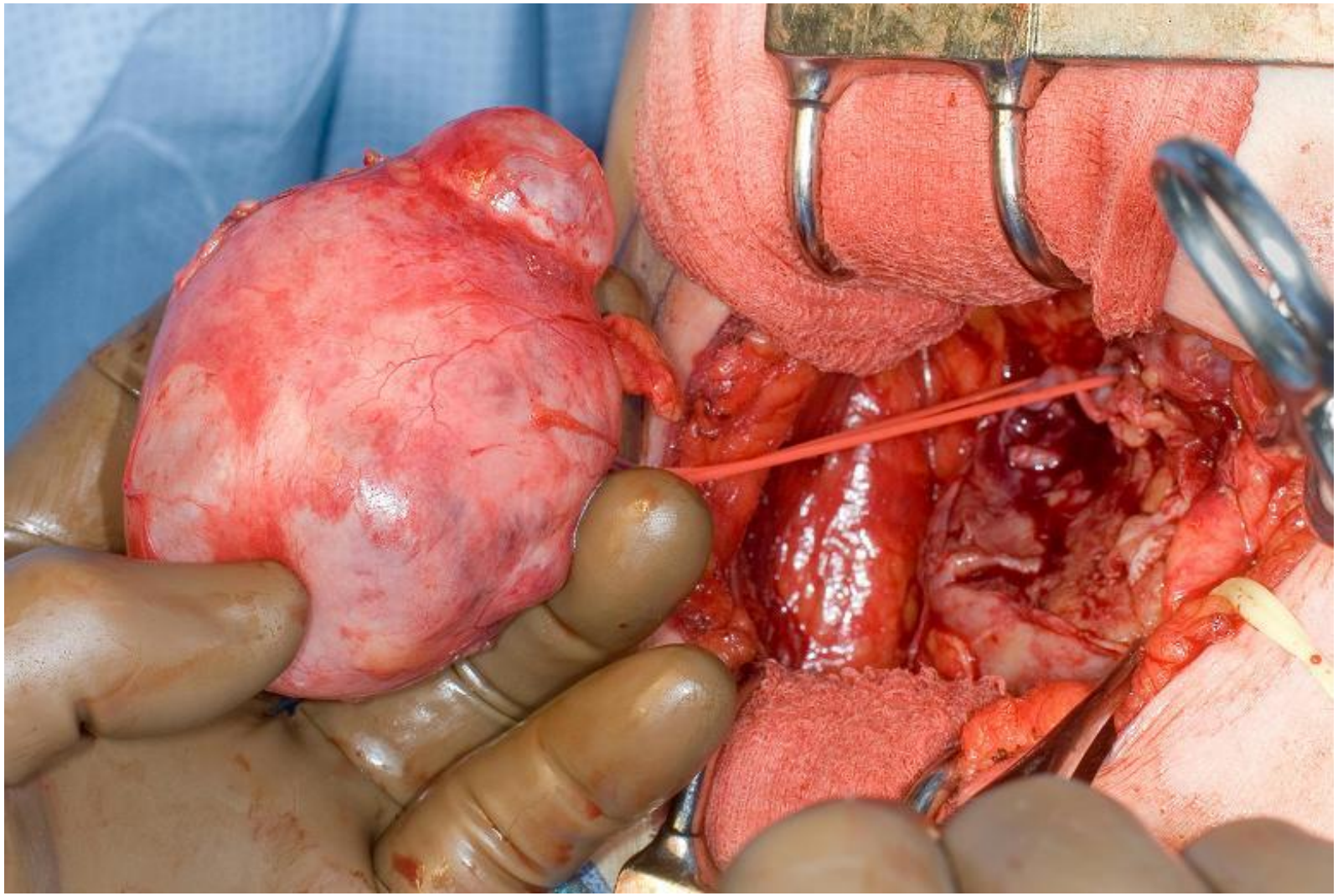
Cystic renal lesion



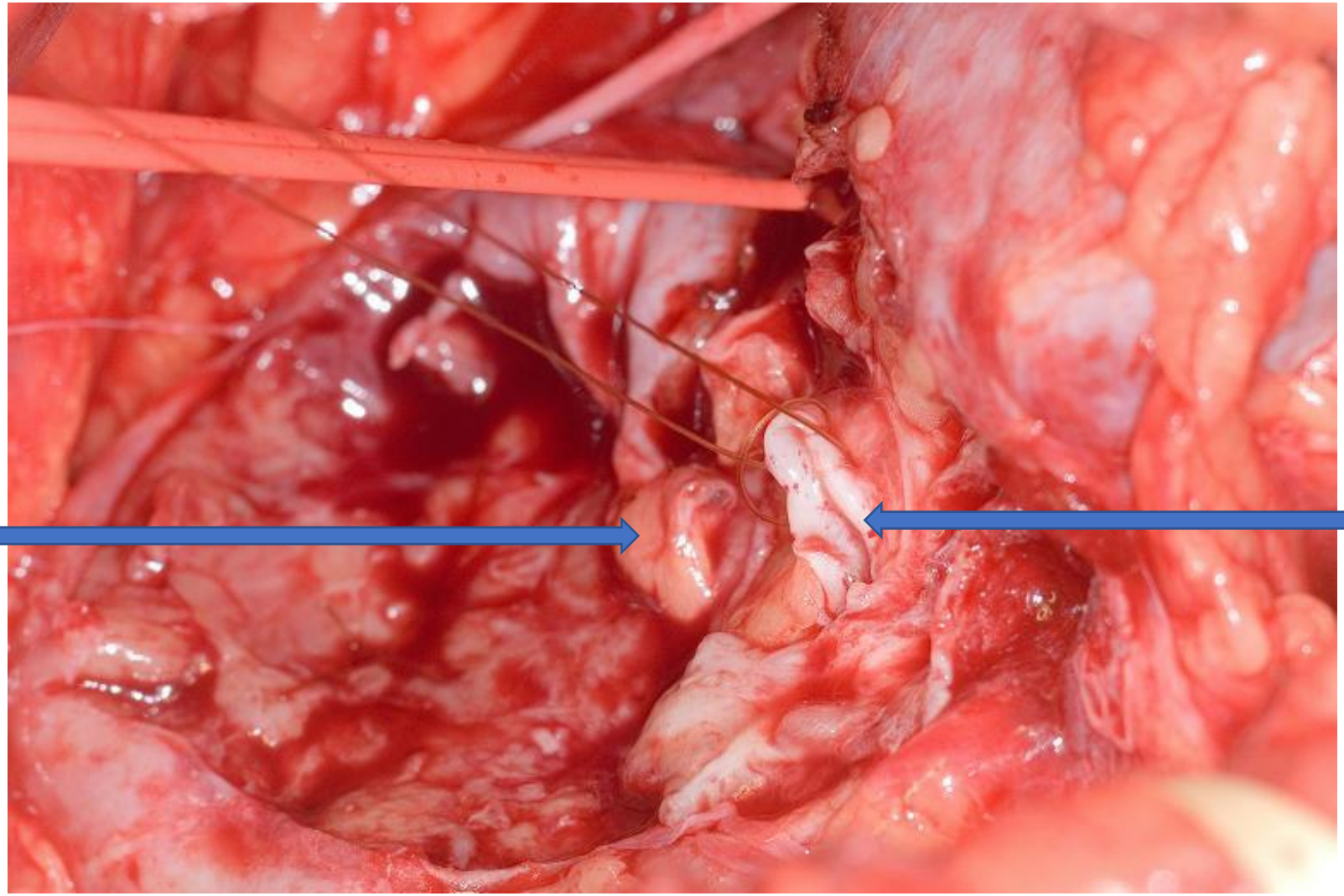
Mini Flank Incision



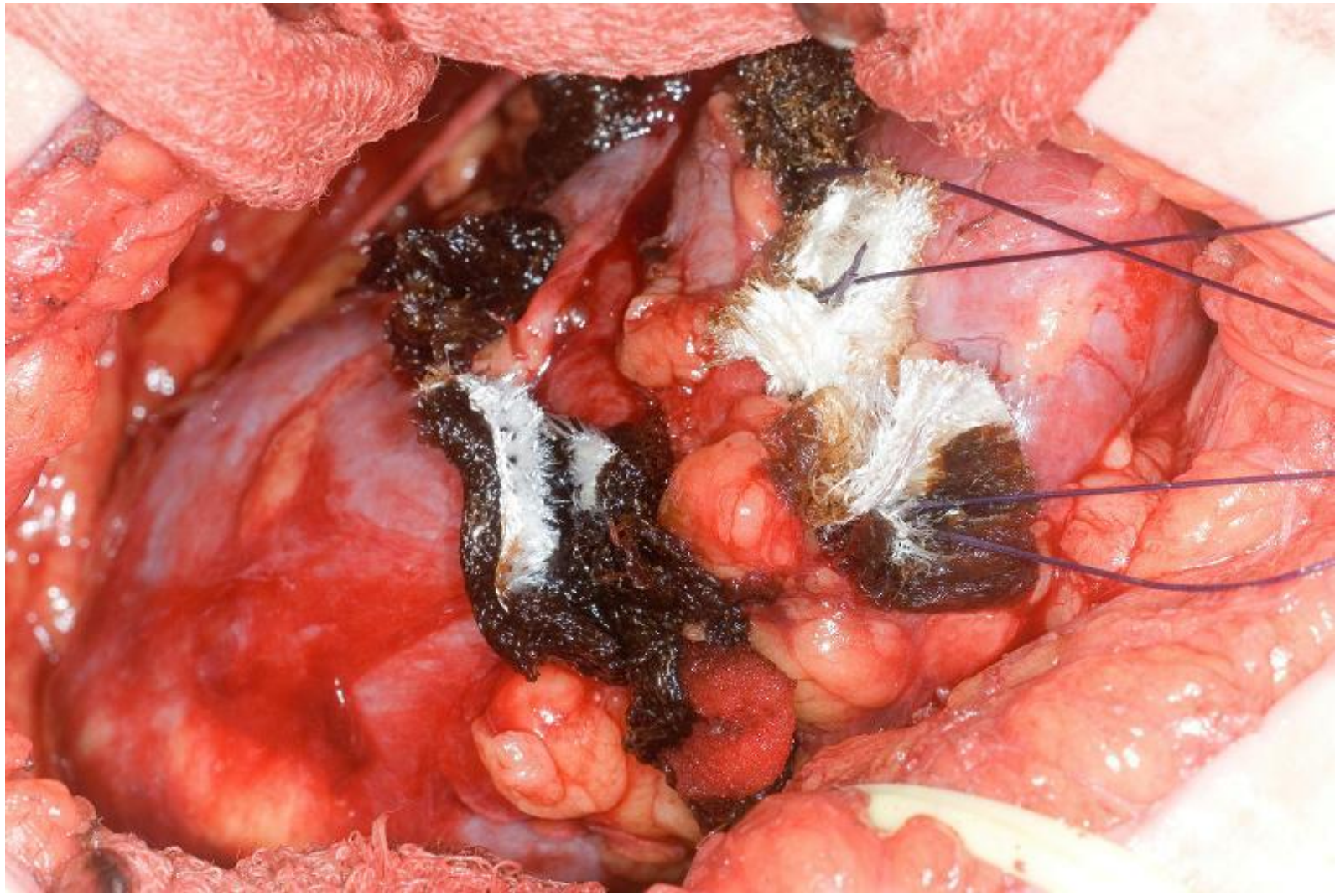
Cyst Enucleation is safe as it is surrounded by fibrous wall



Lack of Perinephric Fat Invasion (pt3a) ensures negative margins



Renorrhaphy



FG2 Cystic ccRCC

3 Month Follow Up - Normal eGFR

Surgical Resection Provides Excellent Outcomes for Patients With Cystic Clear Cell Renal Cell Carcinoma

Webster; et al.. *Urology*. 2007 70(5):900-904

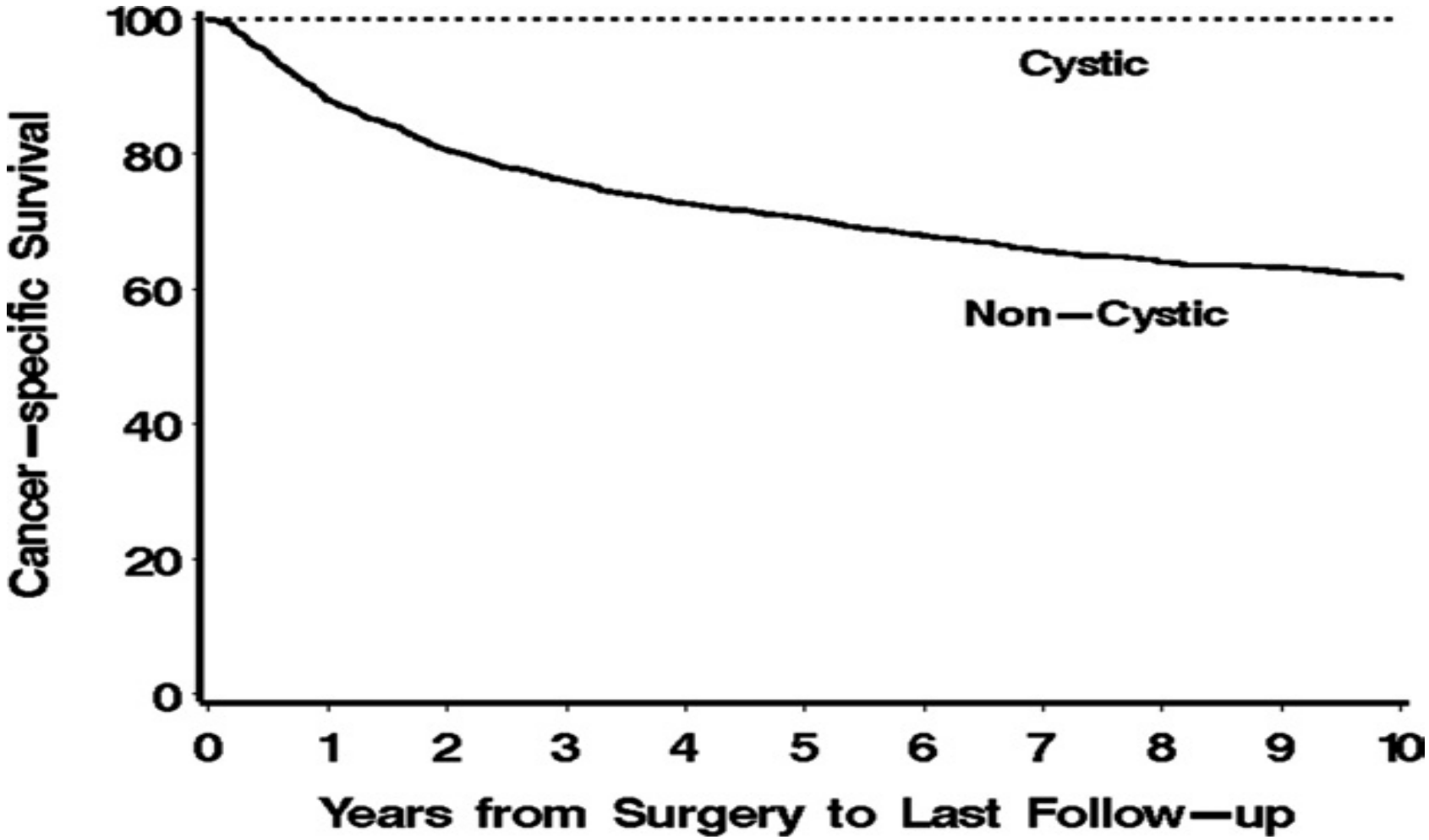
Comparison of clinical and pathologic features by cystic architecture for 2431 patients with clear cell RCC

		Cystic architecture	
Feature	Yes n 85 n (%)	No (n 2346)	*P*-Value
Primary tumor size			
<5 cm	59 (69.4)	761 (32.4)	<0.001
5 to <7 cm	17 (20.0)	465 (19.8)	
7 to <10 cm	7 (8.2)	575 (24.5)	
≥10 cm	2 (2.4)	545 (23.2)	
2002 Primary tumor pathologic stage			
pT1a	54 (63.5)	579 (24.7)	<0.001
pT1b	22 (25.9)	566 (24.1)	
pT2	8 (9.4)	459 (19.6)	
pT3a	1 (1.2)	218 (9.3)	
pT3b	0 (0.0)	475 (20.3)	
pT3c	0 (0.0)	19 (0.8)	
pT4	0 (0.0)	30 (1.3)	
Regional lymph node pathologic stage			
pNx and pN0	85 (100.0)	2219 (94.6)	0.021
pN1 and pN2	0 (0.0)	127 (5.4)	
Distant metastases (clinical stage)			
cM0	85 (100.0)	1990 (84.8)	<0.001
cM1	0 (0.0)	356 (15.2)	

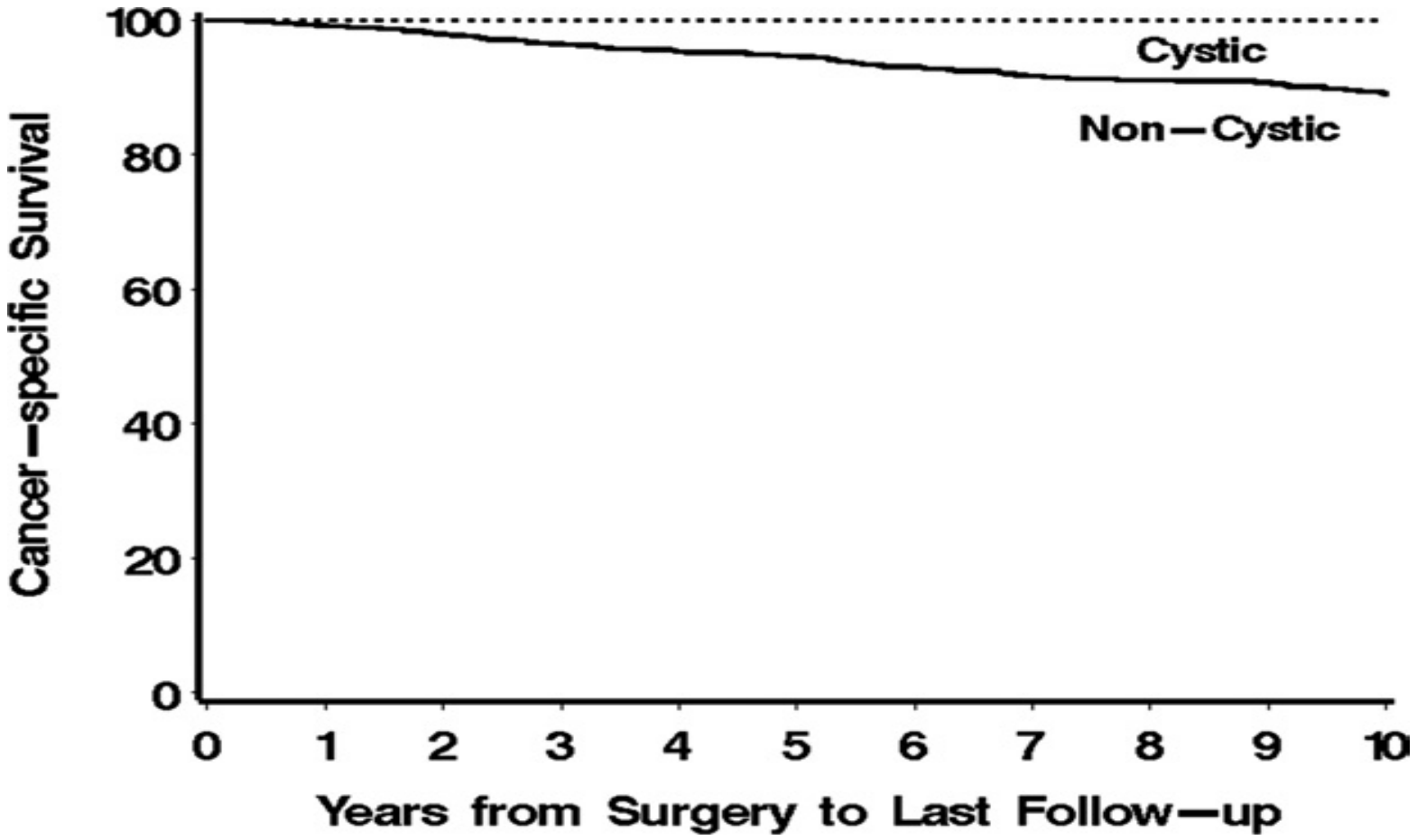
Comparison of clinical and pathologic features by cystic architecture for 2431 patients with clear cell RCC

Feature	Cystic architecture: Yes n 85 n (%)	No (n 2346)	*P*-Value
2002 TNM stage groupings			
I	76 (89.4)	1078 (46.0)	<0.001
II	8 (9.4)	363 (15.5)	
III	1 (1.2)	510 (21.7)	
IV	0 (0.0)	395 (16.8)	
Nuclear grade			
1	35 (41.2)	227 (9.7)	<0.001
2	49 (57.7)	1007 (42.9)	
3	1 (1.2)	908 (38.7)	
4	0 (0.0)	204 (8.7)	
Coagulative tumor necrosis			
No	83 (97.7)	1650 (70.3)	<0.001
Yes	2 (2.4)	696 (29.7)	
Sarcomatoid differentiation			
No	85 (100.0)	2222 (94.7)	0.021
Yes	0 (0.0)	124 (5.3)	

Cancer-Specific Survival



Cancer-Specific Survival PT1



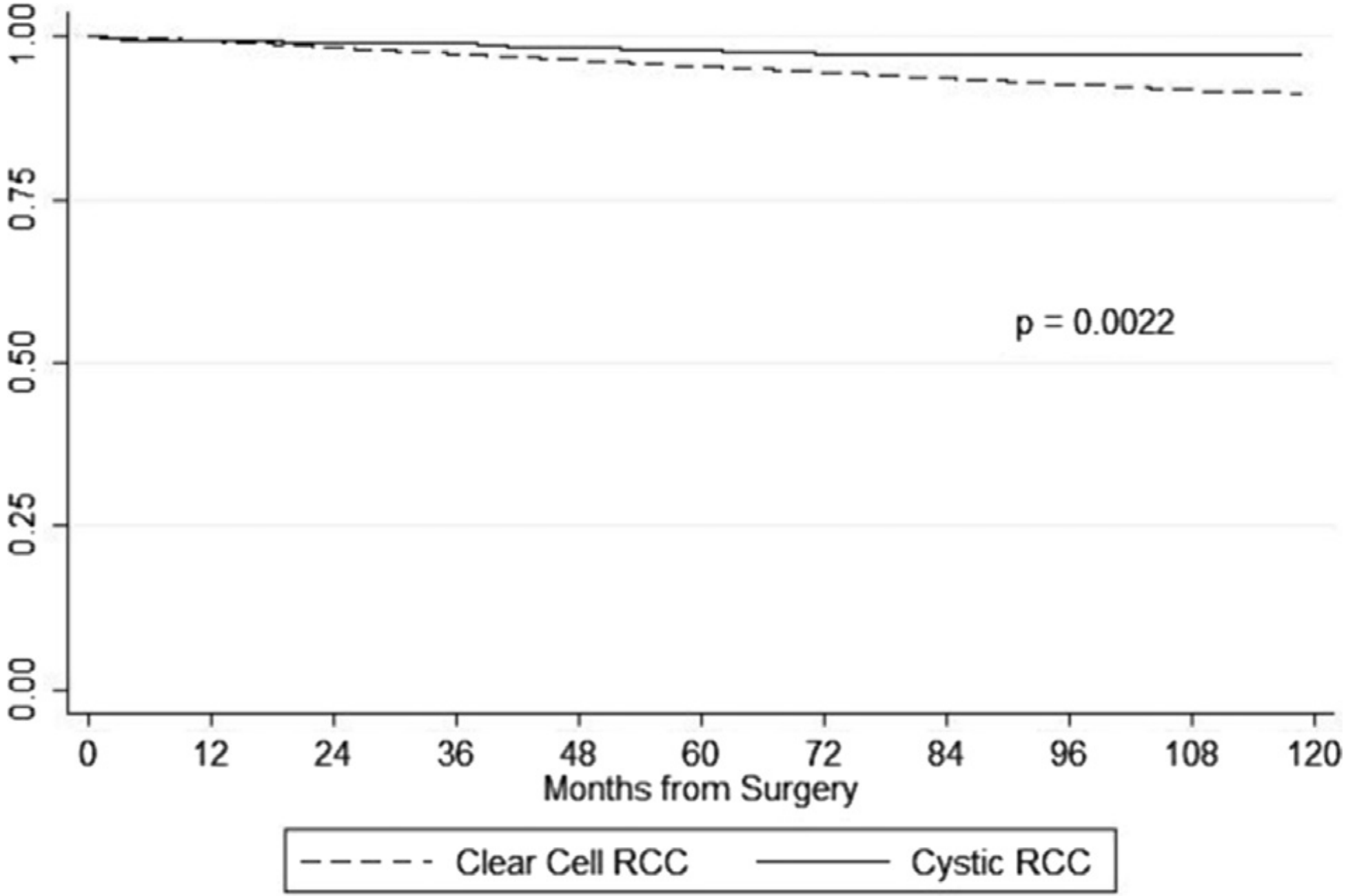
Cystic renal cell carcinoma carries an excellent prognosis regardless of tumor size

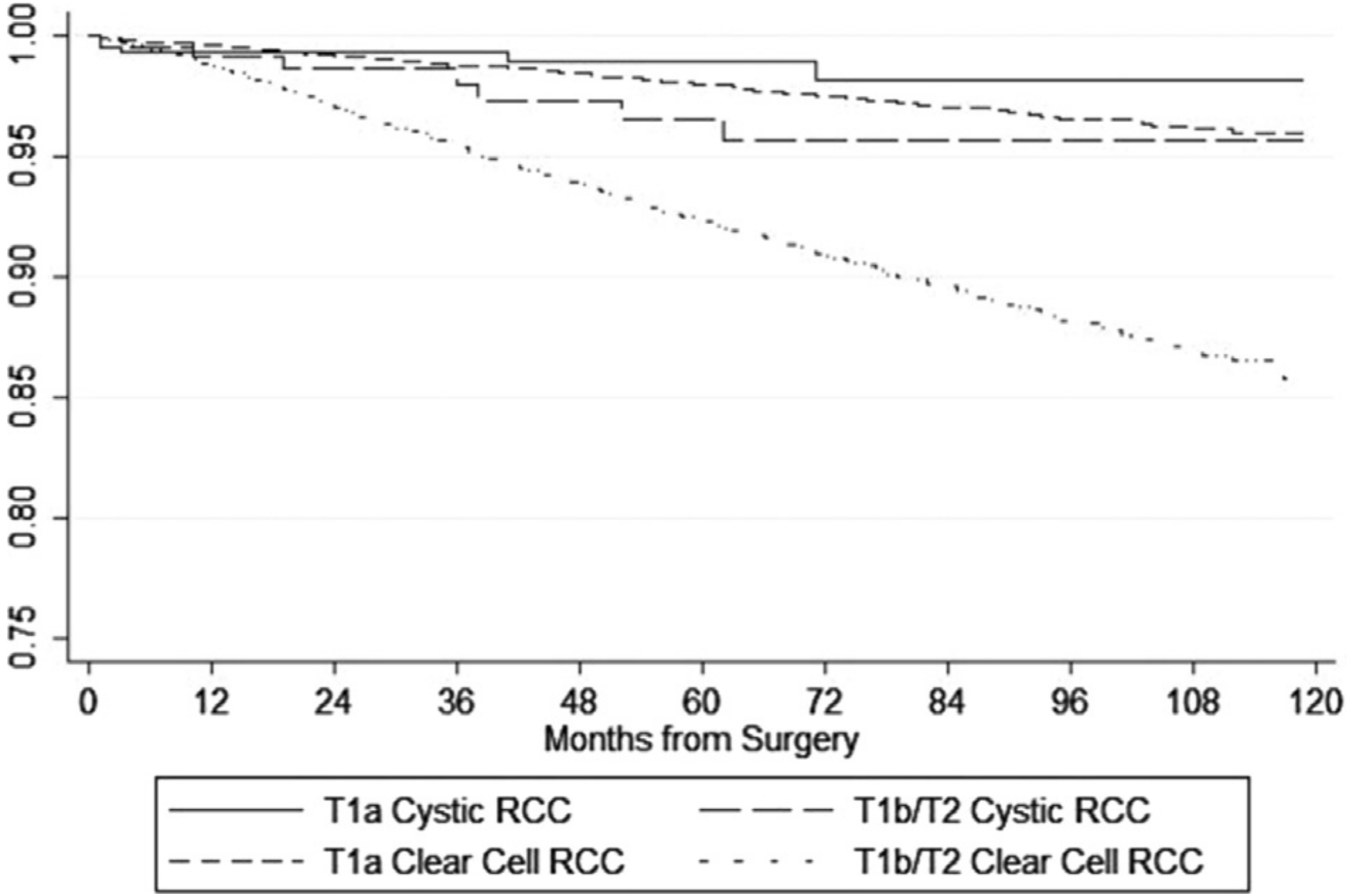
Winters; et al..*Urol Oncol.*, 2015 Jun; 33 (12): 505

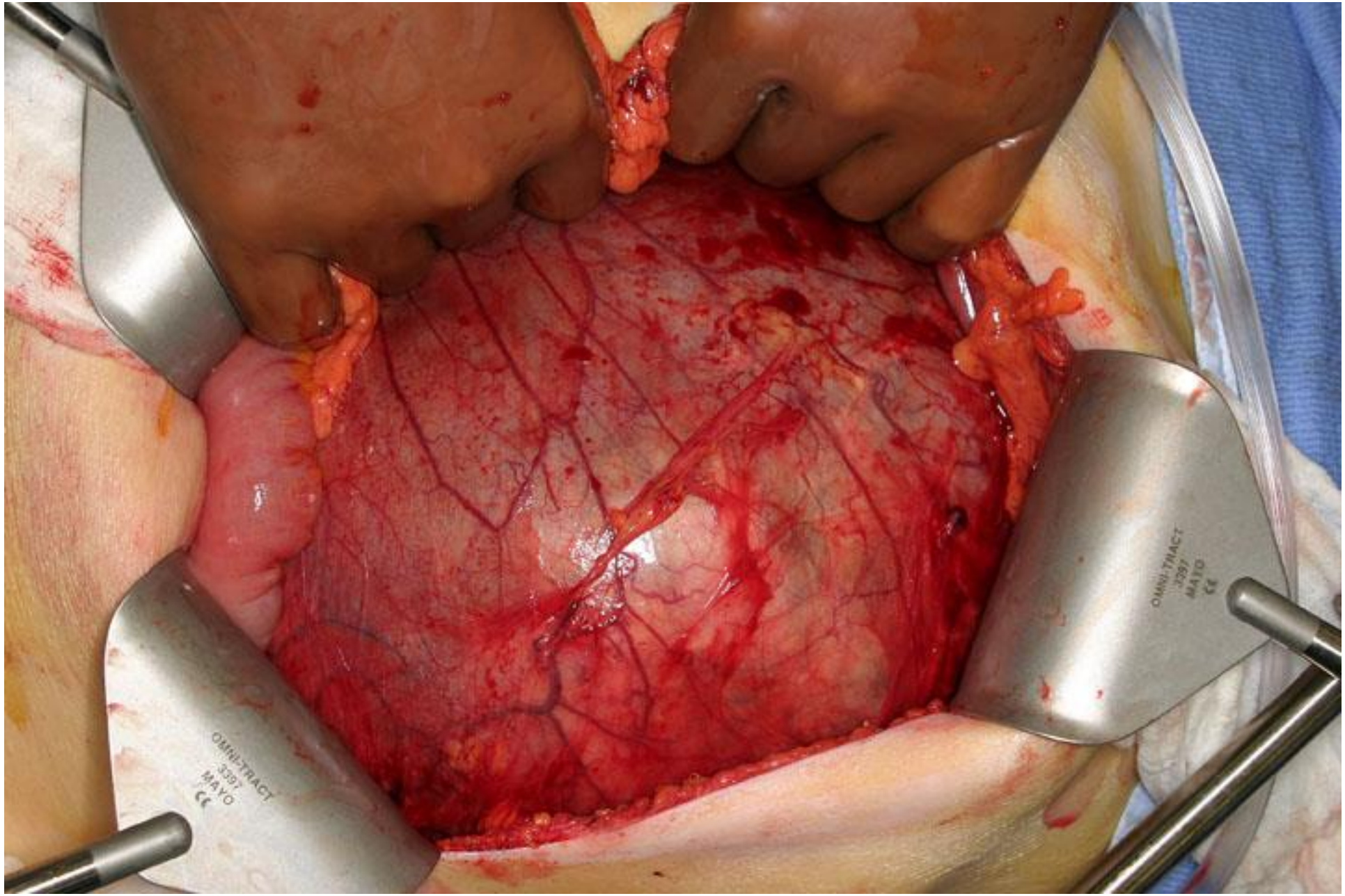
SEER Database

n=678 cystic clear cell cancer

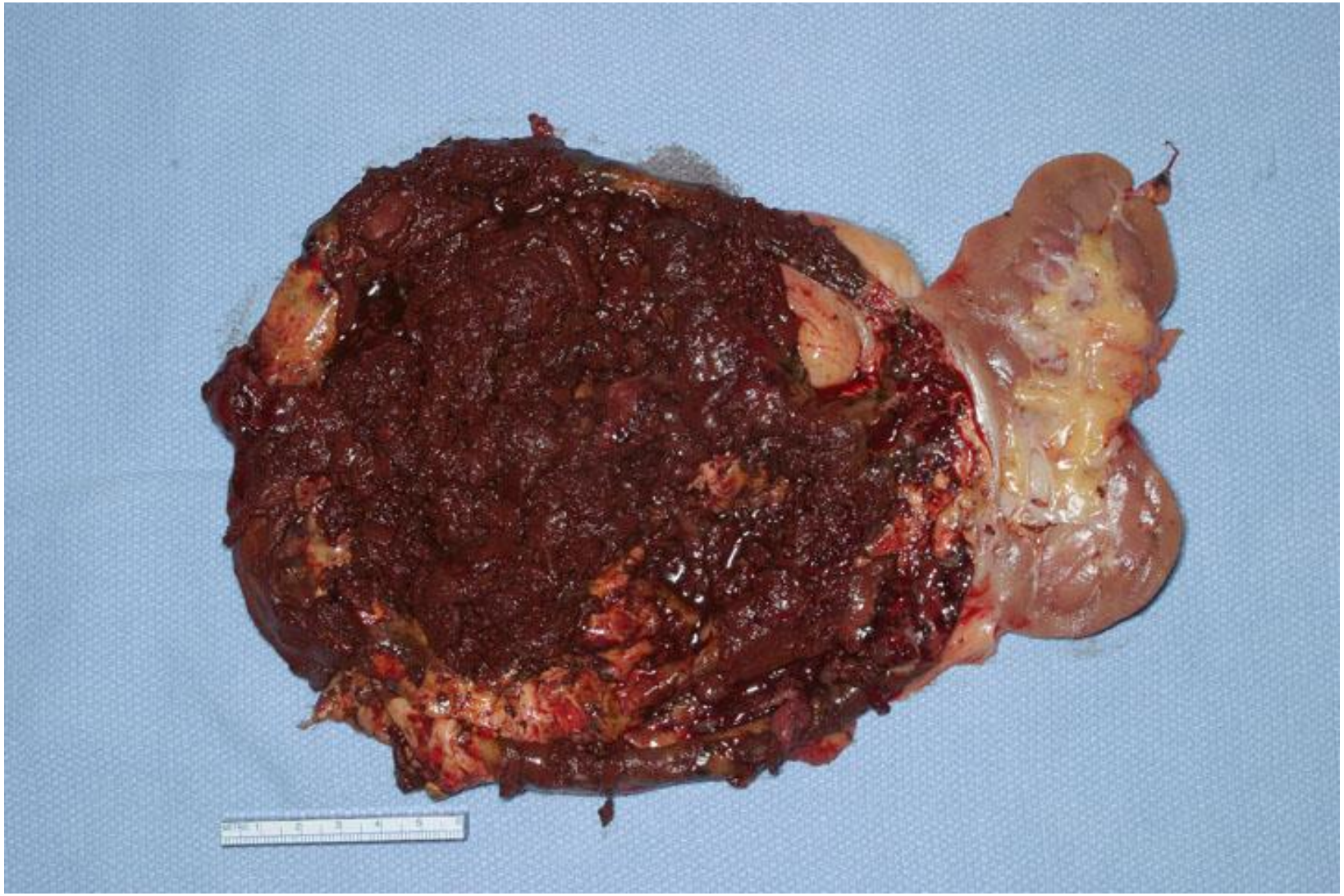
n= 46,677 cc RCC (solid)


1.00
0.75
0.50
0.25
0.00
p = 0.0022
0
12
24
36
48
60
72
84
96
108
120
Months from Surgery
Clear Cell RCC
Cystic RCC

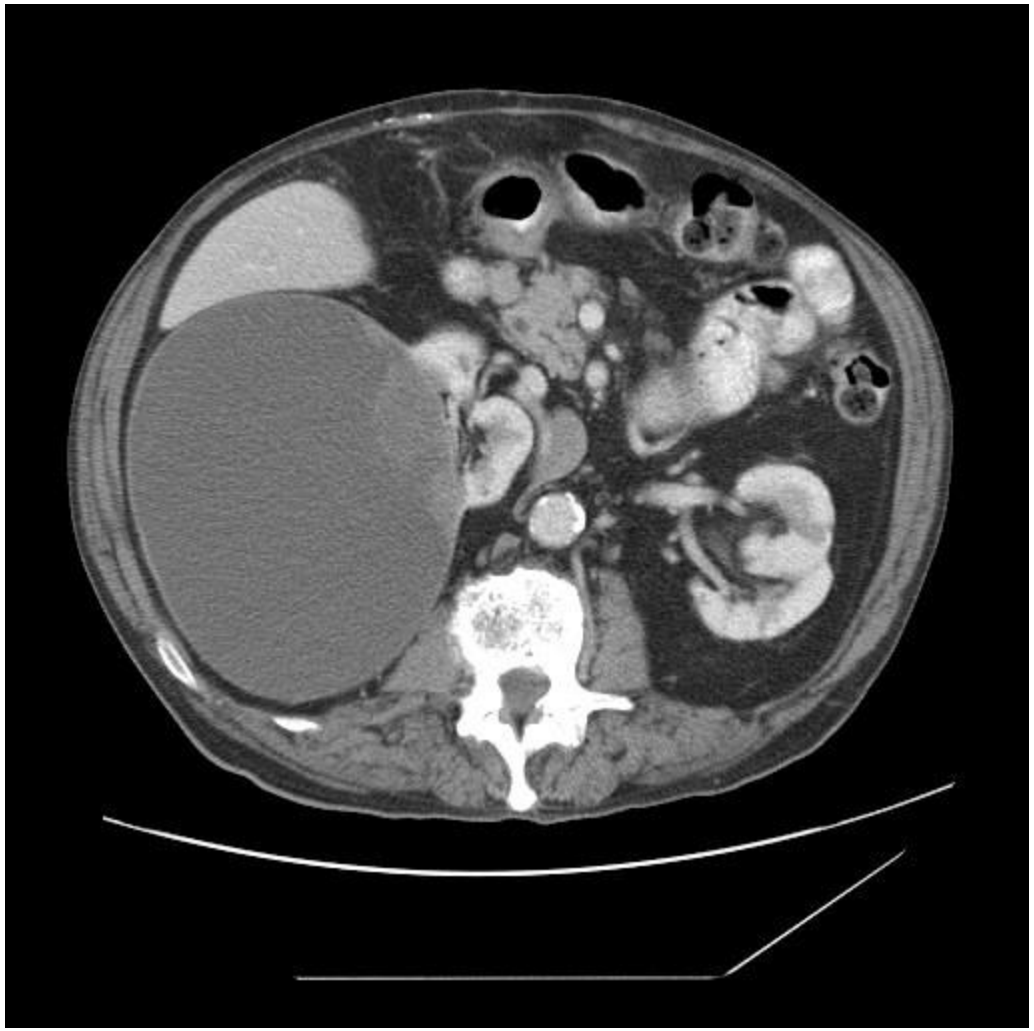

1.00
0.95
0.90
0.85
0.80
0.75
0
12
24
36
48
60
72
84
96
108
120
Months from Surgery
T1a Cystic RCC
T1b/T2 Cystic RCC
T1a Clear Cell RCC
T1b/T2 Clear Cell RCC


OMNI-TRACT
3397
MAYO
OMNI-TRACT
3397
MAYO

Hemorrhagic Cystic ccRCC

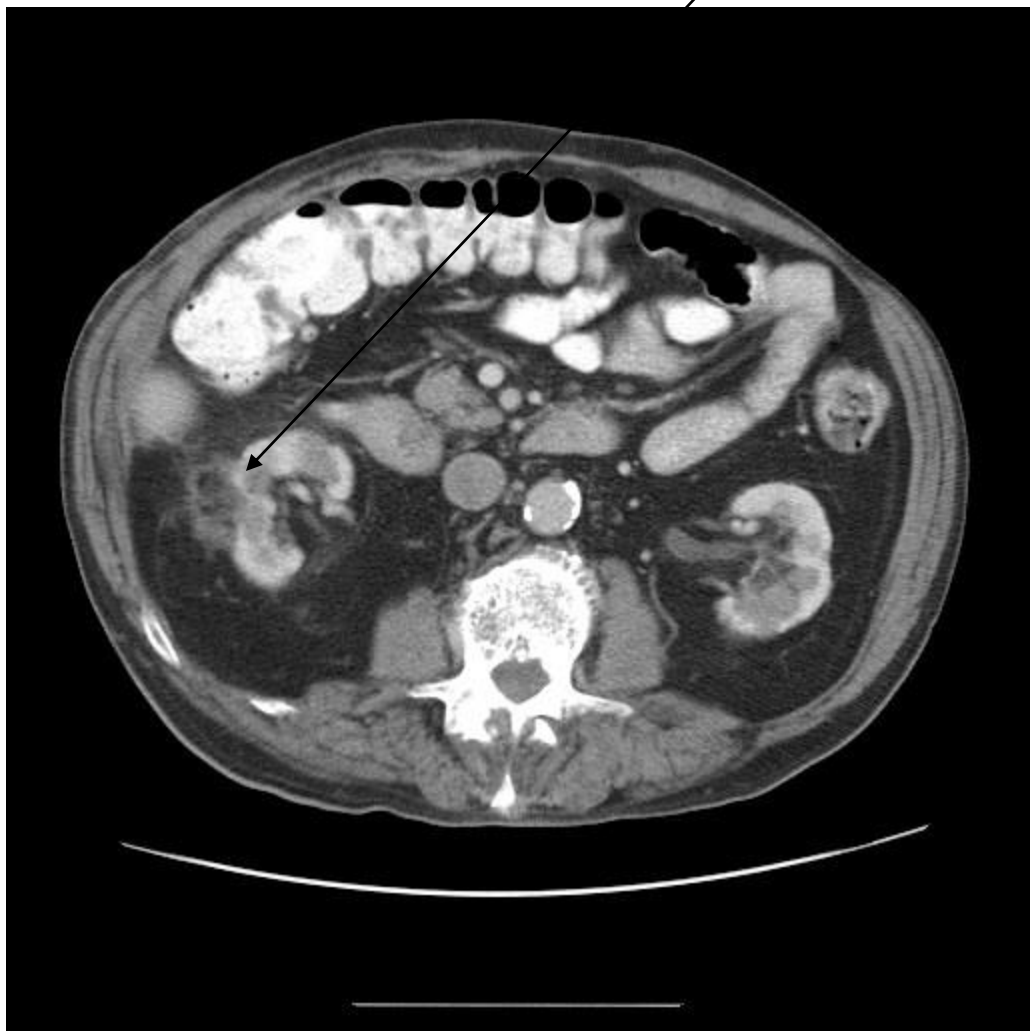


54-year-old male complains of right upper quadrant bulge.



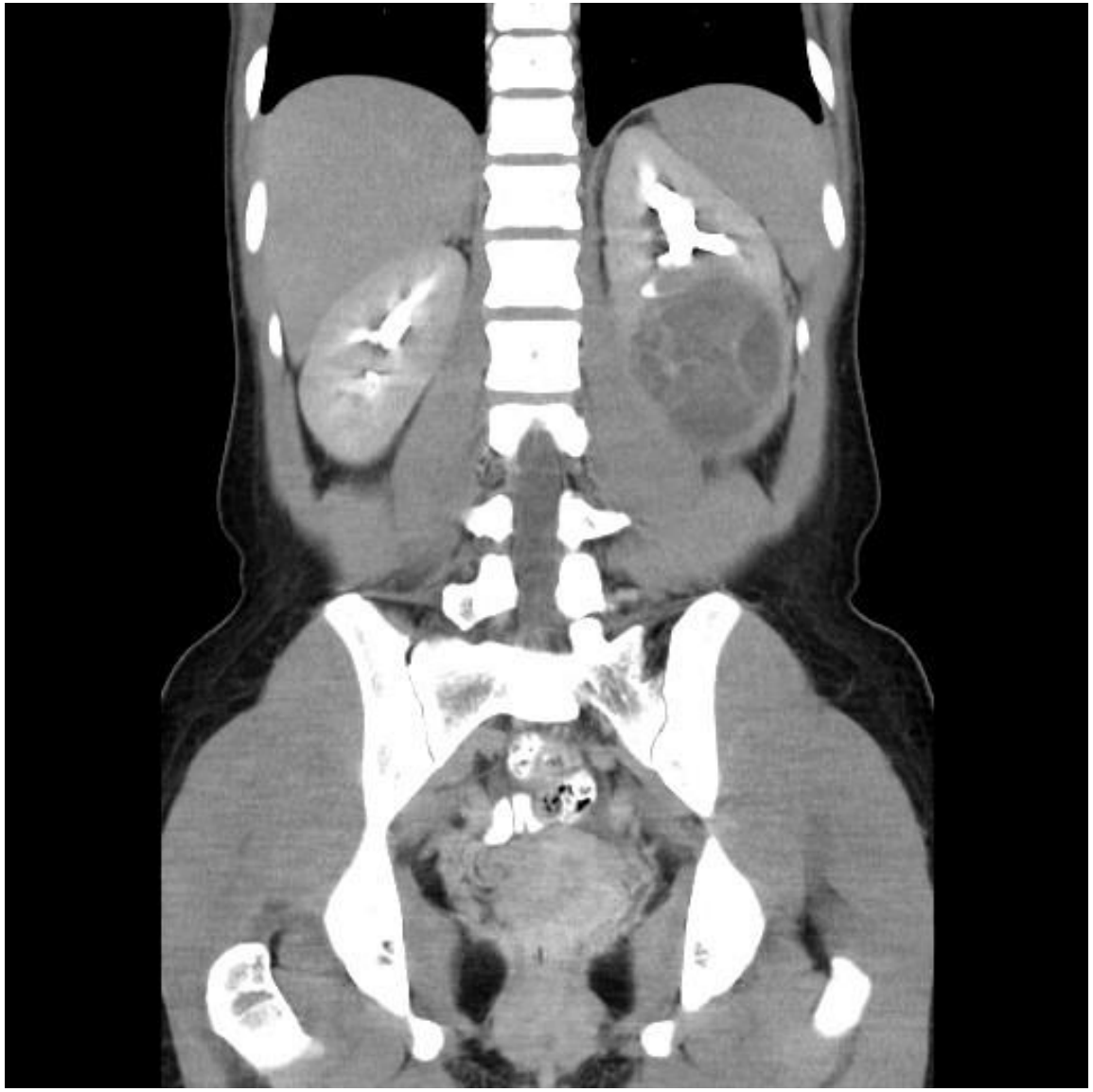
Pre-op

54-year-old male complains of right upper quadrant bulge. Resected cystic ccRcc.



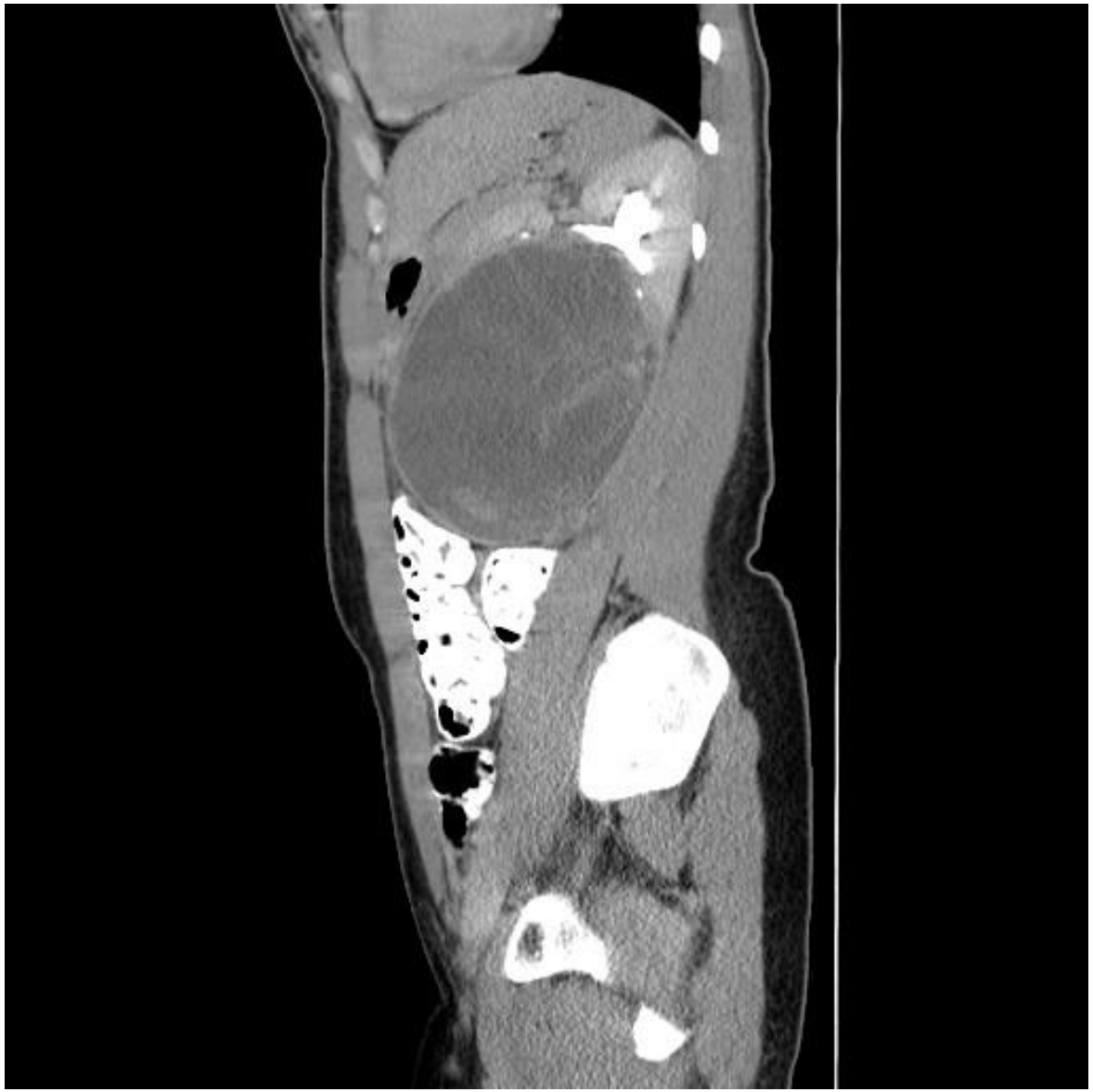
Post-op

30 yo female felt bulge and left upper quad pain at volleyball

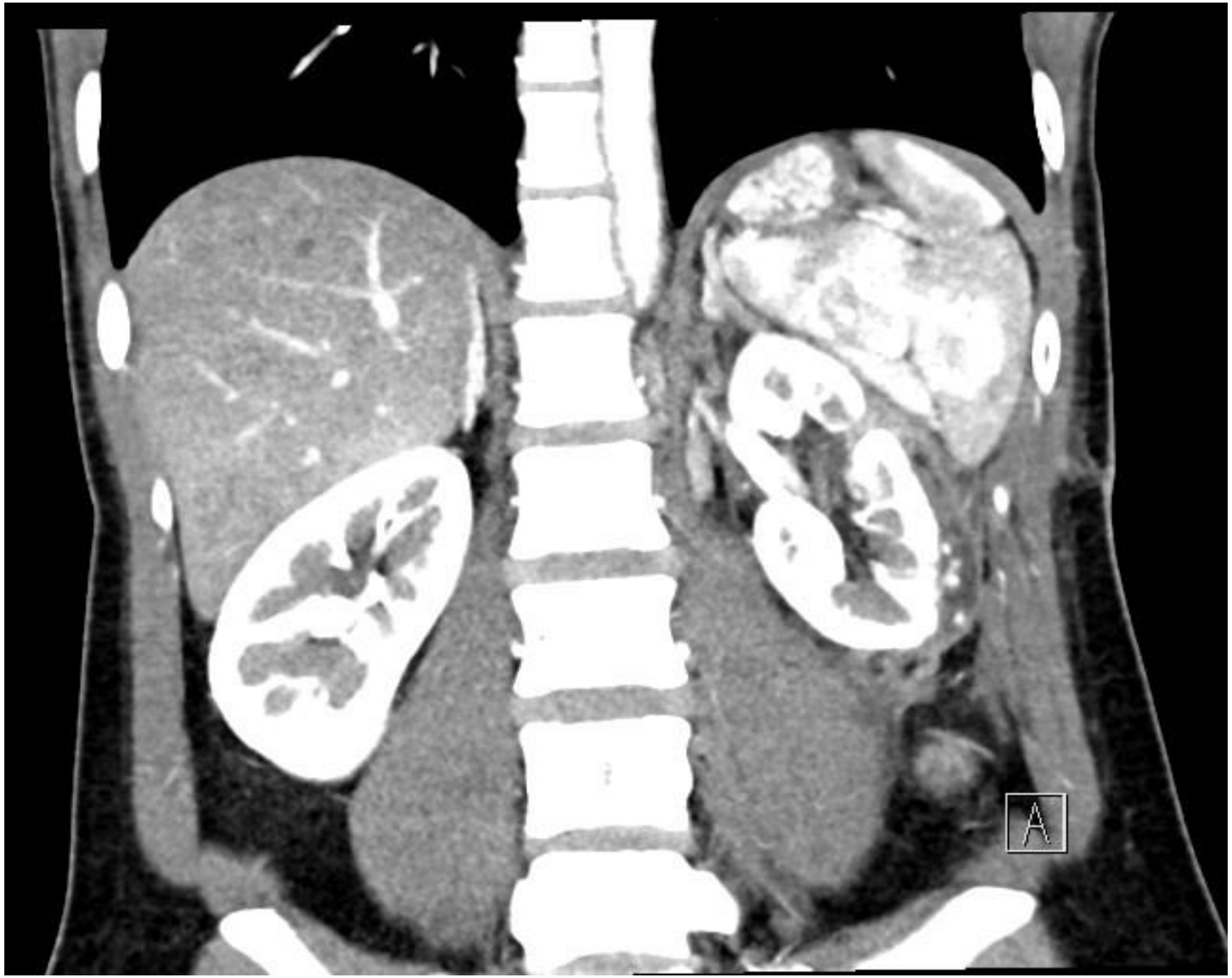


30 yo female with left upper quad pain

30 yo female with left upper quad pain



3 month Post-Op
Epithelioid AML



Conclusion

- incidence of complex (HR) cystic renal lesions increasing with increasing cross-sectional imaging
- RMB is accurate and prevents unnecessary surgery or changes management elderly/comorbidity
- the rate of malignancy for Bosniak III/IV is high but surgical outcomes are excellent. Bosniak classification does not predict aggressiveness (FG) and cures for Bosniak IV lesions are high as compared to solid clear cell renal cell cancer ; favor NSS when possible
- obey oncologic surgical principles (laprascopic unroofing not acceptable)
- consider extending surveillance beyond midterm (5yrs) for high risk Bosniak lesions, especially young and healthy