Contemporary Management of Renal Masses

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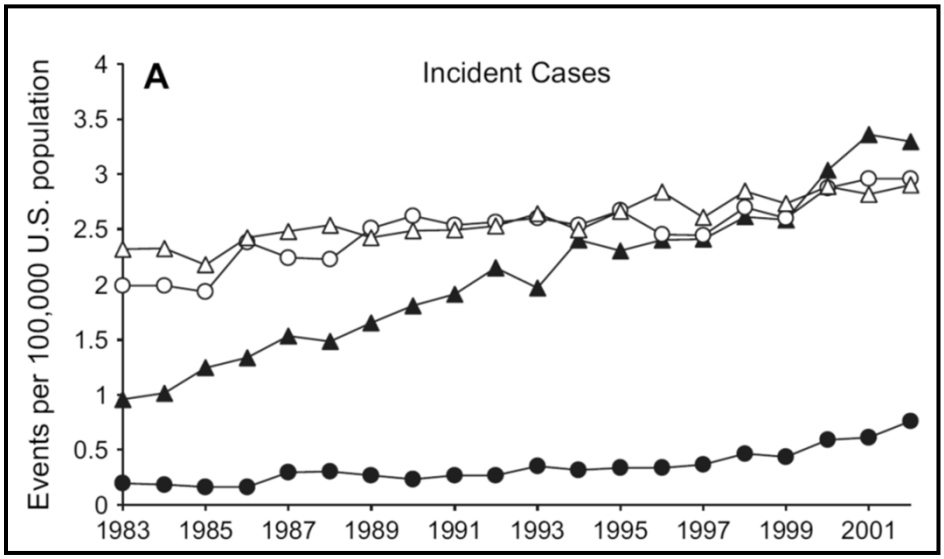
Outline

- Epidemiology
- Differential Diagnosis
- Evaluation
  - Imaging
  - Role for Biopsy
- Treatment
  - Surveillance
  - Surgery
  - Ablation
- Follow-up
- Cases

Renal Mass

- **Increasing incidence with widespread use of cross-sectional imaging**
- **Renal lesions are seen in 15-25% of abdominal imaging studies**
  - **Most are benign cysts**
- **Majority are detected incidentally.**



● = <2 cm, ▲ = 2 – 4 cm, ○ = >4 – 7 cm, and Δ = >7 cm

Renal Mass- Differential Diagnosis

Malignant	Benign	Inflammatory
Renal Cell Carcinoma -Clear Cell -Papillary -Chromophobe -Collecting duct Urothelial Based -Urothelial carcinoma -Squamous cell -Adenocarcinoma Sarcoma Wilms tumor Carcinoid Lymphoma Leukemia Metastasis	Simple cyst Angiomyolipoma Oncocytoma Metanephric adenoma Cystic Nephroma Mixed epithelial/stromal tumor Reninoma Leimyoma Pseudotumor	Abscess Focal pyelonephritis Xanthogranulomatous pyelonephritis Tuberculosis

Renal Mass- Differential Diagnosis

Malignant	Benign
Renal Cell Carcinoma **-Clear Cell** **-Papillary** **-Chromophobe**	**Simple cyst** **Angiomyolipoma** **Oncocytoma**

Is it Benign or Malignant?

- **The question at hand.**
- **This can frequently determined by radiographic assessment.**
- **Size Matters**
- **Current trend is to biopsy more renal masses <4cm.**

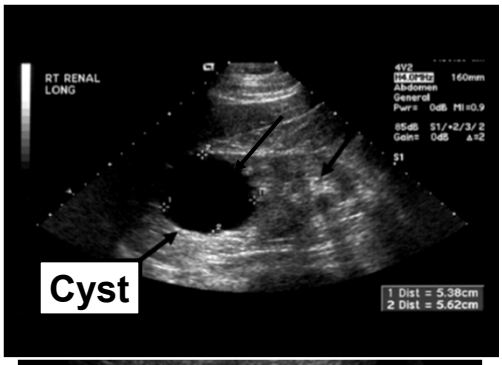
Radiographic Assessment

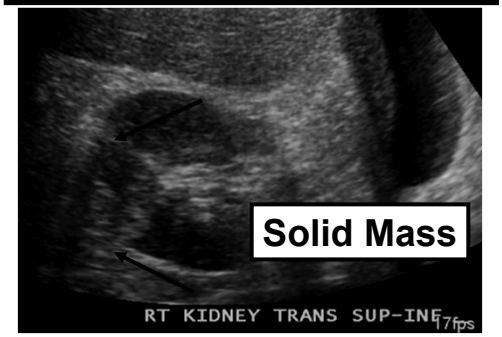
- **Ultrasound**
- **CT**
- **MRI**

- **<u>Key Point</u>:**
  - **Need to determine enhancement**

Ultrasound

- Reliable for differentiation of a solid lesion from fluid.
- Can establish the diagnosis of a simple cyst.





CT Scan

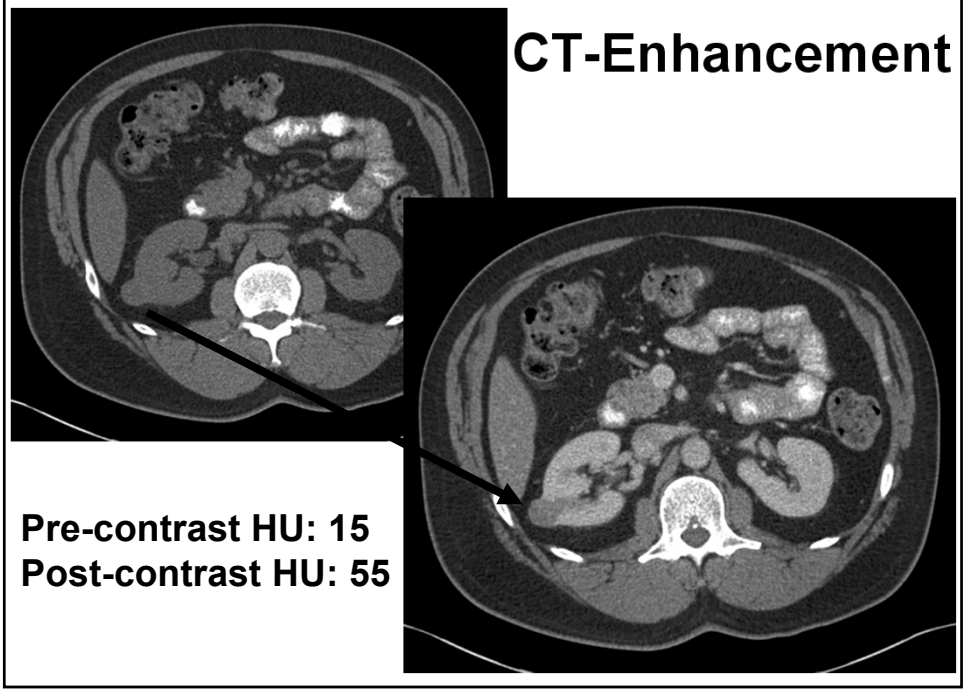
- Triple Phase (Renal Protocol)
  - Pre-contrast
  - Post-contrast (venous phase)
  - Delayed (10 min)
- Hounsfield Units (HU)
  - Represents the density of tissue

Tissue	HU
Bone	+1000
Blood	40
Kidney	30
Water	0
Fat	-50
Air	-1000

Enhancement

- Can only be determined if a <u>contrast agent</u> is used
  - CT – iodonated contrast
    - Enhancing Lesion = Pre-contrast to Post-contrast change in HU >15-20
  - MRI – Gadolinium
    - Slightly more subjective

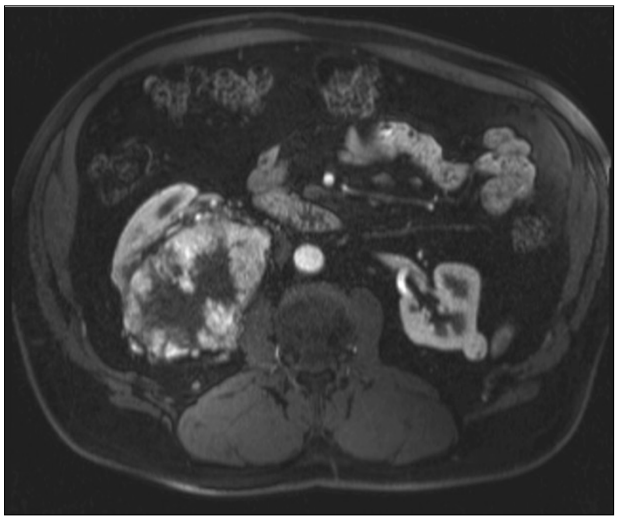
CT-Enhancement



Pre-contrast HU: 15
Post-contrast HU: 55

MRI

- Pre and Post Gadolinium



Risk of Contrast Agents

- IV Contrast (CT)
  - Contrast Allergy
  - Nephrotoxicity
    - Avoid with severe renal impairment
    - Risk reduction: Hydration
- Gadolinium (MRI)
  - No nephrotoxicity
  - Risk of Nephrogenic Systemic Fibrosis in those with severe renal impairment (EGFR<30).

cG250 PET/CT: Radiolabeled Antibody

- 124I-cG250 (REDECTANE®)
  - Binds carbonic anhydrase IX
  - Clear cell RCC
  - Radiographic diagnosis
- No role for CT PET-FDG with renal tumors.

^{18}F-FDG

^{124}I-cG250

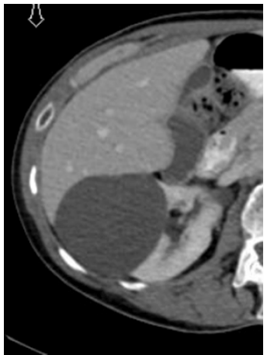
Wilex AG, Munich, Germany

Fat

- Solid masses with areas of negative HU (<-20) indicate the presence of fat and are diagnostic of AMLs.
- AML = Angiomyolipoma
- AML is a benign tumor.

Renal Cysts

- The kidney is one of the most common locations in the body for cyst formation.
- Renal cysts are cavities derived from renal tubules.
- Composed of a layer of epithelial cells enclosing a cavity filled with urine-like liquid or semi-solid material.
- 20% by age 40
- 50% by age 60

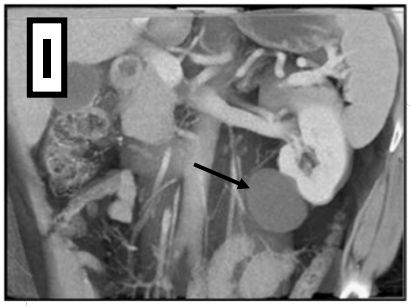


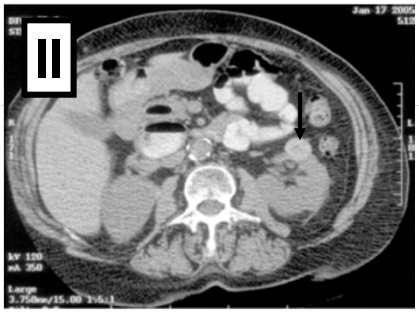
Renal Cysts: Bosniak Classification

Bosniak Class	Description	Cancer Risk	Management
I	No enhancement Smooth Wall No Septa No Calcifications	0%	None
II	No enhancement Hairline Septa Fine Calcifications	Minimal	None
IIF	No enhancement Hyperdense lesion Multiple Septa Thicker Calcifications	<10%	Surveillance
III	Thickened Wall with Enhancement	50%	Surgery
IV	Enhancing Nodule	90%	Surgery

Adapted from Campbell-Walsh Urology 10th Ed.

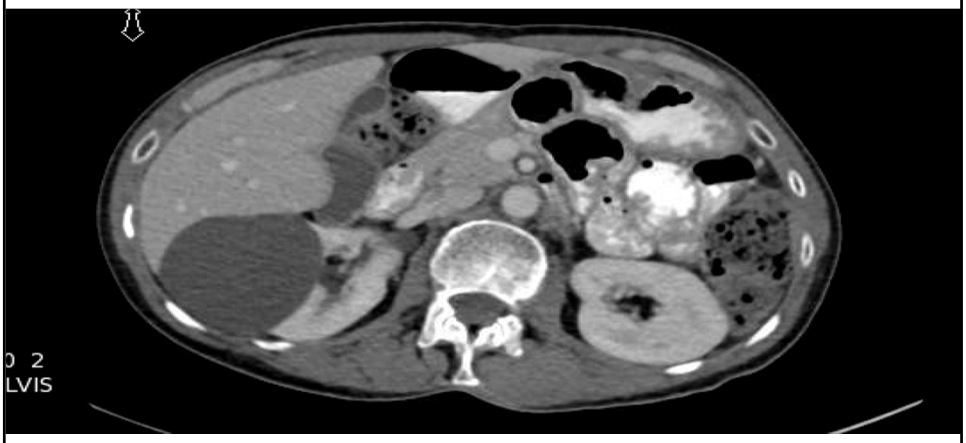
Renal Cysts – Bosniak Classification





III Pictures of each

Case- Simple Renal Cyst



Imaging Interpretation

- Enhancing renal masses are most likely malignant.
- Simple Cysts (Bosniak Type I):
  - Can be diagnosed by U/S or CT.
  - Do not need follow-up.
- AMLs are benign and can be followed
  - >4cm = greater risk for spontaneous bleeding
    - Selective angioembolization vs. surgery

AML = Angiomyolipoma

Role for Biopsy

- Historically, renal masses have not been biopsied.
  - Most are malignant
  - Issues with accuracy/non-diagnostic rates
  - Fear of needle tract seeding
  - High reported complication rates

Role for Biopsy

- Current role for biopsy is expanding
  - Especially for masses <4cm
- Updated date on biopsy results are much improved.

Role for Biopsy

- Contemporary results of renal mass biopsy:
  - Diagnostic rate: 92%.
    - RCC Subtype Concordance: 80-100%
    - Fuhrman Grade Concordance: 50-70%
  - Complications: <5%
    - Hematoma most common

Marconi et al. Eur Urol 2015

Indications: Renal Mass Biopsy

- R/o non-renal primary (mets or lymphoma)
- +/- R/o benign lesions
- Confirm diagnosis and histologic subtype in patients with metastases or unresectable lesions
- Confirm diagnosis:
  - Prior to ablative therapy
  - In patients considering observation when surgery is high risk

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Biopsy only if it will change management

- Confirm diagnosis and histologic subtype in patients with metastases or unresectable lesions
- Confirm diagnosis:
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Tumor Size and Pathology

Tumor Size	RCC	Benign*	High Grade
≤2.0	75%	25%	4%
2.1-3.0	80%	20%	5%
3.1-4.0	84%	16%	25%

*Oncocytoma and AML – 75%

J Urol 2006; 176:896

Renal Cancer 2015

- Incidence
  - 61,560 new cases
  - 14,080 deaths
- Peak incidence 5th-7th decades
- Men > Women
- Lifetime Probability of Developing Renal Cancer:
  - 1 in 49 male (#7)
  - 1 in 84 female (#10)

American Cancer Society. *Cancer Facts & Figures 2015*. Atlanta: American Cancer Society; 2015

Renal Cell Carcinoma – Risk Factors

- Tobacco Exposure
  - May account for ~20% of cases
- Obesity
  - May account for ~40% of cases in US
  - Risk increases ~30% for every 5kg/m^2 increase in BMI
- Hypertension
- Low socioeconomic status and urban background
- More than 100 chemicals have been investigated but none have been definitively established as causative in RCC

Renal Cancer – Mortality

Site	Incidence/yr	Deaths 2015
Prostate Cancer	220,800	27,540 (12%)
Bladder Cancer	74,000	16,000 (22%)
Kidney Cancer	61,560	14,080 (23%)

American Cancer Society. *Cancer Facts & Figures 2015*. Atlanta: American Cancer Society; 2015

Renal Cancer – Presentation and Survival

Stage at Diagnosis	Distribution	5-yr Survival
Localized	61%	91%
Regional (lymph nodes)	17%	63%
Distant (metastatic)	18%	11%

Seer Database

Clinical Presentation

- 80% incidental

- Flank pain
- Gross hematuria
- Palpable mass

← "Classic Triad" <10%

- Microhematuria

- Paraneoplastic syndromes (10-20%)

Paraneoplastic syndromes

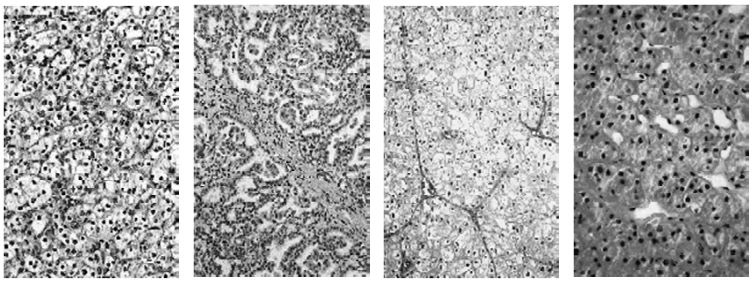
- "Internist's Tumor"
  - Elevated ESR 55%
  - HTN 38%
  - Anemia 36%
  - Cachexia 35%
  - Pyrexia 17%
  - Elevated LFTs 14%
  - Hypercalcemia 5%
  - Polycythemia 4%
  - Neuromyopathy 3%

Campbell-Walsh Urology 10th Ed.

Clinical Presentation - RCC

- Local Tumor Growth
  - Hematuria
  - Flank Pain
  - Abdominal Mass
- Metastasis
  - Persistent Cough
  - Bone Pain
  - Cervical Lymphadenopathy
  - Constitutional Symptoms
- Obstruction of IVC
  - Bilateral Lower Extremity Edema
  - Right-sided Varicocele (or nonreducing Varicocele)

Renal Cell Carcinoma: Histologic Subtypes



Type:	Clear cell	Papillary	Chromophobe	Oncocytoma
Freq (%):	75	15	5	5

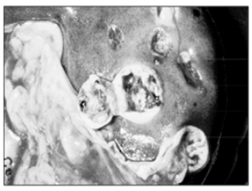
Hereditary RCC

Disease	Gene (chromosome)	Histology	Frequency
von Hippel-Lindau	VHL (3)	Clear Cell	75%
HLRCC*	FH (1)	Papillary Type 2	10%
Birt-Hogg-Dube	BHD (17)	Chromophobe/Oncocytoma	10%
Hereditary papillary RCC	Met (7)	Papillary Type 1	5%

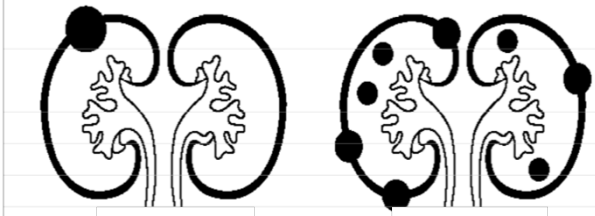
*HLRCC = Hereditary Leiomyomatosis Renal Cell Carcinoma

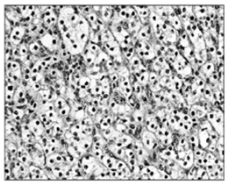
VHL: Renal Cell Carcinoma

- RCC occurs in 50% of VHL patients
  - Males=females in VHL
  - 4th to 5th decade (39)
  - Now most common cause of death



Multiple Renal Cysts Containing RCC





Clear Cell RCC

Renal Cell Carcinoma: Staging

Stage	Tumor	Lymph Nodes	Metastasis
I	T1 (<7cm)	N0	M0
II	T2 (>7cm)	N0	M0
III	T1 or T2 T3 (vein/fat)	N1 N0 or N1	M0
IV	T4 (outside Gerota's) Any T	Any N Any N	Any M M1

Treatment Options

- Surveillance
- Surgical Excision ← Gold Standard
  - Radical Nephrectomy
  - Partial Nephrectomy
- Needle Ablation
  - Cryoablation or Radiofrequency Ablation
- RCC does NOT respond to chemotherapy or radiation

Decision Making

- Tumor Characteristics:
  - Size
  - Location
  - Appearance
- Patient Characteristics
  - Comorbid disease
  - Life expectancy
  - Patient desire

Active Surveillance (AS)

- Incidentally detected tumors:
  - Small size (<4cm)
  - Elderly
  - Patients with significant comorbidity unfit for surgery
- Opportunity to observe the natural history of these small tumors.

Tumor Size and Pathology

Tumor Size	RCC	Benign*	High Grade
≤2.0	75%	25%	4%
2.1-3.0	80%	20%	5%
3.1-4.0	84%	16%	25%

*Oncocytoma and AML – 75%

J Urol 2006; 176:896

Active Surveillance

- Tumors <3cm
  - Risk of developing metastasis in 3 years is ~1%
- Average growth rate ~0.3cm/yr
- Most studies only have limited follow-up
- Follow-up protocol is not defined
  - Repeat imaging every 6-12 months

Active Surveillance

- AUA Guidelines:
  - "AS is a reasonable option for patients with a limited life expectancy or for those who are unfit for or do not desire intervention."

Risk-adapted Management

- Biopsy can be helpful
- More favorable histology:
  - Papillary type 1
  - Chromophobe
  - Low grade:
    - Fuhrman grade 1 and 2.

Risk-adapted Management

- 5 yr Cancer specific survival:
  - Fuhrman Grade (clear cell RCC):
    - I: 94%
    - II: 88%
    - III: 63%
    - IV: 39%

    - Low (I&II): 90%
    - High (I&II): 61%

Becker et al. Eur J Surg Oncol 2015

Surgery

- Approach?
  - Open vs. Laparoscopic vs. Robotic

- Radical vs. Partial Nephrectomy?
  - Nephron preservation

PARTIAL NEPHRECTOMY

- **Partial nephrectomy oncologically equivalent to radical nephrectomy.**

  Leibovich et al. J Urol 2004; 171:1066
  Breau et al. J Urol 2010; 183:903

- **L/S PN equivalent to Open PN with less morbidity.**
  - **Technical obstacles**
  - **MIS- more likely to have radical nephrectomy**

  Gill et al. J Urol 2007; 178:41

- **More attention has been given to the significant morbidity associated the chronic kidney disease (GFR<60).**
  - **Surgical vs. Medical** Go, et al: NEJM 2004; 351: 1296
  - **Nephron-preservation**

Chronic Kidney Disease (CKD)

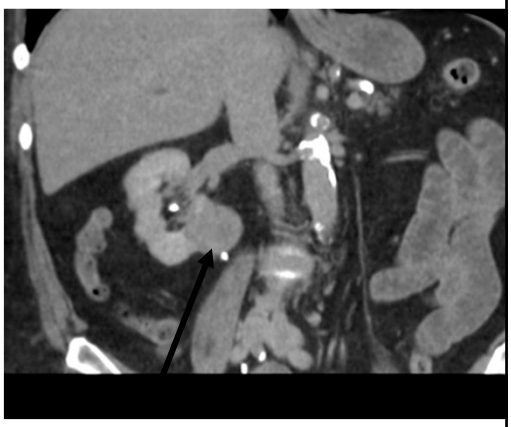
- **GFR <60 ml/min/1.73m^2 for at least 3 months**
- **Important consideration with significant associated morbidity and mortality**
- **RCC patients are NOT donor nephrectomy patients**
  - **Often have HTN and/or DM**
- **Median survival after starting dialysis is 2-2.5 years**

Renal Cancer – Nephron Preservation

CKD Stage (Estimated GFR (ml/min/1.73m^2))	Death from Any Cause	Any Cardiovascular Event	Any Hospitalization
CKD III (30-44)	1.8	2.0	1.5
CKD IV (15-29)	3.2	2.8	2.1
CKD V (<15)	5.9	3.4	3.1

Go et al: NEJM 2004;351:1296.

Is the tumor amenable to a partial nephrectomy?



Indications for Nephron Sparing Surgery

- ***Absolute/Imperative***: **To prevent anephric state**
  - **Anatomic/Functional solitary kidney**
  - **Bilateral RCC**
- ***Relative***: **Contralateral kidney is threatened by local, systemic, genetic conditions that may affect function**
  - **DM, HTN, stones, RAS, VHL**
- ***Elective***: **NSS with a normal contralateral kidney**

Uzzo: AUA Review Course

Partial Nephrectomy

- **GOALS**
  - **Cancer Control**
    - **Margins**
    - **CSS**
  - **Preservation of renal function**
    - **Technical ability to perform NSS**
    - **↓ Warm Ischemia time**
    - **Selective/no ischemia**
  - **↓ Complications**
  - **↓ Convalescence**
- **Robotics facilitates very difficult partial nephrectomies**

Partial Nephrectomy

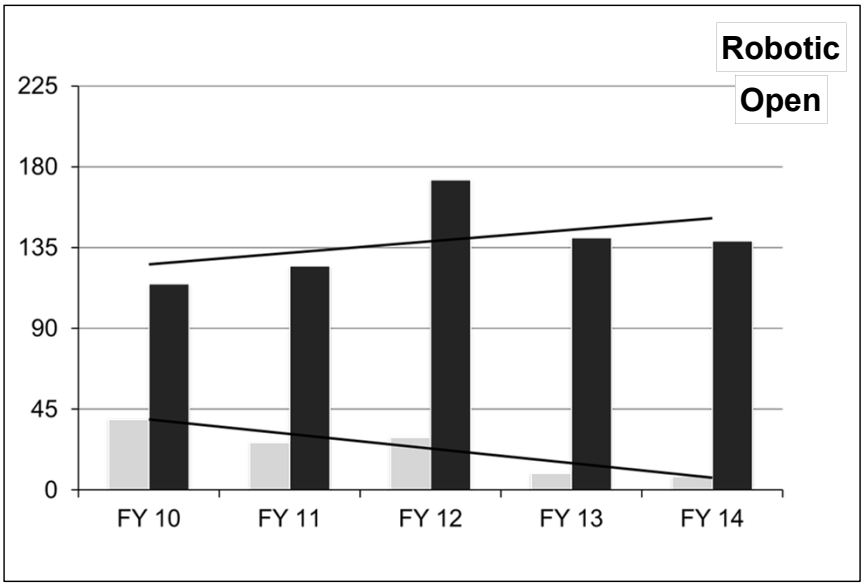
- **Open**
- **Laparoscopic**
- **Robotic**
- **Approach is not as important as preserving nephrons ➔ partial nephrectomy**

RAPN - Nationwide Inpatient Sample

	RAPN	OPN	P value
N (2008-2010)	**9095**	**25461**	
Transfusion	**5.8%**	**10.6%**	***<0.001***
Post-op Complications	**22.1%**	30.5%	***<0.001***
LOS	**3**	4	**ns**
Prolonged LOS (>75th %ile)	**12.4%**	**34.8%**	***<0.001***

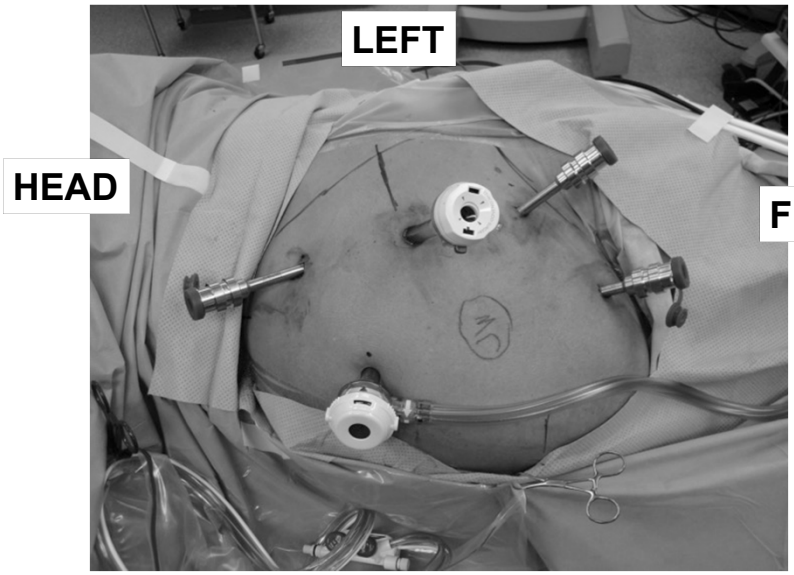
Ghani et al. J Urol 2014;191:907

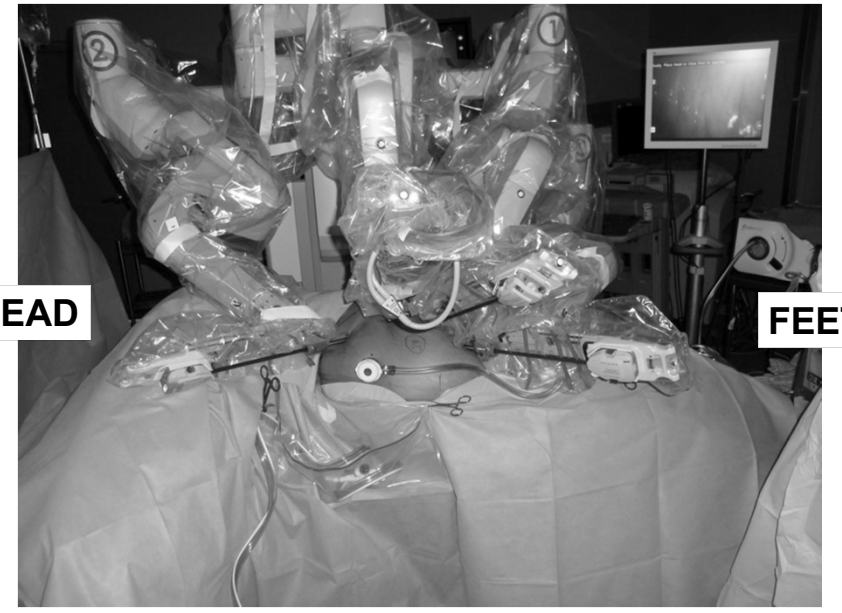
OSU Partial Nephrectomy



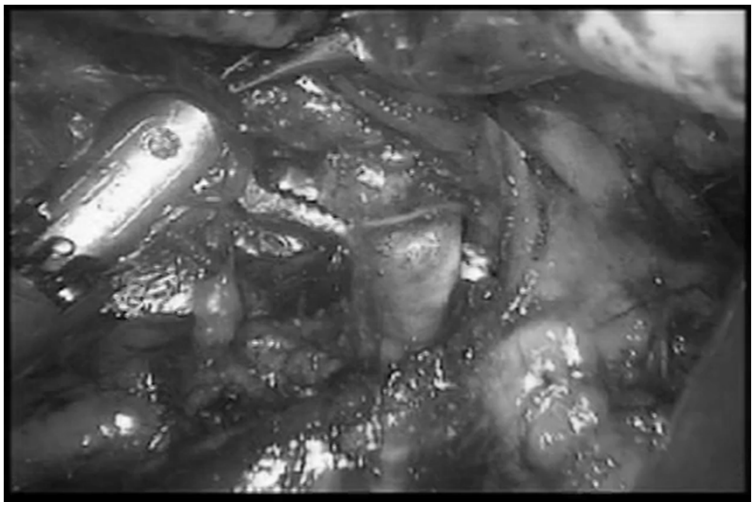
Robotic Partial Nephrectomy

Robotic Partial Nephrectomy





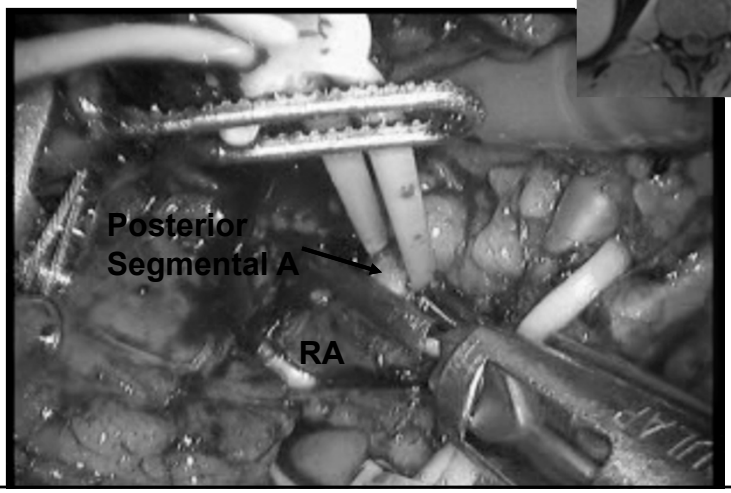
RIGHT ROBOTIC PARTIAL NEPHRECTOMY



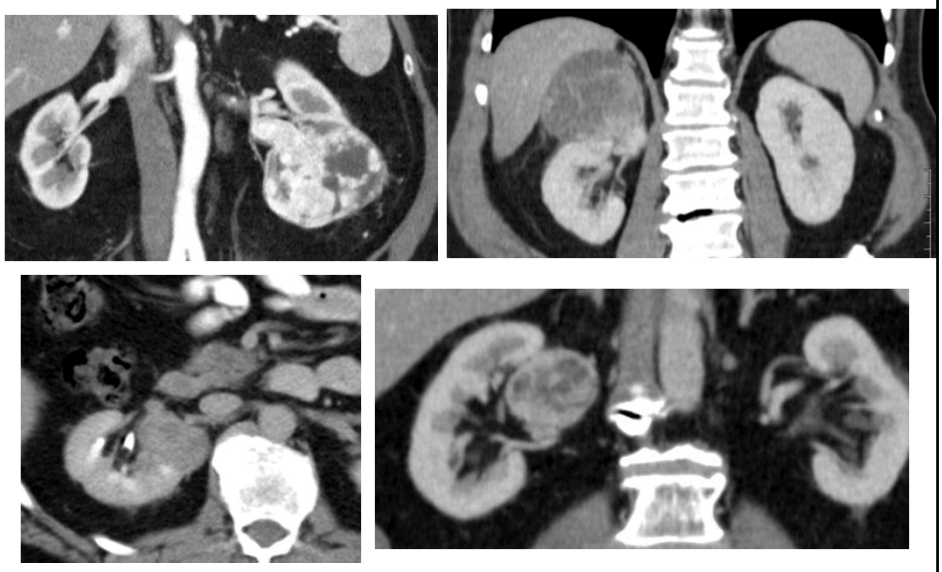
Margin Assessment

ROBOTICS –RAPN

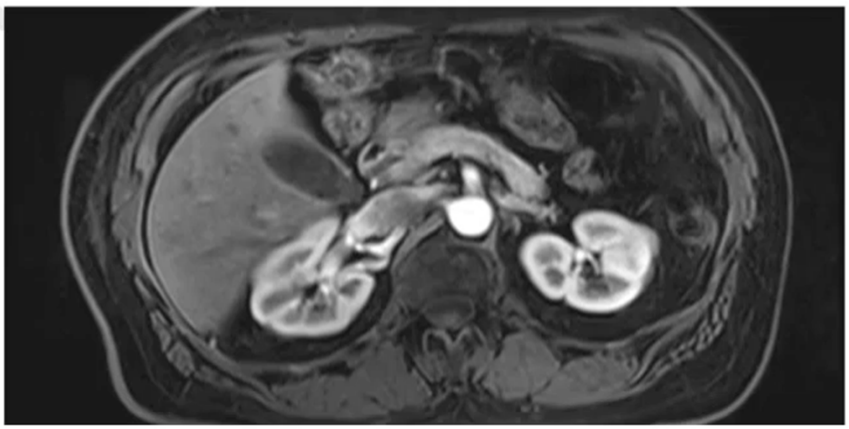
-Solitary Kidney
-BMI: 48
-Pre-op Cr: 2.03 (eGFR-37)
-Post op Cr: 2.10

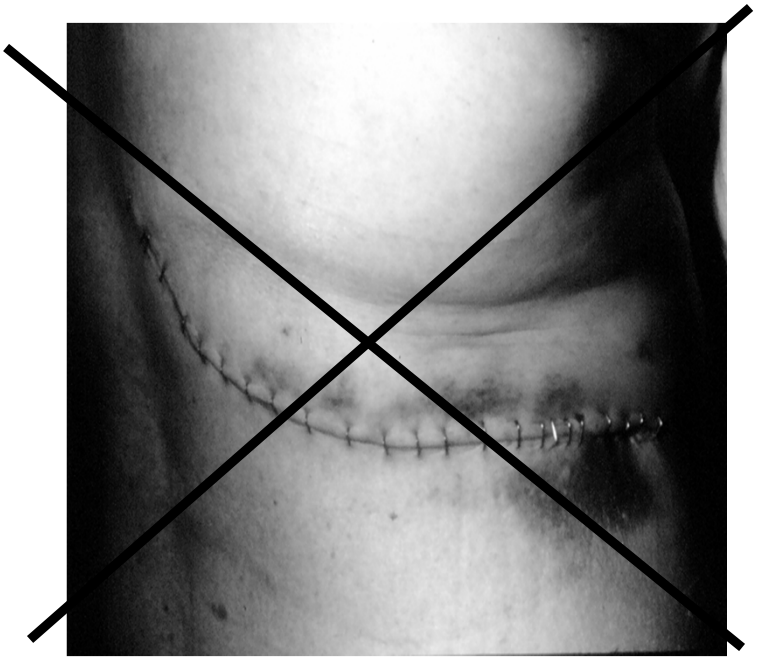


ROBOTICS – Partial Nephrectomy



RAPN with unexpected venous thrombus video





Laparoscopic Radical Nephrectomy

Laparoscopic surgery is the preferred approach for most tumors

Renal ablative techniques

- **Potential for less morbidity/complications**
- **Allows treatment of older patients who are not good surgical candidates**
- **Potential for similar efficacy to partial nephrectomy for select masses**

Indications for ablation of renal masses

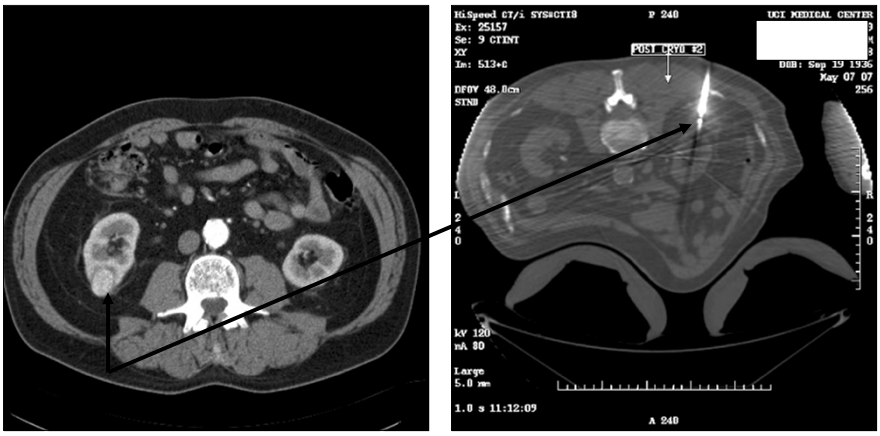
- Solid renal lesion <3cm (T1a)
  - Not good candidates:
    - Tumor deep in the renal sinus
    - Adjacent to the renal hilum or ureter
    - Anterior tumors with adjacent bowel
- Best suited to treat renal lesions in patients with comorbidities that preclude a major surgical procedure
  - i.e. elderly, severe COPD, CV disease
- Renal insufficiency
- Solitary kidney
- Multifocal/Recurrent tumors secondary to VHL, BHD etc

Leveilee R, Wingo M. Ablation technologies for renal cell carcinoma: Oncology spectrum 1(2)

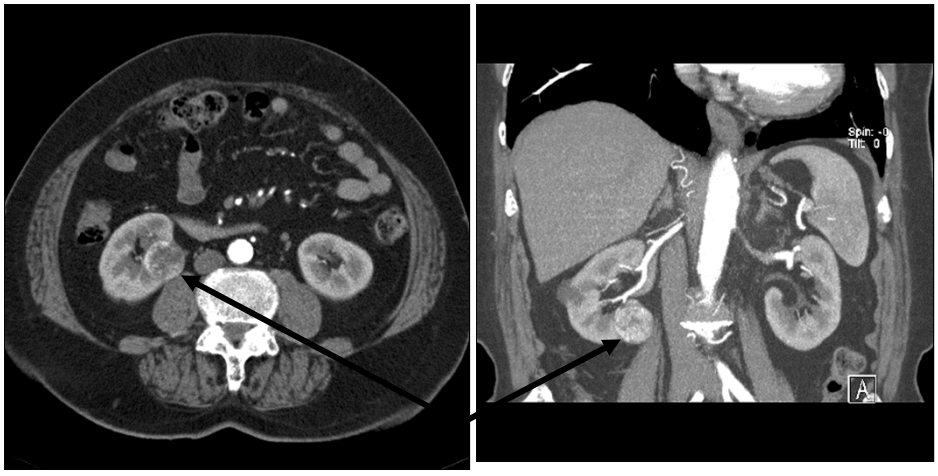
Ablative Modalities

- Radiofrequency Ablation (RFA)
- Cryoablation
- Generally performed percutaneously with CT, MRI or U/S guidance.

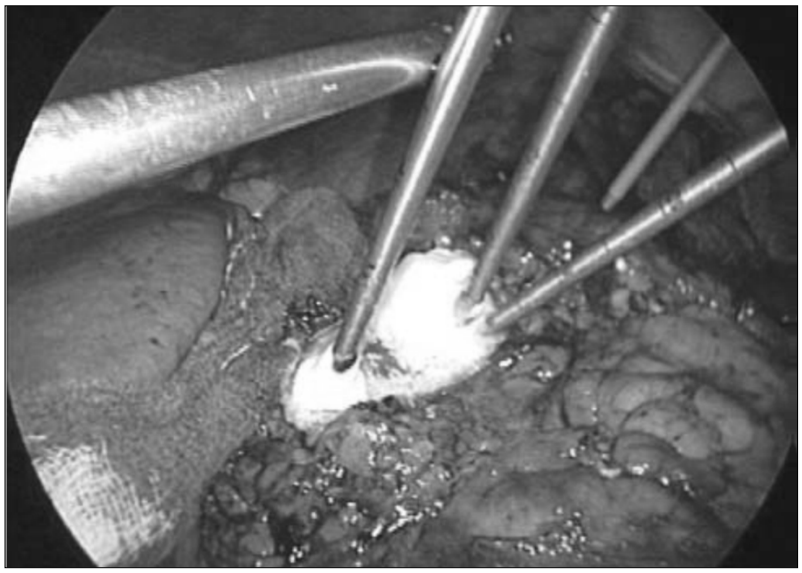
Percutaneous cryoablation



Laparoscopic cryoablation



Laparoscopic cryoablation



Post-ablation imaging

2 weeks 6 weeks 3 months

Treatment Options:
LOCAL RECURRENCE FREE SURVIVAL

Treatment	Survival	Tumor Size (cm)	F/U (mo)
RFA	87.0%	2.7	19
Cryo	90.6%	2.6	18
LPN	98.4%	2.6	15
OPN	98.0%	3.1	47
LRN	99.2%	4.6	18
ORN	98.1%	4.8	58

RFA=radiofrequency ablation; Cryo=cryoablation;
LPN=laparoscopic partial nephrectomy; OPN=open partial nephrectomy
LRN=laparoscopic radical nephrectomy; ORN=open radical nephrectomy

Adapted from Campbell-Walsh Urology 10th Ed.

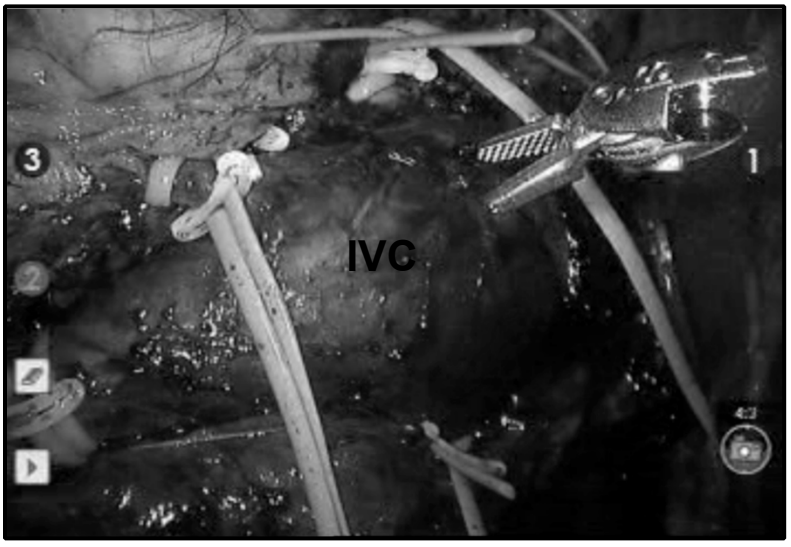
Treatment Options - Summary

- Surgery
  - Gold Standard
  - Suitable for tumors of all sizes
  - Nephron-sparing when possible
  - Minimally invasive approaches available
- Needle Ablation
  - Tend to have higher local recurrence rates
- Active Surveillance
  - Long term outcomes unknown
  - Not best for younger/healthier patients

Advanced Disease

- Surgery remains an integral part of the management of these patients.
  - Tumor thrombus in IVC
  - Regional Lymphadenopathy
  - Metastatic disease
- Surgery is the only treatment that offers the opportunity for cure

Robotic Nephrectomy with IVC Thrombectomy



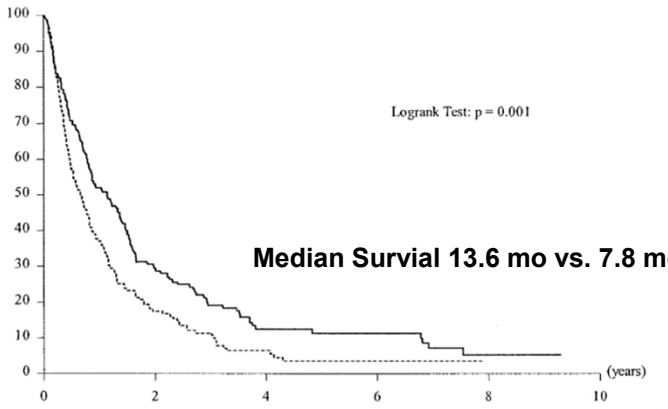
Robotic Nephrectomy with IVC Thrombectomy

Robotic Nephrectomy with IVC Thrombectomy


Omni-Tract®
REF 3536

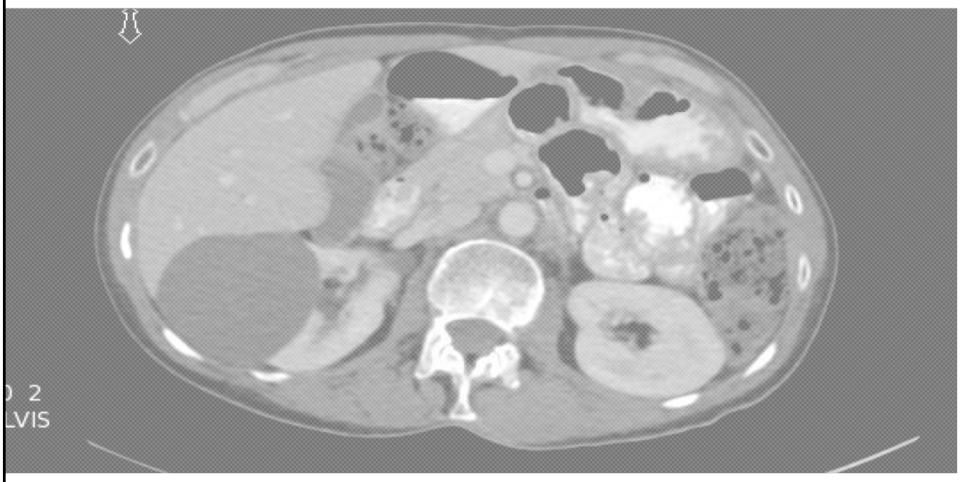
Metastatic Renal Cell Carcinoma

- **Cytoreductive nephrectomy**

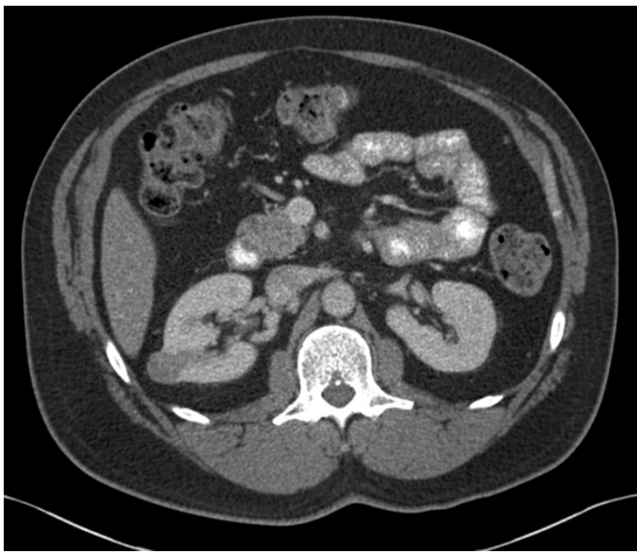


J Urol 2004; 171:1071

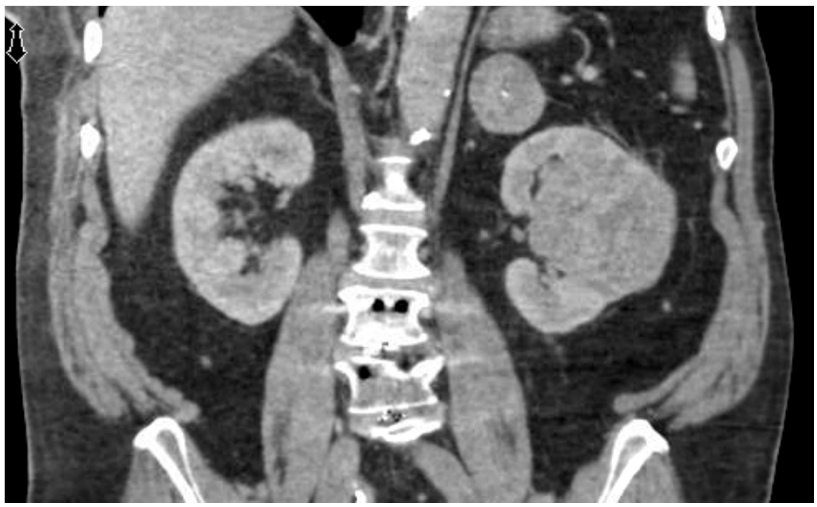
Case: Simple Renal Cyst



Case:
2 cm Enhancing Renal Mass



Case:
Left 9 cm Renal Mass & 4 cm Adrenal Mass



Conclusion

- **Renal masses are typically found incidentally**
- **A simple renal cyst can be diagnosed by U/S or CT and does not need follow-up**
- **Most solid renal masses represent renal cell carcinoma**
- **Nephron-sparing surgery should be perform when technically feasible.**
- **Most surgery can be performed in a minimally invasive fashion (laparoscopic/robotic)**