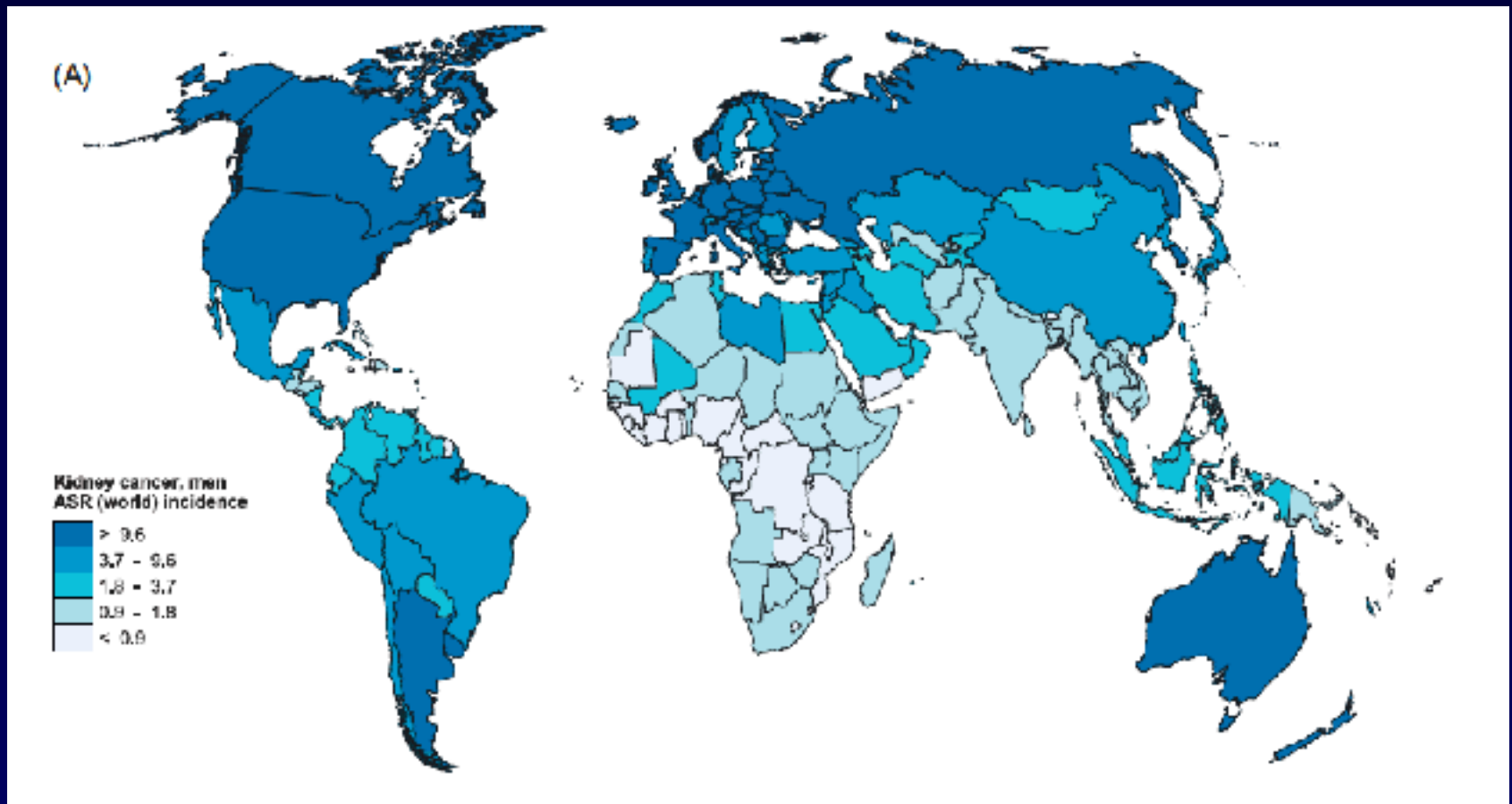*Odense, 2018*

DETECTION & CHARACTERIZATION OF SMALL RENAL MASSES

Nicolas Grenier
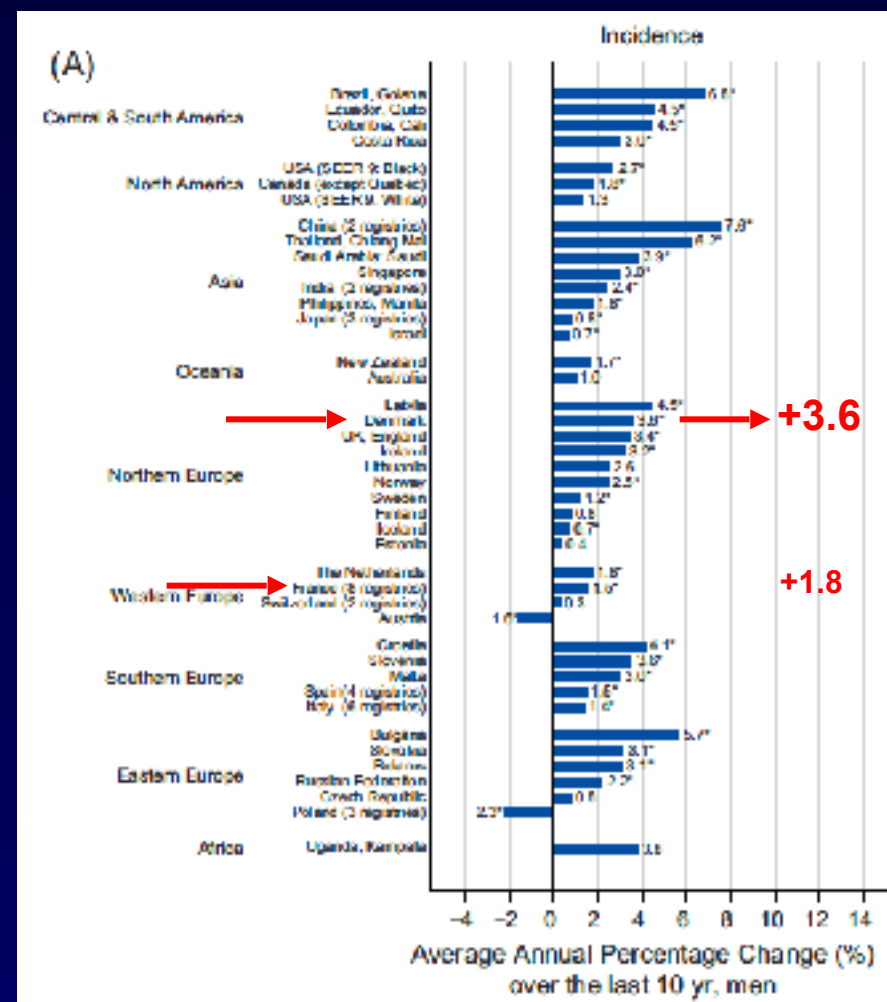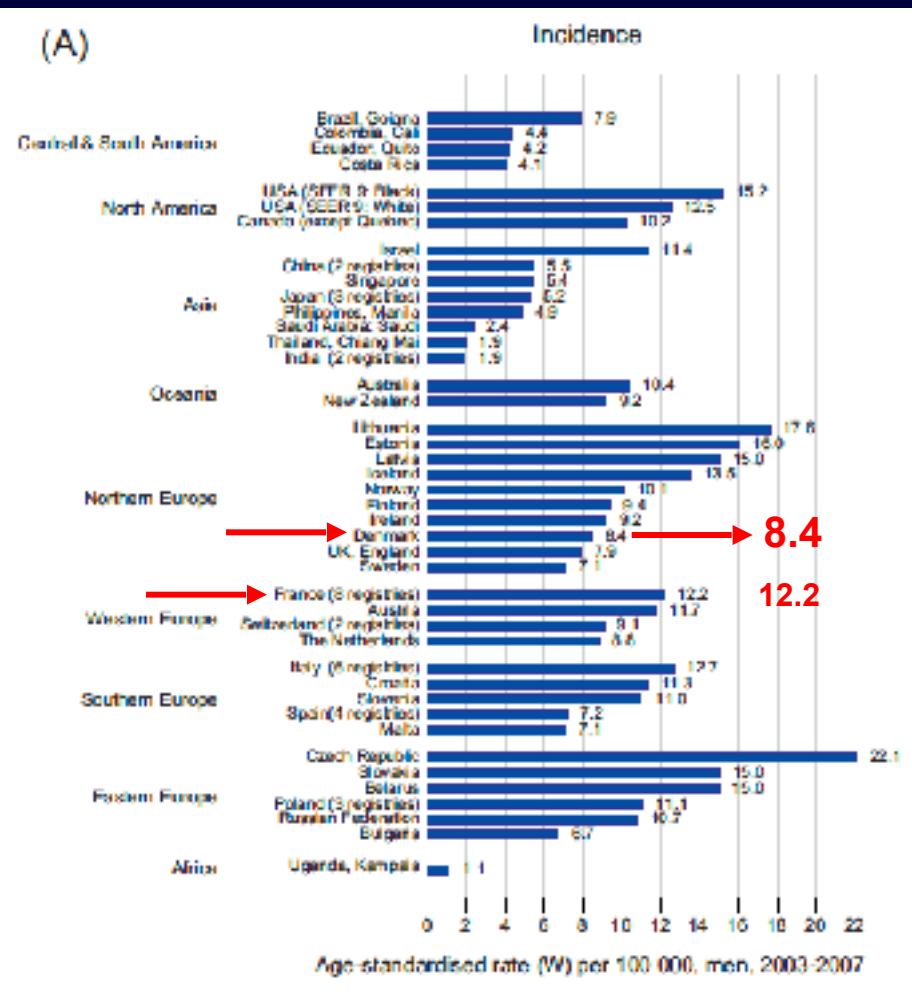
Université de Bordeaux
Service de Radiologie, Groupe Hospitalier Pellegrin, Bordeaux

nicolas.grenier@chu-bordeaux.fr

université
de BORDEAUX

CHU
Hôpitaux de
Bordeaux

Renal cancer : *International variations of incidence (2003-2007)*
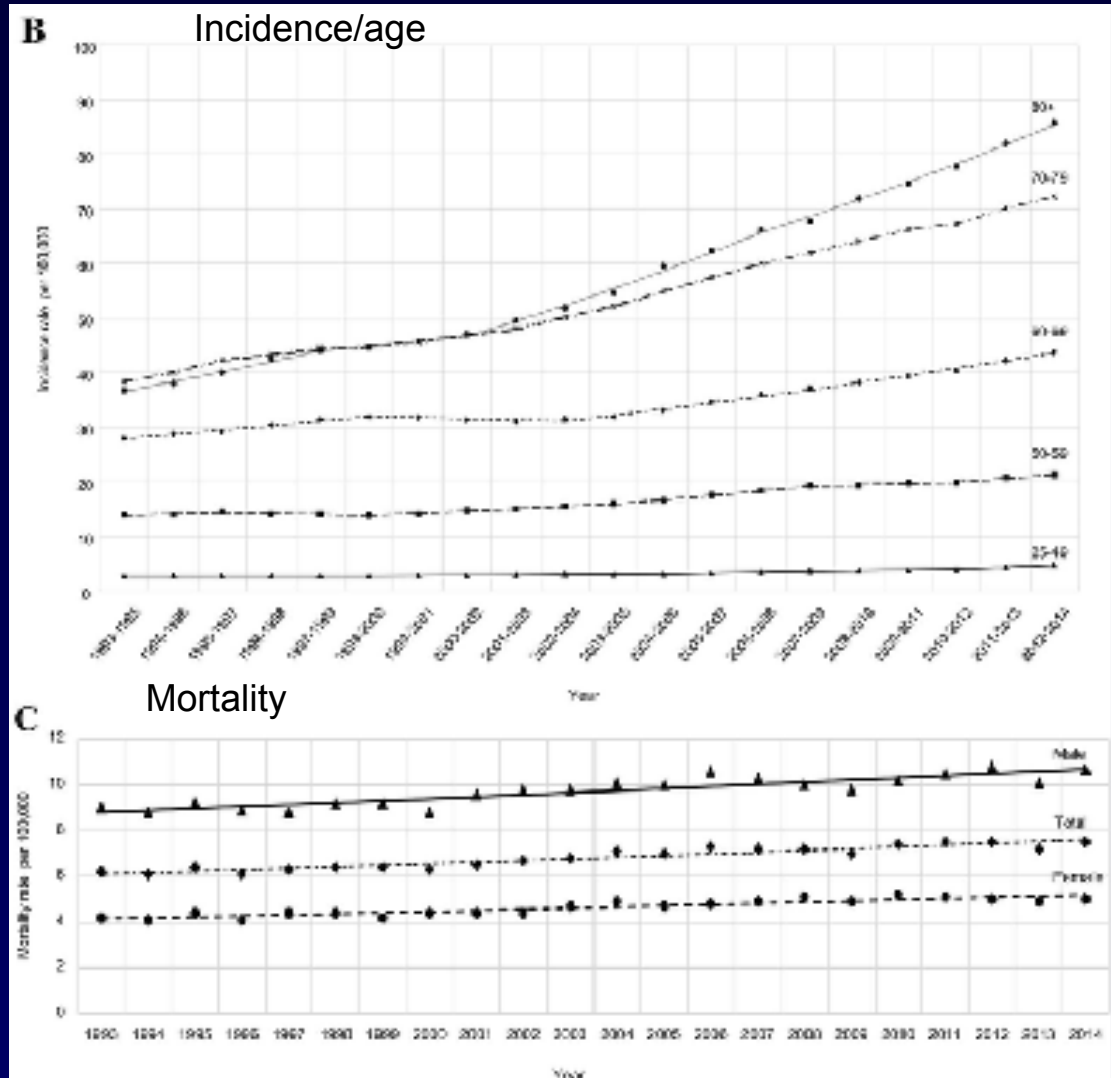

Znaor A et al, Eur Urol 2015

# Renal cancer : *International variations of incidence* (2003-2007)

Renal cancer : *Incidence*

- **RCC is the 9th most common cancer in men and 14th most common cancer in women worldwide**

- **RCC is the most lethal urological malignancy**

Incidence/age

Mortality

Rossi SH et al, World J Urol 2018

Renal cancer : *Incidence*

- **More than 60% discovered incidentally by imaging**

- **Over 25% of individuals with RCC have evidence of metastases at presentation**

According to stage

According to grade

King SC et al, J Urol 2014
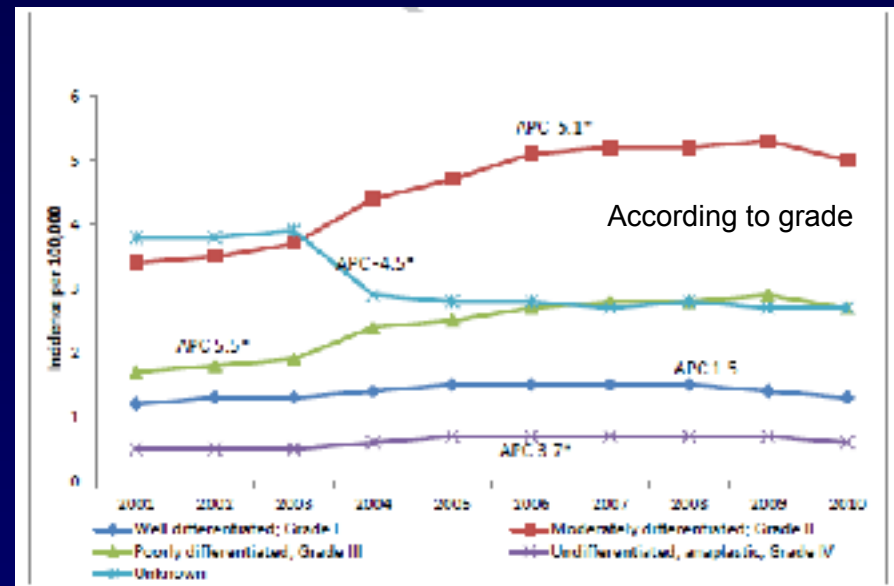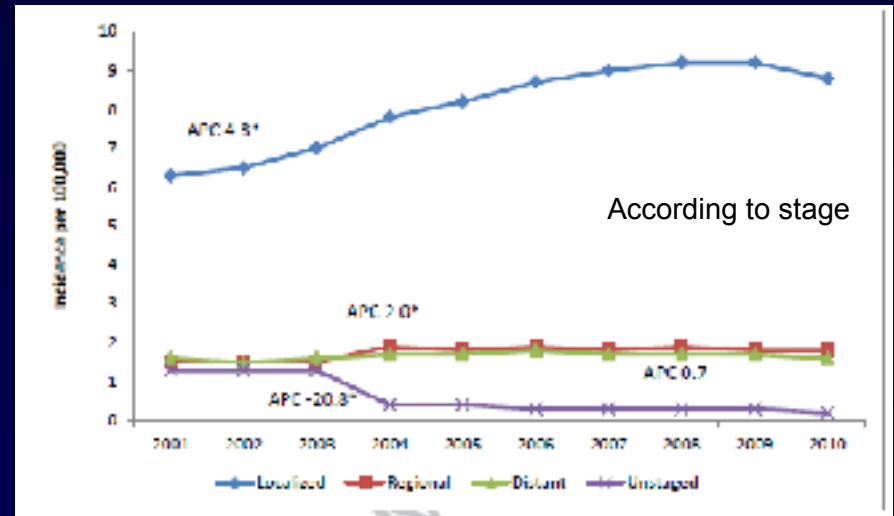
Detection of small renal tumors with US

Meta-analysis of the prevalence of renal cancer detected by abdominal ultrasonography

S. H. Rossi[1], R. Hsu[1], C. Blick[4], V. Goh[5], P. Nathan[7], D. Nicol[6], S. Fleming[8], M. Sweeting[2], E. C. F. Wilson[3] and G. D. Stewart[1]

Fig. 4 Infographic delineating comparative detection ability of established UK screening programmes compared with screening for renal cell carcinoma. The present meta-analysis suggests that screening 1000 individuals would detect at least one renal cell carcinoma.

Detection of small renal tumors with CT

CT is the main imaging technique able to detect SRMs
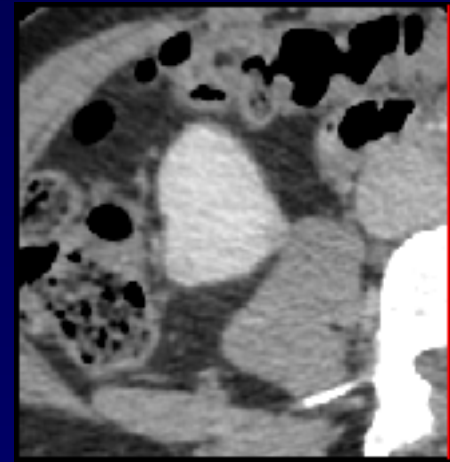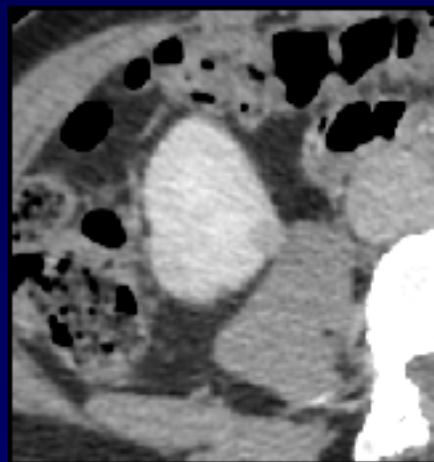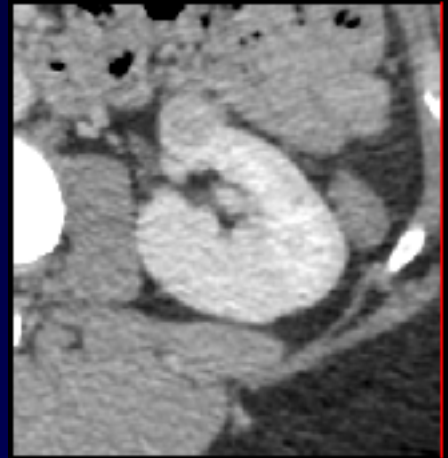

- <u>Perfect technique</u> :
  - Unenhanced phase
  - Contrast-enhanced vascular phase
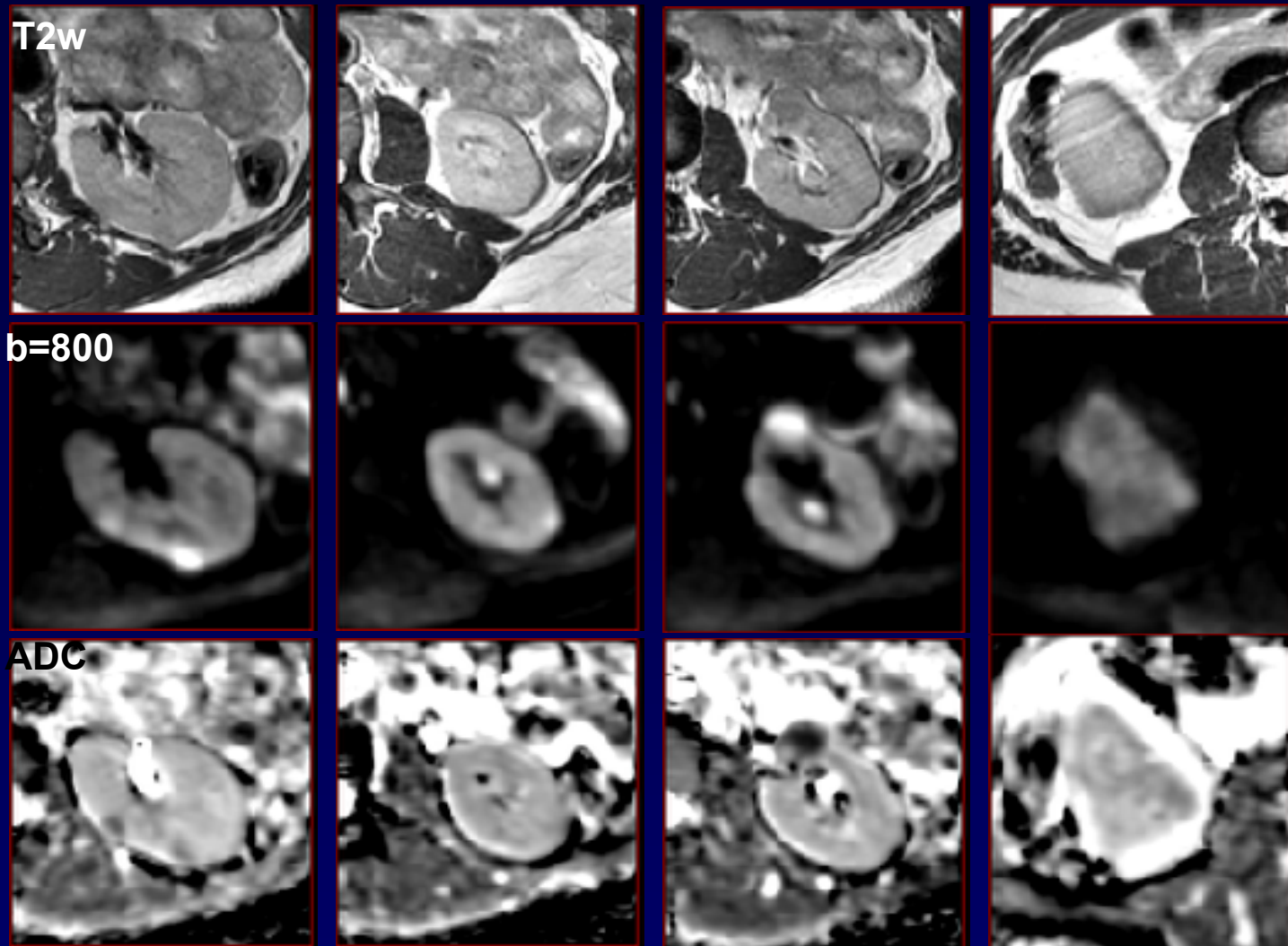 - Contrast-enhanced tubular phase

Detection of small renal tumors with CT

Value of the tubular phase +++

Detection of small renal tumors with MRI

MRI is very sensitive, but rarely used as first step, except for high risk patients

Value of DWI

Small renal masses : *nature*

- Of small solid renal masses, approximately 80% are malignant and 20% are benign. But, when stratified by size, <u>proportion of benign is</u>:
    - 25% among masses smaller than 3 cm,
    - 30% among masses smaller than 2 cm,
    - 44% among masses smaller than 1 cm

    Frank I et al, J Urol 2003

- Many renal masses are either too small to be fully characterized

- Renal mass management guidelines recommend additional imaging for many of these lesions

Silverman SG et al, Radiology 2015

Decrease number of tumor biopsy ?

- Increased incidence of discovering SRMs have provided the rationale for expanding the indications for renal tumour biopsy.

Size is a predictive factor of failure

- Repeat biopsy is successful in 80%

Table 3 – Current indications and contraindications of percutaneous renal tumour biopsies

Indications	• SRMs that are indeterminate on abdominal imaging (including selected indeterminate cystic lesions)
	• Renal masses that are suspicious for metastatic disease in the presence of a known extrarenal malignancy
	• Incidentally diagnosed SRMs in patients who are potentially candidates for active surveillance or minimally invasive ablative therapy to support treatment decisions
	• Renal tumours during follow-up of thermal ablation to confirm histologic success and monitor for recurrence
	• Primary renal tumours in the setting of metastatic disease to select the optimal biologic systemic therapy, particularly when a cytoreductive nephrectomy is not indicated or neoadjuvant systemic therapy is planned
	• Unresectable retroperitoneal renal tumours involving the kidney

Volpe A et al, Eur Urol 2015

Table 4 – Multivariate analysis of predictors of a diagnostic small renal mass biopsy

Predictor	Odds ratio	95% CI	p value
Size, cm (per 1-cm increase)	3.11	1.54–6.28	0.002
Tumor type: solid vs cystic	13.9	3.78–50.7	<0.0001
Image guidance: US vs CT or US plus CT	1.48	0.54–4.09	0.48
Location Mid vs lower pole	0.78	0.24–2.47	0.91
Upper vs lower pole	0.91	0.25–3.32	

Leveridge MJ et al, Eur Urol 2011

Objectives of imaging of renal tumors

- Is the mass solid or cystic ?

- Is the cystic mass benign or malignant ?

- Is the solid mass benign or malignant ?

- Can we discriminate RCC subtypes ?

- Can we improve the tumor staging ?

Characterization of renal tumors

- Is the mass solid or cystic ?

- Is the cystic mass benign or malignant ?

- Is the solid mass benign or malignant ?

- Can we discriminate RCC subtypes ?

- Can we improve the tumor staging ?

Characterization of renal tumors

- Actually, imaging of renal tumors is based on :
  - Ultrasonography (B mode and color doppler)
  - CT
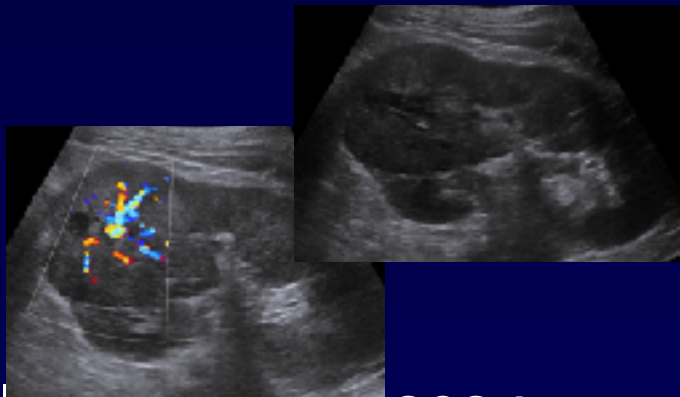
- In selected cases :
  - CEUS
  - MRI
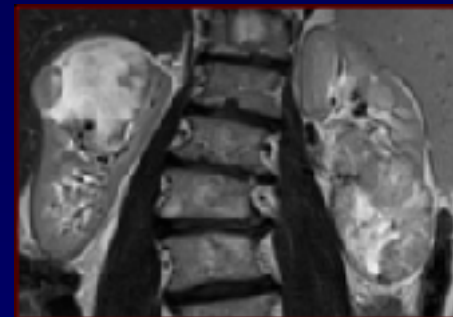
Multiparametric MRI

- Main sequences:
  - T1w Ip-Op
  - T2w
  - DCE (0-4mn)
  - Late post-Gd T1w
  - Diffusion-weighted
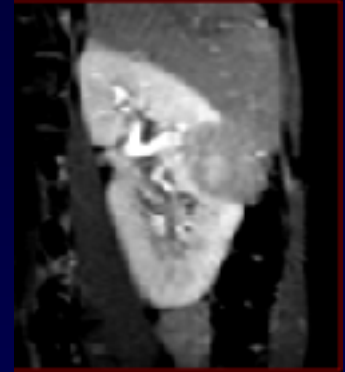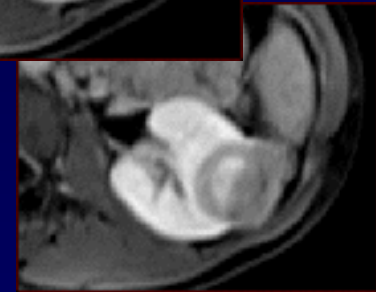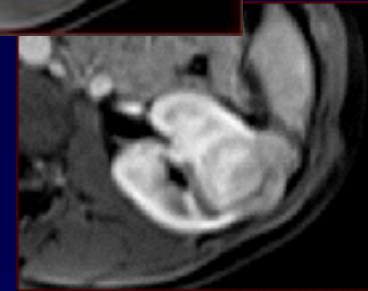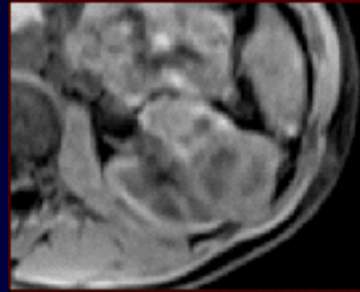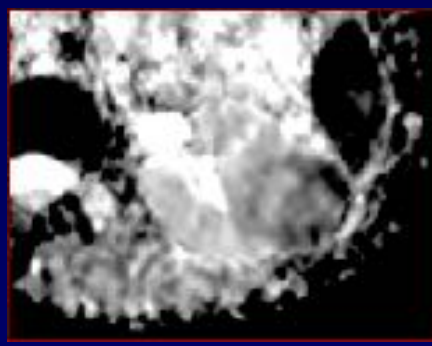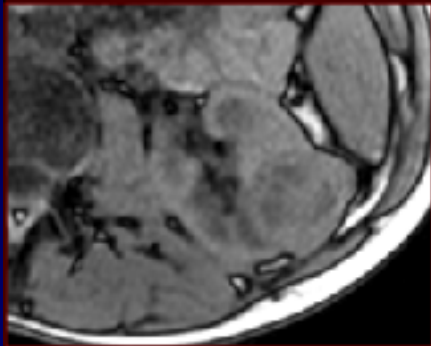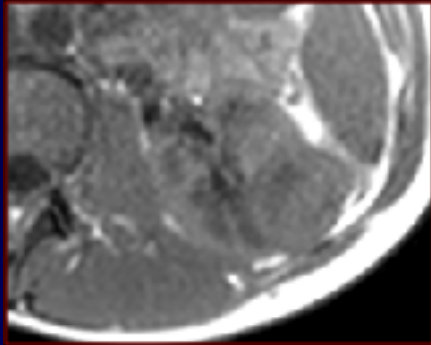
Characterization of renal tumors

- Is the mass solid or cystic ?

- Is the cystic mass benign or malignant ?

- Is the solid mass benign or malignant ?

- Can we discriminate RCC subtypes ?

- Can we improve the tumor staging ?

Is the mass solid or cystic ?

- <u>Post-contrast enhancement</u> :
  - significant when > 15 HU
  - unsignificant when < 10 HU
  - undeterminate when between 10 and 15 HU
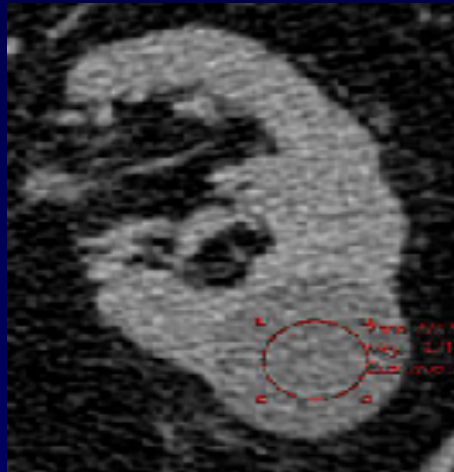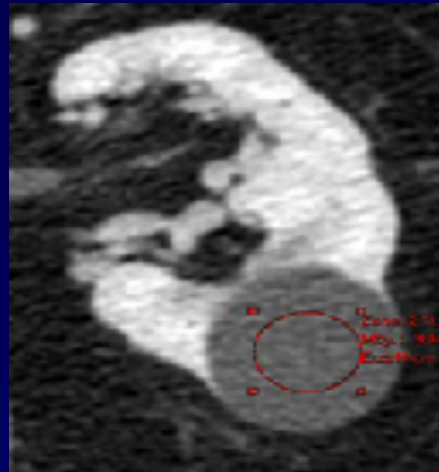
3HU   9HU

Is the mass solid or cystic ?
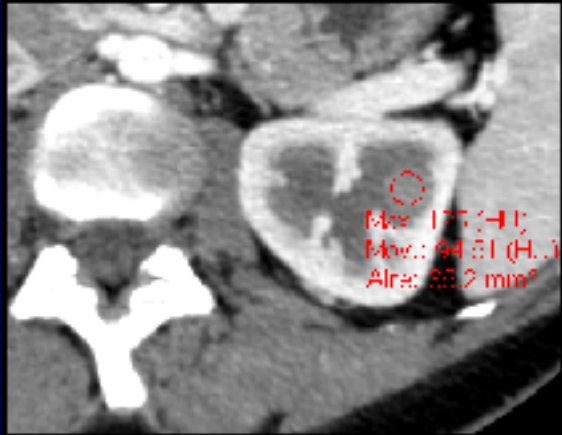
95HU

103HU
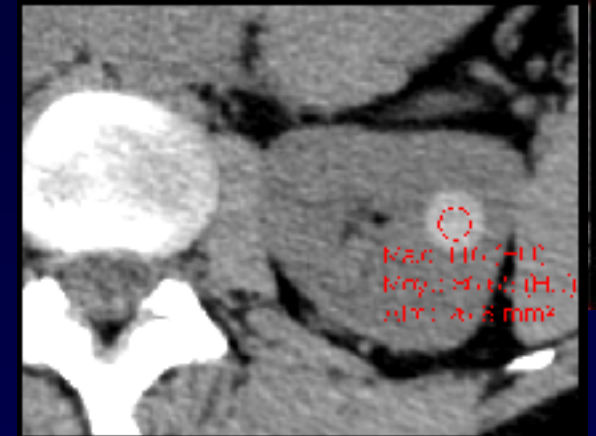
86HU
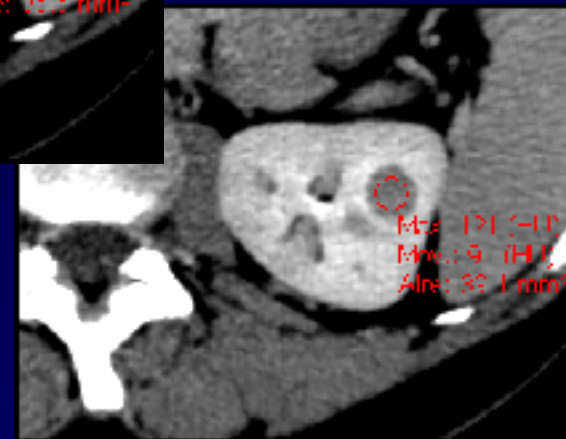
91HU
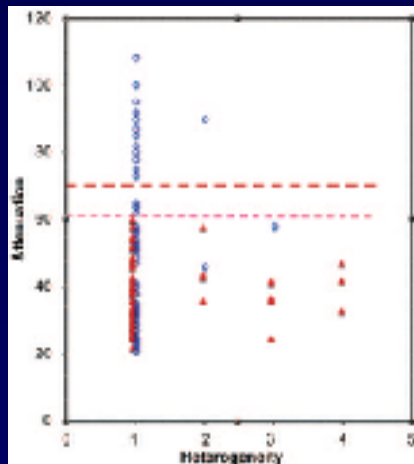
More than 99% of lesions with a density > 70 UH are cysts

Jonisch AI et al, Radiology 2007

Is the mass solid or cystic ?

22HU   38HU   41HU
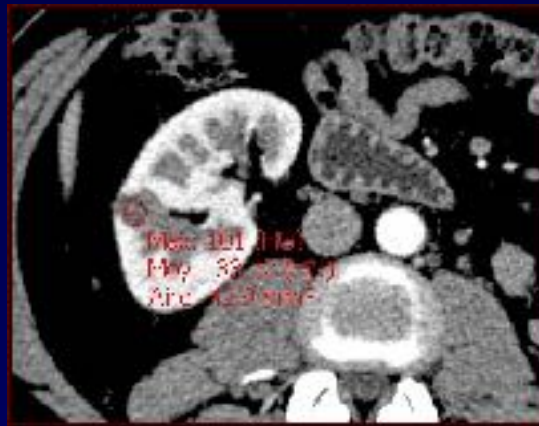
Please measure and do an US…

Very small masses: *cystic or solid ?*

Role for MRI +++ : T2w & DWI

- When infracentimetric, US and CT may be inconclusive (**mainly in at-risk patients**)
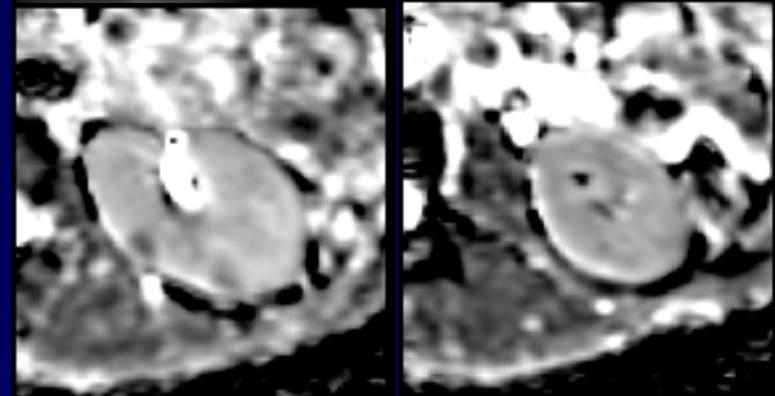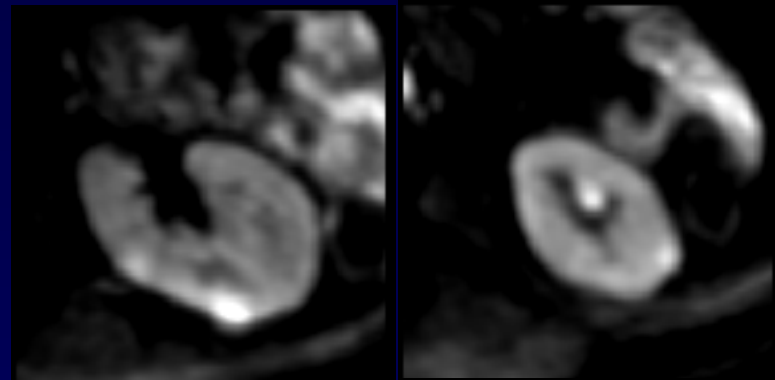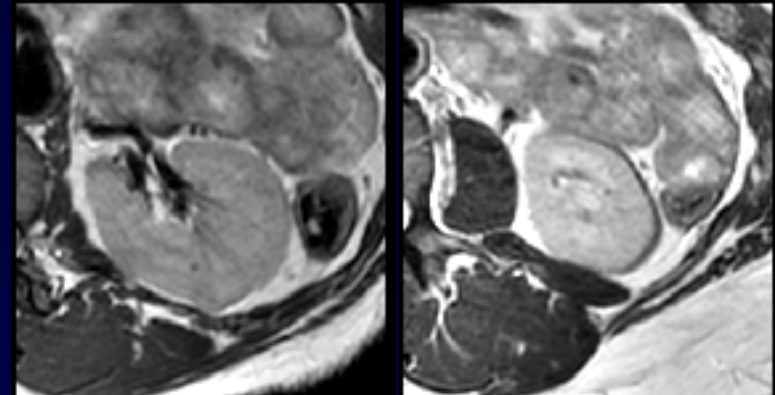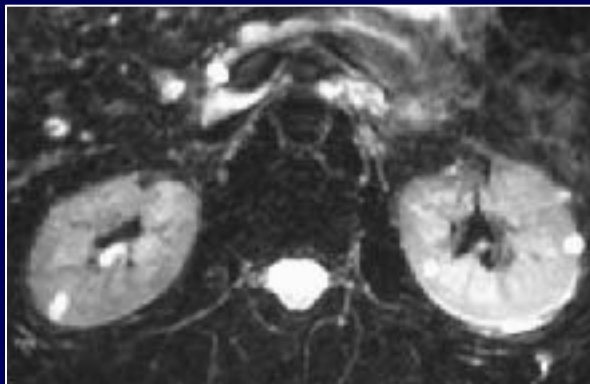
Is the mass solid or cystic ?

Role for MRI +++
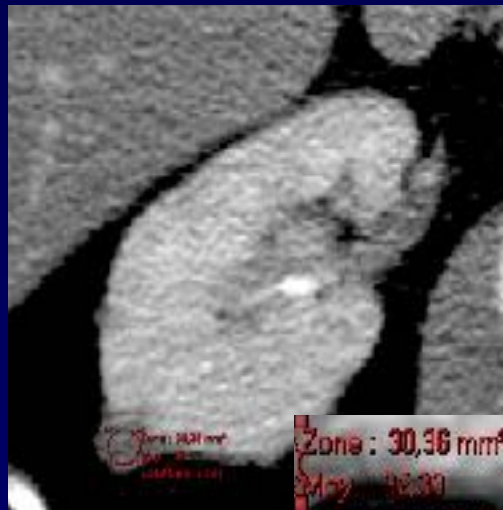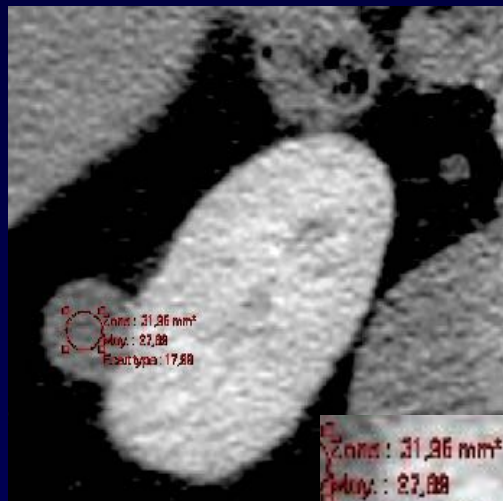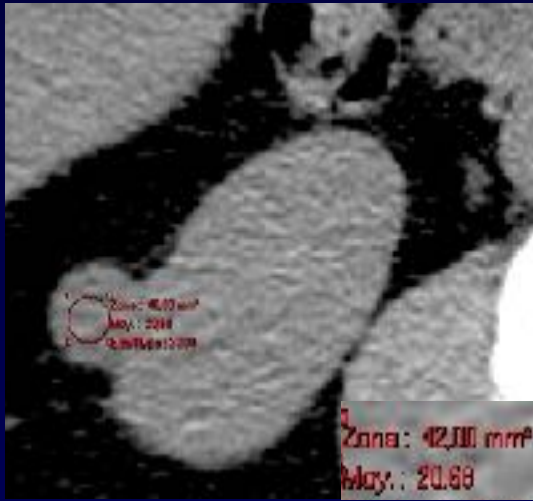
- ♂ 52 yo
- Left nephrectomy for papillary carcinoma
- 1 year fo

Courtesy O Hélénon, Paris

Is the mass solid or cystic ?
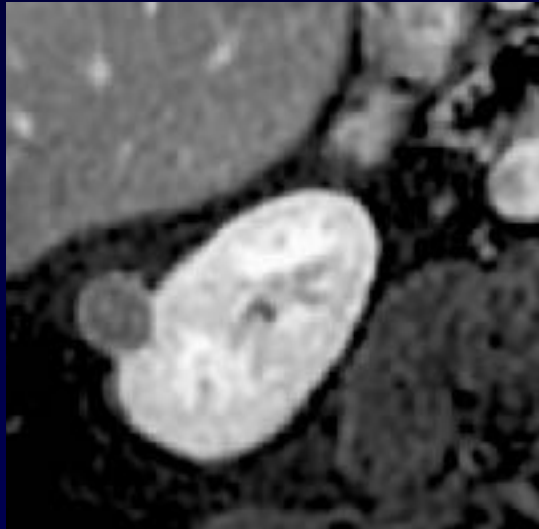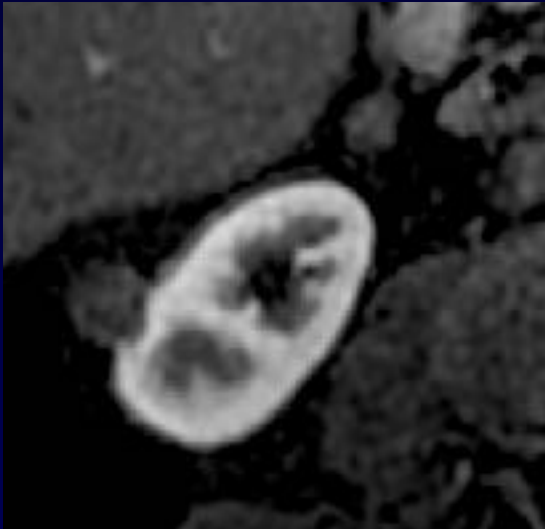
Recurrent papillary carcinoma

Any SRM with a non-fluid density before injection, even wo significant contrast enhancement must be imaged with CEUS or CE-MRI
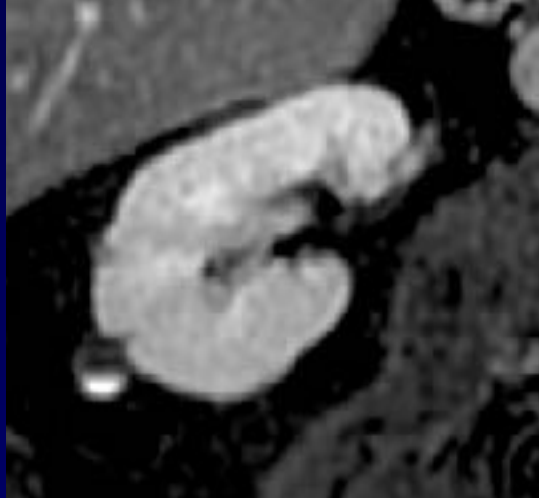
Haemorrhagic cyst

Hyperintensity on T1 or fluid-fluid level = hemorrhagic cyst

Courtesy O Hélénon, Paris

Is the mass solid or cystic ?

A new role for CEUS

Hemorrhagic cyst

RCC in a cyst
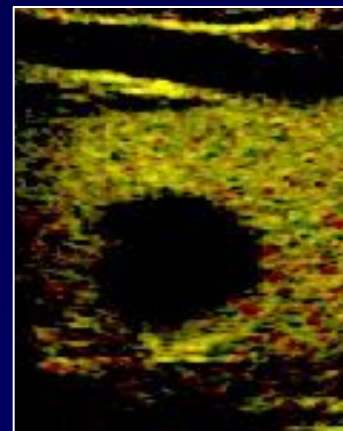
Courtesy Simon Freeman, Plymouth

Courtesy JM Correas, Paris

Is the mass solid or cystic ?

Solid Renal Cell Carcinoma
Measuring Water Attenuation
(−10 to 20 HU) on Unenhanced CT
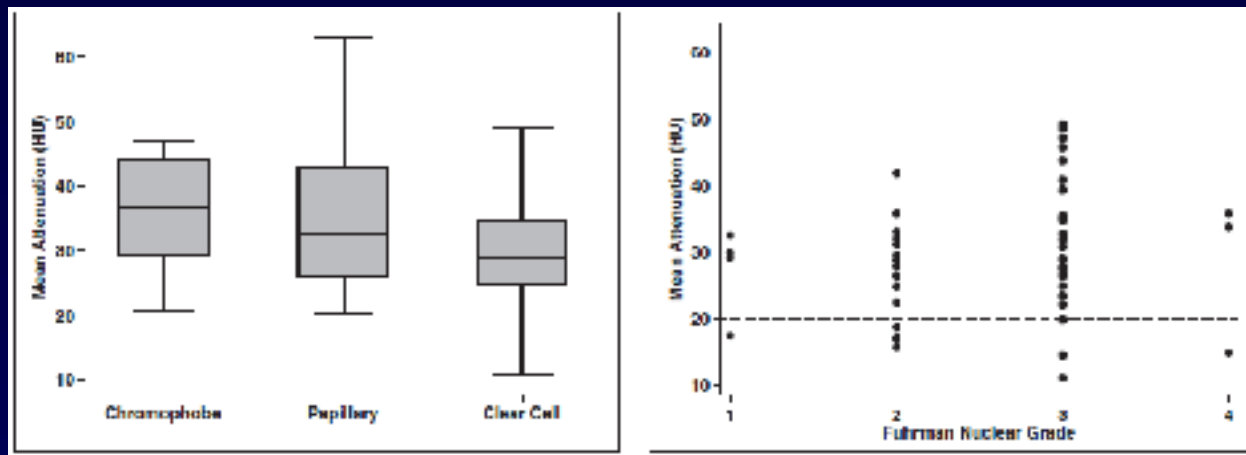
Schieda N et al, AJR 2015
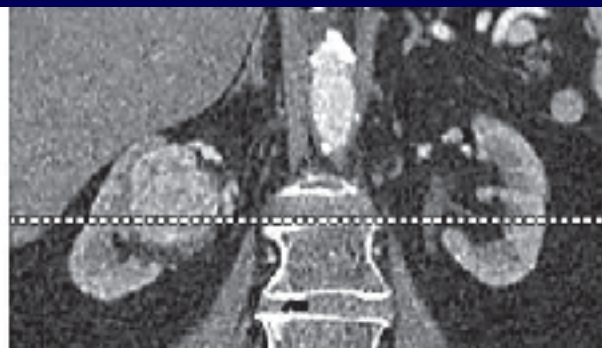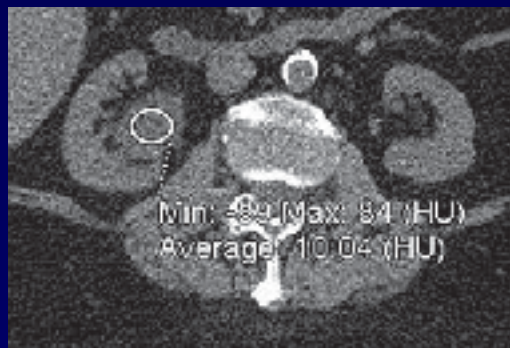
But : heterogeneous ± irregular margins

Explanation : lipid content ?

Objectives of imaging of renal tumors

- Is the mass solid or cystic ?

- **Is the cystic mass benign or malignant ?**

- Is the solid mass benign or malignant ?

- Can we discriminate RCC subtypes ?

- Can we improve the tumor staging ?
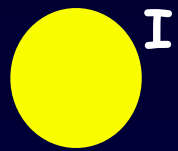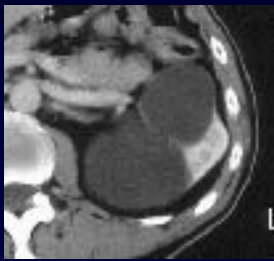
Bosniak's classification
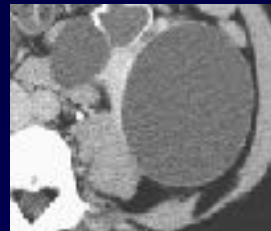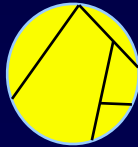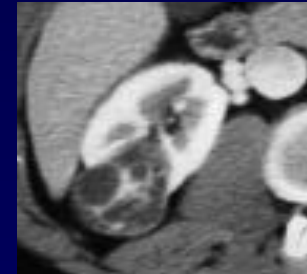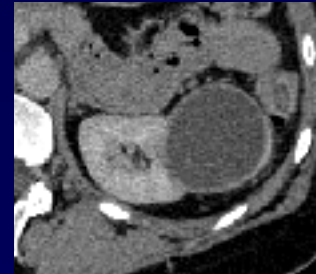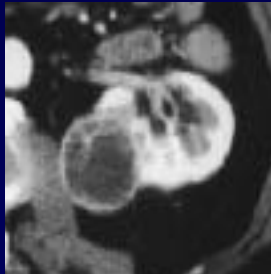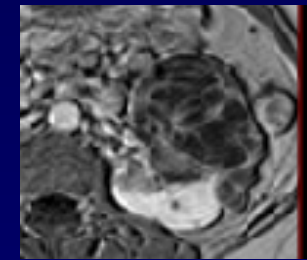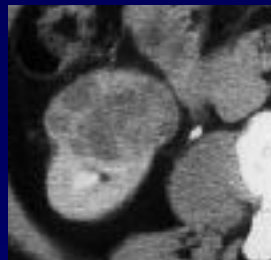
Bosniak : a role for MRI ?

- Helps to reclassify lesions IIF into III

IIF

III-IV
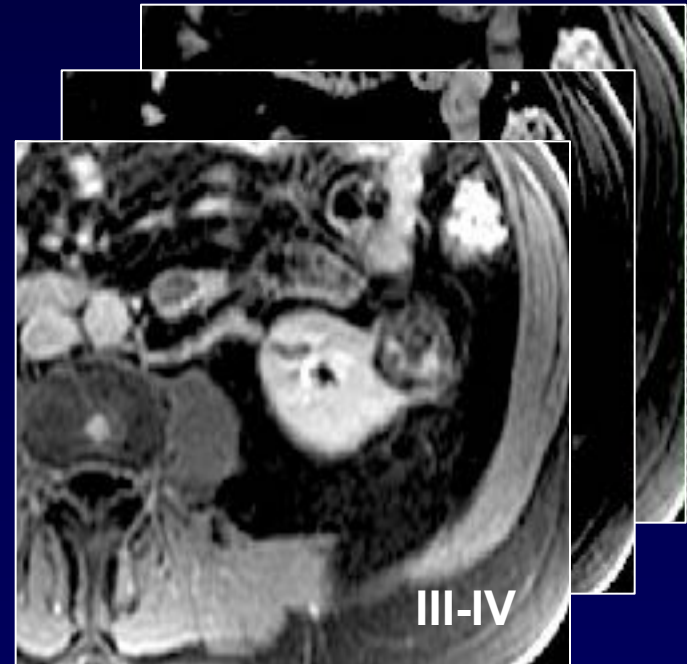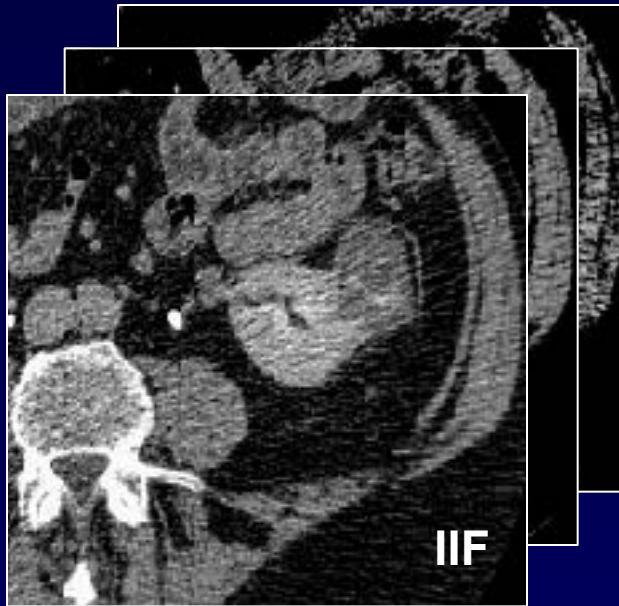
- Smith AD et al, Radiology 2012 :
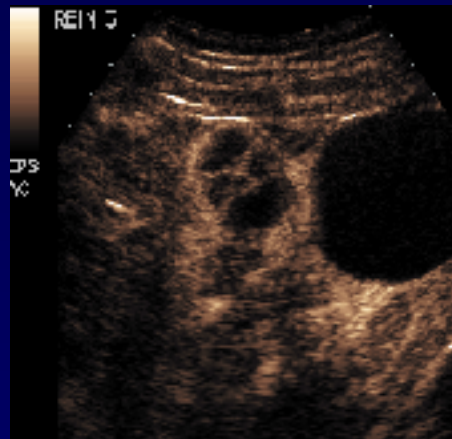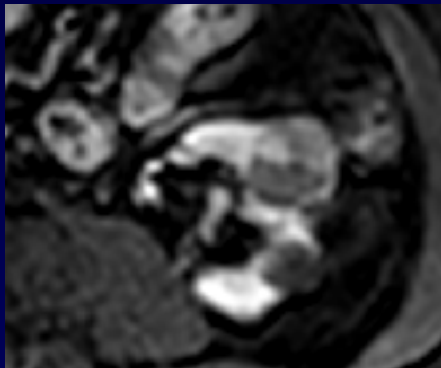 25% of Bosniak IIF were malignant !

Courtesy O. Hélénon, Paris

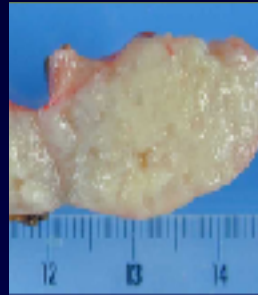# Bosniak : a role for CEUS
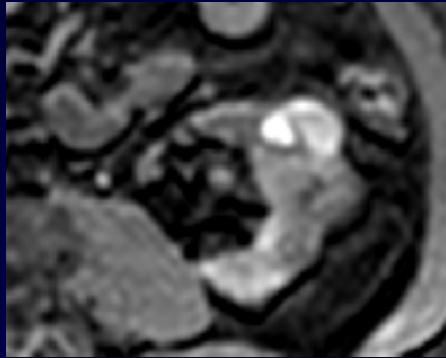
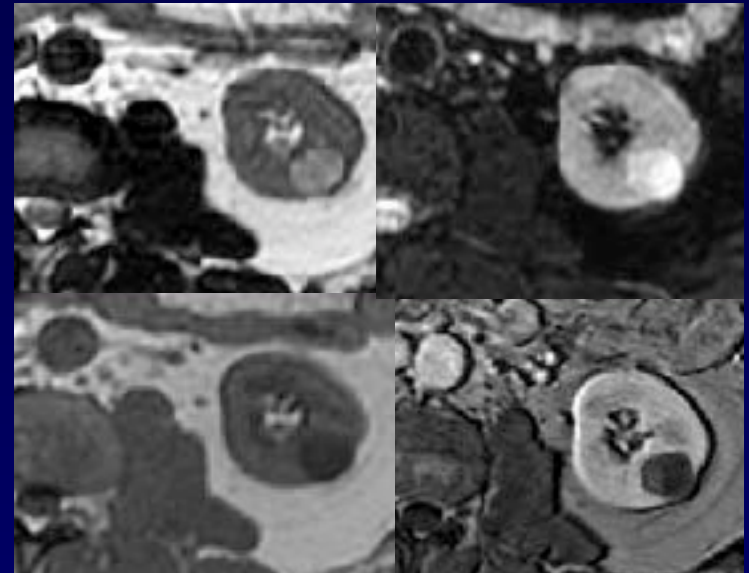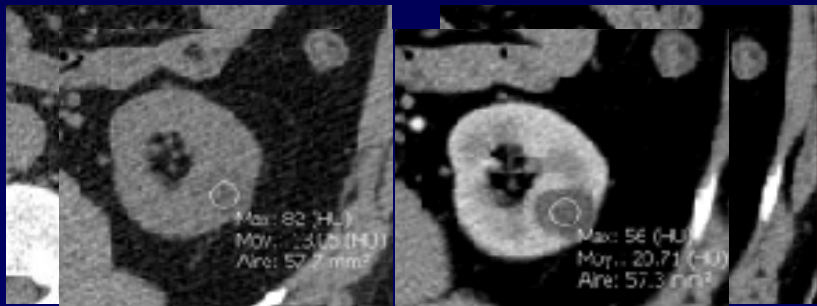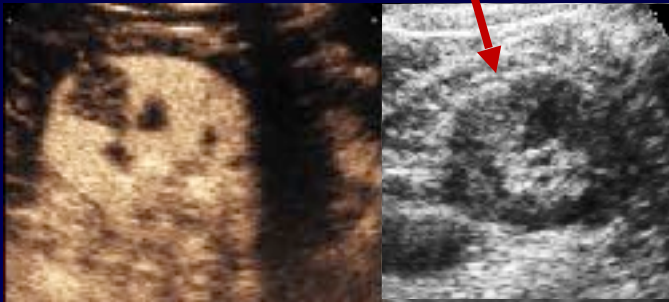**Cystic carcinoma**
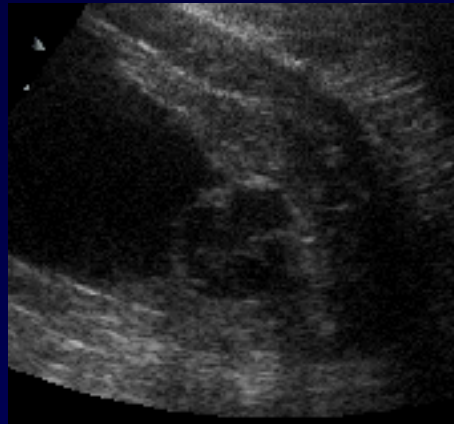
Hemorrhagic cyst
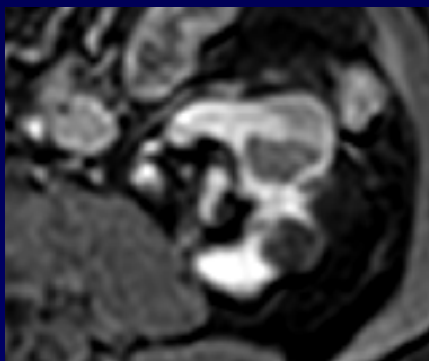
Tubulocystic carcinoma

- **Characteristics :**
  - Low grade malignant tumor
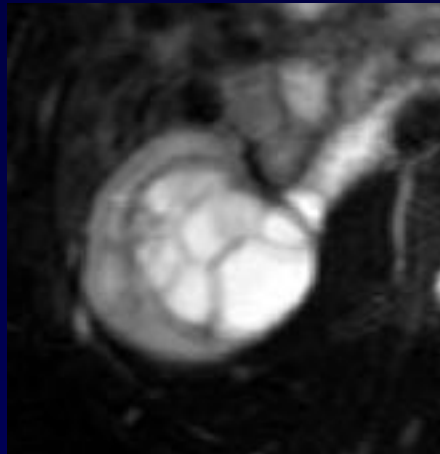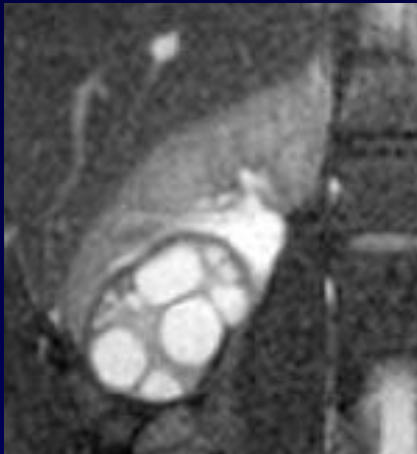 - > 50 years, sex ratio M/F 7:1
  - microcystic
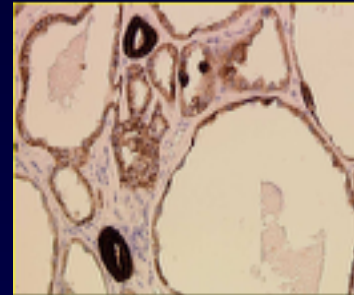
Combination of high echogencity and Bosniak II, IIF or III on CT or MRI
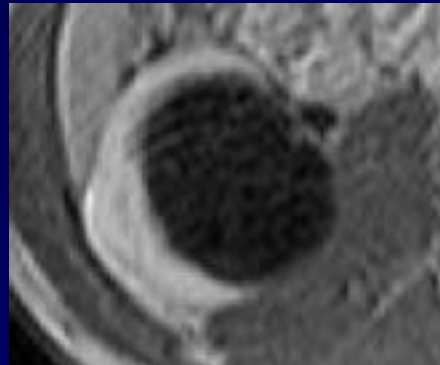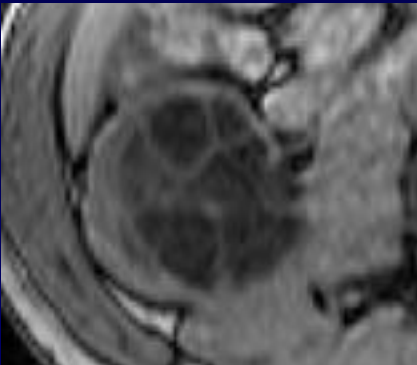

Cornelis F et al, Eur Radiol 2015
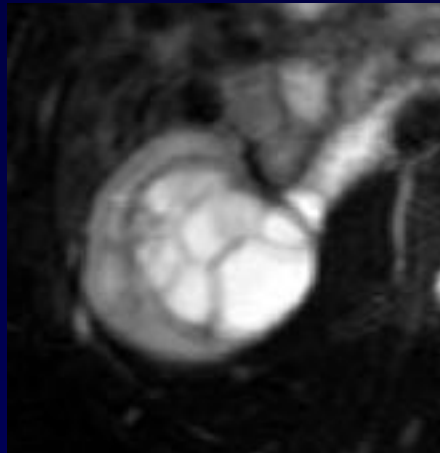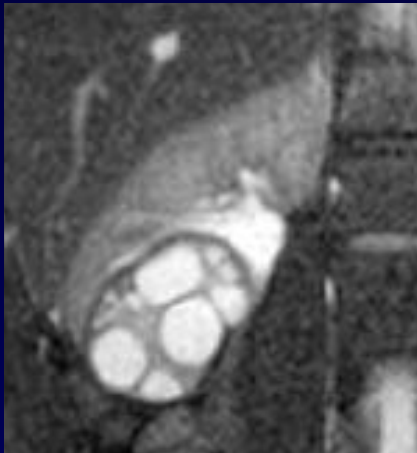
Question

- What is the Bosniak class of this lesion ?

- A- Bosniak II
- B- Bosniak IIF
- C- Bosniak III
- D- Bosniak IV
- E- not applicable

- What is the Bosniak class of this lesion ?

- A- Bosniak II
- B- Bosniak IIF
- C- Bosniak III
- D- Bosniak IV
- E- not applicable

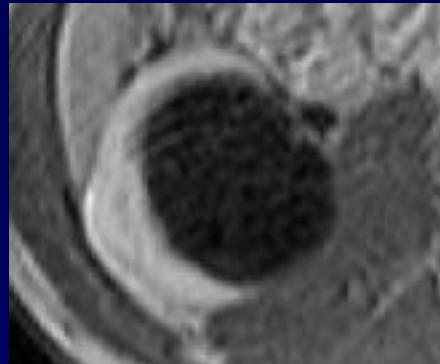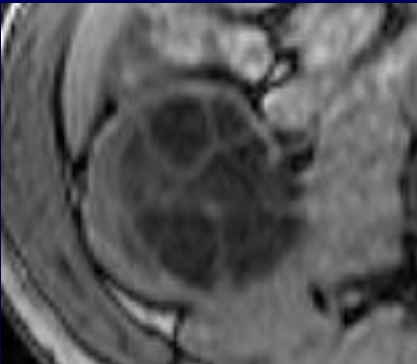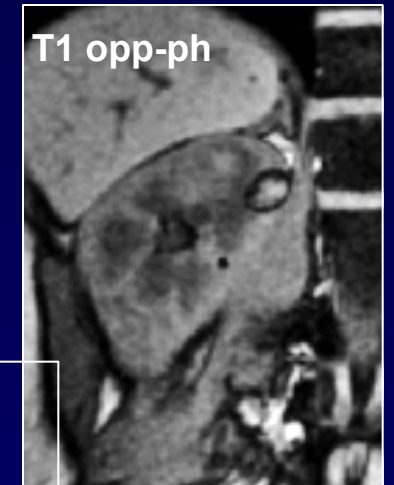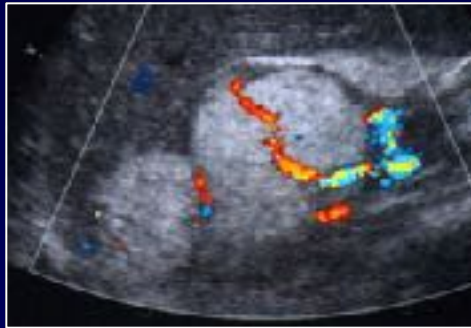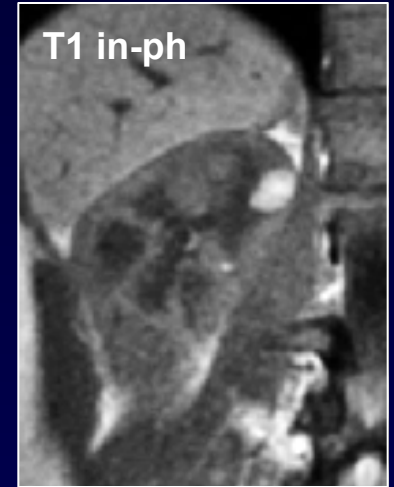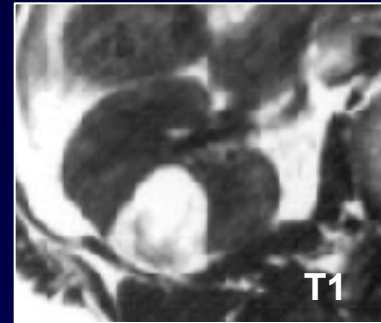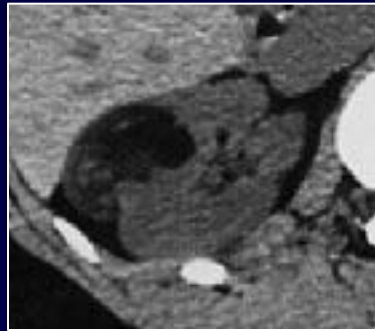*Volders, RadioGraphics 2001*

Objectives of imaging of renal tumors

- Is the mass solid or cystic ?

- Is the cystic mass benign or malignant ?

- Is the solid mass benign or malignant ?

- Can we discriminate RCC subtypes ?

- Can we improve the tumor staging ?

Angiomyolipomas

Typical patterns

T1 in-ph

T1

T1 opp-ph

T1 FS
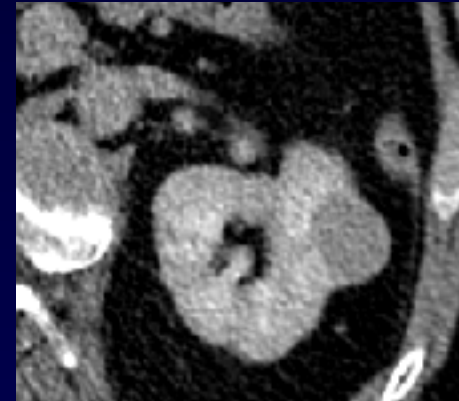
Sonography :
-Hyperechoic
-Hyperattenuating
-Homogeneous

CT :
-Density < -30UH
-No calcification
-No necrosis

MRI:
-High SI on T1w
-Drop of SI on FS T1
-India ink artifact on OPP

Characterization of solid renal masses

A large proportion of small renal tumors are « indeterminate » :
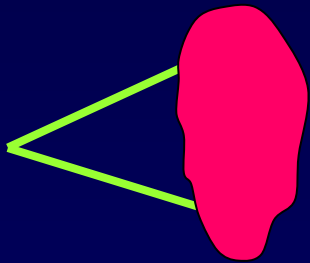T1 or T2 stage, wo fat or necrosis

→

- RCC : CCC, PC, ChC
- Oncocytoma
- Fat-poor AML
- ….

- **Can we identify benign tumors ?**
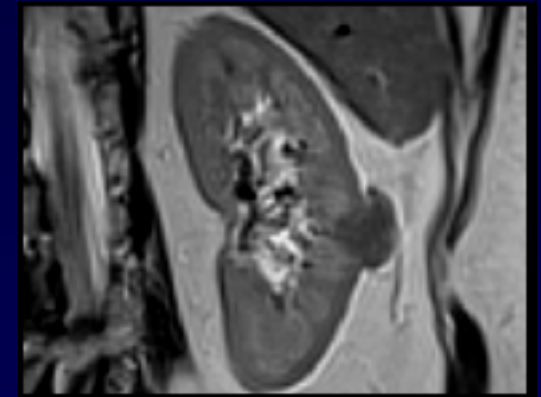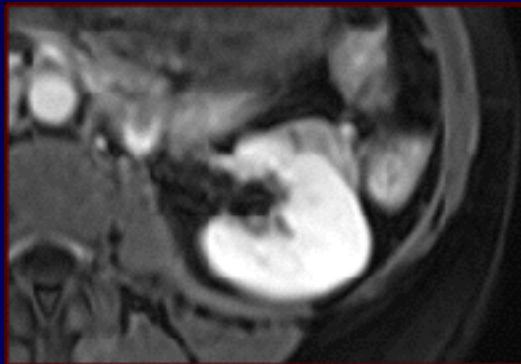 - Fat-poor AMLs
  - Oncocytomas

Morphological features in favor of Fat-poor AML

- **<u>Typically</u> :**
  - Ice cream cone
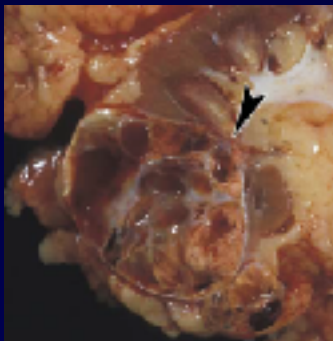 - No necrosis
  - No calcification
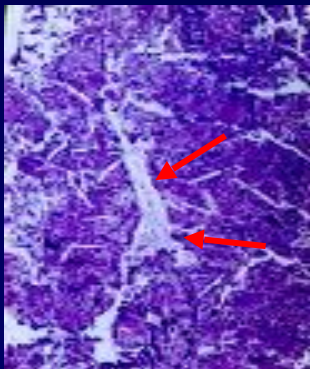 - No pseudocapsule

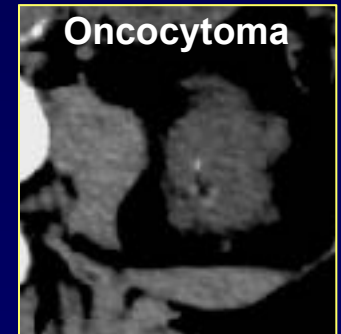Ice cream cone

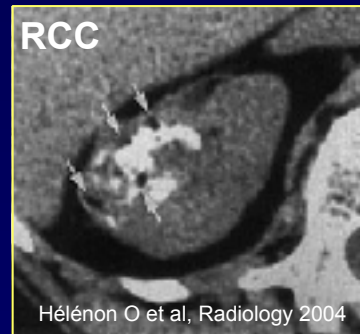# Morphological features ruling-out AML

A « **Pseudocapsule** », only visible on T2w sequences **rules-out AML**

Roy C et al, AJR 2005

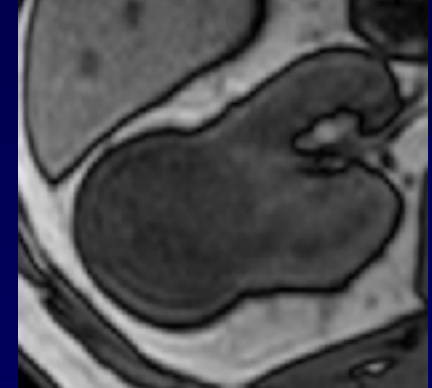Fat & necrosis **rules-out AML**

Fat & calcifications **rules-out AML**

RCC

Hélénon O et al, Radiology 2004

Oncocytoma

Fat-poor AMLs

- **Chemical-shift MRI may help**
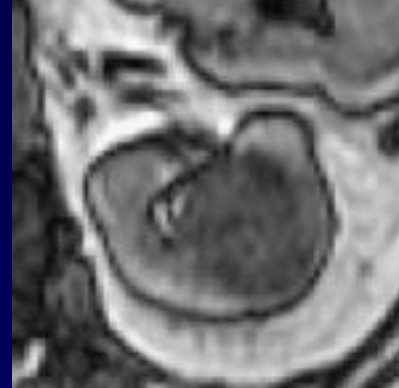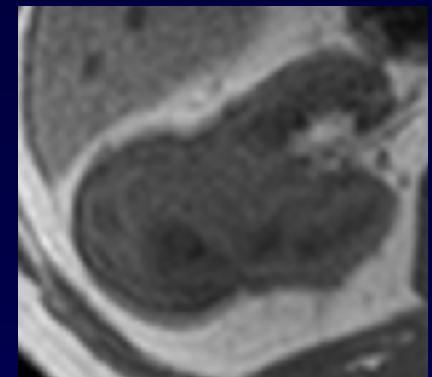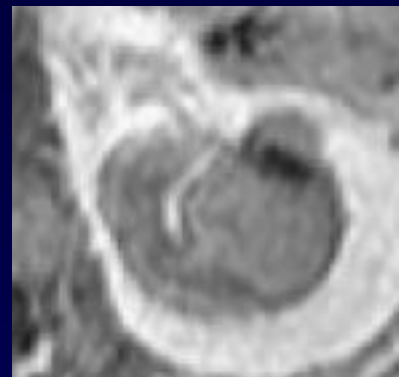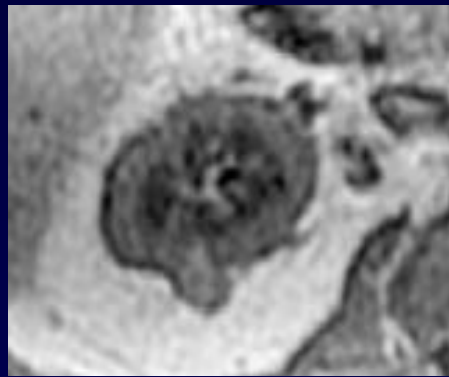
fpAML

fpAML

RCC
CC cytoplasm

PC
spumous macrophages
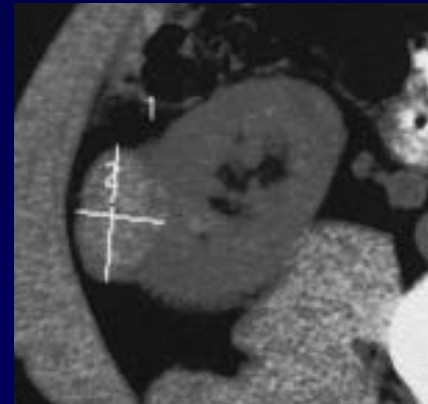
But not specific and no discriminant threshold !

Fat-poor AMLs

HES
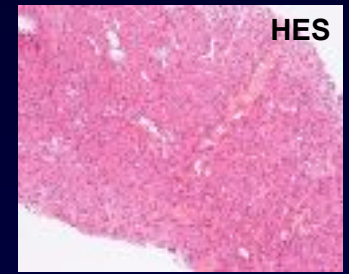
- **Chemical-shift MRI may NOT help :**

  Fat-poor AMLs with a high density of smooth muscle cells don't show any OPP drop of SI but a hyperattenuation on   unenhanced CT & a high vascularity after contrast
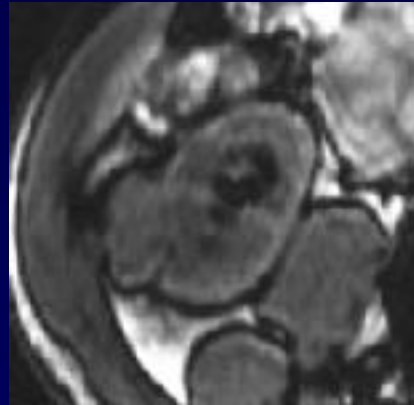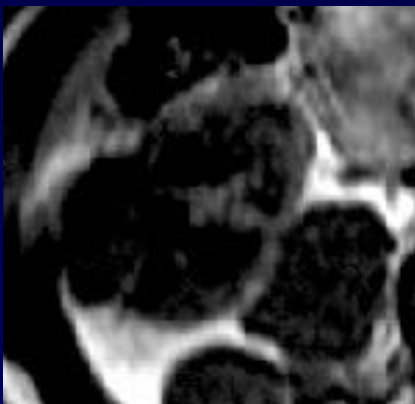
No signal drop on OPP-phase T1

=> *Hyperattenuating fat-poor AMLs*

Jinzaki M et al. Abdom Imaging 2014

Fat-poor AMLs

- **mpMRI may help +++**
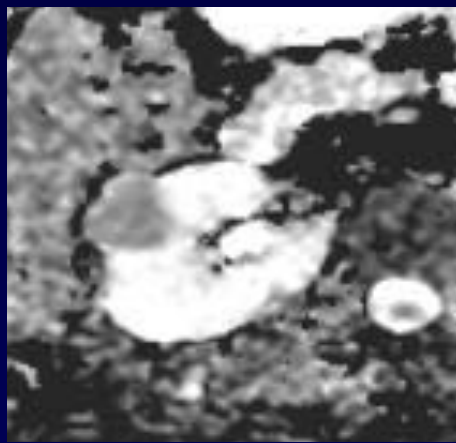
Low SI on T2 **Low ADC** **High wash-in / wash-out**
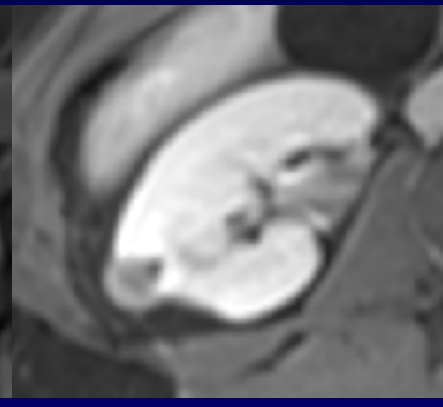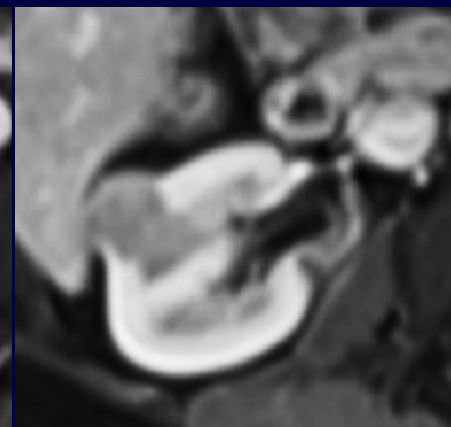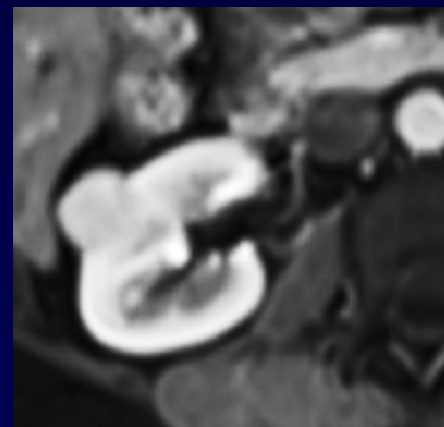
Oncocytomas

- **<u>Typical patterns:</u>**
  - Well defined, even when large
  - Fibrous central scar : observed in 40% of cases of oncocytomas
  - Spoke wheel enhancement

E. Comperat, Paris
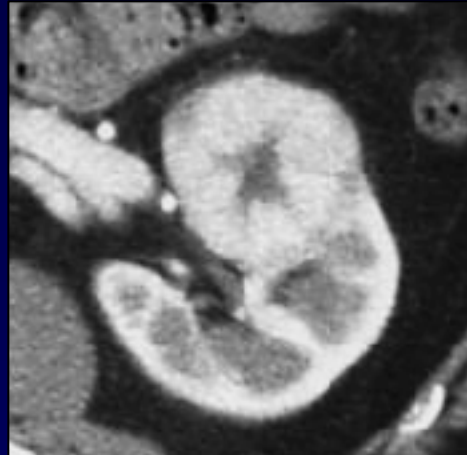
But:
-Usually large tumors !
-is this central area always a fibrous scar versus necrosis ?
-is a fibrous scar specific for oncocytomas ?

Oncocytomas

- **A central fibrous scar is not specific of oncocytoma** :
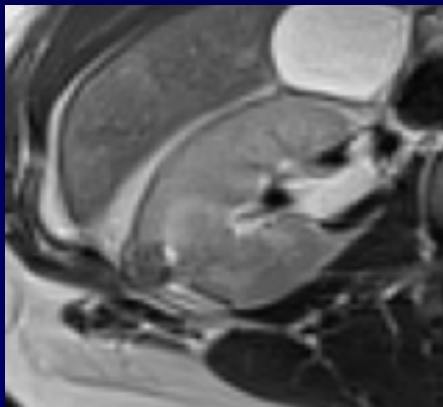 - Also observed in carcinomas : CCC and ChC
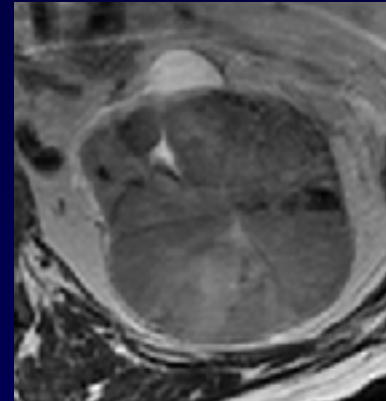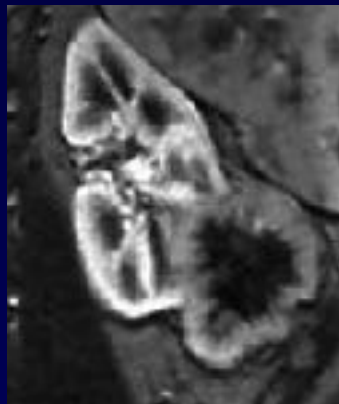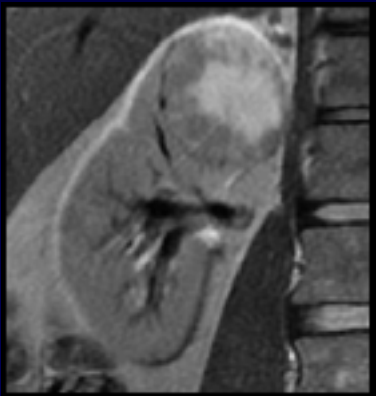
CCC   Oncocytoma   ChC

Oncocytomas

- **Central scar ? MRI may help**

A central hyperintense area on T2 :
central fibrous scar or central necrosis ?
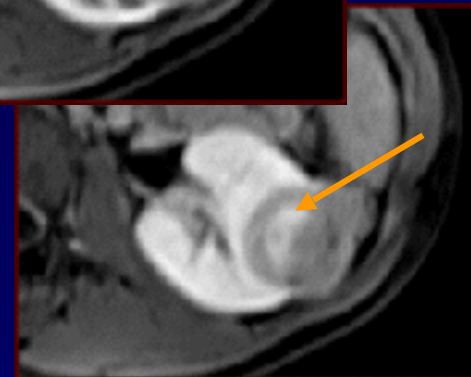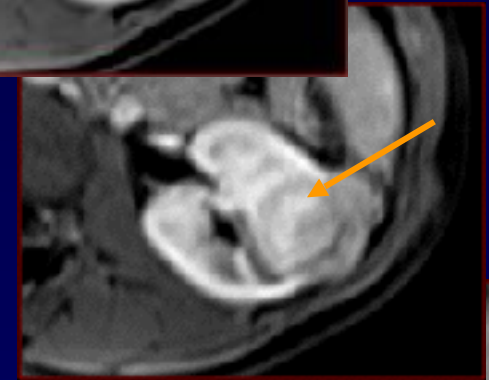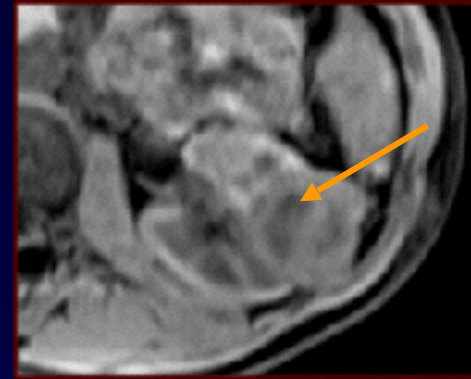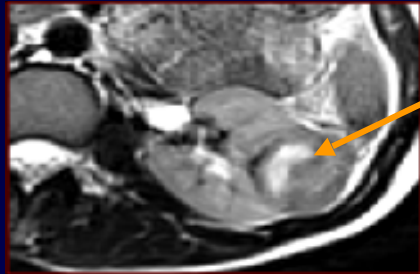
DCE may help to make the difference

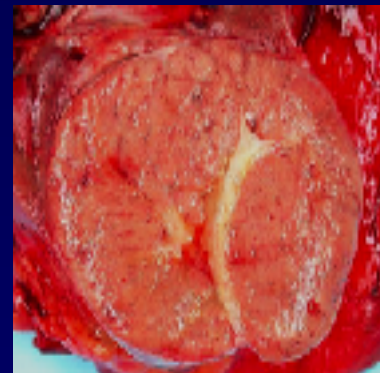- **Enhancement => vascularized central fibrous scar :**
  - early enhancement if hypervascularized
  - late enhancement if hypovascularized

- **No enhancement : ?**

15'

?
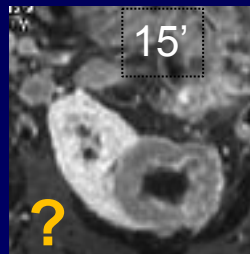
*Oncocytomas
with fibrous scar*

Morphological criteria

- **If HYPOvascularized central area : fibrous scar vs necrosis needs late T1 imaging**
    - **but NOT SPECIFIC :** oncocytoma vs CCC

Fibrous scar in oncocytoma

T = 50 s T = 2.1 mn T = 15 mn

Fibrous scar in CCC

T = 50 s T = 2.1 mn T = 15 mn
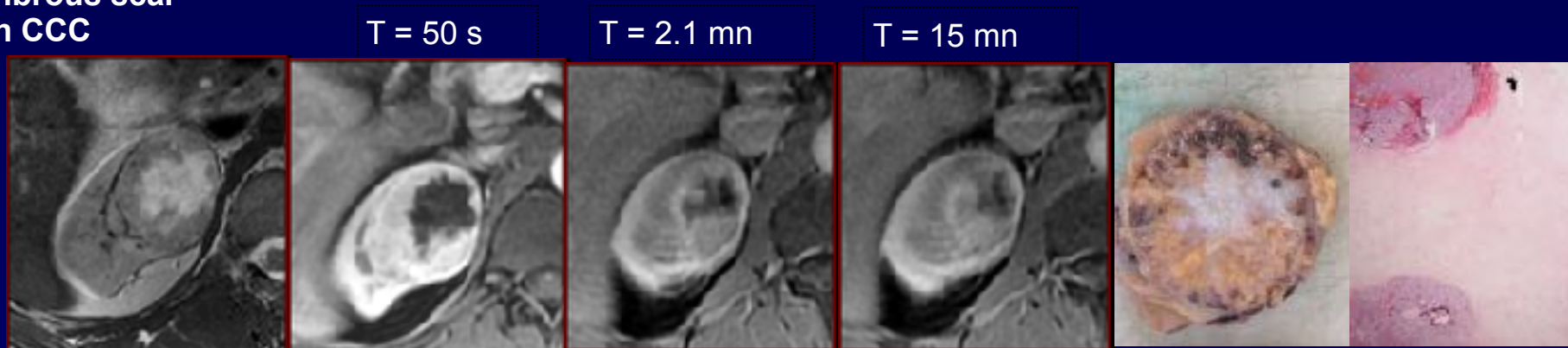
Oncocytomas

- ## If no central area evocative of scar :
    - Segmental enhancement inversion on CT ?

Segmental Enhancement Inversion at Biphasic Multidetector CT: Characteristic Finding of Small Renal Oncocytoma[1]

Kim JI et al. Radiology 2009

    - But also observed in CCC
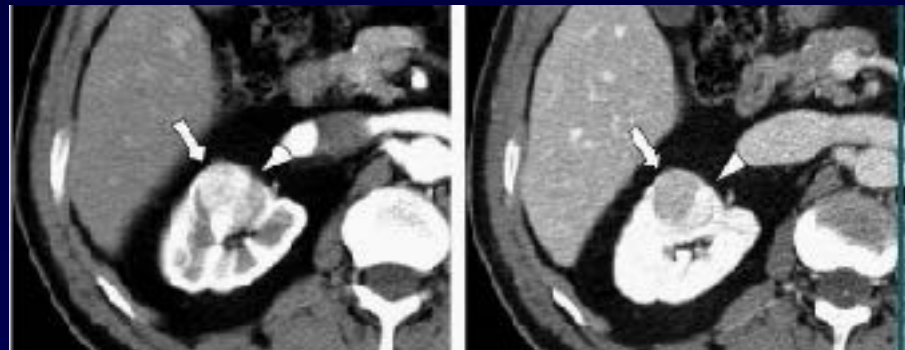
O'Malley ME et al, AJR 2012

- ## Undetermined patterns:
    - Well defined homogeneous tumor on CT: Oncocytoma or RCC ?

Oncocytomas
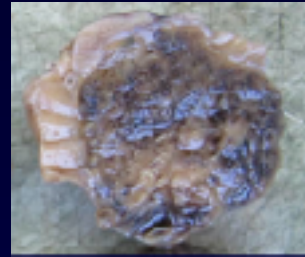
- **mpMRI may help : Typical patterns**

High SI on T2 ≥ T2 kidney
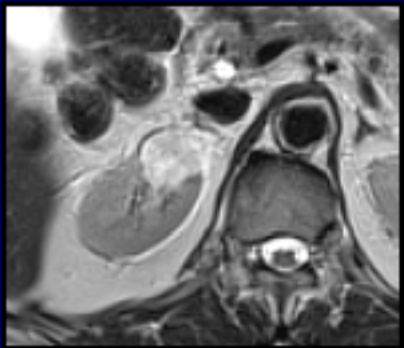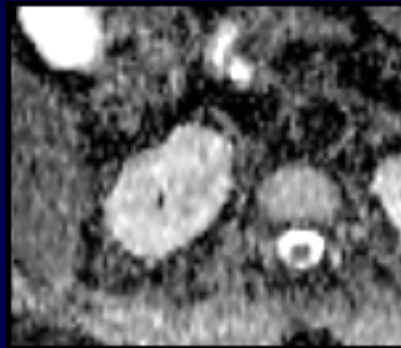
high ADC ≥ T2 kidney
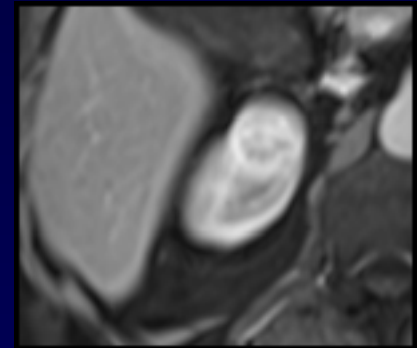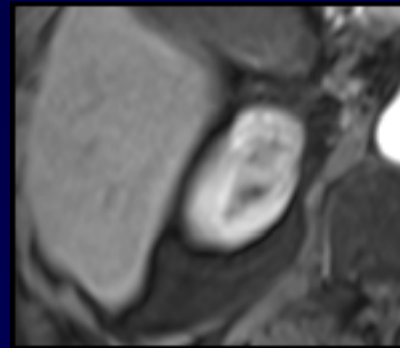
High wash-in

No change of SI on chemical shift

T1w IN
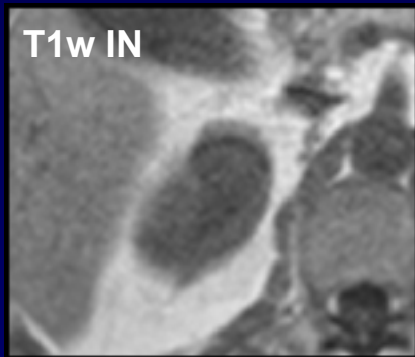
T1w OPP
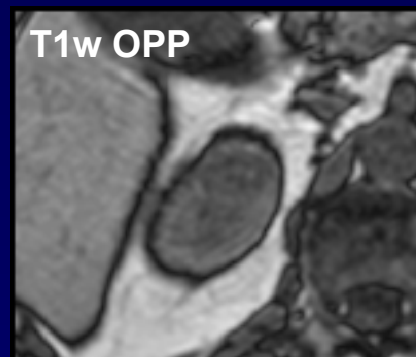
Clear cell carcinomas

- **Typical patterns**

**High SI on T2
≥ T2 kidney**
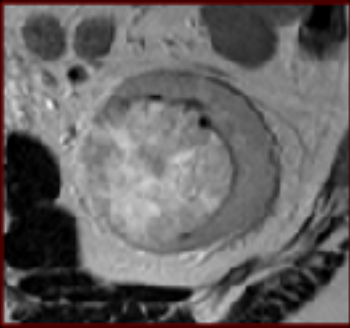
**high ADC
≥ T2 kidney**
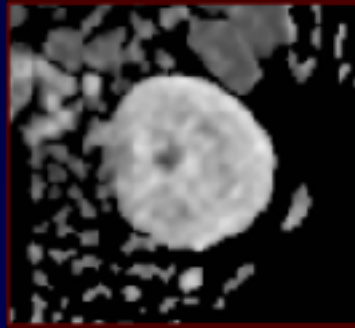
High wash-in
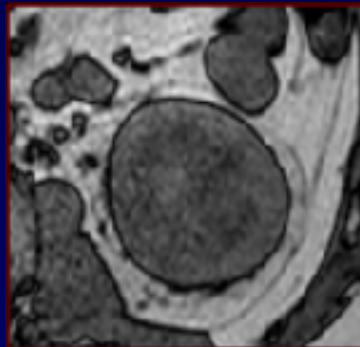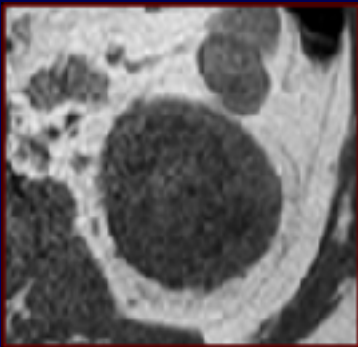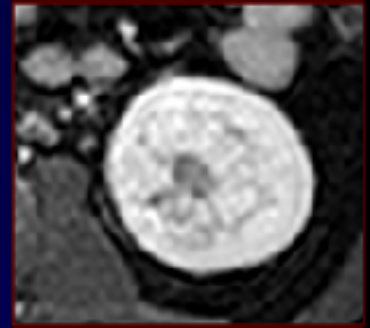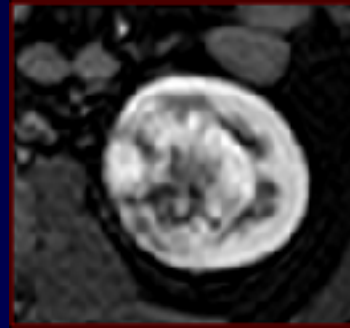
No change of SI on chemical shift

Unfortunately, CCC and oncocytomas may have the same features …

Clear cell carcinomas
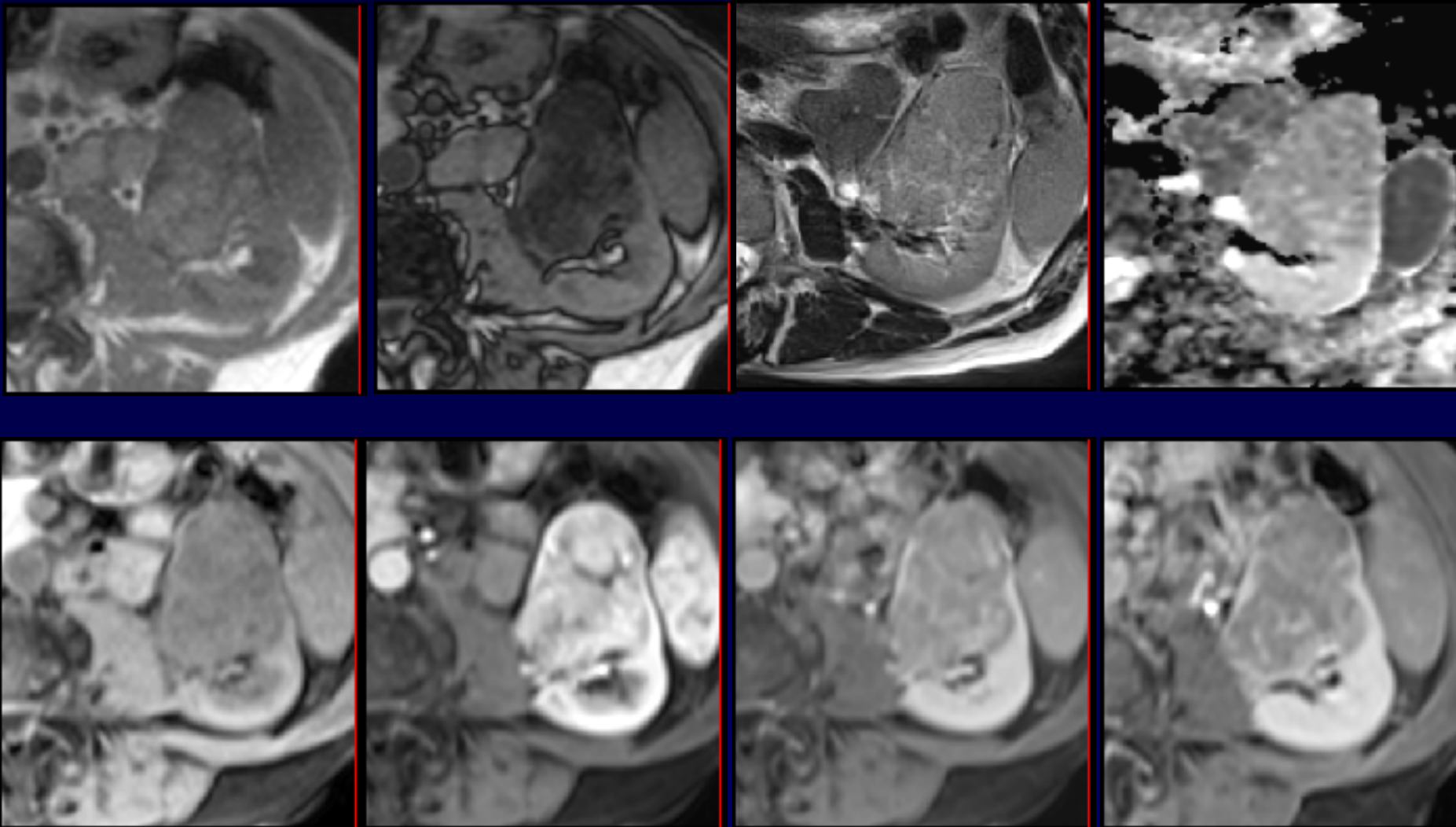
A drop of SI on OPP is the only feature able to separate both tumors

Type 1 Papillary carcinomas

- **Typical patterns** :
  - Homogeneous
  - Hypovascularized
  - Sometimes necrotic or cystic

- **MRI may help**

Low SI on T2

May show a drop of SI on OPP
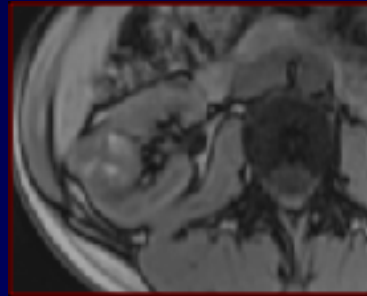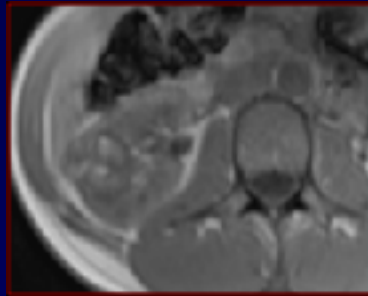
Low ADC
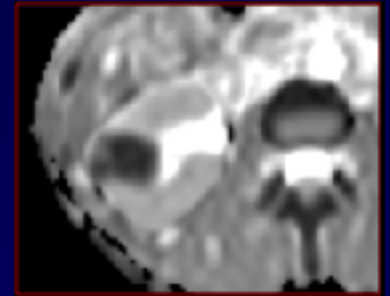
Low wash-in / wash-out
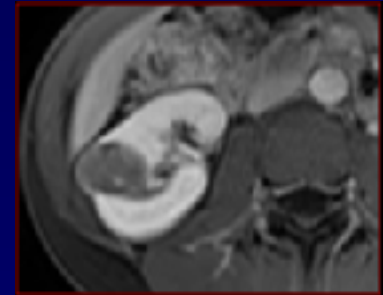
Type 1 Papillary carcinomas

- **Typical patterns :**

Low SI on T2
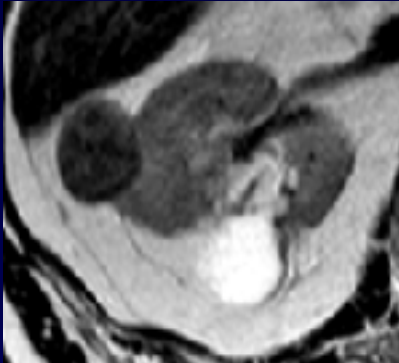
Low ADC
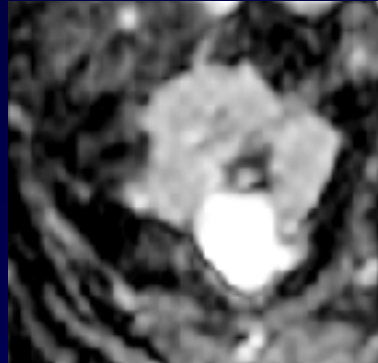
Low wash-in / wash-out
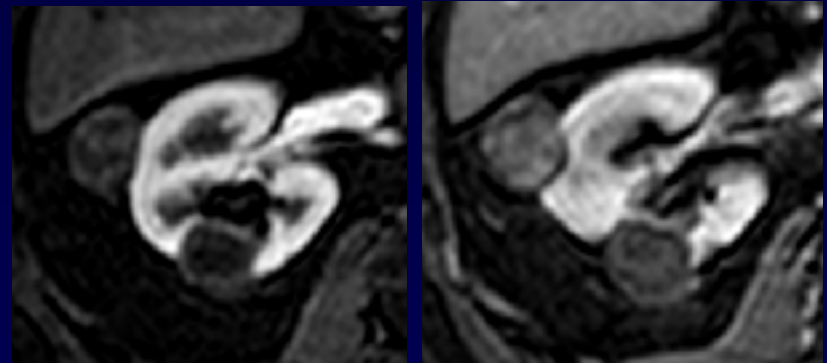
May show a drop of SI on IN (hemosiderin)

T1w IN

T1w OPP

Chromophobe carcinomas

T1w

T2w

T1after Gd

- **Typical patterns:**
  - Homogeneous, even when large (no necrosis)
  - Sharp margins
  - Central scar in 10% of cases
  - Intermediate to high vascularization
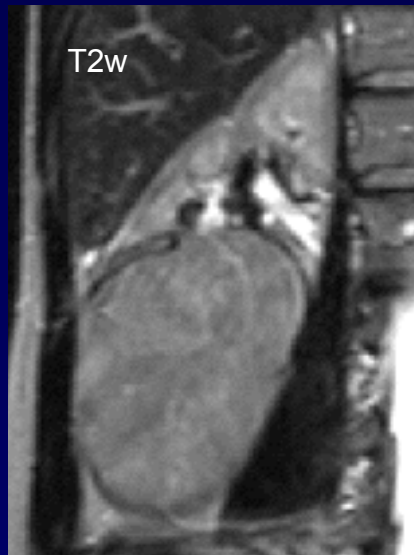
T2w

T1w

T1after Gd

Chromophobe carcinomas

- **Typical patterns**

Intermediate to low T2/kidney
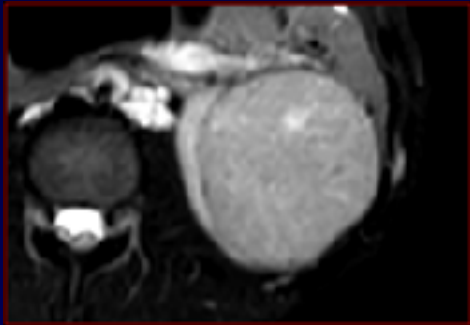
Intermediate to low ADC/kidney
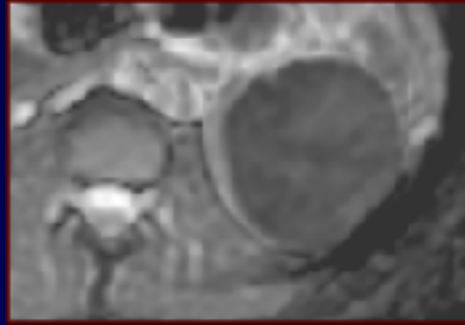
Intermediate to high WI & WO

No change of SI on chemical shift

T1w IN

T1w OPP
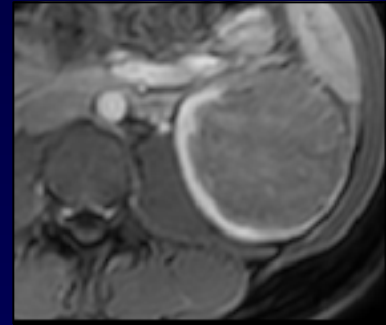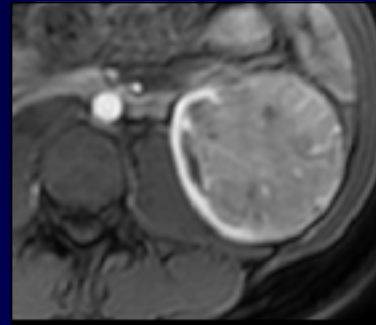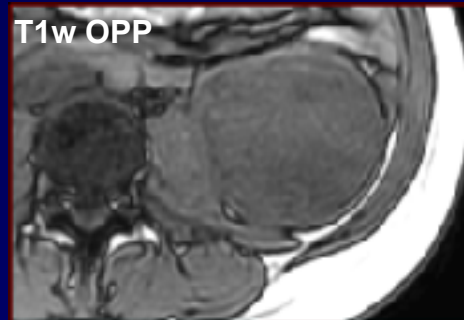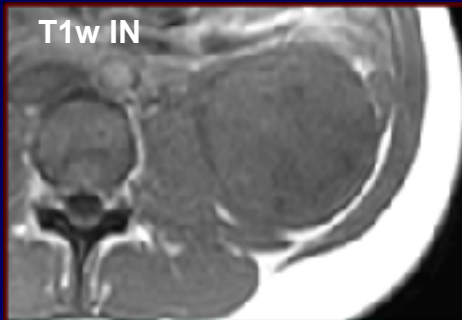
Young pregnant woman 26 yo

Differenciation Oncocytoma vs ChC

Oncocytoma
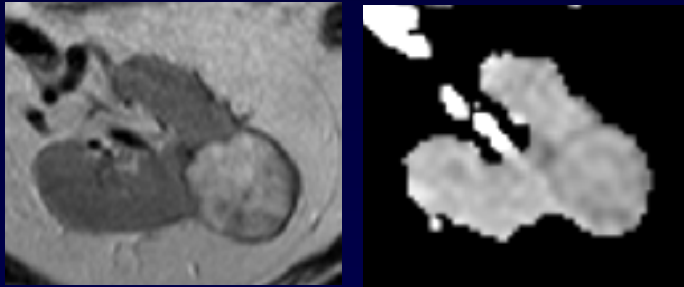
Chromophobe carcinoma
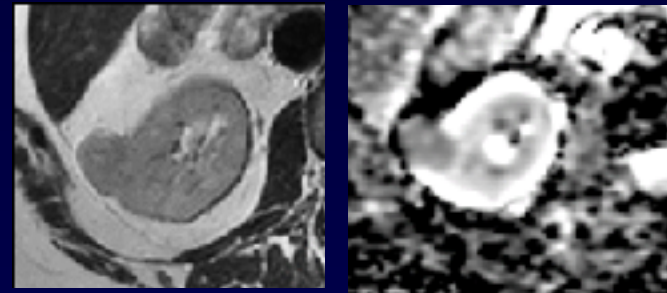
Oncocytomas show higher T2, higher ADC, and higher arterial inflow

p=0.02
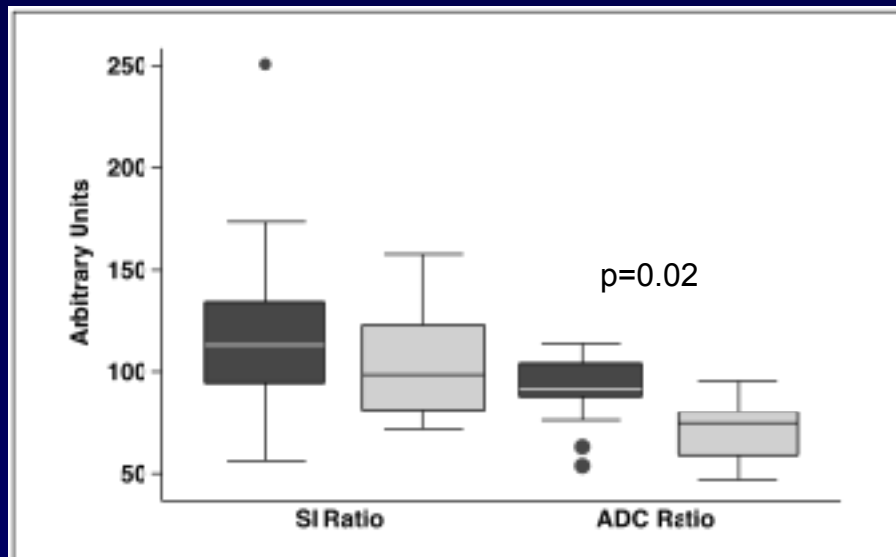
ADC index was the most discriminant :
88 cut-off : 85% SP

Combination of ADC index, SII and WI :
92.3% SS, 92.3% SP, 92.9% accuracy for oncocytomas

Galmiche C et al, AJR 2016
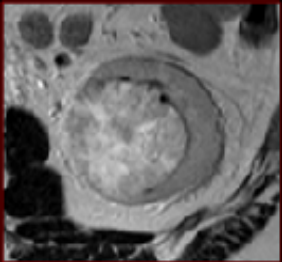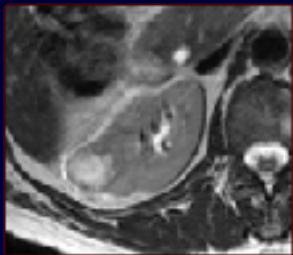
High SI on **T2w**

Intermediate SI on **T2w**
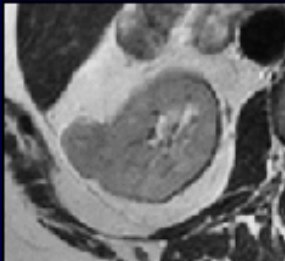
Low SI on **T2w**
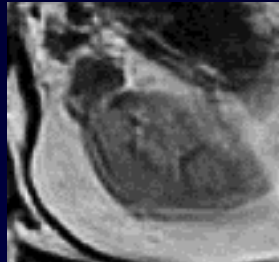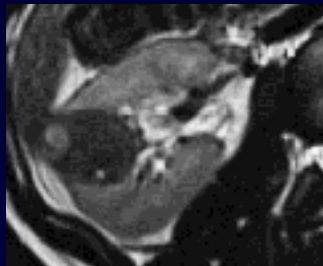
CC RCC   Oncocytoma   Ch RCC   LfcAML   Pap RCC

High **ADC**-value
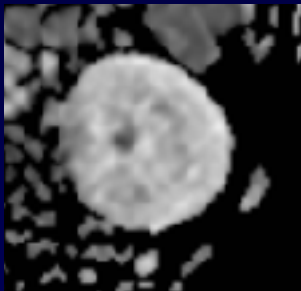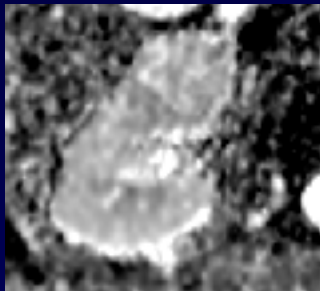
Intermediate **ADC**-value
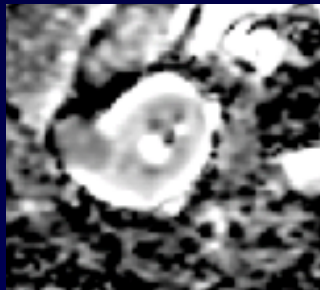
Low **ADC**-value
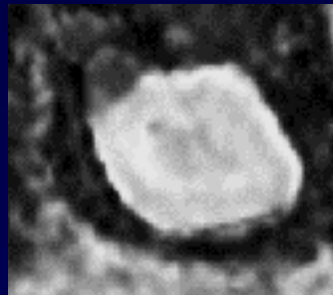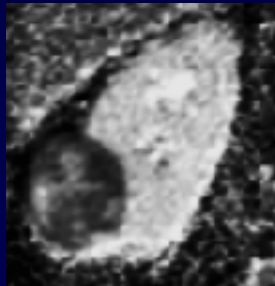
CC RCC   Oncocytoma   Ch RCC   LfcAML   P RCC

High perfusion
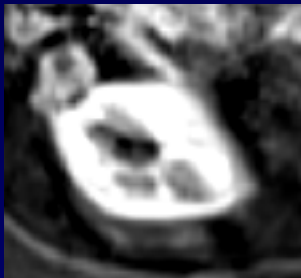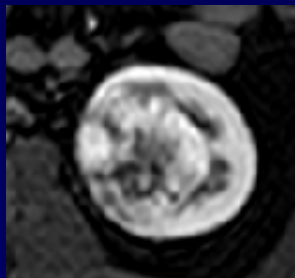
Intermediate perfusion
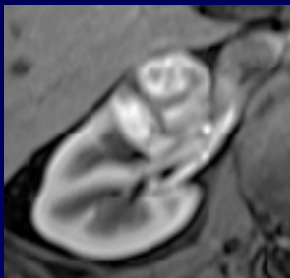
Low perfusion
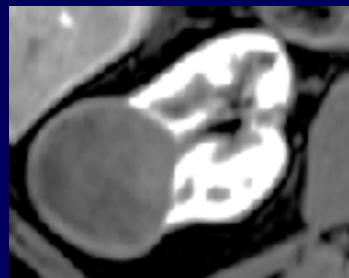
LfcAML   CC RCC   Oncocytoma   Ch RCC   Pap RCC

mpMRI : *summary*

CC RCC

High T2
High ADC
High perfusion
May drop on OUT

Pap RCC

Low T2
Low ADC
Low perfusion
May drop on OUT
May drop on IN

Ch RCC

Intermediate T2
Low ADC
Low perfusion

IfAML

Angular interface ± ice cream
Low T2
Low ADC
High perfusion
May drop on OUT

Oncocytoma

Enhancing central area
Intermediate T2
High ADC
High perfusion

Combination of multiple criteria : mpMRI

Subtypes	Subtypes			
	Oncocytoma ($n=16$)	AML ($n=4$)	Clear cell RCC ($n=57$)	Chromophobe RCC ($n=7$)
AML ($n=4$)	SIR ($P=0.01^*$, 0.92^{**}) SII ($P=0.002$, 0.98)			
Clear cell RCC ($n=56$)	SII ($P=0.01$, 0.65) WiI2 ($P<0.01$, 0.71)	SIR ($P=0.0007$, 0.88)		
Chromophobe RCC ($n=7$)	TSR ($P=0.02$, 0.87) WiI2 ($P=0.03$, 0.74) WiI3 ($P=0.02$, 0.77) WoI1 ($P=0.03$, 0.8) WoI2 ($P=0.04$, 0.78)	SIR ($P=0.02$, 0.92) SII ($P=0.01$, 0.95)	TSR ($P=0.01$, 0.79) WiI3 ($P=0.03$, 0.73) WoI2 ($P=0.01$, 0.79)	
Papillary RCC ($n=16$)	SIR ($P<0.001$, 0.94) ADCr ($P=0.02$, 0.75) WiI1 ($P<0.001$, 0.89) WiI2 ($P<0.001$, 0.92) WiI3 ($P=0.001$, 0.90)	SII ($P=0.004$, 0.98) WiI1 ($P=0.003$, 0.98) WiI2 ($P=0.009$, 0.98) WiI3 ($P=0.02$, 0.97) WoI1 ($P=0.04$, 0.83) WoI2 ($P=0.01$, 0.90)	SIR ($P<0.001$, 0.88) SII ($P=0.01$, 0.75) ADCr ($P<0.001$, 0.84) WiI1 ($P<0.001$, 0.93) WiI2 ($P<0.001$, 0.93) WiI3 ($P<0.001$, 0.89) WoI1 ($P<0.001$, 0.71) WoI2 ($P<0.001$, 0.80)	SIR ($P=0.002$, 0.95) WiI1 ($P=0.004$, 0.92) WoI1 ($P=0.002$, 0.87) WoI2 ($P<0.001$, 0.97)

" *Papillary RCCs were distinguished from other tumours (SS 37.5 %, SP 100 %) and oncocytomas from chromophobe RCCs (SS 25 %, SP 100 %) and clear cell RCCs (SS 100 %, SP 94.2 %)* »

Cornelis et al. Eur Radiol 2014

Case
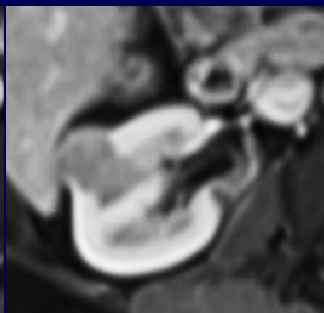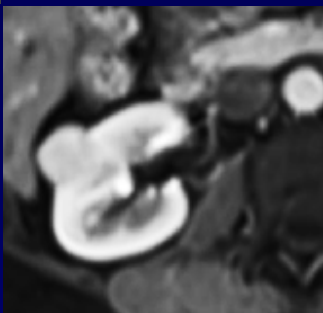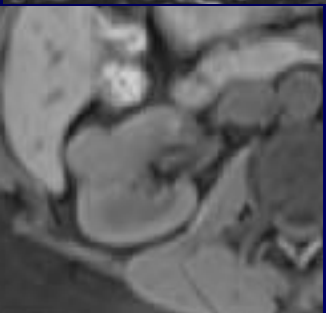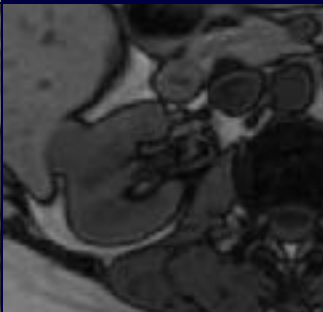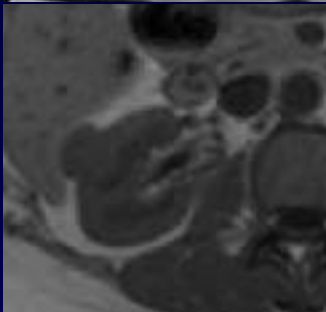
1- T2W	HIGH *CCC / Oncocytoma*	MID *Chromophobe*	LOW *AML / PT*
2- IPOP Signal Drop	YES *CCC / AML*		NO *Any*
3- DWI	HIGH *Oncocytoma / CCC*	MID *Chromophobe*	LOW *AML / PT*

4- WASH-IN	FAST *CCC / AML*	MID *Chromophobe / Oncocytoma*	SLOW *PT*
5- WASH-OUT	YES *CCC / AML*	MID *Chromophobe / Oncocytoma*	NO *PT*

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very encouraging

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Diagnostic Performance and Interreader Agreement of a Standardized MR Imaging Approach in the Prediction of Small Renal Mass Histology[1]

Table 3

Diagnostic Performance by Pathologic Subtype

Pathologic Subtype	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	κ Value
Clear cell RCC	85 (71–98)	76 (69–85)	77 (74–87)	83 (74–98)	81 (75–92)	0.55 (0.33–0.71)
Papillary RCC	80 (68–96)	94 (90–98)	79 (71–92)	94 (91–98)	91 (88–97)	0.73 (0.61–0.81)
Chromophobe RCC	14 (14–29)	99 (95–100)	50 (17–100)	94 (94–95)	94 (90–95)	0.23 (-0.02–0.80)
Oncocytoma	33 (17–83)	97 (91–99)	38 (25–63)	96 (95–99)	94 (90–96)	0.25 (0.07–0.80)
Minimal fat AML	67 (33–83)	98 (95–100)	67 (44–100)	98 (95–98)	98 (95–98)	0.43 (0.19–0.65)

Note—Data are medians among all reviewers, with the range in parentheses. AML = angiomyolipoma, NPV = negative predictive value, PPV = positive predictive value, RCC = renal cell carcinoma.

- **Diagnostic accuracy** : 81% (88 of 109) and 91% (99 of 109) in diagnosis of clear cell RCC and papillary RCC
- Moderate to substantial **interreader agreement** among seven radiologists
- **Limitations** :
  - Retrospective, monocentric
  - Diffusion-weighted imaging was not included
  - Only qualitative assessments

Conclusion

- Imaging sequences and parameters have to be perfect, either for detection or for characterization of renal masses

- Imaging techniques are often complementary; we have to use them all before to conclude to benign or before to propose a biopsy

- Many pitfalls are present

Conclusion

- Multiparametric MRI may help in characterizing undeterminate solid renal tumors :
  - Using classical MR imaging sequences
  - Better than CT

- Could avoid a certain number of biopsies

- Significant threshold have still to be better defined and prospectively evaluated