Imaging in RCC
Can we tell what's malignant

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Radboudumc

Baus oncology, London 2014

Introduction

- Renal Cell Carcinoma (RCC) 2-3% of all cancers
- ~85% is ccRCC
- Estimated incidence in European Union per 100.000 (2012):
    - Men 15.8
    - Women 7.9
- Currently majority of detected solid renal masses is incidentaloma <4cm
- Still up to 30% mRCC at initial staging
- On initial imaging tumor size is important predictor of malignancy, more benign lesions expected in small renal masses.
- In surgical series, up to 20% of small renal masses shows benign histology.

Ljungberg, Mulders et al Eur Urol 201 0 Kang et al. AJR Am J Roentgenol 2014, Frank et al. J Urol 2010
Remzi et al.World J Urol 2010

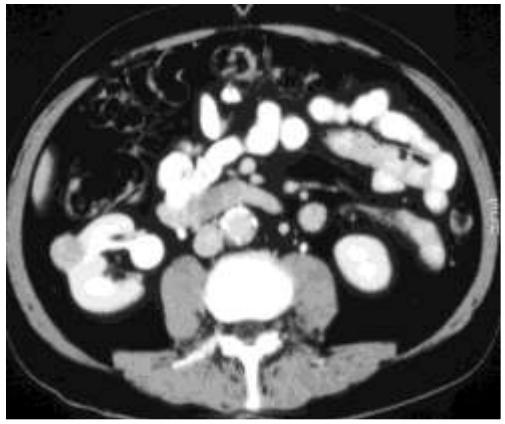
Imaging

- Guidelines recommend contrast enhanced CT or MRI for primary lesion assessment
- On CT high-density (40-70 HU) and contrast enhancement (increase in attenuation ≥20 HU) depicts RCC
- MRI may also complement CT where CT is limited in identification of enhancing soft tissue and defining its characteristics
- No place for PET scanning due to low diagnostic accuracy for detecting primary RCC

Ljungberg, Mulders et al. Submitted Eur Urol 2014, Kang et al. AJR Am J Roentgenol 2014, Wang Cancer et al. Imaging 2012

Imaging drawbacks

- With current used techniques, both CT and MRI can not reliably distinguish benign (lipid poor angiomyolipoma and oncocytoma) from malignant lesions
- Mainly problem in SRMs
- Histological confirmation of metastasis based on imaging is impossible



Biopsy

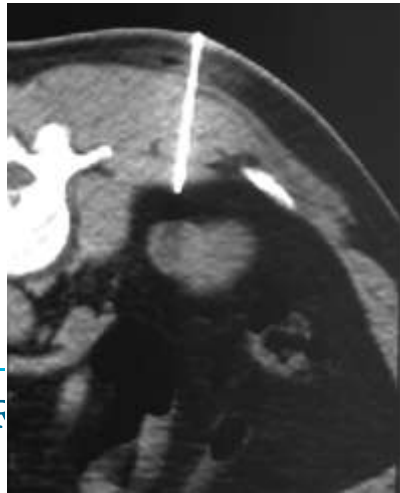
- In case of radiologically indeterminate renal masses biopsy may be warranted
- Biopsy sensitivity 86-100%, however up to 20% are inconclusive
- Especially biopsy in SRMs may be technically demanding
- In histological biopsy assessment, oncocytoma are hard to distinguish from well differentiated RCCs due to oncocytic features
- Biopsy is invasive procedure

SEP. PROCEDURE IN LOCAL ANEST.

CT-FLUOROSCOPY

17G SHEATH ON TUMOR

18G CORE 3-4 CORE BIOPSIES TROUGH SHEATH



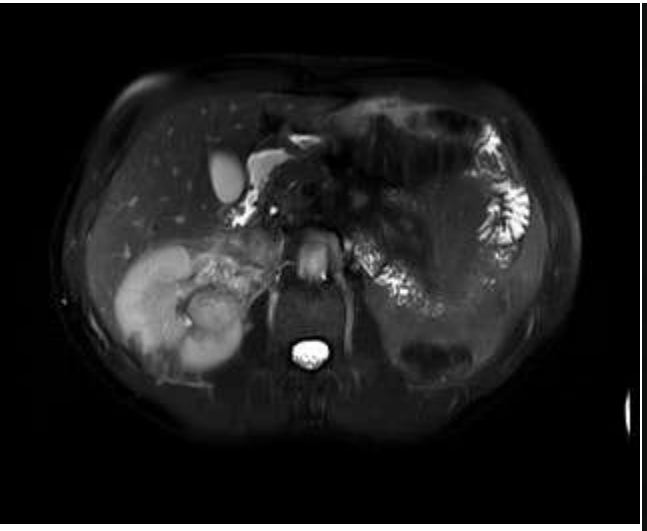
Ljungberg, Mulders et al. Eur Urol 2010, Somani et al. Eur Urol 2007, Rosenkrantz et al. AJR Am J Roentgenol 2010

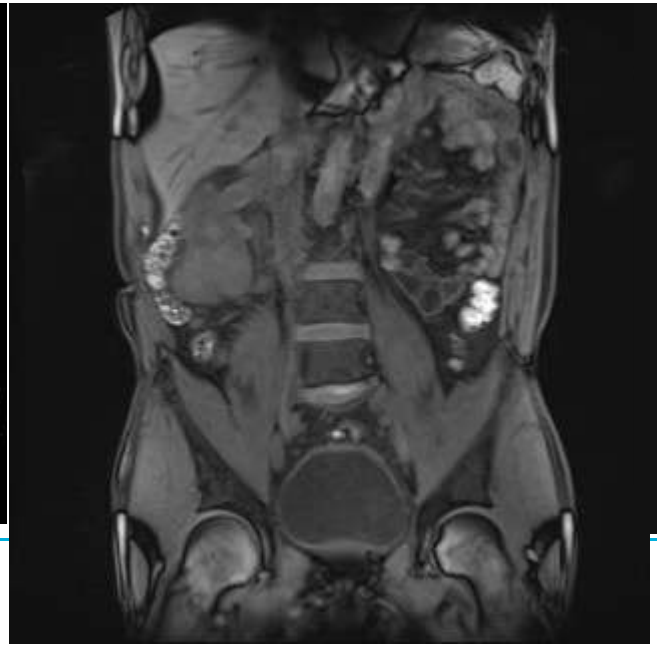
Diagnostic challenges

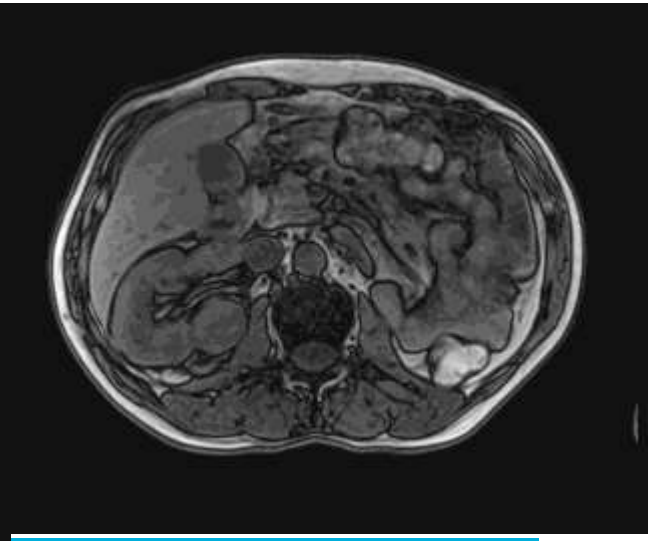
- Diagnostics based on imaging especially challenging in distinguishing benign from malignant SRMs and in case of suspected metastasis
- For all renal masses when administration of contrast agent is contra indicated (impaired renal function or previous allergic reactions)
- New imaging modalities are evaluated

Diffusion Weighted MRI

- Technique to assess restriction of diffusion (movement of water molecules)
- Due to high cellularity diffusion in tumours is restricted
- Currently in clinical use for prostate and other organs







Diffusion Weighted MRI

Eur Radiol (2014) 24:241–249
DOI 10.1007/s00330-013-3004-x

MAGNETIC RESONANCE

Diffusion-weighted imaging of focal renal lesions: a meta-analysis

E. A. Lassel · R. Rao · C. Schwenke · S. O. Schoenberg · H. J. Michaely

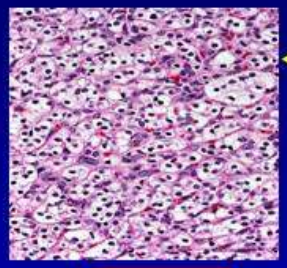
- 1181 measurements used: 450 RCCs, 132 cysts, 521 benign lesions (including normal parenchyma), 13 oncocytoma's, 65 uroepithelial tumours

Diffusion Weighted MRI

- Conclusions:
  - “Evaluation of ADC values can help to determine between benign and malignant lesions in general but also seems able to differentiate oncocytomas from malignant tumours…”
  - Differentiation of AMLs from RCC not possible

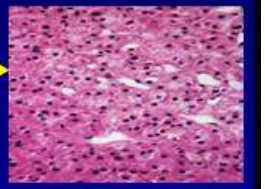
- Main drawback is data heterogenity mainly due to non standardized scanning protocols

RCC : Histologic and Molecular Characteristics



Proximal Nephron

Distal Nephron

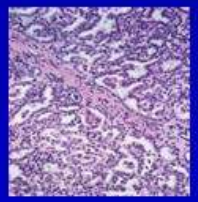


Oncocytoma (5%)

Clear Cell Carcinoma (75%)

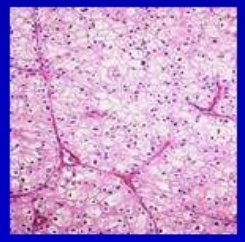
- LOH - 3p25
- VHL mutation (50-80%)
- Hypermethylation (5-20%)
- Anti-VEGF and VEGFr therapy

Papillary Carcinoma (15%)



Type 1 c-met mutation

Type 2 FH mutation



Chromophobe (5%)

Collecting Duct, Undifferen-tiated (rare)

More RCC specific imaging

- 1986: antibody “G250” discovered
- Antigen later found: Carbonic Anhydrase IX (CAIX)

CAIX expression

NO expression

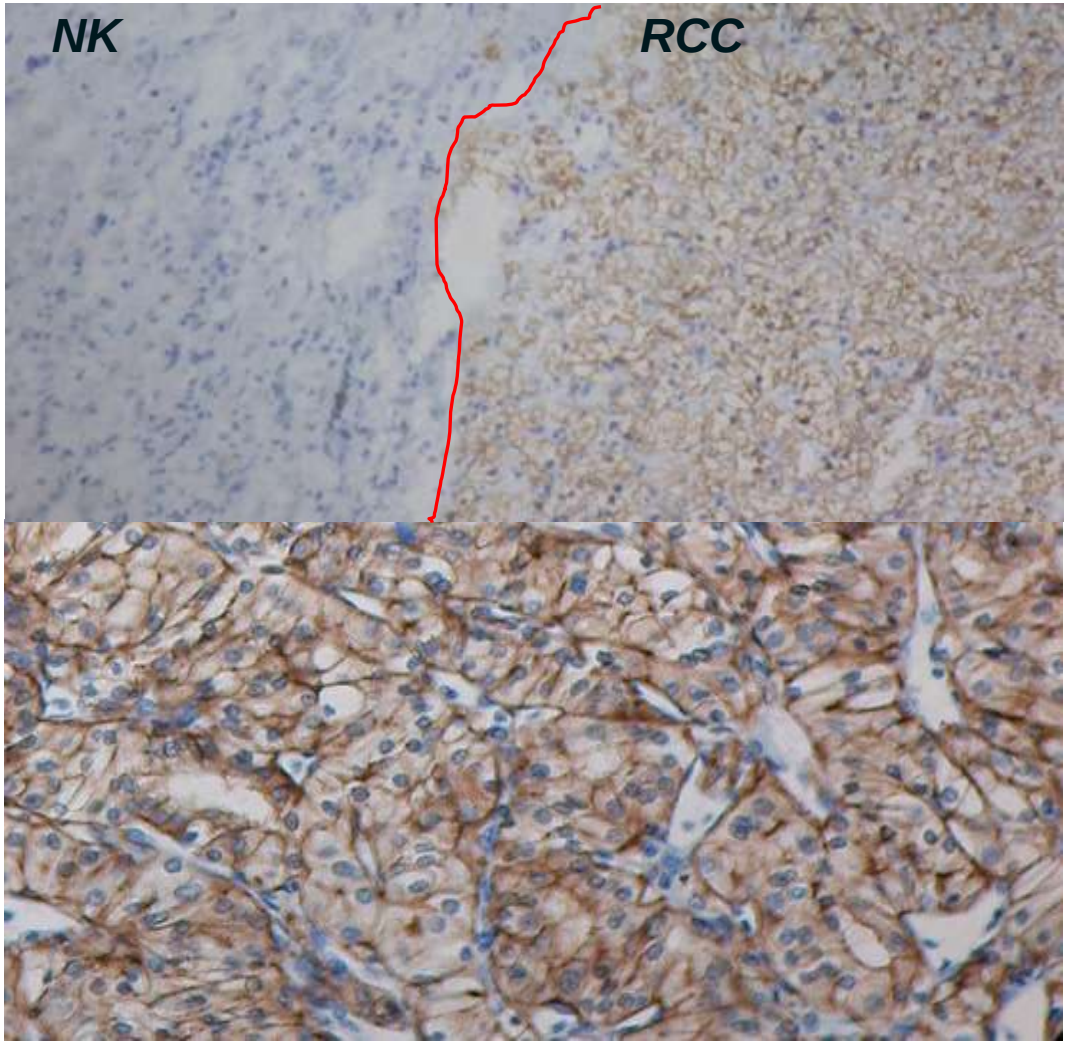
- Normal kidney tissue
- Most normal tissues

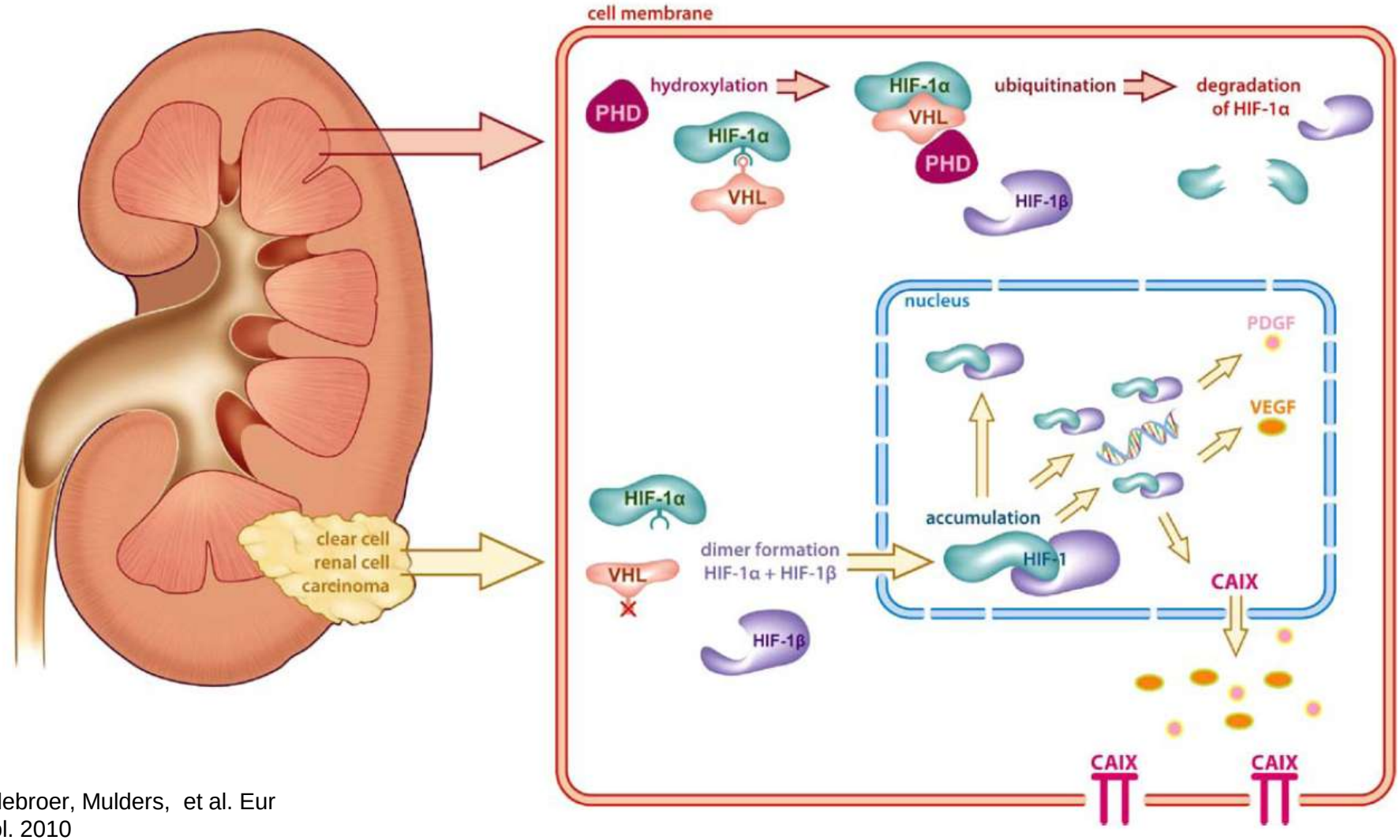
Exceptions:

- Larger bile ducts, upper GI tract

Expression ccRCC: high, homogeneous
Expression non-ccRCC: heterogeneous

CAIX staining in ccRCC and normal kidney tissue



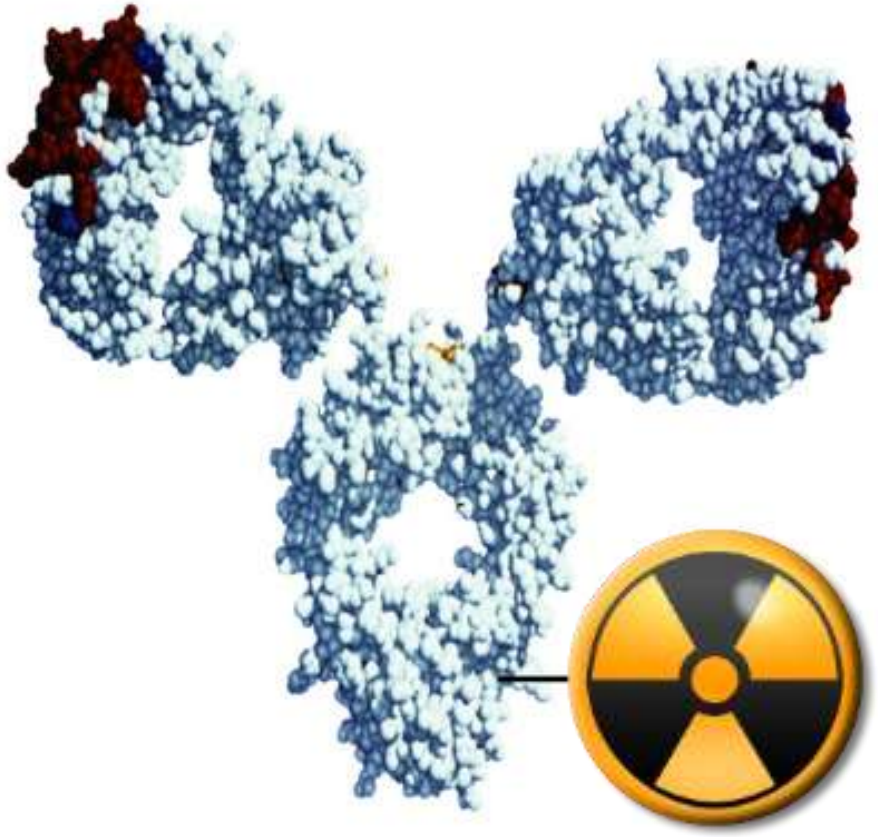


Stillebroer, Mulders, et al. Eur Urol. 2010

ImmunoSPECT imaging

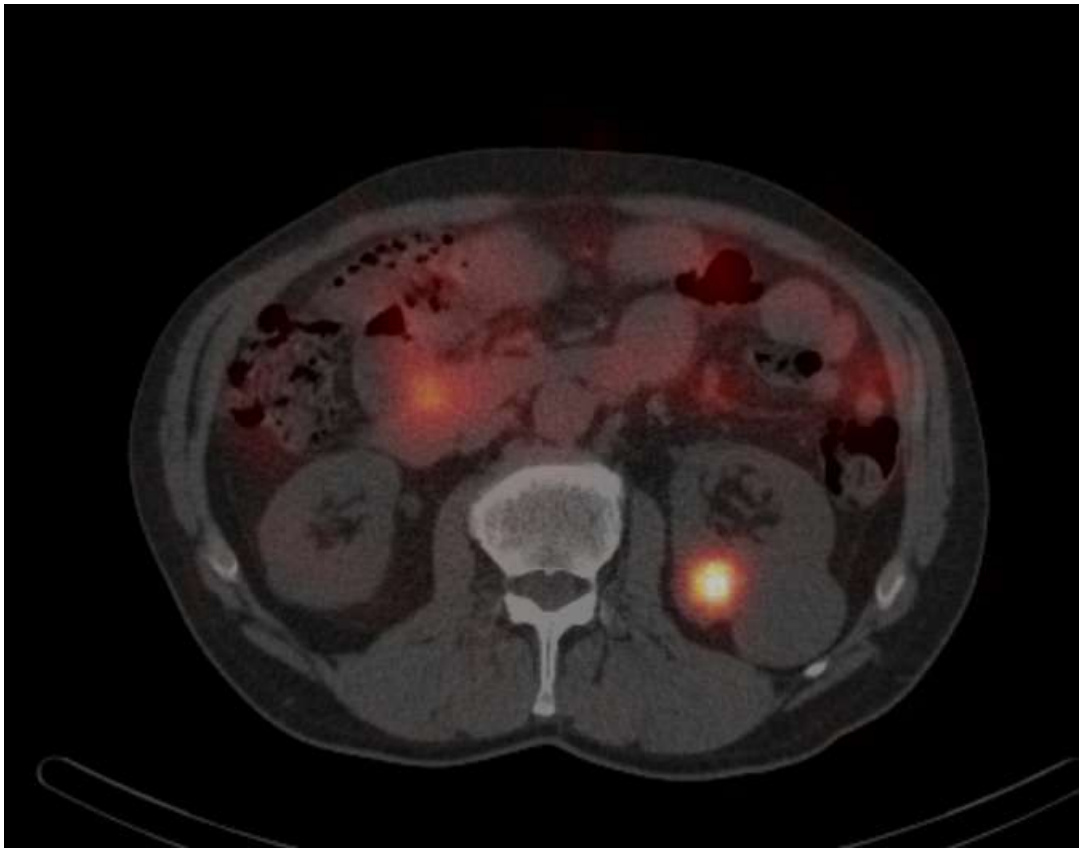
- Carbonic Anhydrase IX (CAIX) specific antigen for ccRCC
- Not found in normal renal tissue nor in benign cysts
- High levels of expression are reported in up to 94% of ccRCC
- Very low levels are expressed in other organs, mainly in the upper gastrointestinal tract
- CAIX is an excellent target for imaging ccRCC lesions with monoclonal antibody (mAb) girentuximab (G250)

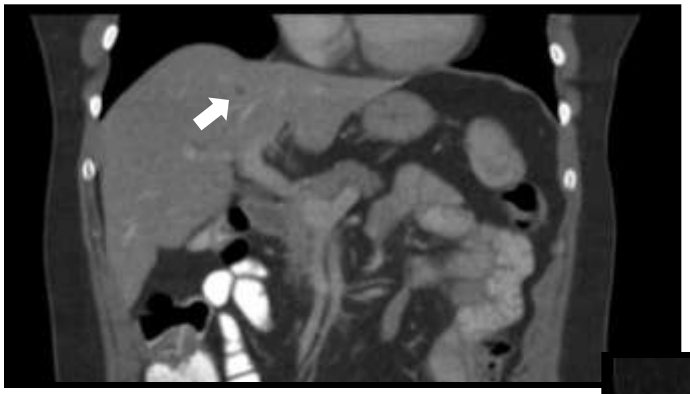
Principle



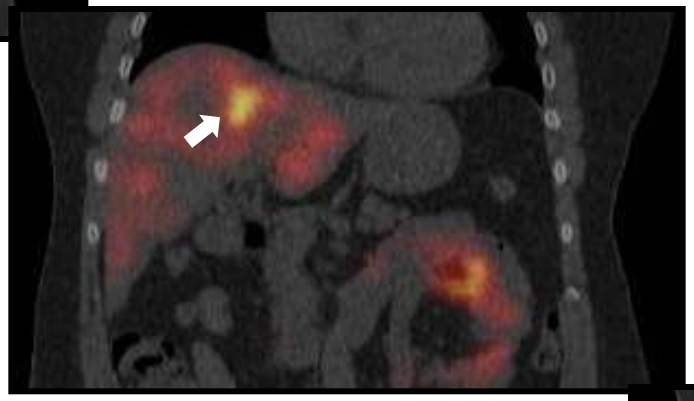
Radioimmunodetectie: ^{111}Indium (γ-straler, SPECT imaging)
Radioimmunotherapie: ^{177}Lutetium (β-straler, therapie)

Radioimmunodetectie met ^{111}In-girentuximab





March 2012



April 2012

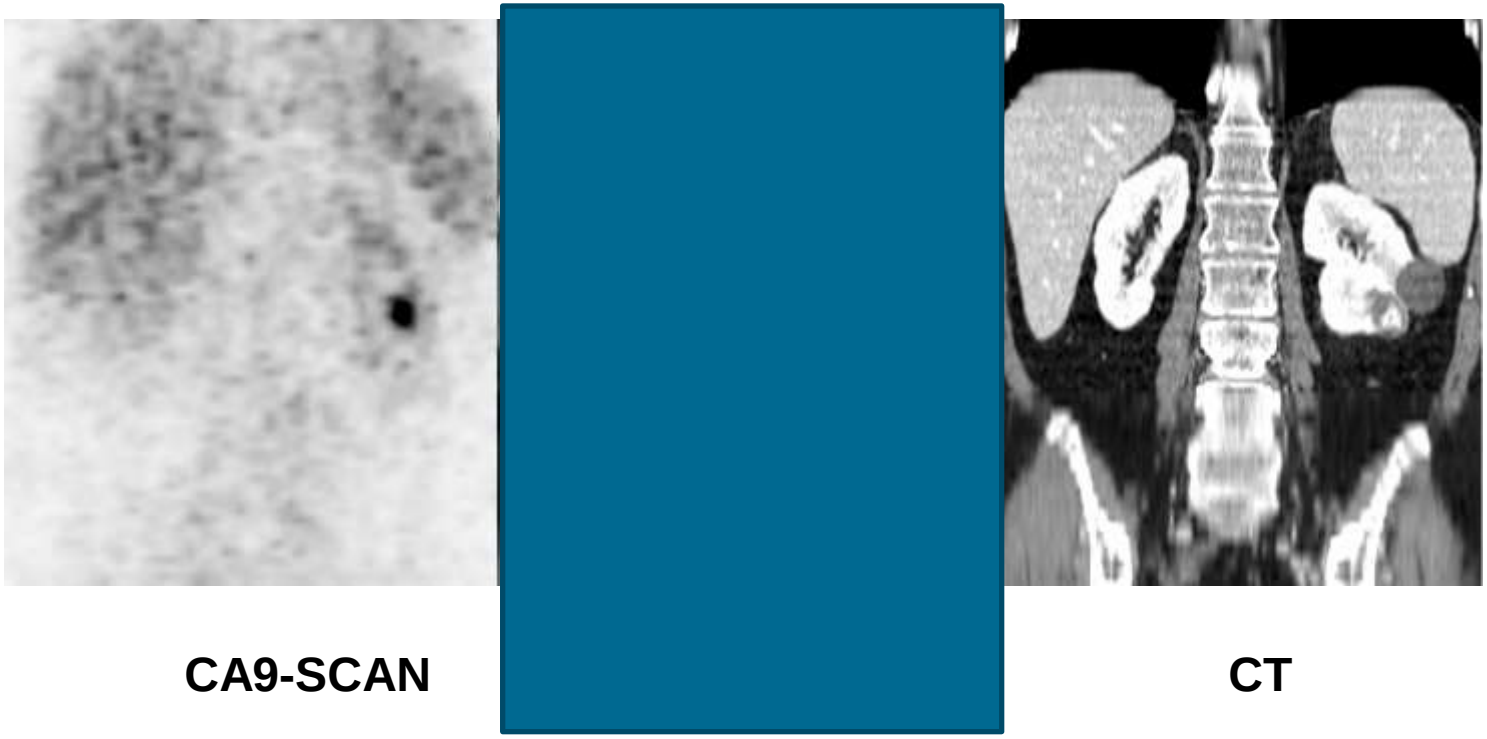
June 2012

Radboudumc

Muselaers, Oosterwijk, Mulders et al. Eur Urol 2013

Clinical usefulness - imaging

CA9-SCAN adds biological information to anatomical information



CA9-SCAN **CT**

ImmunoSPECT imaging

European Association of Urology

Kidney Cancer

Indium-111–labeled Girentuximab ImmunoSPECT as a Diagnostic Tool in Clear Cell Renal Cell Carcinoma

Constantijn H.J. Muselaers[a,b,*], *Otto C. Boerman*[b], *Egbert Oosterwijk*[a], *Johannes F. Langenhuijsen*[a], *Wim J.G. Oyen*[b], *Peter F.A. Mulders*[a]

[a] *Department of Urology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands;* [b] *Department of Nuclear Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands*

Immunospect imaging

- Evaluation of 29 patients using 111In-girentuximab
- immunoSPECT

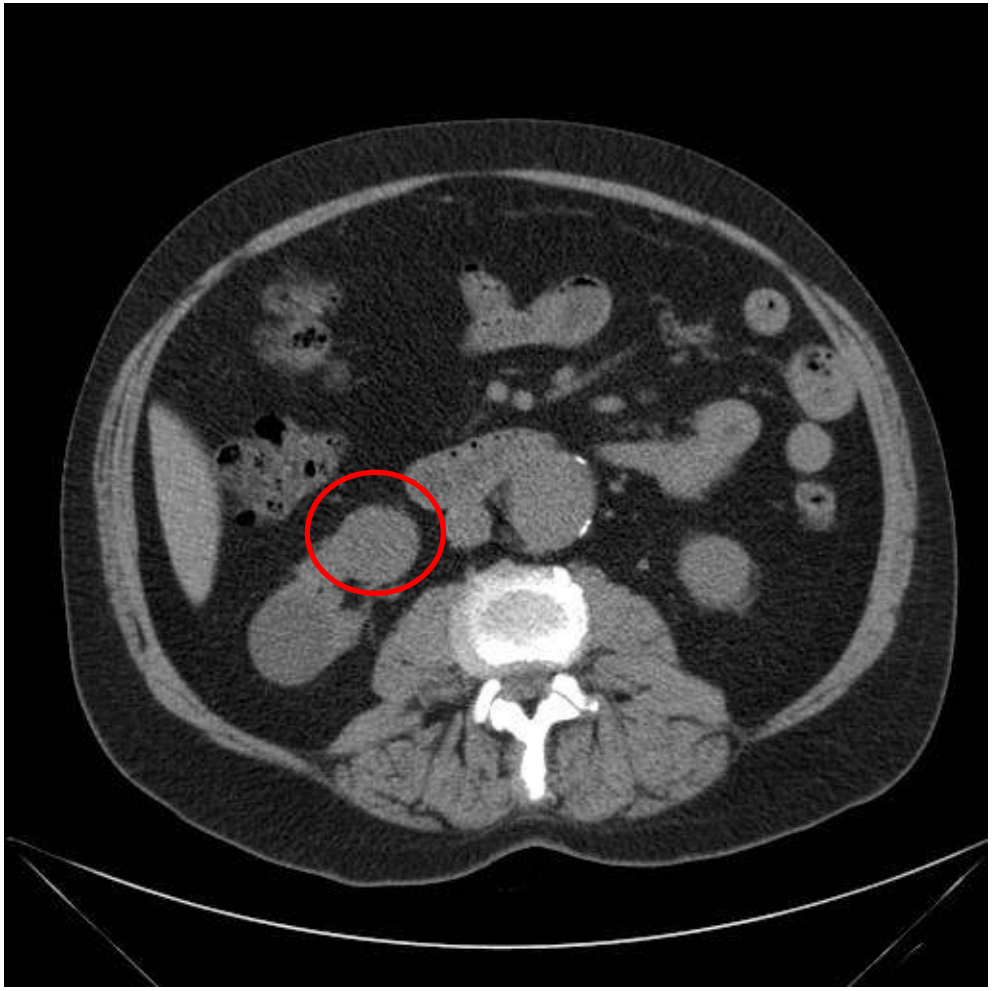
- 22 localized diseased:
  - 16 positive scans: 15 ccRCC, 1 papillary RCC
  - 6 negative scans: no ccRCC found (4) nor progression (2)

- 7 patients with metastatic disease:
  - 4 positive scans: systemic therapy initiated
  - 3 negative scans: 1 progression and 2 no progression

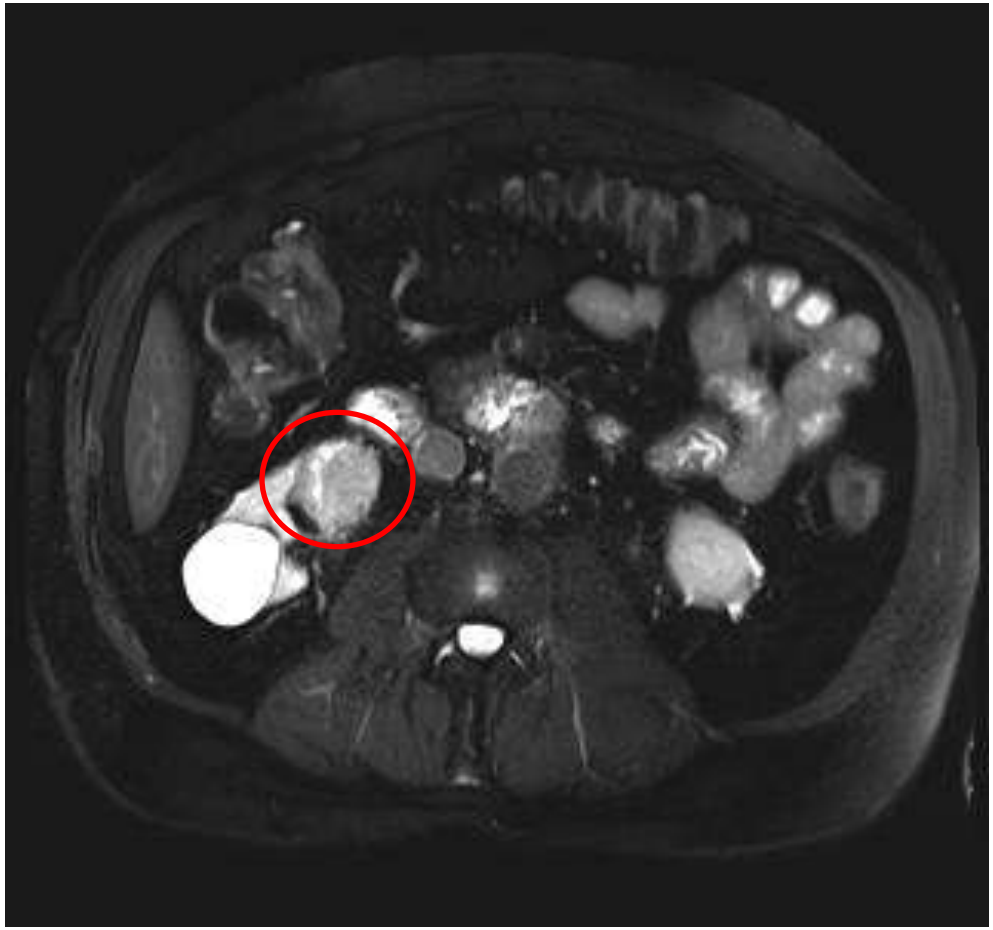
Case 1 Localized disease?

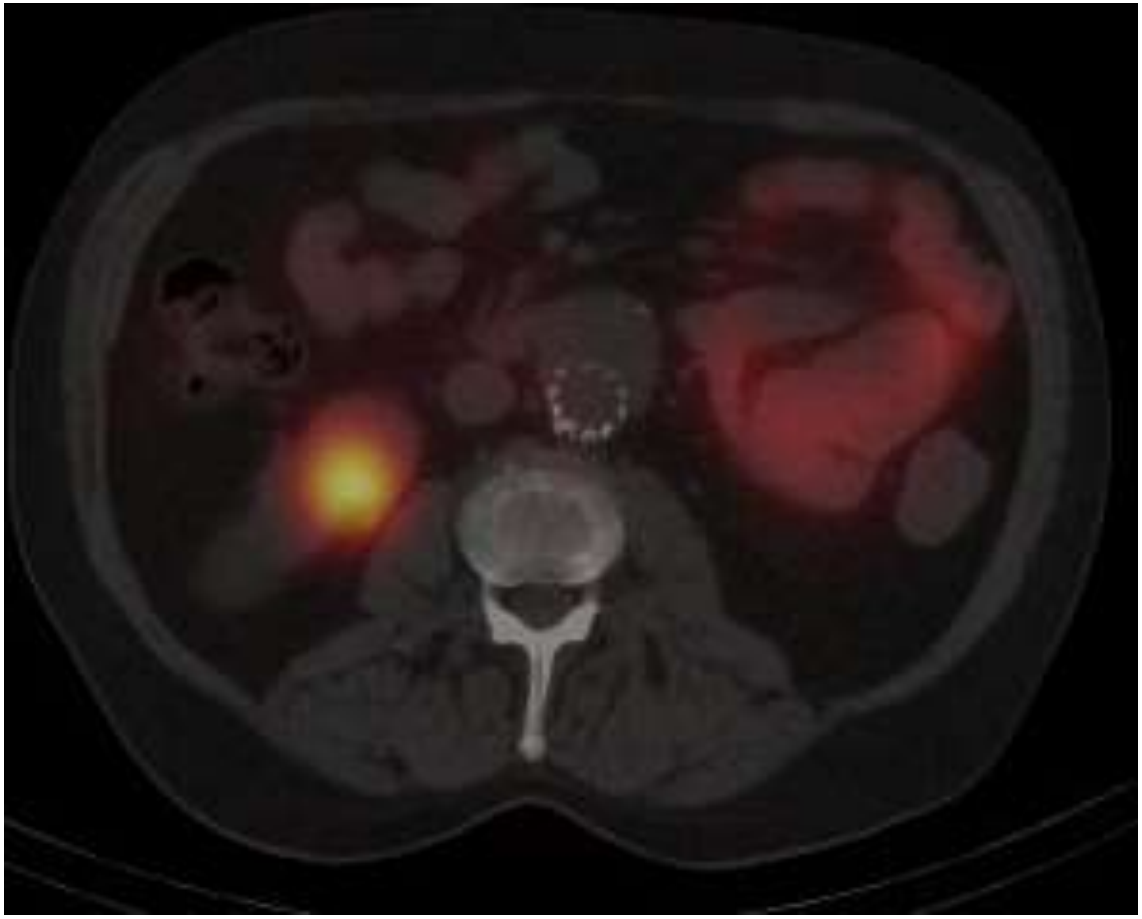
- 66 year old male referred to our clinic with diagnostic dilemma tumor lower pole right kidney
- Impaired renal function, eGFR 19 mL/min/1,73m2
- On ultrasound incidentaloma
- Due to renal function only non contrast enhanced CT performed
- Further diagnostics warranted

Case 1



Case 1





Case 2 Metastatic disease?

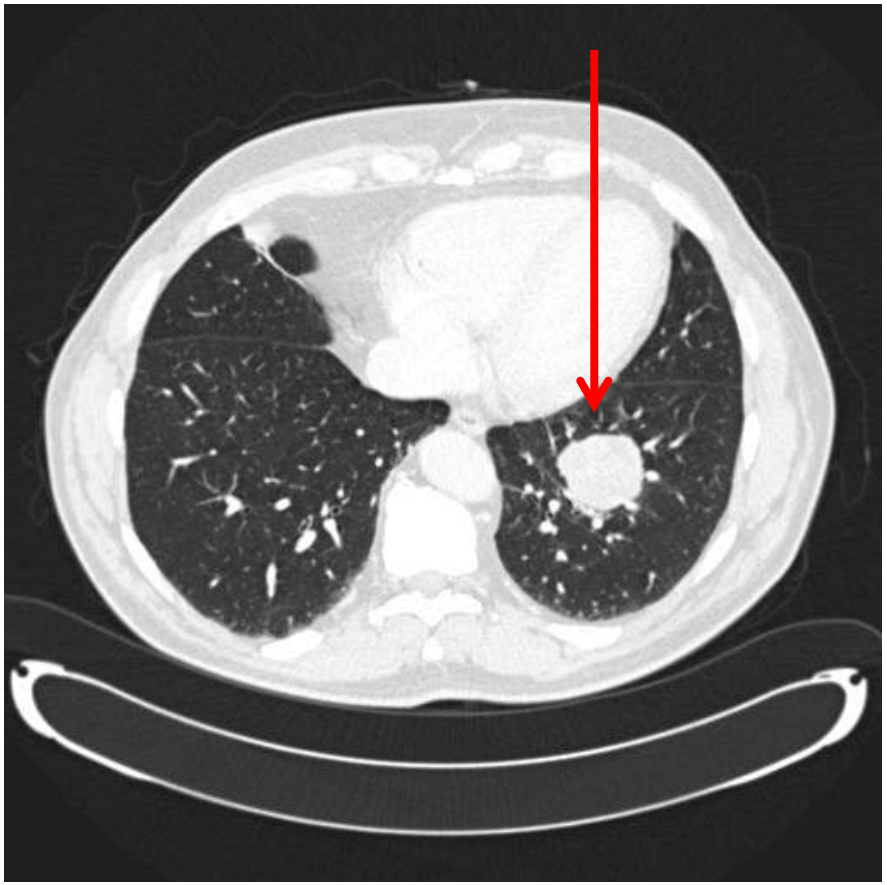
- 1952: TBC

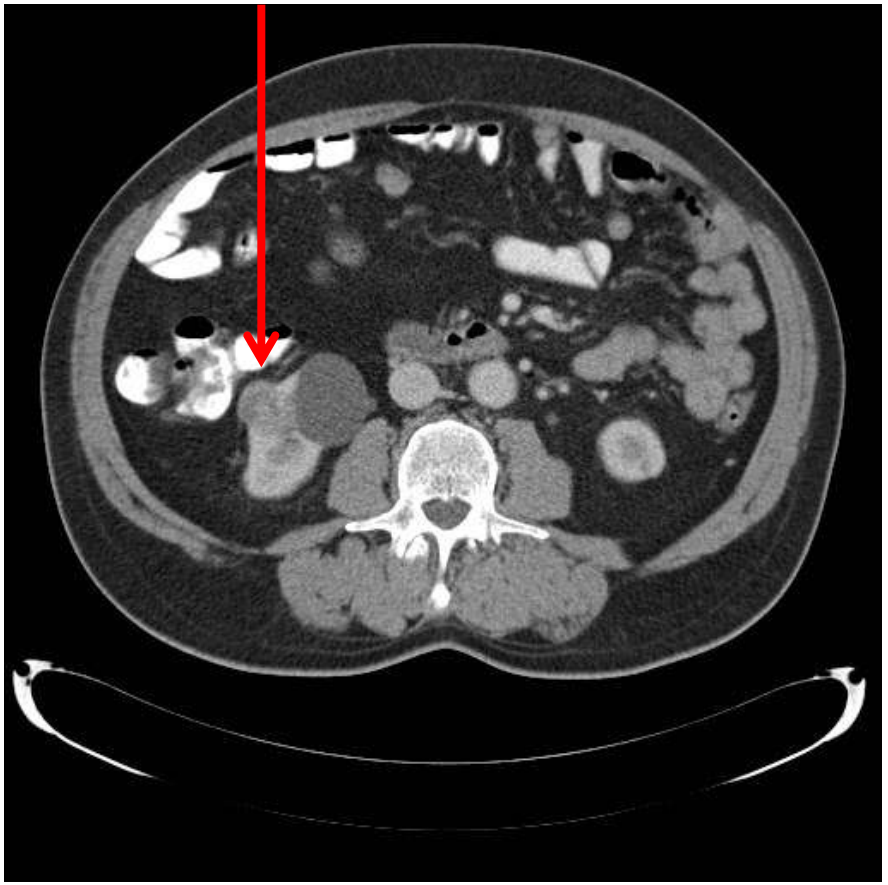
- Hematologist:
  - Auto immune hemolysis with decreasing Hb, primary disease or due to malignancy? → imaging

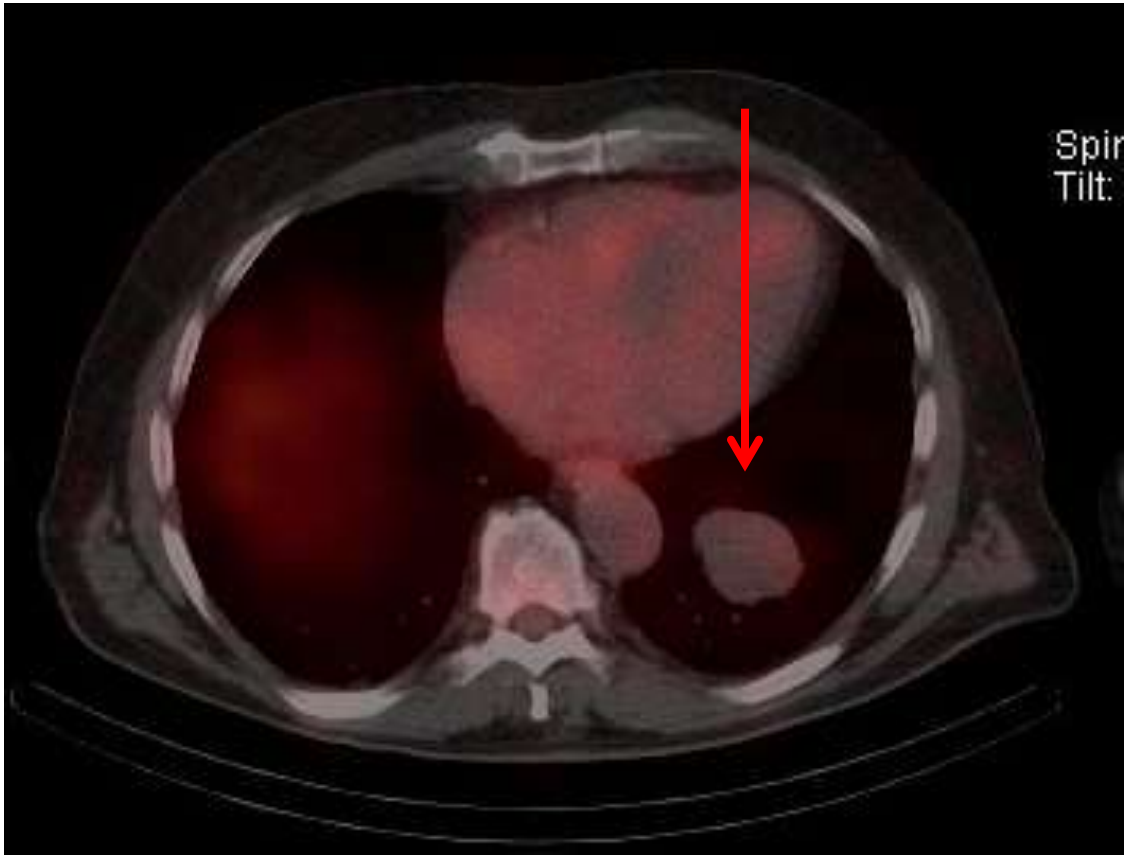
- CT thorax abdomen → lesion left lung and right kidney → referred to lung specialist

- Consultation lung specialist:
  - PET scan: both lesions FDG negative
  - Pathology lung flush, no malignancy (representative?)

- Consultation of the urologist



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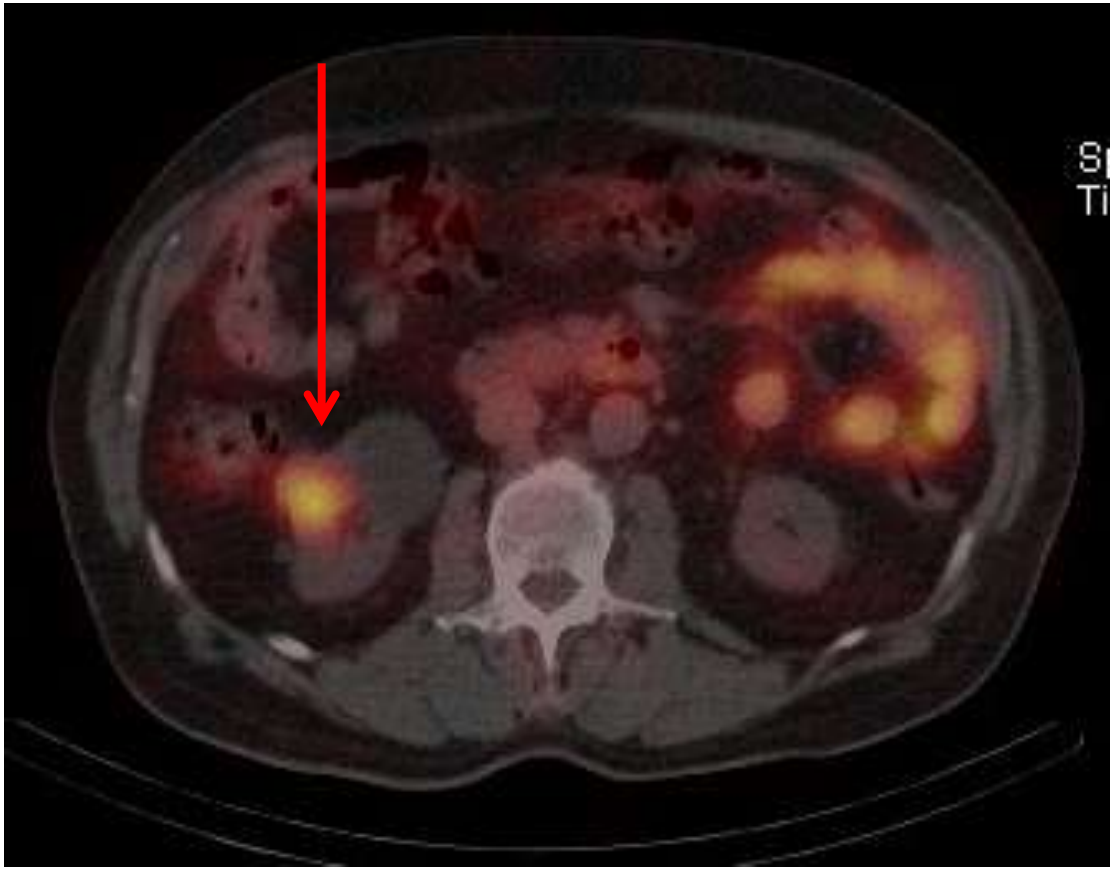


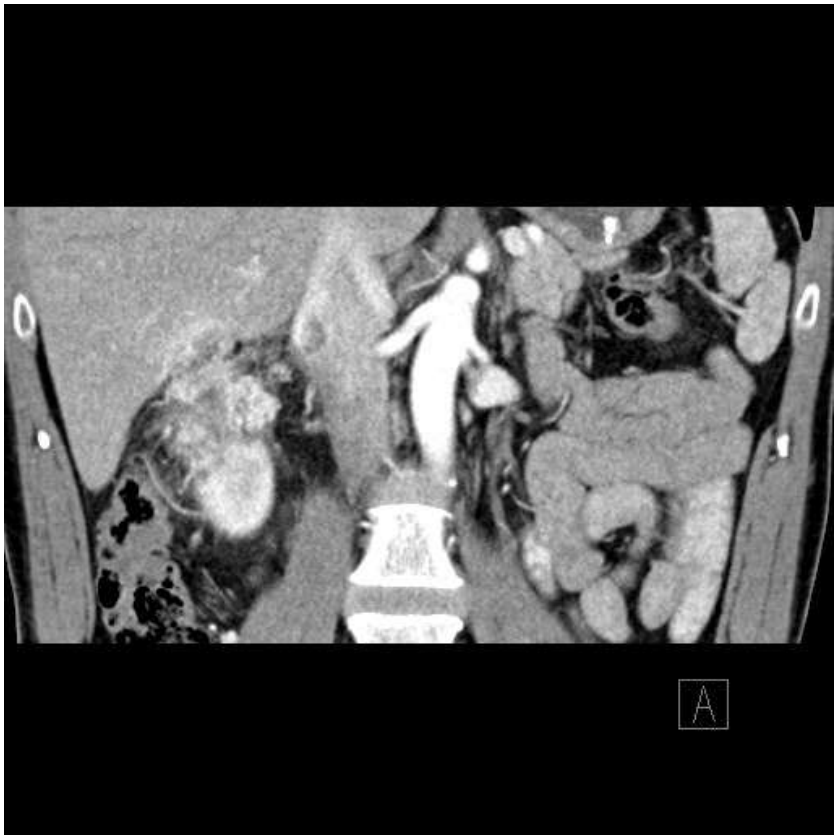
Conclusions

- Conventional CT and MRI sufficient in larger RCC.

- In case of SRMs new modalities necessary to distinguish benign from malignant lesions :
  - DW MRI → promising, uniformity required
  - Immuno SPECT using 111-In-Girentuximab very helpfull in case of ccRCC

- In evaluating possible metastatic disease Immuno SPECT using 111-In-Girentuximab valuable non invasive diagnostic tool

Thank you



Introductie

Beoordeling primaire tumor:

- vaak rijk aan vaten
- aankleuring na iv contrasttoediening
- kleine tumor vaak homogeen
- grote tumor vaak inhomogeen tgv necrose en bloeding
- verkalkingen in tumor bij 30%

Introductie

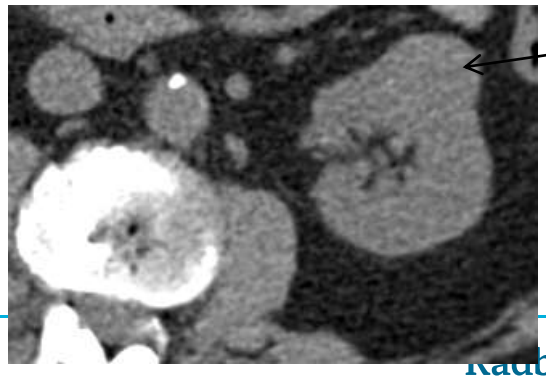
Beoordeling primaire tumor:

- CT nier 3 fasen met iv contrast
  - blanco
  - corticomedullaire fase
  - nefrogene fase

Introductie

Beoordeling primaire tumor:

- CT blanco
  - HU waarde laesie
  - vergelijk met HU na iv contrast
  - verkalkingen

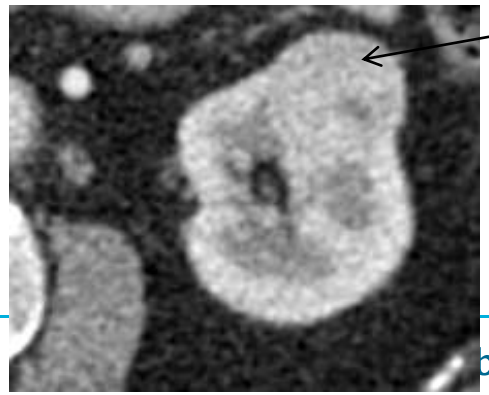


HU 38

Introductie

Beoordeling primaire tumor:

- CT corticomedullaire fase
  ingroei in vaten
  aankleuring hypervasculaire laesies

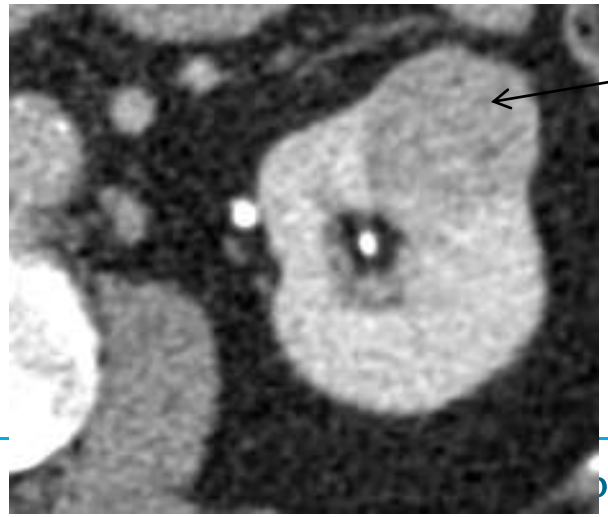


HU 125

Introductie

Beoordeling primaire tumor:

- CT nefrogene fase
  onderscheid massa's en normaal nierweefsel



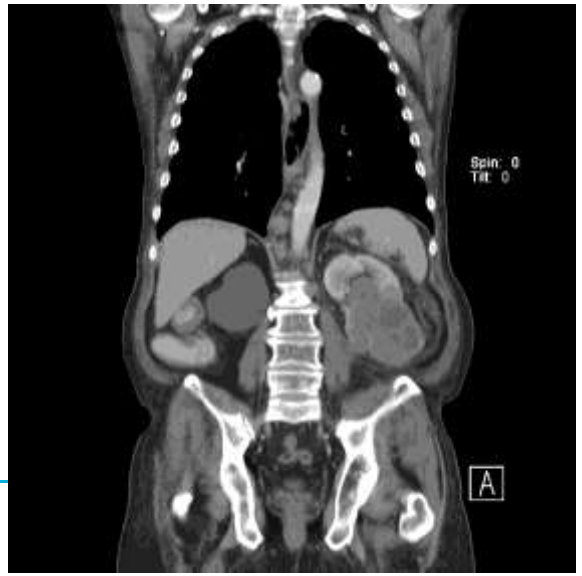
Partiële nefrectomie
PA: heldercellig niercelcarcinoom

HU 96

Introductie

Beoordeling metastasen: (stadiëring)

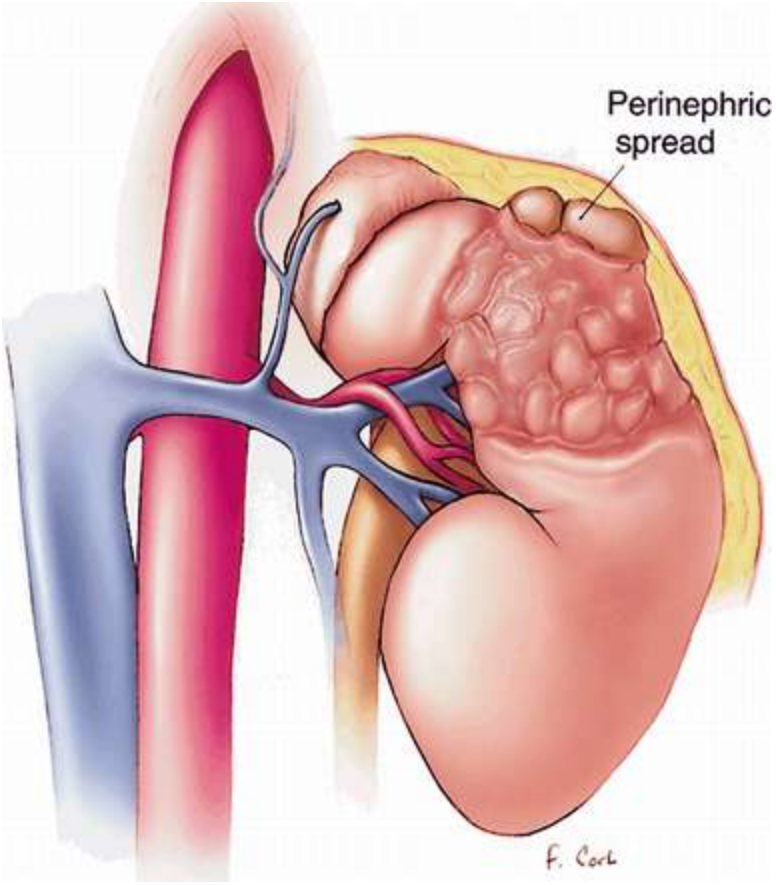
- combineer CT nier 3-fase met scan van gehele thorax en abdomen



Stadiëring

TNM stadium T3a

Niercelcarcinoom met kapseldoorbraak en uitbreiding in vet rond nier

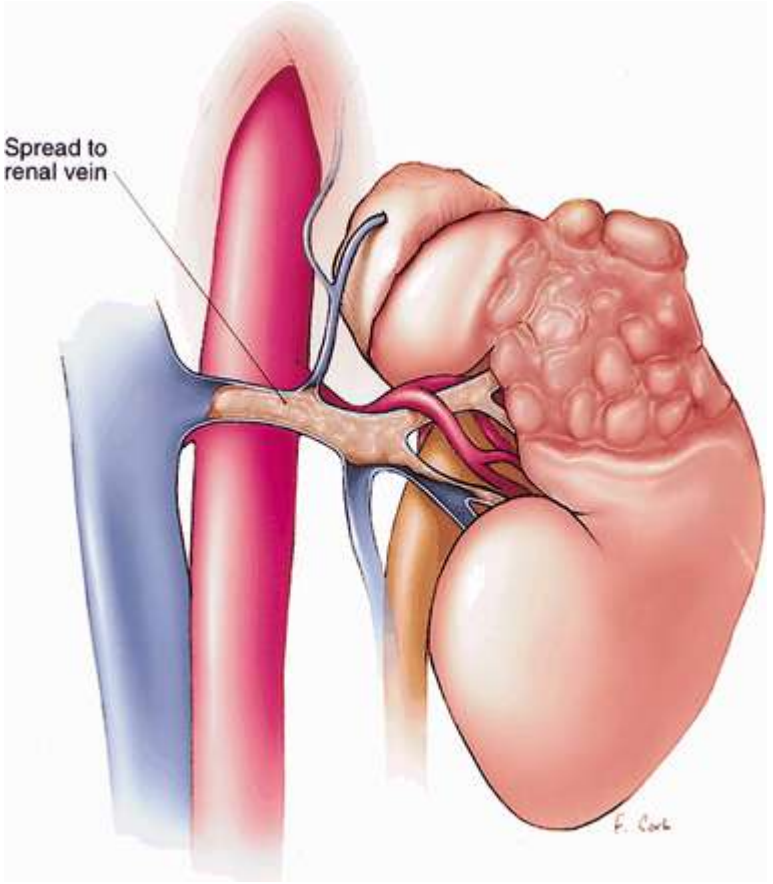


Radiographics 2001; 21: S237-S254

Stadiëring

TNM stage T3b

Niercelcarcinoom met tumor uitbreiding in de linker vena renalis



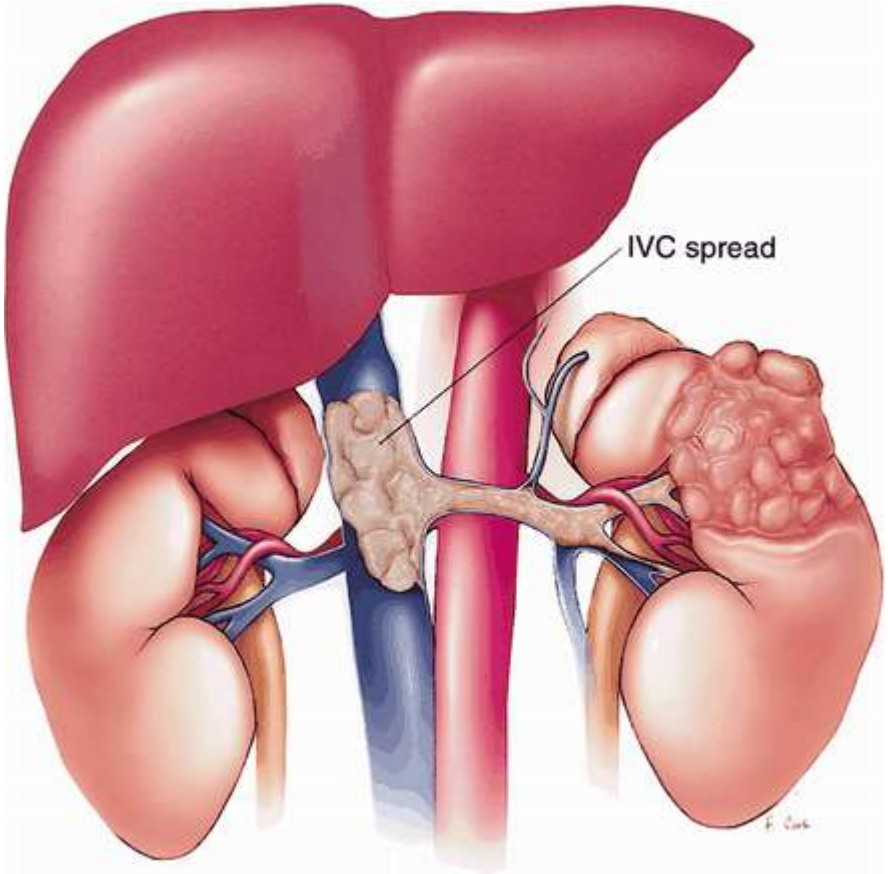
Radiographics 2001; 21: S237-S254

Stadiëring

TNM stage T3b

Niercelcarcinoom met tumor uitbreiding in de linker vena renalis en vena cava inferior

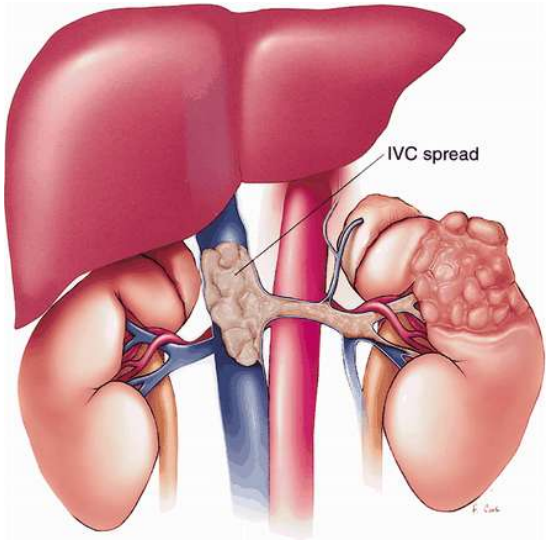
Bij 4-10%, meer bij rechtszijdige laesies



Radiographics 2001; 21: S237-S254

Stadiëring

TNM stage T3b

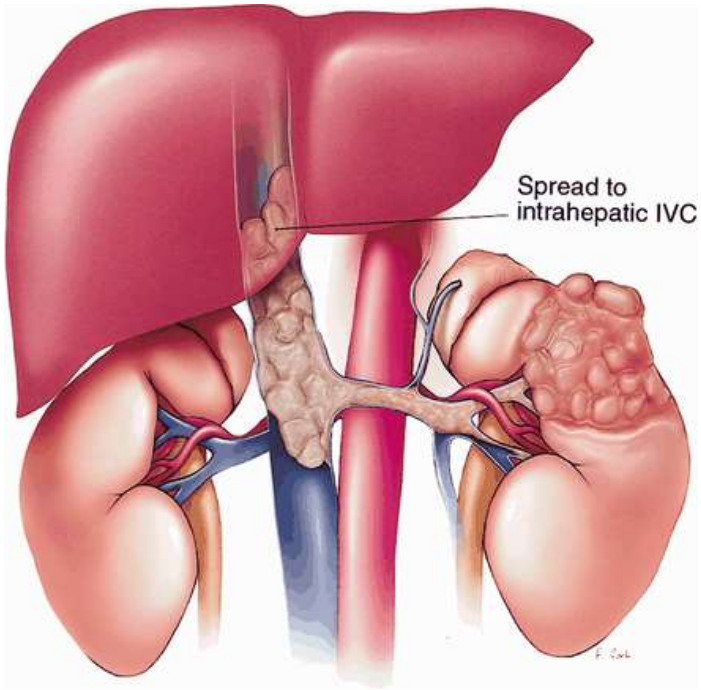


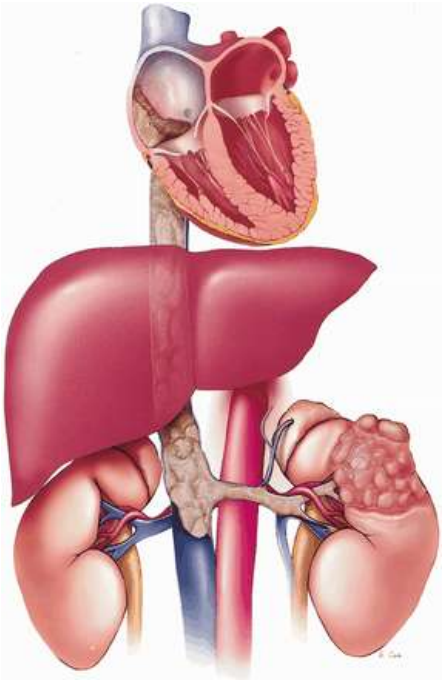
Radiographics 2001; 21: S237-S254

Stadiëring

TNM stage T3b
intrahepatisch

TNM stage T3c
supradiafragmaal

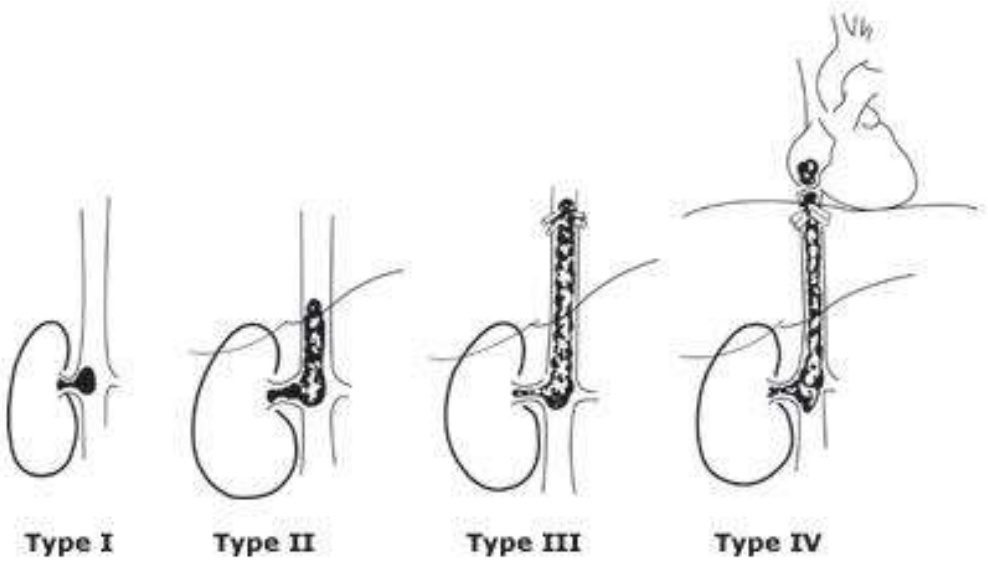




Radiographics
2001; 21: S237-
S254

Niercelcarcinoom met tumor uitbreiding in de linker vena renalis, vena cava inferior en rechter atrium

Stadiëring



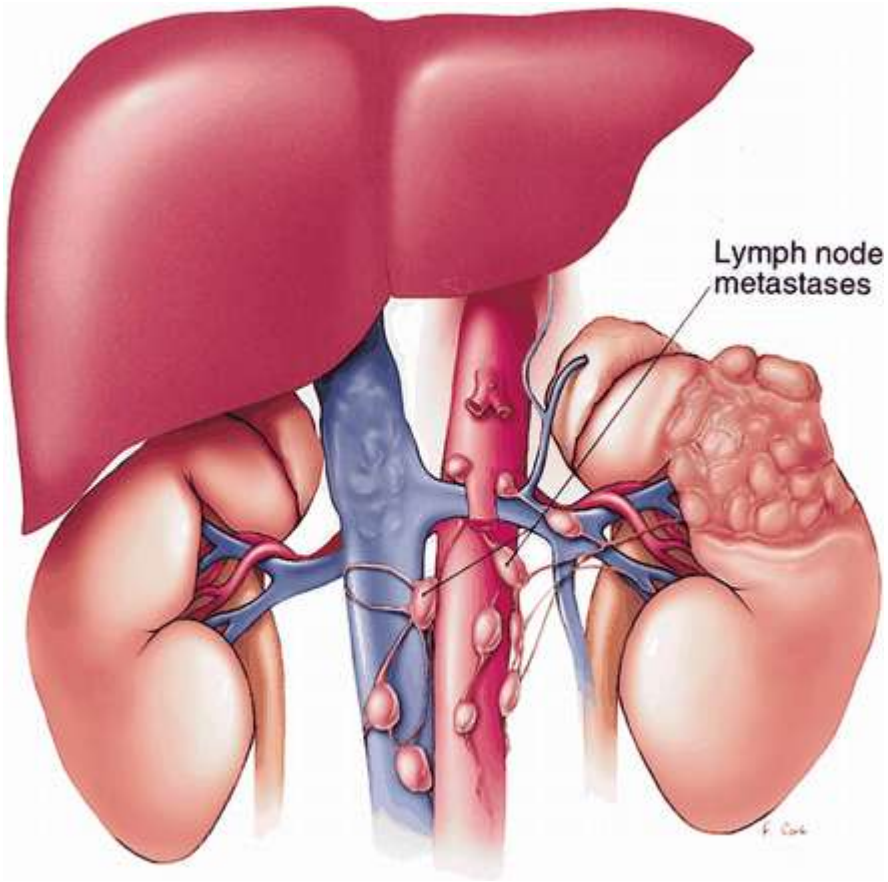
4 stadia van cavoatriale tumor extensie

Chiappini, Savini, Marinelli et al. Cavoatrial tumor thrombus: single-stage surgical approach with profound hypothermia and circulatory arrest, including a review of the literature.. J Thor Cardiovasc Surg 2002; 124: 684.

Stadiëring

Lymfklieren korte-as diameter > 1 cm

Let wel: reactief of maligne adenopathie



Radiographics 2001; 21: S237-S254

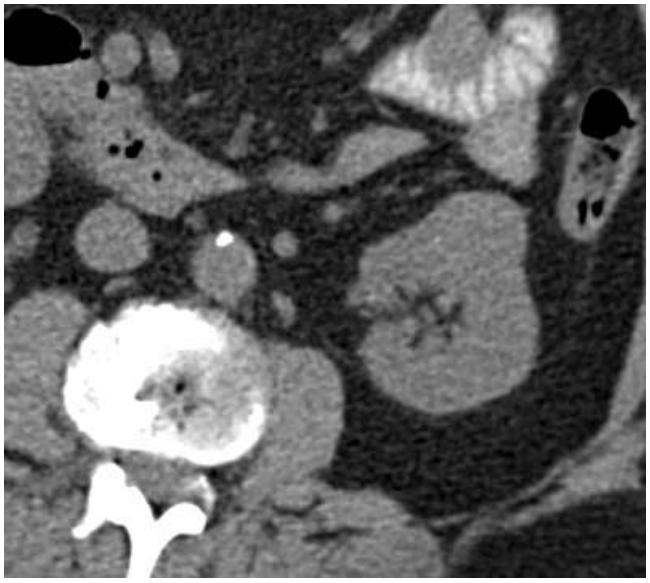
CT scan is de modaliteit

Type scan:

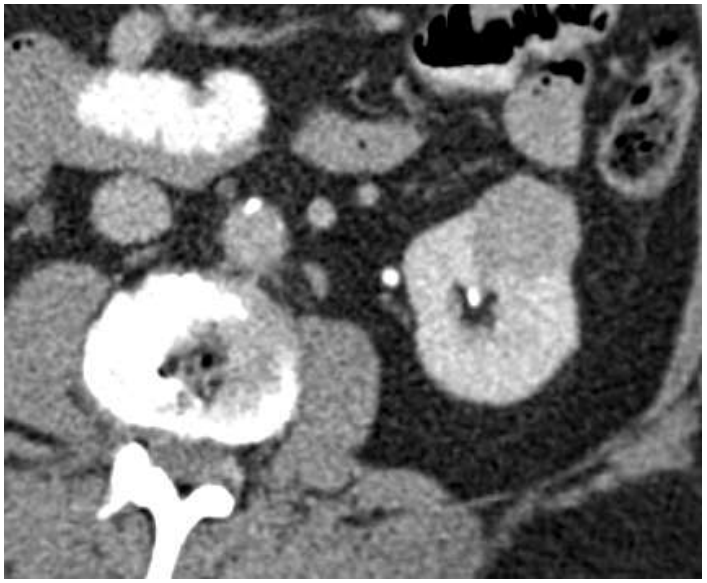
- met i.v. contrast
- portaal veneuze contrastfase
- coupe dikte
- reconstructie kernel

MDCT – contrastfase

Patient –



blanco

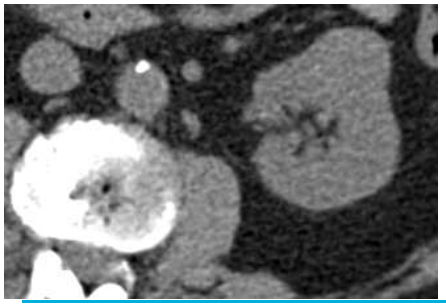
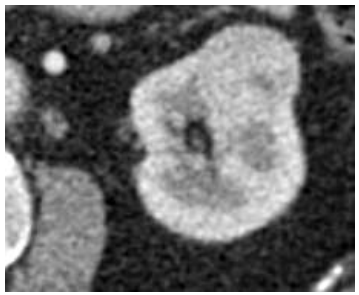
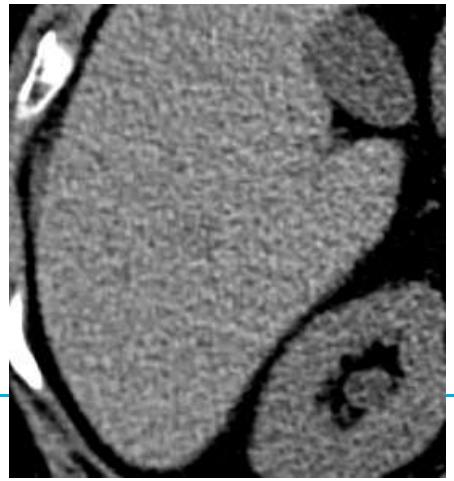
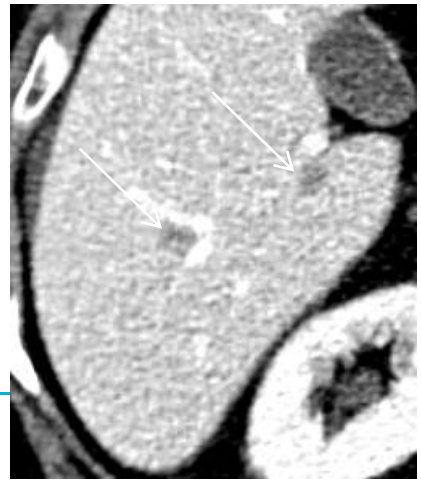


veneus

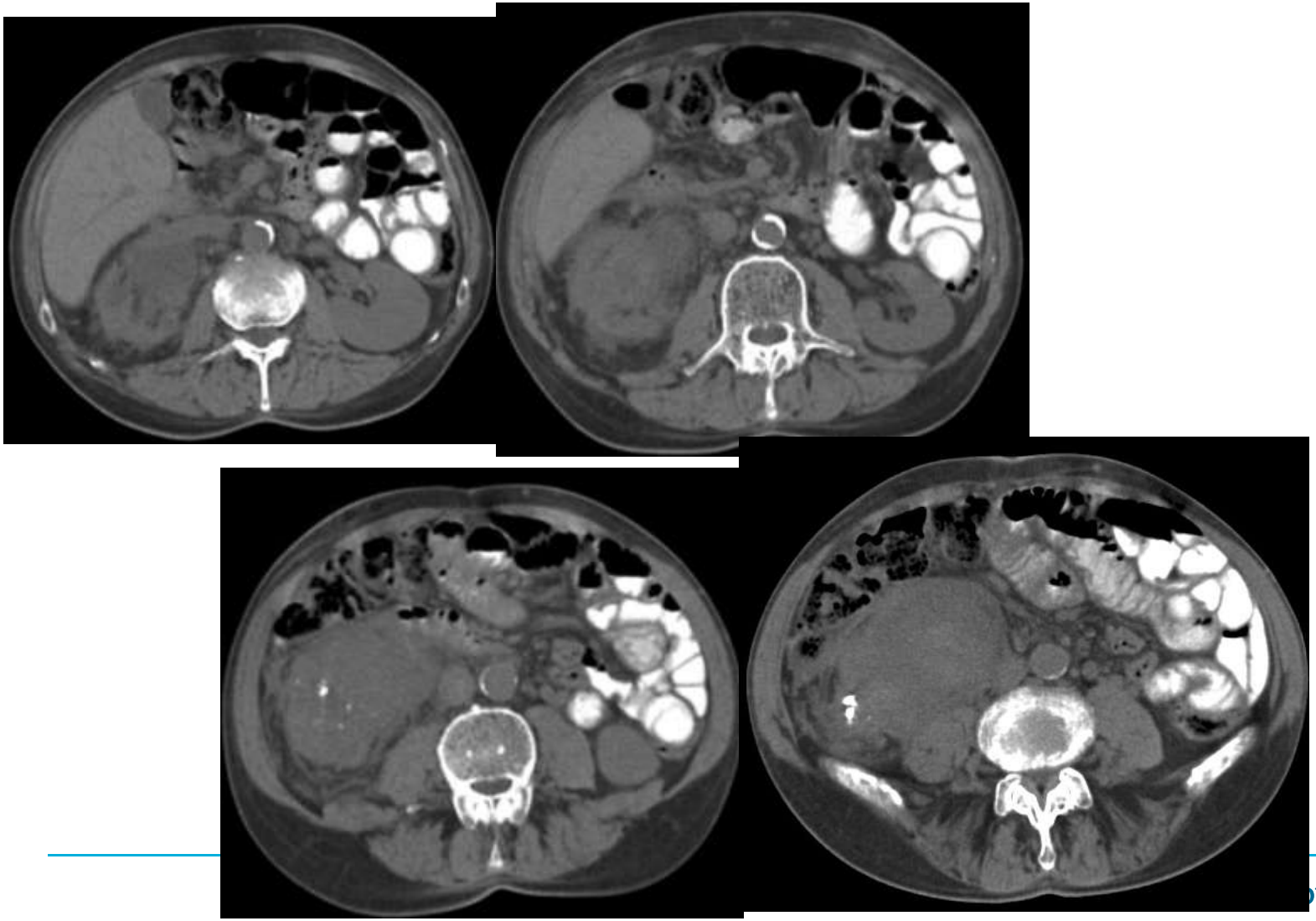
Discussie

CT zonder iv contrast:

- missen van (kleine) metastatische laesies in solide organen
- missen (kleine) klieren

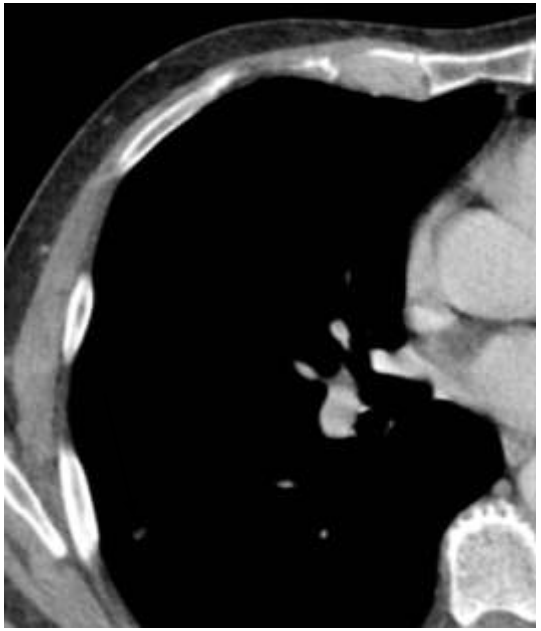
CT zonder iv contrast



MDCT – reconstructie kernel

Patient

longsetting



weke delen setting

Scan parameters zeer belangrijk !!!

- MDCT
- dunne coupes (≤ 5 mm)
- met intraveneus contrast
  (veneuze fase)
- weke delen setting / longsetting
- hoge mate van reproduceerbaarheid

Conclusie

Metingen op CT scan betrouwbaar, indien:

- metingen op CT beelden van goede en vergelijkbare kwaliteit gedurende een therapie

- metingen op dezelfde settings