Nyrekreft

Epidemiologi
Patologi
Kirurgisk Behandling

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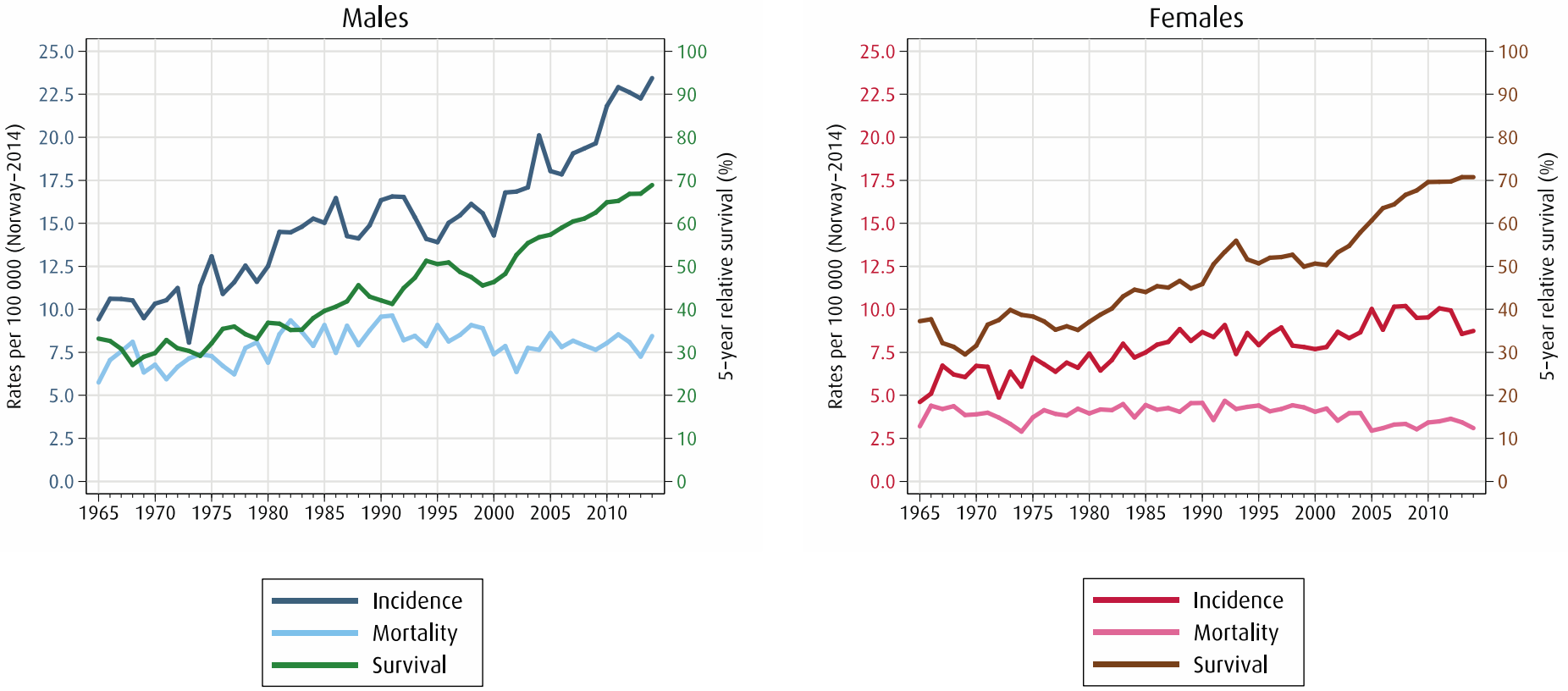
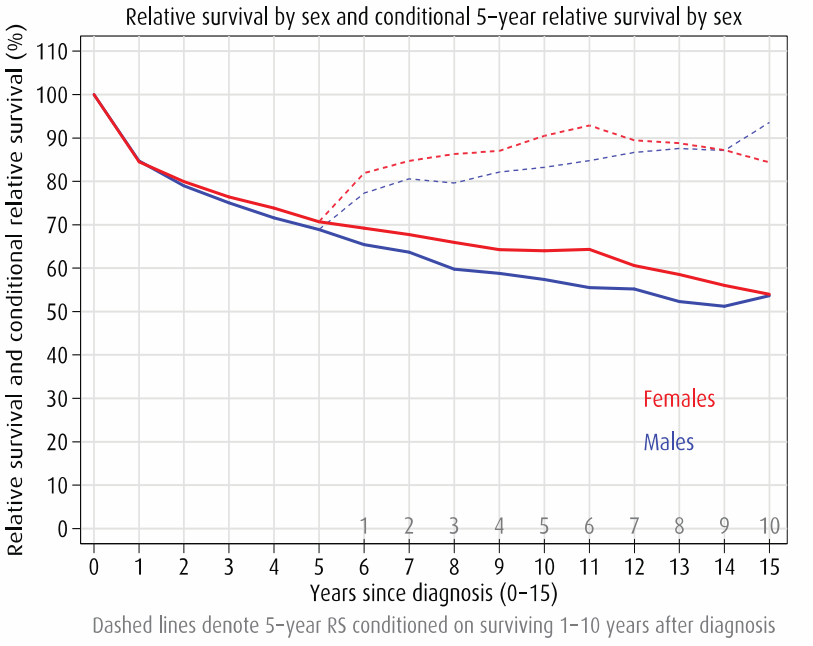
Trender i insidens, mortalitet og 5 års overlevelse

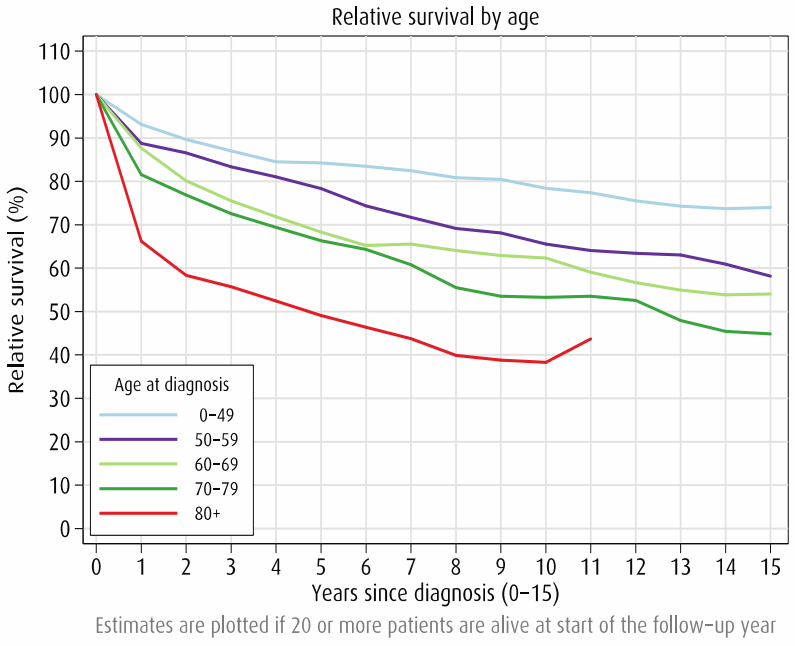
Figure 11-L: Kidney excluding renal pelvis (ICD-10 C64)



Mortalitet/Overlevelse

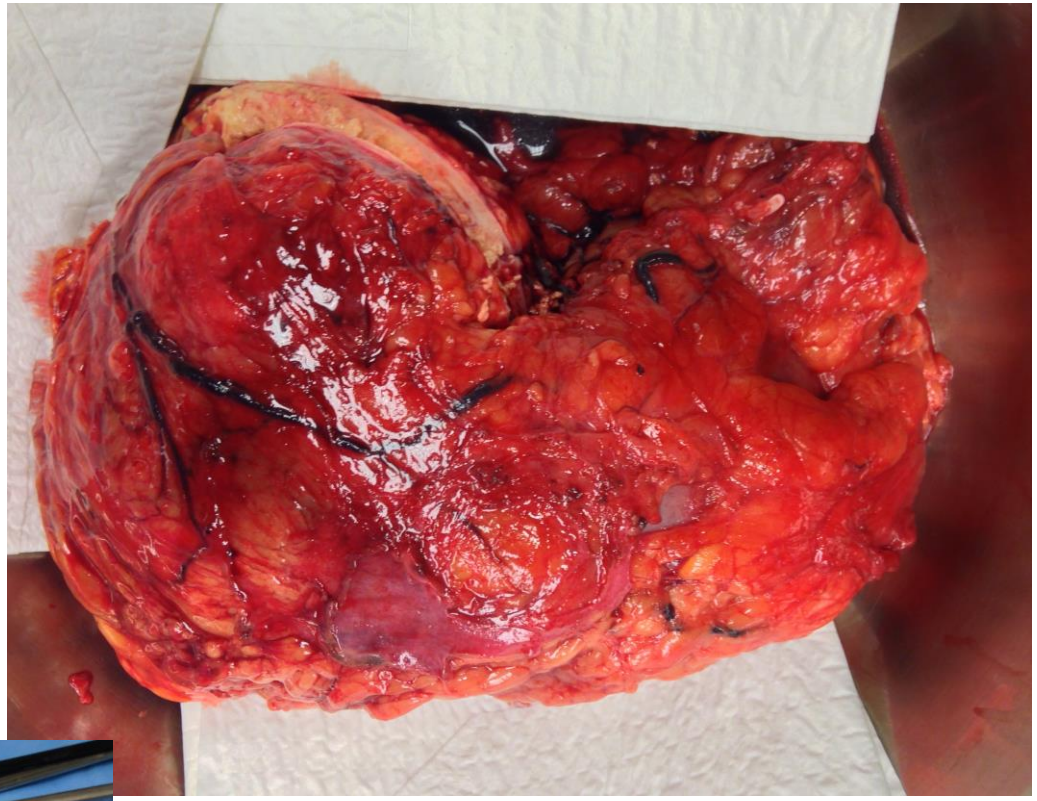
- 2014: 286 død av of RCC (død av cancer er 10 971)
  - » 2,6 % of alle cancer relaterte dødsfall i Norge
  - » 0,6% av alle dødsfall
- Ca. 50% relativ 15 års overlevelse

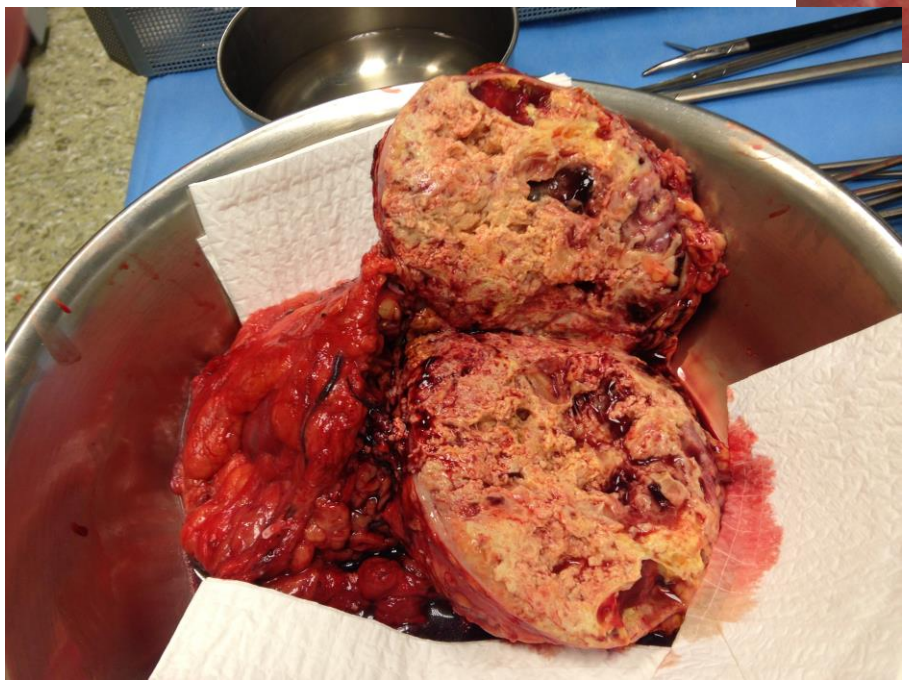




Generelt

- RCC 80 -90 % av maligne nyresvulster
- Grawitz tumor – hypernefrom-rcc





Epidemiologi RCC

- 2 % av cancer i Norge

- Diagnostisert 2013; 760 fordelt på 5 mill (2014 ; 815)
- 13 :100 000 i 2013 (2004; 9,8)

- Fem års overlevelse ca 70 %
- 6006 i live 2014 mot 3560 i 2004 med RCC
- 286 døde av RCC i 2014 (195 menn, 91 kvinner)

- Jevn mortalitet /overlevelse på landsbasis
- Incidensen av avansert cancer stabil(menn 1,9 og 3,6, kvinner 0,6 og 1,3)
- 2% årlig økt forekomst siste ti år

Alder og kjønn - Røyk og tobakk

- **Hyppigere** hos menn enn kvinner
  - 579 menn og 234 kvinner (2014: incidens er henholdsvis 2,4 og 8,8)
  - 60-70-80 åra, men kan også oppstå hos barn
- **Tobakk** forårsaker 20 -30% av RCC hos menn og 10 til 20 % hos kvinner (RR 1,4-2,5)
  - mengde røykt, røykeslutt reduserer risiko
- **Overvekt** RR 1.07 for hver økte enhet på bmi
  - 40 % av nyrekreft i us er koblet mot overvekt
  - Også beskyttende
- **Hypertensjon** (diuretika og antihypertensiva beh ht)

Etiologi og risikofaktorer

- Endestadie nyresvikt
- Trikloretylen (løsemiddel) (RR2-6)

- Sosiøkonomisk status (mer i lavstatus)
- Ernæring; ugunstig med fett og proteinrik kost på bekostning av grønsaker

- RR 2,9 for første eller andregradslektning med RCC
- Familiæresyndromer (tuberøs sklerose)

- Strålebehandling tidligere
- Tidligere Wilms tumor (stråling/kjemo)
- Geografi –Europa og Nord Amerika på topp

Symptomer

- «klassisk triade» for RCC
  - Hematuria
  - Flanke smerter
  - Palpabel tumor

Senkning
Hypertensjon
Anemi
Cachexi
Pyrexi
Leverfunksjon
Hypercalcemi
Necromyopati
amyloidose

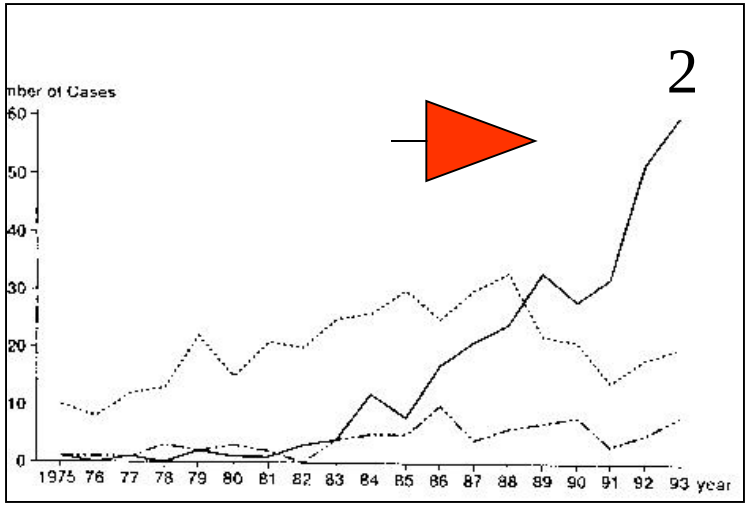
”Metastaser”
Vedvarende hoste
Beinsmerte
Cervikale glandler
Vekt tap/feber/slapphet

Paraneoplasi
Hypercalcemi
Hypertensjon
Polycytemi
Stauffers syndrome

”Obstruksjon av vena cava”
Bilaterale perifere ødemer
Høgresidig varcocele

Incidental detection

- 1971; Skinner[1] (USA) - 7%
- 1995; Homma[2] (Japan) - 66%



Norge;

1978-1987	: 21 %	(3)
1988-2000	: 35 %	(3)
1997-2004	: 45 %	(4)
2005-2010	: 57 %	(4)

1. Skinner et al. Cancer 1971;28:1165-77.
2. Homma et al. Int J Urol 1995; 2: 77-80.
3. Beisland et al, Scand J Urol Nephrol 2002; 36: 414-8
4. Sand et al, SJU 2013

Incidentally detected RCC:

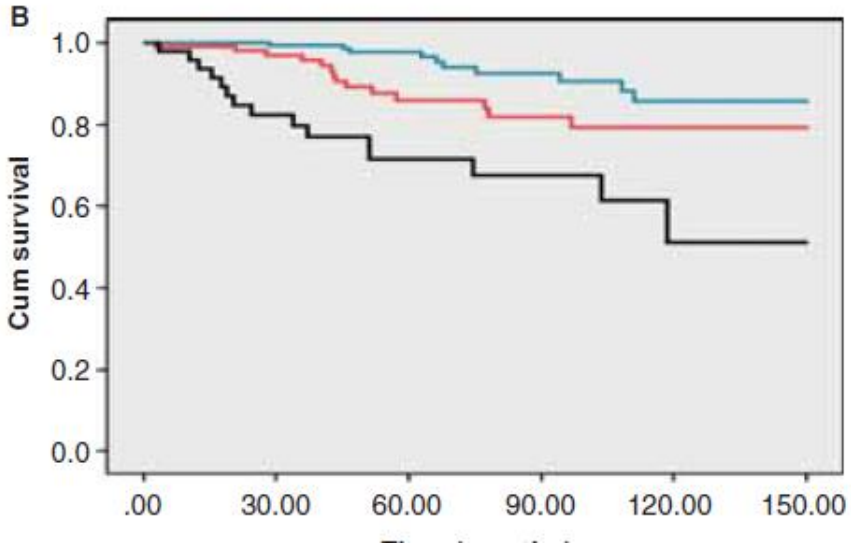
- Lower stage
- Less mets.
- Lower grade
- Smaller
- Less necrosis and sarcomatoid components

pT stage[c]				< 0.001
pT1a	160 (39)	37 (19)	123 (56)	
pT1b	105 (25)	42 (22)	63 (29)	
pT2a	50 (12)	40 (21)	10 (5)	
pT2b	18 (4)	16 (8)	2 (1)	
pT3a	69 (17)	49 (25)	20 (9)	
pT3b	4 (1)	4 (2)	0 (0)	
pT4	7 (2)	7 (4)	0 (0)	
Metastatic disease				< 0.001
N0 or M0	381 (92)	164 (84)	217 (99)	
N+ and/or M+	32 (8)	31 (16)	1 (.5)	
TNM stage[c]				< 0.001
I	261 (64)	76 (39)	185 (85)	
II	56 (14)	44 (23)	12 (6)	
III	58 (13)	38 (19)	20 (9)	
IV	38 (9)	37 (19)	1 (.5)	
Nuclear grade (n = 392)				< 0.001
G1	17 (4)	1 (.5)	16 (8)	
G2	195 (50)	67 (36)	128 (62)	
G3	116 (30)	66 (36)	50 (24)	
G4	64 (16)	51 (28)	13 (6)	
Tumour size				< 0.001
<5 cm	204 (49)	50 (26)	154 (71)	
5.0–6.9 cm	75 (18)	38 (19)	37 (17)	
7.0–9.9 cm	83 (20)	60 (31)	23 (11)	
>10 cm	51 (12)	47 (24)	4 (2)	
Tumour size (cm)				< 0.001
	5.8 (5.0; 1–20)	7.5 (7.2; 1.1–20)	4.2 (4.0;1–18)	
Histological necrosis				< 0.001
Present (n = 404)	146 (36)	95 (51)	51 (24)	
Sarcomatoid components				0.001
Present (n = 405)	25 (6)	20 (11)	5 (2)	

Sand et al, SJU 2013

HUS 1997-2010

Cancer specific survival for incidental, classical and general symptoms group



1. Sand et al, SJU 2013

Some facts to reflect over

- RCC - Most common solid tumor at autopsy (1)
- More use of imaging (CT, MRI, US)
- Older population with more chronic diseases
- Rapid rising incidence of RCC
- Stable mortality

Some quite interesting questions emerges

1. Hellsten, Eur Urol 1981

What is incidental detection in Norway today??

- 63% found as the result of diagnostic work-up or follow-up for a ***DEFINITE*** other medical condition
- 37% were diagnosed due to unspecific complaints leading to imaging

  - The first group have significantly higher levels of comorbidity (CCI, ASA, PS)

Sand et al , Scand J Urol 2013

Diagnostikk standard

- **CT Nyre**
- **CT Thorax**
- **Blodprøver**

- **Symptomretta undersøkelser**

Biopsi aktuelt ved

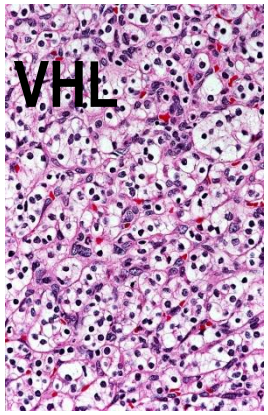
- Komorbiditet
- Fleire primærsvulstar
- Spørsmål om lymfom el
- Metastaser

Malignitetssuspekte nyrelesjoner har tetthetsauke på min 15 HU

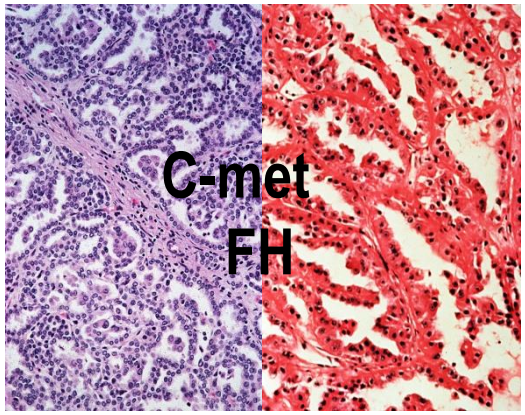
-men 20 -30 % av desse er benigne

Histologic subgroups

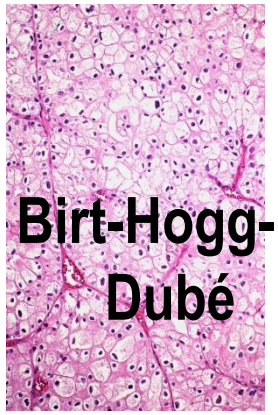
- RCC is a mainly sporadic (noninherited) disease that occurs in 5 histologic subtypes, each caused by a different gene



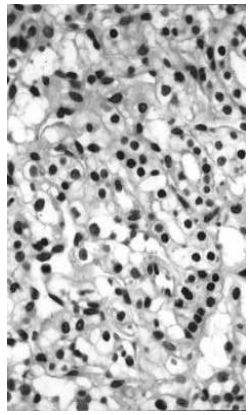
Clear cell (75-85%)



Papillary (Type I + II) (12-14%)



Chromo phobic (4-6%)

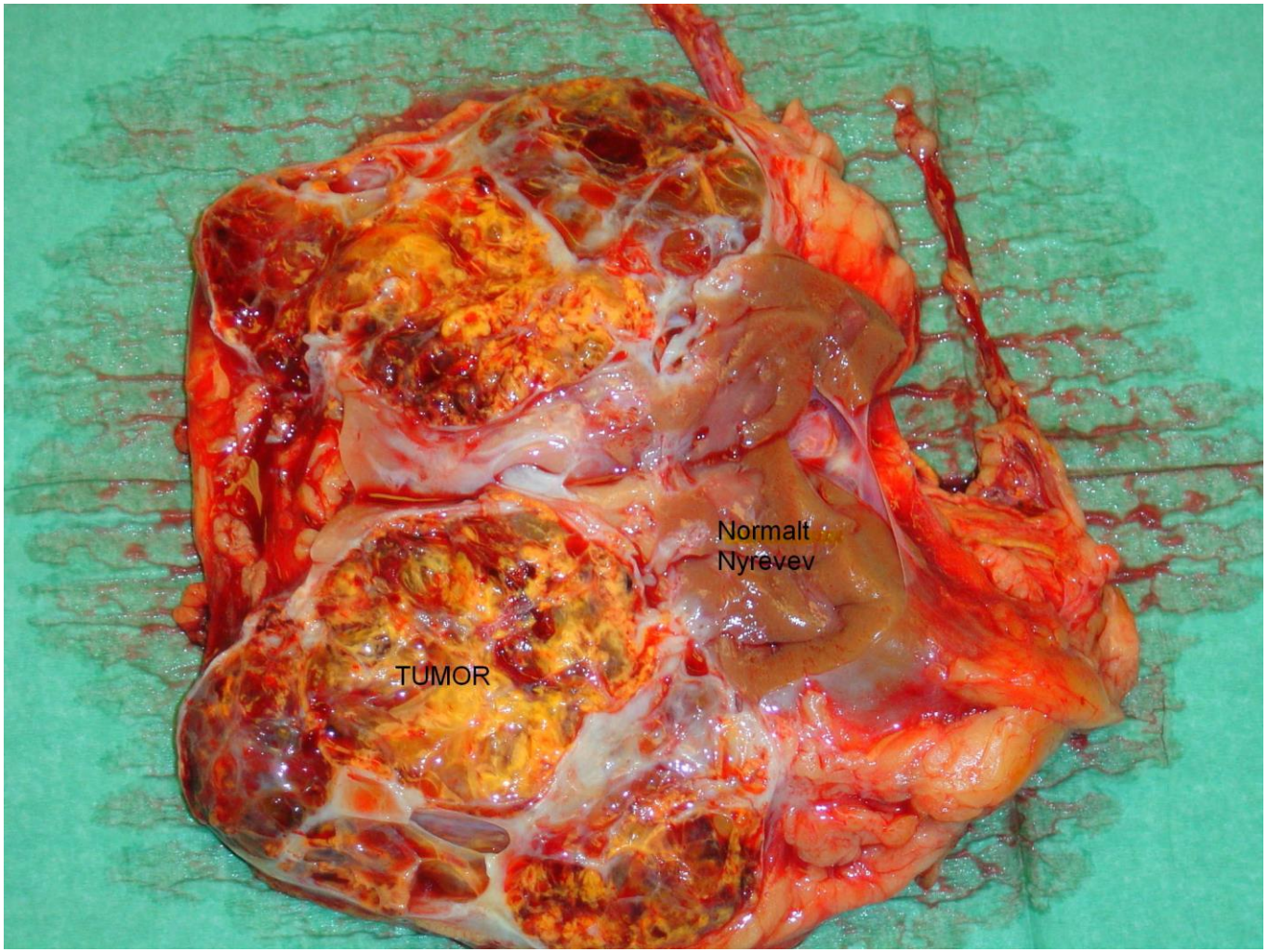


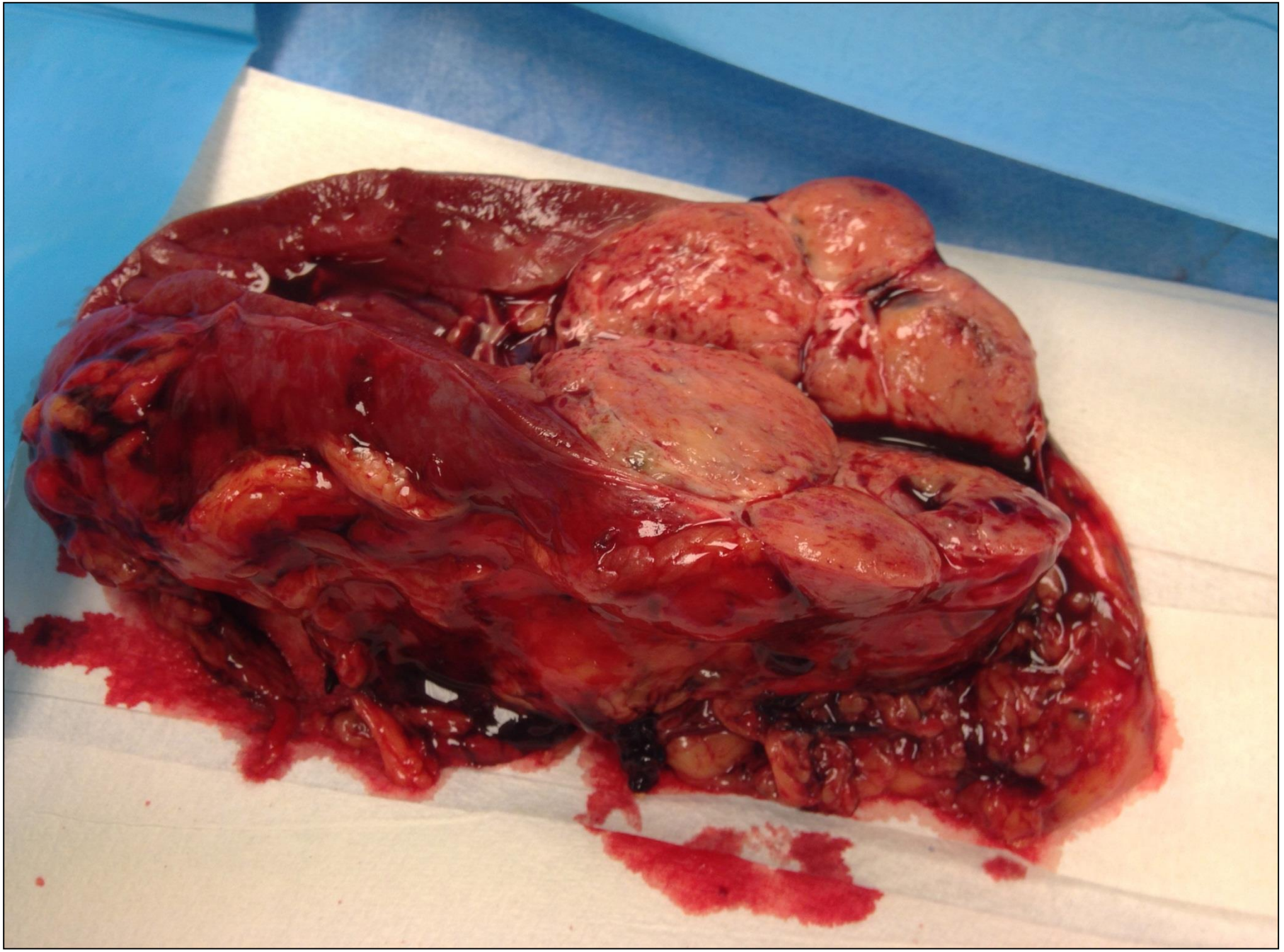
Collecting duct (1%)

Adapted from:
Motzer RJ, et al. N Engl J Med 1996;335:865-75 and
Linehan WM. Educational Book of the 41st Annual ASCO Meeting 2005:362-7

Arveleg Syndrom	Element	Kromosom	Presentasjon	Tillegg
Von Hippel Lindau	VHL gen	3p25-26	Klarcellet Bilateral Multifokal 30-50 år 50 %	Hemangiblastomer CNS Retina angiom Feokromocytom Cyster pancreas
Hereditary papillary	C-MET protoonco	7q31	Papillær type1 Multifokal 40-50 år	
Familiær leiomyomatose og RCC	Fumarat hydratase	1q42	Papillær type 2 Solitær, unilateral aggresiv Tidlig 40 åra 20 %	Kutan leiomyom Uterusleiomyom
Birt-Hogg -Dubé	BHD1	17p12q11	Kromofobe Oncocytom Hybrider Bilaterale, multiple 20-40%	Lungecyster Pneumothorax Hud fibrofollikulom

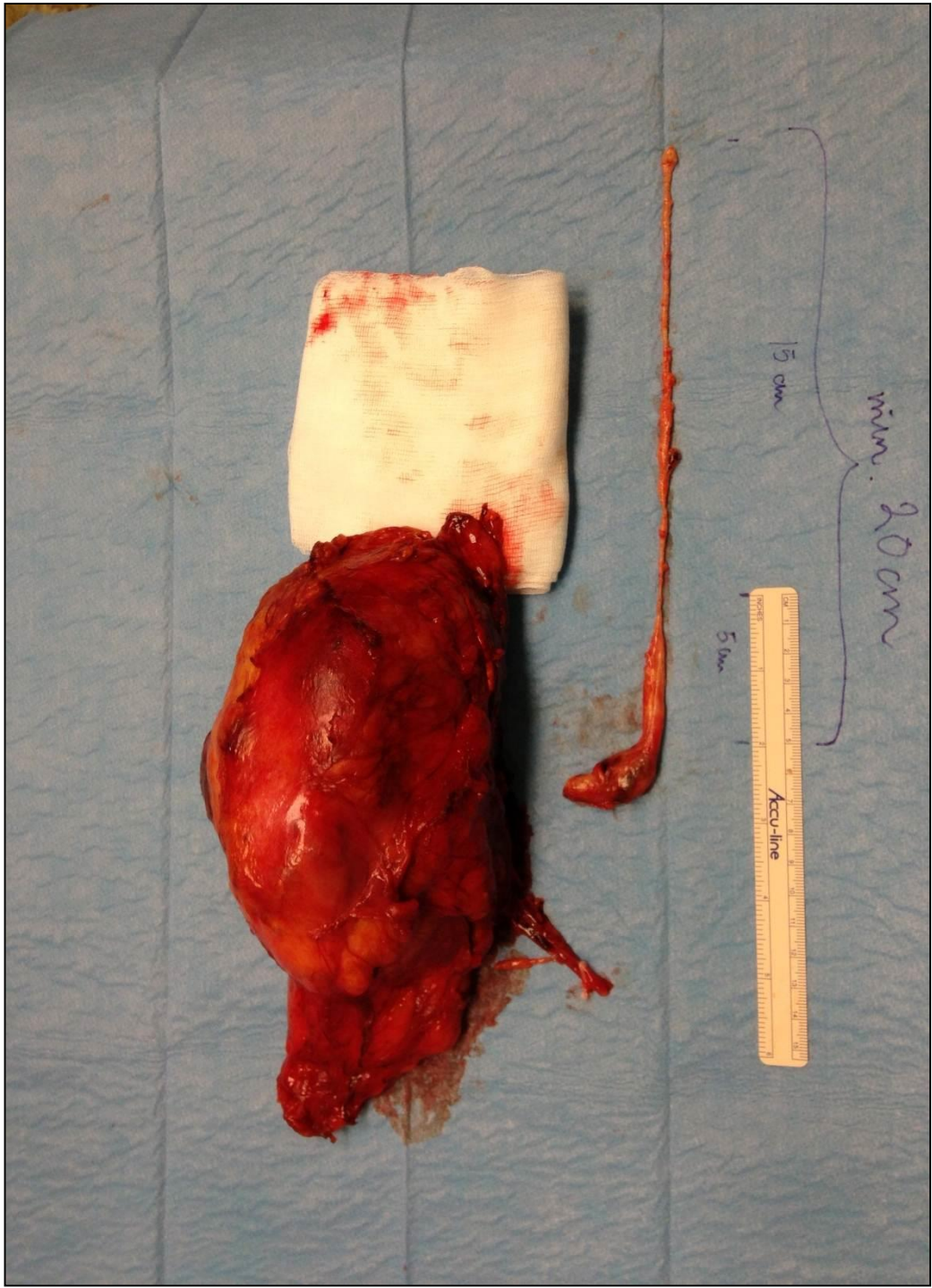
Klarcellede RCC graderes etter Fuhrman 1-4



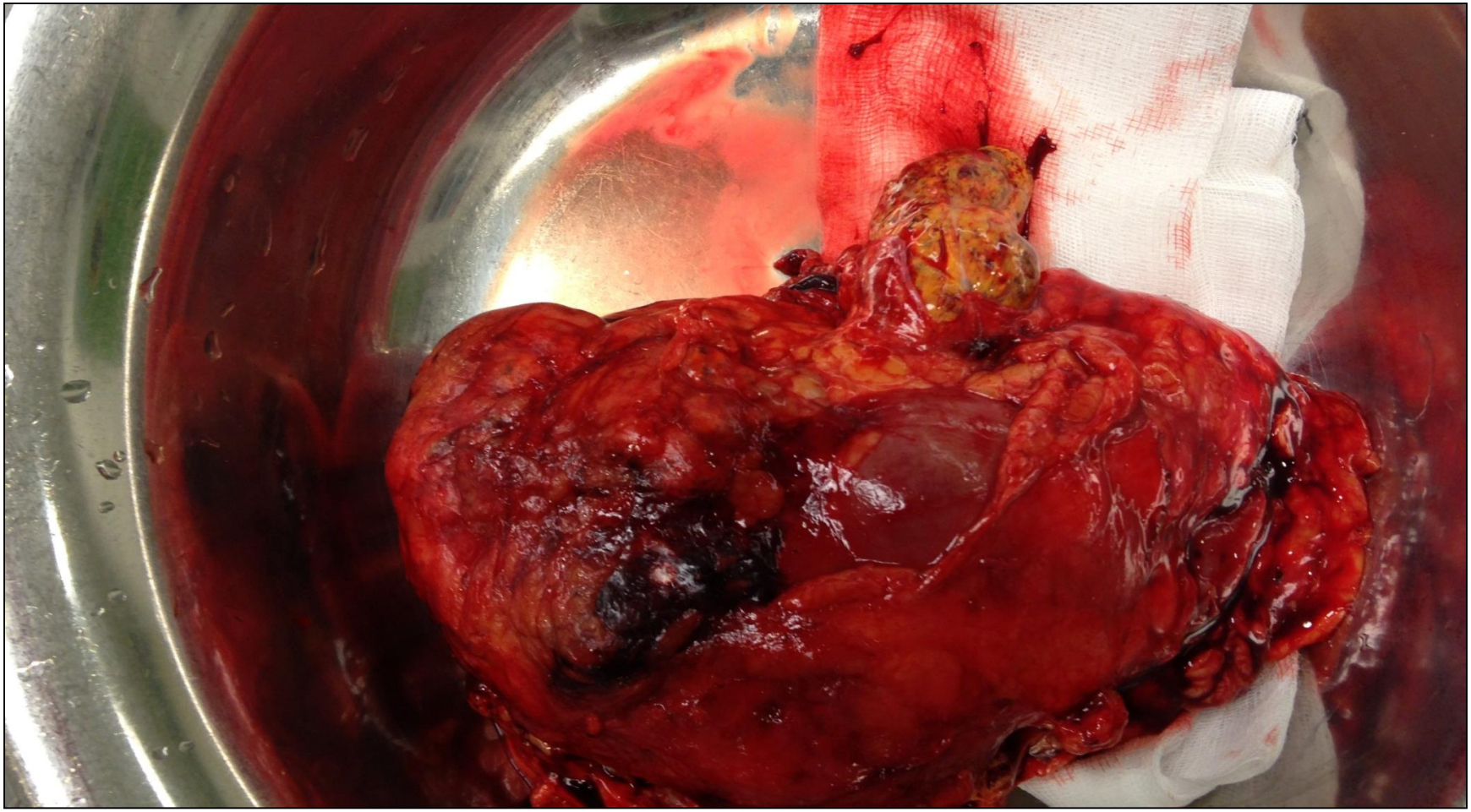


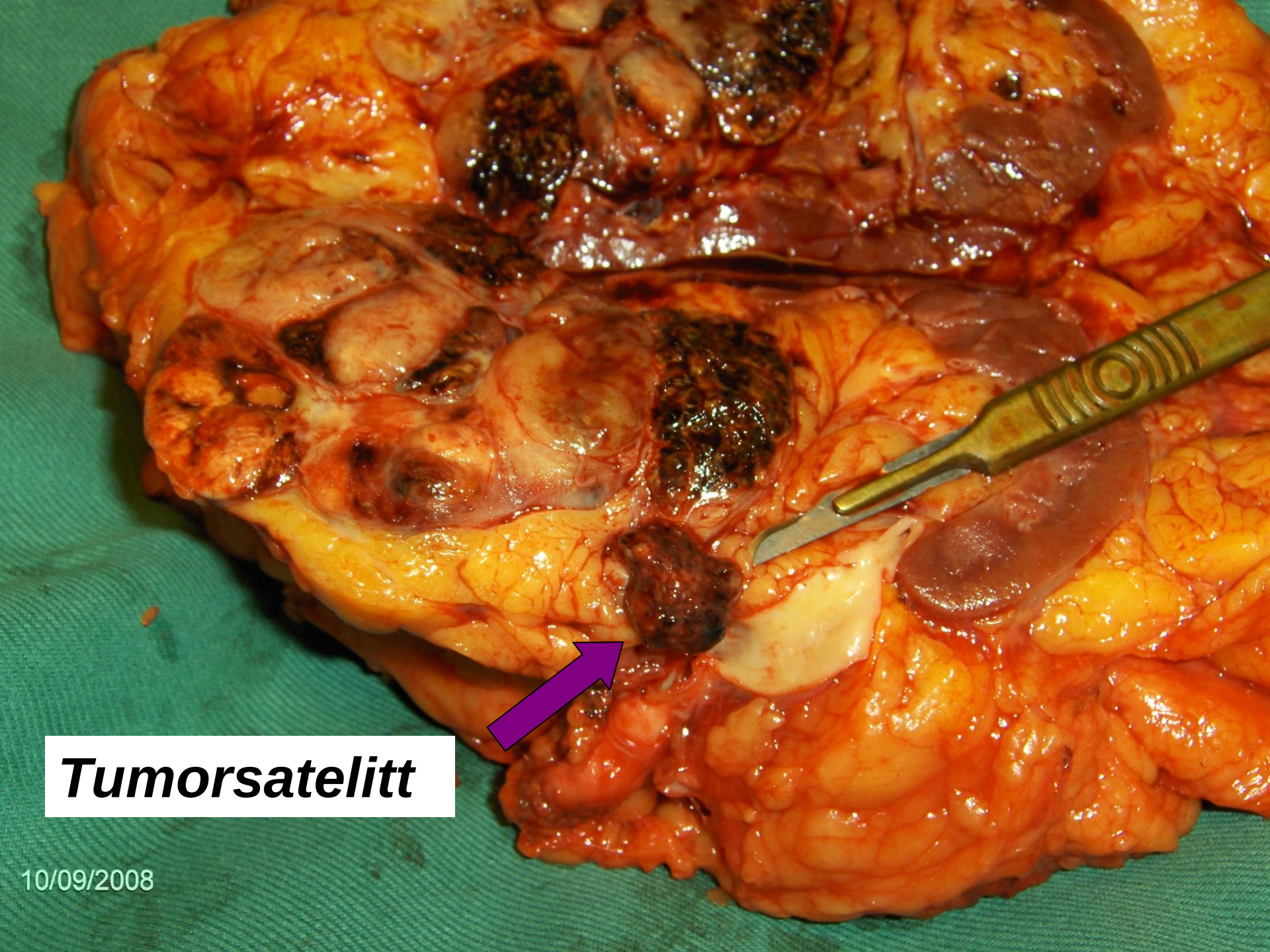
Tumor thrombus in the renal vein or Vena Cava

1-5 % av nyresvulster har sarcomatoide komponenter, Infiltrative, aggressive, median overlevelse 1 år, cytostatika forsøkes



Tumortrombe i vena renalis uten innvekst




Tumorsatelitt
10/09/2008

International TNM Staging System for Renal Cell Carcinoma

T: Primary Tumor

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤7.0 cm and confined to the kidney
T1a	Tumor ≤4.0 cm and confined to the kidney
T1b	Tumor >4.0 cm and ≤7.0 cm and confined to the kidney
T2	Tumor >7.0 cm and confined to the kidney
T2a	Tumor >7.0 cm and ≤10.0 cm and confined to the kidney
T2b	Tumor >10.0 cm and confined to the kidney
T3	Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond the Gerota fascia
T3a	Tumor grossly extends into the renal vein or its segmental (muscle containing) branches or tumor invades perirenal and/or renal sinus fat but not beyond the Gerota fascia
T3b	Tumor grossly extends into the vena cava below the diaphragm
T3c	Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond the Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)

N: Regional Lymph Nodes

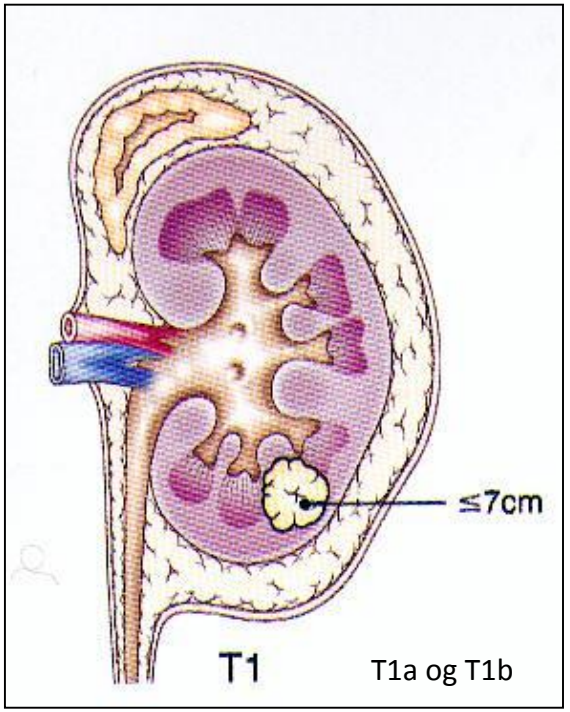
NX:	Regional lymph nodes cannot be assessed
N0:	No regional lymph nodes metastasis
N1:	Metastasis in regional lymph node(s)

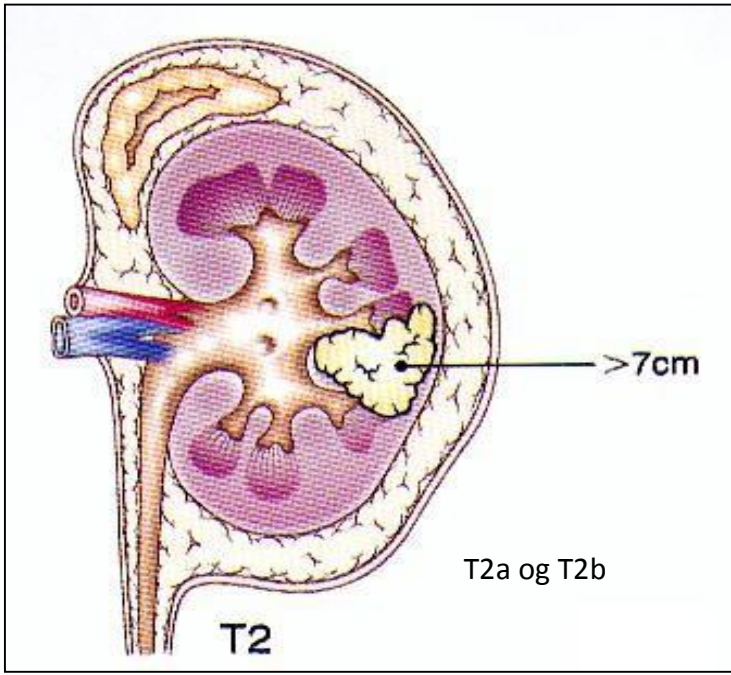
M: Distant Metastases

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis present

Stage Grouping

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1 or T2	N1	M0
	T3	Any N	M0
Stage IV	T4	Any N	M0
	Any T	Any N	M1





Treatment modalities

- **Active Surveillance / Observation**
- **Nefronsparing Surgery (partial nephrectomy)**
  - Open
  - Lap. NSS
  - Robotic assisted
  - Lap. Cryoablation
  - Percutanous Radiofrequency Ablation
- **Radical nephrectomy**
  - Open
  - Laparoscopic

SURGERY IS THE CURE FOR RCC!!

- But to do nothing might be even better for many patients

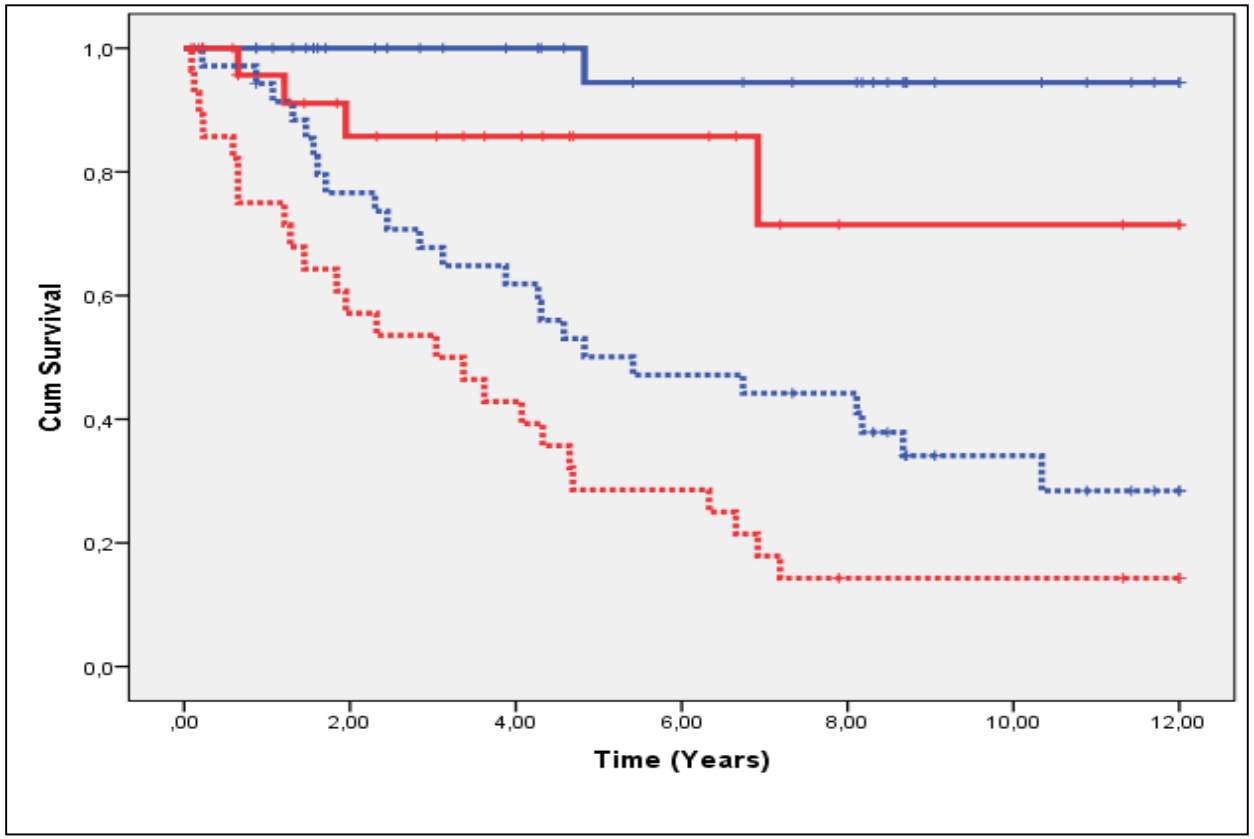
EAU 2015 Abstract No: 1025

12-year follow-up of a cohort of 63 old and comorbid patients with renal masses primarily treated with observation

- In this study, we report long-term follow-up data (up to 12 years after initial detection) for a cohort of patients with renal masses initially managed by observation.
- In addition, we have compared the long-term survival results for the initially observed group of patients with the patients initially surgically treated at our hospital during the same period (2002-2007)

Beisland C[1,4], Reisaeter LAR[2,4], Bostad L[3,4], Hjelle KM[1,4]
Departments of Urology[1], Radiology[2] and Pathology[3], Haukeland University Hospital;
Department of Clinical Medicine[4] , University of Bergen, Norway

Results I



94%

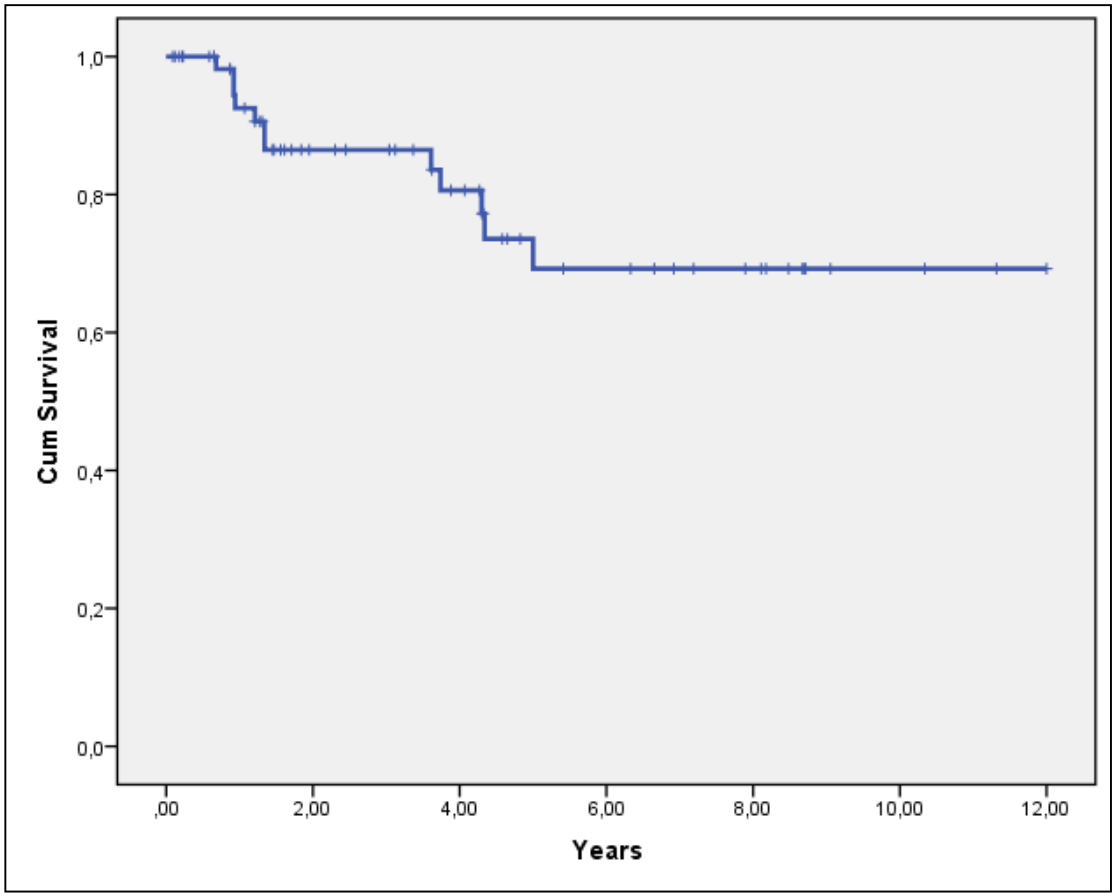
71%

28%

14%

Blue line:	CSS <4 cm
Red Line:	CSS >4 cm
Blue dotted Line:	OS <4 cm
Red dotted Line:	OS >4 cm

Results II

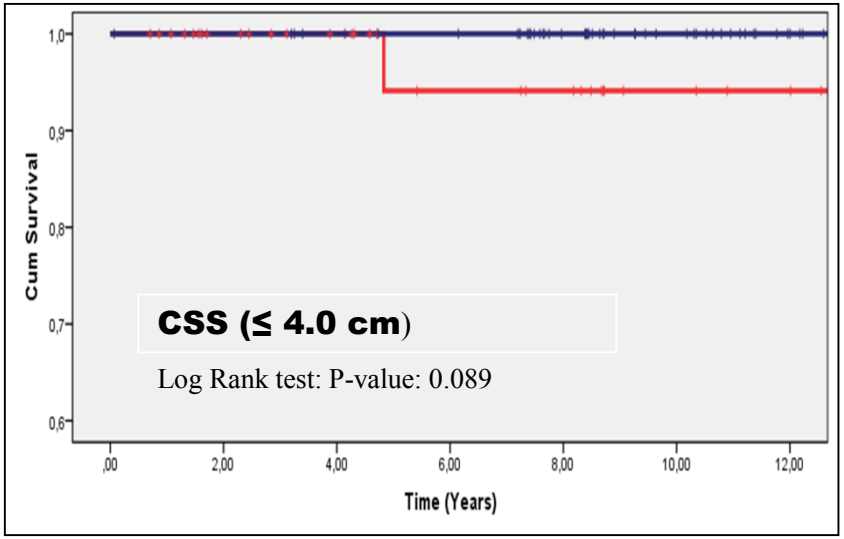


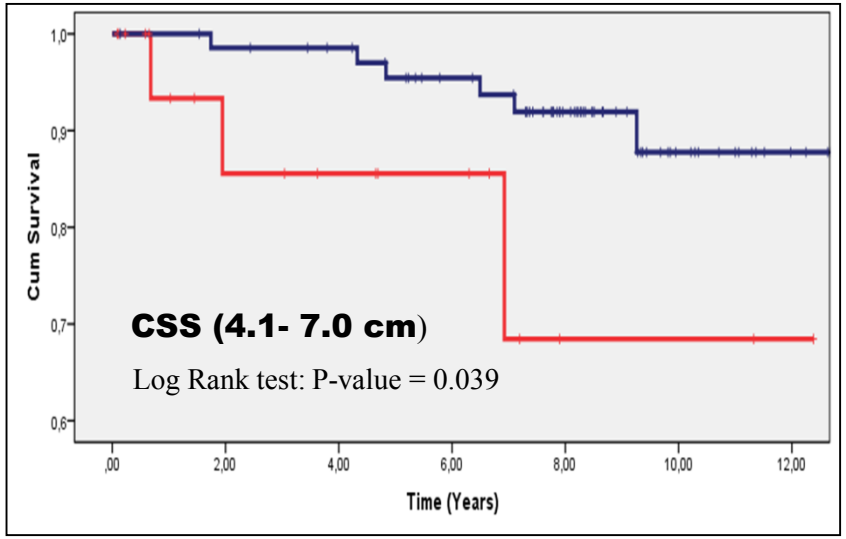
- Eleven patients (17%) have received delayed radical treatment
- No later progression of the disease.

Results III

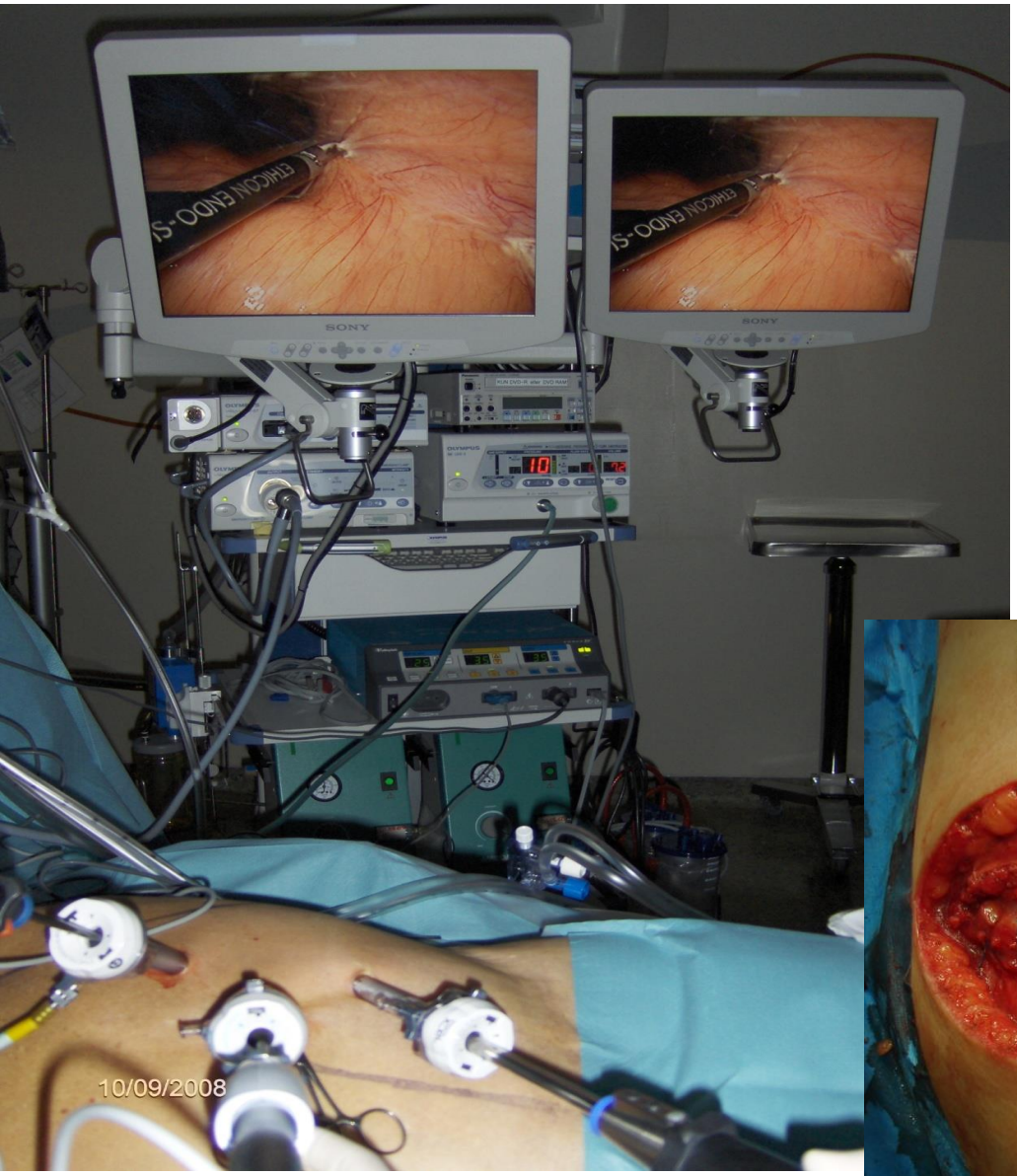
Comparison of patients with SRM ≤ 7.0 cm treated initially with observation (**red**) or initial surgery (**blue**)

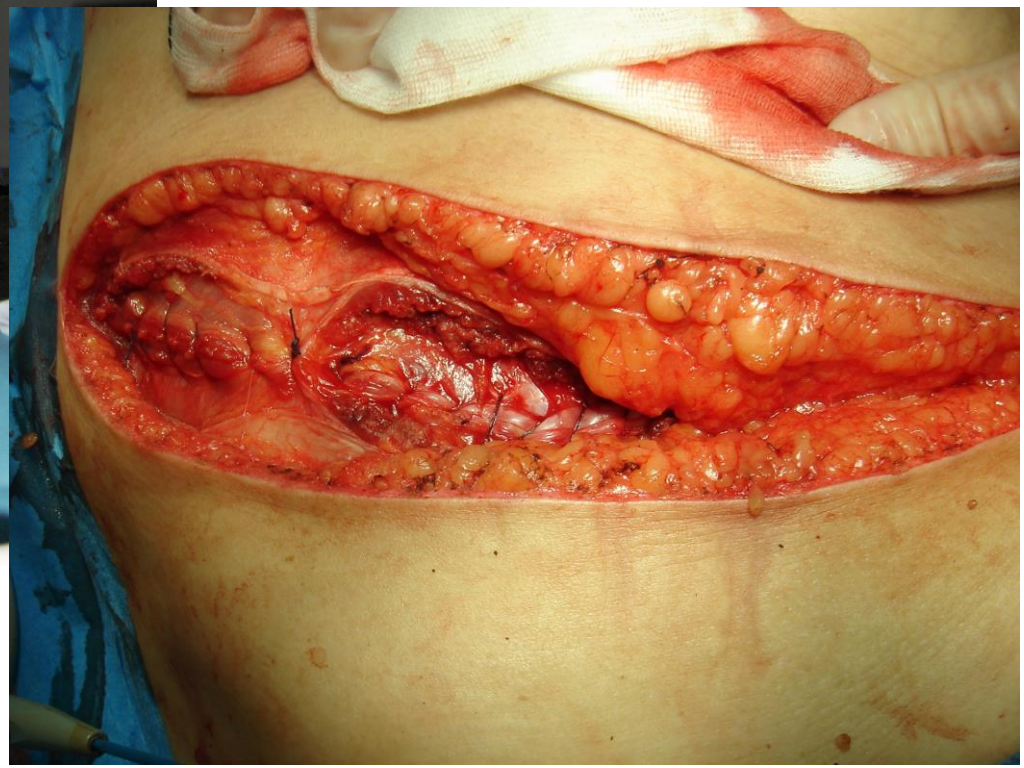
	Surgery (n=127)(%)	Observed (n=53)(%)	p-value
Size in cm (+SEM)	4.2 (± 0.1)	3.8 (± 0.2)	0.086
Age in years (+SEM)	64.8 (± 1.0)	76.3 (± 1.1)	< 0.001
ASA - Score			
I - II	91 (72)	12 (23)	< 0.001
III - IV	36 (28)	41 (77)	
Gender			
Males	82 (57)	30 (65)	0.399
ECOG			
0	102 (80)	7 (13)	< 0.001
1-3	25 (20)	46 (87)	

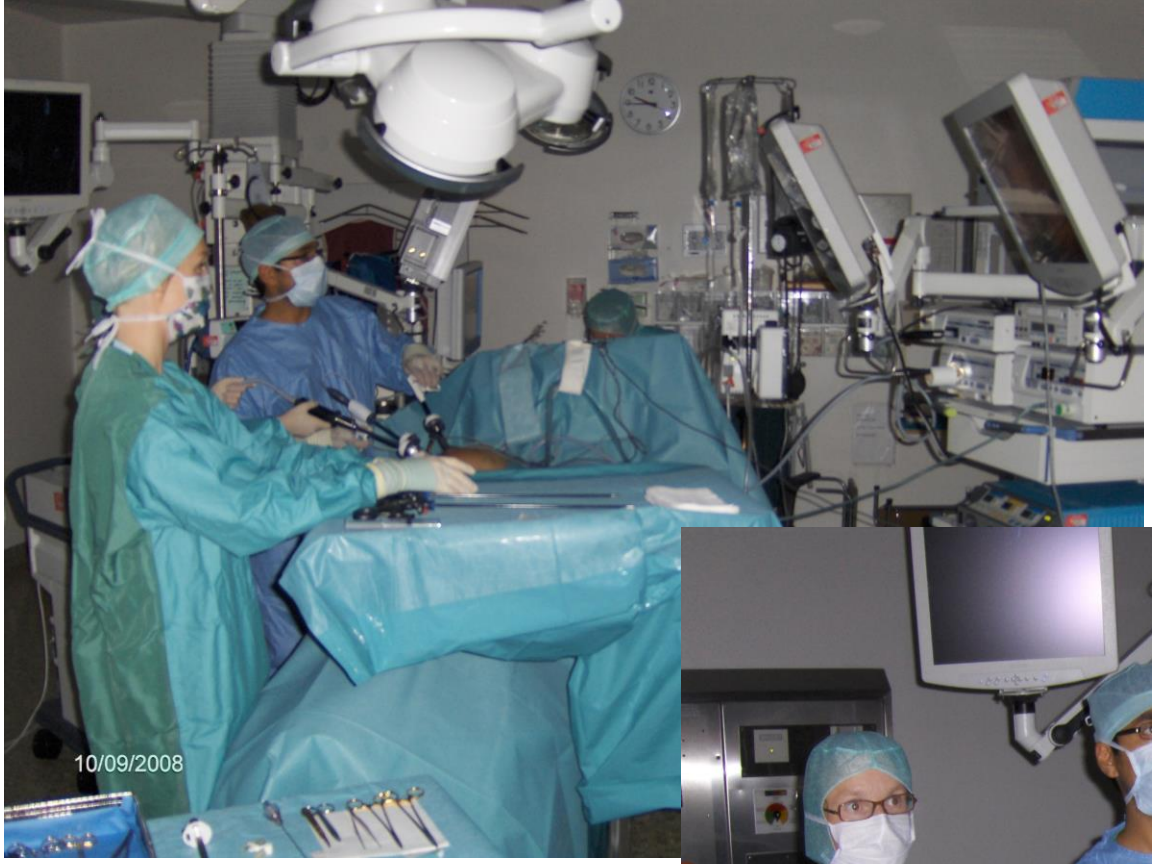


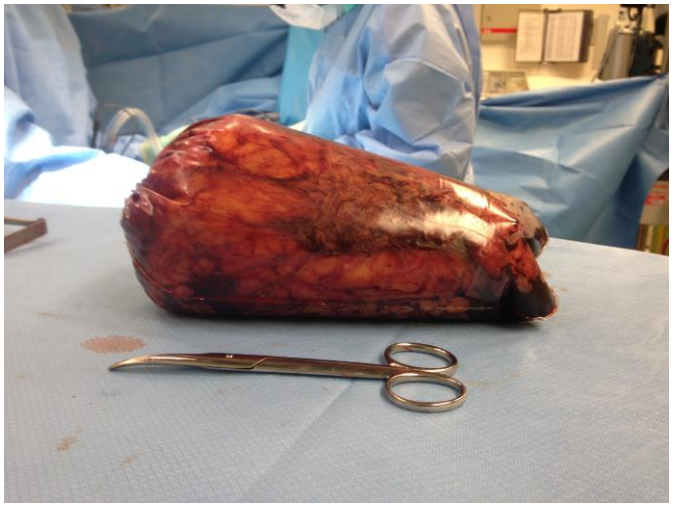


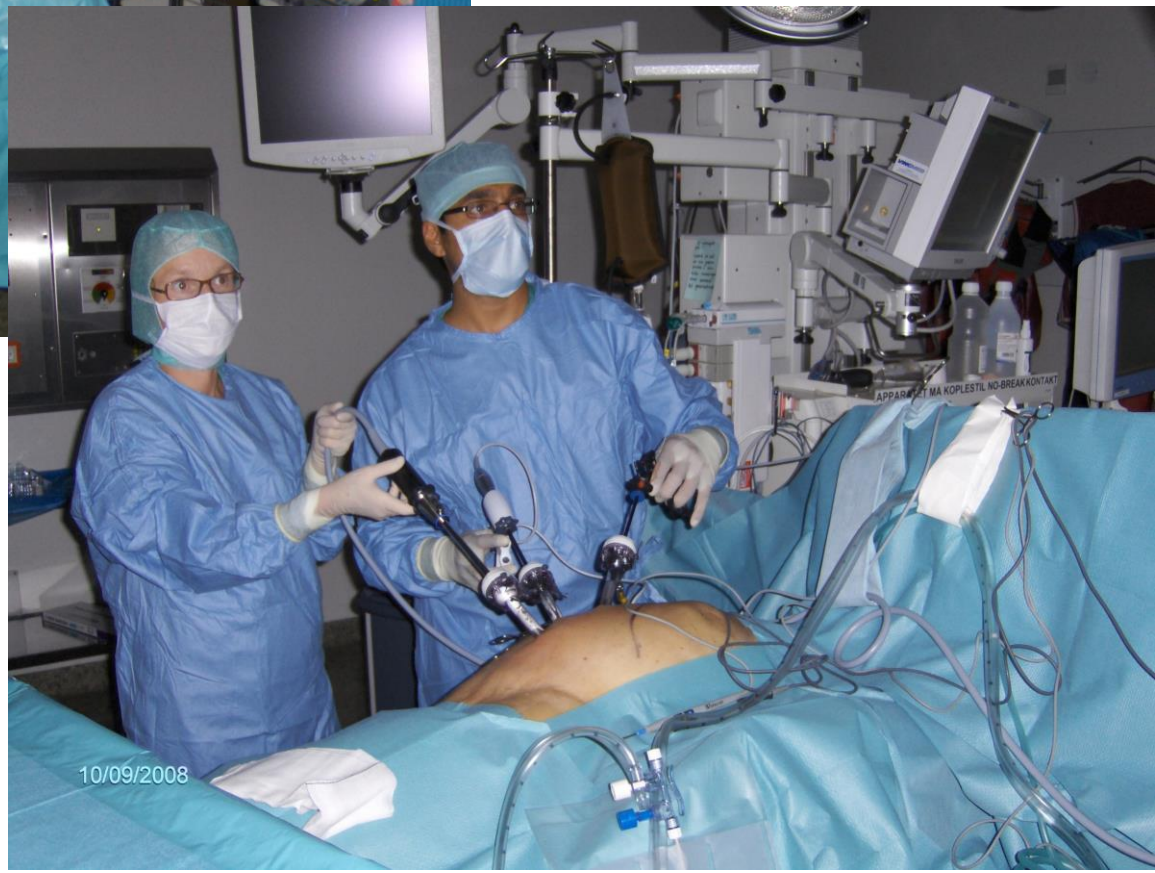
Kirurgi



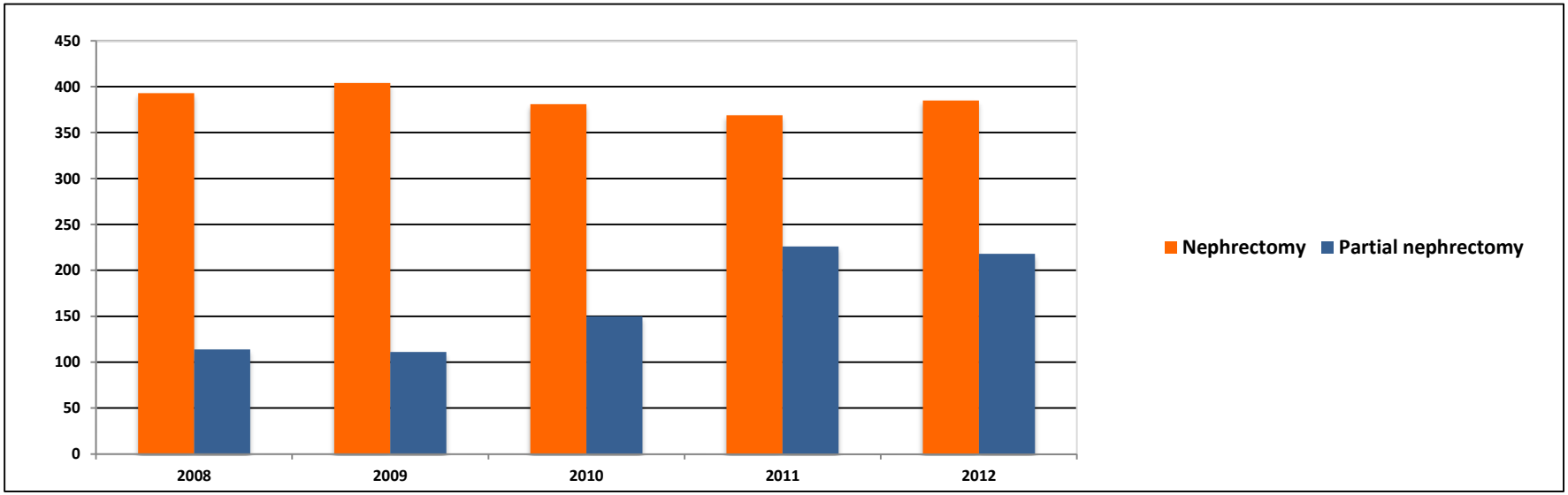


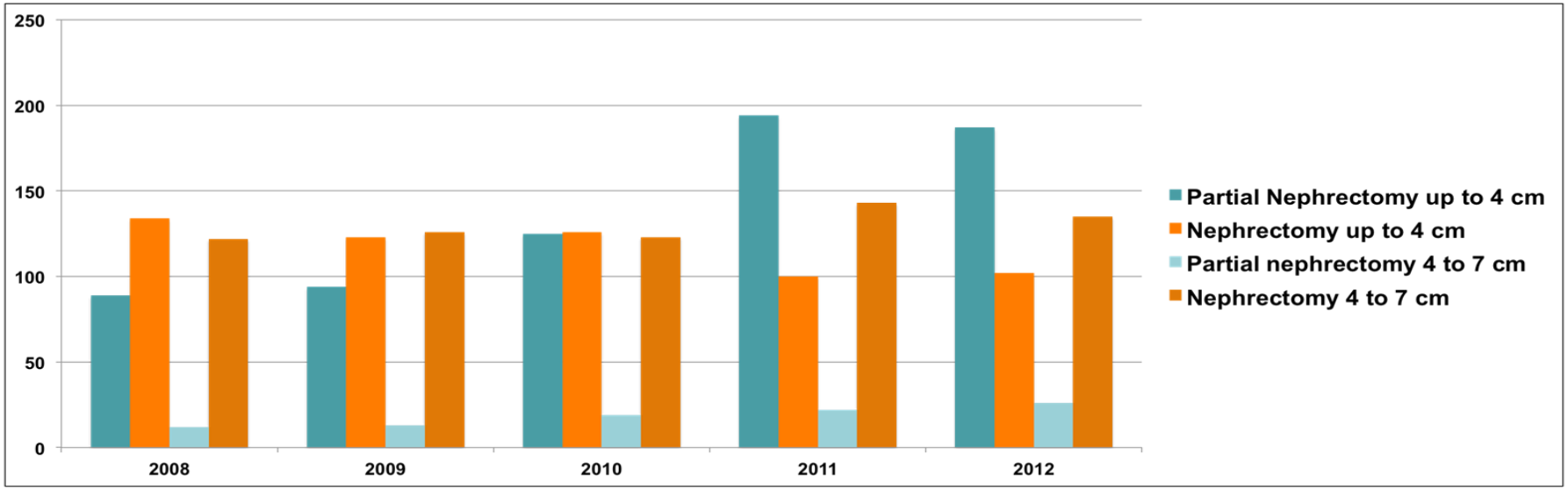

10/09/2008




10/09/2008

Nasjonalt





Hjelle et al. 2015

Partiell eller ei? (T1a T1b T2a)

Vurdere Ct bilder

- Størrelse
- Perifer/sentral
- Affeksjon av kar
- Glandler
- Samlesystem
- Resterende nyrevev
- Kontrastopptak
- CT nyrer

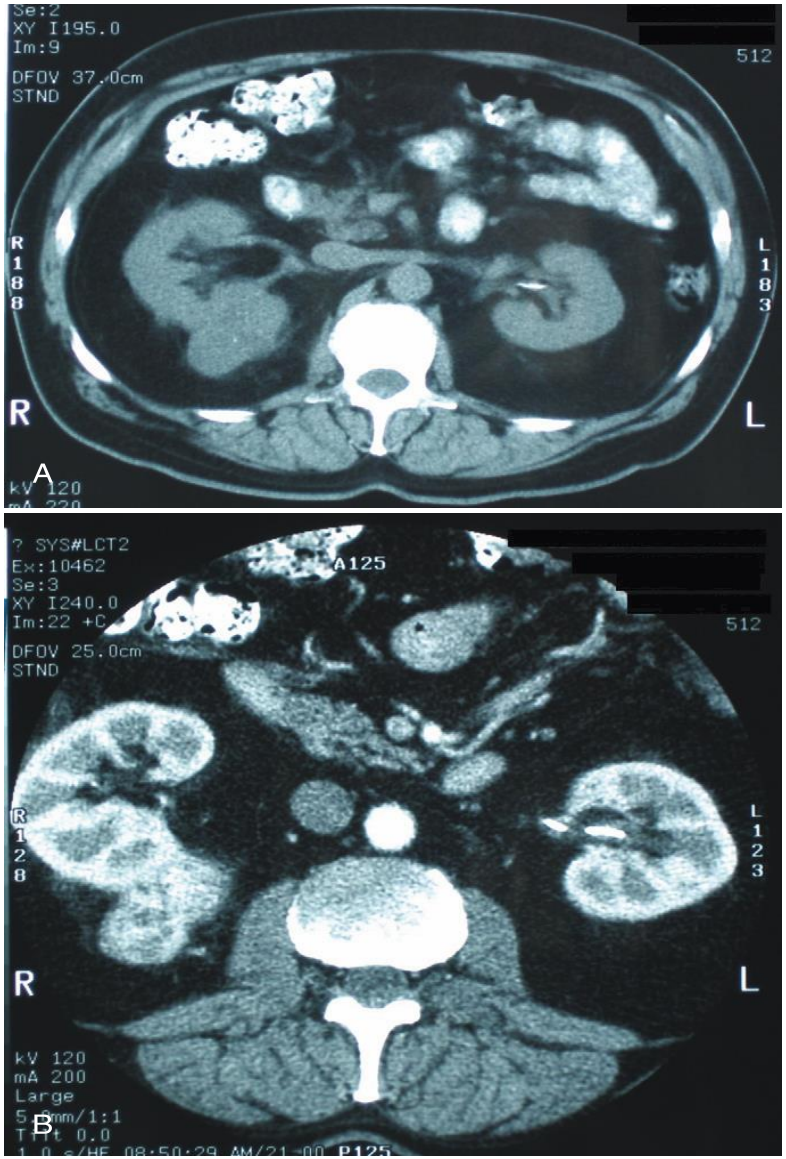
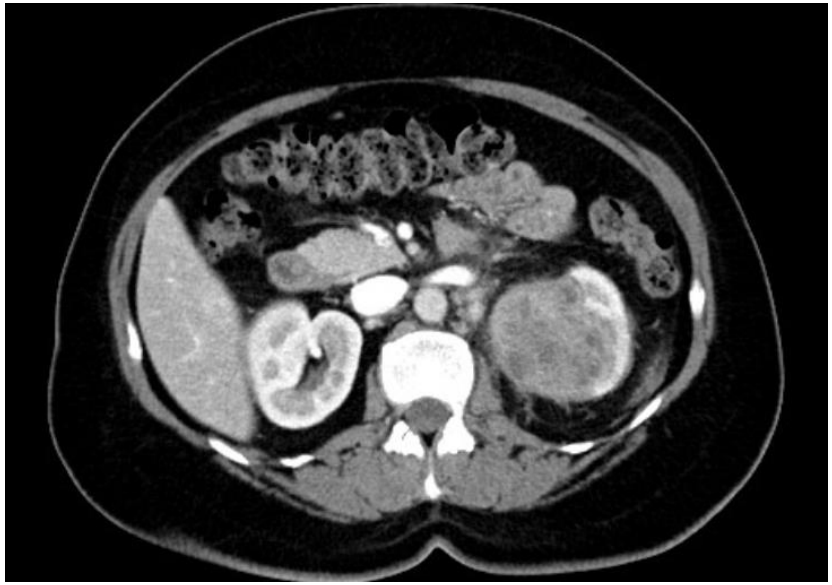
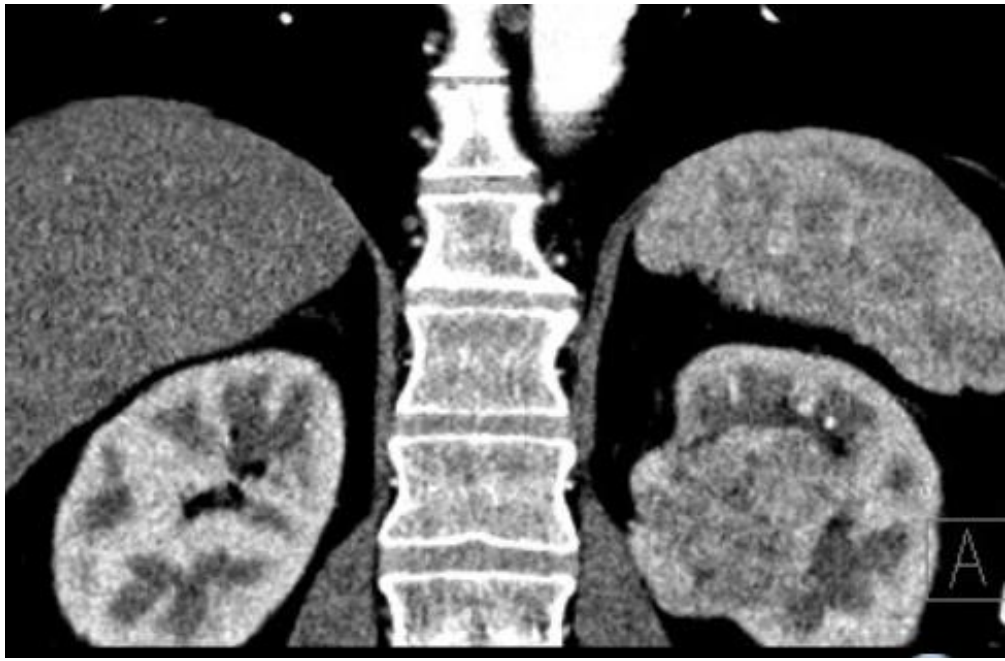


Figure 49–2. **A,** Unenhanced CT scan shows solid, right posterior renal mass. **B,** After administration of the contrast agent, CT scan shows that the mass enhances more than 20 HU and is thus highly suggestive of RCC. This mass was excised and confirmed to be a clear cell renal cell carcinoma. (Courtesy of Dr. Terrence Demos, Maywood, IL.)

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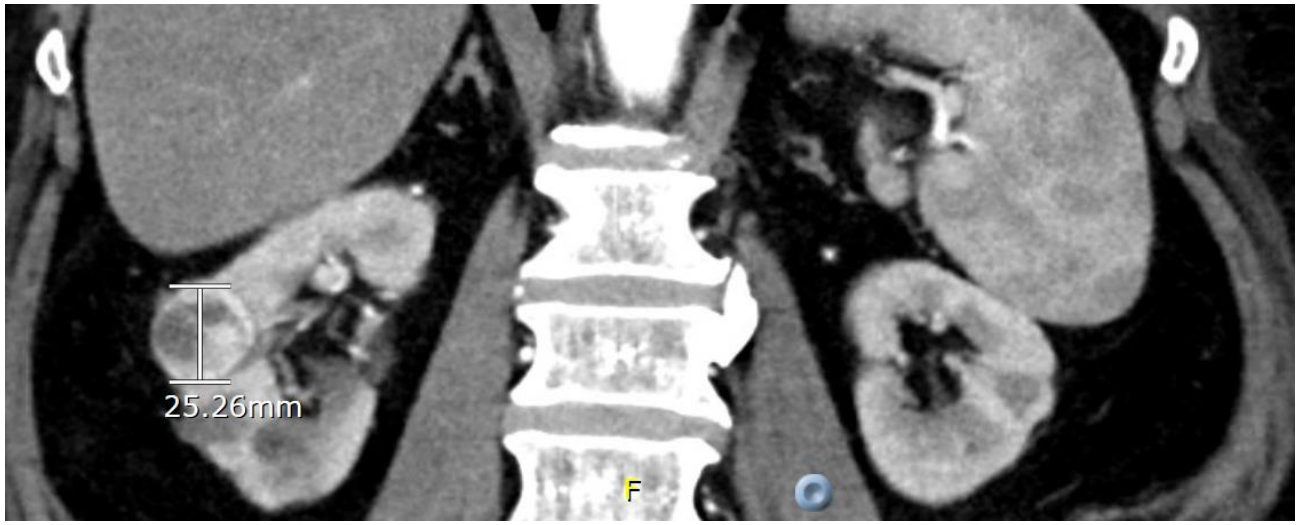
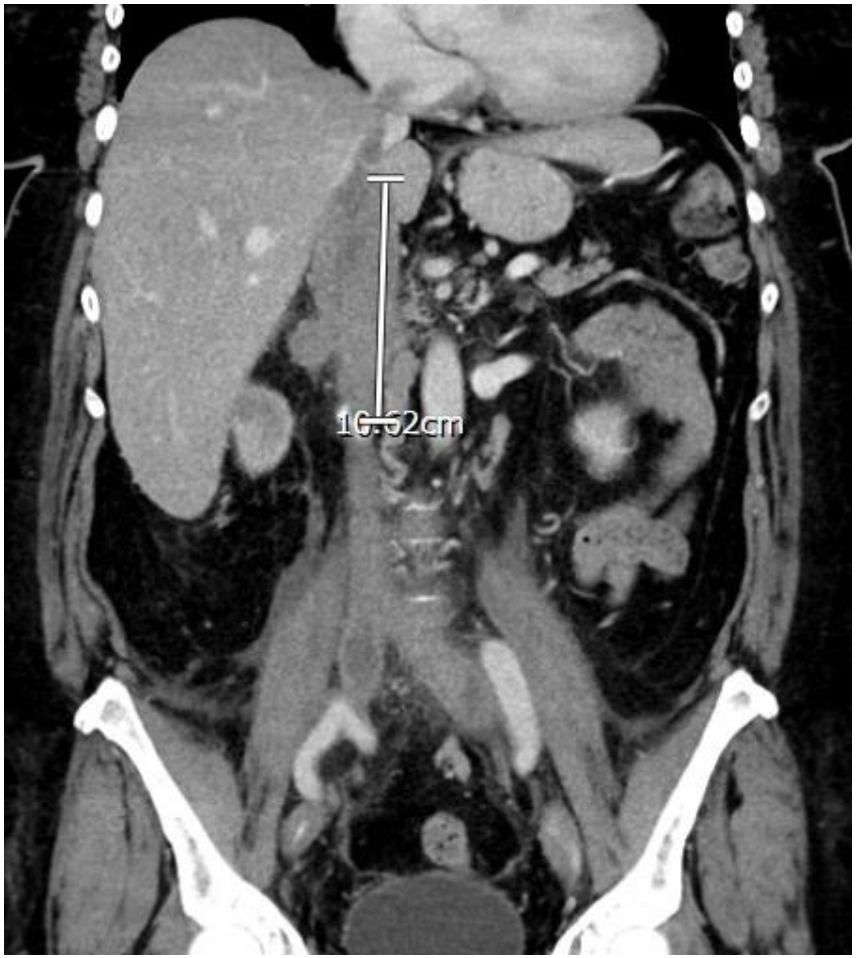
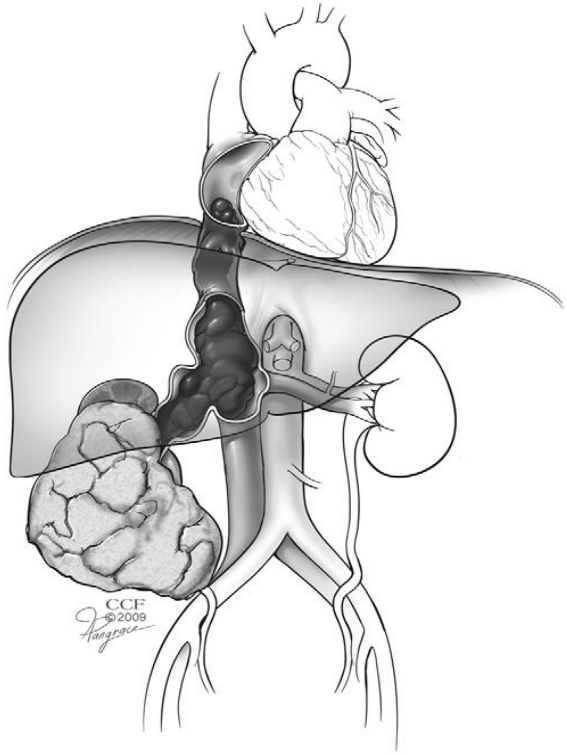
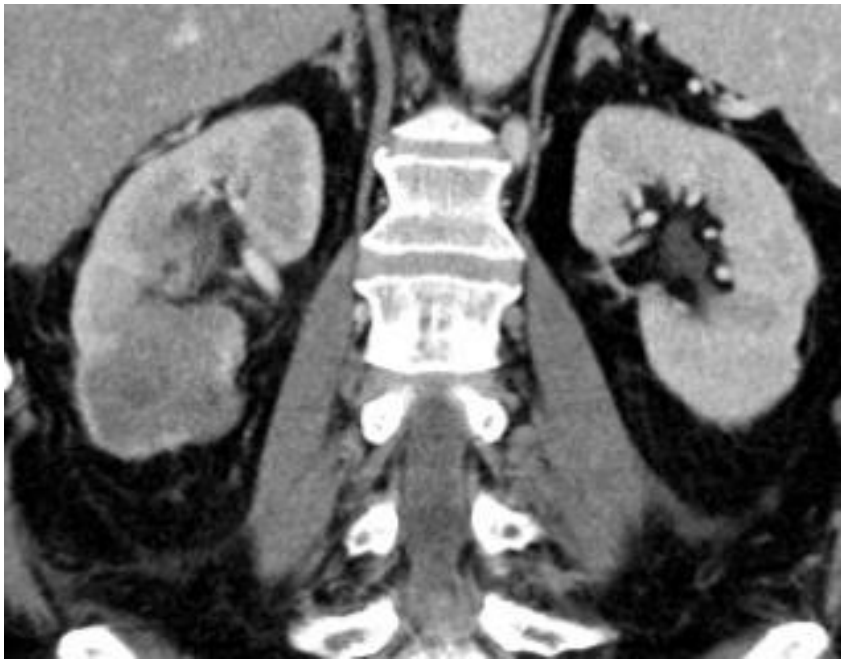

25.26mm
F

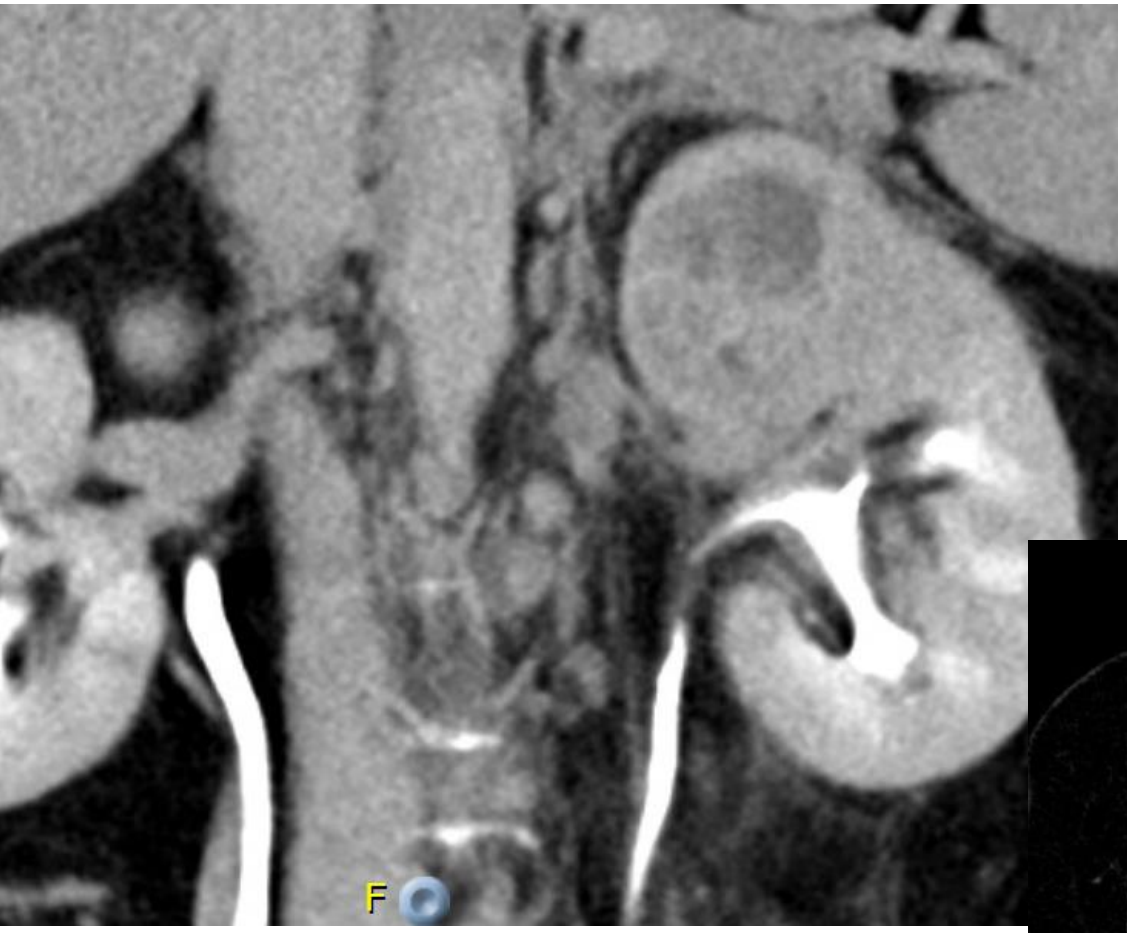
Hva kan vi gjøre her ?

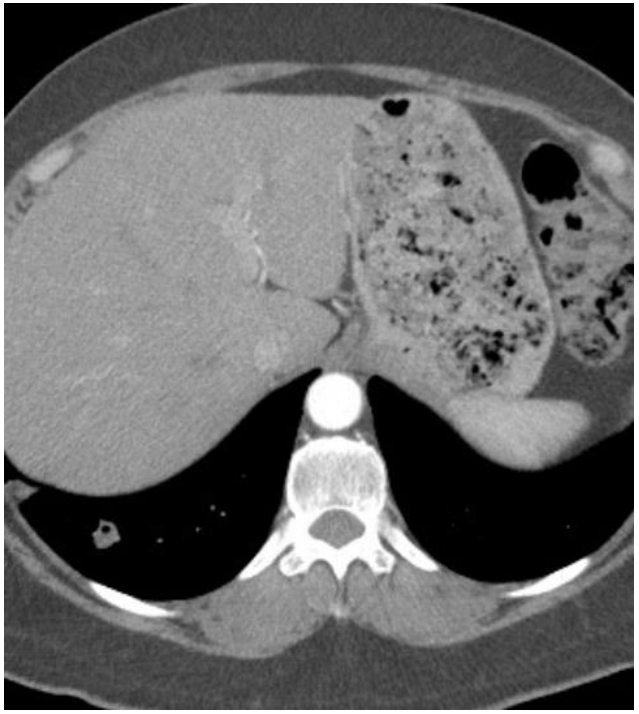


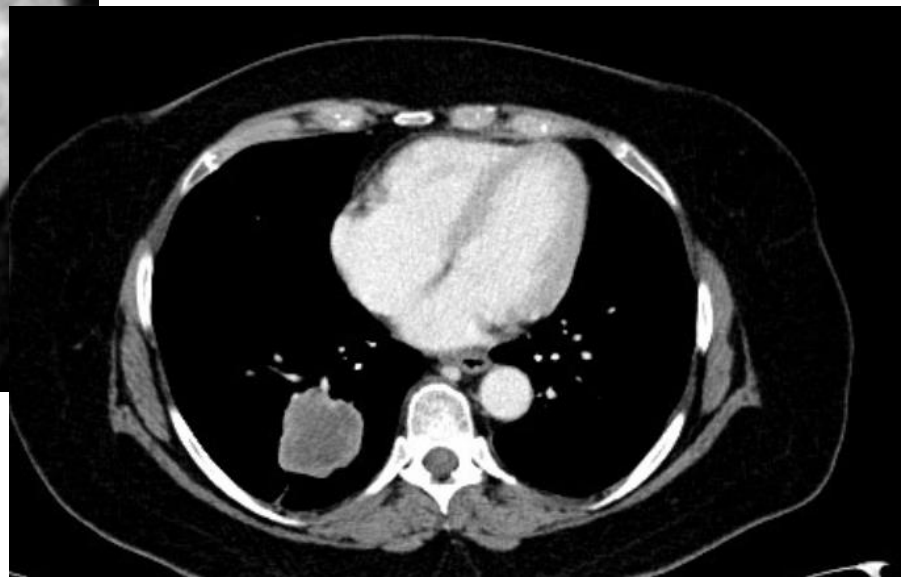




Collecting duct RCC







Complications – preoperative planning

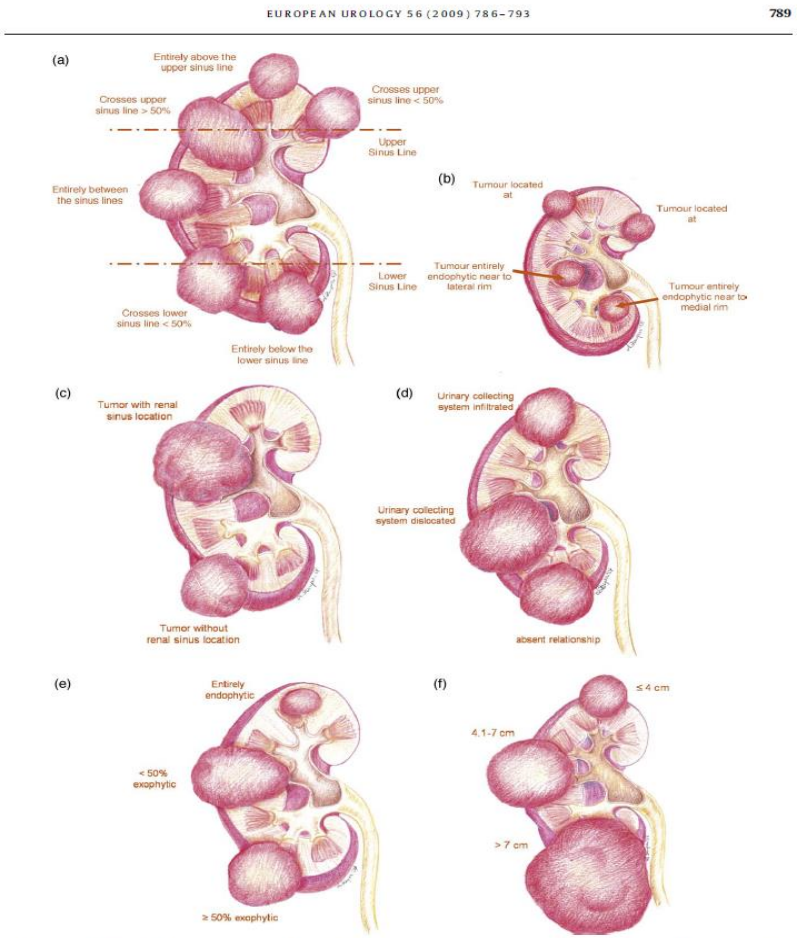
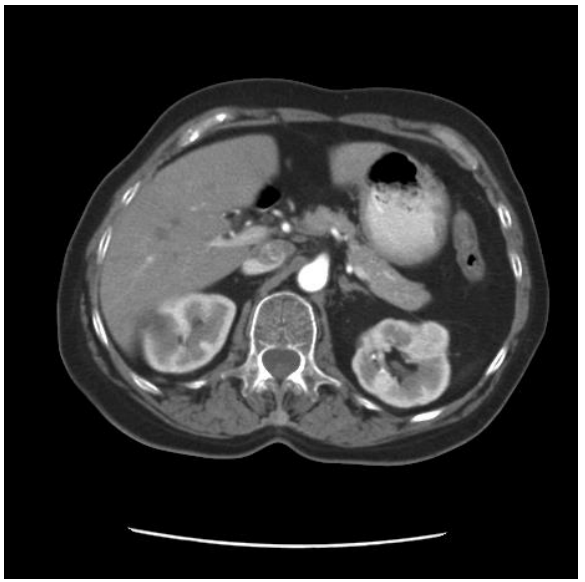
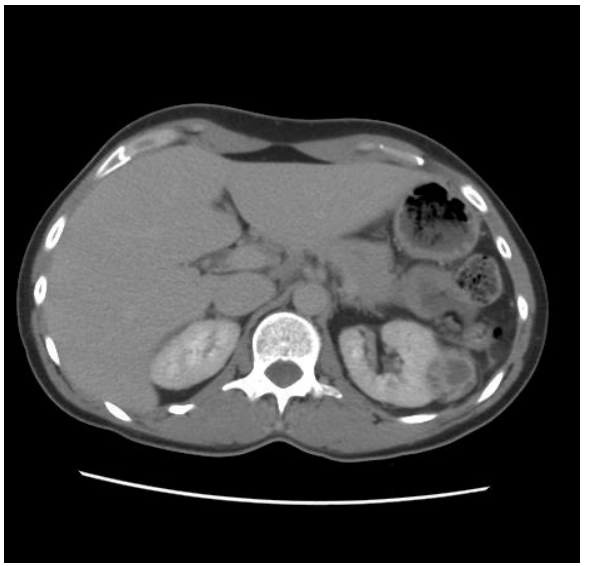


Fig. 3 – (a) Longitudinal classification of the tumours; (b) margin location of the tumours; (c) tumour relationship with renal sinus; (d) tumour relationship with urinary collecting system; (e) tumour deepening into the parenchyma; (f) tumour size classification.



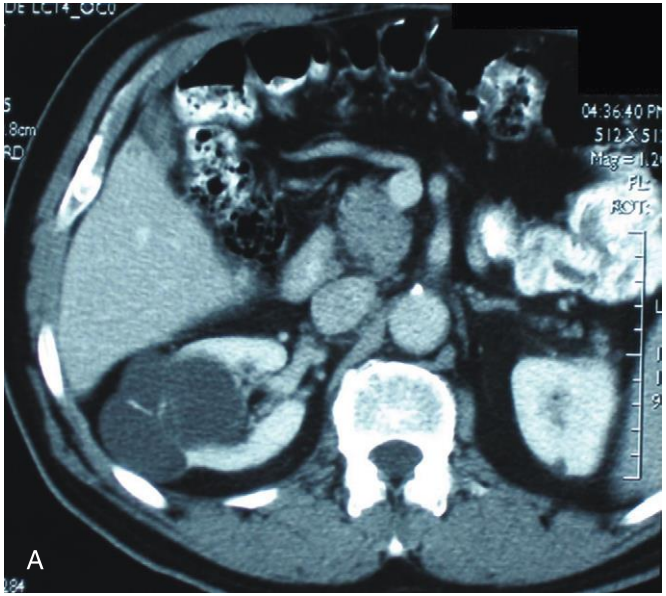


Bosniak klassifisering av komplekse cyster – hvordan følge opp og behandle

Classification of Complex Renal Cysts

BOSNIAK CLASSIFICATION	RADIOGRAPHIC FEATURES	RISK OF MALIGNANCY	MANAGEMENT
I	Water density Homogeneous, hairline thin wall No septa No calcification No enhancement	None	Surveillance not necessary
II	Few hairline thin septa in which "perceived" enhancement may be present Fine calcification or short segment of slightly thickened calcification in wall or septa No unequivocal enhancement	Minimal	Surveillance not necessary
IIF	Hyperdense lesion (≤3 cm), well marginated, with no unequivocal enhancement Multiple hairline thin septa Minimal smooth wall thickening "Perceived" enhancement of wall or septae may be present Calcification may be thick and nodular but must be without enhancement Generally well marginated No unequivocal enhancement	Minimal 3%-5%	Periodic surveillance
	Hyperdense lesion >3 cm or totally intrarenal, with no enhancement	5%-10%	Periodic surveillance
III	"Indeterminate," thickened irregular or smooth walls or septa in which measurable enhancement is present	50%	Surgical excision
IV	Clearly malignant lesions that can have all the criteria of category III but also contain enhancing soft tissue components	75%-90%	Surgical excision

Israel & Bosniak 2005, Bosniak 1986, Muglia 2014,Park 2007



Bosniak Type II

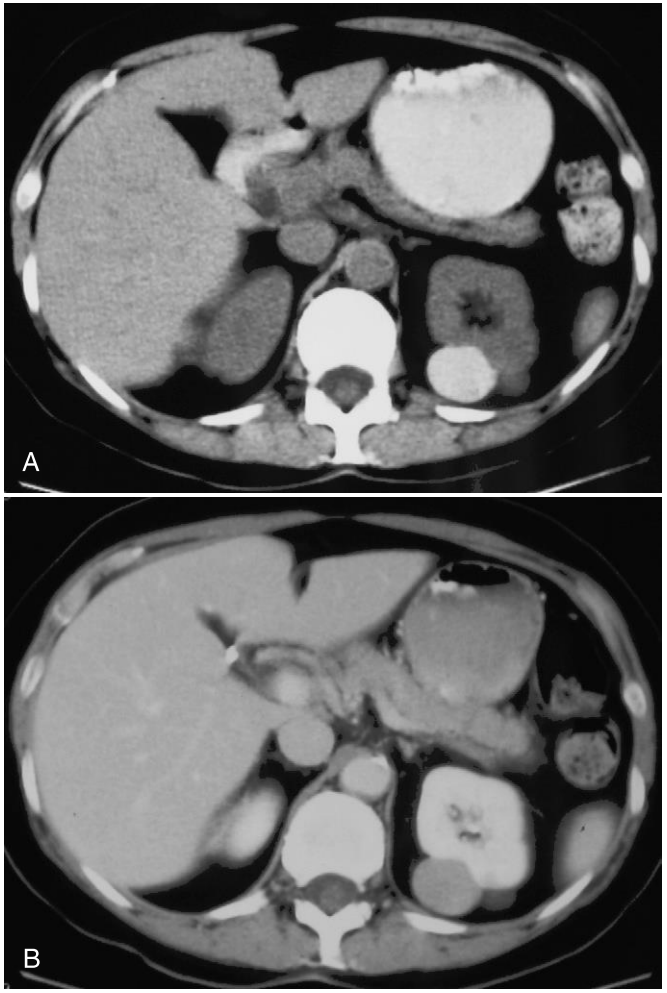
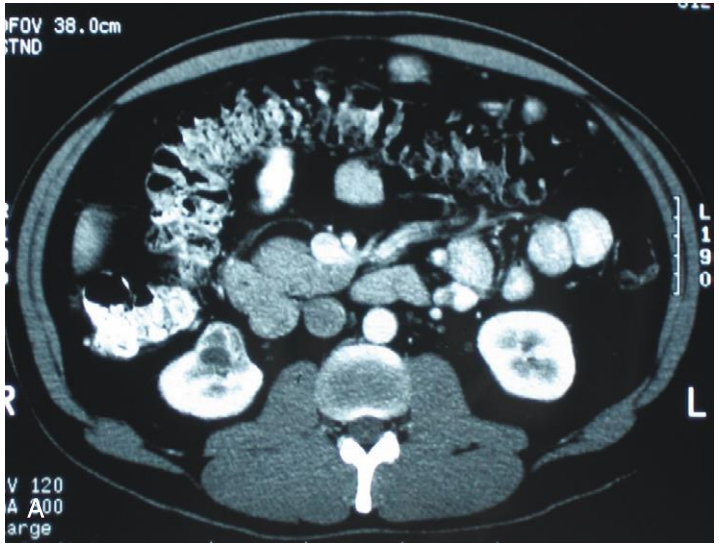
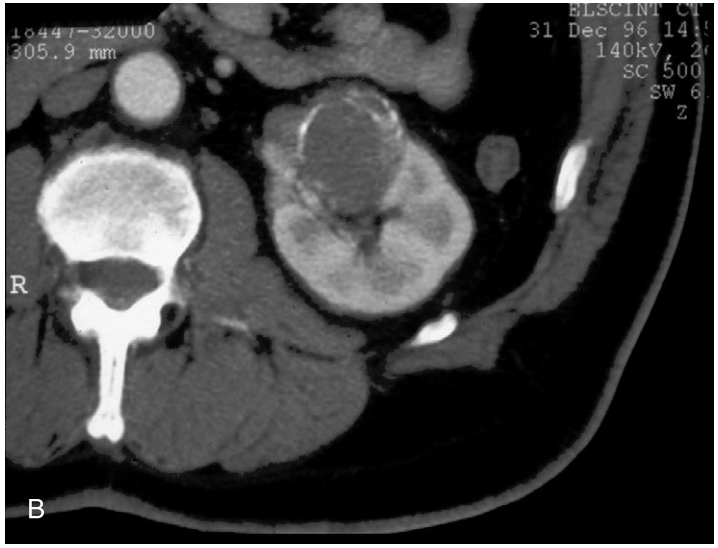
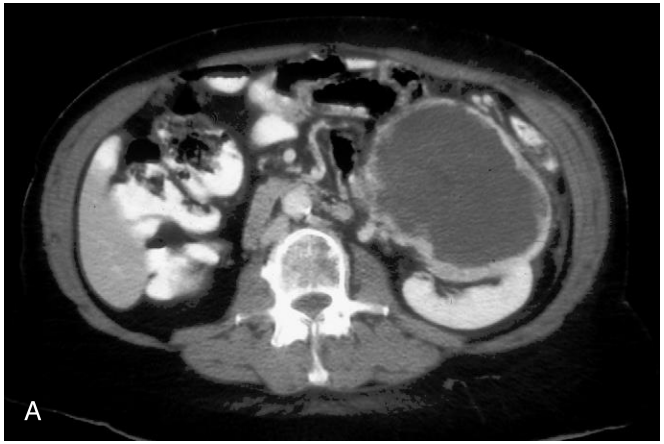


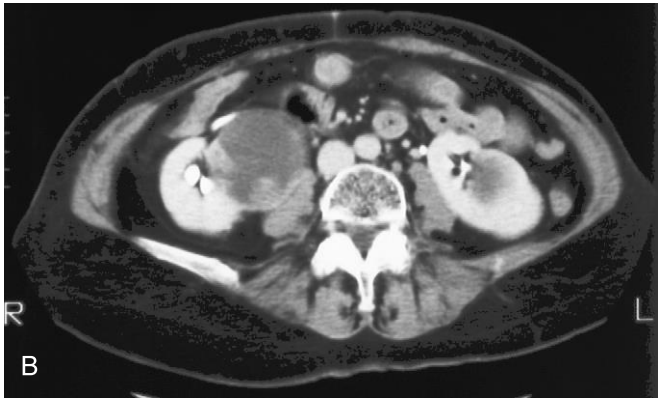
Figure 49–6. Bosniak class II hyperdense cyst. **A,** Unenhanced CT scan shows small, smooth-walled, high-density left renal cyst. **B,** CT scan after administration of contrast material shows no enhancement of the cyst. This is an extreme example of a hyperdense cyst. (Courtesy of Dr. Terrence Demos, Maywood, IL.)





Bosniak type 3





Bosniak type 4

Valg av operasjonsmetode 2000 - 2012

Tabell	LRNx av RNx	Åpen RNx	LRNx	NSS
2000-05	1 %	7,1 cm	-	2,9 cm
2006-09	28 % [2]	8,3 cm	5,0 cm	3,0 cm
2010-12	41%	9 cm	6 cm	4 cm

1) Patologisk tumorstørrelse etter fiksering

2) LRNx ble innført som metode Ultimo oktober 2006

Beisland et al , Kir. Høstmøte

Fraksjon RCC behandla ved HUS med NSS

	≤3,0 cm (1)	3,1 – 5,0 cm	> 5,1 cm
1999-2001	27	13	7
2002-2004	86	35	9
2005-2007	90	29	0
2008-2010	91	46	12

pT1a= 75% NSS

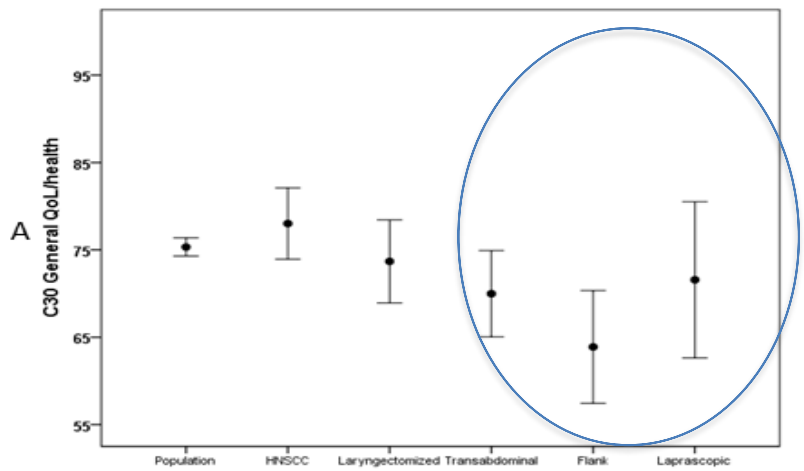
(1) Patologisk tumorstørrelse etter fiksering

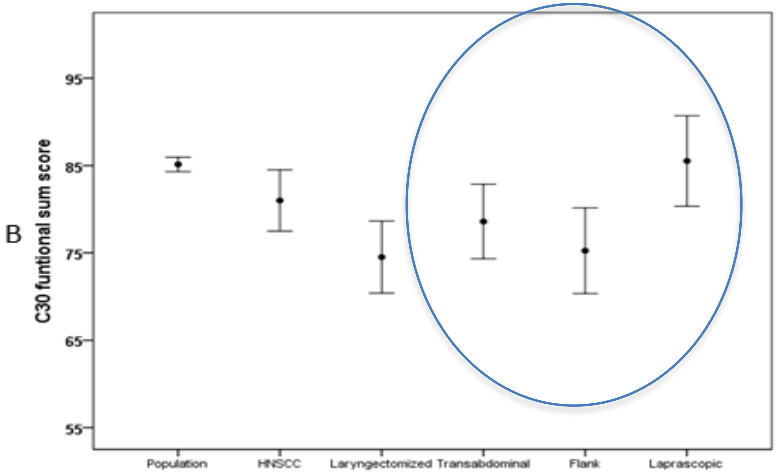
Komplikasjoner

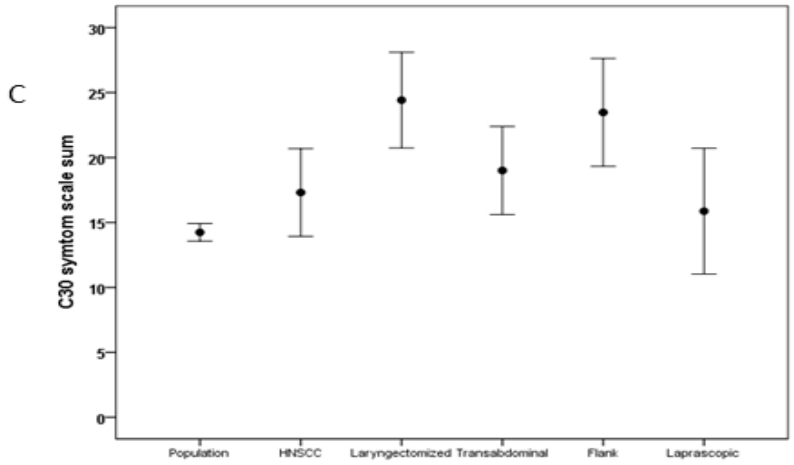
- Postoperative: 15-30% (15-25%)
- Reoperasjoner: 2-3% (2,2%)
- Mortalitet: 0-4% ila 30 dager (0,4%)

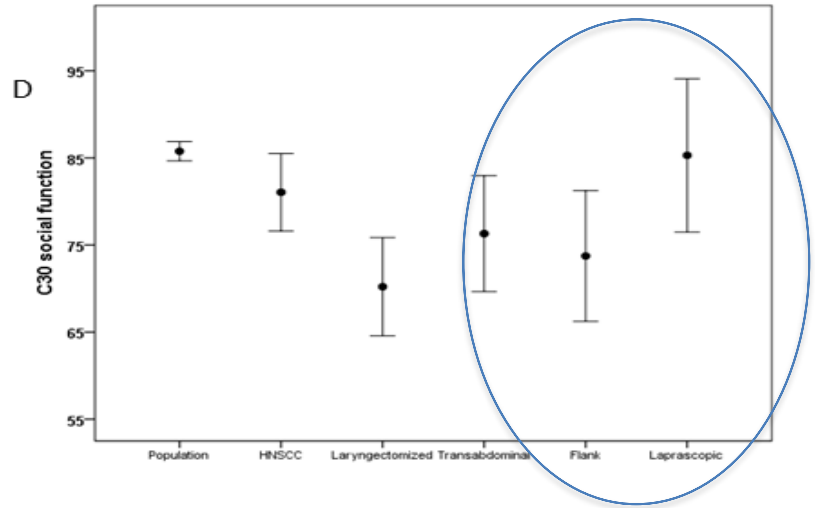
Mini-invasive metoder som Cryo, RFA og Hifu er aktuelle, men lite brukt i Norge så langt

Long-term QoL in surgically treated RCC









E Beisland et al. SJU 2014

Oppfølgings-program

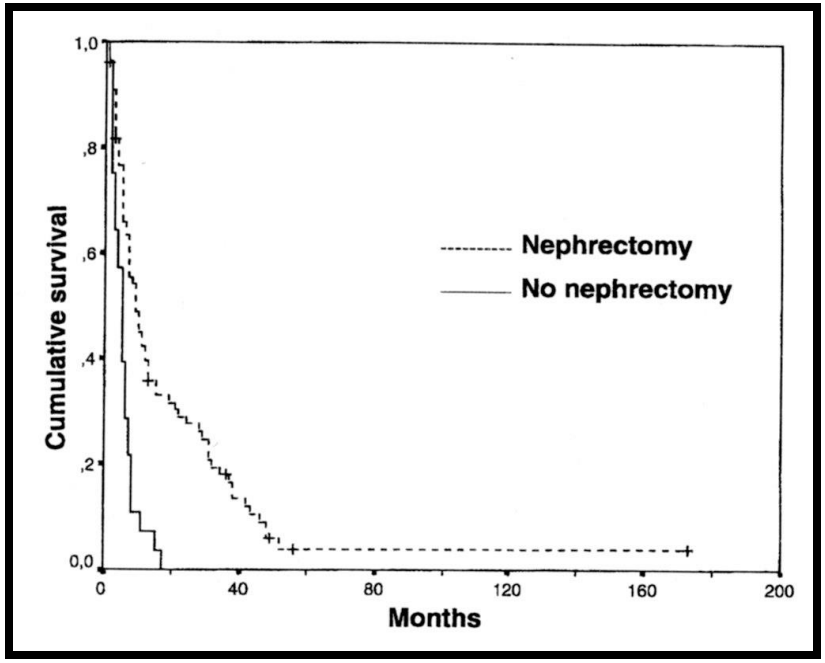
- 5 år
  - Sykehus
  - Allmennpraktiker

    - Avhengig av risiko for tilbakefall(Leibovich)
      - Størrelse
      - T stadium
      - glandler
      - Fuhrman grad
      - Påvist histologisk nekrose

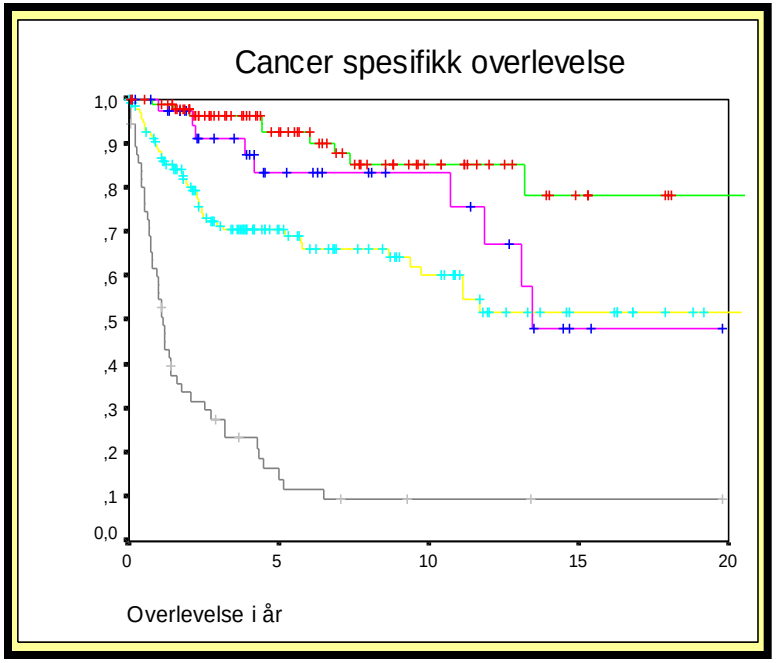
Ca 10 % risiko for residiv etter 5 år

Pasienter med primært metastaserende nyrecancer

Leveutsikter for pasienter med primær MRCC med og uten Nx



Ljungberg, Sc J Urol Nephrol 2000



Beisland, Tdnlf 2002

K-M plott som fremstiller forskjell i overlevelse mellom de ulike stadier 1-4

Nx ved primært MRCC

- Som gruppe har disse pasientene kort levetid igjen
  - Mange av dem er i dårlig almentilstand
- Nefrektomi bør derfor kun tilbys pasienter for å palliere lager/symptomer eller der hvor man mener å kunne tilby livsforlengende annen behandling i tillegg.

- (NCI-rapport 1993: 4,4% komplett regresjon av metastaser
  - » Kun lungemet. (Marcus J Urol 1993))

Grupper av indikasjoner for Nx ved primær MRCC

1. Intraktable lokalsymptomer fra tumor
   - Smerte
   - Blødninger (Intraarterieal coiling)
   - Lokal direkte påvirkning av naborgan (inkl. IVC)

2. Sjeldne systempåvirkninger fra tumor
   - Hyperkalsemi
   - Hjertesvikt pga shunting av blod i tumor
   - Dysfunksjon i gastrointestinal tractus

Indikasjoner for Nx ved primær MRCC II

3. Ved samtidig reseksjon av solitær metastase

Aggressiv kirurgi mht både den solitære metastasen og primærtumor angis i litteraturen å gi 5-års overlevelse på ~35-50%

Best ved solitære metastaser til hjerne, skjellett og lunge (1-3)

MD Anderson/ Texas: 179 solitære metastaser hos 2100 MRCC pas.(1984-97)

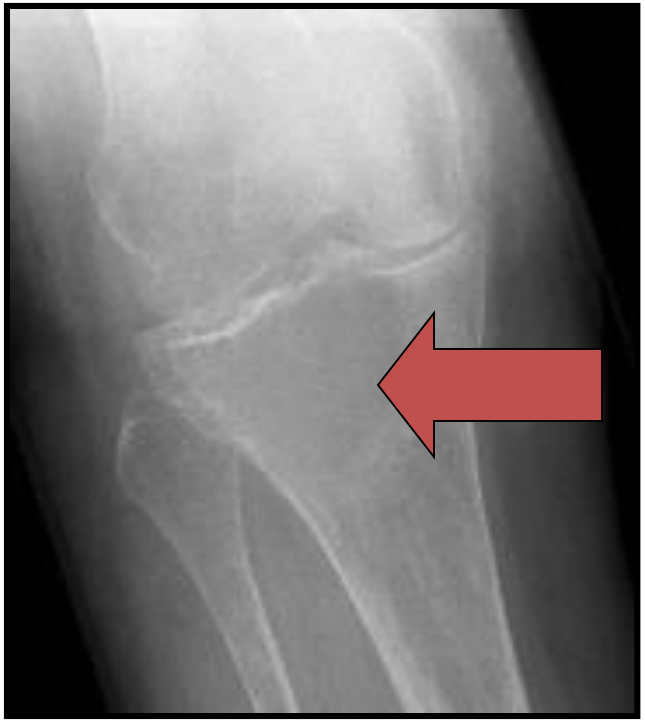
22% 5-års overall survival ved synkrone solitære matastaser (organuavhengig). (4)

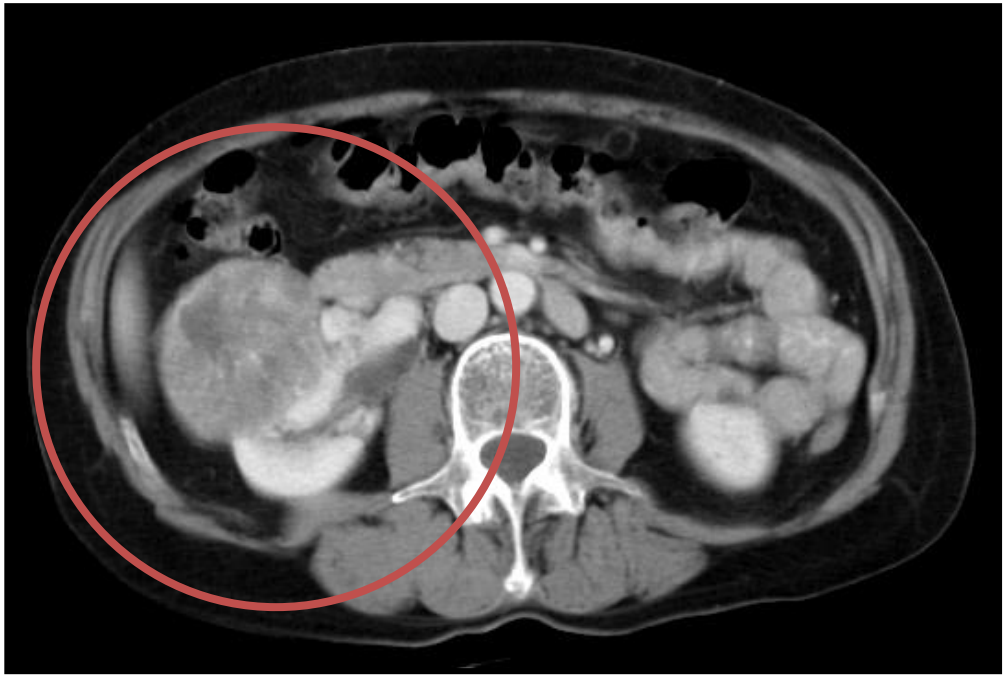
1. Montie, J Urol 1977
2. Trasher, J Urol 1990
3. Klugo, J Urol 1977
4. Swanson, Symposiumabstrakt Hamburg 11-2003

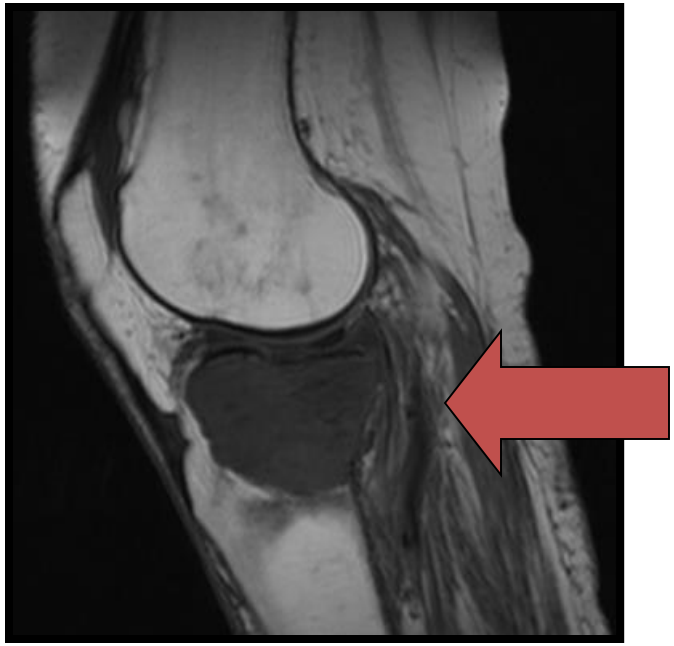
Kasus, Kvinne 67 år

Synkron tibiametastase og RCC 6,5 cm

- Behandlet med preop. stråling av metastasen
- 6 mndr observasjonstid
- Samtidig Nx og metatasektomi

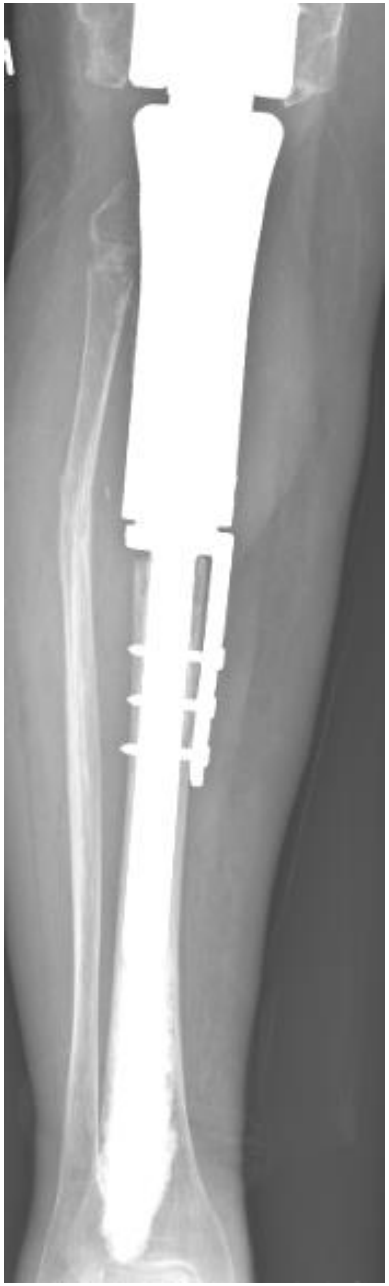


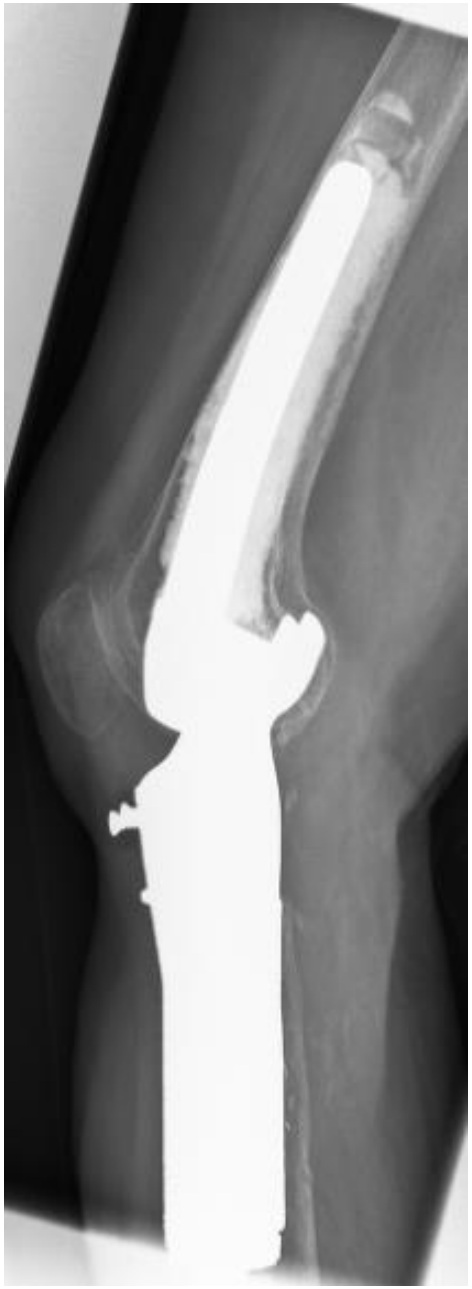




Postoperativt

- PT3b (TT til IVC)
- Ukomplisert per og postoperativt forløp
- Strålefibrose i lårmuskulatur
- Recidiv etter 3 år





MEN !!!!

- Seleksjon er viktig ved cytoreduktiv Nx
- Høyere forekomst av perioperative komplikasjoner
  - 30-dagers mortalitet: 0-17% (1-6)
  - Komplikasjonsrate: 10-50% (1-6)
  - % manglende systemisk beh p.o.: 2-77% (1-6)
  - Ikke økt komplikasjons ved cytoreduktiv Nx ved TT (7)
  - Men ikke høyere enn for N0M0 dersom selekterer etter performance status (ECOG 0-1) og lokalisasjon og mengde av metastatisk sykdom

1. Mickisch, Lancet 2001
2. Flanigan, NEJM 2001
3. Bennett, J Urol 1995
4. Fallick, J Urol 1997
5. Franklin, Sem Urol Oncol 1996
6. Wood, J Urol 2001
7. Zisman, J Urol 2002