Minimally invasive surgery using ablative modalities for the small renal mass

Prof. Dr.
Özcan ATAHAN
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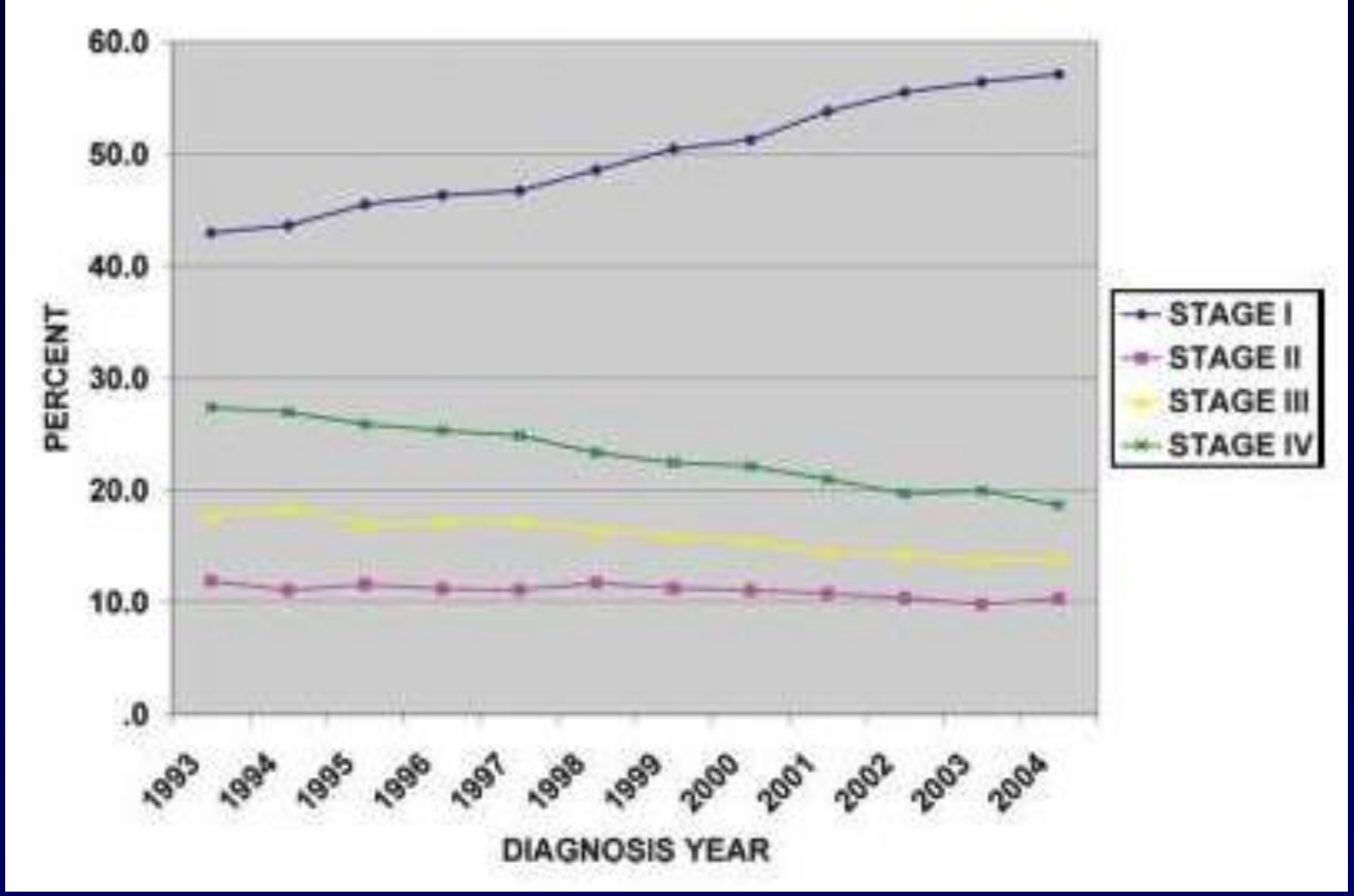
Renal Cell Carcinoma

- RCCs represents 2–3% of all cancers
- More than 50% of these are detected incidentally
- Small renal masses are defined as renal masses less than 4 cm in diameter
- RCC incidence has been rising
  - Annual increase:2.3-4.3 %
  - Greatest ↑ in small, localized tumor
  - Largest ↑ in patients aged 70-89
  - patients ~ 50 % aged 65 ↑



- Incidental detection of smaller volume tumors ↑
  - 1962 → 13%
  - 2004 → 66 %

Kane CJ et al., Cancer, 113: 78, 2008

Small Renal Mass 2013

- Since the greatest increase in RCC incidence is in small, curable renal tumors, why is the mortality rate not declining?
- Are we finding lethal tumors earlier when they are curable, or are we just finding insignificant tumors of no clinical significance?
- Should we treat all small renal masses?
- Can these small renal tumors be treated as well with ablation?
- Do we need to treat them all?

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SOLID RENAL TUMORS: AN ANALYSIS OF PATHOLOGICAL FEATURES RELATED TO TUMOR SIZE

IGOR FRANK, MICHAEL L. BLUTE, JOHN C. CHEVILLE, CHRISTINE M. LOHSE, AMY L. WEAVER AND HORST ZINCKE

From the Departments of Urology (IF, MLB, HZ), Pathology (JCC), and Health Sciences Research (CML, ALW), Mayo Medical School and Mayo Clinic, Rochester, Minnesota

TABLE 3. *Proportion of benign versus RCC tumors according to tumor size*

Tumor Size (cm)	No. Benign (%)	No. RCC (%)
0.0–Less than 1.0	37 (46.3)	43 (53.8)
1.0–Less than 2.0	38 (22.4)	132 (77.7)
2.0–Less than 3.0	75 (22.0)	266 (78.0)
3.0–Less than 4.0	71 (19.9)	285 (80.1)
4.0–Less than 5.0	37 (9.9)	336 (90.1)
5.0–Less than 6.0	40 (13.0)	267 (87.0)
6.0–Less than 7.0	11 (4.5)	232 (95.5)
7.0 or Greater	67 (6.3)	998 (93.7)

Percentages indicate the proportion of tumors in each size category that are benign or RCC, respectively.

20-46 % of small tumours were benign

small renal tumours (< 3 cm) grow slowly and
only progress to metastatic disease in 1-2 % of cases [

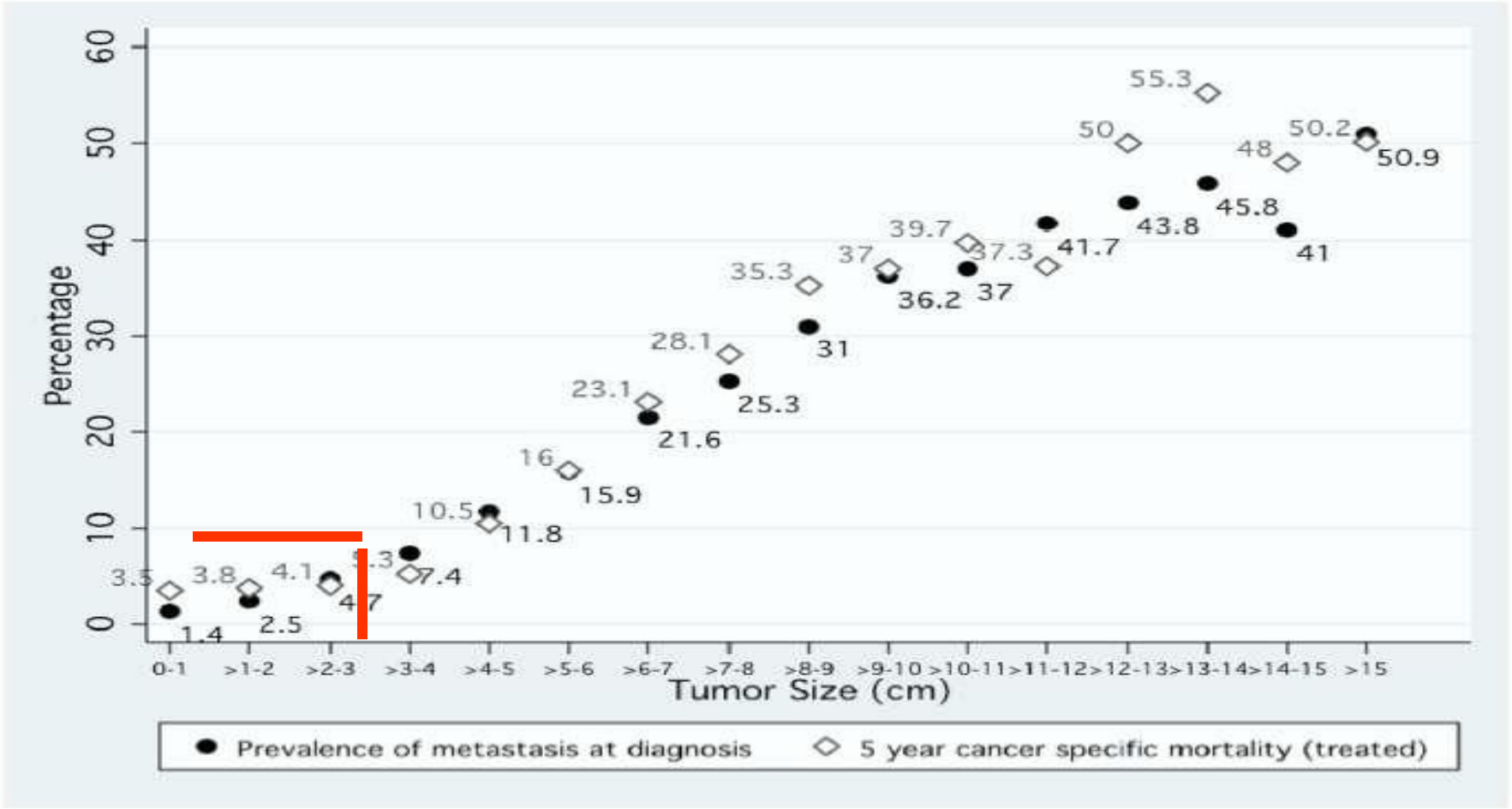


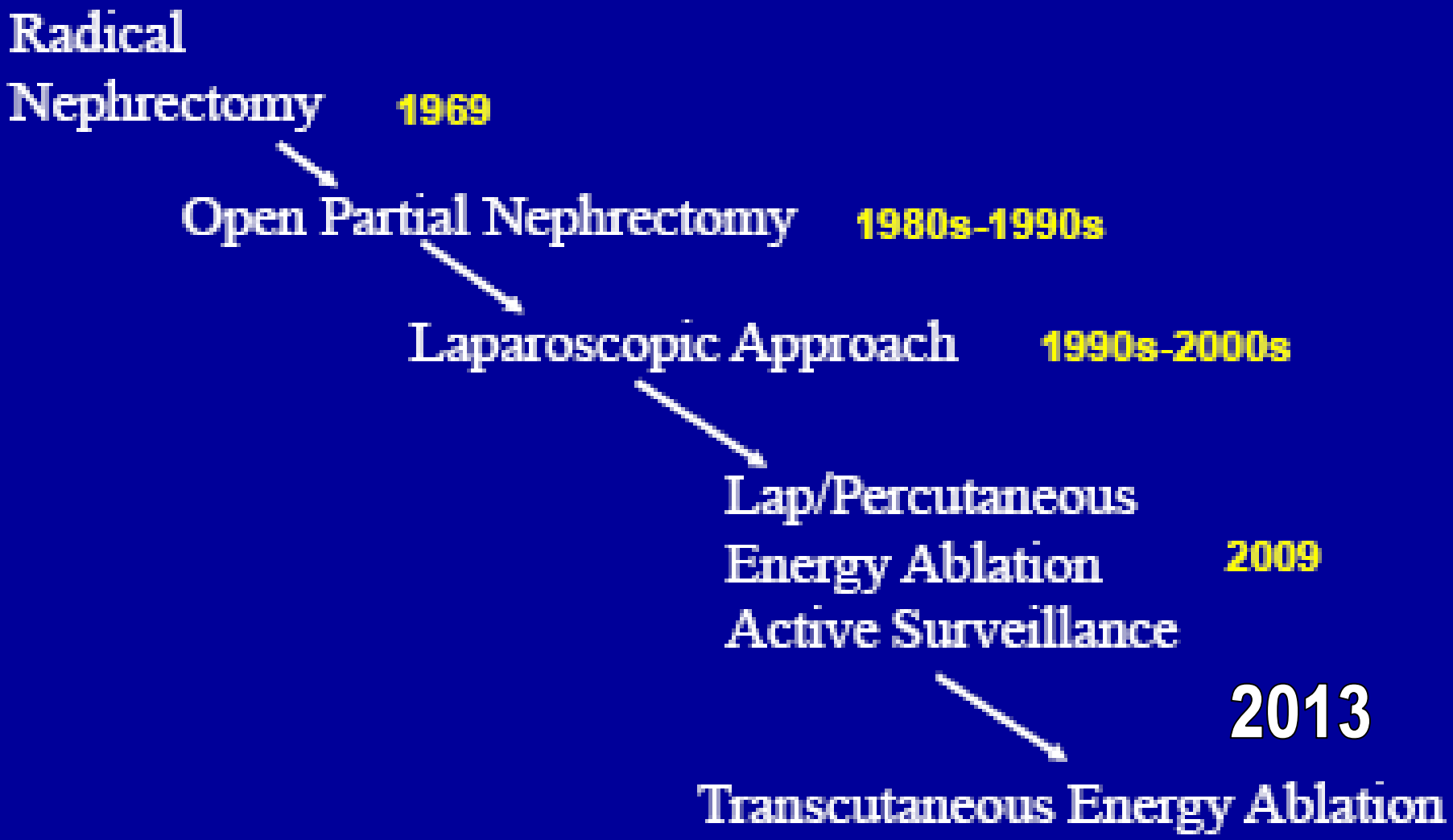
Figure 2. Percent of patients with metastasis at presentation (circles) and 5-year cancer specific mortality in treated patients (diamonds) by tumor size category.

Nguyen MM and Gill IS, J Urol 2009

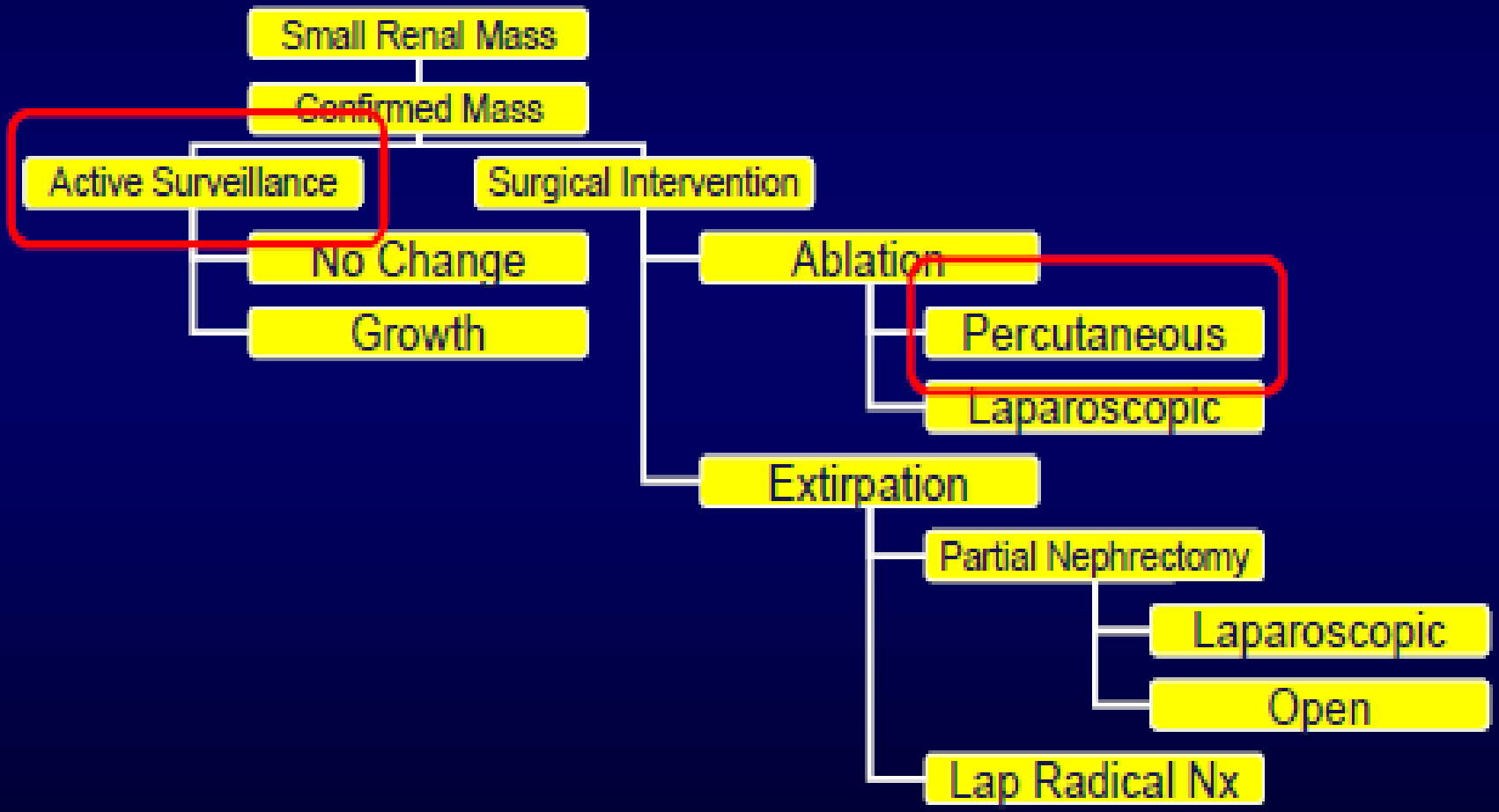
Treatment of Localised Tumors

- Active surveilance
- Surgery
  - Radical nephrectomy
  - Minimally invasive nephron-sparing surgery (NSS)
    - open-laparoscopic-robotic
- ***Others minimally invasive treatments***
  - ***Radiofrequency ablation (RFA)***
  - ***Cryoablation***
- Novel treatments
  - High-intensity focused ultrasound (HIFU),
  - Laser interstitial thermotherapy (LITT),
  - Microwave thermotherapy (MWT),
  - Pulsed cavitational ultrasound (PCU),
  - Radiosurgery ***("Cyberknife")***

Treatment of Localised Tumors



Small Renal Mass Algorithm



Guidelines on Renal Cell Carcinoma

B. Ljungberg, N. Cowan, D.C. Hanbury, M. Hora, M.A. Kuczyk, A.S. Merseburger, P.F.A. Mulders, J-J. Patard, I.C. Sinescu

European Association of Urology

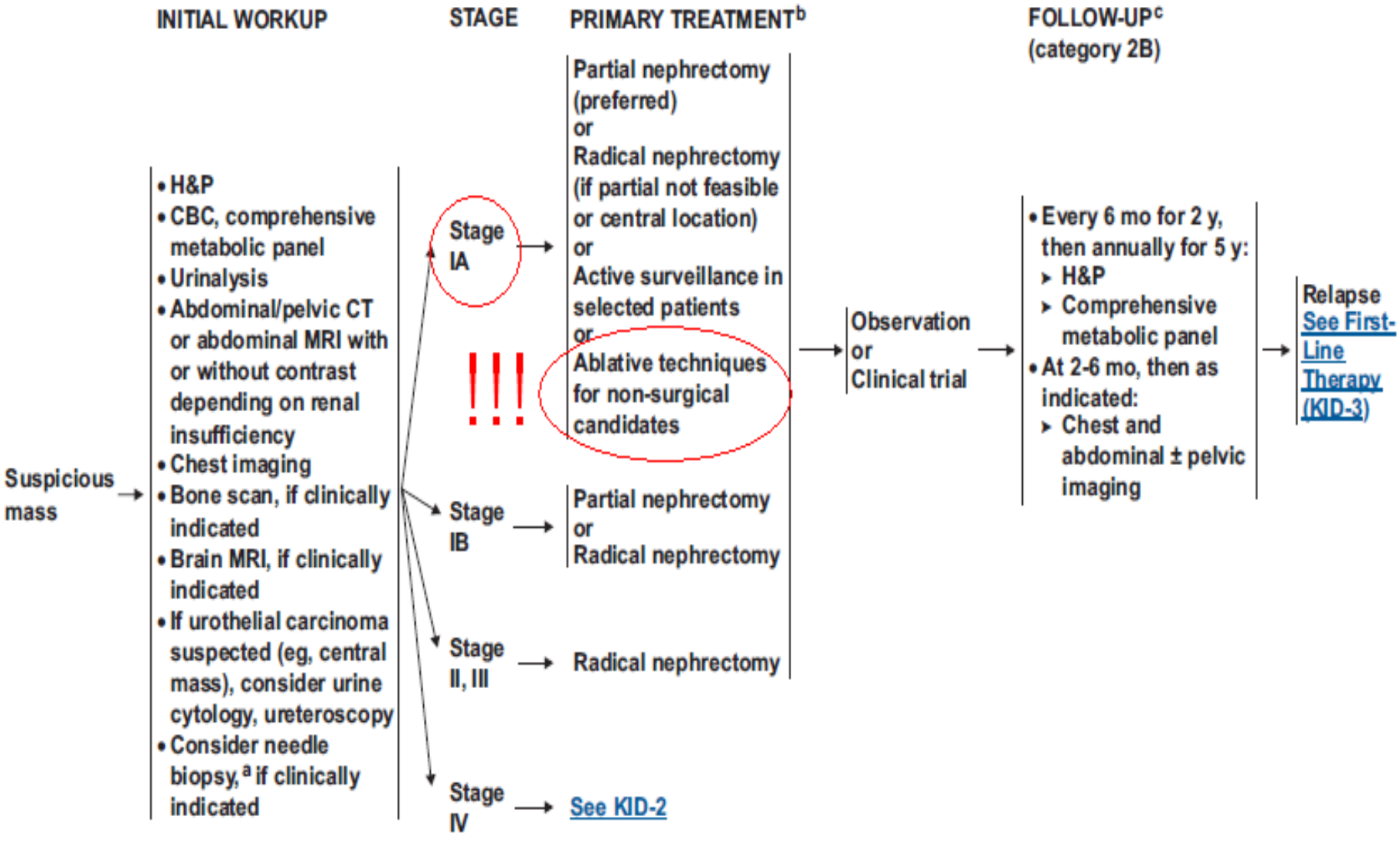
6. TREATMENT OF LOCALISED RCC

6.3.2.3 Recommendations

	GR
Patients with small tumours and/or significant co-morbidity who are unfit for surgery should be considered for an ablative approach, e.g. cryotherapy and radiofrequency ablation.	A
Pre-treatment biopsy has to be carried out as standard.	C
Other image-guided percutaneous and minimally invasive techniques, such as microwave ablation, laser ablation, and high-intensity focused ultrasound ablation are still experimental in character. The experience obtained with radiofrequency ablation and cryoablation should be considered when using these related techniques.	B

NCCN Guidelines Version 1.2013
Kidney Cancer

NCCN Guidelines Index
Kidney Cancer TOC
Discussion



Why ablative treatments ?

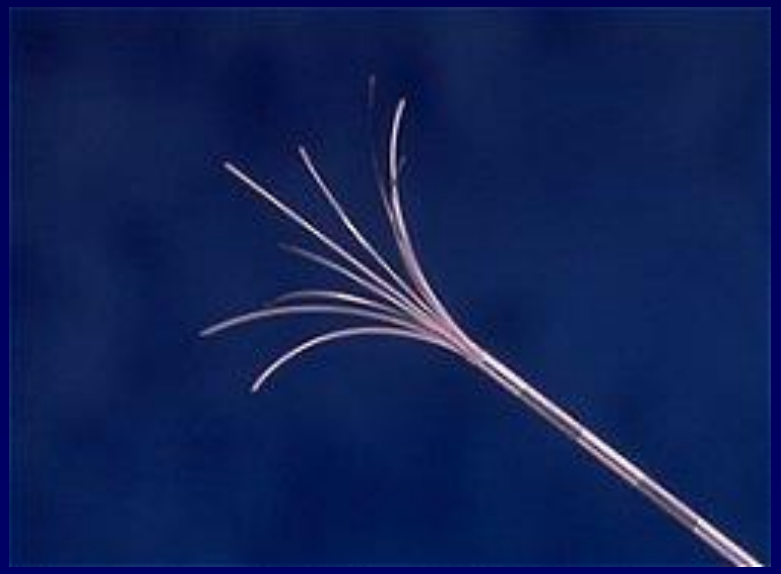
- Minimally aggressive, therapeutic alternative for renal tumors
  - The standard management of SRMs has been partial nephrectomy (PN)
  - PN is associated with an overall complication rate of about 20%
- Alternative to nephrectomy in patients with
  - previous nephrectomy,
  - bilateral tumors,
  - von Hippel-Lindau disease,
  - or small renal carcinomas and in those with contraindications for surgery.

Why Ablative Treatments ?

- Decreased morbidity
- Shorter hospitalisation
- Earlier return to normal activities
- Preservation of renal function
- Potentially lower costs
- Reintervention
- Ability to treat patients who are poor surgical risks.

Radiofrequency Ablation

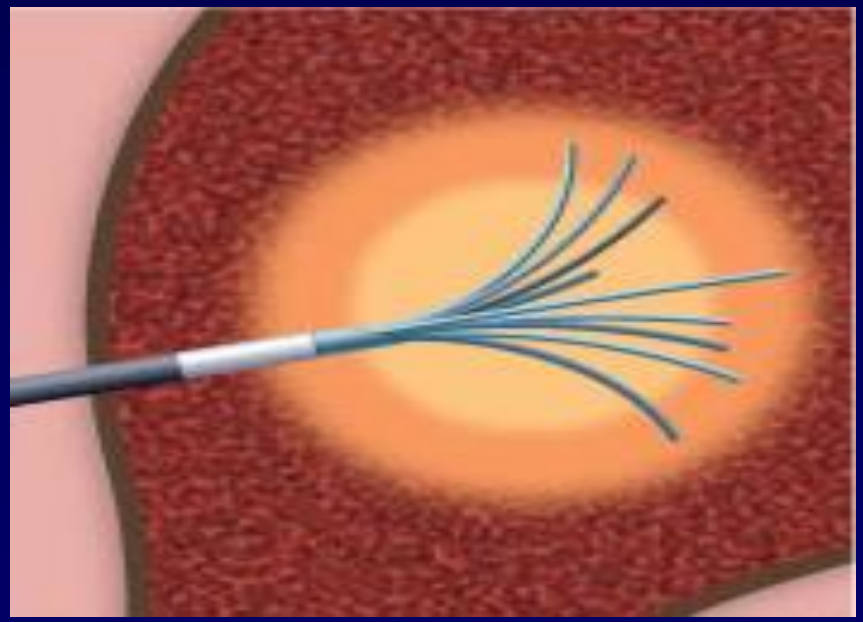
- Radiofrequency generators 250 W
  - Alternating electrical current
  - Frequencies 150 KHz-1MHz
  - Needle applicator of 1.6-2.5 mm in diameter
  - Monopolar&bipolar
- Tumour tissue is destroyed by creating temperatures in 48-50°C
- Coagulation necrosis and cellular death



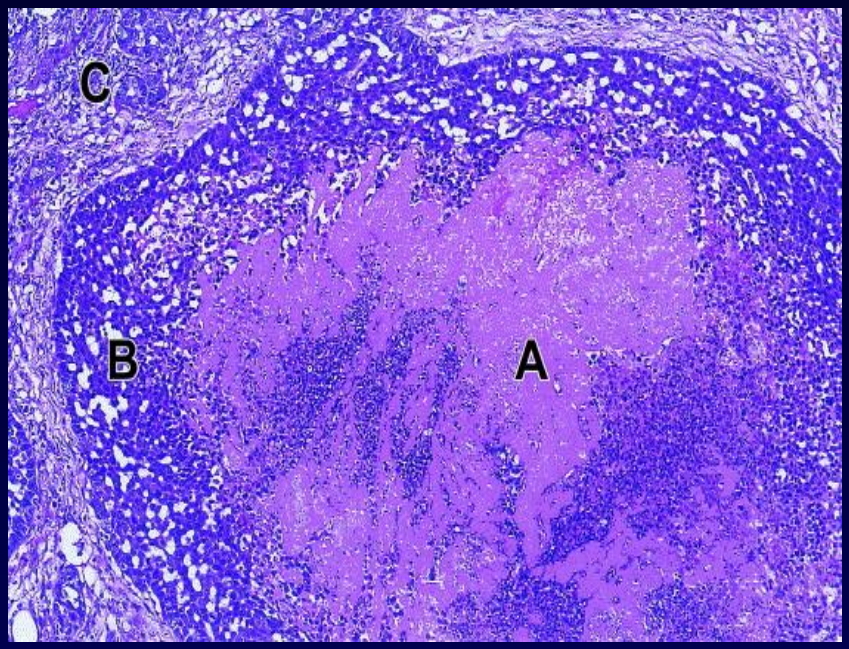
Pathophysiology of RFA

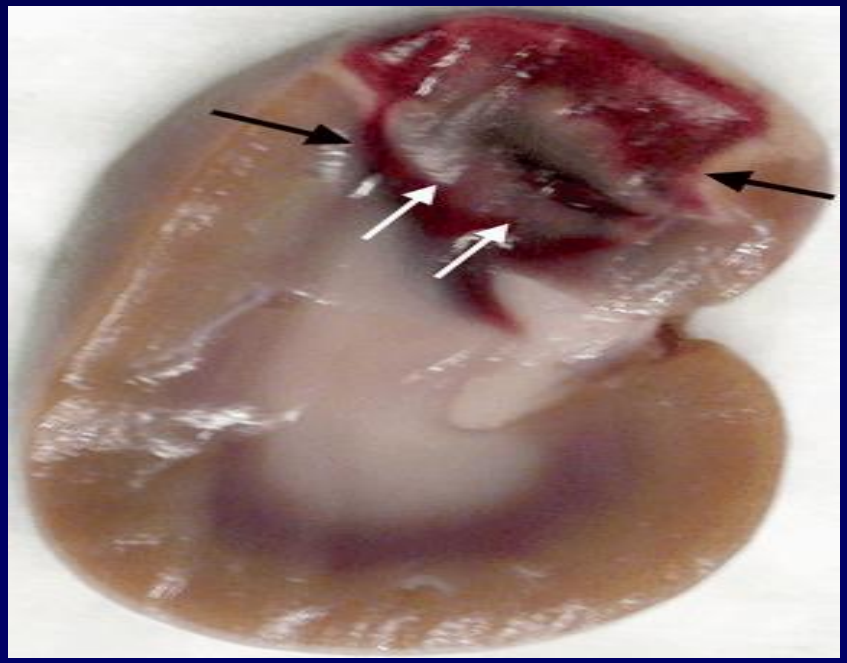
- 45 °C → cellular functions are disabled
- 60 °C → proteins are denatured
- 100 °C → cells are vaporized
- Supraphysiologic temperature
  - Direct cytotoxic effects on cellular components
  - Microvascular and arteriolar occlusion
  - Secondary ischemic injury

- Dry RFA
  - Energy → target tissue
- Wet RFA
  - Energy → ionic solutions perfused into tissues
- Applicator needle 1-2 mm
- 3 cm spheric necrosis



- 4 zones from the centre to periphery of the lesion:
  - Carbonization
  - Complete coagulation necrosis
  - Surrounding rim of inflammation and haemorrhage
  - Normal renal parenchyma





Different Approaches in Renal RFA

- Intraoperative open surgical
- Laparoscopic
  - Probe insertion under direct vision
  - Avoiding adjacent organ damage
- Percutaneous imaging-guided treatment
  - Preferred for posterior tumours
  - Well tolerated, performed under sedation, outpatient basis

Tumour Size

complete ablation achieved

- in all tumors less than 3 cm in size
- in 92% of tumors between 3 and 5 cm
- but in only 25% of tumors larger than 5 cm

- <3 cm → one treatment
- >3 cm → multiple treatments

Tumor Location

- Exophytic tm → succsess ↑ 92-100%
- Central tm → succsess ↓ 44%
  - More than one treatment
  - hemorrhagie ↑
- Cystic tm → succsess ↓
- Surgical resection
  - central
  - >5 cm
  - Adjacent to ureter

Indications of RFA

- Small, incidentally found, renal cortical lesions in elderly patients
- Patients with a genetic predisposition for developing multiple tumours
- Patients with bilateral tumours
- Patients with a solitary kidney at high risk of complete loss of renal function following surgical tumour resection (LE: 2b)

Contraindications of RFA

- Poor life expectancy of < 1 year
- Multiple metastases
- Low possibility of successful treatment due to size or location of tumour
  - > 3 cm
  - In the hilum
  - Near the proximal ureter or the central collecting system
    - Are not typically recommended for ablative techniques via a percutaneous approach
- Absolute contraindications
  - Irreversible coagulopathies
  - Severe medical instability, such as sepsis

Imaging guidance and ablation monitoring

- US
  - Steam bubbles produced by the vaporization
- CT
  - Residual tumor (administration of contrast medium)
- MRI
  - Patients
    - Renal insuffiency with serum cre > 2.0 mg/dL
    - A history of contrast reactions

Follow-up

- Tumor remains in situ, follow-up imaging is important
  - Residual tumor & relaps
- CT or MR follow-up at
  - 6-monthly intervals to approximately 2 years
  - After 2 years annually to 5 years,
- Tumor recurrency, within 3 months (70%)
  in the first year (92%)

Complications

2.8-17.6%

most common comp. is hemorrhage and perinephritic haematom

- Major 2.8-3.1%
  - Ureteral stricture
  - Pyelocalyceal injury
  - Bowel injury
  - Colonephric fistül
  - Pneumothorax
  - Gross hematuria
- Minor 3.5-17.6%
  - Pain
  - Paresthesias
  - Small volume hematuria
  - Pneumonia
  - Urinary infections
  - Cre ↑
  - Limited perinephric hematoma
  - Burns
  - Anesthetic-related

	Approach	Tumours, No.	Median tumour size	Follow-up, mo	CSS, %	Tumour recurrence after one ablation, %
Zagoria et al [51]	Percutaneous	125 (125 RCCs)	2.7	13.8 (mean)	98	13*
McDougal et al [52]	Percutaneous	20 (all RCCs)	3.2	55.2 (median)	94	5
Hegarty et al [57]	Percutaneous	82 (no. of RCC not given)	2.5	12 (median)	100	11.1
Park et al [83]	Laparoscopic/ percutaneous	94 (65 RCCs)	Mean: 2.4	25 (mean)	98.5	3.2

CSS = cancer-specific survival; RCC = renal cell carcinoma.
* All tumours recurring were >3.7 cm.

Published series of percutaneous radiofrequency ablation of renal tumors

Authors	Tumors, *n*	Patients, *n*	Therapeutic success (%)	Guidance	Major and minor complications (%)	Follow-up, mo
Pavlovich et al (2002) [3]	24	21	79	US/CT	19	2
Ogan et al (2002) [4]	13	12	93	CT	8	1–13
Farrell et al (2003) [5]	35	20	100	US	20	1–23
Su et al (2003) [6]	35	29	100	CT	7	0–23
Roy-Choudhury et al. (2003) [7]	11	8	88	US/CT	0	10–26
Mayo-Smith et al (2003) [8]	32	32	87	US/CT	9	1–36
Lewin et al (2004) [9]	10	10	100	MRI	0	6–42
Gervais et al (2005) [10,11]	100	85	91	US/CT	11	3.5–72
Matsumoto et al (2005) [12]	63	63	98	CT	11	12–33
Ahrar et al (2005) [13]	30	29	96	CT	18	1–33
Weizer et al (2005) [14]	32	24	92	CT	21	1–28
Arzola et al (2006) [15]	27	23	90	CT	4	7–53
Sabharwal et al (2006) [16]	18	11	100	CT	0	1–24
Veltri et al (2006) [17]	44	31	89	US	18	1–54
Breen et al (2007) [18]	105	97	90	US/CT	4	1–76
Zagoria et al (2007) [19]	125	104	91	CT	8	1–76
Rouvière et al (2008) [20]	30	22	95	US/CT	9	3–84
Levinson et al (2008) [21]	56	46	90	CT	21	41–80
Cura (2010)	65	58	91	US	13	10–50

US = ultrasound; CT = computed tomography; MRI = magnetic resonance imaging.

Original Article

Durable Oncologic Outcomes After Radiofrequency Ablation

Experience From Treating 243 Small Renal Masses Over 7.5 Years

Chad R. Tracy, MD[1]; Jay D. Raman, MD[2]; Chester Donnally, MS[3]; Clayton K. Trimmer, MD[4]; and Jeffrey A. Cadeddu, MD[3]

- 208 patients with 243 SRMs
- Tumor size ~ 2.4 cm,
- Follow-up 1.5 - 90 months (mean, 27months).
- Of the 227 tumors (93%) preablation biopsy, RCC was confirmed in 79%.
- The initial treatment success rate was 97%,
- Overall 5-year recurrence-free survival rate was 93%
- 5-year cancer-specific survival rates 99%
- 3 patients developed metastatic disease, and 1 patient died of RCC

Cancer 2010;116:3135–42.

Impact on renal function

- Ablative procedures provide ‘renal protection’
- Lucas SM et al. (J Urol 2008 179:5-9)
  - Pretreatment and 3th years GFR →stage 3 CKD
  - RFA- PN-RN 95.2%-70.7 %-39.9%
- Raman JD ve ark. (Can J Urol 2008 15:3980-85)
  - 21renal masses in solitary kidneys → RFA → at mean of follow-up 30.7 months → GFR had only declined by 11.8 %

Tumor Size > 5 cm

- In attempting to treat larger tumors by RFA
- Combined approach:
  - renal artery embolization
  - direct ethanol injection
  - use of the antiangiogenic drug sorafenib

Cryoablation

Pathophysiology of Cryoablation

Freezing with argon gas

- Extracellular ice crystal formation
- Increases the osmolarity in the extracellular space
- Intracellular osmotic Pressure ↑
- Shift of fluid from the intracellular to extracellular compartment → dehidratation
- Proteins denaturation
- Intracellular ice crystal formation → lethal to the cell

Pathophysiology of cryoablation

Thawing Helyum gas

- Water back to intracellular ⇨ damage and rupture of the cell membrane ⇨ cell lysis
- Dilatation ⇨ endotelium injury ⇨ oedema ⇨ platelet aggregation ⇨ microtrombus ⇨ microvascular occlusion ⇨ ischemia

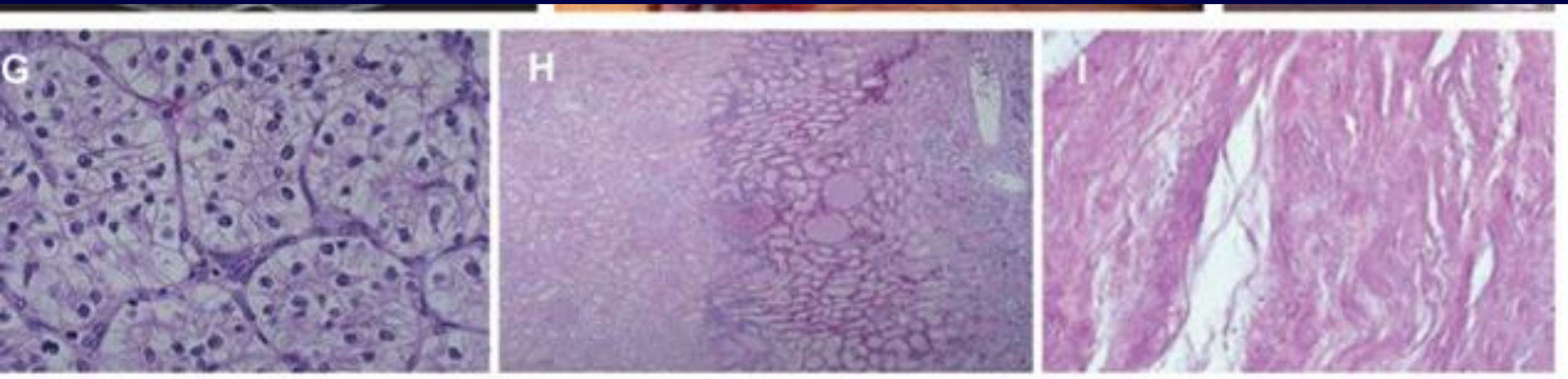
Review Article

International Braz J Urol Vol. 34 (6): 676-690, November - December, 2008

Localized Renal Cell Carcinoma Management: An Update

Flavio L. Heldwein, T. Casey McCullough, Carlos A. V. Souto, Marc Galiano, Eric Barret

Department of Urology, Institut Montsouris, Paris, France

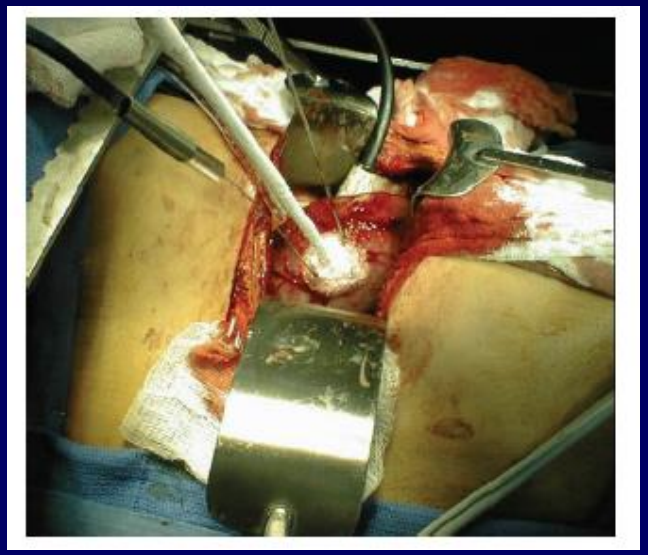


renal cell carcinoma (G), an infarction area after cryotherapy (H) and fibrosis in a follow-up biopsy

- Chosy et al. (J Urol 1998 159:1370-4)
  - In a porcine kidney model
  - A temperature of -19.4-0°C → 80% of tissue had complete necrosis
  - A temperature ≤ -19.4 °C → resulted in complete cell death
- Campbell et al. (Urology 1998 52:29-34)
  - In canine kidney model
  - A temperature <-20 °C →edge of the ice-ball had to extend at least 3.1 mm beyond the edge of the target lesion
- Nakada et al. (BJU Int 2004 94:632-6)
  - A rabbit model with a transplanted renal tumour, long-term results
  - Compared cryoablation and radical nephrectomy
  - Disease-free survival was no different
  - Equivalency of the two treatments in an in vivo model

Approach

- Open surgical approach
- Laparoscopic
- Percutaneous



Open Surgical Approach

- Delworth et al. (J Urol 1996 155:252-5)
  - Two patients with solitary kidney, succesfull cryoablation
- Rukstalis et al. (Urology 2001 57:34-9)
  - Treated 29 tumours (median 2.2 cm) with open renal cryoablation using a small 6–8 cm incision.
  - Double freeze-thaw cycle
  - Found that 91% of patients had no enhancement of their cryolesion on follow-up imaging.

Laparoscopic Approach

- Preferred method
- Anterior ve anteromedial tumors →laparoscopic
- Posterior ve posteromedial →retroperitoneoscopic approach
- Advantages of lap.
  - mobilization of vital structures away from the treatment area, including bowel, liver, spleen,ureter, etc
  - Biopsy of tumor
  - Careful visual monitoring of probe placement
  - ice-ball progression in relation to the mass
  - establishment of haemostasis if necessary.

Percutaneous approach

- Increasingly more reported

- The advantages of a percutaneous approach
  - a less-invasive procedure
  - shorter hospitalization
  - excellent ice-ball monitoring with cross-sectional imaging (MRI or CT)
  - less requirement for pain medication
  - cost-effectiveness over the laparoscopic approach

- Disadvantages
  - the lack of direct visual cues for probe placement,
  - inability to separate vital structures from the treatment area
  - radiation exposure during CT guided treatment

Percutaneous approach

- Biopsy of tumor
- Cryoprobe placement into the renal mass using imaging modalities
- Double freeze-thaw

Selected Series of Cryoablation

	Approach	Tumours, No.	Median size, cm	Follow-up, mo	CSS, %	Tumour recurrence after one ablation, %
Gill et al [77]	Laparoscopic	56 (36 proven RCCs)	2.3	36	98	3.6
Schwarz et al [78]	Open/laparoscopic	85 (50 proven RCCs)	2.6	10 (mean)	–	2.4
Davol et al [79]	Open/laparoscopic	48 (38 proven RCCs)	2.6	64 (median)	100	12.5, 2.5*
Hegarty et al [57]	Laparoscopic	179 (no. of RCC not given)	2.5	36 (median)	98	1.7
Cestari et al [80]	Laparoscopic	37 (29 proven RCCs)	Mean: 2.6	20.5 (mean)	–	5.7
Silvermann et al [81]	Percutaneous	26 (24 proven RCCs)	2.6	14 (mean)	–	13
Aron et al [82]	Laparoscopic	88 (no. of RCC not given)	2.3	83 (median) (range: 60–120)	At 5 yr: 95	At 5 yr: 22

CSS = cancer-specific survival; RCC = renal cell carcinoma.
* After first and after repeat treatment cycle.

Complications
14%

Most common comp: hemorrhage, Paresthesias

- Major comp.4.9%
  - CHF
  - MI
  - Pancreatic injury
  - Ureteral obstruction
  - Hemothorax
- Minor comp.
  - Pain
  - Paresthesias
  - Urinary leakage
  - Perirenal fluid
  - Pneumothorax,
  - Haematuria
  - Infection

Kidney Functions

- Cryoablation has minimal effects on renal function

- Gill:
  - Long-term data on renal function after LCA (3 years)
  - Before procedure: sCre: 1.2 mg/dl
  - After 43 months: sCre: 1.4 mg/dl
  - Patients with a solitary kidney had comparable renal function after ablation
    - 2.2 mg/dl
    - 2.6 mg/dl
  - In patients with impaired renal function demonstrated a slightly improved creatinine after LCA (3.0 vs. 2.7 mg/dl).

J Urol 2005 173:1903-7

Excise, Ablate or Observe: The Small Renal Mass Dilemma—A Meta-Analysis and Review

David A. Kunkle, Brian L. Egleston and Robert G. Uzzo*

From the Departments of Urologic Oncology and Biostatistics (BLE), Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, Pennsylvania

	Percentage of patients	**Local Recurrence (%)**	**Development of mets %**
PN	77.8	2.6	5.6
RFA	9.4	11.7	2.3
CRYO	7.7	4.6	1.2
Active surv.			0.9

Significantly higher incidence of local tumor progression following cryoablation and RFA therapy compared with PN.

	Mean Age (years)	Mean tumor size (cm)
PN	60.1	3.40
RFA	67.2	2.69
CRYO	65.7	2.56

Tumor size is smaller in ablated patients

Patients treated with energy ablative techniques are significantly older

Complications

	RN	PN	RFA&Cryo
Number of patients	18575	3019	1103
Comp. %	18.20	17.16	11&1.8

Columbia University Experience
Partial Nephrectomy vs Cryoablation (≤3cm)

Parameter	LPN	LCA	P-value
Number	N=75 (91 lesions)	N=92 (95 lesions)	
Tumor Size (cm)	1.9	2.0	0.45
Patient age (yrs)	58.8	69.2	<0.001
ASA (3 or 4)	17%	48%	<0.001
Ischemia time (min)	24.5 (11-40)	0	
EBL	168.4	66.0	0.005
Overall Complications	11.9	9.3	<0.001
Follow-up (months)	21.8 (1-48)	14 (1-34)	<0.001
Recurrence (n,%)	1 (1.1%)	2 (2.6)	0.588

Haramis et al, J Endourol, 2010 Jul;24(7):1097-100

EUROPEAN UROLOGY 60 (2011) 435–443

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Review – Kidney Cancer
Editorial by Giacomo Novara and Vincenzo Ficarra on pp. 444–445 of this issue

Laparoscopic Cryoablation Versus Partial Nephrectomy for the Treatment of Small Renal Masses: Systematic Review and Cumulative Analysis of Observational Studies

Tobias Klatte[a,], Bernhard Grubmüller[a], Matthias Waldert[a], Peter Weibl[a], Mesut Renzi[b]*

[a] *Department of Urology, Medical University of Vienna, Vienna, Austria*
[b] *Department of Urology, Landesklinikum Weinviertel, Korneuburg, Austria*

- Patients undergoing LCA were significantly
  - older, mean tumor sizes were lower,
  - mean follow-up duration was shorter
- the risk of metastatic progression was similar.
- Compared with PN, LCA results in a higher risk of local tumor progression.
- The risk of perioperative complications appears to be lower following LCA;
- PN is the gold standard for SRMs,
- but LCA may be indicated in selected patients with significant comorbidity.

Klatte T et al Eur Urol 2011

Cryoablation or Radiofrequency Ablation of the Small Renal Mass

A Meta-analysis

David A. Kunkle, MD
Robert G. Uzzo, MD

CANCER November 15, 2008 / Volume 113 / Number 10

- 47 studies and the ablation of 1375 renal masses
- CA 65% laparoscopicaly, RFA 94% percutaneously
- Pretreatment biopsy rate CA>RFA (82.3% & 62.2%)
- repeat ablation was performed more often after RFA (8.5% vs. 1.5%)
- local tumor progression RFA > CRA, 12.9% vs. 5.2%
- Metastasis RFA > CA (%2.5 & %1)

Conclusions

- RFA and cryroablation are a minimally invasive treatment option for localized renal masses
- For the patient at high surgical risk who is not a candidate for observation or
- Who wants proactive treatment
- Who accepts with full understanding the need for lifelong radiographic surveillance and repeat biopsy after treatment.
- Provide patient-related benefits such as
  - Reduction in blood loss,
  - Post-operative pain,
  - Shorter hospital stay.

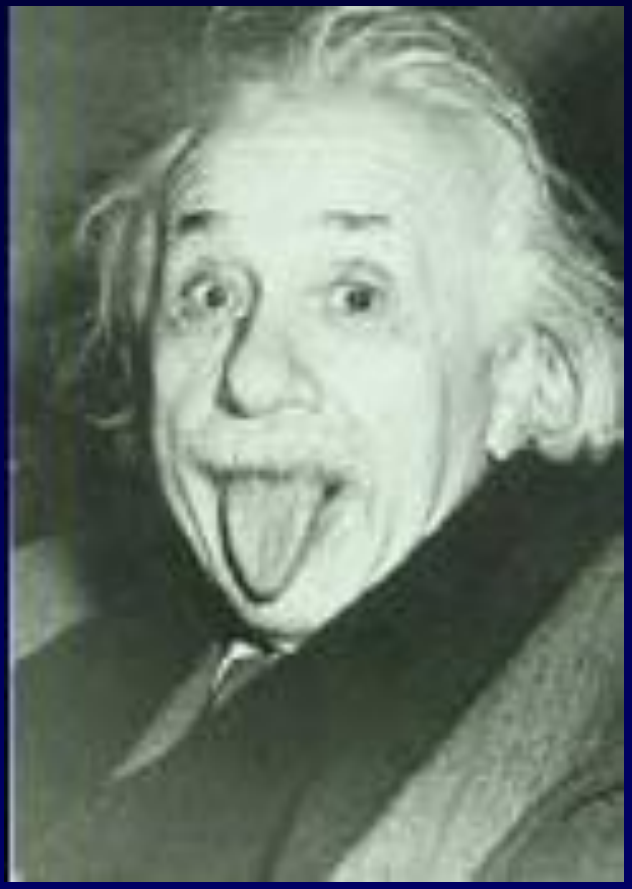
Conclusion

- The rates of local recurrence of the tumour were not very high
- demonstrate near equivalent oncological outcomes compared to extirpative surgeries
- Decline in renal function is minimal

Conclusion

- Cryoablation may result in significantly better local tumor control rates than RFA
- Cryoablation was associated with a significantly lower rate of incomplete ablation (4.8%) than RFA (14.2%)
- Percutaneous ablation studies had significantly higher incomplete ablation rates than laparoscopic studies (13.9% vs. 2.1%)
- Percutaneous cryoablation studies were compared to laparoscopic cryoablation studies (10.5% vs. 2.2%)
- Survival
  - cryoablation total RFS rates were lower than rates for LPN, OPN and LRN, and relatively similar to RFA and ORN rates,
  - Metastatic RFS and CSS also were lower for cryoablation than for LPN

Renal Mass Management



"The questions may be the same. However,

the answers have changed."

Thank You
благодарение