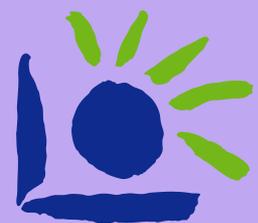


Traitements loco-régionaux actuels et à venir

F. DESCHAMPS

Service de Radiologie Interventionnelle



Institut de cancérologie
GUSTAVE ROUSSY
VILLEJUIF - www.igr.fr

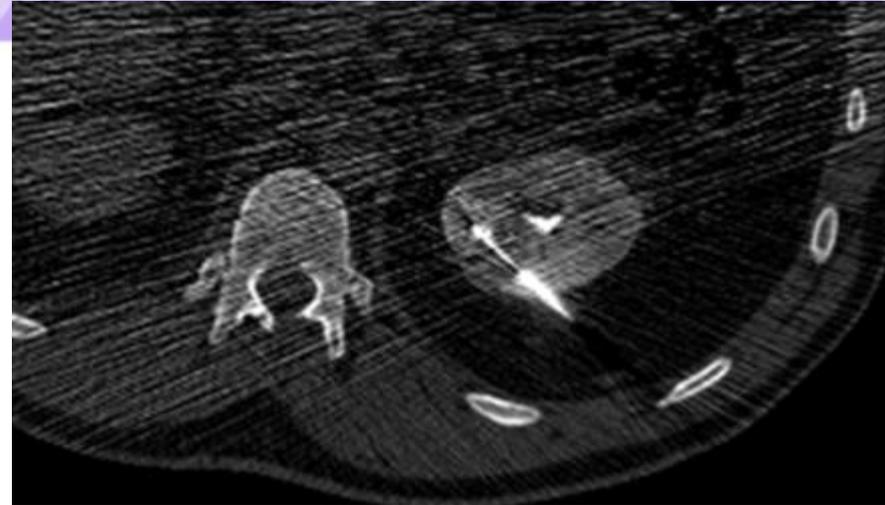
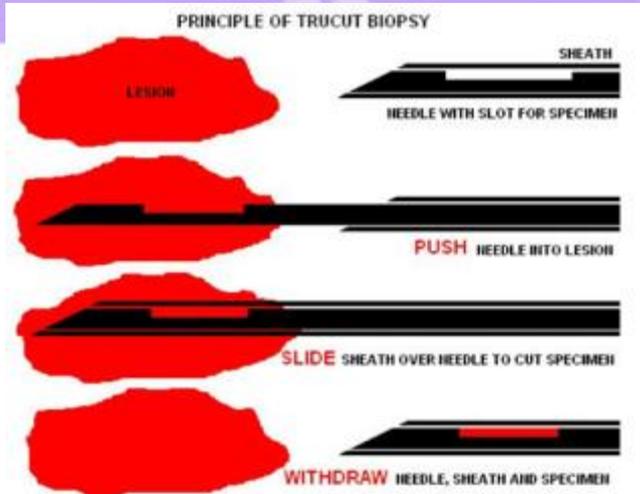
Radiologie Interventionnelle

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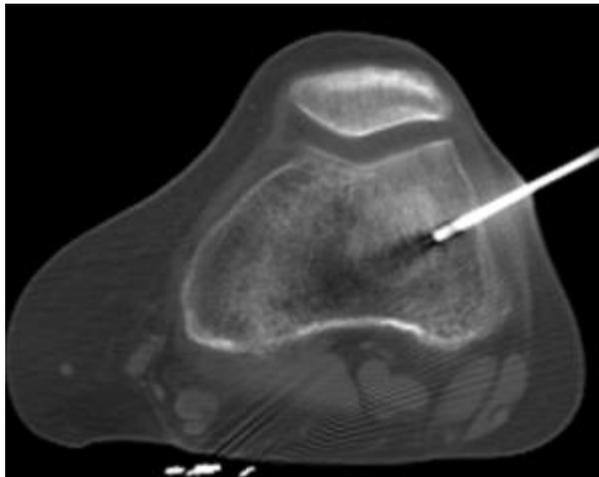
- Techniques chirurgicales « mini-invasives »
- Voies percutanée ou endo-vasculaire
- Sous contrôle imagerie : Radiologie, angiographie, TDM ou écho
- Blocs opératoires spécifiques



Biopsie percutanée



Association A.R.Tu.R.



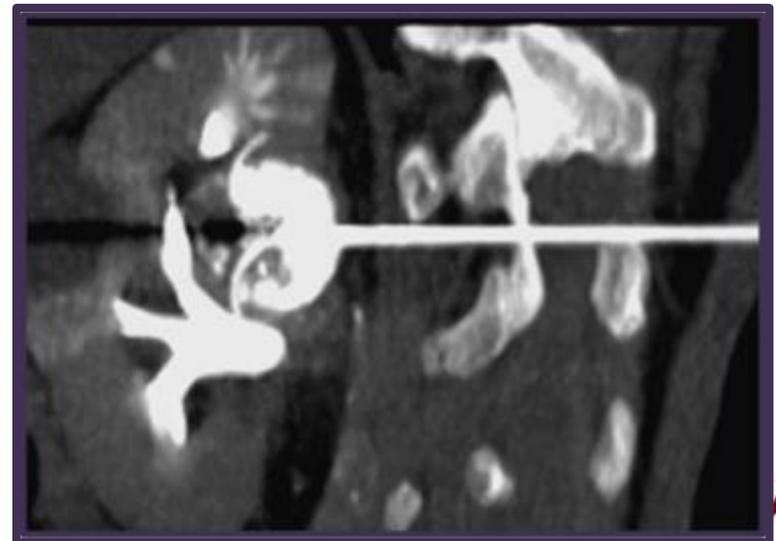
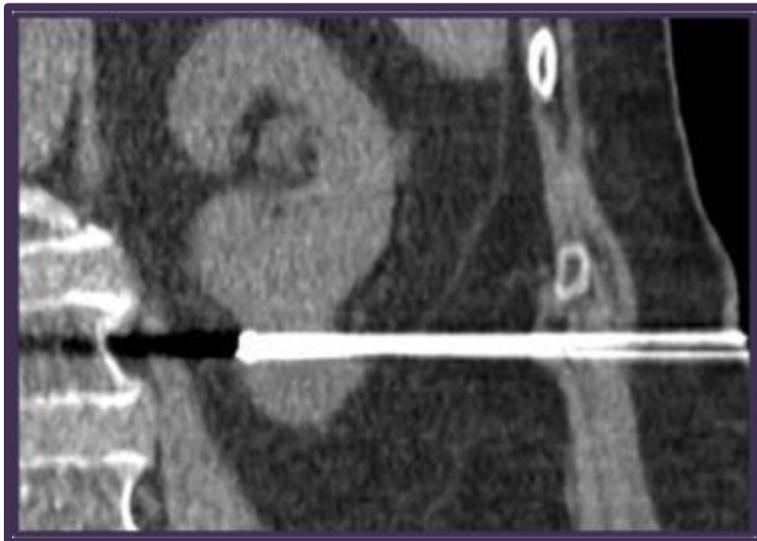
Techniques d'ablation thermique

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Traitements loco-régionaux actuels

Destruction thermique (tumeur de petite taille)

- Radiofréquence
- (Micro-ondes)
- Cryothérapie



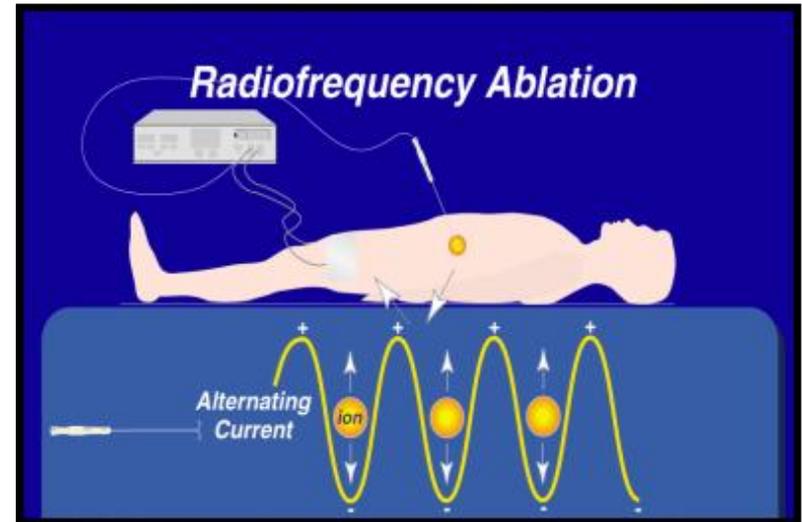
Radiofréquence

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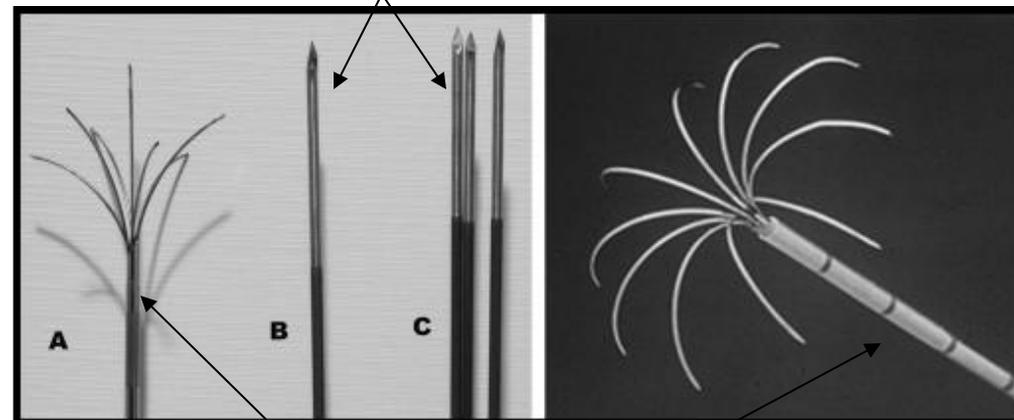
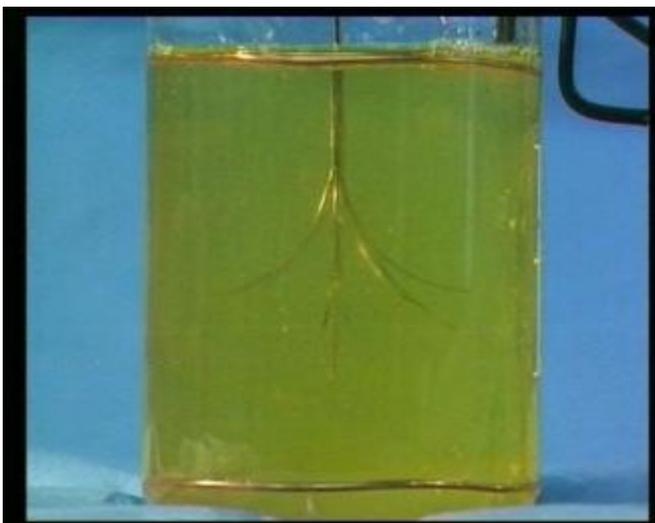
= Aiguille "électrode"

Courant sinusoïdal (420-500 kHz)

- Agitation ionique (friction)
- Elevation T C tissus
 - $T > 60$ C, mort cellulaire



Aiguilles droites
refroidies

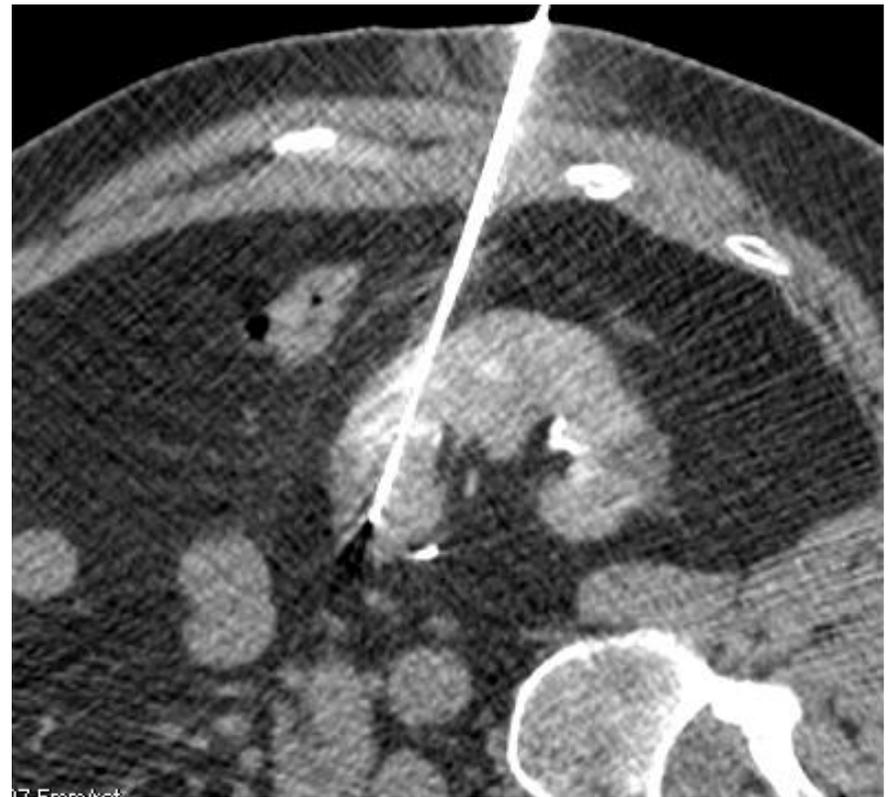
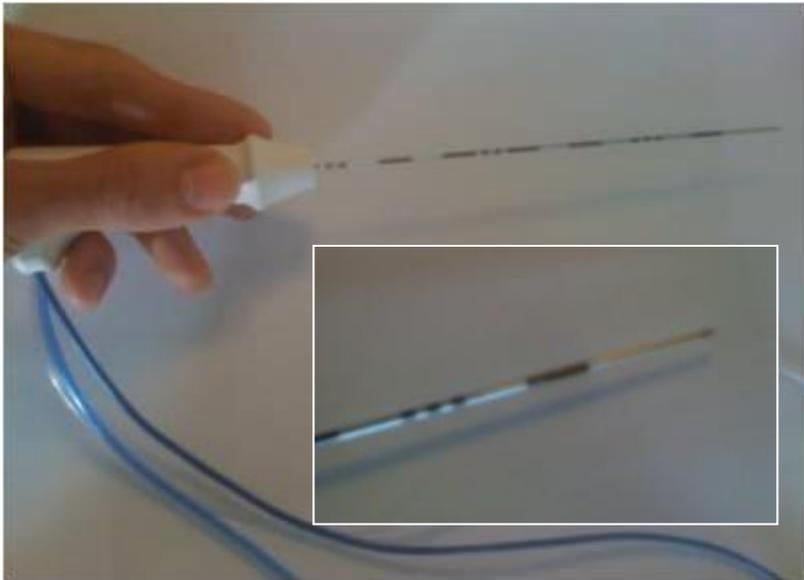


Aiguilles déployable

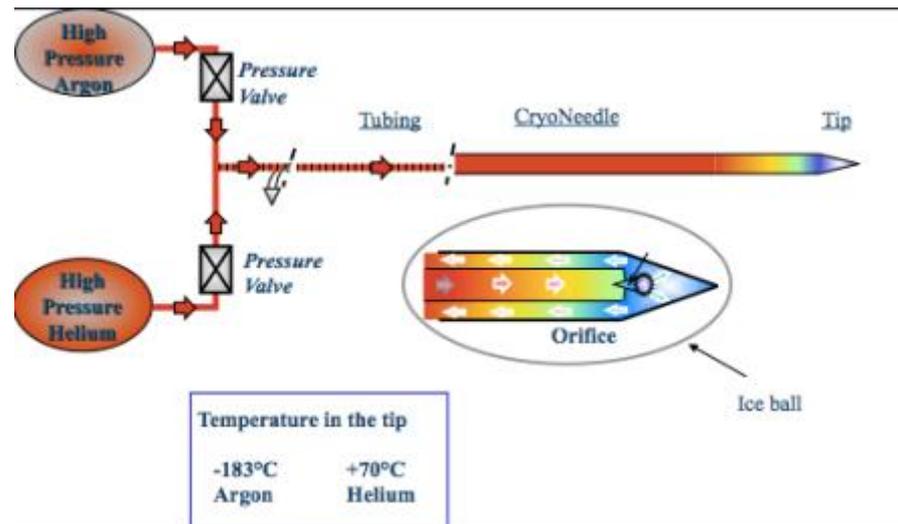
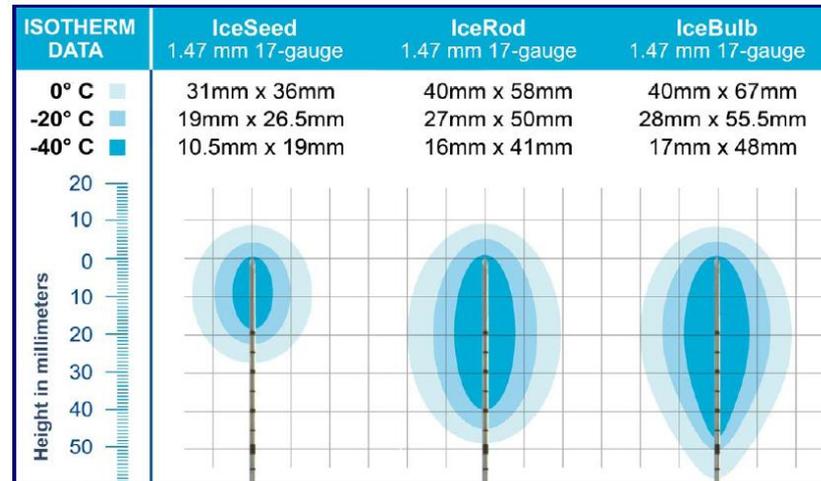
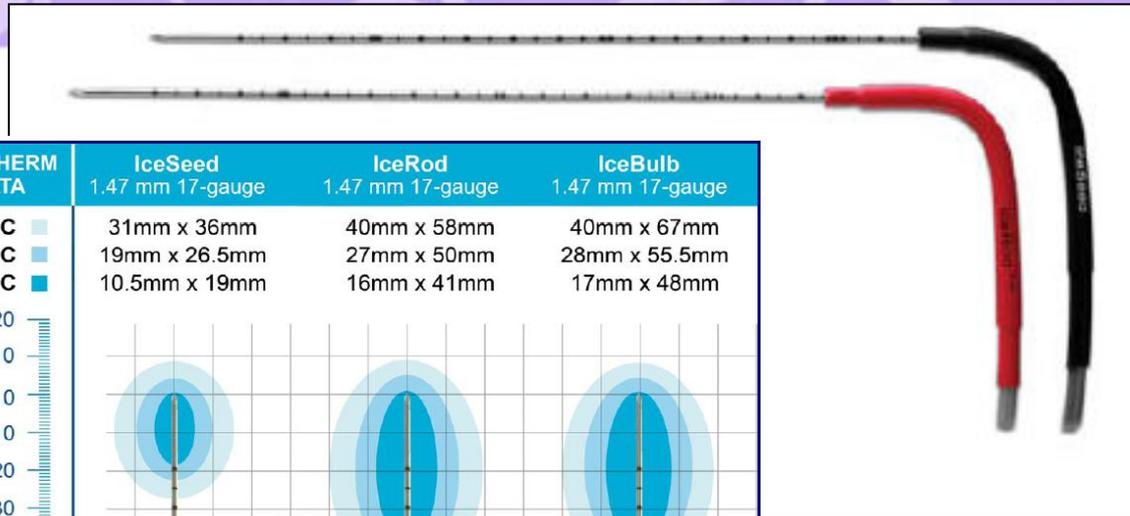
Radiofréquence

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Anesthésie générale

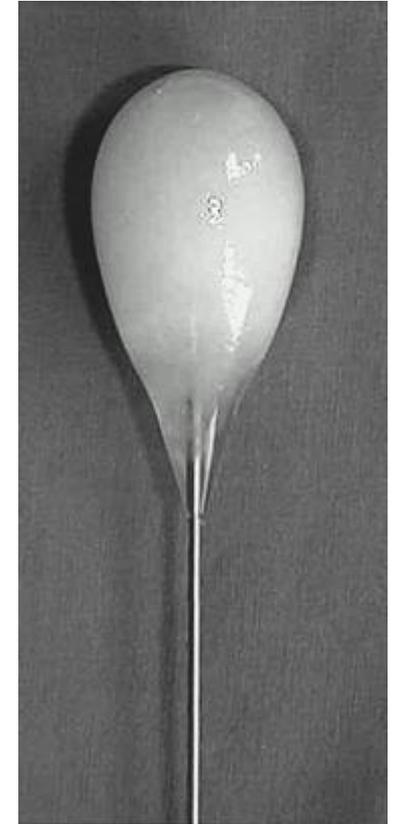
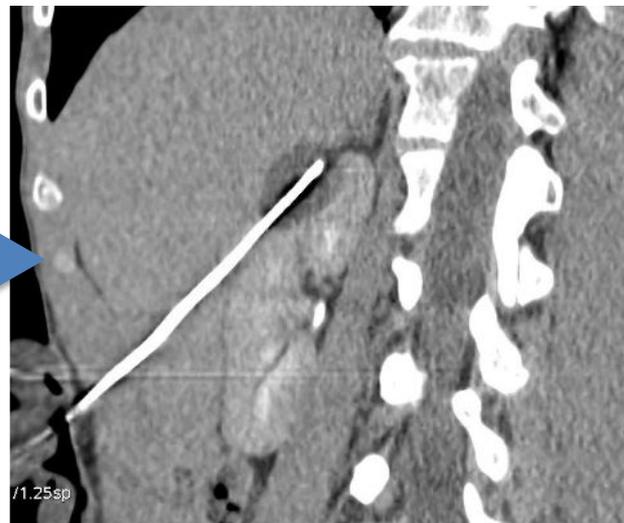
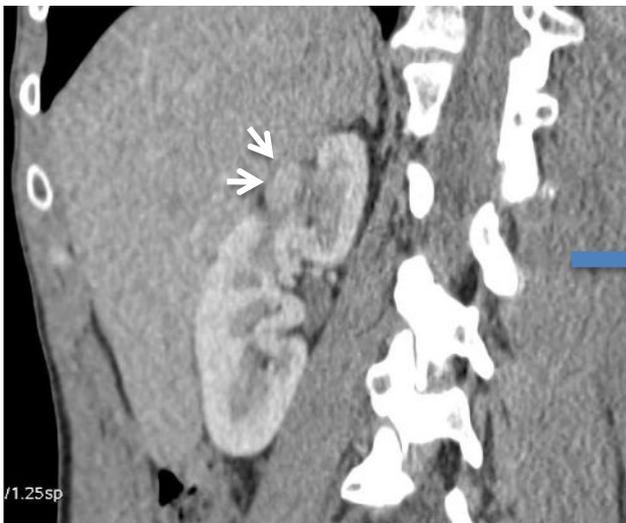
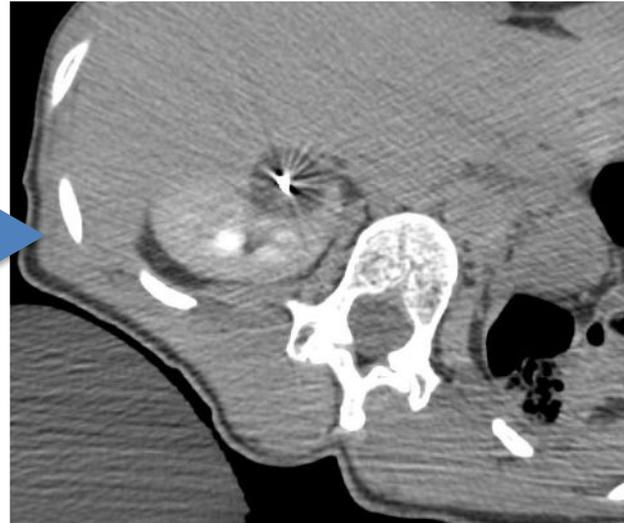


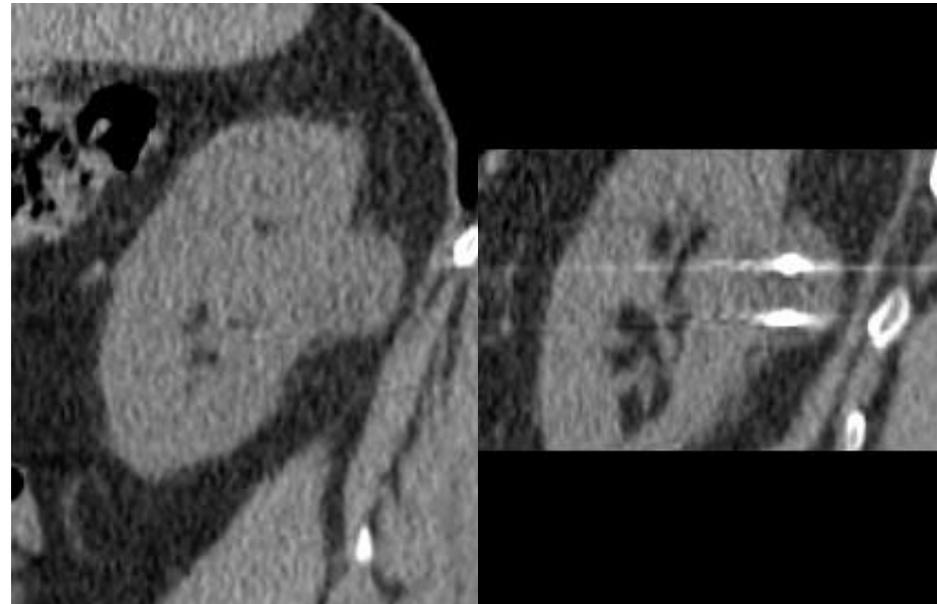
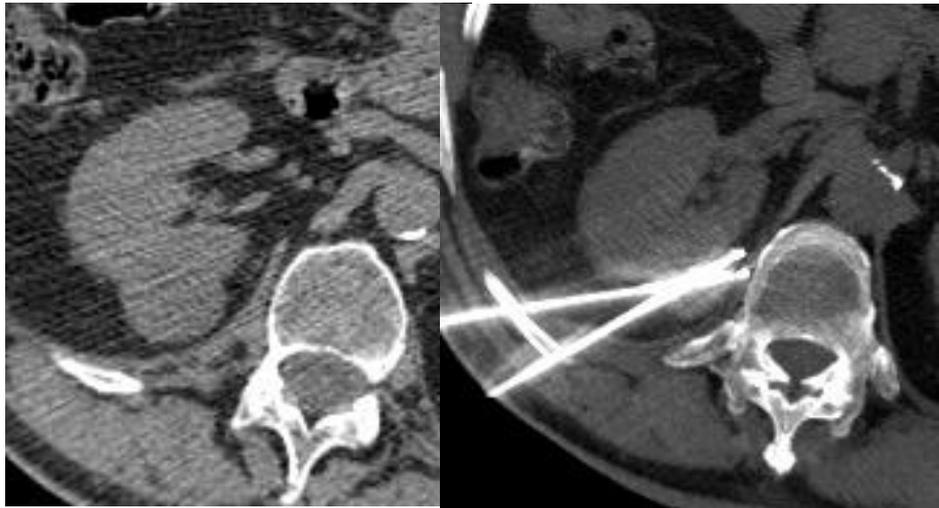
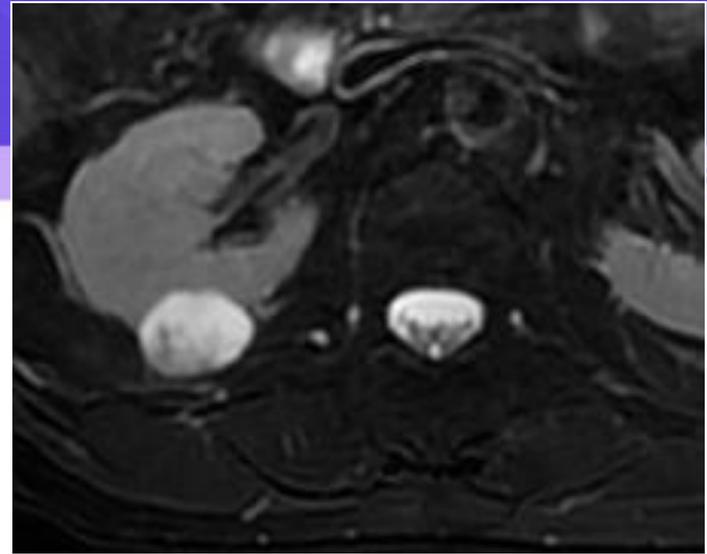
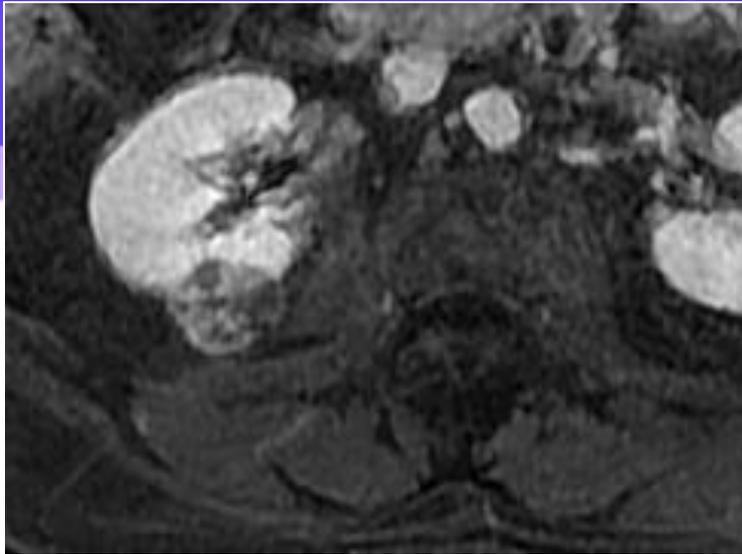
Cryothérapie

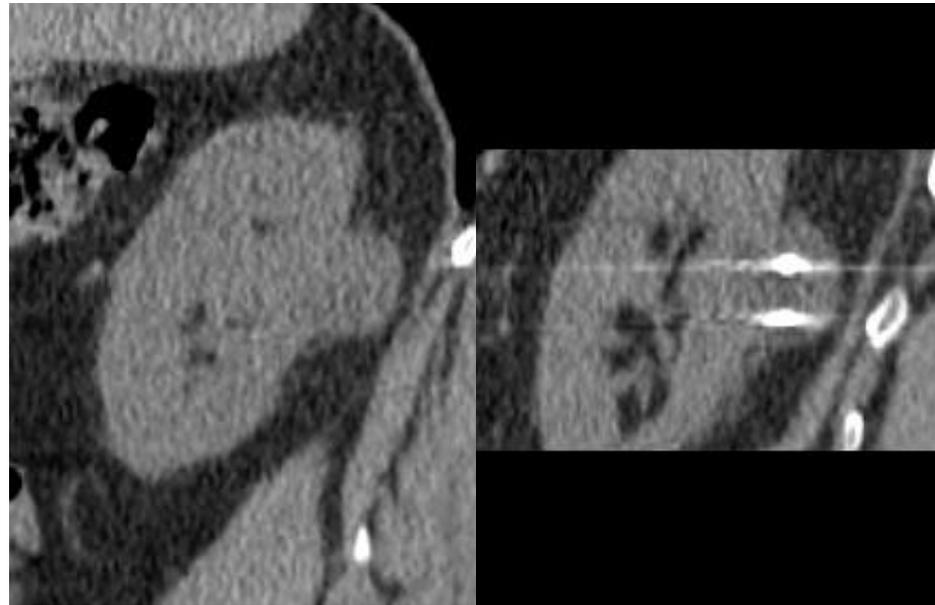
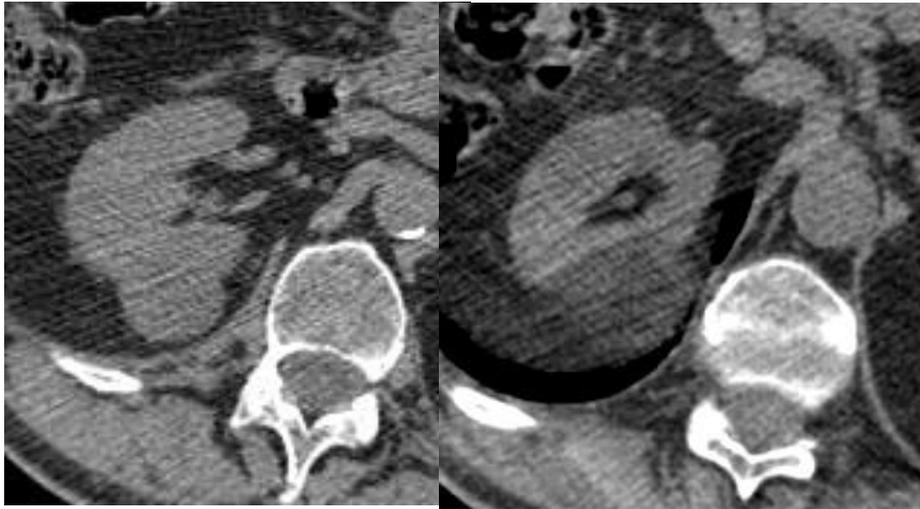
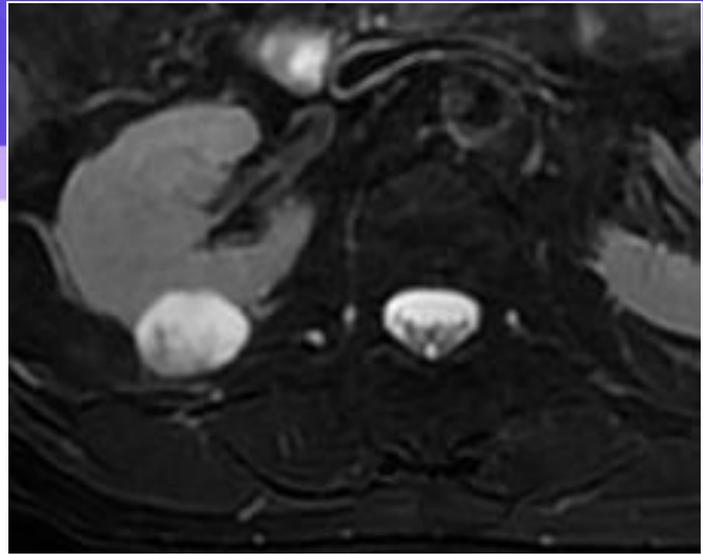
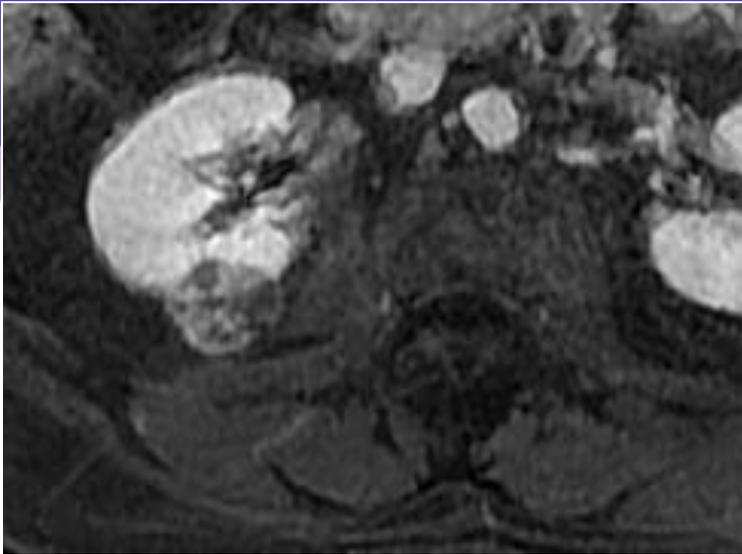


Cryothérapie

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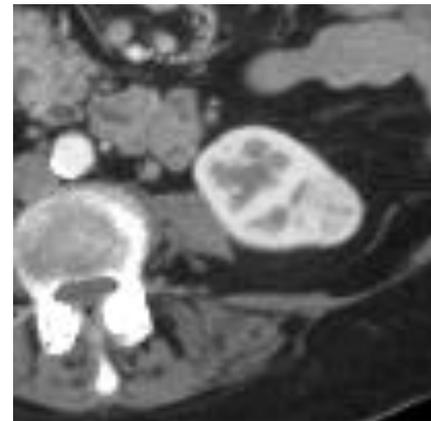
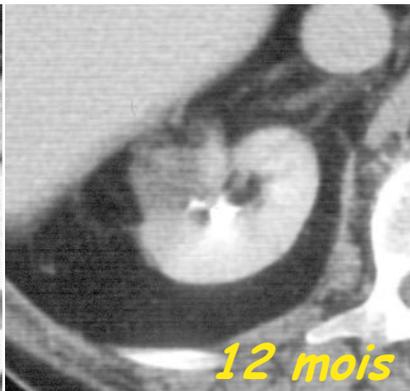
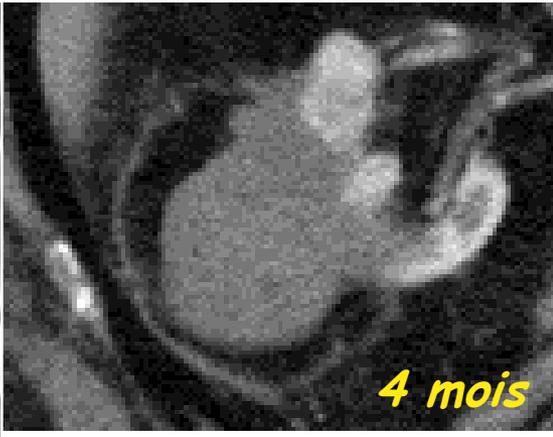
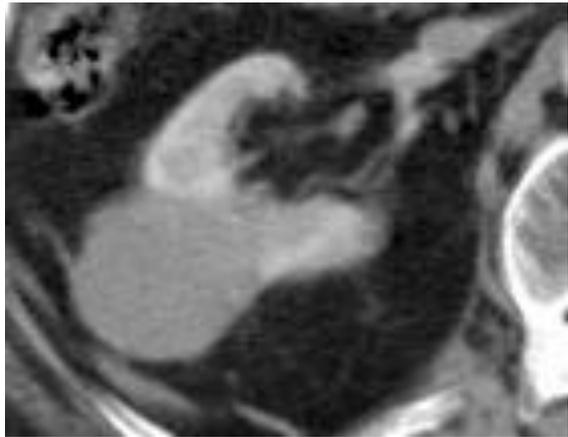




Imagerie post traitement:

Cicatrice, involution lente et retardée: 10-20% / 6 mois

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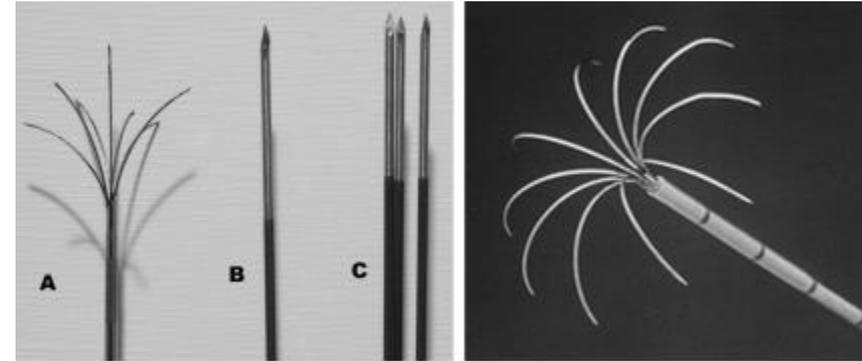
(de Baère T, J Urol 2002 Gervais, DA, RSNA 2002)



Techniques d'ablation

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Radiofréquence: quelle aiguille?



Cryothérapie:

- 1/ succès local > RF (traitement incomplet= 5.2% vs. 12.9%, $p < 0.0001$ *)
- 2/ complications < RF (structures pyeliques)**: intérêt pour tumeur centrale.

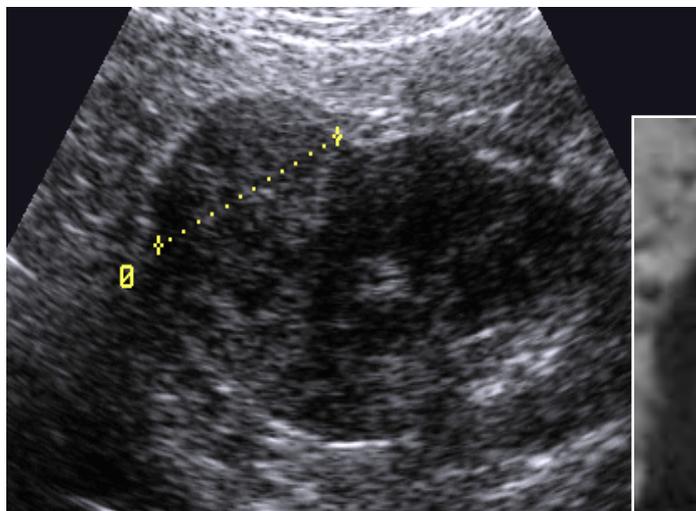
* David A. Chochrane 2008.

1375 tumeurs, mean= 2.6 cm, mean follow-up= 19 mois

** Janzen, J Urol 200, Sung, J Urol 2003.



Visibilité



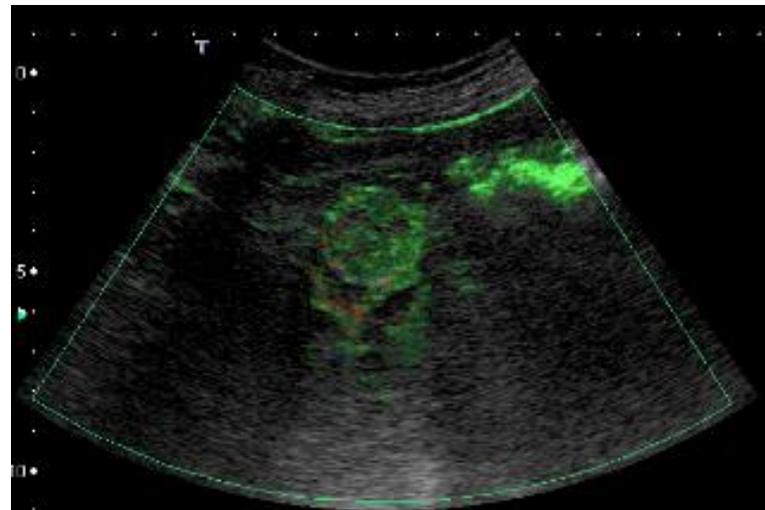
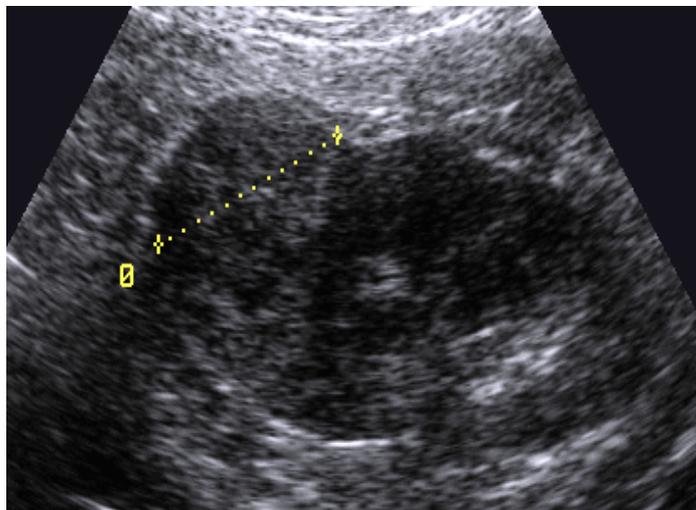
Cryo. Gangi. strasbourg

- Succès local/ complications
- US = TDM (IV-) = IRM*

* Veltri. CVIR 2009.

Visibilité

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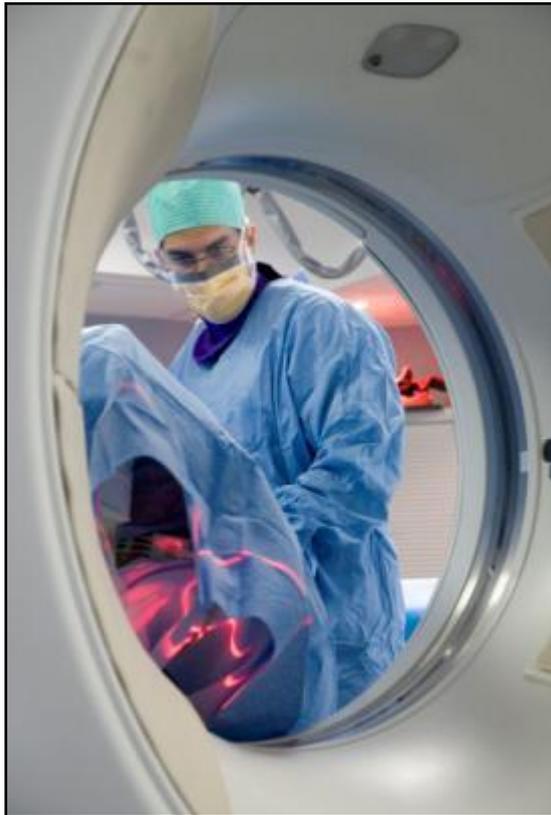
US +++

- non irradiant
- Accessibilité machine
- Ponction temps réel
- Approche 3D



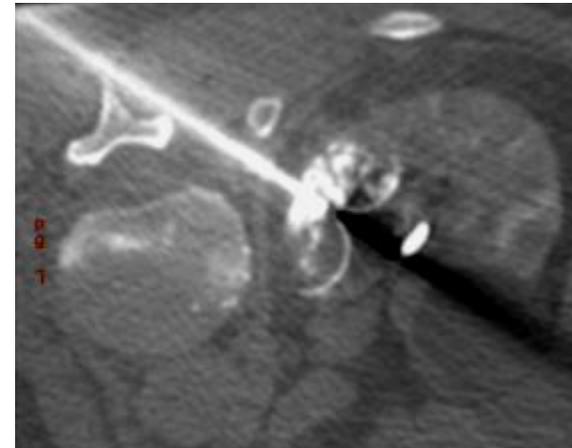
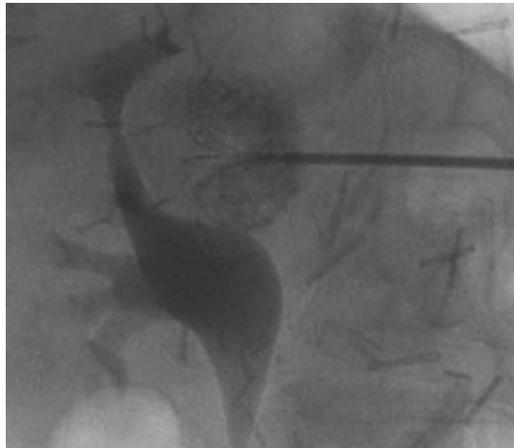
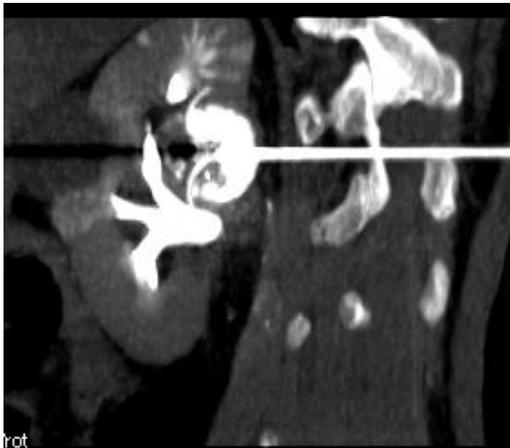
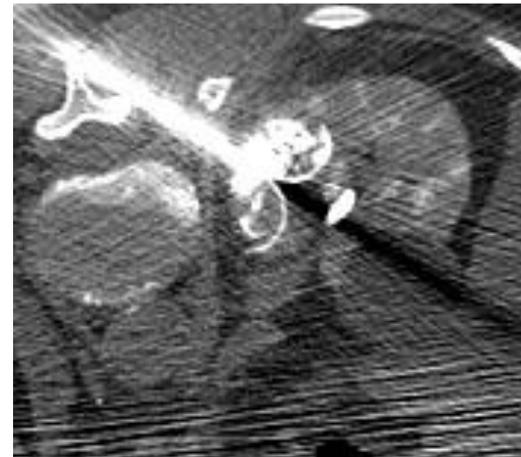
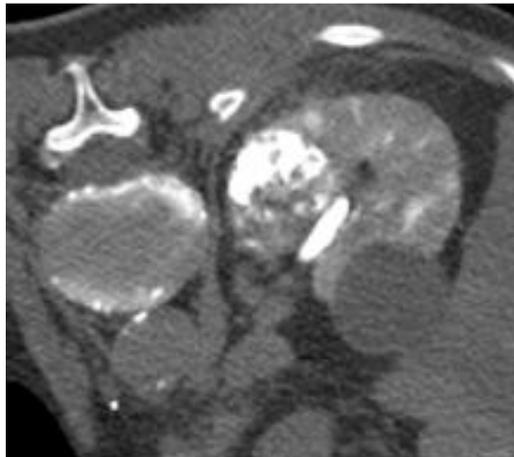
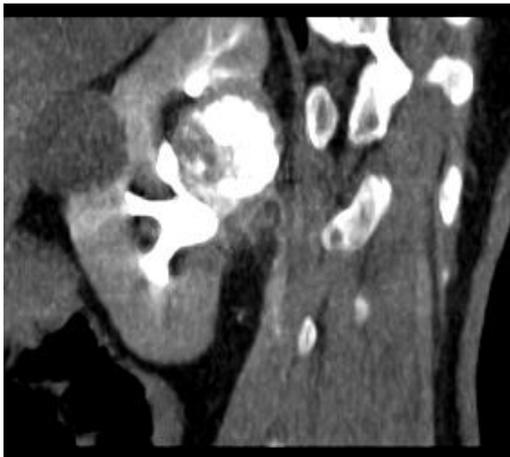
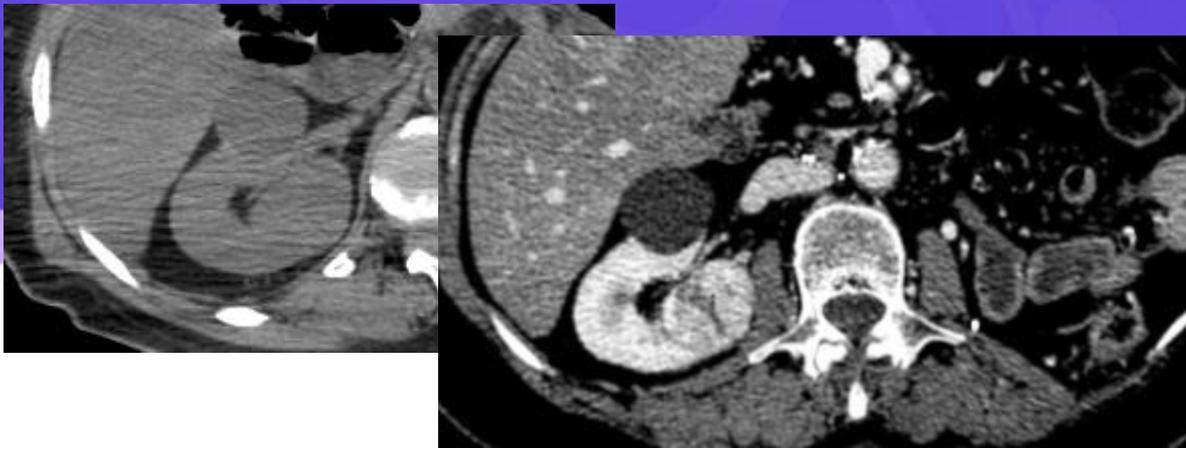
Visibilité

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Scanner







IRM



Pr A. Gangi
CHU de Strasbourg



Trends in the surgical management of localized renal masses: thermal ablation, partial and radical nephrectomy in the USA, 1998–2008

Jeffrey M. Woldrich*†, Kerrin Palazzi*†, Sean P. Stroup*†, Roger L. Sur*†, J. Kellogg Parsons*†, David Chang† and Ithaar H. Derweesh*†

*Division of Urology, †Department of Surgery, University of California San Diego School of Medicine, La Jolla, CA, USA

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Fig. 1 Change in renal procedures over time: percentages indicate the proportion that each individual modality constitutes with respect to the total annual renal procedures. RFA, radiofrequency ablation.

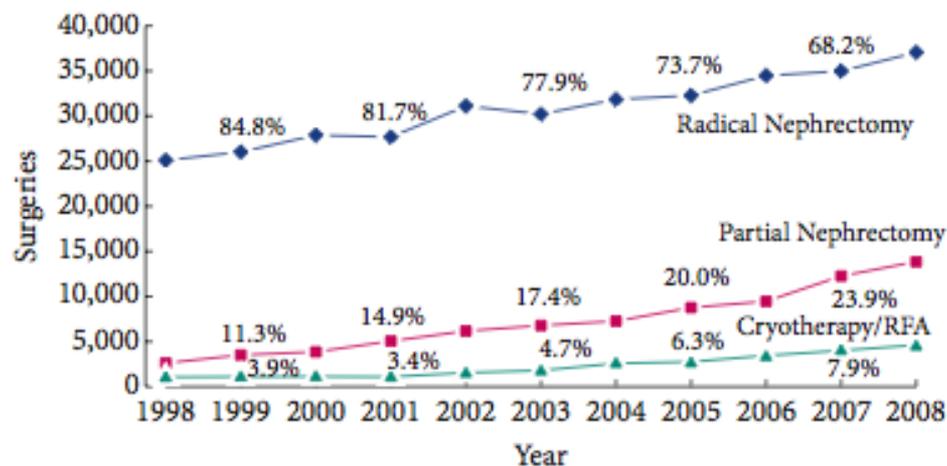


Table 3 Multivariate analysis of undergoing cryotherapy/radiofrequency ablation (RFA) compared to partial and radical nephrectomy.

Variable	Cryo/RFA vs partial nephrectomy (referent)				Cryo/RFA vs radical nephrectomy (referent)			
	Odds ratio	95% CI	P	Odds ratio	95% CI	P		
Age group (≥ 70 years; < 70 years referent)	2.154	1.974	2.349	<0.001*	1.613	1.493	1.744	<0.001*
Sex (female, male referent)	1.116	1.039	1.199	0.003*	1.102	1.032	1.177	0.004*
Hypertension	1.111	1.013	1.218	0.026*	1.146	1.046	1.257	0.004*
Diabetes mellitus	1.261	1.067	1.490	0.007*	1.351	1.163	1.568	<0.001*
Chronic kidney disease	1.275	1.056	1.541	0.012*	0.630	0.532	0.745	<0.001*

Taille de la tumeur

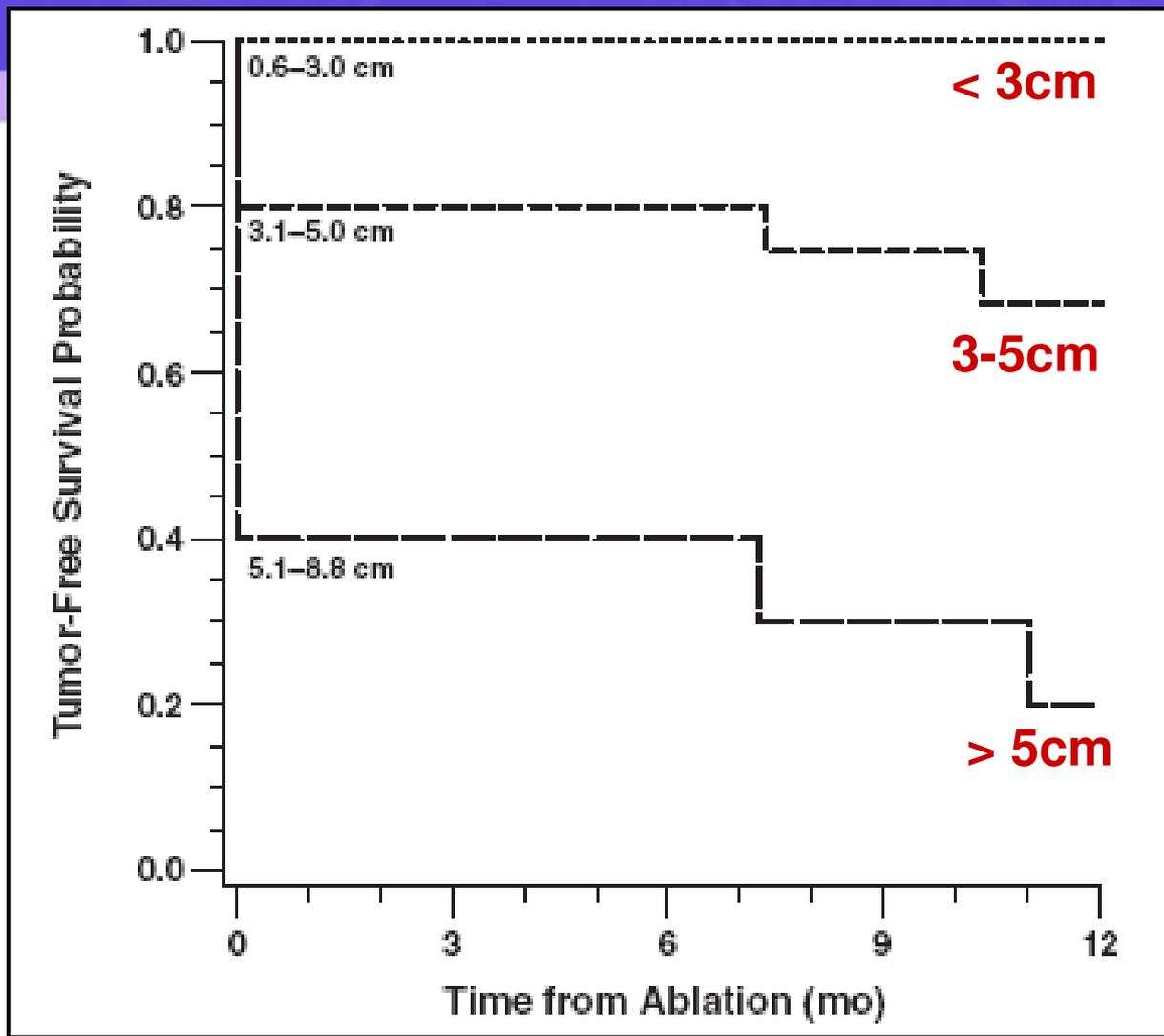
7e Rencontre Patients de l'Association A.R.Tu.R.

Taille tumeur	Nécrose tumorale complète	n session(s) nécessaire(s)		
		1	2	3
<3 cm	100%	92%	8%	0%
3-5 cm	92%	53%	44%	3%
>5 cm	25% !!!	0%	50%	50%

Gervais. AJR 2005. 100 tumeurs.
Mean follow-up: 28 months



Taille de la tumeur



Rencontre Patients de l'Association A.R.Tu.R.

Survie sans récurrence



Radiofrequency Ablation Versus Partial Nephrectomy in Patients with Solitary Clinical T1a Renal Cell Carcinoma: Comparable Oncologic Outcomes at a Minimum of 5 Years of Follow-Up

Ephrem O. Olweny^a, Samuel K. Park^a, Yung K. Tan^a, Sara L. Best^a, Clayton Trimmer^b, Jeffrey A. Cadeddu^{a,*}

^a Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA; ^b Department of Radiology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Janvier 2012

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Table 1 – Demographic and clinical characteristics

	RFA	PN	p value
n	37	37	
Follow-up, yr, median (IQR)	6.5 (5.8–7.1)	6.1 (5.4–7.3)	0.68
Age, yr, median (IQR)	63.8 (56.3–69.1)	54.8 (47.8–59.1)	0.0001
Male/female	24/13	20/17	0.34
Ethnicity, n (%)			
White	27 (72.9)	29 (80.6)	0.25
African American	6 (16.2)	2 (5.4)	0.13
Hispanic	1 (2.7)	2 (5.4)	0.56
Other	3 (8.1)	3 (8.1)	1.0
ASA score, n			0.03 [*]
1	2	9	0.02
2	21	21	1.0
3	14	7	0.07
Tumor size, cm, median (IQR)	2.1 (1.8–2.8)	2.5 (1.7–3.1)	0.44
Surgical approach, n (%)			
Percutaneous	25 (67.6)	–	–
Laparoscopic	12 (32.4)	28 [†] (75.6)	–
Open	–	9 (24.4)	–
Tumor histology, n (%)			
Clear cell	25 (67.6)	28 (77.8)	0.34
Papillary	9 (24.3)	3 (8.3)	0.06
Chromophobe	1 (2.7)	3 (8.3)	0.29
Not specified	2 (5.6)	2 (5.6)	1.0

RFA = radiofrequency ablation; PN = partial nephrectomy; IQR = interquartile range; ASA = American Society of Anesthesiology.

^{*} The p value is for comparison of ASA categories for RFA versus PN using the chi-square test.

[†] Includes one patient who was converted to open PN.

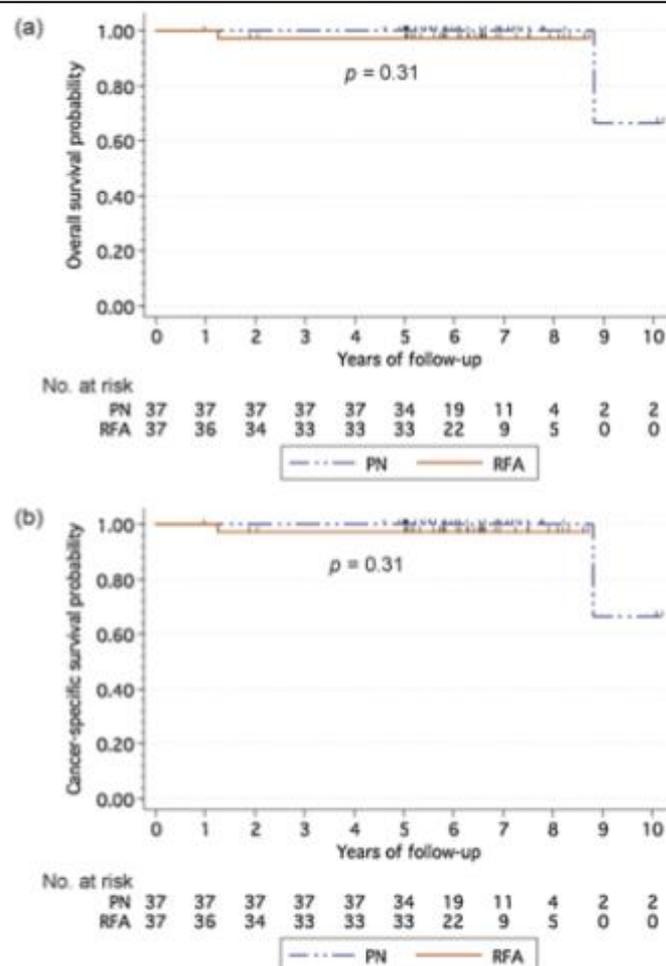


Fig. 2 – (a) Overall survival and (b) cancer-specific survival for radiofrequency ablation (RFA) versus partial nephrectomy (PN).



Radiofrequency Ablation Versus Partial Nephrectomy in Patients with Solitary Clinical T1a Renal Cell Carcinoma: Comparable Oncologic Outcomes at a Minimum of 5 Years of Follow-Up

Ephrem O. Olweny^a, Samuel K. Park^a, Yung K. Tan^a, Sara L. Best^a, Clayton Trimmer^b, Jeffrey A. Cadeddu^{a,*}

^a Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA; ^b Department of Radiology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Janvier 2012

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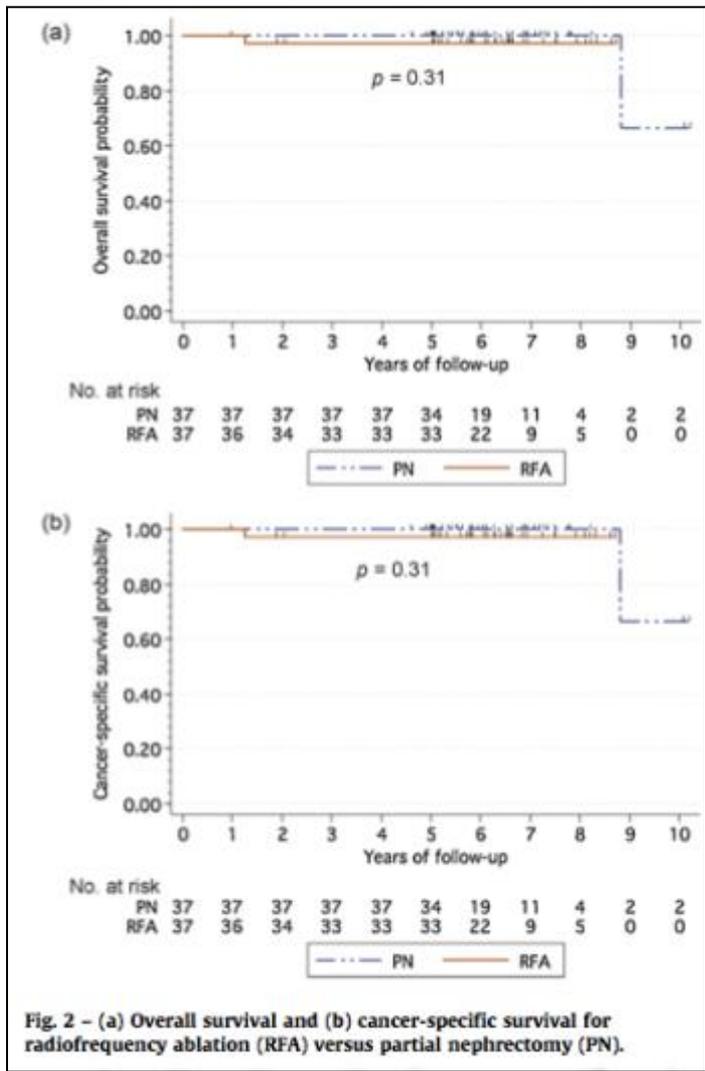
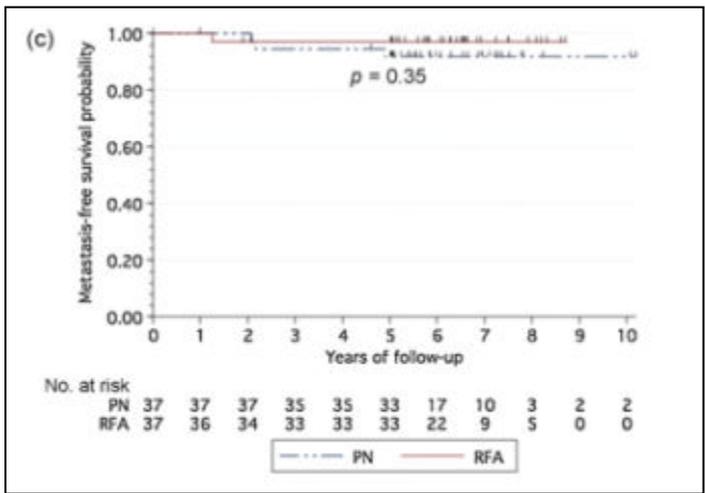
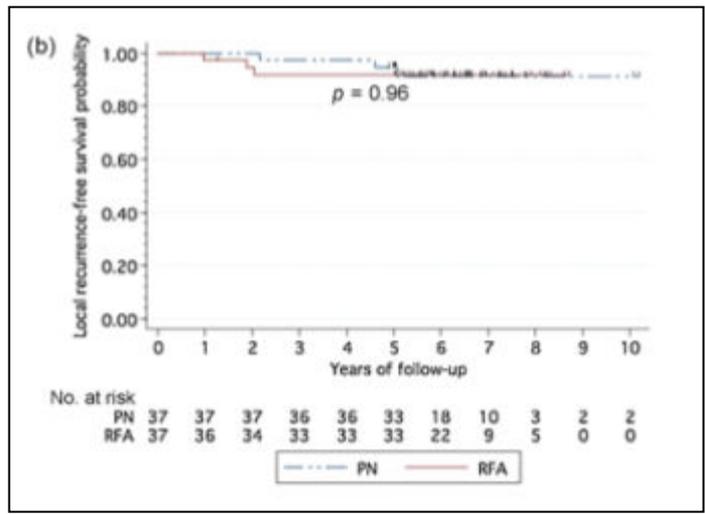
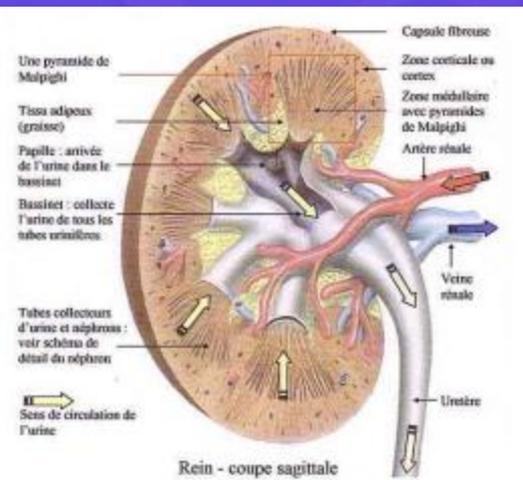


Fig. 2 – (a) Overall survival and (b) cancer-specific survival for radiofrequency ablation (RFA) versus partial nephrectomy (PN).



Localisation de la tumeur



Localisation	Exophytique	Parenchymale	centrale	mixte
nécrose complète	100% n=67/67	100% n=5/5	78% n=7/9	61% n=11/18

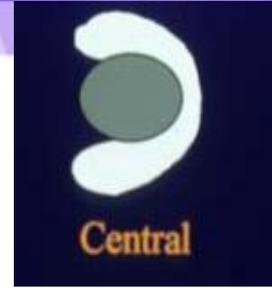
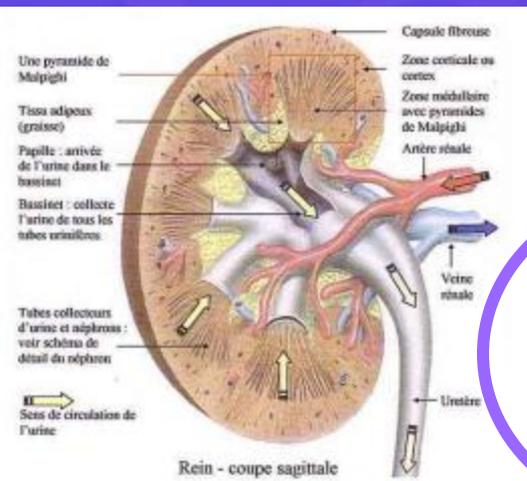
Facteur prédictif **indépendant** de traitement incomplet^{1,2}

1/ Gervais AJR 2007: p= 0.005

2/ Veltri CVIR 2006: p=0.007

- Effet « four » de la graisse péri-rénale
- Refroidissement central par les vaisseaux hilaires: « heat-sink effect »
- « Peur » des complications

Localisation de la tumeur



Localisation	Exophytique	Non-exophytique	
Complications	7%* n=2/27	35%	6/17

*p=0.04

Localisation	Non-centrale		centrale	
Complications	15%** n=6/39		40%	2/5

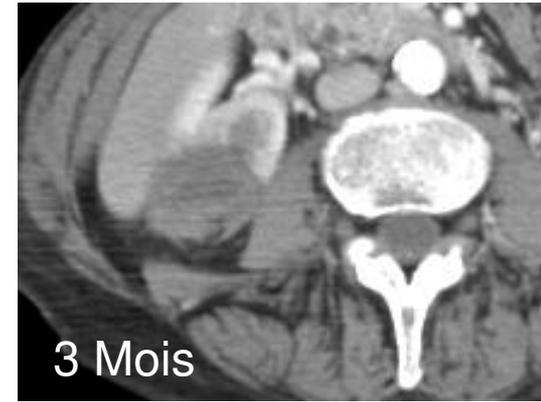
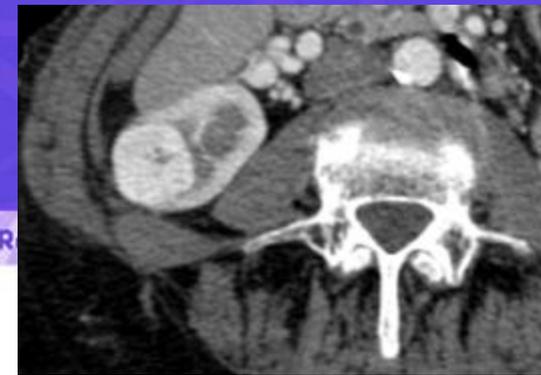
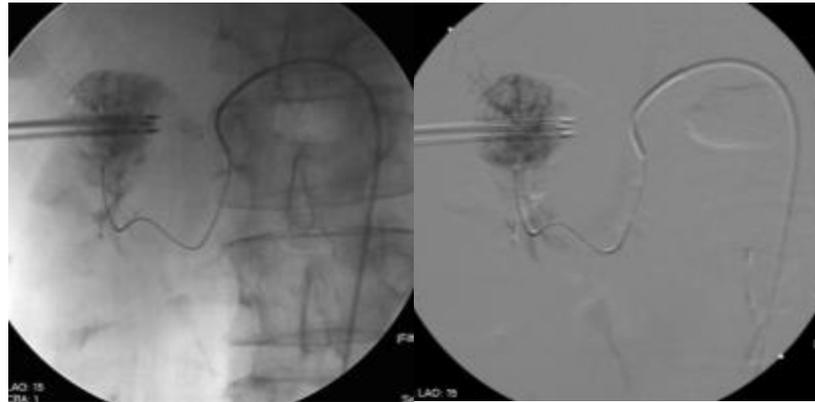
**p=NS

Diminution significative des complications (stenose, fistule)

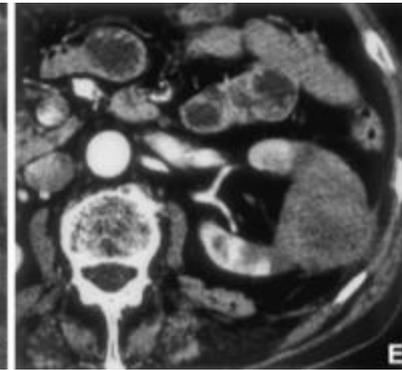
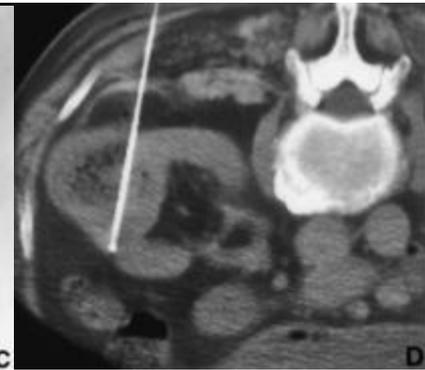
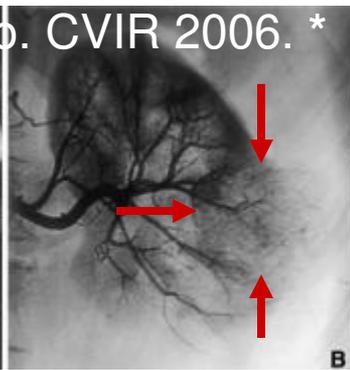
Micro-circulation tumorale

→ « Heat-sink effect »

Embolisation vasculaire hyperselective



Koichiro Yamakado. CVIR 2006. *



* RF + embolisation artérielle. 12 tumeurs, mean= 5.2 cm (3.5 à 9 cm).

Follow-up 13 mois. Succès: 70% (1 session), 87% (2 sessions) et 100% 4 (sessions)

Micro-circulation tumorale

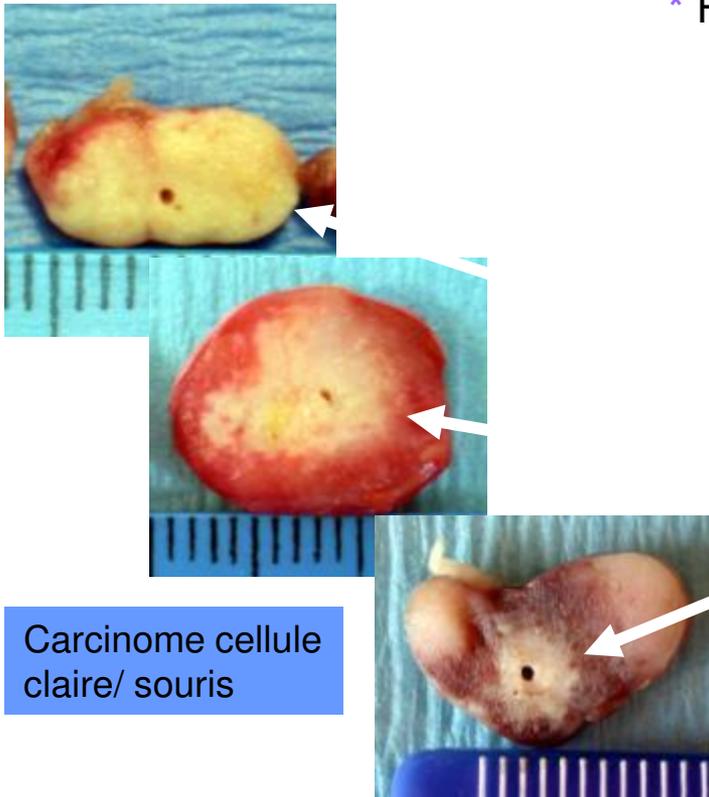
→ « Heat-sink effect »

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Pré-traitement par anti-angiogéniques IV

- Expérimentation animale (Carcinome cellule claire/ souris) *
- Cases reports (x3) **

* Hakime. Radiology 2005. ** Grenier. Urology 2009.



Carcinome cellule claire/ souris

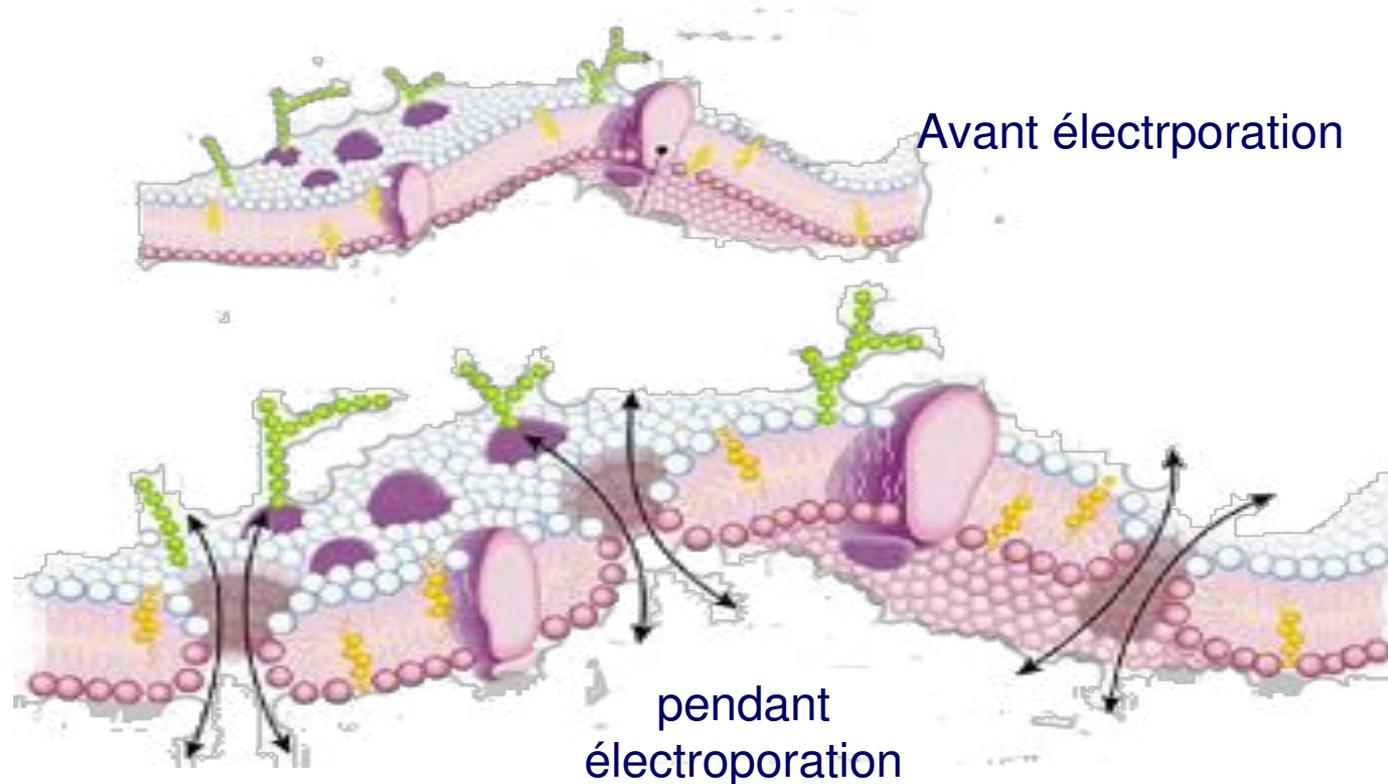
Sorafenib*	<u>Tumor size</u>	<u>RF Ablation</u>
80 mg	11.1 ± 1.0 mm	11.1 ± 0.3 mm
20 mg	12.2 ± 1.2 mm	8.5 ± 0.4 mm
0 mg	15.2 ± 1.6 mm	6.7 ± 0.7 mm



Electroporation?

= application de pulses électriques (2250–3000 V) répétés (50–100), de
courte durée (50–100 msec)

→ Augmenter la perméabilité des pores cellulaires



Electroporation

REVERSIBLE (*Début des expérimentations 1960*)

7^e Rencontre Patients de l'Association A.R.Tu.R.

- **Electro-chimiothérapie**

- Entrée dans la cellule de drogue ne pénétrant pas

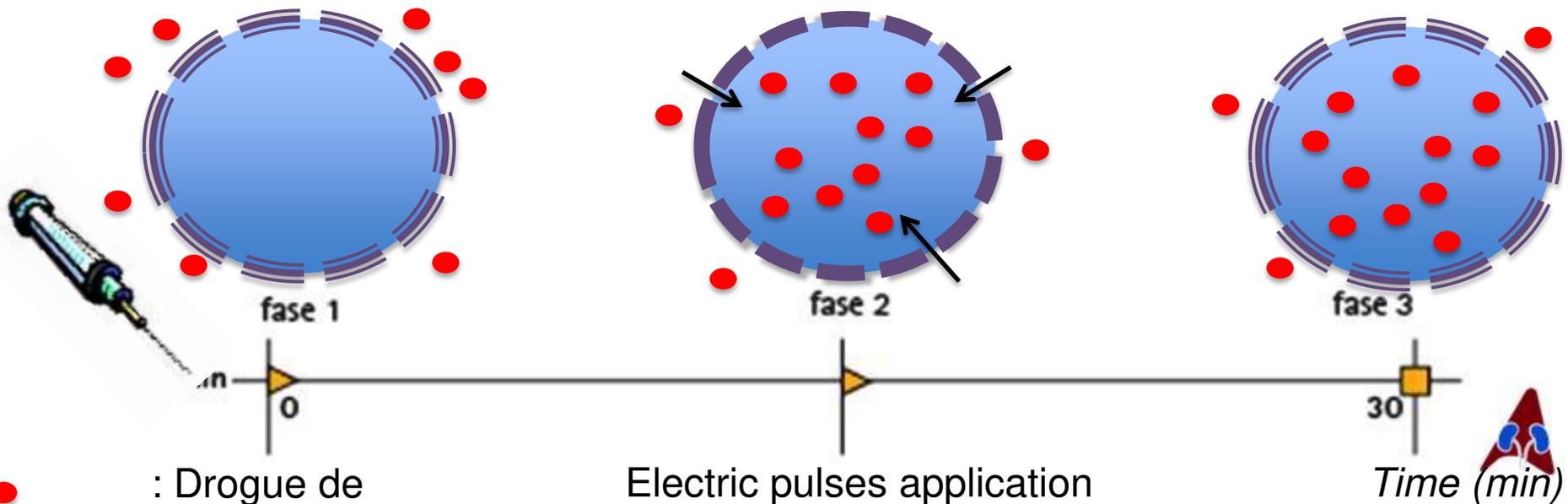
- **Electro-genetherapie**

- Incorporation d'acide nucléique / DNA

Chimiothérapie
autour de la cellule

Augmentation de la
perméabilité membranaire
permet l'accès au cytosol

Fermeture des pores
**Action spécifique sur
cellules tumorales**



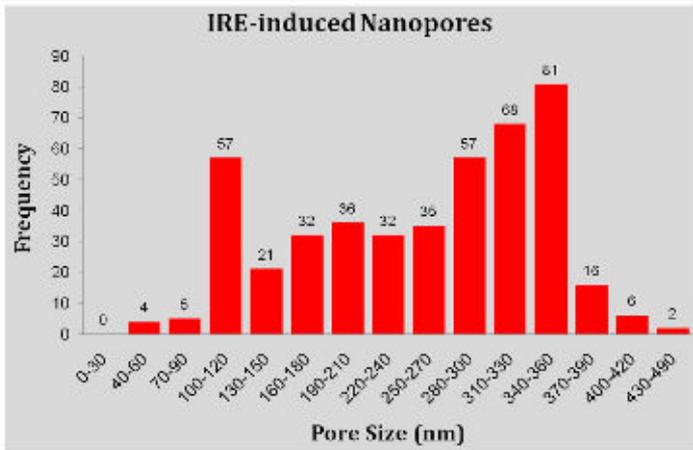
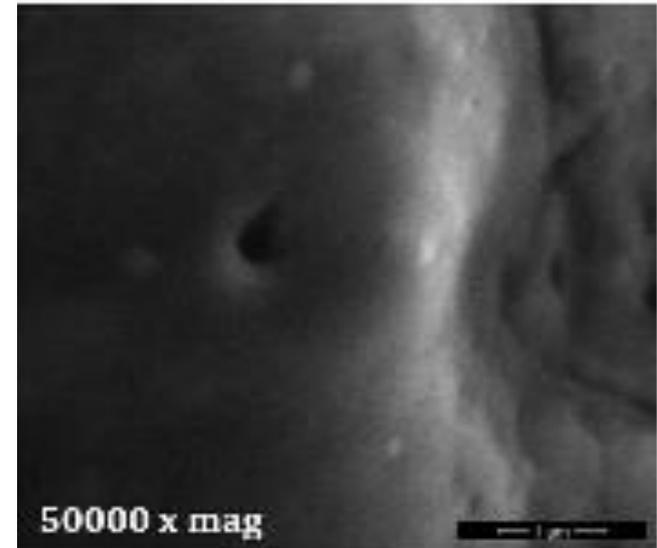


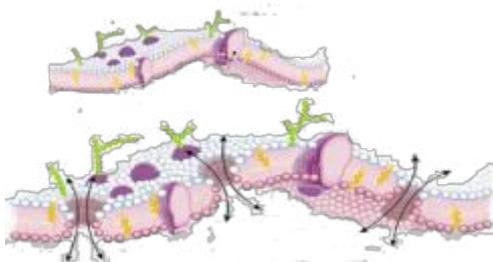
Figure 5. Bar graph showing the range and frequency of the size of nanopores in the IRE-ablated zone; sizes ranged from 40–490 nm and the highest frequency of pore size was noted to be in bimodal distribution at the size of 340–360 nm followed by 310–330 nm, 280–300 nm, and 100–120 nm. (Available in color online at www.jvir.org.)

Average nanopore size:

- RE-induced= 49.7 nm (10–120 nm)
- IRE-induced= 254.7 nm (0–490 nm)



- (i) the distance from the energy source,
- (ii) the strength of the electrical field,
- (iii) the duration of the treatment



Electron Microscopic Demonstration and Evaluation of Irreversible Electroporation-Induced Nanopores on Hepatocyte Membranes

Edward W. Lee, MD, PhD, Daphne Wong, BS, Sergey V. Prikhodko, PhD, Alejandro Perez, BS, Cassidy Tran, BS, Christopher T. Loh, MD, and Stephen T. Kee, MD

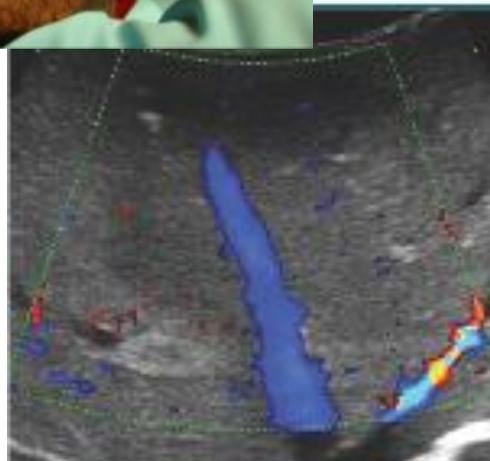
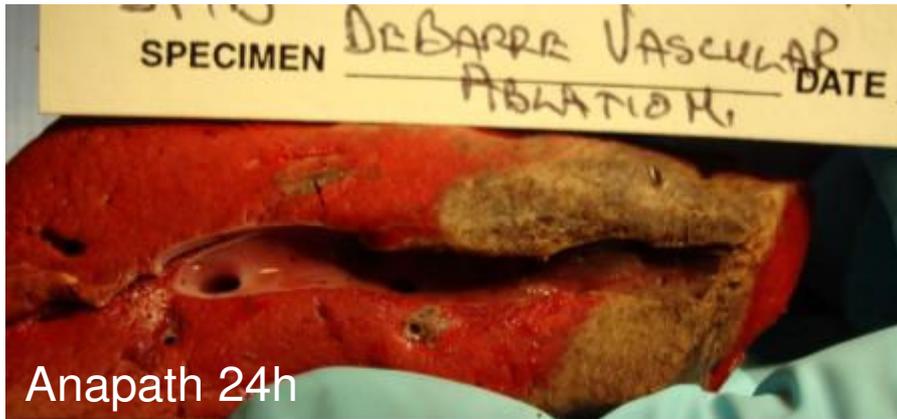


Electroporation

IRREVERSIBLE (IRE)

7e Rencontre Patients de l'Association A.R.Tu.R.

- non thermal ablation (no heat sink effect???, more predictable ablation area???)

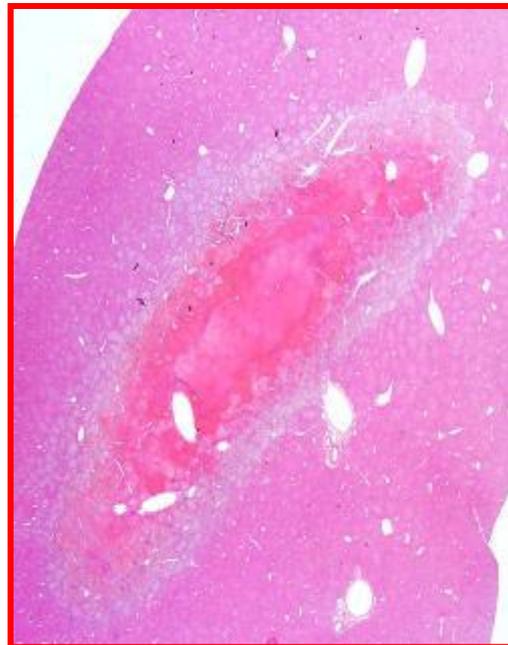


Electroporation

IRREVERSIBLE (IRE)

7e Rencontre Patients de l'Association A.R.Tu.R.

- non thermal ablation (no heat sink effect???, more predictable ablation area???)
- hypoechoic area of ablation during and immediately after IRE
- sharp line of demarcation (ablated/ non-ablated areas)



Electroporation

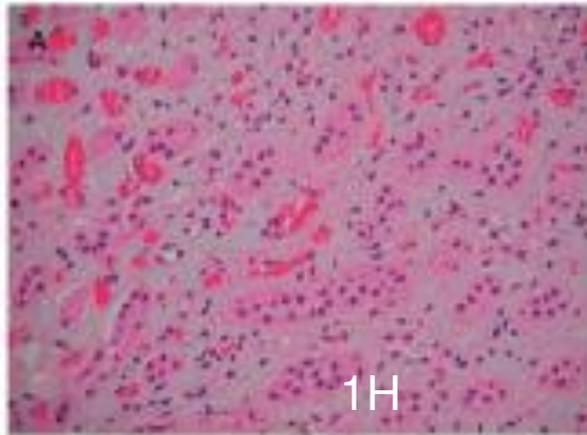
IRREVERSIBLE (IRE)

7e Rencontre Patients de l'Association A.R.Tu.R.

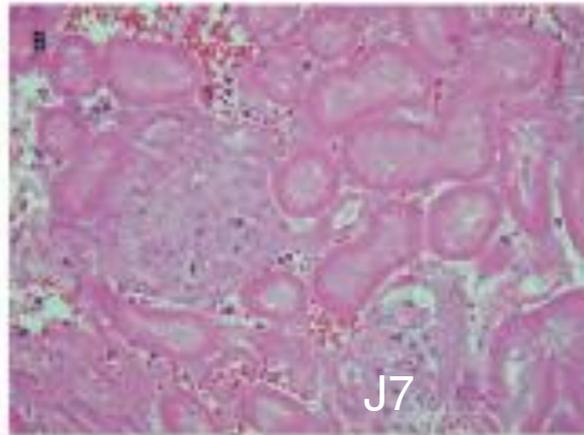
- non thermal ablation (no heat sink effect???, *more predictable ablation area???*)
- hypoechoic area of ablation during and immediately after IRE
- sharp line of demarcation (ablated/ non-ablated areas)
- cellular destruction, preservation of underlying collagen network of tissue (basic tissue structure preserved)



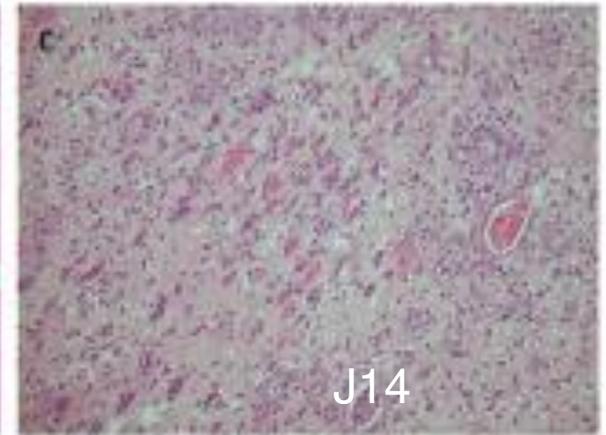
IRE for renal ablation?



Cellular apoptosis



Necrosis,
Minimal inflammation



Stromal fibrosis,
Chronic inflammation



24 IREs/ 8 pigs

BJUI Irreversible electroporation (IRE): a novel method
for renal tissue ablation

Chad R. Tracy, Wareef Kabbani* and Jeffrey A. Cadeddu[†]

Department of Urology, University of Iowa, Iowa City, IA, and Departments of *Pathology and [†]Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Accepted for publication 7 May 2010

Urothelial sparing?

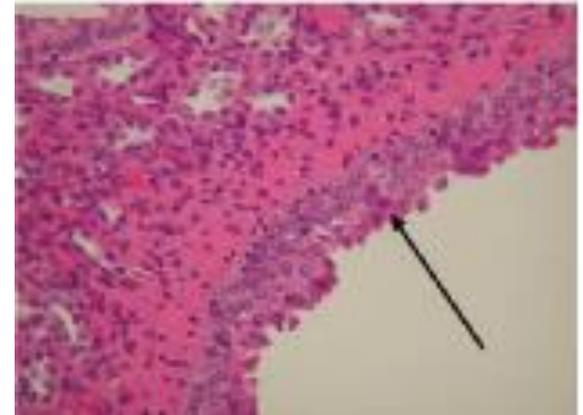
7e Rencontre Patients de l'Association A.R.Tu.R.

16 direct involvement during ablation:

40% urothelial damages (n=6)

- ulceration, necrosis
- with repair/regrowth by 14 days
- no urinoma at sacrifice

FIG. 5. H&E stained porcine renal tissue at 1 h after IRE, the urothelium (arrow) appears normal with adjacent tissue showing effective ablation, as shown by nuclear pyknosis and eosinophilia.



24 IREs/ 8 pigs

BJUI
BJUI INTERNATIONAL

Irreversible electroporation (IRE): a novel method for renal tissue ablation

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Urothelial sparing?

7e Rencontre Patients de l'Association A.R.Tu.R.



Urinary Tract Effects After Multifocal Nonthermal Irreversible Electroporation of the Kidney: Acute and Chronic Monitoring by Magnetic Resonance Imaging, Intravenous Urography and Urinary Cytology

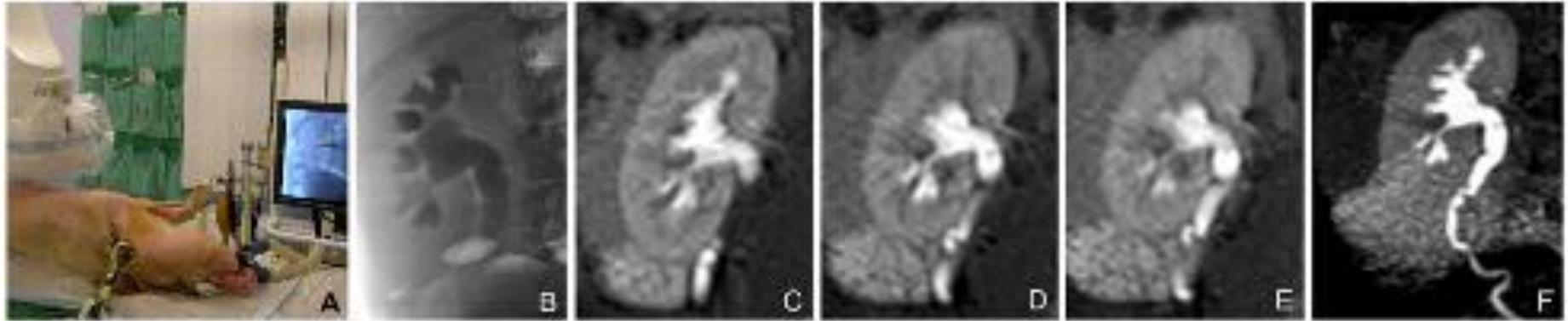
24 IREs/ 8 pigs

Johann Jakob Wendler · Maciej Pech · Markus Porsch · Andreas Janitzky ·
Frank Fischbach · Peter Buhtz · Klaus Vogler · Sarah Hühne · Katrin Borucki ·
Christof Strang · Dirk Mahnkopf · Jens Ricke · Uwe-Bernd Liehr

CVIR
2011

Urothelial sparing?

Blood test (Creatinine), UIV at 3 days, MRI at 7 and 28 days



- 1 macrohaematuria with transient increase of creat
- No renal failure
- No extravasation, no fistula, no ulceration, no shrinkage

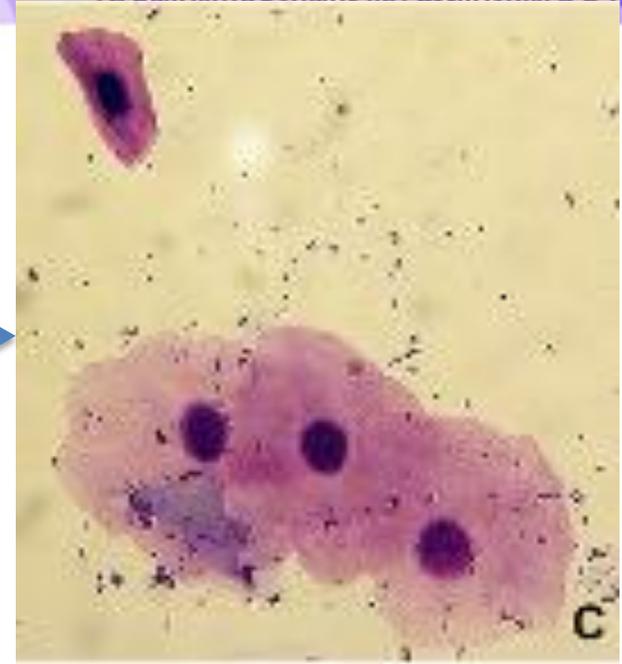
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Urothelial sparing?



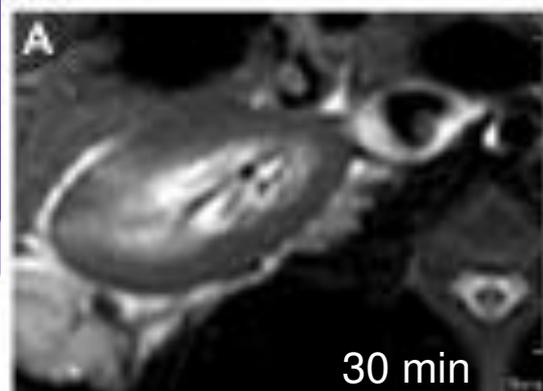
J1: degenerated transitional urothelium cell nuclei

J3: normal cytology

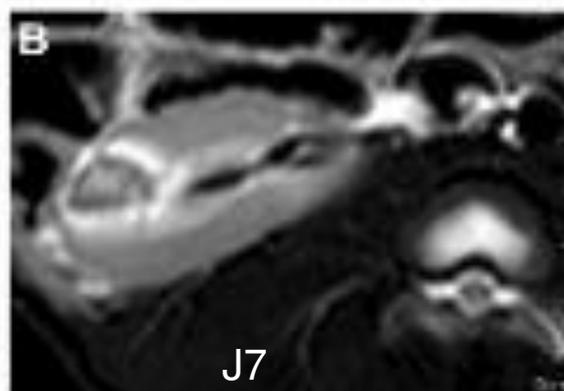
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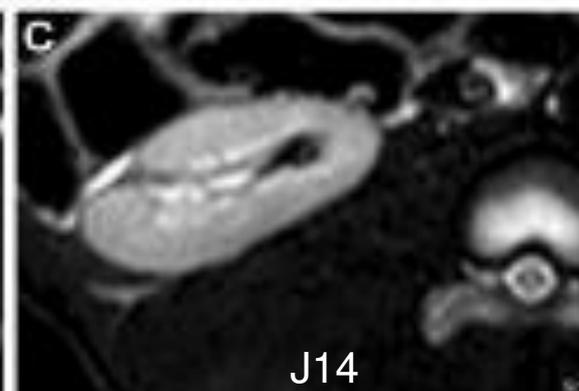
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30 min



J7



J14

R.

Pig no.	NTIRE, technique, electrodes	Renal position of ablation zone	Lesion size on MRI at day 7 (mm)	Lesion size on MRI at day 28 (mm)	Macroscopic lesion shape on surface at day 28 (mm)	Macroscopic lesion size on surface at day 28 (mm)	Microscopic lesion size at day 28 (mm)
1	1 Bipolar	UP, ventrolateral	26 × 13 × 13	13 × 10 × 5	Elongate	15 × 3	15 × 8 × 4
1	1 Bipolar	MP, ventrolateral	19 × 16 × 12	5 × 6 × 6	Circular	6 × 6	8 × 6 × 4
1	3 monopolar	LP, ventrolateral	15 × 17 × 10	4 × 10 × 4	Star-shaped	6 × 6 × 5	6 × 8 × 4
2	1 Bipolar	UP, dorsolateral	15 × 14 × 13	8 × 10 × 6	Circular	9 × 9	9 × 9 × 8
2	3 Monopolar	MP, dorsolateral	17 × 14 × 13	10 × 8 × 4	Circular	12 × 11	12 × 10 × 6
3	1 Bipolar	UP, ventrolateral	21 × 9 × 9	12 × 5 × 4	Elongate	20 × 4	20 × 6 × 5
3	1 Bipolar	MP, ventrolateral	10 × 13 × 12	7 × 7 × 7	Circular	5 × 4	5 × 9 × 7
3	1 Bipolar	LP, ventrolateral	9 × 11 × 9	6 × 6 × 4	Circular	6 × 4	8 × 8 × 7

Length × width × depth. Upper pole with upper principal calyces (UP), lower pole with lower principal calyces (LP), and middle part with medium principal calyces and renal pelvis (MP)

Evolution cicatrice rapide
IRM= Macro=
microscopique

8 IREs/ 3 pigs

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Tu.R.

- No changes in cardiac function after IRE
- One case of supraventricular extrasystole
- No immediate adverse effects of IRE

Irreversible Electroporation of Renal Cell Carcinoma: A First-in-Man Phase I Clinical Study

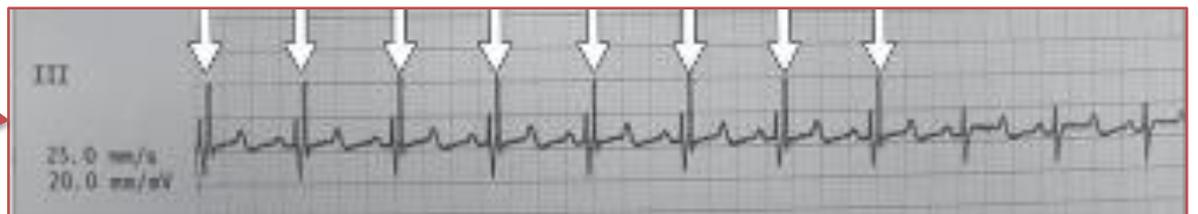
n= 6

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Christof Strang · Simon Blaschke · Oliver Dudeck ·
Jens Ricke · Uwe-Bernd Liehr

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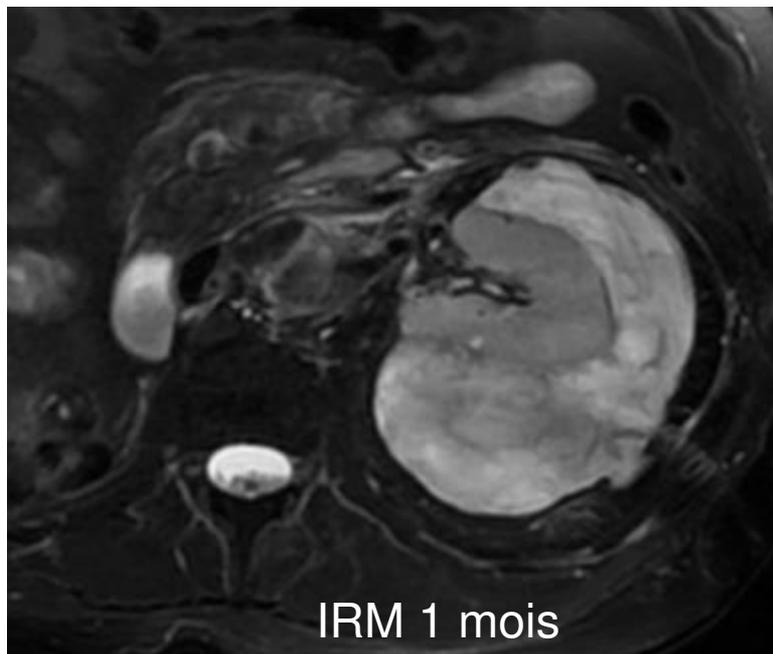


High voltage generator (1000–3000 V per pulse)





Récidive à 1



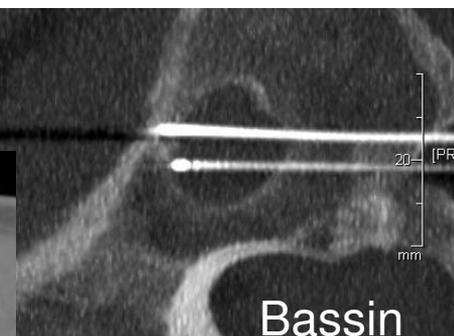
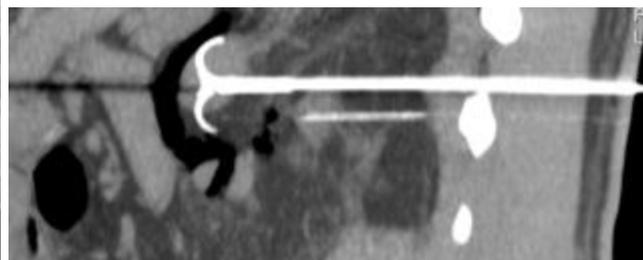
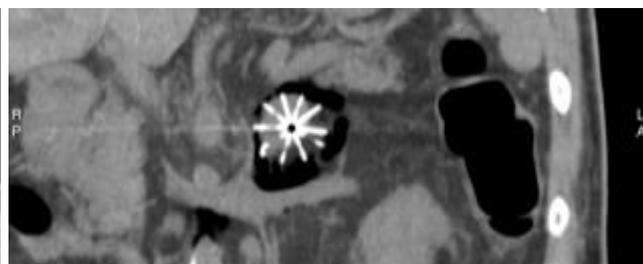
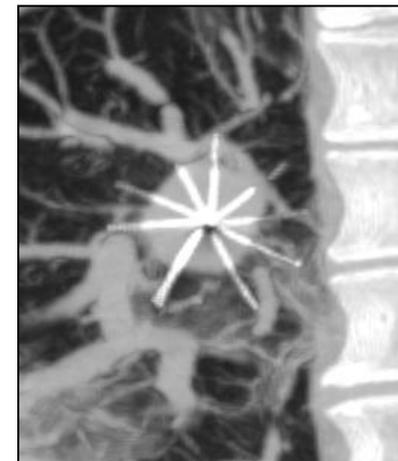
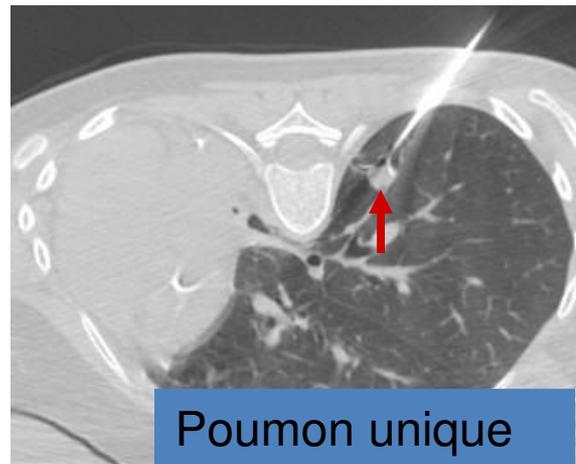
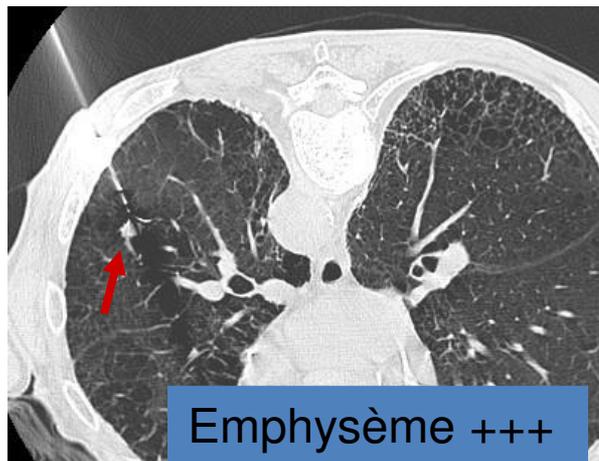
IRM 1 mois

	Créatininémie (micromol/l)
J0	90
J1	169
J2	202
J3	241
J6	160
J10	111
J30	100



Technique « ablathermie » percutanée → curatif des métastases: < 3-4 cm

7e Rencontre Patients de l'Association A.R.Tu.R.



Conclusion

7e Rencontre Patients de l'Association A.R.Tu.R.

- Radiofrequence et cryotherapie:
 - technique mini-invasive
 - efficace pour petite tumeurs (< 4cm)
 - épargne « néphronique »
- Association à embolisation artérielle ou anti-angiogénique pour tumeur plus volumineuse?
- Electroporation?

