Cancer bronchiques primitifs inopérables : radiofréquence pulmonaire

(indications, contrindications, complications, alternatives)

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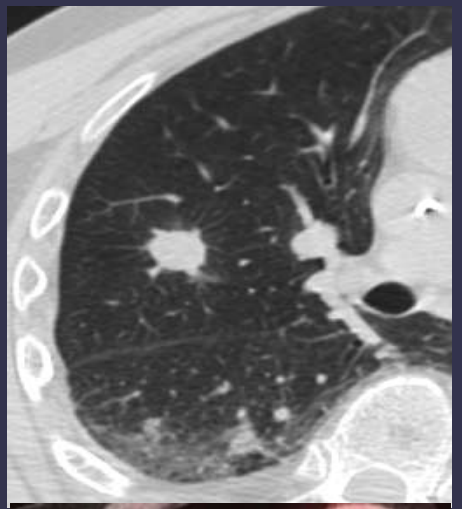
VILLEJUIF - www.igr.fr

Biopsies ? Oui

Avant Ttt ? Pendant Ttt (avant / après) ?



La radiofréquence

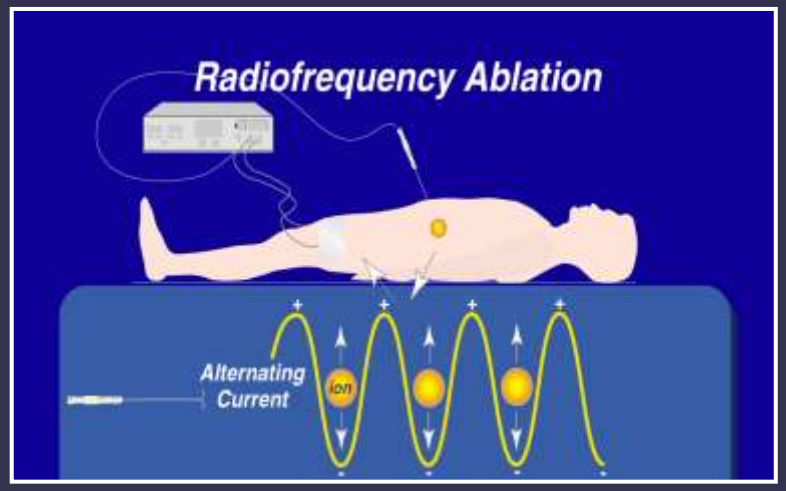
comment ça marche

Destruction thermique

Temp > 60°C

Mort cellulaire immédiate

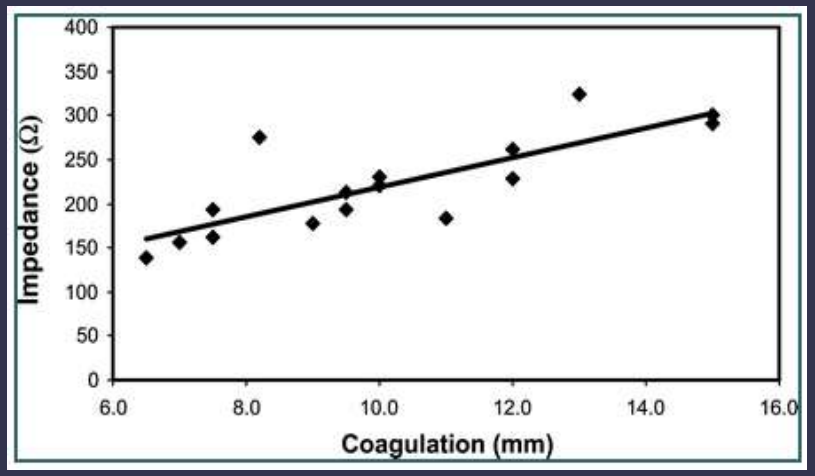
- 420 - 500kHz courant sinusoïdal
  - agitation ionique
  - Echauffement par friction
  - Coagulation des tissues



Lung is RF friendly

- **Volume of ablation for a given quantity of RF energy**
  - **Lung (13 ± 3.5 mm)**
  - **Soft tissue (9.8 ± 1.0 mm)**
  - **Kidney (7.3 ± 0.6 mm)**

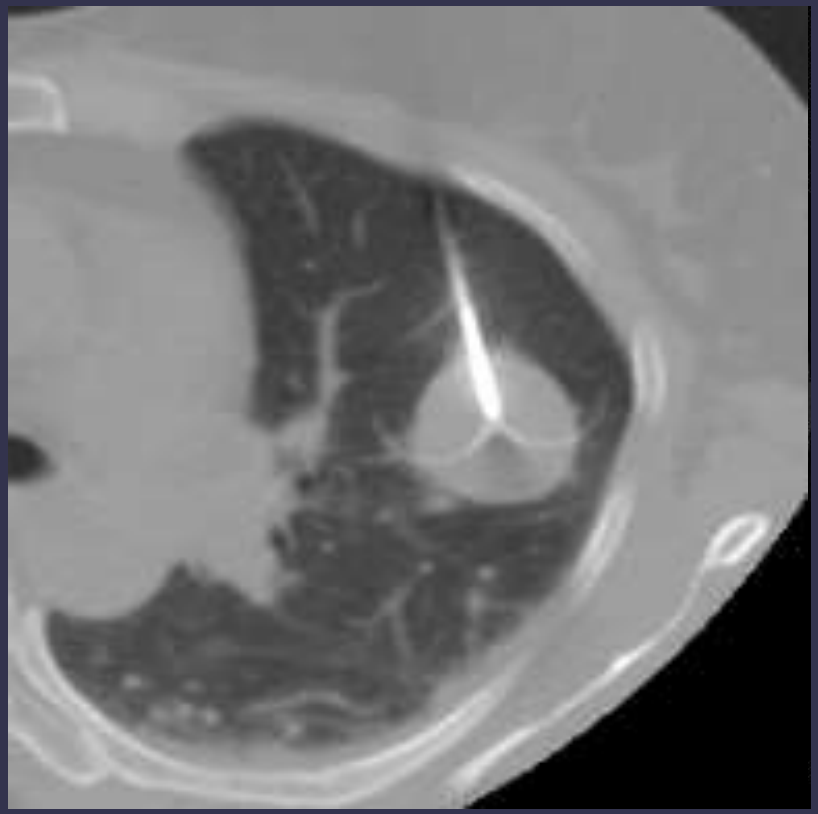
(Ahmed M, Radiology 2004)



- **Lung tissue provides high degree of thermal and electric insulation**

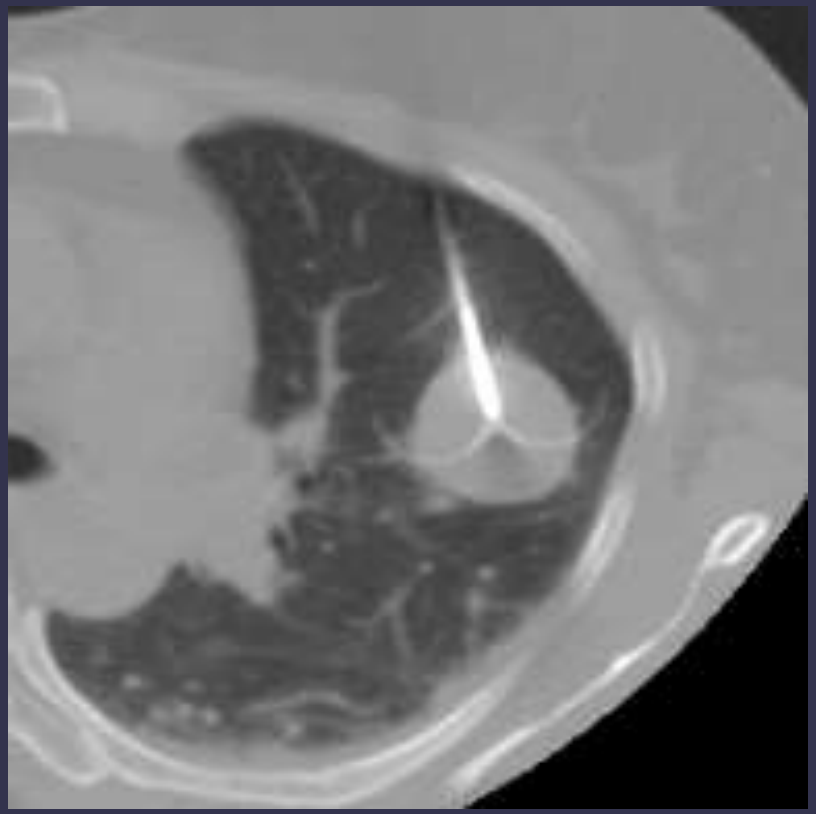
La radiofréquence (RFA)

en pratique



La radiofréquence (RFA)

en pratique



La radiofréquence (RFA)

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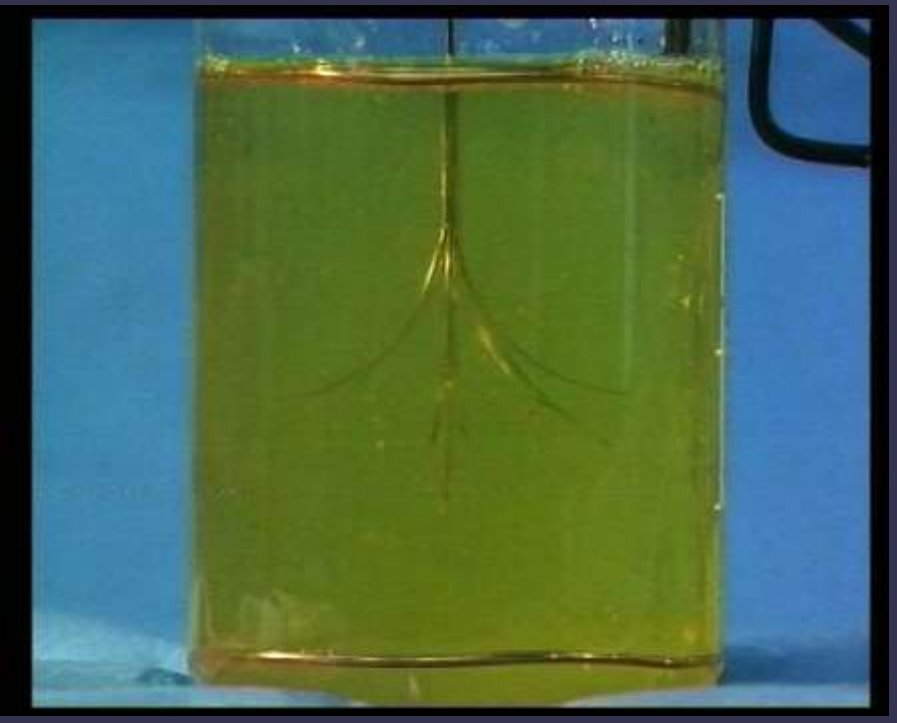
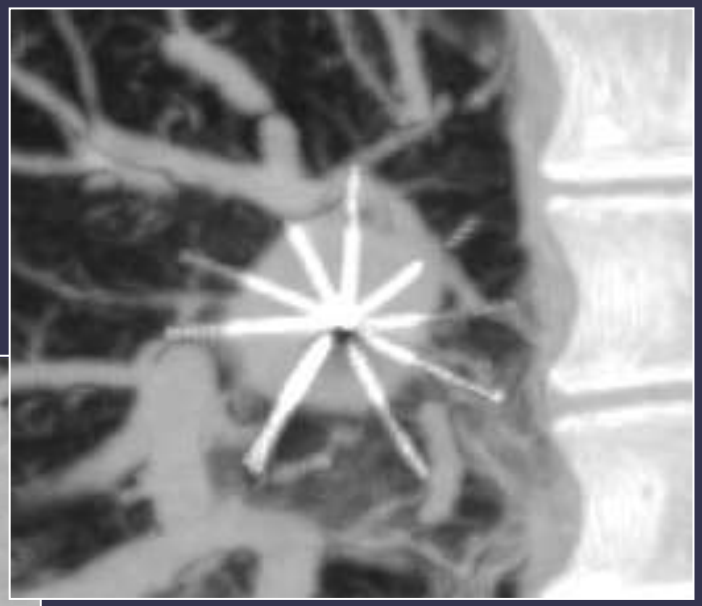


La radiofréquence

comment ça marche

le poumon est un milieu favorable



La radiofréquence détruit complètement des tumeurs pulmonaires

- **Destruction complète de tumeurs chez l'animal**
  - **Modéme VX2 lapin (foie et poumon)**

(Goldberg SN, Acad Radiol 1996)

Pathologic Assessment of Radiofrequency Ablation of Pulmonary Metastases

Jeffrey D. Jaskolka, MD, FRCPC , John R. Kachura, MD, FRCPC , David M. Hwang, MD, FRCPC, Ming S. Tsao, MD, FRCPC, Thomas K. Waddell, MD, FRCSC, Murray R. Asch, MD, FRCPC, Gail E. Darling, MD, FRCSC, and Michael R. Johnston, MD, FRCSC

Patient Demographics

Primary Tumor	Lesion size (cm)
Colorectal carcinoma	2.2
Osteosarcoma	1.2
Colorectal carcinoma	2.5
Leiomyosarcoma (uterus)	1.5
Colorectal carcinoma	3.0
Colorectal carcinoma	2.1
Synovial sarcoma	1.7
Malignant fibrous histiocytoma	2.6
Osteosarcoma	2.5

- Ablation/résection de 9 métastases pulmonaires

100% nécrose coagulation sur toutes les métastases

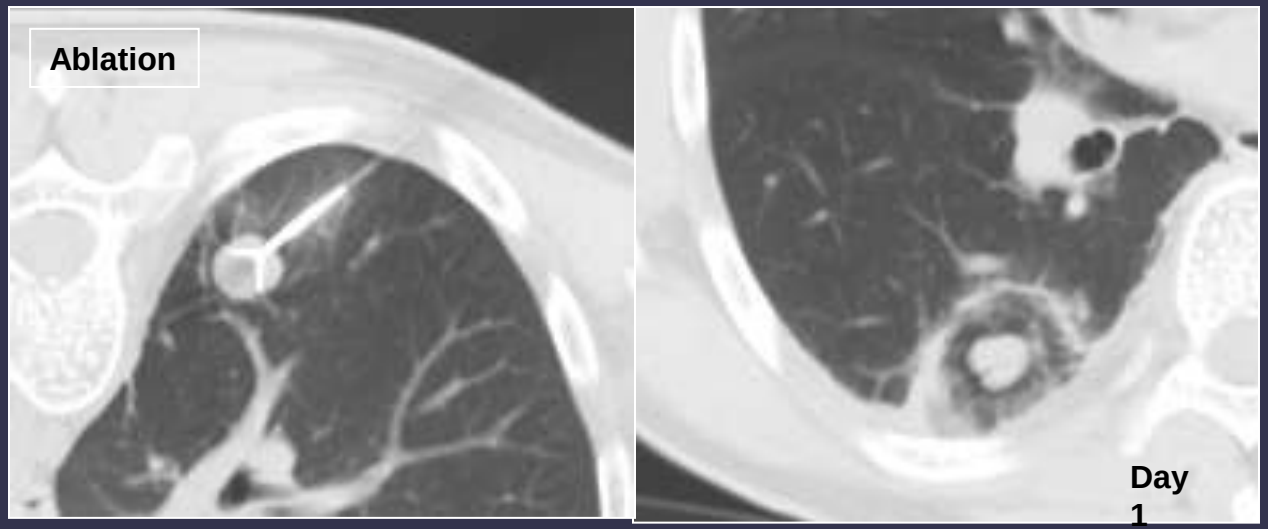
(Jasolka JD, JVIR 2010)

La radiofréquence détruit complètement des tumeurs pulmonaires

Marges d'ablation

4% ablation incomplète si ratio surface ablation / surface tumeur ≥ 4
19% ablation incomplète si ratio surface ablation / surface tumeur < 4

(p=0.02)
(de Baere T, Radiology 2006)



	Nb of tumors	Effectiveness		
Estimated ratio of ablation volume to tumor volume		1 year	2 years	<.0001
≥3	188	83	70	
<3	154	61	50	

(Hiraki T, Cancer 2006)

La radiofréquence détruit complètement des tumeurs pulmonaires

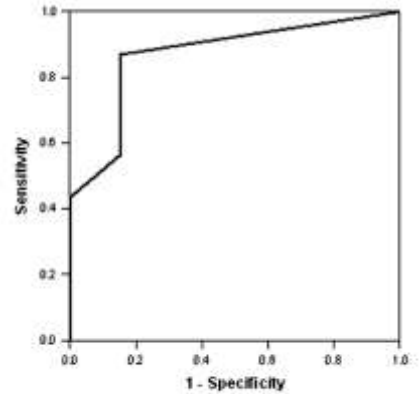


Fig. 1 Receiver operating characteristic curve constructed from recurrence at ground glass opacification margin minimal width. Area under curve 0.868 ± 0.124 (95% confidence interval)

Table 3 Multivariate analysis

Characteristic	*p*-Value	Hazard ratio for recurrence (95% CI)
Minimal GGO margin depth (mm)	0.005	0.460 (0.267–0.794)
Adjacent vessel <3 mm ($n = 11$)	0.017	15.54 (1.63–148.58)
Maximal GGO margin depth (mm)	0.314	–
Size of lesion	0.415	–
Lobar location[a]	0.169	–
Adjacent bronchus	0.351	–
Zonal location by thirds	0.169	–

95% CI—95% confidence interval, *GGO* ground glass opacification

[a] Upper $n = 16$, middle/lingula $n = 2$, lower $n = 18$

Ground glass opacity margin width (p=0.005)

Receiver Operator Characterixtics suggest a cut off of 4.5 mm for 100% specificity (no recurrence)

(Gillams A CVIR 2009)

La radiofréquence détruit complètement des tumeurs pulmonaires

Traitement des petites tumeurs

3% to 38.1% (med = 11.2%) : review 24 publications, 1.7 cm med size

(Zhu JC, Annals surg oncol. 2008)

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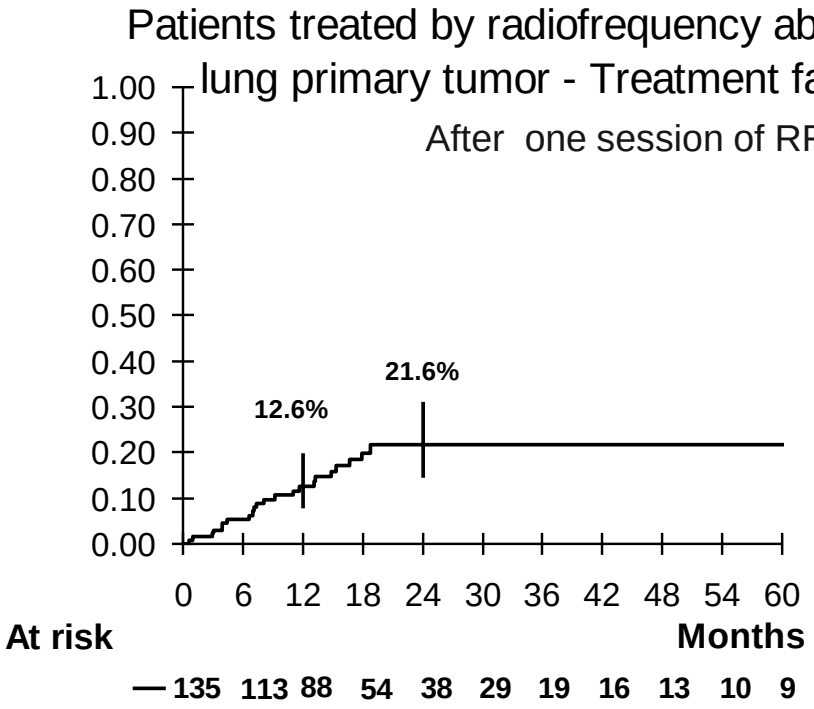
131 NSCLC T1/T2; N0
Tumeurs (125/131 preuve histo.)
T1a : 59 45%
T1b : 45 34%
T2a : 27 21%



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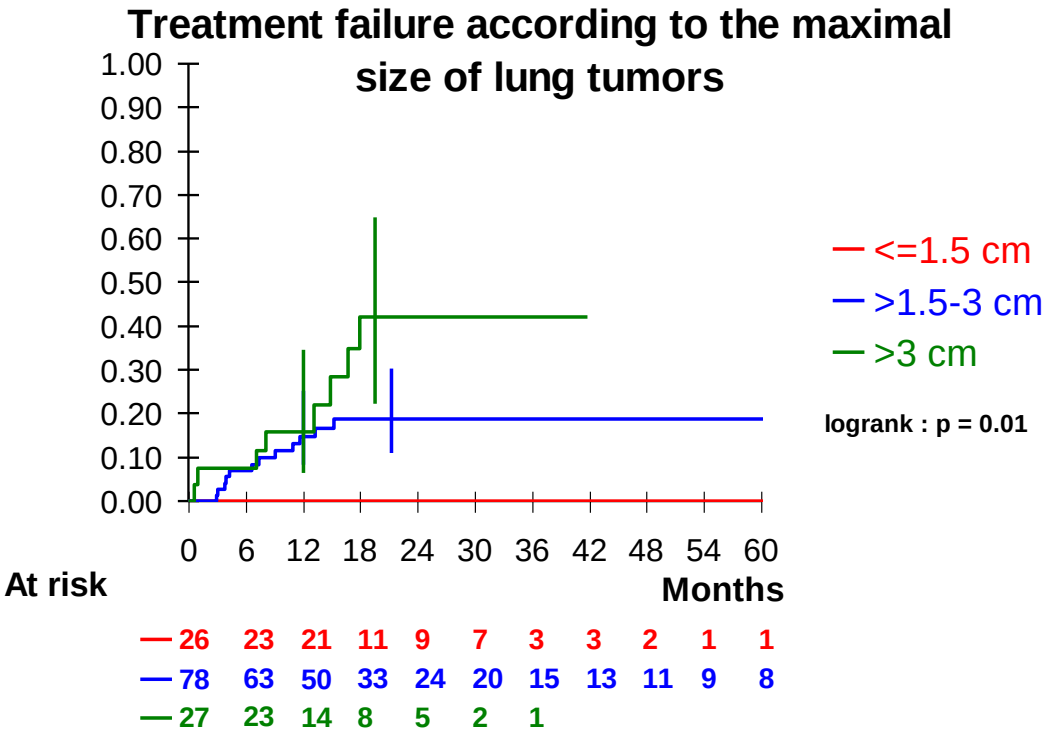
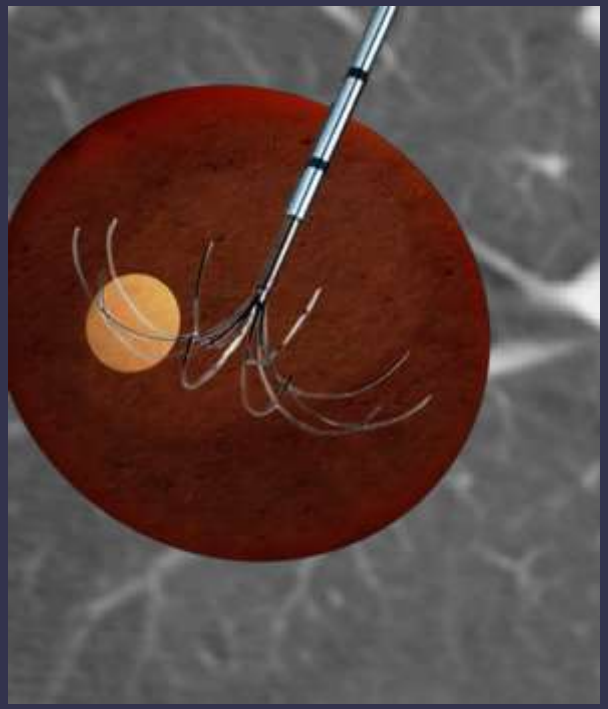
	<=1.5 cm (n=26)	>1.5-2 cm (n=33)	>2-3 cm (n=45)	>3 cm (n=27)
2 years	0%	21.9% (8.1)	16.4% (6.2)	42.1% (12)



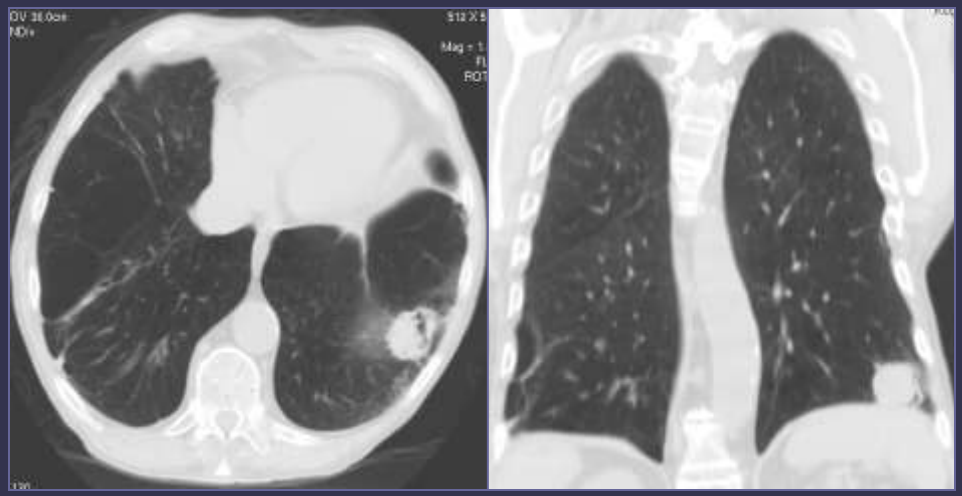
La radiofréquence détruit complètement des tumeurs pulmonaires

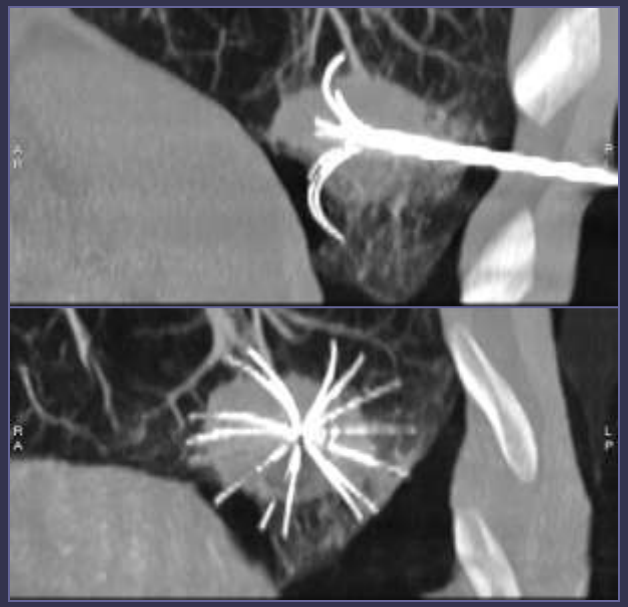
- **Trop petit pour la radiofréquence ?**



Mal situé pour la radiofréquence ?

- **Contact vaisseaux > 3mm**
- **Sommet du poumon si poumon accolé**
- **Contact mediastin supérieur (nerf phrénique)**





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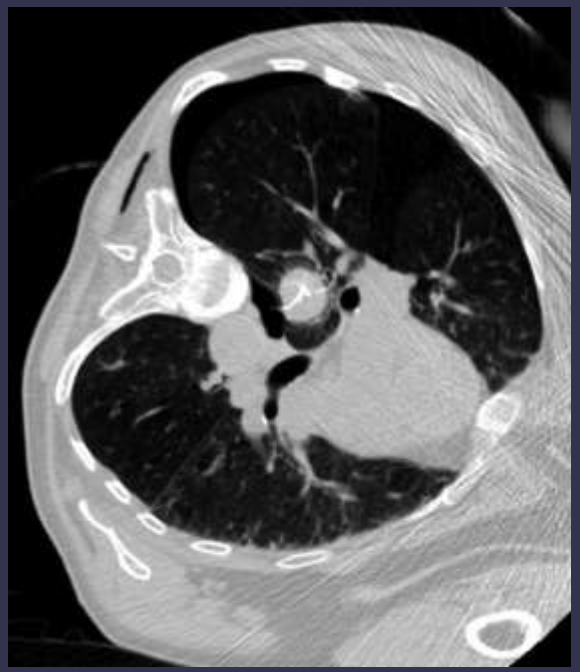

Radiofréquence et survie NSCLC

Population 131 NSCLC T1/T2; N0
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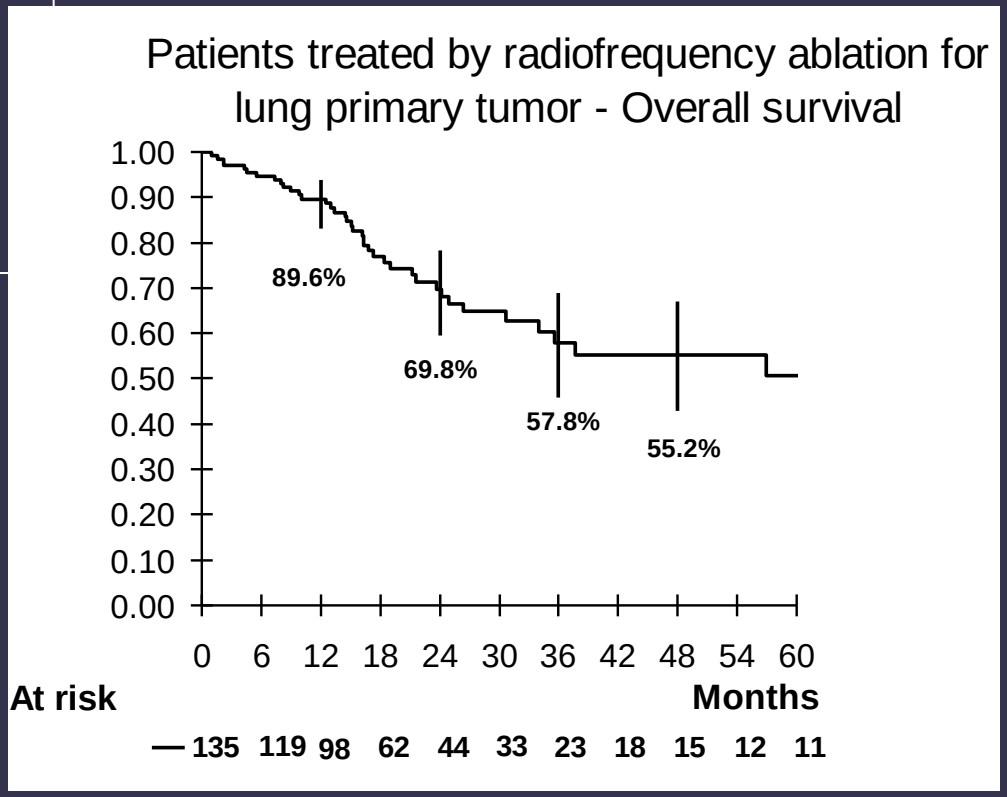


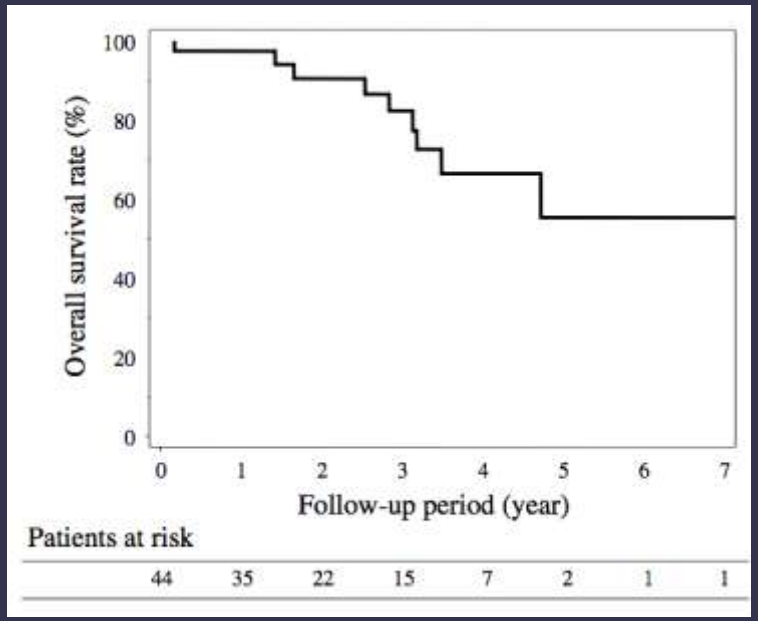
1st NSCLC or DFI > 1 year	YES (n=87)	NO (n=12)	
4 year OS	62.2% ± 6.8	39.7% ± 16	0.08

CLINICAL INVESTIGATION INTERVENTIONAL ONCOLOGY

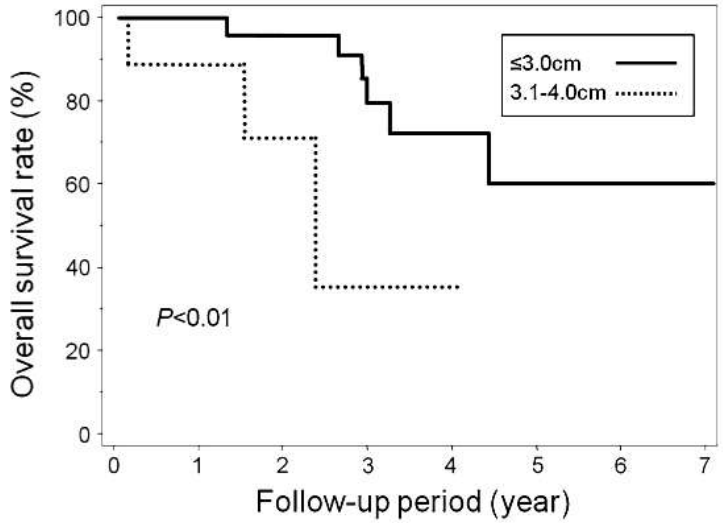
Lung Radiofrequency Ablation for the Treatment of Unresectable Recurrent Non-Small-Cell Lung Cancer After Surgical Intervention

44 patients (26 male and 18 female)
51 recurrent NSCLC
mean diameter 1.7 ± 0.9 cm, range 0.6 to 4.0)

1-, 3-, and 5-year overall survival rates were 97.7, 72.9, and 55.7%



	Hazard ratio	95% CI	*P*
Tumor size >3 cm	12.37	4.63–33.02	0.01



Patients at risk

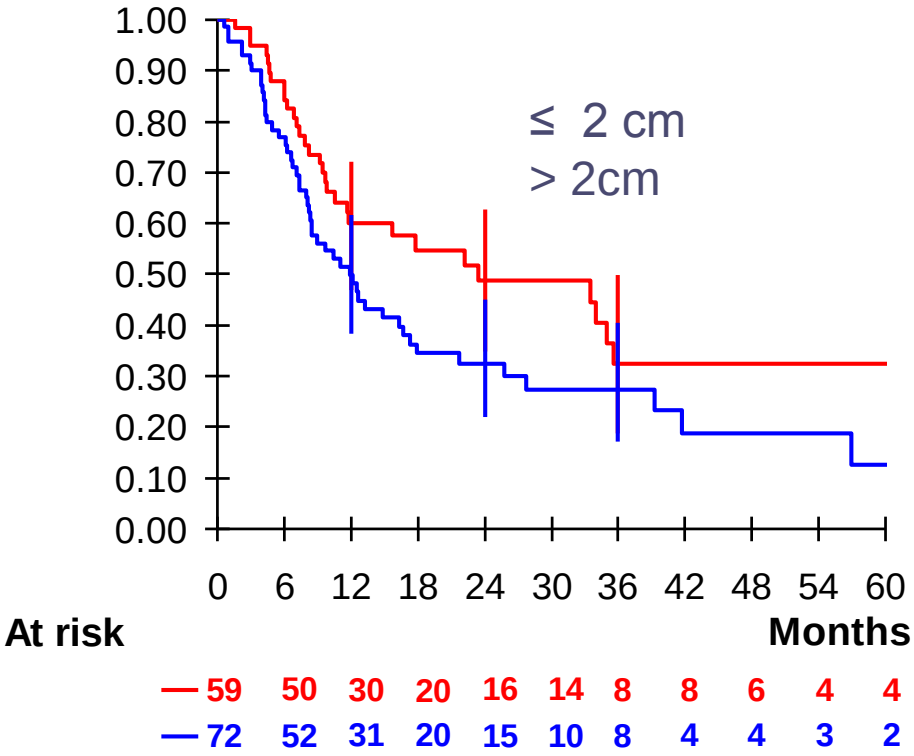
≤3.0cm	38	30	21	14	6	2	1	1
3.1-4.0cm	6	4	2	1				

(Kodama H, Cardiovasc Intervent Radiol 2012; 35:563–56

Radiofréquence et survie NSCLC

- **Size of the target tumor**

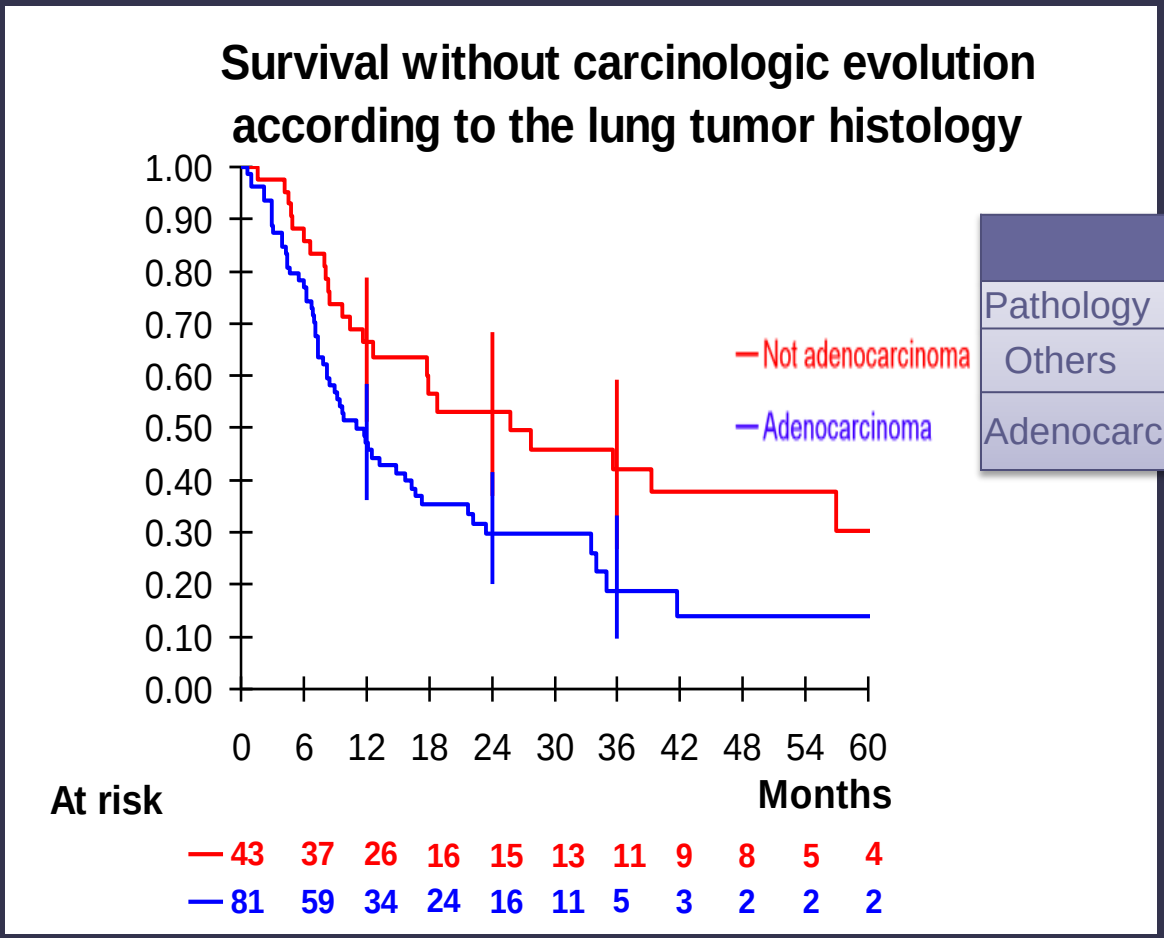
Survival without carcinologic evolution according to the maximal size of lung tumors



	HR	IC95%	p
Max Size			
<=2 cm	1		
>2 cm	1.6	1.00-2.5	0.050

Radiofréquence et survie NSCLC

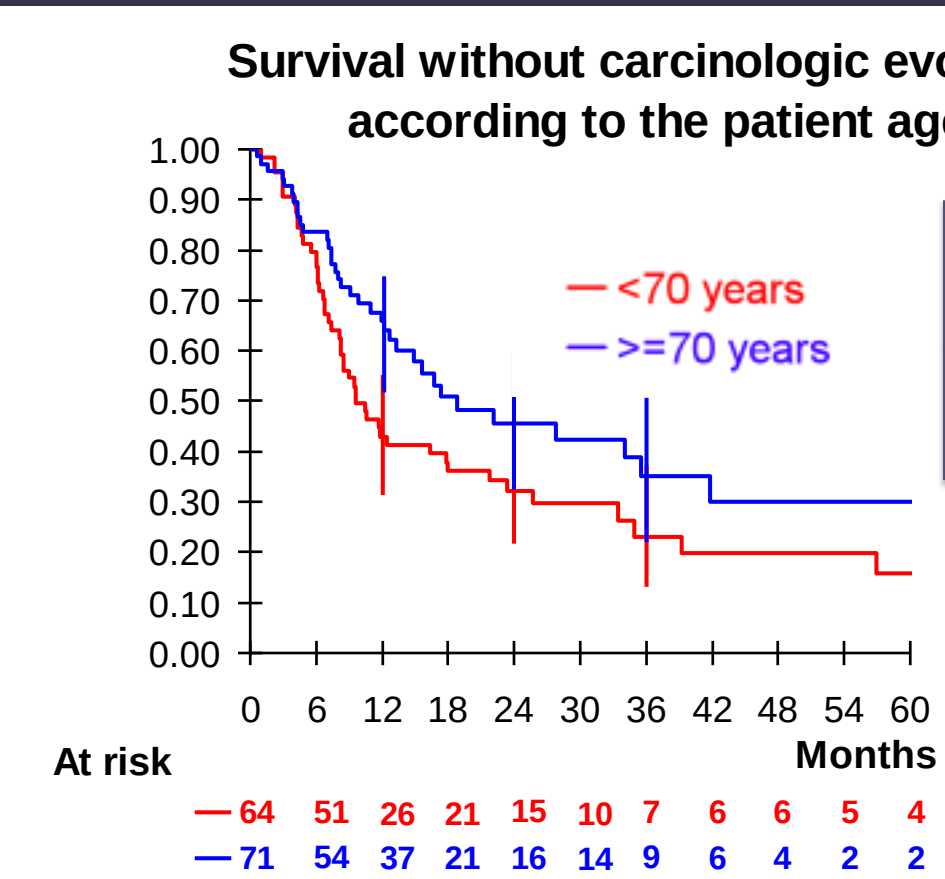
Disease Free Survival mutivariate analysis



	HR	IC95%	p
Pathology			
Others	1		
Adenocarcinoma	1.95	1.17-3.2	0.011

Radiofréquence et survie NSCLC

Disease Free Survival mutivariate analysis



	HR	IC95%	p
Age			
<70 ans	1		
>=70 ans	0.62	0.39-0.96	0.033

lussiére J, de Baere T. CIRSE 2011)

La radofréquence n'altère pas la fonction respiratoire

	Before RF	1 month after RF
FEV1	**2.2 (0.62-3.75)**	**2.1 (0.72-3.61)**
VC	**2.77 (0.8-7.9)**	**2.6 (0.83-5.43)**

(de Baere T, Radiology 2006)

	Baseline	1 month	3 months	6 months	12 months
NSCLC (n=22)					
FEV, L	1·9 (0·9)	1·7 (1·1)	1·7 (0·9)	1·6 (0·9)	1·5 (0·7)
FEV % of predicted	68·8 (26·9)	65·3 (24·6)	71·0 (27·2)	62·5 (18·5)	63·4 (20·7)
FVC, L	2·9 (0·9)	2·6 (1·1)	2·8 (0·8)	2·7 (0·9)	2·7 (1·0)
FVC % of predicted	82·4 (18·1)	77·2 (16·2)	82·0 (19·5)	76·7 (12·4)	74·5 (18·3)
CRC metastases (n=41)					
FEV, L	2·3 (0·9)	2·1 (0·8)	2·2 (1·1)	2·5 (0·9)	2·3 (1·2)
FEV % of predicted	86·0 (23·2)	84·0 (20·8)	87·0 (18·7)	88·6 (24·3)	86·6 (22·9)
FVC, L	2·9 (1·1)	2·9 (0·8)	3·3 (1·0)	3·2 (1·2)	3·0 (0·9)
FVC % of predicted	90·2 (22·3)	85·7 (20·6)	86·9 (21·2)	95·7 (17·7)	94·8 (19·7)
Other metastases (n=16)					
FEV, L	2·1 (0·7)	2·1 (0·8)	1·9 (1·1)	1·9 (0·9)	1·7 (0·9)
FEV % of predicted	92·9 (25·9)	87·8 (33·5)	82·0 (41·1)	84·0 (30·8)	81·5 (32·3)
FVC, L	2·6 (1·2)	2·3 (1·4)	2·9 (1·1)	3·0 (1·1)	2·8 (1·3)
FVC % of predicted	99·3 (22·1)	84·1 (34·9)	88·9 (29·2)	90·8 (16·3)	93·6 (22·5)

Data are mean (SD). Differences were not statistically significant for any of the findings at different follow-up times compared with baseline. NSCLC=non-small-cell lung cancer. FEV=forced expiratory volume. FVC=forced vital capacity. CRC=colorectal carcinoma.

Table 3: Findings of pulmonary function tests before and after radiofrequency ablation in 79 patients followed for 12 months

(Lencioni R, Lancer Oncol 2008)

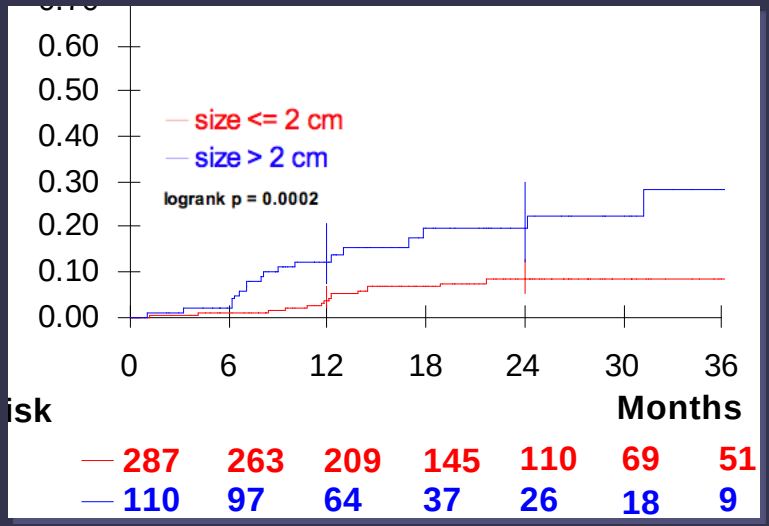
- Traitement à but curateur des malades non opérables

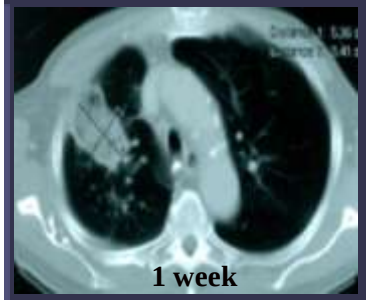
  Seuil inférieur inconnu?

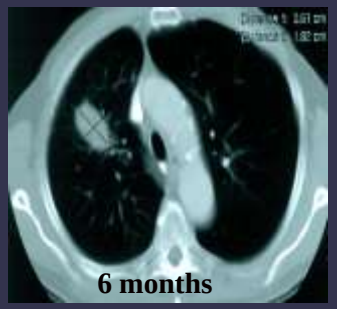
La radofréquence : imagerie de suivi

CT méthode classique

Difficulté à évaluer la prise de contraste
analyse morphologique
➔ découverte tardive des ablations incomplètes





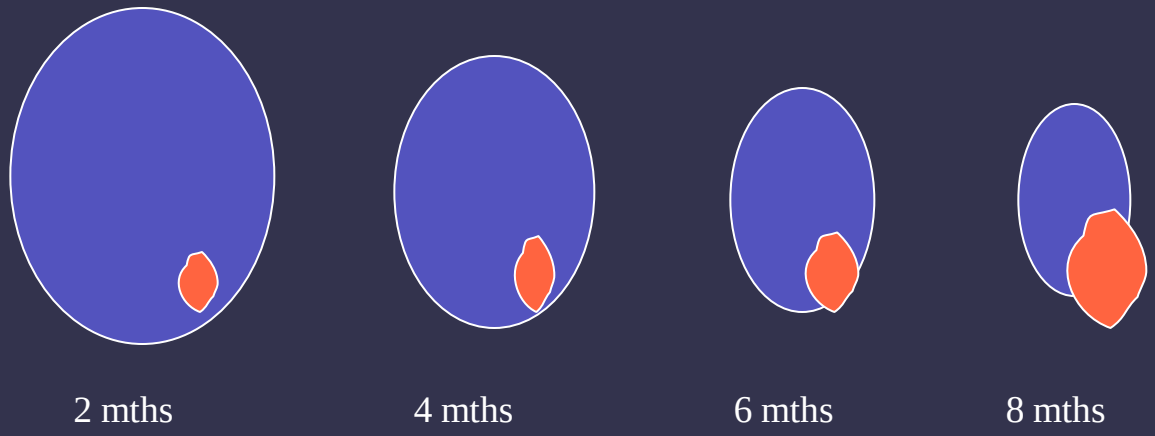


La radofréquence : imagerie de suivi

CT méthode classique

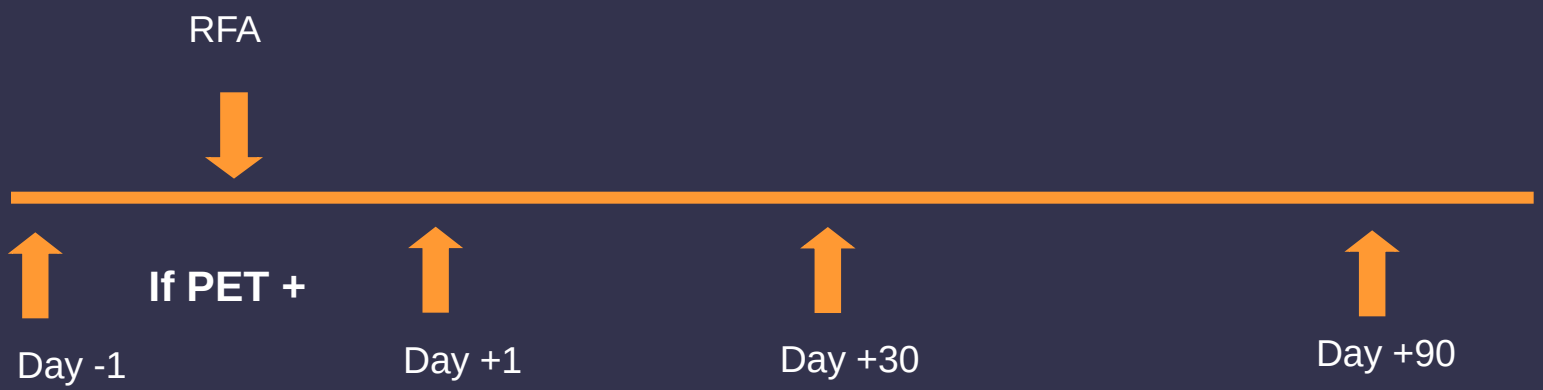
Difficulté à évaluer la prise de contraste
analyse morphologique
➔ découverte tardive des ablations incomplètes

Diminution lente de la zone d'ablation



La radofréquence : imagerie de suivi

- PET-CT ?
- Etude prospective monocentrique (Feb 2004 - Mars 2007)



	TEP D1	TEP D30	TEP M3
28 patients	27	28	24

(De Andreis D. Radiology *2011*)

La radofréquence : imagerie de suivi

PET/CT

28 patients/ 48 RFA	1 month	3 months	6 months	18 months	Overall
PET recurrence	3TP+1FP	4TP+2FP	6TP+1FP	7TP+ 0FP	7/7
CT recurrence	0	1TP+1FP	2TP+1FP	3TP+0FP	3/7**

- 4 fo 7 incomplete ablation detected at 3 months
- 6 of 7 incomplete ablation detected at 6 months

•TP = True positive, FP = False positive
*** patient shave been retreated*

(de Andreis D, Radiology 2011)

1 - 4 days Early PET Tumor Response	Clinical Outcome at 1 y[a] No Event	 Event
Complete response (*n* = 14)	8 (57)	6 (43)
Partial or no response (*n* = 12)	4 (33)	8 (67)

Note—Values in parentheses are percentages. Fisher exact test, $p = 0.27$.
[a]Event is death, progression, or repeat ablation.

6-Month PET Tumor Response	Clinical Outcome at 1 y[a] No Event	 Event
Complete response (*n* = 7)	7 (100)	0 (0)
Partial response (*n* = 9)	2 (22)	7 (78)
Progressive disease (*n* = 7)	2 (29)	5 (71)

Note—Values in parentheses are percentages. Chi-square, $p = 0.004$; Fisher exact test, $p = 0.001$ (complete response vs partial response or progressive disease).
[a]Event is death, progression, or repeat ablation.

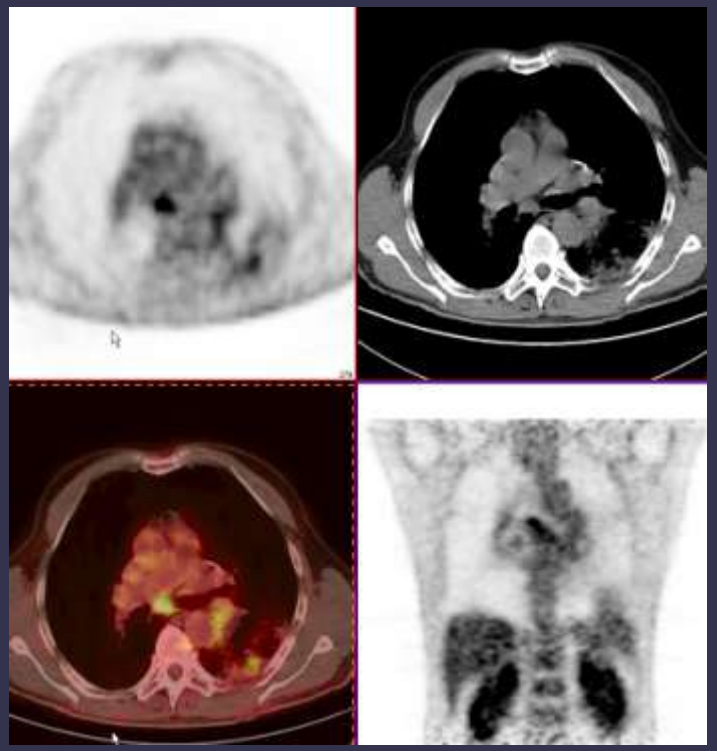
(Yoo DC, AJR 2011)

La radofréquence : imagerie de suivi

PET/CT

Fixation FDG ganglions mediastinaux

J 1 : 15%, 1 mois : 21%, 3 mois : 15%



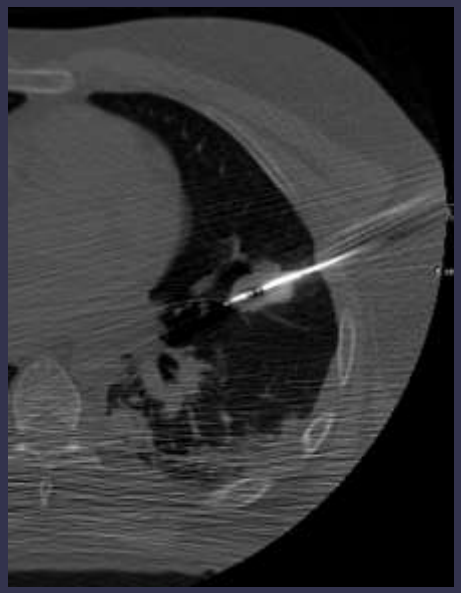
(de Andreis D, Radiology 2011)

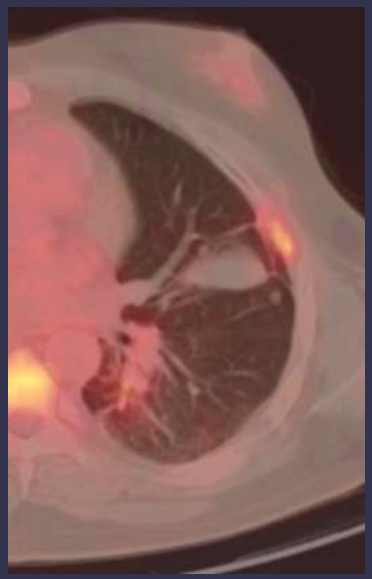
La radofréquence : imagerie de suivi

PET/CT

Fixation FDG du point de ponction

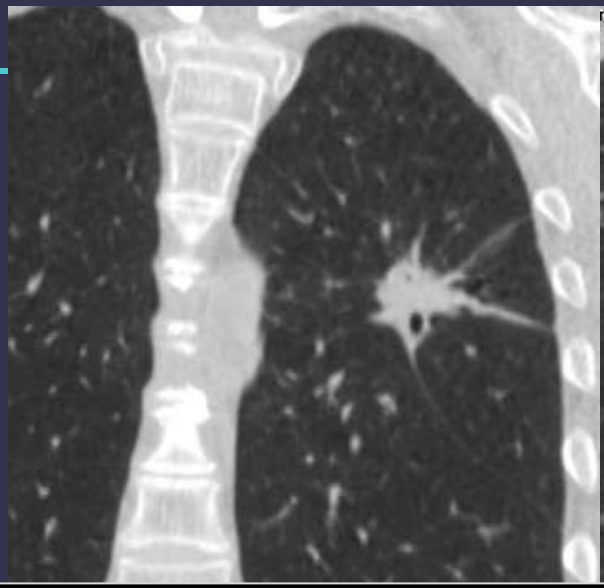
J 1 : 19%, 1 mois : 11%, 3 mois : 15%

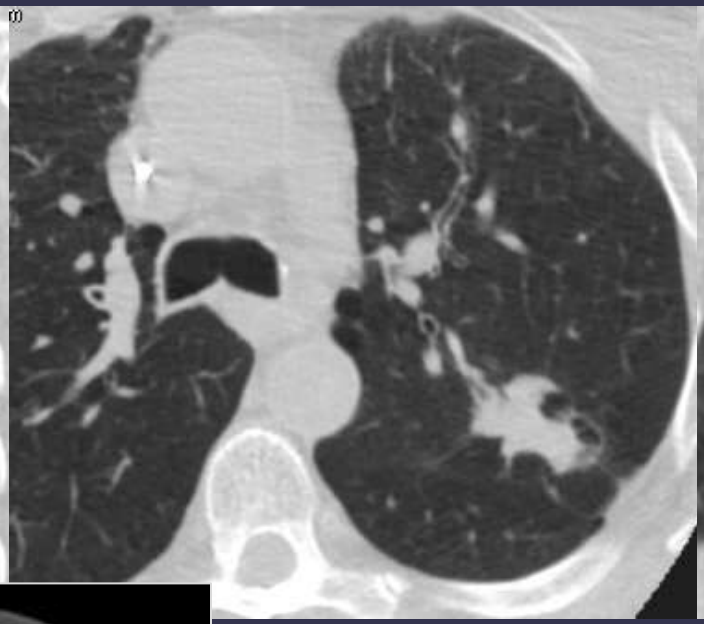


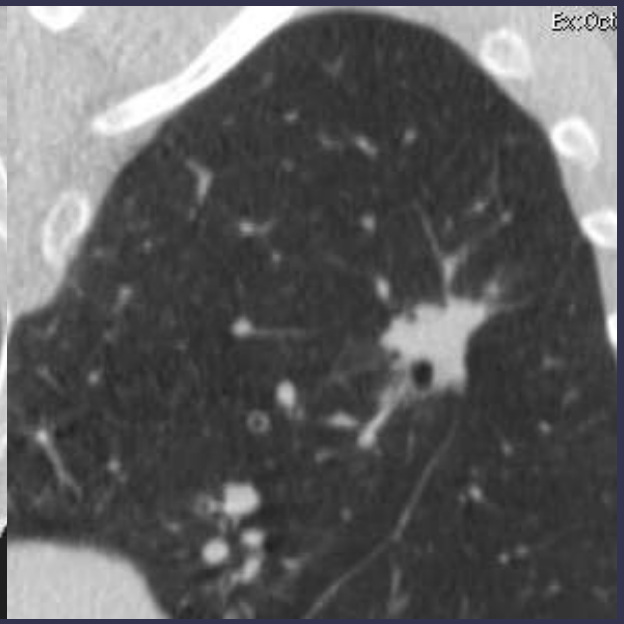


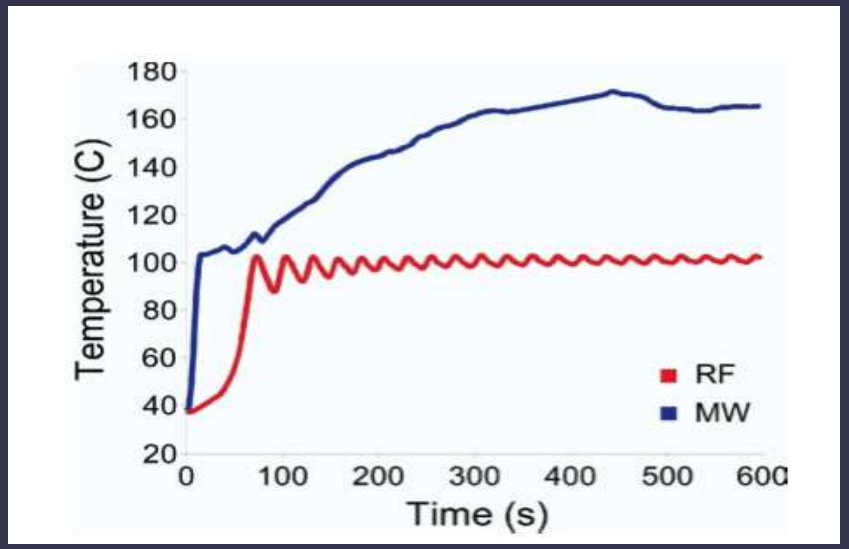
(de Andreis D, Radiology 2011)

Micro-ondes pulmonaire

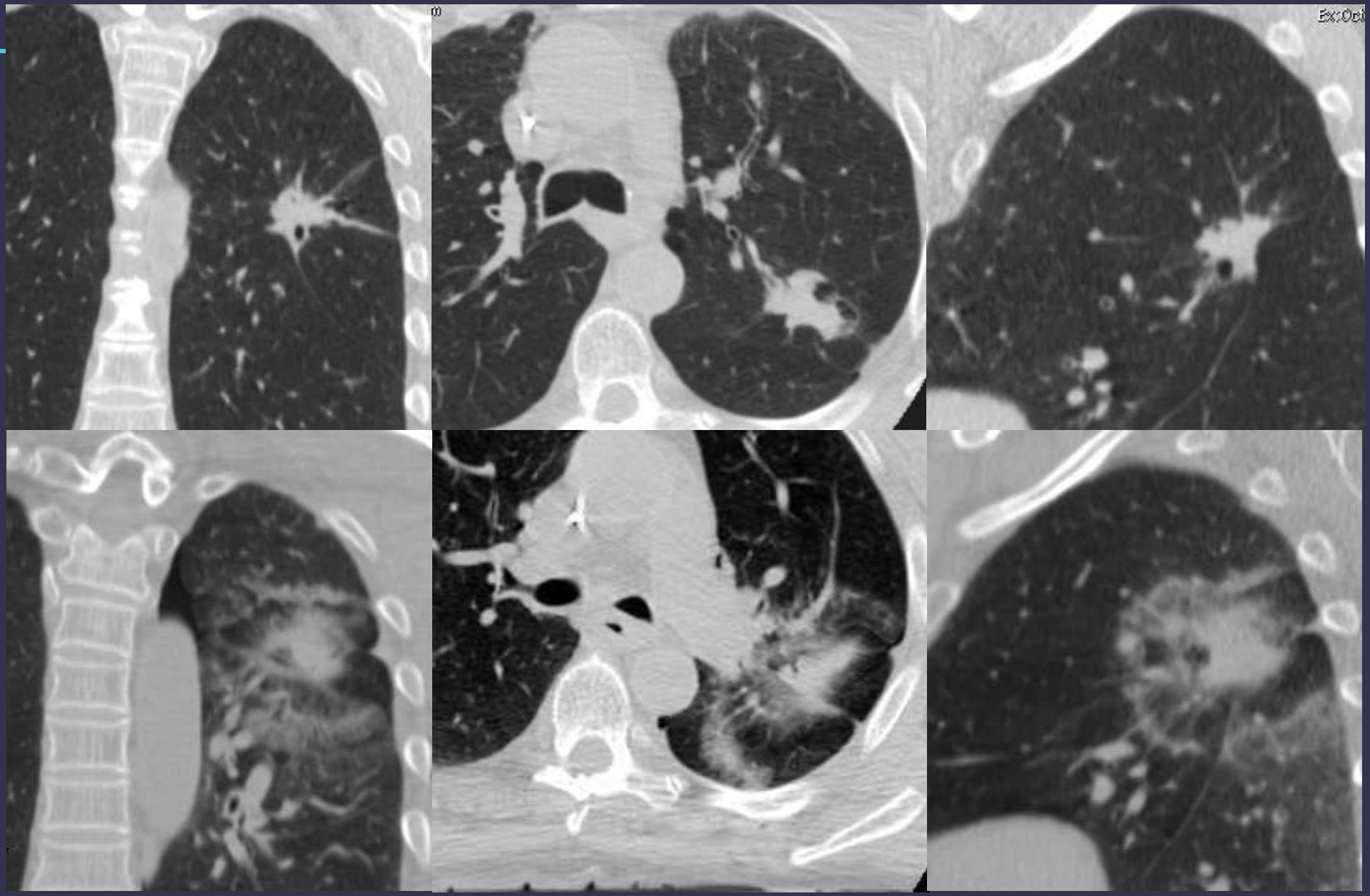








Micro-ondes pulmonaire



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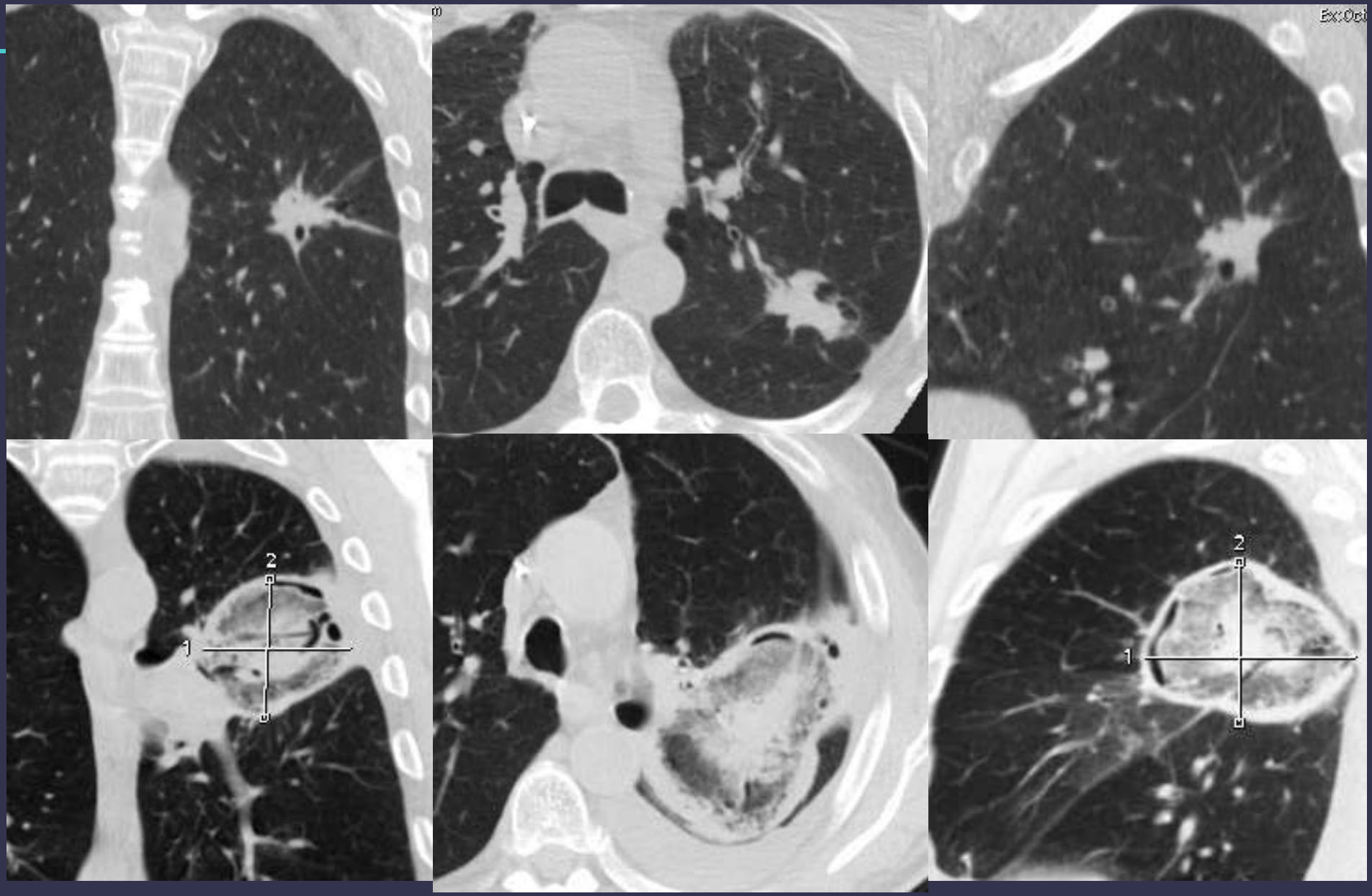
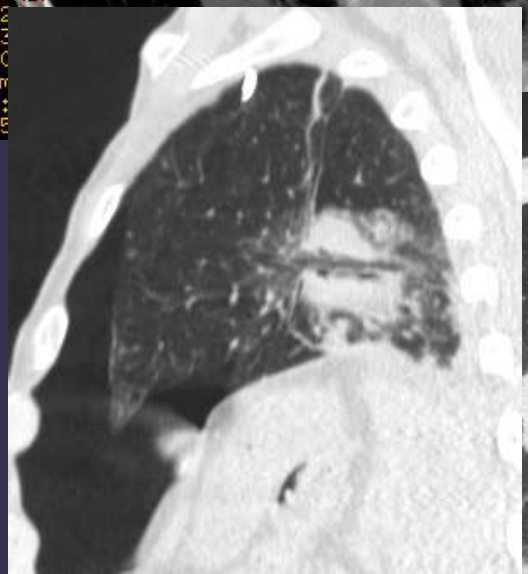
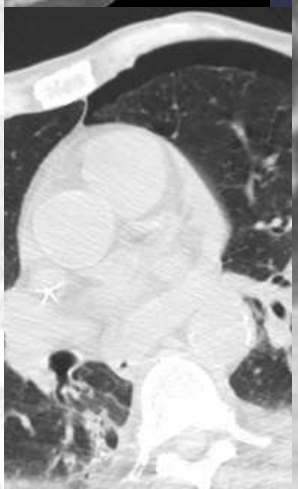
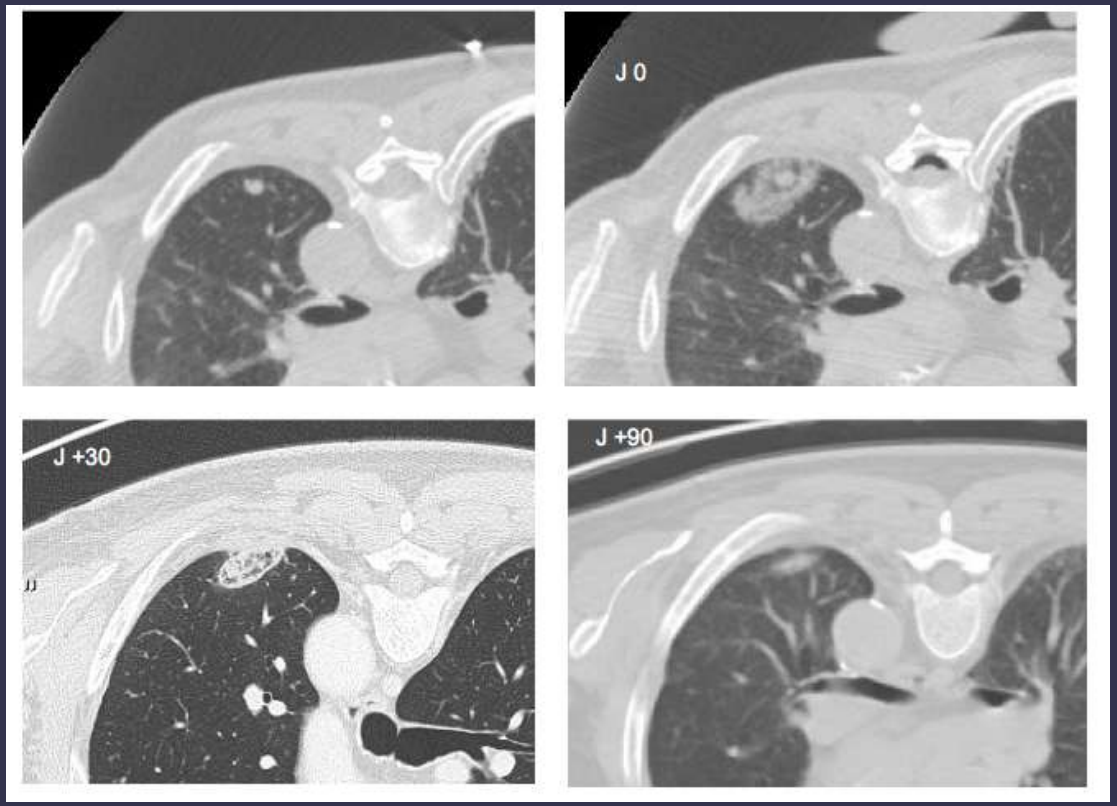


Micro-ondes pulmonaire

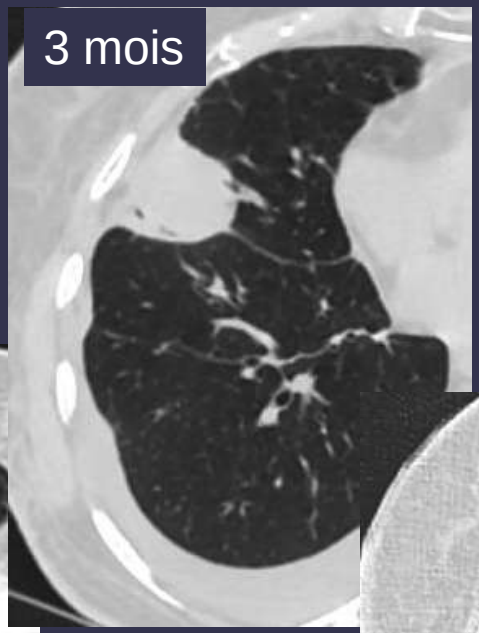




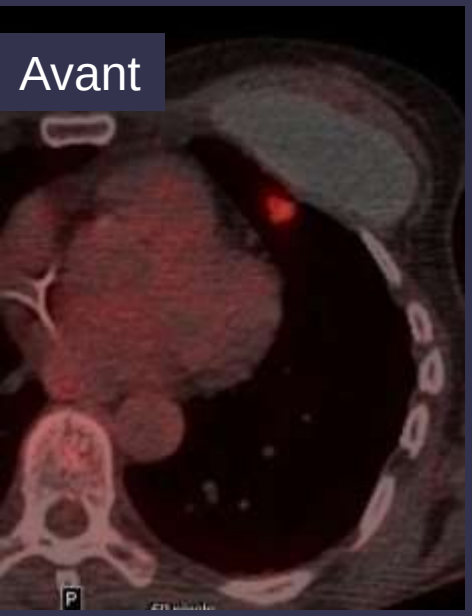
Cryothérapie pulmonaire

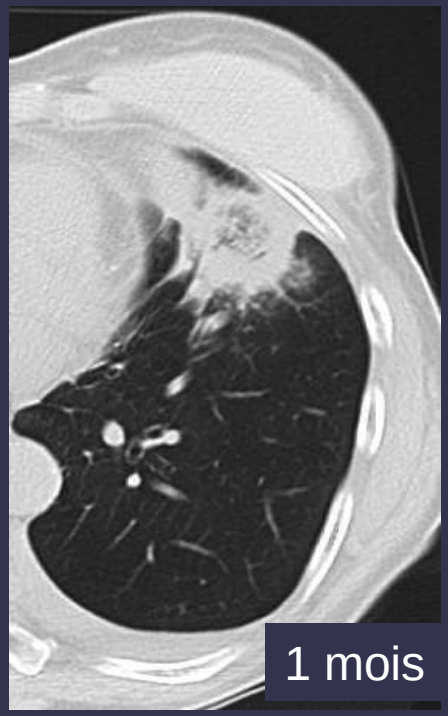


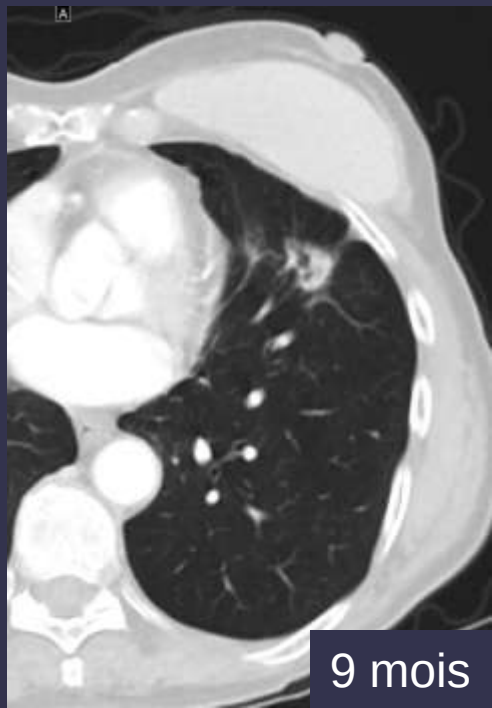
Cryothérapie pulmonaire



Cryothérapie pulmonaire





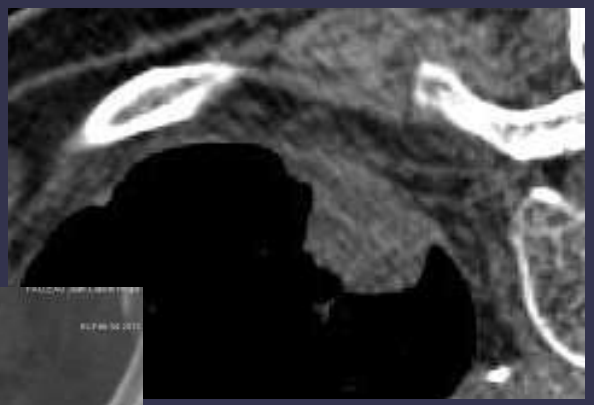


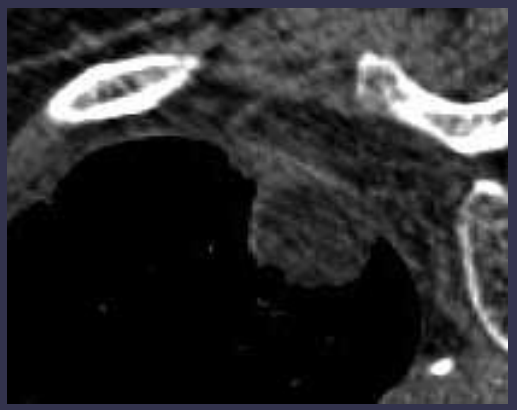
Cryothérapie pulmonaire

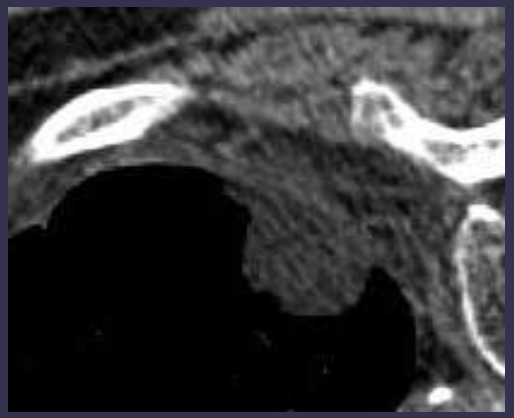
Before treat

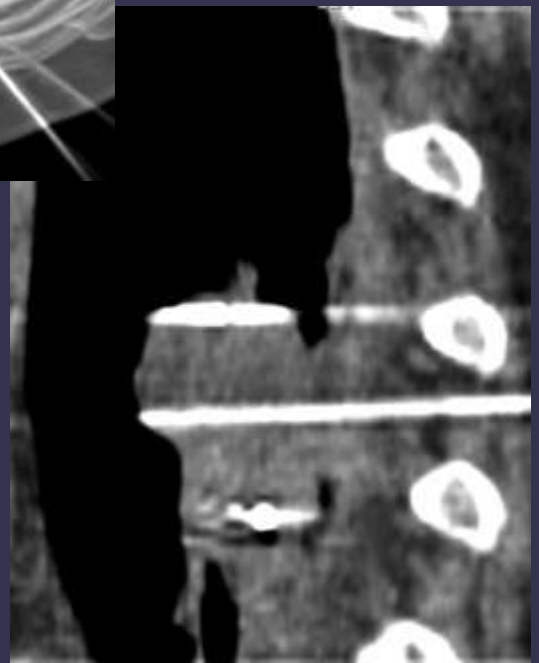
3+5 min treat

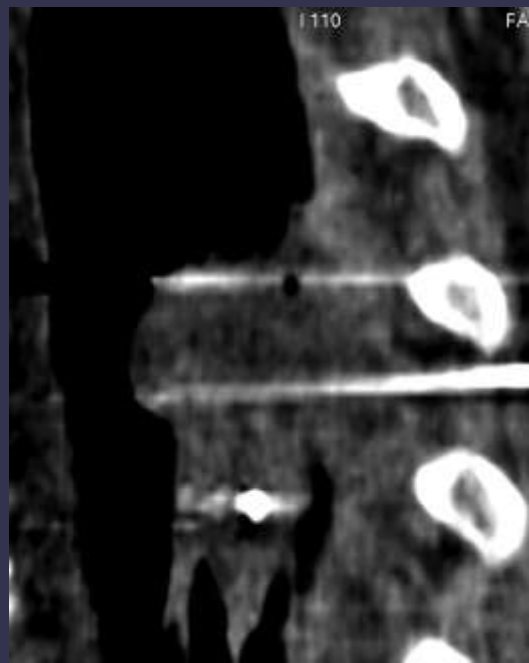
3+5+10 min treat











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European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

CT-guided conformal cryoablation for peripheral NSCLC: Initial experience

Xiao Zhang[a,1], Jinlin Tian[a,2], Lei Zhao[b,3], Bin Wu[a,4], Daniel S. Kacher[c,5], Xuyang Ma[a,6], Shurong Liu[a,7], Chao Ren[a,8], Yue-Yong Xiao[a,*]

- 46 patients : biopsy proven NSCLC
- ADK (n=32,) SCC (n=12), LCC (n=2)
- d≤3 cm (n=19) ---- 2 probes
- 3<d<5cm (n=27) ----- more than 2 probes
  - RECIST at 24 months (3 patients died due to multiple metastases)
    - 36 complete response (83.7%),
    - 7 partial response (16.3%)
    - 0 stable disease or progressive

(Zhang X, Eur J Radiol 2012; 81:3354–3362)

- 35 tumors, 13,3 mm mean diam. in 20 patients
- Incomplete ablation : 20% / tumor, 35 % / patients (after 21 mths)
- Size larger than 3 cm predictive of incomplete ablation (p=0,01)

(Kawamira, M. J thorac Cardiovasc Surg 2006)

REVIEW ARTICLE

Cryosurgery for lung cancer

Lizhi Niu[1,2], Kecheng Xu[1,2], Feng Mu[1,2]

[1]Department of Oncology, Affiliated Fuda Hospital, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Science, No. 91-93 Judezhong Road, Haizhu District, Guangzhou 510305, China; [2]Guangzhou Fuda Cancer Hospital, Jinan University School of Medicine, No. 2 Tangdexi Road, Tianhe District, Guangzhou 510305, China Fuda Cancer Hospital Guangzhou, China

625 NSCLCpercutaneous cryoablation

150 patients (followed 12-36 months)

1-, 2-, and 3-year OS : 64%, 45% and 32%

No cryoshock / renal insufficiency
Pleural effusion 16.2%
Hemoptysis 22.5%

(Niu L. J Thorac Dis 2012;4:408-419)

Hongwu Wang, MD, PhD
Peter J. Littrup, MD
Yunyou Duan, MD
Yanqun Zhang, MD
Huasong Feng, MD
Zhoushan Nie, MD

Published online
10.1148/radiol.2351030747
Radiology 2005; 235:289–298

Thoracic Masses Treated with Percutaneous Cryotherapy: Initial Experience with More than 200 Procedures[1]

TABLE 4
Complications of PCT

Complication	No. of Procedures*	Comments†
Cough	171 (79)	Only five (3%) cases exaggerated after cryotherapy
Hemoptysis	134 (62)	Stopped within 1 week; no intervention (embolization) required
Fever	91 (42)	Slight or moderate (<38.5°C); resolved within 1–5 days with antiinflammatory medication
Hypertension	72 (33)	Self limited and mild to moderate; occurred only during lesion freezing
Pleural effusion	30 (14)	More frequent with pleura-based tumors; five (17%) effusions drained
Pneumothorax	26 (12)	Twelve (46%) cases required periprocedural evacuation, 11 (42%) cases clinically unimportant, three (12%) cases required catheter drainage for 5–7 days
Subcutaneous emphysema	11 (5)	Commonly occurred in elderly patients; absorbed in 3–5 days
Skin injury	10 (5)	Minimal at puncture site; easily prevented by using water-filled glove
Death	2 (1)	Neither intraprocedural; one case owing to ARDS and one case owing to pulmonary embolus
Arm paralysis	1 (.5)	Brachial plexus damage from direct approach
Loss of speech	1 (.5)	Temporary aphasia from recurrent laryngeal nerve damage
All	217 (100)	. . .

(Wang H, Radiolgy 2005)

No cryoshock / renal insufficiency
Pleural effusion 16.2%
Hemoptysis 22.5%

(Niu L. J Thorac Dis 2012;4:408-419)

Conclusion

- La destruction tumorale percutanée a 15 ans
  - Evolution de l'imagerie
  - Evolution des outils de traitement
- RF permet un taux de succès de 85/90% dans les meilleures indications
- 60% survie à 3ans pour cancer bronchique primitif

- Intérêt de traitements combinées (chimiothérapie, anti-angiogéniques)
- Comparaison avec chirurgie
- Comparaison/combinaison avec radiothérapie stéréotaxique


Interactive CardioVascular and Thoracic Surgery 15 (2012) 258–265
doi:10.1093/icvts/ivs179 Advance Access publication 10 May 2012

BEST EVIDENCE TOPIC - THORACIC

Is radiofrequency ablation more effective than stereotactic ablative radiotherapy in patients with early stage medically inoperable non-small cell lung cancer?

Haris Bilal[a], Sarah Mahmood[b], Bala Rajashanker[c] and Rajesh Shah[a,*]

Interactive CardioVascular and Thoracic Surgery 15 (2012) 258–265
doi:10.1093/icvts/ivs179 Advance Access publication 10 May 2012

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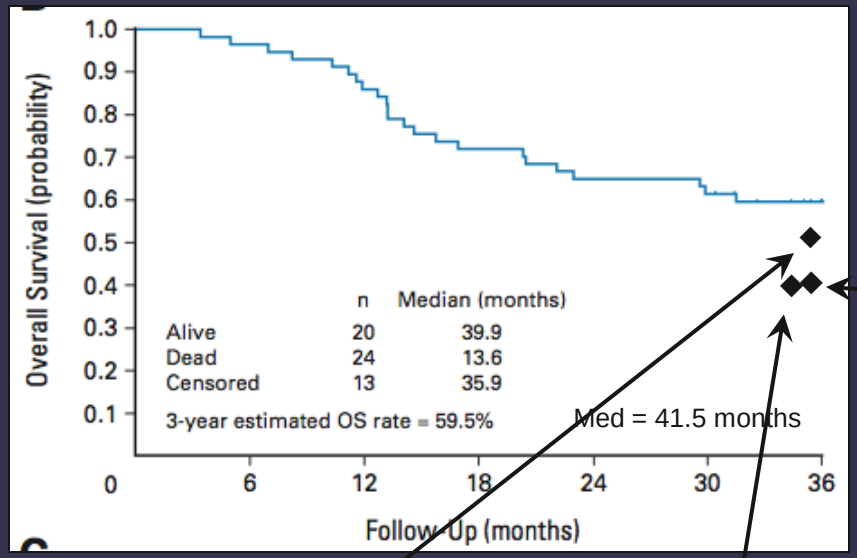
Haris Bilal[a], Sarah Mahmood[b], Bala Rajashanker[c] and Rajesh Shah[a,*]



Outcome in a Prospective Phase II Trial of Medically Inoperable Stage I Non–Small-Cell Lung Cancer Patients Treated With Stereotactic Body Radiotherapy

Pia Baumann, Jan Nyman, Morten Hoyer, Berit Wennberg, Giovanna Gagliardi, Ingmar Lax, Ninni Drugge, Lars Ekberg, Signe Friesland, Karl-Axel Johansson, Jo-Åsmund Lund, Elisabeth Morhed, Kristina Nilsson, Nina Levin, Merete Paludan, Christer Sederholm, Anders Traberg, Lena Wittgren, and Rolf Lewensohn

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

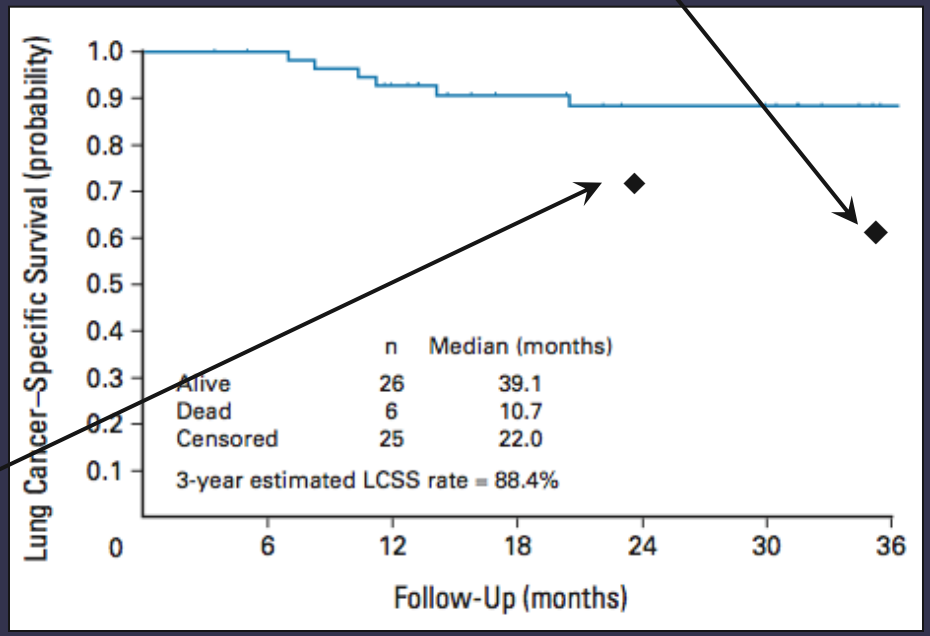
T1a (n=11), T1b (n=29) , T2a (n=17)
Tumor volume 16 cm^3 (≠ d=3.1cm) [1–51cm3]

Long-Term Results of Radiofrequency Ablation Treatment of Stage I Non-small Cell Lung Cancer
A Prospective Intention-to-Treat Study
Ambrogi MC, J Thor Oncol 2011

Med = 41.5 months

Lung Radiofrequency Ablation for the Treatment of Unresectabl Recurrent Non-Small-Cell Lung Cancer After Surgical Intervention
Kodama R, CVIR 2011

Charlson Comorbidity index predicts patient outcome, in cases of inoperable non-small cell lung cancer treated with radiofrequency ablation
Simon TG, Dupuy D, 2012



Response to radiofrequency ablation of pulmonary tumours: a prospective, intention-to-treat, multicentre clinical trial (the RAPTURE study)
Lencioni R, Lancet Oncol 2008

(Baumann P, Jclin Oncol 2009, 27 : 3290-3296)


2004