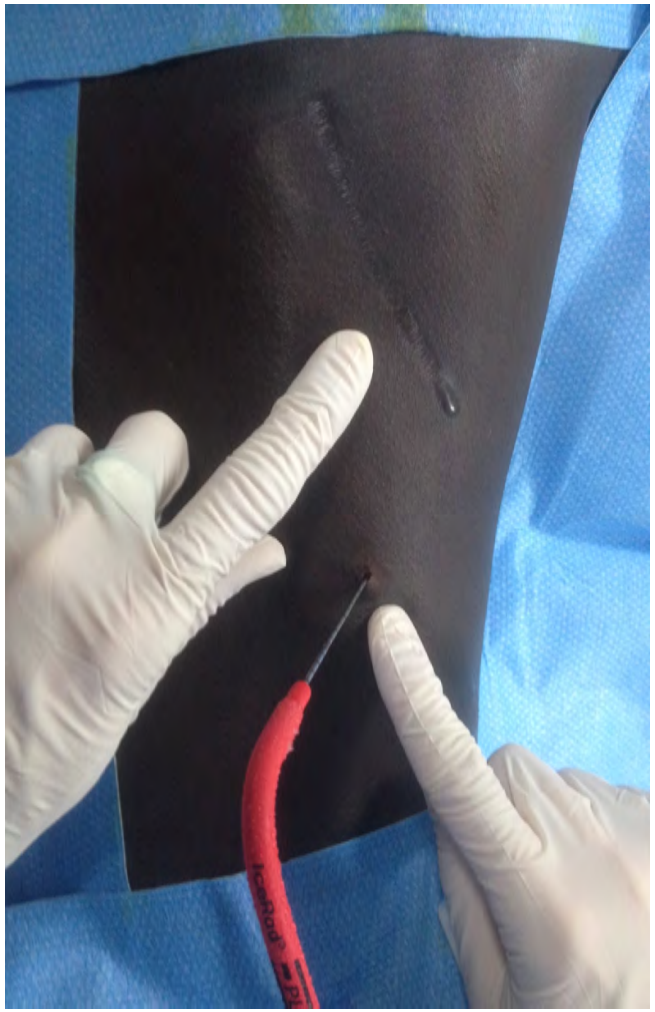
IOT | Institut d'Oncologie Thoracique

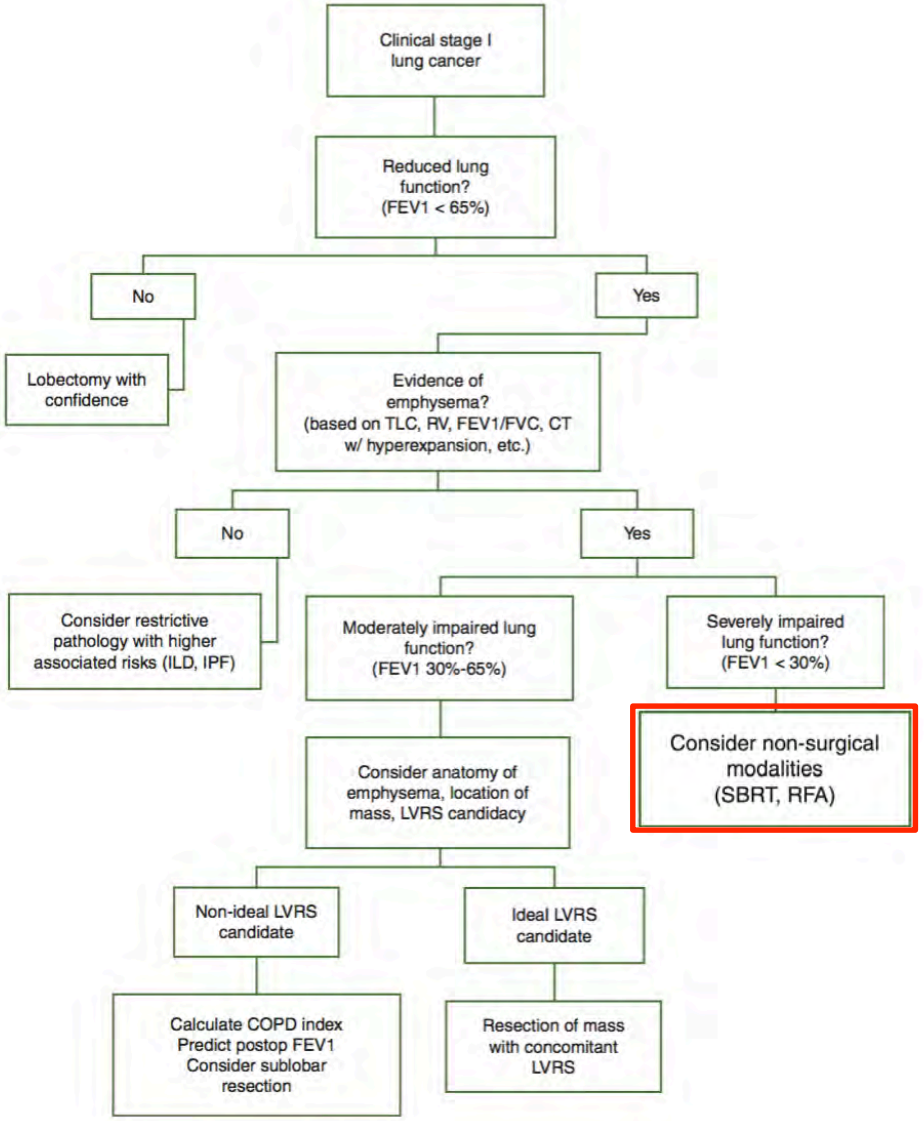
GUSTAVE ROUSSY

LES CBPN DE STADE PRECOCE

Alternatives à la chirurgie thoracique dans les stades précoces ?

Lambros TSELIKAS





ESMO
Annals of Oncology 28 (Supplement 4): iv1–iv21, 2017
doi:10.1093/annonc/mdx222

CLINICAL PRACTICE GUIDELINES

Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

RADIOTHERAPIE

- “conventionnelle”
- stéréotaxique

ABLATIONS PERCUTANNEES

- radiofréquence
- micro-ondes
- cryothérapie

Postmus, ESMO Guidelines 2017, Annals of Oncology

ANESTHESISTE

CHIRURGIEN

NON opérable…mais pourquoi ?

PNEUMOLOGUE

LE PATIENT

≃ 25% des patients avec un CBPNPC à un stade précoce

RADIOTHERAPIE

NSCLC T1,T2N0 in XXth century

Patients inopérables : place de la RT co nelle

- Résultats moins bon / chirurgi ations différentes+++
- Survie Globale (OS) ans = 22–72%, 0–42%.
- Survie s) at 2 ans et 5 ans = 54–93% et 13–39%.
- Re corégionale (LRR)= 6–70%

Very poor results

Rowell, Systematic Review, Chest 2001

SABR / SBRT

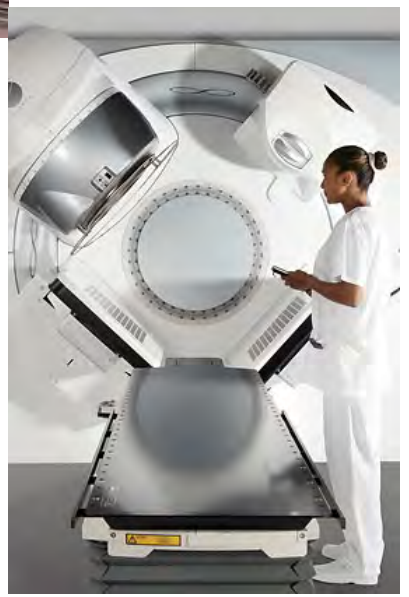
- Depuis 10 ans, **utilisation croissante** de la SBRT/SABR (extra-encéphalique)
- **Radiothérapie stéréotaxique:**
  - Administration de **hautes doses** d'irradiation
  - En **peu de fractions** (1-10, le plus souvent **3-5**)
  - Dégrée de **précision élevé**
  - Gradients de dose pour **limiter la toxicité** (organes adjacents)
- **Taux de control local: ≥ 90% à 3 ans** pour les tumeurs périphériques

(≃ résultats de la chirurgie)

Plusieurs systèmes différents
Fractionnement différents

Equipe pluridisciplinaire ++++

- Physicists
- Dosimetrists
- Technicians
- Radiotherapists
- Radiation Oncologits

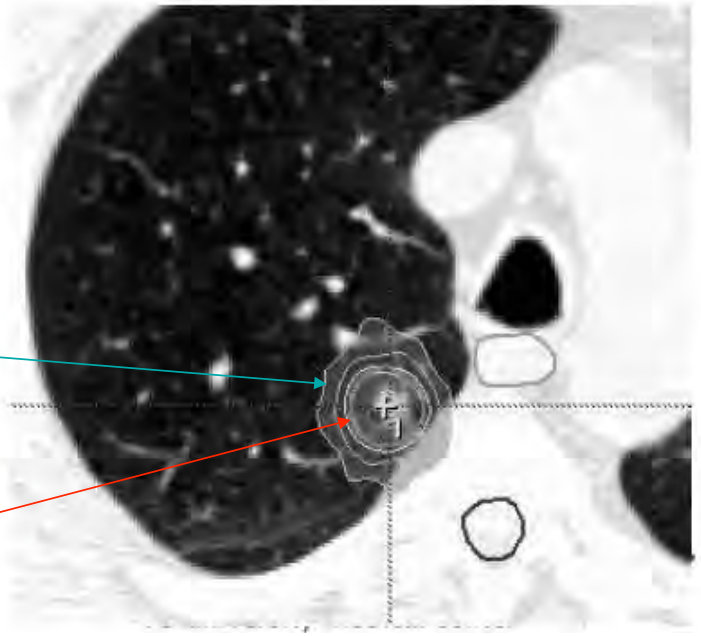


Principe de la SBRT: dose élevée dans un petit volume

Thus allowing for:

- **Steep dose-gradients**
- **Hypofractionation (3-5x)**
- **High biological effective dose**

40% isodose = BED 60 Gy
60% isodose = BED 112.5 Gy
80% isodose = BED 180 Gy
100% isodose = BED 262 Gy



Avant SBRT:

- Scan Thorax (IV+),
- PET-CT récent,
- Preuve histologique,
- FP + DLCO

Décision en RCP +++

Patients Inopérable : SBRT vs Surveillance

National Cancer Database Analysis, 2003-2006

SBRT : N=248 , Surveillance : N= 2889

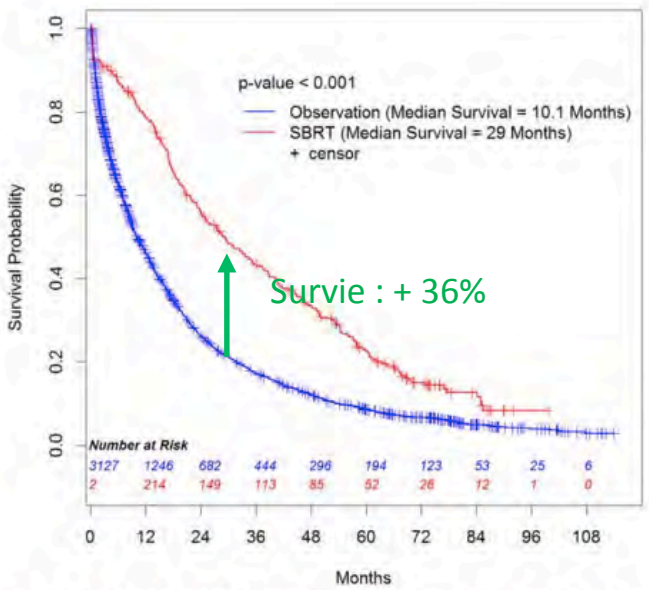


Figure 2. Kaplan-Meier curves illustrate the survival of all patients. SBRT indicates stereotactic body radiation therapy.

TABLE 3. Multivariable Interaction Model for Treatment Effect by Age or Charlson/Deyo Score

Strata	Treatment	HR (95% CI)	HR *P*
Age, y			
70-74	SBRT vs observation	0.72 (0.53-0.97)	.028[a]
75-79	SBRT vs observation	0.66 (0.49-0.88)	.004[a]
80-84	SBRT vs observation	0.59 (0.42-0.83)	.003[a]
≥85	SBRT vs observation	0.56 (0.37-0.85)	.006[a]
Charlson/Deyo score			
0	SBRT vs observation	0.64 (0.52-0.78)	<.001[a]
1	SBRT vs observation	0.79 (0.56-1.11)	.173
≥2	SBRT vs observation	0.51 (0.33-0.77)	.002[a]

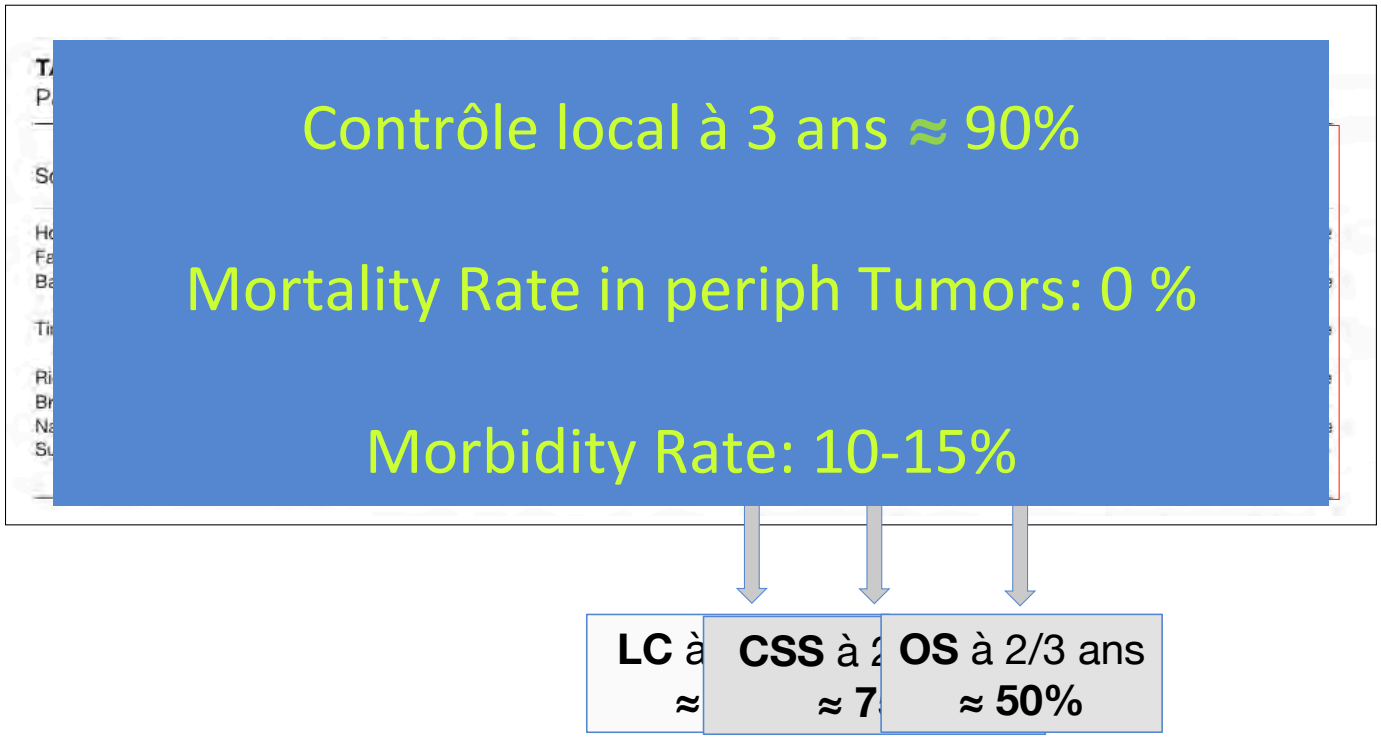
Abbreviations: CI, confidence interval; HR, hazard ratio. SBRT, stereotactic body radiation therapy.

[a]These *P* values indicate a statistically significant difference.

Nanda et al, Cancer 2015

Patients Inopérable : SBRT

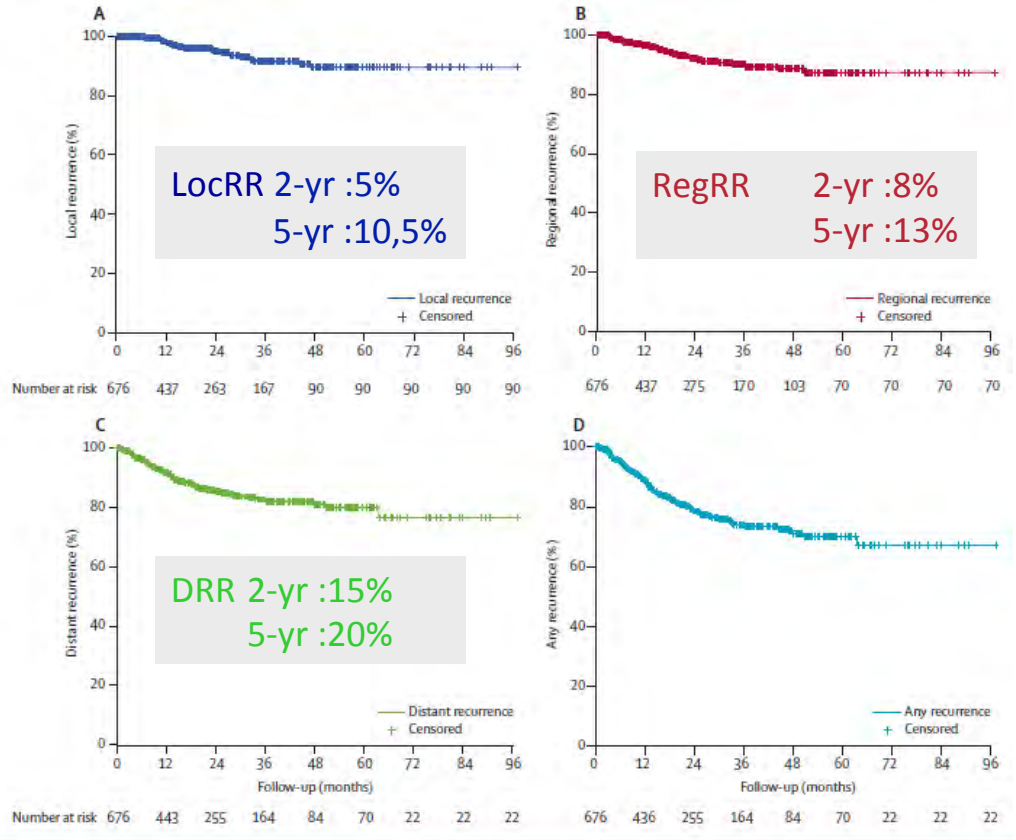
Phase II, études prospectives



Tandberg et al, Cancer 2017

SABR : Patterns of recurrence

Actuarial rates at 2 and 5 years

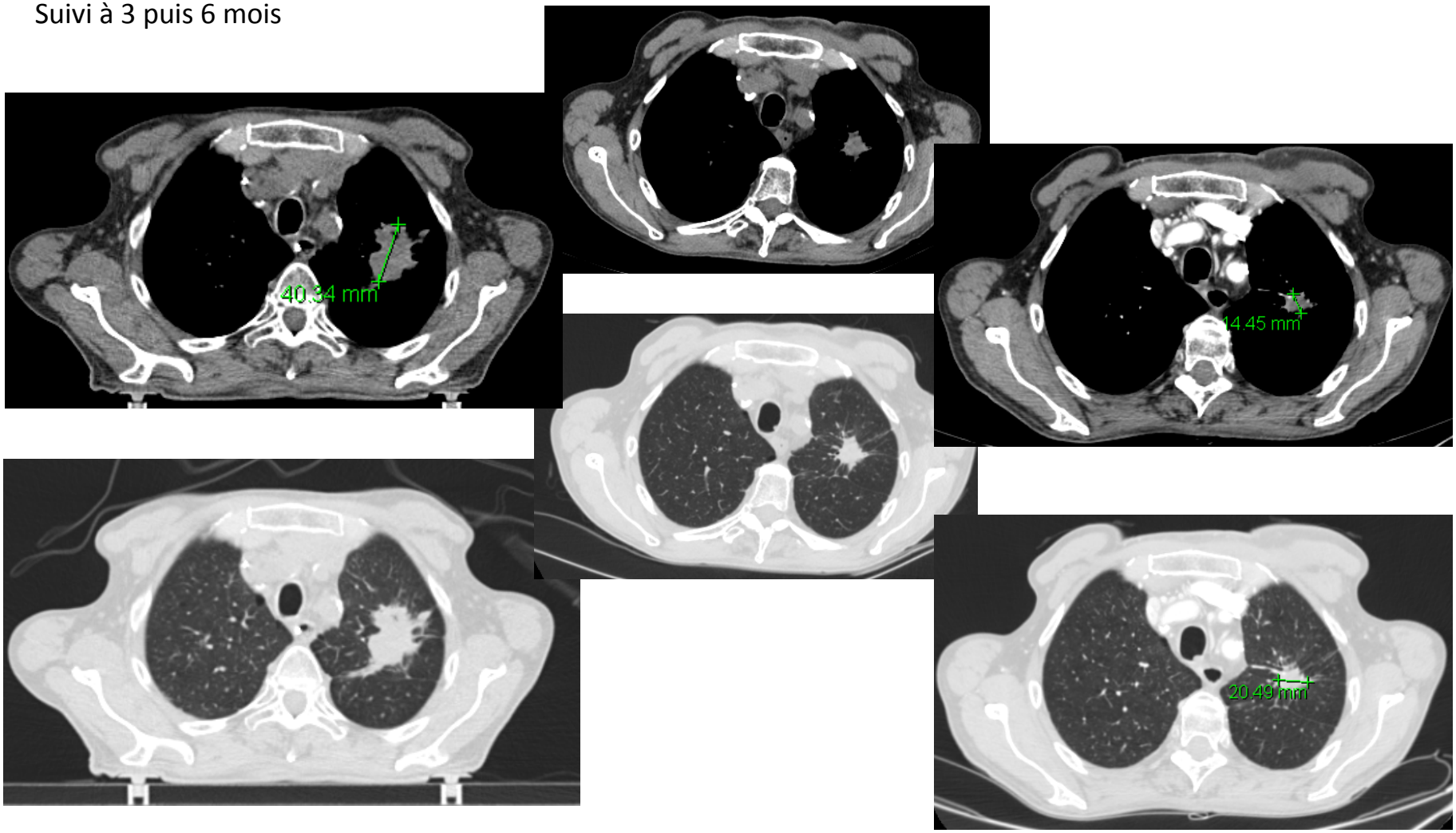


- **676 pts** 2003-2011
- Suivi Median: 33 mois
- Median time to LR: **14·9 months**
- Median time to RR : 13·1 months
- Median time to DR: 9·6 months
- 2eme primitif: 6%

Senthi et al, Lancet Oncol 2012

M GM, traité pour un carcinome épidermoïde T2aN0M0 60 Gy (5 x 12 Gy)

Suivi à 3 puis 6 mois



Dose et fractionnement optimal?

- **Pas de dose standard**
- **BED >100 Gy**.
- Schéma les plus « classiques »
  - Stade I, T périphérique : 3X18-20 Gy, 3X15 Gy 4X12 Gy
  - T plus volumineux, proche de la paroi: 5X12 Gy, 5X11 Gy
- **Adapter la SBRT en fonction de la taille, localisation, organe adjacents** (médiastin++++)
  - Tumeurs centrales: 8X7,5 Gy, 8X7 Gy, 5X10 Gy
  - Tumeurs hyper-centrales: 10X5 Gy

Organes adjacents et contraintes

Tab. 1 Normal tissue constraints according to published major clinical studies. Radiation Therapy Oncology Group (RTOG) protocols can be found on the RTOG website at http://www.rtog.org/ClinicalTrials/ProtocolTable.aspx

Organ at risk	Single fraction (RTOG 0915)	Three fractions (RTOG 0618/1021)	Four fractions (RTOG 0915)	Five fractions (RTOG 0813)	Eight fractions (Haasbeck et al. 2011 [76])
Trachea and large bronchus	D_{max} 20.2 Gy	D_{max} 30 Gy	D_{max} 34.8 Gy 15.6 Gy <4 cc	D_{max} 105%[a] 18 Gy <5 cc[b]	D_{max} 44 Gy
Heart	D_{max} 22 Gy 16 Gy <15 cc	D_{max} 30 Gy	D_{max} 34 Gy 28 Gy <15 cc	D_{max} 105%[a] 32 Gy <15 cc	–
Esophagus	D_{max} 15.4 Gy 11.9 Gy <5 cc	D_{max} 25.2 Gy 17.7 G <5 cc	D_{max} 30 Gy 18.8 Gy <5 cc	D_{max} 105%[a] 27.5 Gy <5 cc[b]	D_{max} 40 Gy
Brachial plexus	D_{max} 17.5 Gy 14 Gy <3 cc	D_{max} 24 Gy 20.4 Gy <3 cc	D_{max} 27,2 Gy 23.6 Gy <3 cc	D_{max} 32 Gy 30 Gy <3 cc	D_{max} 36 Gy
Chest wall	D_{max} 30 Gy 22 Gy <1 cc	30 Gy <30 cc 60 Gy <3 cc [77, 78]	D_{max} 27,2 Gy 32 Gy <1 cc	30 Gy <30 cc 60 Gy <3 cc [77, 78]	–
Spinal cord	D_{max} 14 Gy 10 Gy <0.35 cc	D_{max} 18 Gy (RTOG 0236)	D_{max} 26 Gy 28.8 Gy <0.35 cc	D_{max} 30 Gy 22.5 Gy <0.25 cc	D_{max} 28 Gy

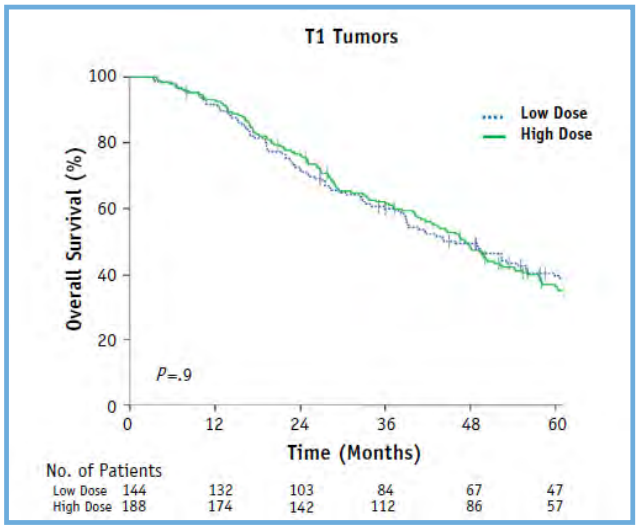
Increasing Radiation Therapy Dose Is Associated With Improved Survival in Patients Undergoing Stereotactic Body Radiation Therapy for Stage I Non–Small-Cell Lung Cancer

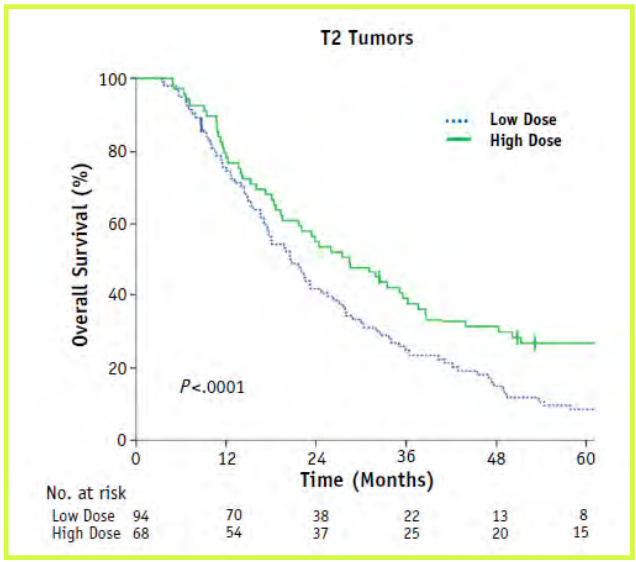
IJROBP 2015

Matthew Koshy, MD,*,† Renuka Malik, MD,† Ralph R. Weichselbaum, MD,*,† and David J. Sher, MD, MPH‡

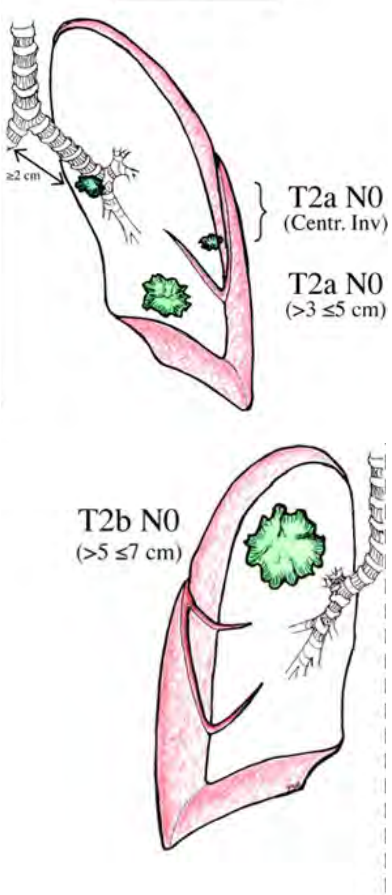
N=498 pts *2003-2006*	HD >BED 150 Gy	LD <150 Gy	p
3 yr OS	55%	46%	**0,03**
T1	61%	60%	0,9
T2	37%	24%	**0,01**
Prognostic factors: gender (HR 0,76), T2(HR 0,68) and HD (HR 1,99)			

- Increasing BED is associated with improved OS.
- Many confounding factors… Higher BED in pts with smaller T
- Need for prospective trials





SBRT pour des T > 3 cm

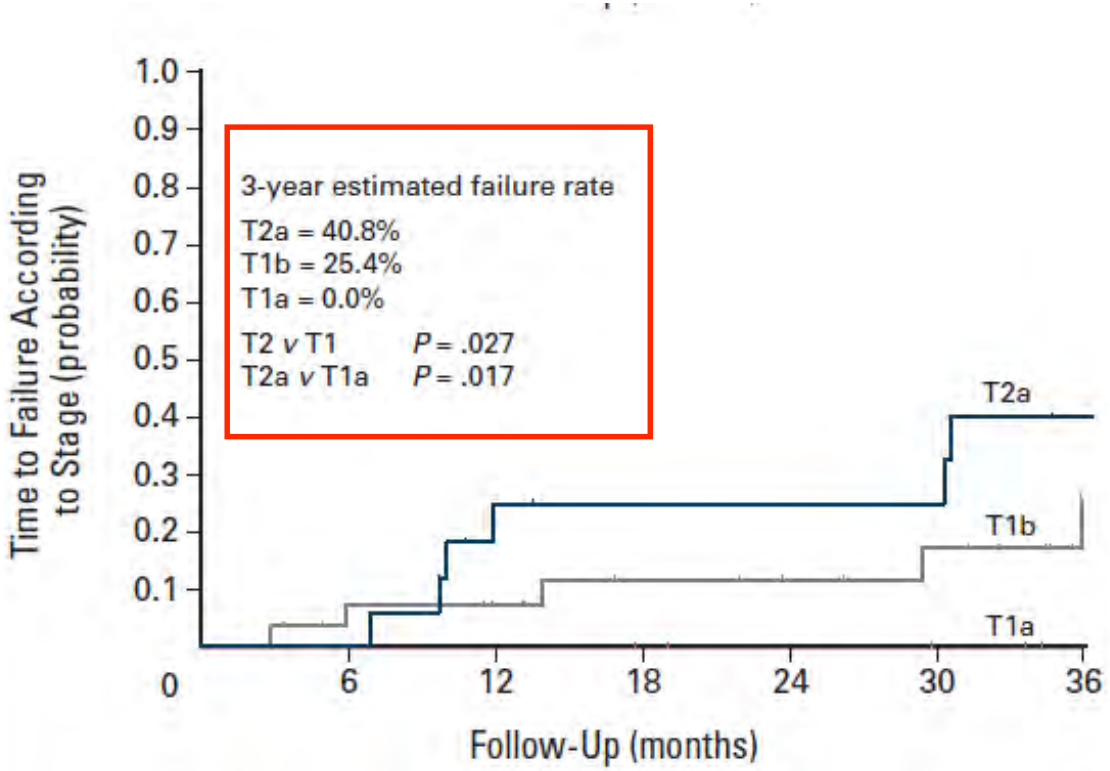


- Local control at 3 years: ~ 85-90%
- Increased local failure frequently in T2 lesions / T1
- Less evidence of SBRT for T > 5 cm
- Some authors suggest higher doses for larger T (BED prescribed to encompassing isodose >100 Gy needed)
- Higher risk also of regional /distant recurrence

Timmerman JAMA 2010, Baumann JCO 09, Acta Onco 06; Chi systematic review 2010

SABR : Résultats en fonction de la taille

- N=57 pts
- T1 ou T2N0 (70%)
- **Dose=45 Gy (15 GyX3)**
- BED periph: 112
- Estimated risk of failure:
  - T1 : 18%
  - T2 : 41%



Baumann JCO 2009

The Impact of Tumor Size on Outcomes After Stereotactic Body Radiation Therapy for Medically Inoperable Early-Stage Non-Small Cell Lung Cancer

- 185 pts with T1: n=133 ; T2: n=52
- 82% biopsy proven NSCLC
- Dose **T1: 48 Gy/4fr** **Larger T: 54** to **60 Gy/3 fr**

  and **T adjacent to mediastinum: 60 Gy/8 fr** or **50 Gy/10 fr**

  - **BED <100 Gy →LFR of 16.7%**
  - **If BED >100 Gy → LFR of 2.3%**

- GTV larger than 100 cm^3 or T>5,7 cm are at higher risk of regional and distant failure

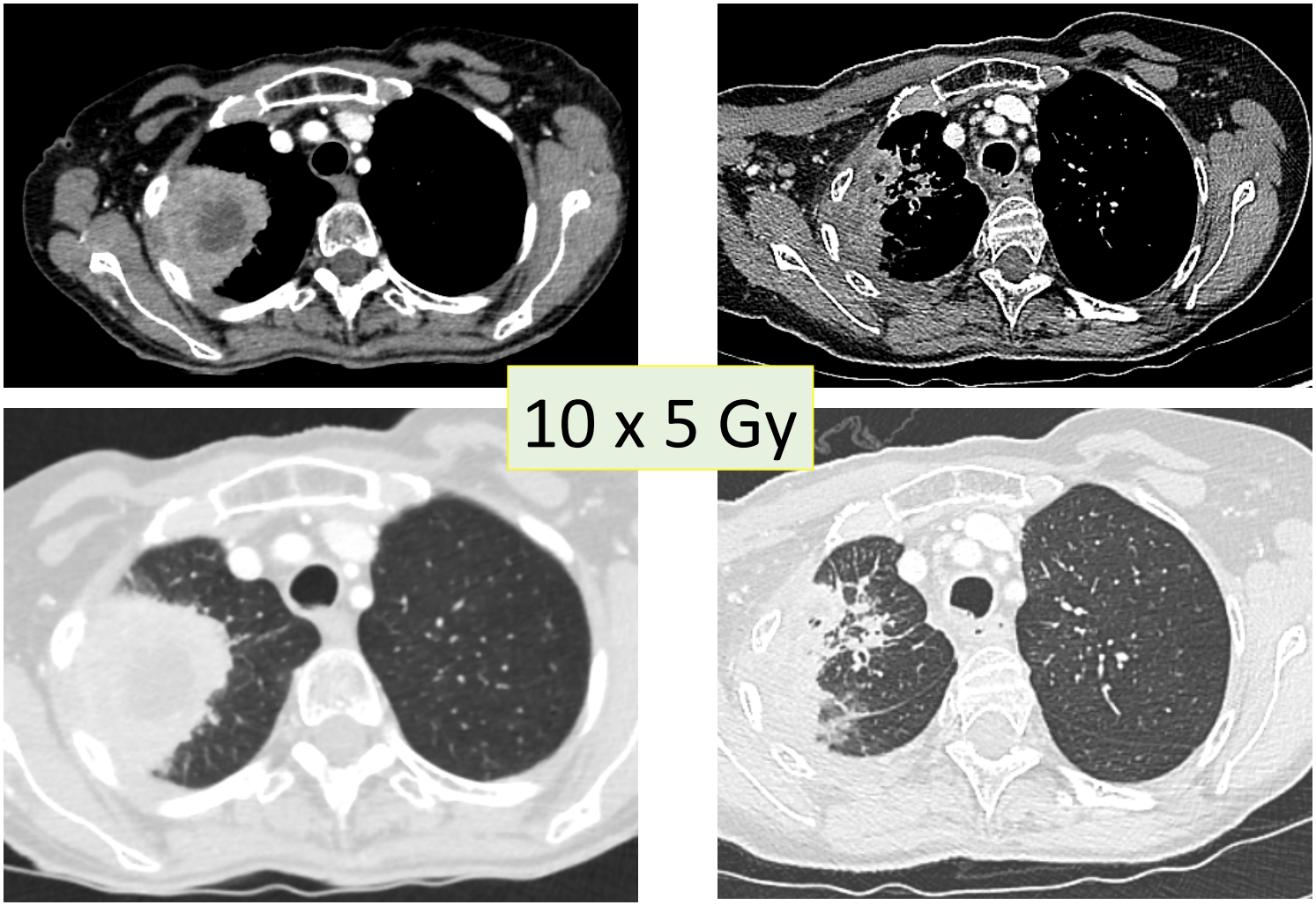
Alibhai et al, PMH experience IJROBP 2013

♂ 65 ans

Epidermoïde

CI chir : médicale

- OMS
- comorbidités



10 x 5 Gy

Pré-Ttt

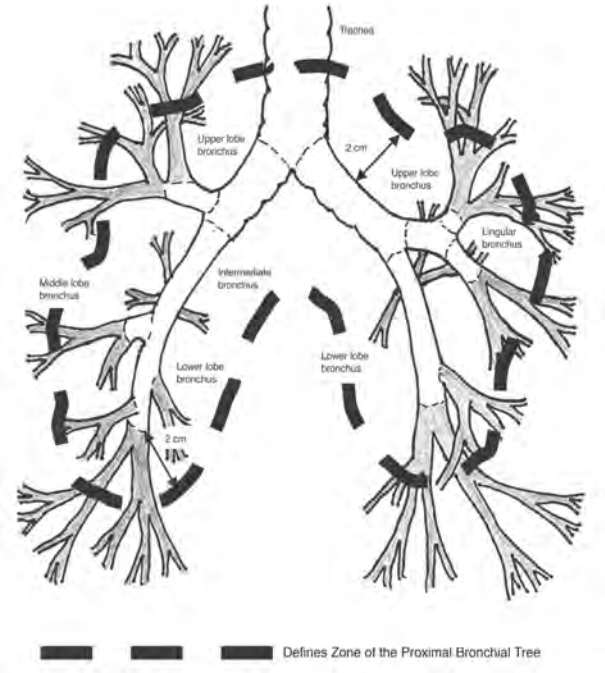
9 mois post SBRT

Limites SABR : tumeurs centrales

- 70 pts : 60-66 Gy/3Fr
- 2-yr local control 95%
  - Peripheral tumors

    2-year free from severe toxicity : 83%
  - Central tumors:

    2-year freedom from severe toxicity: **54%**



Severe bronchial stenosis and fistula may occur
≥2 yrs when large bronchi have received >80 Gy

Necessité d'une surveillance prolongée ++

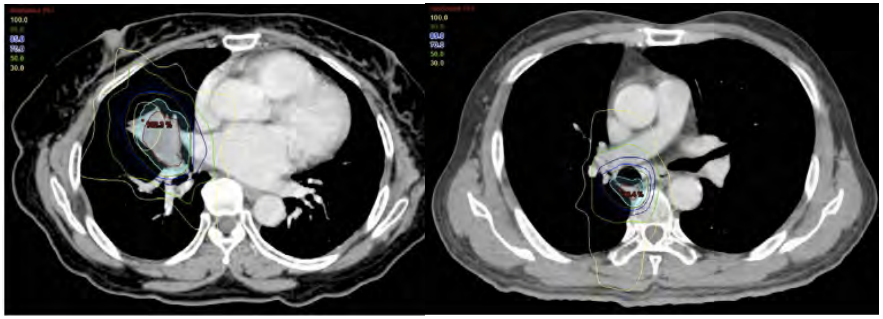
Timmerman JCO 2010, Miller 2005

Toxicités supérieures / inhabituelles pour les T. centrales

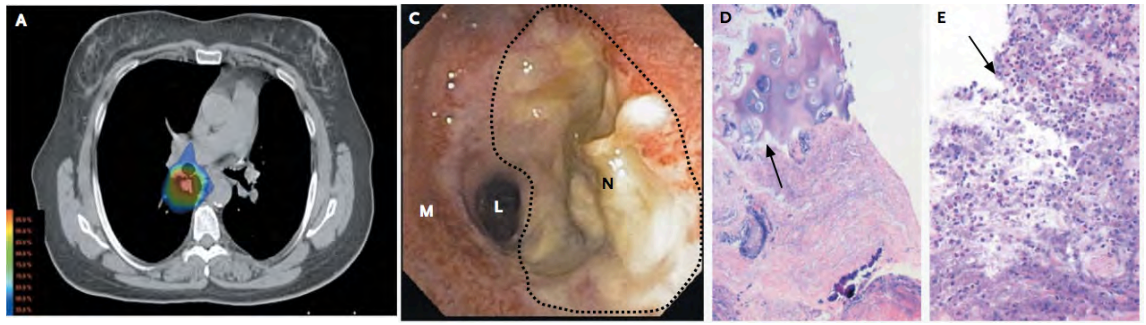
Table 2
Bronchial stricture after SBRT.

	Site of primary tumor		
	Bronchial tumor[a] (%)	Peribronchial tumor[b] (%)	Peripheral tumor[c] (%)
No stricture	0(0)	1(33)	23(100)
Partial stricture	3(50)	2(67)	0(0)
Complete stricture	3(50)	0(0)	0(0)

Sténoses Bronchiques



40Gy/4F, 48Gy/4F, 60Gy/3F

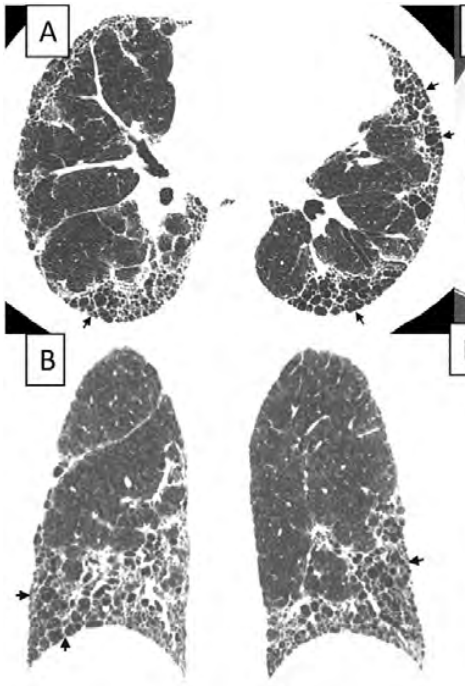


Bronchial Necrosis 8 months after SBRT (5x10Gy)

Concept of Risk adapted SBRT

Song, Lung Cancer 2006 *Lageerwald, IJROBP 2008* *Coradetti, NEJM 2012*

Interstitial Pulmonary Fibrosis (IPF): **seule CI** au SABR



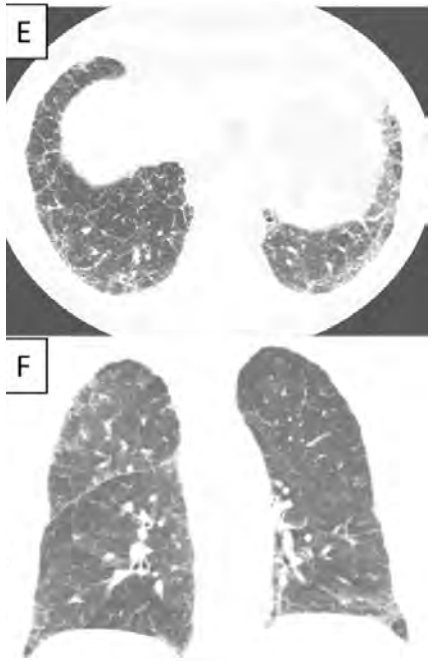
UIP pattern, with extensive honeycombing: basal predominant, peripheral predominant reticular abnormality, with multiple layers of honeycombing.

IPF is a chronic, progressive fibrotic interstitial lung disease of unknown origin

HRCT images: usual interstitial pneumonia (UIP) pattern

IPF représente CI à RT stéréotaxique si sévère

Mais pronostic plutôt dépendant **de la fibrose**



Possible UIP pattern; peripheral predominant, basal predominant reticular abnormality with moderate amount of ground glass abnormality, but without honeycombing.

Raghu G, AJRCCM 2011

SBRT vs Chirurgie

Systematic review

Stereotactic radiotherapy (SABR) for the treatment of primary non-small cell lung cancer; Systematic review and comparison with a surgical cohort

Francesca Soldà [a], Mark Lodge [b], Sue Ashley [c], Alastair Whitington [d], Peter Goldstraw [e], Michael Brada [f,*]

[a] Harley Street at University College Hospital, London, UK; [b] INCTR UK, Oxford, UK; [c] Keswick, Cumbria, UK; [d] SE London Cancer Network, Guy's Hospital, London, UK; [e] Academic Department of Thoracic Surgery, Royal Brompton Hospital, London, UK; [f] Leaders in Oncology Care, London, UK

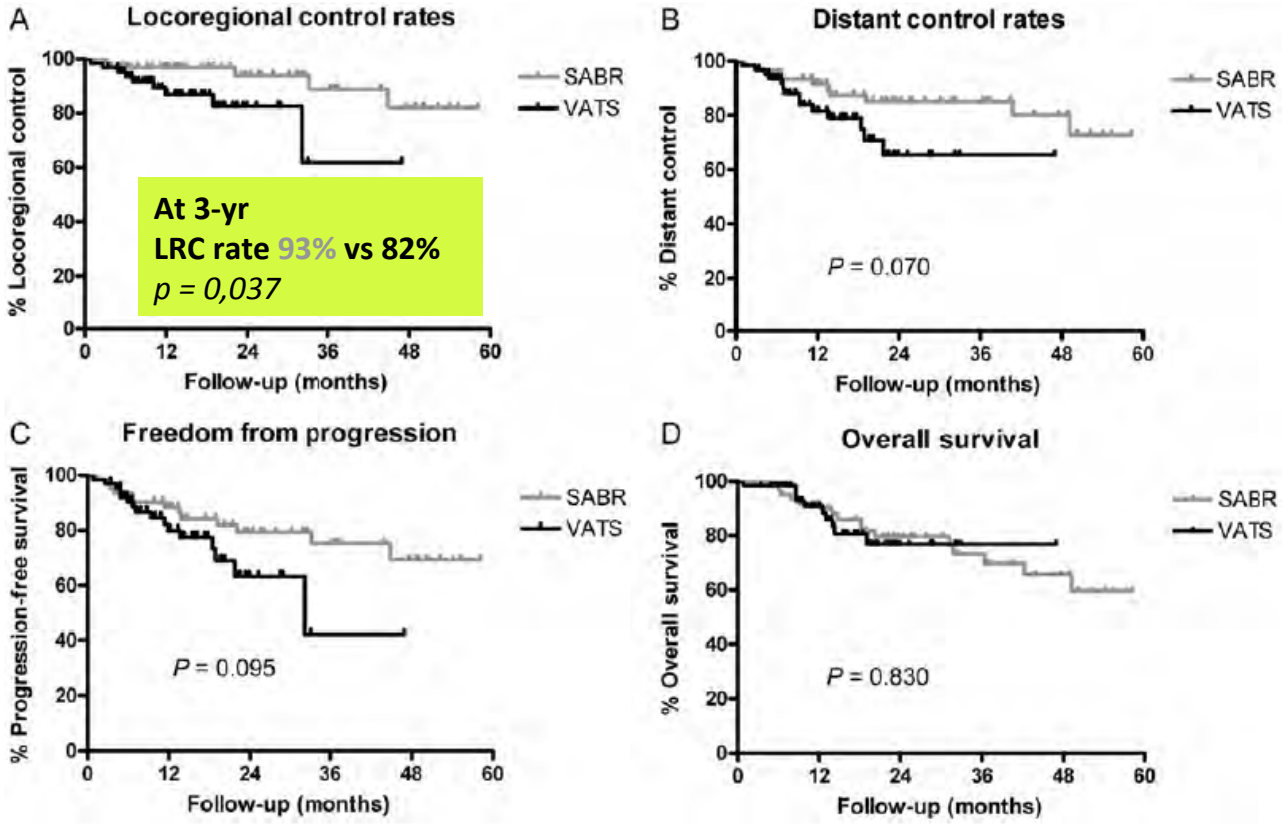
- **3201** patients stage I NSCLC treated **with SABR**
  - **2-yr OS was 70%** (95% CI: 67–72%)
  - 2 yr local control = 91% (95% CI: 90–93%).
  - No survival or local PFS difference with different RT technologies used for SABR
- **2038** stage I patients treated **with surgery**
  - **2yr-OS 68%** (95% CI: 66–70)

Solda et al, Rad & Onc 2013

Stage I–II non-small-cell lung cancer treated using either stereotactic ablative radiotherapy (SABR) or lobectomy by video-assisted thoracoscopic surgery (VATS): outcomes of a propensity score-matched analysis

SABR : n = 64

VATS : n = 64



Verstegen et al, Ann of Onc 2013

SBRT vs Chirurgie : et chez les patients opérables alors?

Attempts of randomized trials have failed (ROSEL, STARS, ACOSOG/RTOG)

Several projects planned to meet this challenge…

Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials

Joe Y Chang, Suresh Senan*, Marinus A Paul, Reza J Mehran, Alexander V Louie, Peter Balter, Harry J M Groen, Stephen E McRae, Joachim Widder, Lei Feng, Ben E E M van den Borne, Mark F Munsell, Coen Hurkmans, Donald A Berry, Erik van Werkhoven, John J Kresl, Anne-Marie Dingemans, Omar Dawood, Cornelis J A Haasbeek, Larry S Carpenter, Katrien De Jaeger, Ritsuko Komaki, Ben J Slotman, Egbert F Smit†, Jack A Roth†*

Chang et al, Lancet Oncol 2015

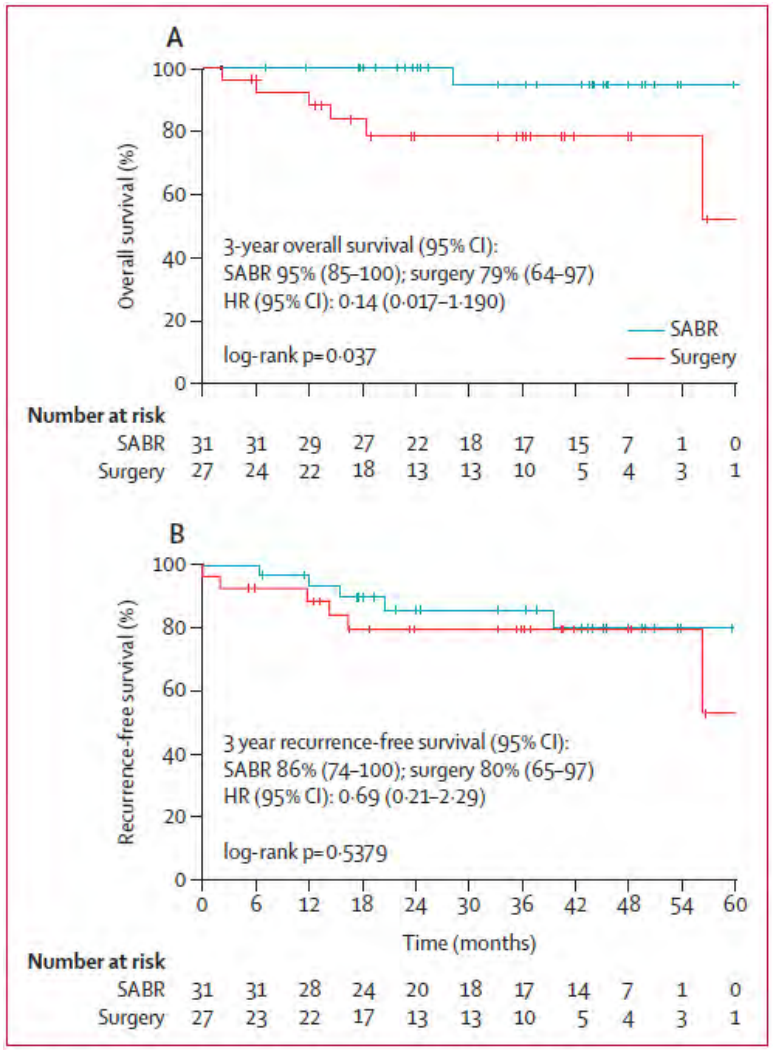


Figure 2: **Overall survival (A) and recurrence-free survival (B)**

	SABR	**Chir**	***p***
N pts	31	27	
Est 3yr OS	95%	79%	**0,037***
Est 3yr RFS	86%	80%	0,54
Récurrence	1 Local R 4 Nodal R 1 DM	1 Nodal R 2 DM	
Grade 3/4 AE	3 gr 3(10%) *3 chest wall pain* *2 dyspnea* *1 rib fracture*	12 (44%) *4 chest pain* *4 dyspnea* *2 lung infections*	
Gr 5 AE	0	1 death *Surg cpl*	

Chang et al, Lancet Oncol 2015

Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials

Lettres à l'éditeur

- we believe these findings can only be thought to be exploratory and hypothesis-generating.

Christopher Cao, Thomas D'Amico, Todd Demmy, Joel Dunning, Dominique Gossot,, Tristan D Yan, on behalf of the International VATS Interest Group **tristanyan@annalscts.com**

- Additional studies are needed to substantiate the results.

Lei Zhang, Jingru Tian, *Changli Wang / **raymd728@qq.com**

- Much larger trials are needed to achieve balanced treatment groups. In the analysis by Chang and colleagues, discrepancy exists between the p value shown in figure 2 (p=0·037) and the 95% CI (0·017–1·190)

Isabelle Opitz, Gaetano Rocco, Alessandro Brunelli, Gonzalo Varela, Gilbert Massard, Walter Weder, on behalf of the European Society of Thoracic Surgeons **isabelle.schmitt-opitz@usz.ch**

- it is based on an unjust comparison of modern SABR techniques to outdated surgical approaches, and due to methodological limitations of the pooled data.

Masatsugu Hamaji, Shawn S Groth, David J Sugarbaker, *Bryan M Burt **bryan.burt@bcm.edu**

- The report by Chang and colleagues was underpowered to study overall survival and it was also underpowered to evaluate recurrence-free survival.

Masatsugu Hamaji, Shawn S Groth, David J Sugarbaker, *Bryan M Burt bryan.burt@bcm.edu

- As a participating centre for the STARS trial of stereotactic ablative radiotherapy (SABR) versus lobectomy for stage I non-small-cell lung cancer (NSCLC), we have grave concerns about how the recent report by Joe Chang and colleagues1

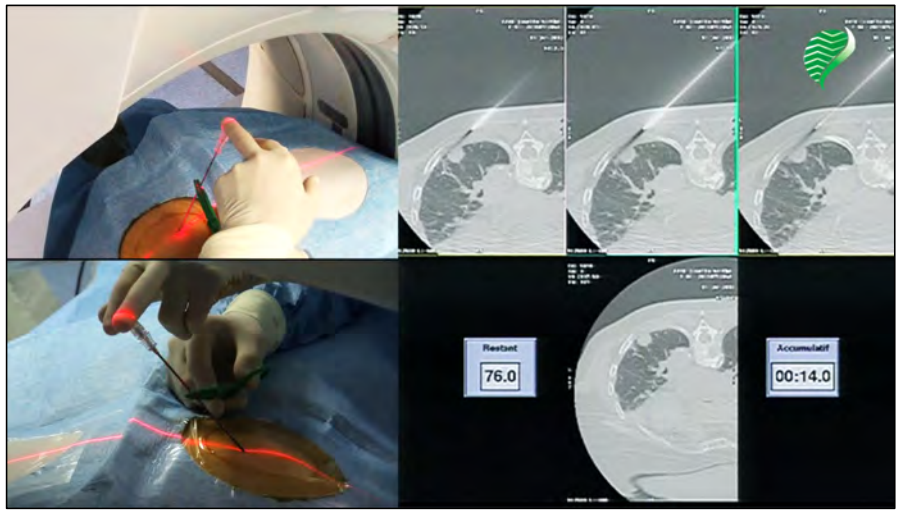
****David Rice, Boris Sepesi, John Heymach, Stephen Swisher, Ara Vaporciyan*** **drice@mdanderson.org**

RADIOLOGIE INTERVENTIONNELLE

RFA, MWA, CRYO

IMAGERIE

ENVIRONNEMENT DE BLOC-OPERATOIRE



MINI-INVASIVES

La radiofréquence : RFA

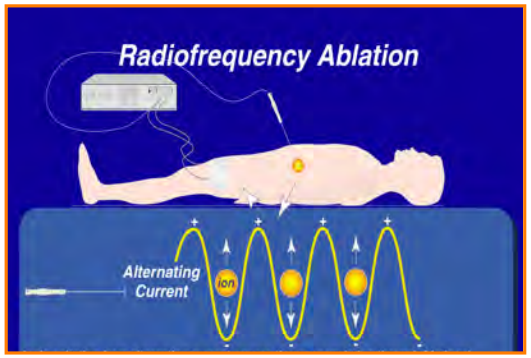
- Sinusoidal current

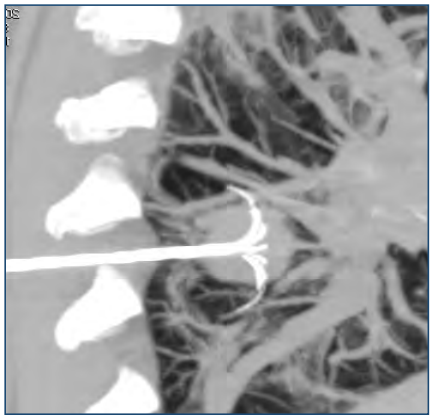
  (420 - 500kHz)

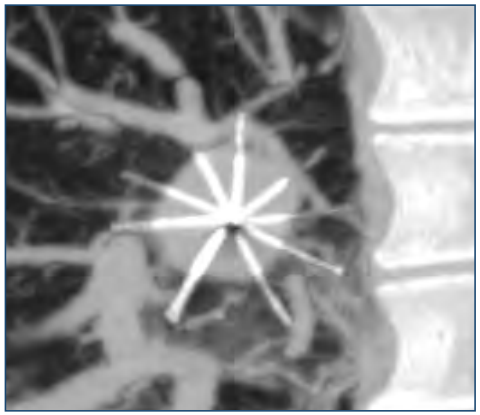
  ➔ Ionic movement

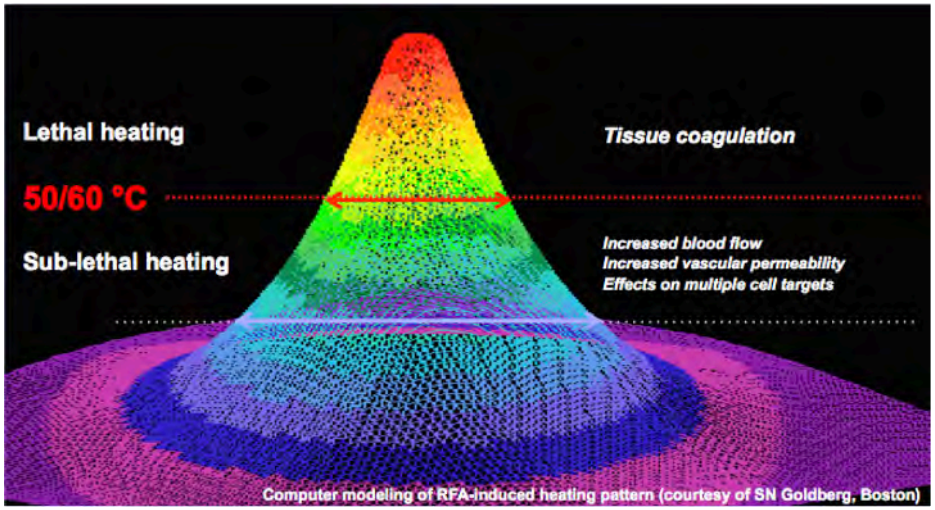
  ➔ Frictional heating

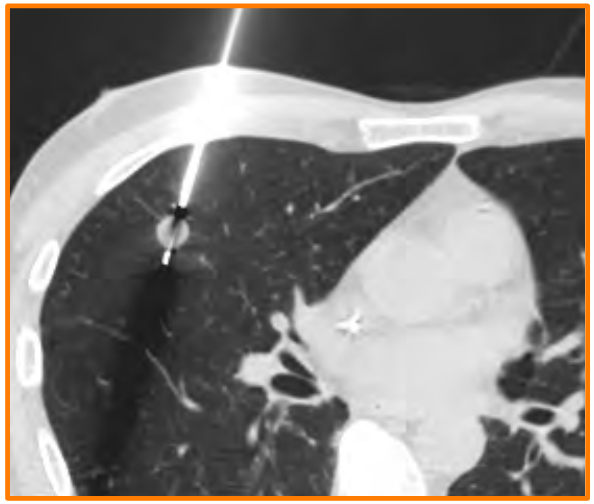
  ➔ Tissue Coagulation

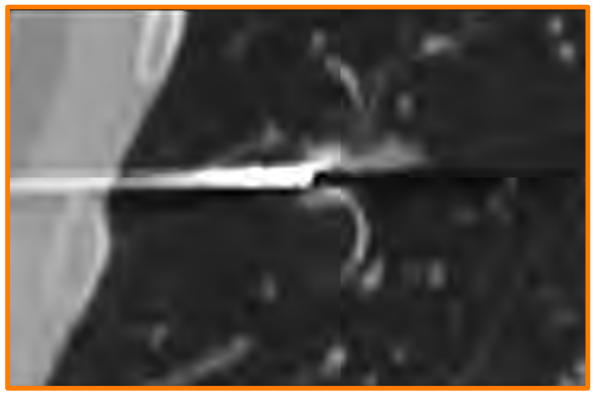








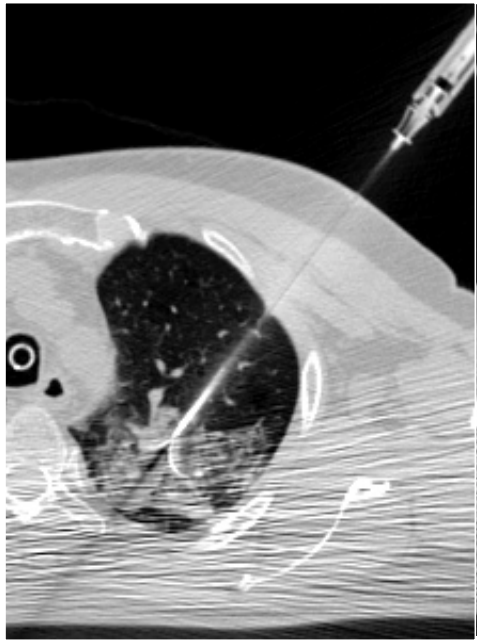




BIOPSIE & ABLATION PENDANT LA MEME PROCEDURE

BIOPSIE ET ABLATION DANS LE MEME TEMPS OPERATOIRE

Immédiatement AVANT



Immédiatement APRES

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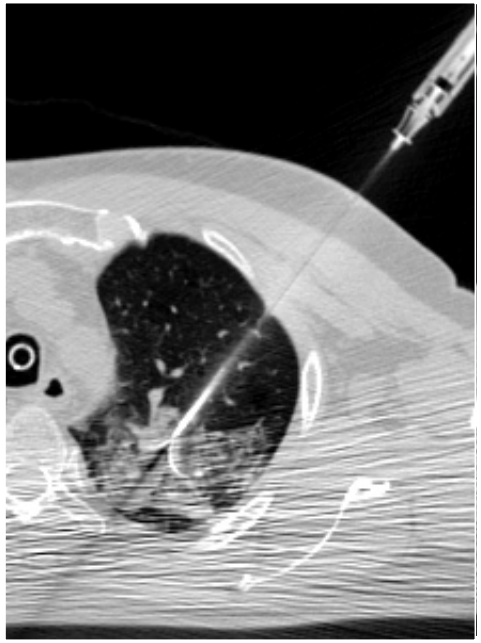

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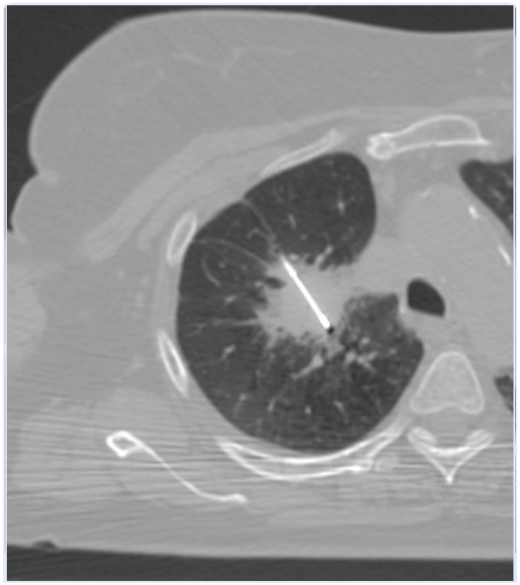

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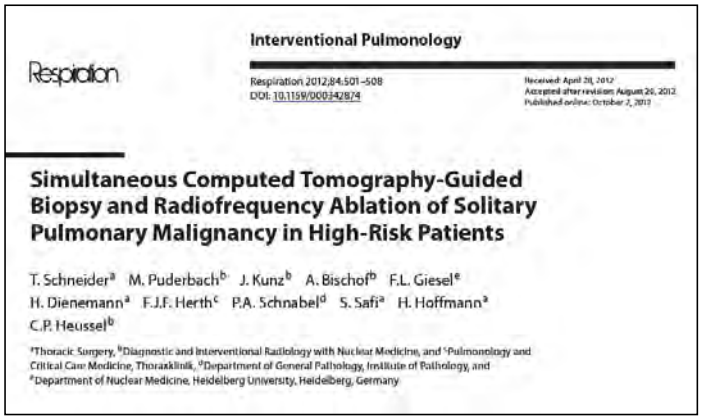

Respiration

Interventional Pulmonology

Respiration 2012;84:501–508
DOI: 10.1159/000342874

Received: April 26, 2012
Accepted after revision: August 26, 2012
Published online: October 2, 2012

Simultaneous Computed Tomography-Guided Biopsy and Radiofrequency Ablation of Solitary Pulmonary Malignancy in High-Risk Patients

T. Schneider[a] M. Puderbach[b] J. Kunz[b] A. Bischof[b] F.L. Giesel[e]
H. Dienemann[a] F.J.F. Herth[c] P.A. Schnabel[d] S. Safi[a] H. Hoffmann[a]
C.P. Heussel[b]

[a]Thoracic Surgery, [b]Diagnostic and Interventional Radiology with Nuclear Medicine, and [c]Pulmonology and Critical Care Medicine, Thoraxklinik, [d]Department of General Pathology, Institute of Pathology, and [e]Department of Nuclear Medicine, Heidelberg University, Heidelberg, Germany

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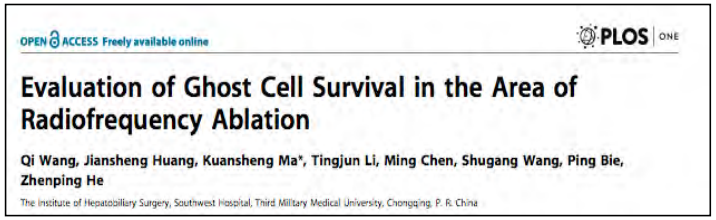

OPEN ACCESS Freely available online

PLOS ONE

Evaluation of Ghost Cell Survival in the Area of Radiofrequency Ablation

Qi Wang, Jiansheng Huang, Kuansheng Ma*, Tingjun Li, Ming Chen, Shugang Wang, Ping Bie, Zhenping He

The Institute of Hepatobiliary Surgery, Southwest Hospital, Third Military Medical University, Chongqing, P. R. China

OPINION

Thermal ablation of tumours: biological mechanisms and advances in therapy

Katrina F. Chu and Damian E. Dupuy — *Nature reviews cancer 2014*

BIOPSIE ET ABLATION DANS LE MEME TEMPS OPERATOIRE

Immédiatement AVANT

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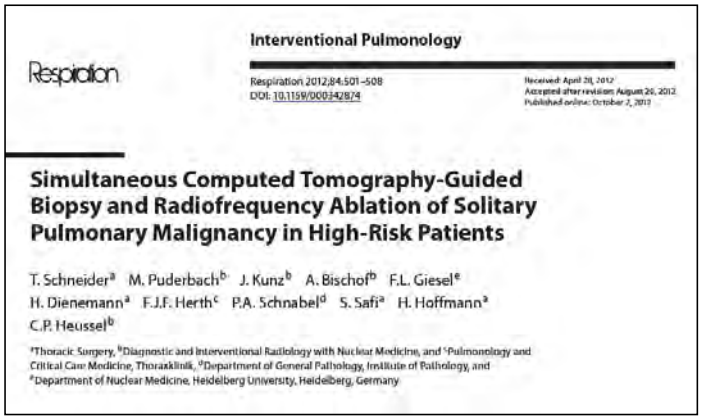

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PATHOLOGICAL EXAMINATION (N = 20)			
Sample size	(mm)	8.4 ± 3.7	[4 – 20]
Sample coagulative necrosis*	%	89.2 ± 19.4	[43 – 100]
Coagulative necrosis artifacts	Mild	7	(35 %)
	Moderate	9	(45 %)
	Important	4	(20 %)
Cancer diagnosis	Yes	18	(90 %)
	No	2	(10.5 %)
Cancer characterization	Possible	14	(70 %)
	Not possible	5	(30%)

Tselikas, Eur Radiol 2016

RFA chez patients non chirurgicaux (Institut Gustave Roussy / Institut Bergonié)

CLINICAL INVESTIGATION INTERVENTIONAL ONCOLOGY

Percutaneous Lung Thermal Ablation of Non-surgical Clinical N0 Non-small Cell Lung Cancer: Results of Eight Years' Experience in 87 Patients from Two Centers

Jean Palussiere · Philippe Lagarde · Anne Aupérin · Frédéric Deschamps · François Chomy · Thierry de Baere

87 CBPNPC, N0
Taille moyenne : 21mm [10-54]

Preuve histologique pour toutes les tumeurs (Adenocarcinoma = 59 %).
T1 : 74% (n=64)
T2 : 26 % (n=23)
- T2a : 25% (n= 22)
- T2b : 1% (n=1) (diam = 54mm)

87 patients avec 97 tumeurs
- One tumeur (n=80)
- Two tumeurs (n=6)
  - Ipsilateral tumeur (n=2)
  - Bilateral tumeur (n=4)
- Five tumeurs (n=1)

Palussiere J, CVIR 2015

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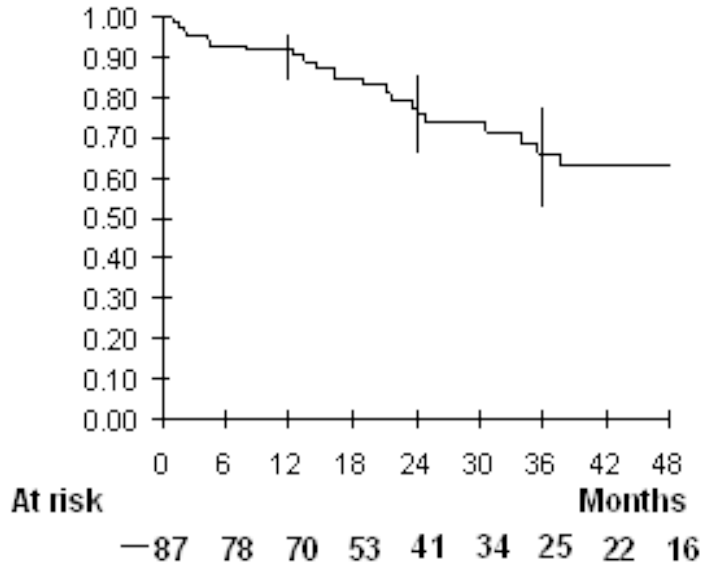
87 CBPNPC, N0 (age µ 69.1 ans)

Taille : µ = 21 mm [10-54]



Taille >2 cm

seul facteur associé à échec de contrôle local

(p = 0.015)

HR = 4.30

(95 % CI, 1.20–15.4)

Time	1 year	2 years	3 years	4 years	5 years
OS	91.9%	77.5%	**66.1%**	63.4%	**58.1%**

Palussiere J, CVIR 2015

Charlson Comorbidity Index predicts patient outcome, in cases of inoperable non-small cell lung cancer treated with radiofrequency ablation

Tracey G. Simon[a], Michael D. Beland[a], Jason T. Machan[b], Thomas DiPetrillo[c], Damian E. Dupuy[a,*]

- 82 non surgical NSCLC
- Survival : 77%, 62%, 50% and 20% @ 1,2, 3, and 5 years

Risk factor	Charlson comorbidity score by grade		Charlson comorbidity score by threshold	
	HR (95% CI)	*p*-Value	HR (95% CI)	*p*-Value
Age (per year)	1.00 (0.95, 1.04)	0.8097	1.00 (0.96, 1.04)	0.9973
Gender (male vs. female)	2.45 (1.20, 5.02)	0.0139		0.0034
Tumor stage (>IB vs. I)	2.85 (1.18, 6.90)	0.0205		0.011
Histology (squamous vs. no)	0.44 (0.23, 1.50)	0.1898		0.1395
Charlson comorbidity score		<0.0001		<.0001
3–4 vs. 1–2	2.77 (0.54, 14.38)[‡]	n.s.		
≥5 vs. 1–2	12.08 (2.35, 62.10)[‡]	<0.05		
≥5 vs. 3–4	4.36 (1.61, 11.76)[‡]	<0.05		
≥5 vs. <5			5.43 (2.64, 11.19)	<.05

Simon, Eur J Radiol 2012

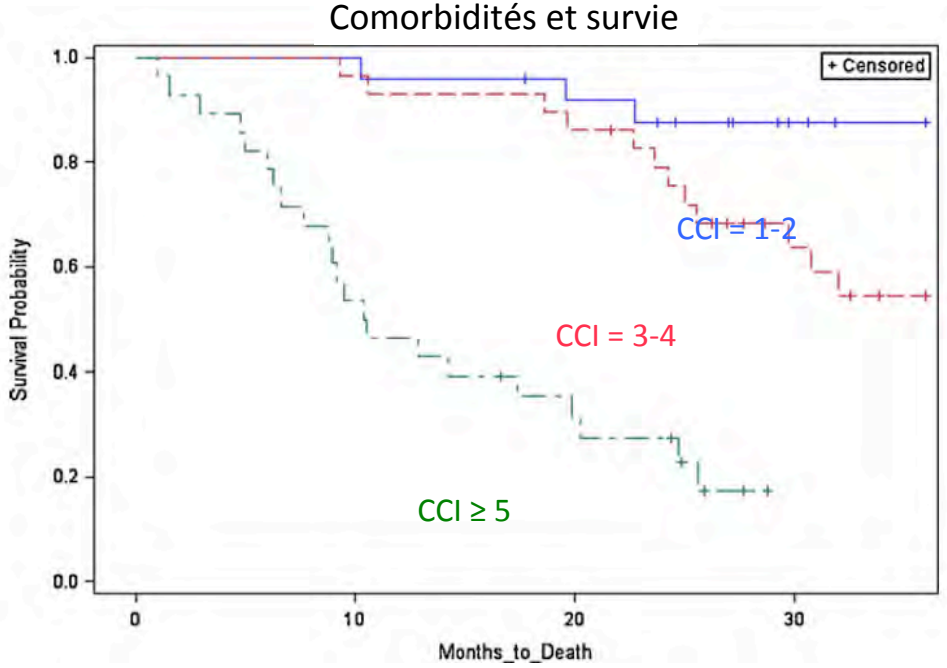
Charlson Comorbidity Index predicts patient outcome, in cases of inoperable non-small cell lung cancer treated with radiofrequency ablation

Tracey G. Simon[a], Michael D. Beland[a], Jason T. Machan[b], Thomas DiPetrillo[c], Damian E. Dupuy[a,*]

- 82 non surgical NSCLC
- Survival : 77%, 62%, **50%** and 20% @ 1,2, **3**, and 5 years

40 décédés
- 19 de NSCLC
- 21 d'autre causes

Comorbidités et survie



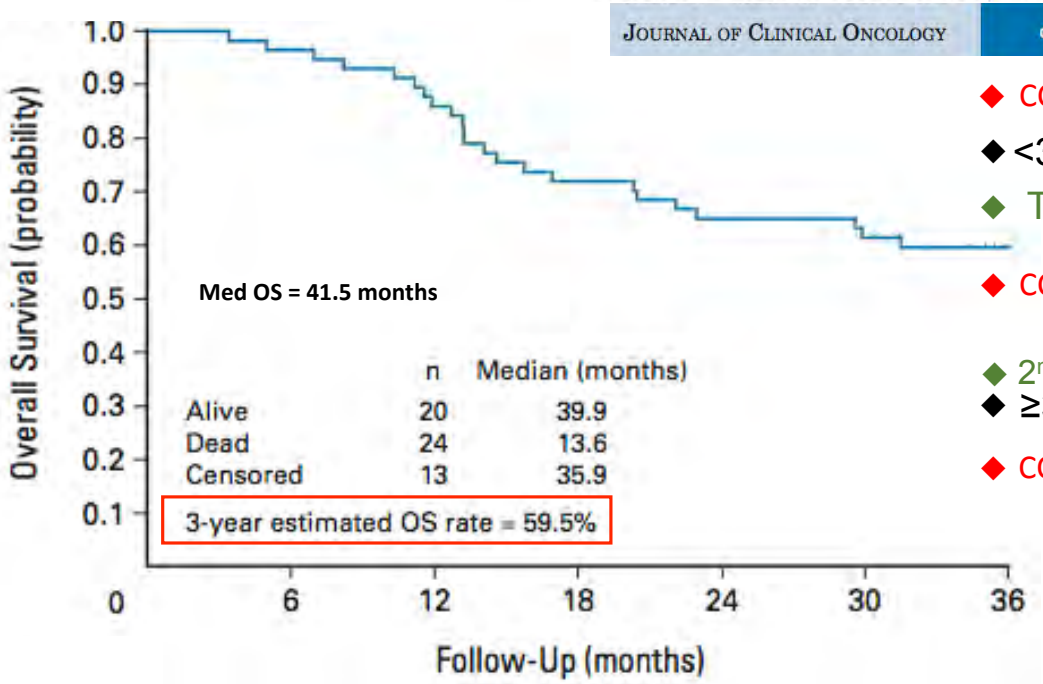
CCI : Charlson comorbidity index

(Simon TG, Eur J Radiol 2012)

SBRT vs RFA

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

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

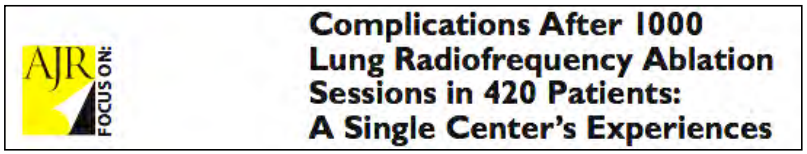


- ◆ CCI = 1-2
- ◆ <3cm
- ◆ T1N0
- ◆ CCI = 3-4
- ◆ 2nd cancer / DFI<1 year
- ◆ ≥3cm
- ◆ CCI ≥ 5

- Kodama H, Cardiovasc Intervent Radiol 2012;
- Simon TG, Eur J Radiol 2012;
- Palussiere J, CVIR 2015;

Baumann P, J Clin Oncol 2009

Tolérance



- Death : 0.4% including interstitial pneumonia (0.3%), Hemothorax (0.1%).
- Major complications : 9.8% (*Grade **4** : 0.4%, Grade **3** : 9.4%)*

  aseptic pleuritis (2.3%),

  pneumonia (1.8%),

  lung abscess (1.6%),

  bleeding re-quiring blood transfusion (1.6%),

  pneumothorax with pleural sclerosis (1.6%),

  bronchopleural fistula (0.4%),

  brachial nerve injury (0.3%),

  tumor seeding (0.1%),

  diaphragm injury (0.1%).

Khasima T et al, AJR 2011

Respiratory test	Before RFA	1 mth post RFA
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)

* FEV1 : Forced Expiratory Volume in 1 second
** VC : Vital Capacity

de Baere T, Radiology 2006

NO CHANGES OF RESPIRATORY FUNCTION

	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

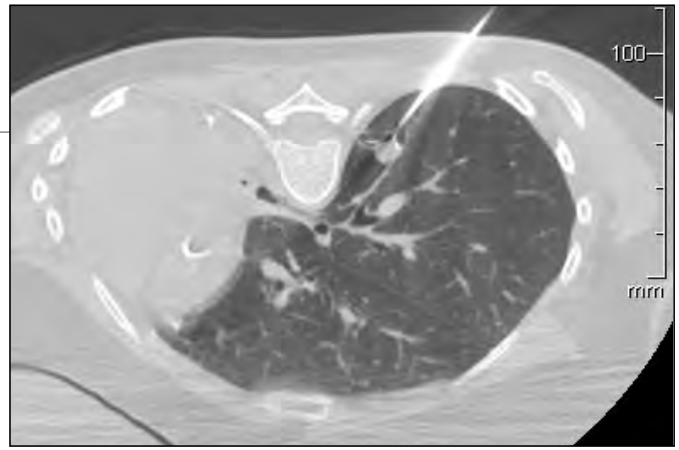
Lencioni R, Lancet Oncol 2008

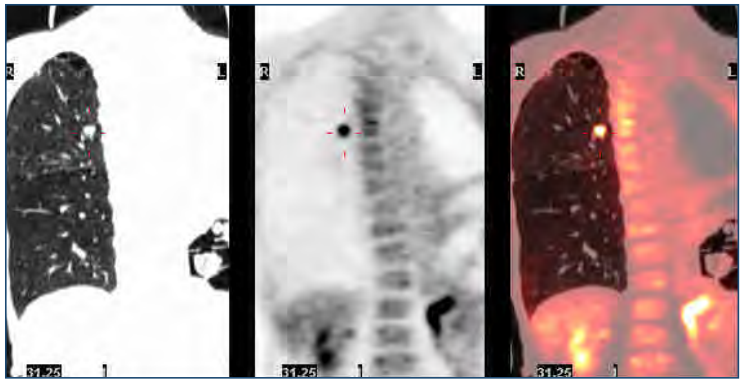
LIMITATIONS ?

FAISABILITE SUR POUMON UNIQUE

- 15 patients (64 ans)
  - Primitifs (n=11)
  - Métastases (n=4)

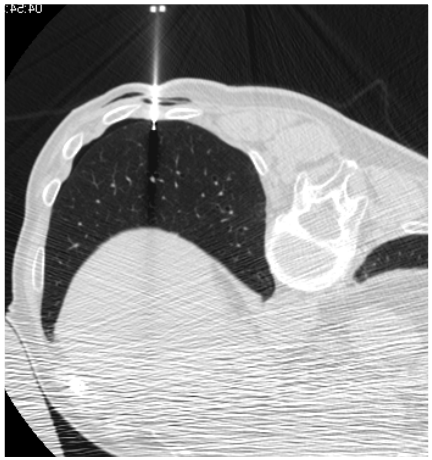
  CCR (n=3), sarcome (n=1)
- 21 tumeurs :15.5 mm [4-37]
- Delais / pneumonectomie: [5m-14y]
- FEV = 30 – 70% (m: 56%)

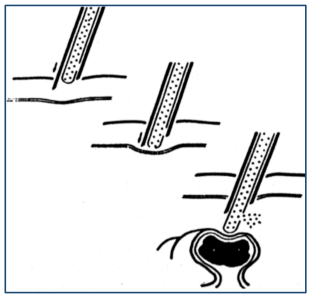




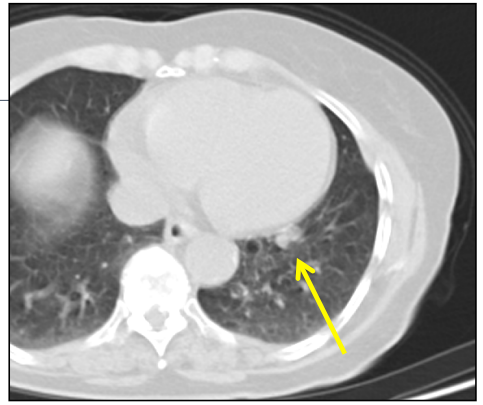
Hess A et al, Radiology 2010

TECHNICAL CHALLENGES?

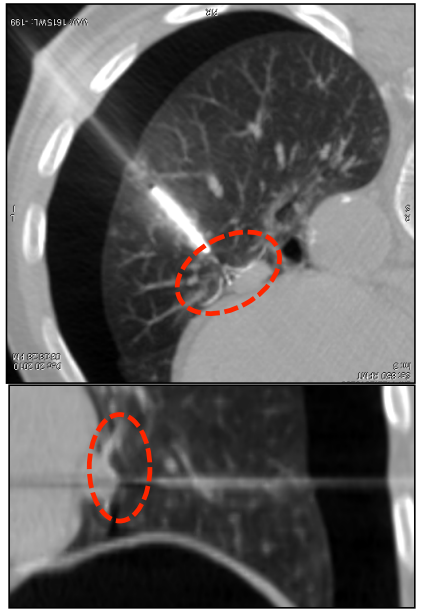


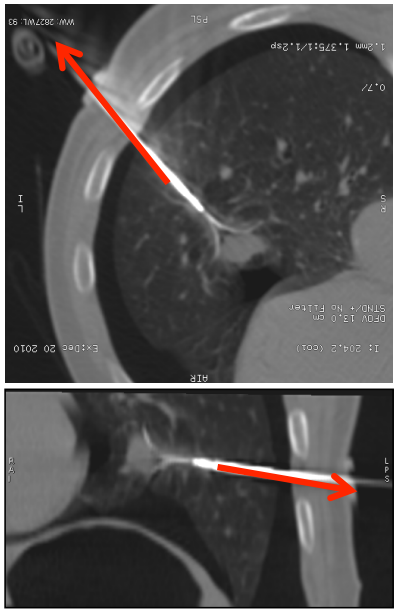


Pneumothorax induit après insertion de l'aiguille de RF



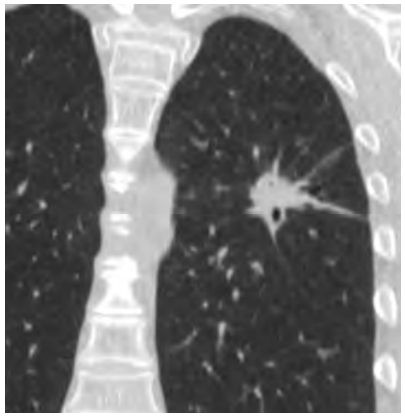
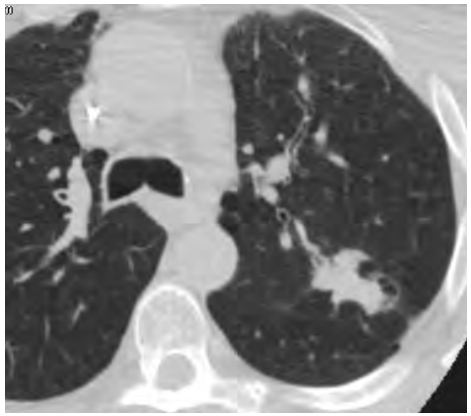
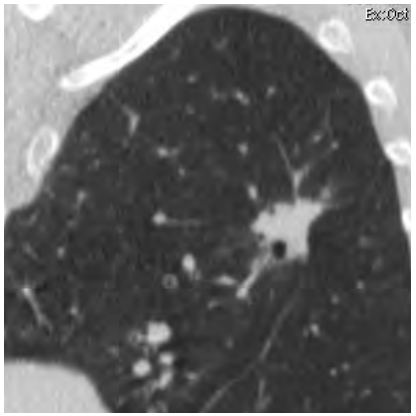
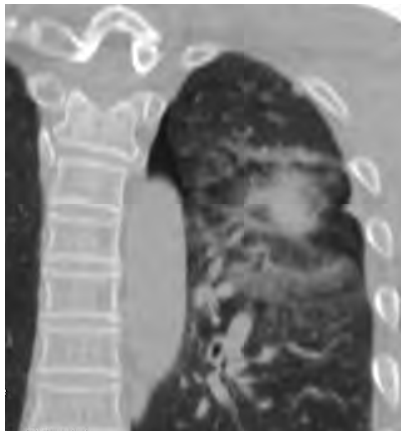
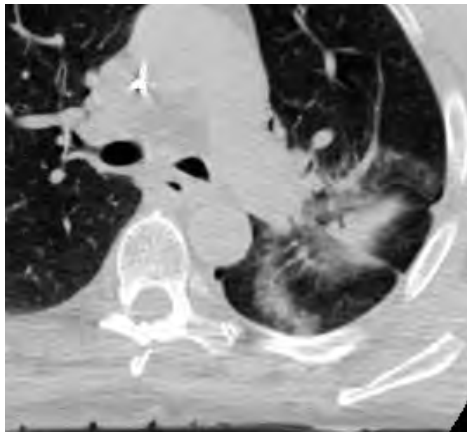
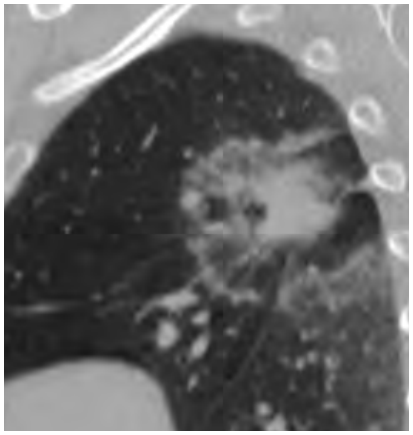
Traction prudente sur l'aiguille de RF





Les micro-ondes: MWA

Reproducibilité ?

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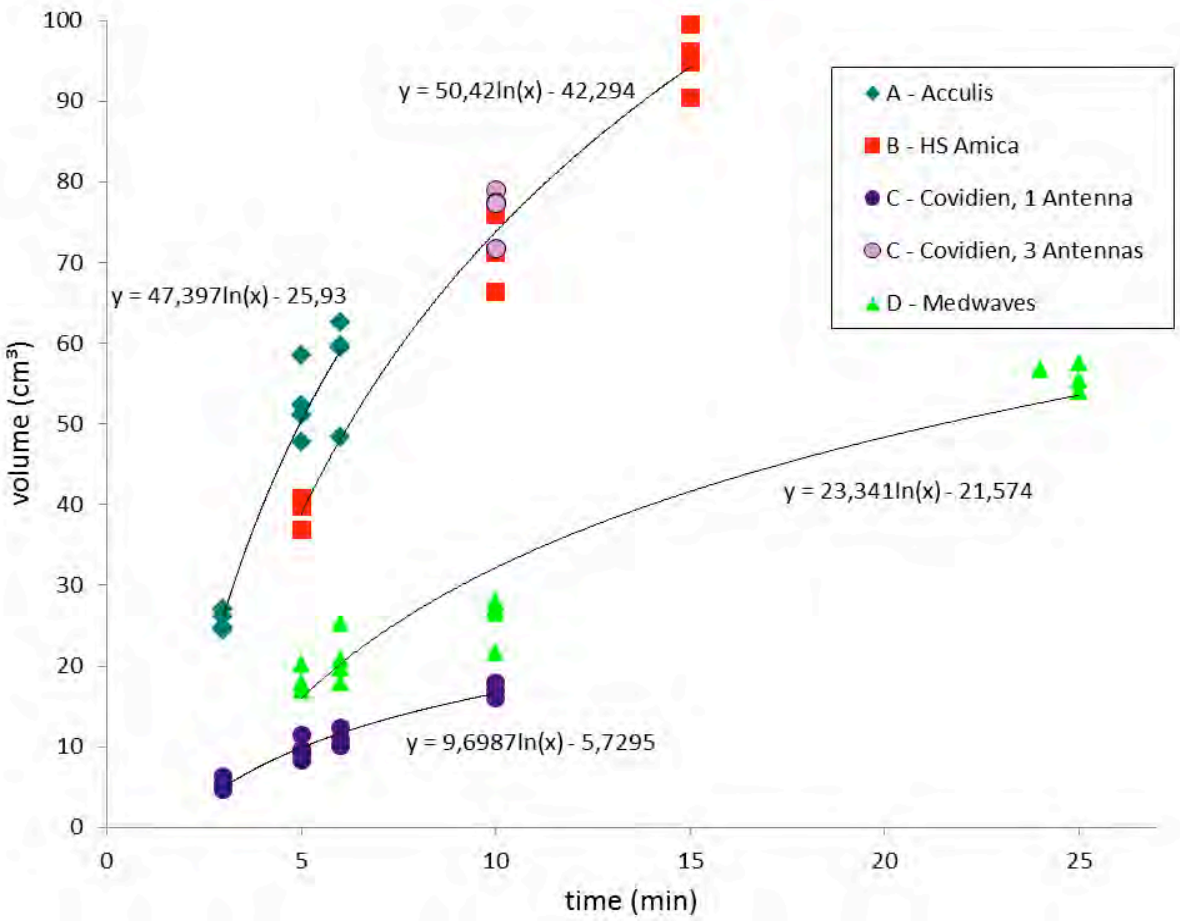
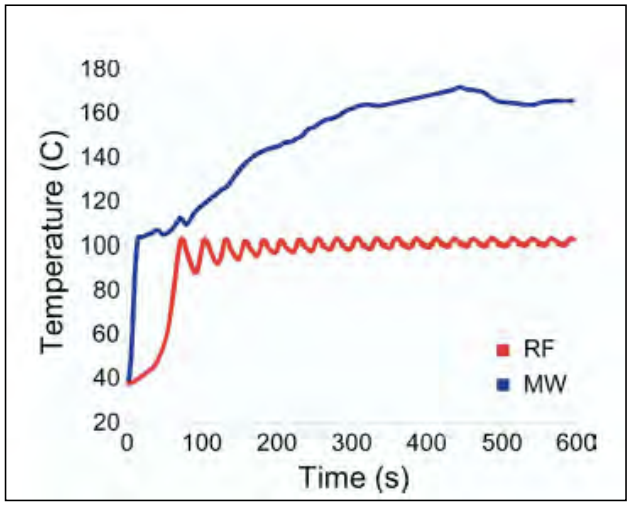




Hoffmann R. Radiology 2013 Brace, Curr Probl Diagn Radiol 2009

Major complications of high-energy microwave ablation for percutaneous CT-guided treatment of lung malignancies: Single-centre experience after 4 years

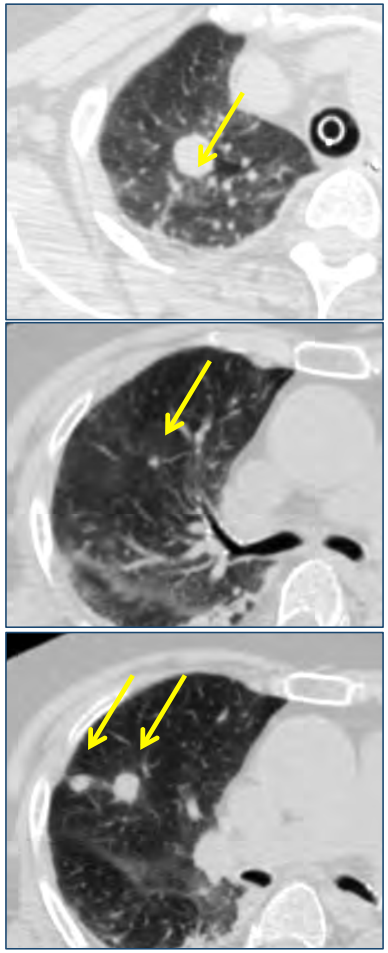
Alexander M Splatt[1] and Karin Steinke[1,2]

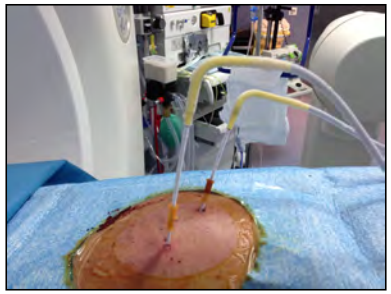
- 20% Complications ≥ grade 3 (14 / 70 ablations)
  - 1.4% décès dans les 30 jours
  - 12.9% pneumothorax avec drainage,
  - 55.7% épanchement nécessitant une aspiration
  - 2.9% hémorragie pulmonaire significative
  - 2.9% infections
  - 1.4% brulure de la paroi thoracique
  - 1.4% ensemencement

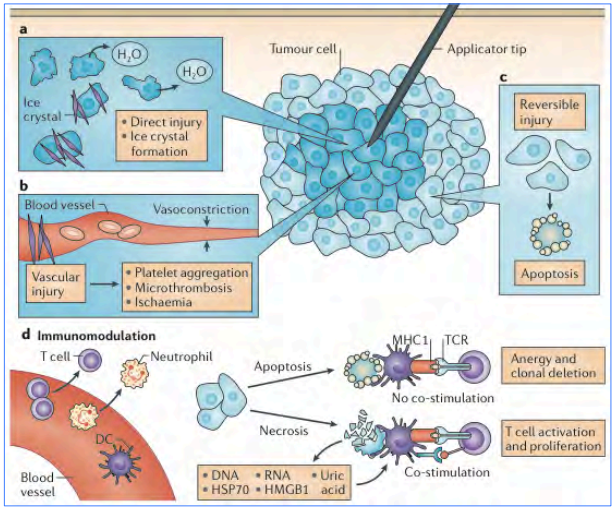
- Plus de complications pour nodule **<7 mm** de la plèvre.

Splatt, Journal of Medical Imaging and Radiation Oncology 2015

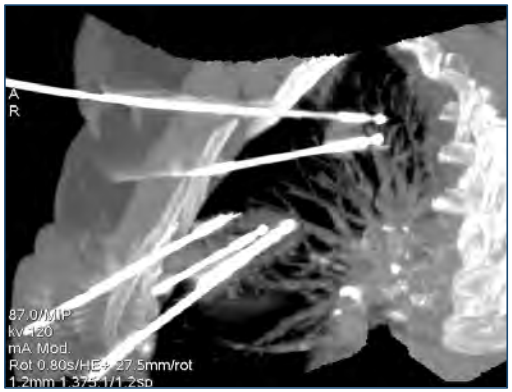
Cryothérapie

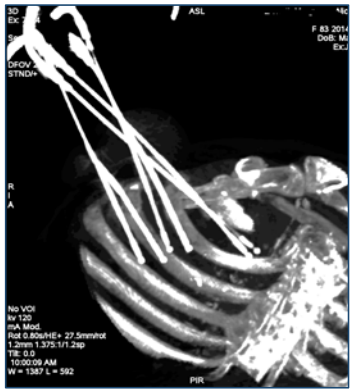




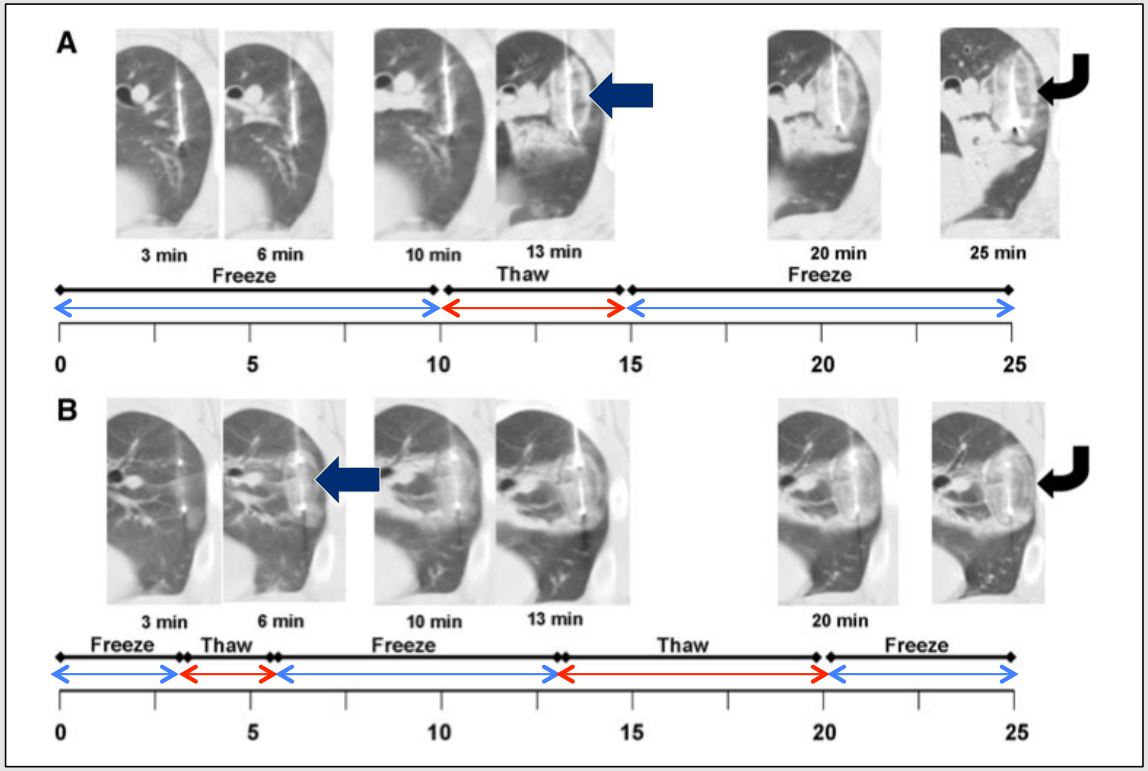


(Chu, Nature reviews Cancer 2014)





Hemorrhage during the thaw => thermal conductivity **20 X** aerated lung



JL. Hinshaw, CVIR 2010

Treatment cycles :

3 / 2+1 / 7 / 2+1 / 10 / 2

< 30'

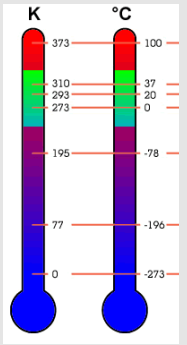
Niu, Techn in Cancer Res and Treat. 2012

Thomson-Joule Effect

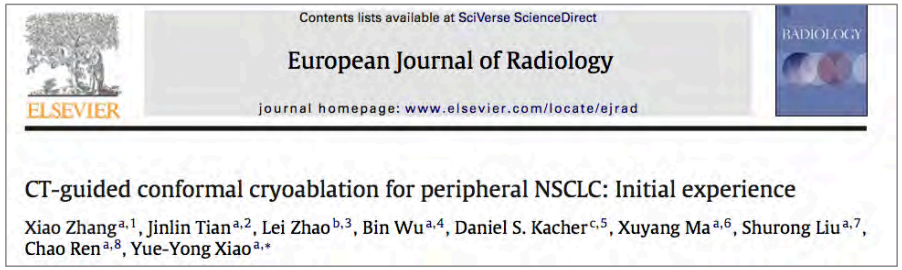
ARGON => Freeze

*HELIUM => thaw

** Or Electrical thawing : **CX***



Faisable sous anesthésie locale ou sédation



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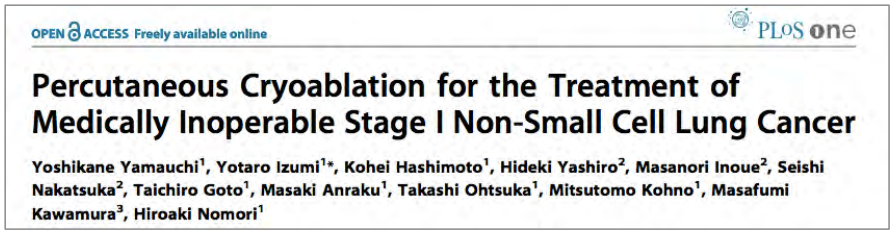
CT-guided conformal cryoablation for peripheral NSCLC: Initial experience

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,*]

X Zhang, Eur J Radiol, 2012

n = 46 biopsy proven **NSCLC** (32 ADK, 12 SCC, 2 LCC)

- d ≤ 3 cm (n=19) ---- 2 probes
- 3 < d < 5cm (n=27) ----- more than 2 probes



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PLoS one

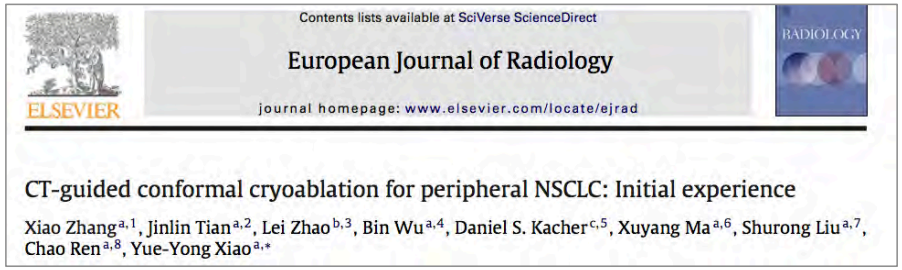
Percutaneous Cryoablation for the Treatment of Medically Inoperable Stage I Non-Small Cell Lung Cancer

Yoshikane Yamauchi[1], Yotaro Izumi[1]*, Kohei Hashimoto[1], Hideki Yashiro[2], Masanori Inoue[2], Seishi Nakatsuka[2], Taichiro Goto[1], Masaki Anraku[1], Takashi Ohtsuka[1], Mitsutomo Kohno[1], Masafumi Kawamura[3], Hiroaki Nomori[1]

Y Yamauchi, Plos ONE 2012

n = 22 Stage I biopsy proven **NSCLC**

- Charlson comorbidity ≥ 3
- 34 tumors with 25 cryoablation sessions



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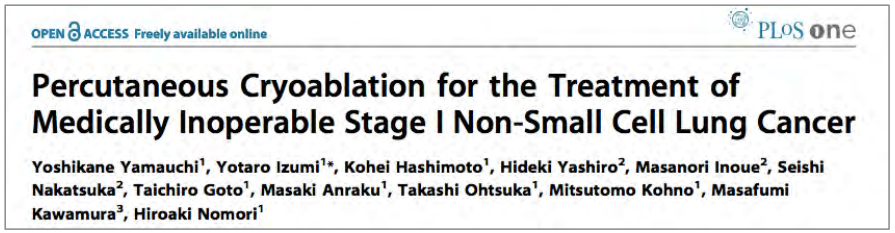
X Zhang, Eur J Radiol, 2012

RECIST at 24 months:

- 36 complete response (83.7%)
- 7 partial response (16.3%)
- 3 patients died due to multiple metastases



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Y Yamauchi, Plos ONE 2012

	Baseline	Post cryo
VC	2.72 ± 0.82	2.64 ± 0.74
FEV1	1.81 ± 0.53	1.77 ± 0.5

- Med OS : 68 months
- DFS @ 2- and 3-year : 78% and 67%
- 3% local progression *(med F-Up: 23 months)*
- Mean time to progression : 69 ±4 months

Pneumothorax **28%**, Chest tube **4%** , Pleural effusions **31%**

Before treatment

3 / 3 / 7

3 / 3 / 7 / 3 / 10

I 110

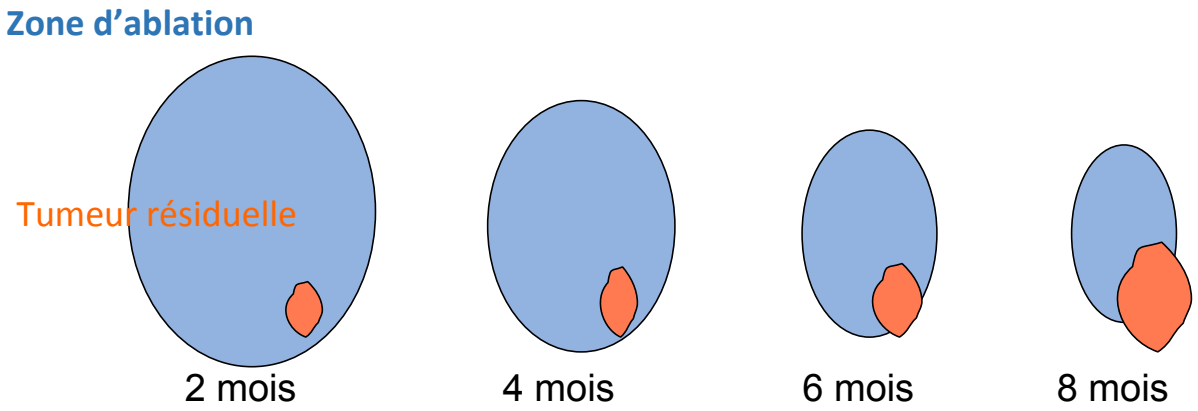
FA

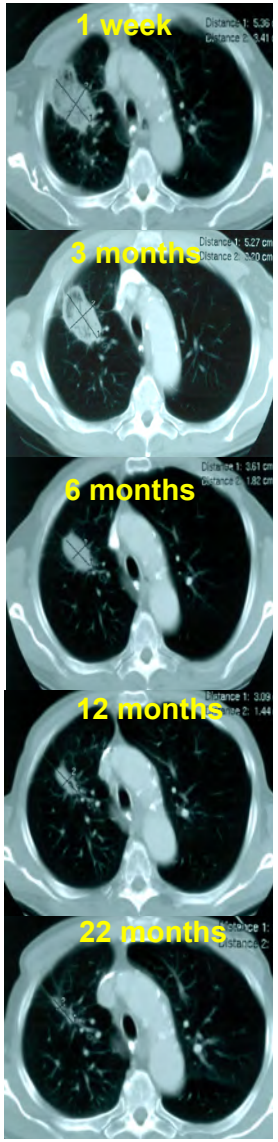
Ablation zone visualization

Suivi en Imagerie : scanner

Evaluation Morphologique

➔ Découverte tardive des traitements incomplets





Pour résumer :

- Alternatives efficaces, peu morbides
- Place de chaque technique a établir
  - **SBRT :**
    - **plus de données, pas de pneumothorax**
    - **Preuve histo, Localisation, taille > 5cm**
  - **RF/Cryo :**
    - **Histo per-op, moyen « physiques » de protection, imagerie, retraitements**
    - **Taille > 3cm, Pneumothorax**
  - Vs Chir pour patients opérables???

LES CBPN DE STADE PRECOCE