Advances in percutaneous ablation for hepatocellular carcinoma

P. Nahon1,2,3

1 Hepatology, Jean Verdier Hospital, APHP, Bondy, France

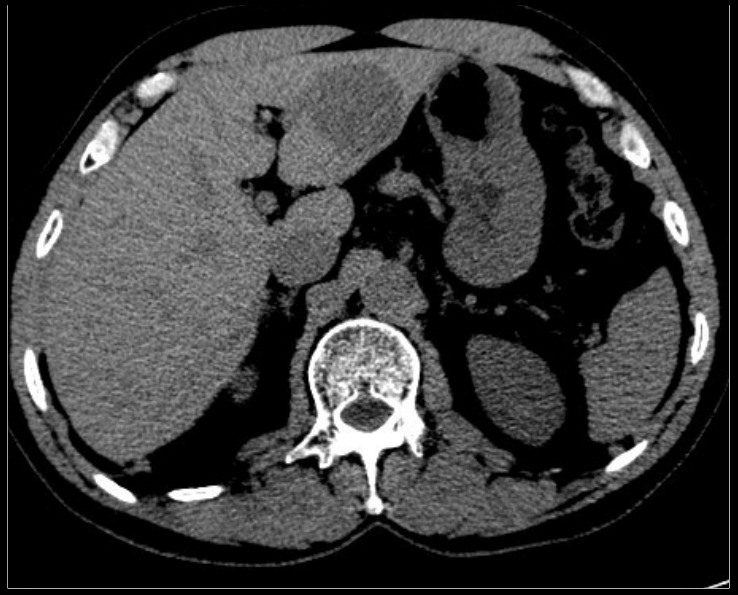
2 Paris 13 university, Sorbonne Paris Cité, UFRSMBH, Bobigny, France

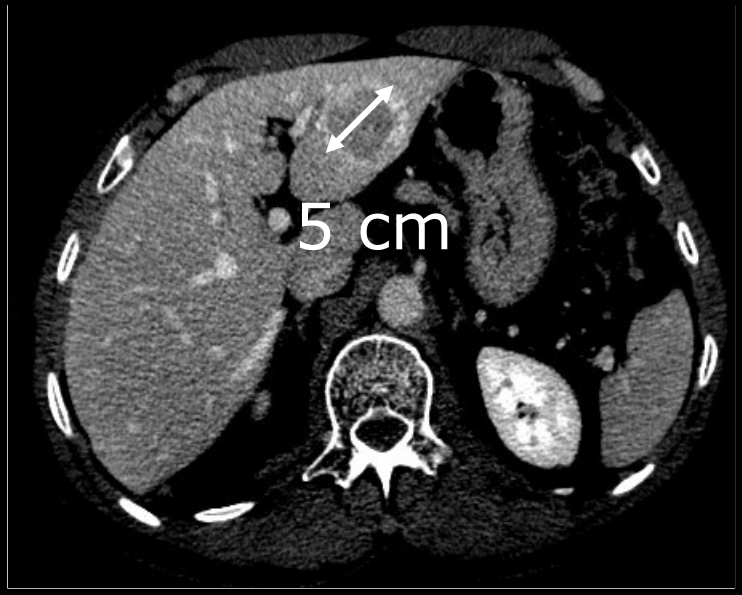
3 Inserm, UMR-1162, Génomique fonctionnelle des tumeurs solides, Paris, nce

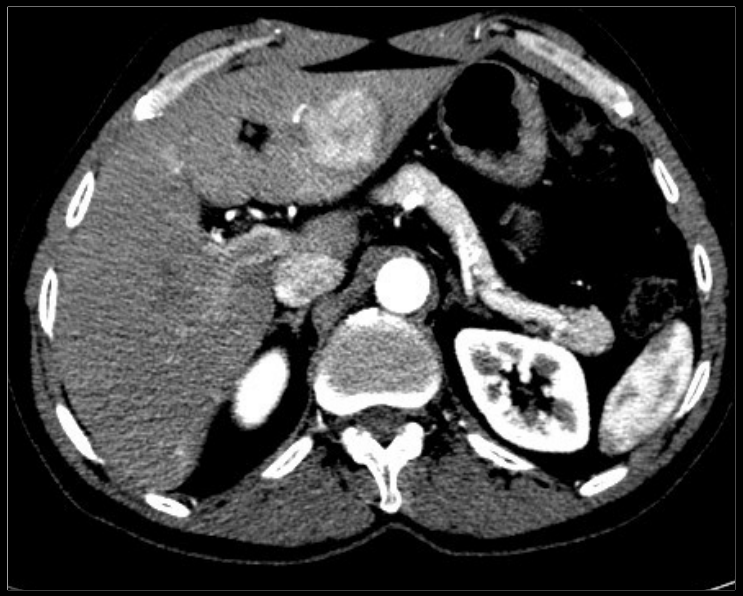
First case

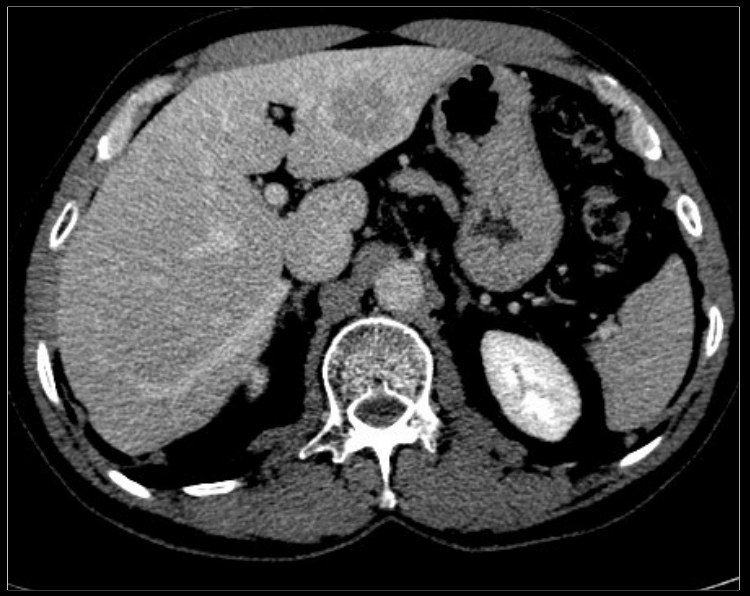
- 59 years old male
- Child-Pugh A6 HBV related cirrhosis (treated)
- Grade II esophageal varices
- Platelets count: 98 000 / mm3
- Bilirubin: 9 mg/L
- Albumin: 34 g/L
- Prothrombin time: 77%
- Liver stiffness: 22 Kpa
- Alpha-fetoprotein: 478 ng/ml
- PS 0, ECOG 0

Pretherapeutic imaging





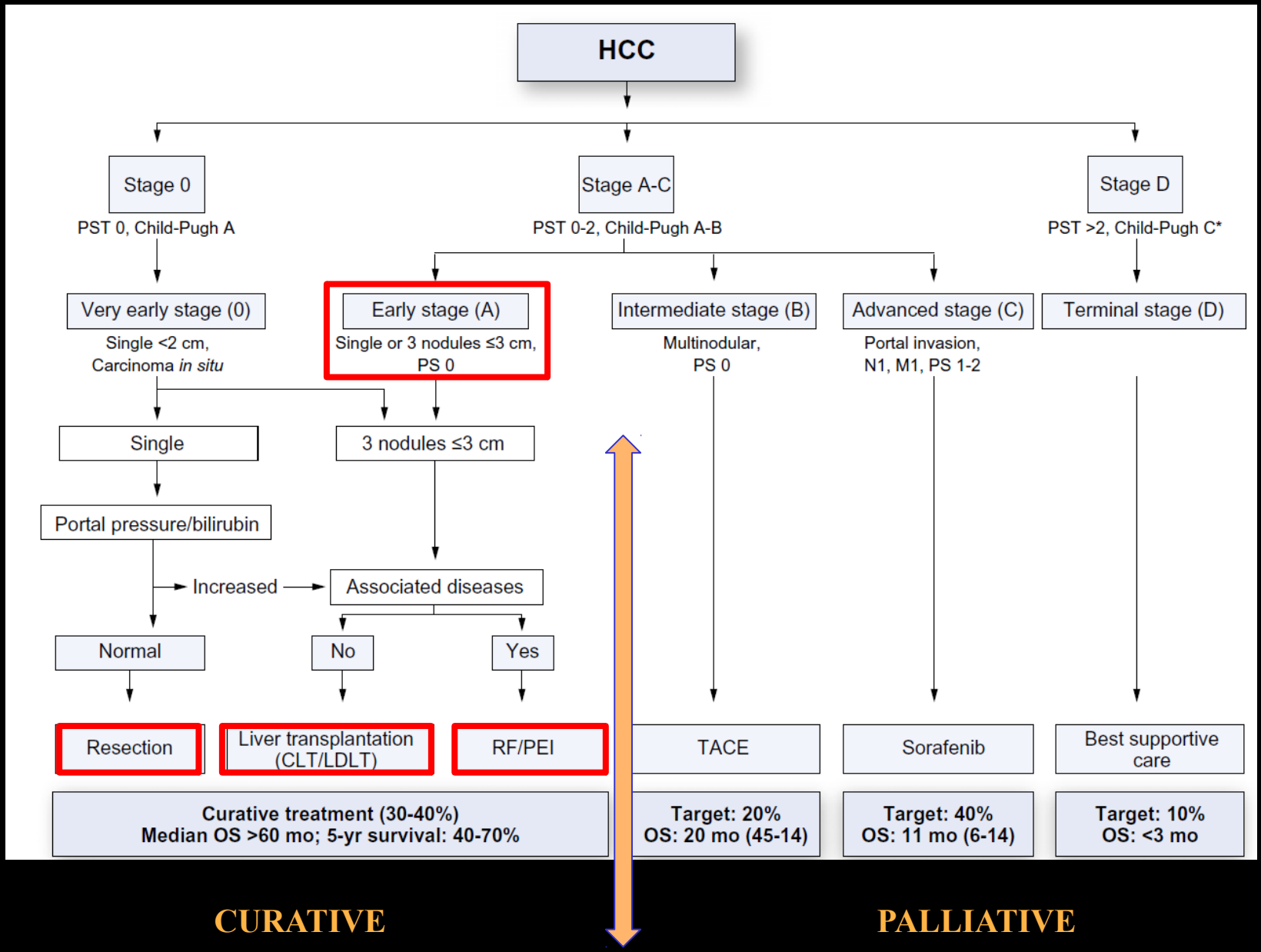




Which treatment?

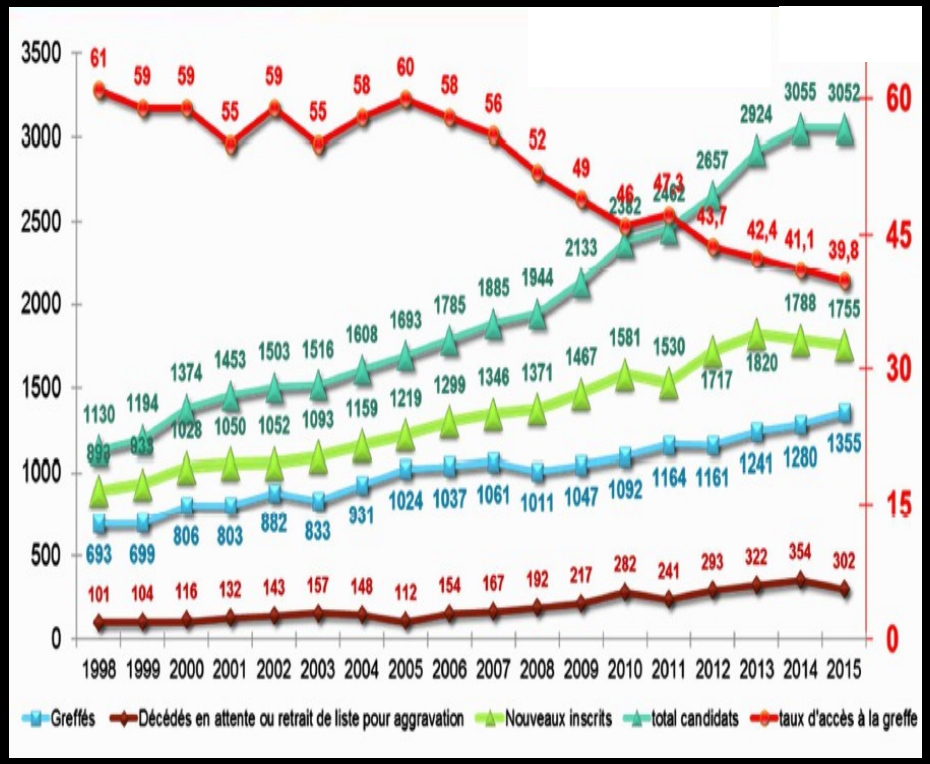
1. Transplantation
2. Resection
3. Ablation
4. TACE
5. Other

BCLC staging

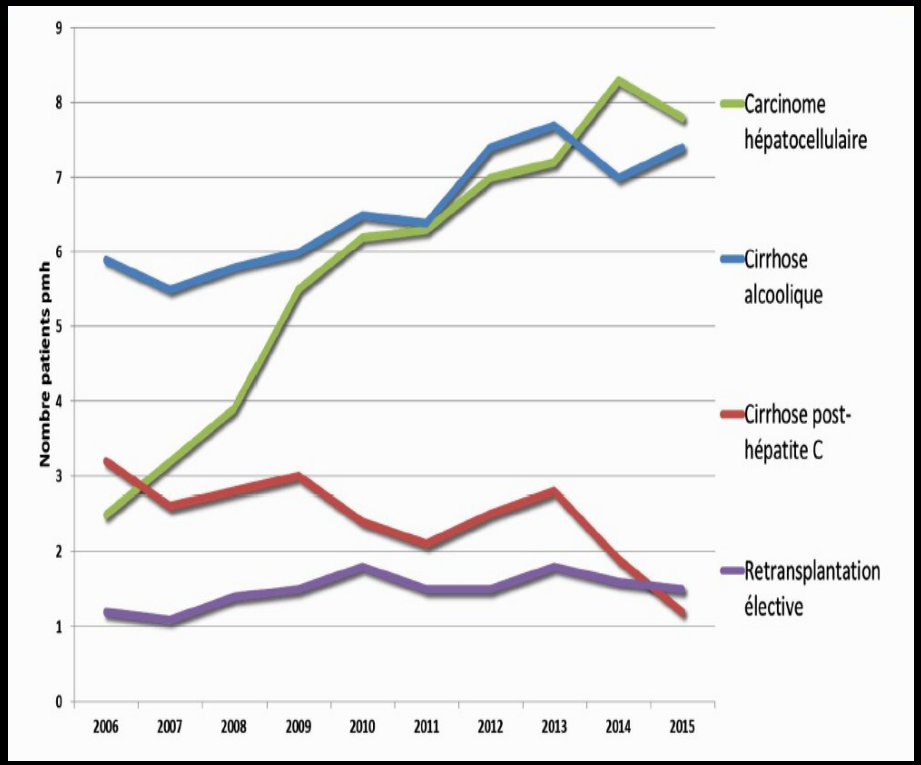


Transplantation not realy possible in first line

2.3 Patients / graft



LT indications

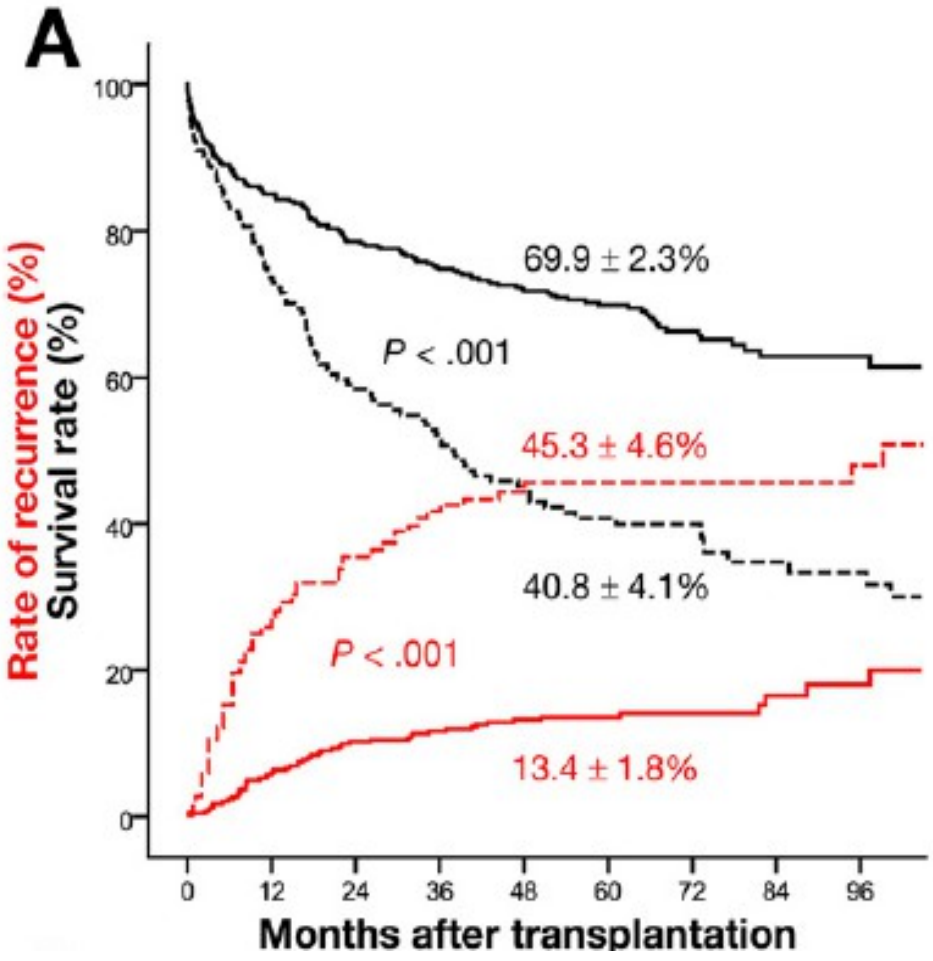


Mean time to LT for HCC in France : 12.2 months

Scoring for liver graph allocation : MELD & Risk of post LT recurrence

Score AFP	**Pts**
Diameter (cm)	
≤3	**0**
3-6	**1**
>6	**4**
Number of nodules	
1-3	**0**
≥4	**2**
AFP (µg/L)	
≤100	**0**
100-1000	**2**
>1000	**3**

Duvoux C et al. Gastroenterology 2012



Risk of recurrence post-LT

— ≤ 2 : low --- > 2 : high

Our patient?

Score AFP	**Pts**
Diameter (cm)	
≤3	**0**
3-6	**1**
>6	**4**
Number of nodules	
1-3	**0**
≥4	**2**
AFP (µg/L)	
≤100	**0**
100-1000	**2**
>1000	**3**

$5 \Rightarrow 1$

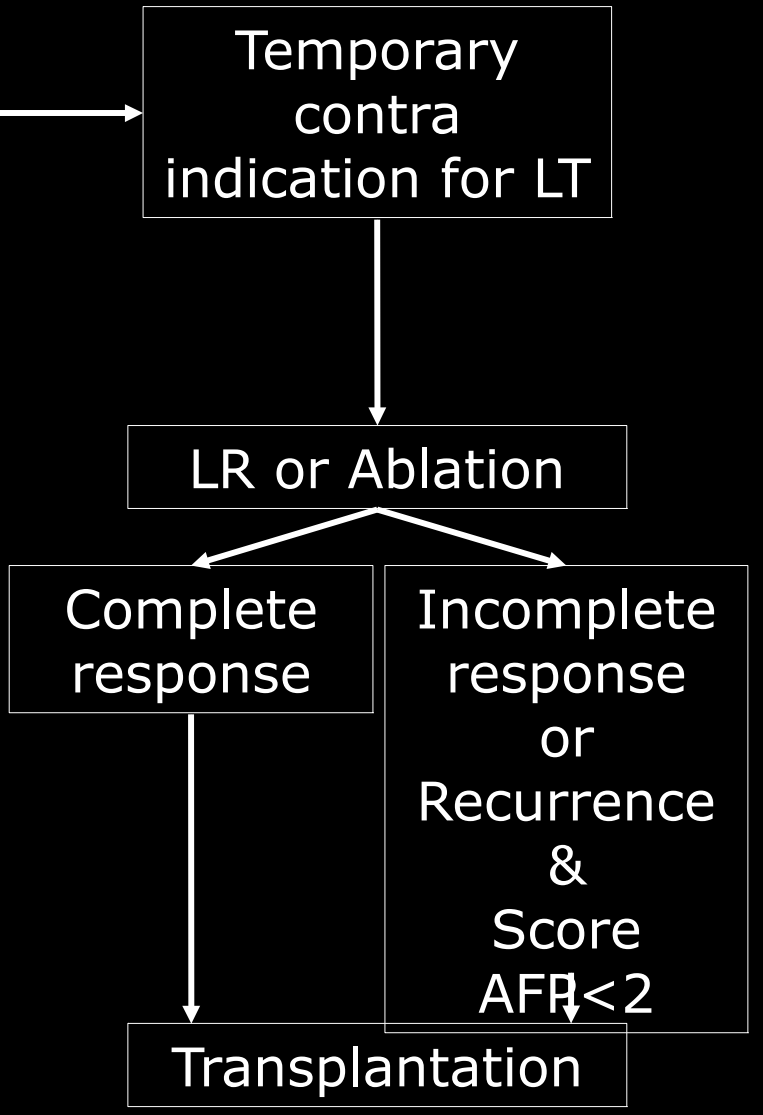
$+$

$< 4 \Rightarrow 0$

$+$

$478 \Rightarrow 2$

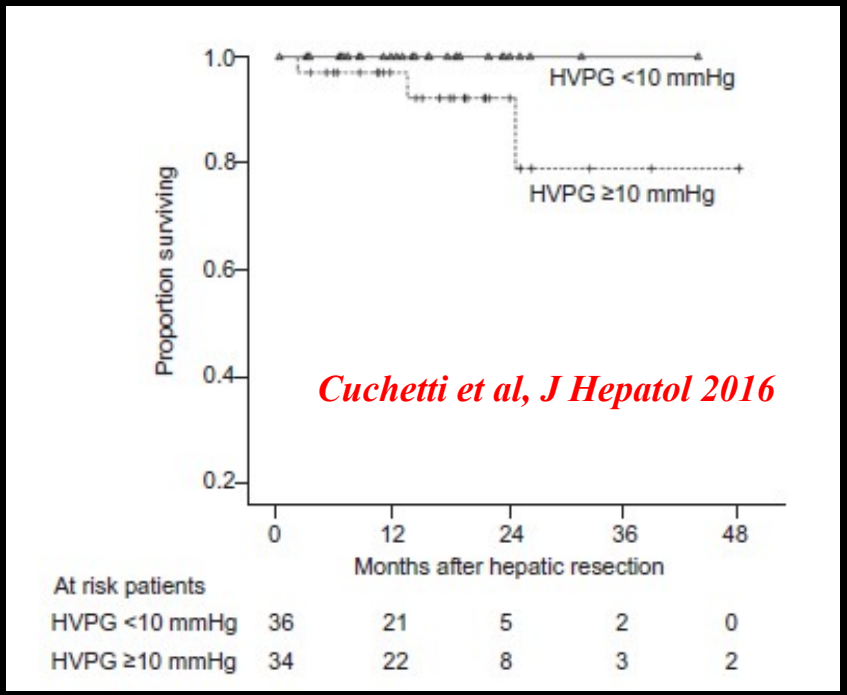
Score AFP $= 3 > 2$



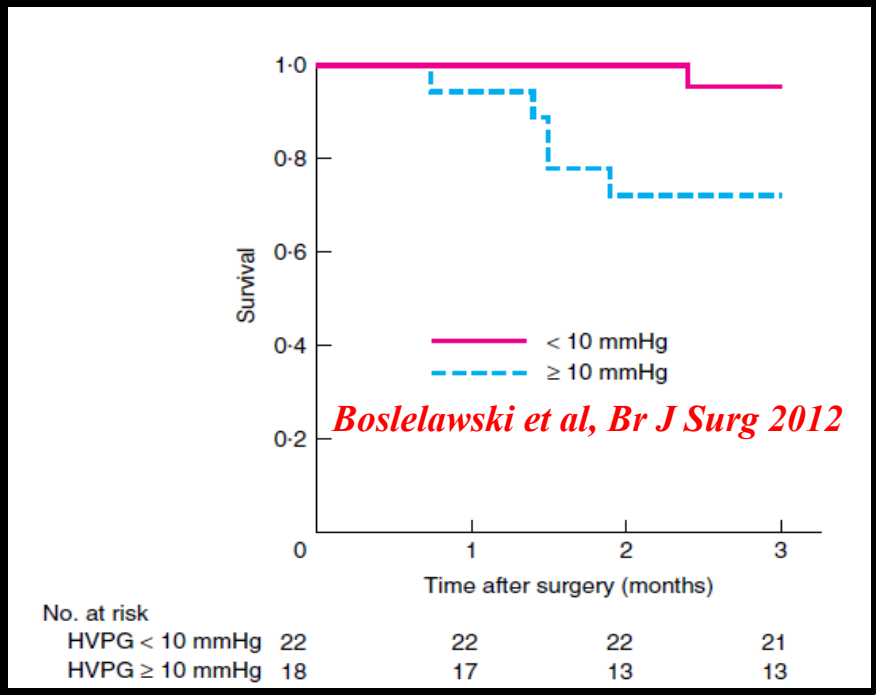
Surgical Resection of Hepatocellular Carcinoma in Cirrhotic Patients: Prognostic Value of Preoperative Portal Pressure

Gastroenterology 2006

Conclu-sions: Cirrhotics with increased portal pressure are at high risk of hepatic decompensation after resection of hepatocellular carcinoma. Surgical resection should therefore be restricted to patients without portal hypertension.



Cuchetti et al, J Hepatol 2016



Boslelawski et al, Br J Surg 2012

Portal hypertension (CSPH): Resection?

1108 patients (386 with *vs* 722 without HP) in **8** studies

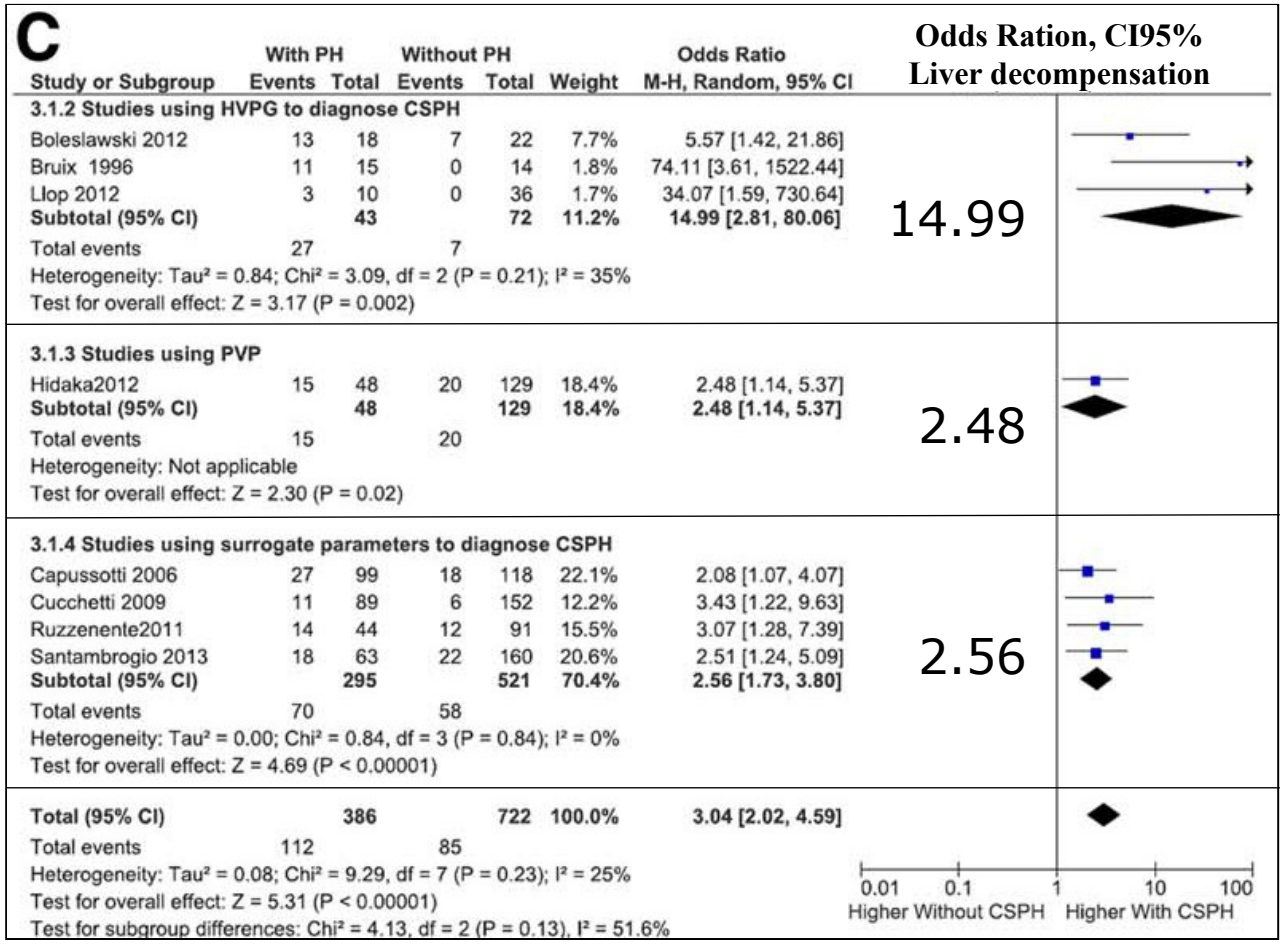
Berzigotti, Bruix, Hepatology 2015

HVPG:
≥ 10 mm Hg

PVP:
≥ 20 cm H2O

Surrogate:
GEV or
Plt.< 105/ml or
Spleen > 12 cm

Pooled

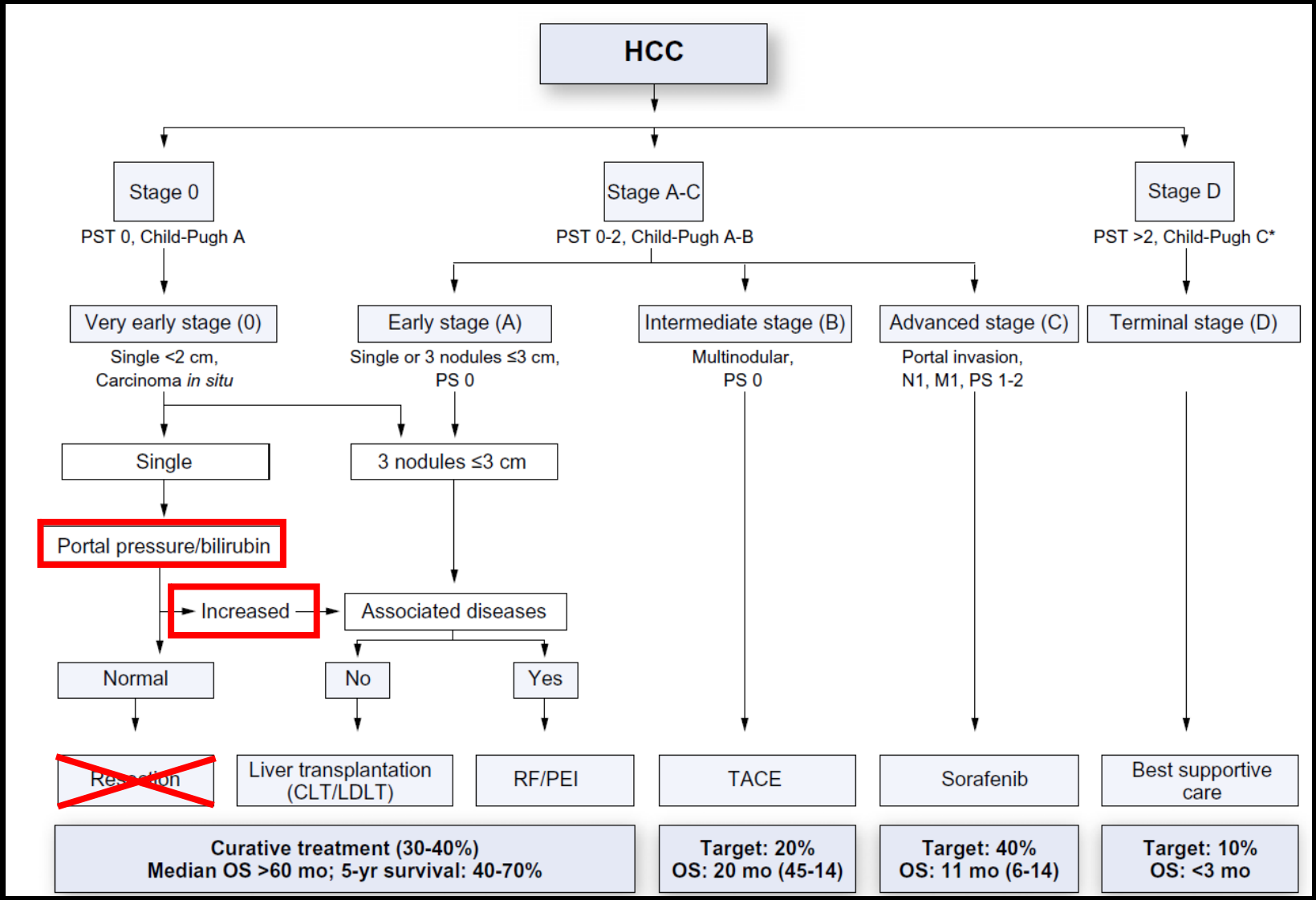


Ablation or resection ?

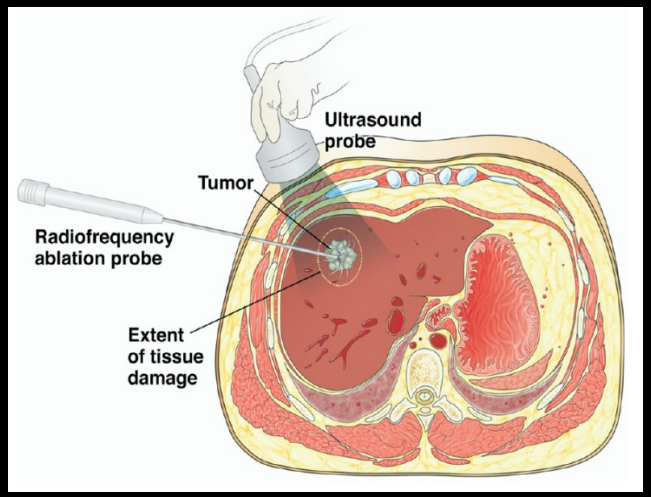
	Ablation	Resection
2 or 3 nodules	Distant	Same segment
Localization	Deep	Superficial
Liver function	Gooda	Excellentb
Portal Hypertension	Yes	No
Mortality	0.3%	1%
5-yrs survival	76% in patients eligible for resection	75%

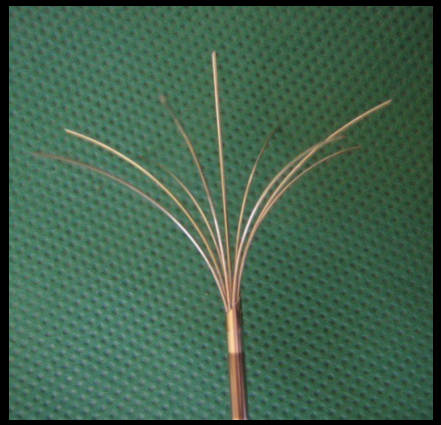
a Malades appartenant principalement à la classe A ou B de Child-Pugh
b Malades appartenant principalement à la classe A de Child-Pugh.avec bilirubine normale et sans hypertension portale

BCLC (AASLD/EASLD)



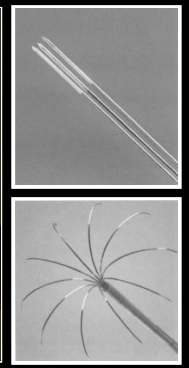
Percutanous ablation



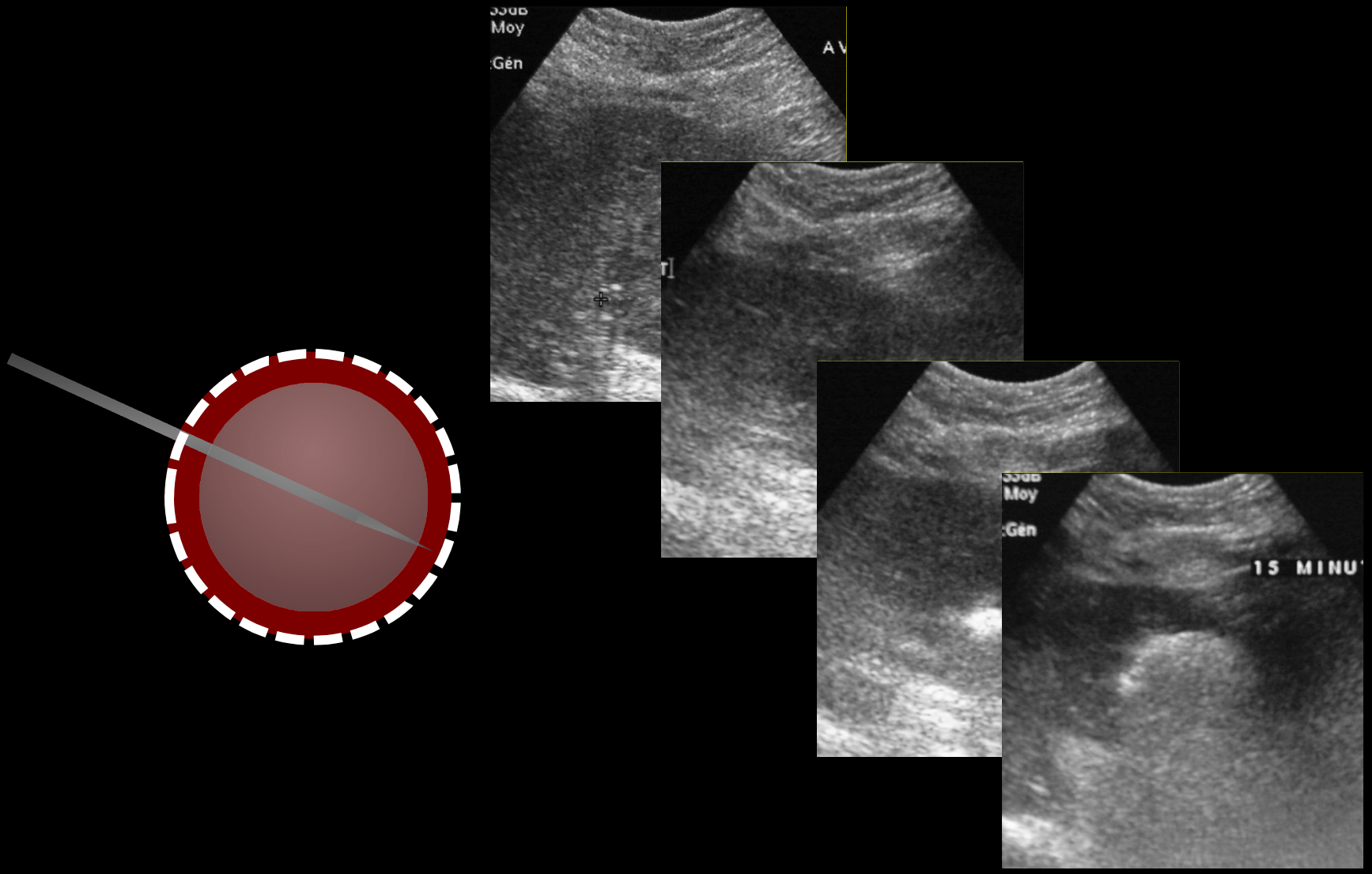


US control

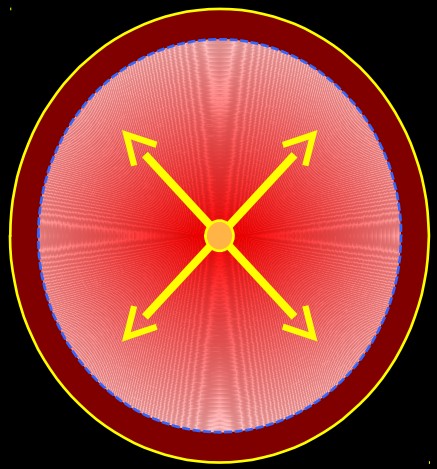
Radiofrequency ablation



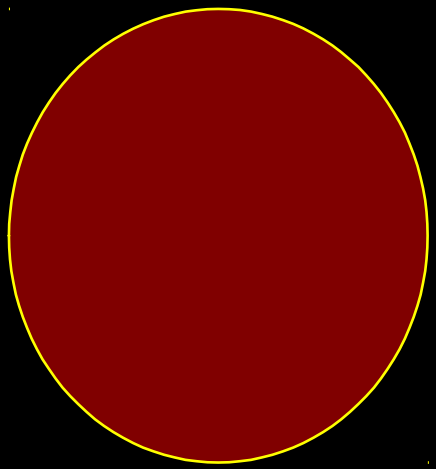
>3 cm: with centrifugal ablation methods no safety margin can be reliably achieved



Principles for large ablations

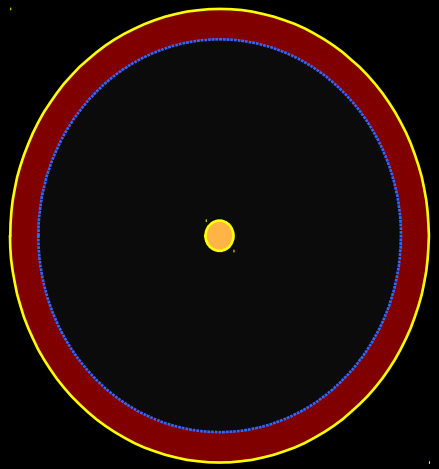


Monopolar RFA

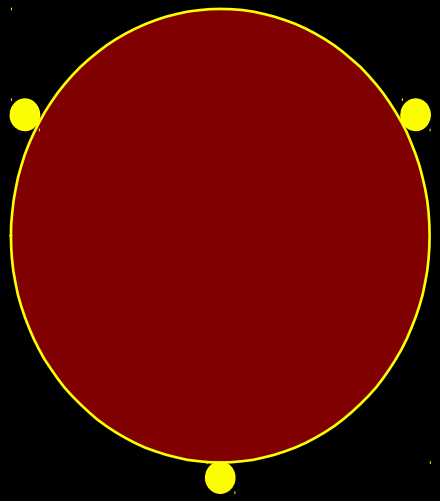


Multibipolar « no touch »

Principles for large ablations

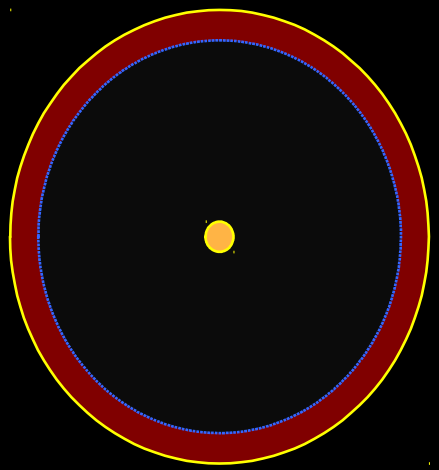


Monopolar RFA

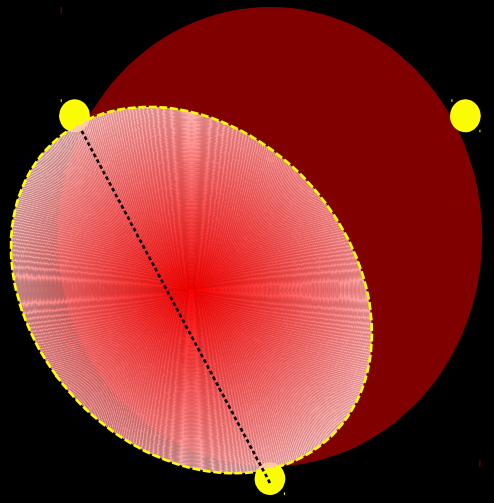


Multibipolar « no touch »

Principles for large ablations

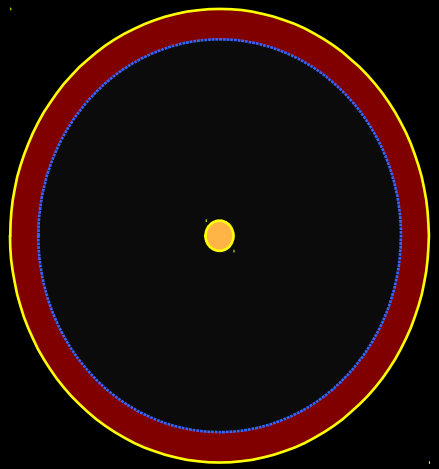


Monopolar RFA

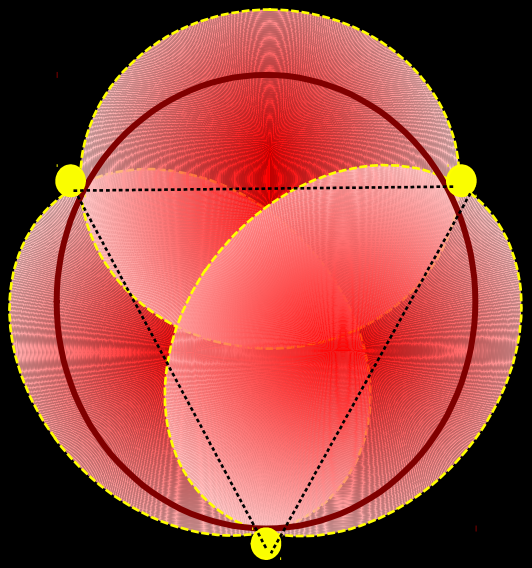


Multibipolar « no touch »

Principles for large ablations

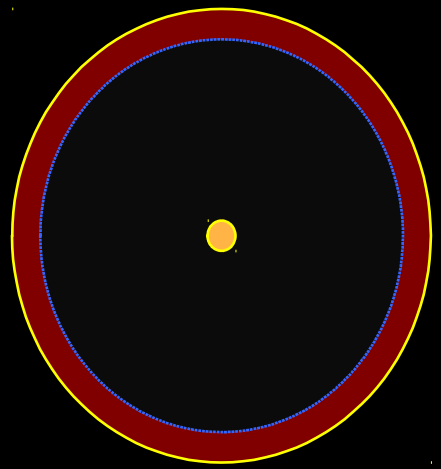


Monopolar RFA

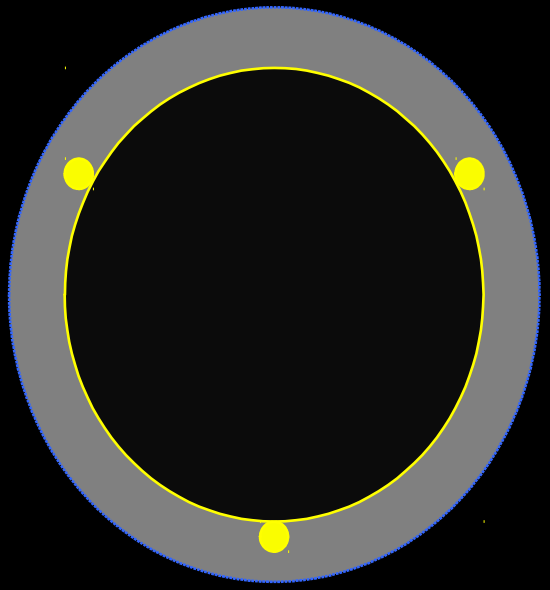


Multibipolar « no touch »

Principles for large ablations



Monopolar RFA



Multibipolar « no touch »

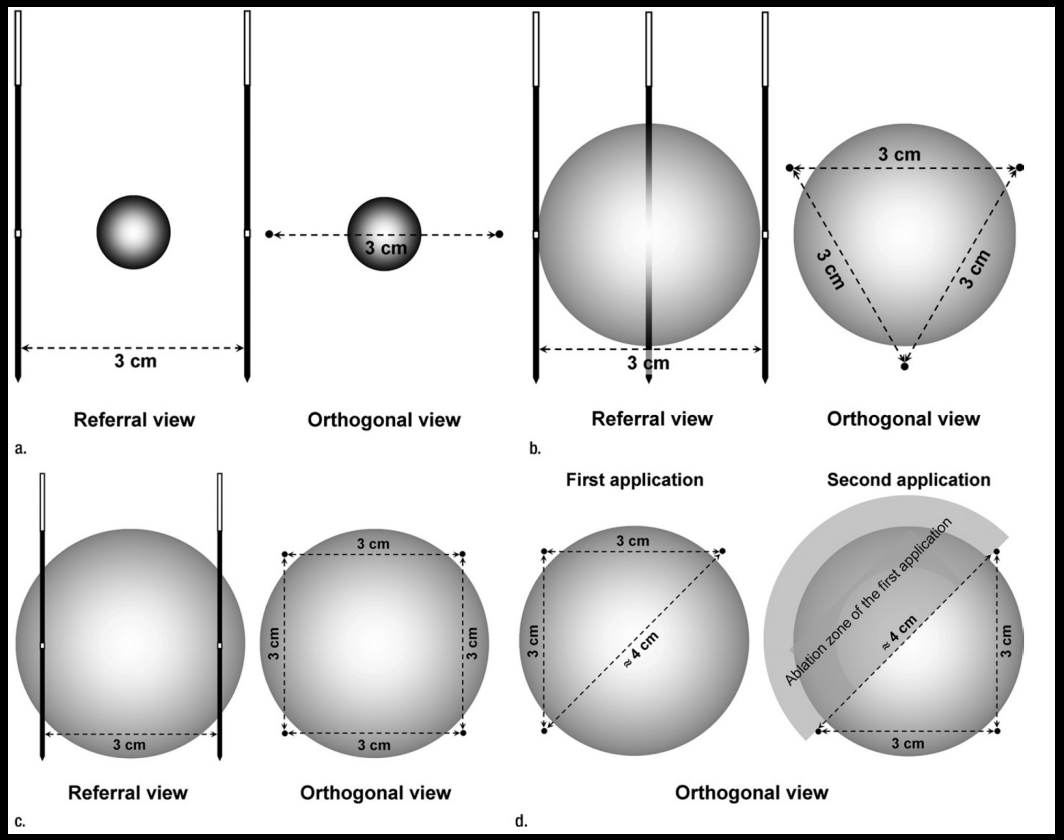
No touch multibipolar RFA for HCC within Milan criteria

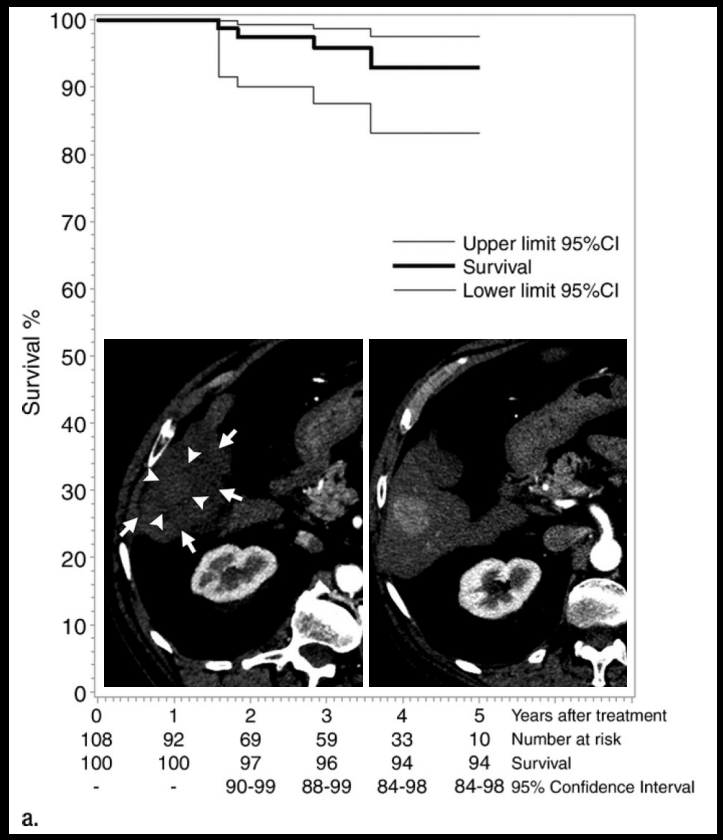
Radiology

Radiology: Volume 280: Number 2—August 2016

Olivier Seror, MD, PhD
Gisèle N'Kontchou, MD
Jean-Charles Nault, MD
Yacine Rabahi, MD
Pierre Nahon, MD, PhD
Nathalie Ganne-Carrié, MD, PhD
Véronique Grando, MD
Nora Zentar, MD
Michel Beaugrand, MD
Jean-Claude Trinchet, MD, PhD
Abou Diallo, MD
Nicolas Sellier, MD

Hepatocellular Carcinoma within Milan Criteria: No-Touch Multibipolar Radiofrequency Ablation for Treatment—Long-term Results[1]





Research Article

EASL JOURNAL OF HEPATOLOGY

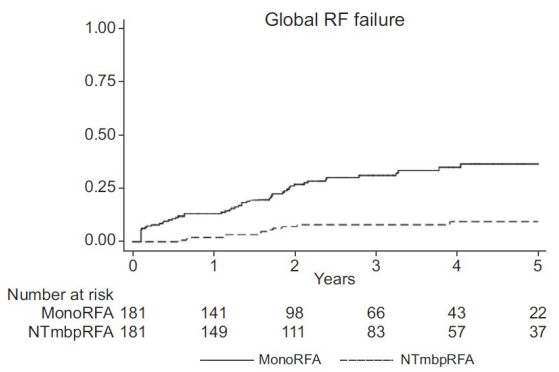
http://dx.doi.org/10.1016/j.jhep.2016.07.010

Comparison of no-touch multi-bipolar *vs.* monopolar radiofrequency ablation for small HCC

Arnaud Hocquelet[1,2,*], Christophe Aubé[3,4], Agnès Rode[5], Victoire Cartier[3], Olivier Sutter[6,7], Anne Frederique Manichon[5], Jérome Boursier[4,8], Gisèle N'kontchou[9], Philippe Merle[10], Jean-Frédéric Blanc[11], Hervé Trillaud[1,2], Olivier Seror[6,7,12]

Table 1. Baseline characteristics of patients treated either by monopolar or no-touch multi-bipolar radiofrequency ablation.

	MonoRFA n = 181 (%)	NTmbpRFA n = 181 (%)	*p* value
Age in years (SD)	64 (10)	65 (9)	0.110
Male	149 (82.3)	144 (79.5)	0.503
Cirrhosis aetiologies			0.196
Non-viral hepatitis	103 (57)	98 (54)	
Viral Hepatitis	66 (36)	61 (34)	
Mixed	12 (7)	22 (12)	
Child-Pugh A	156 (86.1)	156 (86.1)	1
Platelet count ≤100 G/L	72 (40)	72 (40)	1
Alpha fetoprotein serum level (categorized)			1
<10 ng/ml	122 (67.4)	122 (67.4)	
10-100 ng/ml	52 (28.7)	52 (28.7)	
>100 ng/ml	7 (3.9)	7 (3.9)	
Mean tumour size in mm (SD)	24 (8)	25 (8)	0.279
≤30 mm	149 (82.3)	149 (82.3)	
>30 mm	32 (17.7)	32 (17.7)	1
Multiple tumours	36 (19.9)	36 (19.9)	1
Subcapsular tumour	22 (12.1)	22 (12.1)	1
Tumour near large vessel	24 (13.2)	24 (13.2)	1



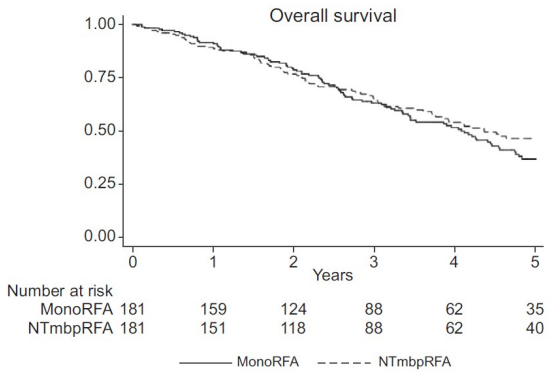
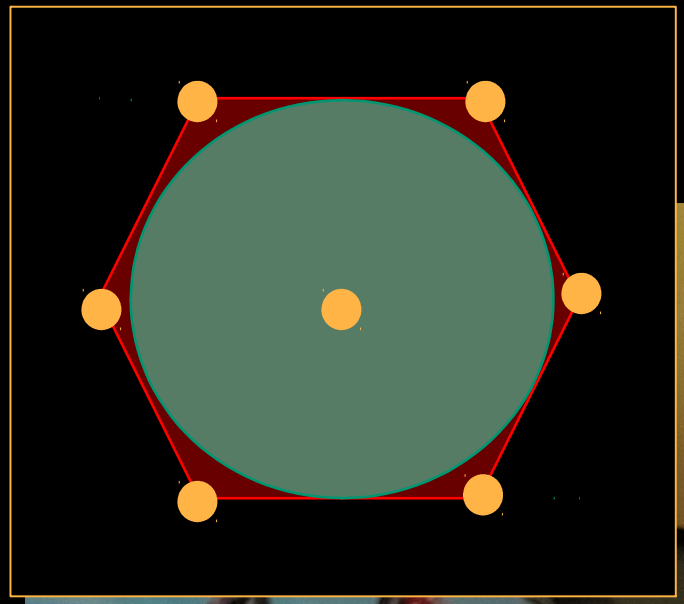


Table 2. Global radiofrequency ablation (RFA) failure, primary RFA failure and local tumour progression according to tumour size and RFA technique.

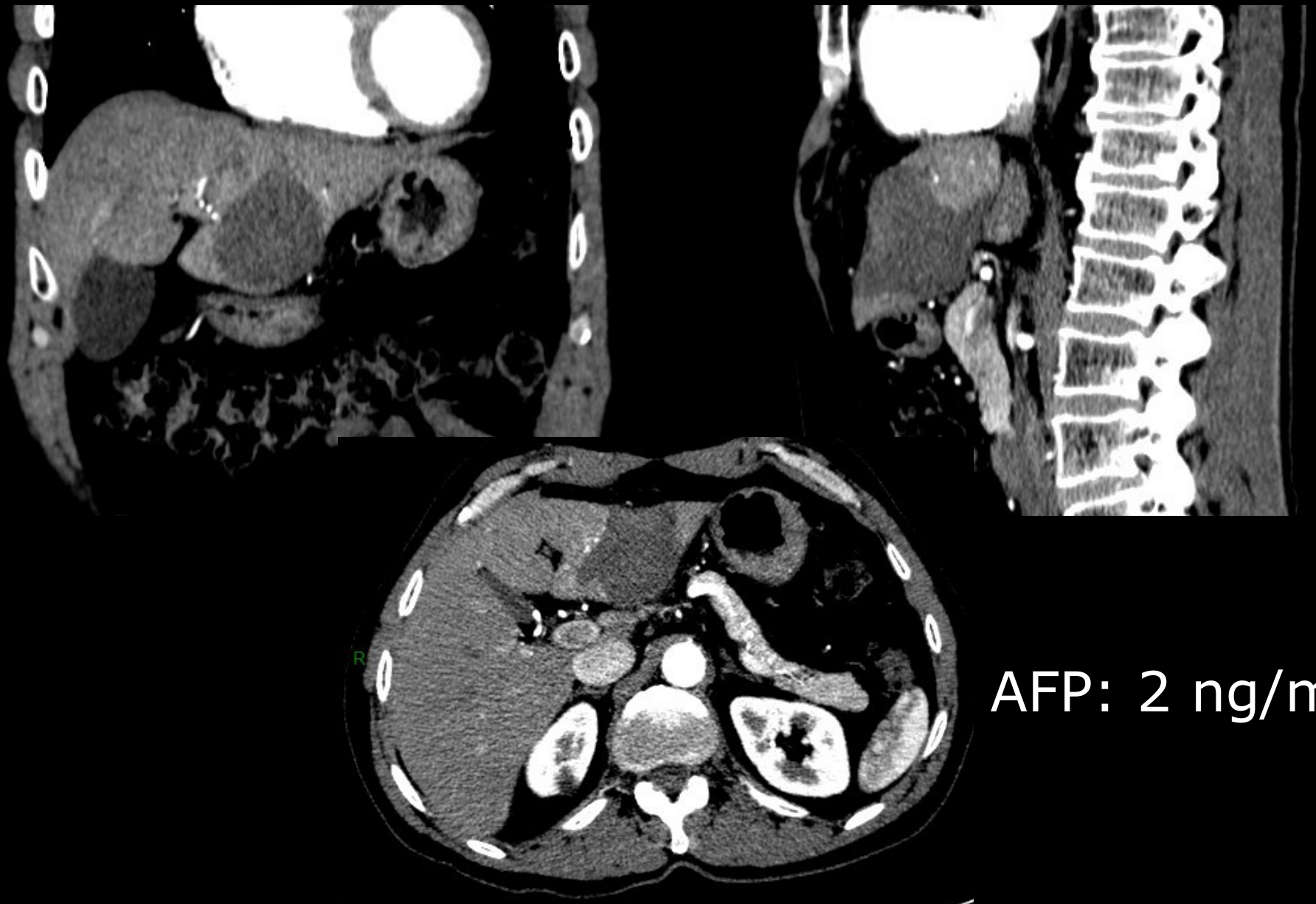
	<20 mm n (%)			20-30 mm n (%)			31-40 mm n (%)			>40 mm n (%)		
RF	MonoRFA n = 47	NTmbpRFA n = 39	*p* value	MonoRFA n = 102	NTmbpRFA n = 110	*p* value	MonoRFA n = 25	NTmbpRFA n = 24	*p* value	MonoRFA n = 7	NTmbpRFA n = 8	*p* value
Primary RFA failure	0	0	n.a.	6 (5.9)	0	0.011	3 (12)	0	0.235	1 (14)	0	0.467
LTP*	10 (21)	1 (2.6)	0.019	19 (20)	9 (8.4)	0.024	8 (36)	2 (8)	0.032	5 (83)	1 (12.5)	0.026
Global RFA failure	10 (21)	1 (2.5)	0.01	25 (25)	9 (8.2)	0.001	11 (44)	2 (8.3)	0.008	6 (86)	1 (12.5)	0.01

On October 2009 :

- Near no touch RFA consisting in inserting 7 straight electrodes with 4 cm active tips: 6 in square configuration at periphery of the tumor and 1 in its center.
- 200 kJ in 42’ minute of application time has been delivered
- 2 days of hospital stay

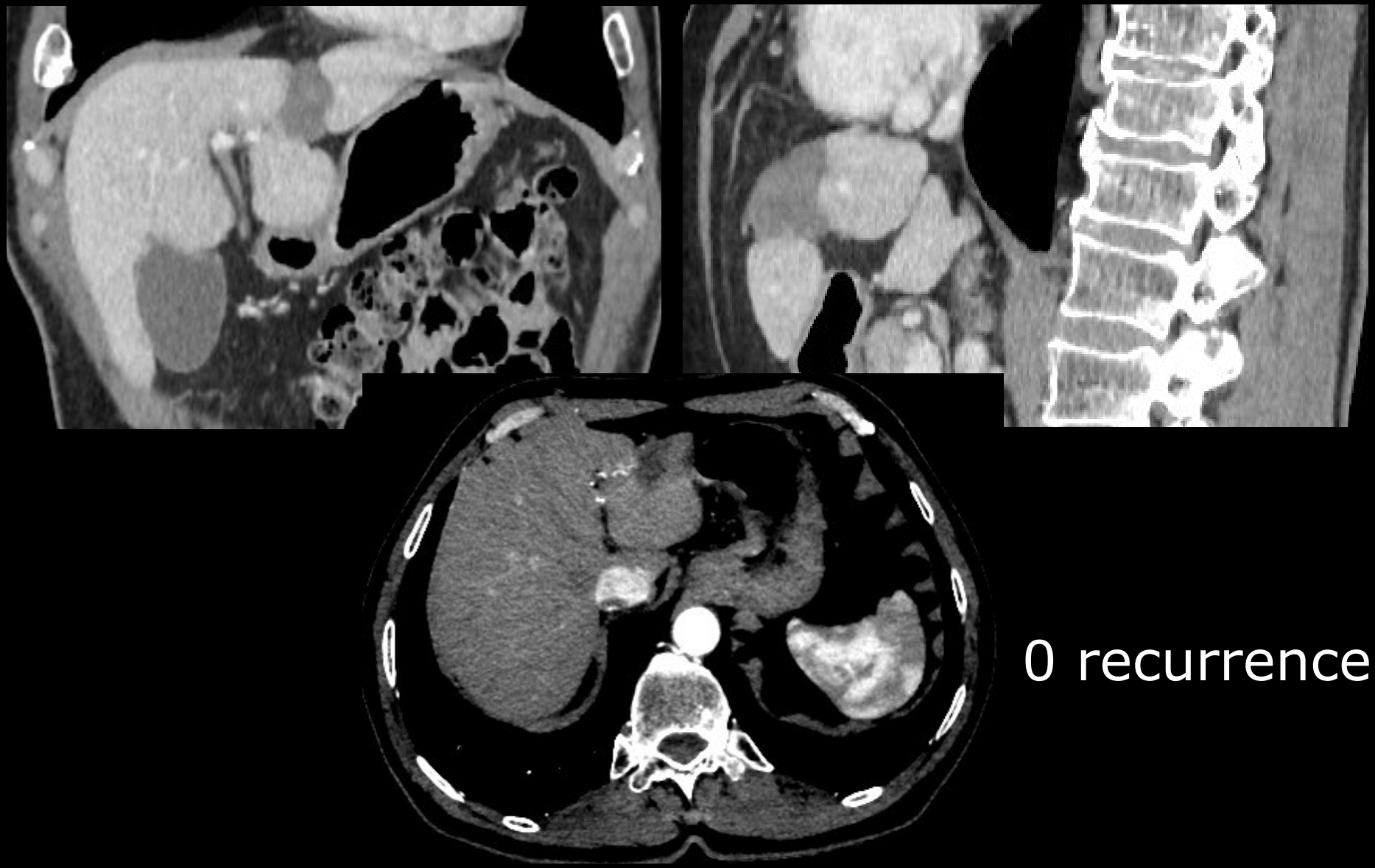


One month later



AFP: 2 ng/ml

5 years later

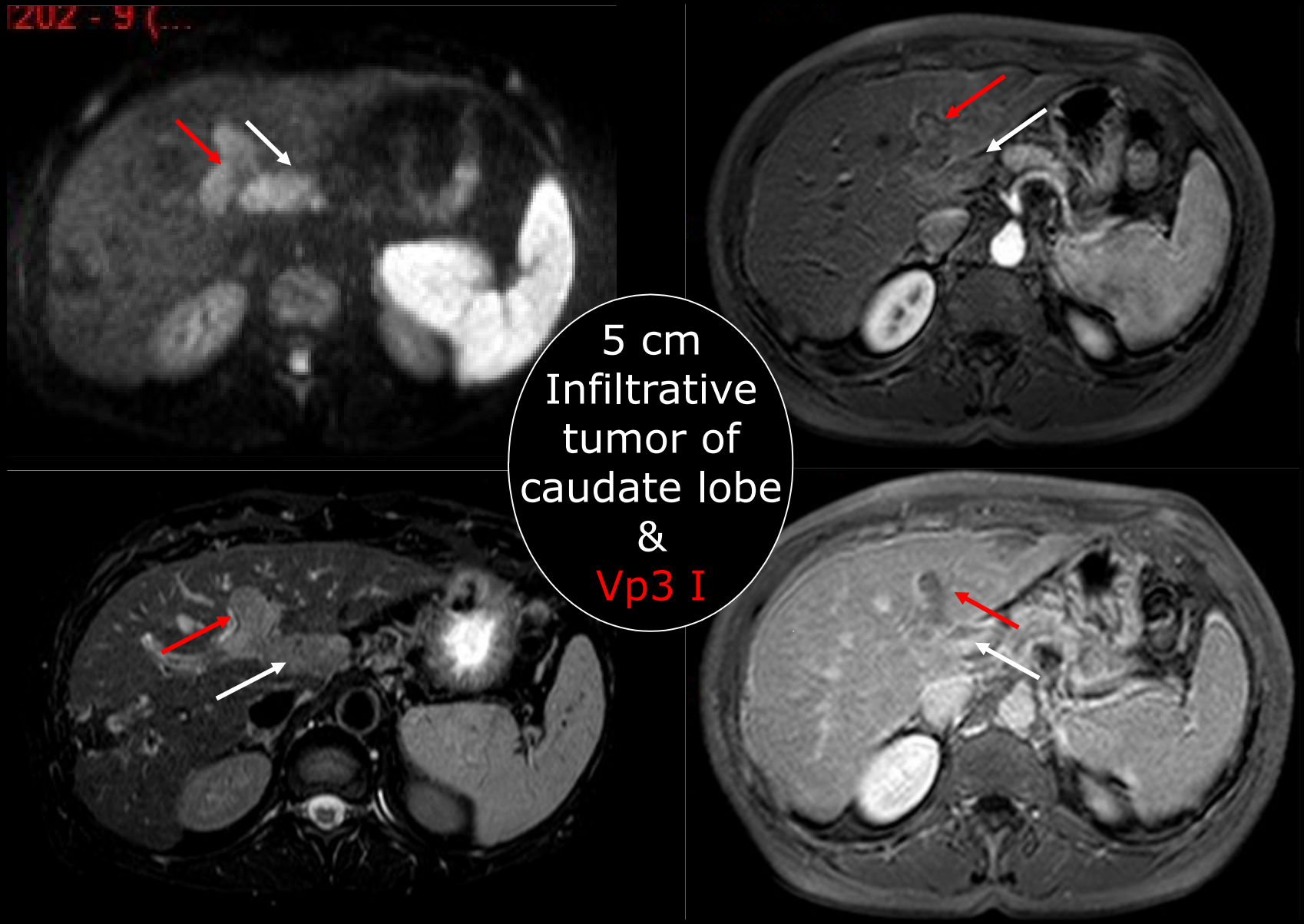


0 recurrence

2nd case

- 56 years old female
- Child-Pugh A6 HCV (treated) and alcohol related cirrhosis (alcohol up-take non stopped)
- 2 years ago successfully treated by NTmbpRFA for binodular HCC (grade III, AFP 25 ng/ml)
- HVPG = 10 mm Hg
- Platelets count: 94 000 / mm3
- Bilirubin: 24 µmol/L
- Albumin: 32 g/L
- Prothrombin time: 75%
- Alpha-fetoprotein: 69 ng/ml
- PS 0, ECOG 0

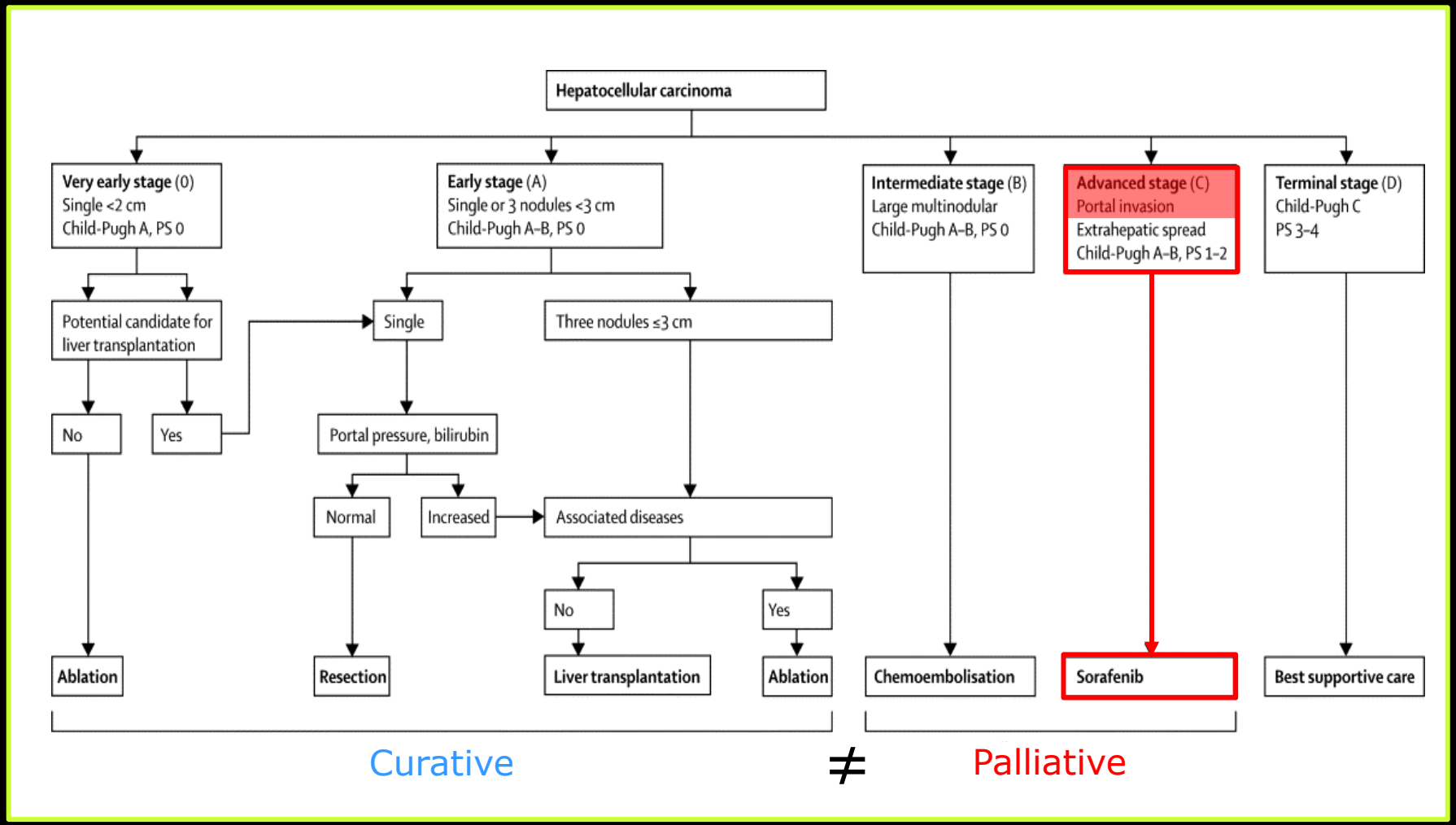
Pretherapeutic imaging



Which treatment?

1. Transplantation
2. Resection
3. Ablation
4. TACE
5. Other

Which BCLC stage?



What could we expect from sorafenib?

The outcome of sorafenib monotherapy on hepatocellular carcinoma with portal vein tumor thrombosis

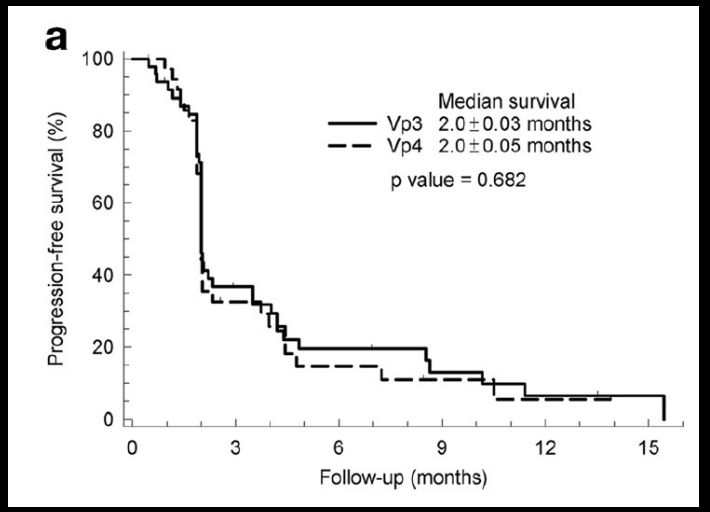
Yuan-Hung Kuo[1] · I-Pei Wu[1,2] · Jing-Houng Wang[1] · Chao-Hung Hung[1] · Kun-Ming Rau[3] · Chien-Hung Chen[1] · Kwong-Ming Kee[1] · Tsung-Hui Hu[1] · Sheng-Nan Lu[1]

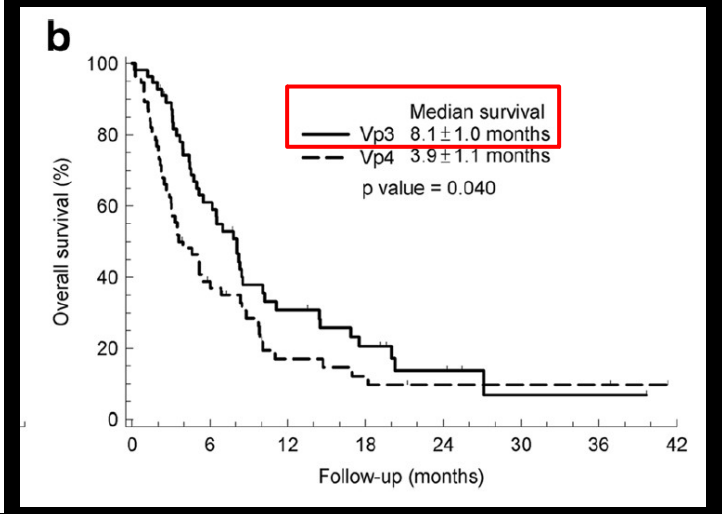
Invest New Drugs
DOI 10.1007/s10637-017-0468-6

Table 4 Associated factors with overall survival in 113 BCLC-C HCC patients with MVI

Variable	Comparison	Univariate analysis		Multivariate analysis	
		HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age	Per 1 year increase	0.99 (0.97–1.02)	0.6		
Sex	Female vs. Male	0.99 (0.58–1.68)	0.969		
Child-Pugh score	6 vs 5	1.22 (0.8–1.86)	0.368		
AFP ≥ 200 ng/mL	Yes vs No	1.74 (1.13–2.67)	0.012	2.06 (1.24–3.44)	0.005
HBV infection	Yes vs No	1.15 (0.75–1.78)	0.515		
HCV infection	Yes vs No	0.69 (0.44–1.07)	0.096		
Tumor Number	≥ 4 vs < 4	2.03 (1.32–3.13)	0.001	3.05 (1.72–5.43)	<0.001
Tumor type	Infiltration vs nodule	1.62 (0.74–3.51)	0.227		
Tumor size	Per 1 cm increase	1.07 (1.02–1.12)	0.003		
MVI pattern	Vp4 vs Vp3	1.54 (1.02–2.34)	0.042	2.3 (1.44–3.67)	0.001
Dosage reduction	Yes vs No	0.49 (0.32–0.77)	0.002		
Hepatic decompensation	Yes vs No	2.65 (1.66–4.23)	<0.001	2.03 (1.17–3.5)	0.011
Concurrent treatment after sorafenib failure	Yes vs No	0.21 (0.12–0.37)	<0.001	0.17 (0.09–0.33)	<0.001

Abbrevation *MVI* Macroscopic vascular invasion; *HCC* Hepatocellular carcinoma; *BCLC-C* Barcellora classification of liver cancer stage C; *HR* Hazard ratio; *CI* Confidence interval; *HBV* Hepatitis B virus; *HCV* Hepatitis C virus





Radiology

Olivier Seror, MD
Giselle N'Kontchou, MD
Djamel Haddar, MD
Marius Dordea, MD
Yves Ajavon, MD
Nathalie Ganne, MD
Jean Claude Trinchet, MD
Michel Beaugrand, MD
Nicolas Sellier, MD

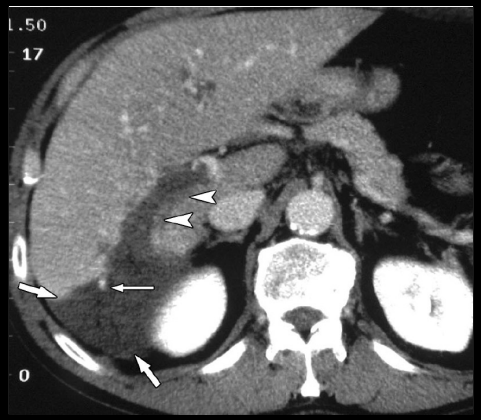
Published online before print
10.1148/radiol.2341031008
Radiology 2005; 234:299–309

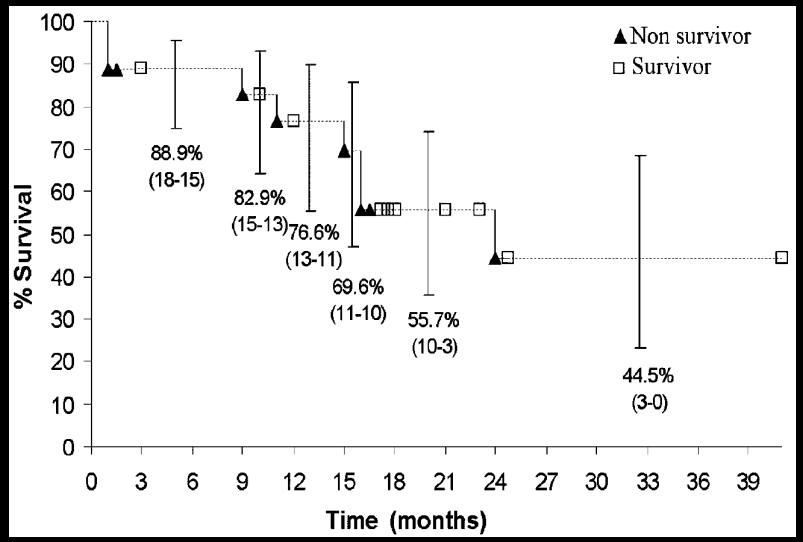
Abbreviations:
AFP = α-fetoprotein
HCC = hepatocellular carcinoma
PEI = percutaneous ethanol injection
PIAEI = percutaneous intraarterial

Large Infiltrative Hepatocellular Carcinomas: Treatment with Percutaneous Intraarterial Ethanol Injection Alone or in Combination with Conventional Percutaneous Ethanol Injection[1]

Radiology · January 2005

- 18 Patients
- 35-90 mm (52mm±16)
- 12 (66%) infiltrative
- 4 (22%) (Vp2/Vp3)



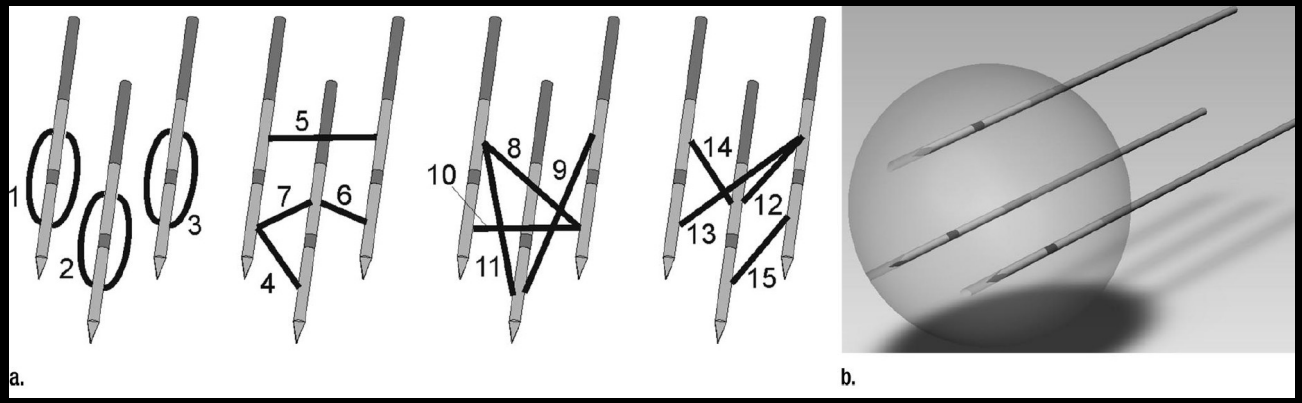


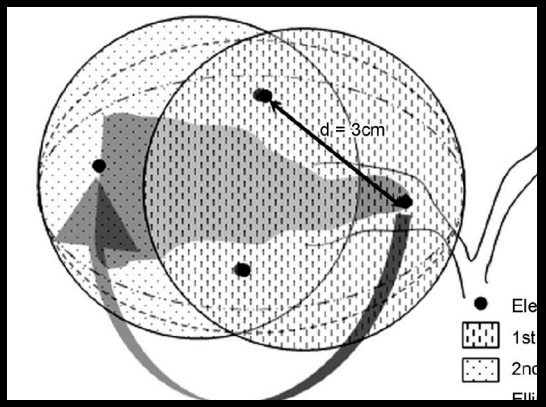
Olivier Seror, MD, PhD
Gisèle N'Kontchou, MD
Medhat Ibraheem, MD
Yves Ajavon, MD
Corinne Barrucand, MD
Nathalie Ganne, MD
Emmanuelle Coderc, MD
Jean Claude Trinchet, MD
Michel Beaugrand, MD
Nicolas Sellier, MD

Large (≥5.0-cm) HCCs: Multipolar RF Ablation with Three Internally Cooled Bipolar Electrodes—Initial Experience in 26 Patients[1]

Radiology

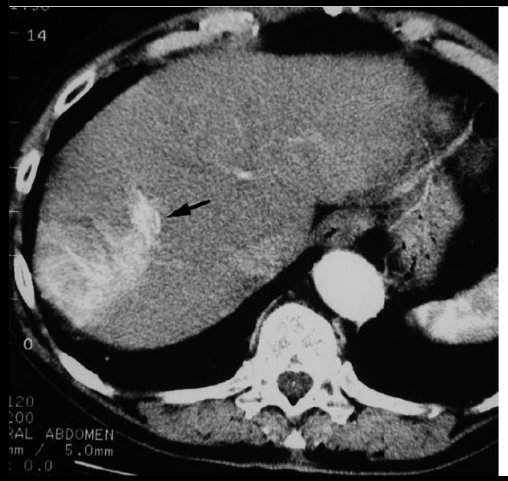
Radiology: Volume 248: Number 1—July 2008





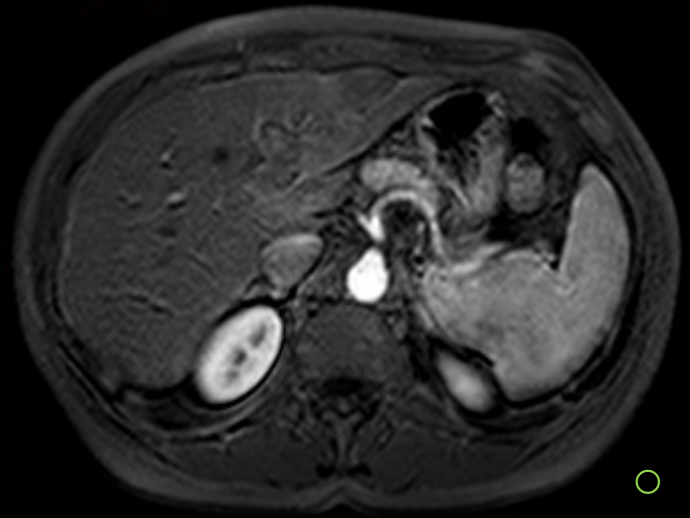
Characteristics of Tumors and Treatments in 27 HCCs 5.0 cm or Larger according to Early Response to Multipolar RF Ablation

Parameter	Complete Ablation (*n* = 22)	Incomplete Ablation (*n* = 5)
Tumor characteristic		
Diameter (cm)*	5.9 ± 0.9 (5.0–8.0)	6.2 ± 1.7 (5.0–8.5)
Multifocality†	4 (18)	2 (40)
Contact with vessels†‡	15 (68)	4 (80)
Subcapsular location†	18 (82)	5 (100)
Infiltrative form†	8 (36)	4 (80)
Portal invasion†§	3 (14)	1 (20)
Serum α-fetoprotein level greater than 400 μg/L†	6 (27)	5 (100)
Treatment characteristic		
No. of procedures*	1.2 ± 0.4 (1–2)	1.25 ± 0.5 (1–2)
No. of applications*	2.5 ± 2.1 (1–10)	3 ± 2.4 (1–7)
Amount of energy (kJ)*	205 ± 95 (90–435)	192 ± 103 (50–270)



Which technique of ablation could be selected for our patient?

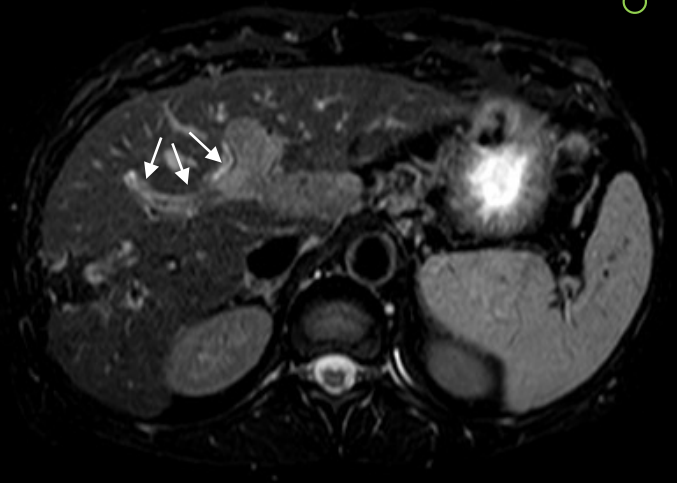
- ~~Intra arterial ethanol injection~~



No punctionable arterial feeder

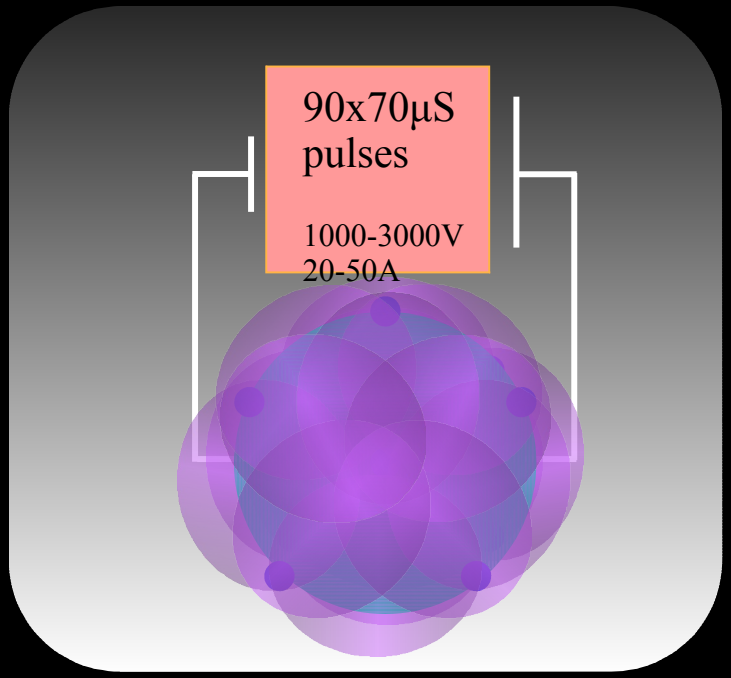
- Sum of size of nodules < 7 cm
- Bilirubin > 20µmol/L

- ~~Multibipolar RFA (abla-thermy)~~



Main bile duct confluence in vicinity

Principle of Irreversible Electroporation (IRE)



According to tumor size

- from 2 to 6 electrodes
- From 1.5 to 2.5 cm spaced

At cell scale

Apoptosis and necrosis

Minimal thermal effect (<30%) :

↘ risks of collateral damages,

No treatment failure due to cooling effect of blood flow

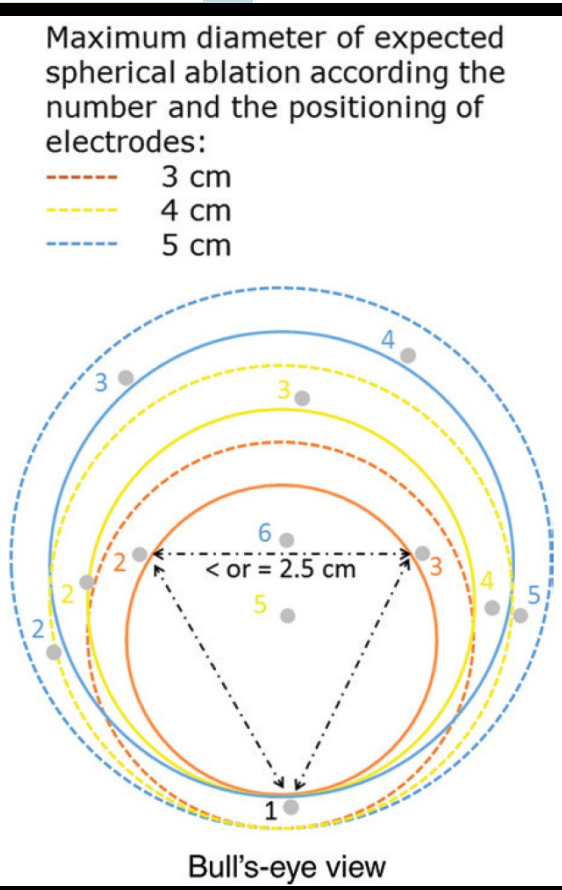
IRE: a non thermal ablation

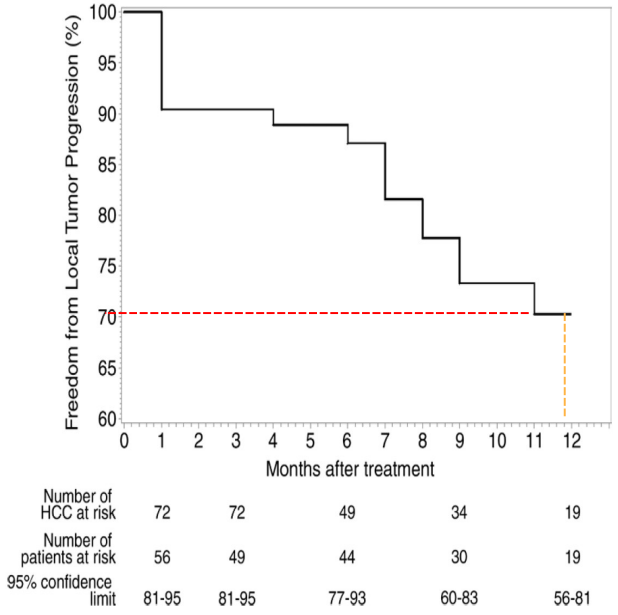
Olivier Sutter, MD
Joyce Calvo, MD
Gisèle N'Kontchou, MD
Jean-Charles Nault, MD
Raffik Ourabia, MD
Pierre Nahon, MD, PhD
Nathalie Ganne-Carrié, MD, PhD
Valérie Bourcier, MD
Nora Zentar, MD
Fatna Bouhafs, MD
Nicolas Sellier, MD
Abou Diallo, MD
Olivier Seror, MD, PhD

Safety and Efficacy of Irreversible Electroporation for the Treatment of Hepatocellular Carcinoma Not Amenable to Thermal Ablation Techniques:

A Retrospective Single-Center Case Series[1]

Radiology.
2017 Apr
28:161413.
doi: 10.1148/
radiol.2017161413.





Overall freedom of local tumor progression of 75 HCC in 58 patients

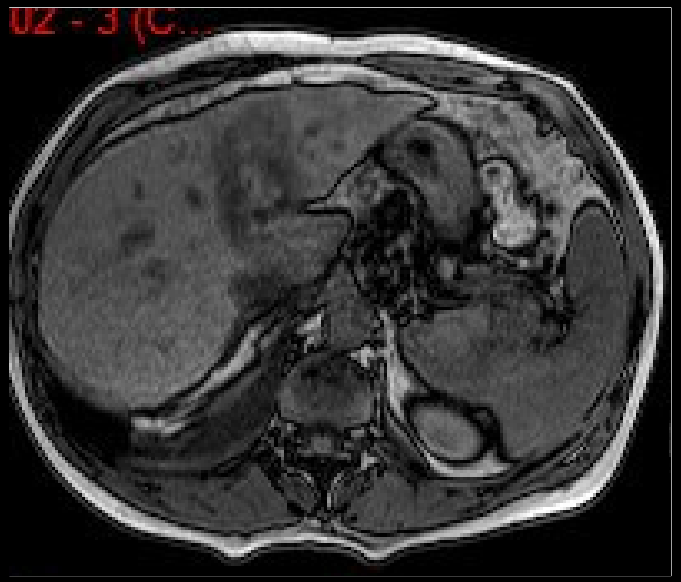
58 Patients with 75 HCC treated by IRE

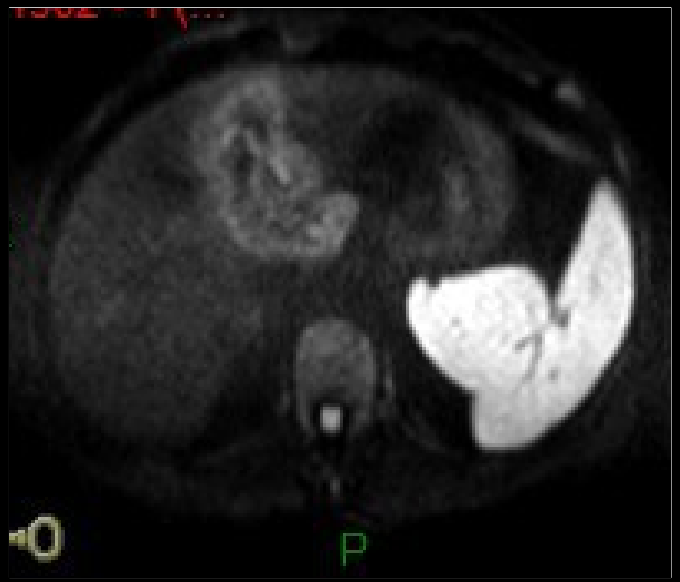
Patients	
No. of patients	58 (100)
Age (y)†	65.4 (41.6–90)
Age >75 y	16 (33.3)
Male	43 (74)
No previous treatment	24 (41.4)
Cause of cirrhosis	
Alcohol	20 (34.5)
Hepatitis C virus	18 (31)
Hepatitis B virus	5 (9)
NASH	11 (19)
Other	4 (6.5)
History of decompensation	13 (22)
Esophageal varices	36 (62)
Ascites‡	20 (34.5)
Platelet count <75 g/L	18 (31)
Prothrombin activity <75%	23 (39.6)
Albumin level <35 g/L	13 (22.4)
Total bilirubin level >15 μg/mL	12 (20.7)
α-Fetoprotein level (ng/mL)†	29 (2–1662)
α-Fetoprotein level >100 ng/mL	8 (16.7)
ECOG performance status >1	20 (34.5)
ASA score	
1	0
2	21 (36)
3	37 (64)
4	0
Nodules	
No. of nodules	75 (100)
Longest diameter (mm)†	24 (6–90)
Longest diameter >30 mm	16 (21.3)
Location	
Hilar	47 (62.7)
Peripheral	13 (37.3)
Infiltrative form	7 (9.3)
Portal invasion	10 (13.3)

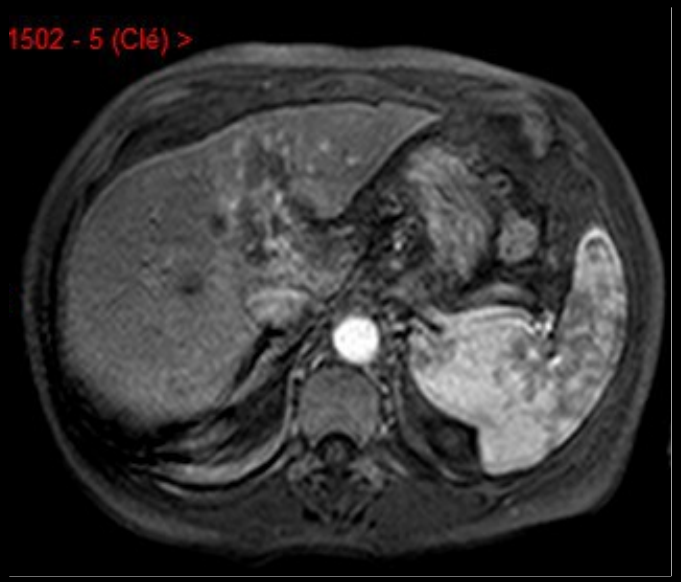
On July 2013 :

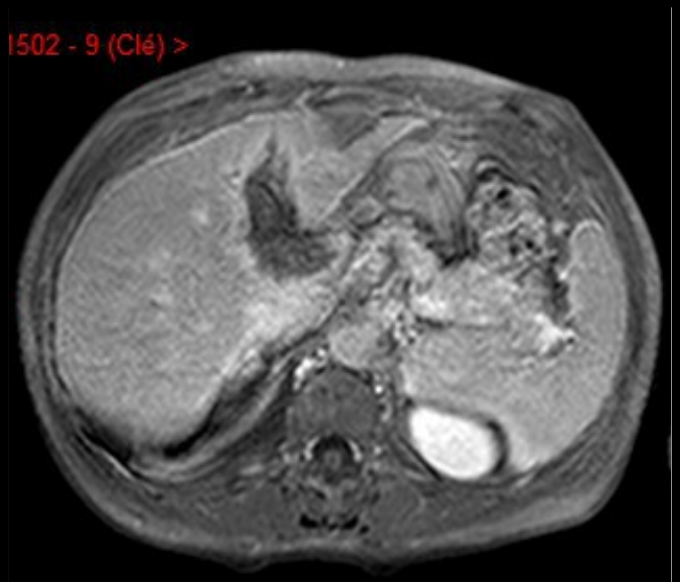
- 6 straight electrodes with 2 cm active tips (2 cm distance) inserted under fused US/MR guidance along the main axis of left portal vein tumor invasion up to caudate lobe.
- 90 RF pulses of 90µs between each pair of electrodes combinations (n = 15) at > 2000 V reaching at least 20 A.
- 2 additional cycles after pull-back of 2 cm

Early MR follow-up (72h)

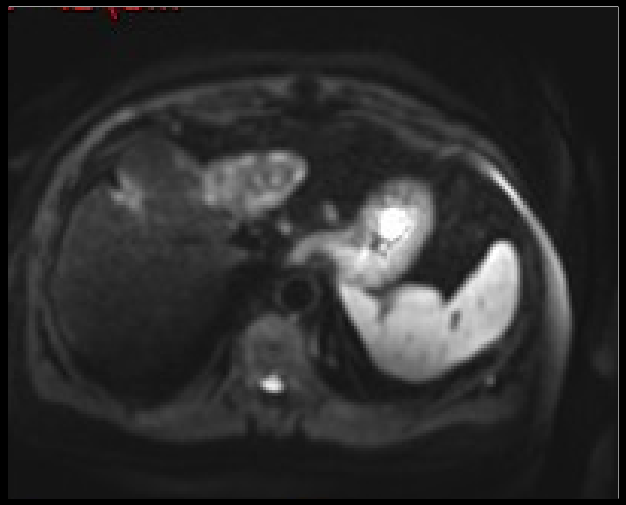


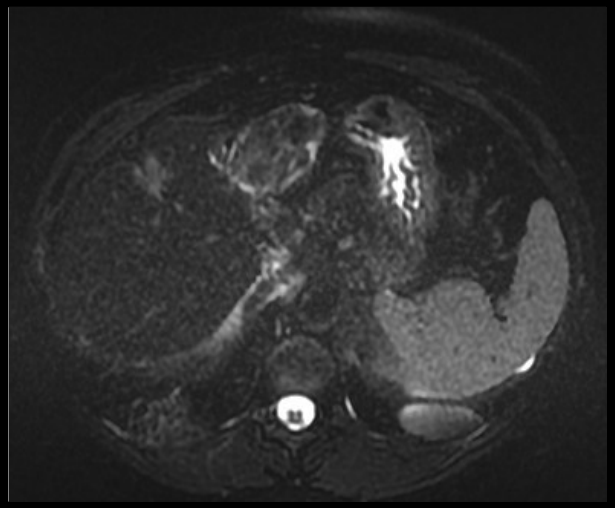


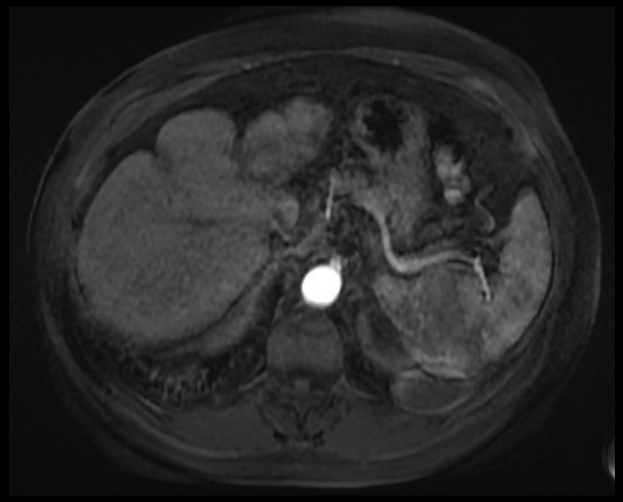




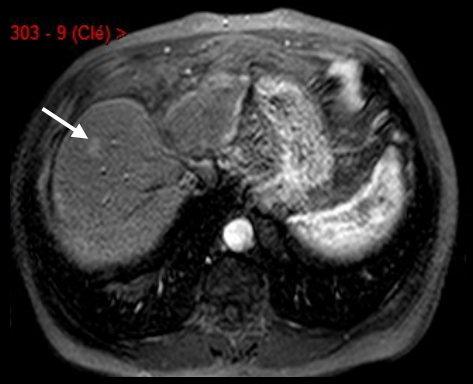
May 2017 last news (57 months after IRE)







- 23 months after IRE FU showed distant 8 mm recurrence in segment VIII successfully treated by IRE



- Since tumor progression free
- Last AFP: 7 ng/mL

Summary

- ✓ Advances in ablative techniques and technologies offer new aggressive therapeutic managements for large and more locally advanced tumor.

- ✓ Wide range of procedures allow safe and efficient ablation of all tumors including:
  - Large HCC
  - Abutting or invading biliary/vascular structures

- ✓ Patients with large/locally advanced tumors must be referred to expert centres to benefit from these procedures in order to allow a possible “switch” from palliative to curative management