Image-Guided Ablation: Current Status and Future Prospects

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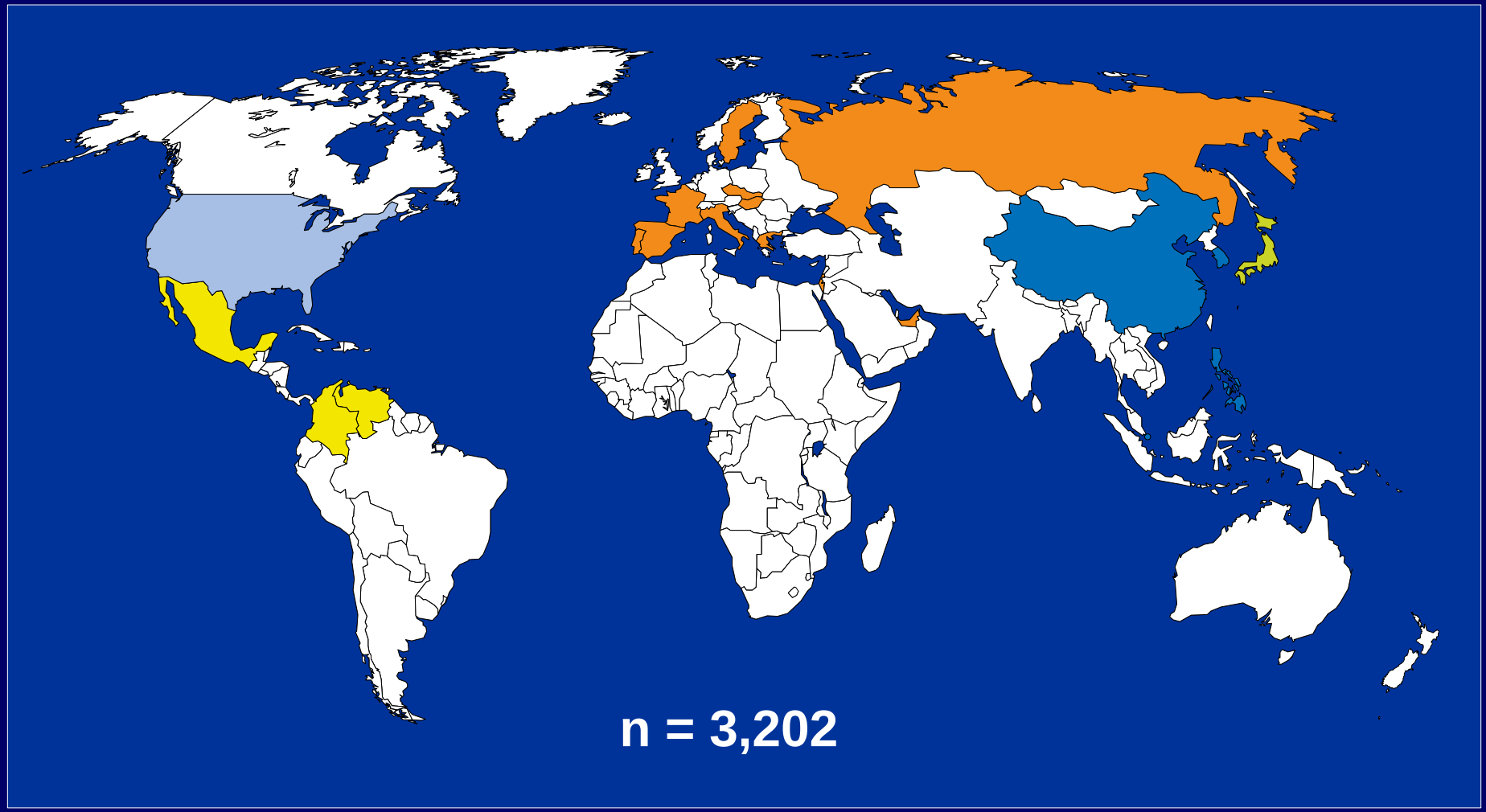
GIDEON: The Largest Global Observational Study Completed in HCC (n = 3,202)



Lencioni R et al. Int J Clin Pract 2014;68:609-617

GIDEON: The Largest Global Observational Study Completed in HCC (n = 3,202)

Pre-Sorafenib Therapy for HCC by Geographical Region

%	AP *n*=928	EU *n*=1113	LA *n*=90	USA *n*=563	Japan *n*=508	Overall *N*=3202
All LRTs	67.2	43.5	27.8	49.4	84.4	57.5
TACE	60.3	33.1	13.3	37.1	71.3	47.2
Conventional TACE (Lipiodol) *	90.2	59.2	83.3	40.7	82.3	73.9
DEB-TACE *	2.9	36.1	16.7	39.7	1.7	15.9
Surgical treatment	24.2	15.5	5.6	9.4	43.3	21.1
Ablation	15.5	20.2	17.8	12.6	50.0	22.2

* For patients who received TACE: n=1511; AP=560, EU=368, LA=12, USA=209, Japan=362;
AP, Asia-Pacific; LA, Latin America; LRTs, Loco-Regional Therapies

Lencioni R et al. Int J Clin Pract 2014;68:609-617

EASL-EORTC Clinical Practice Guidelines: Management of HCC

EORTC Clinical Practice Guidelines EASL

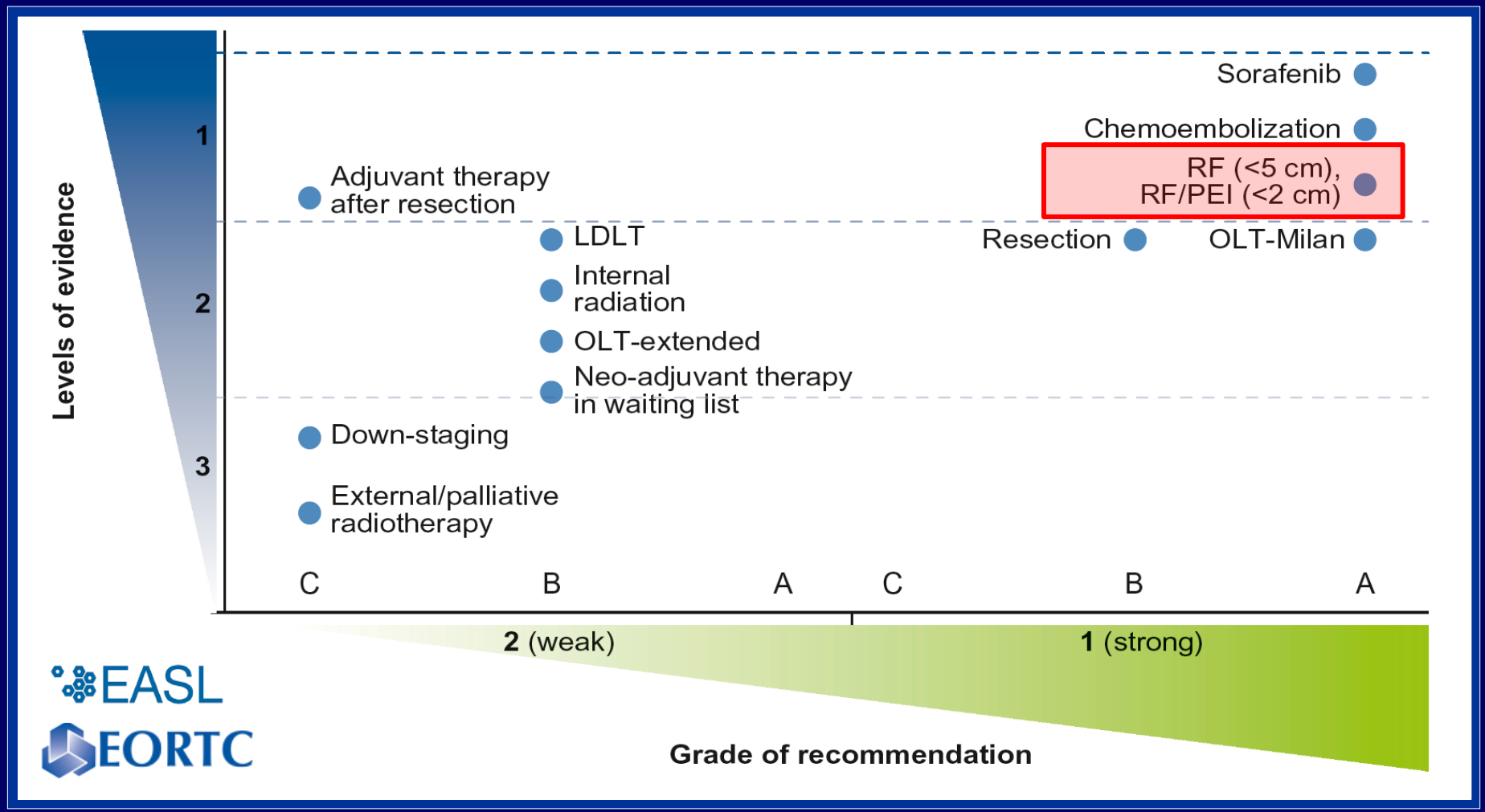
EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma

European Association for the Study of the Liver*,
European Organisation for Research and Treatment of Cancer

Contributors: Chairmen: *Josep M. Llovet (EASL); Michel Ducreux (EORTC).* ***Clinical Practice Guidelines Members:*** *Riccardo Lencioni; Adrian M. Di Bisceglie; Peter R. Galle; Jean Francois Dufour; Tim F. Greten; Eric Raymond; Tania Roskams; Thierry De Baere; Michel Ducreux; and Vincenzo Mazzaferro.* ***EASL Governing Board Representatives:*** *Mauro Bernardi.* ***Reviewers:*** *Jordi Bruix; Massimo Colombo; Andrew Zhu.*

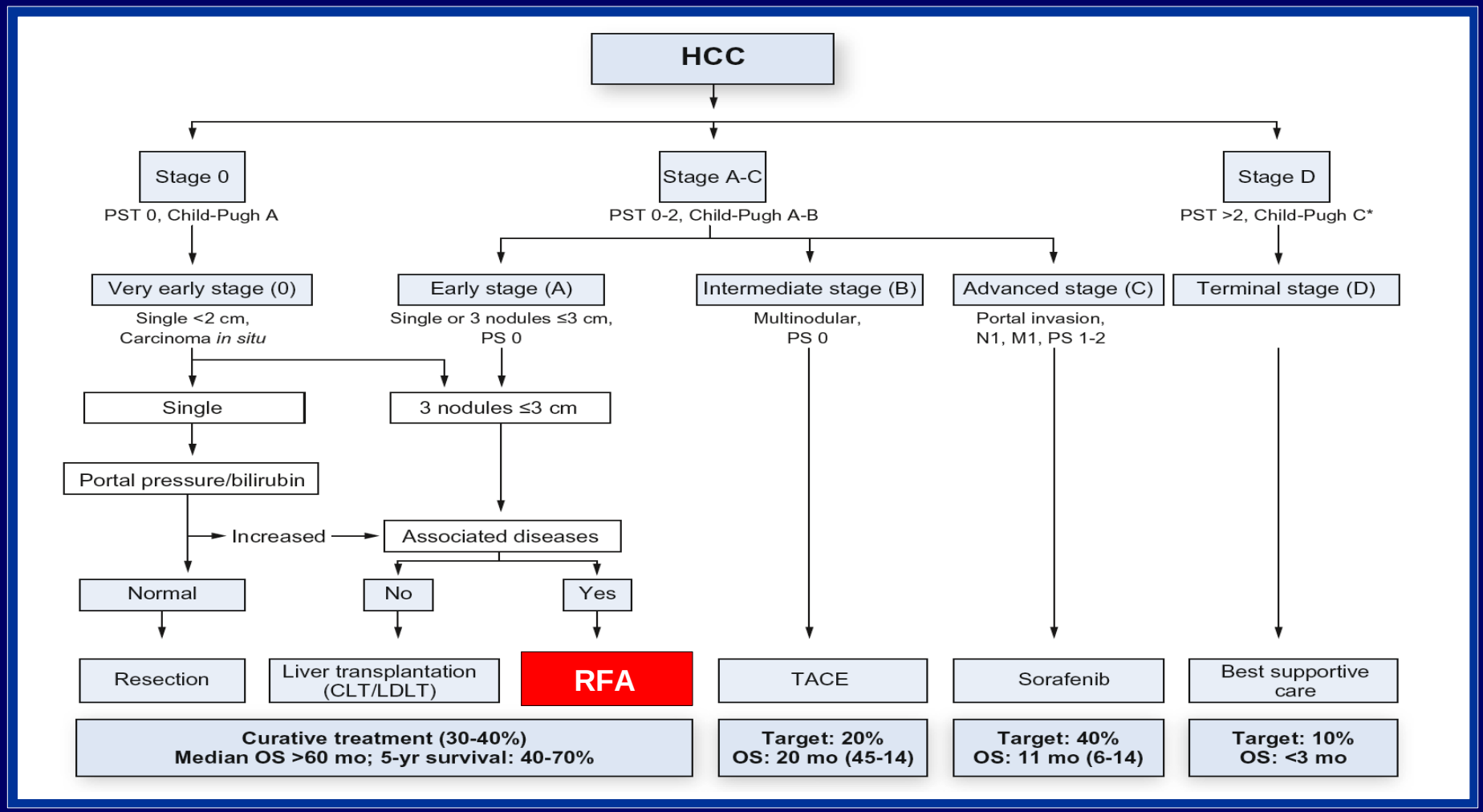
EASL-EORTC. J Hepatol 2012;56:908-943 - Eur J Cancer 2012;48:599-641

Treatment Options for HCC: Levels of Evidence and Grade of Recommendation



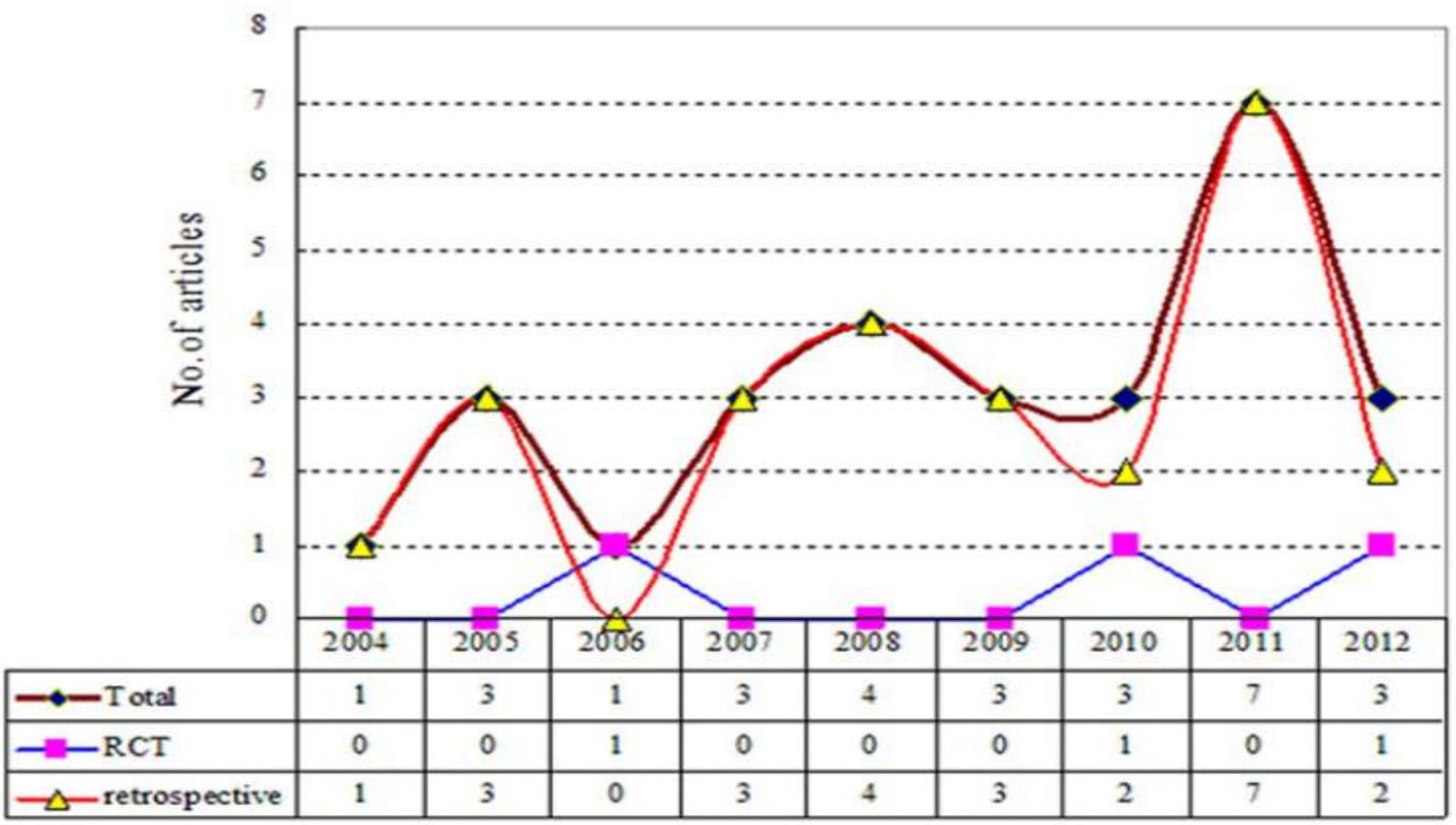
EASL-EORTC. J Hepatol 2012;56:908-943 - Eur J Cancer 2012;48:599-641

EASL-EORTC Clinical Practice Guidelines: BCLC Staging and Treatment Strategy



EASL-EORTC. J Hepatol 2012;56:908-943 - Eur J Cancer 2012;48:599-641

Resection versus RFA for Early-Stage HCC: Bibliometric Map of Clinical Trials

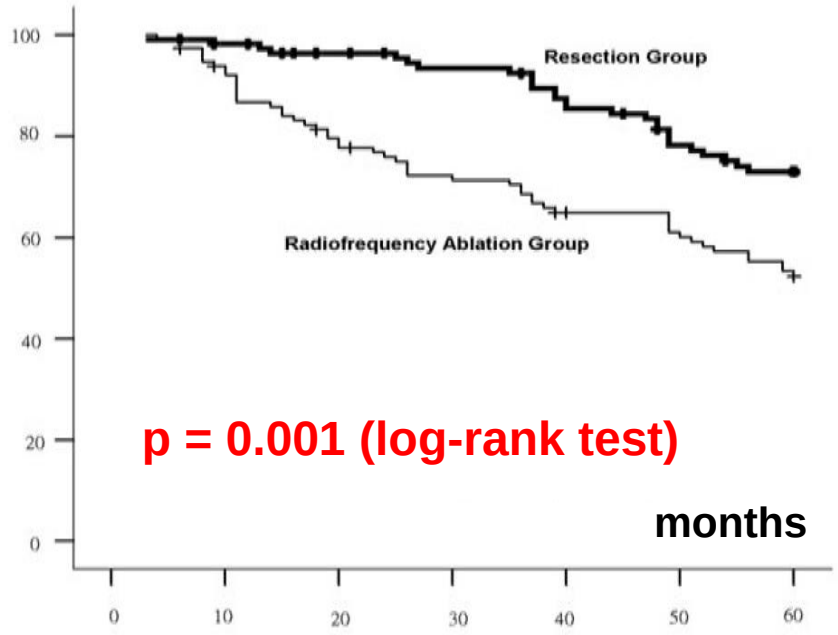


	2004	2005	2006	2007	2008	2009	2010	2011	2012
Total	1	3	1	3	4	3	3	7	3
RCT	0	0	1	0	0	0	1	0	1
retrospective	1	3	0	3	4	3	2	7	2

Wang Y et al. PlosOne 2014;9:e84484

Resection vs RFA: Randomized Clinical Trials Included Tumors of Different Stages

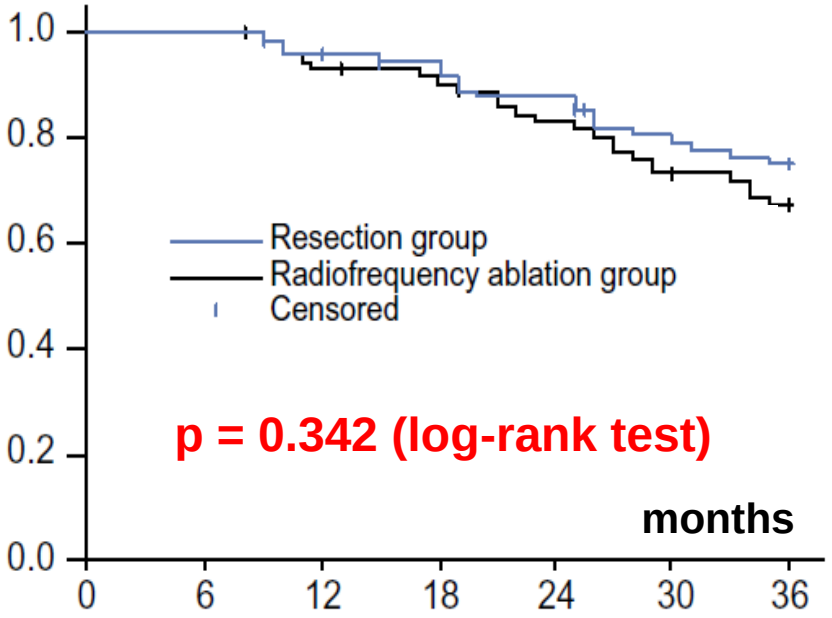
Overall Survival



- 230 patients, 94% Child A
- Single ≤ 5 cm, up to 3 ≤ 3 cm

Huang J et al. Ann Surg 2010;252:903-912

Overall Survival



- 168 patients, 49% Child A
- Up to 2 HCC tumors ≤ 4 cm

Feng K et al. J Hepatol 2012;57:794-802

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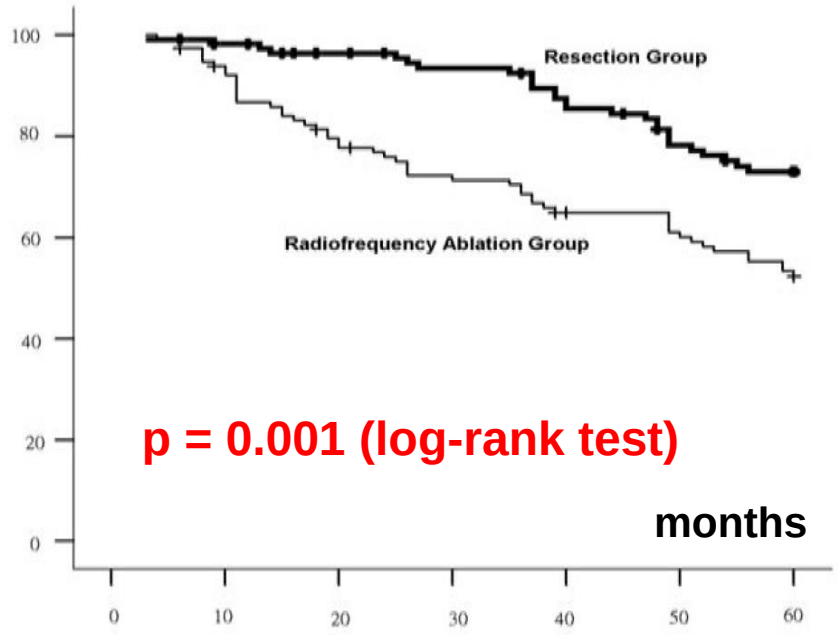

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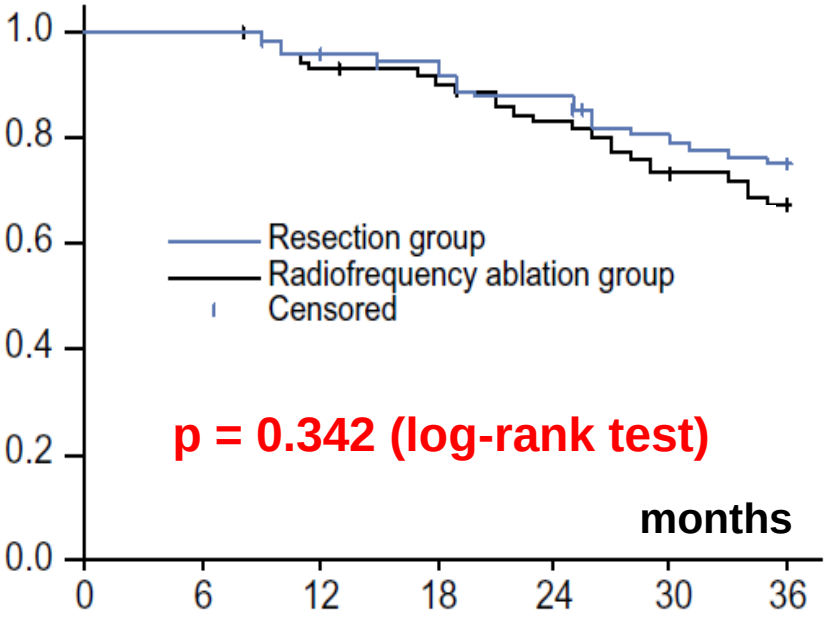

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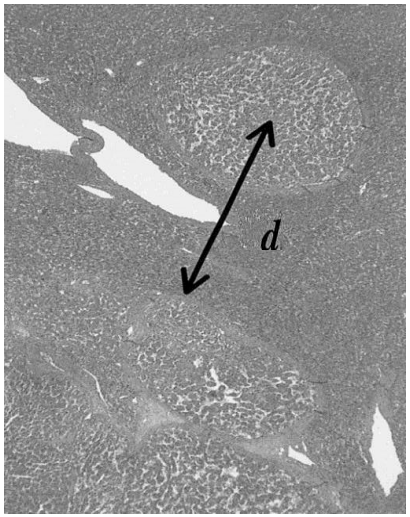
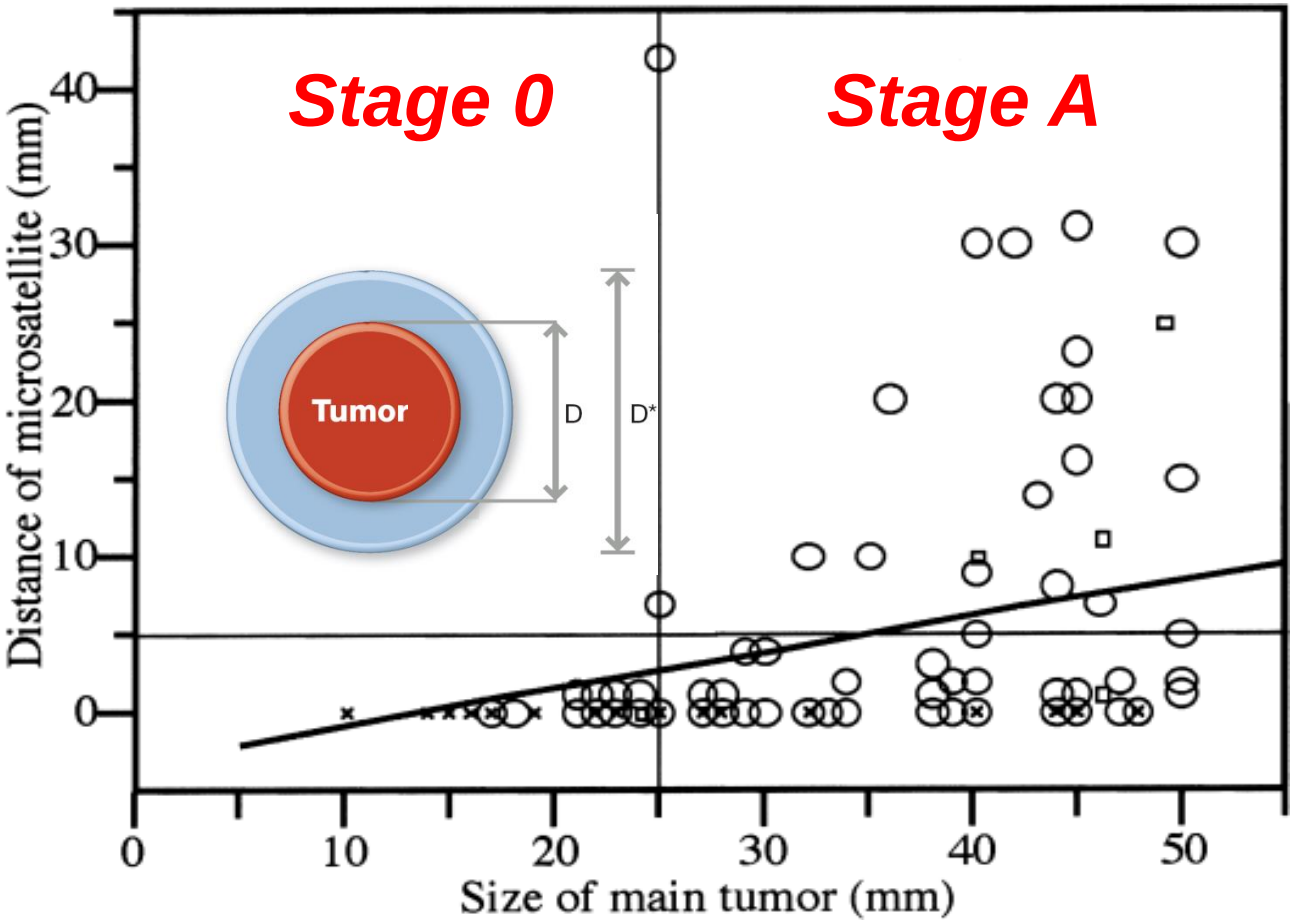
Huang J et al. Ann Surg 2010;252:903-912

Feng K et al. J Hepatol 2012;57:794-802

Stage 0 (Very Early) vs Stage A (Early) HCC: Frequency and Distribution of Microsatellites

- **46% of patients with single HCC < 5**





Sasaki A et al. Cancer 2005;103:299-306

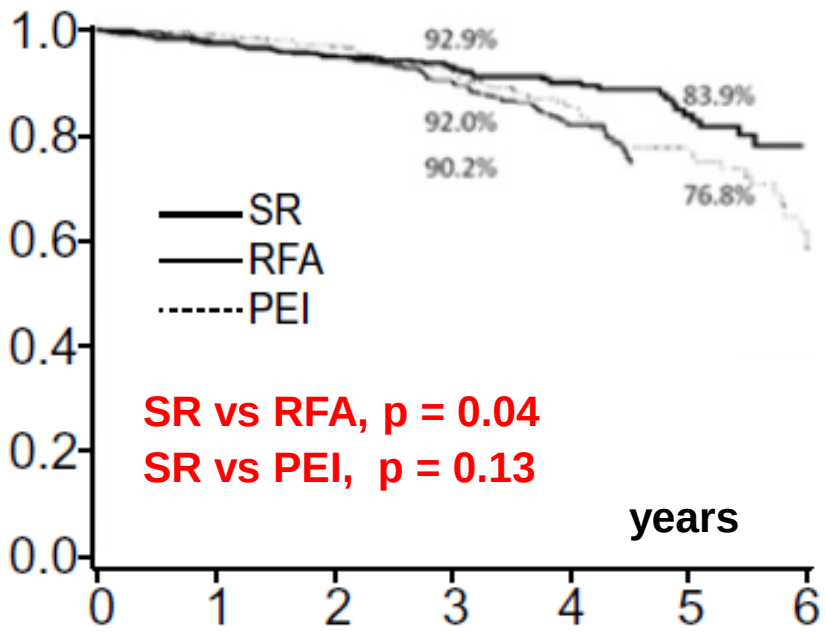
RFA: Histologic Outcome in Explanted Liver Specimens

Variables	Histologic Outcome		*P* Value*
	Successful RF Treatment	Unsuccessful RF Treatment	
Tumor size			
≤2.5 cm	26 (87)	4	.017
>2.5 cm	9 (53)	8	
≤3.0 cm	29 (83)	6	.050
>3 cm	6 (50)	6	
Location			.009
Nonperivascular	28 (88)	4	
Perivascular	7 (47)	8	
Sex			.29
Male	22	10	
Female	13	2	
RF device			.66
Cool-tip†	7	1	
Expandable‡	28	11	
Patient age (y)			.32
Mean	54.5	57.4	
Standard deviation	±10.6	±7.9	

Lu DSK et al. Radiology 2005;234:954-960

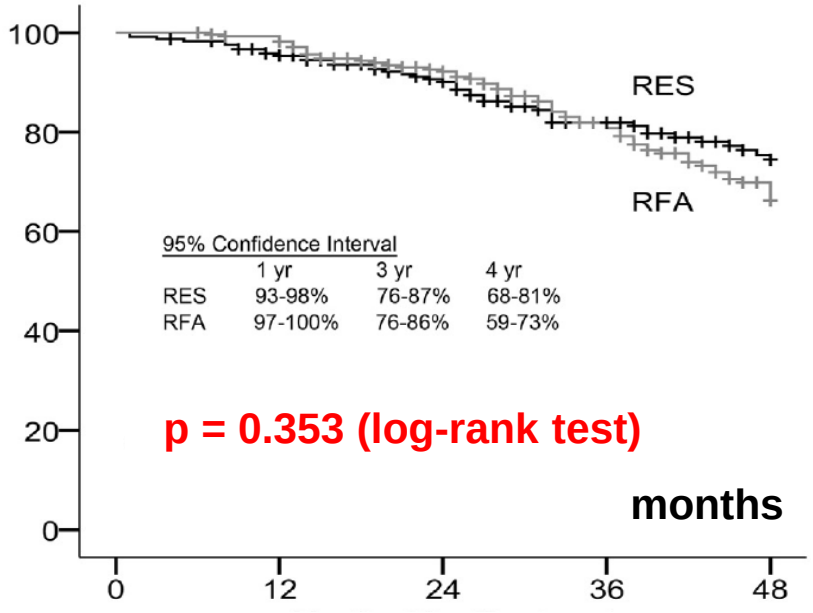
Resection vs RFA for Solitary Small Tumors: Nationwide Surveys

Overall Survival



- Japanese Survey (n = 2,560)
- Single HCC ≤ 2 cm, Child A

Overall Survival

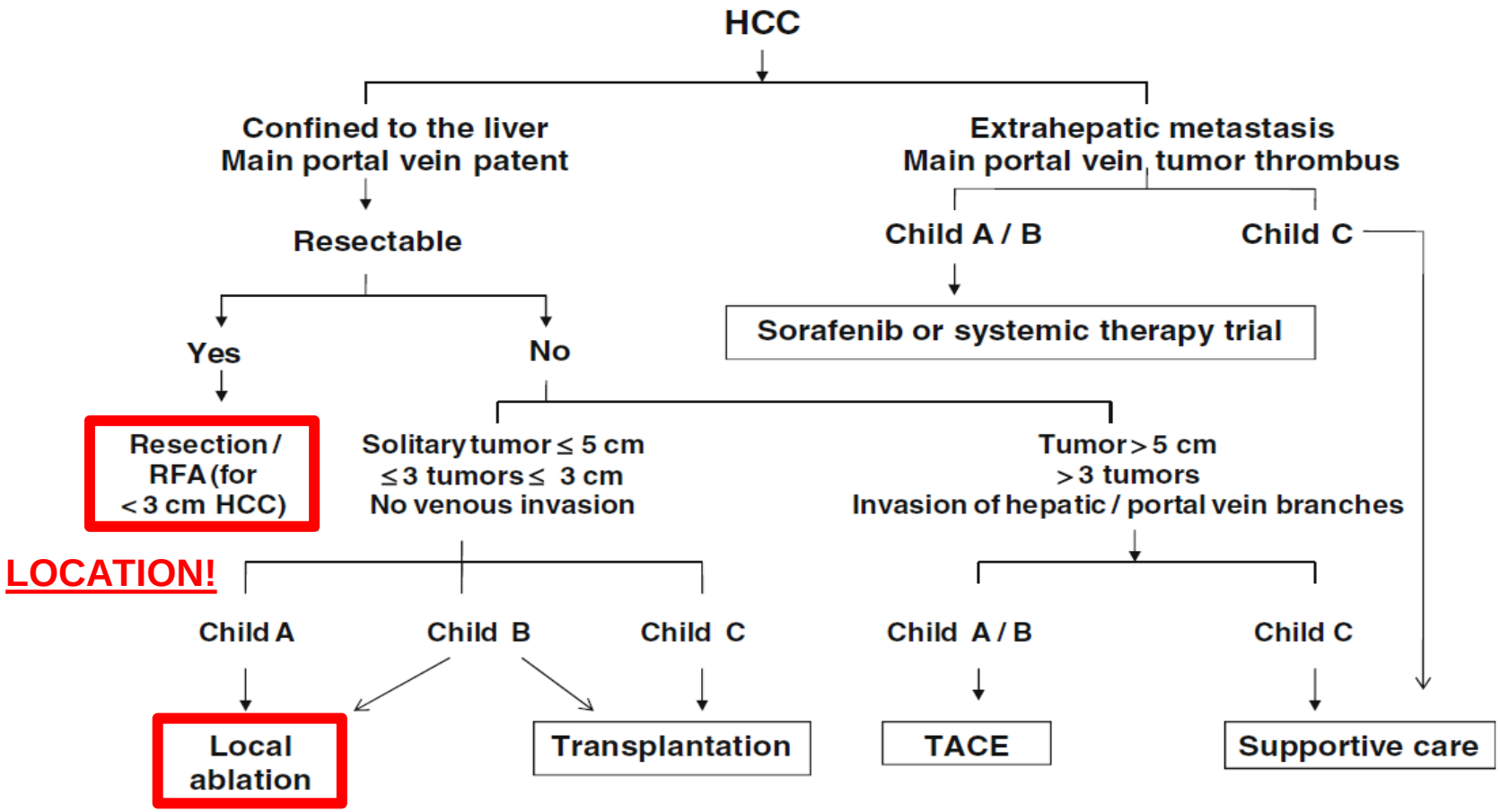


- Italian Survey (n = 544)
- Single HCC ≤ 3 cm, Child A

Hasegawa K et al. J Hepatol 2013;58:724-729

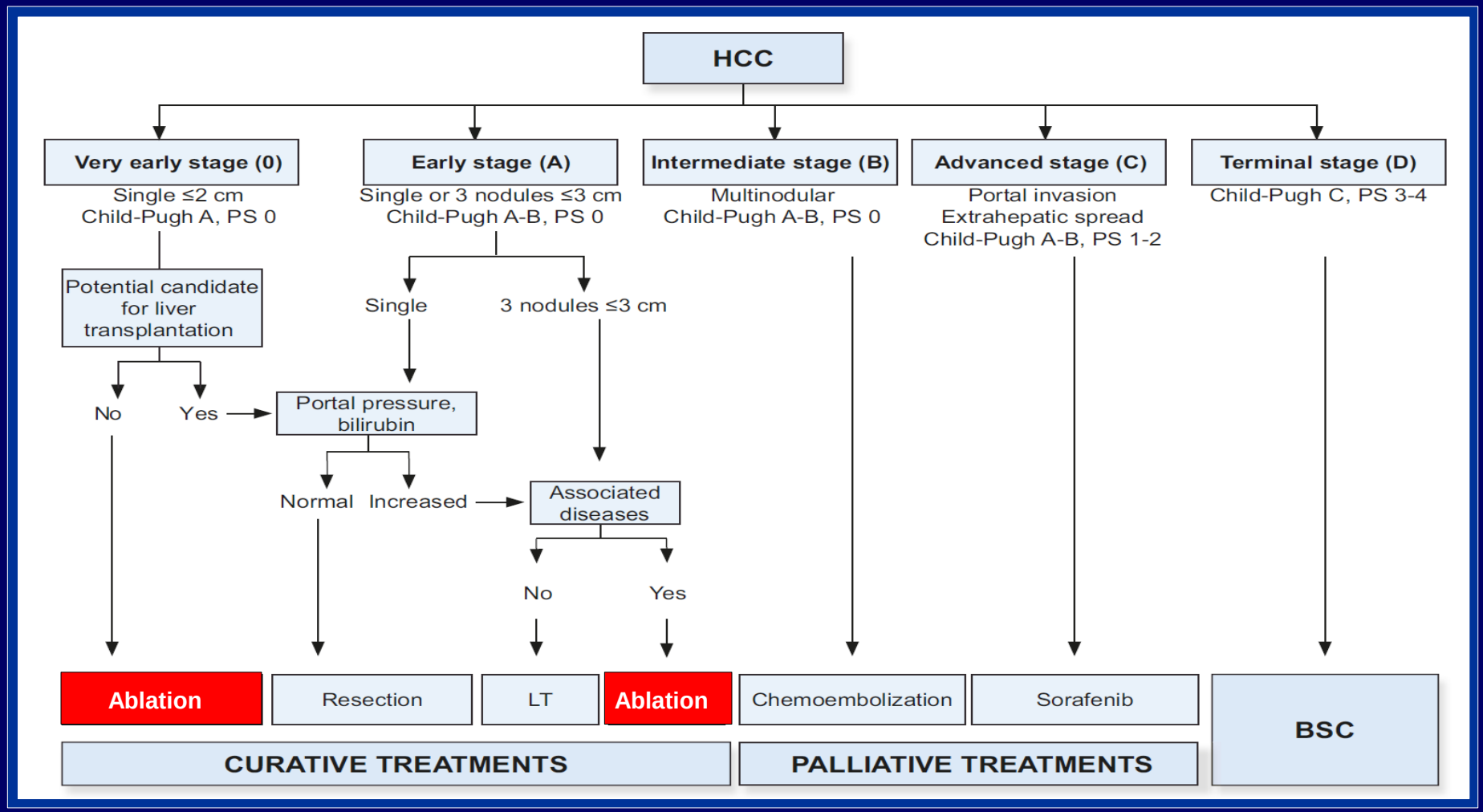
Pompili M et al. J Hepatol 2013;59:89-97

APASL Consensus Recommendations: The Two Roles of Ablation in HCC Treatment



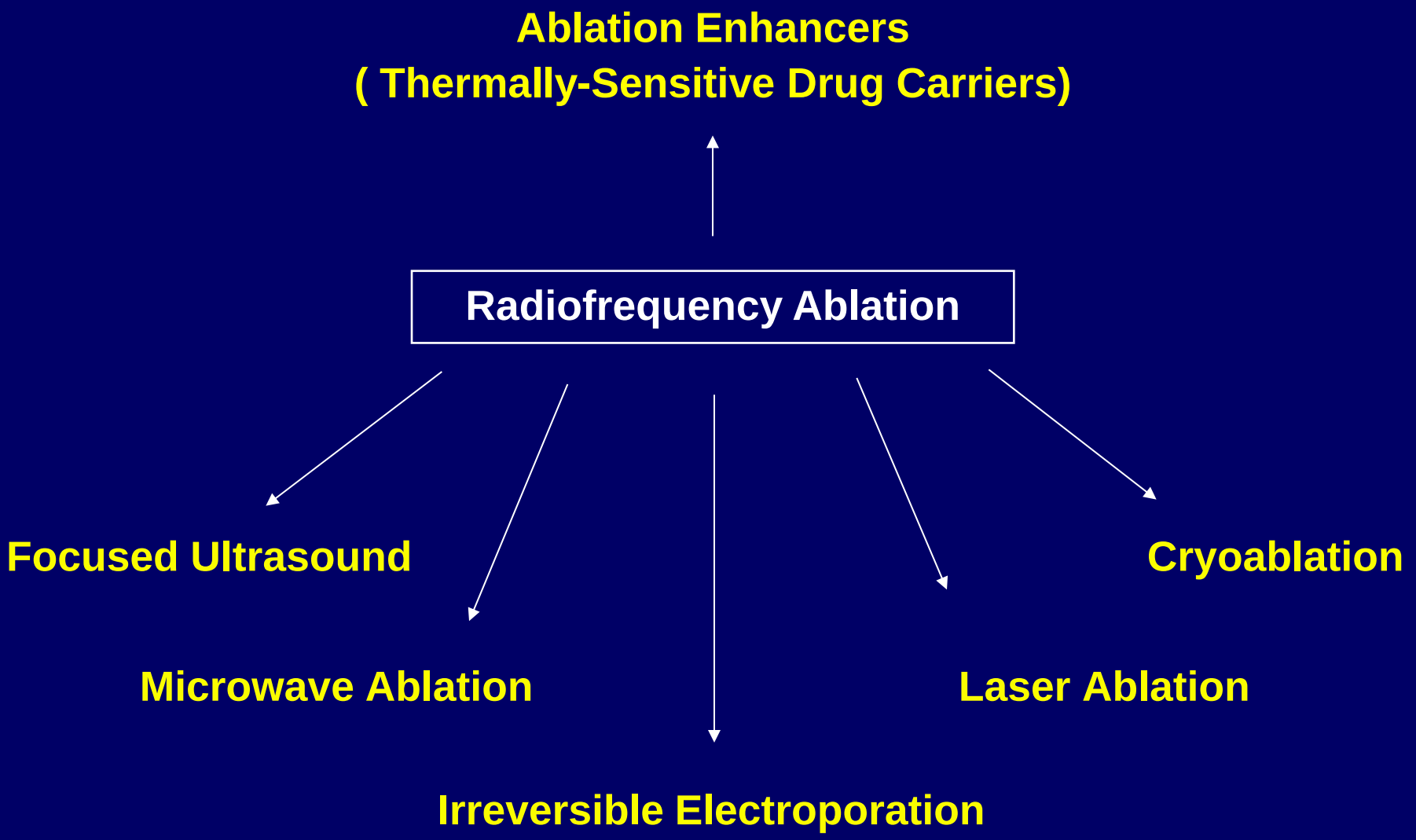
Omata M et al. Hepatol Int 2010;4:439-474

Barcelona Clinic Liver Cancer (BCLC): Staging System – Update 2011

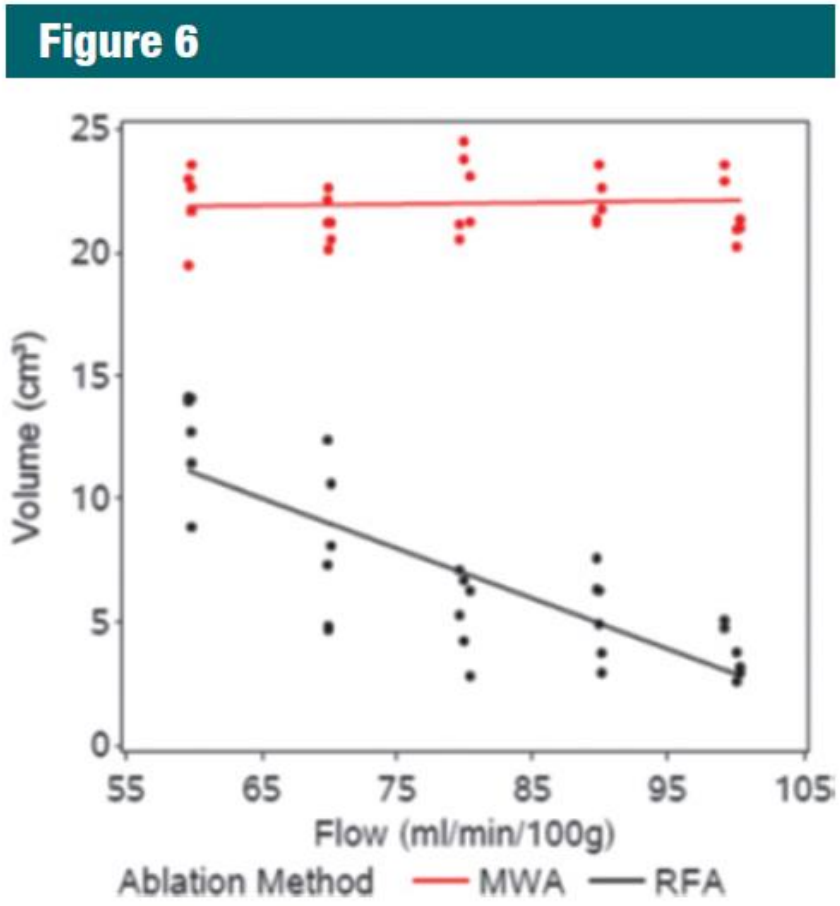


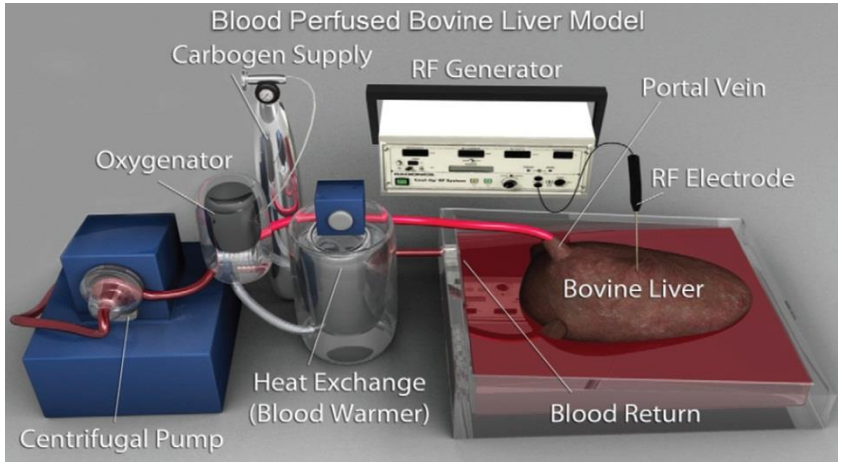
Forner et al. Lancet 2012;379:1245-1255 – de Lope CR et al. J Hepatol 2012;56 Suppl 1:S75-87

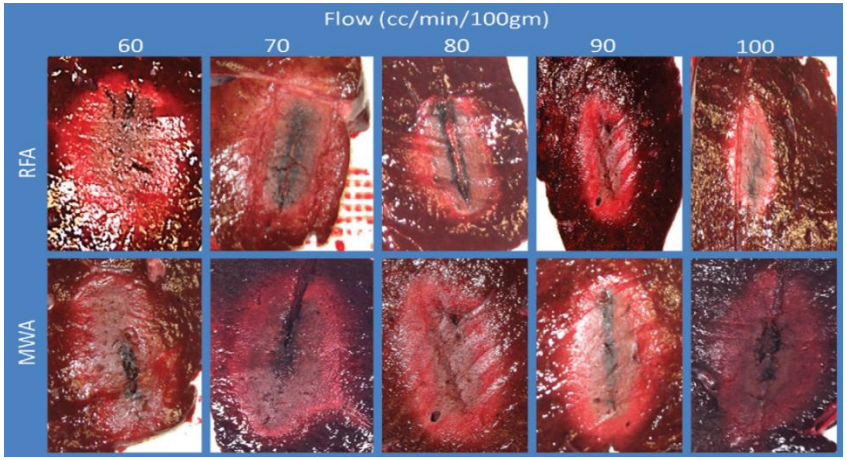
Image-Guided Ablation of HCC: Evolving Methods and Techniques



Microwave vs Radiofrequency Ablation: Experimental Findings



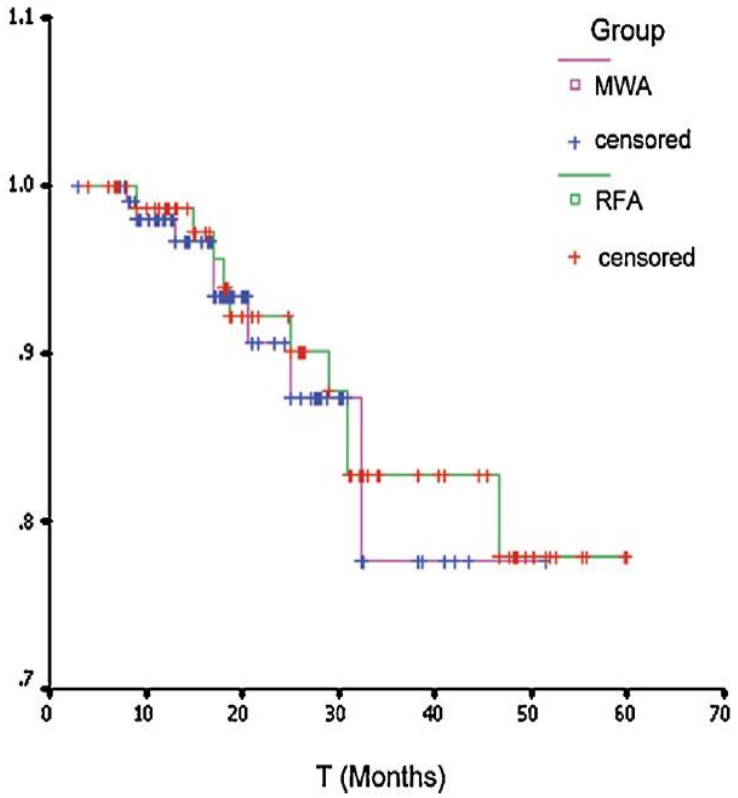




Dodd GD III et al. Radiology 2013;267:129-136

Microwave vs Radiofrequency Ablation: Retrospective Studies

Overall Survival (*n* = 198)

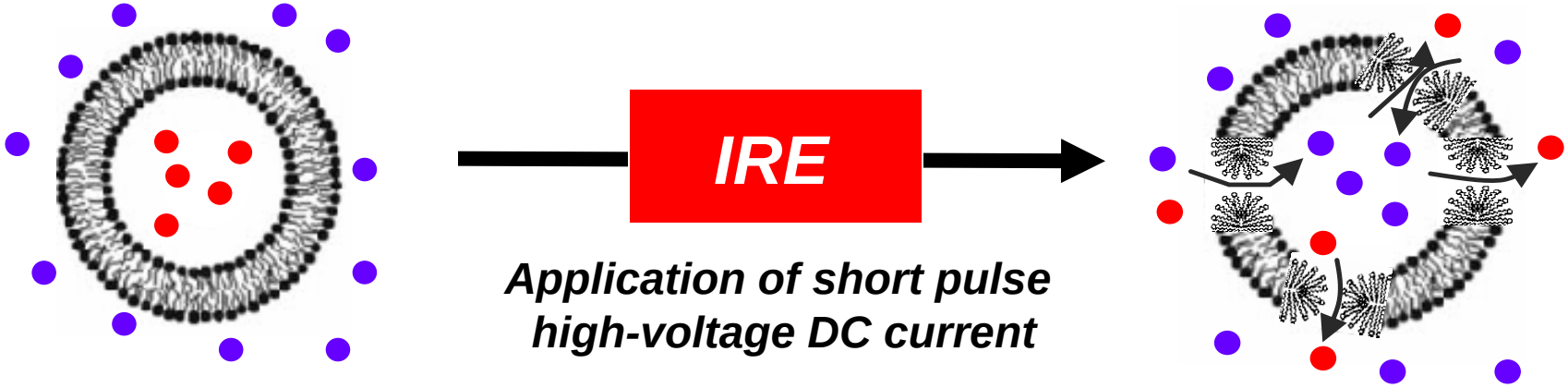


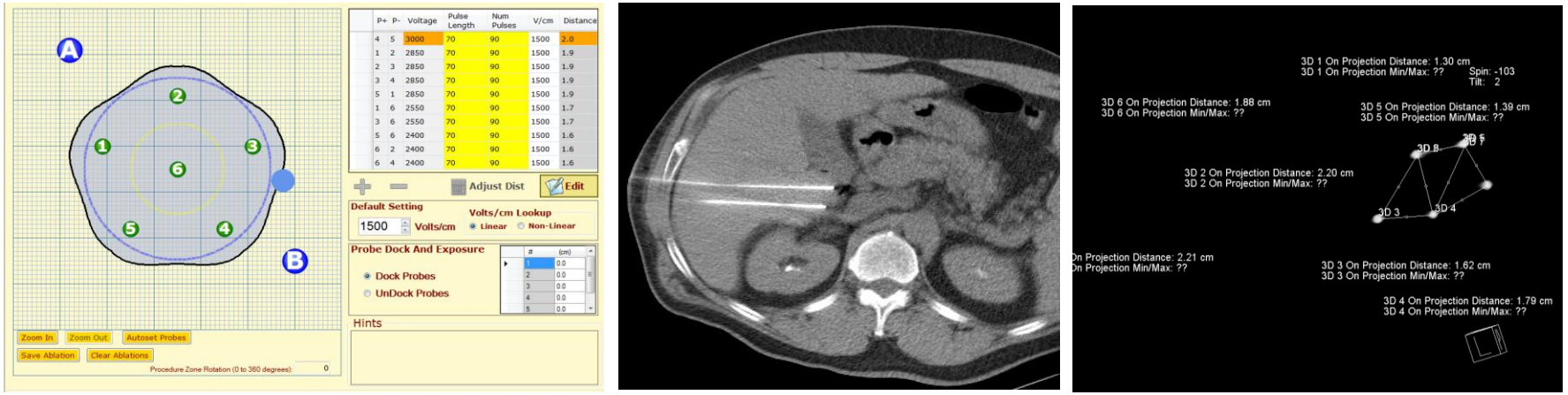
Complications (*n* = 879)

Serious complication	RFA (%)	MWA (%)
Intra-peritoneal bleeding	1 (0.27)	2 (0.31)
Portal vein thrombosis	ND	1 (0.15)
Intra-hepatic haematomas	1 (0.27)	ND
Bile leak	1 (0.27)	2 (0.31)
Biloma	ND	1 (0.15)
Bile duct injury	ND	1 (0.15)
Liver dysfunction	1 (0.27)	4 (0.61)
Liver abscess	3 (0.80)	1 (0.15)
Intestinal perforation	1 (0.27)	ND
Diaphragmatic hernia	ND	2 (0.31)
Haemothorax	2 (0.53)	1 (0.15)
Intractable pleural effusion	2 (0.53)	5 (0.76)
Tumour implantation	1 (0.27)	ND
TOTAL	13 (3.5)	20 (3.1)

Ding J et al. Eur J Radiol 2013;82:1379-1384

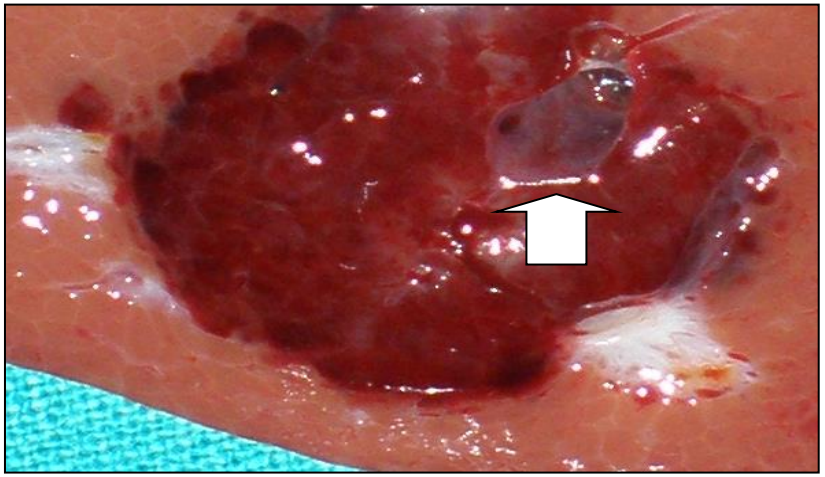
Irreversible Electroporation (IRE): A Novel, Non-Thermal Ablation Technique

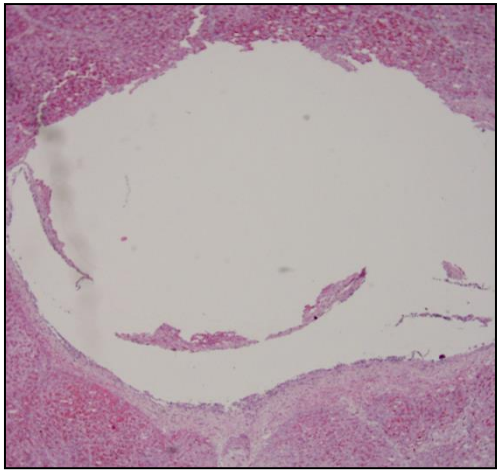


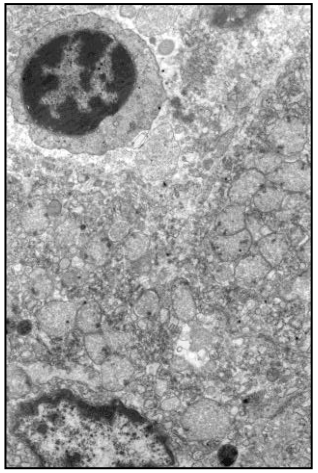


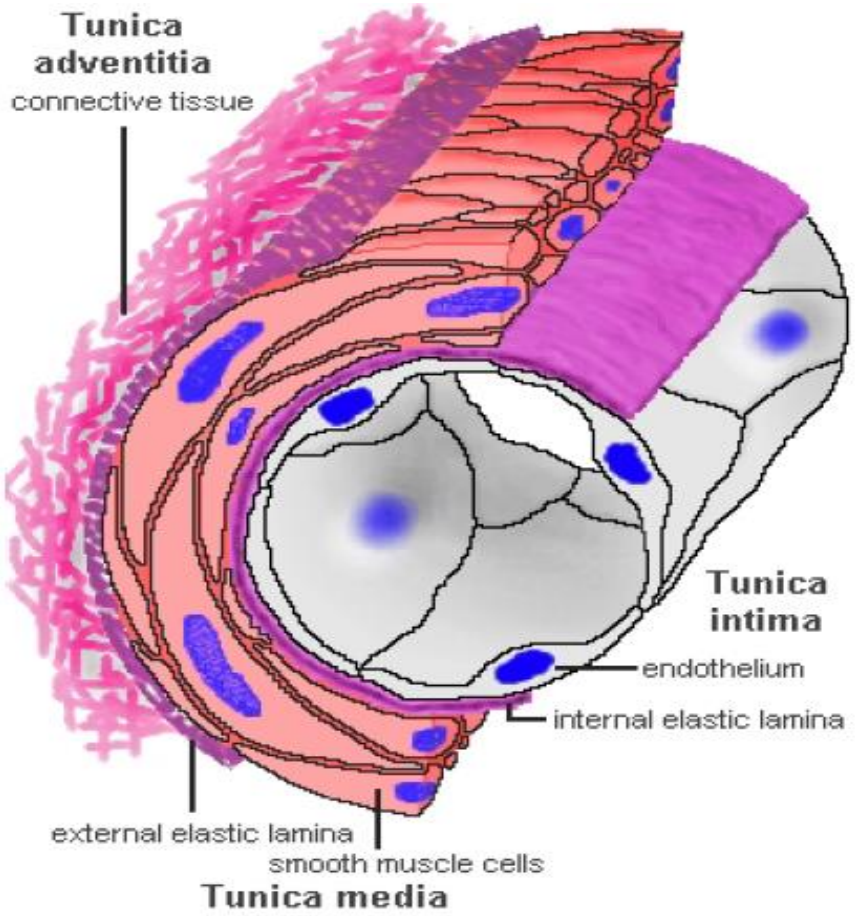
Lencioni R et al. Radiology 2012;262:43-58

Irreversible Electroporation (IRE): Experimental Findings





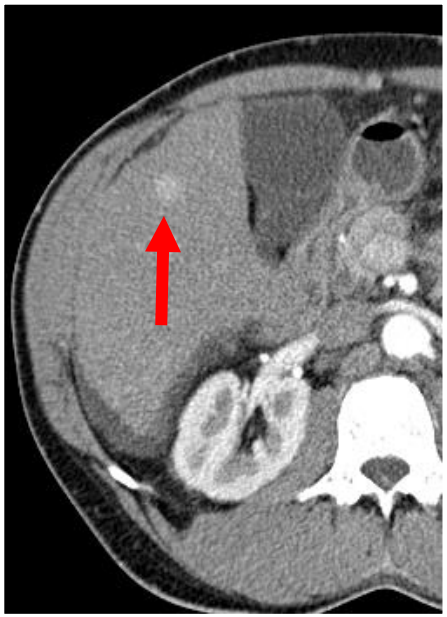




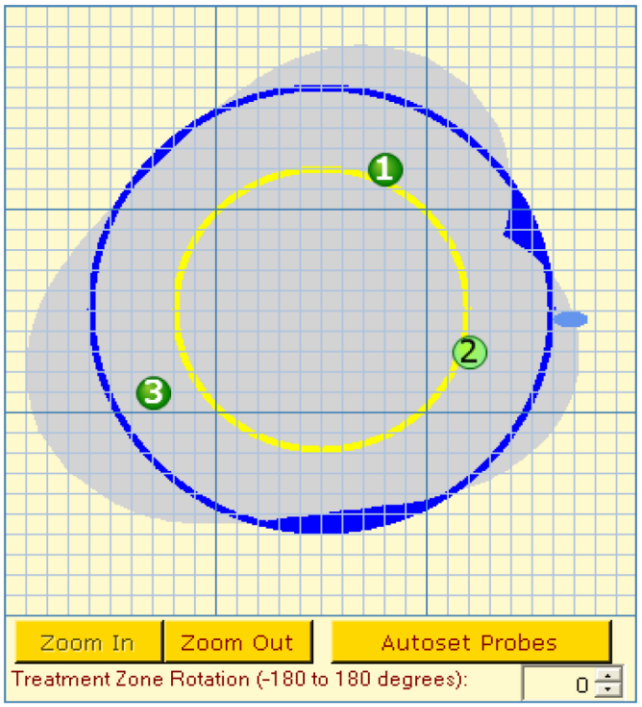
Lencioni R et al. Radiology 2012;262:43-58

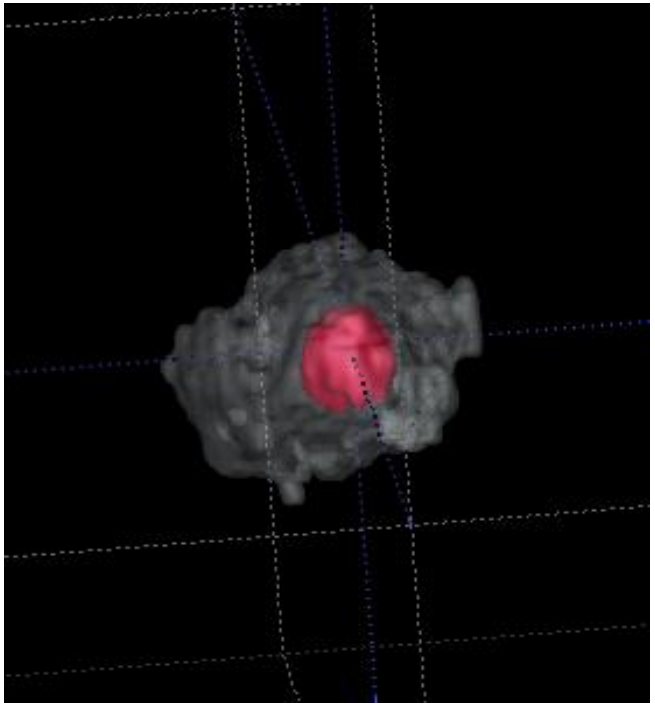
A Prospective Phase II Trial Using IRE for the Treatment of Early-Stage HCC

- **Multicenter study (26 subjects, 5 European centers)**
- **Primary endpoint: response by mRECIST, 2-year follow-up**



Baseline





Lencioni R, Bruix J (unpublished data)

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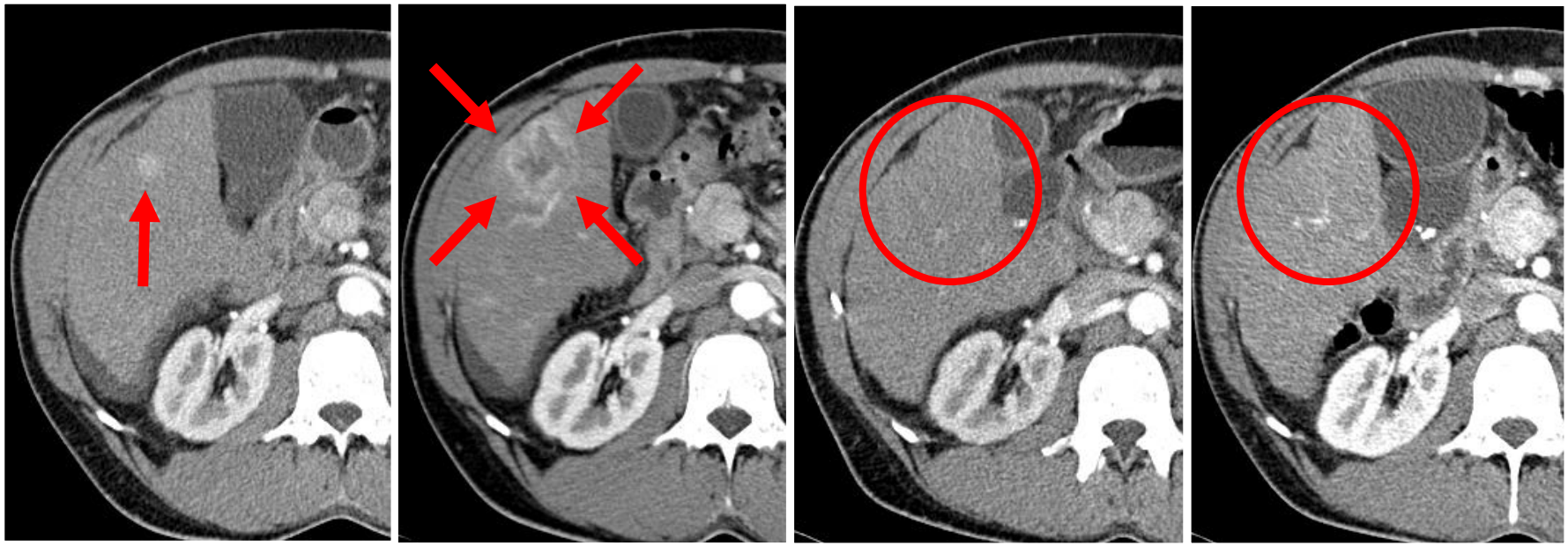
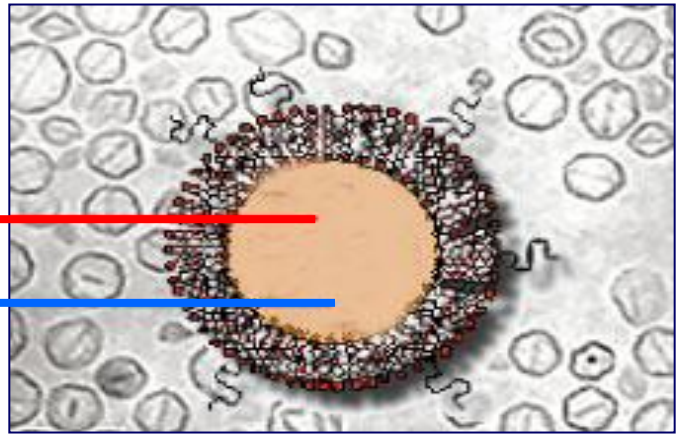
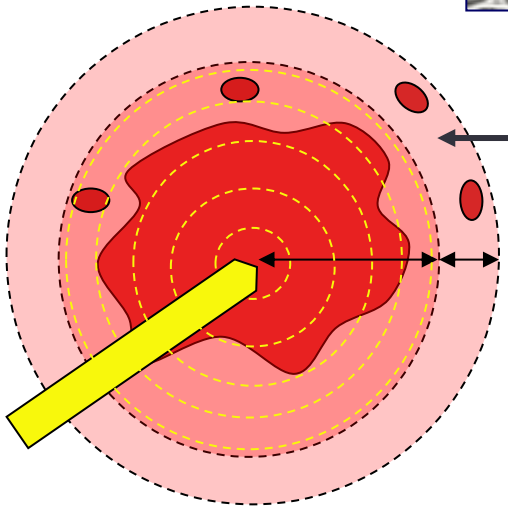


Lencioni R, Bruix J (unpublished data)

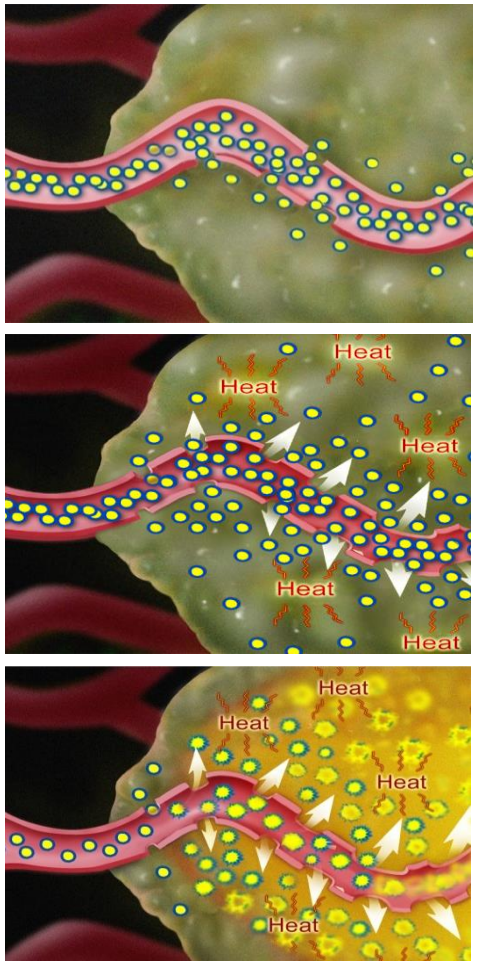
RFA in Combination with Heat-Activated Liposomal Encapsulation of Doxorubicin





39- 50°C

high concentration of doxorubicin deposited by ThermoDox (Celsion Corporation)



Presented at ILCA 2013

HEAT Trial: A Phase III Randomized Controlled Study of RFA + ThermoDox vs RFA Alone

HEAT

A Phase III, Randomized, Double-Blinded, Dummy-Controlled Study of the Efficacy and Safety of ThermoDox® in Combination with RFA Compared to RFA Alone in the Treatment of HCC

Inclusion Criteria

- HCC 3-7 cm
- ≤ 4 tumors
- Candidate for RFA
- Child-Pugh A-B
- No prior treatment

Randomization

n = 701

- 50 mg/m² ThermoDox
- Dummy infusion

Primary Endpoint
- PFS

Secondary Endpoints
- OS
- TTLR
- Safety
- Others

Presented at ILCA 2013

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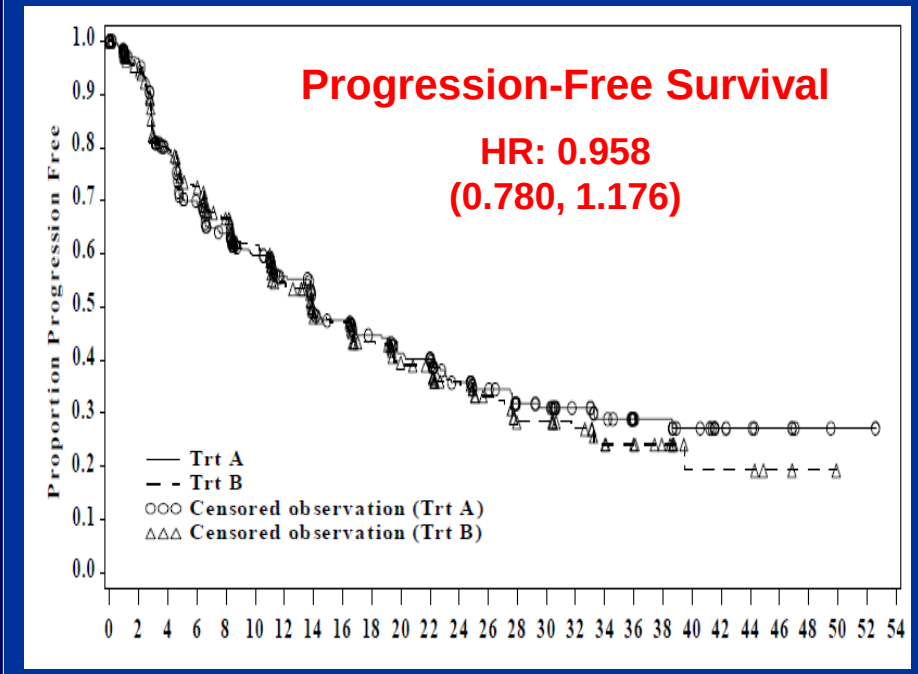

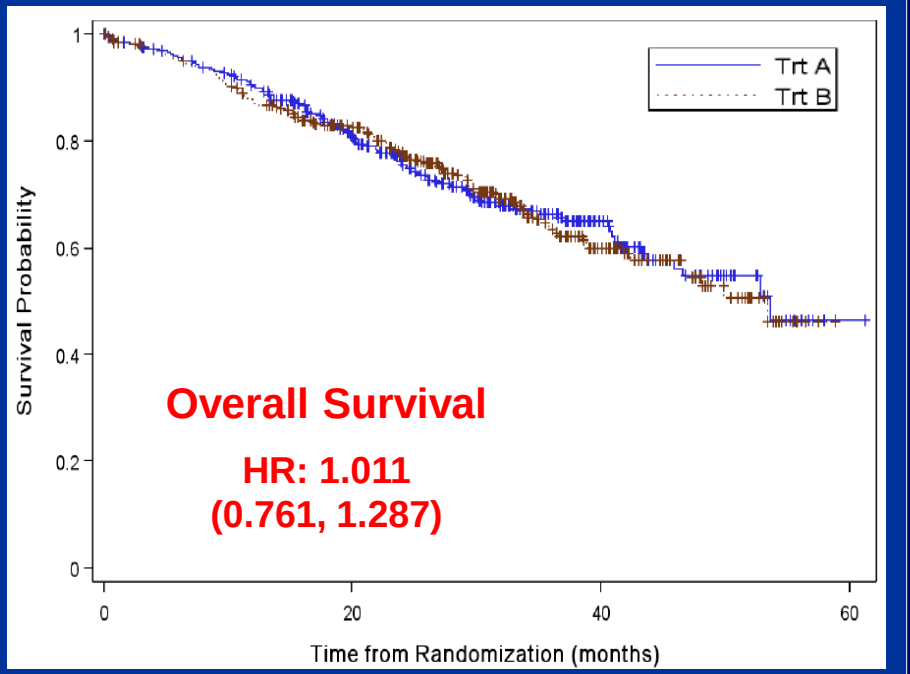

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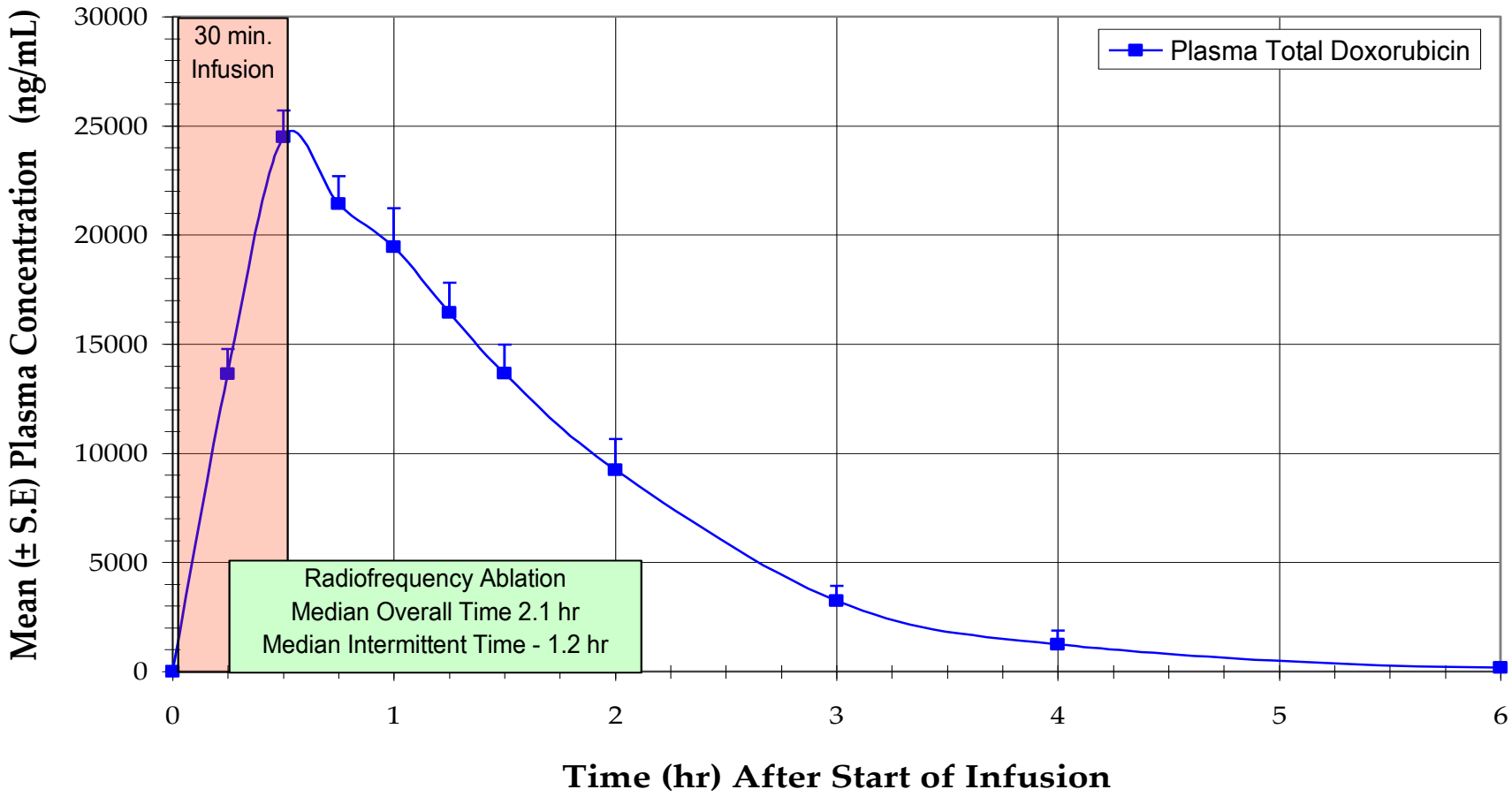

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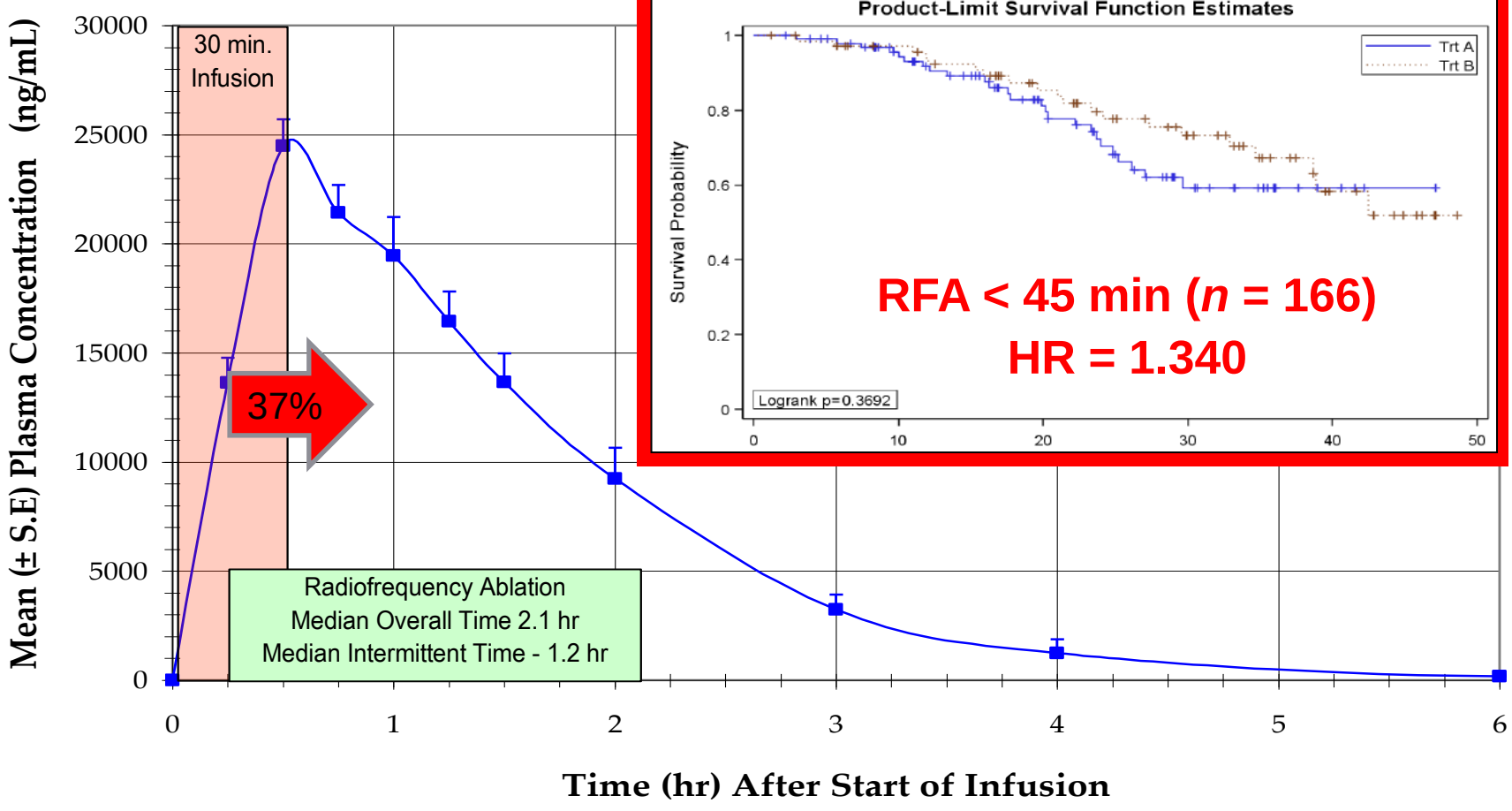

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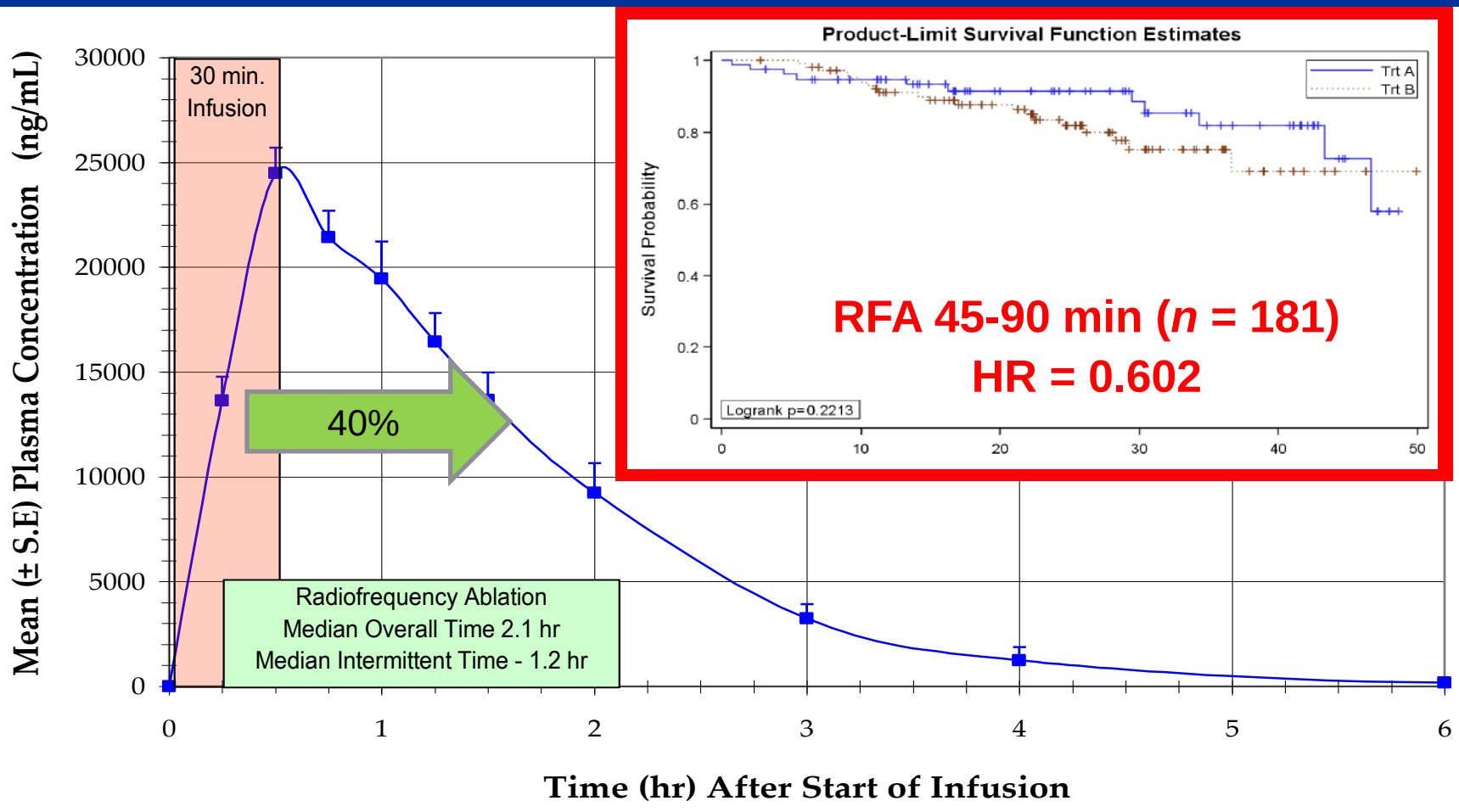

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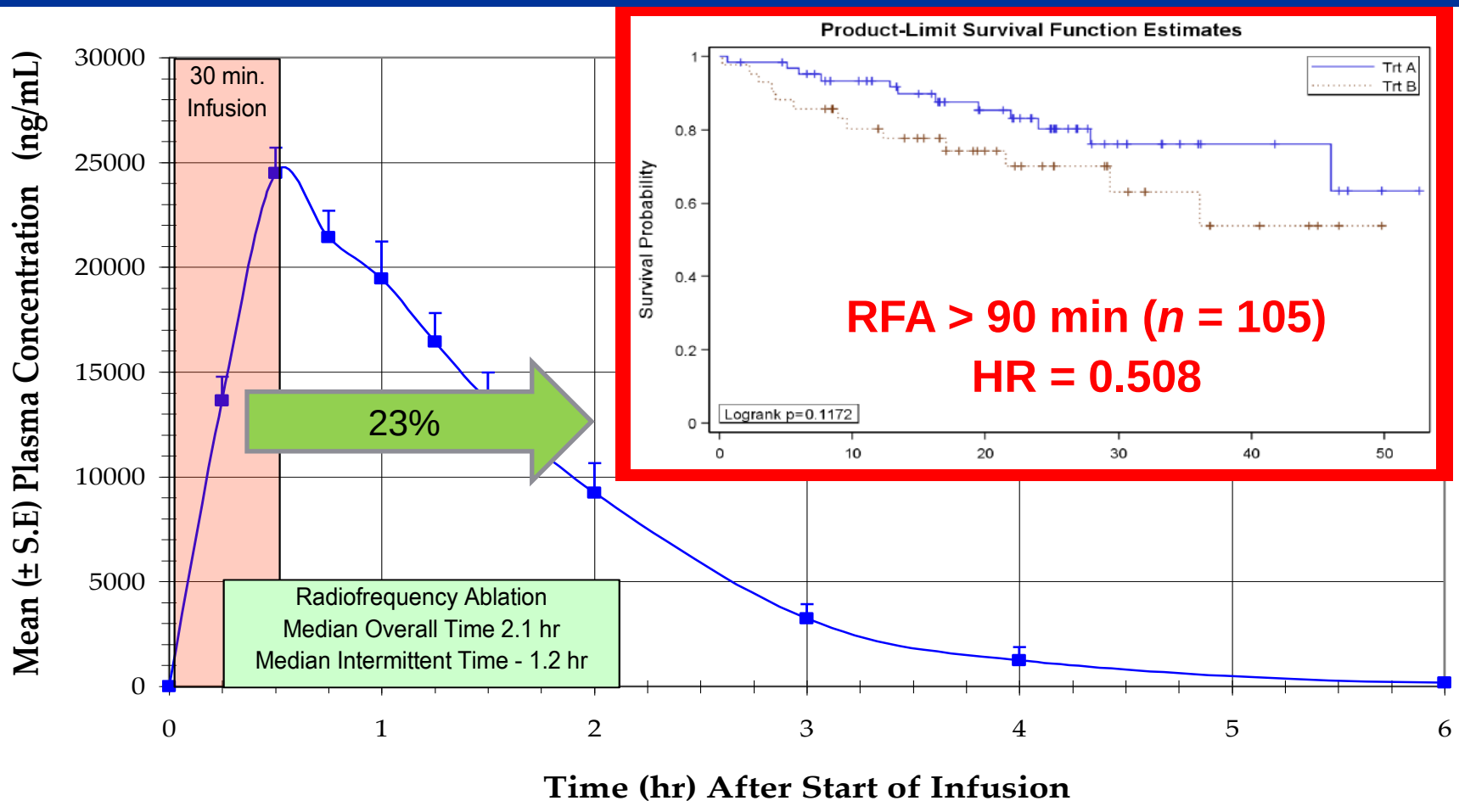
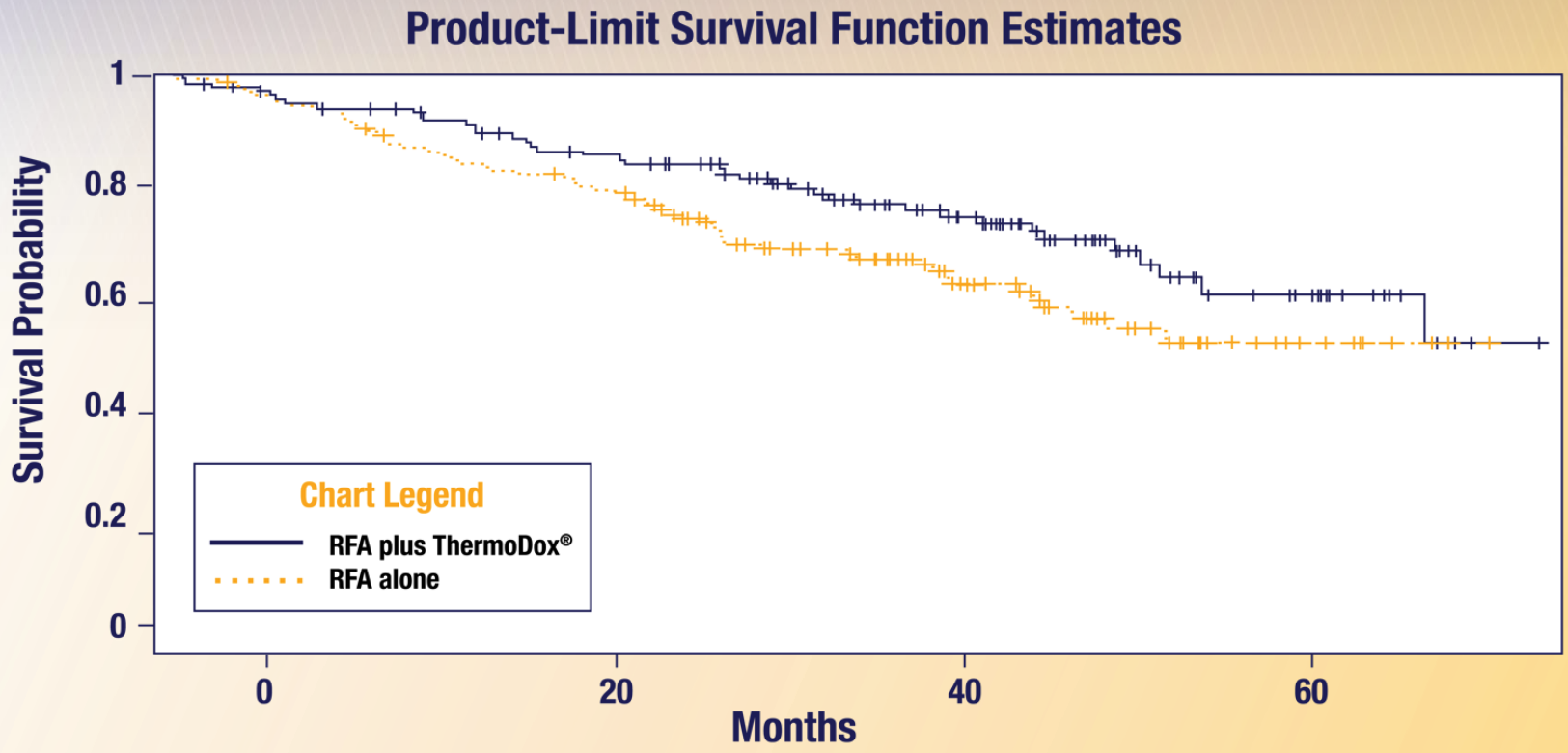


Presented at ILCA 2013

Sub-Group Analysis of HEAT Study Data: 285 Patients with Optimized RFA (>45 mins)



Overall Survival as of 6/30/2014	HR=0.639 (95% CI 0.419–0.974) *P* Value=0.037

Celsion•EGEN

The Study Design Difference- Optimizing both RFA & Chemo

The new OPTIMA protocol

104-13-302

differs substantially

from the earlier 700 patient

Phase III trial

- **Optimized thermal ablation**
  (by requiring multiple overlapping RFA ablation cycles)
- **Optimized doxorubicin tumor tissue concentration**
  (by heating the target area for at least 45 minutes to concentrate a therapeutic amount of doxorubicin in tumor tissue)
- **Eligibility limited to patients with a single HCC lesion**
- **Overall Survival is the primary endpoint**

Percutaneous Ablation for HCC in 2014: Take-Home Points

- **Resection and RFA are equally effective for stage 0 (very early) HCC tumors**
  - ***Complementary vs competitive: location, location, location!***

Percutaneous Ablation for HCC in 2014: Take-Home Points

- **Resection and RFA are equally effective for stage 0 (very early) HCC tumors**
  - ***Complementary vs competitive: location, location, location!***
- **Ablation is recommended for stage A (early) HCC in patients who are not optimal surgical candidates**
  - ***Novel technologies (MWA, IRE) seem to be able to overcome some of the limitations of RFA: data, data, data!***

Percutaneous Ablation for HCC in 2014: Take-Home Points

- **Resection and RFA are equally effective for stage 0 (very early) HCC tumors**
  - ***Complementary vs competitive: location, location, location!***
- **Ablation is recommended for stage A (early) HCC in patients who are not optimal surgical candidates**
  - ***Novel technologies (MWA, IRE) seem to be able to overcome some of the limitations of RFA: data, data, data!***
- **The high rate of incomplete response / recurrence after RFA remains a major unmet medical need**
  - ***Research on novel drugs / new carriers is a top priority***