saint 2012

8. Symposium für angewandte interventionsradiologische Techniken

Radiologische Interventionen

TUMORZENTRUM CANCER CENTER | heilbronn-franken

SLK-Kliniken

Baustelle Leber bei Tumorpatienten-

Wer blickt da noch durch?

Prof. Dr. med. Philippe L. Pereira

Chairman of the Dept of Radiology,
Minimally invasive Therapies and Nuclearmedicine
SLK-Clinics, am Gesundbrunnen, Heilbronn
Ruprecht-Karls University of Heidelberg
Research Director, Tumor therapies and interventional MRI
Eberhard-Karls University of Tübingen, Germany

Potential conflict of interests

(Honoraria, Advisor, Consultant, Travel grants, Research grants)

Acculis

Bayer Global

Bayer (Germany)

Biocompatibles, BTG

Bracco

Terumo

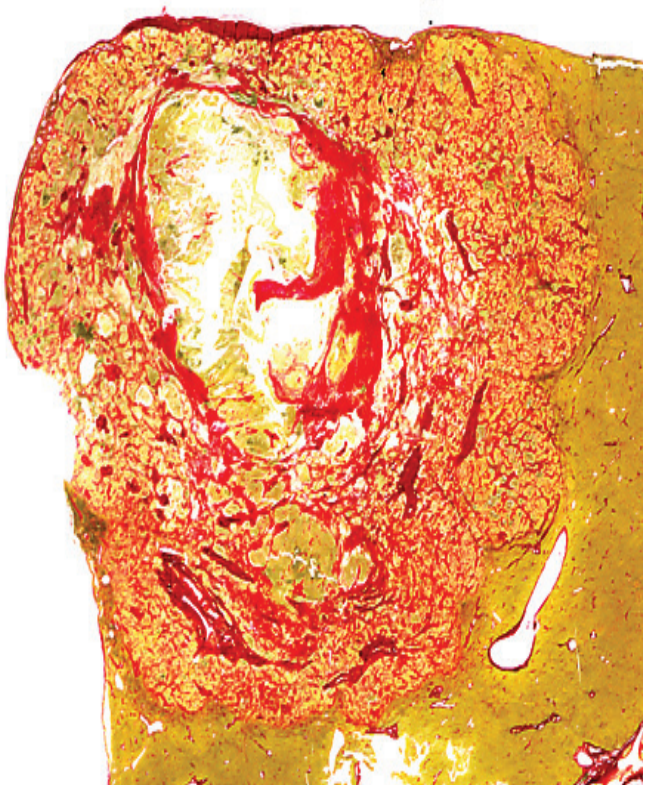
Celo Nova

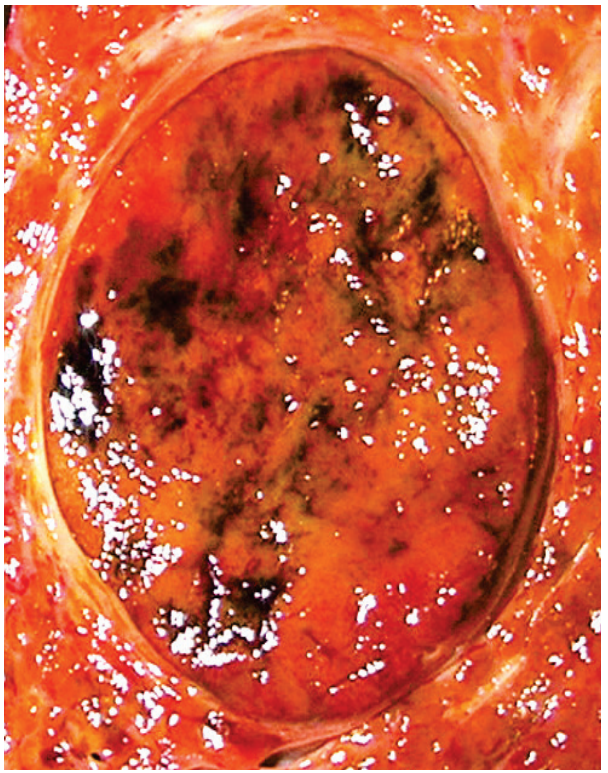
Celon Olympus

Pharmacept

Siemens Medical Solutions

Baustelle Leber bei Tumorpatienten



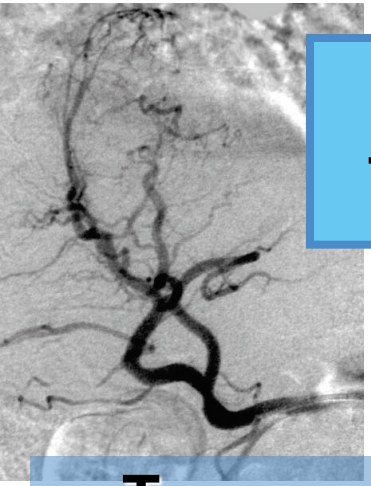


CRLM *versus* HCC?

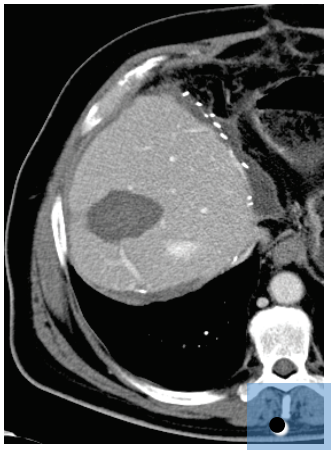
„different underlying diseases and different tumor biology“

Interventionelle Onkologie

Leber



palliative Therapien



Potenziell kurative Therapien

- **Transcatheter therapies**
  - Transarterial bland embolization
  - Transarterial chemoembolization
  - Intraarterial chemoperfusion
  - I-131 lipiodolization
  - Y-90 radioembolization
  - Drug-eluted embolization
  - Chemosaturation

- **Percutaneous therapies**
  - Ethanol injection
  - Acetic acid injection
  - Cryoablation
  - Laser
  - Radiofrequency ablation
  - Microwave
  - Light activated therapy
  - High focused US
  - Electrolytic therapy
  - Irrev. Electroporation
  - Cyberknife

S3 Leitlinien HCC

AWMF

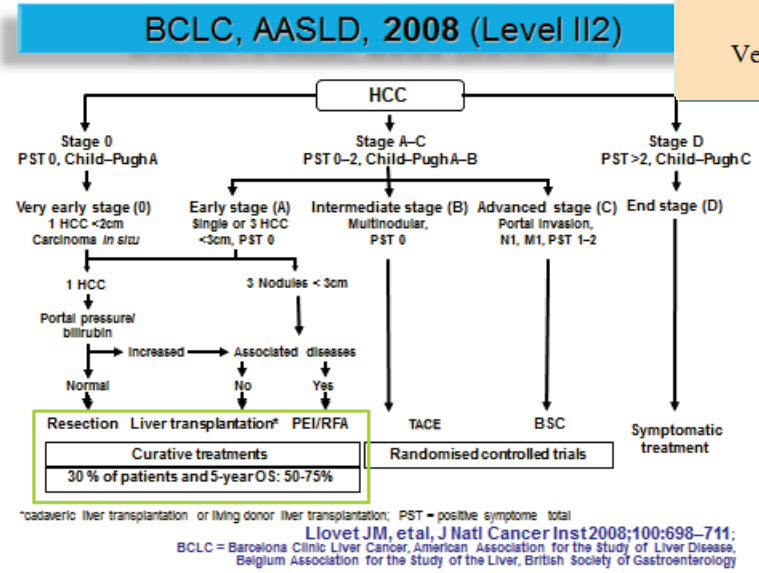
DKG KREBSGESELLSCHAFT

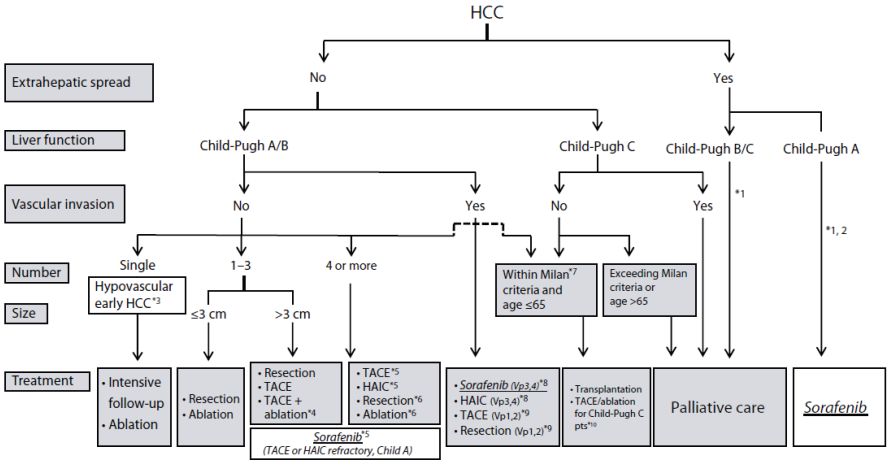
S3 Leitlinie

"Kolorektales Karzinom"

AWMF-Register-Nummer (021-007OL)

Version 1.0 09.2012





THE COCHRANE COLLABORATION®

S3-Leitlinien
Kolorektales Karzinom: Mets

Aktualisierung 2008

Hintergrund:

Zur lokalen Tumorkontrolle bei funktionell inoperablen Metastasen gibt es eine Reihe von Verfahren wie Lasertherapie und Radiofrequenzablation, die eine lokale Tumorablation ermöglichen und für die Fallserien vorliegen, deren Stellenwert im gesamten onkologischen Behandlungskonzept jedoch ungeklärt ist (Solbiati L and 2001; Vogl TJ 2002). Daher sollte bei diesen Patienten primär eine systemische Chemotherapie durchgeführt werden. Die regionale (HAI, SIRT) ist der systemischen Chemotherapie nicht überlegen und sollte daher nicht außerhalb von Studien eingesetzt werden (Kerr DJ 2003).

Bei der selektiven intravaskulären Radionuklidtherapie handelt es sich um ein weitgehend experimentelles Verfahren, welches nur in Frage kommt, wenn alle anderen Optionen ausgeschöpft sind. Zur SIRT sind nur relativ kleine Kohortenstudien veröffentlicht. (Lim, Gibbs et al. 2005; Mancini, Carpanese et al. 2006; Welsh, Kennedy et al. 2006)

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S3-Leitlinien Kolorektales Karzinom: Mets Aktualisierung 2013

3.5.16	Empfehlung
Empfehlungsgrad 0	Eine RFA kann durchgeführt werden, wenn nicht resektable Lebermetastasen vorliegen oder der Allgemeinzustand des Patienten eine Resektion nicht zulässt, insbesondere nach vorangegangener Leberresektion.
Level of Evidence 3a	De Novo: [568-570]
	Starker Konsens

568. (NICE), N.I.f.C.E., *Radiofrequency ablation for the treatment of colorectal metastases in the liver.* 2011: London.
569. Kim, K.H., et al., *Comparative analysis of radiofrequency ablation and surgical resection for colorectal liver metastases.* J Korean Surg Soc, 2011. **81**(1): p. 25-34.
570. Mulier, S., et al., *Radiofrequency ablation versus resection for resectable colorectal liver metastases: time for a randomized trial?* Ann Surg Oncol, 2008. **15**(1): p. 144-57.

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Understanding NICE guidance

Information for people who use NHS services

Radiofrequency ablation for the treatment of colorectal metastases in the liver

What has NICE said?

This procedure can be offered routinely as a treatment option for people with colorectal metastases in the liver who have already had or who cannot have more invasive surgery (liver resection) provided that doctors are sure that:

- the patient understands what is involved and agrees to the treatment, and
- the results of the procedure are monitored.

A team of specialists in hepatobiliary (liver) cancer should be involved in ensuring the right patients are offered the procedure.

Other comments from NICE

NICE noted that the evidence was not consistently reported and therefore difficult to interpret.

Radiofrequency Ablation Versus Resection for Resectable Colorectal Liver Metastases: Time for a Randomized Trial?

Stefaan Mulier,[1,2] Yicheng Ni,[2] Jacques Jamart,[3] Luc Michel,[4] Guy Marchal,[2] and Theo Ruers[5]

[1]Department of Surgery, Leopold Park Clinic, Froissartstraat 34, B-1040 Brussels, Belgium
[2]Department of Radiology, University Hospital Gasthuisberg, Catholic University of Leuven, Herestraat 49, B-3000 Leuven, Belgium
[3]Department of Biostatistics, University Hospital of Mont-Godinne, Catholic University of Louvain, Avenue du Dr. Thérasse 1, B-5530 Yvoir, Belgium
[4]Department of Surgery, University Hospital of Mont-Godinne, Catholic University of Louvain, Avenue du Dr. Thérasse 1, B-5530 Yvoir, Belgium
[5]Department of Surgery, Antoni van Leeuwenhoek Hospital, The Netherlands Cancer Institute, Postbus 90203, 1006 BE Amsterdam, The Netherlands

Background: Surgical resection is the gold standard in the treatment of resectable colorectal liver metastases (CRLM). In several centers, resection is being replaced by radiofrequency ablation (RFA), even though there is no evidence yet from randomized trials to support this. The aim of this study was to critically review the oncological evidence for and against the use of RFA for resectable CRLM.

Methods: An exhaustive review of RFA of colorectal metastases was carried out.

Results: Five-year survival data after RFA for resectable CRLM are not available. Percutaneous RFA is associated with worse local control, worse staging, and a small risk of electrode track seeding when compared with resection (level V evidence). For tumors ≤3 cm, local control after surgical RFA is equivalent to resection, especially if applied by experienced physicians to nonperivascular tumors (level V evidence). There is indirect evidence for profoundly different biological effects of RFA and resection.

Conclusions: A subgroup of patients has been identified for whom local control after RFA might be equivalent to resection. Whether this is true, and whether this translates into equivalent survival, remains to be proven. The time has come for a randomized trial.

J Korean Surg Soc 2011;81:25-34
DOI: 10.4174/jkss.2011.81.1.25

JKSS
Journal of the Korean Surgical Society

pISSN 2233-7903 • eISSN 2093-0488

ORIGINAL ARTICLE

Comparative analysis of radiofrequency ablation and surgical resection for colorectal liver metastases

Kyung Ho Kim, Yong Sik Yoon, Chang Sik Yu, Tae Won Kim[1], Hye Jin Kim[2], Pyo Nyun Kim[2], Hyun Kwon Ha[2], Jin Cheon Kim

Departments of Surgery, [1]Oncology, and [2]Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Purpose: To evaluate the comparative therapeutic efficacy of radiofrequency ablation (RFA) and hepatic resection for the treatment of colorectal liver metastasis (CRLM). **Methods:** Between 1996 and 2008, 177 patients underwent RFA, 278 underwent hepatic resection and 27 underwent combination therapy for CRLM. Comparative analysis of clinical outcomes was performed including number of liver metastases, tumor size, and time of CRLM. **Results:** Based on multivariate analysis, overall survival (OS) correlated with the number of liver metastases and the use of combined chemotherapy ($P < 0.001$, respectively). Disease-free survival (DFS) also correlated with the number of liver metastases ($P < 0.001$). In the 226 patients with solitary CRLM < 3 cm, OS and DFS rates did not differ between the RFA group and the resection group ($P = 0.962$ and $P = 0.980$). In the 70 patients with solitary CRLM ≥ 3 cm, DFS was significantly lower in the RFA group as compared with the resection group ($P = 0.015$). **Conclusion:** The results indicate that RFA may be a safe alternative treatment for solitary CRLM less than 3 cm, with outcomes equivalent to those achieved with hepatic resection. A randomized controlled study comparing RFA and resection for patients with single small metastasis would help to determine the most efficient treatment modalities for CRLM.

S3-Leitlinien
Kolorektales Karzinom: Mets
Aktualisierung 2013

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Level of Evidence 3a	De Novo: [568-570]
	Starker Konsens

Neither experimental nor case studies nor mixed studies nor escalation trial nor post marketing studies nor registry studies……

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Neither experimental nor case studies
studies nor trial
t marketing r
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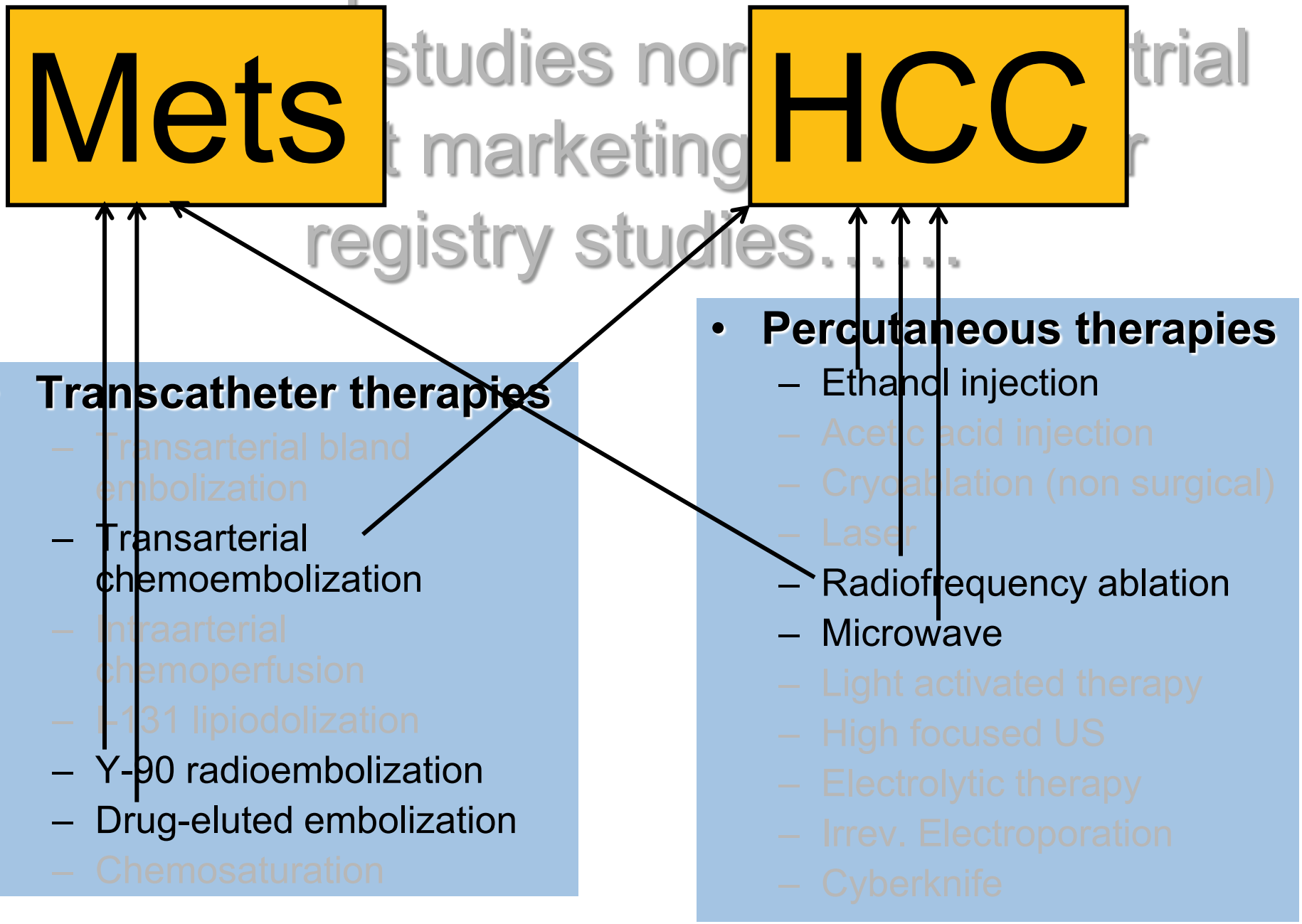
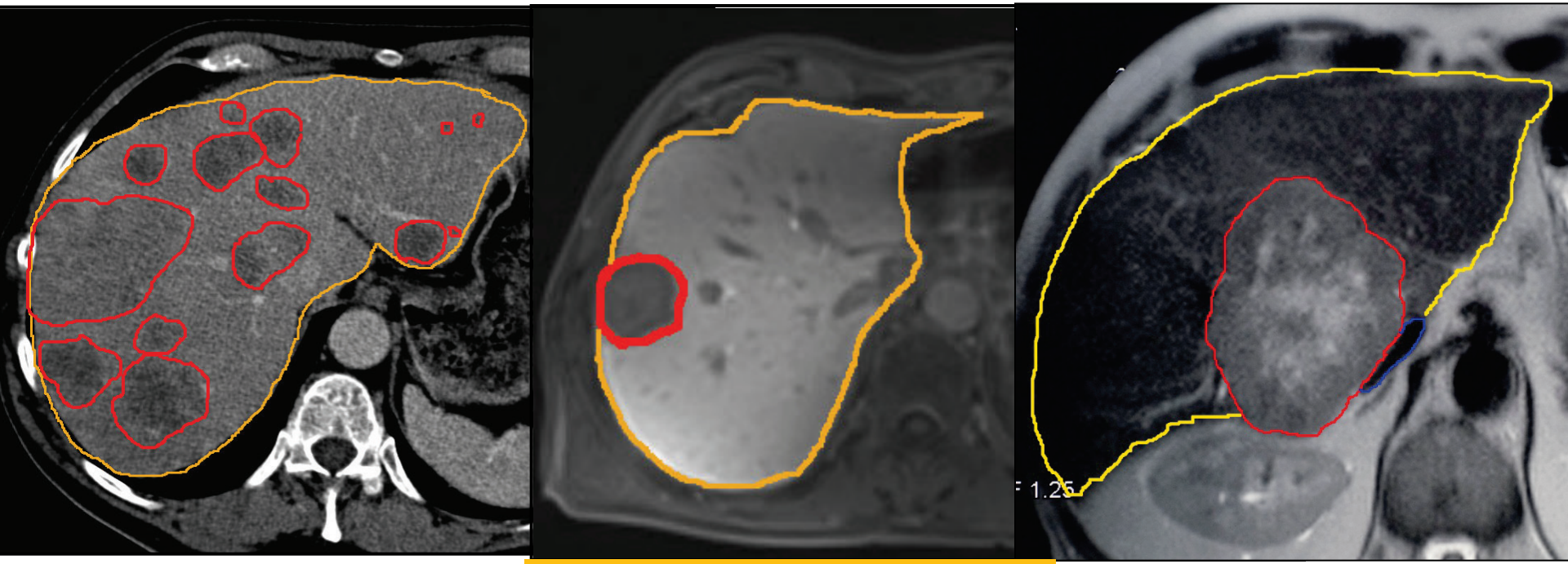


RFA: 14-55% at 5 years for colorectal liver metastases

„mainly due to patient selection criterias“

CRLM: Different clinical situations determine treatment aim and therapeutic strategy



Primary resectable or abladable
5y-OSR: 14-55%

non resectable CRM: Patients'selection

	Approach	Size of tumor	Nb of tumor	CEA	EHD	Varia
Solbiati 2001	perc.	**>4.1cm**	n.s.	-	-	-
Gillams 2004	perc.	**>5cm**	**>5 mets**	-	**significant**	-
Abdalla 2004	iOP	n.s.	**>3 mets**	n.s.	-	RF ablation* vs resection
Berber 2005	iOP	**>5cm**	**>3 mets**	**>200ng/ml**	**n.s.**	
Van Duijnhoven 2006	iOP	**>5cm**	n.s.	-	-	metachronous & central location
Aloia 2006	iOP	**>3cm**	n.s.	-	-	RF ablation* vs resection
Amersi 2006	Perc./lap.	**>3cm**	n.s.	-	-	-
Wang 2012	Perc	**>2.5cm**	n.s.	-	-	**Minimal margin 5mm**

5J.-Überleben nach RFA von nicht resektablen CRLM bei selektierten Patienten: 14-55%

„RFA versus Chirurgie und Vergleichstudien“

Author	Entity	Method	Patients [n]	Overall Survival			p	Local Recurrence [%]	Complication [%]
				2y [%]	3y [%]	5y [%]			
Aloia 2006	CRLM	Surgery	150	n.a.	79	71	**0.001**	5	death 1
		RFA	30	n.a.	57	27		30	death 0
Pawlik 2006	Sarcoma	Surgery	35	n.a.	n.a.	n.a.	**0.19**	n.a.	n.a.
		Surgery + RFA	18	n.a.	n.a.	n.a.		n.a.	n.a.
		RFA	13	n.a.	n.a.	n.a.		n.a.	n.a.
Park 2007	CRLM	Surgery	59	n.a.	n.a.	48	**0.0002**	2	n.a.
		RFA	30	n.a.	n.a.	19		9	n.a.
White 2007	CRLM	Surgery	30	100	82	65	**n.a.**	12	14
		RFA	22	100	28	0		59	4
Leblanc 2008	Various	Surgery	37	83	n.a.	n.a.	**0.763**	5.4	11
		Surgery + RFA	28	68	n.a.	n.a.		7.1	11
		RFA	34	75	n.a.	n.a.		11.7	9
Berber 2008	CRLM	Surgery	90	n.a.	n.a.	40	**0.35**	2	31.1
		RFA	68	n.a.	n.a.	30		16	2.9
Lee 2008	CRLM	Surgery	116	n.a.	n.a.	65.7	**0.227**	6.9	n.a.
		RFA	37	n.a.	n.a.	48.5		29.7	n.a.
Hur 2009	CRLM	Surgery	42	n.a.	70	60	**0.026**	9.5	14.3
		RFA	25	n.a.	50.1	25.5		28	0
Reuter 2009	CRLM	Surgery	192	n.a.	n.a.	23	**n.s.**	2	major 29
		RFA	66	n.a.	n.a.	21		17	major 10
McKay 2009	CRLM	Surgery	58	n.a.	n.a.	43	**0.021**	7	59
		RFA	43	n.a.	n.a.	23		60	43
Otto 2010*	CRLM	Surgery	28	n.a.	67	51	**0.721**	4	36.6; death 0
		RFA	82	n.a.	60	48		32	25; death 0

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Radiofrequency Ablation for Metachronous Liver Metastasis from Colorectal Cancer after Curative Surgery

In Ja Park, MD,[1] Hee Cheol Kim, MD,[1] Chang Sik Yu, MD,[1] Pyo Nyun Kim, MD,[2] Hyung Jin Won, MD,[2] and Jin Cheon Kim, MD[1]

TABLE 1. *Clinicopathological characteristics of patients and primary tumors*

	RFA (n = 30)		Resection (n = 59)		p
Mean age, yr (range)	61	(41–61)	54	(21–77)	0.72
Sex (%)					0.71
Male	22	(73.3)	41	(69.5)	
Female	8	(26.7)	18	(30.5)	
Mean preoperative CEA (range), ng/mL	13.4	(< 1–119)	7.7	(1–114.6)	0.02
Comorbidity (%)	14	(46.7)	18	(30.5)	0.13
Stage (%)					0.55
I	1	(3.3)	1	(1.7)	
II	11	(36.7)	16	(27.1)	
III	18	(60.0)	42	(71.2)	
Location (%)					0.71
Colon	17	(56.7)	31	(52.5)	
Rectum	13	(43.3)	28	(47.5)	
Time to liver metastasis, months	14.4	(4–40)	18.1	(3–98)	0.10
CEA at diagnosis of liver metastasis, ng/mL	10.3	(0.6–70.2)	14.5	(0.6–122)	0.39
No. of liver metastases					
Mean	1.2	(1–3)	1.4	(1–5)	0.04
Single	25	(83.3)	43	(72.9)	
Multiple	5	(16.7)	16	(17.1)	
Mean size of liver metastases	2.0	(0.6–4)	3.1	(0.5–8)	0.001
≤3 cm	26	(86.7)	34	(57.6)	
> 3 cm	4	(13.3)	25	(42.4)	
Location of liver metastases					0.16
Unilateral	29	(96.7)	51	(86.4)	
Bilateral	1	(0.3)	6	(13.6)	
Chemotherapy after treatment of liver metastases					0.38
No	8	(26.7)	11	(18.6)	
Yes	22	(73.3)	48	(81.4)	

Radiofrequency Ablation for Metachronous Liver Metastasis from Colorectal Cancer after Curative Surgery

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	Pat. n=	Tumor Size [cm]	Median Survival (months)	Approach	Survival Rates
Park 2007	RFA 30 OP 59	2 3.1	**36** **56**	Perc.	**5y-SR: 19%** **5y-SR: 48%**

1. Mets in RFA-Group were non resectable because of comorbidity or too large resection
2. **Single RFA session**
3. **Single RF-applicator for CRLM up to 3cm**
4. **Only 12 minutes energy application & US-Monitoring !!!**
5. **Some mets treated with RF were in „difficult locations“, R0 not possible**

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Neither experimental nor case studies nor mixed studies nor escalation trial nor post marketing studies nor registry studies……

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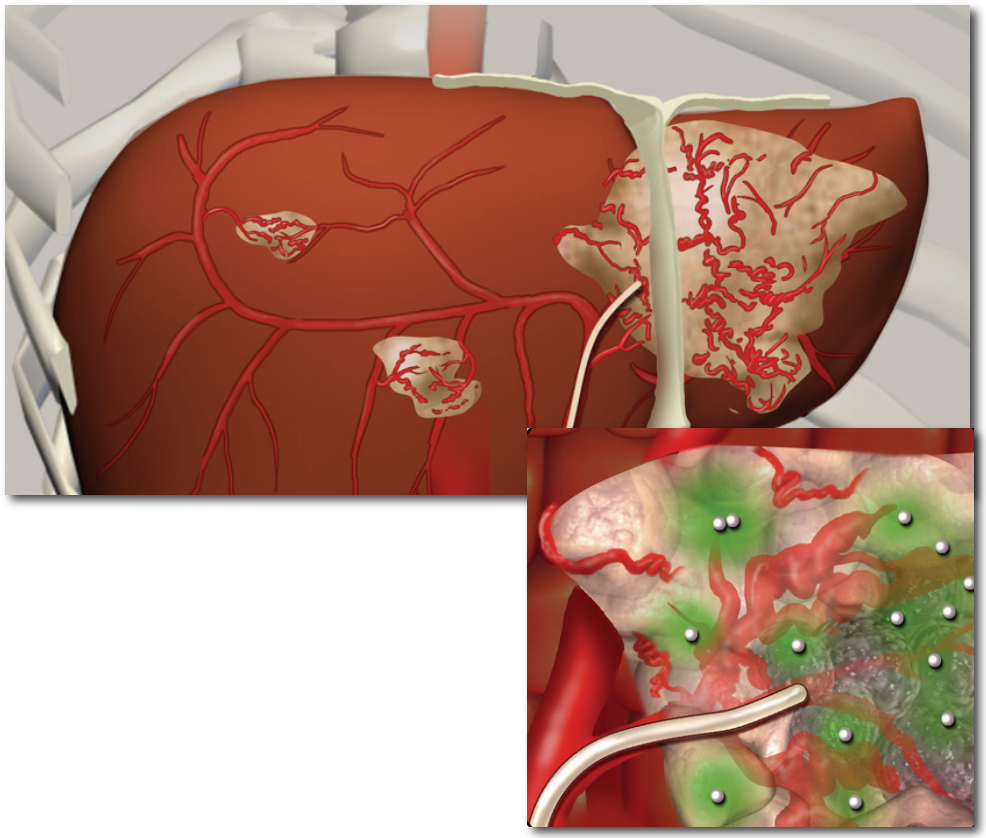
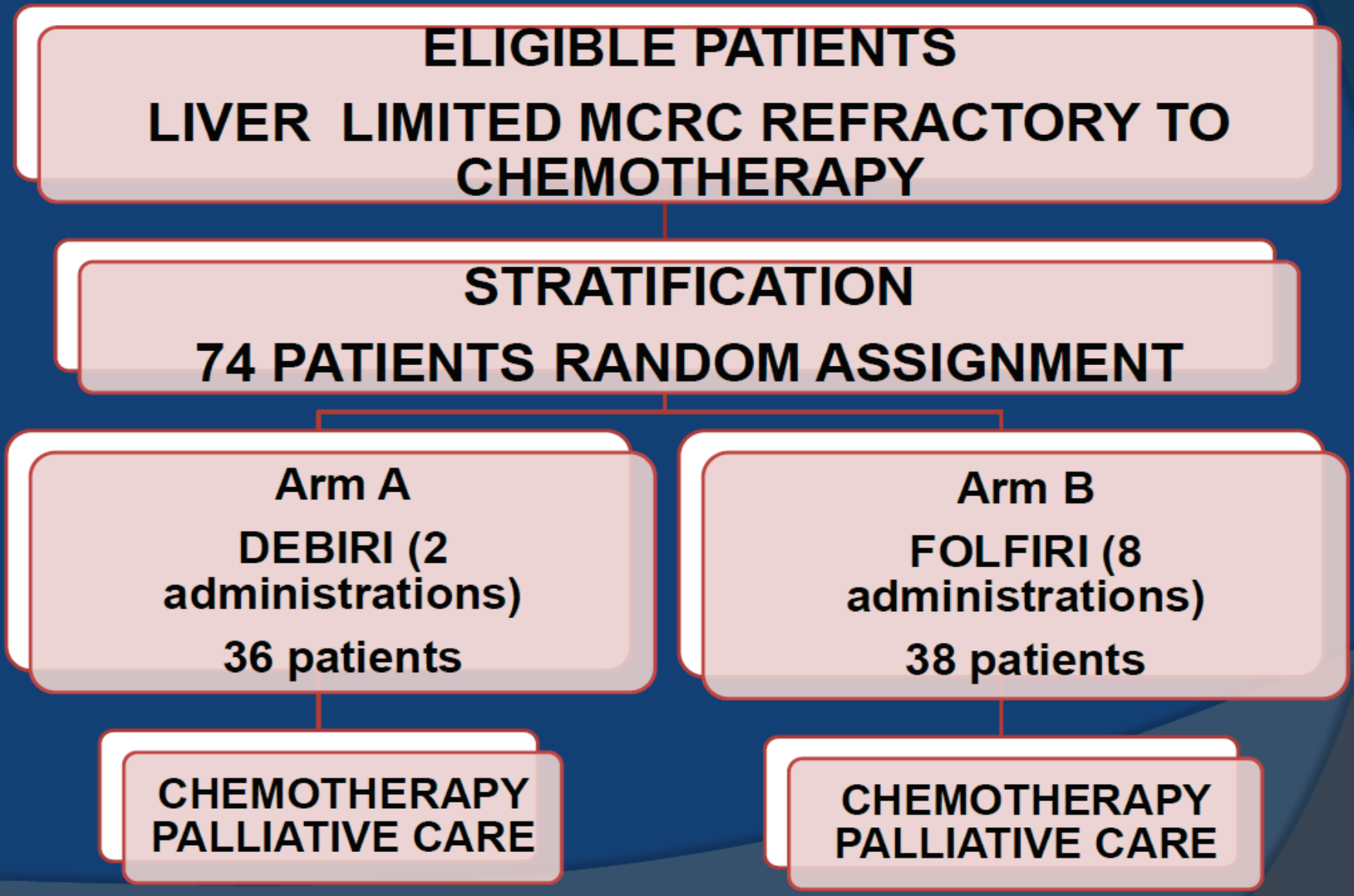


STUDY DESIGN: DEBIRI vs FOLFIRI



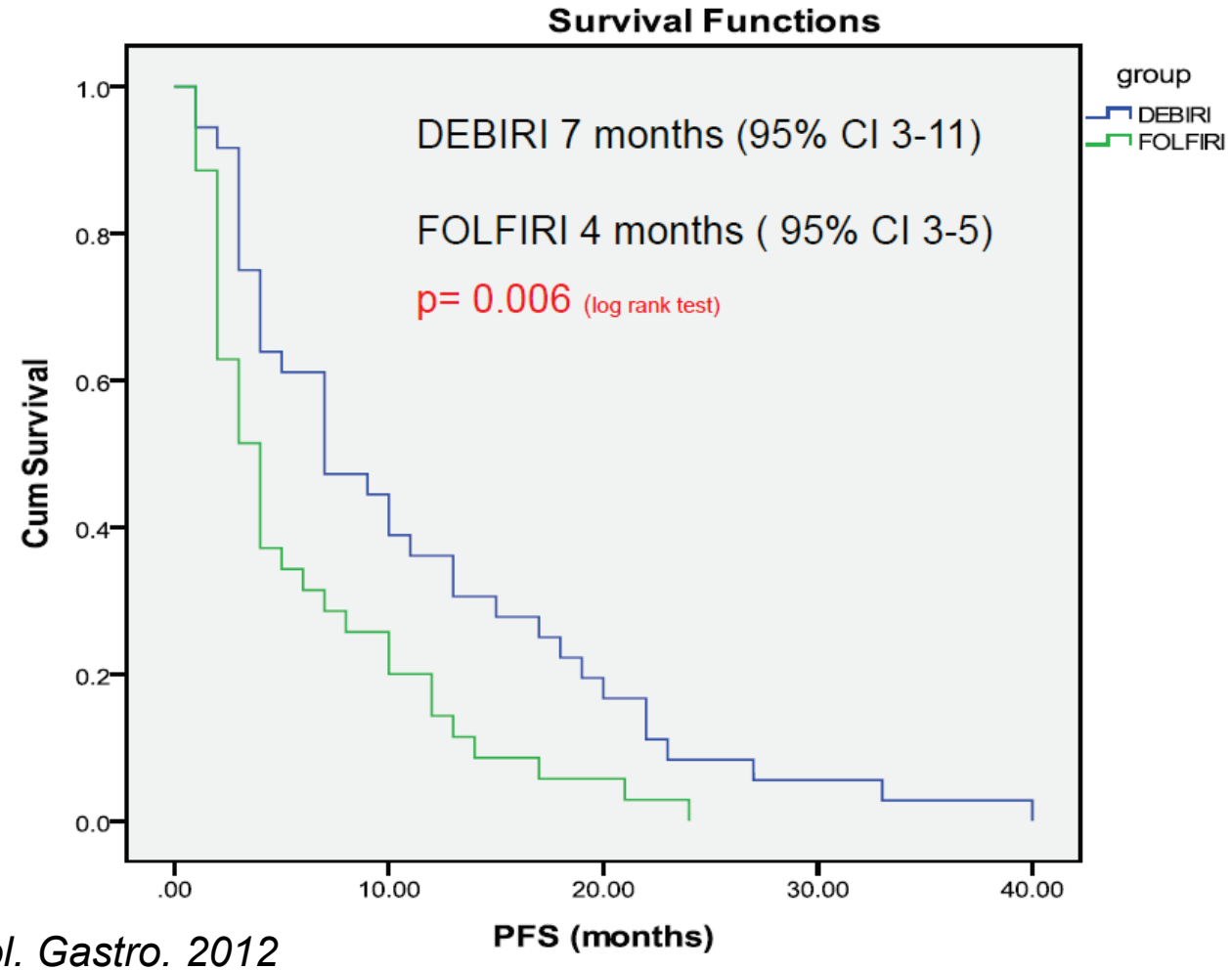
ANNALS OF GASTROENTEROLOGY & HEPATOLOGY

ORIGINAL ARTICLE

Hepatic Arterial Chemoembolization Adopting Dc Bead®, Drug-Eluting Bead Loaded with Irinotecan (Debiri) Versus Systemic Therapy for Hepatic Metastases from Colorectal Cancer: A Randomized Study of Efficacy and Quality of Life

Giammaria Fiorentini[1], Camillo Aliberti[2], Giorgio Benea[2], Massimo Tilli[2], Francesco Graziano[1], Andrea Mambrini[3], and Stefano Guadagni[4]

Affiliations: [1]Department of Oncology and Hematology, Ospedali Riuniti Marche Nord – sede Muraglia, Pesaro, Italy; [2]Department of Radiology, Delta Hospital, Ferrara, Italy; [3]Department of Oncology, General Hospital, Carrara, Italy and [4]Department of Surgery, University of L'Aquila, L'Aquila, Italy



Fiorentini G et al: Ann Hepatol. Gastro. 2012

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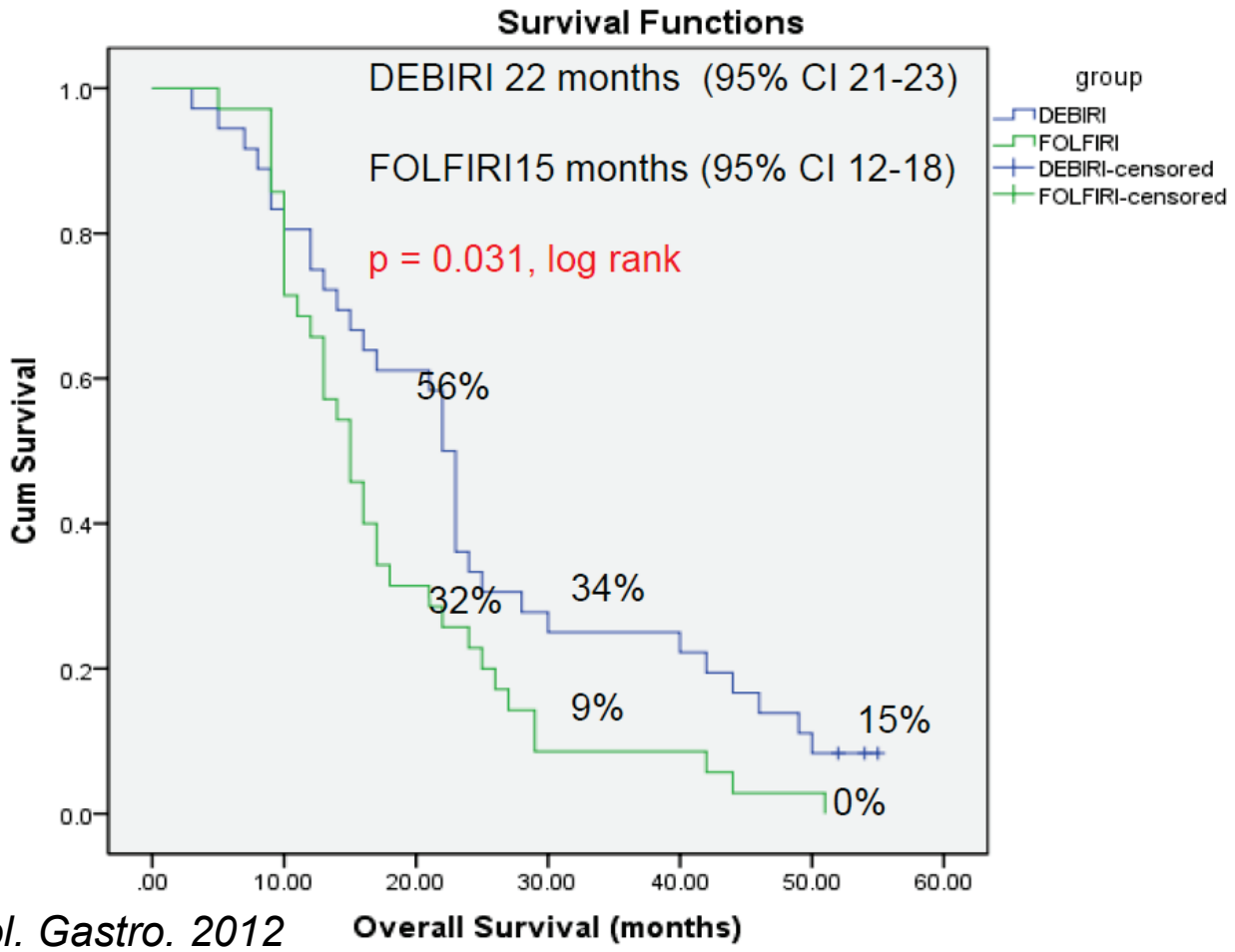
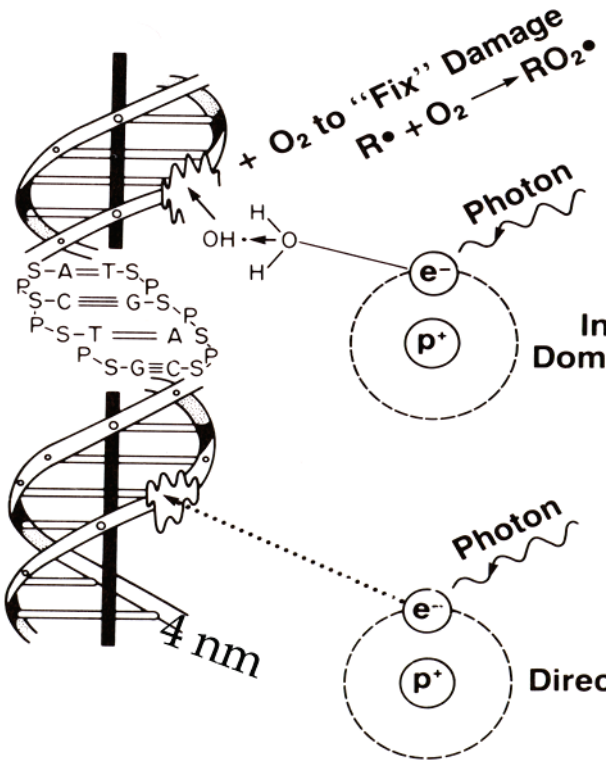
Affiliations: [1]Department of Oncology and Hematology, Ospedali Riuniti Marche Nord – sede Muraglia, Pesaro, Italy; [2]Department of Radiology, Delta Hospital, Ferrara, Italy; [3]Department of Oncology, General Hospital, Carrara, Italy and [4]Department of Surgery, University of L'Aquila, L'Aquila, Italy



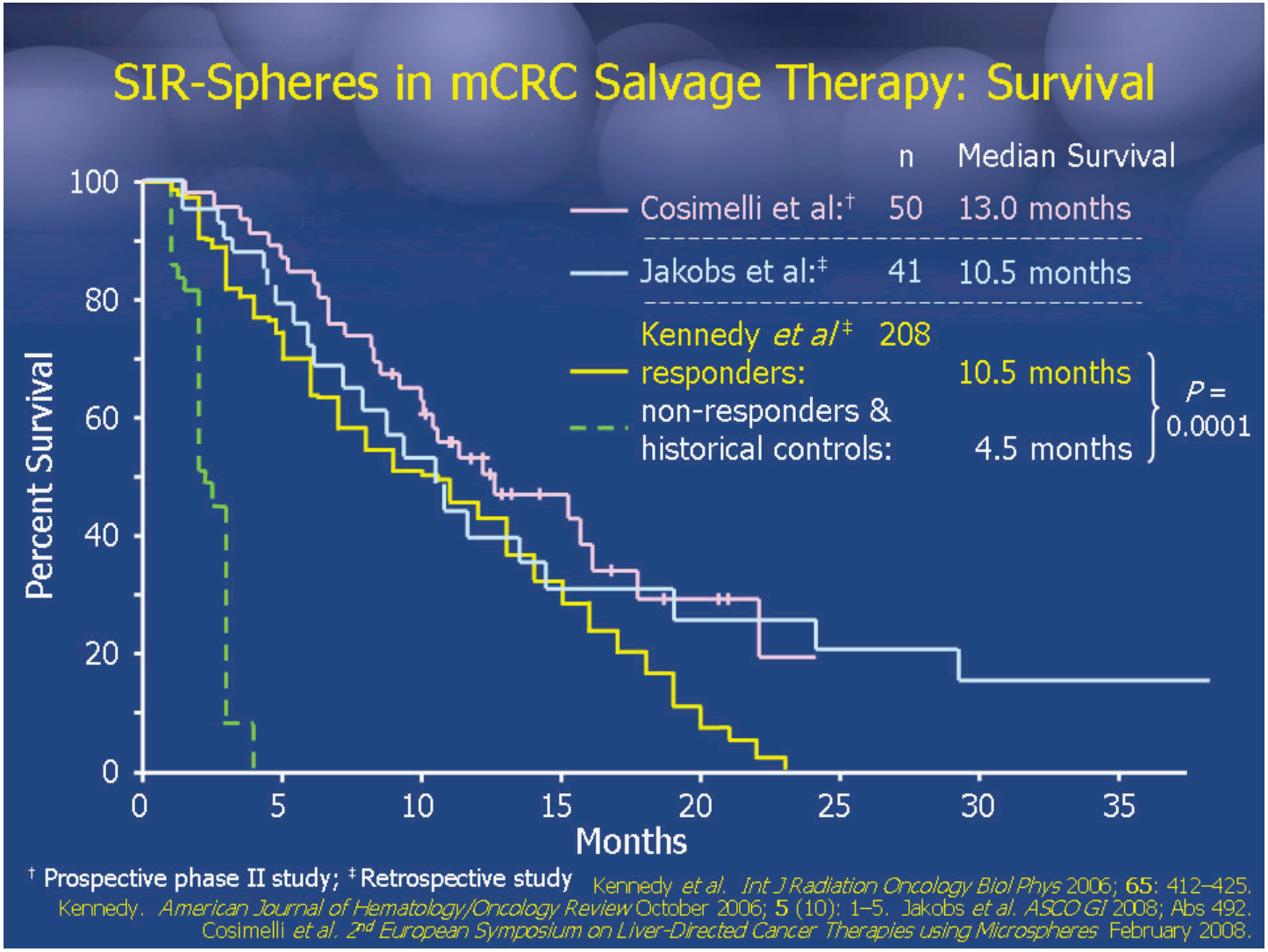
Fiorentini G et al: Ann Hepatol. Gastro. 2012

Neither experimental nor case studies nor mixed studies nor escalation trial nor post marketing studies nor registry studies……

- **Transcatheter therapies**
  - Transarterial bland embolization
  - Transarterial chemoembolization
  - Intraarterial chemoperfusion
  - I-131 lipiodolization
  - Y-90 radioembolization
  - Drug-eluted embolization
  - Chemosaturation

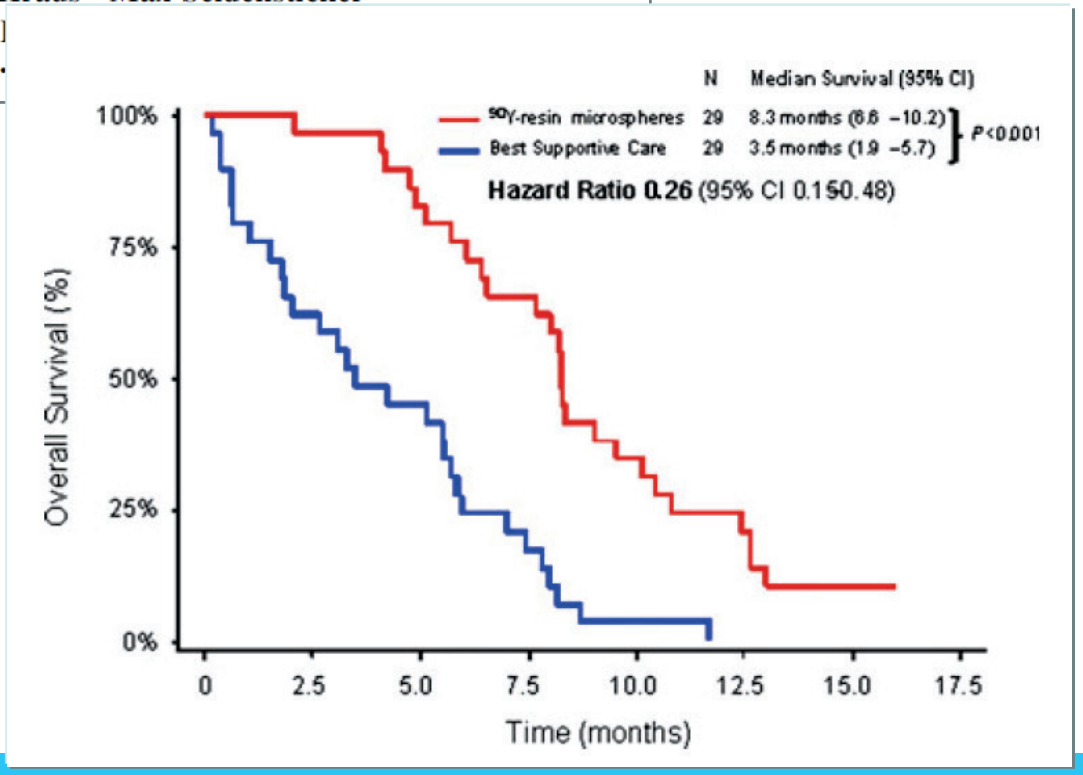


Radioembolisation and CRLM as 3rd Line/Salvage Therapy



Matched-Pair Comparison of Radioembolization Plus Best Supportive Care Versus Best Supportive Care Alone for Chemotherapy Refractory Liver-Dominant Colorectal Metastases

Ricarda Seidensticker · Timm Denecke · Patrick Kraus · Max Seidensticker · Konrad Mohnike · Jörg Fahlke · Erika Kettner · [illegible] · Oliver Dudeck · Maciej Pech · Holger Amthauer ·



Conclusions: Radioembolization offers a promising addition to BSC in treatment-refractory patients for whom there are limited options. Survival was prolonged and adverse events were generally mild-to-moderate in nature and manageable.

In CVIR 2012

Phase III Trial Comparing Protracted Intravenous Fluorouracil Infusion Alone or With Yttrium-90 Resin Microspheres Radioembolization for Liver-Limited Metastatic Colorectal Cancer Refractory to Standard Chemotherapy

Alain Hendlisz, Marc Van den Eynde, Marc Peeters, Geert Maleux, Bieke Lambert, Jaarke Vannoote, Katrien De Keukeleire, Chris Verslype, Luc Defreyne, Eric Van Cutsem, Philippe Delatte, Thierry Delaunoit, Nicola Personeni, Marianne Paesmans, Jean-Luc Van Laethem, and Patrick Flamen

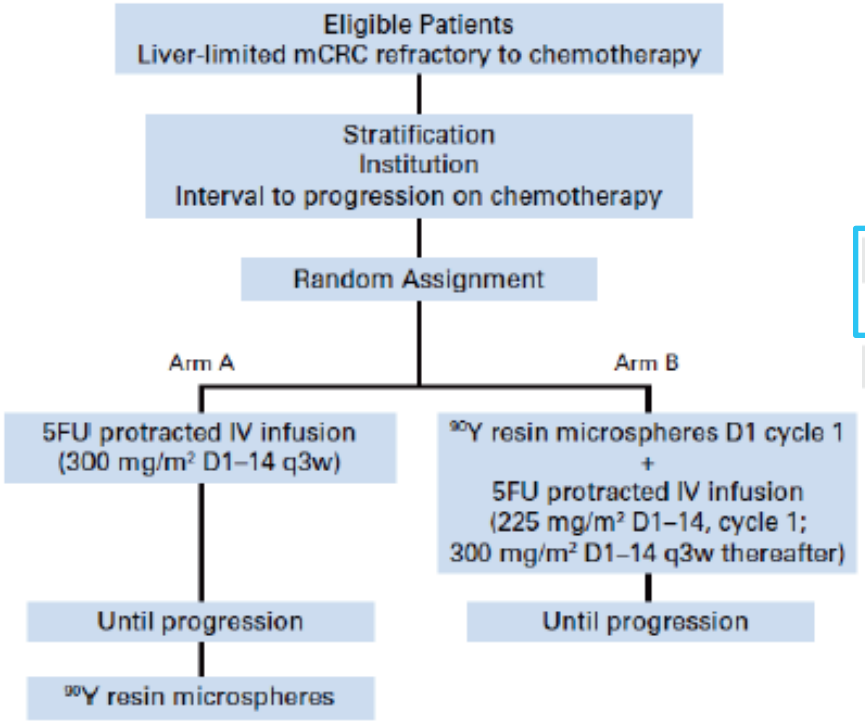


Table 2. Best Overall Hepatic Response

Response	FU Alone (n = 23) No.	%	Radioembolization + FU (n = 21) No.	%
Partial response	0	0	2	10
Stable disease	8	35	16	76
Progressive disease	14	61	2	10
Nonevaluable	1	4	1	5

NOTE. Comparison of response rates: 0 of 23 versus two of 21, $P = .22$ (95% CI for the difference between arms B and A ranging from −0.10 to 0.32). Comparison of stabilization rates: eight of 23 versus 18 of 21, $P = .001$ (95% CI for the difference ranging from 0.19 to 0.71).

Abbreviation: FU, fluorouracil.

MST: 10.0 months vs 7.3 mo. n.s.

SIR-Spheres microspheres in 1st-line Treatment of CRLM

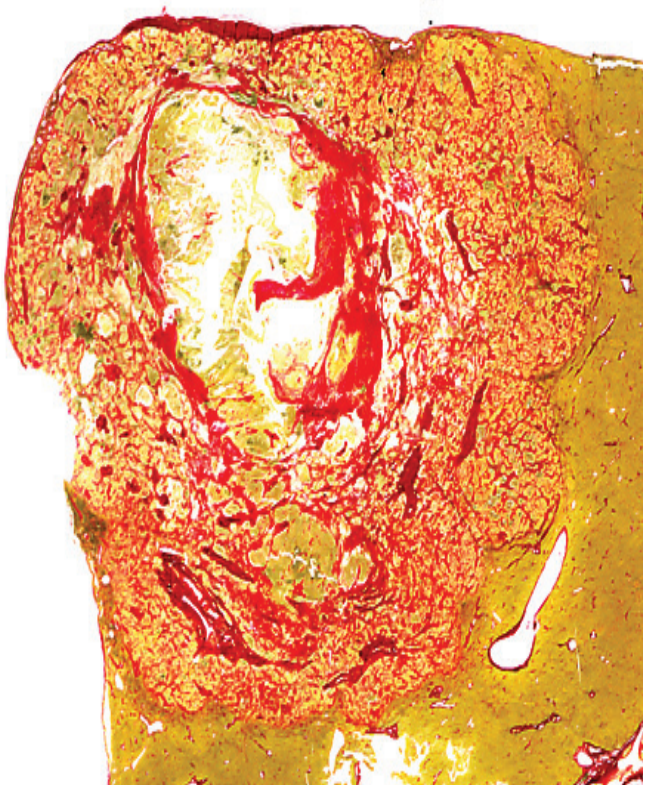
Investigator	n	Treatment	ORR	TTP/PFS	Survival
Gray	74	SIR-Spheres† + HAC	44%	15.9 mo	39% at 2 yr
		HAC (FUDR)	18%	9.7 mo	29% at 2 yr
van Hazel	21	SIR-Spheres† + 5FU/LV	91%	18.6 mo	29.4 mo
		5FU/LV	0%	3.6 mo	12.8 mo
			P<0.001	*P*<0.0005	HR 0.33; *P*=0.025

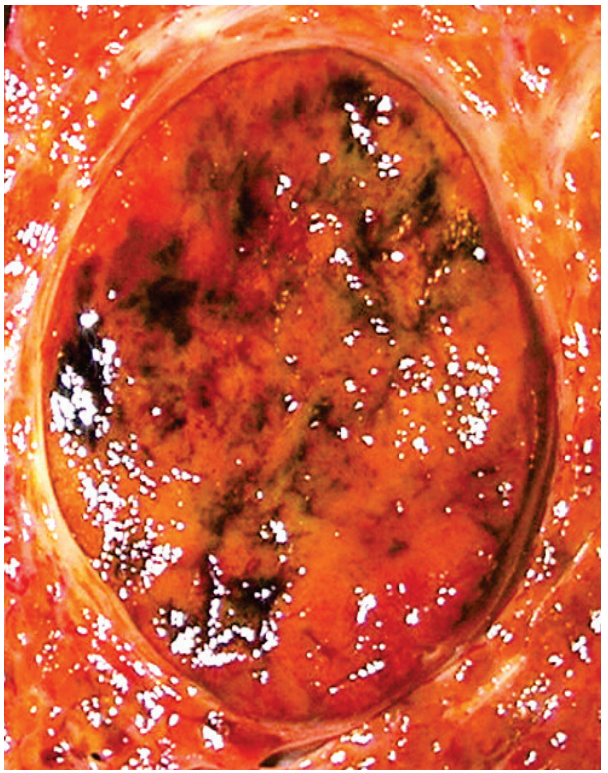
Gray *et al*. *Ann Oncol* 2001. van Hazel *et al. J Surg Oncol* 2004

Interventionelle Onkologie und CRLM

- ✓ **RFA:** Verbessertes Überleben mit geringer Toxizität, wiederholung möglich.
- ✓ **RFA: Kurative Intention in selektierten Patienten (<3 oder <3.5cm)**
- ✓ **RFA: kurativ in Kombination mit SR bei primär nicht resektablen Patienten (10-25%)**
- ✓ **SIRT nur bei Chemorefraktären CRM**
- ✓ **SIRT in Kombination mit syst. CTx?**
- ✓ **TACE ? Drug eluted beads? Combined?**

Baustelle Leber bei Tumorpatienten



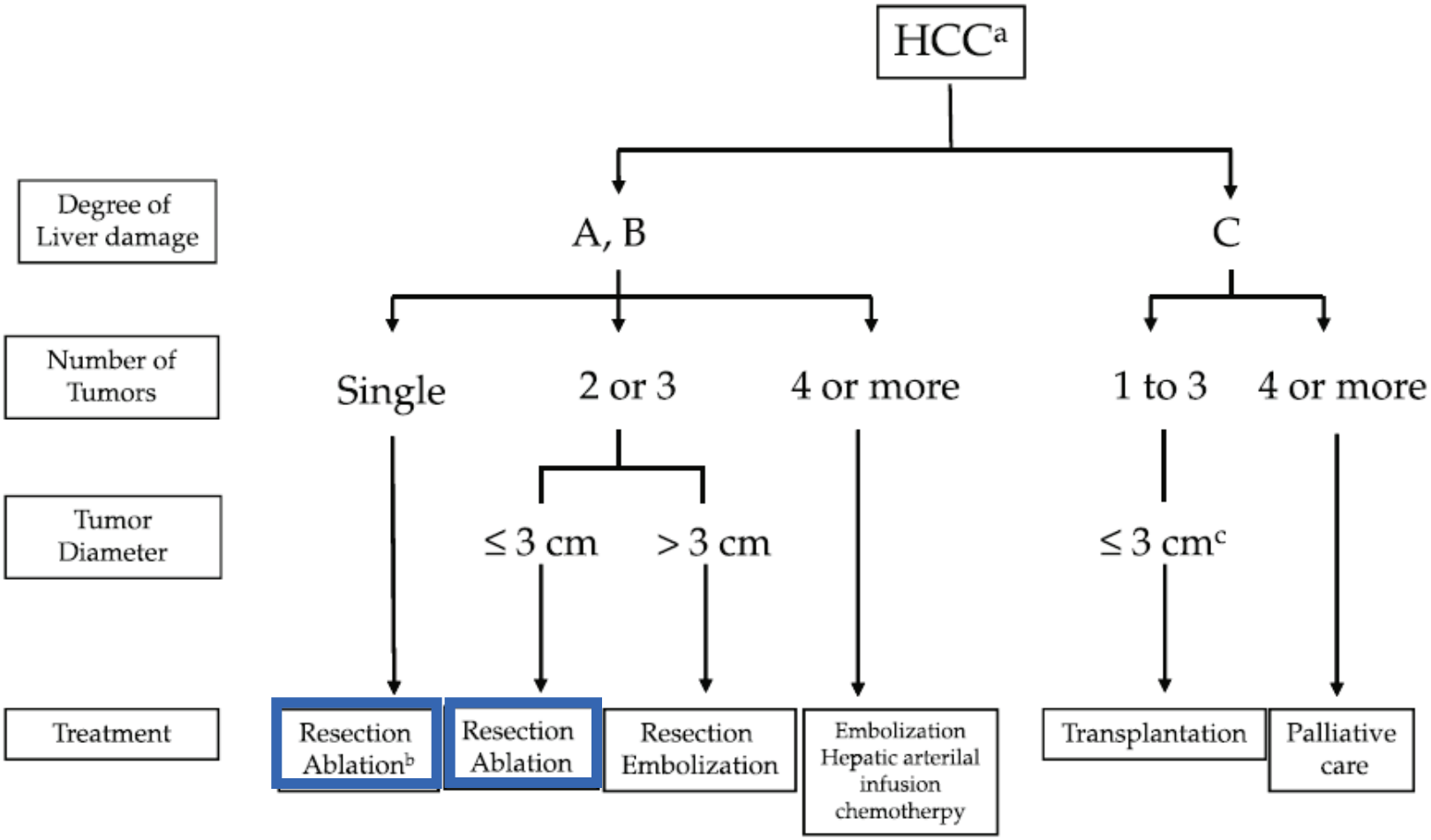


CRLM *versus* HCC?

„different underlying diseases and different tumor biology“

J-HCC and RFA

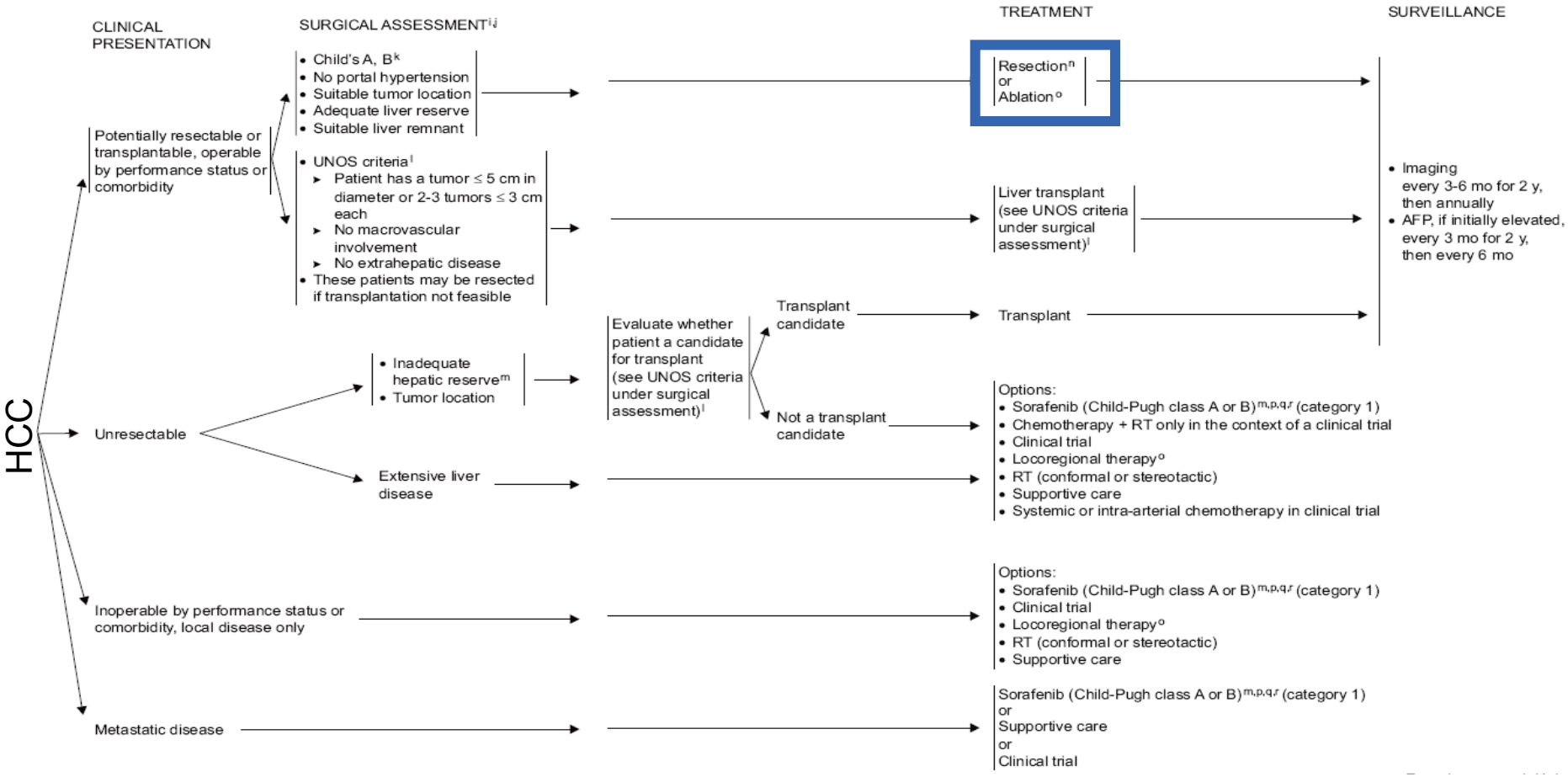
„HCC<3cm & CPT A/B“



Kokudo, N. and M. Makuuchi, Evidence-based clinical practice guidelines for hepatocellular carcinoma in Japan: the J-HCC guidelines. J Gastroenterol, 2009. 44 Suppl 19: 119-121

NCCN (AASLD) and RFA

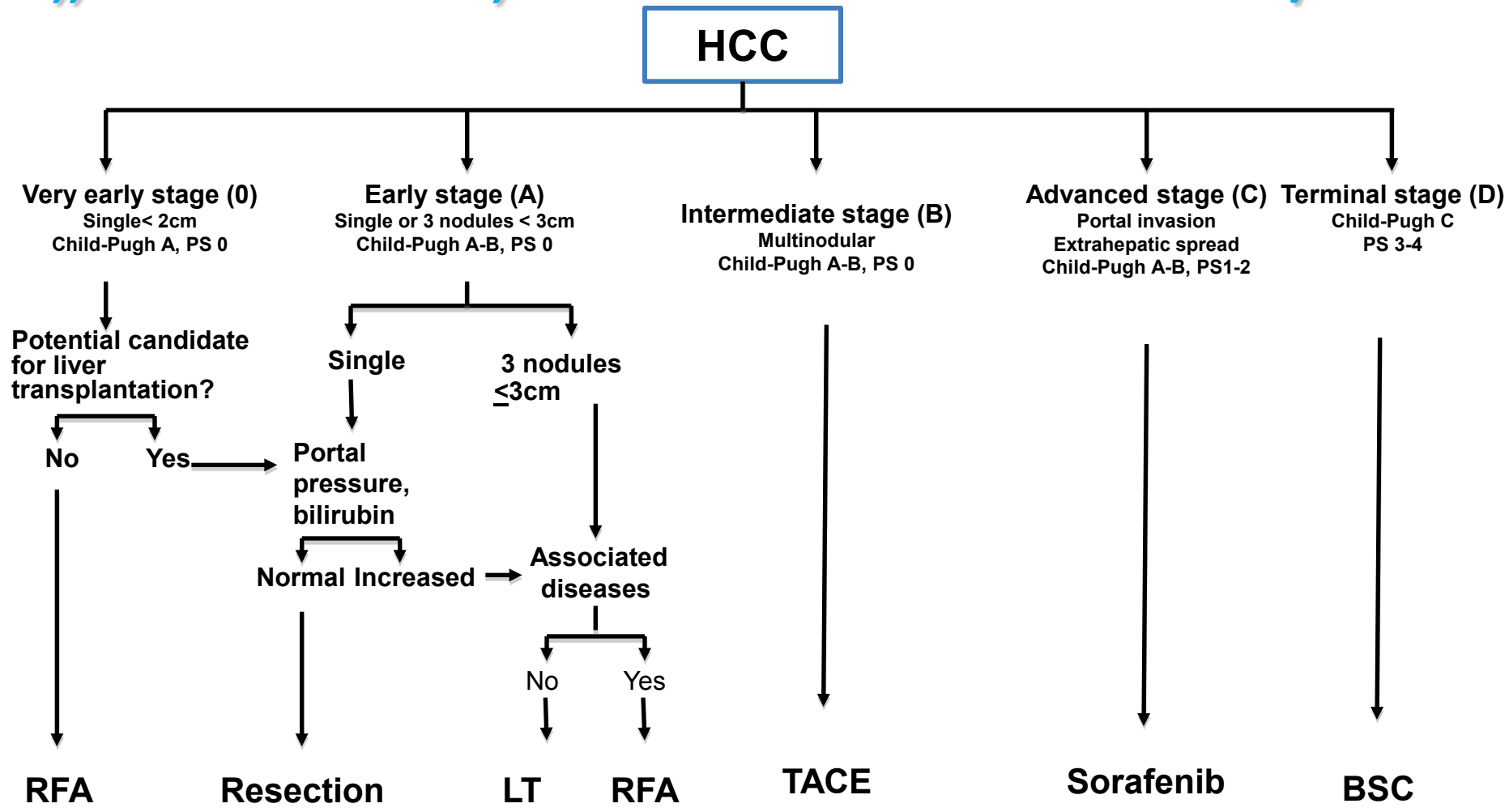
„potentially resectable & CPT A/B“



Benson Al B et al., NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network, 2009, Volume 7 (4): 350-391

BCLC and EASL 2012

„resectable, 3 x <3cm and CPT A/B“



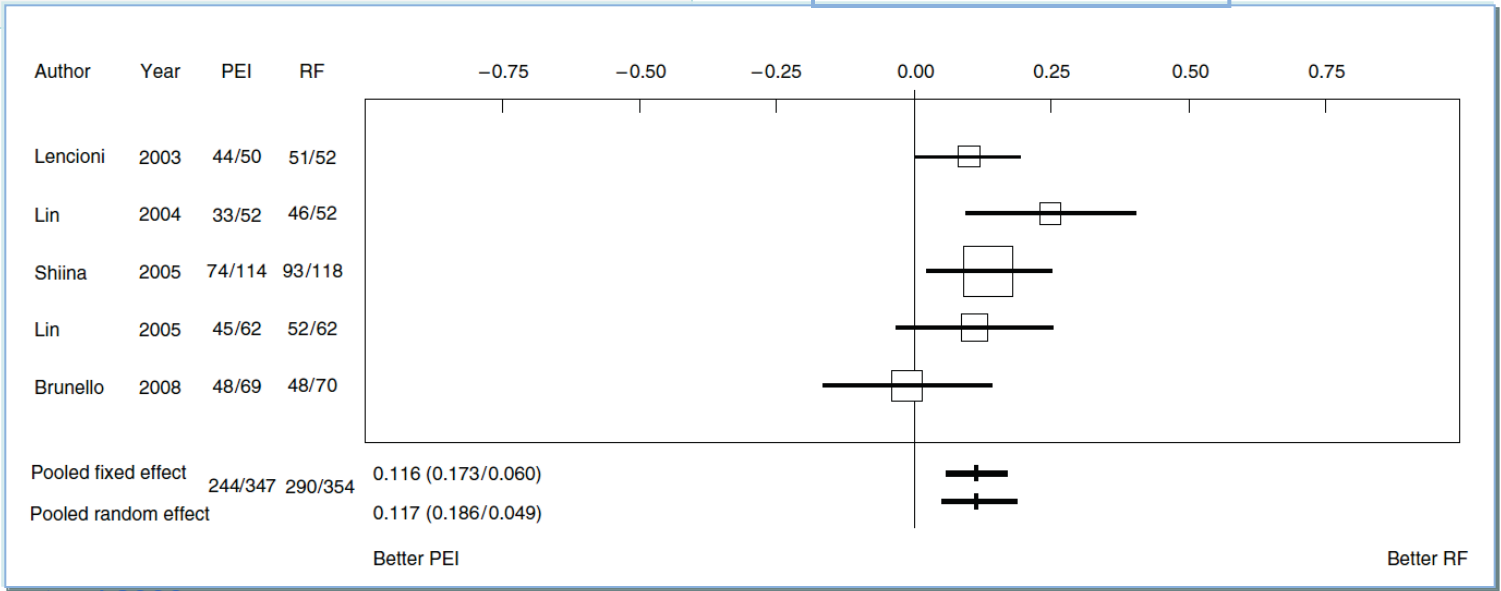
Courtesy of Jordi Bruix

Forner et al Lancet 2012

Radiofrequency Thermal Ablation vs. Percutaneous Ethanol Injection for Small Hepatocellular Carcinoma in Cirrhosis: Meta-Analysis of Randomized Controlled Trials

- Overall survival: RFA > PEI *p<.05*
- Local relapse rate: RFA > PEI *p<.05*
- 1-year DFS: RFA > PEI *p<.05*
- 2-year DFS: RFA > PEI *p<.05*
- 3-year DFS: RFA > PEI *p<.05*

Overall Survival



Orlando A et al, Am J Gastroenterol 2009

Level 1a Evidences: RFA > PEI/ PAI for early stage HCC in cirrhosis

Germani et al, J Hepatology 2010

Conclusion
RFA seems to be a superior ablative therapy than PEI for HCC, particularly for tumours >2 cm. PAI did not differ significantly from PEI for all the outcomes evaluated.

Orlando A et al, Am J Gastroenterol 2009

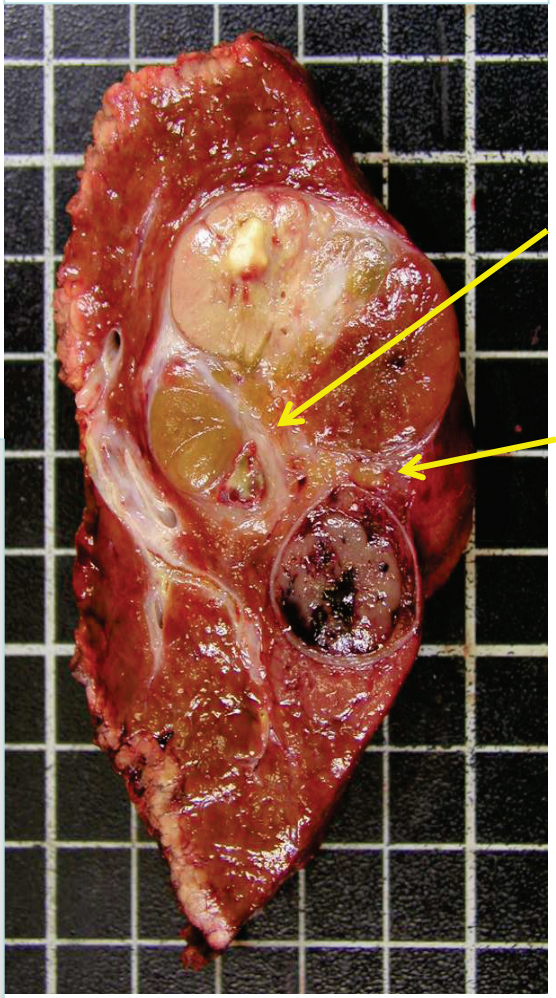
Conclusion
The available data is sufficient to conclude that RF significantly improves survival, cancer-free survival and, in addition, reduces the percentage of local recurrence compared to PEI.

Bouza C et al, BMC Gastroenterology 2009

Conclusion
Despite limitations, available evidence from adequate quality controlled studies support the superiority of RFA versus PEI in terms of better survival and local control of the disease for the treatment of patients with relatively preserved liver function and early-stage non-surgical HCC.

RFA > PEI or PAI for early stage HCC in cirrhosis: Why?

Photo: Dr D. Cherqui



1. The tumor size and the presence of **intratumoral septa** prevented diffusion of the ethanol/acetoacid within the HCC
2. RFA induces a safety ablation margin that causes **necrosis of satellites at periphery** and **microscopic vascular invasions**.

percutaneous RF-Ablation *versus* liver resection

HCC <5cm or 3 x HCCs < 3cm

*p<.005	RFA Total n=202 pats			Resection Total n=224 pats		
Local recurrence rate	18%	0%		10%	0%	
3-year overall survival	80%	87%	71%	77%	86%	73%
3-year "Disease free"		51%	64%		82%	69%
Hospital stay		5.2 d*			19.1d*	

Cho et al, 2005 ***n=151 patients****; Lu et al, 2006 with* ***n=105 patients****; Chen et al, 2006 with* ***n=180 patients***

percutaneous RF-Ablation *versus* liver resection

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RFA in HCC and pronostic factors:

Size and number of HCC

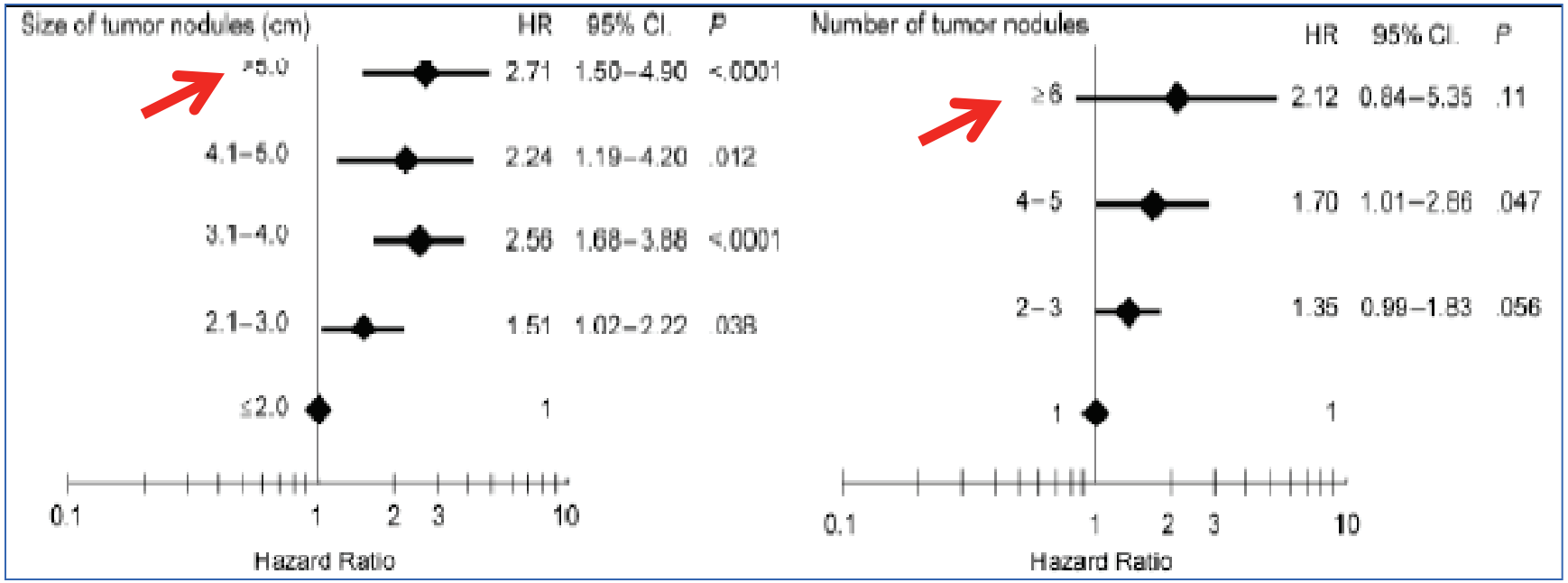
Tateishi R et al, J Gastroenterol 2009

- N= 663 patients with HCC
- Tumor size and number were stratified:
  - <2cm, 2.1-3cm, 3.1-4cm, 4.1-5cm, >5cm
  - 1, 2-3, 4-5, >5 HCCs
- Multivariate Cox proportional Regression Analysis with tumor size and number as covariate

RFA in HCC and pronostic factors:

Tumorsize and number

Tateishi R et al, J Gastroenterol 2009



„The prognosis of patient worsened gradually as the number or size of HCC nodule increases. **RFA can be applied beyong the conventional indications with increased risk of failure**“

Patients with 5y-OS > 40% presented with

- maximum 3 HCCs
- HCC size < 5cm

Table 3. Estimated 5-year survival based on the size and number of tumor nodules

	Number of tumor nodules			
Tumor size (cm)	1 (%)	2–3	4–5 (%)	>5 (%)
≤2.0	75	68	61	54
2.1–3.0	65	55	47	39
3.1–4.0	48	37	28	21
4.1–5.0	52	42	33	25
>5.0	46	35	26	19

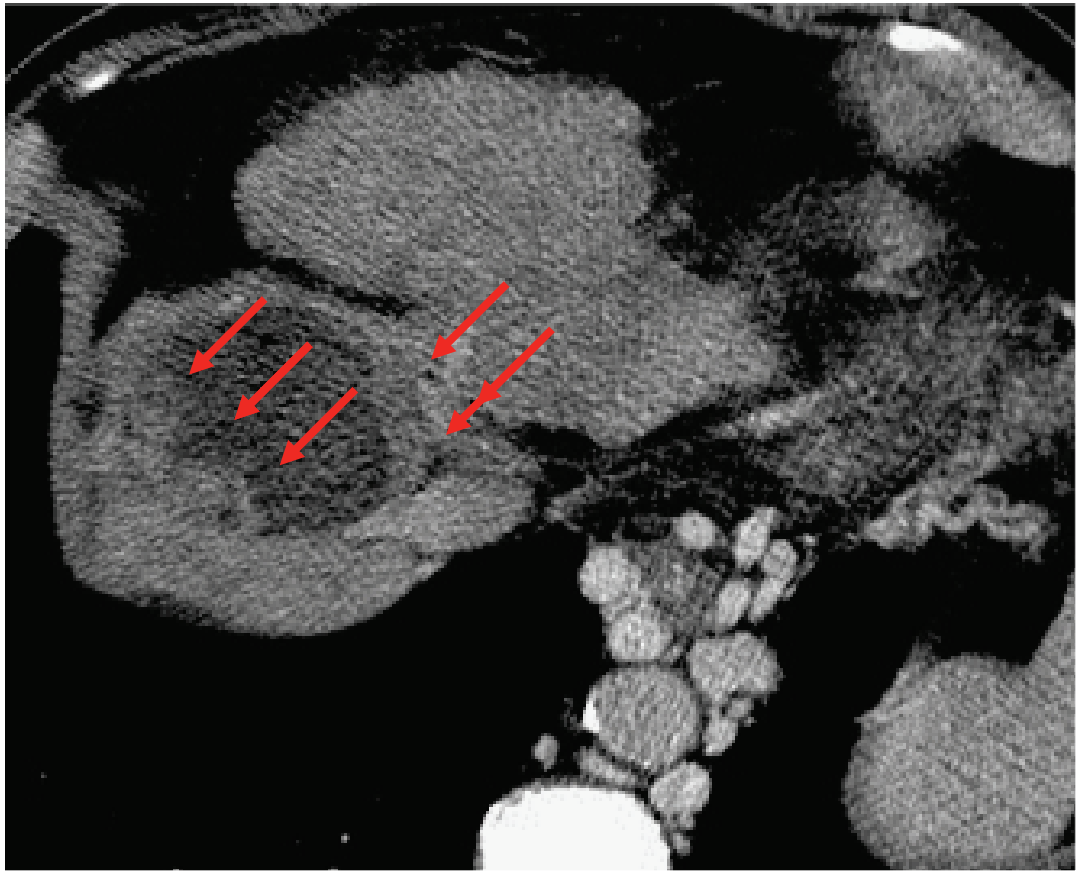
Clinical trial: Ablative therapy alone for **3cm>HCC>7cm**

Yin XY et al, Cancer 2009

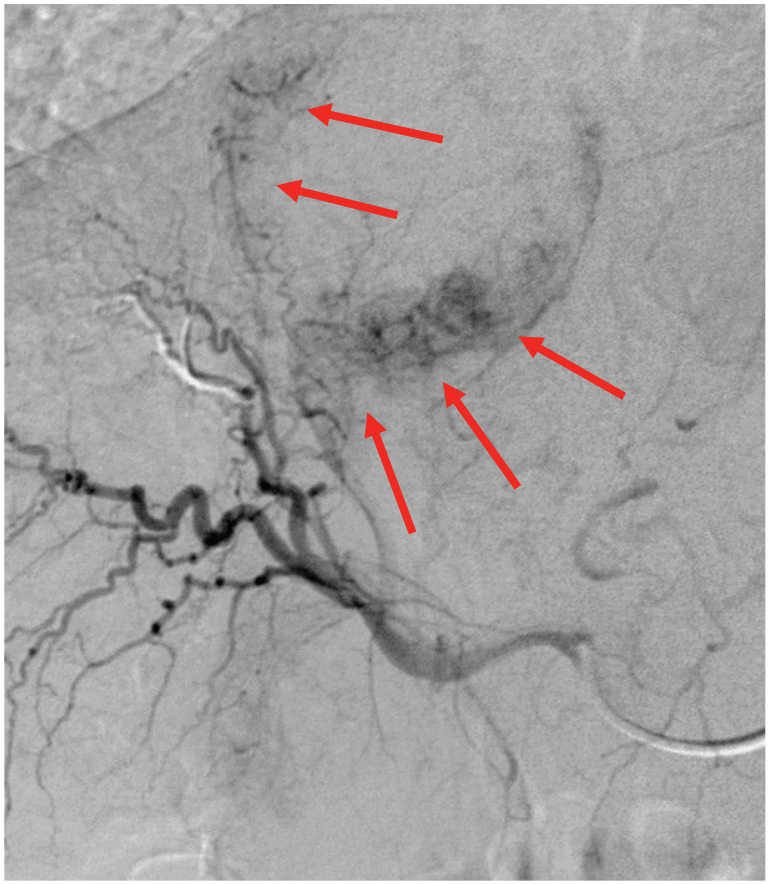
- Major complications: 9.2%
- Complete Ablation: 92,6%
- **Local tumor relapse (LTP): 22%**
- Median time for LTP: 4,6 Months
- Overall survival:
  - 1-year OSR: 75,8%
  - 3-year OSR: 30,9%
  - **5-year OSR: 15,4%**

Monopolar RFA in HCC > 3cm

CT prior to RFA

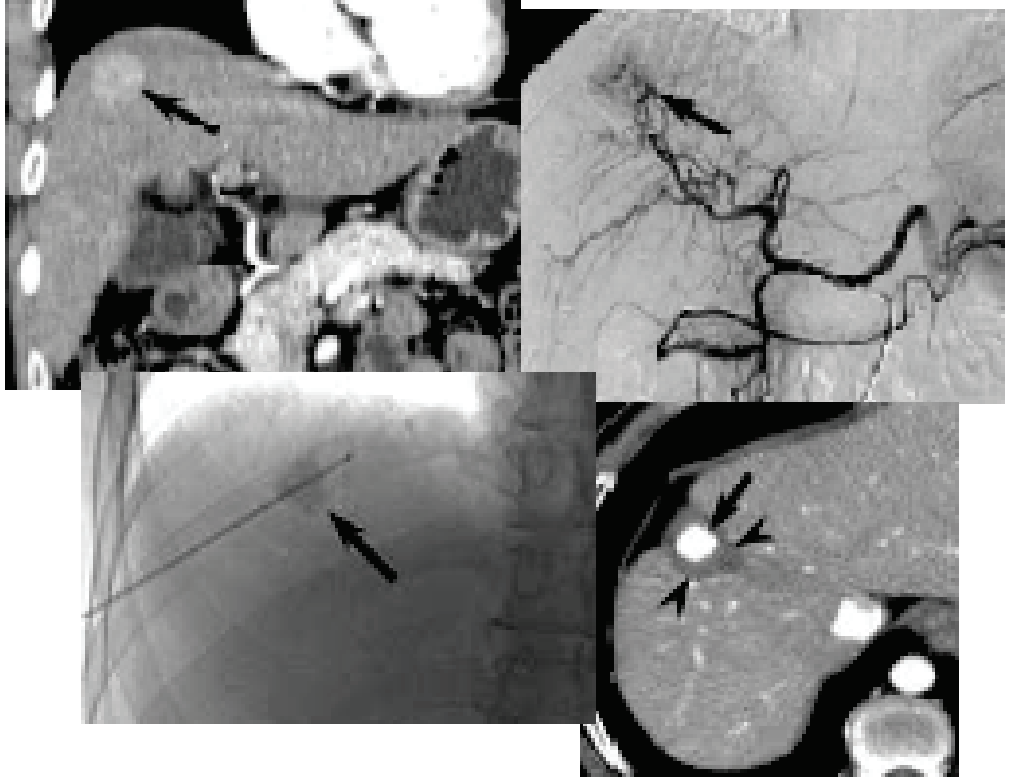


Angio after RFA



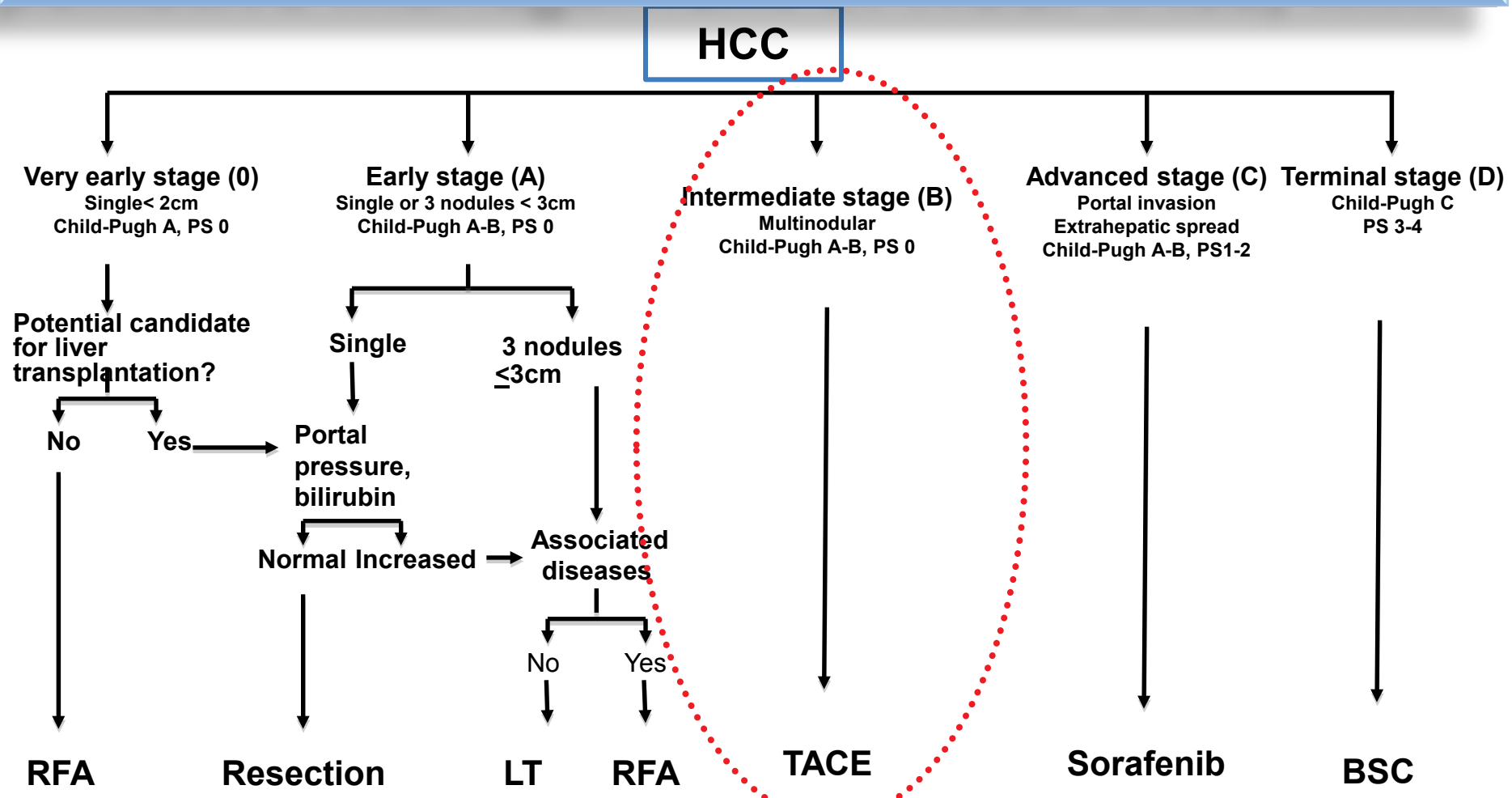
Courtesy of R. Lencioni

1. Buscarini L, Ultraschall Med, 1999
2. Rossi S, Radiology 2000
3. Yamasaki T, Cancer 2001
4. Yamakado K et al,JVIR 2002
5. Gasparini D, Radiol Med 2002
6. Kitamoto M, AJR 2003
7. Akamatsu M, Liver Int 2004
8. Luo BM, World J Gastroenterol 2005
9. Maluccio M, JVIR 2005
10. Shen SQ, Hepatogastroenterology 2005
11. Yamasaki T, J Gastroenterol 2005
12. Liu YM, World J Gastroenterol 2006
13. Veltri A, Eur Radiol 2006
14. Kurokohchi K, Oncol Rep 2006
15. Lim HS, AJR 2006
16. Takaki H, JVIR 2007
17. Kobayahi M, Liver Int 2007
18. Helmberger T, Digestion 2007
19. Wang JB, Qual Life Res 2007 *
20. Liao GS, Eur J Surg Oncol 2008
21. Fuke H, Aliment Pharmacol Ther 2008
22. Yamakado K, Radiology 2008
23. Takaki H, J Vasc Interv Radiol 2008
24. Kang, JVIR 2009
25. Shibata T, Radiology 2009
26. Peng ZW, Eur J Surg Oncol 2010 *
27. Morimoto M Cancer, 2010
28. Zhao M, Zhonghua 2010*
29. Guang C, Jpn J Radiol 2011*
30. Clasen S, Pereira PL, J V I R 2011
31. Yan S, Xu D, Dig Dis 2012….



(*Randomized) Clinical trials have shown the benefit of combining **TACE-RFA > RFA** alone for the treatment of **HCC>3cm.**

Evolving treatment paradigm in the palliative management of HCC: TACE, MKI

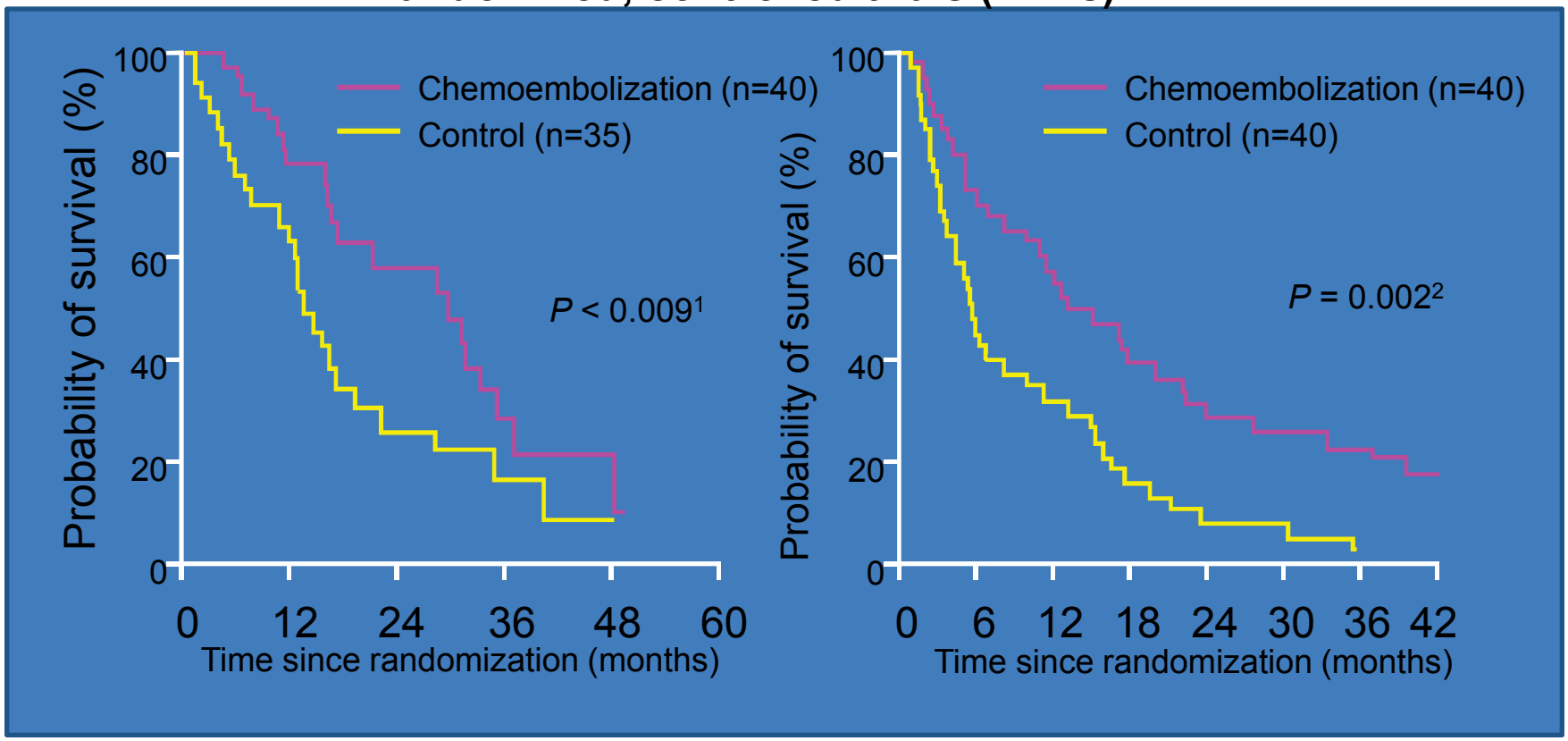


Courtesy of Jordi Bruix

Forner et al Lancet 2012

Conventional TACE (cTACE) improved survival in intermediate-stage HCC> 24 months

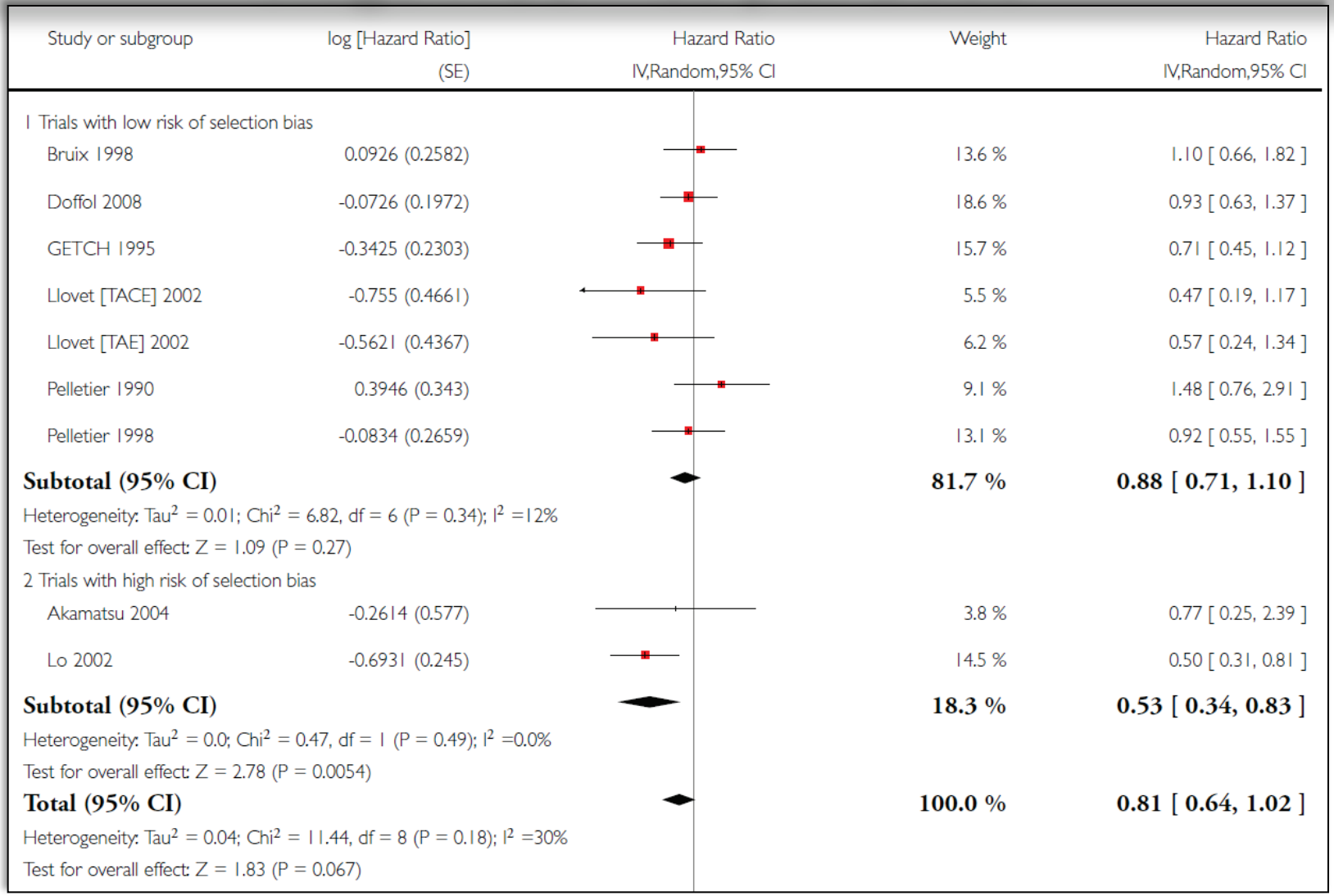
Randomized, controlled trials (RCTs)[1,2]



- 3-year OS: 26[2]–29%[1]
- Sustained overall response rate (ORR; 3–6 months): 35[1]–39%[2]

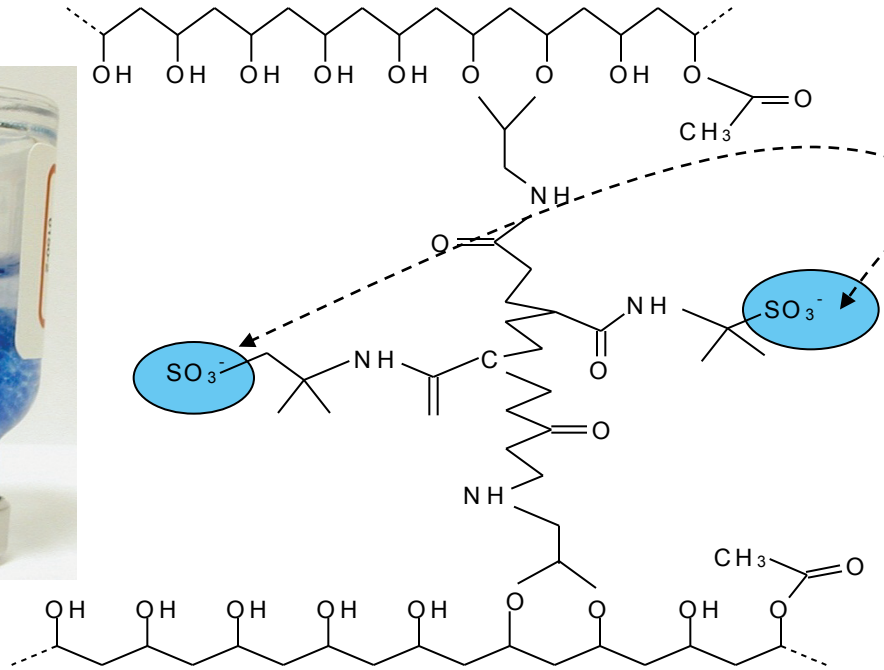
1. Llovet et al. Lancet 2002;359:1734. 2. Lo et al. Hepatology 2002;35:1164.

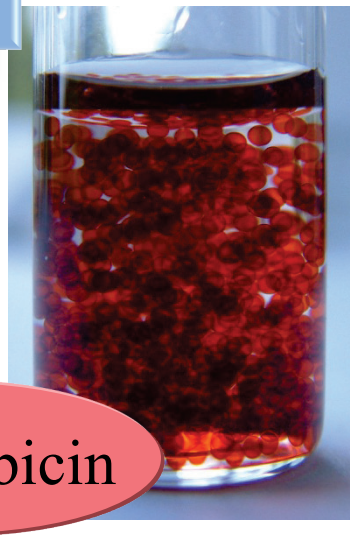
TACE is standard of care for intermediate-stage HCC[1,2] as per BCLC



[1]Bruix J, Sherman M. Hepatology. 2011;53:1020-2; [2]Llovet JM, Bruix J. *Hepatology* 2003;37:429-442.;Oliveri RS et al. Cochrane Metaanalysis 2011

Drug Eluted Beads offen new standards for intraarterial therapies in HCC



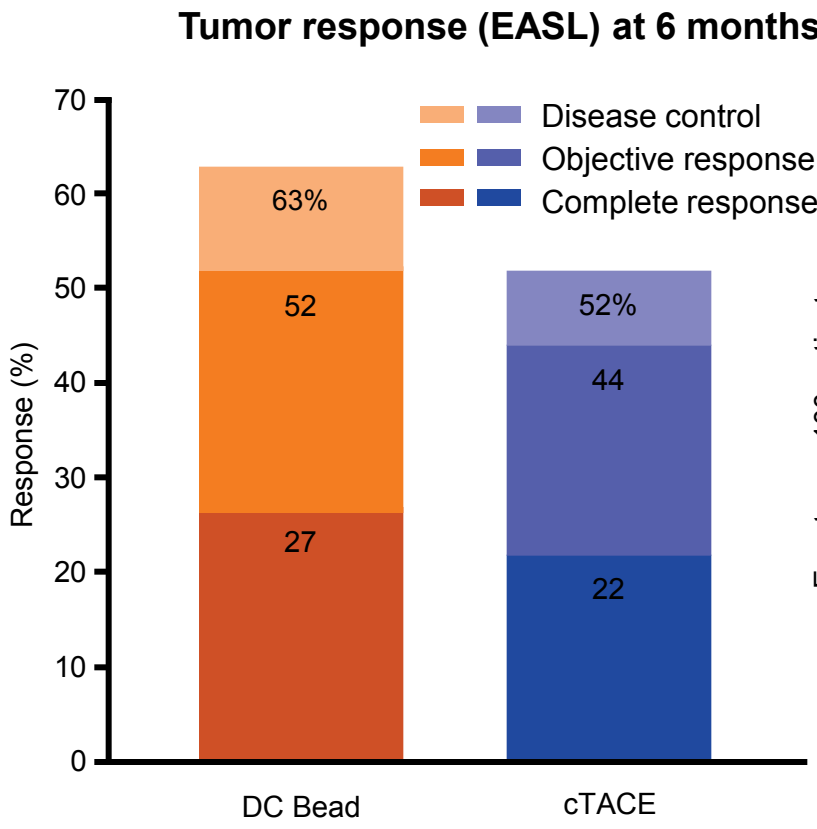


Embolic microspheres that **may be loaded with cytotoxic or cytostatic anticancer drugs** (e.g. IRI) that may be released into the cancer

more targeted therapies in HCC

PRECISION V

'Compared with cTACE, DEB has a standardized methodology, is more reproducible, and offers improved response and a significantly better safety profile'[1]

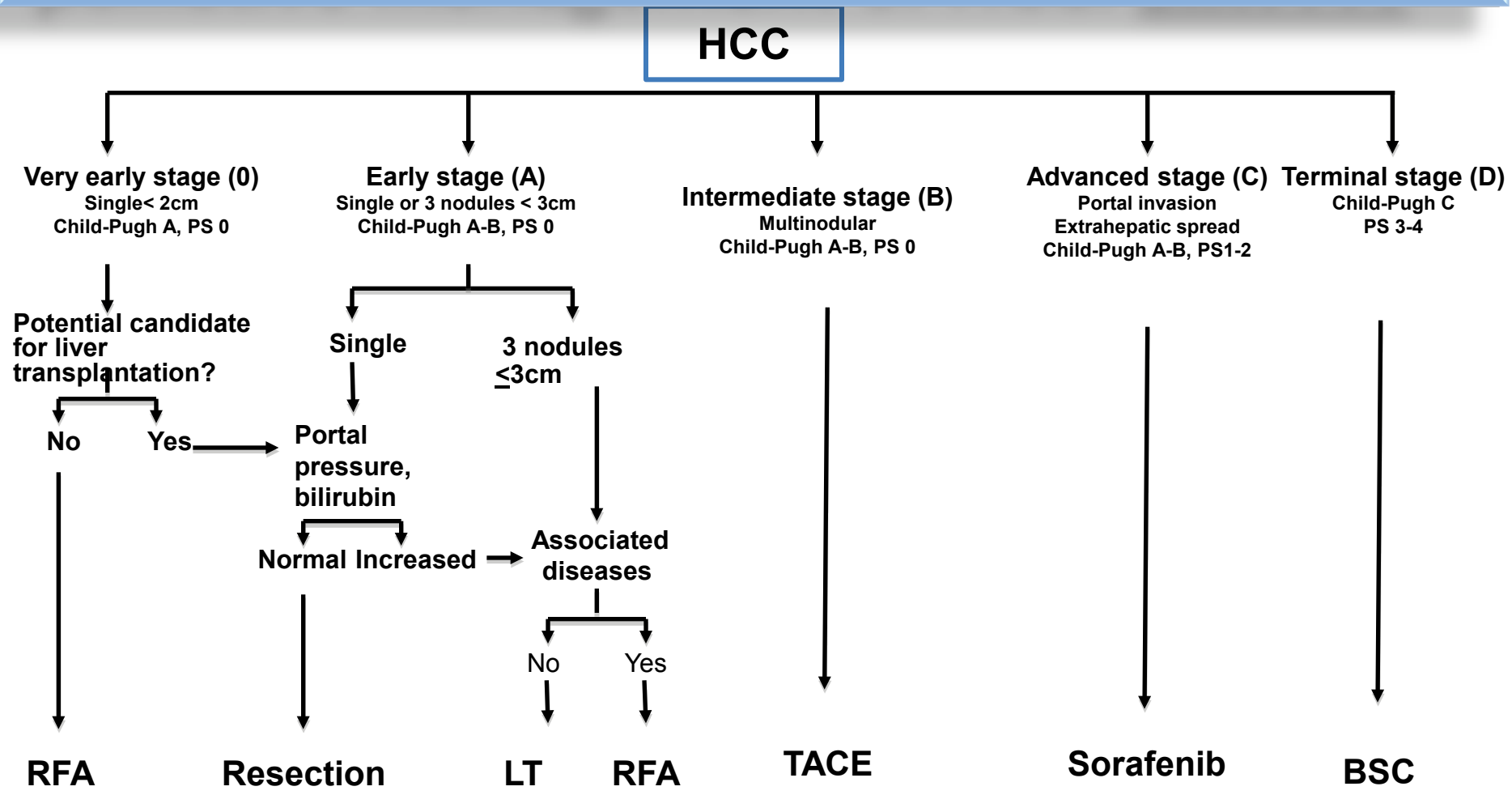


	ORR
Malagari (Abd Im 2007)	71 %
Malagari (CVIR 2009)	73 %
Varela (J Hepatol 2007)	75 %
Nicolini (JVIR 2011)	77 %

Events per 100 patients

1. Raoul et al. Cancer Treat Rev 2011;37:212.
Lammer et al. Cardiovasc Intervent Radiol 2010;44:41.

Evolving treatment paradigm in the palliative management of HCC: **SIRT???**



Courtesy of Jordi Bruix

Forner et al Lancet 2012

Yttrium-90 Microspheres (TheraSphere®) Treatment of Unresectable Hepatocellular Carcinoma: Downstaging to Resection, RFA and Bridge to Transplantation

LAURA M. KULIK,[1] BASSEL ATASSI,[2] LODEWIJK VAN HOLSBEECK,[2] TAMEEM SOUMAN,[2] ROBERT J. LEWANDOWSKI,[2] MARY M. MULCAHY,[3] RUSSELL D. HUNTER,[4] ALBERT A. NEMCEK JR.,[2] MICHAEL M. ABECASSIS,[5] KENNETH G. HAINES III,[6] AND RIAD SALEM, MD, MBA[2]*

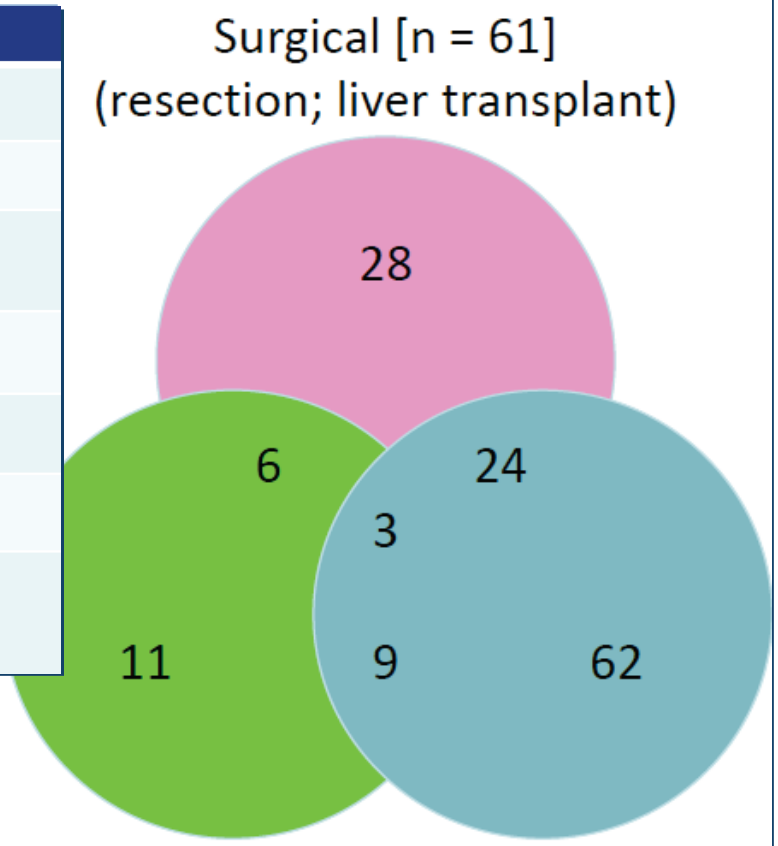
- N=155 Pats with HCC, 35 Pats. with T3 stade (results with 34 pats)

		Survival 1 y	Survival 2 y	Survival 3 y
Downstaging to T2	56% (19)			
….to resection	3% (1)			
….to ablation	32% (11)			
Bridge to LTx	8			
Rad-Path correlation	2 out of 7 explants			
Survival		84%	54%	27%
Median survival	800 d			

J Surg Oncol 2006

Radioembolisation and HCC
The ENRY Study in 325 pats

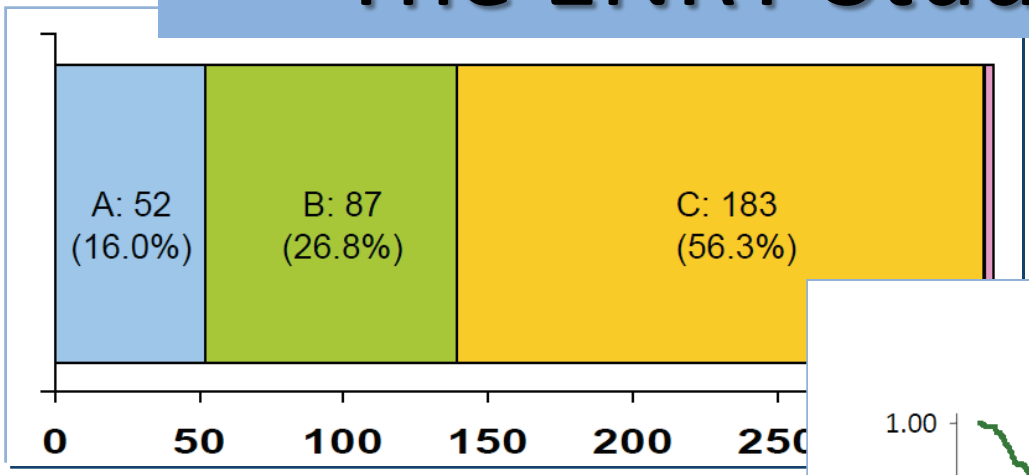
Variable		%
Tumour nodules > 5		38.6 %
Bilobar disease		53.1 %
Extra-hepatic Metastases		9.2 %
Portal Vein Occlusion		23.3 %
Alpha-fetoprotein > 400 ng/mL		34.9 %
ECOG Performance Status > 0 [a]		45.6 %
Child-Pugh class	A B	82.5 % 17.5 %



- **Any procedure: 143 (44.0%)**
- 2-3 procedures: 42 (12.9%)

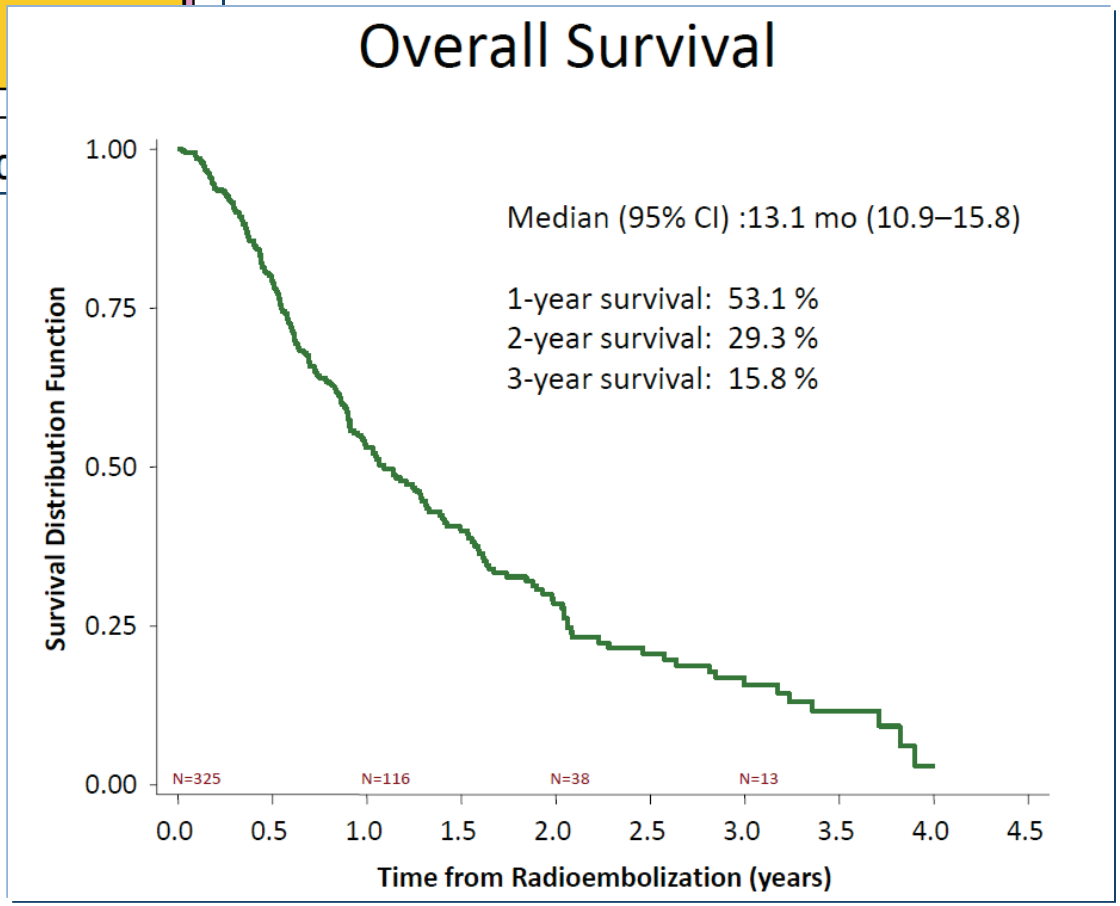
Sangro B et al, Hepatology 2011

Radioembolisation and HCC
The ENRY Study in 325 pats



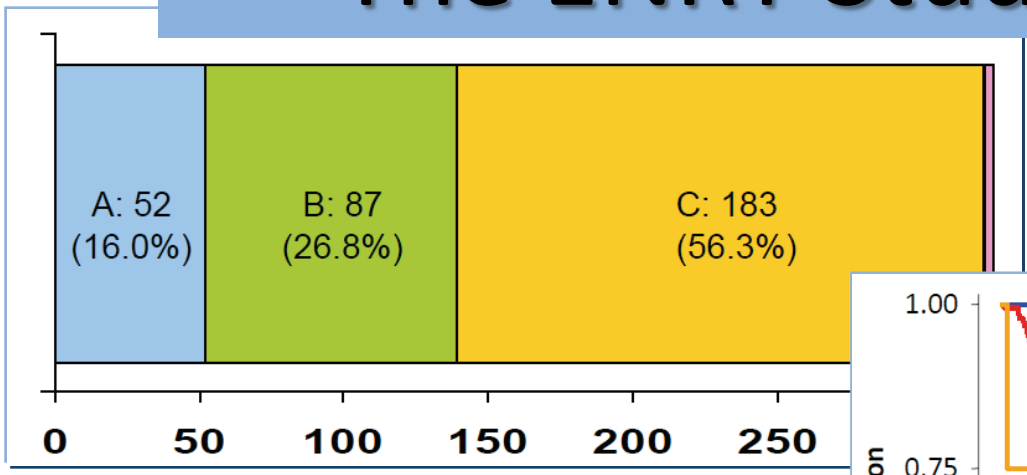
Multivariate analysis

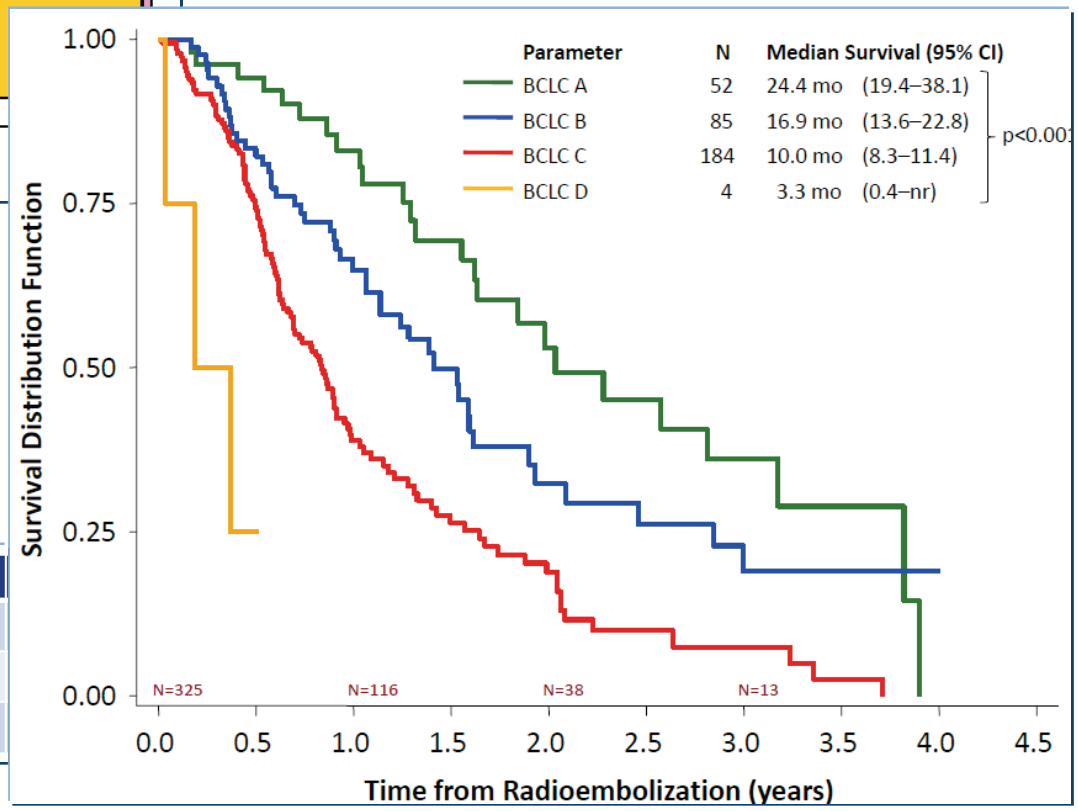
Variable	Hazard Ratio	95% CI
Number of Nodules	1.76	1.32 – 2.35
ECOG	1.39	1.14 – 1.70
Extra-Hepatic Disease	1.91	1.17 – 3.13
INR >1.2	1.47	1.04 – 2.09



Sangro B et al, Hepatology 2011

Radioembolisation and HCC
The ENRY Study in 325 pats



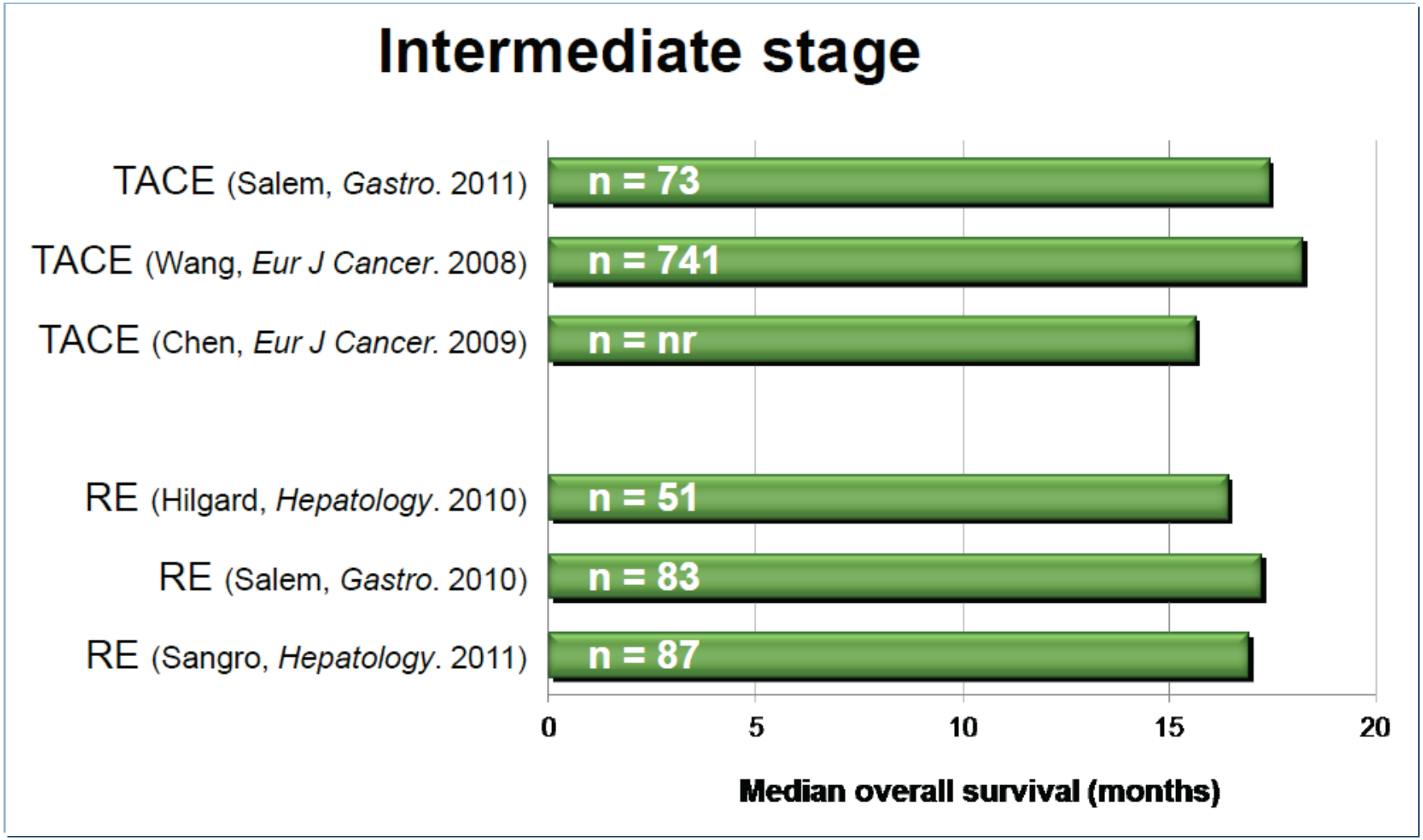


Multivariate analysis

Variable	Hazard Ratio	95% CI
BCLC stage	1.74	1.41 – 2.16
Bilobar disease	1.36	1.02 – 1.82
INR > 1.2	1.46	1.05 – 2.01

Sangro B et al, Hepatology 2011

Radioembolisation or TACE in HCC?



Sangro B et al, J Hepatology 2012

Interventionelle Onkologie und HCC

- ✓ **PEI/PAI nicht mehr indiziert**
- ✓ **RFA: Kurative Intention in selektierten Patienten (HCC < 3cm)**
- ✓ **RFA + TACE (welche?) bei 3cm<HCC<5cm**
- ✓ **TACE bei HCC nicht BCLC C und weder abladierbar oder resezierbar oder LTx**
- **SIRT: Evidenzen bei HCC basieren auf retrospektive Studien oder nicht-kontrollierte prospektive Studien**

Danke für Ihre Aufmersamkeit !!

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