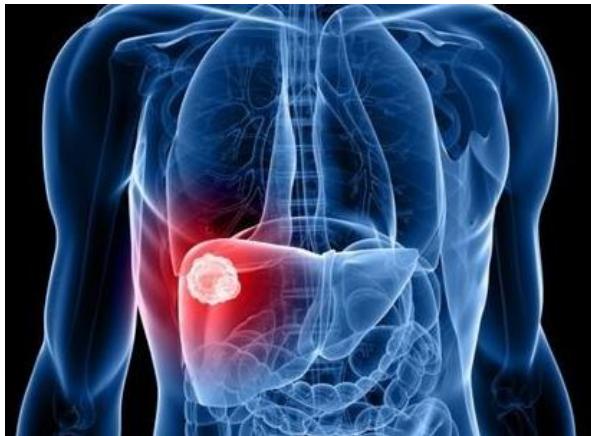


# Trattamento degli epatocarcinomi e delle metastasi epatiche: chirurgia vs. trattamenti loco-regionali

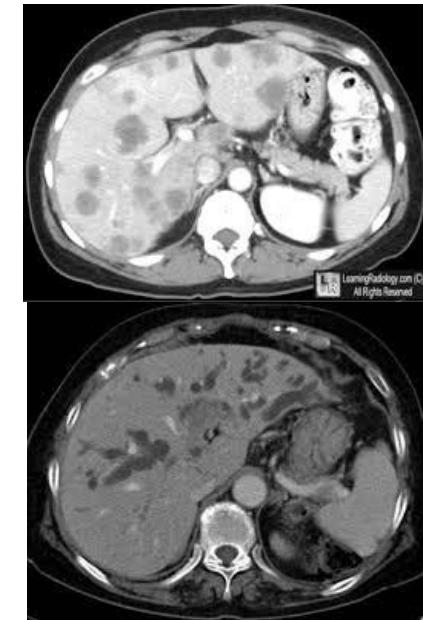
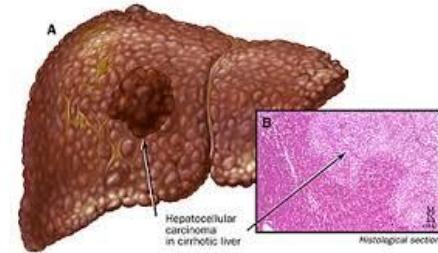


A Cristaudi  
**Capoclinica Servizio Chirurgia**  
Ospedale Regionale di Lugano



# Epidemiologia

- Epatocarcinoma (HCC) **50%**
- Metastasi (colorettali. - CRLM) **30%**
- Colangiocarcinoma **10%**
- Carcinoma colecisti **2%**
- Altre lesioni **8%**



# Approccio multidisciplinare

Tipo di tumore

Numero di noduli

Localizzazione dei noduli

Status paziente

Funzione epatica

Epatopatia vs chemio

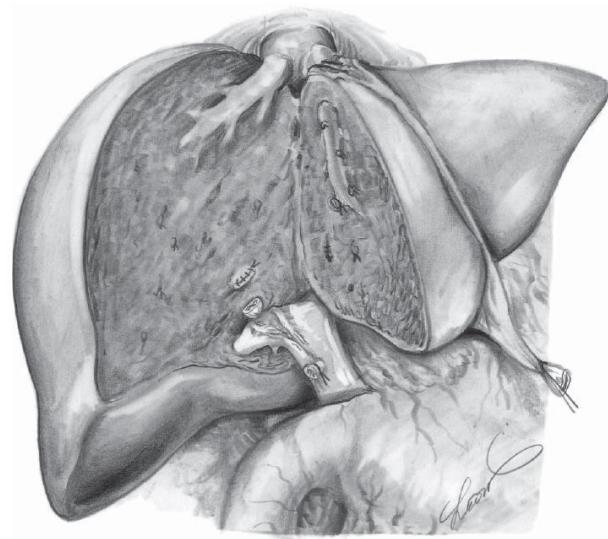
Trattamento

Fegato residuo?



# Funzione epatica

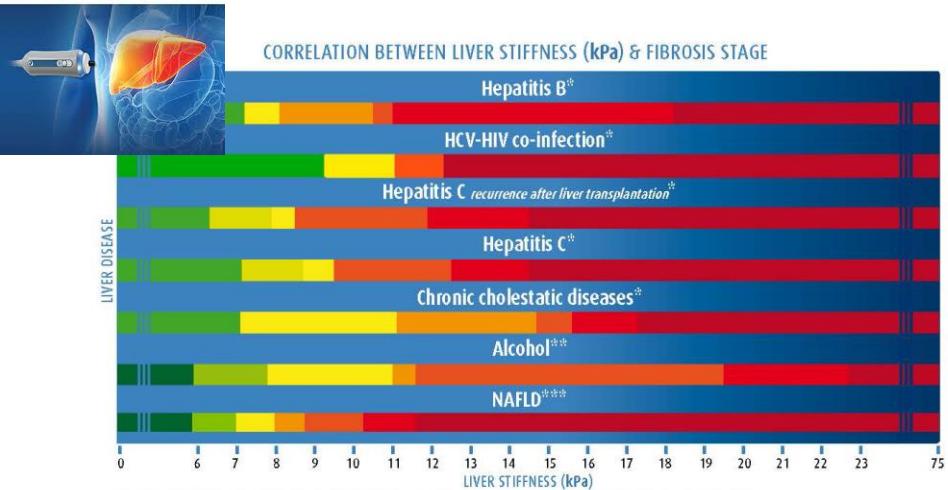
- Child-Pugh (bili, TP/INR, albumina, ascite, encefalopatia )
- MELD (bili, TP/INR, crea, Na)
- Volumetria
- Gradiente pressorio (portale/sistemico)
- Fibroscan
- ICG test



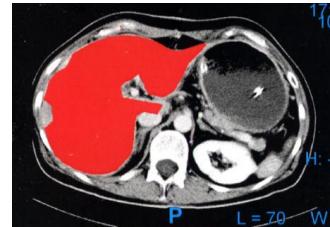
# Funzione epatica

>20-30 % fegato sano  
 >40% fegato cirrotico/post chemio

FibroScan®



Total liver : 1350 cm<sup>3</sup>

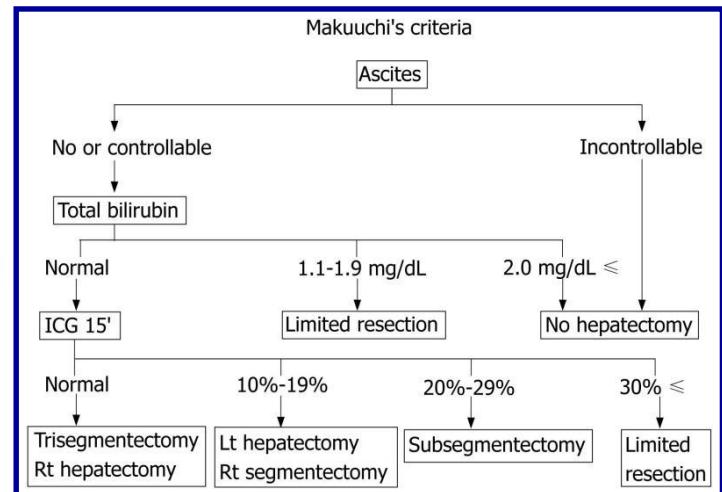


Right liver : 1000 cm<sup>3</sup>



Volume of right/left volume – tumoral volume

Total hepatic volume – tumoral volume

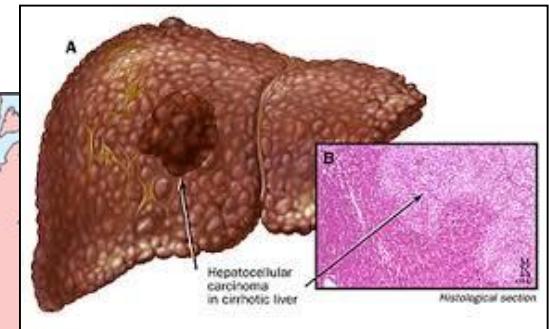
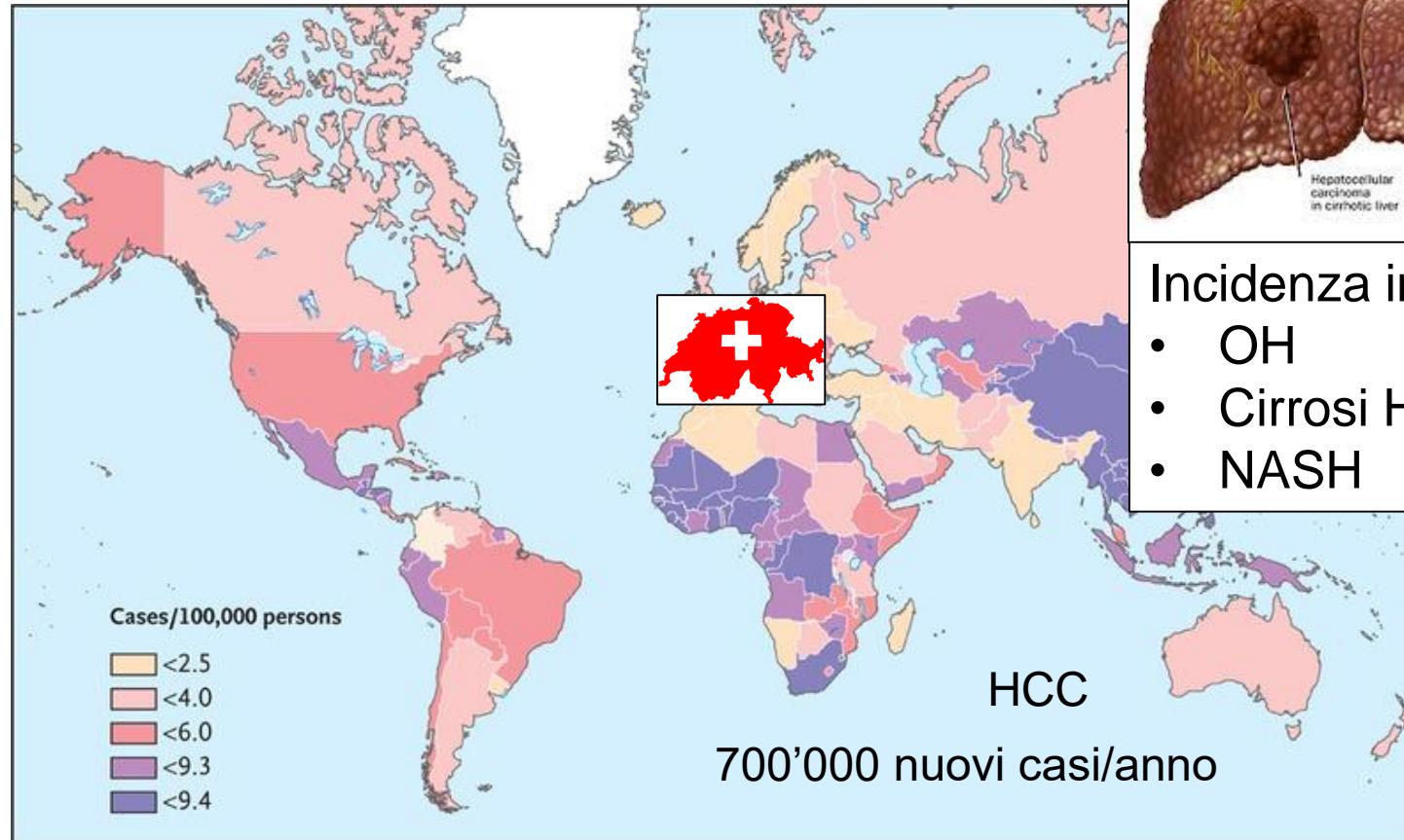


# Chirurgia vs trattamenti locali

- Terapie complementari / consecutive
- Trattamenti radiologici bridge alla chirurgia
- Trattamenti combinati con radiologia intra-operatoria



# Epatocarcinoma

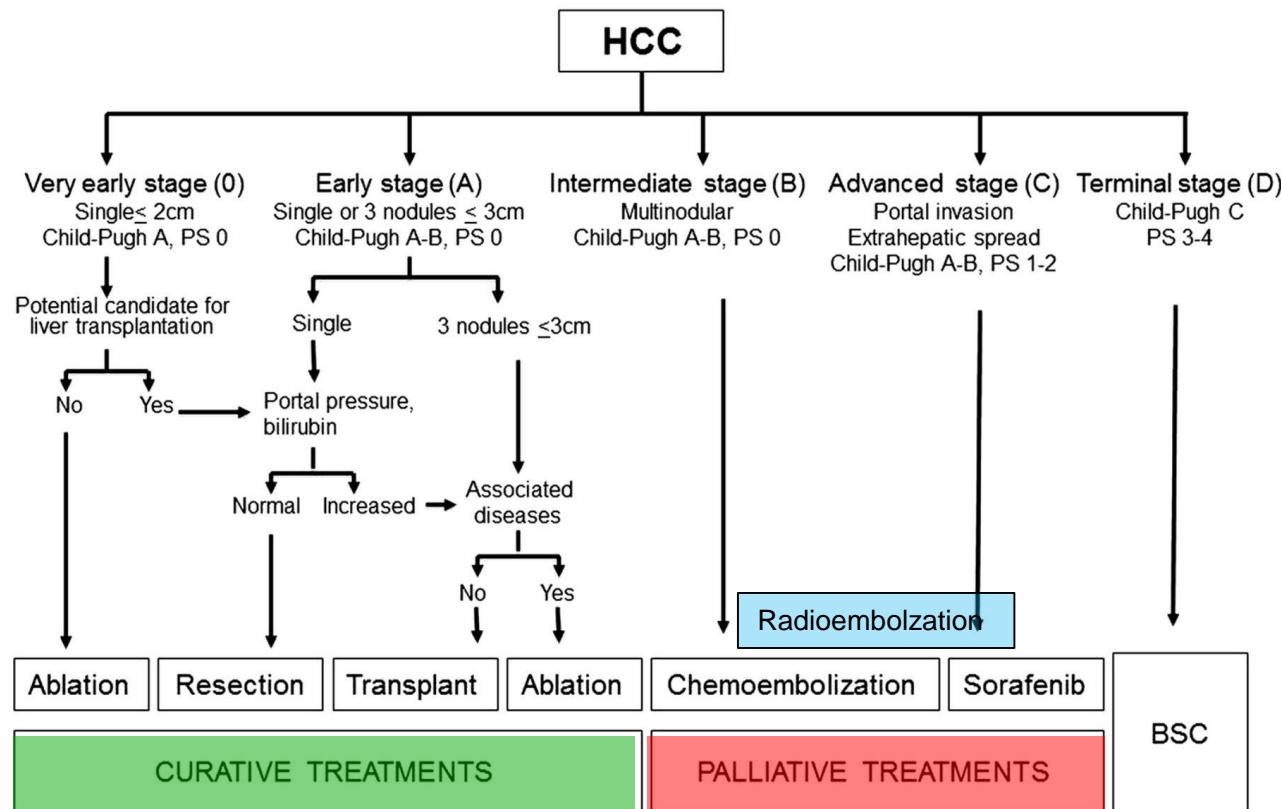


Incidenza in aumento

- OH
- Cirrosi HCV
- NASH

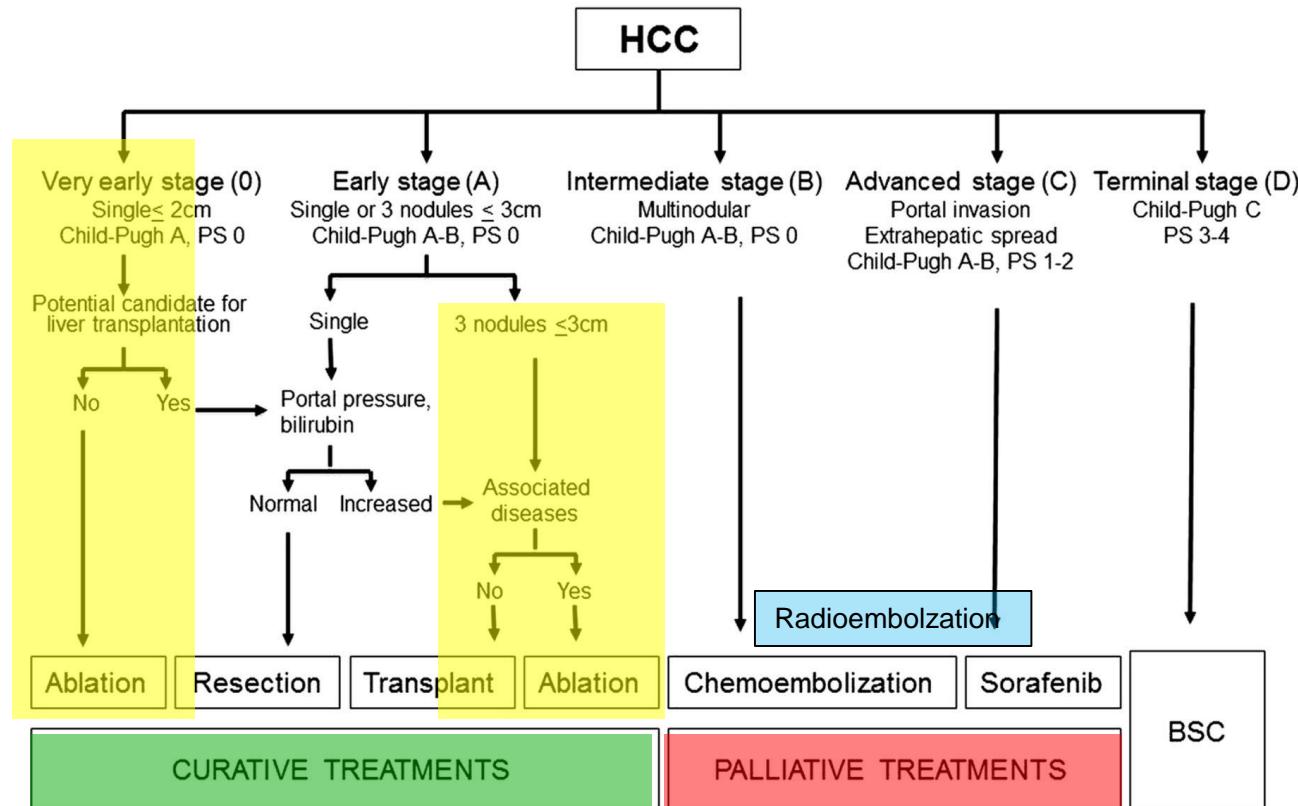
# Epatocarcinoma

## BCLC Barcelona Clinic Liver Cancer

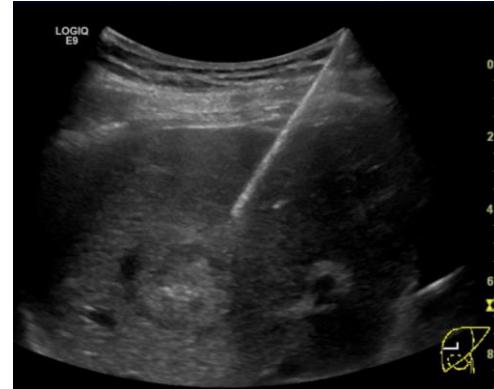
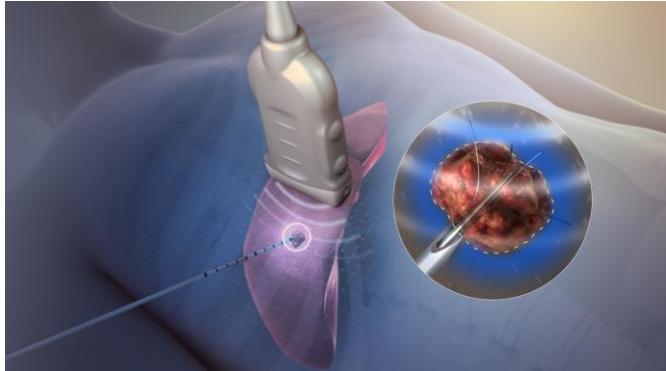


# HCC – Termoablazioni

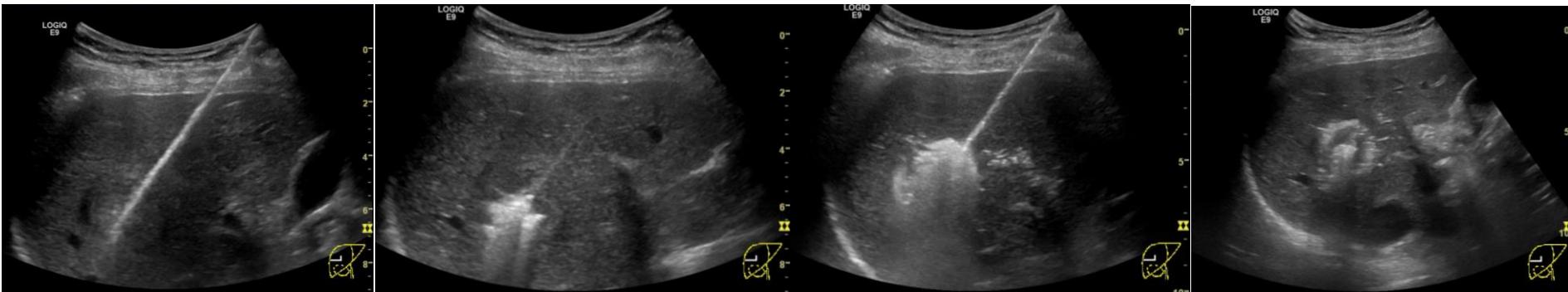
## BCLC Barcelona Clinic Liver Cancer



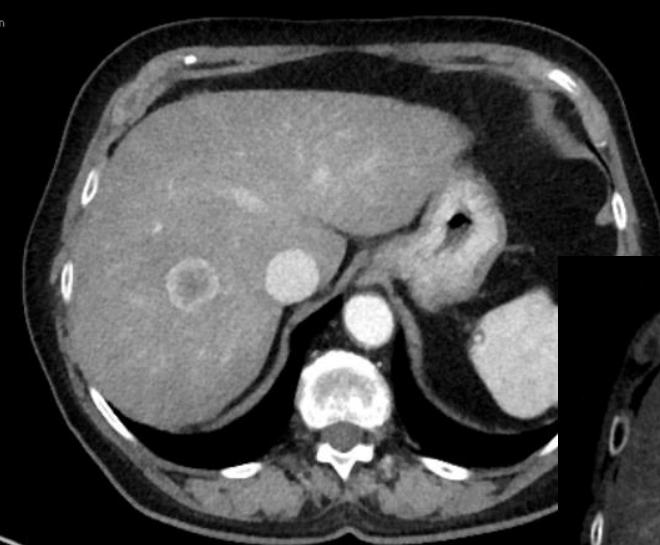
# Termoablazioni



- Radiofrequenza
- Microonde



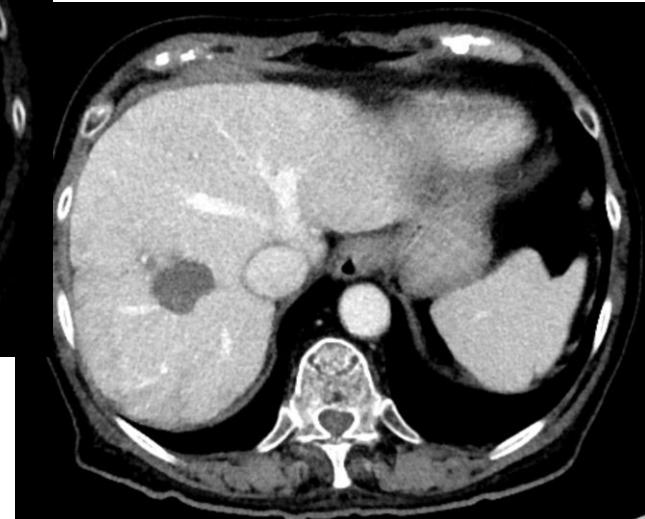
**Situazione ideale:** noduli piccoli (<3cm) e centrali



19.01.2016



08.08.2016



11.08.17

# RF vs chirurgia

European Radiology  
https://doi.org/10.1007/s00330-018-5902-4

INTERVENTIONAL



Radiofrequency ablation versus surgical resection of hepatocellular carcinoma: contemporary treatment trends and outcomes from the United States National Cancer Database

Johannes Uhlig<sup>1,2</sup> · Cortlandt M. Sellers<sup>1</sup> · Stacey M. Stein<sup>3,4</sup> · Hyun S. Kim<sup>1,3,4</sup>

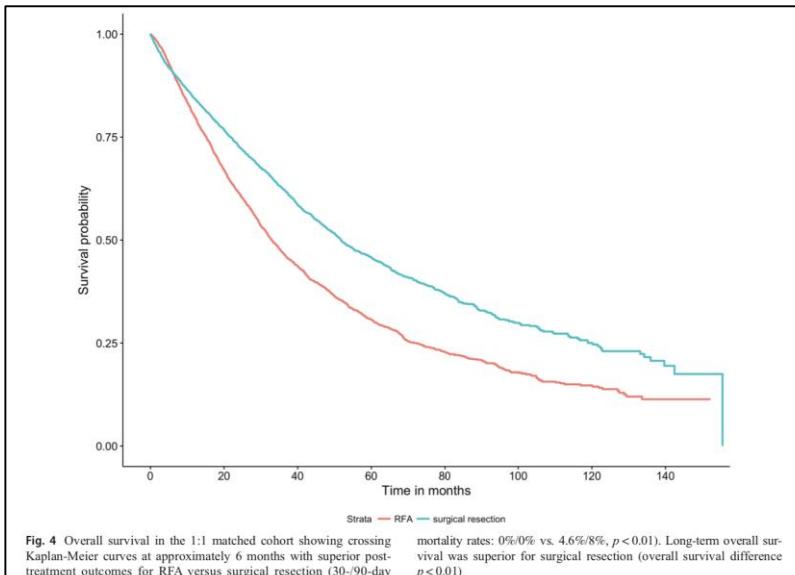
18000 pazienti  
HCC <3 cm (RF); < 5 cm (chir)

Vantaggio significativo RF:

- ↓ complicanze post-procedurali
- ↓ durata di ricovero

**Table 3** Adjusted 5-year overall survival rates by RFA and surgical resection, showing increasing treatment effectiveness from 2004 to 2014

	RFA: adjusted 5-year OS (%)	Surgical resection: adjusted 5-year OS (%)
2004–2006	21.8	37.2
2007–2010	26.7	45.7
2011–2014	36.2	54.0



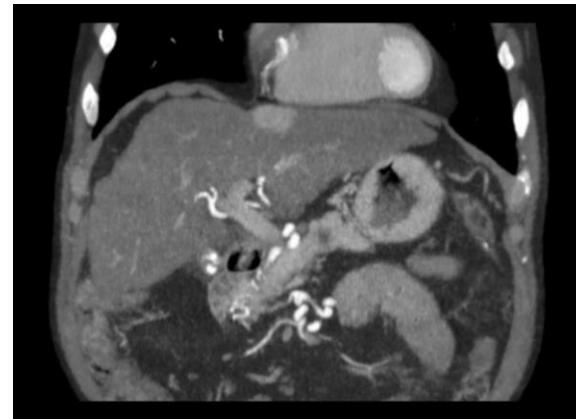
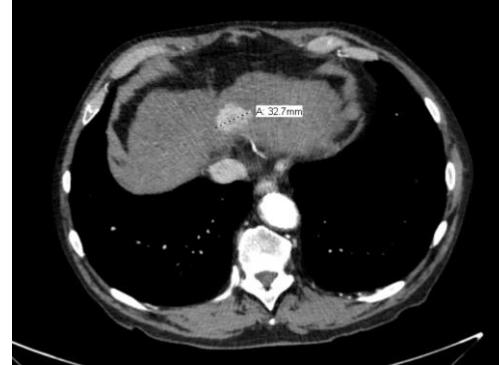
# RF + chirurgia

77 anni, polimorbidio

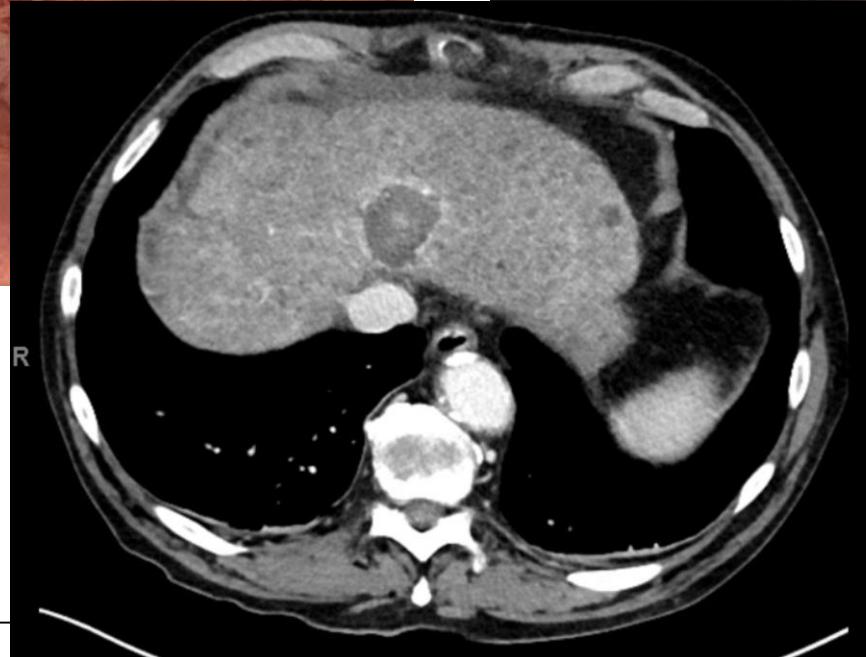
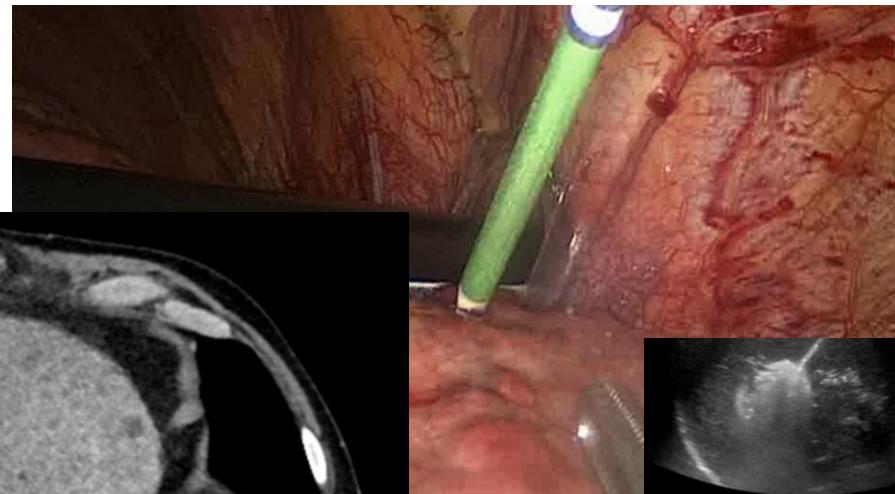
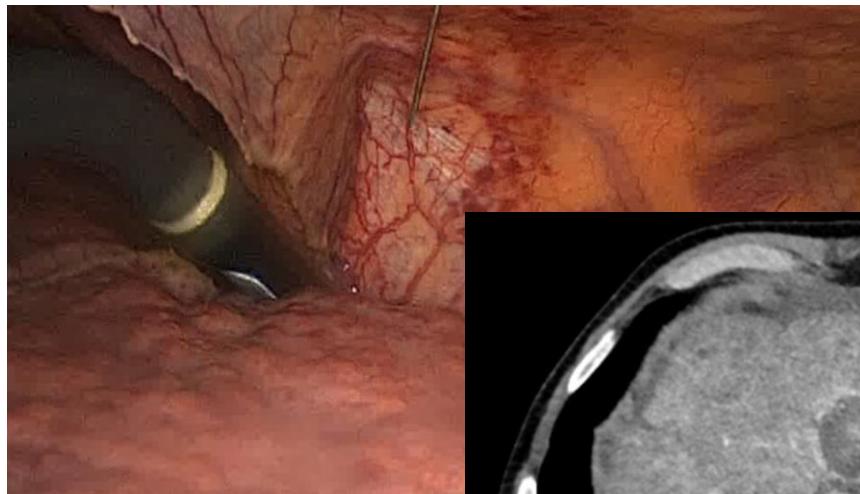
Cirrosi OH, consumo attivo

Child A (recente scompenso Child B)

Oncoboard: ablazione con RF

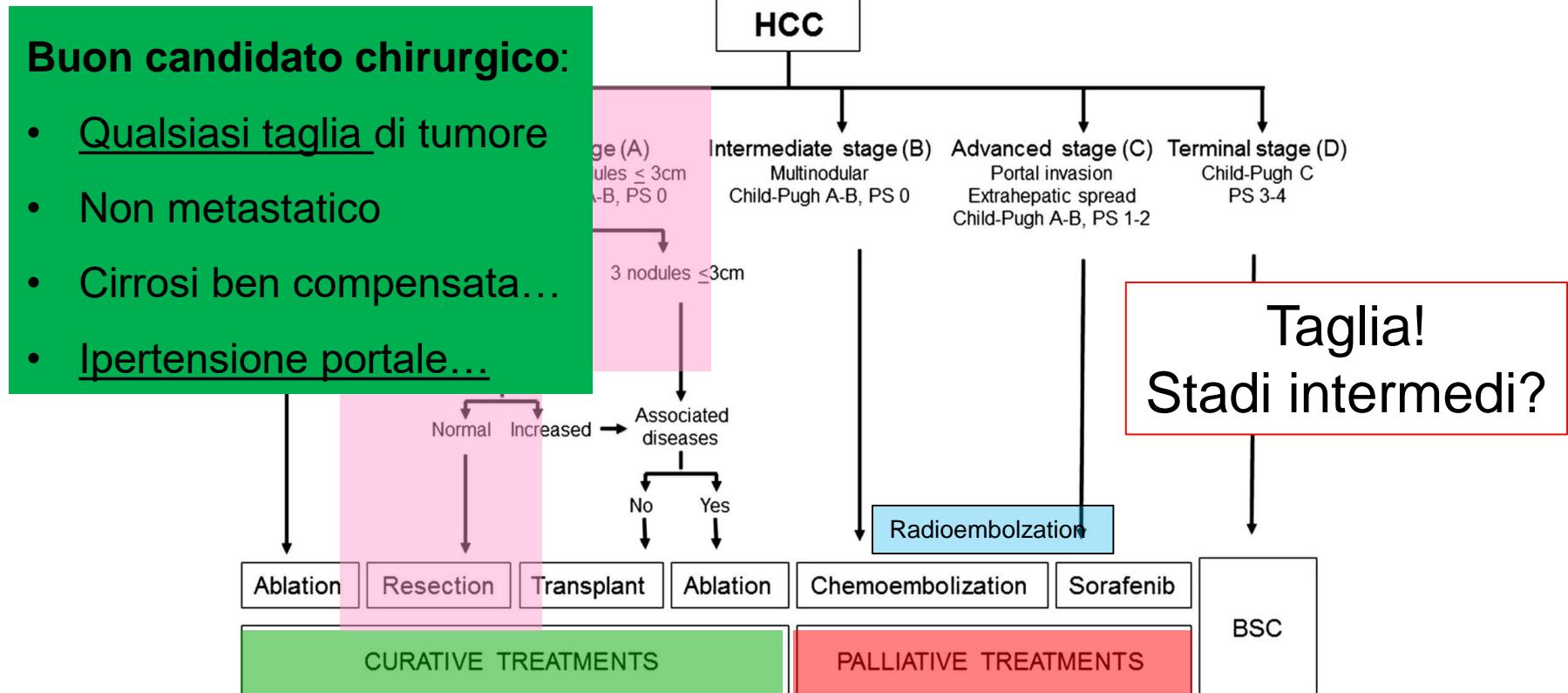


# RF + chirurgia



# HCC – Chirurgia

## BCLC Barcelona Clinic Liver Cancer



# A Snapshot of the Effective Indications and Results of Surgery for Hepatocellular Carcinoma in Tertiary Referral Centers: Is It Adherent to the EASL/AASLD Recommendations?

An Observational Study of the HCC East-West Study Group

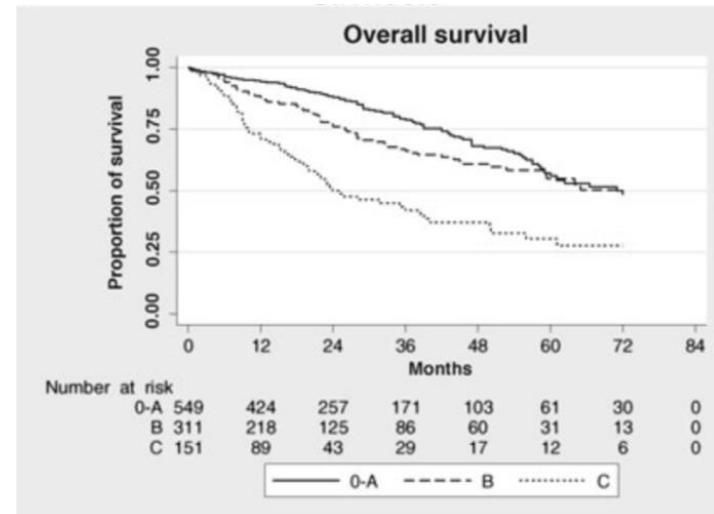
Guido Torzilli, MD, PhD,\* Jacques Belghiti, MD,† Norihiro Kokudo, MD, PhD,‡ Tadatoshi Takayama, MD, PhD,§  
Lorenzo Capussotti, MD,¶ Gennaro Nuzzo, MD,|| Jean-Nicolas Vauthey, MD,\*\* Michael A. Choti, MD,††  
Eduardo De Santibanes, MD,††† Matteo Donadon, MD,\* Emanuela Morenghi, §§  
and Masatoshi Makuchi, MD, PhD¶¶



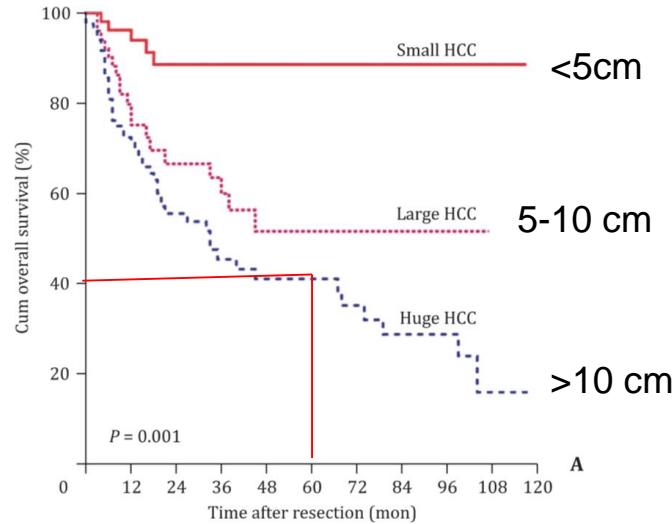
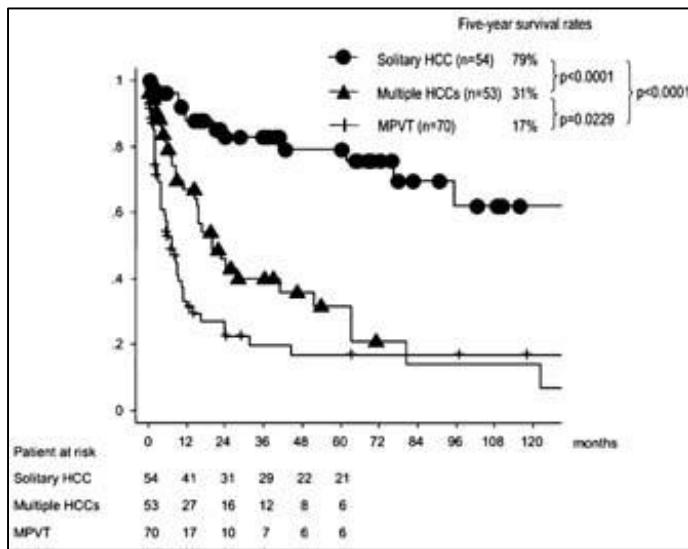
Ann Surg. 2013;257(5):929-37

**TABLE 2.** Pattern of Presentation According to the BCLC Classification

BCLC Class	n (%)
<i>BCLC 0-A [n = 931]*</i>	
Single ≤2 cm	204 (22)
Single ≤5 cm	604 (65)
Up to 3 tumors, none >3 cm	123 (13)
<i>BCLC B [n = 666]</i>	
Single >5 cm	456 (68.5)
Multiple	210 (31.5)



# Taglia del tumore

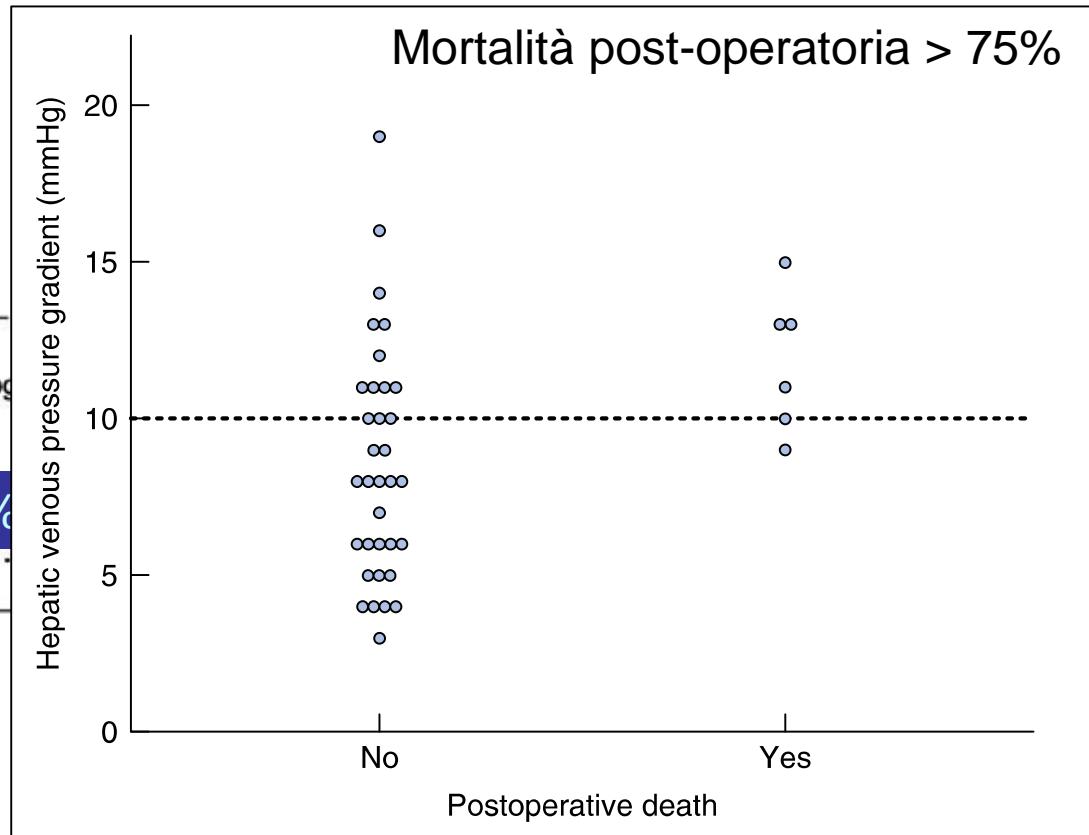
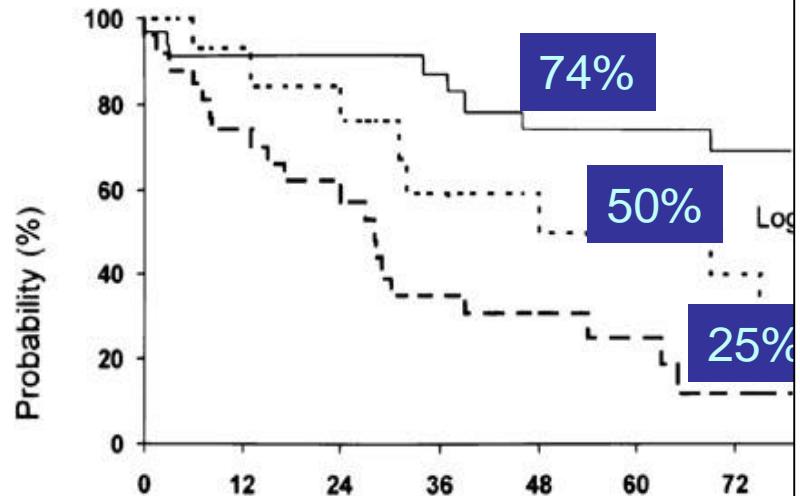


**Table 3**

Comparison of 5-year DFS and overall DFS among different HCC subgroups.

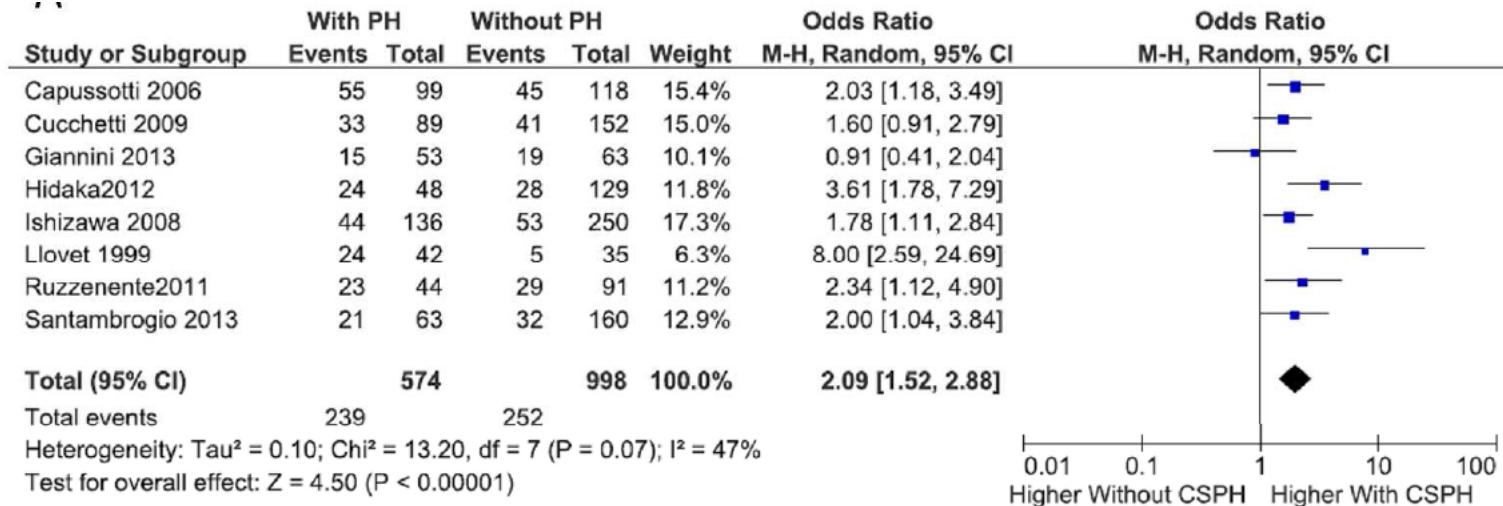
Groups	P value	
	5-year DFS	Overall DFS
Small HCC versus Large HCC	0.069	0.088
Small HCC versus Huge HCC	<b>0.041</b>	<b>0.029</b>
Large HCC versus Huge HCC	0.951	0.831

# Ipertensione portale



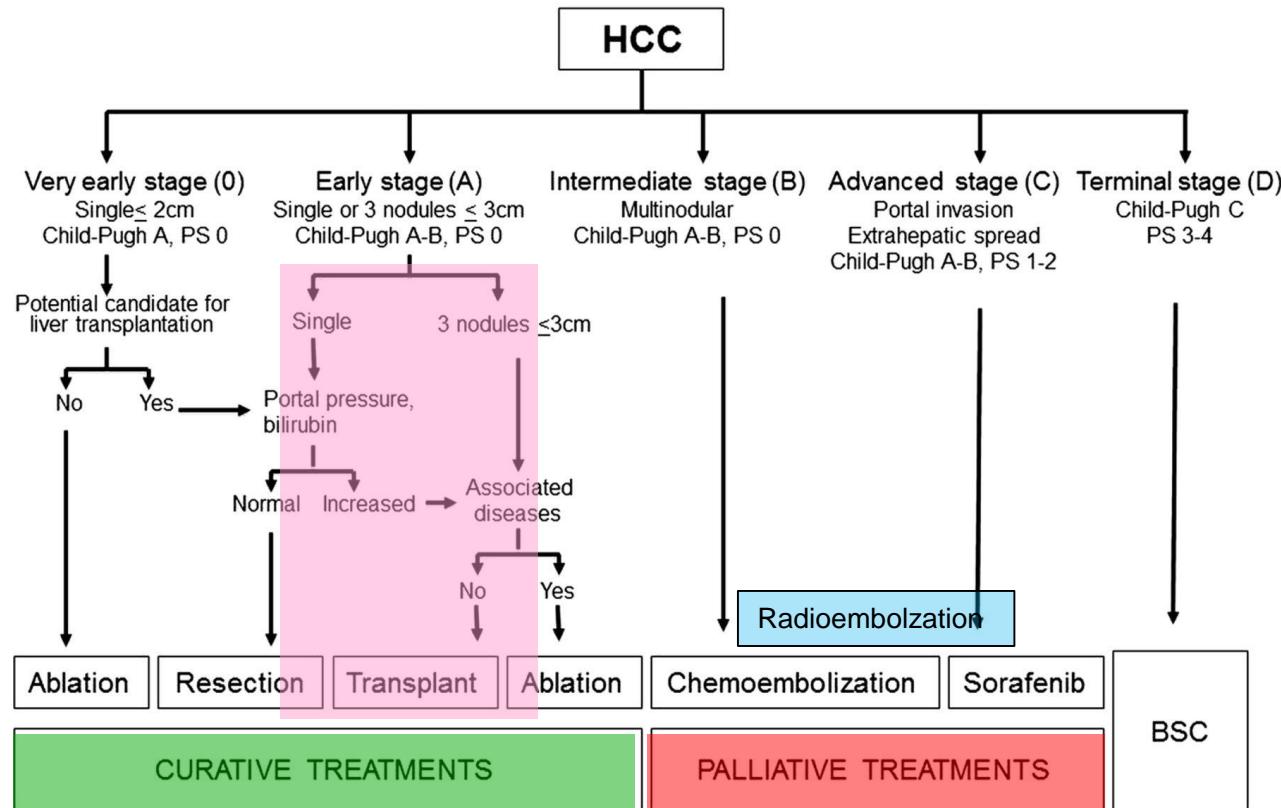
# Ipertensione portale

## Meta-analisi, sopravvivenza a 3 anni



# HCC - trapianto

## BCLC Barcelona Clinic Liver Cancer



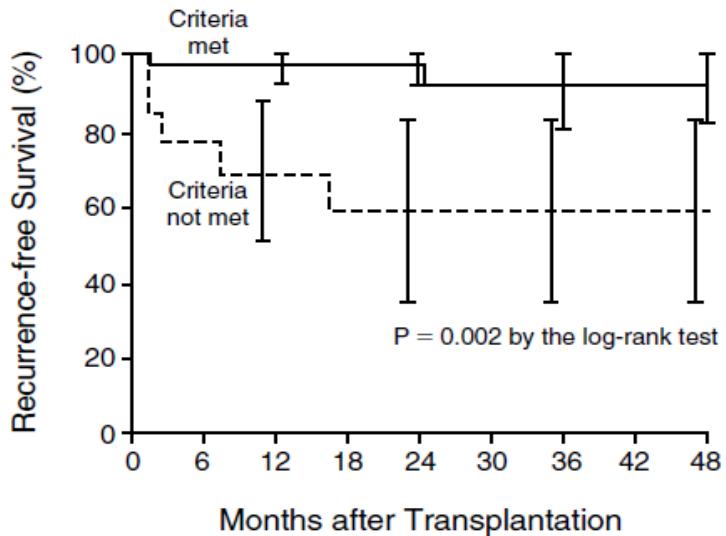
# Criteri di Milano

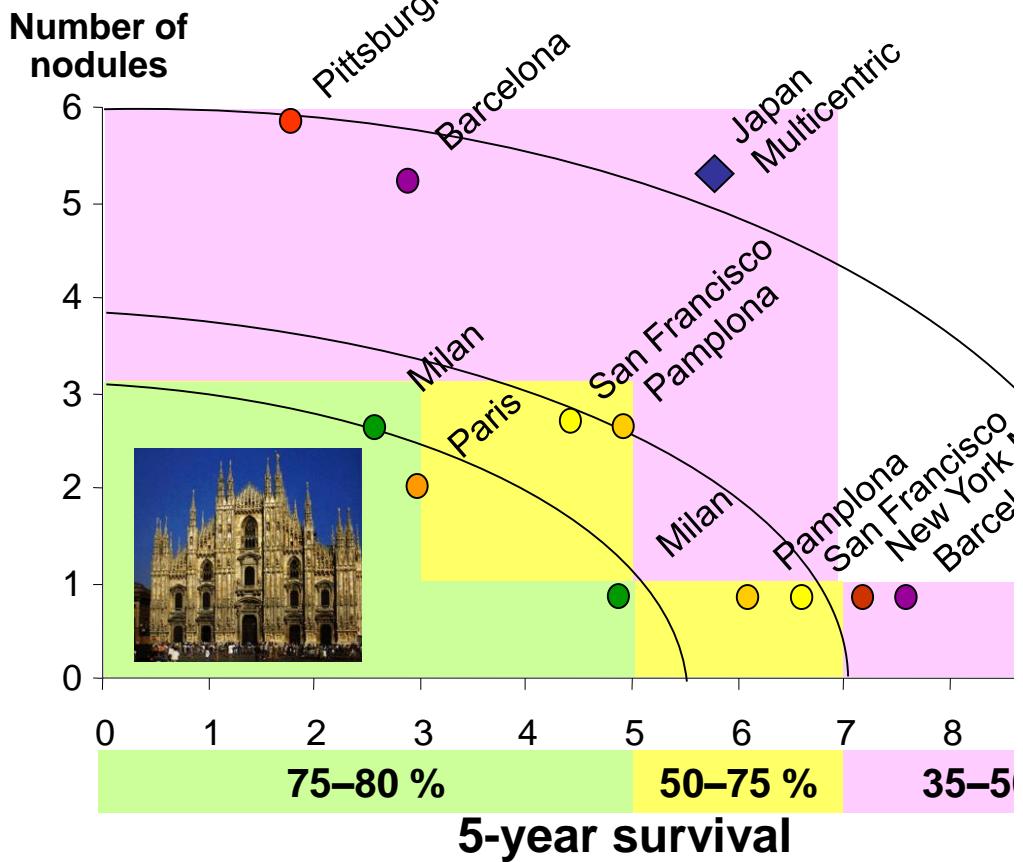
## LIVER TRANSPLANTATION FOR THE TREATMENT OF SMALL HEPATOCELLULAR CARCINOMAS IN PATIENTS WITH CIRRHOSIS

VINCENZO MAZZAFERRO, M.D., ENRICO REGALIA, M.D., ROBERTO DOCI, M.D., SALVATORE ANDREOLA, M.D., ANDREA PULVIRENTI, M.D., FEDERICO BOZZETTI, M.D., FABRIZIO MONTALTO, M.D., MARIO AMMATUNA, M.D., ALBERTO MORABITO, PH.D., AND LEANDRO GENNARI, M.D., PH.D.

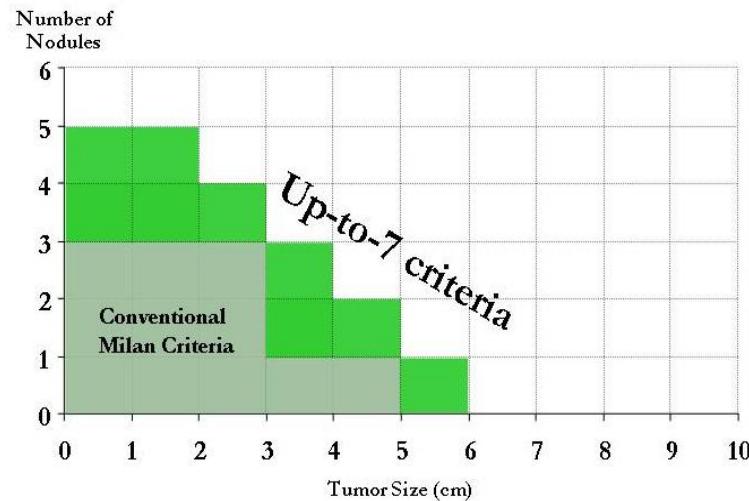


- singolo HCC  $\leq 5$  cm
- $\leq 3$  HCC  $\leq 3$  cm



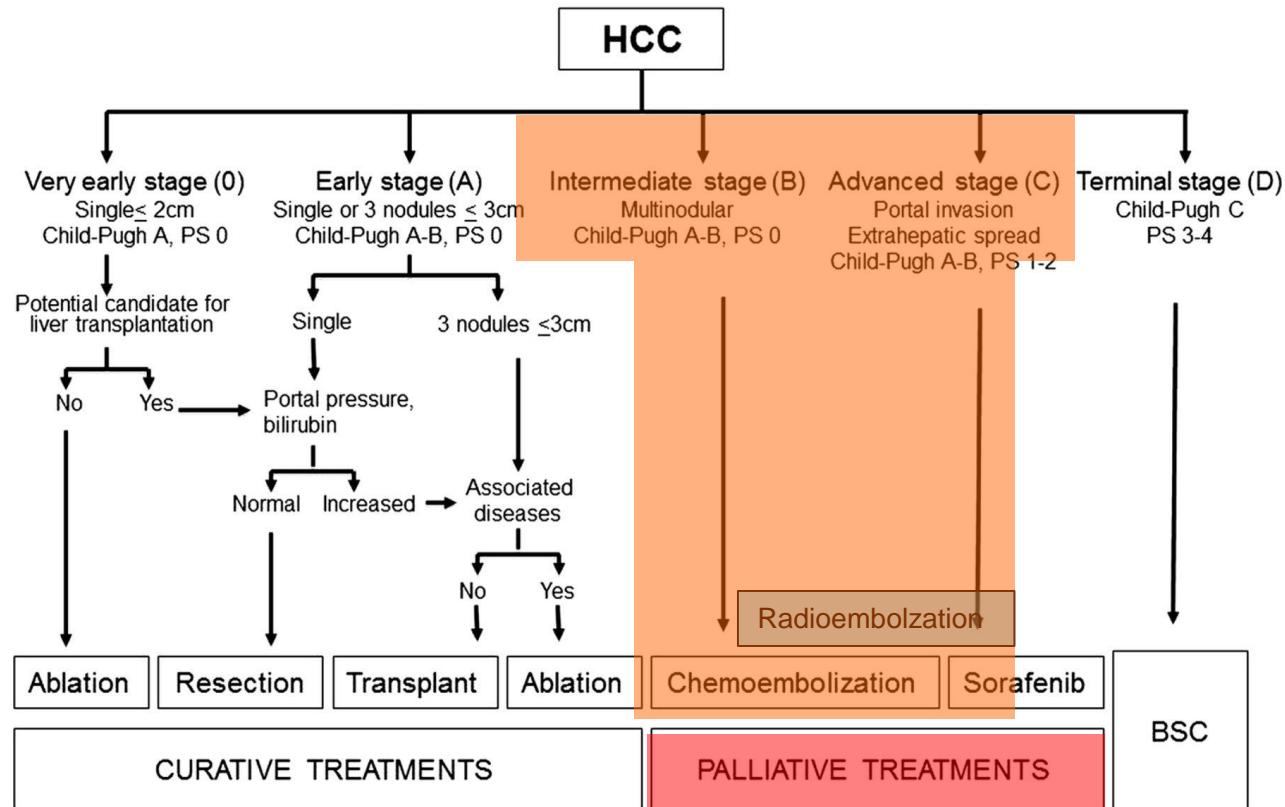


The longer the trip,  
the higher the price  
“Metroticket”

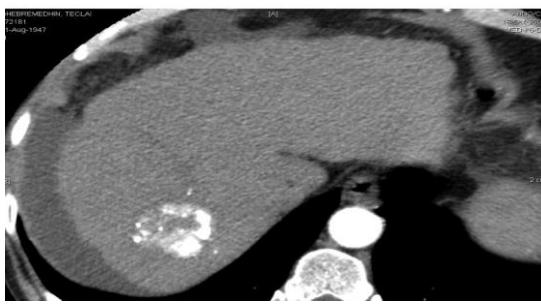
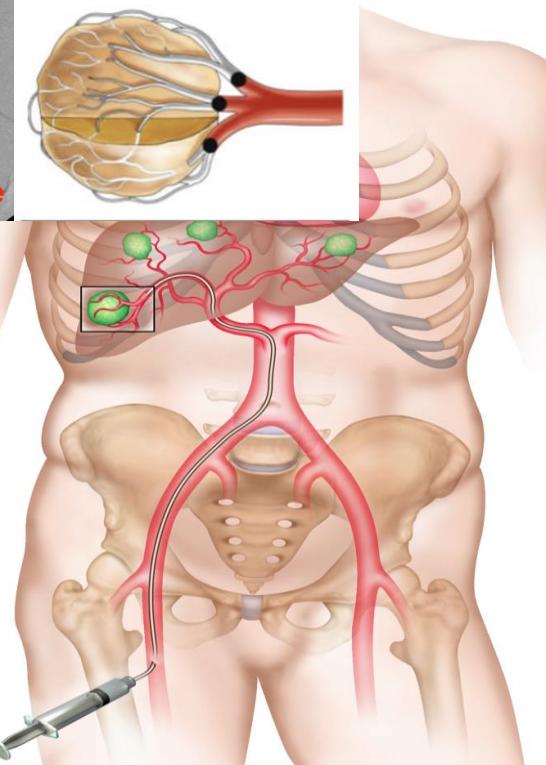
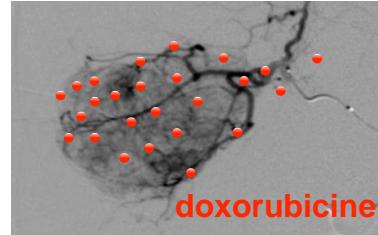


# HCC – stadi avanzati

## BCLC Barcelona Clinic Liver Cancer



# Chemioembolizzazione



# Chemioembolizzazione - TACE

Paziente ideale:

- non resecabile
- senza invasione vascolare
- Child A- B < 8

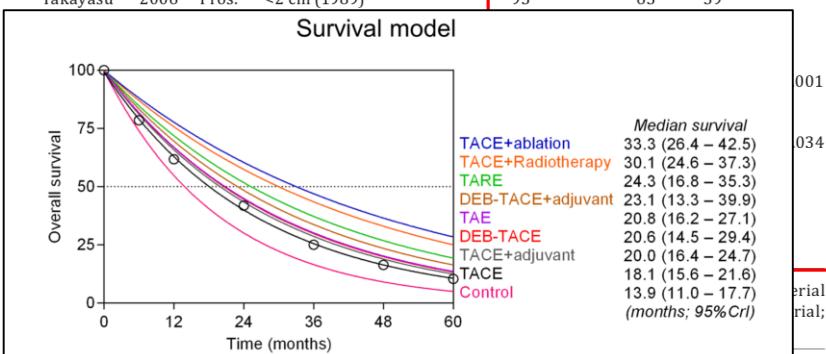
Possibile indicazione «bridging»  
prima di trapianto

CI assolute:

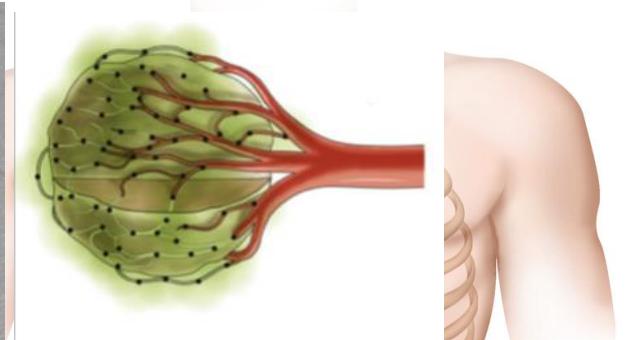
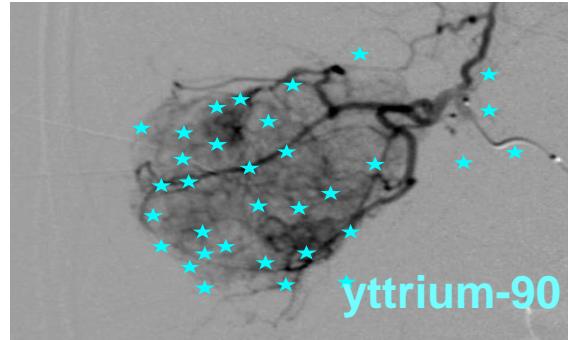
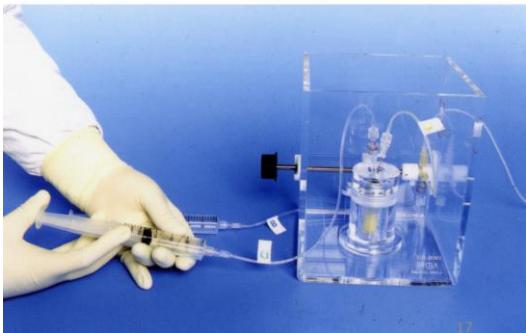
- Child B > 8
- occlusione flusso portale

**Table 1.** Response and Survival Rates of HCC Patients in Past Trials of TACE alone, or Comparing TACE/TAE versus Inactive Treatments

Author	Year	Study Design	Treatment Arms (No. of Patients)	Response Rate (%)	Survival (%)			
					1-year	2-year	3-year	5-year
Yamada [2]	1983	Ret.	TAE (66)		44	29	15	
Matsui [4]	1993	Ret.	Subseg TACE (100)		100		73	53
Nishimine [5]		Ret.	Seg TACE (98)		89		59	30
GETCH [7]	1995	RCT	TACE (50)	16	62	38		NS
			Control (46)	5	43	26		
Llovet [8]	2002	RCT	TAE (37)	43	75	50	29	
			TACE (40)	35	82	63	29	P=0.009
			Control (35)	0	63	27	17	
Lo [9]	2002	RCT	TACE (40)	27	57	31	26	P=0.002
			Control (39)	2.6	32	11	3	
Takayasu	2006	Pros.	<2 cm (1989)		93	63	39	



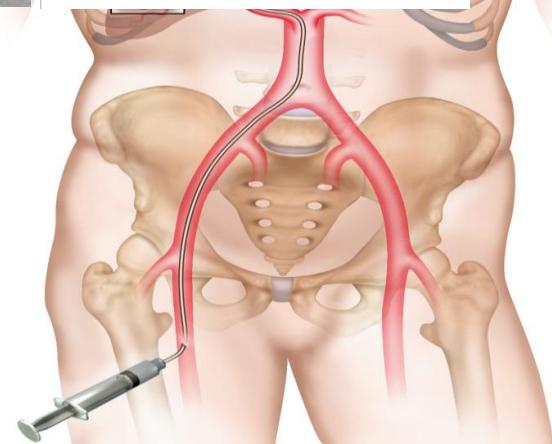
# Radioembolizzazione



Microsfere resina/vetro

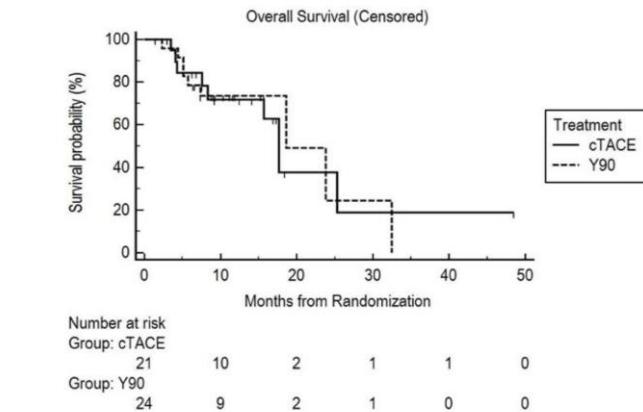
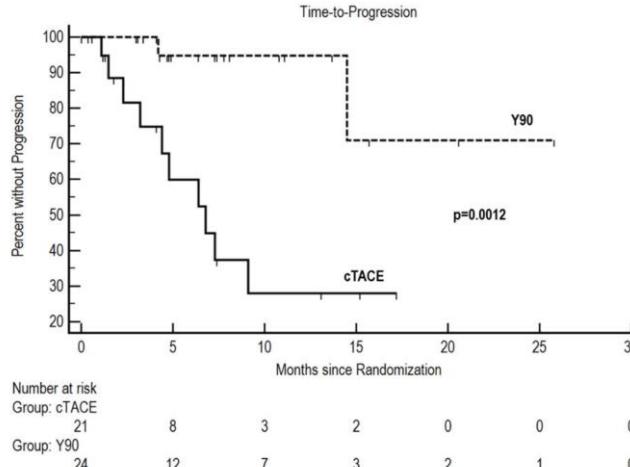
Alte dosi radioterapia locale

2 sessioni (test MMA)



# Radioembolizzazione - SIRT

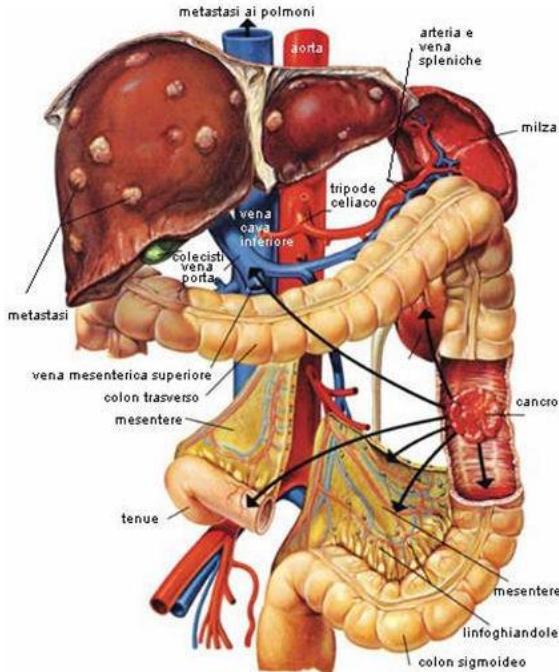
- Indicazioni in crescita
- Possibile se trombosi VP
- Ben tollerato
- Ripetibile
- Possibile terapia «bridge»
- Downstaging
- CI: shunt polmonare > 30Gy



# UCEP – Radiologia

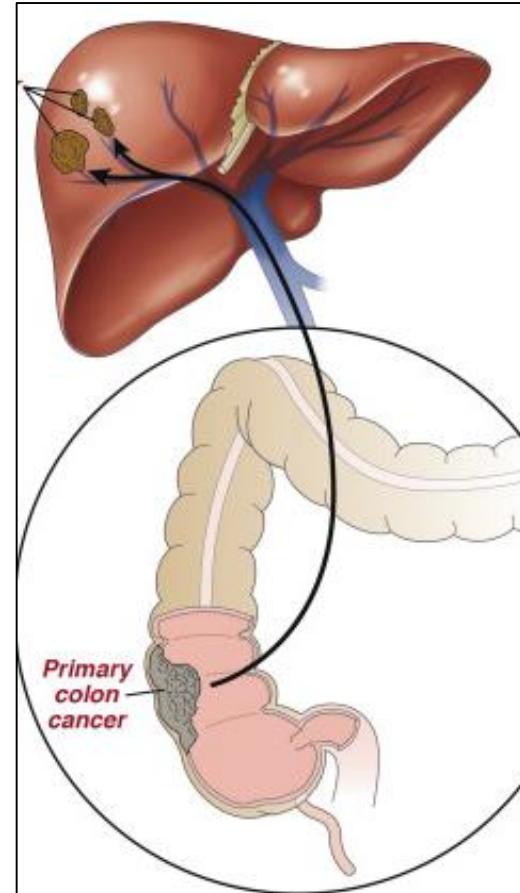


# Trattamento delle metastasi epatiche

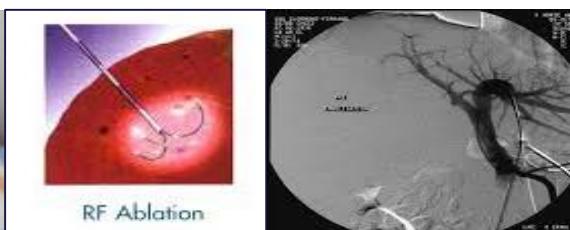


# Metastasi colorettali

- 50-60% dei tumori colorettali primari → metastasi sincrone/metacrone
- Chirurgia gold standard
- **20% → 60% operabilità pazienti M1**
- **Sopravvivenza a 5 aa fino al 50%**



Evoluzione delle indicazioni alla resezione chirurgica!



# Strategia terapeutica

## Metastasi sincrone:

- Operabili d'emblée
  - Potenzialmente operabili
  - Non operabili
- 
- Tumore primario sintomatico
  - Tumore primario asintomatico

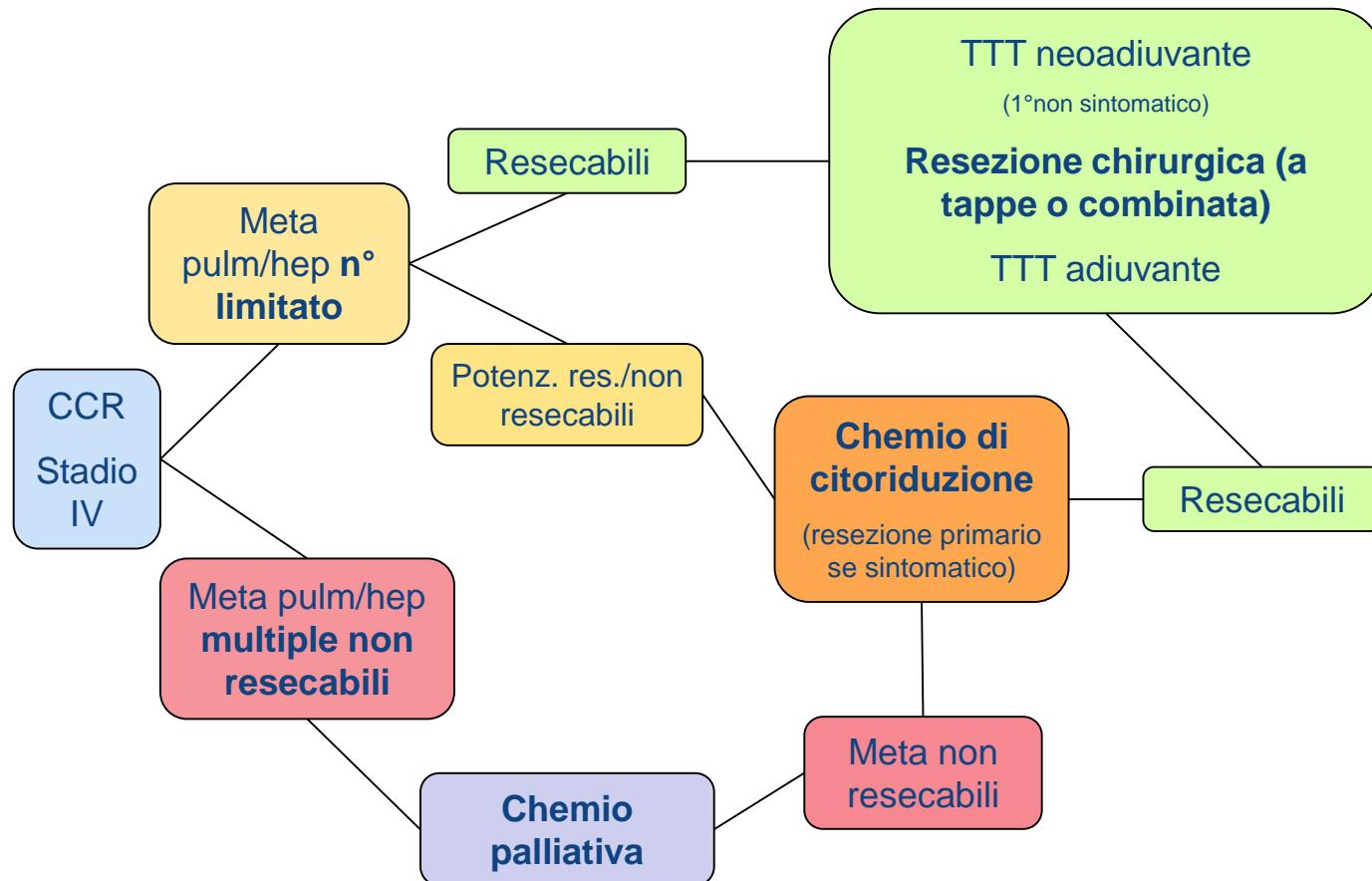


## Metastasi metacrone

- Operabili (potenzialmente) d'emblée
- Non operabili

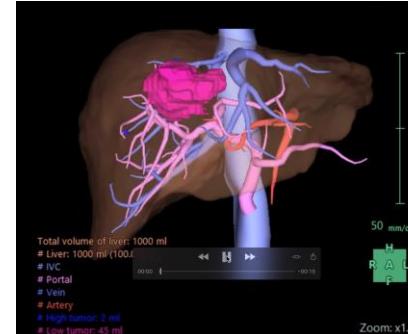
## Malattia metastatica extra-epatica

# Carcinoma Colorettale Stadio IV



# Metastasi resecabili d'emblee

- 20% dei pazienti
- **Obiettivo: R0 + >30% fegato restante**
- R1 vascolare di necessità accettato
- Studio imaging pre-op e funzione ++
- No malattia extra-epatica non resecabile
- Chimioterapia peri-op vs resezione up-front



# Metastasi potenzialmente resecabili

- Nuovi schemi chemioterapia (+/- terapie target)
- Strategie chirurgiche: OSH vs TSH
- Embolizzazione portale/ALPPS
- Approcci combinati RF/chir

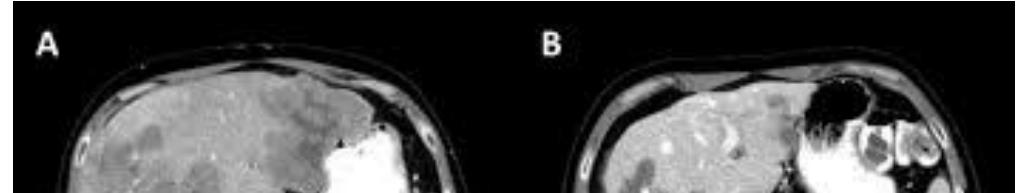


# Chemioterapia per-op

FOLFOXIRI +/- anti-EGFR/VEGF

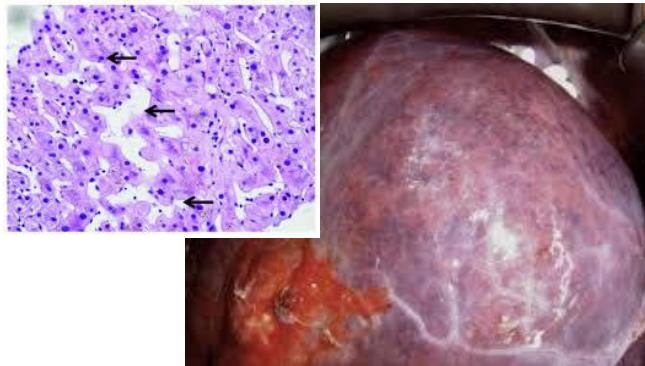


epatotossicità!

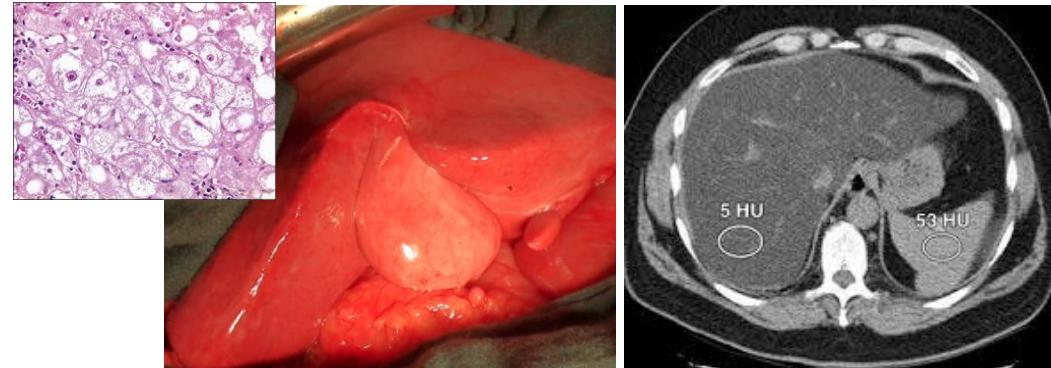


Aumento della morbidità intra e post-operatoria  
Rischio di insufficienza epatica post-op  
Almeno 4 settimane intervallo

Oxaliplatin: SOS/«blue liver»

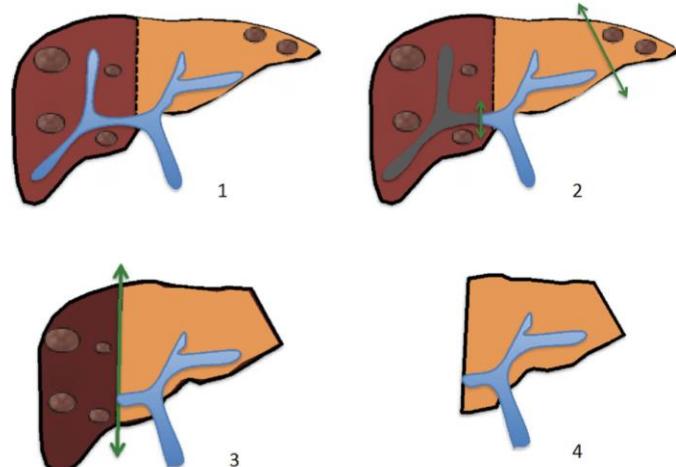
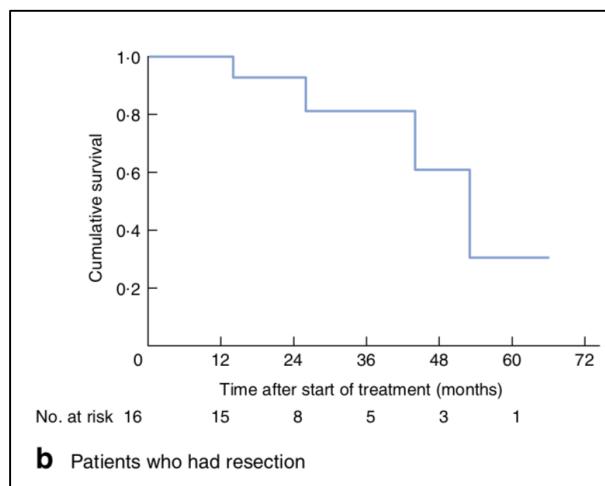


IRInotecan: CASH/ «yellow liver»



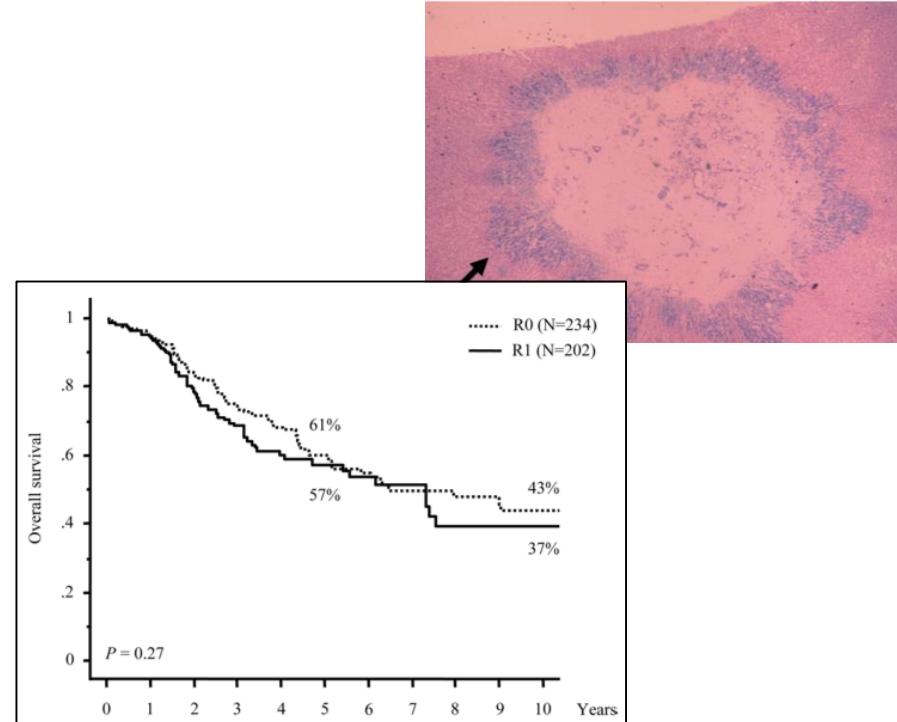
# Considerazioni chirurgiche

- Parenchima Sparing Hepatectomies (re-epatectomie possibili)
- ONE stage vs TWO stage
- Trattamento «Reverse»



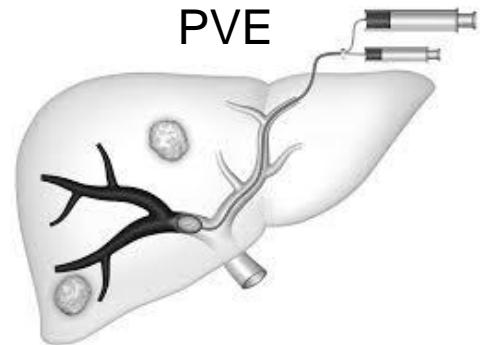
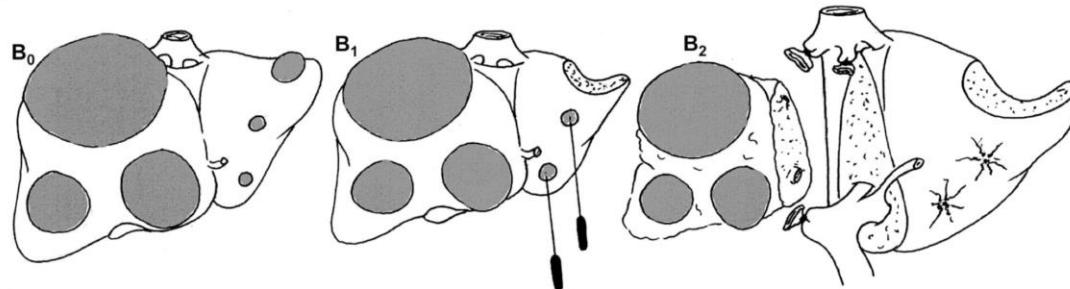
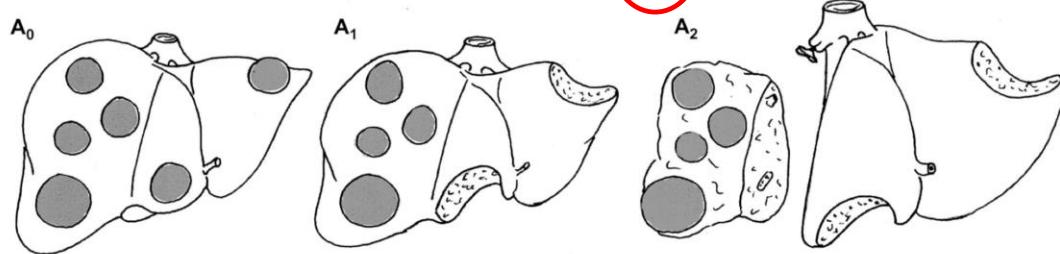
# Considerazioni chirurgiche

- Parenchima Sparing Hepatectomies (re-epatectomie possibili)
- ONE stage vs TWO stage
- Trattamento «Reverse»
- Margini 1cm – 1mm
- Dangerous Halo
- R1 vascolare possibile

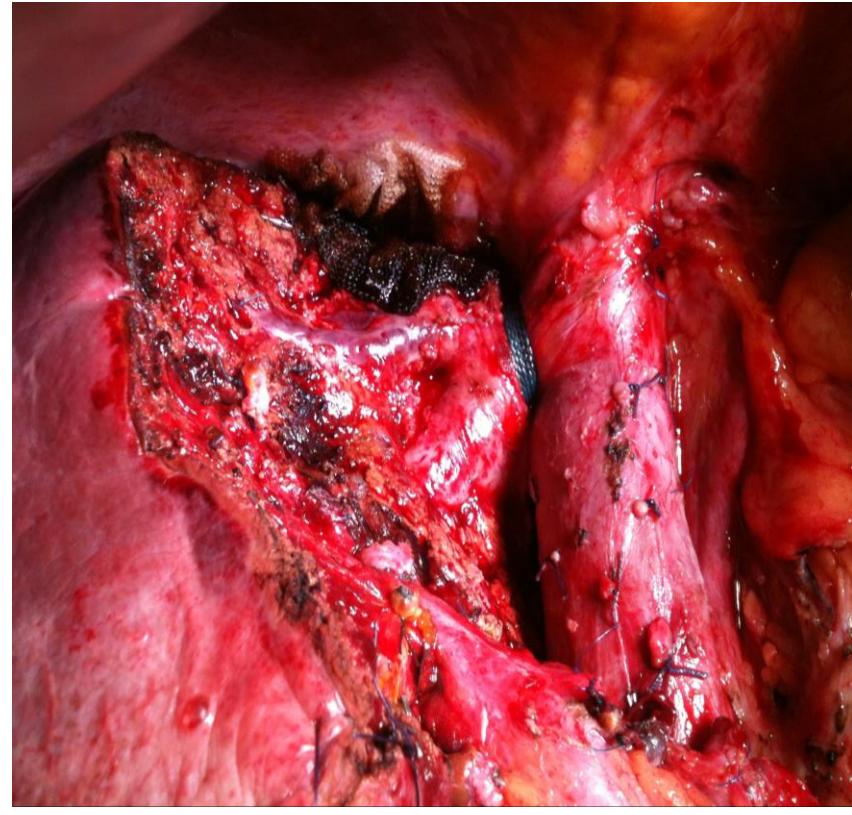
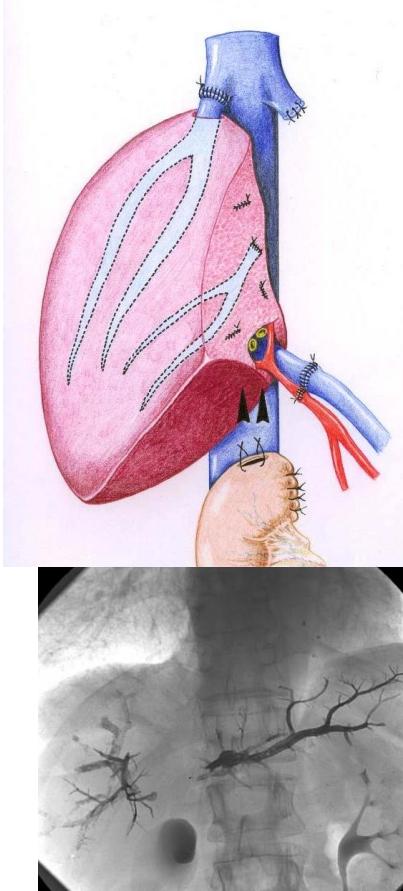


# Embolizzazione portale

MBCLM patients → First-stage hepatectomy (non anatomical resection ± radiofrequency ablation) PVE Second-stage hepatectomy Right or extended right hepatectomy

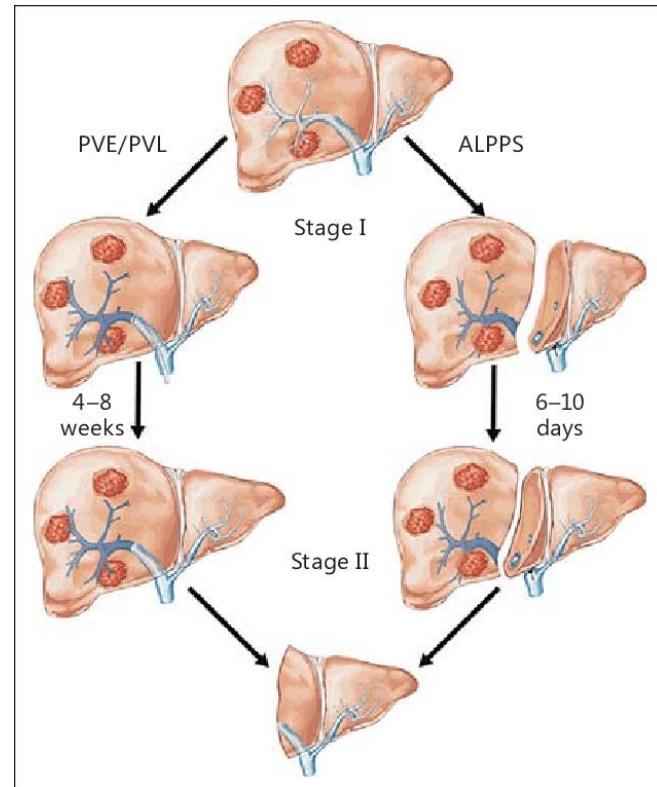
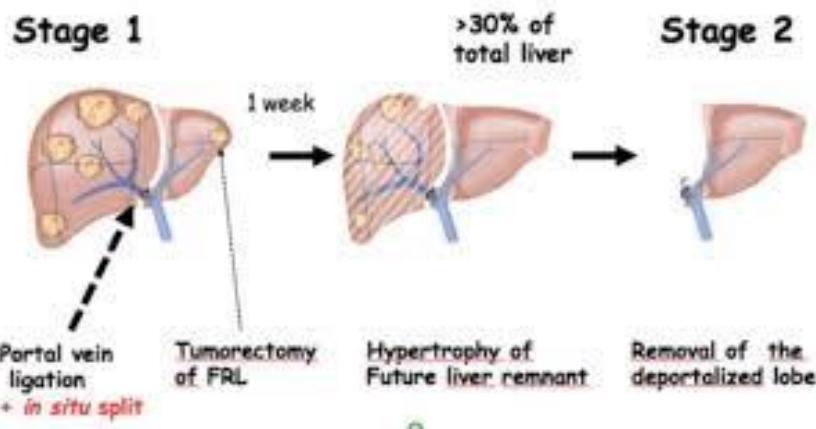


> 85% di resecabilità





# ALPPS - Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy



# ALPPS - Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy

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Short Report

The HPB controversy of the decade: 2007–2017 – Ten years of ALPPS

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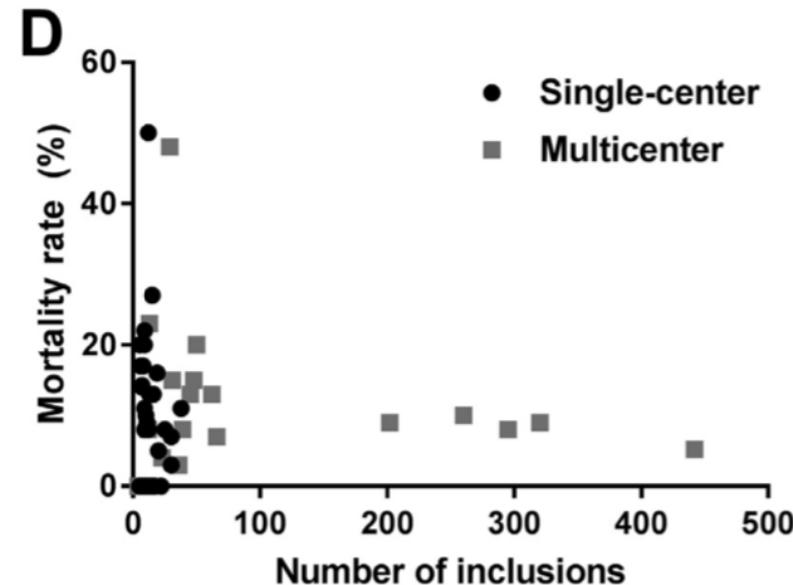
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Mortalità fino al 50%!

Procedura limitata a centri esperti

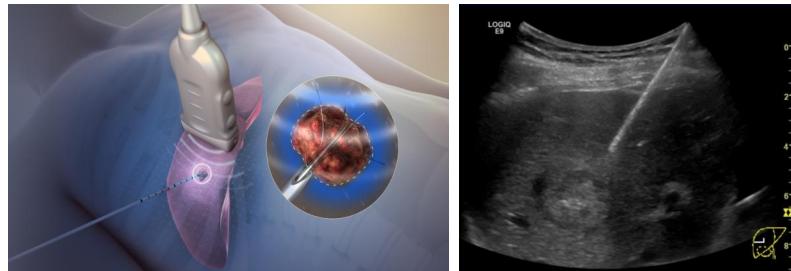


# Missing metastases

- Fino al 6% delle metastasi
- Risposta radiologica ✗ Risposta istologica : residui microscopici 80%!
- Da evitare e resecare se possibile
- Trattamento conservativo: recidiva locale 19-77%
- Considerare interruzione chemio/anticipazione chirurgia/marcaggio

# Trattamenti locali

- RF / MWA
- Lesioni < 3 cm
- Meno complicanze
- Alto tasso recidiva locale! (60%)
- Pazienti ad alto rischio chirurgico
- Combinata alla resezione (TSH)



# Trattamenti locali

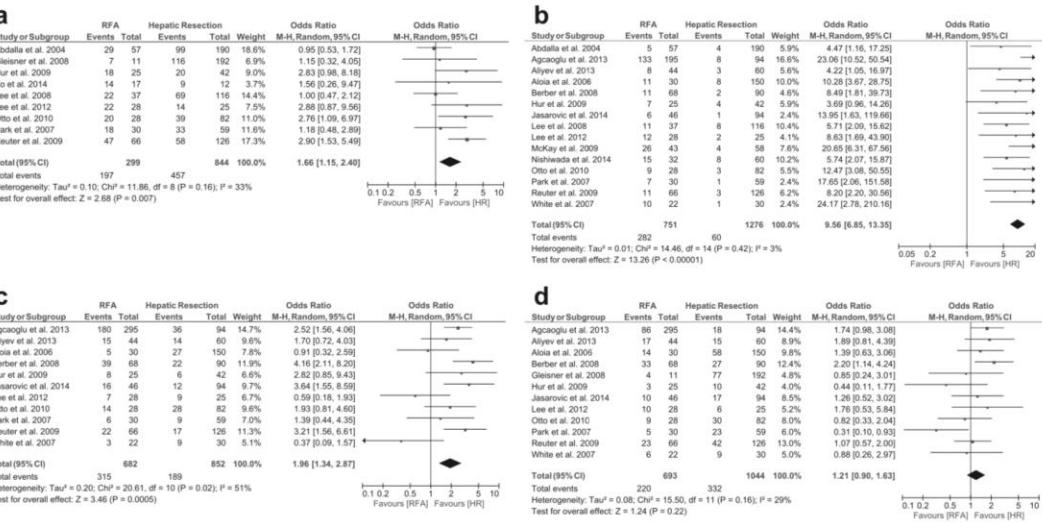


Figure 2 Recurrence rates. a: Any recurrence, b: Local recurrence, c: 'De novo' intrahepatic recurrence, d: Extrahepatic recurrence

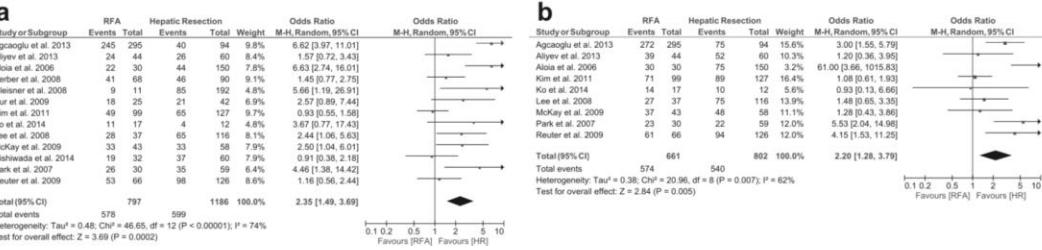
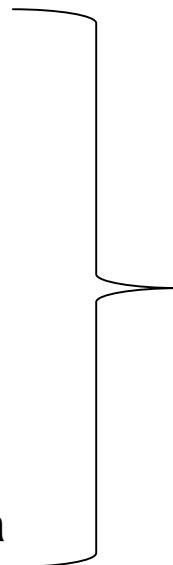


Figure 3 Survival rates. a: 5-year overall survival, b: 5-year disease free-survival

# Metastasi non resecabili

- Chemioterapia
- RFA
- TACE
- Dab-TACE
- SIRT
- RT stereotassica



Risposte RECIST  
fino al 35%

Table 5 Survival and follow-up

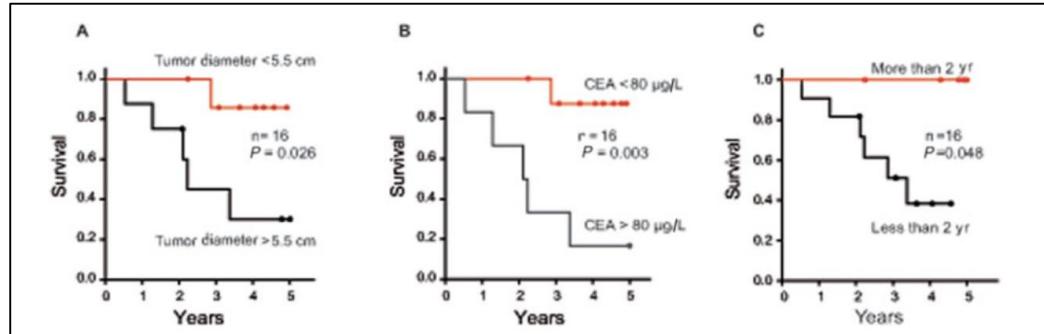
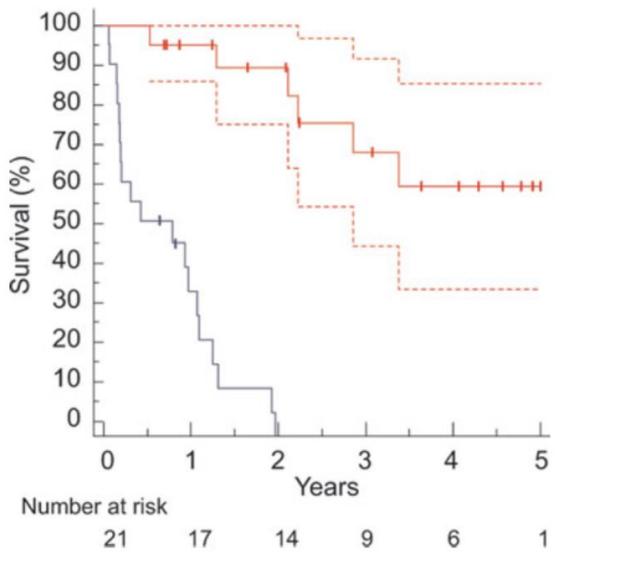
References	Median Survival, months (95% CI)	1-Year Survival (%)	Median Follow-Up, months (Range)
<b>cTACE</b>			
Popov 2002	9 (4–16) <sup>a</sup>	–	–
Salman 2002	10 (8–11)	54	–
Vogl 2009	14	62	–
Vogl 2012	23	88	11 <sup>b</sup>
Nishiofuku 2013	21 (8–34)	67	17 <sup>b</sup>
<b>DEB-TACE</b>			
Alberti 2011	25 (6–34) <sup>a</sup>	83	29 (7–48)
Martin 2011	19	75	18 (12–40)
Fiorentini 2012	22 (21–23)	81	50
Huppert 2014	8 (2–38)	–	8 (1–54)
Iezzi 2015	7	–	11 <sup>b</sup> (5–18)
<b>Y-90</b>			
Lim 2005	7	27	18
Sato 2008	15	54	–
Van Hazel 2009	12 (3–60) <sup>a</sup>	–	–
Cosimelli 2010	13 (7–18)	50	11 <sup>b</sup> (2–29)
Hendlisz 2010	10	–	25 (2–41)
Seidensticker 2012	8	24	–
Benson 2013	9 (7–12)	–	30
Cohen 2014	8 (4–43) <sup>a</sup>	–	–
Lewandowski 2014	11 (9–15)	–	–
Sofocleous 2014	15 (6–26)	52	31 (19–41)
Golfieri 2015	11 (8–14)	–	7 (1–72)
Edalat 2016	9 (2–16)	–	14 <sup>b</sup> (3–35)
Van den Hoven 2016	9 (5–12)	–	–

# Trapianto

## Liver Transplantation for Nonresectable Liver Metastases From Colorectal Cancer

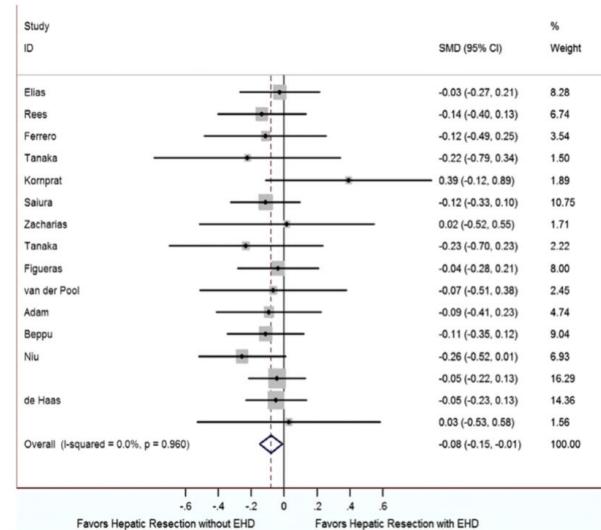
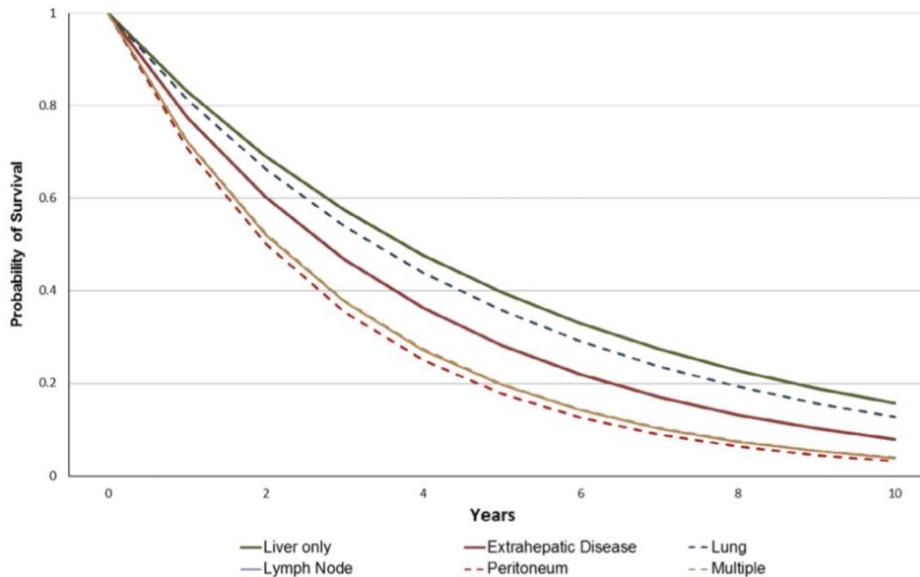
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# Metastasi extra-epatiche

- Non CI se tutta la malattia è resecabile/controllabile
- Aumento della OS 0→28% (31m media)



# Conclusioni



- Chirurgia offre migliori possibilità lungo termine
- Studio accurato della funzione epatica e dell'anatomia
- Multiple opzioni di trattamento, «à la carte»



**Discussione multidisciplinare con team esperto (UCEP)**

Grazie

