



29 ottobre 2011

MALATTIA METASTATICA DEL CARCINOMA DEL GROSSO INTESTINO .

TECNICHE E TERAPIE INNOVATIVE

TERAPIA INTRARARTERIOSA



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DEFINIZIONE DI RESECABILITA'

Defining Resectable Metastatic Colorectal Cancer

Table 1. Criteria defining resectability for surgical resection

1. Macroscopic and microscopic (R0) treatment of the disease is feasible with either resection alone or resection combined with radiofrequency ablation.
 2. At least two adjacent liver segments can be spared.
 3. Adequate vascular inflow, outflow, and biliary drainage can be preserved.
 4. Sufficient remnant liver volume (>20% of the total estimated liver volume in normal liver, >40% of total estimated liver volume in cirrhotic liver).
-

RESECCABILITA'

Resectability of Colorectal Cancer

Table

1. Initially resectable
2. Initially unresectable but *likely* convertible
 - Preoperative portal vein embolization
 - Resection plus ablation
3. Initially unresectable but *likely* convertible
4. Initially unresectable and *unlikely* convertible



DEFINIZIONE DI RESECABILITA'

Defining Resectable Metastatic Colorectal Cancer

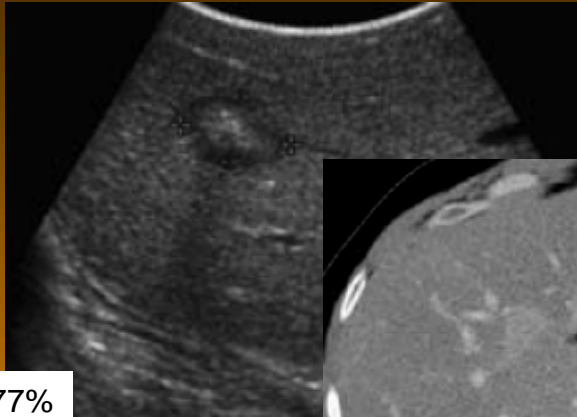
Table 2. Categories of resectability

1. Initially resectable disease by *standard*
2. Initially resectable but *not*
 - Staged resection plus embolization
 - Staged resection plus ablation
3. Initially unresectable but *likely convertible* with tumor response
4. Initially unresectable and *unlikely convertible*

RADIOLOGIA DIAGNOSTICA

RADIOLOGIA DIAGNOSTICA

US



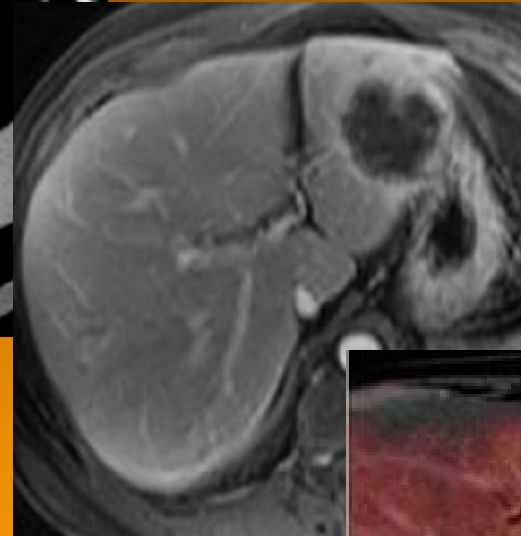
Sensibilità 53%-77%

TC



Sensibilità 70%-95%

RM



Sensibilità 73%-95%

TC - PET

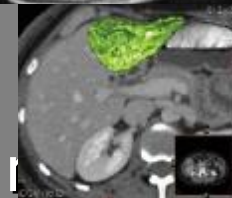
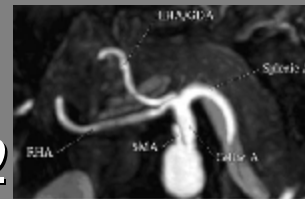
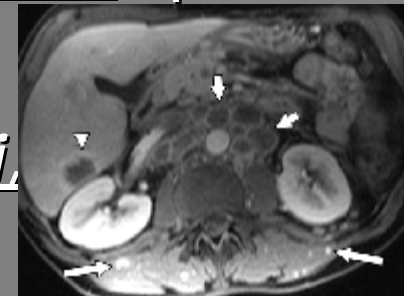
Sensibilità 90%-95%

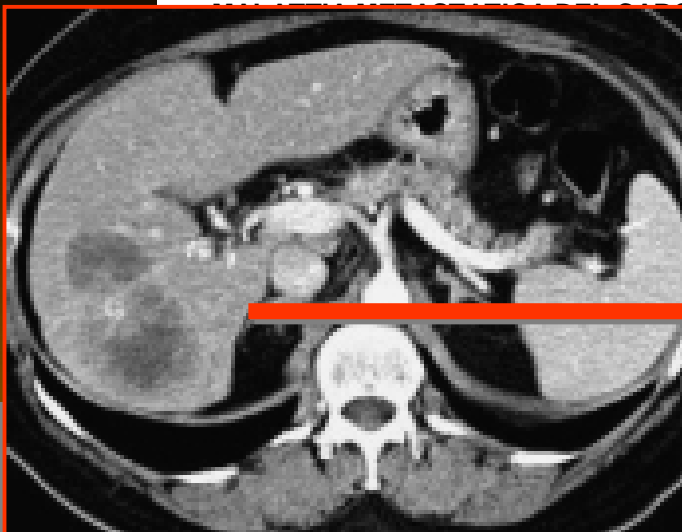


RADIOLOGIA DIAGNOSTICA

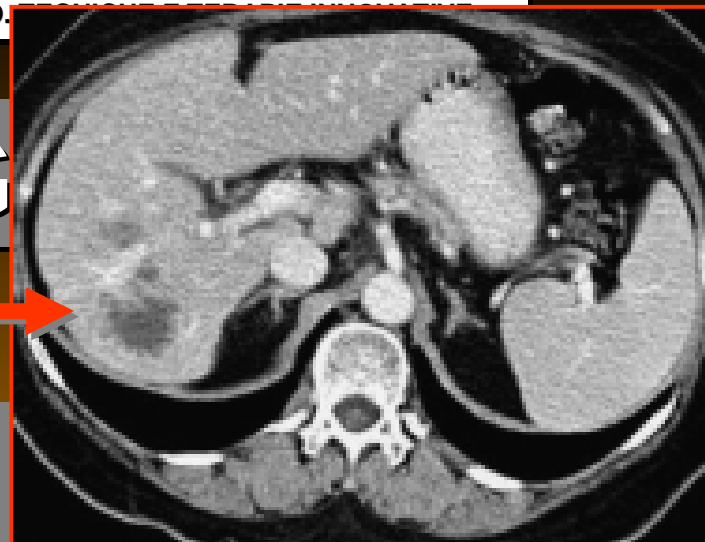
GOALS

- Definire il numero e l'estensione delle metastasi epatiche con riguardo all'estensione segmentaria e lobare
- Identificare le sedi extraepatiche, linfonodali, peritoneali, a distanza
- Assistere il planning chirurgico
- Valutare il volume residuo del fegato (in caso di resectione)
- Valutare il risultato delle terapie neoadiuvanti nel downstaging di lesioni inizialmente non resecabili





GIA DIAG



GOALS

- Valutare il risultato delle terapie palliative nelle lesioni non resecabili

- Criteri WH
- Criteri Rec
- Criteri Pre
- Criteri mR

Table 2 Assessment of Target Lesion Response: Conventional RECIST and mRECIST Assessment for HCC Following the AASLD-JNCI Guideline

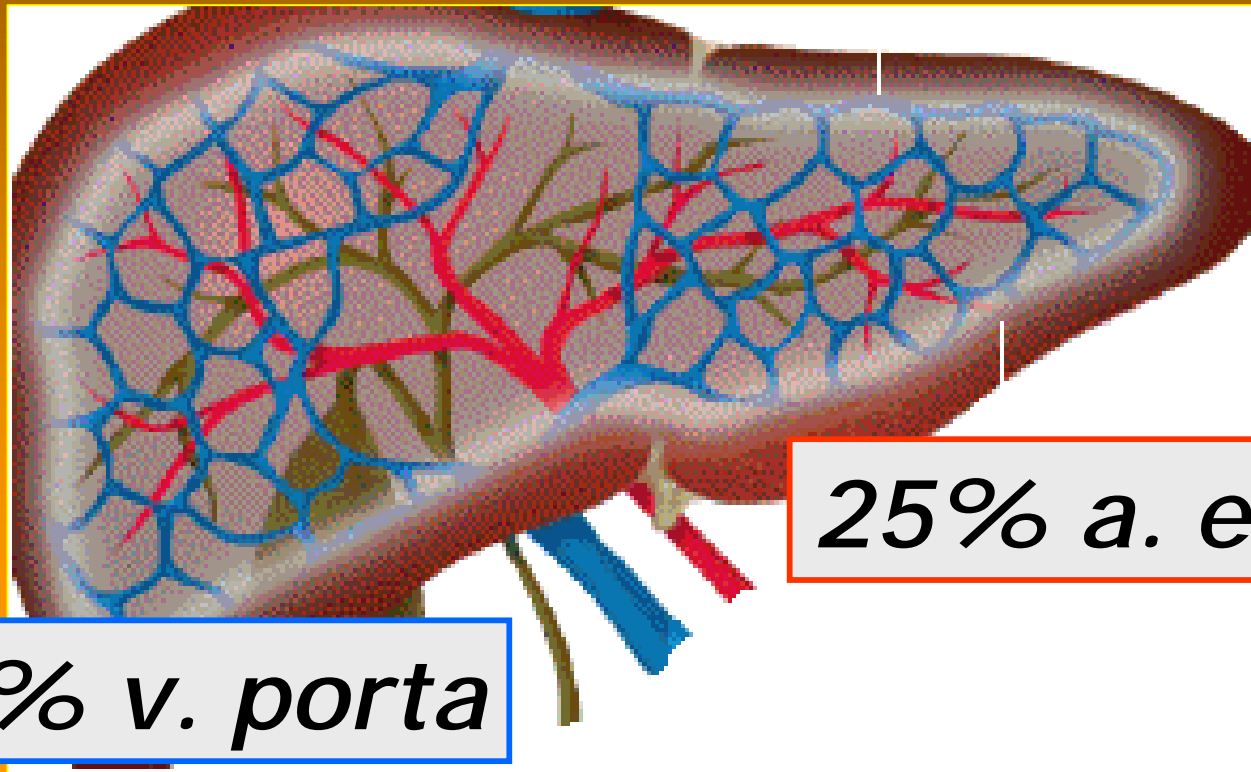
RECIST	mRECIST for HCC
CR = Disappearance of all target lesions	CR = <u>Disappearance of any intratumoral arterial enhancement in all target lesions</u>
PR = At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of the diameters of target lesions	PR = At least a 30% decrease in the sum of diameters of viable (enhancement in the arterial phase) target lesions, taking as reference the baseline sum of the diameters of target lesions
SD = Any cases that do not qualify for either partial response or progressive disease	SD = Any cases that do not qualify for either partial response or progressive disease
PD = An increase of at least 20% in the sum of the diameters of target lesions, taking as reference the smallest sum of the diameters of target lesions recorded since treatment started	PD = An increase of at least 20% in the sum of the diameters of viable (enhancing) target lesions, taking as reference the smallest sum of the diameters of viable (enhancing) target lesions recorded since treatment started

AASLD, American Association for the Study of Liver Diseases; JNCI, Journal of the National Cancer Institute; HCC, hepatocellular carcinoma; mRECIST, modified Response Evaluation Criteria in Solid Tumors; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.

TERAPIA INTRARARTERIOSA

RATIONALE

1 – Doppia vascolarizzazione epatica



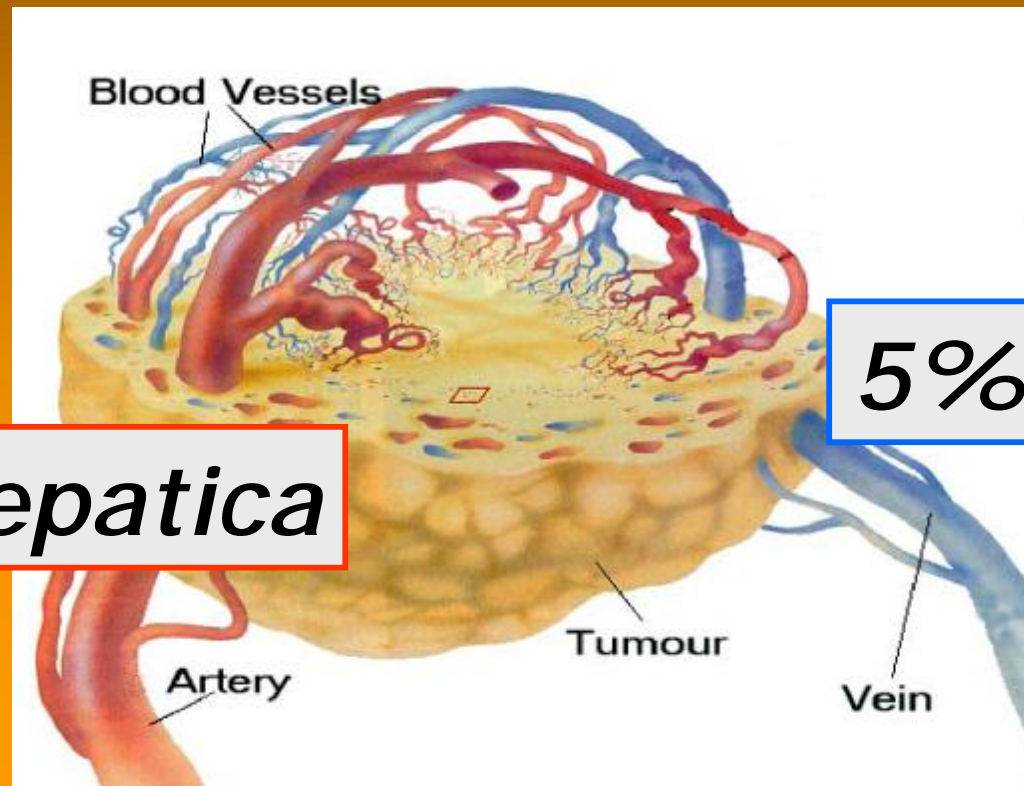
25% a. epatica

75% v. porta

TERAPIA INTRARTERIOSA

RATIONALE

2 - Vascolarizzazione tumorale (>5 mm)



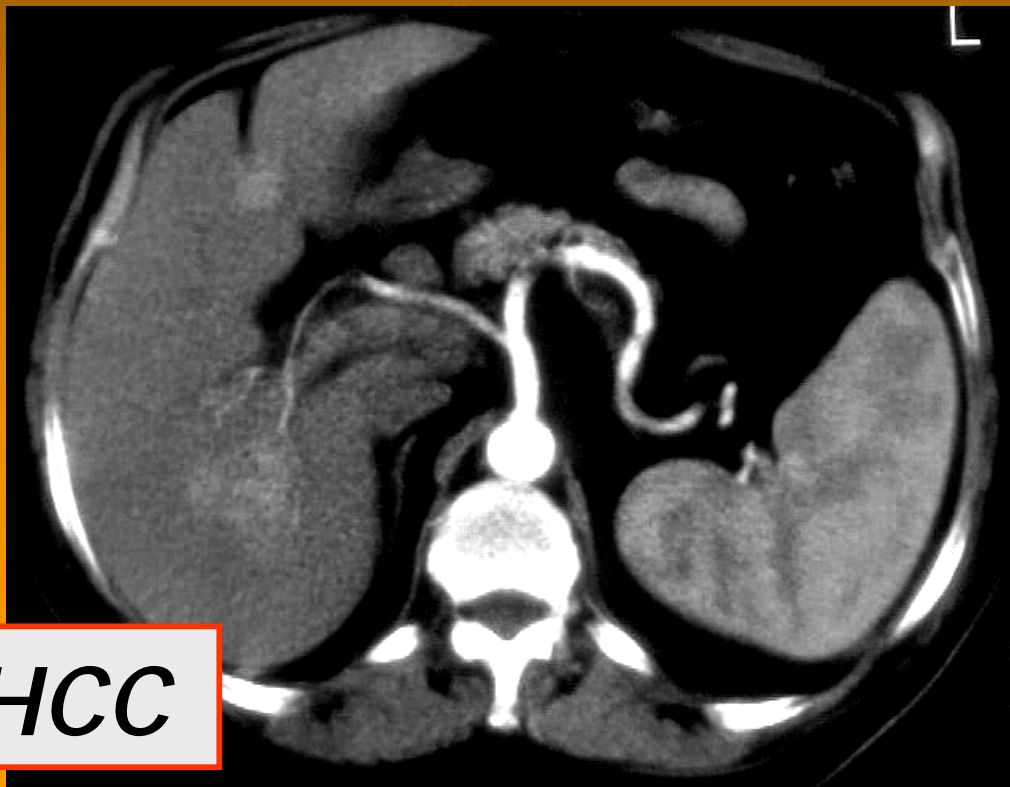
95% a. epatica

5% v. porta

TERAPIA INTRARTERIOSA

RATIONALE

2 - *Vascularizzazione tumorale*



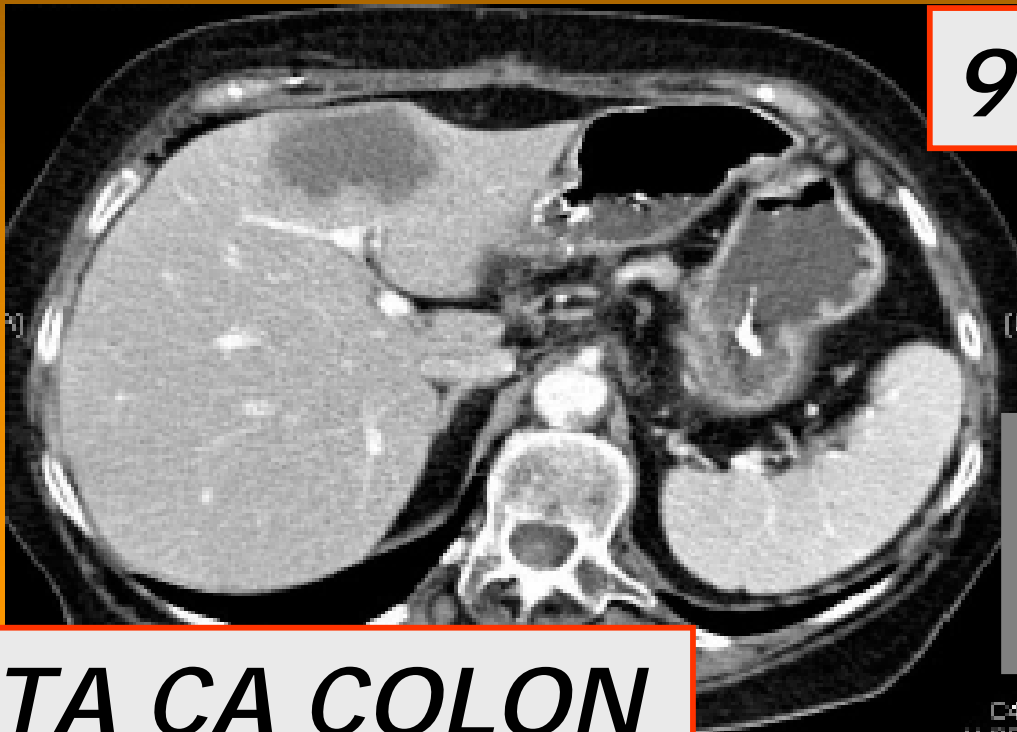
HCC

95% a. epatica

TERAPIA INTRARTERIOSA

RATIONALE

2 - Vascolarizzazione tumorale (>5 mm)



95% a. epatica



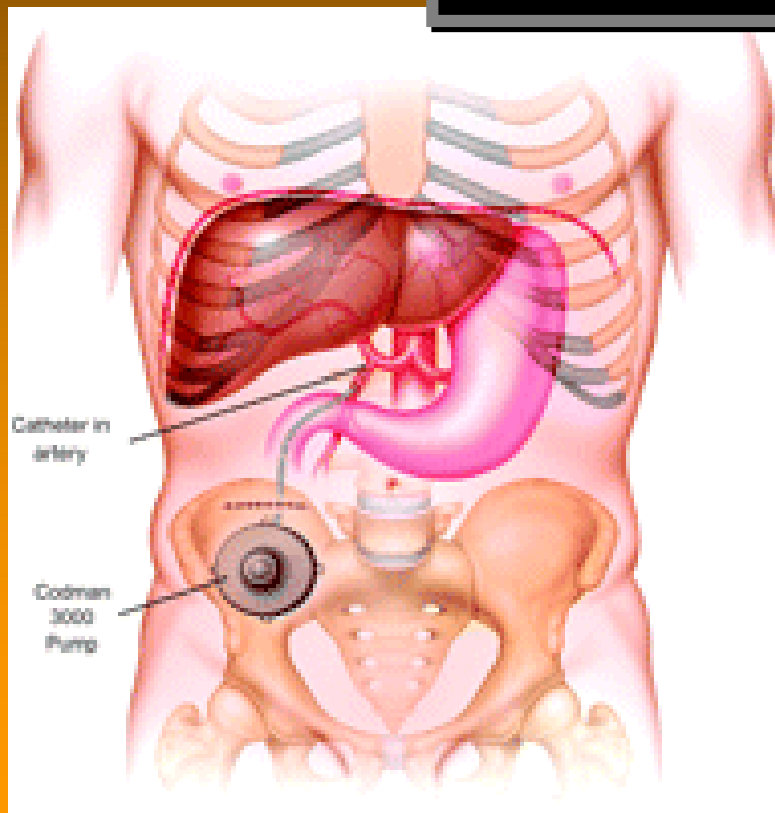
30% ipervascolari
40% isovascolari
30% ipovascolari

META CA COLON

TERAPIA INTRARTERIOSA

BACKGROUND

Cateteri Port



TERAPIA INTRARTERIOSA

BACKGROUND

Infusione arteriosa epatica (HAI)

[REDACTED] as a first-line treatment option for patients with unresectable CRLM . One apparent reason is that HAI [REDACTED]

[REDACTED] A recent meta-analysis of 10 randomized controlled trials comparing HAI chemotherapy alone with systemic chemotherapy did not find fluoropyrimidine-based HAI was associated with an overall survival advantage when compared with fluoropyrimidine- based systemic chemotherapy

Mocellin S, Pilati P, Lise M, Nitti D. Meta-analysis of hepatic arterial infusion for unresectable liver metastases from colorectal cancer [REDACTED]
[REDACTED] *J Clin Oncol* 2007;25(35):5649–5654.

TERAPIA INTRARTERIOSA

BACKGROUND

TACE o CEAT

Chemioembolizzazione convenzionale

TACE of Colorectal Cancer Liver Metastases

	pts.	line	drugs	embx.	ORR(%)	PFSV(mo)	mOSV (mo)
Tellez '98	30	SL	C/D/M	collagen	n.r.	n.r.	9

-No improvement of local oRR compared to historical HAI studies

Salman '02	24	SL	FU/INF	PVA	21	n.r.	11
Müller '03	66	FSL	FU/Mel	IO/GF	43	8	8
Hong '09	21	FSL	C/D/M	PVA	n.r.	n.r.	8
Vogl '09	463	SL	M/Gem/I	IO/DSM	15*	n.r.	14

TERAPIA INTRARTERIOSA

TECNICHE E TERAPIE INNOVATIVE

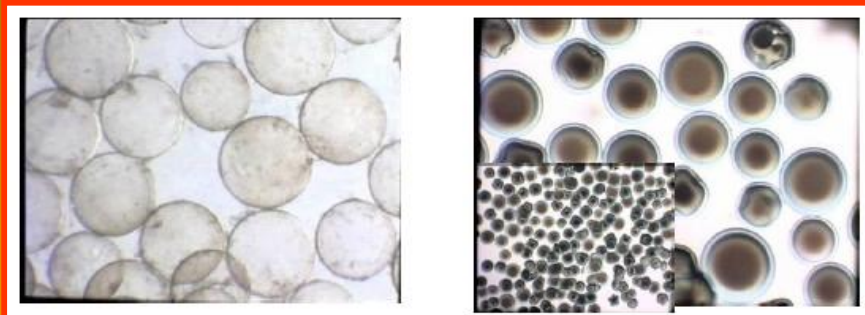
*Chemioembolizzazione DEB
(Drug Eluting Beads)*

Radioterapia interna (SIRT)

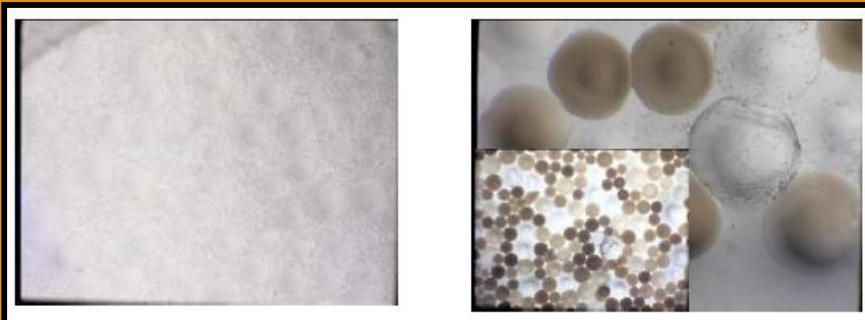
TERAPIA INTRARTERIOSA

TECNICHE E TERAPIE INNOVATIVE

Chemoembolizzazione DEB (Drug Eluting Beads)



DC beads™



Hepaspheres™

TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

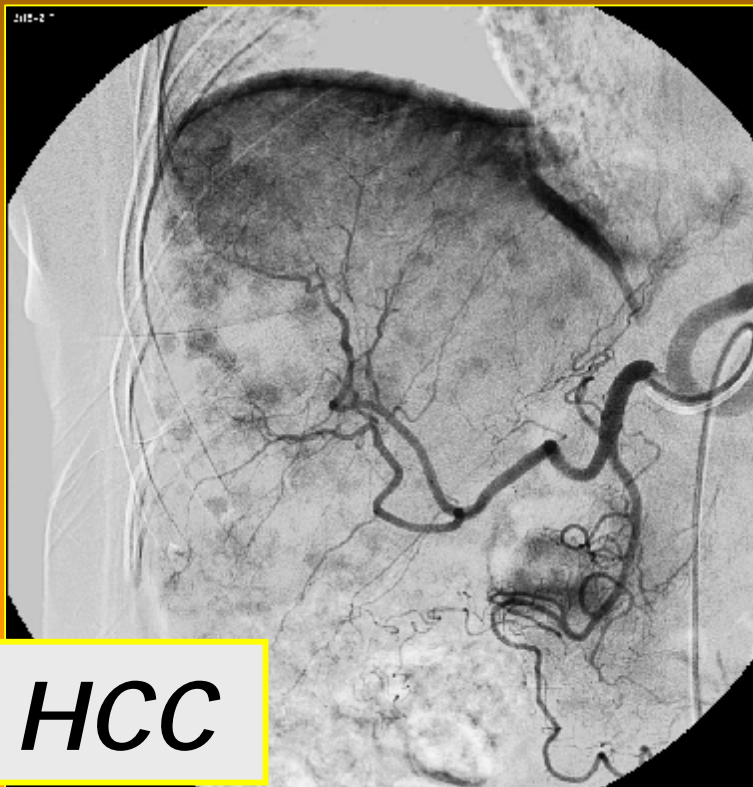
Microparticelle (100–500 μm), in Hydrogel PVA, idrofile , capaci di legare i chemioterapici (Doxorubicina, Irinotecan, Oxaliplatino) con legame ionico reversibile



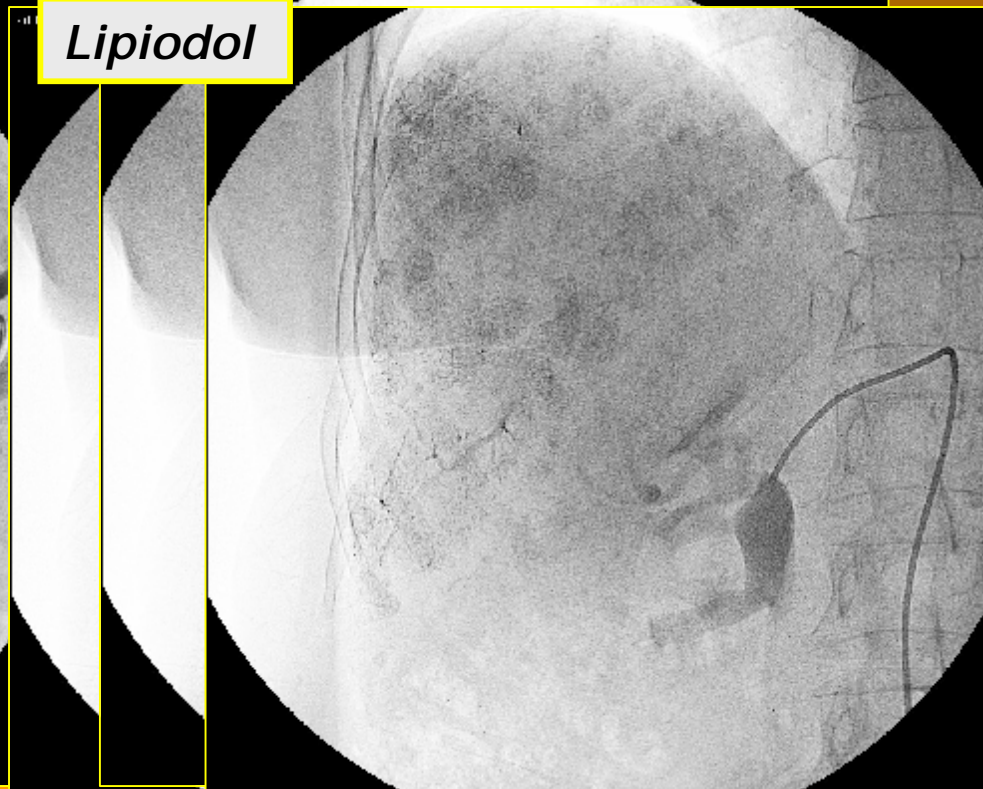
TERAPIA INTRARARTERIOSA

Chemioembolizzazione DEB

A differenza del Lipiodol non hanno tropismo elettivo per le neoformazioni, ma embolizzano i rami arteriosi in cui sono iniettati



Lipiodol



TERAPIA INTRARARTERIOSA

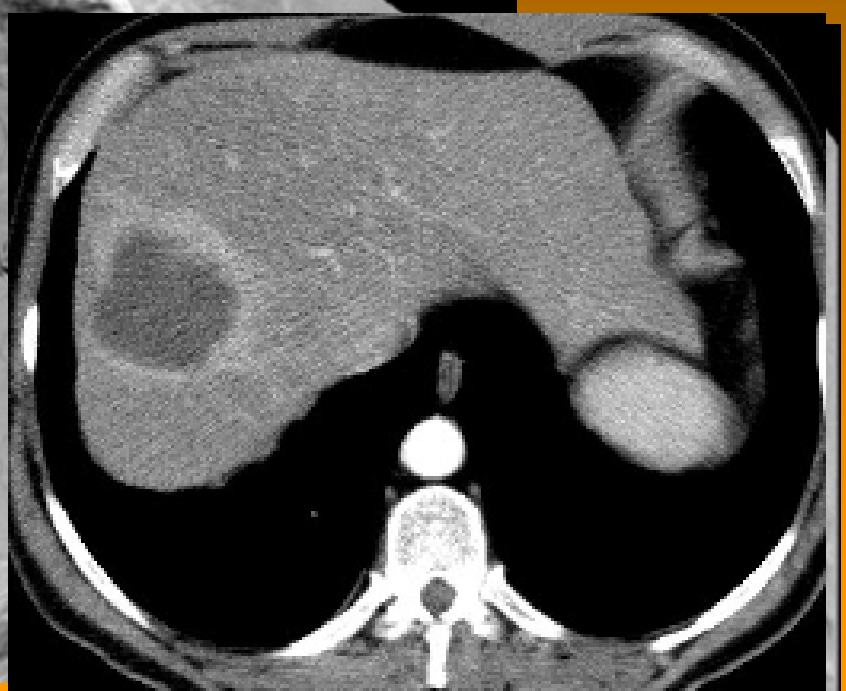
Chemioembolizzazione DEB

A differenza del Lipiodol non hanno tropismo elettivo per le neoformazioni, ma embolizzano i rami arteriosi in cui sono iniettati



META CA COLON

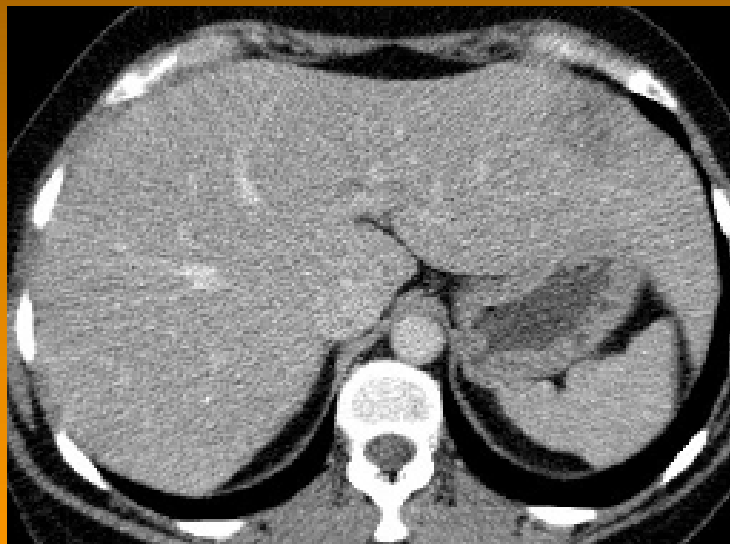
DEB



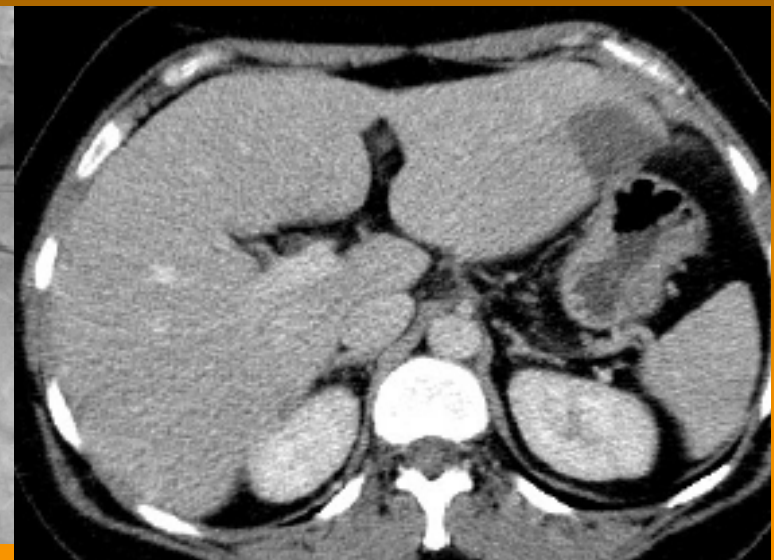
TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

Necessità di trattamenti multipli, segmentari o lobari, a distaza di settimane



DEB



TERAPIA INTRARARTERIOSA

Chemioembolizzazione DEB

Doppio effetto: ischemia + chemioterapia locale, risparmio del fegato normale e riduzione dei livelli sistemici di chemioterapico



Distribuzione del farmaco

TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

GEST 2011

E U R O P E



Global Embolization
Symposium and Technologies

First Announcement

April 27-30
Paris | France

www.gest2011.eu

10:15-12:00

Liver embolization: non HCC

Colorectal liver metastasis: treatment options

Colorectal liver metastasis: TACE

Colorectal liver metastasis: radioembolization

Colorectal liver metastasis: drug eluting beads

Portal vein embolization: technique and results

Treatment of benign liver tumours

Treatment of neuroendocrine tumours: medical therapy

Treatment of neuroendocrine tumours: embolization options

W.S. Rilling (Milwaukee/US)

J. Taieb (Paris/France)

Q&A: panel discussion

TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

Transarterial chemoembolisation (TACE) using irinotecan-loaded beads for the treatment of unresectable metastases to the liver in patients with colorectal cancer: an interim report

Background: Following failure of standard systemic chemotherapy, the role of hepatic transarterial therapy for colorectal hepatic metastasis continues to evolve as the experience with this technique matures. The aim of this study to gain a better understanding of the value of drug eluting bead therapy when administered to patients with unresectable colorectal hepatic metastasis.

Methods: This was an open-label, multi-center, single arm study, of unresectable colorectal hepatic metastasis patients who had failed standard therapy from 10/2006-10/2008. Patients received repeat embolizations with Irinotecan loaded beads(max 100 mg per embolization) per treating physician's discretion.

Results: Fifty-five patients underwent 99 treatments using Irinotecan drug eluting beads. The median number of total treatments per patient was 2(range of 1-5). Median length of hospital stay was 23 hours(range 23 hours - 10 days). There were 3 [REDACTED]. The median disease free and overall survival from the time of first treatment was 247 days and 343 days. Six patients(10%) were downstaged from their original disease status. Of these, four were treated with surgery and two with RFA. Neither number of liver lesions, size of liver lesions or extent of liver replacement($\leq 25\%$ vs $>25\%$) were predictors of overall survival. Only the presence of extrahepatic disease($p = 0,001$), extent of prior chemotherapy (failed 1st and 2nd line vs > 2 line failure)($p = 0,007$) were predictors of overall survival in multivariate analysis.

Conclusion: [REDACTED] in the treatment of patients as demonstrated by [REDACTED]

TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

DEBIRI on colorectal cancer liver metastases: personal experience and tips & tricks

- 148 patients treated
- 254 TACE
- 100% technical success
- 1 major complication (acute pancreatitis)

TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

DEBIRI on colorectal cancer liver metastases: personal experience and tips & tricks

Only DEBIRI 53/116

- Median survival time 15,7months
- Median duration of response 3,2months
- Median time to progression 4,6months

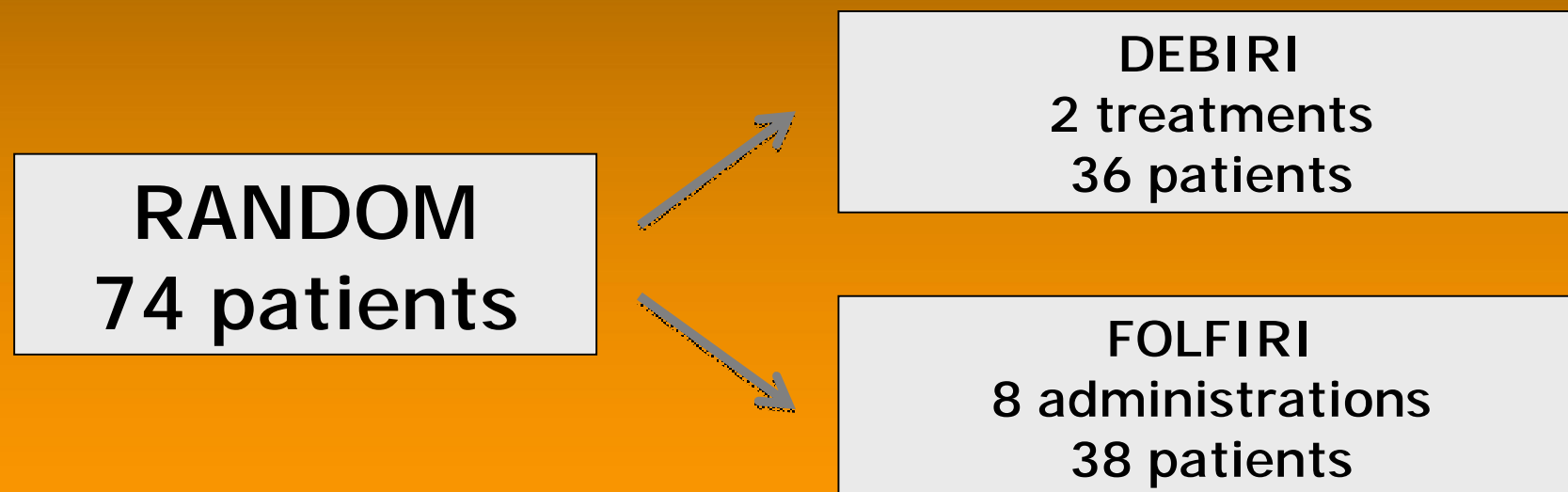
DEBIRI + Sistemic therapy 63/116

- Median survival time 24,6months
- Median duration of response 8,2months
- Median time to progression 10,2months

TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL ASSESSING SURVIVAL AT 3 YEARS OF POLYVINYL ALCOHOL MICROSPHERES PRELOADED WITH IRINOTECAN (DEBIRI) VS. FOLFIRI IN PATIENTS WITH HEPATIC METASTASES FROM COLORECTAL CANCER



TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL ASSESSING SURVIVAL AT 3 YEARS OF POLYVINYL ALCOHOL MICROSPHERES PRELOADED WITH IRINOTECAN (DEBIRI) VS. FOLFIRI IN PATIENTS WITH HEPATIC METASTASES FROM COLORECTAL CANCER

	DEBIRI 35 pts	FOLFIRI 35 pts
COMPLETE & PARTIAL RESPONSES	24 (68.6%)	7 (20%)
STABLE DISEASE	4 (11.4%)	12 (34,3%)
PROGRESSION	7 (20%)	16 (45,7%)

TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL ASSESSING SURVIVAL AT 3 YEARS OF POLYVINYL ALCOHOL MICROSPHERES PRELOADED WITH IRINOTECAN (DEBIRI) VS. FOLFIRI IN PATIENTS WITH HEPATIC METASTASES FROM COLORECTAL CANCER

- [redacted] reported [redacted] (pain, nausea, fever, vomiting) than FOLFIRI. These symptoms can be controlled with periprocedural medications
- [redacted] (mainly leukopenia, anaemia, diarrhoea, asthenia and alopecia) were [redacted]
- Our study is the [redacted] an intra-arterial hepatic therapy (DEBIRI) over systemic chemotherapy (FOLFIRI) in patients failing at least 2 lines of chemotherapy.
- [redacted] when compared to systemic FOLFIRI

TERAPIA INTRARTERIOSA

Chemoembolizzazione DEB

Feasibility of neoadjuvant transarterial chemoembolization (TACE) using irinotecan beads (DEBIRI) before hepatectomy (HPX) for easily resectable colorectal liver metastases (RCLM): A phase II study.

Conclusions [REDACTED] pre-HPX for RCLM
and is [REDACTED]

TERAPIA INTRARTERIOSA

Chemioembolizzazione DEB

DC BEAD MANAGING METASTATIC COLORECTAL CANCER CLINICAL EXPERIENCE FROM GERMANY

- TACE using Irinotecan-eluting DC-Beads is [redacted] and [redacted] of colorectal liver metastases.
- The extend of [redacted] seems to [redacted] in the grade of tumor [redacted]
- [redacted] surrounding tumor necrosis were seen [redacted] in the majority of [redacted] despite complete necrosis in CT
- [redacted] is associated with [redacted]

TERAPIA INTRARTERIOSA

Chemoembolizzazione DEB

**DC BEAD MANAGING METASTATIC
COLORECTAL CANCER
CLINICAL EXPERIENCE FROM GERMANY**

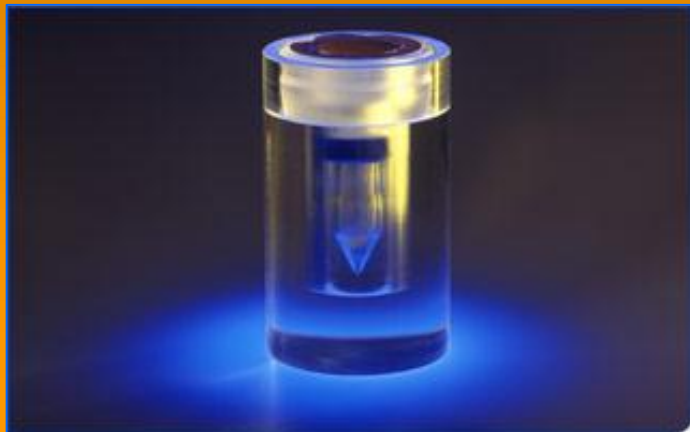
- [redacted] and HIF-1 α [redacted] and incomplete necrosis
[redacted] use of Bevacizumab?

TERAPIA INTRARTERIOSA

Radioterapia interna (SIRT)



SIR-Spheres®

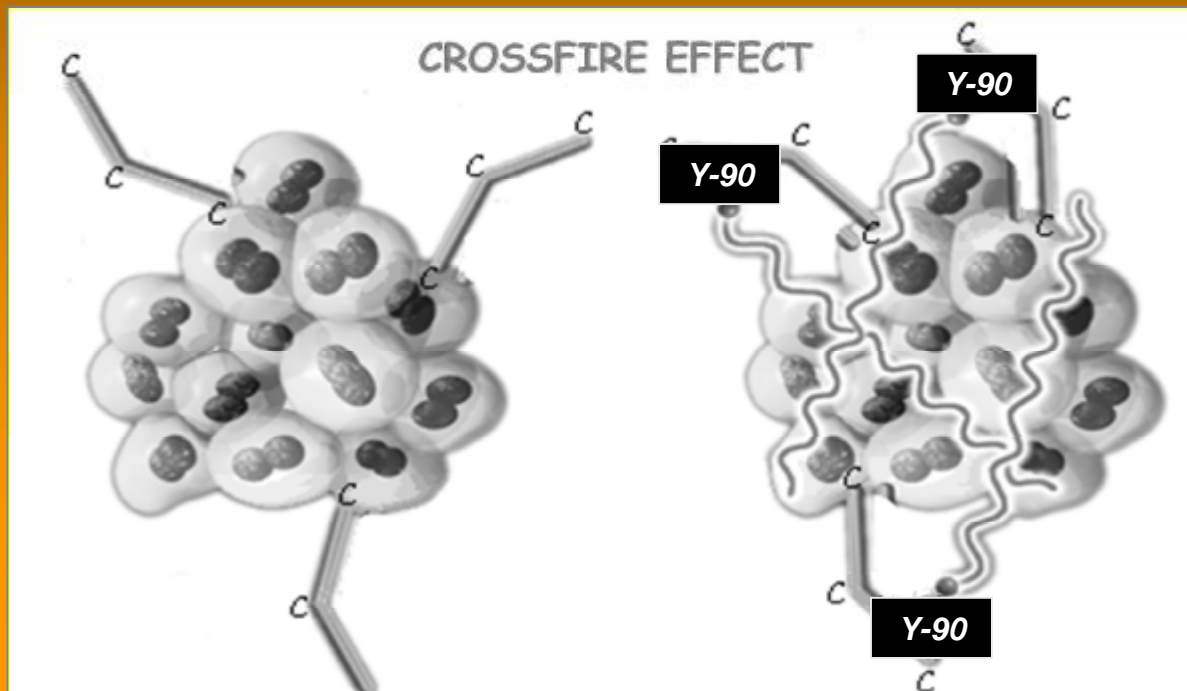


TheraSphere®

TERAPIA INTRARTERIOSA

Radioterapia interna (SIRT)

Microsfere (15–35 μm), di resina o vetro impregnate di Yttrio-90 (Y-90), β emittente, con penetrazione tissutale 1,1 cm



TERAPIA INTRARTERIOSA

Radioterapia interna (SIRT)

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

CONCLUSION: Radioembolization with (90)Y-resin microspheres plus FU is **more effective and better tolerated** than FU alone. This procedure is a valid therapeutic option for chemotherapy-refractory liver-limited mCRC.

TERAPIA INTRARTERIOSA

Radioterapia interna (SIRT)

Multi-centre phase II clinical trial of yttrium-90 resin microspheres alone in unresectable, chemotherapy refractory colorectal liver metastases.

RESULTS: 1 patient [redacted], 11 [redacted], 12 [redacted], 22 [redacted]; 4 (8%) were non-evaluable. Median overall survival was 12.6 months (95% CI, 7.0-18.3); 2-year survival was 19.6%

CONCLUSION: Radioembolisation produced [redacted] and [redacted] in patients with advanced, unresectable and chemorefractory mCRC

TERAPIA INTRARTERIOSA

Radioterapia interna (SIRT)

Radioembolization of colorectal hepatic metastases using yttrium-90 microspheres

CONCLUSIONS: [REDACTED] appears to provide sustained disease stabilization with [REDACTED] [REDACTED] with [REDACTED] at the time of Y90 appeared to [REDACTED]

TERAPIA INTRARTERIOSA

Radioterapia interna (SIRT)

Recommendations for radioembolization of hepatic malignancies using yttrium-90 microsphere brachytherapy: a consensus panel report from the radioembolization brachytherapy oncology consortium

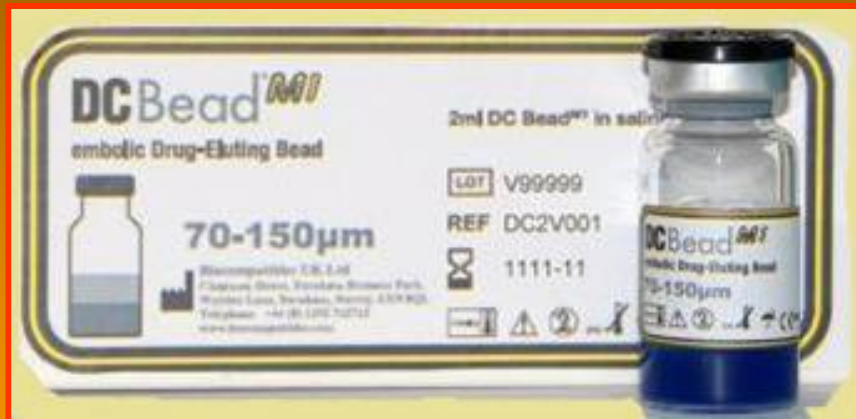
There are only [REDACTED]
Among the changes that are described are [REDACTED]
[REDACTED] with [REDACTED]
(a phenomenon that has been termed "radiation lobectomy"), induction of [REDACTED]
and [REDACTED]
The [REDACTED] actors for development of these adverse effects,
and their influence on liver insufficiency [REDACTED]

Relative [REDACTED]
irreversibly elevated serum bilirubin levels

TERAPIA INTRARATERIOSA

Work in progress

DEB Ultrasmall (70-150 μm)



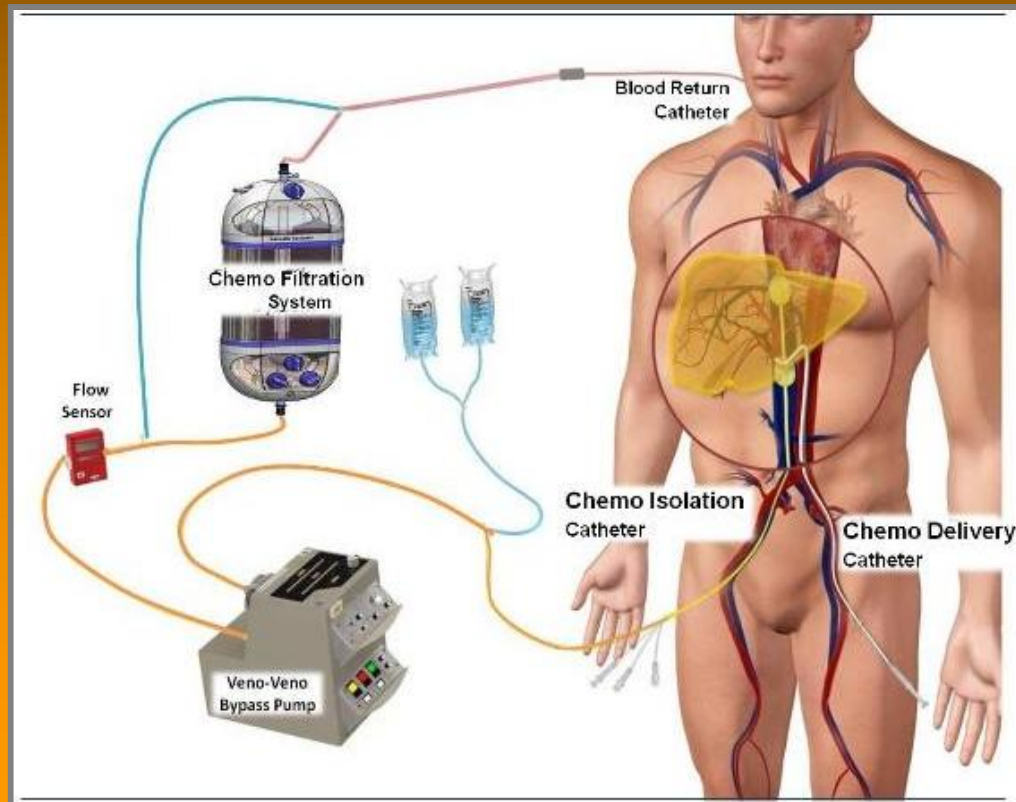
DC Bead^{MI}

- Maggiore penetrazione nel letto vascolare tumorale
- Trattamento metastasi ipovascolari
- Trattamento micrometastasi satelliti

TERAPIA INTRARTERIOSA

Work in progress

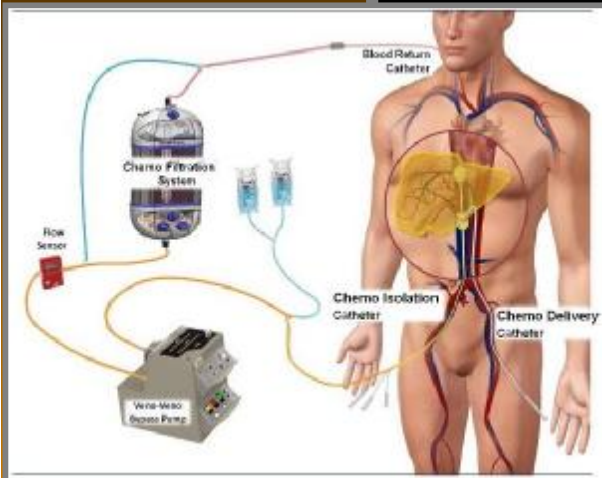
Chemosaturation



TERAPIA INTRARARTERIOSA

Work in progress

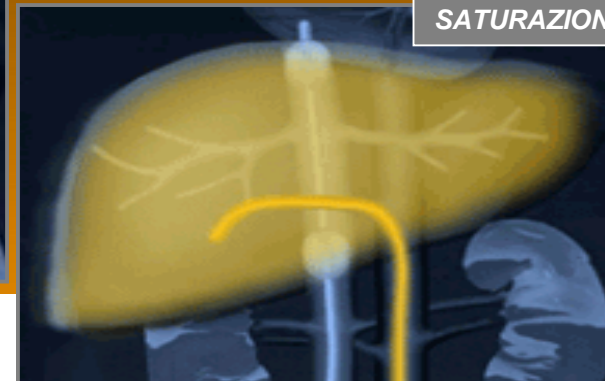
Chemosaturation



ISOLAMENTO



SATURAZIONE



- **ISOLAMENTO** Tratta l'intero parenchima epatico
- **SATURAZIONE** Permette una dose 100x di chemioterapico nella sede tumorale
- **FILTRAZIONE** Controllo della tossicità sistemica

FILTRAZIONE



TERAPIA INTRARTERIOSA



Azienda Ospedaliero-Universitaria , Ferrara, Italy - VASCULAR AND INTERVENTIONAL RADIOLOGY UNIT



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Alberta Manservigi
Silvia Giorgi
Patrizia Busi
Mara Simoni
Isabella Veronesi

Daniela Fagjoli

GRAZIE PER L'ATTENZIONE

GRAZIE PER L'ATTENZIONE