



*Società
Medico Chirurgica
di Ferrara*



dal 1846

AGGIORNAMENTI NELL'APPROCCIO DIAGNOSTICO-TERAPEUTICO AI TUMORI NEUROENDOCRINI GASTRO-ENTERO-PANCREATICI

Ablazione non chirurgica delle metastasi epatiche

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET

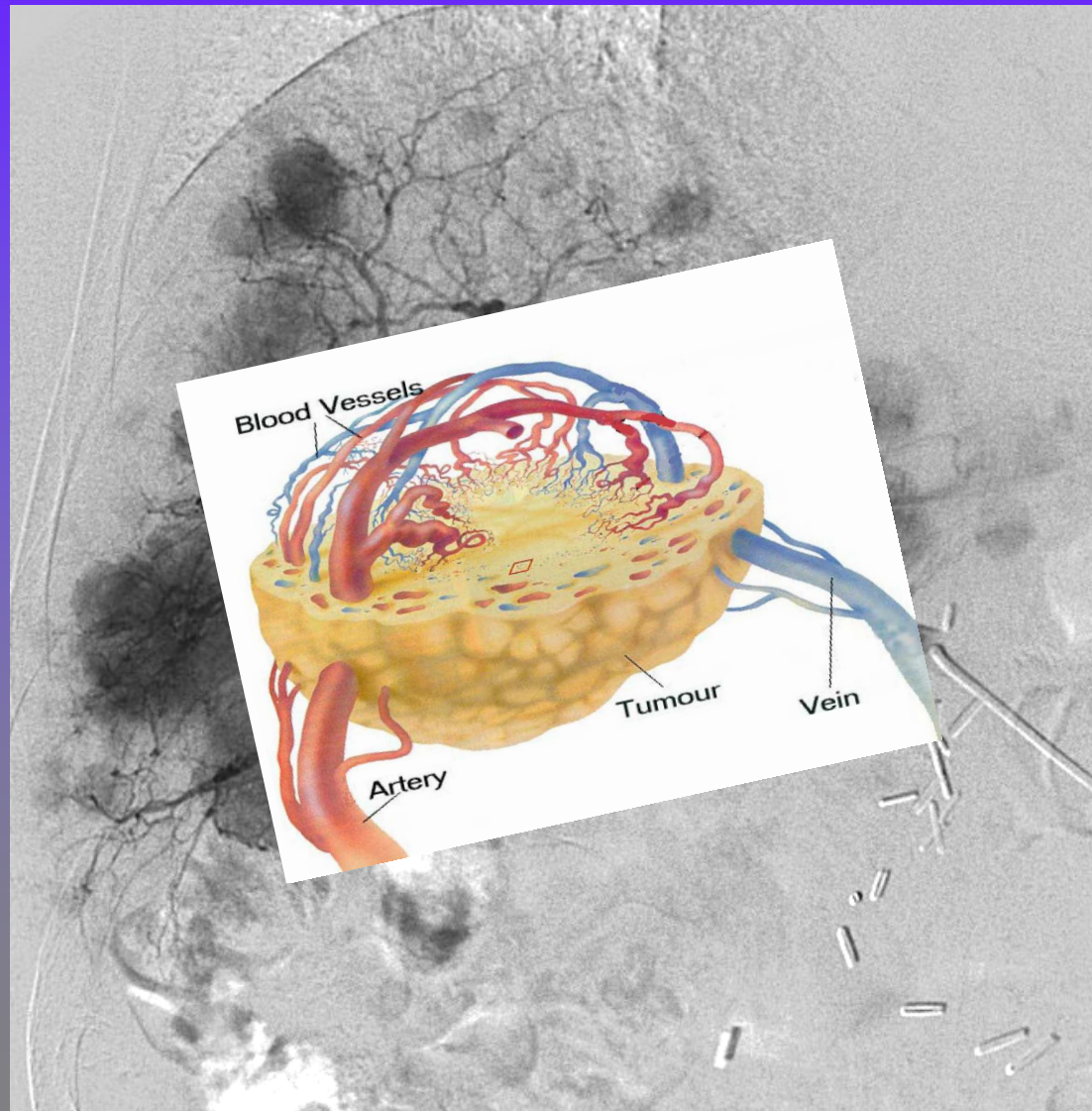
Roberto Galeotti

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Dipartimento di Diagnostica per Immagini e Medicina di Laboratorio

U.O.S. Radiologia Vascolare ed Interventistica



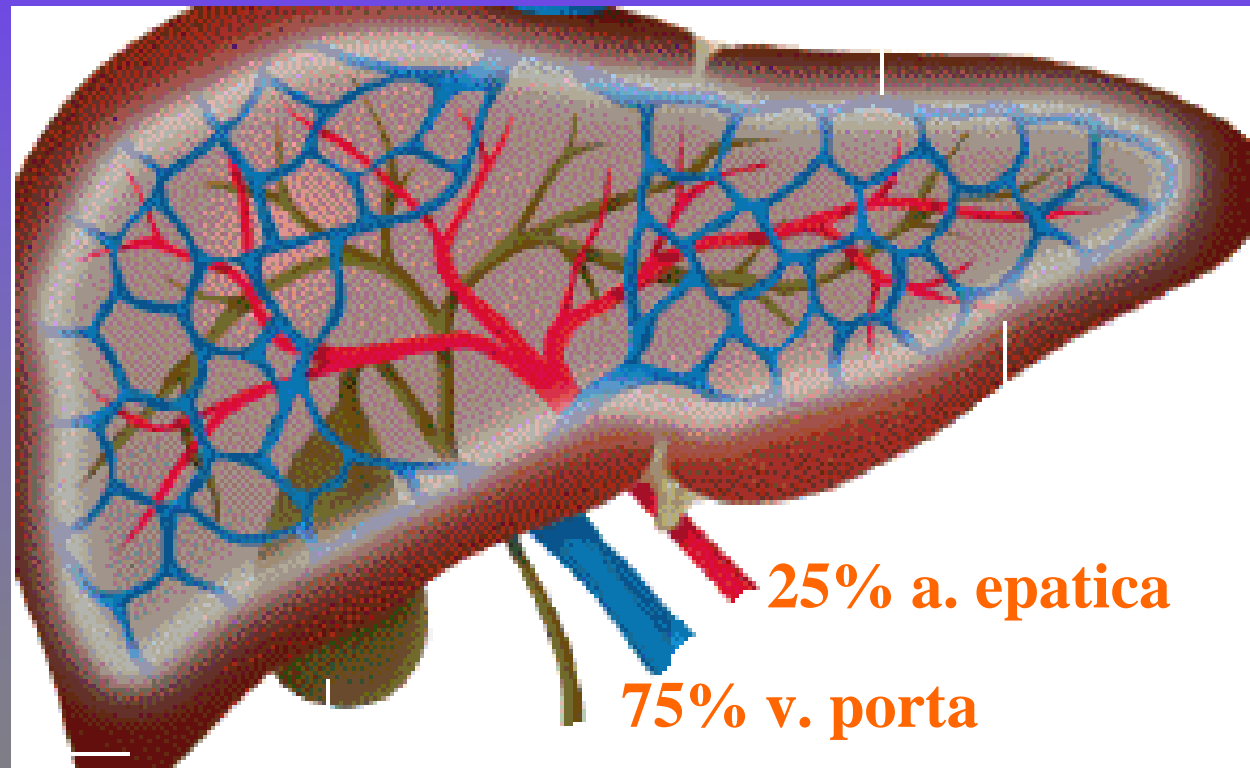
TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET



TERAPIA TRANSARTERIOSA
METASTASI EPATICHE DA NET

- PRESUPPOSTI -

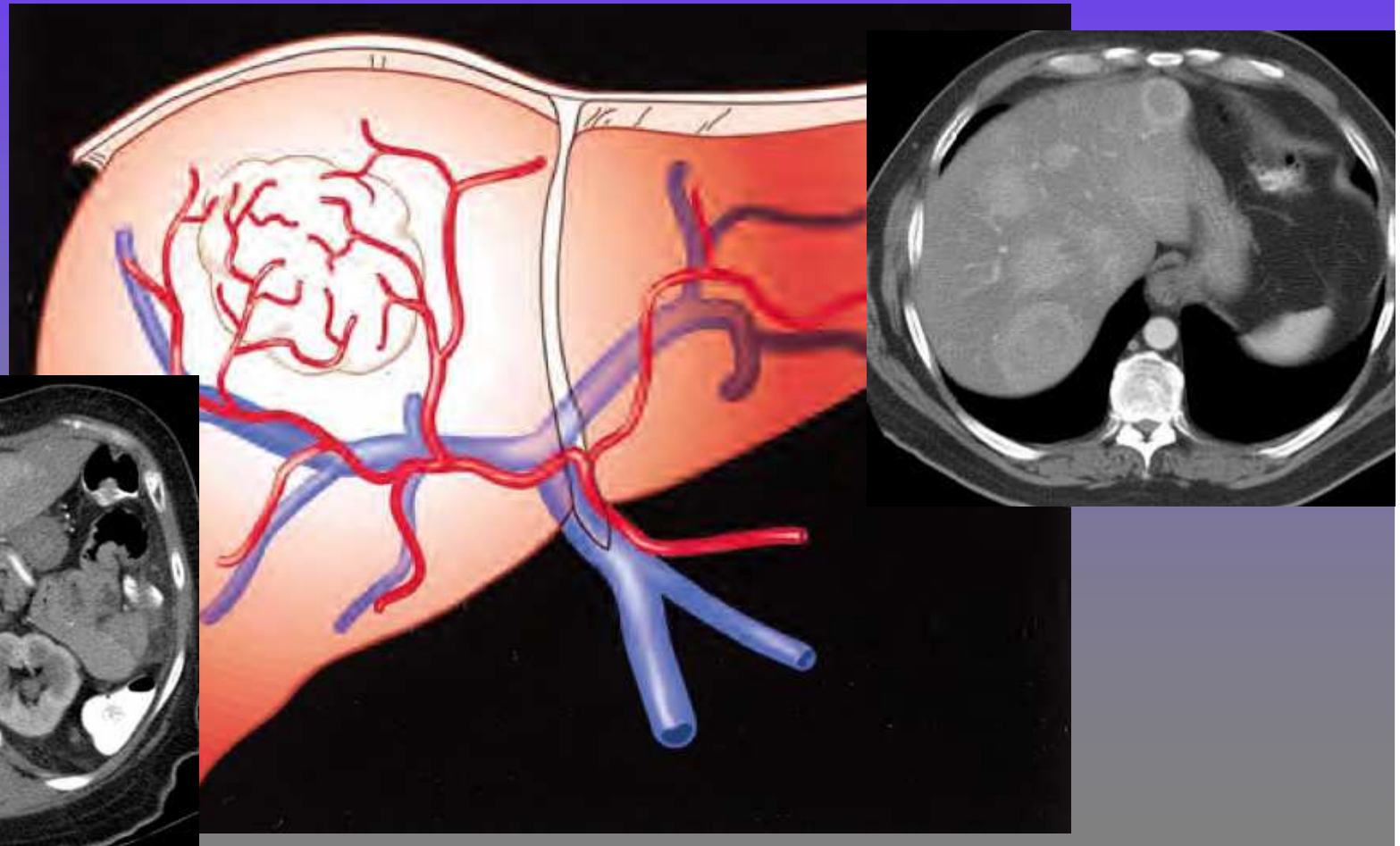
1 – Doppia vascolarizzazione epatica



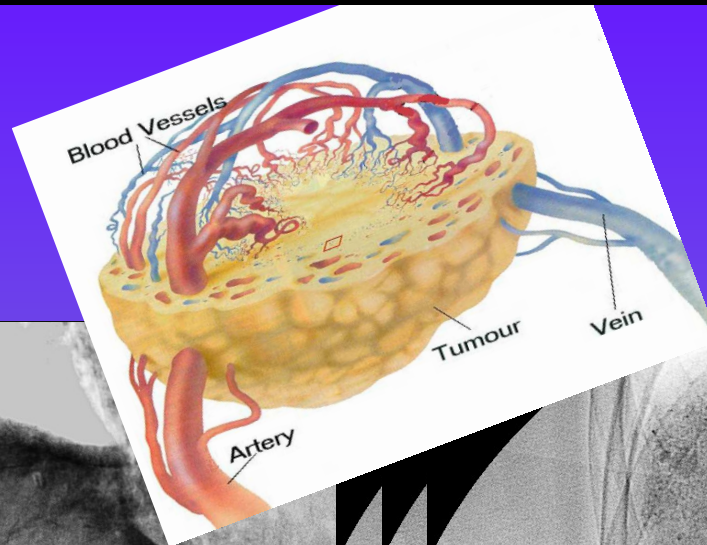
TERAPIA TRANSARTERIOSA
METASTASI EPATICHE DA NET

- PRESUPPOSTI -

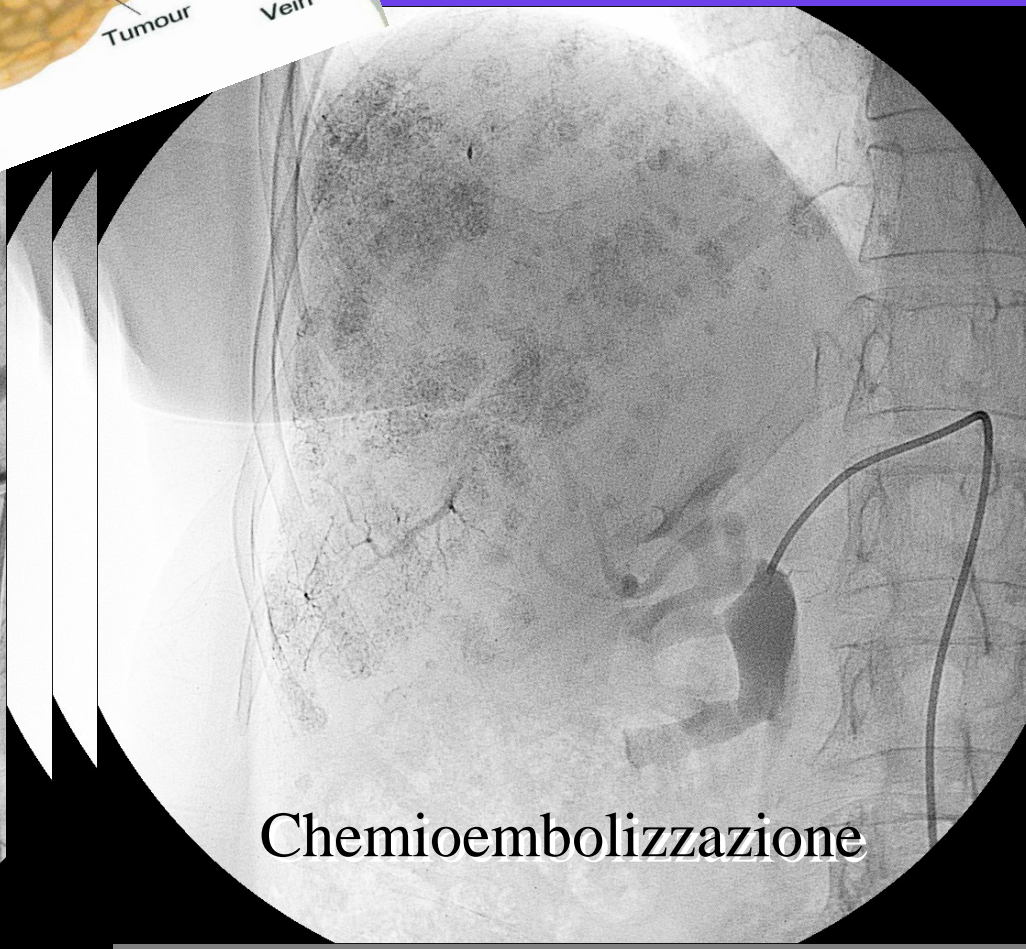
2 – Vascolarizzazione arteriosa delle metastasi epatiche da neoplasie neuroendocrine



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215-2 F



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Neuroendocrine tumor metastases to the liver:
radioembolization, TACE, bland embo or drug eluting
particles

T. de Baère (Villejuif/FR)

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET

TECNICHE

- BLAND EMBOLIZATION (TAE)
- CHEMOEMBOLIZATION (TACE)
- DRUG ELUTING BEADS (DEB TACE)
- RADIOEMBOLIZATION

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BLAND EMBOLIZATION (TAE)



Microsfere



Spugna gelatinica



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CHEMOEMBOLIZATION (TACE)

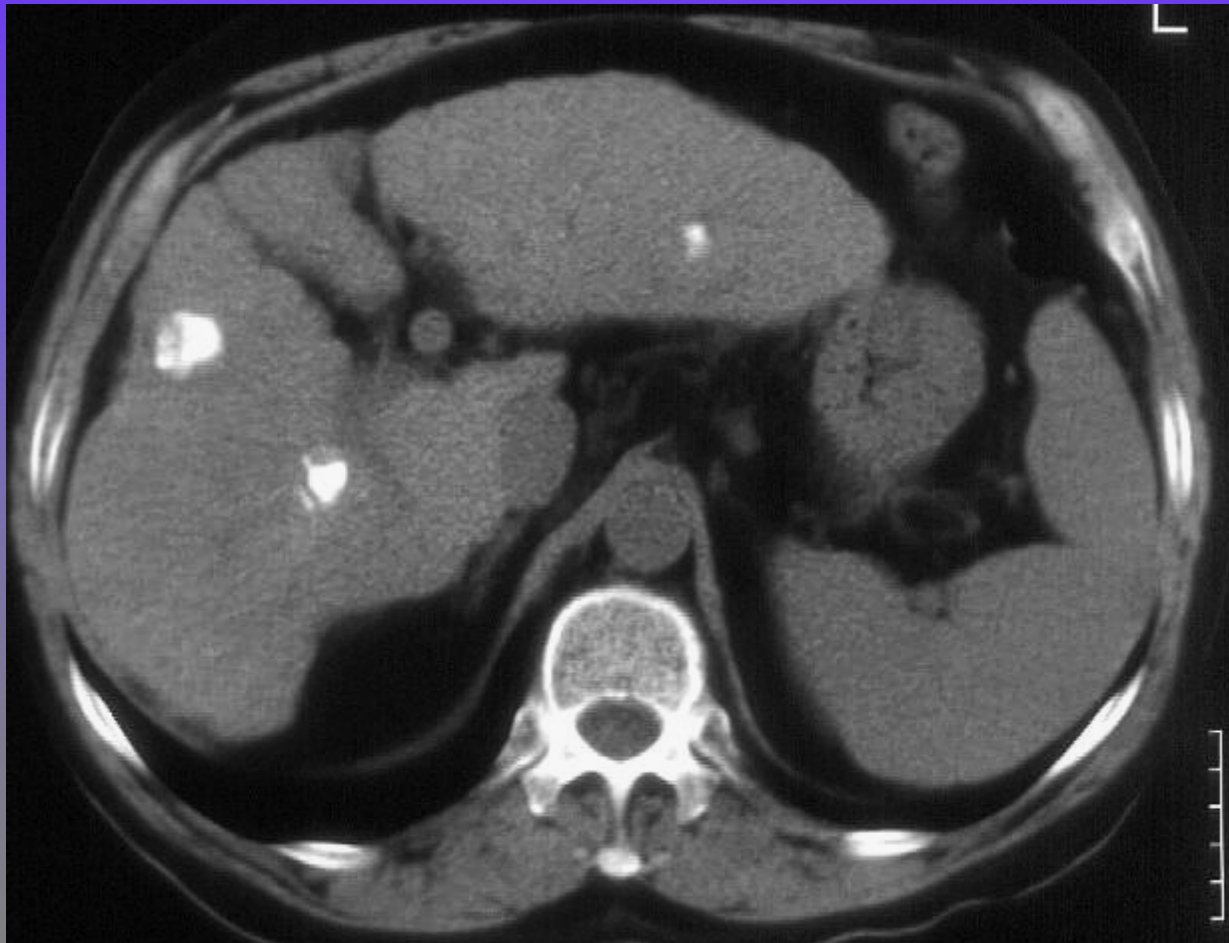
Tropismo del Lipiodol Ultrafluid (LUF) per i tumori vascolarizzati dall'arteria epatica



Kanematsu T., Inokuchi K.
*Treatment of liver cancer and concomitant
esophageal varices*
Nippon Geka Gakkai Zasshi 1983;84(9) :923-6

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CHEMOEMBOLIZATION (TACE)



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• DRUG ELUTING BEADS (DEB TACE)



Microsfere a rilascio di farmaco

Razionale di Utilizzo

- Prolungato rilascio di farmaco all'interno dei rami arteriosi tumorali
- Incremento dell'effetto citotossico sulle cellule neoplastiche senza incremento della tossicità d'organo
- Decremento della dispersione sistemica del chemioterapico con conseguente riduzione degli effetti collaterali



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DC Bead

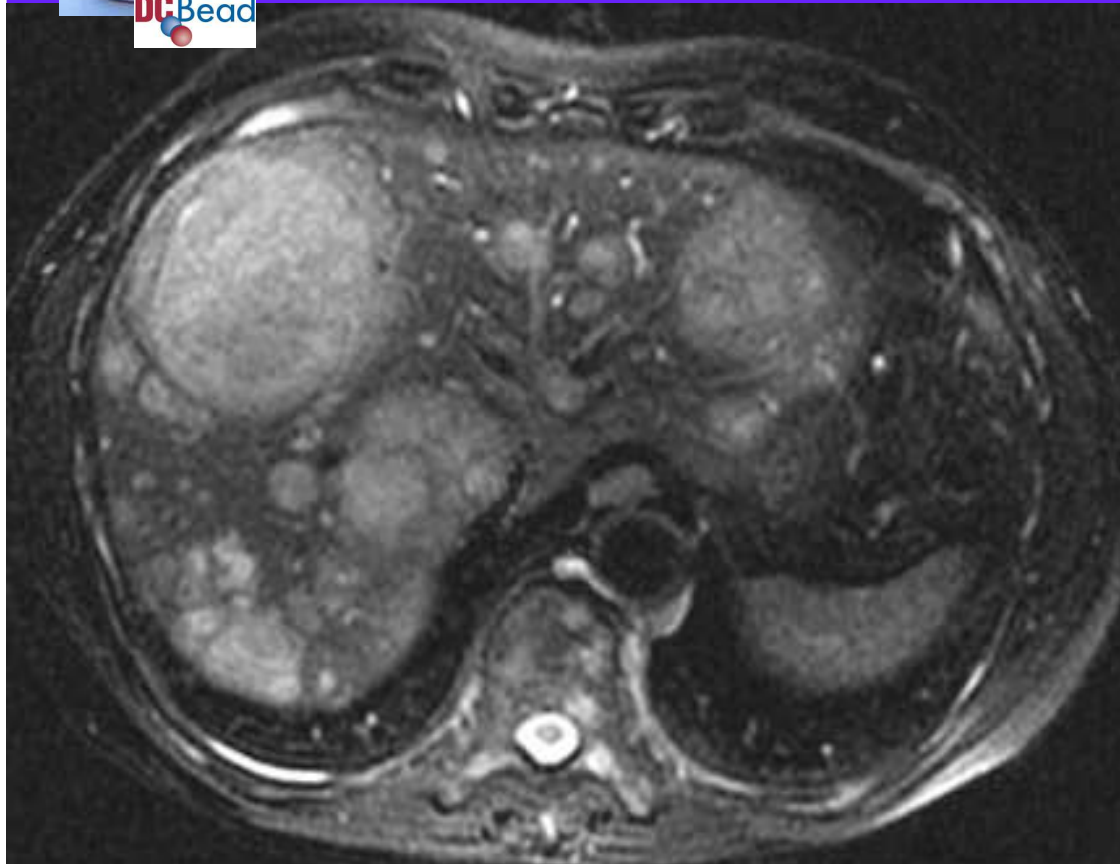


HepaSpheres™
EXPANDING MICROSPHERES

S (DEB TACE)

...e con microsfere
...e superselettiva

~~(Precision TACE)~~



Sulla base dell'estensione tumorale intraepatica (grandezza e numero delle lesioni, estensione mono o bilobare) può essere necessario modulare il trattamento in più sessioni ad intervalli di 30-60 gg

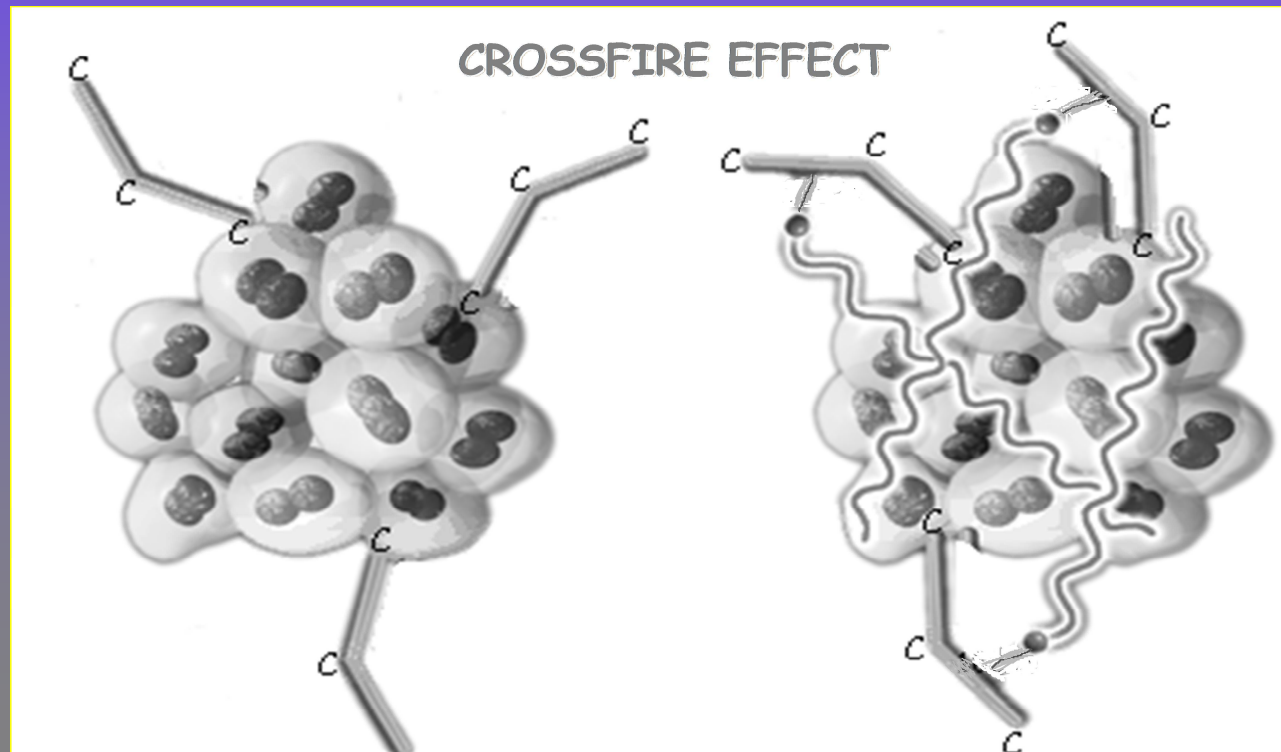
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•RADIOEMBOLIZATION

SIR-Spheres®
Yttrium-90 microspheres
Tomorrow's standard practice in the
treatment of Liver Cancer



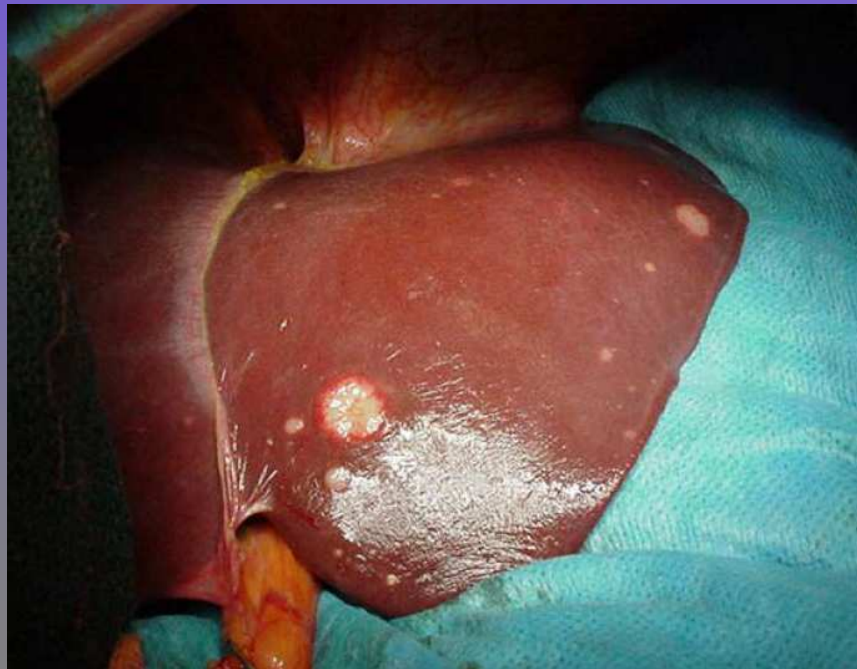
Lipiodol Radioattivo



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CRITERI DI INCLUSIONE

**Controindicazione alla chirurgia e/o
alle procedure ablative locoregionali**



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METASTASI EPATICHE DA NET

CONTROINDICAZIONI

- **Trombosi portale**
- **Bilirubinemia >2-3 ml/dL**
- **Estensione tumorale epatica >75%**

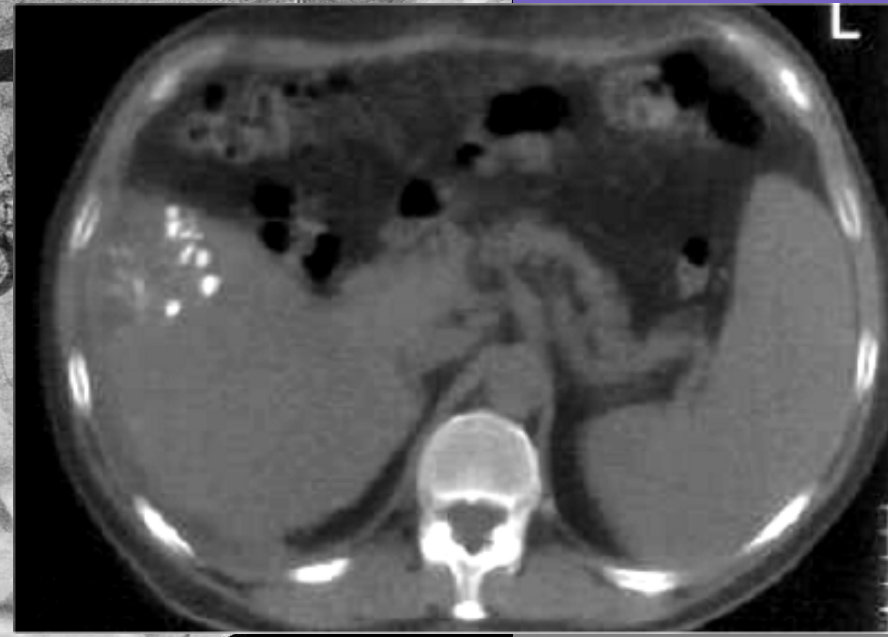
TERAPIA TRANSARTERIOSA
METASTASI EPATICHE DA NET

FATTORI LIMITANTI

- **Metastasi necrotiche e poco vascolarizzate**
- **Patologie o varianti anatomiche vascolari**

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET

- Metastasi necrotiche e poco vascolarizzate



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COMPLICANZE

-Sindrome post-embolizzazione
(dolore, febbre, nausea, ileo)

70%

- Colecistite
- Arterite
- Ascesso epatico
- Stenosi biliari
- Insufficienza epatica
- Sindrome epato-renale
- Pancreatite

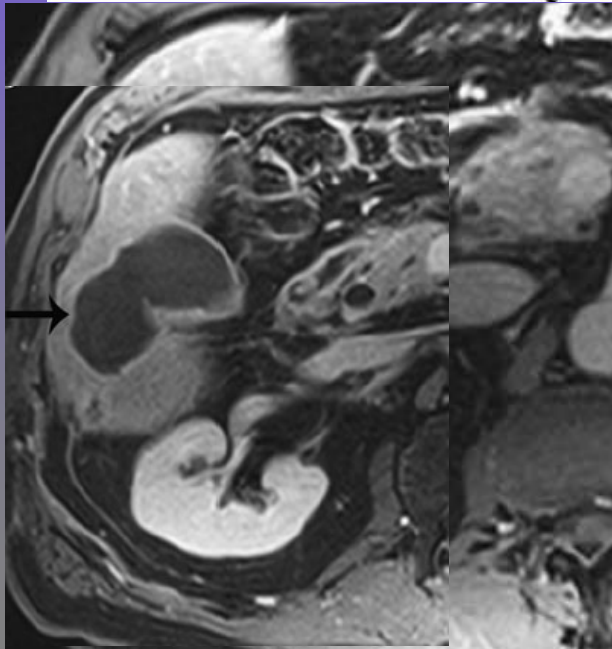
4%

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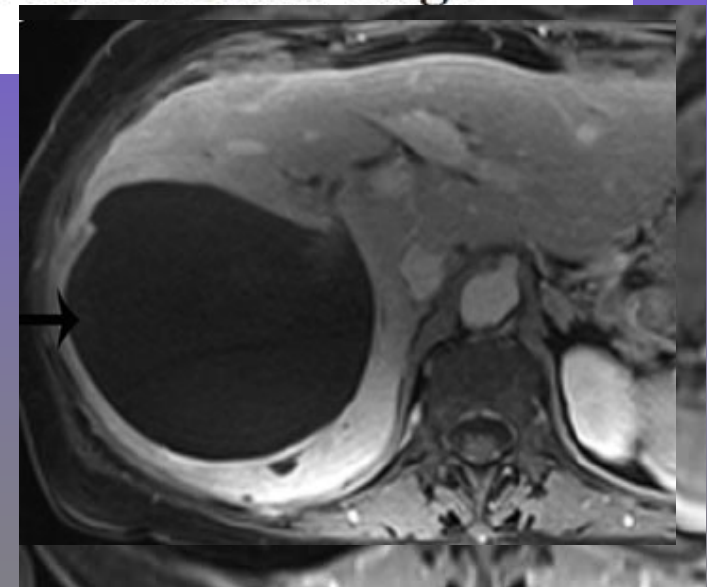
COMPLICANZE

Nikhil Bhagat • Diane K. Reyes • Mingde Lin •
Ihab Kamel • Timothy M. Pawlik • Constantine Frangakis •
J. F. Geschwind

**Phase II Study of Chemoembolization With Drug-Eluting Beads
in Patients With Hepatic Neuroendocrine Metastases: High
Incidence of Biliary Injury**



Bilomas 54%



Cardiovasc Intervent Radiol (2013) 36:449–459

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET

COMPLICANZE

Nikhil Bhagat • Diane K. Reyes • Mingde Lin •
Ihab Kamel • Timothy M. Pawlik • Constantine Frangakis •
J. F. Geschwind

**Phase II Study of Chemoembolization With Drug-Eluting Beads
in Patients With Hepatic Neuroendocrine Metastases: High
Incidence of Biliary Injury**

Conclusions Although biloma and liver abscess are known risks after TACE, the high incidence in our study population was unexpected and forced interruption of the trial.

Cardiovasc Intervent Radiol (2013) 36:449–459

TERAPIA TRANSARTERIOSA
METASTASI EPATICHE DA NET

RISULTATI

EFFETTO SULLA SINTOMATOLOGIA

EFFETTO SULLA MASSA TUMORALE

EFFETTO SULLA SOPRAVVIVENZA

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EFFETTO SULLA SINTOMATOLOGIA

Remissione dei sintomi nel 60% - 100%
dei pazienti trattati

Table 1 Symptoms and hormonal secretion

Reference	No./Type	Chemotherapy	Sustained relief (%) (in symptomatic pts)	5-HIAA decrease > 50% (results only for CT)
Therasse <i>et al.</i> (1993)	23/CT	ADR	100	91
Ruszniewski <i>et al.</i> (1993)	18/CT 5/ICC	ADR	73	57
Clouse <i>et al.</i> (1994)	14/CT*	ADR	90	69
Diaco <i>et al.</i> (1995)	10/CT	CDDP, MMC, ADR**	100	—
Ruszniewski & Malka (2000)	8/CT 7/ICC	STZ (1.5 g/m ²)	67	50
Roche <i>et al.</i> (2003)	10/CT 4/other	ADR	70	75

ICC, islet cell tumor; CT, patients with carcinoid syndrome mostly from midgut origin; ADR, adriamycin; MMC, mitomycin; CDDP, cisplatin.

*Mostly CT; all 14 tumors were functionally active; ** sequential intra-arterial 5-fluorouracil also administered.

D O'Toole, F Marie and P Ruszniewski.

Ablative therapies for liver metastases of endocrine tumors *Endocrine-Related Cancer* (2003) 10 463-468

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EFFETTO SULLA MASSA TUMORALE

Risposta oggettiva **33% – 86 %**

Table 2 Variations in tumor size (according to WHO criteria)

Reference	No./Type	Objective response (%)	Mean duration (months)	Progression rate (%)
Therasse <i>et al.</i> (1993)	23/CT	35	—	12
Ruszniewski <i>et al.</i> (1993)	18/CT 5/ICC	33	21	17
Mavligit <i>et al.</i> (1993)	5/ICC	80	18.5	—
Clouse <i>et al.</i> (1994)	20/CT or ICC	78	6–8.5	—
Diaco <i>et al.</i> (1995)	10/CT	60	42.5	—
Ruszniewski & Malka (2000)	8/CT 7/ICC	53	10.5	26
Roche <i>et al.</i> (2003)	10/CT 4/other	86	—	14

D O'Toole, F Marie and P Ruszniewski.

Ablative therapies for liver metastases of endocrine tumors *Endocrine-Related Cancer* (2003) 10 463-468

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET

RISULTATI

EFFETTO SULLA SOPRAVVIVENZA

Neuroendocrine Hepatic Metastases
Does Aggressive Management Improve Survival?

John G. Touzios, MD, James M. Kiely, MD,* Susan C. Pitt, BA,* William S. Rilling, MD,†
Edward J. Quebbeman, MD, PhD,* Stuart D. Wilson, MD,* and Henry A. Pitt, MD**

(Ann Surg 2005;241: 776–785)

Results: Median and 5-year survival were 20 months and 25% for the Nonaggressive group, >96 months and 72% for the Resection/Ablation group, and 50 months and 50% for the TACE group. The survival for the Resection/Ablation and the TACE groups was significantly better ($P < 0.05$) when compared with the Nonaggressive group. Patients with more than 50% liver involvement had a poor outcome ($P < 0.001$).

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TABLE 1: Outcomes of hepatic arterial embolization in large published case series.

Author	Type of embolization	No. of patients/No. of embolization procedures	Survival	Comments
Bloomston et al. [36]	TACE	122/156	PFS: 10 months OS: 33 months 5-yr survival: 28%	Symptom improvement associated with increase in OS
Swärd et al. [33]	TAE	107/213	OS: 56 months	Increased survival with reduction in 5-HIAA; reduced survival with increased AST or chromogranin A
Pitt et al. [28]	TACE and TAE	100/229	TACE OS: 25.5 TAE OS: 25.7 TACE 5-yr survival: 19% TAE 5-yr survival: 13%	OS and 5-yr survival not statistically different between TAE and TACE; resection of primary tumor increased OS
Kamat et al. [23]	TACE and TAE	60/123	OS: 18 months PFS: 9 months	Patients had greater than 75% hepatic tumor burden; symptom improvement seen in 65%; major complication rate of 29%
Varker et al. [37]	Repeat TACE	27/54	OS: 28 months PFS: 5 months	Repeat TACE associated with similar OS and PFS, and lower complication rates compared to single TACE

Review Article

Eric Lee, H. Leon Pachter, and Umut Sarpel

Hepatic Arterial Embolization for the Treatment of Metastatic Neuroendocrine Tumors

International Journal of Hepatology

Volume 2012, Article ID 471203, 8 pages

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET

Med Oncol
DOI 10.1007/s12032-010-9750-6

ORIGINAL PAPER

Hepatic artery chemoembolization for the treatment of liver metastases from neuroendocrine tumors: a long-term follow-up in 123 patients

Xiang Da Dong · Brian I. Carr

Received: 20 September 2010 / Accepted: 12 November 2010
© Springer Science+Business Media, LLC 2010

Chemoembolization for unresectable NETs metastatic to liver is useful for tumor size reduction, symptom palliation and can be associated with prolonged survival.

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META-ANALISI della LETTERATURA
Informazioni tecniche

Cicli ripetuti di trattamento, modulati sulla risposta morfologica e sulla tolleranza clinica, aumentano l'efficacia terapeutica.

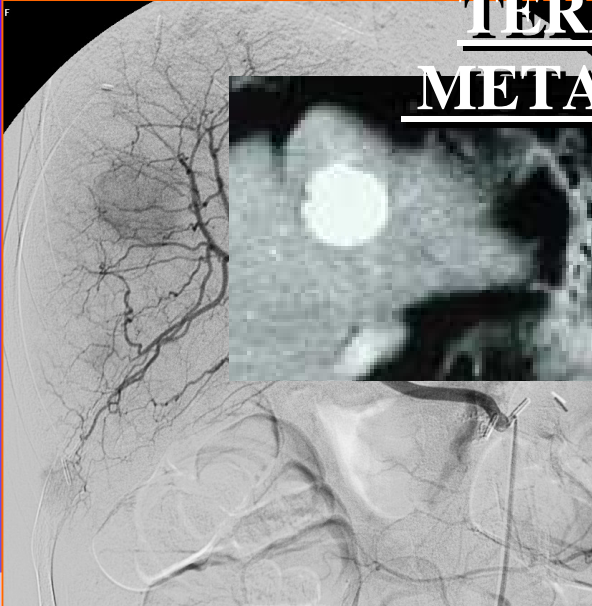
Steward M.J., et al.

Neuroendocrine Tumors: Role of Interventionale Radioogy in Therapy
RadioGraphics 17:1235-1250 (2008)

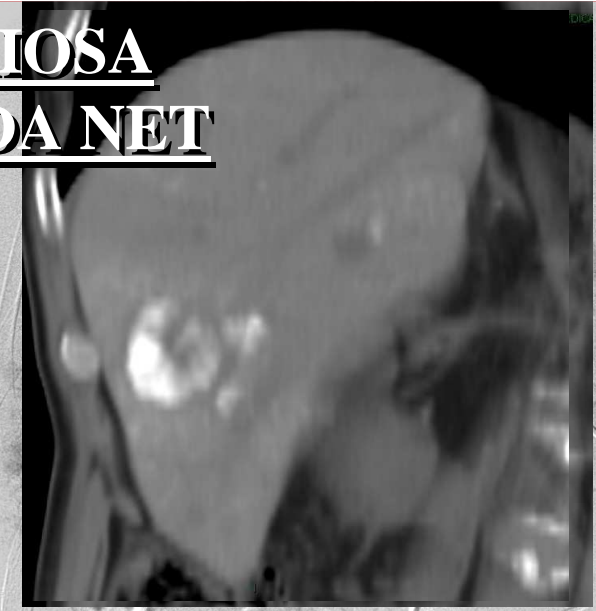
Madoff D C, et al.

Update in the Management of Neuroendocrine Hepatic Metastases
JVIR 17:1235-1250 (2006)

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET



ANALISI della LET
formazioni tecniche



I pazienti con coinvolgimento del parenchima epatico superiore al 50% - 75% hanno un outcome peggiore

Steward M.J., et al.

Neuroendocrine Tumors: Role of Interventionale Radioogy in Therapy
RadioGraphics 17:1235-1250 (2008)

Touzios, et al.

Neuroendocrine Hepatic Metestases: Does Aggressive Management improve survival?
Ann Surg 241: 776-785 (2005)

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET

META-ANALISI della LETTERATURA ***Informazioni tecniche***

**L'Associazione con altre terapie aumenta
l'efficacia terapeutica :**

- Chirurgia
- PEI
- RF
- Radioterapia interna
- Immunoterapia
- Terapia genica
- Terapia antiangiogenetica

Madoff D C, et al.

Update in the Management of Neuroendocrine Hepatic Metastases
JVIR 17:1235-1250 (2006)

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METASTASI EPATICHE DA NET

CONCLUSIONI

“It is in the management of refractory, unresectable, or recurrent disease that the interventional radiologist have the primary role”

Steward M.J., et al.
Neuroendocrine Tumors: Role of Interventionale Radiology in Therapy
RadioGraphics 17:1235-1250 (2008)

TERAPIA TRANSARTERIOSA METASTASI EPATICHE DA NET

CONCLUSIONI

Liver metastases of neuroendocrine tumours; early reduction of tumour load to improve life expectancy

Liesbeth M Veenendaal¹, Inne HM Borel Rinkes¹, Cornelis JM Lips² and Richard van Hillegersberg*¹

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* Corresponding author

Published: 26 June 2006

World Journal of Surgical Oncology 2006, 4:35 doi:10.1186/1477-7819-4-35

Received: 07 April 2006

Accepted: 26 June 2006

Conclusion: Treatment for patients with neuroendocrine hepatic metastases must be tailored for each individual patient. When local ablative therapies are used early in the course of the disease, the occurrence of carcinoid syndrome with end stage hepatic disease can be postponed or prevented.

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CONCLUSIONI



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GRAZIE PER L'ATTENZIONE