

Terapia locoregionale: approcci ecoguidati

*Sergio Sartori
Ecografia interventistica*

Metastasi epatiche

- Frequenti
- Determinanti sulla sopravvivenza
- Impatto positivo di una citoriduzione aggressiva



La chirurgia è la terapia di elezione MA solo il < 25 % è elegibile

Le recidive a 5 anni si verificano nell'80-95 % casi

Termoablazioni e trattamenti transcatetere rappresentano un'opzione terapeutica

Non esistono trial clinici randomizzati di confronto

Approccio multidisciplinare



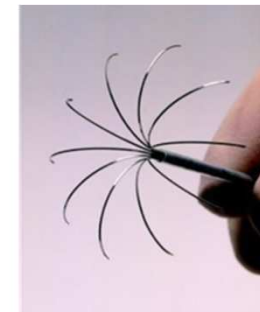
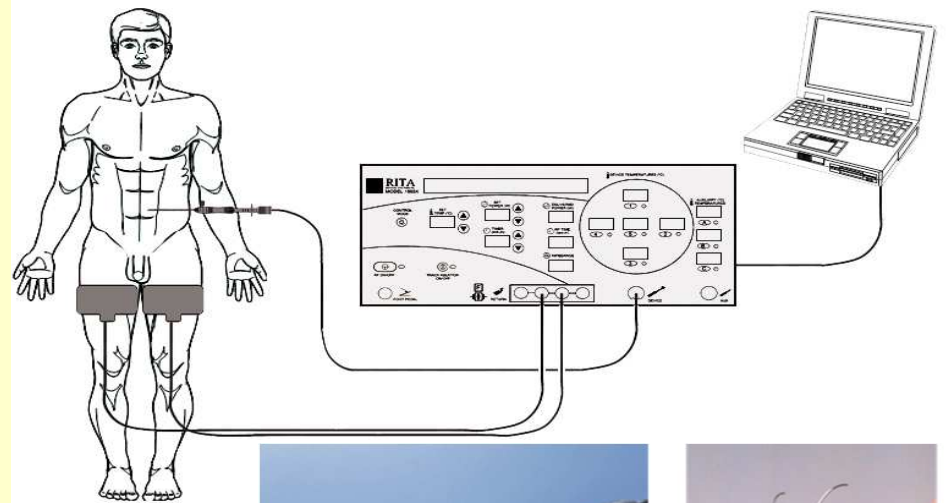
PAT's

Introduzione diretta all'interno di un tessuto di un agente lesivo chimico o termico

- Efficaci
- Basso rischio di complicanze
- Basso costo
- Risparmio del parenchima sano
- Agevole ripetizione dell'intervento
- Efficacia della terapia di associazione con altri trattamenti citoreduuttivi

RF

- ❖ Temp >46° necrosi coagulativa
- ❖ L'entità' del calore prodotto dipende dalla conduttività' del tessuto e dalla dissipazione per convezione (sink effect dei vasi)
- ❖ I nuovi elettrodi consentono di ottenere diametri di necrosi fino a 3-4 cm



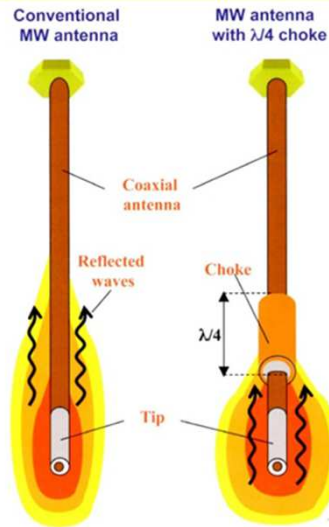
PRO

Efficacia e sicurezza validate
Facile utilizzo

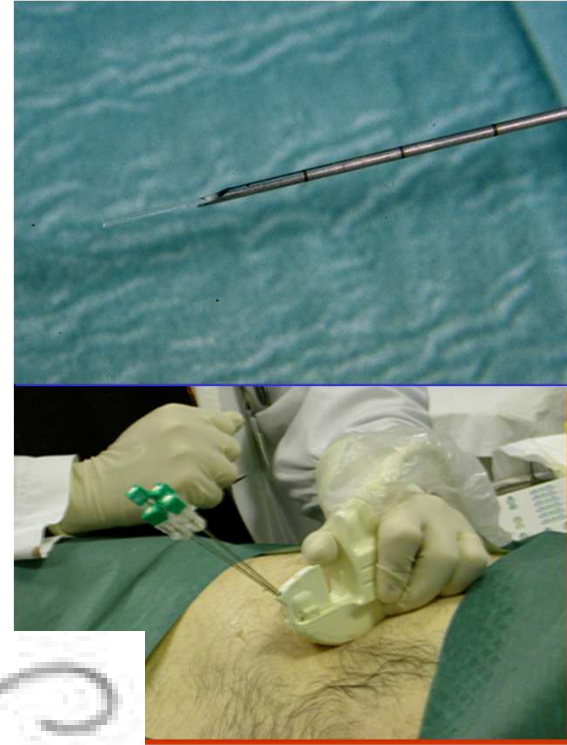
Contro

Heat sink effect
>3 cm multiple infissioni

“Nuove” tecnologie



MW LASER
Crioablazione



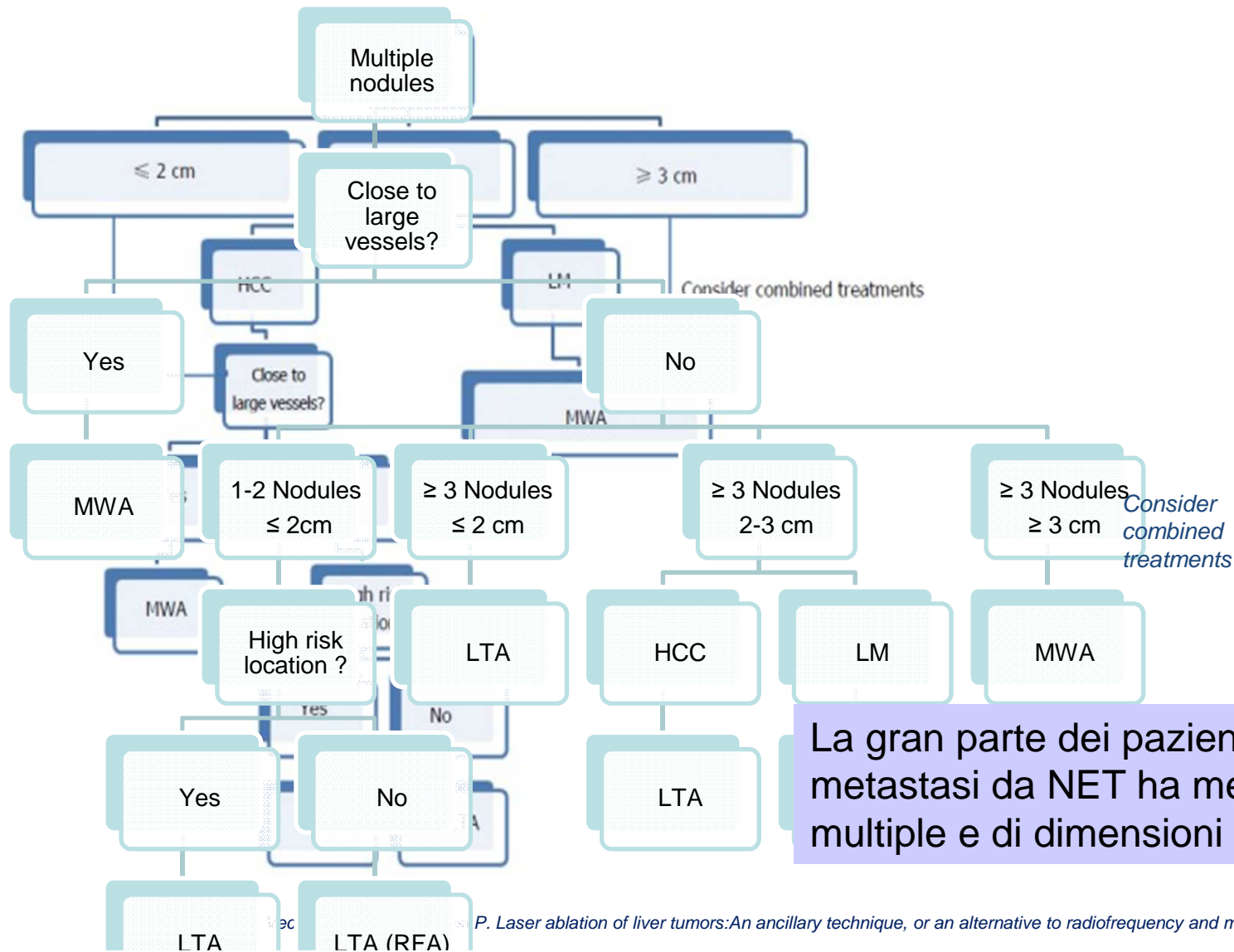
- ❖ Non necessita di circuito elettrico
- ❖ Buona conducibilità
- ❖ Scarsa dispersione di calore
- ❖ Temperature maggiori in minor tempo
- ❖ Diametri maggiori



a 4 fibre (diametri di
n a 4 cm)
male

- ❖ Distribuzione dell'energia meno prevedibile
- ❖ Difficoltà intrinseca maggiore
- ❖ Costi più elevati

Tailored therapy



La gran parte dei pazienti con metastasi da NET ha metastasi multiple e di dimensioni variabili

P. Laser ablation of liver tumors: An ancillary technique, or an alternative to radiofrequency and microwave? WJR 2017

Neuroendocrine gastro-entero-pancreatic tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[†]

K. Öberg¹, U. Knigge², D. Kwekkeboom³ & A. Perren⁴ on behalf of the ESMO Guidelines Working Group*

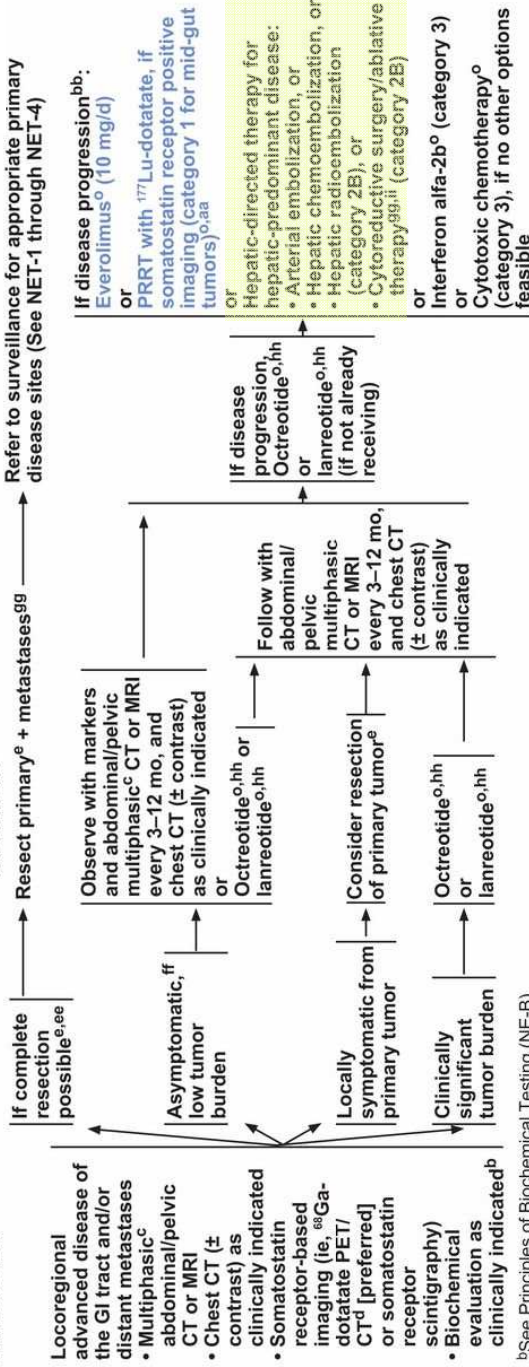
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and might help to improve systemic treatment. There are no randomized clinical trials comparing the efficacy of locoregional therapies and palliative liver surgery [15]. The choice of the ablative or locoregional procedure such as radiofrequency ablation (RFA), laser-induced thermoablation or selective hepatic transcatheter arterial embolization (TAE), chemoembolization (TACE) and selective internal radiotherapy (SIRT) depends on the local expertise, number and size of lesions and location of liver involvement. These types of

tumors and is used for down-staging of the disease. RFAs in tumors <5 cm in size have shown 70%–80% symptomatic responses with control of symptoms up to 1 year (III, B).

MANAGEMENT OF LOCREGIONAL ADVANCED DISEASE AND/OR DISTANT METASTASES^c
GASTROINTESTINAL TRACT
EVALUATION^{b,c}



^bSee Principles of Biochemical Testing (NE-B).
^cMultiphasic imaging studies are performed with IV contrast.
^d⁶⁸Ga-dotatate PET/CT is more sensitive than somatostatin receptor scintigraphy for determining somatostatin receptor status. PET/CT of skull base to mid-thigh; CT with IV contrast when possible. PET/CT of skull base to mid-thigh; CT with IV contrast when possible. Data are limited on the optimal timing of scans following administration of somatostatin analogs.
^eSee Surgical Principles for Management of Neuroendocrine Tumors (NE-C).
^fSee Principles of Systemic Anti-Tumor Therapy (NE-D).
^gSee Principles of PRRT with ¹⁷⁷Lu-Dotatate (NE-E).
^hIf disease progression, treatment with octreotide or lanreotide should be continued in patients with functional tumors and may be used in combination with any of the subsequent options. For details on the administration of octreotide or lanreotide with ¹⁷⁷Lu-dotatate, see NE-E.
ⁱⁱNoncurative debulking surgery might be considered in select cases.
^{jj}Resection of a small asymptomatic (relatively stable) primary in the presence of unresectable metastatic disease is not indicated. However, taking a careful history is recommended as surgery may be an option for asymptomatic patients with previous, intermittent obstructions.
^{kk}Includes ablative techniques such as radiofrequency, microwave, and cryotherapy. There are no randomized clinical trials and prospective data for these interventions are limited. However, data on the use of these interventions are emerging.
^{ll}Treatment with octreotide or lanreotide will likely only benefit those patients who are somatostatin receptor positive.
^{mm}Only if near complete resection can be achieved.

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Hepatic-Directed Therapies

For patients with unresectable, hepatic-predominant, progressive gastrointestinal tract NETs, hepatic-directed therapies may be considered, mainly with the palliative goals of extending life and relieving hormonal symptoms.^{13–16}

Cytoreductive surgery or ablative therapies such as radiofrequency ablation or cryoablation may be considered if near complete treatment of tumor burden can be achieved (category 2B).^{44–48} For unresectable liver metastases, hepatic regional therapy (arterial embolization,⁴⁹ chemoembolization,^{50–52} or radioembolization [category 2B])^{53–55} is recommended. No single modality of embolization therapy has been shown to be superior to another, but there is a difference in both long- and short-term toxicities among the different modalities.

Guidelines for the management of gastroenteropancreatic neuroendocrine (including carcinoid) tumours (NETs)

John K Ramage,¹ A Ahmed,² J Ardill,³ N Bax,⁴ D J Breen,⁵ M E Caplin,⁶ P Corrie,⁷ J Davar,⁸ A H Davies,⁹ V Lewington,¹⁰ T Meyer,¹¹ J Newell-Price,¹² G Poston,¹³ N Reed,¹⁴ A Rockall,¹⁵ W Steward,¹⁶ R V Thakker,¹⁷ C Toubanakis,¹⁸ J Valle,¹⁹ C Verbeke,²⁰ A B Grossman¹⁷

- ▶ Treatment choices for non-resectable disease include somatostatin analogues, biotherapy, targeted radionuclide therapy, locoregional treatments including ablation and (chemo) embolisation and chemotherapy. Level of evidence 4, Grade of recommendation C.
- ▶ External beam radiotherapy may relieve bone pain from metastases. Level of evidence 4, Grade of recommendation C.
- ▶ Chemotherapy may be used for inoperable or metastatic pancreatic NETs. Level of evidence 1, Grade of recommendation A.
- ▶ Chemotherapy may be used for poorly differentiated NETs and in selected non-pancreatic NETs of high grade or aggressive clinical course. Level of evidence 2, Grade of recommendation B.
- ▶ Sunitinib or everolimus may be used as a line of therapy for patients with advanced (inoperable or metastatic), progressive (radiological evidence of disease progression within 12 months), well-differentiated pancreatic NETs. Level of evidence 1, Grade of recommendation A.
- ▶ If possible, patients with NETs should be entered into formal trials of new drug treatments. Level of evidence 4, Grade of recommendation C.

Ablation

- ▶ In the setting of metastatic NET, ablation most commonly has a role in small volume tumours, paucifocal disease or in combination with resection. Level of evidence 3, Grade of recommendation C.
- ▶ Ablation, in common with resection, has been shown to be useful in symptom relief. Level of evidence 3, Grade of recommendation C.
- ▶ Image-guided ablation can contribute to the cytoreductive approach to metastatic disease. Level of evidence 3, Grade of recommendation C.

BMJ



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NIH-PA Author

Consensus Guidelines for the Management and Treatment of Neuroendocrine Tumors


Progression of liver metastases is the predominant cause of mortality in many NET patients.

Median survivals of 24–128 months are reported with treatment.^{15–17} For this reason, hepatic resection, radiofrequency ablation, and hepatic arterial embolization have been used to control tumor burden. In those patients in whom all hepatic metastases seem to be

resectable and in whom no (or mild non clinically significant) extrahepatic disease is



Percutaneous Laser Ablation of Liver Metastases from Neuroendocrine Neoplasm. A Retrospective Study for Safety and Effectiveness

Sergio Sartori¹  · Paola Tombesi¹ · Francesca Di Vece¹ · Lara Bianchi¹ · Rosaria Ambrosio²

Analisi retrospettiva di sicurezza ed efficacia del trattamento Laser (LA) delle metastasi epatiche (LM) da NET

Dal 2004 al 2017 : 21 pazienti con almeno 3 LM < 4cm
189 LM trattate in 41 sessioni utilizzando Tecnica Laser multifibre

Tutti i pazienti avevano già effettuato chirurgia sul T ed era stata effettuata l'analisi immunoistochimica del Ki-67

FU con TC ad un mese ed alternanza di TC e CEUS ogni 3 mesi per i primi 2 anni

Risultati

FU medio 39 mesi

1 complicanza di grado 4 (0,53 %)

Technical efficacy 100%

Primary efficacy rate 94.7%

Secondary efficacy rate 100%

Scomparsa dei sintomi in tutti i pazienti sintomatici

Local tumor progression 10/189 pz

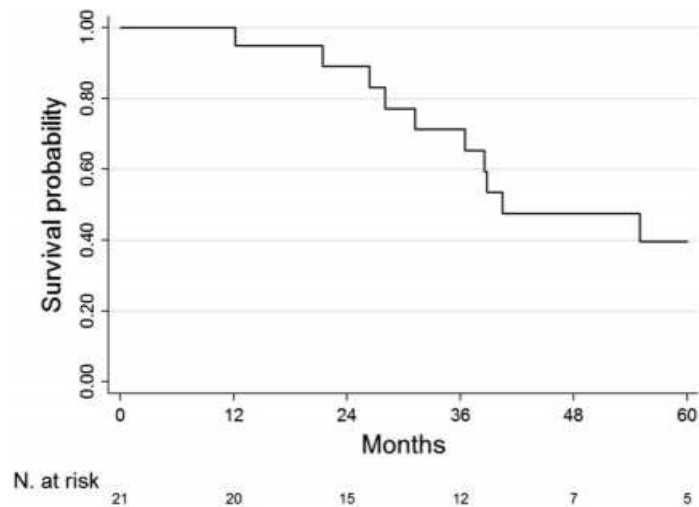


Fig. 3 Overall survival curve for all patients from the first LA session to death or April 30, 2019

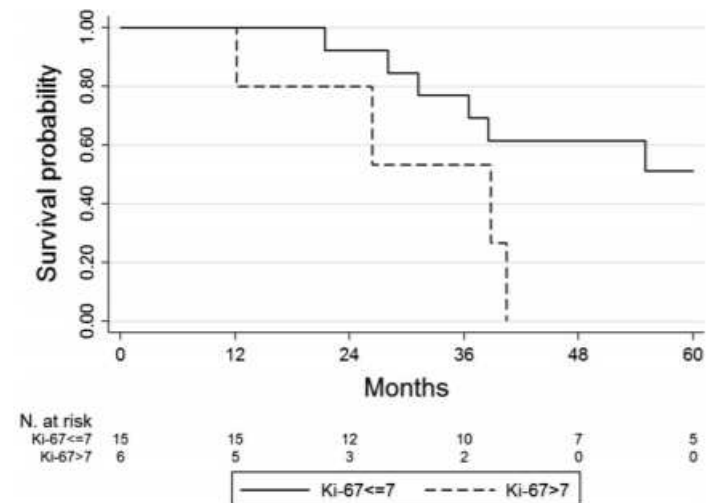
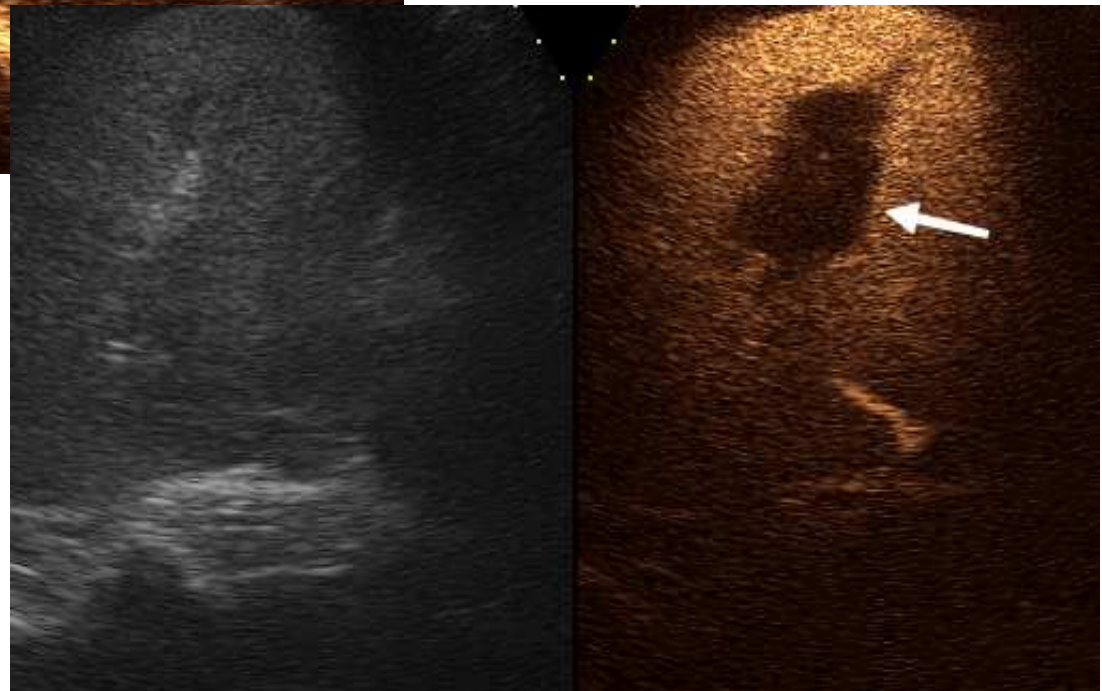
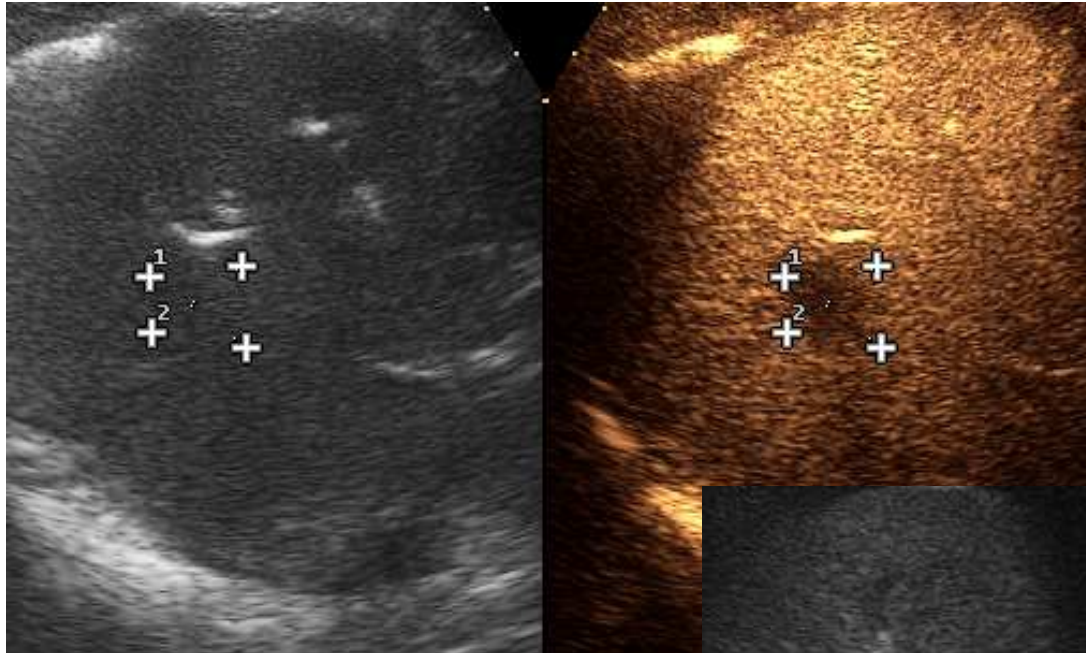
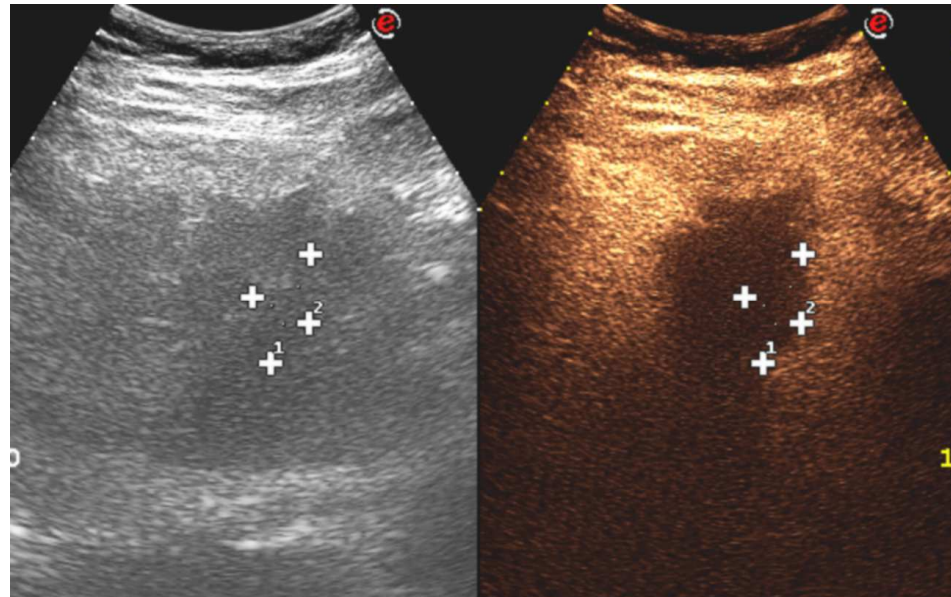
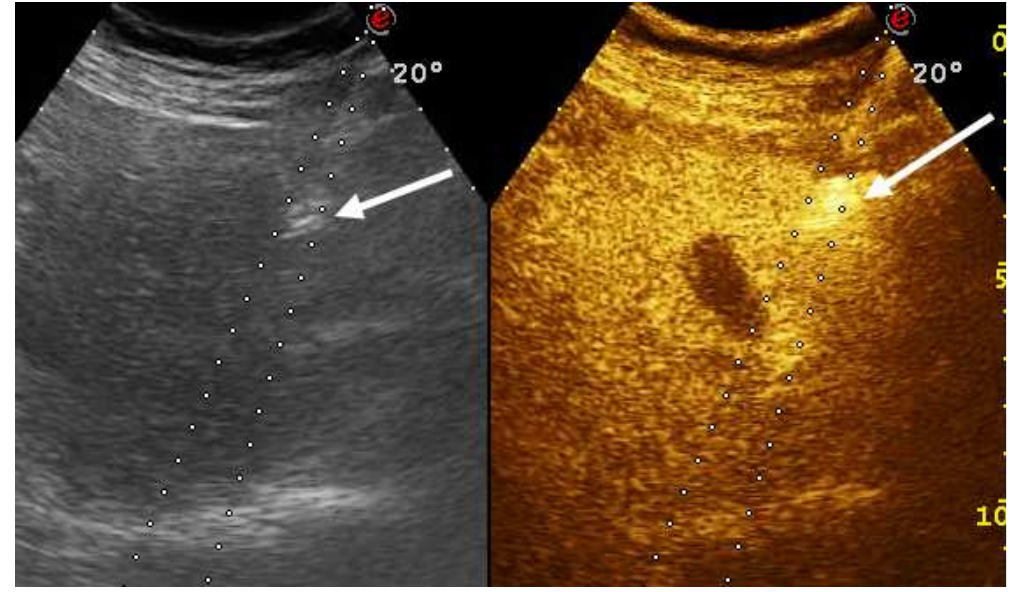
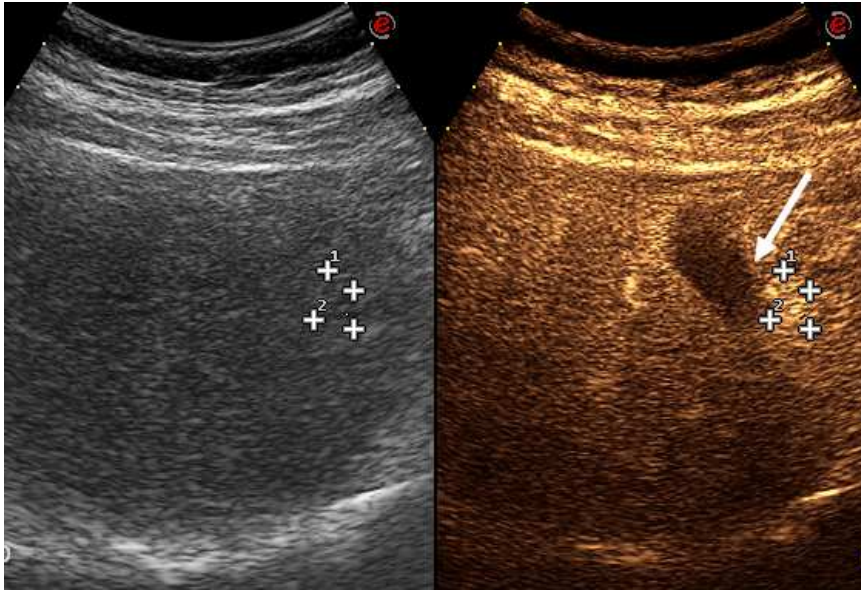


Fig. 4 Overall survival curves for patients with Ki-67 $\leq 7\%$ and $> 7\%$

Complete ablation



Incomplete ablation: retreatment





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EDITORIAL

Thermal ablation in colorectal liver metastases: Lack of evidence or lack of capability to prove the evidence?

Sergio Sartori, Paola Tombesi, Francesca Di Vece

Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials

Smith, Pell. *BMJ* 2003



Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials