

**CARCINOMA
DIFFERENZIATO
DELLA TIROIDE:
DALLA DIAGNOSI
AL FOLLOW-UP**

Le questioni aperte,
le risposte possibili

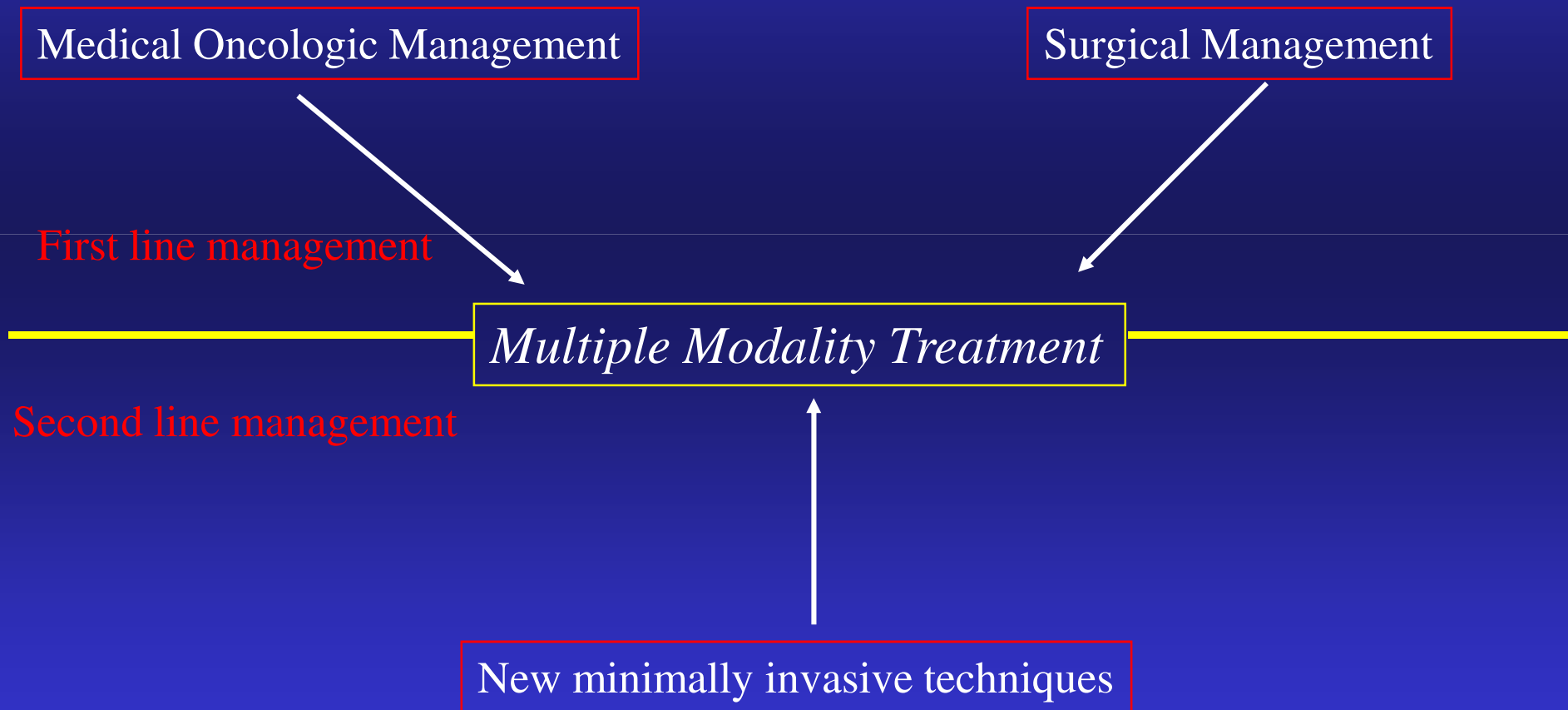
Ruolo della interventistica per le secondarietà epatiche e di altre sedi

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Introduction

Therapeutic Approaches



Introduction

background to interventional procedures

- Hepatic resection is possible in fewer than 10% of patients
- The disease can become refractory to somatostatin analogues
- additional therapies such as external radiation or systemic chemotherapy have limited effectiveness
- these forms of non-operative treatments are not curative, and the disease will eventually spread further and become lethal.

Introduction

the role of radiologists

- It is in this scenario radiologists have an established primary role
- In this case the treatment has to be tailored to the goal (i.e.: reduction of tumor bulk, hormonal palliation, conversion to resectable status) and to take account of the extension and distribution of disease

Introduction

Radiological Interventional Approach

- From the radiological standpoint the minimally invasive metastases directed therapies can be classified in two groups:
 - a) Local ablation therapies
 - b) Percutaneous transcatheter treatments

Local Ablation Therapies

Radiological Interventional Approach

Injective

~~Percutaneous Injection~~

~~(Alcohol, Acetic Acid,
Hot Water, Gene Therapy)~~

Physical Ablation

Laser Ablation

Radio Frequency

Micro-Wave

Cryo Ablation

HIFU

Rationale for Local Ablation Therapies

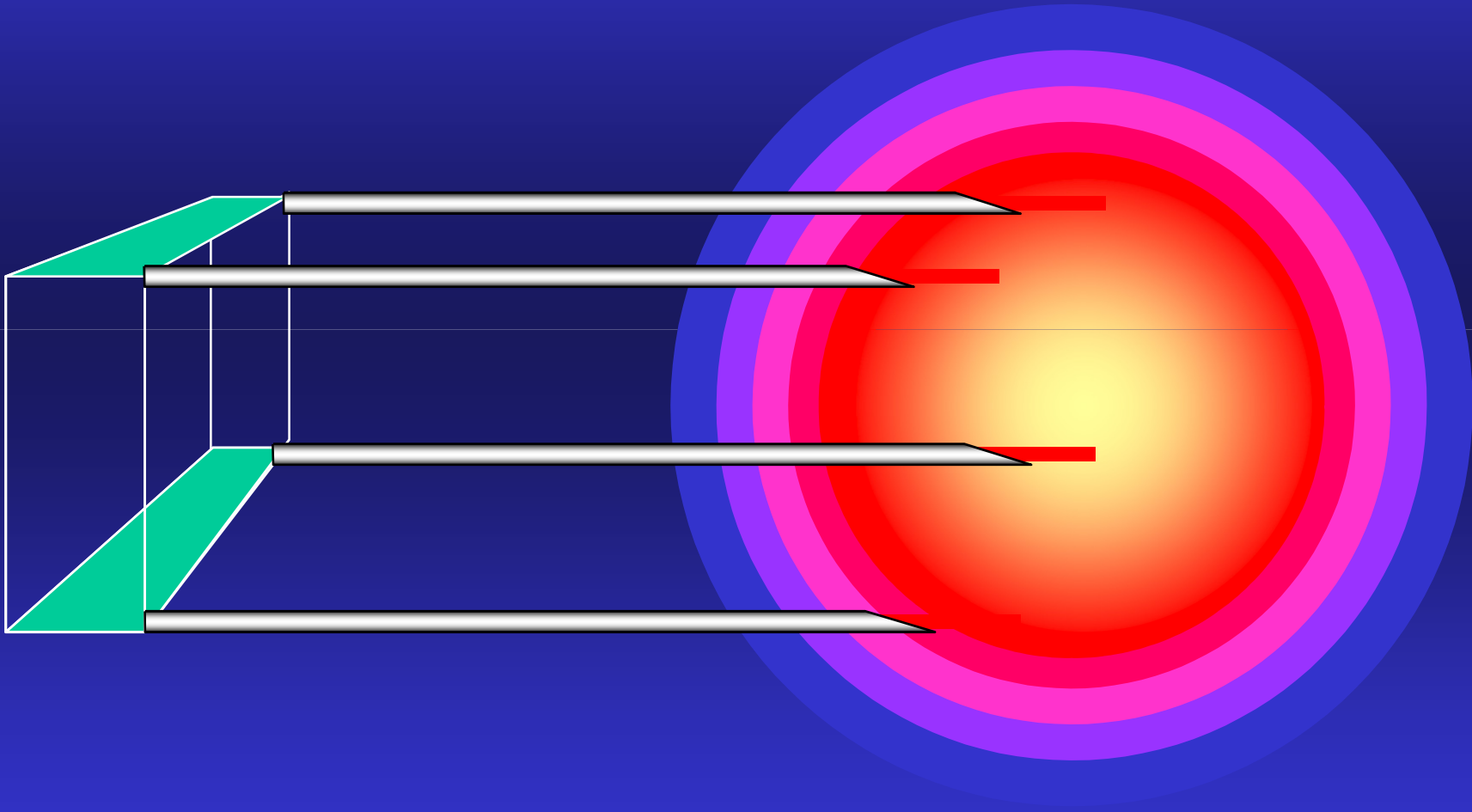
- Efficacious in tumor killing
- Rapid
- Safe
- Inexpensive
- Selective



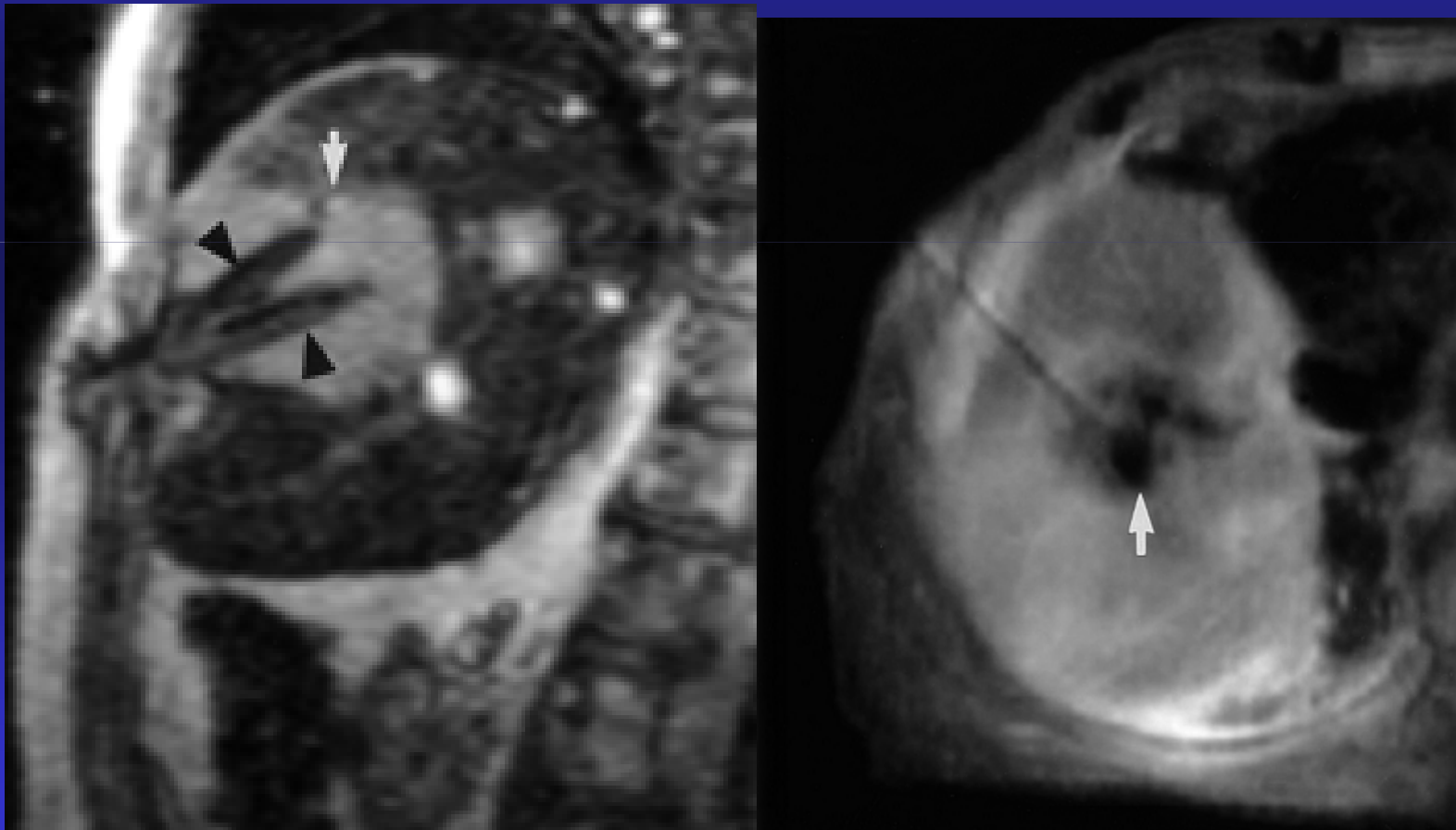
Local Ablation Therapies: drawbacks

- Local efficacy similar to surgical resection
- Lesions detectable on one imaging modality
- Not indicated for large and multiple lesions when curative ablation is required (Less than 5 lesions smaller than 4 cm.)

Laser Ablation (multifiber technique)

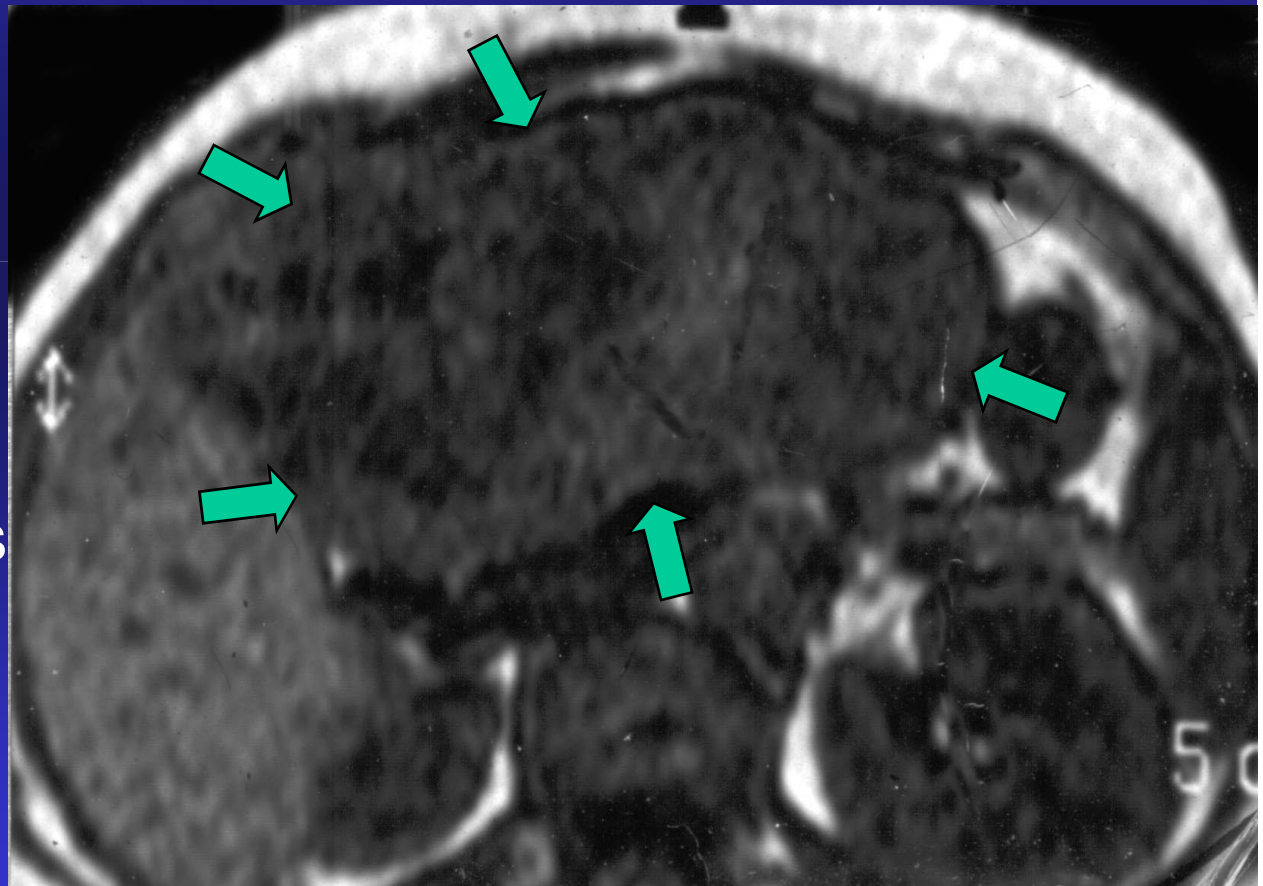


Laser Ablation (multifiber technique) MRI guidance



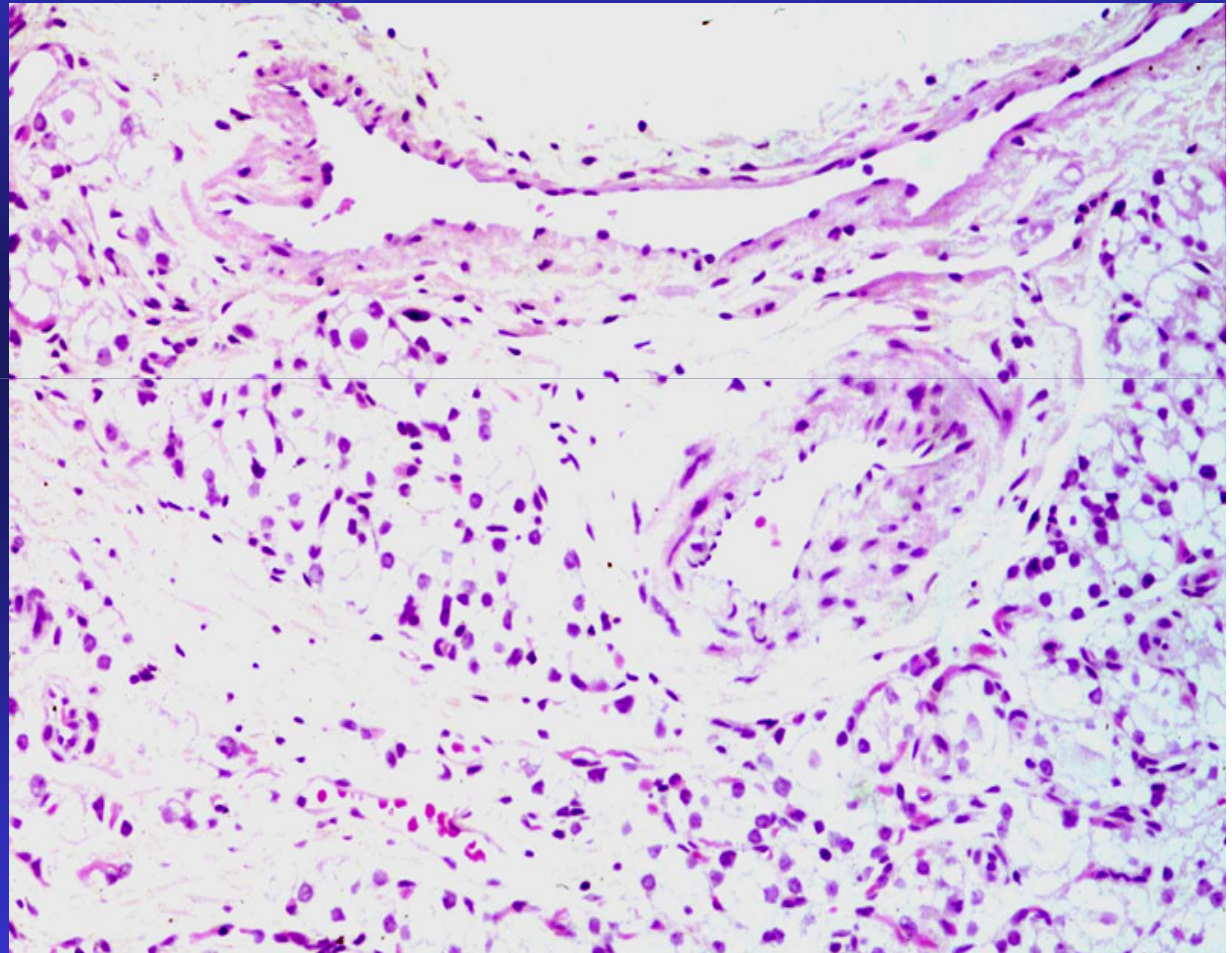
Massive liver metastasis of follicular carcinoma: MR T1-weighted transverse image of the abdomen

- left lobe of the liver (segments 1-4)
- large hypointense and inhomogeneous area (17 cm in diameter)



Percutaneous liver biopsy

- metastasis from well differentiated follicular carcinoma
- severe thyrotoxicosis due to massive hyperfunctioning metastatic tissue

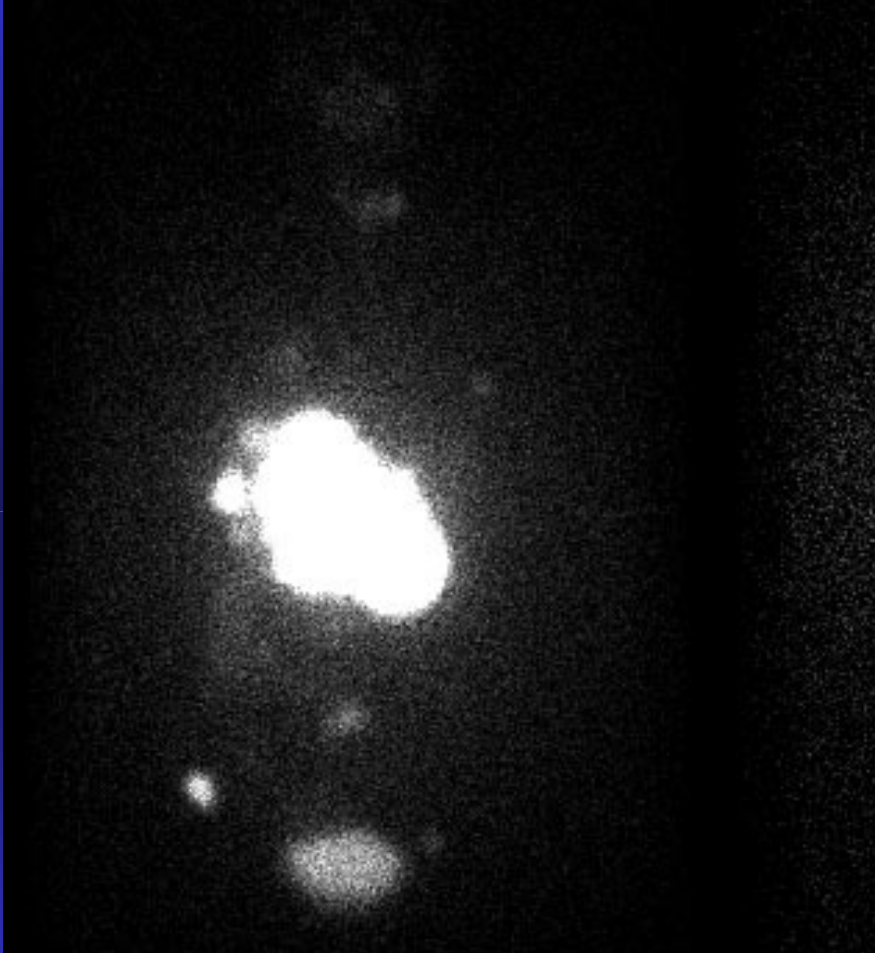


MRI T1-weighted transverse image of the upper abdomen after ILTA treatment

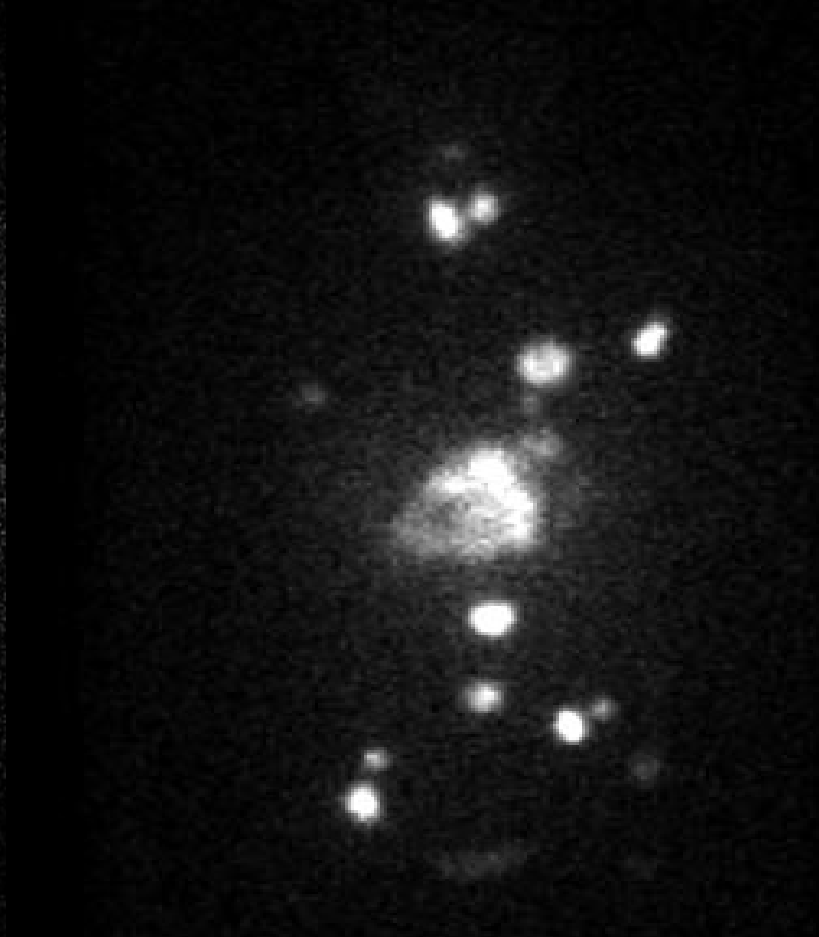
- large hypointense area of the liver due to coagulative necrosis induced by LTA treatment
 - improvement of hormonal levels and general conditions



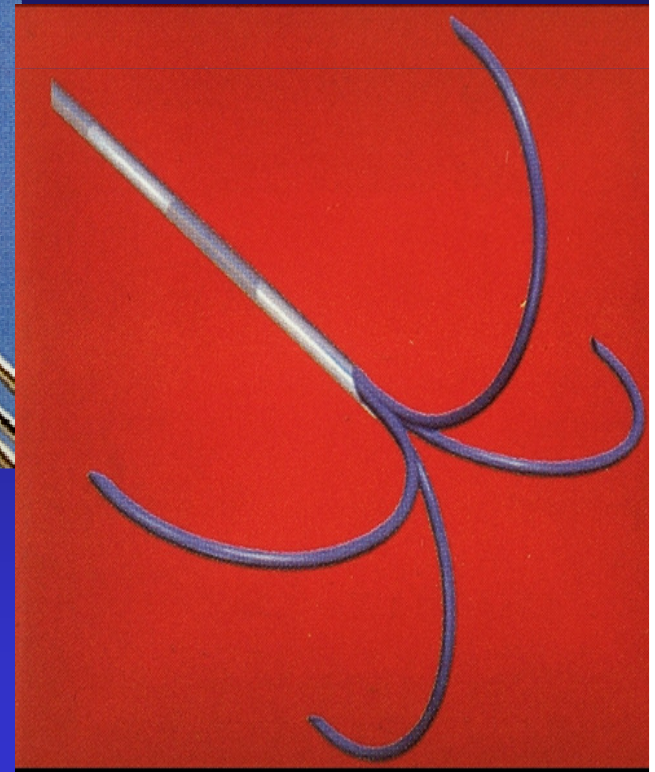
Baseline ^{123}I whole body scan



^{123}I whole body scan after PLA



RadioFrequency Ablation



RadioFrequency Ablation

- Despite the large use of this ablation technique for liver cancer and liver metastases there are limited reports about its use on hepatic metastases from DTCs

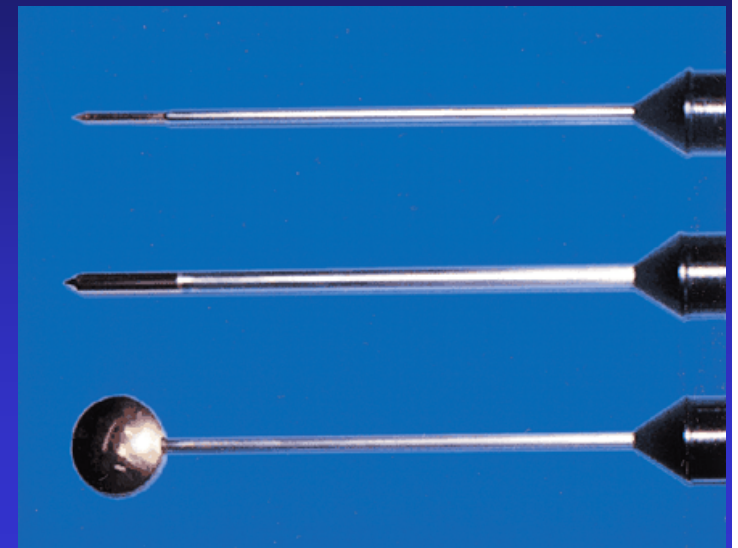
RadioFrequency Ablation

(palliative ablation)



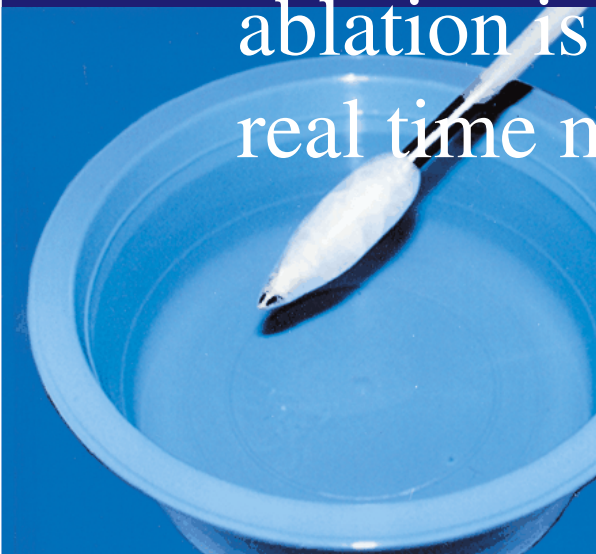
Cryoablation “the iceball”

- Large-diameter applicators frequently requiring intraoperative settings
- Higher rates of complications for large liver tumor especially hemorrhage



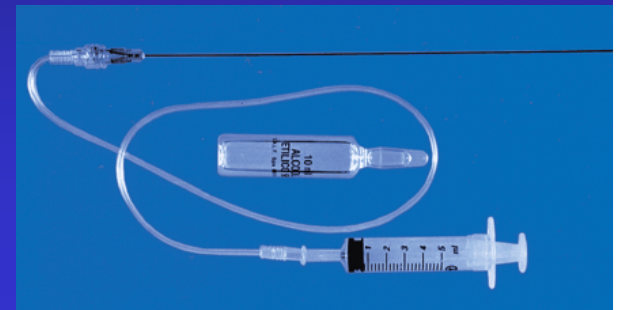
Cryoablation and “the iceball”

- More recently smaller caliber applicators has become available allowing safer percutaneous approach
- One advantage of cryoablation like Laser ablation is MRI compatibility that permits a real time monitoring of the ablated area



Percutaneous Ethanol Ablation

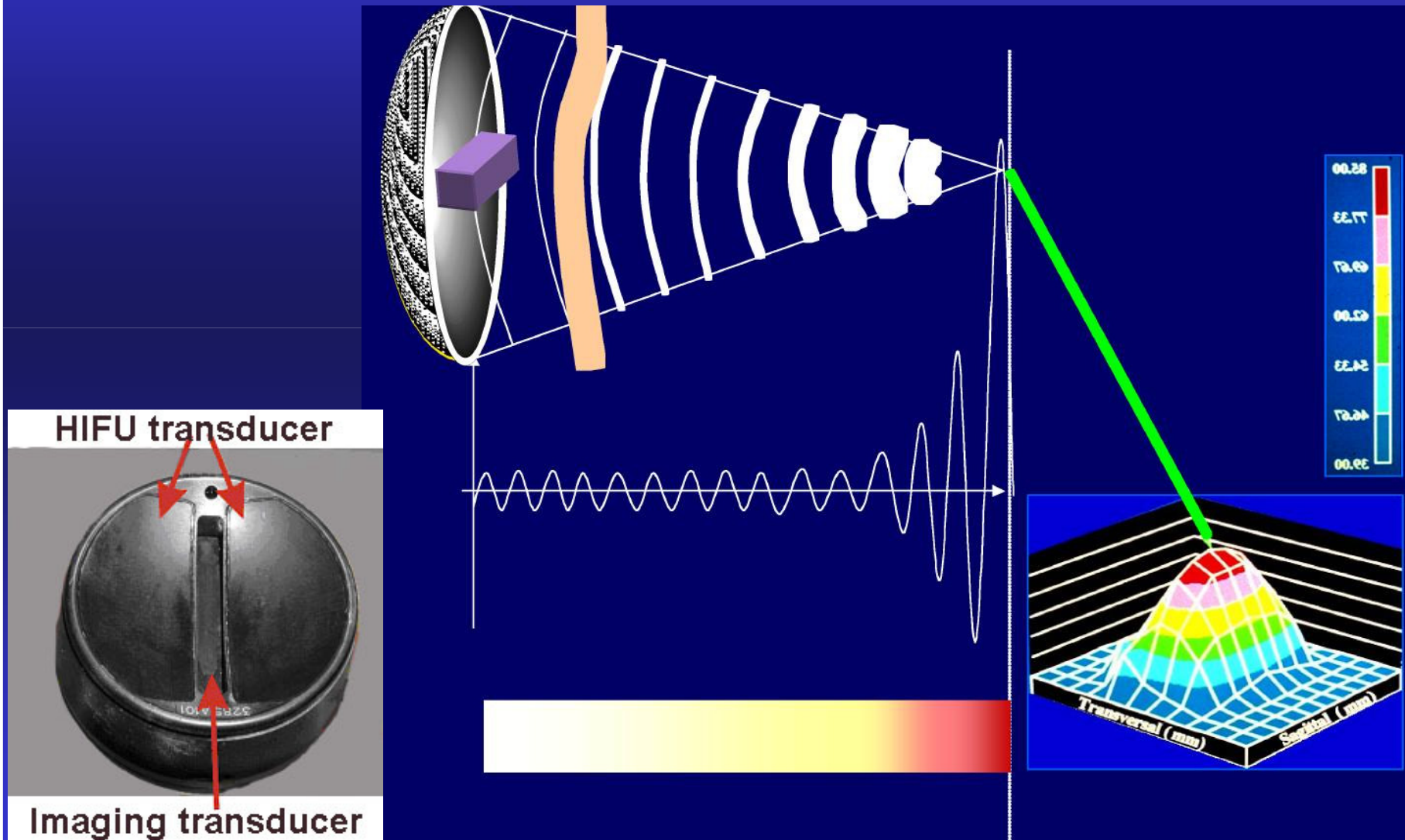
- Considered the reference treatment for HCCs, PEI has been essentially replaced by other ablation techniques
- In fact PEI demonstrated reduced efficacy on liver metastases
- Today its use is limited to particular conditions (lesion adjacent to vital structures, lesion in difficult location or close to the central bile ducts)



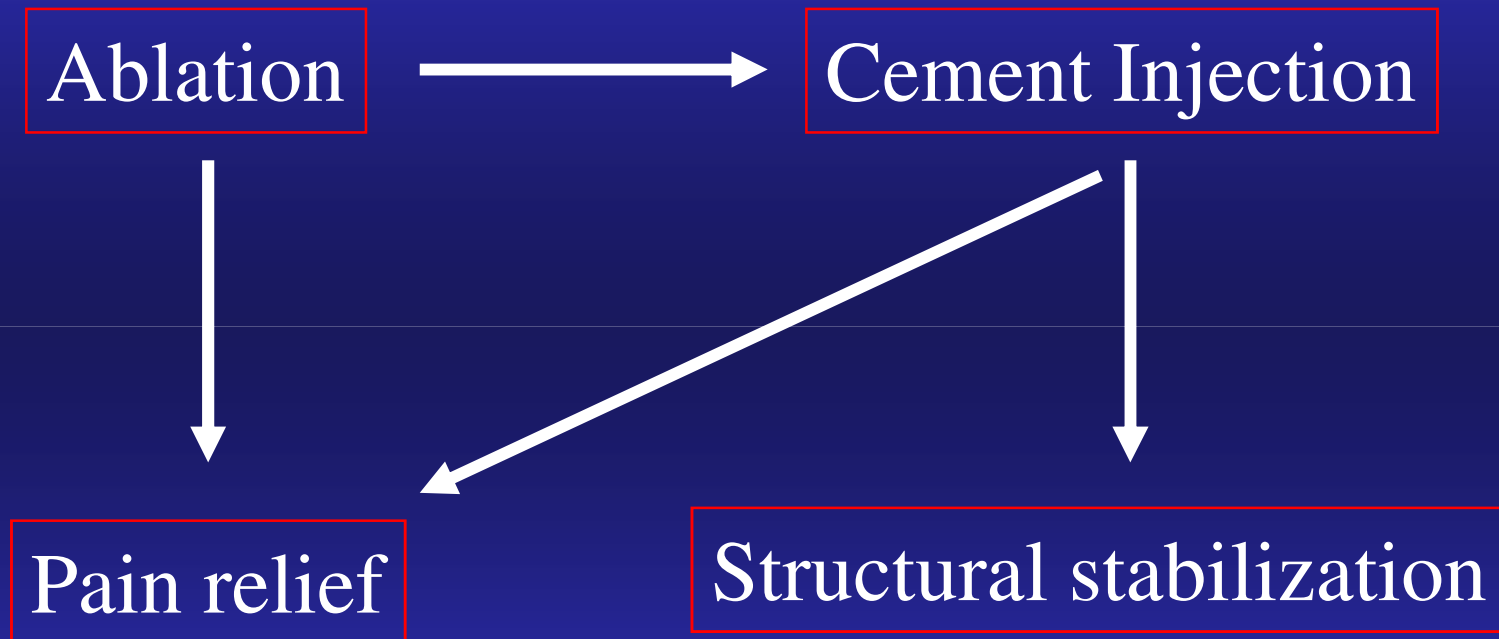
High Intensity Focused Ultrasound (HIFU):

Principles of Action

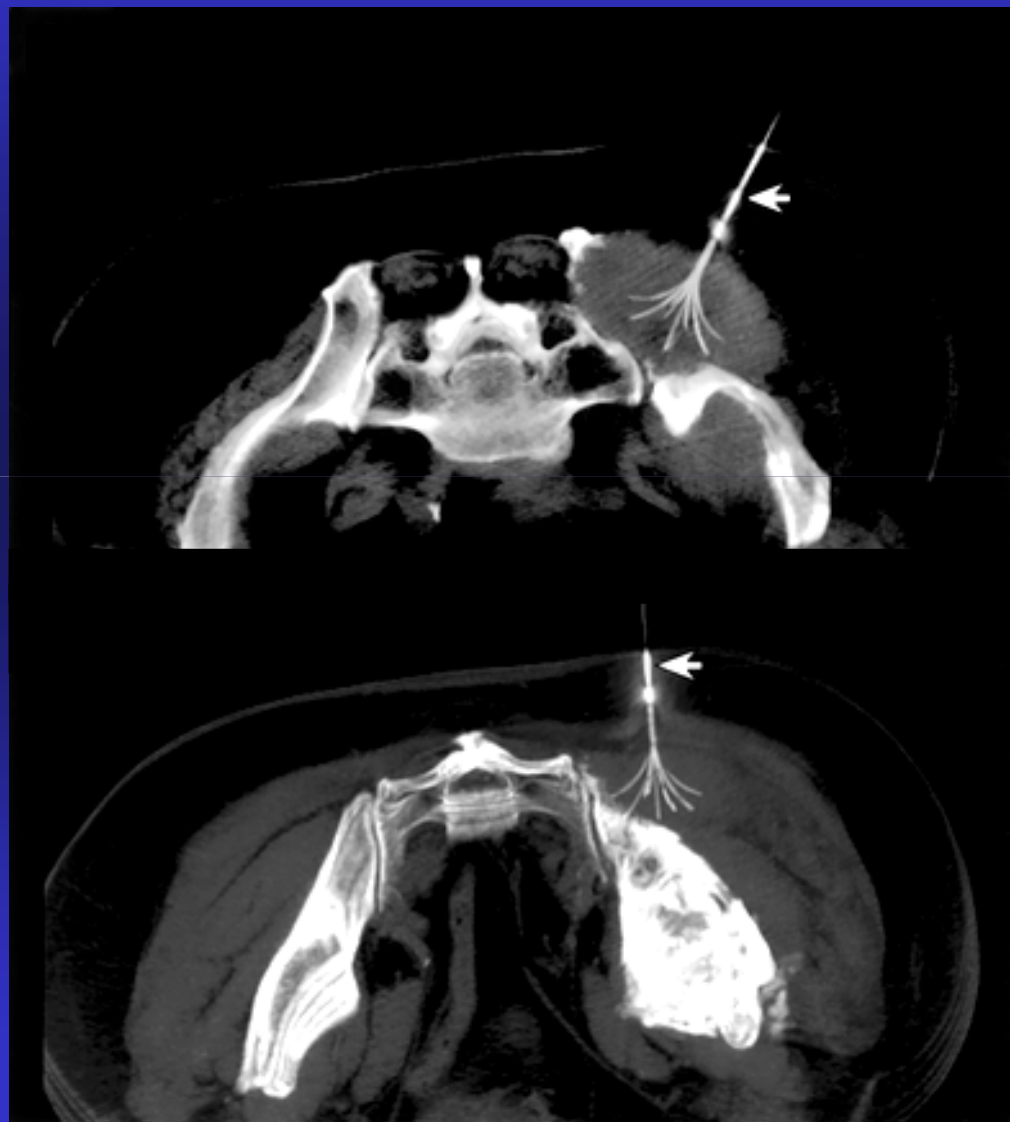
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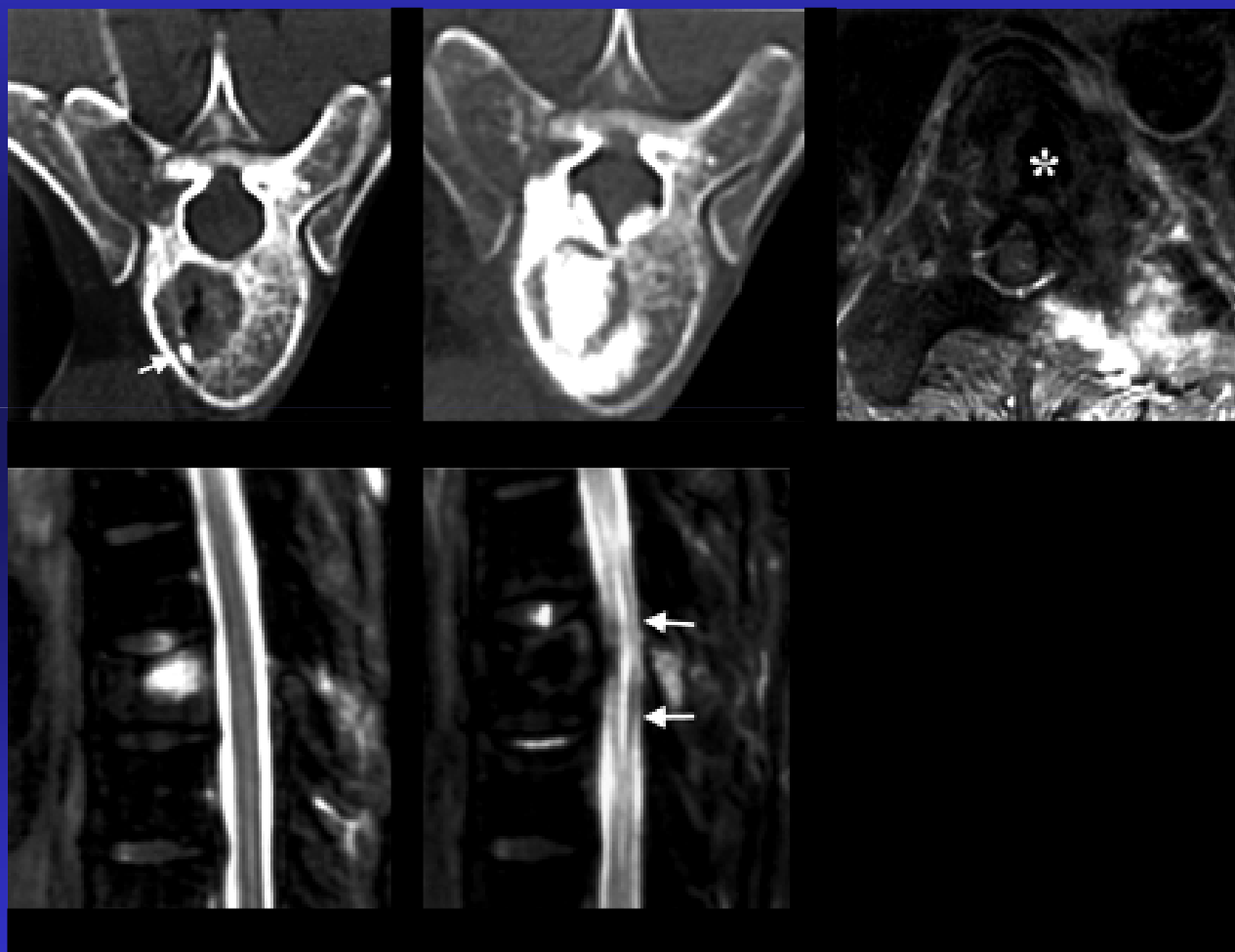
Ablation Therapies: bone mets



Ablation Therapies: bone mets



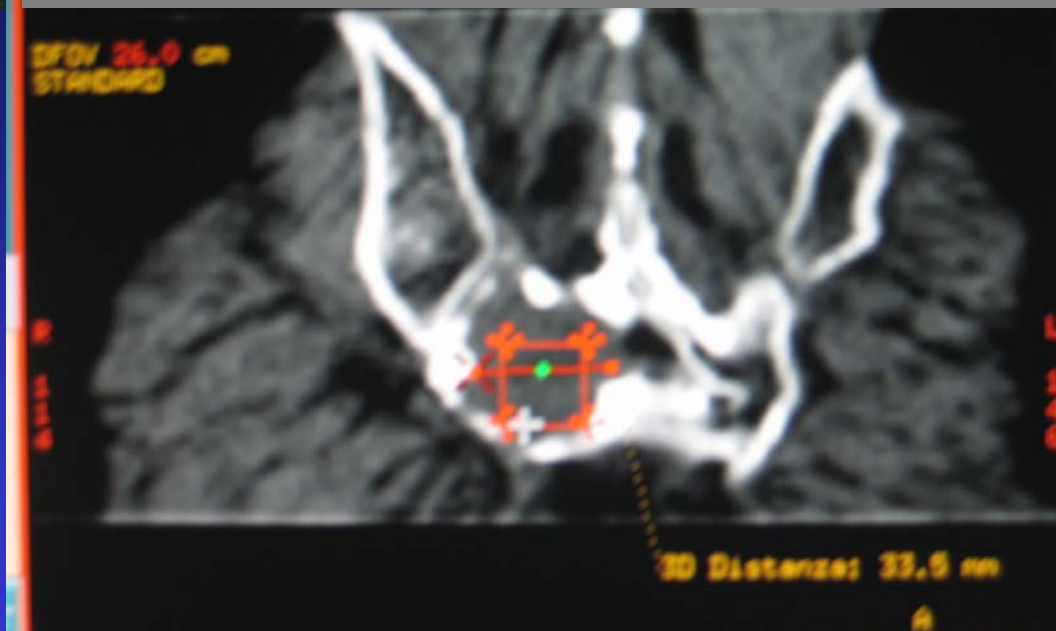
Ablation Therapies: bone mets





Follicular thyroid carcinoma. Local control of the disease. Bone metastasis with a dominant pelvic lesion. No ^{131}I uptake.

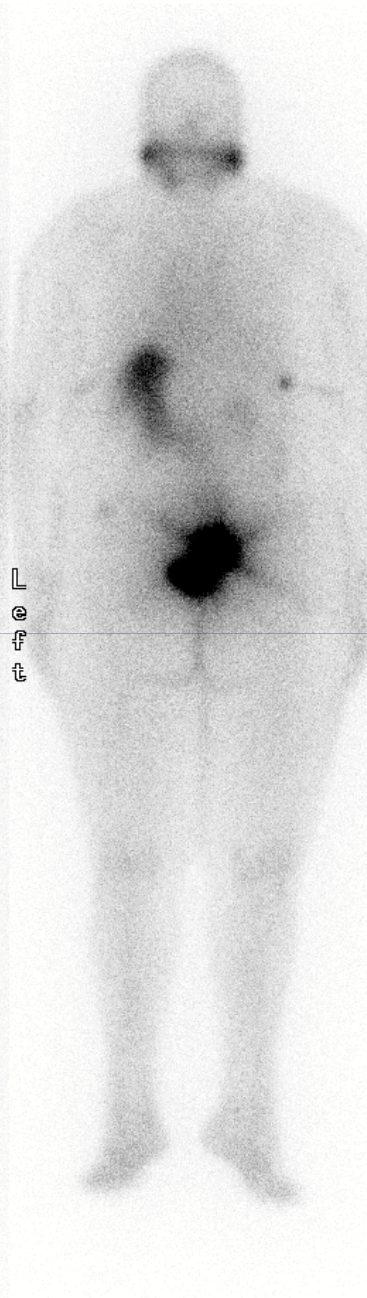
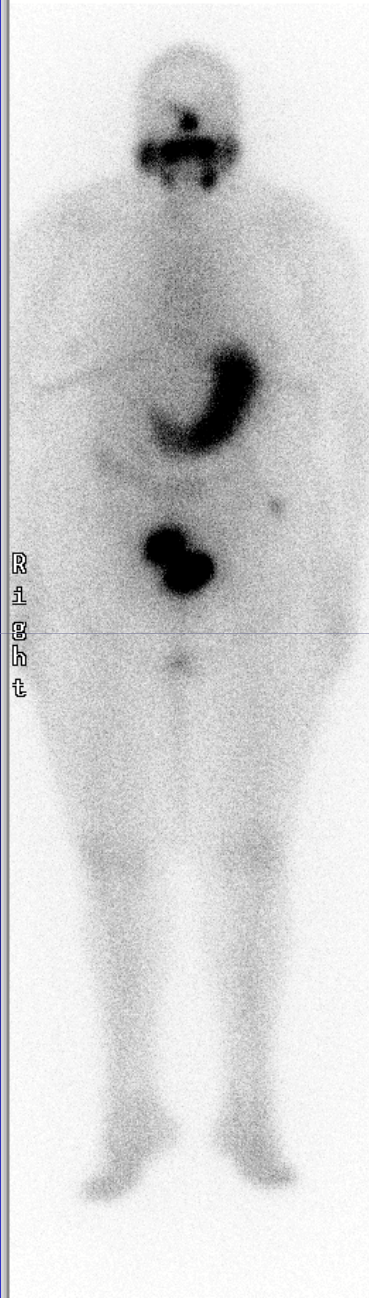
Continuous severe pain that was not relieved by external RT. Increasing use of opioids (oxycodone, 60 mg/d)





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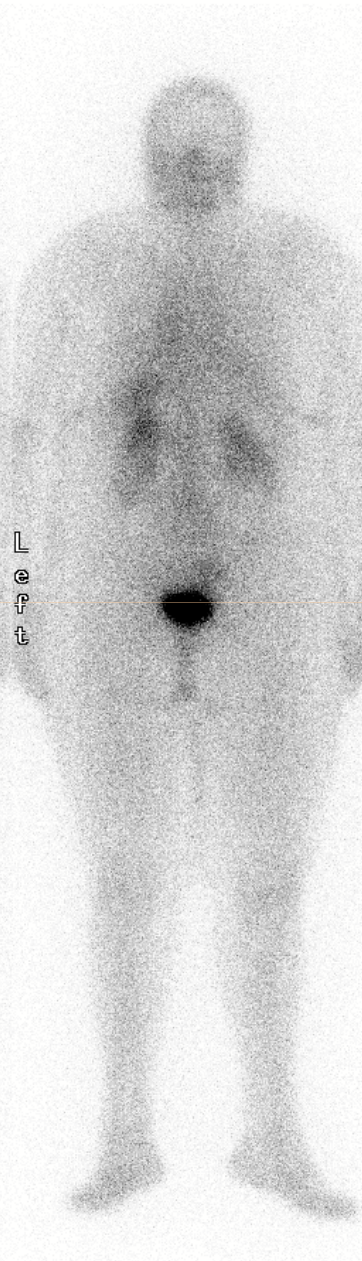
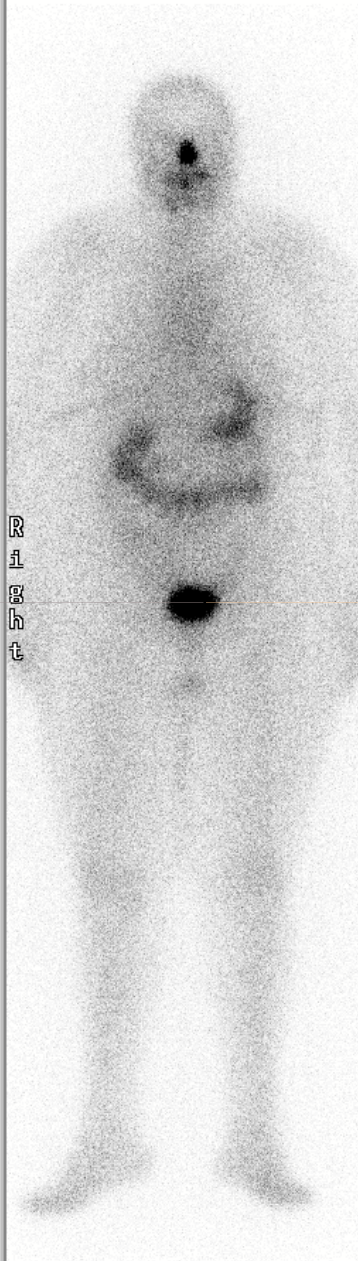


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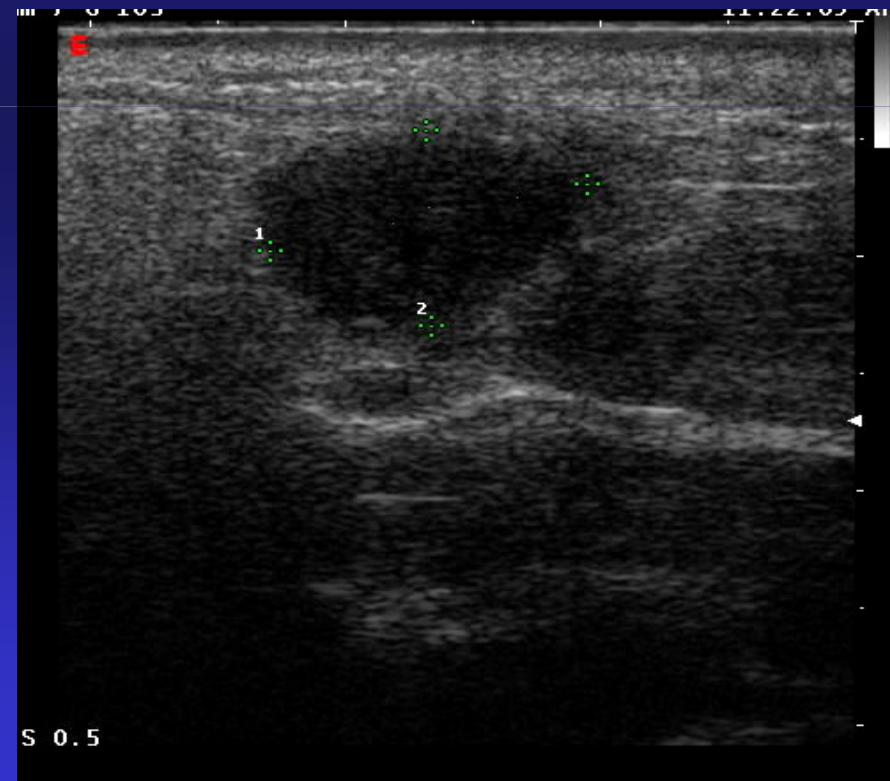
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Laterocervical nodal metastasis



before LTA treatment



3 months after LTA treatment

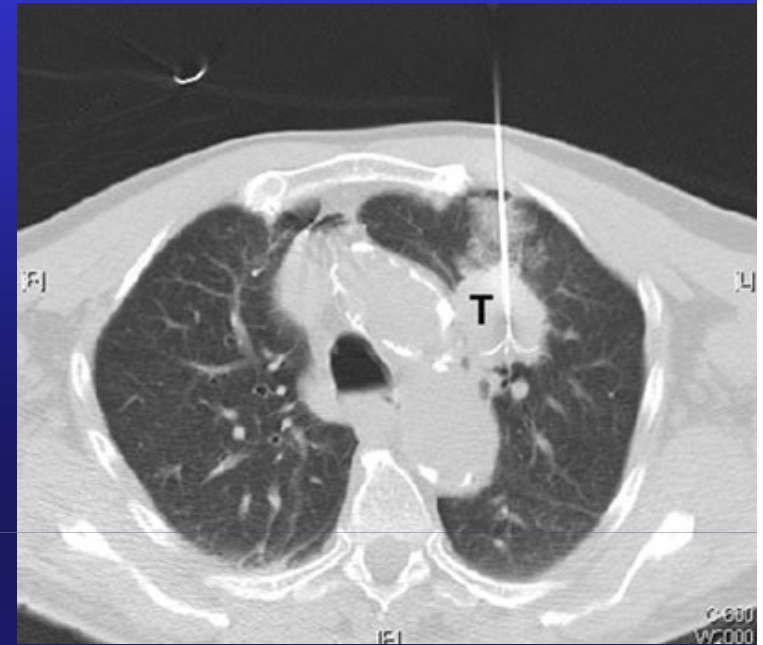
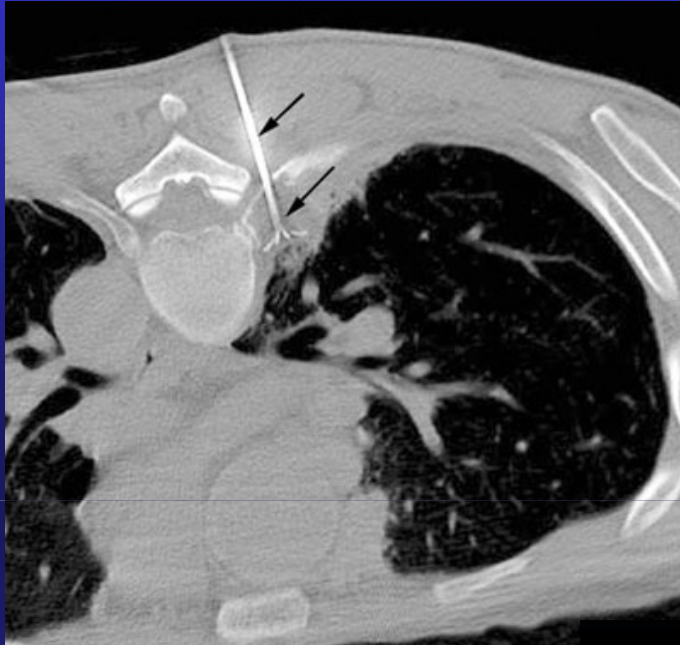
Percutaneous image-guided radiofrequency ablation of painful metastasis involving bone

Goetz MP et al. J Clin Oncol 2004; 22: 300-06

Painful metastases involving bone: Percutaneous image-guided Cryoablation

Callstrom MR et al. Radiology 2006; 241: 572

Ablation Therapies: chest and lung mets



Ablation Therapies:

Take-home points

- In the case of small liver metastases Percutaneous Ablation Techniques (PATs) are expected to obtain results similar to curative liver resection probably with lower morbidity and mortality
- Percutaneous treatments can be preferred to surgery for cytoreduction with some exception

Ablation Therapies:

Take-home points

- Local ablation and cement injection are proved to give pain relief and structural stabilization
- Pain relief can be faster than after radiation therapy
- Chest and lung mets can be accessible to local ablation

Vascular Liver Directed Therapies

Vascular Therapies



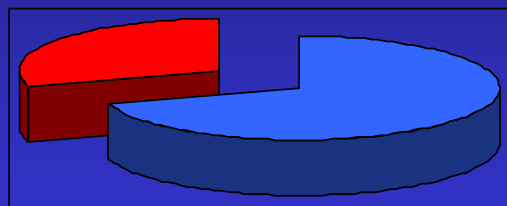
Hepatic artery ligation
Intraarterial bland embolization
Transcatheter Arterial Chemo Embolization
Selective Internal Radiation Therapy
Drugs-Eluting-beads

Rational for vascular Therapies

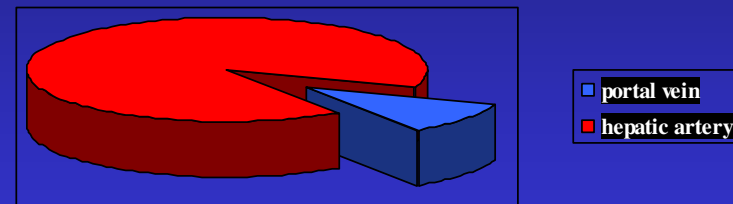
- In theory, vascular therapies can be applied to every location mets
- Practically, most of the vascular therapies are aimed to liver mets

Rational for vascular Therapies

- Liver vascular supply depends on portal vein (70%) and hepatic artery (30%)
- Mets vascularity originates mainly from hepatic artery (90%)



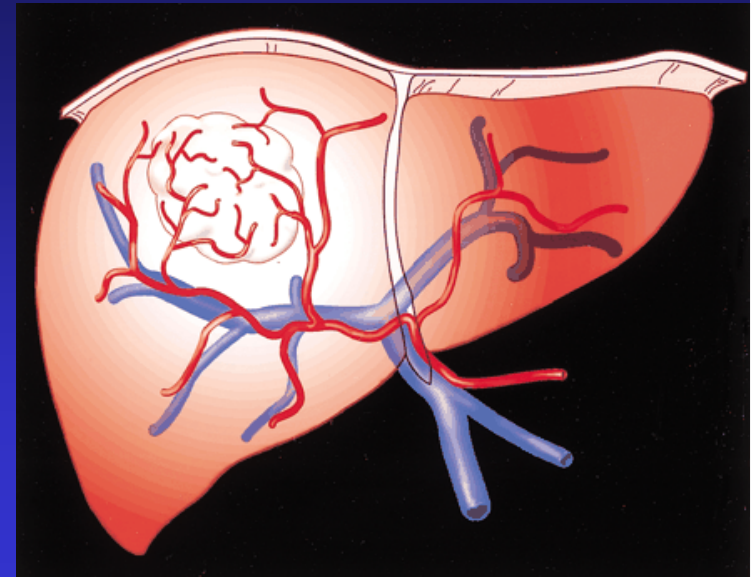
Liver vascular supply



metastases vascular supply

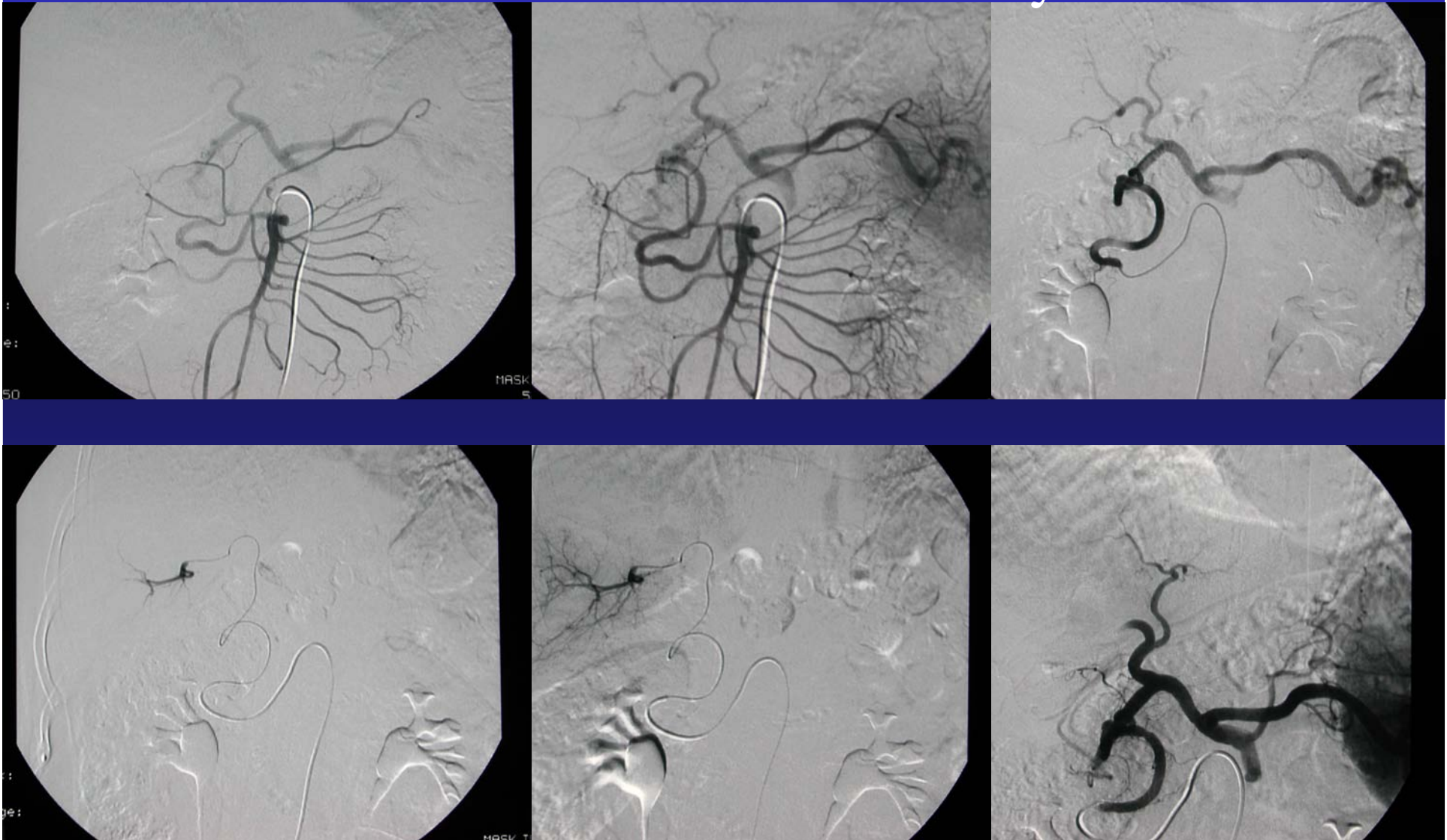
Vascular Therapies: drawbacks

- Collateralization of arterial supply
- Variable arterial anatomy
- Increase of tumor aggressivity (upregulation of angiogenesis factors; Bevacizumab?)
- Vessel stricture or dissection preventing further treatments



Vascular Therapies: drawbacks

Variable arterial anatomy



Rational for vascular Therapies

- Several reports have established that induction of tumor ischemia can increase the response to systemic chemotherapy and can reduce hormone levels, palliate symptoms and reduce tumor burden

Rational for TACE over TAE

- Increased efficacy of local delivered chemotherapy (increased concentration and exposure time)
- Enhanced biological effects of chemotherapy by hypoxia (doxorubicin, Mitomicin C, Streptozocin)



TACE over TAE: evidence based?

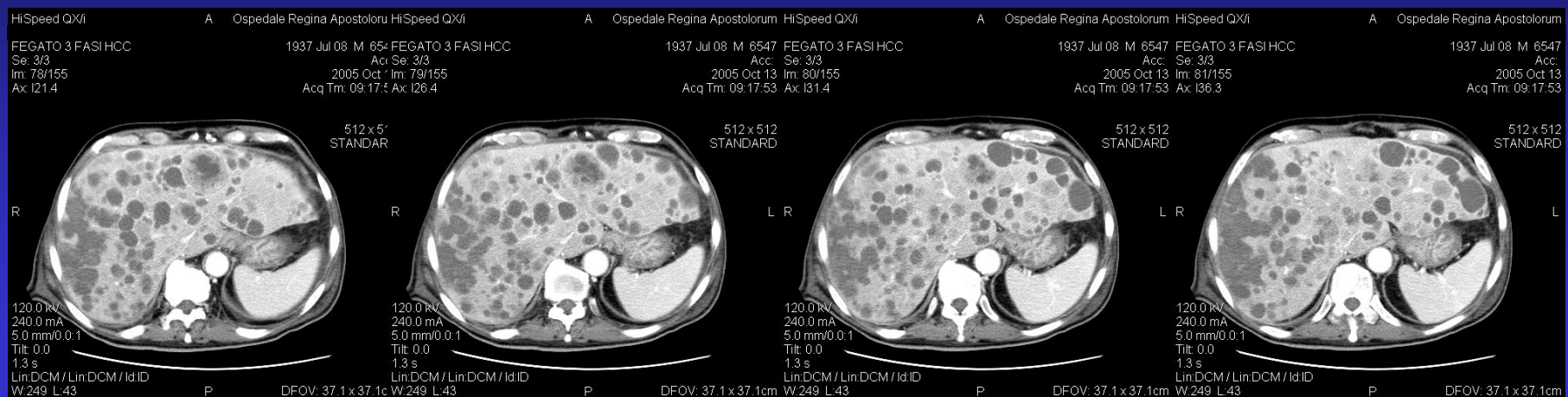
- It is unclear whether chemoembolisation offers any therapeutic advantage over bland embolization
- No consensus on which chemotherapeutic agent or association have to be used

TACE and TAE: indications

- Symptoms related to hormonal excess
- Symptoms related to tumor bulk
- Patients with progressive and dominant liver disease

TACE and TAE: how much of the liver should be embolized?

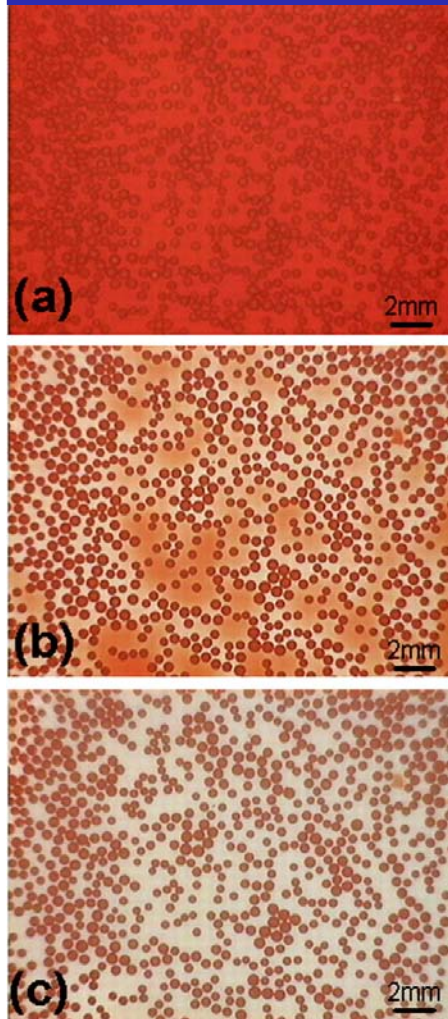
- Embolization of the whole liver in a single session should be avoided
- To avoid liver failure in patients with extensive disease (>75%) only a small portion of liver lobe should be embolised during each session



TACE and TAE: complications

- Despite selective embolisation there may occur:
 - a) liver failure (4% mortality)
 - b) tumor lysis syndrome (postembolic syndrome) in 86% of cases

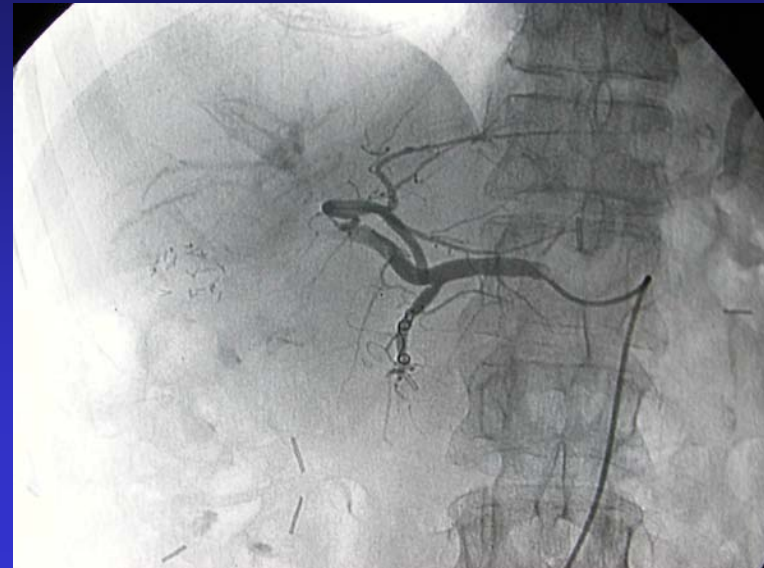
Transcatheter Arterial ChemoEmbolization (TACE) with Drug Eluting Beads (Precision TACE)



- It consists of injecting drug loaded beads in the hepatic vasculature
- It represents an evolution of standard TACE
- drug elution is controlled and sustained unlike the rapid separation of the drug from lipiodol

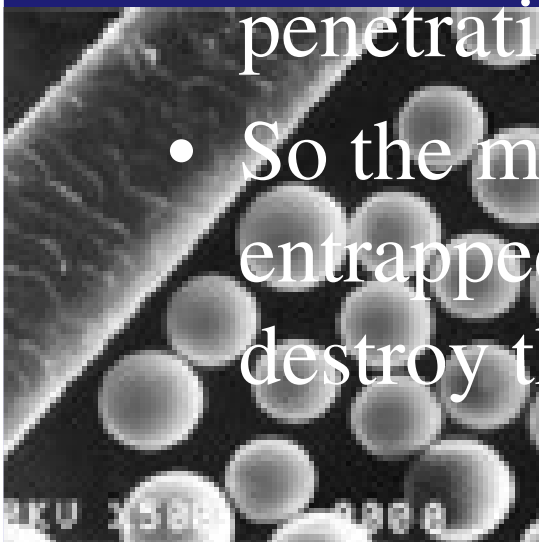
Loading of 300–500- μ m beads with 25 mg/mL doxorubicin at 1 minute (a), 10 minutes (b), and 20 minutes (c).

Transcatheter Arterial ChemoEmbolization (TACE) with Drug Eluting Beads (Precision TACE)



Selective Internal Radiation Therapy SIRT

- Consists of injecting ^{90}Y ttrium loaded glass or resin microsphere (20-40 μm) in the hepatic vascular bed
- ^{90}Y ttrium is a pure high energy β emitter (0.9367 MeV) with a mean tissue penetration of 2.5 mm.
- So the microspheres preferentially entrapped in hepatic metastasis irradiate and destroy the surrounding cells



SIRT: possible advantages vs TACE

- The treatment produce minimal or bland embolisation (\uparrow O² tension increase the efficacy !!!!!)
- Large portion or the entire liver can be treated in a single session
- Acute and subacute toxicity appear to be more tolerable than for other hepatic embolisation procedures
- Less arterial endothelium toxicity

SIRT: possible disadvantages vs TACE

- The introduction of microsphere into the vasculature of organs other than liver can produce chronic pain, ulceration or bleeding
- Extrahepatic shunting needs to be identified through the injection of Tc-99m MAA into the hepatic artery
- Coiling of collaterals often required
- Hepatic fibrosis

SIRT and Precision TACE: results

- The introduction of SIRT and Drug-Eluting -Beads aroused new interest in Transcatheter Arterial Therapies and larger series of patients have been enrolled
- Preliminary results appear to be promising

Liver Directed Therapies as a bridge therapy to curative liver resection

- Tumor ablation or embolization can be used to improve performance status before resection
- Combined hepatic artery and portal vein embolization can increase number of patients amenable to extended liver resection
- Synchronous and asynchronous curative resection and curative ablation can be used in the same patient

Minimally Invasive Therapies for metastases to the liver: take home points

- Data suggest that aggressive management of hepatic metastases does improve survival
- Minimally Invasive Treatments increase the patient population eligible for this strategy
- Patients with more than 30-50% liver involvement may not benefit from an aggressive approach.

Minimally Invasive Therapies for metastases to the liver: future directions

- Eluting beads with new drugs
- SIRT associated with radiosensitizing chemotherapy
- Laser Ablation with sensitizing nanoparticles
- Combination of novel molecular targeted therapies with liver directed therapies