



ANNUAL

**Advances and Innovations in Endoscopic Oncology
and Multidisciplinary Gastrointestinal Cancer Care**

Pioneering Progress: Next-Gen Liver Directed Therapies Unveiled

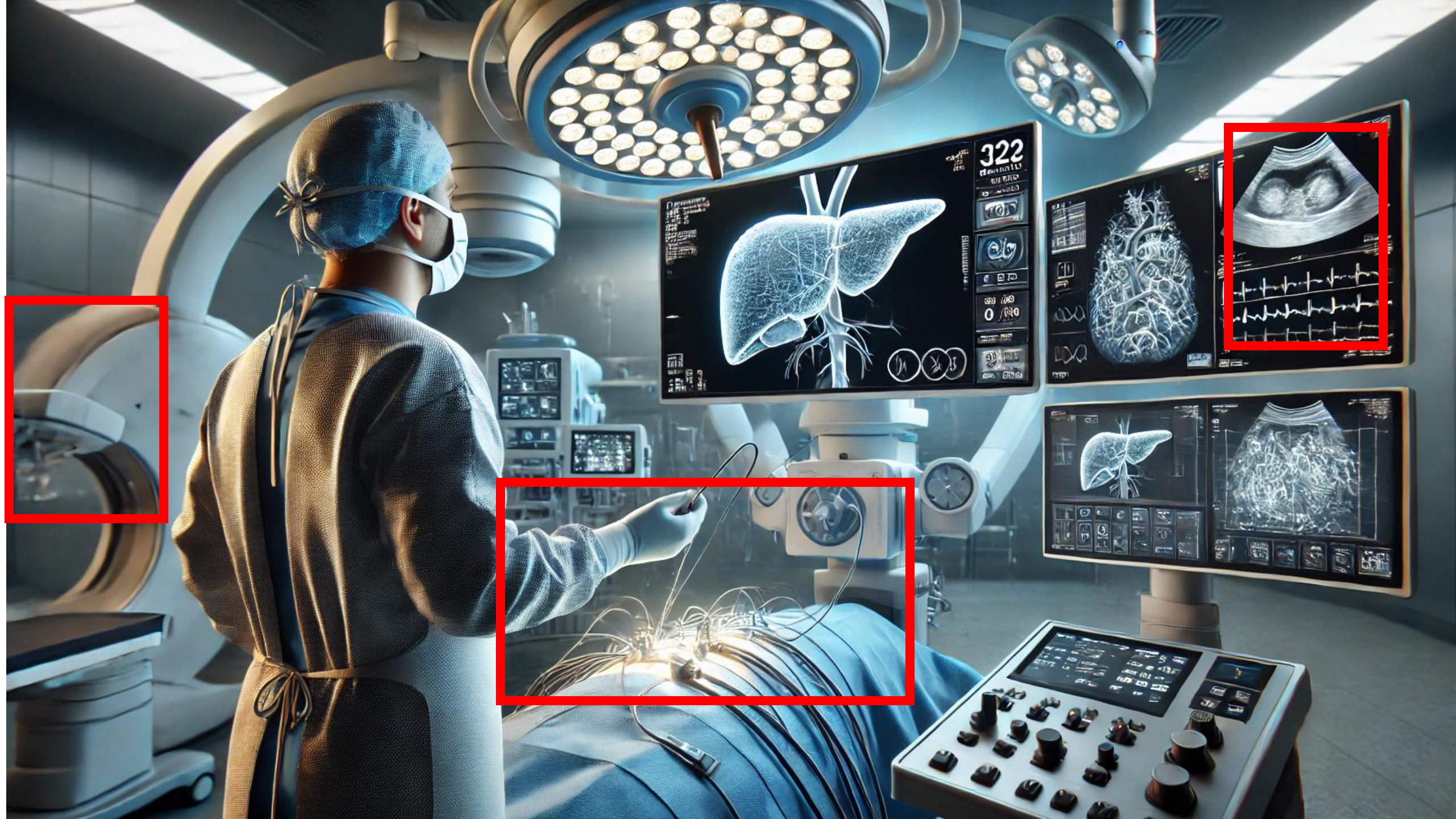
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Chief of Division of Interventional Radiology

City of Hope Duarte





Disclosures

- Consultant Boston Scientific, Ethicon, Galvanize Therapeutics, and Sirtex Medical

The presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed [Assembly Bill \(AB\) 1195](#), which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed [AB 241](#), which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

What's New...Where Are We Going?

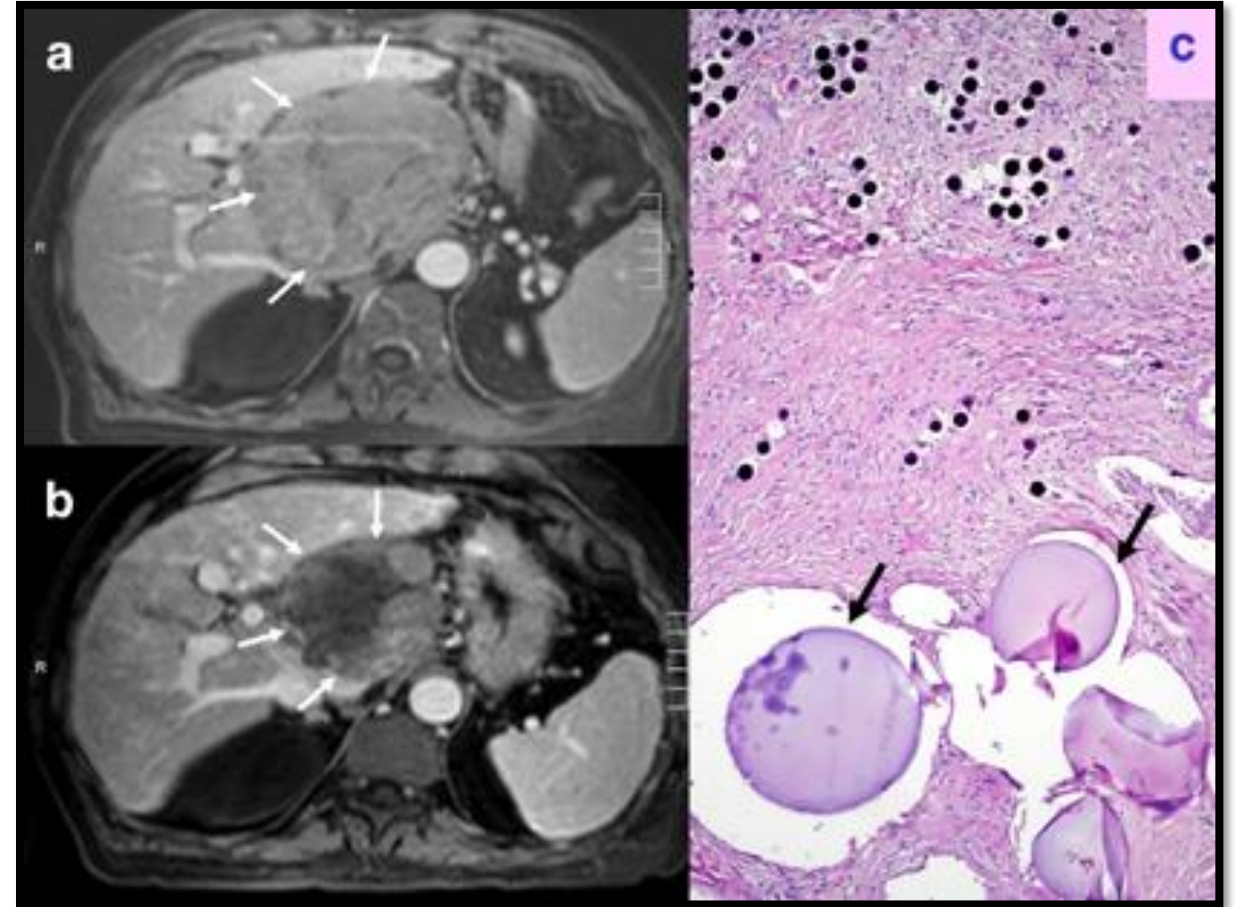
- Y-90 and the future of radioembolization
 - Dosimetry and high dose selective treatment
- Isolated Hepatic Perfusion
- Trans-arterial Microperfusion
- Histotripsy



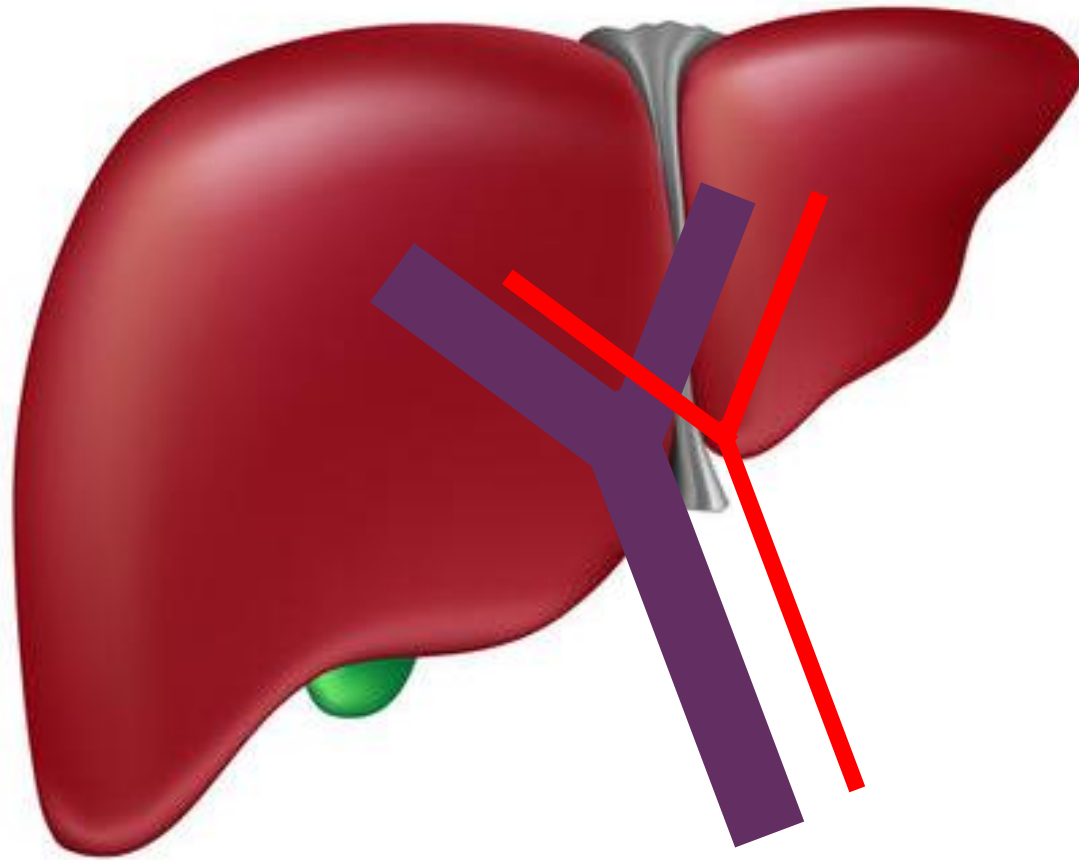
Radioembolization

Yttrium 90

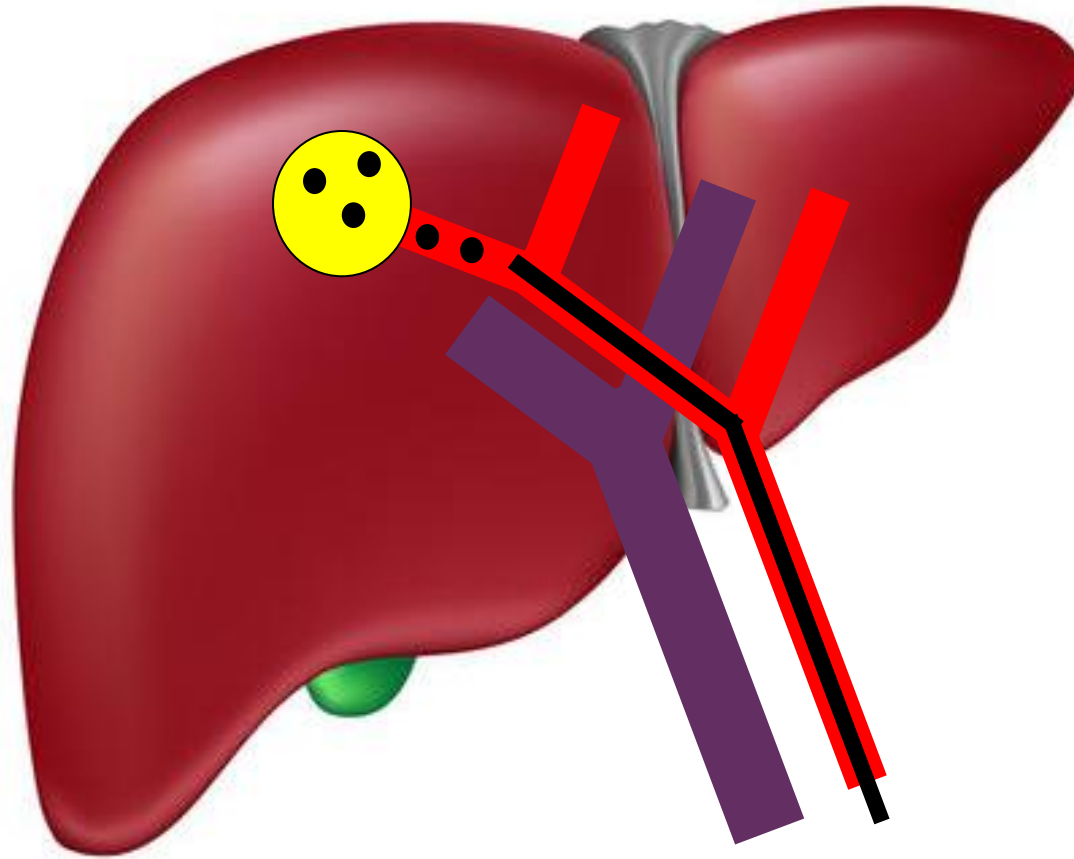
- pure beta-emitter with a half-life of 64.2 hours.
- Tissue penetration of the emissions is 2.5 to 11 mm
- Emits local high dose of radiation to tumor with little embolic effect.
- Treatment done as outpatient procedure
- May deliver 200- 1000Gy to tumor!!!



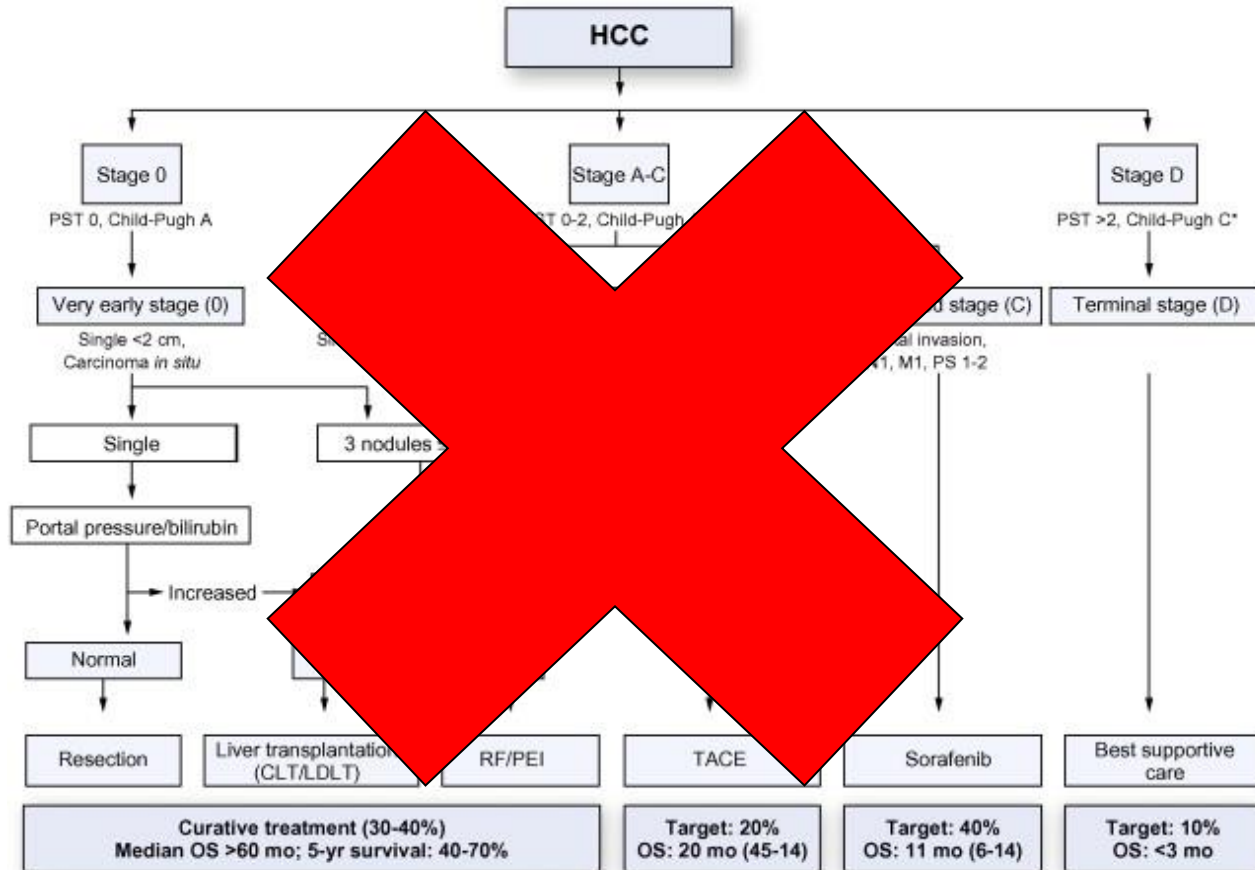
Liver Directed Therapy



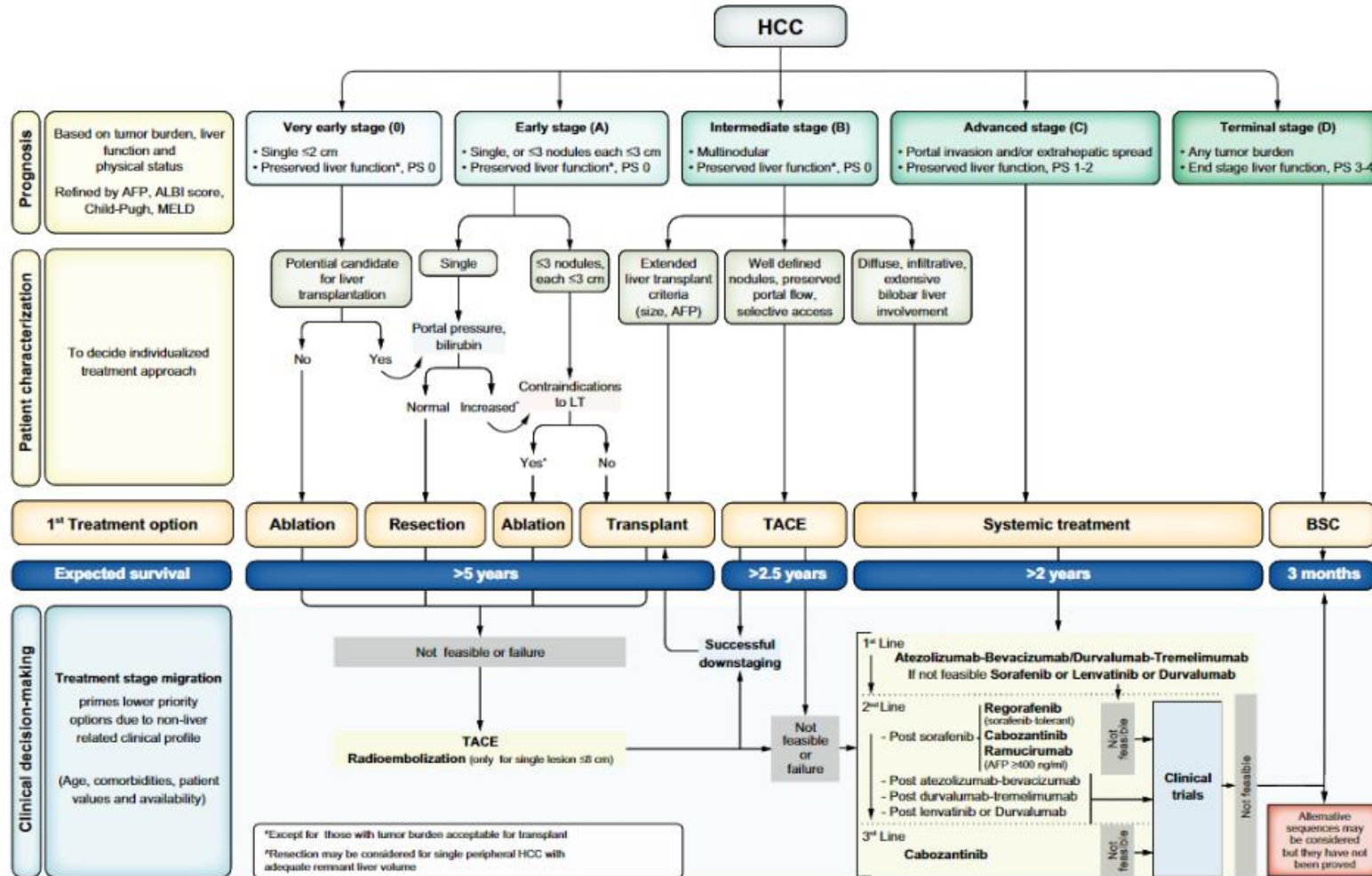
Liver Directed Therapy



HCC- Where were we



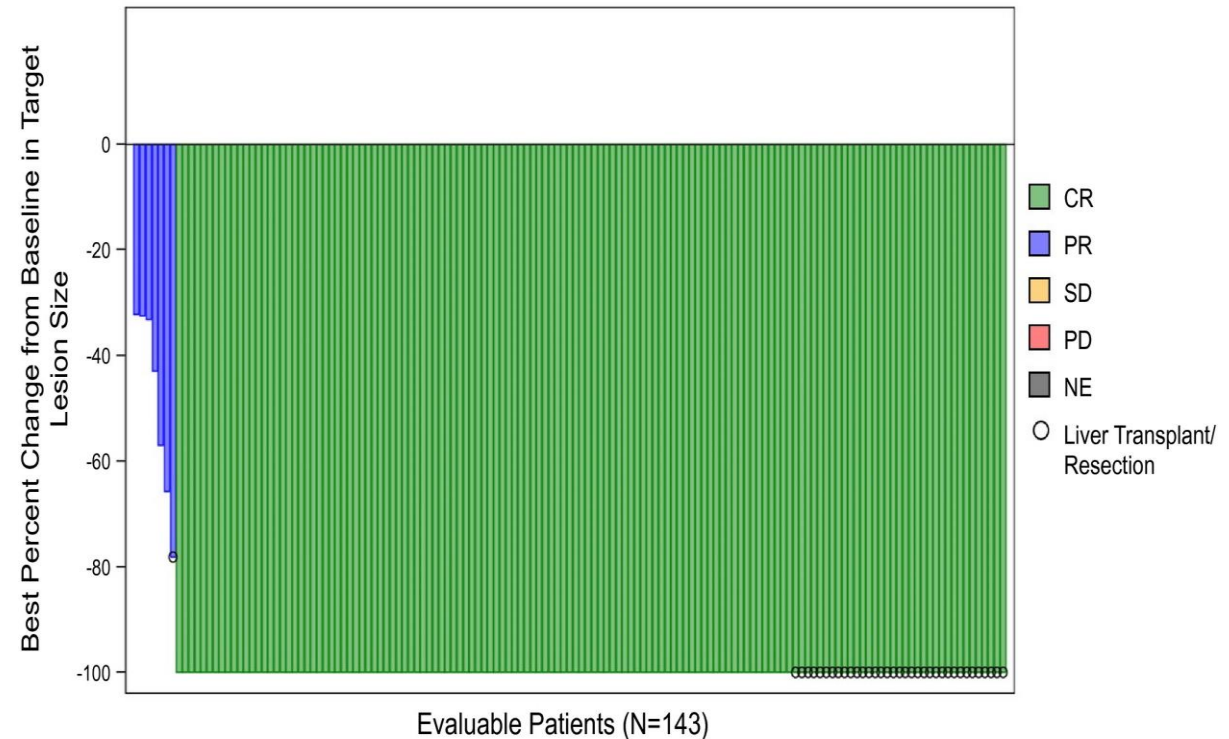
HCC- Where are we



Legacy Study

■ Can we cure large tumors?

- Multicenter single arm 162 pts
 - Solitary Tumor up to 8 cm
 - Median Dose 410 Gy!
 - ORR 88.3%
 - PFS 93.9% at 24 months
 - 84% 3 yr OS without surgery
 - 93% 3yr OS when downstaged to surgery/txplt



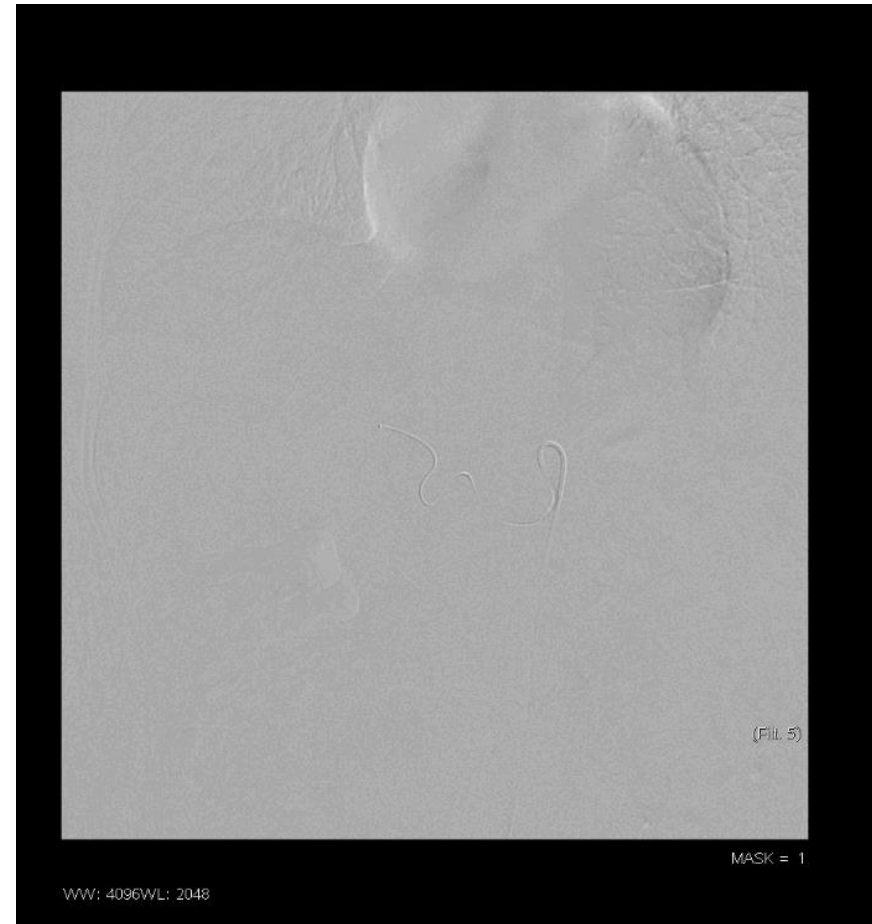
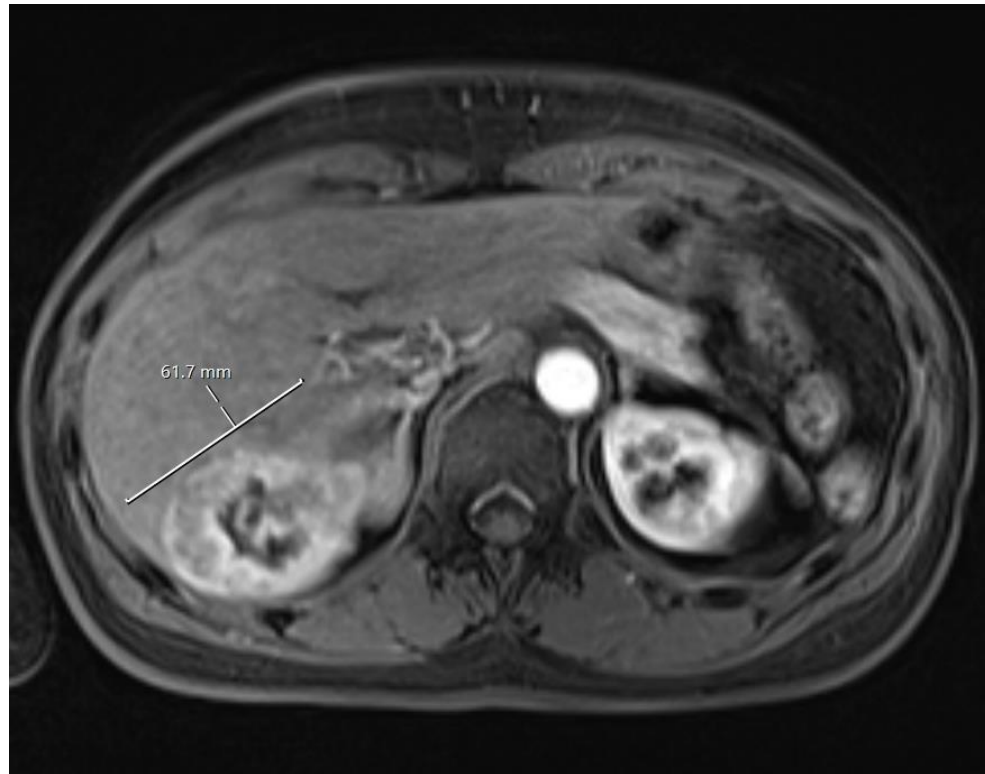
Complete Pathologic Necrosis

Voxel-based tumor dose correlates to complete pathologic necrosis after transarterial radioembolization for hepatocellular carcinoma

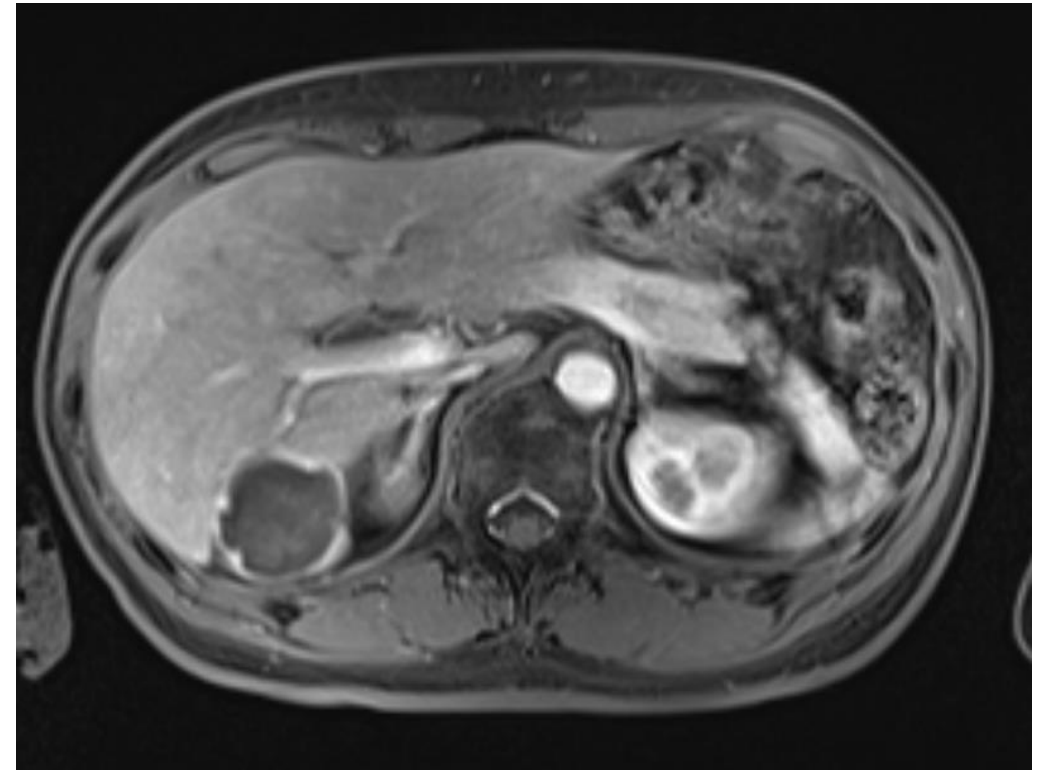
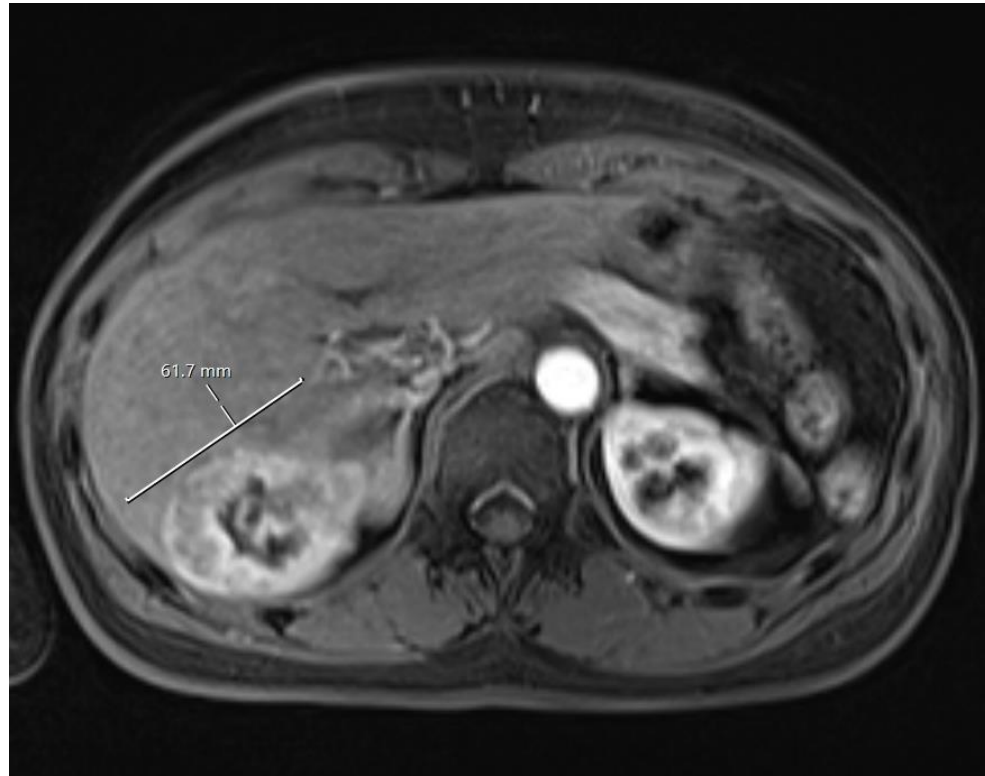
Hepatocellular carcinoma radiation segmentectomy treatment intensification prior to liver transplantation increases rates of complete pathologic necrosis: an explant analysis of 75 tumors

- Pianka et al EJNMMI 2024
 - 26 pts with complete pathologic response post Y90
 - D95 of 719 Gy
 - 87% spec for CPN
- Montazeri et al EJNMMI 2022
 - 38 pts with segmentectomy intent
 - 76% achieved CPN
 - 446 Gy predictive of CPN (OR 5.5)

Curative Y90



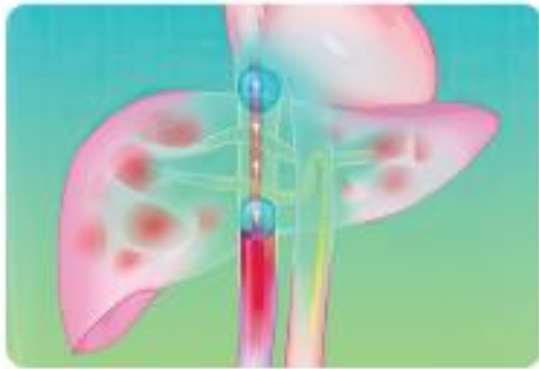
Curative Y90



1 yr later

Isolated Hepatic Perfusion

Isolation



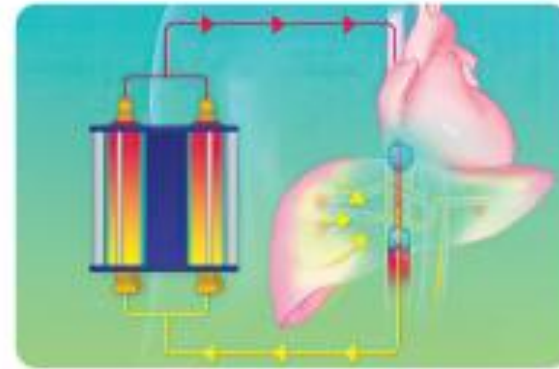
Isolating the liver blood supply allows for the benefits of high-dose melphalan while reducing systemic toxicity^{3,4}

Saturation



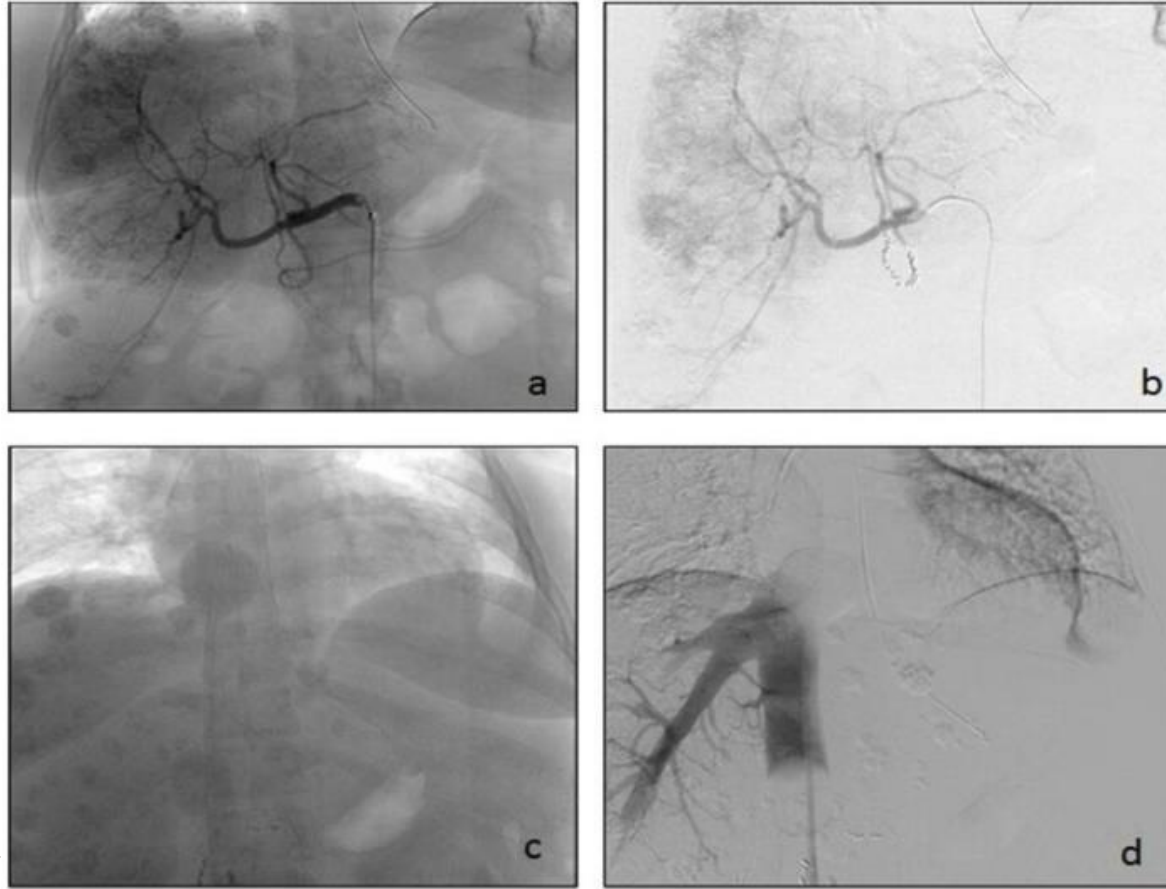
A 30-minute infusion of high-dose melphalan effectively delivers treatment to the entire organ^{1,3}

Filtration



A 30-minute washout period removes >80% of the melphalan, thereby limiting systemic drug exposure (mean [SD] filter efficiency of 82.7% [14.4%] for the total filtration period)¹

Isolated Hepatic Perfusion



Quadri et al. Hepatoma Research
July 2016

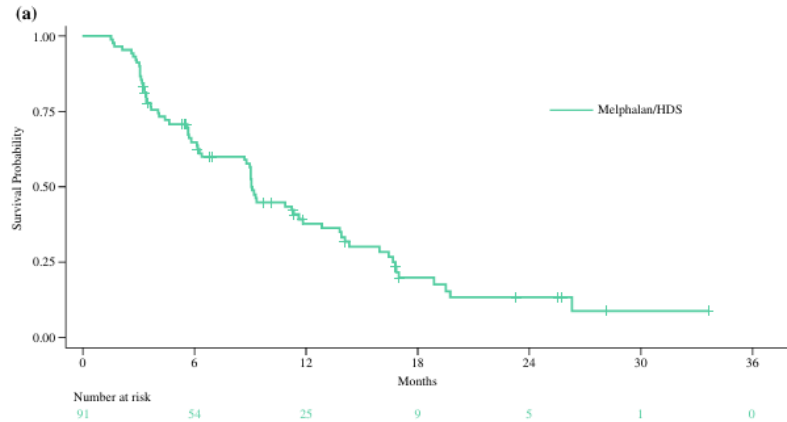
Isolated Hepatic Perfusion

■ Focus Trial

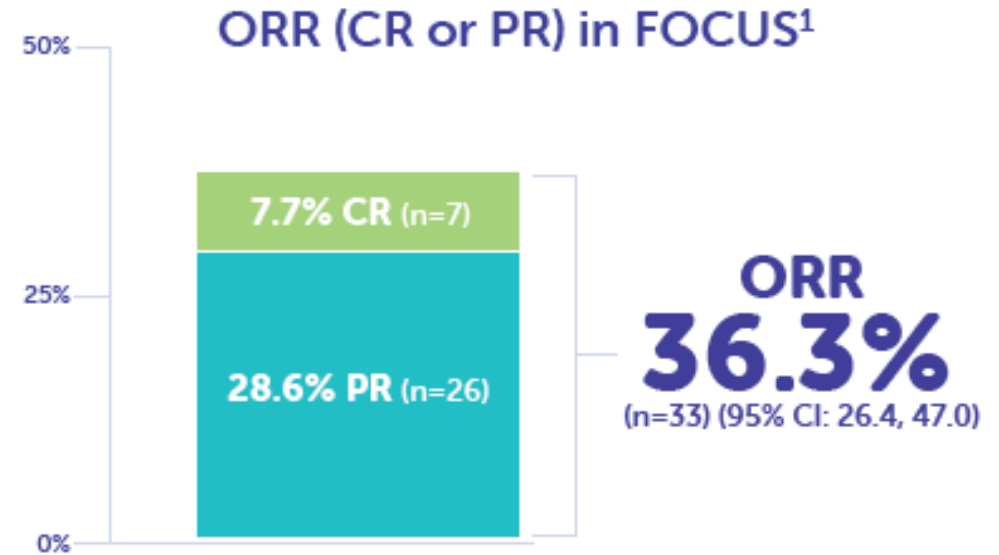
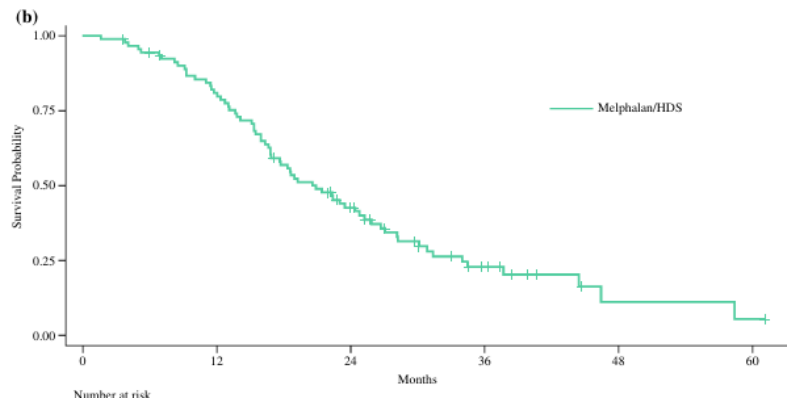
- Uveal melanoma 3-5% of melanoma cases
- Liver primary site of metastatic disease in 90 % of patients
- Median OS 12 months
- Multicenter Study 91 pts with metastatic uveal melanoma
- 3mg/kg melphalan q6-8 weeks for up to 6 cycles
- Open label single arm study

Isolated Hepatic Perfusion

mPFS - 9 months



mOS – 20.5 months



CR: Disappearance of all target lesions^a

PR: $\geq 30\%$ Decrease in the sum of the long axis diameter of tumor target lesions^b

TransArterial MicroPerfusion



Hypervascular tumors are adequately treated with current therapies

Tumors that are highly vascularized

- Large tumor feeders – excellent targets for systemic therapy
- Can be accessed and treated with current local therapy techniques

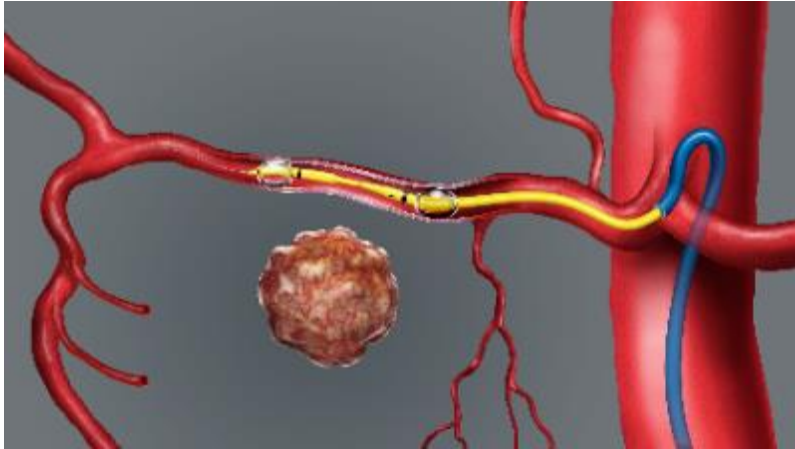


Hypovascular tumors = major barrier to chemotherapy treatment success

Tumors that have poor blood supply

- No visible tumor feeder vessels
- Systemic therapy does not reach tumor tissue
- Inability to identify or engage tumor feeder vessels: local therapy is ineffective

TAMP

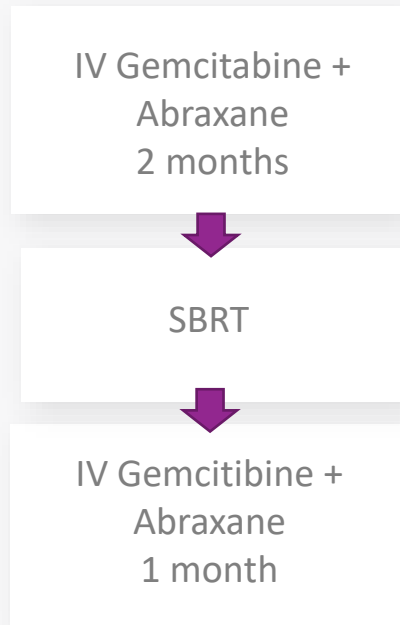


Mechanism: after vessel isolation, increase in pressure forces drug across the artery wall into the micro-vasculature into tissue



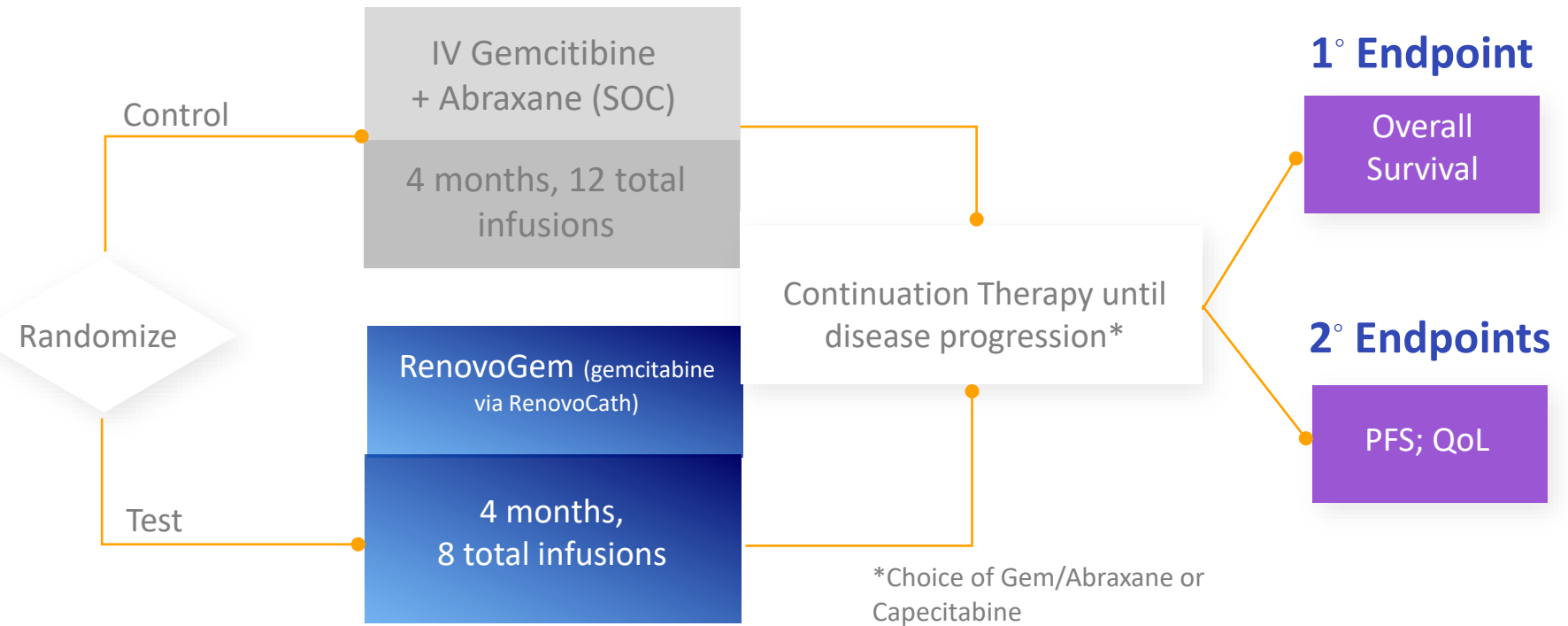
RR3 TIGeR-PaC: Randomized Combo Product Clinical Trial

INDUCTION PHASE



1:1 RANDOMIZATION PHASE

4-Months Maintenance Treatment:
SOC vs RenovoGem

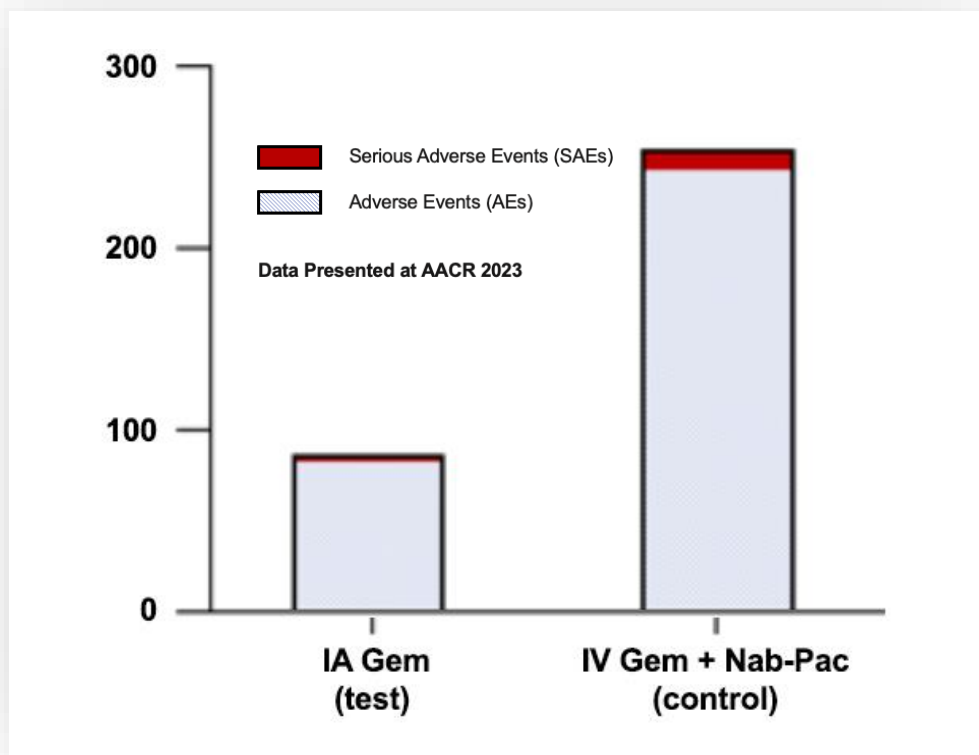


TIGeR-PaC 1st of Two Pre-Planned Interim Analyses: Tolerability and Safety

Tolerability during active treatment:

- 61% of IA patients received all planned treatments at the pre-specified dose vs. 18% of IV (primarily due to AEs or SAEs)
- Patients receiving IV therapy had more myelosuppression, fatigue, dehydration, neuropathy, and metabolic derangements
- Patients receiving IA therapy had more nausea and abdominal pain events

65% fewer total AEs and SAEs in IA vs. IV arm

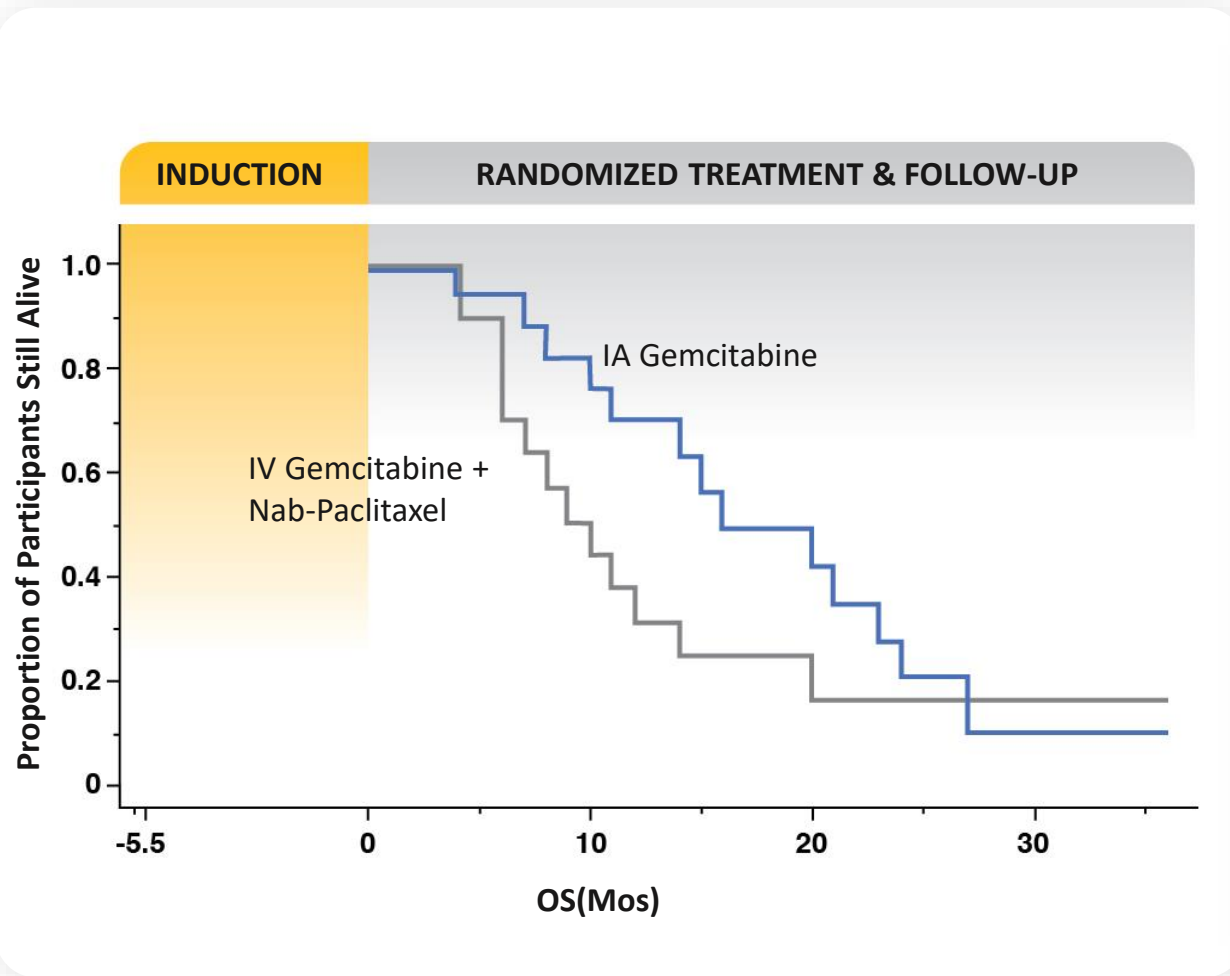


AEs with greater than 10% frequency in each arm (All Grades)

Adverse Events	IV Gem + Nab-Pac	IA Gemcitabine
Neutropenia	81%	21%
Anemia	48%	8%
Thrombocytopenia	38%	4%
Elevated AST	33%	4%
Elevated ALT	29%	13%
Fatigue	19%	8%
Neuropathy	19%	0%
Dehydration	19%	8%
Hypertension	14%	4%
Hypokalemia	14%	4%
Hypoalbuminemia	14%	4%
Abdominal Pain	0%	21%
Nausea	10%	17%

Adverse event prevalence: ● IA ● IV

TIGeR-PaC 1st of Two Pre-Planned Interim Analyses: median Overall Survival

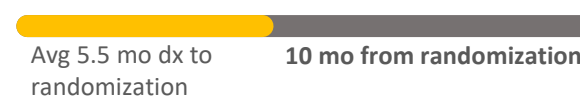


Data on 45 patients randomized

- 23 randomized to IA gemcitabine
- 22 randomized to IV gem + nab-pac

Median Overall Survival (OS) Difference: **6-months**

IV Gem + Nab-Pac (control arm)



10
Months from
randomization

~15.5 months from diagnosis

IA Gemcitabine (test arm)



16
Months from
randomization

~21.5 months from diagnosis

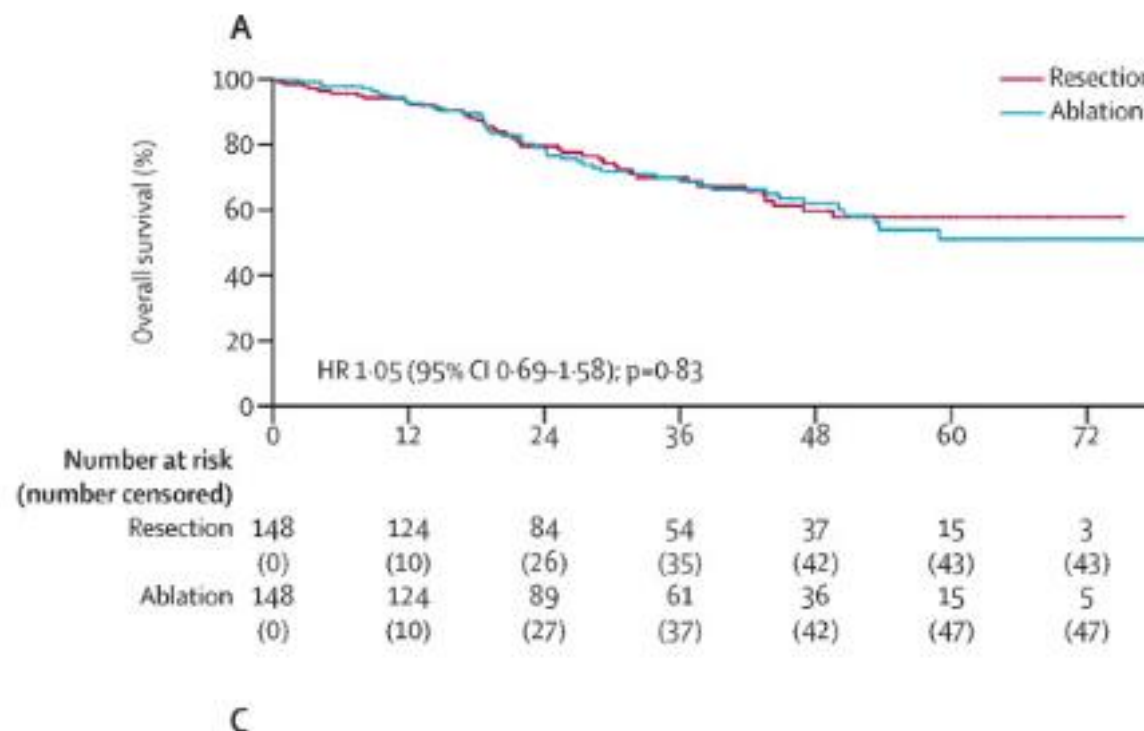
Statistical significance not reached to stop the study early; however, meets continuation requirements by DMC [HR: 0.48 (95% CI: 0.2-1.12)]. The efficacy and safety of delivering FDA approved gemcitabine combined with FDA cleared RenovoCath has not been established.

Thermal ablation versus surgical resection of small-size colorectal liver metastases (COLLISION): an international, randomised, controlled, phase 3 non-inferiority trial

Van der Lei et al. Feb 2025

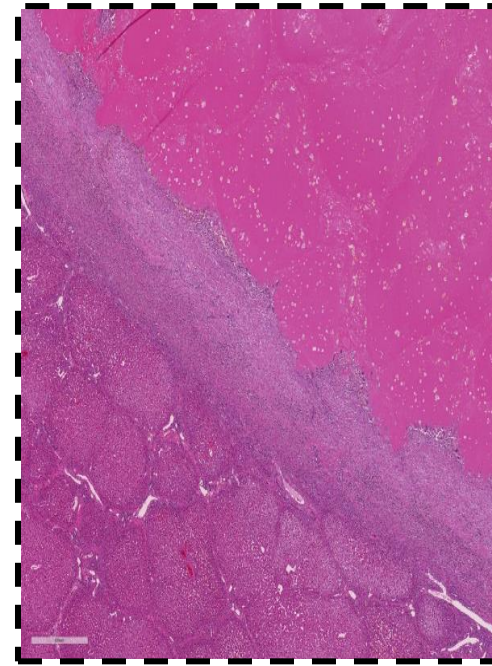
THE LANCET
Oncology

- Phase 3 randomized study metastatic CRC ablation VS surgery
 - 341 patients enrolled
 - Fewer than 10 tumors
 - Under 3 cm in size
 - No difference DFS or OS
 - Mortality
 - 2.1% surgery vs 0% ablation
 - Ablation favored
 - Adverse events
 - Length of stay
 - Local control

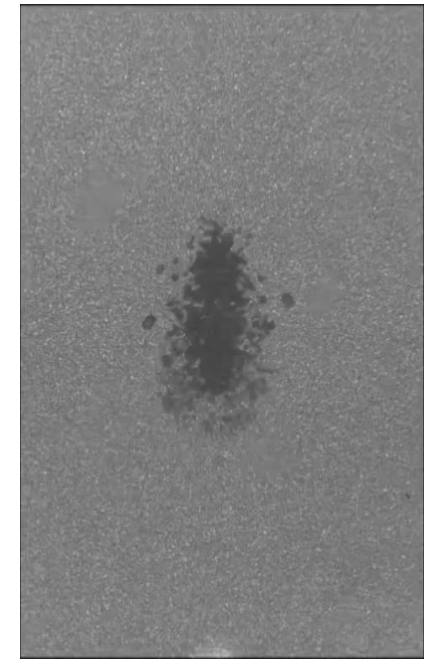


WHAT IS HISTOTRIPSY

- Histotripsy is a noninvasive ablation modality
- Mechanically destroys tissue using US target beam
- Liquifies tissue and causes instantaneous cell death

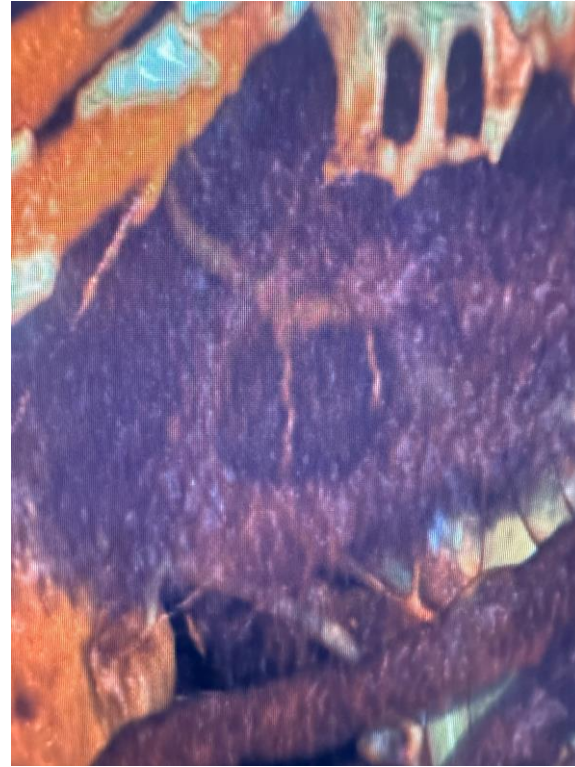
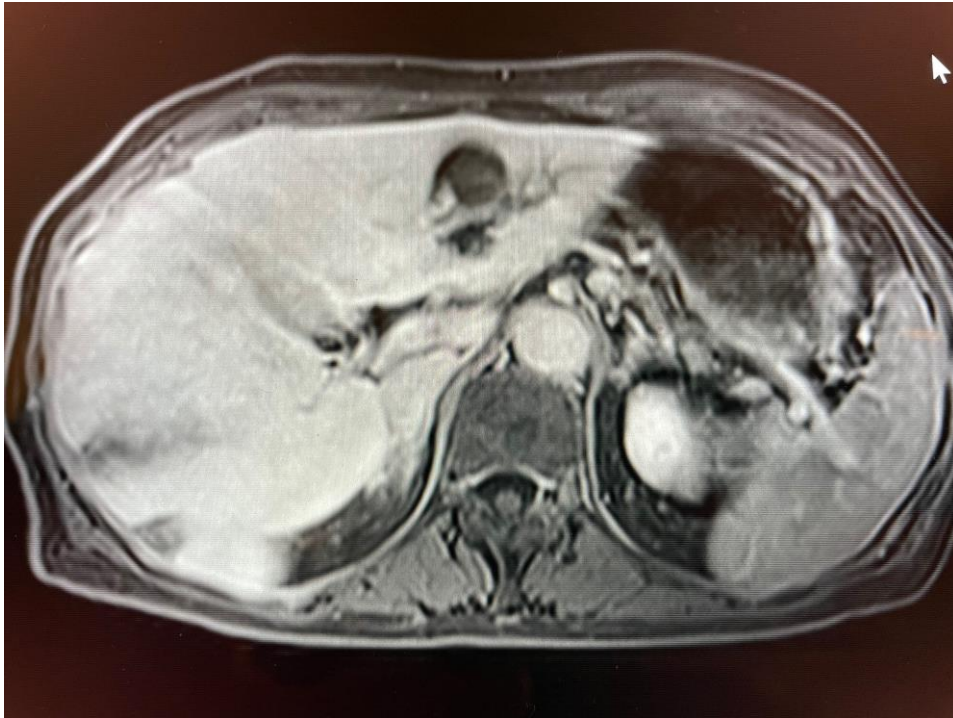


Histopathological image of histotripsy treatment in porcine liver showing uniform treatment effect within the treatment zone with a well-demarcated transition to healthy, unaffected tissue.



Red Blood Cell Phantom

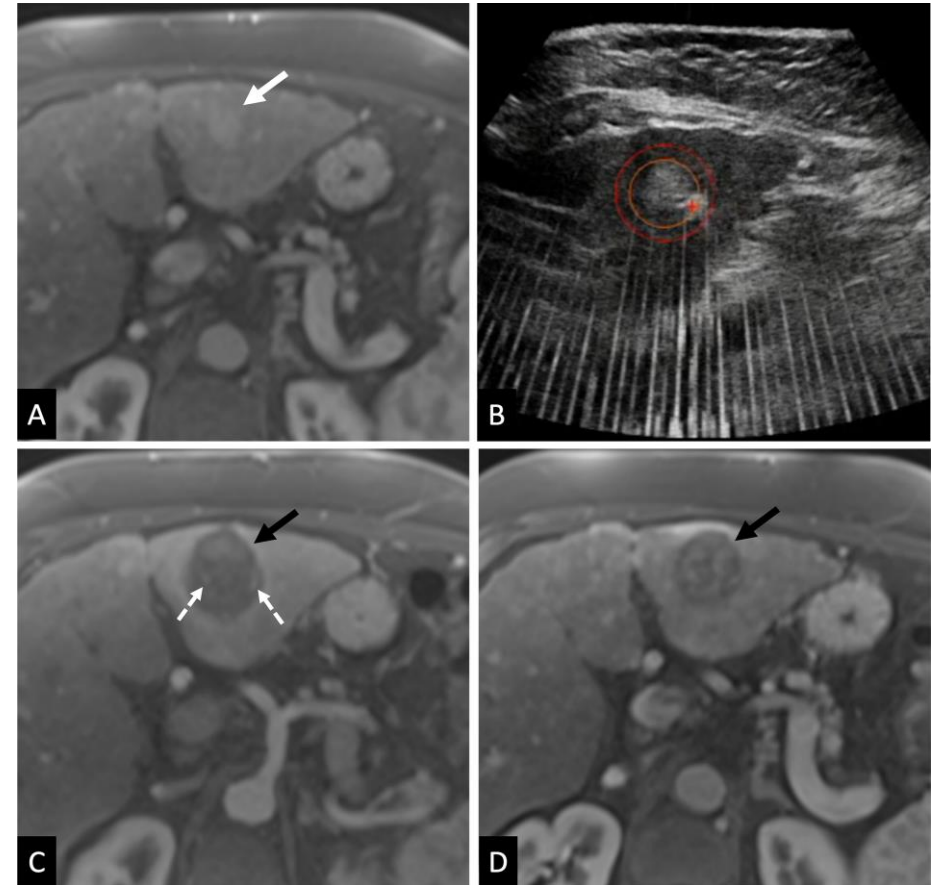
Histotripsy preservation of Support structures



HOPE4LIVER Study

Mendiratta-Lala et al Radiology sept 2024

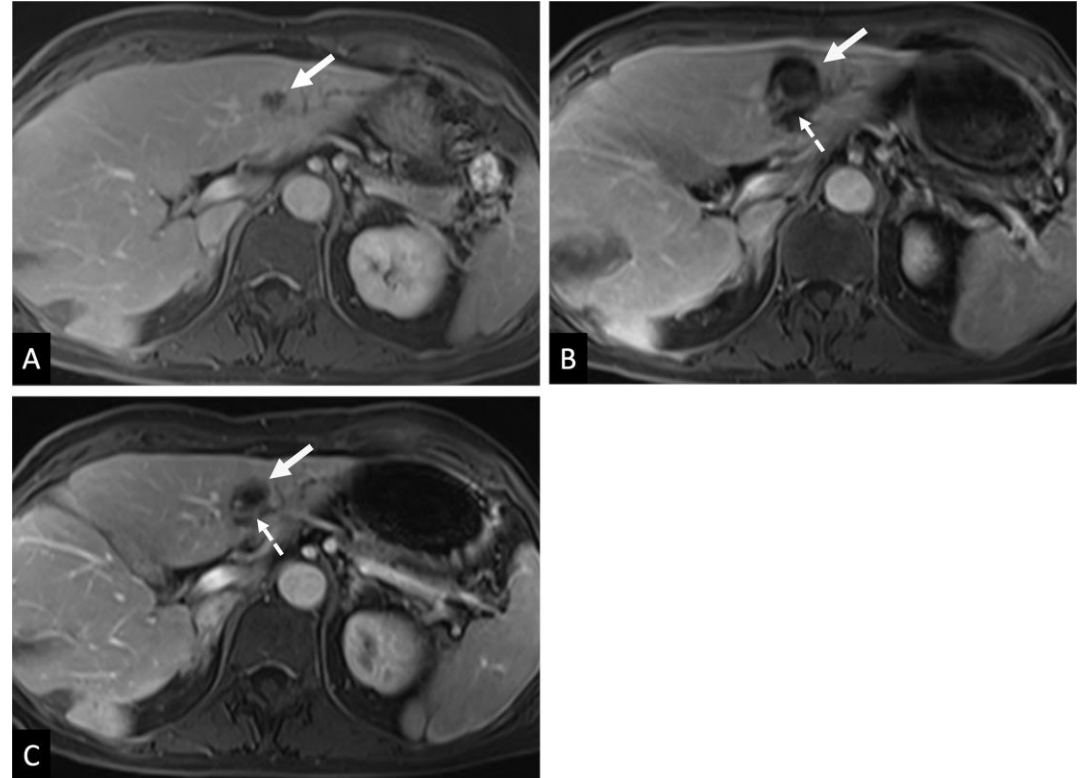
- Multicenter, single arm trial
- 3 tumors up to 3 cm in size
- 44 patients with 49 tumors treated
- 41% HCC: 59% Metastatic disease
- Endpoints- technical success and safety



HOPE4LIVER Study

Mendiratta-Lala et al Radiology sept 2024

- Technical success achieved in 42/44 tumors
- Technical efficacy at 30 days 83%
- 3 grade 3 or > complications
 - Infection, pain, liver failure (disease progression?)



Thank you!

