Role of Interventional Radiology in Oncology Care

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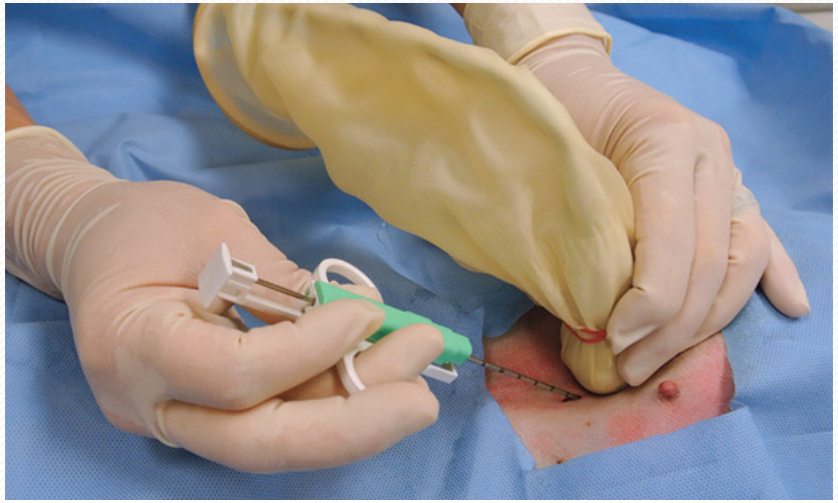
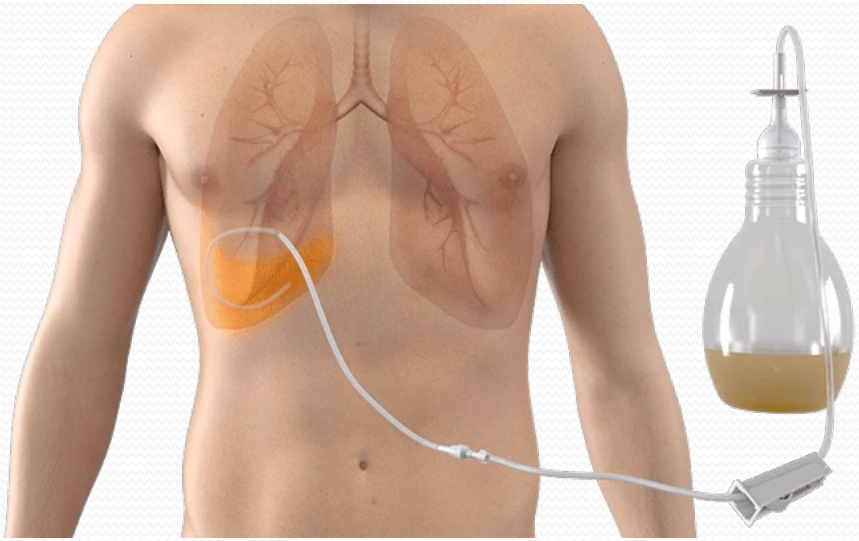
IntelliRad Imaging

Objectives

- Introduction to Interventional Radiology and its role in oncologic care
- Briefly review percutaneous and transcatheter ablation methods employed by interventional radiology in the locoregional control of malignancy
- Discuss several commonly encountered malignancies and the possible role of Interventional Radiology in co-treatment

Interventional Radiology





Interventional Radiology

- Offers minimally invasive image guided targeted treatment of cancer, often outpatient
- Broad categories of procedures
  - Neo-adjuvant (pre-operative) procedures
    - Port placement, biopsies, etc
  - Intra-arterial therapy
    - TARE and TACE
  - Ablative therapy
    - Microwave/radiofrequency ablation, Cryoablation
  - Pain palliation
    - Vertebral tumor ablation with vertebroplasty

Interventional Radiology

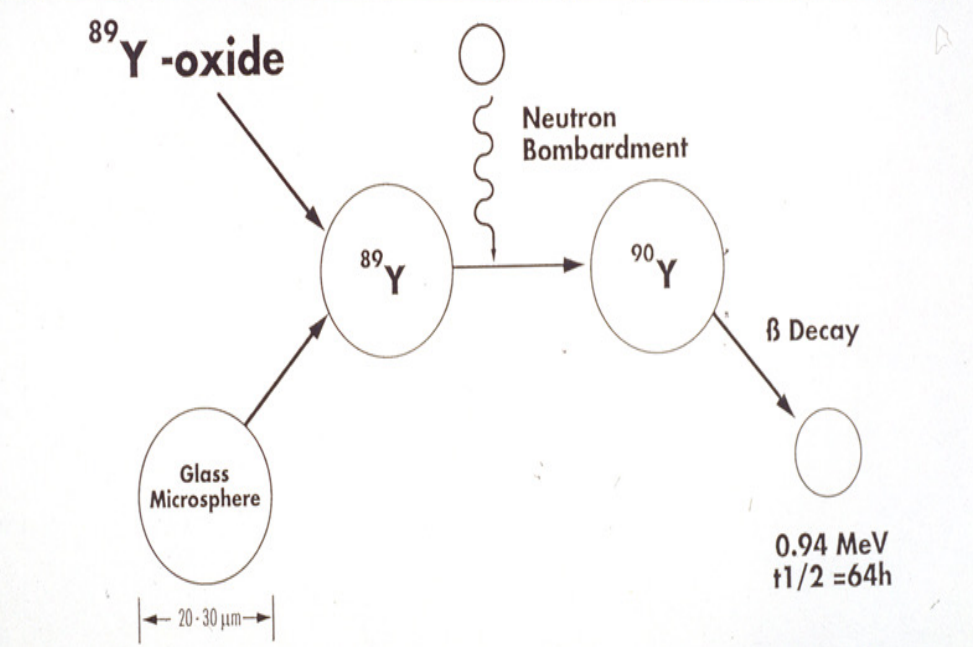
- Component of MDTB
- Often for poor surgical candidates, when systemic therapy fails, or as a supplement to systemic treatment
  - However increasingly being investigated as a first line therapy

Intra - Arterial Therapy: Chemoembolization

- Transarterial delivery of drug eluting microspheres
- Drug eluting beads loaded with chemotherapeutic
  - Provides sustained controlled release
  - Ex: doxorubicin in HCC
- Higher local drug concentration
- Lower systemic drug exposure
  - Compared with systemic treatment
- Used for hepatic malignancies
- May require post-procedure overnight hospitalization
  - Pain control
  - Post embolic syndrome

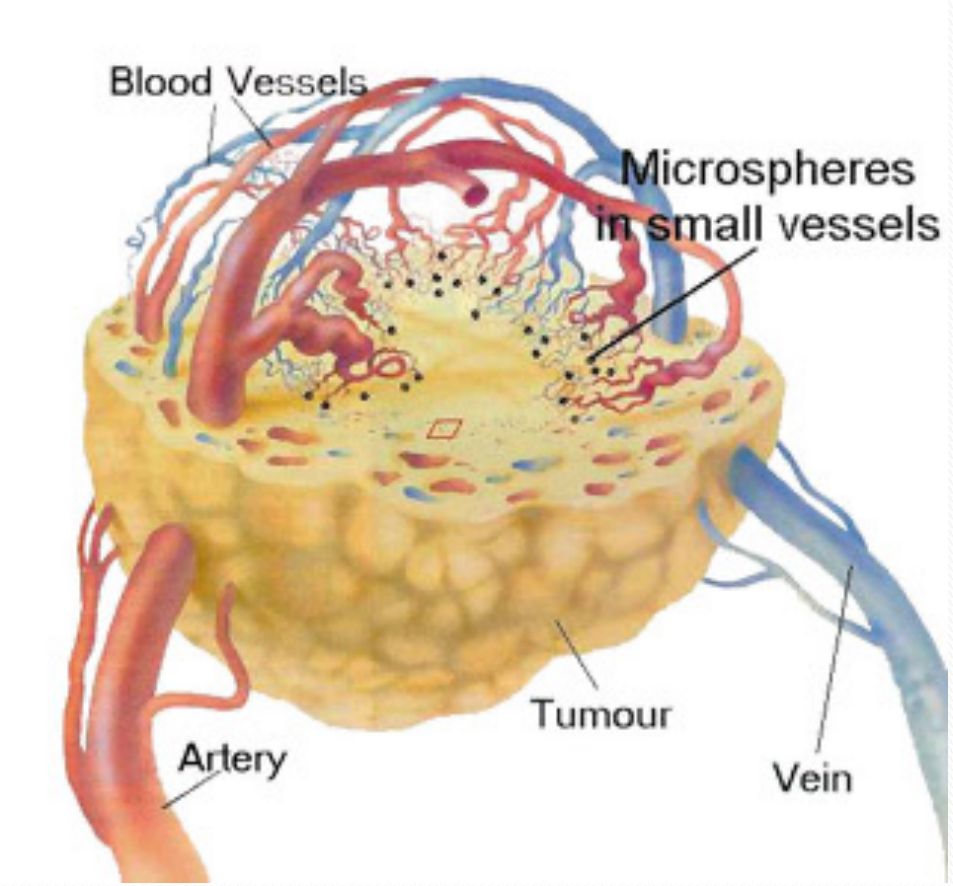
Intra - Arterial Therapy: Radioembolization

- Outpatient procedure
- FDA approved
  - mCRC (2002) and HCC (2021)
- Transarterial liver directed therapy
  - ECOG and Bili most important predictors
- Microspheres loaded with Y90
- Undergoes beta decay to Zirconium-90
- 100% beta emitter
  - Half life of 64.2 hours
  - Average range in tissue of 2.5 mm



Intra - Arterial Therapy: Radioembolization

- Microspheres 32 um in diameter
  - Size comparison
    - WBC 12-15 um
    - RBC 8 um
- Particles lodge in tumor capillaries
  - Irrespective of tumor size or number
- Preferentially target tumors



Intra - Arterial Therapy: Radioembolization

Recent Trials:

- Radioembolization with Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial (EPOCH) (2021)
  - Unresectable mCRC planned for standard second line chemo (oxaliplatin or irinotecan based) randomized to received adjunct radioembolization vs chemotherapy alone
    - ORR 34% in radioembolization + chemo vs 21% in control arm
    - PFS of 8 months vs 7.2 months, hPFS of 9.1 months vs 7.2 months
    - No difference in OS (14 vs 14.4 months)

Intra - Arterial Therapy: Radioembolization

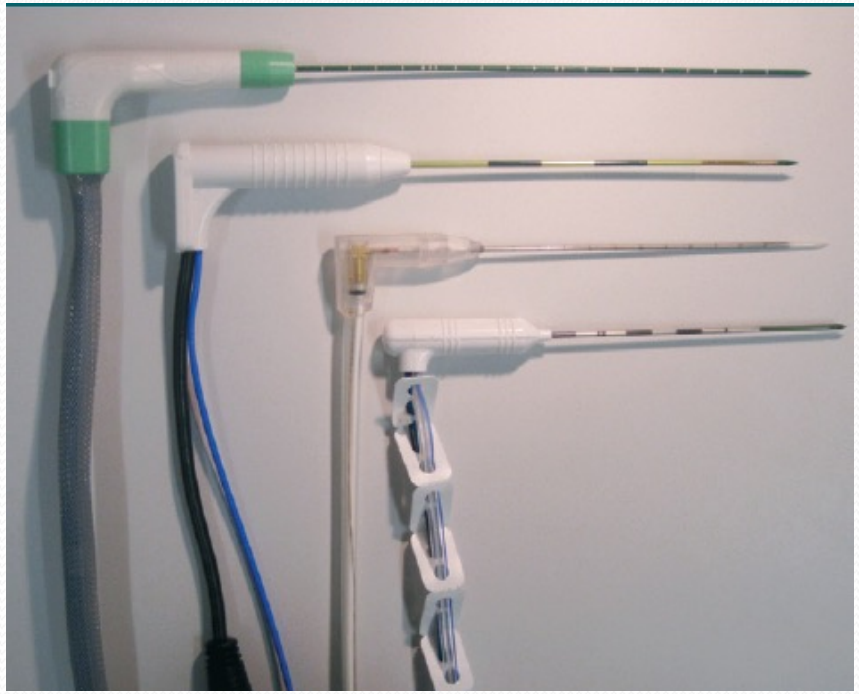
- Survival and Toxicities After Y90 Transarterial Radioembolization of Metastatic Colorectal Cancer in the RESIN Registry (2022)
  - Prospective multicenter registry of 498 unresectable mCRC patients
    - Radioembolization was utilized as first line therapy in 17%, second line in 41%, and third or later in 43%
      - PFS was 7.9, 10, and 5.9 months
      - OS was 13.9, 17.4, and 12.5 months
      - OS 16.2 months if no extrahepatic disease vs 12.6 months if extrahepatic

Intra - Arterial Therapy: Radioembolization

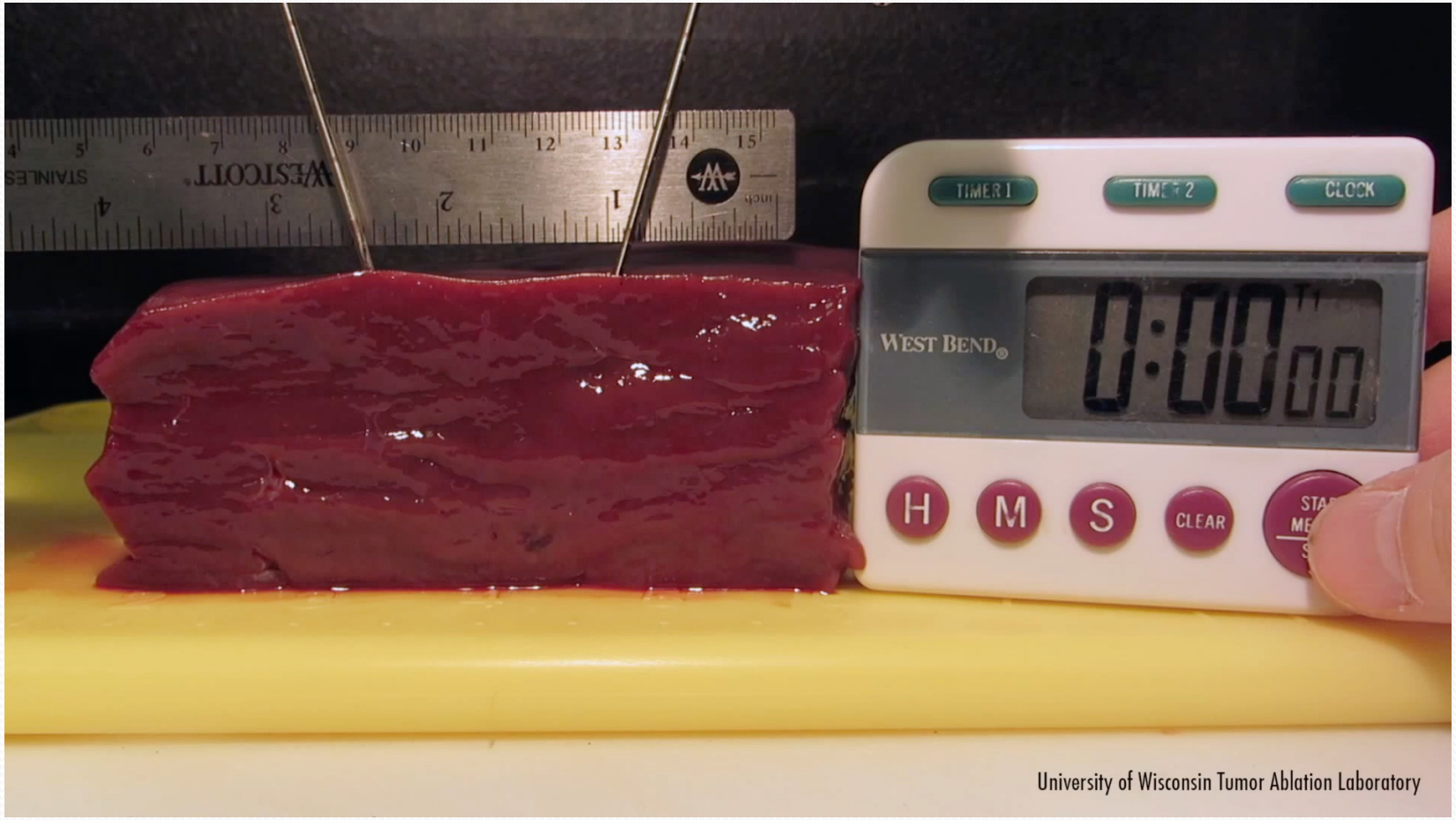
- Radioembolization with Y90 Resin Microspheres Followed by Nivolumab for Advanced Hepatocellular Carcinoma: A Single Arm, Single Centre, Phase 2 Trial (2021)
  - First prospective study reporting on combination of radioembolization and checkpoint inhibition
  - Enrolled patients who were not surgical candidates and had a treatment plan in place for radioembolization
    - Y90 treatment followed by nivolumab at 21 days and then every 2 weeks thereafter
    - Primary endpoint was ORR, with a positive study defined as 41%
      - The study did not meet its primary endpoint with an ORR of 30.6%
        - Subset of patients with liver confined disease ORR was 43.5%
        - ORR improved relative to that of either single agent nivolumab or radioembolization alone

Ablative Therapy

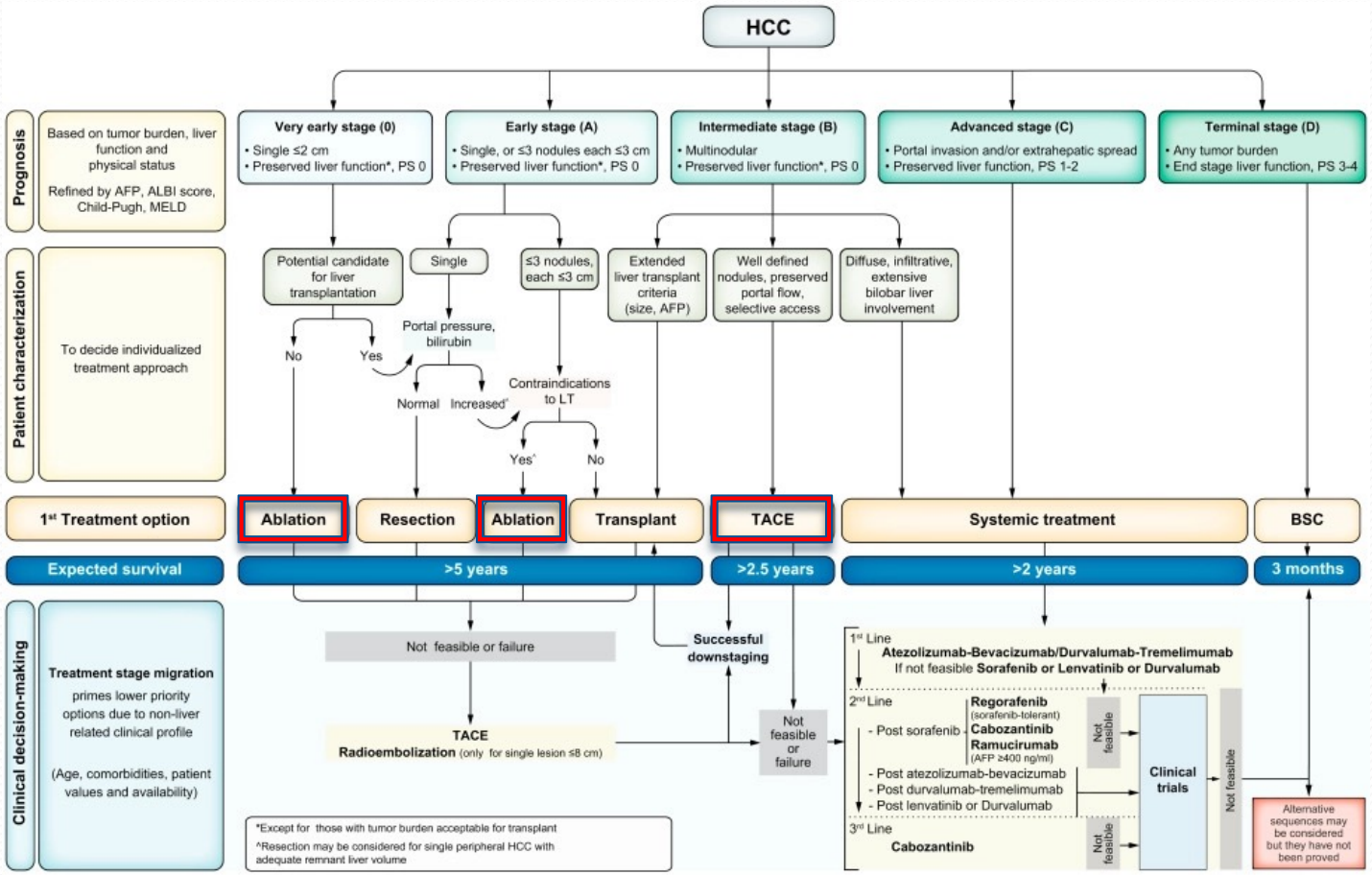
- Percutaneously placed ablation probes
- 2 major modes of thermal ablation
  - Freezing and heating
    - Cell death by freezing <-40° C[1,2]
    - Cell death by heating >60° C[1,2]
      - Radiofrequency ablation
      - Microwave ablation
- Outpatient procedure



Ablative Therapy



Liver Disease - HCC

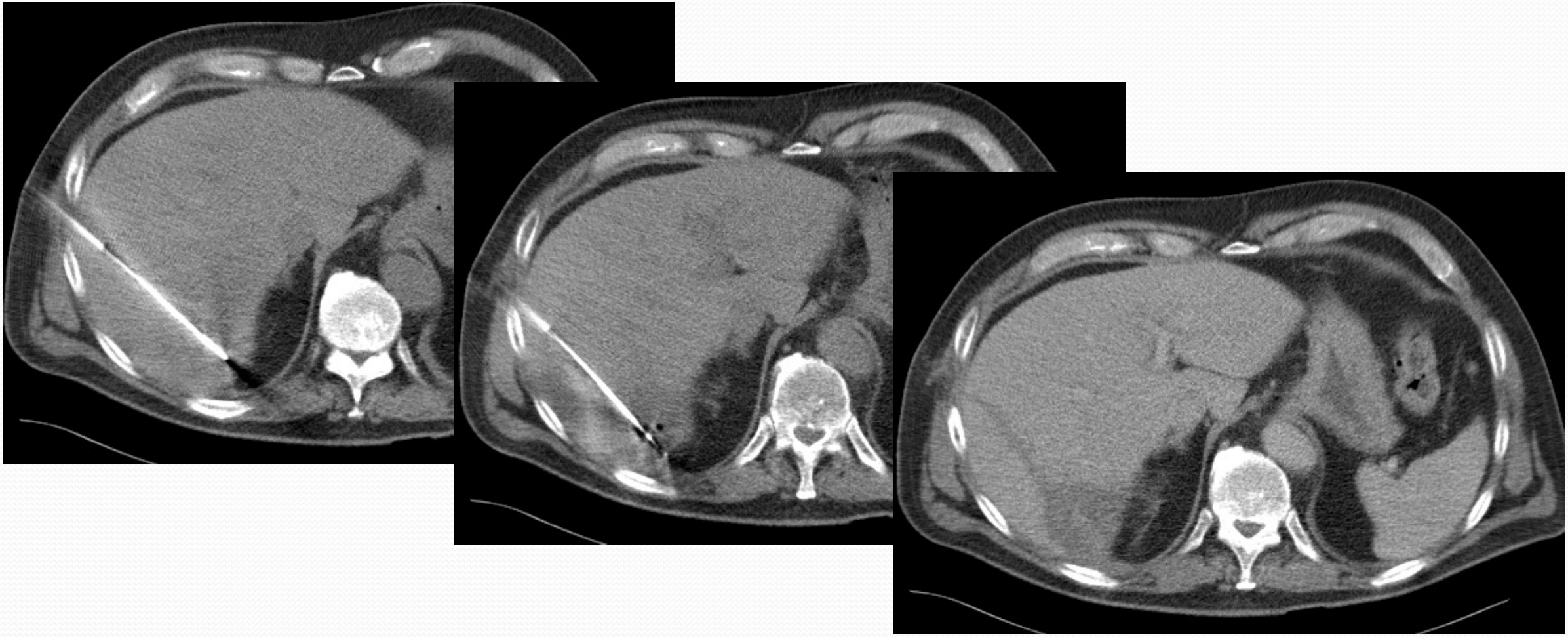


Reig et al. Journal of Hepatology 2022; 76: 681-693

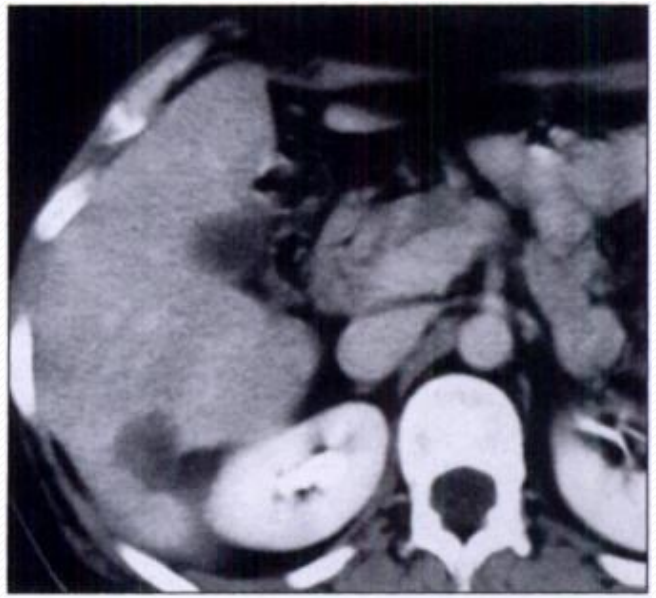
Liver Disease - HCC

- Percutaneous ablation
  - Complete necrosis in 98-100% of lesions <3 cm[1]
    - 83.3% in lesions >3 cm[2]
  - Immune response

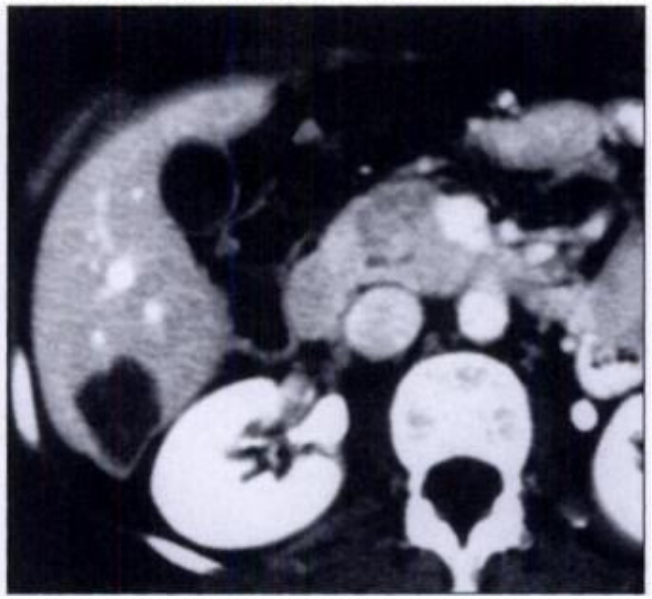
Liver Disease - HCC



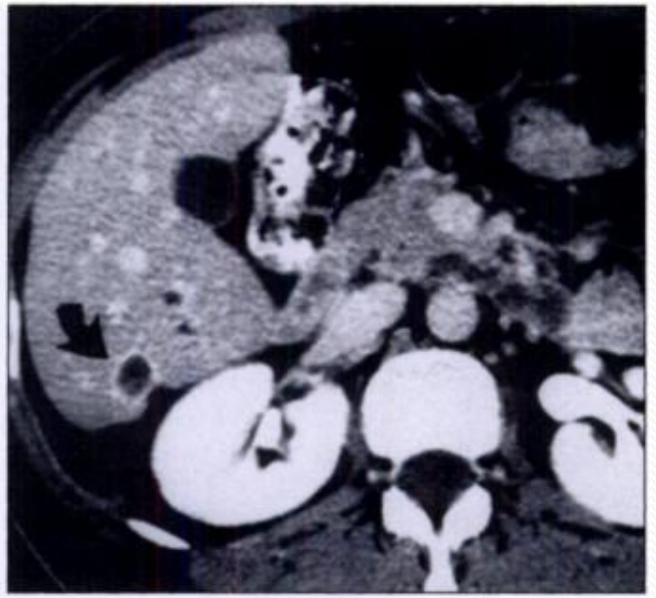
Liver Disease - HCC



Pre-Ablation



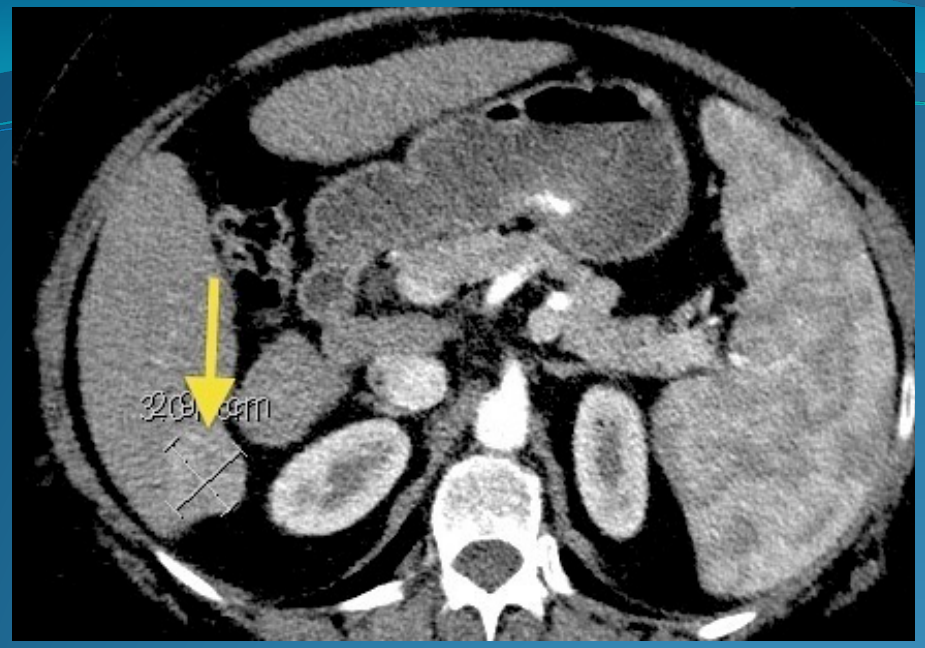
1 Month Post

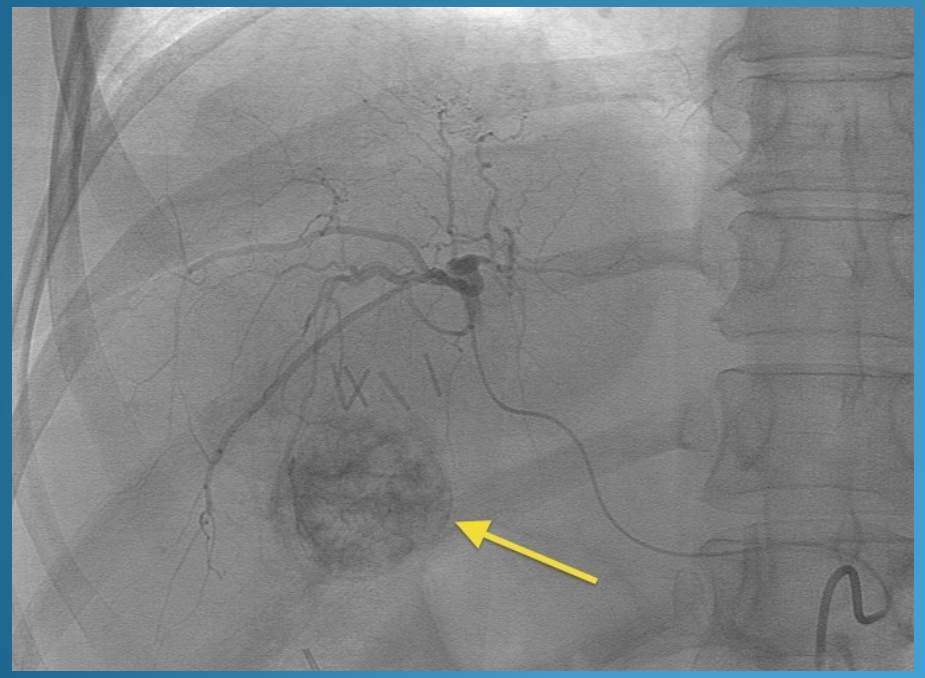


6 Months Post

Liver Disease - HCC

- Transarterial chemoembolization
  - Standard of care in Intermediate BCLC Staging
    - No advanced liver disease, no vascular invasion, no shunting, no extrahepatic disease, largest tumor 4-7 cm
  - Randomized trials and a meta-analysis show survival benefit to chemoembolization
    - LLovet et al, Lancet 2002; 359: 1734-39
    - Lo et al, Hepatology, 2002; 1164

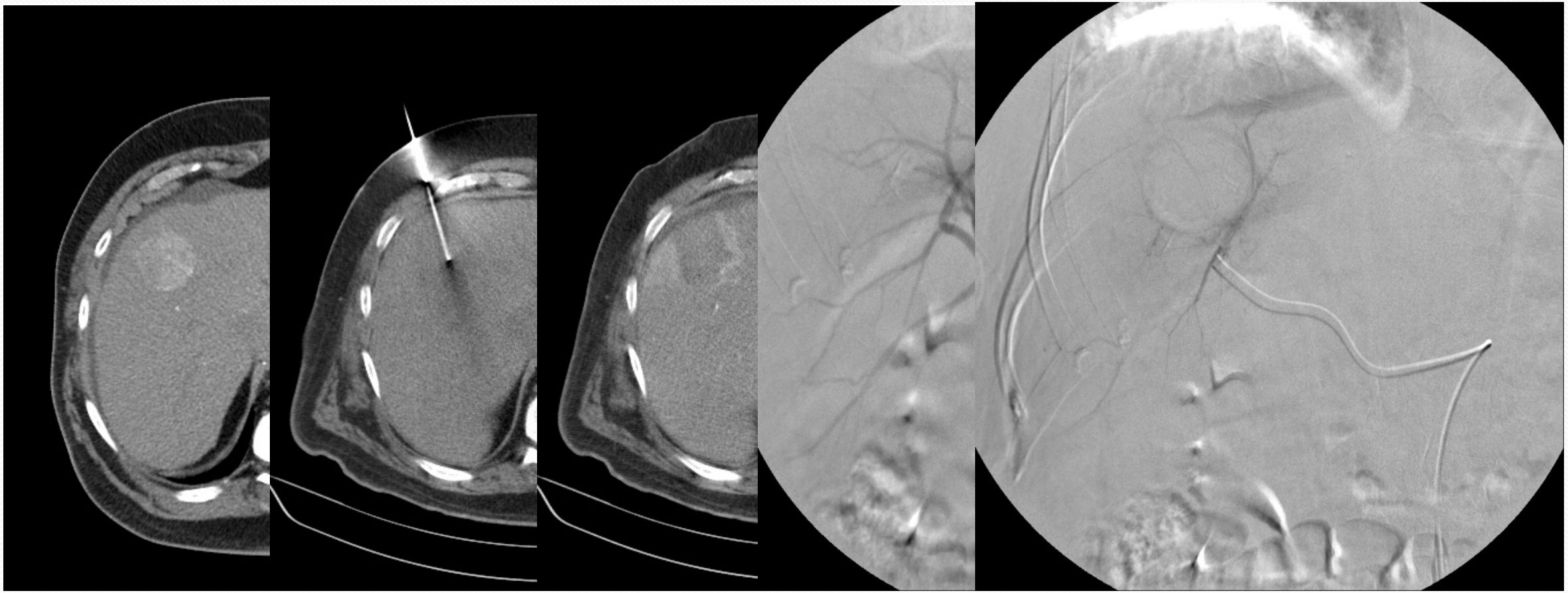




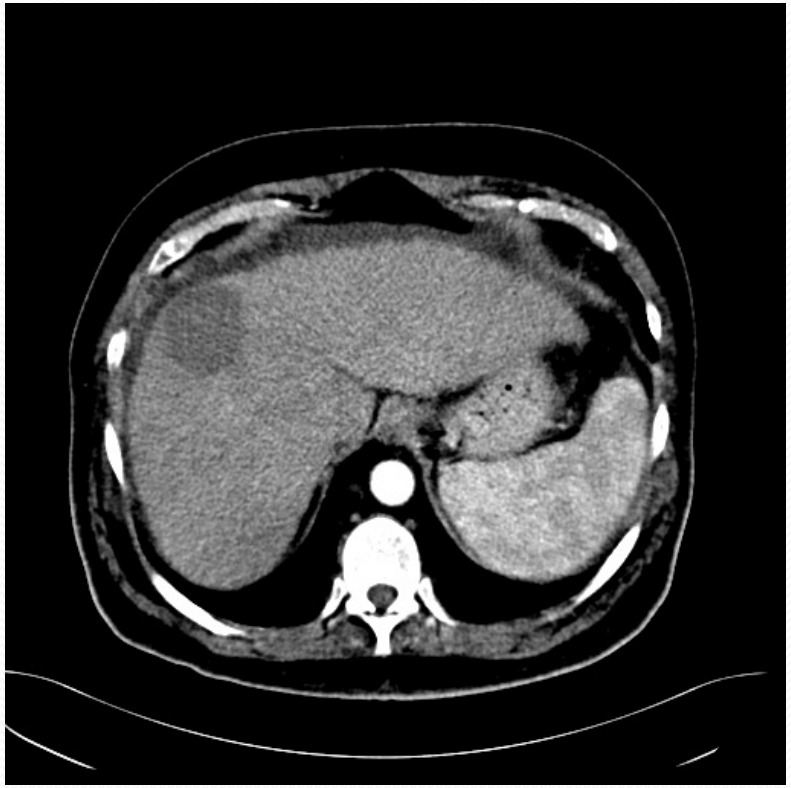
HCC Chemoembolization

This 60 year-old cirrhotic female has a 4.5 cm mass in Hepatic segment 6. She was referred for chemoembolization. The arteriogram demonstrates the targeted mass. Follow-up imaging demonstrates complete tumor necrosis.

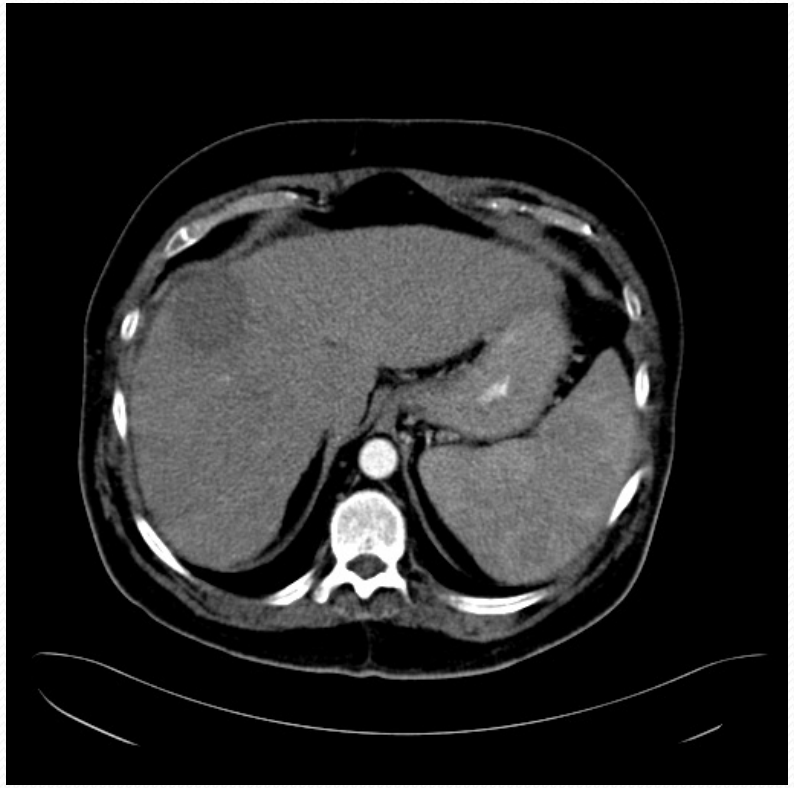
Liver Disease - HCC



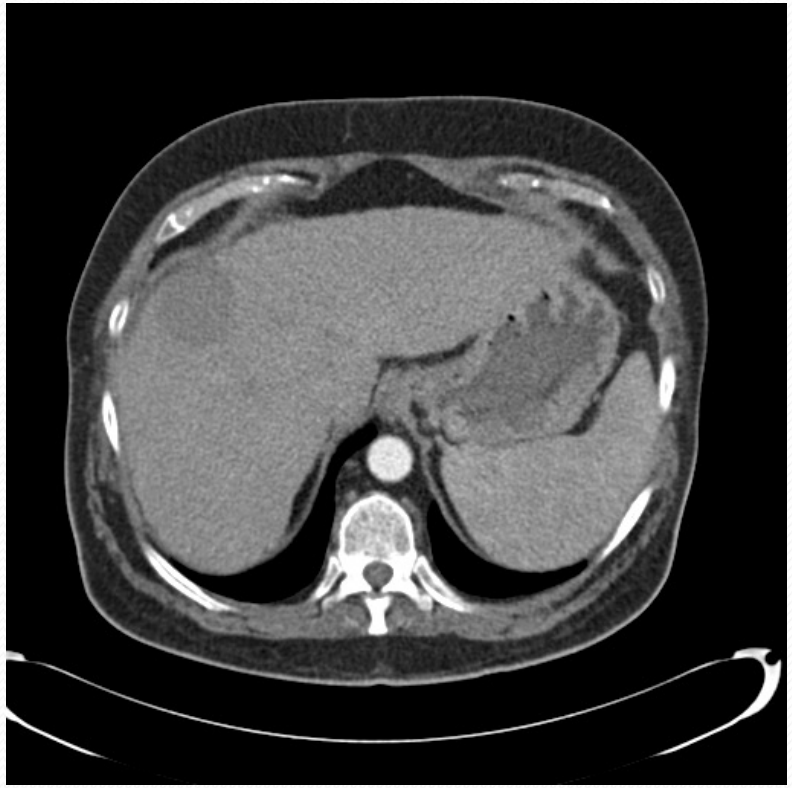
Liver Disease - HCC



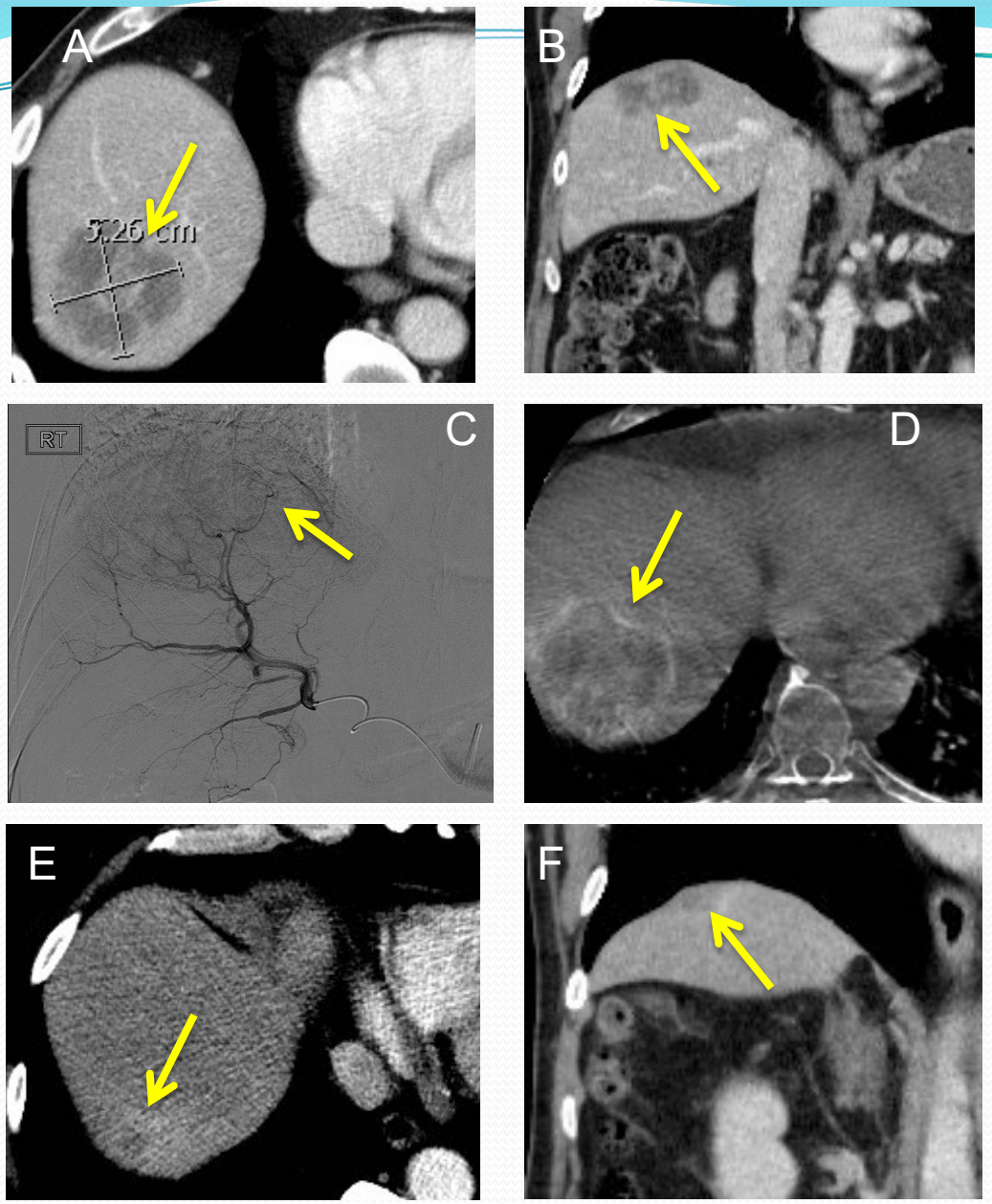
1 Month



3 Months



6 Months

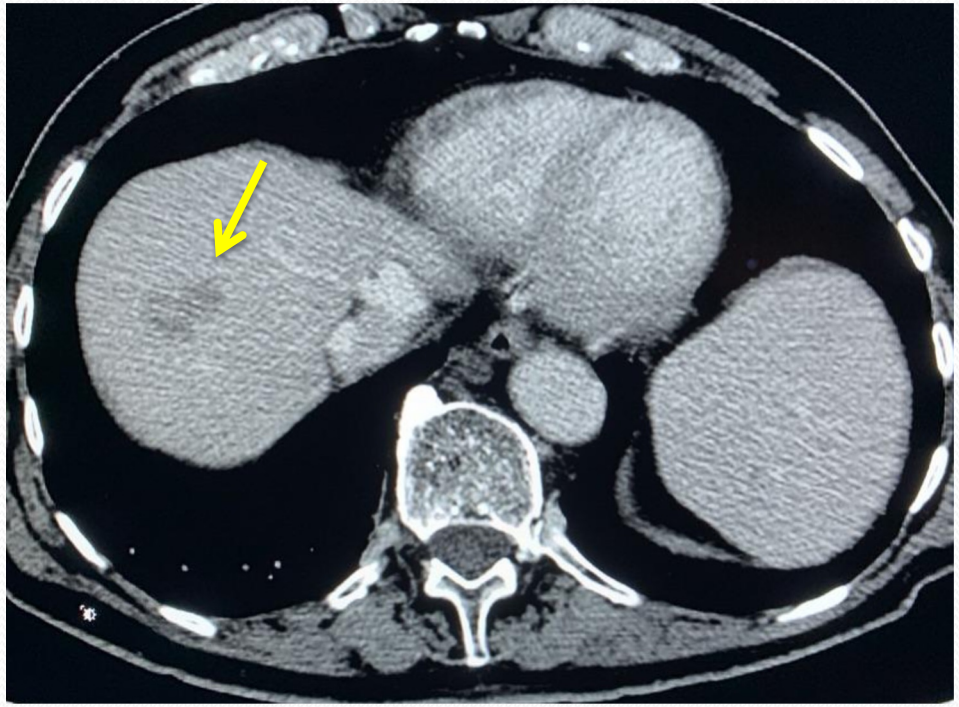


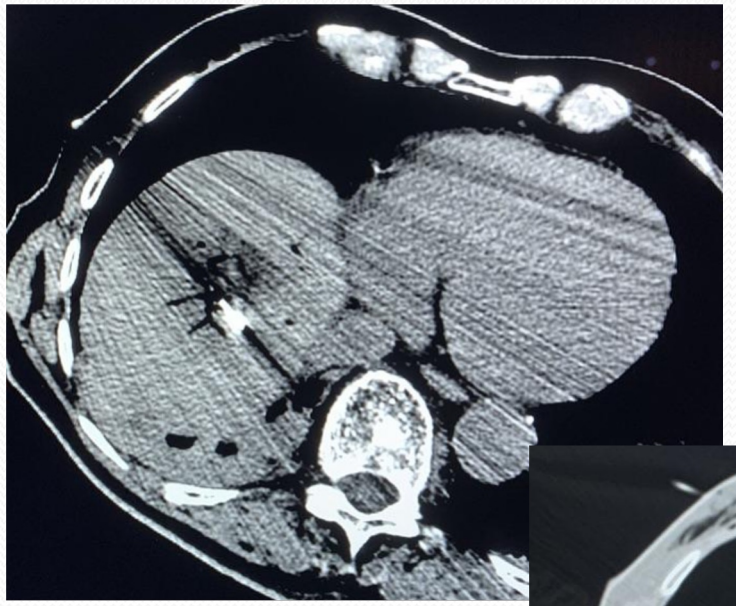
Radioembolization of HCC.

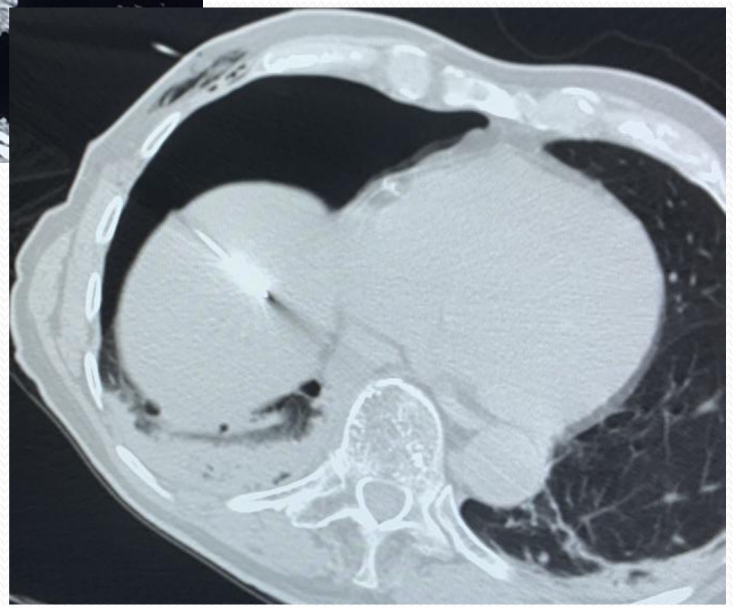
This 66 year old male has HCC restricted to a 5.3 cm segment 7 mass. Poor surgical candidate. Arteriography demonstrated subtle tumor blush (C) which was confirmed with CT reconstruction (D). He was treated with ^{90}Y radioembolization.

Ten months after treatment the tumor has almost completely resolved (E, F).

Liver Disease - HCC







70 year old male with segment VII HCC
typical imaging, elevated AFP, treated with MW

Liver Disease - HCC

3 month followup

Liver Disease - HCC

- Y90 Radioembolization
  - SARAH trial
    - Randomized prospective study conducted in France
    - 459 patients enrolled in 25 centers
    - 70% of patients had advanced HCC (BCLC stage C)
    - Presented in 04/2017 at the European Association for the Study of the Liver congress (EASL)
  - SIRveNIB
    - Randomized prospective study conducted in Asia
    - 360 patients enrolled in 27 centers
    - Presented 06/2017 at the American Society of Clinical Oncology (ASCO)

Liver Disease - HCC

- Sorafenib + Y90 Radioembolization
  - Prospective phase 2 trial presented at ASCO 2017
  - Conducted at MD Anderson
  - 40 patients with advanced HCC (BCLC stage C)
  - Treated with Sorafenib, then after 4 weeks with Y90
  - Associated with longer OS and PFS compared to sorafenib alone
    - Median OS and 95% CI was 18.46 months
    - PFS of 12.29 months
    - SD in 44.74%
    - PR in 28.95%
    - Most common adverse event (CTCAE 3-4) elevated LFTs and HTN (n=4)

Liver Disease - Cholangiocarcinoma

- QOL major consideration
  - Systemic chemotherapy
  - Supportive care
  - Liver directed therapy
    - TACE
    - Y90

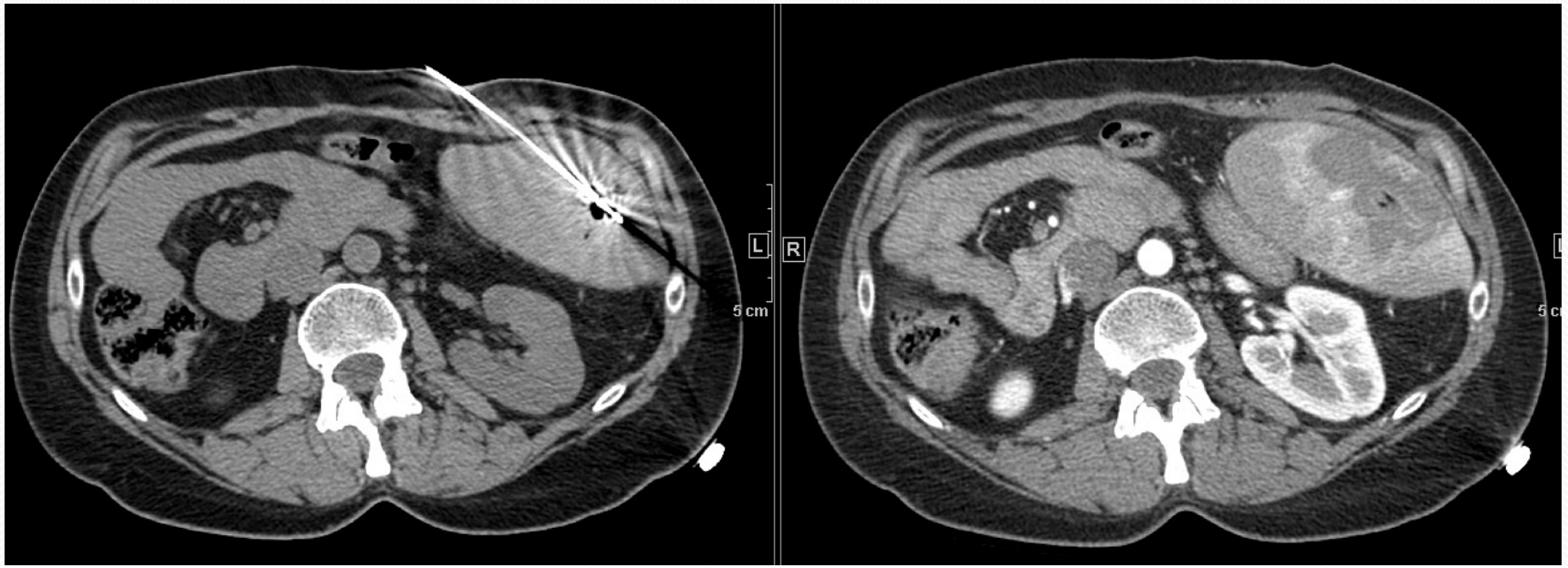
Liver Disease - Cholangiocarcinoma

- Many studies have shown significant survival benefit for liver directed therapy
  - 12-22 mo median survival (or greater) vs 12 mo with gem/cis
  - Combination of liver directed therapy and systemic therapy probably best option
- 17 patients with unresectable ICC (TACE)
  - Patients treated from 1995 – 2004
  - Median survival 23 mo
- 62 patients with unresectable ICC (37) and AUP(TACE)
  - Median survival 22 mo from dx
  - No difference between ICC and AUP
- 33 patients with unresectable ICC (Y90)
  - Median survival 22 mo from tx, 43 mo from dx
  - 12 PR, 17 SD, 5 PD
- 19 patients with unresectable ICC (Y90)
  - Median survival 11.3 mo from tx, 25.1 mo from dx
  - 68% SD

Liver Disease - Cholangiocarcinoma

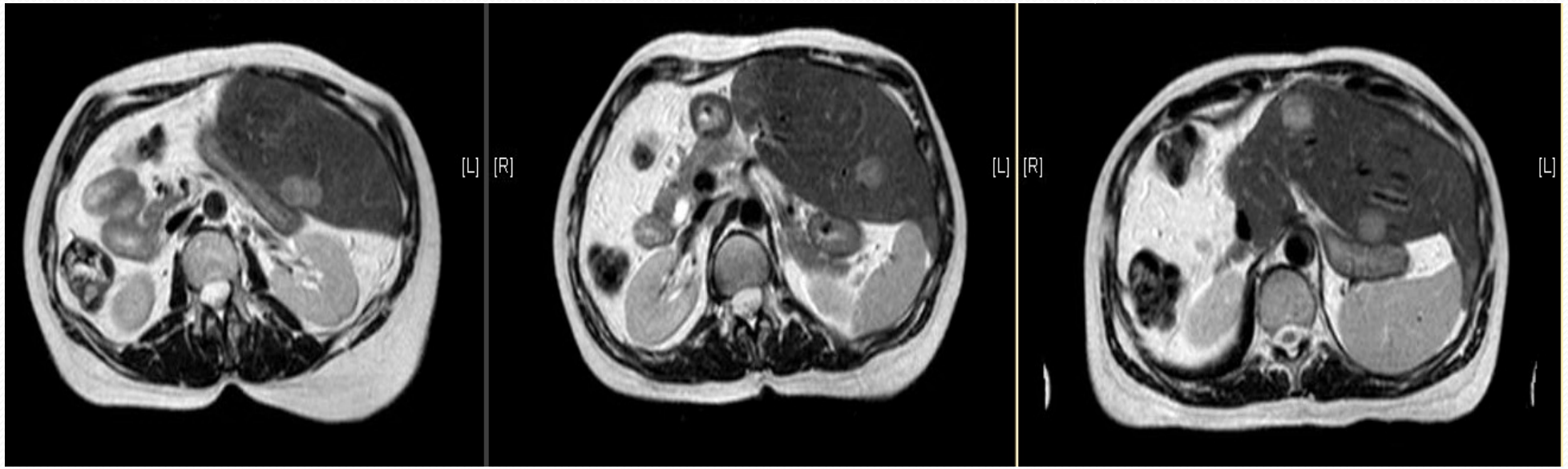
Lead Author	n	Treatment	ORR	SD	Median Survival Post-SIRT	Median Survival Post-Diagnosis	
Treatment of progressive disease or chemo-refractory disease							
Saxena[1]	25	SIR-Spheres§	24.0%	48.0%	9.3 months	20.4 months	
Coldwell[2]	23†	SIR-Spheres§	45.0%	nr	74.0% alive at 14 months	nr	
Khanna[3]	9†	SIR-Spheres§	66.0%		13.5 months	20.0 months	
Hoffmann[4]	33†	SIR-Spheres§	36.4%	51.5%	22.0 months	43.7 months	
Camacho[5]	21	SIR-Spheres§	6.2%	81.3%	16.3 months	nr	
Rafi[6]	19†	SIR-Spheres§	11.0%	68.0%	11.3 months	25.1 months	
Xing[7]	24† 2757†	SIR-Spheres§ *vs.* BSC (non-randomised)	nr	nr	11.5 months	20.8 months 3.0 months	$P < 0.001$
Filippi[8]	17†	SIR-Spheres§	82.4%PET	17.6%PET	14.9 months	nr	
Soydal[9]	16†	SIR-Spheres§	30.0%	nr	9.6 months	nr	

Liver Disease - Cholangiocarcinoma



Segment 3 lesion – during and after ablation

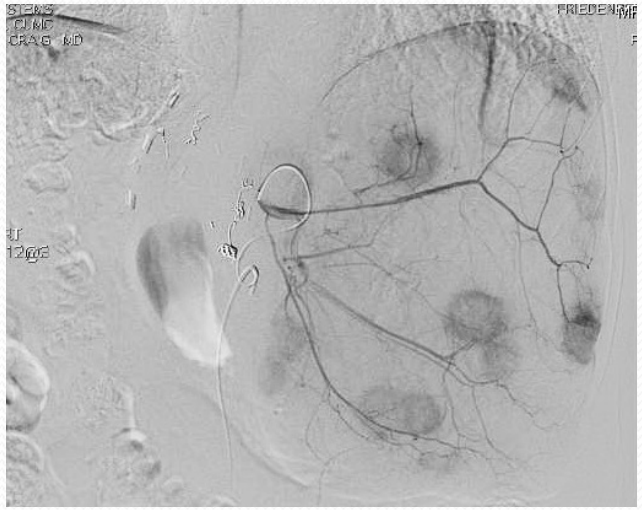
Liver Disease - Cholangiocarcinoma



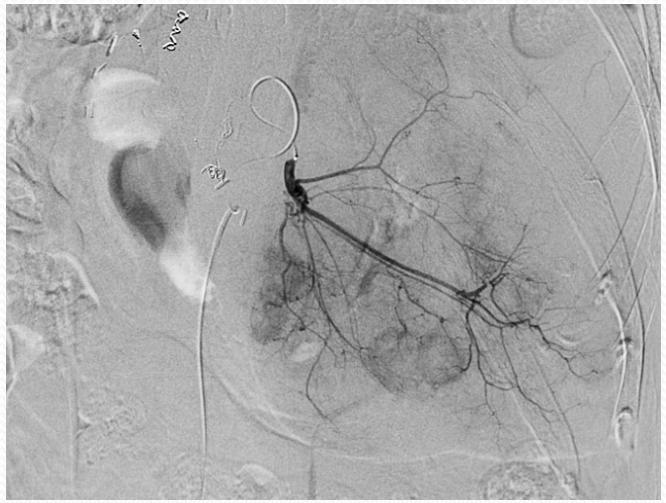
MRI Abdomen – 9m post microwave ablation

- Several new hepatic lesions, S2 & 3, measuring up to 2.9 cm

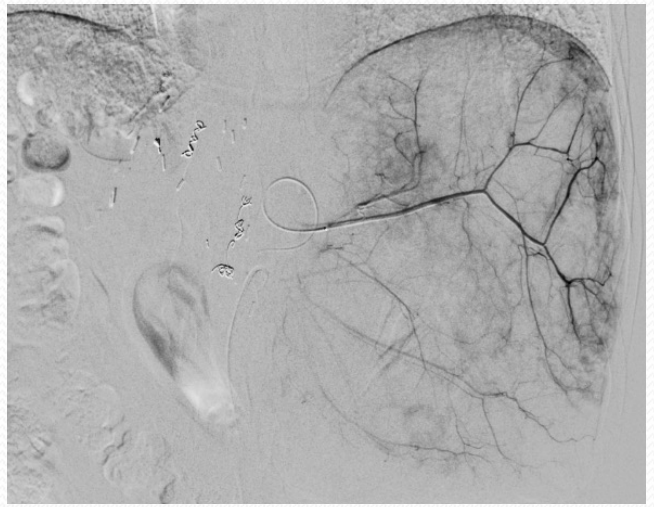
Liver Disease - Cholangiocarcinoma



Mapping



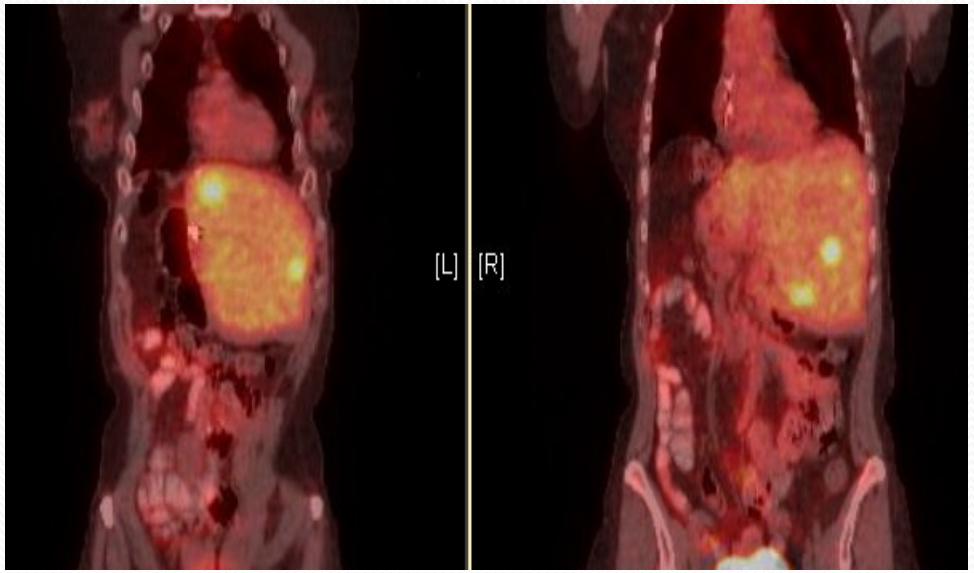
s3 Treatment



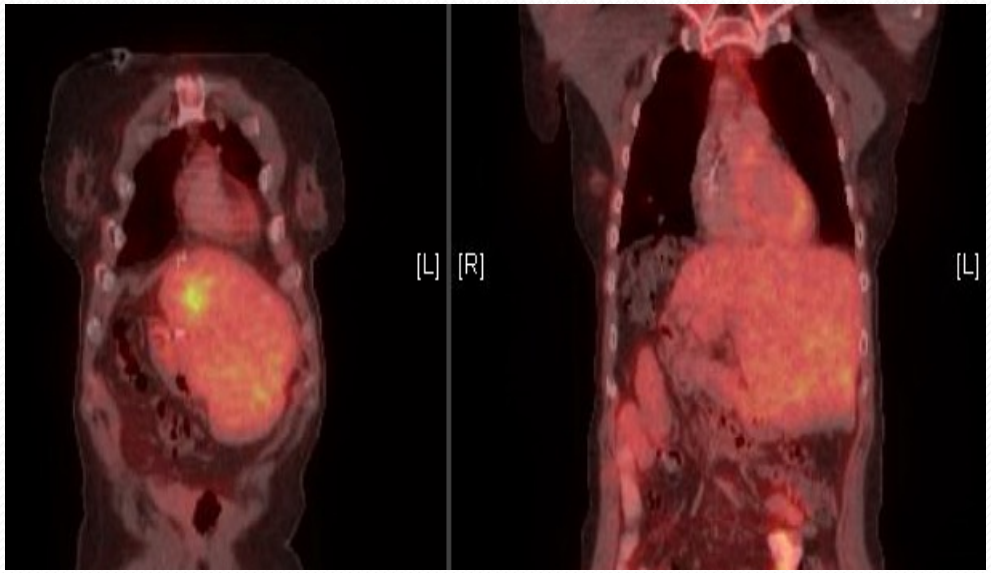
s2 Treatment

Liver Disease - Cholangiocarcinoma

Pre Y90



Post Y90

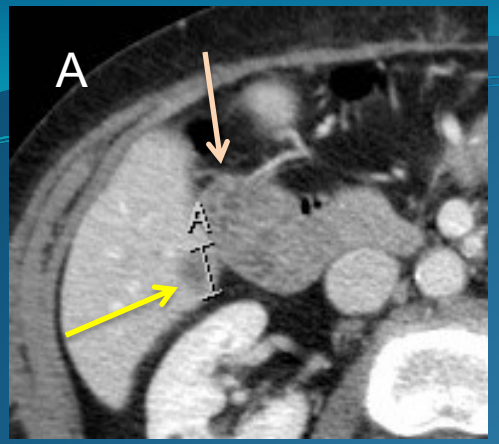


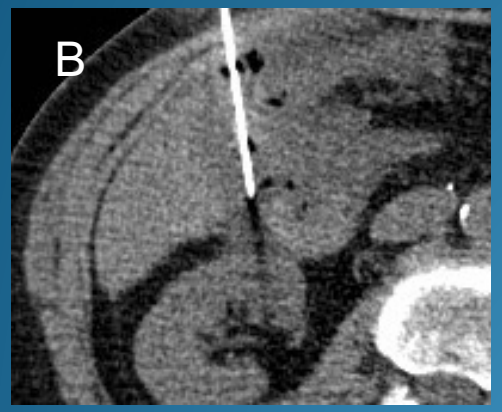
Liver Disease - Metastatic

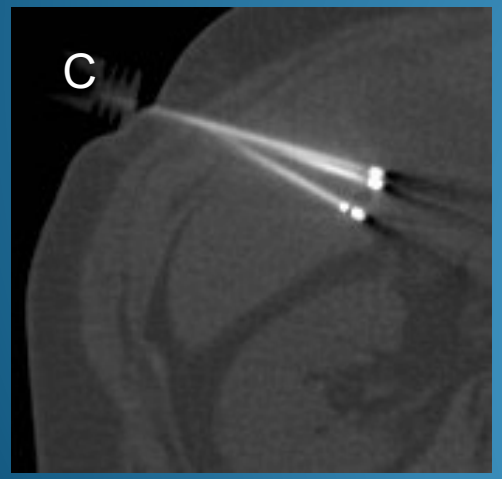
- Colon Cancer
  - 50-60% of patients diagnosed with colorectal cancer develop metastases
    - Liver is most common site
    - 80-90% have unresectable metastatic liver disease
  - 20-34% of patients present with synchronous liver metastases
  - Half of patients who die from colorectal cancer have liver metastases

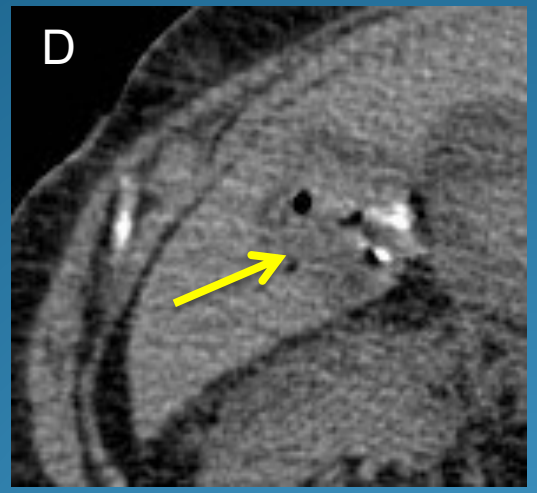
Liver Disease - Metastatic

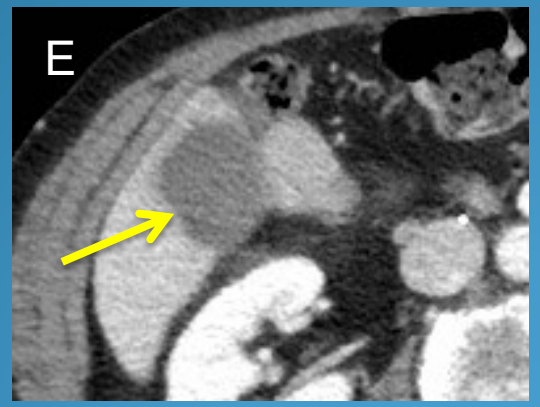
- Colon Cancer (cont'd)
  - SIRFLOX study (ASCO 2015)
    - Phase 3 randomized controlled trial in 530 patients w mCRC to the liver
      - Y90 + FOLFOX +/-bevacizumab vs FOLFOX +/-bevacizumab
    - Prolonged liver PFS (20.5 mo vs 12.6 mo, P=.002)
    - Better selection = better results – 40% enrolled had extrahepatic disease
  - CLOCC study (ASCO 2015)
    - Phase 2 randomized controlled trial in 119 patients w mCRC to the liver
      - Perc ablation + FOLFOX +/-bevacizumab vs FOLFOX +/-bevacizumab
      - Median f/u of 9.7 years
      - Up to nine hepatic mets
      - Prolonged OS (45.6 mo vs 40.5 mo, P=.01)





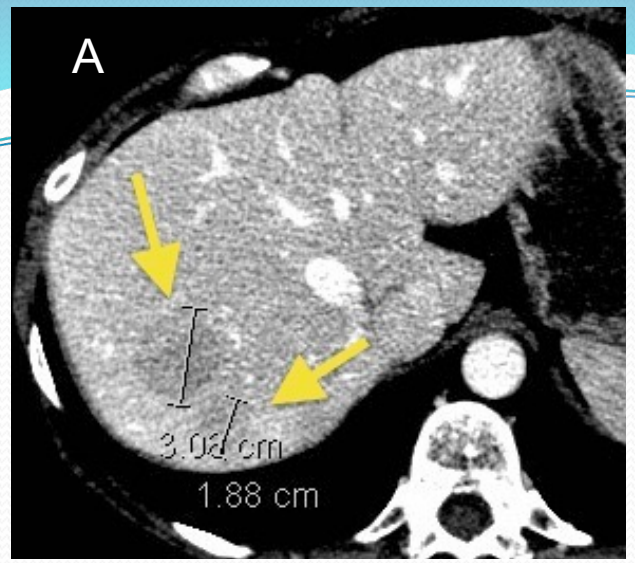


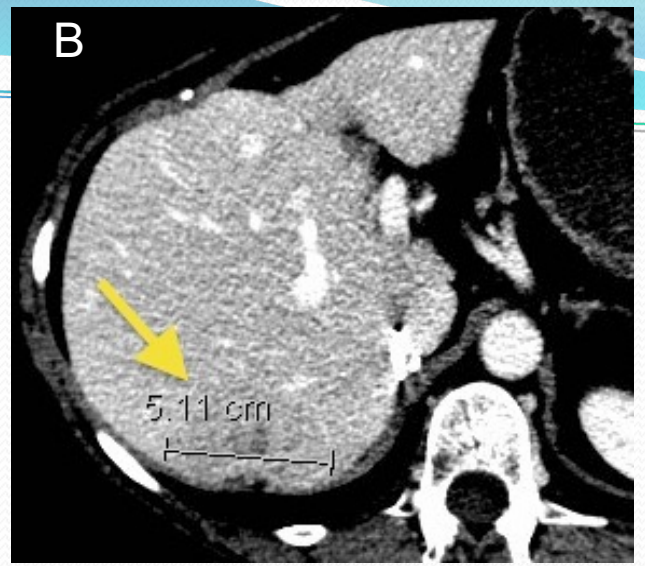


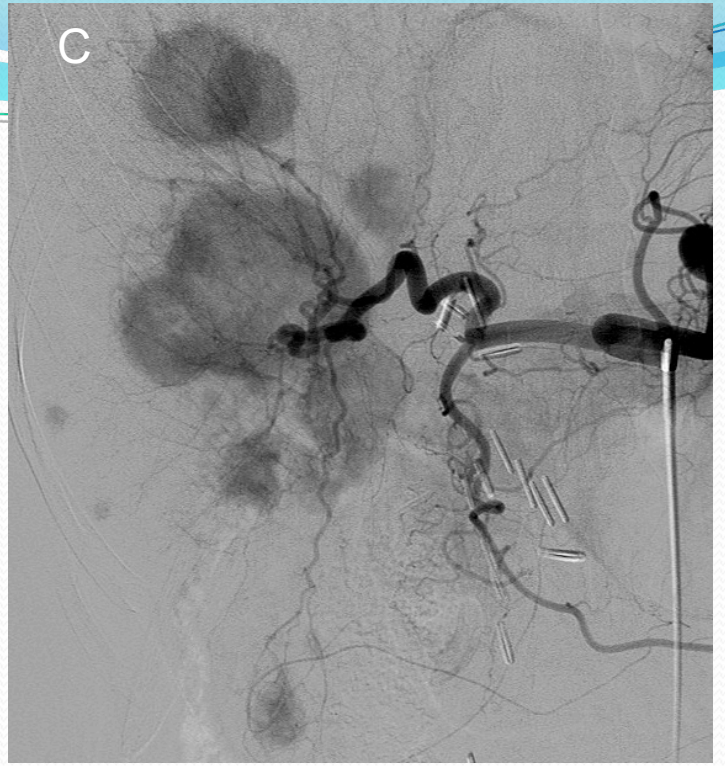


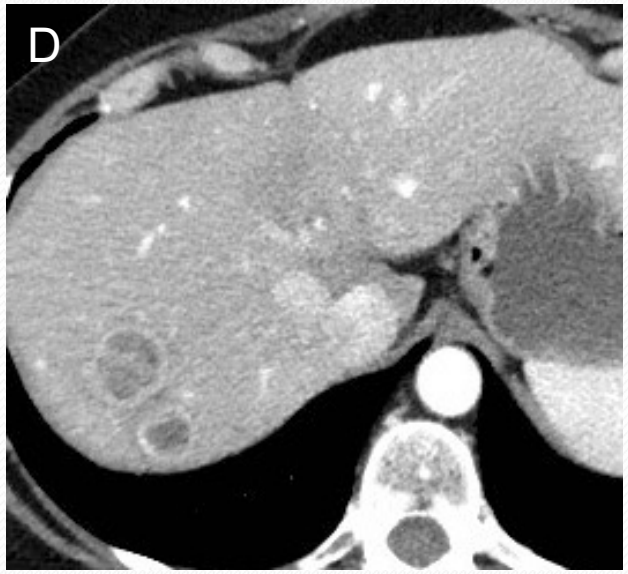
Percutaneous ablation:

57 year-old female developed a solitary liver metastasis following Whipple for Ampullary Carcinoma (Yellow arrow, A). RFA was considered. However, there was nearby bowel (Peach arrow, A). A sheathed needle was advanced between the bowel and liver (B) and D5W infused, providing a safe thermal window. Ablation was performed (C) with a satisfactory area of necrosis on immediate post-ablation imaging (Arrow, D). Follow-up CT in one month confirmed successful treatment with satisfactory margins (Arrow, E).









Radioembolization of Renal Cell Metastases

This 55 year old otherwise healthy female had progressed on systemic therapy.

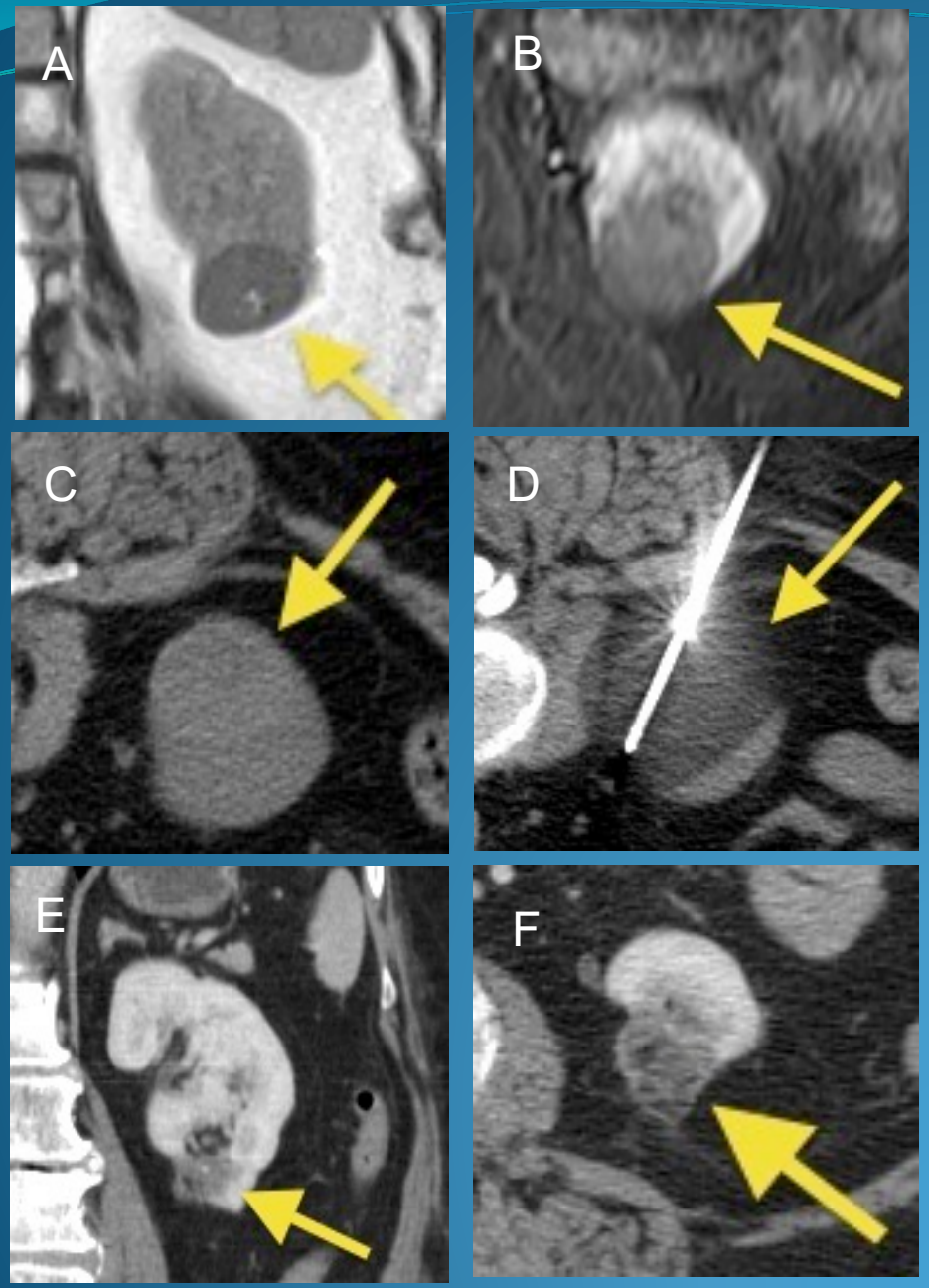
Pre-treatment CT scans (A, B) demonstrate multifocal metastases (Arrows). This finding is confirmed at angiography (C). Three months after radioembolization, there is extensive necrosis in the treated tumors (D, E).

Kidney Cancer

- 5 year survival for localized disease is >92.5%
  - Most important prognostic indicators are stage, grade, local extent, and presence of regional/distant mets
- Stage 1 – pT1a
  - 4cm or less and limited to the kidney (AJCC 2010)
  - NCCN guidelines recommend partial nephrectomy OR if appropriate ablation
    - Distant recurrence free survival rates of ablation and conventional surgery are comparable

Renal Cell Carcinoma

- Ablation
  - 90-95% effective
  - Comparing specifically with partial nephrectomy in T1a (6 yr population based study utilizing SEER)
    - Half rate of renal insufficiency at 1 year follow-up with ablation, half as many CV complications at 30 days, lower blood loss
    - No significant difference in 5 year survival, cancer-specific survival, disease-free survival, local recurrence free survival, or metastasis free survival



Percutaneous Ablation of Renal Cell Carcinoma

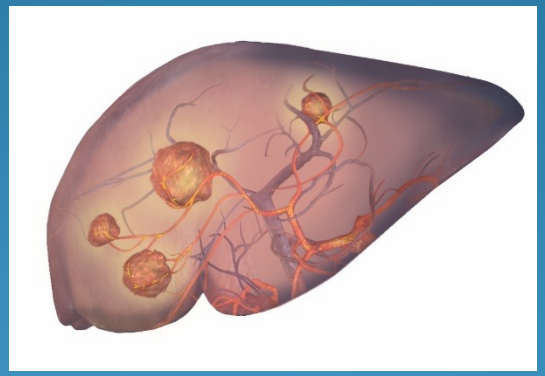
This 72 year-old female was diagnosed with a biopsy-proven renal cell carcinoma (A, B). Her multiple medical comordities limited her surgical options and her Urologist referred her for ablation (C). After placing the probes, the resulting ice ball covered the entire tumor plus a margin of normal kidney (D). At four years from treatment, the mass was no longer enhancing and had decreased significantly in size (E, F).

Lung Cancer - NSCLC

- Poor surgical candidates?
  - Estimated 15% of all patients are considered a poor surgical candidate[1]
- Sub-lobar (wedge) resection?
- Matching for patient, tumor, and treatment differences, thermal ablation is on par with sublobar resection in patients >65 with 1A or 1B NSCLC
- Nonsurgical candidates?
  - Cardiopulmonary comorbidities
  - Poor PFTs

Lung Cancer - NSCLC

Thank You



Integrating interventional radiology into cancer treatment