

Interventional Oncology

Transarterial Therapy In The Management of Primary and Secondary Liver Tumors

Mark F. Abbott, M.D.
Utah Imaging Associates

Disclosures

No financial disclosures

OBJECTIVES

- **Interventional Oncology**
- **Ablation Therapies**
- **Embolic Therapies**
 - **Transarterial therapies in the liver**
 - **Types and techniques**
 - **Evidence and outcomes**
 - **Pt selection**
 - **Potential complication**

Interventional Radiology

“The cutting edge of medicine without the cutting”

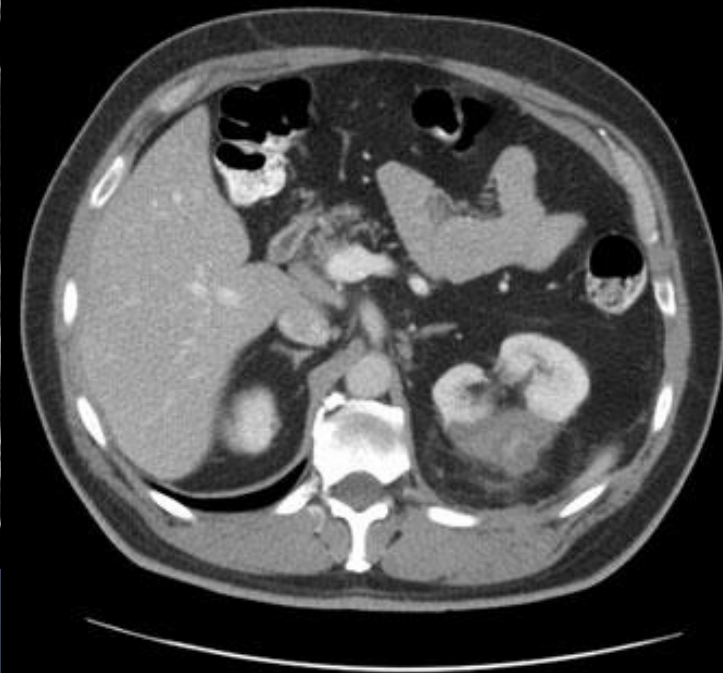
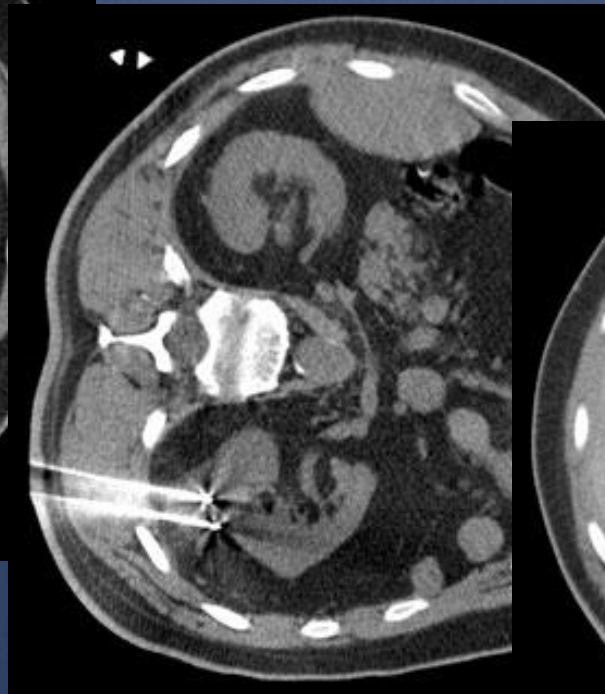
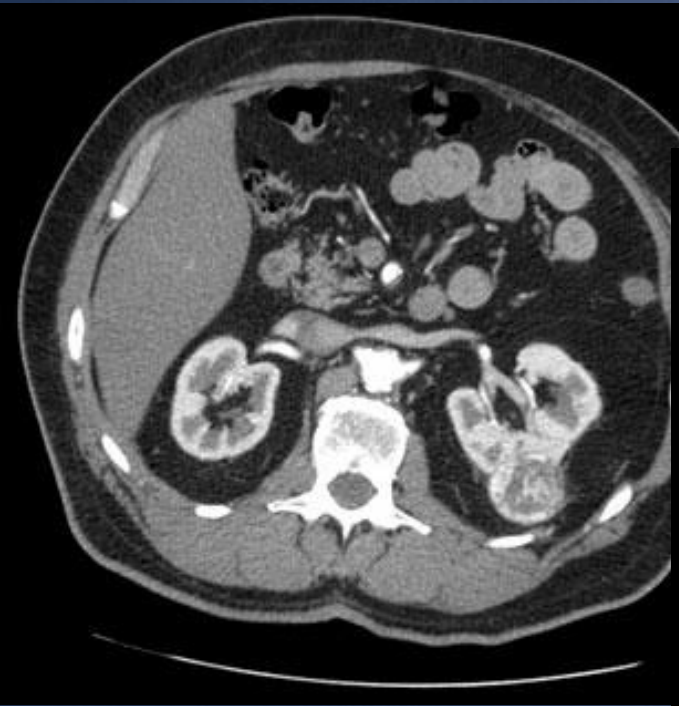
- **Recognized as primary specialty in medicine by ABMS**
- **New Training Pathways**
- **Expanded clinical presence**
 - **Diagnosis, management, treatment and longitudinal care**
 - **Clinic**
 - **Admissions**
- **Use state of the art high tech imaging to perform least invasive diagnostic and therapeutic procedures resulting in fast recovery and few complications**

Interventional Oncology

- Image guided, minimally invasive targeted treatment of cancer
- Part of multidisciplinary approach that includes medical oncology, surgical oncology and radiation oncology
- Vascular delivery of Rx
 - Bland embolization
 - Transarterial chemoembolization (TACE)
 - Selective internal radiation therapy (SIRT) – Intravascular brachytherapy – yttrium 90 (y90) radioembolization
- Direct Puncture of Tumor for Rx
 - Microwave ablation
 - RFA
 - Cryoablation

Ablative Therapies

- Cryoablation
- Renal
 - Increased surgical risk, stage T1a
 - Best results < 3 cm



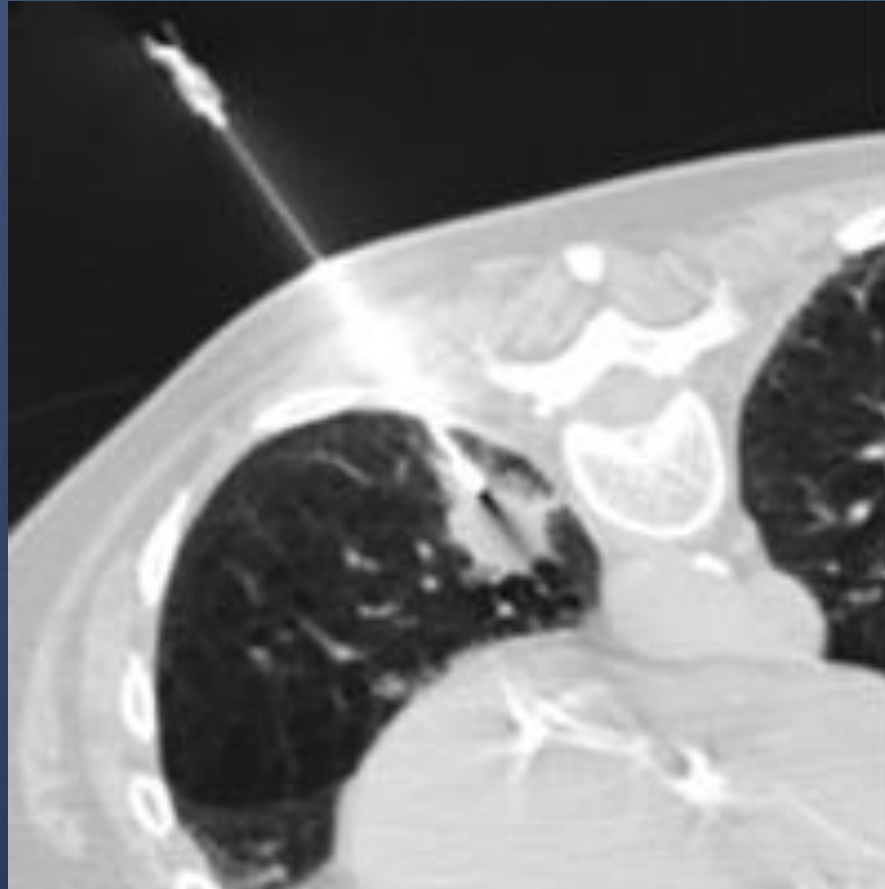
Ablative Therapies

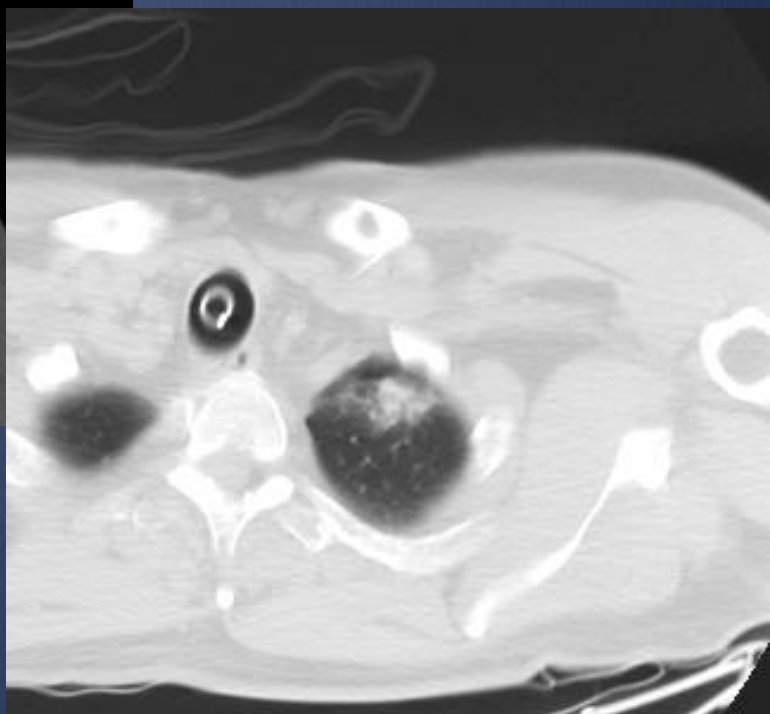
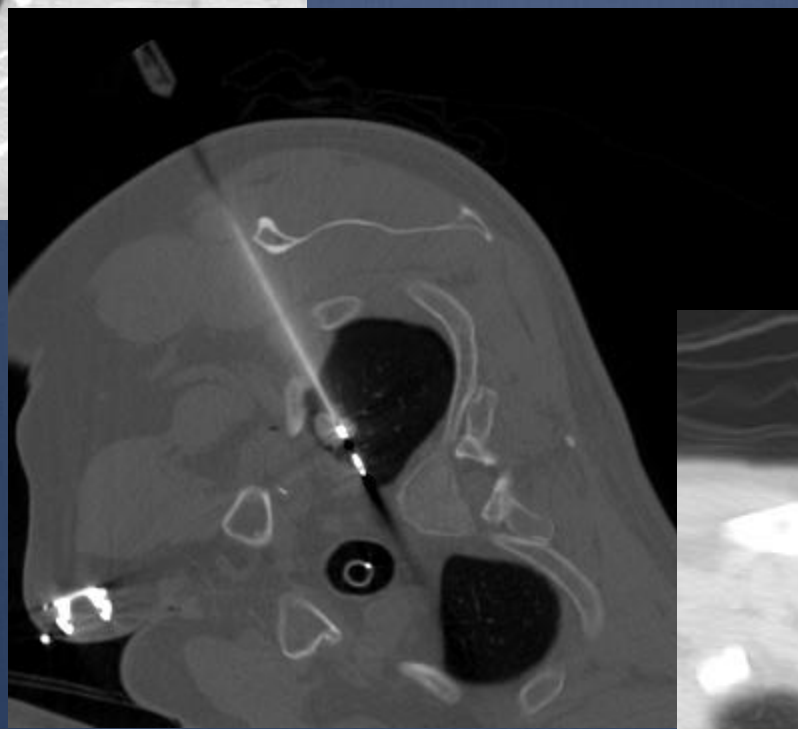
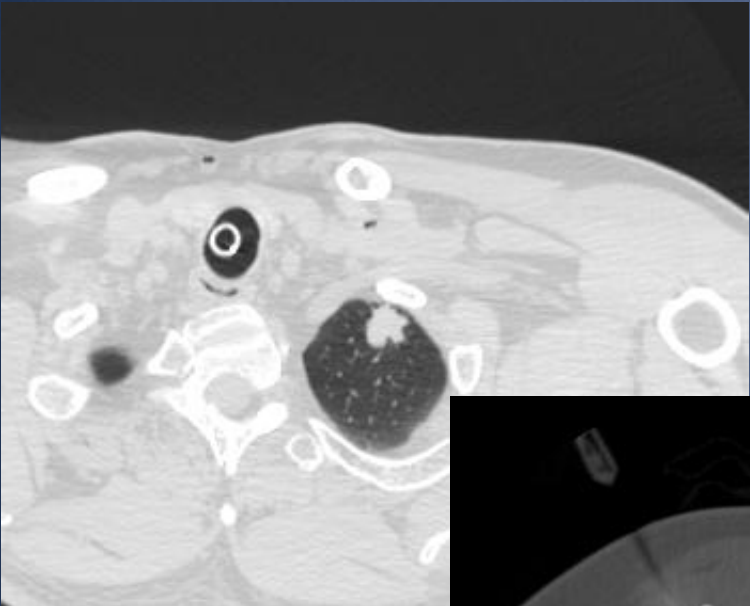
- Microwave
- Hepatic - Poor surgical candidates, pre-transplant, lesions < 3 cm and less than 3 in number



Ablative Therapies

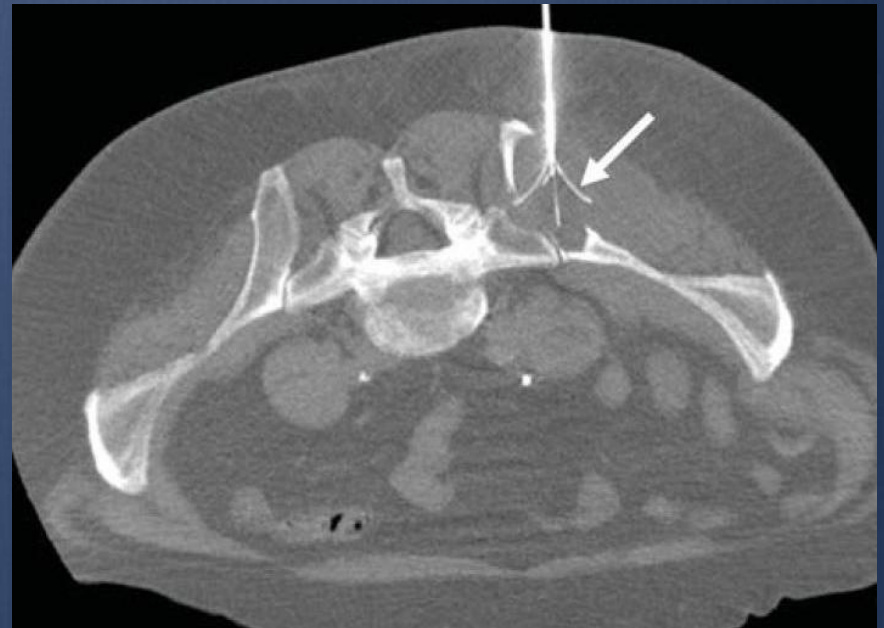
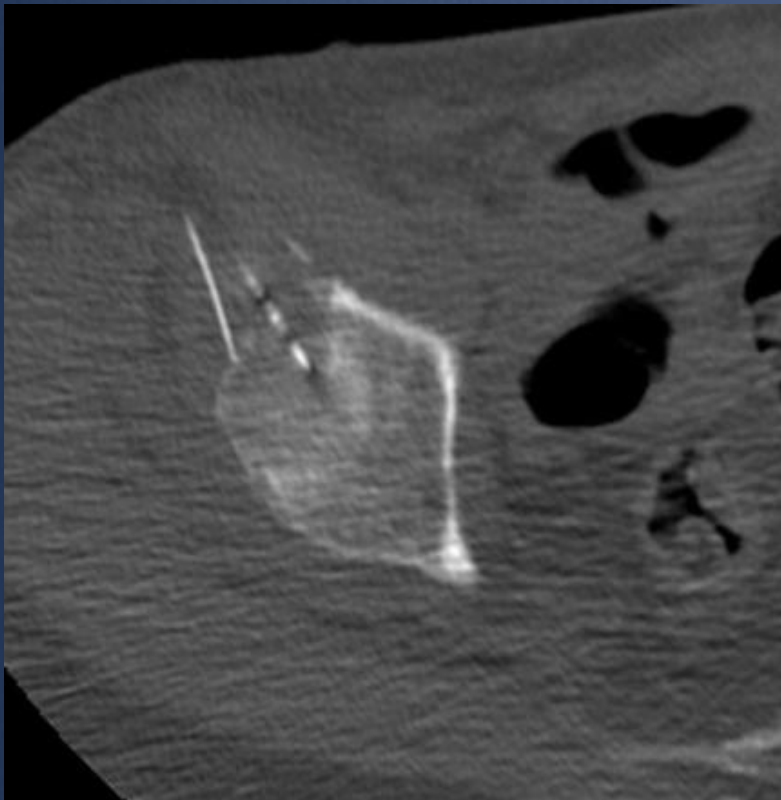
- Lung
 - Pts – high surgical risk, local control, met debulking





Ablative Therapies

- RFA
- Bone
 - Palliative pain control for mets
 - Osteoid osteoma
 - Cement augmentation - STAR



Embolization

- **1949**
 - pea seeds and starch
- **1960s-1970s**
 - Intraarterial vasopressin infusion
 - Mechanical disruption using wires, catheters
 - Sclerosants, Ethanol, etc
 - Plugs – gelfoam, PVA
- **1980s**
 - N-butyl cyanoacrylate (glue), Thrombin
 - Detachable balloons, pushable coils
- **Current**
 - Onyx, drug-eluting spheres, radiolabeled microspheres, detachable coils, amplatzer plug

Embolization

- **Hemorrhage**
 - **Trauma**
 - **Aneurysm/pseudoaneurysm**
 - **Postpartum**
 - **GI bleeds**
 - **Portal HTN**
- **Vascular malformations**
- **Venous disease**
 - **Varicose, gonadal**
- **Nonvascular**
 - **GI, ureteral, fallopian**
- **Neoplastic**
 - **Bland, TACE, radioembolization**

Embolic Therapies

- **Hepatic Embolization**
 - Bland
 - Chemoembolization
 - Radioembolization
- **Presurgical devascularization**
 - Bone mets
 - Large RCC.
- **Prostate & Bladder**
- **Uterine Fibroids**

Hepatic Arterial Embolization

- **Hepatic blood supply favorable for tumor treatment due to tumor hypervascularity and dual hepatic blood supply**
 - **Portal Vein 75-80% supply to liver**
 - **Hepatic artery 20-25%**
- **HCC**
 - **90-100% hepatic arterial supply**

Hepatic Arterial Embolization

F. Fiore, F. Somma, R. D'angelo; Naples/IT

Technique

- **Angiogram**
- **Microcather**
 - **Reduces spasm**
 - **Decreased dissection**
 - **Distal delivery**
- **Selective vs Lobar**
 - **Selective decreases risk of liver failure**



Bland Embolization (TAE)

- **PVA particles delivered locally to disrupt blood supply**
 - **Ischemia and infarction**



Chemoembolization

- Deliver chemotherapy locally and disrupt blood supply
- “getting chemo right where you need it and not where you don’t”
 - Less systemic toxicity
- Conventional TACE – Lipiodol with chemo agent
- Drug eluting beads – doxorubicin, irinotecan, platinum based chemo, etoposides, docetaxel

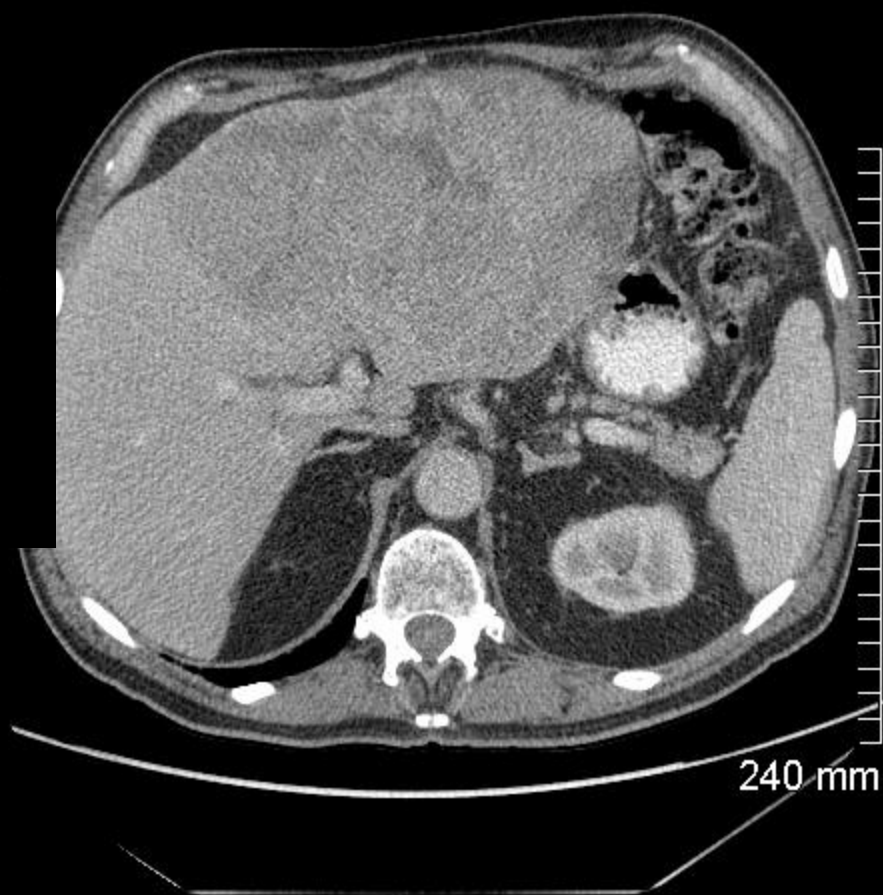
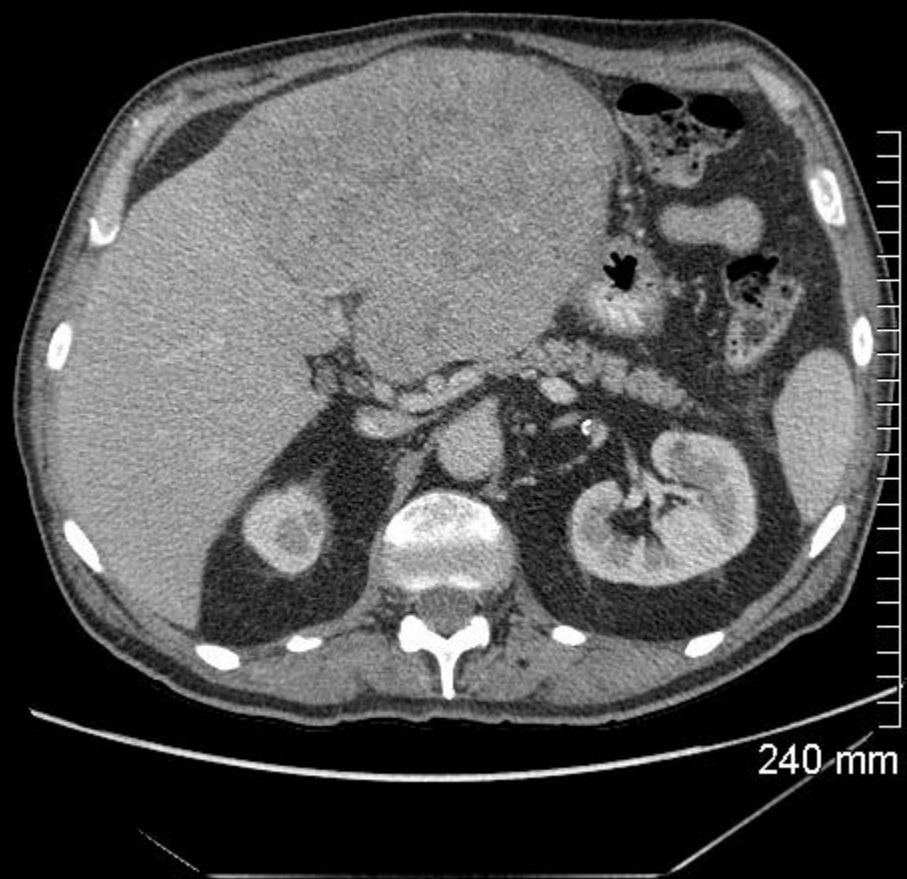
Chemoembolization

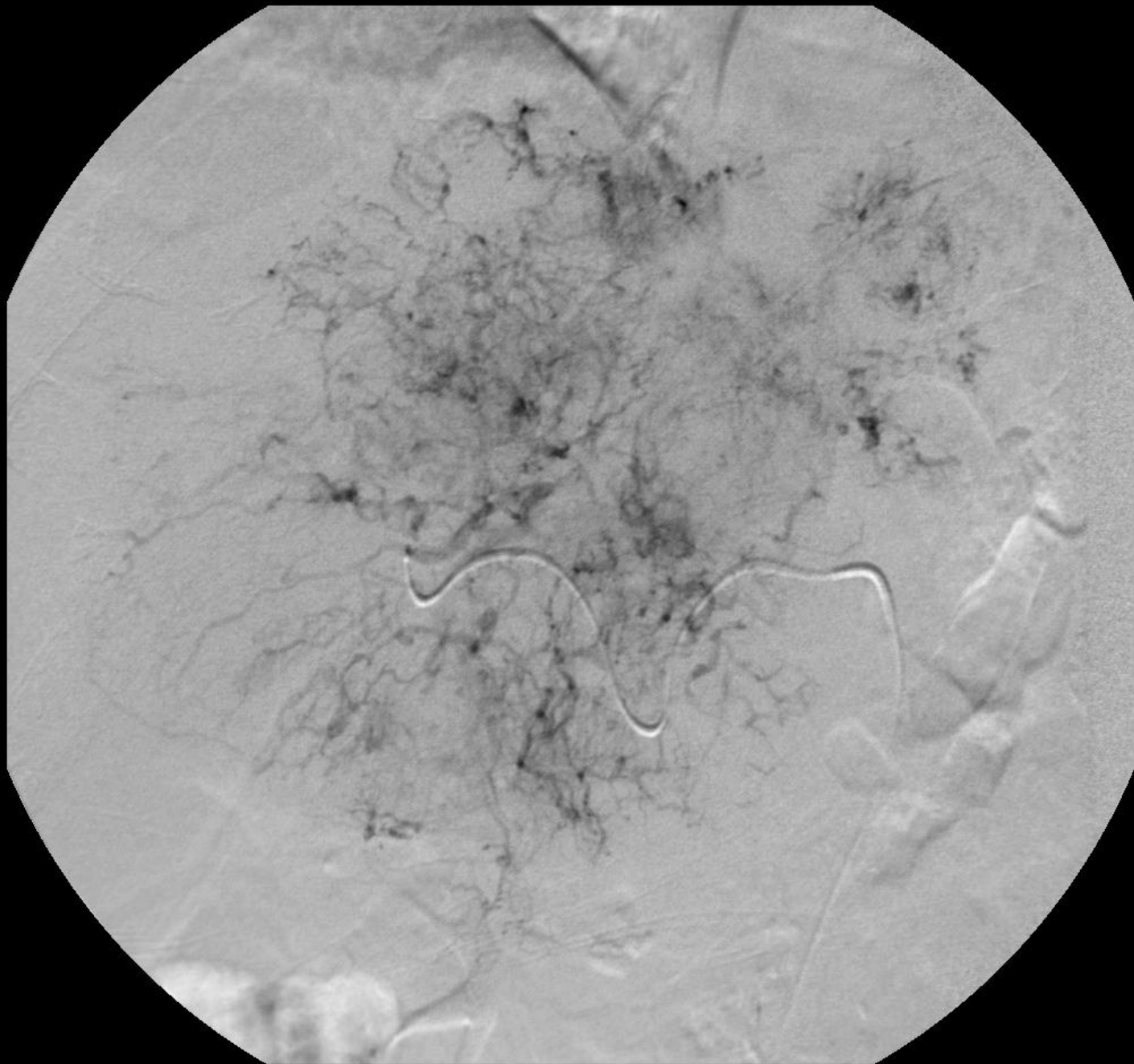
- **TACE**
 - **Chemotherapeutic agent and iodized oil (lipiodol)**
 - **Dox/Cisplatin/mitomycin**
 - **Single agent – Doxorubicin > Epirubicin**
 - **Mixture retained by tumor**
 - **Lipiodol appears as dense persistent stain**
 - **Normal hepatocytes metabolize the lipiodol**
 - **Liver tissue preserved**
- **Embolic and/or chemo effect**
- **Lobar vs subselective**



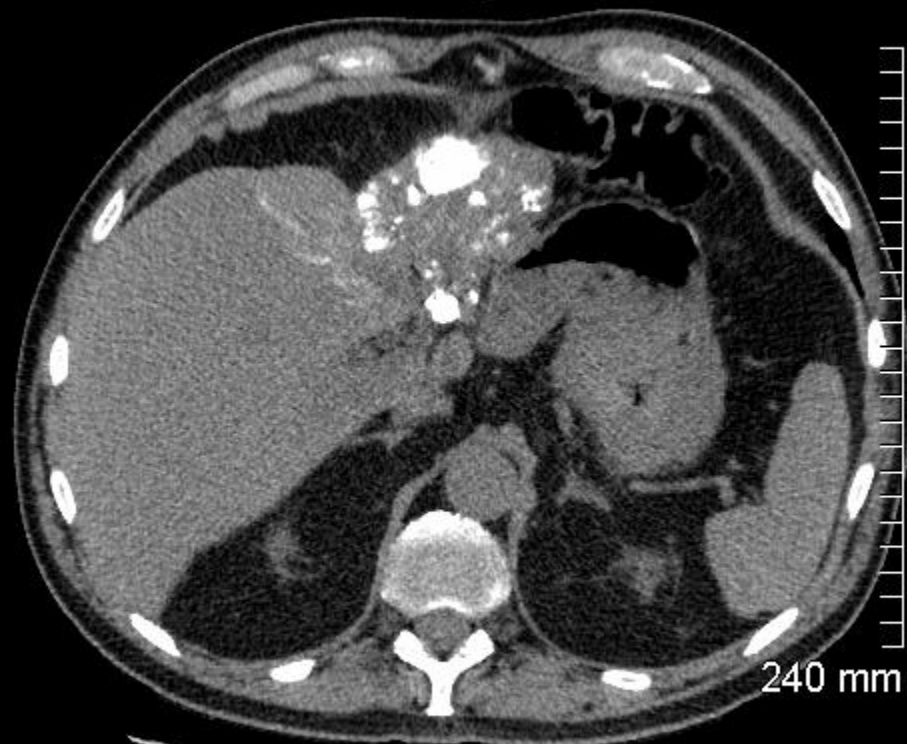
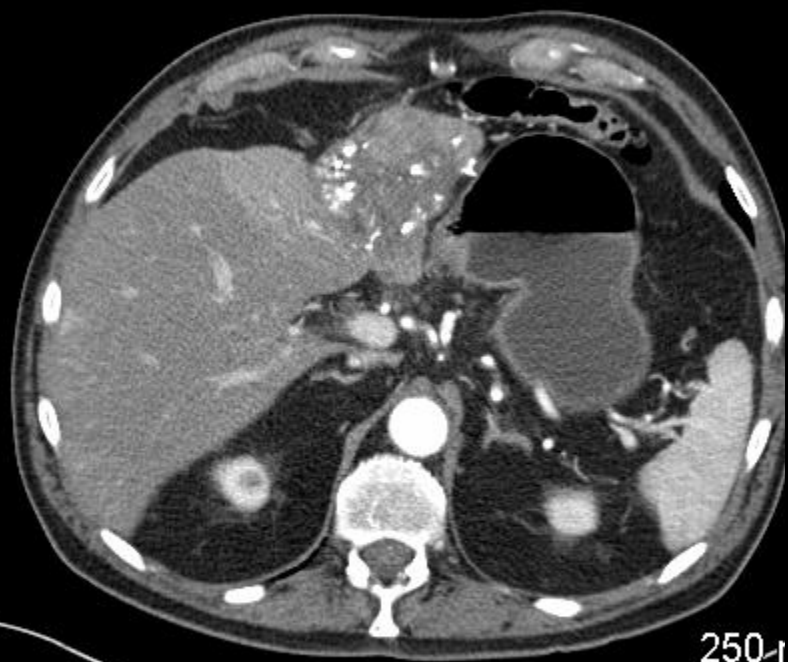
Chemoembolization

- **Drug-Eluting Beads**
 - **Microspheres loaded with chemotherapeutic agents**
 - **Different bead types with diff affinities**
- **Better than TACE for shunting tumors, PV invasion**
- **PRECISION V trial**
 - **Two vials (75 mg doxorubicin each)**
 - **First 300-500**
 - **Second 500-700**
- **Size and dose determined by tumor size and vascularity**
- **Selective > lobar > whole liver**
- **End point – whole dose or sluggish flow**









Patient Selection

- **No absolute guidelines**
- **Child-Pugh A or B**
- **AFP level**
- **Total Bilirubin less than 2 mg/dl**
- **Absence of extrahepatic mets**
- **Less than 50% replacement of liver by tumor**
- **Good overall functional status**
- **Non-surgical lesion or pt**
 - **Transplant, resection, percutaneous ablation**
- **Life expectancy greater than 6 months**
- **Goals – bridge to transplant, resection, palliation**

Patient Selection

- Child-Pugh
 - Perioperative Mortality
 - A is 2-10%
 - B is 12-31%
 - C is 12-82%

Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points) Class A = 5 to 6 points (least severe liver disease) Class B = 7 to 9 points (moderately severe liver disease) Class C = 10 to 15 points (most severe liver disease)			

Patient Selection

- Eastern Cooperative Oncology Group Performance Scale - ECOG
 - 0 Fully active; no performance restrictions
 - 1 Strenuous physical activity restricted; fully ambulatory and able to carry out light work
 - 2 Capable of all self-care but unable to carry out any work activities. Up and about >50% of waking hours
 - 3 Capable of only limited self-care; confined to bed or chair >50% of waking hours
 - 4 Completely disabled; cannot carry out any self-care; totally confined to bed or chair

Contraindications

- **Absolute**
 - **Hepatic failure**
 - **Active liver infection**
 - **Some damage to normal tissue is inevitable**
- **Relative**
 - **Portal vein occlusion**
 - **Subselective treatment**
 - **Biliary tubes**
 - **Biliary obstruction**
 - **Biliary or enteric anastomoses**
 - **Increased risk for abscess**
 - **Antibiotics 5-7 days before and 7-10 after**
 - **25% risk of infection without**

Post treatment

- Admitted
- Hydration
- Pain control
- Nausea
- DC with pain meds, antiemetics, antibiotics
- Watch for fevers, dark urine, yellow eyes, abdominal swelling
- Expect LFTs to be abnormal for 7-10 days
- Post embolization syndrome
 - Low-grade fevers
 - Fatigue
 - nausea
- Systemic effects of chemo

Chemoembolization Complications

- **Liver Failure ~ 2%**
- **Abcess <1% (higher with sphincterotomy)**
- **Cholecystitis <1%**
- **GI Ulcer <1%**
- **Postembolization syndrome requiring extended stay or readmission <5%**
- **Biloma <1%**

Y90 radioembolization

- 20-40 micron particles, β emitters
- Induce cell damage by emitting beta radiation
- Two existing products for trans-arterial use
 - Theraspheres- glass microspheres, FDA approved for HCC in 1999, 2500 Bq/particle and particles 20-30 μm diameter; high specific activity;
 - Sirspheres- resin microspheres, FDA approved for colorectal mets in 2002, 50 Bq/particle and particles 29-35 μm ; greater embolic component to radioembolic effect
- Half-life 64.1 hours (94% of radiation delivered in 11 days)

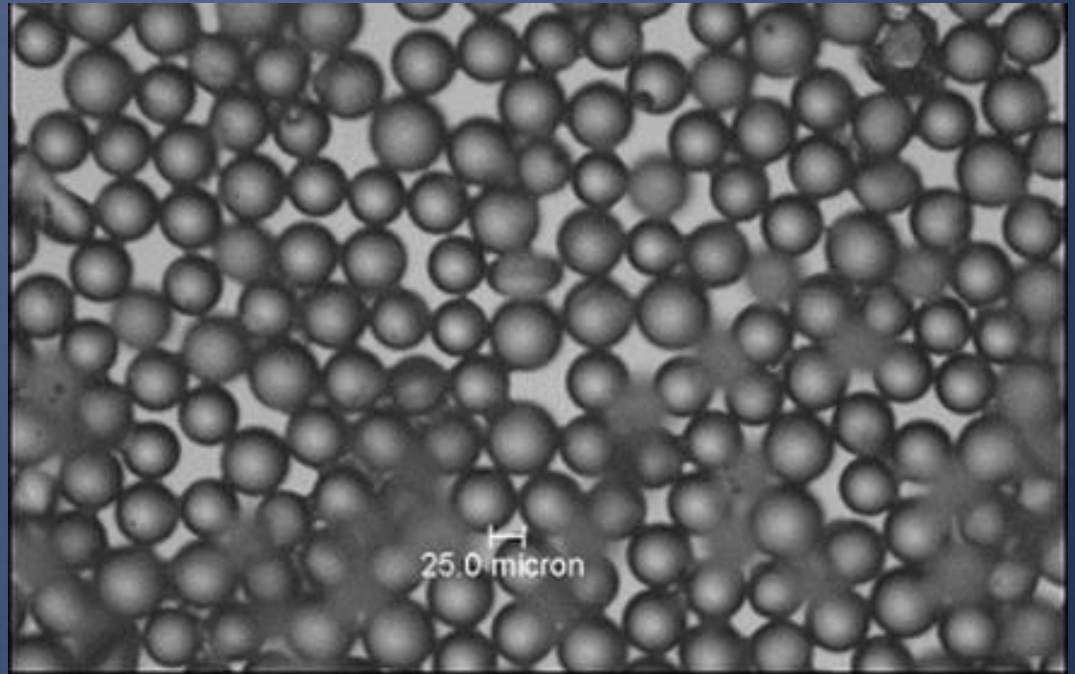
Overview – Y90 radioembolization

Table 5
Comparison of TheraSphere and SIR-Spheres

Characteristic	TheraSphere	SIR-Spheres
Isotope	^{90}Y	^{90}Y
Half-life (h)	64.2	64.2
Time to near-complete decay (3% residual activity), days	13	13
Particle size (μm)	20–30	20–60
Range of spheres per vial	⇒ 1.2–8.0 million	⇒ 40–80 million
Activity per sphere (Bq)	⇒ 2,500	⇒ 50
Specific gravity	High	Low
Activities available (GBq)	3, 5, 7, 10, 15, 20	3
Requires handling for dispensing	No	Yes
Modern delivery route	Transcatheter, intraarterial (hepatic)	Transcatheter, intraarterial (hepatic), hepatic ports (rare)
Embolic effect	⇒ Mild	⇒ Moderate
Indication for use	⇒ Hepatocellular carcinoma with appropriately positioned catheter	⇒ Colorectal metastases with intrahepatic floxuridine
Special radiation precautions upon discharge*	None	Possible urine contamination

* Refer to package insert and to institutional, state, and federal regulations for radiation safety considerations.

Glass
beads,
200X



Resin
beads,
1000X



Y90 radioembolization

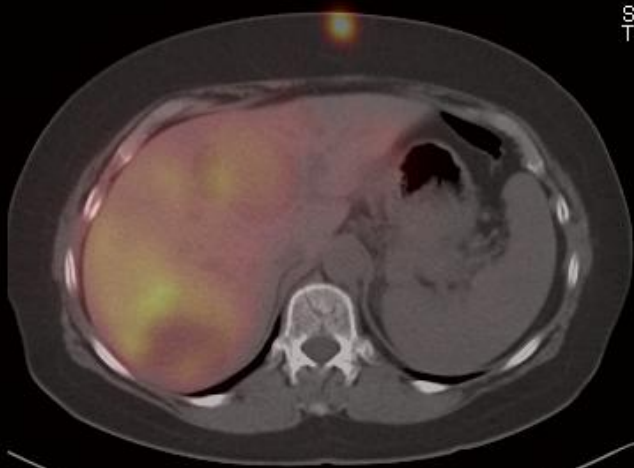
- **Safe, well tolerated and may slow disease progression**
- **Candidates –**
 - **HCC – not surgical or ablation candidates**
 - **Colorectal mets – Nonsurgical candidates who have failed or cannot tolerate chemo**
 - **Neuroendocrine, Ocular melanoma, cholangiocarcinoma**
- **Failed response to chemo – (survival benefit 8 -10 months)**
- **Contraindications – liver failure, t. bili >2.0 mg/dl, tumors amenable to resection, greater than 20% lung shunting, arterial occlusion**

Y90 radioembolization

- Usually very well tolerated
- Out patient procedure
- Side effects/potential complications
 - Post embolization syndrome (20-50%) – Fatigue, anorexia, fever, abdominal pain, N/V
 - Hepatic or biliary dysfunction
 - Lymphopenia
 - Radiation pneumonitis
 - Access site complications
 - Non-target embolization – ulcers, cholecystitis, etc.







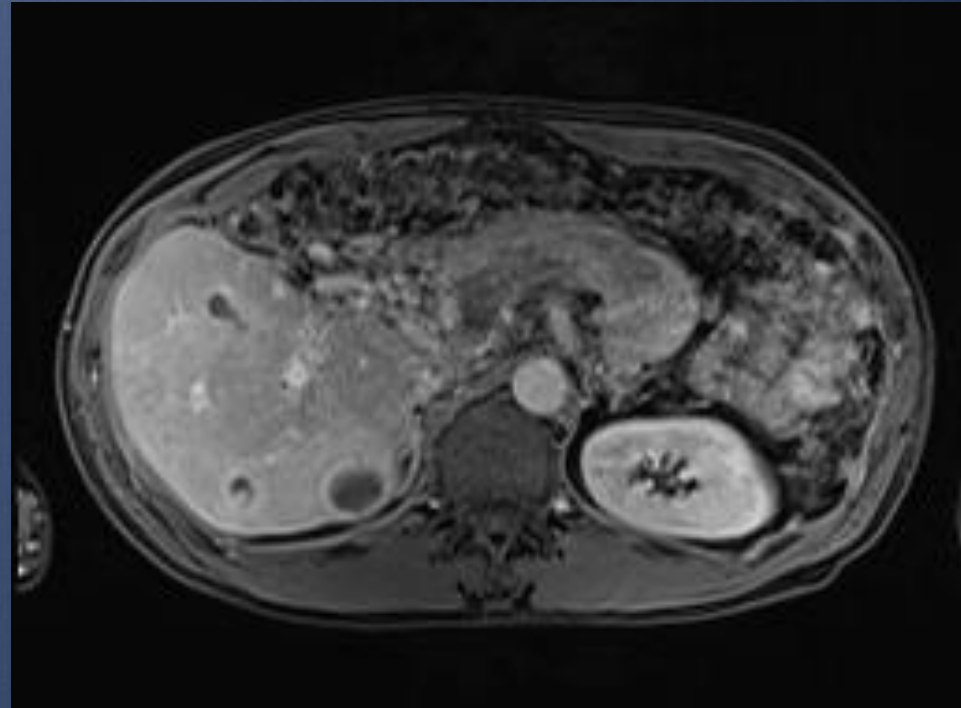
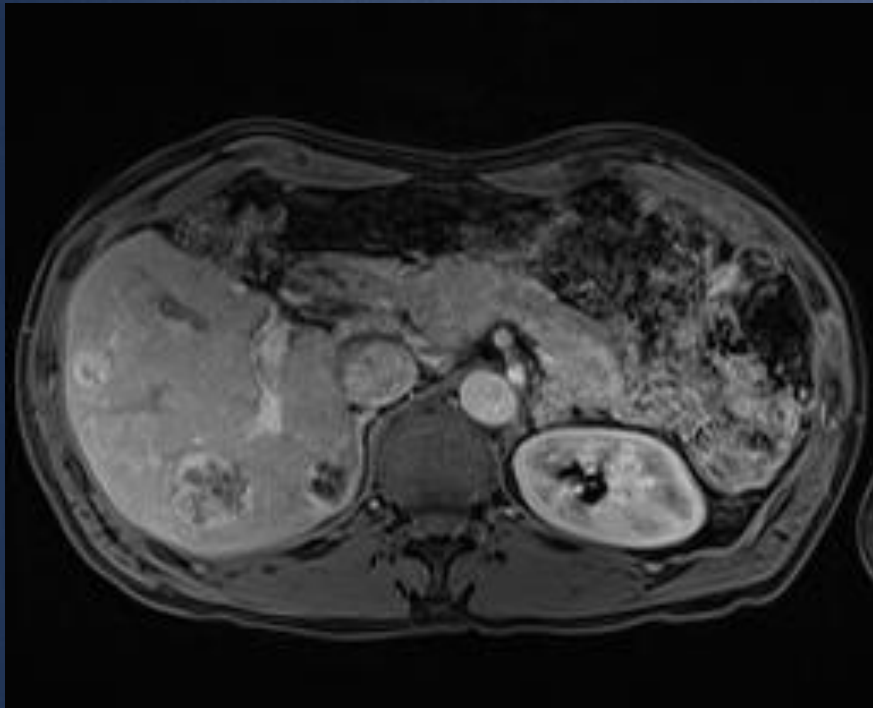
Spin: 0
Tilt: -90

F



Spin: -0
Tilt: -0

A



Y-90 Complications

- Radiation Hepatitis 0-4%
- Cholecystitis 1%
- GI Ulcer <5%
- Postembolization syndrome requiring extended stay or readmission <1%
- Pain, Fatigue, Nausea 20%

Liver Tumor Toolbox

- **500,000 cases/yr worldwisw**
- **Liver resection – open, laparoscopic, staged**
- **Portal vein embolization**
- **Transplant**
- **Tumor ablation**
- **Chemoembolization: cTACE, DEBS**
- **Y90**
- **Radiation Therapy: SBRT**
- **Combined systemic, regional, local therapies**

HCC

- 500,000 cases/yr worldwisw
- 20,000 new cases/yr USA
- 5th leading cause of CA in men, 7th in women
- Major Risk Factors
 - 80-90% pts have cirrhosis
 - HBV & HCV
 - Alcohol related liver dz
 - Non alcoholic fatty liver dz

Treatment for HCC

- **Surgical resection is the gold standard**
 - **Fewer than 20% are surgical candidates**
- **Chemotherapy options limited and largely ineffective**
- **External Beam Radiation – limited due to intolerance of normal liver parenchyma**
- **Ablation – limited for large or multiple lesions**
- **TAE vs Chemoembolization**
 - **Increased survival**

Chemoembolization

- **RCT – Chemoembo vs supportive for unresectable HCC**
 - **Survival 57%, 31% and 26% at 1, 2 and 3 years**
 - **Vs 32%, 11% and 3%**
- **RCT – 112 pts, TAE, TACE or supportive**
 - **Trial stopped early**
 - **TACE and TAE demonstrated clear survival benefit**
 - **82% and 63% at 1 and 2 years**
 - **Vs 63% and 27%**

Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. *Hepatology*.2002; 35:1164-1171.

Llovet JM, Real MI, Montana X, et al. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: A randomised controlled trial. *Lancet*.2002;359:1734-1739

Metastatic Colon Cancer

- **NCCN Guidelines**
 - **1st Line**
 - **FOLFOX, FOLFIRI, FOLFOXIRI, CapeOX +/- Avastin (bevacizumab)**
 - **+/- Vectibix (panitumumab)/Erbitux (cetuximab) for normal type KRAS/NRAS gene**
 - **2nd Line**
 - **Other triplet, +/- EGFR inhibitor, No Avastin**
- **Response rates 40-60%**
- **Downstaging to resectability in 20-25%**

Treatment for Colorectal Mets

- **Surgical resection is the gold standard**
 - **Fewer than 30% have resectable disease**
- **Systemic Chemotherapy**
- **Chemoembolization**
- **Radioembolization**

Current Trials

- **FOXFIRE** – international prospective randomized trial
 - “Assessment of Overall Survival of FOLFOX6m plus SIR-Spheres microspheres versus FOLFOX6m alone as first-line treatment in patients with non-resectable liver metastases from primary colorectal carcinoma in a randomized clinical study”
- **EPOCH** –
 - “Phase III Clinical Trial Evaluating TheraSpheres in Patients with Metastatic Colorectal Carcinoma of the Liver who have Failed First Line Chemotherapy”
 - 2nd line chemo +/- Theraspheres
- **STOP-HCC** –
 - “Phase III Clinical Trial of Intra-arterial TheraSphere in the Treatment of Patients with Unresectable Hepatocellular Carcinoma (HCC)”

Thank you

