IMAGING FOR RADIOACTIVE MICROSPHERE TREATMENT PLANNING

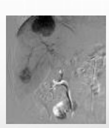
DIAGNOSTIC CT/MR, DSA, FPCBCT, NM

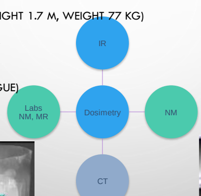
SYSTEMS COVERED

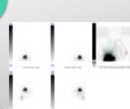
- CT/MR IMAGING FOR DIAGNOSIS
- ANGIOGRAPHY FOR DETERMINING VASCULAR ANATOMY
  - DSA – DIGITAL SUBTRACTION ANGIOGRAPHY
  - FPCBCT – FLAT PANEL CONE BEAM CT
- NM PLANAR IMAGING FOR LIVER TO LUNG SHUNT ESTIMATE (LSF)
- SPECT/CT FOR DETERMINING MICROSPHERE DISTRIBUTION

DOSIMETRY PARAMETERS

- 61-YEAR-OLD MALE WITH CIRRHOSIS AND HCC
- BSA =1.88 (HEIGHT 1.7 M, WEIGHT 77 KG)
- CHILD-PUGH A
- UNOS T3
- ECOG 1 (FATIGUE)
- AFP 809







AFP=alpha-fetoprotein; ECOG=Eastern Cooperative Oncology Group; HCC=hepatocellular carcinoma; UNOS=United Network for Organ Sharing.

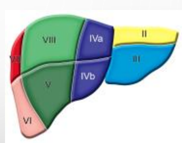
Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

ECOG PERFORMANCE STATUS*

* As published in Am. J. Clin. Oncol.:
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.

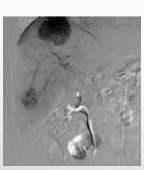
ANGIOGRAPHY

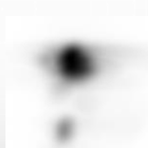
- VASCULAR ANATOMY AND NOMENCLATURE
  - LIVER SEGMENTS
  - STANDARD ANATOMY
  - COMMON VARIANTS
- WHAT DOES THE PHYSICIST REALLY NEED TO KNOW



Catalano, O. A. et al. Radiographics 2008;28:359-378

TREATMENT PLANNING ANGIOGRAM + MAA

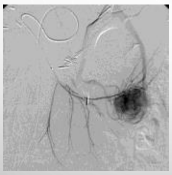




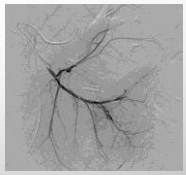
- Treatment of right hepatic lobe with microcatheter to be placed in the RHA distal to the cystic artery

MAA=macro-aggregated albumin; RHA=right hepatic artery.

TUMOR VASCULARITY



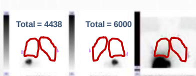
Pretreatment angiogram demonstrating hepatic vein (hyperdynamic) flow



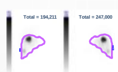
45 day post-treatment angiogram demonstrating elimination of tumor vascularity while preserving normal parenchymal flow

Atassi et al. Radiographics 2008;28 (1): 81-99

LUNG SHUNT FROM NMI USING TC-99M MAA



Lungs = 5160



Liver = 219,021

$$\text{LSF} = \frac{\text{Lungs}}{\text{Liver} + \text{Lungs}}$$

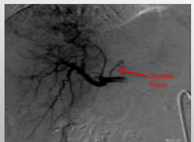
LSF% = 2.3%

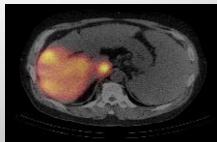
TREATMENT VOLUME IS THE PERFUSED VOLUME

- TREAT EVERYTHING THAT THE VESSEL SUPPLIES
- DOES NOT NECESSARILY CORRESPOND WITH ORGAN GROSS ANATOMY
  - EXAMPLE RHA+4
  - EXAMPLE RHA+1
  - EXAMPLE RHA WITH GALLBLADDER

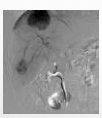
[99MTC]-MAA DISTRIBUTION WITHIN RIGHT HEPATIC LOBE AND CAUDATE LOBE

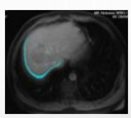
- 50-YEAR-OLD MALE WITH A HISTORY OF HEPATITIS C AND NOW WITH HEPATOCELLULAR CARCINOMA WAS ADMINISTERED 110.7 MBQ OF [99MTC]-MAA THROUGH A CATHETER PLACED IN RIGHT HEPATIC ARTERY; FORTY-FIVE MINUTES FOLLOWING ADMINISTRATION, A SPECT/CT STUDY WAS PERFORMED AND SHOWED DISTRIBUTION WITHIN THE RIGHT HEPATIC LOBE AND THE CAUDATE LOBE.





MICROCATHETER POSITION DETERMINES TREATMENT VOLUME

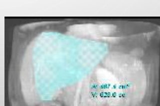




- Microcatheter placement determines treatment volume

PATIENT Z – VOLUMES FROM MRI

Location	Volume (cc)
Right Hepatic Lobe	1075
Left Hepatic Lobe	628
Whole Liver	**1703**
Tumor (segment 8)	134
Tumor (segment 5)	21
Total Tumor	**155**



CONVERSION OF TREATMENT VOLUME TO MASS

Treatment mass = treatment volume • tissue density

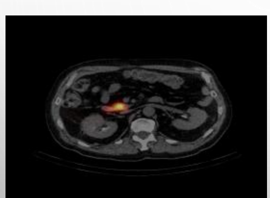
Tissue density = 1.03 g/cc • 1 kg/1000 g

mass (kg) = volume (cc) • 0.00103 kg/cc
= 1075 cc • 0.00103 kg/cc
= 1.10725 kg

VARIANT ANATOMY LEADING TO UNWANTED MICROSPHERE UPTAKE

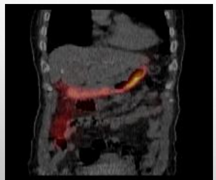
- DESCRIBE MOST COMMON CORRECTABLE VESSELS
- 3 METHODS TO DETECT THESE VESSELS
  - DSA
  - SPECT/CT
  - FPCBCT

DISTRIBUTION FROM GASTRODUODENAL ARTERY



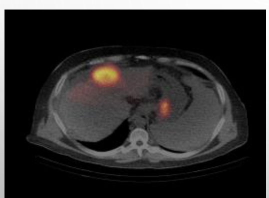
- 63-YEAR-OLD MALE WITH COLON CARCINOMA METASTATIC TO THE LIVER WAS ADMINISTERED 85.1 MBQ OF ^{99M}TC-MAA THROUGH A CATHETER PLACED IN THE RIGHT HEPATIC ARTERY. THERE WAS REFLUX OF TRACER INTO THE GASTRODUODENAL ARTERY; SEVENTY-FIVE MINUTES FOLLOWING ADMINISTRATION, SPECT/CT STUDY WAS PERFORMED. THE TRANSAXIAL SLICE FROM THE RECONSTRUCTED SPECT/CT IMAGE SHOWED ACTIVITY IN THE SECOND PORTION OF THE DUODENUM.

DISTRIBUTION FROM PROXIMAL PROPER HEPATIC ARTERY



- A PATIENT WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA WAS ADMINISTERED 85.1 MBQ OF ^{99M}TC-MAA VIA A MICROCATHETER PLACED JUST PROXIMAL TO THE PROPER HEPATIC ARTERY. THE SAGITAL SPECT/CT IMAGE DEMONSTRATES ACTIVITY WITHIN THE STOMACH, DUODENUM, AND SMALL INTESTINE.

DISTRIBUTION FROM LEFT GASTRIC ARTERY



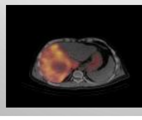
- 76 YEAR-OLD FEMALE WITH A HISTORY OF HEPATITIS C INFECTION AND HEPATOCELLULAR CARCINOMA WAS ADMINISTERED 81.4 MBQ OF ^{99M}TC-MAA THROUGH A CATHETER PLACED IN MIDDLE HEPATIC ARTERY AND REPLACED LEFT HEPATIC ARTERY. SPECT/CT IMAGES WERE SUBSEQUENTLY OBTAINED. TRANSAXIAL RECONSTRUCTED SPECT/CT FUSED IMAGE OF THE MEDIAL LEFT HEPATIC LOBE, STOMACH, AND SPLEEN SHOWS FOCAL ACTIVITY CORRESPONDING WITH THE LEFT LOBE HEPATOMA AND SHOWS FOCAL ACTIVITY IN THE MEDIAL WALL OF THE PROXIMAL STOMACH, INDICATING A SIGNIFICANT ABNORMAL SHUNTING OF THE LIVER ACTIVITY.

DISTRIBUTION FROM THE FALCIFORM ARTERY

58 year-old male with a history of metastatic neuroendocrine disease with hepatic involvement was administered 173.9 MBq of ^{99m}Tc-MAA through a microcatheter placed the middle hepatic artery. The transaxial and sagital reconstructed SPECT/CT image shows ^{99m}Tc-MAA uptake within the anterior abdominal wall due to flow from the falciform artery, which originated from the middle hepatic artery.

FREE TC-99M PERTECHNETATE DISTRIBUTION

45 year-old male with metastatic adenocarcinoma of the gastroesophageal junction with hepatic involvement was administered 155.4 MBq of Tc-99m MAA through a catheter placed in right hepatic artery. The transaxial slice from the reconstructed SPECT/CT image of the abdomen reveals that both the right hepatic and caudate lobes were perfused with an inhomogeneous distribution of activity corresponding to the patient's multifocal intrahepatic lesions. In addition, free Tc-99m pertechnetate can be observed in the lumen of the stomach. Incidentally noted is a focal area of increased uptake in the region of the left upper pole of the thyroid gland.



FLAT PANEL CONE BEAM CT

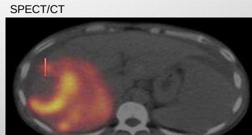
- C-ARM COMPUTED TOMOGRAPHY (CT; ALSO COMMONLY REFERRED TO AS CONE-BEAM CT) IS A THREE-DIMENSIONAL (3D) CT-LIKE FILTERED BACK- PROJECTION RECONSTRUCTION AFTER A ROTATIONAL ANGIOGRAM IS OBTAINED WITH THE USE OF A FLAT-PANEL DETECTOR.
- POTENTIAL ADVANTAGES OF C-ARM CT INCLUDE IMPROVED TUMOR DETECTION AND EXTRAHEPATIC PERFUSION DETECTION, 3D VASCULAR MAPPING, AND REAL-TIME 3D GUIDANCE DURING ANGIOGRAPHIC PROCEDURES
- RADIOLOGY 2015; 274: 320-334.

[^{99M}TC]-MAA DISTRIBUTION WITHIN RIGHT HEPATIC LOBE SHOWING CENTRALLY DECREASED UPTAKE WITHIN TUMOR

- 44 YEAR-OLD FEMALE WITH METASTATIC COLON CARCINOMA WITH HEPATIC INVOLVEMENT AND STATUS POST CHEMOEMBOLIZATION OF THE RIGHT HEPATIC LOBE WAS ADMINISTERED 170.2 MBQ OF [^{99M}TC]-MAA VIA A MICROCATHETER PLACED INTO THE RIGHT HEPATIC ARTERY. THE SPECT/CT IMAGES SHOW FOCAL AREAS OF INCREASED UPTAKE LIKELY CORRESPONDING TO SOME OF THE PATIENT'S FOCAL INTRAHEPATIC LESIONS, INCLUDING PROMINENT UPTAKE IN THE MEDIAL PERIPHERAL ASPECT OF ONE OF THE LARGEST LESIONS IN THE RIGHT LOBE LATERALLY, WITH CENTRALLY DECREASED ACTIVITY, SUGGESTING AN AREA OF NECROSIS OR CYSTIC CHANGE.

Cone Beam CTA

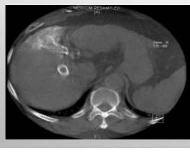
SPECT/CT



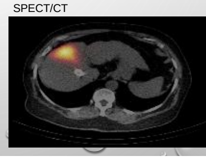
[^{99m}TC]-MAA DISTRIBUTION WITHIN MIDDLE HEPATIC LOBE

- 65-YEAR-OLD FEMALE WITH THE CIRRHOSIS AND HEMOCHROMATOSIS WITH HEPATOCELLULAR CARCINOMA WAS ADMINISTERED 155.4 MBQ OF [^{99m}TC]-MAA VIA A CATHETER PLACED IN THE MIDDLE HEPATIC ARTERY. TRANSVERSE SPECT/CT IMAGE SHOWS MIDDLE HEPATIC LOBE DISTRIBUTION CORRESPONDING TO THE CONE BEAM CT ANGIOGRAM CONTRAST DISTRIBUTION.

Cone Beam CTA

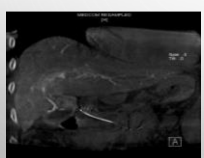


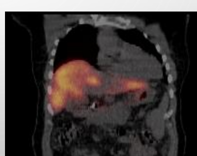
SPECT/CT



RIGHT TO LEFT HEPATIC SHUNT

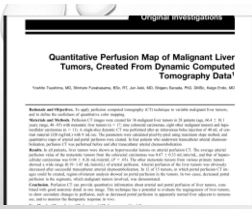
- 56-YEAR-OLD MALE WITH HEPATITIS C VIRUS AND UNRESECTABLE HEPATOCELLULAR CARCINOMA AND PORTAL VEIN TUMOR THROMBOSIS ADMINISTERED 85.1 MBQ OF [^{99m}TC]-MAA VIA A MICROCATHETER PLACED IN THE RIGHT HEPATIC ARTERY. THE CORONAL SPECT/CT IMAGE AND CONE BEAM CTA DEMONSTRATES RIGHT TO LEFT HEPATIC SHUNT MOST LIKELY AS A RESULT OF PORTAL VEIN TUMOR INVASION.

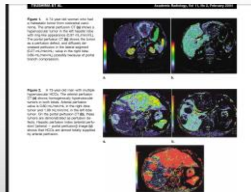




FOLLOW-UP IMAGING

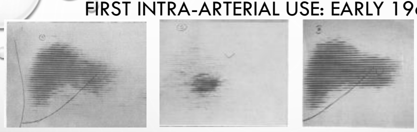
- Y-90 SPECT/CT OR Y90 PET/CT FOR IMMEDIATE DISTRIBUTION/UPTAKE
- CT/MR FOR TUMOR RESPONSE AT 1 MONTH….ETC
- FDG PET/CT FOR SOME METASTATIC DISEASES





MICROSPHERE TREATMENT EFFICACY

FIRST INTRA-ARTERIAL USE: EARLY 1960S



CASE STUDY:

- **A 51-YEAR-OLD MAN WITH A PRIMARY HEPATOMA; A CATHETER WAS INSERTED RETROGRADE THROUGH THE GASTROEPIPLOIC ARTERY INTO THE HEPATIC ARTERY**
- **PATIENT WAS TREATED WITH 60 MCI ^{90}Y MICROSPHERES PLUS 50 MG METHOTREXATE**
- **HEPATIC PHOTOSCANS PRE-TREATMENT AND 4 MONTHS POST-TREATMENT SHOWED SHRINKAGE OF THE HEPATIC CANCER TO A POINT WHERE IT COULD NOT BE PALPATED**
- **THE PATIENT REMAINED WELL 5 MONTHS POST-TREATMENT**

Ariel IM. *Ann Surg*. 1965;162(2):267-278; Ariel IM. *Cancer*. 1967;20(5)793-804.

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CLARENCE CHRISP, DVM,‡ JAMES ANDREWS, MD,§ JACK JUNI, MD,* SARA WARBER, BA,*
JOYCE KLEVERING,§ JAMES CRUDUP,| AND WILLIAM ENSMINGER, MD, PHD*†

A 22-μm glass microsphere called TheraSphere (Theragenics Corp., Atlanta, GA) has been developed in which yttrium 89 oxide is incorporated into the glass matrix and is activated by neutron bombardment to form the beta-emitting isotope yttrium 90 (Y 90) before using the spheres as radiotherapeutic vehicles. The injection of up to 12 times (on a liver weight basis) the anticipated human dose of nonradioactive TheraSphere into the hepatic arteries of dogs was well tolerated and produced clinically silent alterations within centrolobular areas. The hepatic arterial (HA) injection of radioactive TheraSphere also produced portal changes similar to those observed in humans after external beam therapy. While the extent of damage increased with the delivered dose, radiation exposures in excess of 30,000 cGy did not cause total hepatic necrosis and were compatible with survival. No microspheres distributed to the bone marrow and absolutely no myelosuppression was encountered in any animal. Proposed hepatic exposures to humans of 5000 to 10,000 cGy by means of these microspheres, therefore, would appear to be feasible and tolerable. Radiotherapeutic microsphere administration preceded by regional infusion of a radiosensitizing agent and/or immediately following the redistribution of blood flow toward intrahepatic tumor by vasoactive agents can potentially yield a synergistic, highly selective attack on tumors confined to the liver.

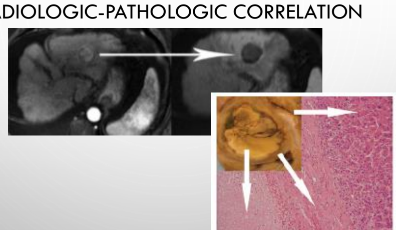
Cancer 61:1336–1344, 1988.

Radiologic–Pathologic Correlation of Hepatocellular Carcinoma Treated with Internal Radiation Using Yttrium-90 Microspheres

Ahsun Riaz,[1] Laura Kulik,[2] Robert J. Lewandowski,[1] Robert K. Ryu,[1] Georgia Giakoumis Spear,[1] Mary F. Mulcahy,[3] Michael Abecassis,[4] Talia Baker,[4] Vanessa Gates,[1] Ritu Nayar,[5] Frank H. Miller,[1] Kent T. Sato,[1] Reed A. Omary,[1] and Riad Salem[1,3]

We present the correlation between radiologic and pathologic findings in HCC patients who underwent radioembolization with yttrium-90 (^{90}Y) microspheres prior to resection or transplantation. Thirty-five patients with a total of 38 lesions who underwent liver explantation after ^{90}Y radioembolization were studied. Imaging surrogates following treatment were evaluated; the explants were examined for assessment of necrosis by pathology. The correlation betwen radiologic and histologic findings of the treated lesions was analyzed. Twenty-three of 38 (61%) target lesions showed complete pathologic necrosis. All target lesions demonstrated some degree of histologic necrosis at explant. Complete histologic necrosis was seen in 89% of lesions with pretreatment size <3 cm. Complete pathologic necrosis was seen in 100%, 78%, and 93% of the lesions that were shown to have complete response by European Association for the Study of the Liver (EASL) necrosis criteria, partial response by World Health Organizaton (WHO) criteria, or thin rim enhancement on post-treatment imaging, respectively. In contrast, complete pathologic necrosis was seen in only 52% and 38% of the lesions that showed partial response by EASL criteria and peripheral nodular enhancement, respectively. *Conclusion:* Post-radioembolization imaging findings of response by EASL and WHO criteria are predictive of the degree of pathologic necrosis. Rim enhancement was an imaging characteristic that correlated well with histologic necrosis. (HEPATOLOGY 2009;49:000-000.)

RADIOLOGIC-PATHOLOGIC CORRELATION



(HEPATOLOGY 2009;49:000-000.)

Fig. 3. Gross and histologic correlation. In a clockwise direction, arrows demonstrate normal parenchyma, fibrosis (peripheral rim), and completely necrotic tumor.

RESPONSE CRITERIA

- WHO CRITERIA
- THE RESPONSE EVALUATION CRITERIA IN SOLID TUMORS (RECIST AND $_{M}$RECIST
- EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER (EASL)DOSE RESPONSE ASSESSMENT
- TUMOR DOSE RESPONSE CHARACTERISTICS BASED ON Y-90 SPECT/CT OR Y-90 PET/CT
- SUMMARY OF VARIOUS TUMOR DOSE RESPONSE STUDIES

STANDARDS OF PRACTICE

CPG

Radioembolization of Hepatic Malignancies: Background, Quality Improvement Guidelines, and Future Directions

Siddharth A. Padia, MD, Robert J. Lewandowski, MD, Guy E. Johnson, MD, Daniel Y. Sze, MD, PhD, Thomas J. Ward, MD, Ron C. Gaba, MD, Mark O. Baerlocher, MD, Vanessa L. Gates, MS, Ahsun Riaz, MD, Daniel B. Brown, MD, Nasir H. Siddiqi, MD, T. Gregory Walker, MD, James E. Silberzweig, MD, Jason W. Mitchell, MD, MPH, MBA, Boris Nikolic, MD, MBA, and Riad Salem, MD, MBA, for the Society of Interventional Radiology Standards of Practice Committee

ABBREVIATIONS

AFP = α-fetoprotein, ECOG = Eastern Cooperative Oncology Group, EASL = European Association for Study of the Liver, FDA = Food and Drug Administration, FDG = fluorodeoxyglucose, HCC = hepatocellular carcinoma, MAA = macroaggregated albumin, mRECIST = modified Response Evaluation Criteria In Solid Tumors, QI = quality improvement, RECIST = Response Evaluation Criteria In Solid Tumors, REILD = radioembolization-induced liver disease, SPECT = single-photon emission computed tomography, 3D = three-dimensional

J Interv Radiol 2017; 28:1-15

Table 1. Outcomes of Radioembolization for Primary Liver Cancer ([10,13-25)

Study, Year	^{90}Y Device	No. of Pts.	CTP Score (No. of Pts.)	BCLC Stage (No. of Pts.)	OR (%)	Median (95% CI) TTP*	Survival
Hepatocellular carcinoma							
Carr, 2004 (13)	Glass	65	NR	NR	NR	NR	649 d (Okuda I), 302 d (Okuda II)
Lewandowski et al, 2009 (14)	Glass	43	A (24), B (19), C (0)	A (0), B (34), C (9), D (0)	61	33.3 mo (17.8– 33.8 mo)	35.7 mo
Riaz et al, 2011 (15)	Glass	84	A (41), B (42), C (1)	A (27), B (25), C (31), D (1)	81	13.6 mo (9.3–18.7 mo)	26.9 mo
Salem et al, 2010 (10)	Glass	291	A (131), B (152), C (8)	A (48), B (83), C (152), D (8)	57	7.9 mo (6–10.3 mo)	17.2 mo (Child-Pugh class A), 7.7 mo (Child-Pugh class B)
Sangro et al, 2011 (23)	Resin	325	A (268), B (57), C (0)	A (52), B (87), C (183), D (3)	NR	NR	12.8 mo
Padia et al, 2014 (16)	Glass	20	A (11), B (8), C (1)	A (2), B (2), C (15), D (1)	95	319 d	90% at 1 y
Mazzaferro et al, 2013 (22)	Glass	52	A (43), B (9), C (0)	A (0), B (17), C (35), D (0)	40	11 mo	15 mo
Kokabi et al, 2015 (24)	Glass	30	A (20), B (10), C (0)	A (0), B (0), C (30), D (0)	NR	9 mo (6.2–13.1 mo)	13 mo
Saxena et al, 2014 (25)	Resin	40	A (30), B (10), C (1), unknown (4)	NR	48	NR	27.7 mo
Gramenzi et al, 2015 (21)	Resin	63	A (58), B (5), C (0)	A (0), B (26), C (37), D (0)	73	5 mo	13.2 mo
Cholangiocarcinoma							
Saxena et al, 2010 (18)	Resin	25	NR	NR	24	NR	9.3 mo
Hoffman et al, 2012 (19)	Resin	33	NR	NR	36	9.8 mo	22 mo
Mouli et al, 2013 (20)	Glass	46	NR	NR	73	NR	14.6 mo

BCLC = Barcelona Clinic Liver Cancer; CI = confidence interval; CTP = Child-Turcotte-Pugh; NR = not reported; OR = objective response; TTP = time to progression.
*TTP is presented as overall time to progression unless otherwise stated.

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Table 2. Outcomes of Radioembolization for Metastatic Disease to the Liver (31,33–50)

Study, Year	^{90}Y Regimen	Previous Chemotherapy	No. of Pts.	Objective Response	Survival
Colorectal cancer metastases					
van Hazel et al, 2016 (37)	Resin + FOLFOX	No	267	76.4%	10.7 mo (PFS)
Gray et al, 2001 (31)	Resin + chemotherapy	No	35	44%	72% (1 y)
Sharma et al, 2007 (33)	Resin + FOLFOX	No	20	90%	9.3 mo (PFS)
Mulcahy et al, 2009 (34)	Glass	Yes	72	40%	14.5 mo
Van Hazel et al, 2004 (35)	Resin + 5-FU	No	11	91%	29.4 mo
Murthy et al, 2005 (39)	Resin	Yes	12	0%	4.5 mo
Abbott et al, 2015 (40)	Glass	Yes	68	NR	11.6 mo
Hendlisz et al, 2010 (36)	Resin	Yes	21	9.5%	10 mo
Kalva et al, 2014 (41)	Resin	Yes	45	2%	186 d
Saxena et al, 2015 (42)	Resin	Yes	302	39%	10.5 mo
Kennedy et al, 2015 (43)	Resin	Yes	606	NR	9.6 mo
Lewandowski et al, 2014 (44)	Glass	Yes	214	NR	10.6 mo
Neuroendocrine metastases					
Rhee et al, 2008 (45)	Resin or glass	No	42	52%	25 mo
King et al, 2008 (46)	Resin + 5-FU	15% of patients	34	50%	24.2 mo
Kennedy et al, 2008 (32)	Resin	NR	148	63.2%	70 mo
Saxena et al, 2010 (47)	Resin	52% of patients	48	54%	35 mo
Breast cancer metastases					
Gordon et al, 2014 (48)	Glass	Yes	75	35%	6.6 mo
Saxena et al, 2014 (49)	Resin	Yes	40	31%	13.6 mo
Uveal melanoma					
Gonsalves et al, 2011 (38)	Resin	No	32	6%	10 mo
Klingenstein et al, 2013 (50)	Resin	77% of patients	13	62%	7 mo

5-FU = 5-fluorouracil; FOLFOX = leucovorin/5-fluorouracil/oxaliplatin; NR = not reported; PFS = progression-free survival.

LONG-TERM HEPATOTOXICITY OF YTTRIUM-90 RADIOEMBOLIZATION AS TREATMENT OF METASTATIC NEUROENDOCRINE TUMOR TO THE LIVE
VASC INTERV RADIOL 2017; ▪:1–7

- RESULTS: AMONG PATIENTS WHO UNDERWENT UNILOBAR RADIOEMBOLIZATION, IMAGING FOLLOW-UP AT A MEAN OF 4.1 YEARS (RANGE, 2.0–15.2 Y) REVEALED CIRRHOSIS-LIKE MORPHOLOGY IN 26.7% (4 OF 15), ASCITES IN 13.3% (2 OF 15), VARICES IN 6.7% (1 OF 15), AND A 21.9% INCREASE IN SPLENIC VOLUME. THE RESPECTIVE INCIDENCES IN PATIENTS TREATED WITH WHOLE-LIVER 90Y RADIOEMBOLIZATION WERE 56.4% (22 OF 39), 41.0% (16 OF 39), AND 15.4% (6 OF 39), WITH A 64.7% INCREASE IN SPLENIC VOLUME. PATIENTS TREATED WITH WHOLE-LIVER RADIOEMBOLIZATION EXHIBITED SIGNIFICANTLY DECREASED PLATELET COUNTS (P 1⁄4 .023) AND LOWER ALBUMIN LEVELS (P 1⁄4 .0002). EIGHT PATIENTS (20.5%) TREATED WITH WHOLE-LIVER RADIO- EMBOLIZATION WHO EXHIBITED CIRRHOSIS-LIKE MORPHOLOGY SHOWED CLINICAL SIGNS OF HEPATIC DECOMPENSATION; ONLY 2 OF 39 PATIENTS (5.1%) HAD NO OTHER CAUSES OF HEPATOTOXICITY.
- CONCLUSIONS: WHOLE-LIVER 90Y RADIOEMBOLIZATION FOR PATIENTS WITH MNET RESULTS IN LONG-TERM IMAGING FINDINGS OF CIRRHOSIS-LIKE MORPHOLOGY AND PORTAL HYPERTENSION IN > 50% OF TREATED PATIENTS, BUT THE MAJORITY REMAIN CLINICALLY ASYMPTOMATIC. LONG-TERM HEPA- TOTOXICITY SOLELY ATTRIBUTABLE TO 90Y DEVELOPS IN A SMALL PERCENTAGE OF PATIENTS.

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European Journal of Radiology
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Research papers

Comparative study of post-transplant outcomes in hepatocellular carcinoma patients treated with chemoembolization or radioembolization

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ARTICLE INFO

Keywords:
Transarterial chemoembolization
Radioembolization
Liver transplantation
Downstaging

ABSTRACT

Purpose: To analyze long-term outcomes in patients bridged/downstaged to orthotopic liver transplantation (OLT) by transarterial chemoembolization (TACE) or yttrium-90 radioembolization (Y90) for hepatocellular carcinoma (HCC).
Methods: 172 HCC patients who underwent OLT after being treated with transarterial liver-directed therapies (LDTs) (Y90: 93; TACE: 79) were identified. Pre-LDT and pre-OLT clinical/imaging/laboratory characteristics including United Network for Organ Sharing (UNOS) staging and alpha-fetoprotein values (AFP) were tabulated. Post-OLT HCC recurrence was assessed by imaging follow-up per standard of care. Recurrence-free (RFS) and overall survival (OS) were calculated. Uni/multivariate and sub-stratification analyses were performed.
Results: Time-to-OLT was longer in the Y90 group (Y90: 6.5 months; TACE: 4.8 months; p = 0.02). With a median post-OLT follow-up of 26.1 months (IQR: 11.1–49.7), tumor recurrence was found in 6/79 (8%) TACE and 8/93 (9%) Y90 patients. Time-to-recurrence was 26.6 (CI: 7.0–49.5) and 15.9 months (CI: 7.8–46.8) for TACE and Y90, respectively (p = 0.48). RFS (Y90: 79 months; TACE: 77 months; p = 0.84) and OS (Y90: 57% alive at 100 months; TACE: 84.2 months; p = 0.57) were similar. 54/155 patients (Y90: 29; TACE: 25) were downstaged to UNOS T2 or less. RFS hazard ratios for patients downstaged to ≤T2 versus those that were not were 0.6 (CI: 0.33–1.1) and 1.7 (CI: 0.9–3.1) respectively (p = 0.13). 17/155 patients (Y90: 8; TACE: 9) that were > T2 were downstaged to UNOS T2 or less (within transplant criteria). Distribution (unilobar/bilobar), AFP, and pre-transplant UNOS stage affected RFS on univariate analyses.
Conclusion: Despite longer time-to-OLT for Y90 patients, post-OLT outcomes were similar between patients bridged or downstaged by TACE or Y90. A trend towards improved RFS for downstaged patients was identified.

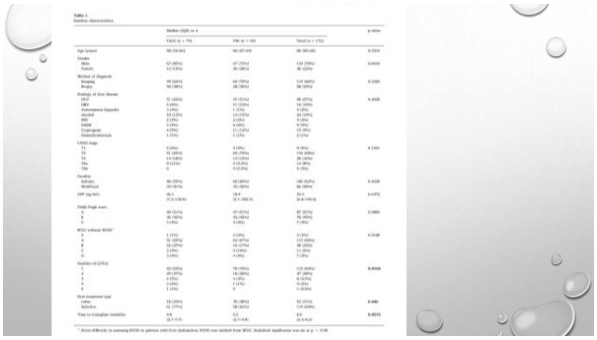

Table 2
Change in AFP.

	Median (IQR)	Pre-treatment	Pre-transplant	*p*-value
AFP	TACE $n = 65$	31.5 (6.8–149.5)	15 (5.8–61.4)	0.0254
	Y90 $n = 90$	22.3 (5.0–277.7)	11.7 (5.3–36.5)	< 0.0001

Table 3
UNOS staging pre-treatment and pre-transplant.

UNOS Stage		Post-LDT		
Pre-LRT	Pre-transplant *	TACE (n=67)	Y90 (n=88)	Total (n=155)
T1	T1	0	3 (4%)	3 (2%)
	T2	5 (7%)	0	5 (3%)
T2	T1	16 (24%)	21 (23%)	37 (24%)
	T2	22 (33%)	41 (47%)	63 (41%)
	T3	3 (5%)	1 (1%)	4 (3%)
	T4a	1 (2%)	1 (1%)	2 (1%)
T3	T1	2 (3%)	2 (2%)	4 (3%)
	T2	7 (10%)	6 (7%)	13 (8%)
	T3	5 (7%)	6 (7%)	11 (7%)
T4a	T3	1 (2%)	1 (1%)	2 (1%)
	T4a	5 (7%)	3 (4%)	8 (5%)
T4b	T3	0	1 (1%)	1 (1%)
	T4b	0	2 (2%)	2 (1%)

*Rows in blue (downstaged), white (bridged) and red (progressed).

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Table 4
Uni/multivariate analysis for recurrence free survival.

Variable	Univariate ($N = 172$)[a]				Multivariate ($N = 149$)[c]	
	Category	Hazard ratio (CI)	p-value	Adjusted p-value[b]	Hazard ratio (CI)	p-value
Gender	Female	0.96 (0.46–2.02)	0.9179	–	0.86 (0.37–2.01)	0.7343
	Male	1.00			1.00	
Age	< 60	0.97 (0.56–1.68)	0.9156	–	1.03 (0.54–1.97)	0.9173
	≥ 60	1.00			1.00	
Liver disease	Other	1.38 (0.78–2.41)	0.2465	–	1.45 (0.75–2.81)	0.2756
	HCV	1.00			1.00	
Distribution	Bilobar	3.01 (1.12–8.12)	**0.0006**	**0.0054**	2.28 (0.87–5.94)	0.0947
	Unilobar	1.00			1.00	
ECOG performance status	0	0.90 (0.50–1.59)	0.7048	–	0.66 (0.33–1.32)	0.2420
	> 0	1.00			1.00	
Treatment group	TACE	1.06 (0.61–1.83)	0.8422	–	0.75 (0.37–1.52)	0.4286
	Y90	1.00			1.00	
Number or LDT	1	0.82 (0.47–1.44)	0.4891	–	0.90 (0.47–1.72)	0.7447
	> 1	1.00			1.00	
Pre-transplant AFP[a]	≤ 13 ng/mL	0.53 (0.29–0.96)	**0.0463**	0.4167	0.65 (0.33–1.27)	0.2076
	> 13 ng/mL	1.00			1.00	
Pre-transplant UNOS stage[a]	≤ T2	0.53 (0.27–1.05)	**0.0360**	0.3240	0.68 (0.33–1.37)	0.2804
	> T2	1.00			1.00	

[a] Univariate analysis on pre-transplant AFP production and UNOS stage was conducted on 155 patients, as pre-transplant AFP values or UNOS stage were not available.
[b] Adjusted for multiple comparison (Bonferroni correction factor = 9).
[c] Multivariate analysis, including all variables used in the univariate analysis, was conducted on 149 patients due to missing values in pre-transplant AFP or UNOS stage. Statistical significance was set at $p < 0.05$.

Gastroenterology 2016;151:1155–1163

Y90 Radioembolization Significantly Prolongs Time to Progression Compared With Chemoembolization in Patients With Hepatocellular Carcinoma

Riad Salem,[1,2,3,*] **Andrew C. Gordon**,[1,*] Samdeep Mouli,[1] Ryan Hickey,[1] Joseph Kallini,[1] Ahmed Gabr,[1] Mary F. Mulcahy,[2] Talia Baker,[3] Michael Abecassis,[3] Frank H. Miller,[4] Vahid Yaghmai,[4] Kent Sato,[1] Kush Desai,[1] Bartley Thornburg,[1] Al B. Benson,[2] Alfred Rademaker,[5] Daniel Ganger,[6] Laura Kulik,[6] and Robert J. Lewandowski[1,2]

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CLINICAL LIVER

This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e24. Learning Objective: Upon completion of this exercise, successful learners will be able to define the role of two commonly used transarterial therapies for Barcelona Clinic Liver Cancer (BCLC) A/B hepatocellular carcinoma (HCC) patients: (1) radioembolization and (2) conventional transarterial chemoembolization (cTACE).

Cardiovasc Intervent Radiol
DOI 10.1007/s00270-017-1648-7

CIRSE CrossMark

CLINICAL INVESTIGATION

Yttrium-90 Radioembolization for Unresectable Combined Hepatocellular-Cholangiocarcinoma

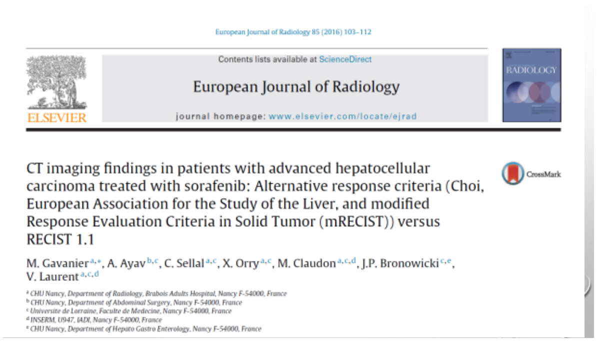
Lauren S. Chan[1] · Daniel Y. Sze[1] · George A. Poultsides[2] · John D. Louie[1] · Mohammed A. Abdelrazek Mohammed[1] · David S. Wang[1]

Received: 16 November 2016 / Accepted: 4 April 2017

Abstract
Purpose Combined hepatocellular-cholangiocarcinoma (cHCC-CC) is a rare mixed cell type primary liver cancer with limited data to guide management. Transarterial radioembolization with yttrium-90 microspheres (RE) is an emerging treatment option for both hepatocellular carcinoma and intrahepatic cholangiocarcinoma. This study explored the safety and efficacy of RE for unresectable cHCC-CC.
Methods Patients with histopathologically confirmed cHCC-CC treated with RE were retrospectively evaluated. Clinical and biochemical toxicities were assessed using the Common Toxicity Criteria for Adverse Events v4.03. Radiological response was analyzed using the Response

before RE showed decreased levels after treatment (median decrease of 72%, range 13–80%). Best hepatic radiological response was 60% partial response and 40% stable disease by modified RECIST, and 100% stable disease by RECIST v1.1. Poor performance status and the presence of macrovascular invasion were identified as predictors of reduced survival after RE.
Conclusion RE appears to be a safe and promising treatment option for patients with unresectable cHCC-CC.
Level of Evidence Level 4.

Keywords Radioembolization · Yttrium-90 microspheres · Combined hepatocellular-cholangiocarcinoma · Cholangiohepatoma · Efficacy ·


European Journal of Radiology 85 (2016) 103–112

Contents lists available at ScienceDirect

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CT imaging findings in patients with advanced hepatocellular carcinoma treated with sorafenib: Alternative response criteria (Choi, European Association for the Study of the Liver, and modified Response Evaluation Criteria in Solid Tumor (mRECIST)) versus RECIST 1.1

M. Gavanier[a,*], A. Ayav[b,c], C. Sellal[a,c], X. Orry[a,c], M. Claudon[a,c,d], J.P. Bronowicki[c,e], V. Laurent[a,c,d]

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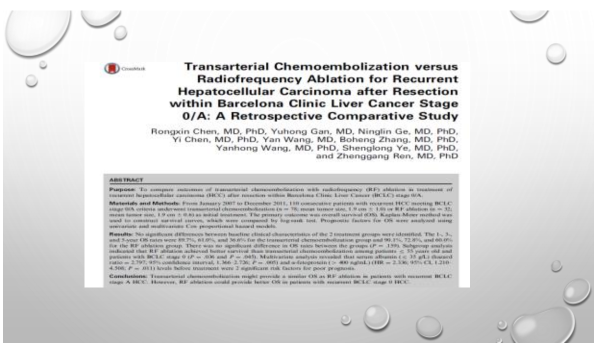
Transarterial Chemoembolization versus Radiofrequency Ablation for Recurrent Hepatocellular Carcinoma after Resection within Barcelona Clinic Liver Cancer Stage 0/A: A Retrospective Comparative Study

Rongxin Chen, MD, PhD, Yuhong Gan, MD, Ninglin Ge, MD, PhD, Yi Chen, MD, PhD, Yan Wang, MD, Boheng Zhang, MD, PhD, Yanhong Wang, MD, PhD, Shenglong Ye, MD, PhD, and Zhenggang Ren, MD, PhD

ABSTRACT


CLINICAL STUDY

Segmental Yttrium-90 Radioembolization versus Segmental Chemoembolization for Localized Hepatocellular Carcinoma: Results of a Single-Center, Retrospective, Propensity Score–Matched Study

Siddharth A. Padia, MD, Guy E. Johnson, MD, Kathryn J. Horton, MD, Christopher R. Ingraham, MD, Matthew J. Kogut, MD, Sharon Kwan, MD, Sandeep Vaidya, MD, Wayne L. Monsky, MD, PhD, James O. Park, MD, Renuka Bhattacharya, MD, Daniel S. Hippe, MS, and William P. Harris, MD

ABSTRACT

Review Article

Complications Following Radioembolization with Yttrium-90 Microspheres: A Comprehensive Literature Review

Ahsun Riaz, MD, Robert J. Lewandowski, MD, Laura M. Kulik, MD, Mary F. Mulcahy, MD, Kent T. Sato, MD, Robert K. Ryu, MD, Reed A. Omary, MD, MS, and Riad Salem, MD, MBA

The past decade has seen significant advancement in the locoregional management of liver tumors; novel and promising therapies such as transarterial chemoembolization, radioembolization, and radiofrequency ablation are now available. The development of new techniques and devices has led to the improved safety and efficacy profiles of external-beam radiation. Radioembolization with yttrium-90 (^{90}Y) microspheres has emerged as a safe and efficacious treatment modality for liver malignancies. The purpose of this article is to present a comprehensive evidence-based review of the complications and adverse events that may be associated with radioembolization with ^{90}Y microspheres. Strategies to mitigate these adverse events are also discussed.

J Vasc Interv Radiol 2009; 20:1121–1130

Abbreviations: GDA = gastroduodenal artery, GI = gastrointestinal, HCC = hepatocellular carcinoma, LSF = lung shunt fraction, MAA = macroaggregated albumin, PRS = postradioembolization syndrome, RILD = radiation-induced liver disease, ^{90}Y = yttrium-90

Table 2
Summary of Complications after ^{90}Y Radioembolization

	Pretreatment Evaluation	
Complication	Risk Factors	Prevention
PRS	High number of microspheres	Steroids, antiemetics, antihistamines
Hepatic dysfunction (ie, RILD)	Age, elevated baseline bilirubin, history of chemotherapy	Avoid whole-liver treatments whenever possible
Biliary adverse events		
Radiation cholecystitis	Injection proximal to cystic artery	Administration distal to origin of cystic artery if possible; coil embolization in rare cases
Other (eg, biliary necrosis, stricture, abscess)	Systemic chemotherapy, noncirrhotic livers; biliary-enteric anastomoses	NA
Portal hypertension	Whole liver treatment, repeat treatment, relatively hypovascular lesions	NA
Radiation pneumonitis	High LSF and high activity	Activity adjustment to decrease lung dose
GI complications (ulcers)	Unrecognized flow to GI tract; rapid injection of ^{90}Y with reflux; proximal injection, eg, common/proper hepatic artery	Identification and prophylactic embolization of arteries communicating with GI tract; prophylactic proton pump inhibitors
Other		
Vascular injury	Previous exposure to systemic chemotherapy	Careful manipulation of wires/catheter, use microcatheters
Anterior abdominal wall injury	NA	Identification and prophylactic embolization of falciform artery

Note.—NA = not applicable; NSAID = nonsteroidal antiinflammatory agent.