

Y90-Microsphere Treatment of Nonresectable Primary and Secondary Liver Malignancies

VA



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INTRODUCTION

Nonresectable primary and secondary liver malignancies have limited treatment options. Curative and palliative treatment of these liver lesions with Y90-labeled resin or glass microspheres has grown in use over the past several years.

PURPOSE

This educational exhibit will compare resin and glass microspheres. It will also review the process of patient selection, treatment planning, and dosimetry related to Y90-Microsphere therapy.

DISCUSSION

Y90 radioembolization for the treatment of primary and secondary liver malignancies offers precise tumor volume targeting, decreased radiation to non-diseased tissues, and decreased morbidity.

CONCLUSION

The treatment of nonresectable primary and secondary liver malignancies has traditionally been a challenge for physicians. The increased utilization of Y90 radioembolization in this setting has proved to be a viable treatment option for these diseases. Several research studies have shown good clinical outcomes and improved survival. Technological advances also allow accurate calculations of radiation administered to diseased and non-diseased tissues.



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NUCLEAR MEDICINE SERVICE

Indications

- **Treatment of Primary Liver Cancer**

- Hepatocellular Cancer (HCC) [11]

**Note: Glass microspheres has recently been approved by FDA for treatment of HCC. It was previously used just as a Humanitarian Device, which limited use to HCC.*

Intrahepatic Cholangiocarcinoma (ICC) [12-16]

- Primary Hepatic Sarcoma [17]

- **Treatment of Secondary Liver Cancer [18]**

- Colorectal Cancer Metastases

***Note: Resin microspheres have been approved for treatment of unresectable metastatic liver tumors from primary colorectal cancer with adjuvant intra-hepatic artery chemotherapy (IHAC) of FUHR (Floxuridine).*

- Neuroendocrine Tumors (NET)

- Pancreatic Cancer Metastases [19,20]

- Breast Cancer Metastases [21-24]

- Cervical Cancer Metastases [25]

- Lung Cancer Metastases [26,27]

- **Extrahepatic Cancers**

- Lung Malignancies [28]



Contraindications

Resin Microspheres

- Ascites or clinical liver failure
- Markedly abnormal synthetic and excretory liver function tests (LFTs), such as total bilirubin > 2.0 mg/dL or albumin < 3.0 g/dL
- $> 20\%$ lung shunting of the hepatic artery blood flow, or > 30 Gy radiation absorbed dose to the lungs, as estimated by the Tc99m-MAA scan
- Pre-assessment angiogram that demonstrates abnormal vascular anatomy that would result in significant reflux of hepatic arterial blood to the stomach, pancreas, or bowel
- Disseminated extra-hepatic malignant disease
- Treatment with capecitabine within the two months prior, or will be treated with capecitabine at any time following microsphere therapy

Glass Microspheres

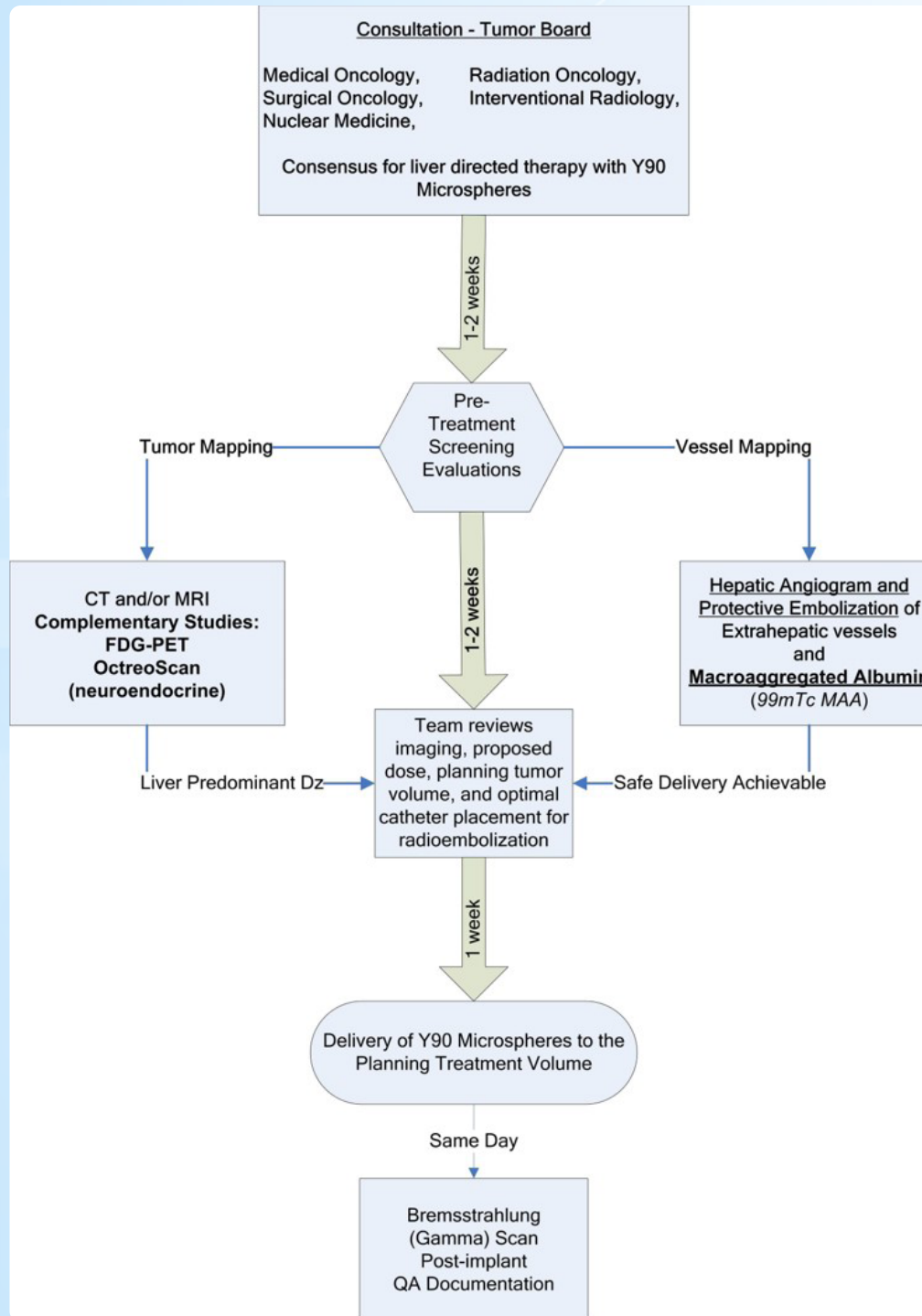
- Tc99m-MAA hepatic arterial perfusion scintigraphy shows any deposition to the gastrointestinal tract that may not be corrected by angiographic technique(s)
- Shunting of blood that could result in delivery of greater than 16.5mCi of Yttrium-90 to the lungs: Radiation pneumonitis has been seen in patients receiving doses to the lungs greater than 30 Gy in a single treatment
- Patients in whom hepatic artery catheterization is contraindicated; such as patients with vascular abnormalities or bleeding diathesis
- Severe liver dysfunction or pulmonary insufficiency
- Complete occlusion of the main portal vein

+High Risk Factors that require pre-treatment consideration:

- Infiltrative tumor type
- Bulky disease $>70\%$ of target liver volume, or tumor nodules too numerous to count
- AST or ALT > 5 times upper limits of normal
- Bilirubin > 2 mg/dL
- Tumor volume $>50\%$ combined with albumin <3 g/dL

Material	Resin	Glass
Brand name	SIR-Spheres	TheraSphere
Isotope is	Attached to the surface	Incorporated into glass matrix
Average size (μm)	32.5	25
Specific gravity (g/ml)	1.6	3.6
Activity per sphere (Bq)	50	2500
Activity per commercially available vial (GBq)	3 (can be divided)	3, 5, 7, 10, 15, 20
Activity calculation	Compartmental MIRD macrodosimetry or empirical formula based on liver volume and tumor volume	Non-compartmental MIRD macrodosimetry
Estimated dose to central vein area (Gy) in Montecarlo simulation*	59	58

MIRD, Medical Internal Radiation Dose Committee. *From Gulec *et al.* [42].



POTENTIAL SIDE EFFECTS

GASTROINTESTINAL

-NAUSEA

-EMESIS

-PAIN

-ULCER

CONSTITUTIONAL

-WEIGHT LOSS

-FATIGUE

-FEVER

LIVER FUNCTION

-BILIRUBIN

-ALKALINE PHOSPHATASE

-ALANINE AMINOTRANSFERASE

-ASPARTATE AMINOTRANSFERASE

-AMMONIA

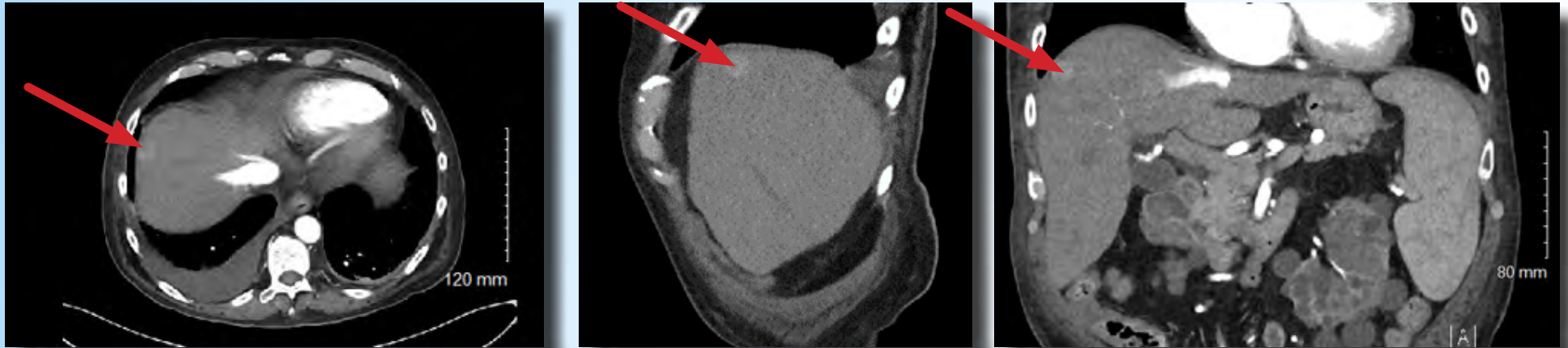


Fig 4. 71 year old male with history of cirrhosis with abdominal pain and fever undergoes contrast enhanced CT imaging. There is a 1.7 x 2.1 x 1.8 cm hypervascular enhancing mass at the periphery of the right hepatic lobe that was biopsy proven hepatocellular carcinoma

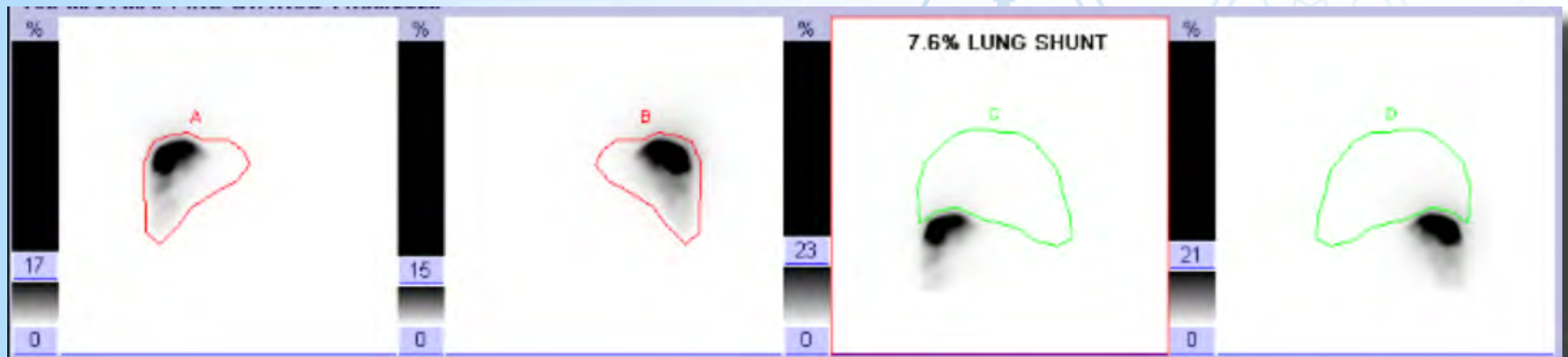
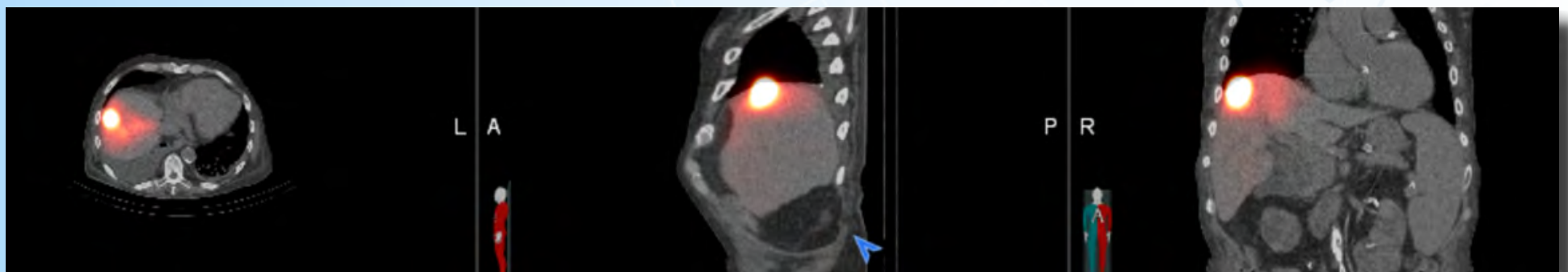


Fig 5. He was discussed at Liver Tumor Board then referred for Y90 Glass Microsphere therapy. Nuclear Medicine MAA Shunt Study A) Planar and B) SPECT-CT images demonstrates expected right hepatic lobe deposition of radioactive particles with a Lung Shunt Fraction of 7.6%.



Pre-Treatment Planning		This section must be approved by the Authorized User.	
Target Tissue (Treatment site)	R Lobe Mass	Lung Shunt Fraction (% LSF)	7.60%
Target Volume (cc)	170	Cumulative Previous Dose to the Lungs (Gy)	0.00
Mass (kg)	0.175	Contract Manufacturer:	Nordion
Desired Dose to Target Volume (Gy)	150	Device:	Y-90 TheraSphere
Treatment date and time	Tue, Dec 08, 2020 10:00 AM	Required Total Activity at time of Treatment (GBq)	0.589
Time zone of Hospital	Central Standard Time (CST)	Number of vials to be administered to Target Tissue	1
Dose Vial A			
Ordered/Received Dose Size (GBq)	6.0		
Calibration Date	Sunday, November 29, 2020		
Hours from Calibration to Treatment (hrs)	215.0		
Nominal Activity in Vial at time of Treatment (GBq)	0.587		
Sum of Nominal Activity in Vial(s) at time of Treatment (GBq)		0.587	
Calculated dose to lungs at Treatment time, assuming 1kg lungs (Gy)	2.2	Cumulative dose to lungs (Gy)	2.23
Dose to Target Volume at Treatment, accounting for lung shunt (Gy)	155	Authorized User signature & date	
Pre-treatment Dose Calibrator (DC) Measurement		Measure the received dose vial(s) in a dose calibrator using TheraSphere setting and correction factor	
Dose Vial A: 6 GBq			
Manufacturer's Lot Number and Vial Number	2099565, 35		
Date and Time of DC measurement	Tue, Dec 08, 2020 8:26 AM		
DC Measured Activity, with correction factor (GBq)	0.581		
Hours from Calibration to DC Measurement (hrs)	213.43		
DC Measured Activity referenced to Calibration time (GBq)	5.85		
OPTIONAL: Manufacturer's Activity at Calibration (GBq)	5.92		
Value to be used in Delivery calculations below:	Dose Calibrator Measurement	Measured by (Initials):	SSD
Pre-treatment Template Measurement		Measure the dose vial (no lead pot) @ 30 cm with ion chamber meter on Template	
Dose Vial A: 6 GBq			
Date and Time of Template measurement	Tue, Dec 08, 2020 8:28 AM		
Measurement of Dose vial on Template (mR/h)	2.000		
Background Measurement (mR/h)	0.020		
Net dose rate of Dose vial on Template (mR/h)	1.980		
		Measured by (Initials):	SSD
Treatment / Administration		Treatment proceeded as planned	
Methods used to confirm Patient Identity (select two)	[X] NAME	[X] Birth Date	
Dose Vial A: 6 GBq			
Confirm Lot number and Vial number (on label) matches Line 23 above	<input checked="" type="checkbox"/> Check if Lot # & Vial # match	<input type="checkbox"/> Check if Lot # & Vial # match	<input type="checkbox"/> Check if Lot # & Vial # match
Administration Start Date & Time	Tue, Dec 08, 2020 10:18 AM		
Patient dose rate, maximum on contact (mR/h)	2		
Patient dose rate, maximum at 1 meter (mR/h)	0.08	Measured by (Initials):	SSD
AU / ADMINISTERING PHYSICIAN comments (sign & date):	<input checked="" type="checkbox"/> None		
Post-treatment Template measurements		Measure the waste jar in beta shield @ 30 cm with ion chamber meter on Template	
Waste Jar - Vial A			
Date and Time of Template measurement	Tue, Dec 08, 2020 10:36 AM		
Waste Container Measurement in Beta shield (mR/h), 4 Cylinder Orientations on Template	Background Measurement (mR/h)	0.020	
	0°	0.040	
	90°	0.050	
	180°	0.050	
	270°	0.040	
Average of 4 Orientations minus Background (mR/h)	0.025		
Hours between Pre- and Post- Treatment Measures (hrs)	2.1		
Pre-Treatment Net Rate decayed to Post- Treat time (mR/h)	1.935		
Percent delivery per Vial (%)	98.7%		
Hours between Calibration and Treatment (hrs)	215.3		
Activity Administered per Vial at time of Treatment (GBq)	0.562		
Ratio: Actual Radiation Dose to Target Tissue vs. Desired Dose	98.9%	Measured by (Initials):	SSD
Final Calculations		Calculated values below use formulas from the TheraSphere package insert. The AU must confirm accuracy.	
Total Activity Delivered to Patient at time of Treatment (GBq)	0.562	Lung shunt fraction (%)	7.6%
(mCi)	15.2	Activity to Lungs (GBq)	0.043
Activity Delivered to Perfused Liver Tissue (GBq)	0.52	(mCi)	1.15
(mCi)	14.0	Radiation to Lungs (Gy)	2.14
Radiation dose to Perfused Liver Tissue (Gy)	148.4	Cumulative radiation to Lungs (Gy)	2.14
Physicist/RSO/CNMT signature & date	Authorized User signature & date		

Target Volume (cc): **170.0** Target Liver Mass (kg): 0.175
 Desired Dose (Gy): **150**
 Time Zone Variance (h): **1** (see Time Zones tab for details) Places in this Time Zone: Dallas Texas
 Lung Shunt Fraction (% LSF): **7.60%** 1-LSF = 0.92 Mexico city Mexico
 Anticipated Residual Waste (%): **1.00%** Optional estimated value 1-Residual = 0.99
 Previous Dose to the Lungs (Gy): **0**

Required Activity at Administration (GBq): **0.57** This value is corrected for LSF and Residual Waste if values are entered above.

Calculated Dose to Lungs (Gy):	2.16	Dose Limit to the Lungs per treatment (Gy):	30	See Package Insert or Instructions for Use
Lung Dose within recommended limit for treatment				
Cumulative Dose to Lungs (Gy):	2.16	Cumulative Dose Limit to the Lungs (Gy):	50	
Lung Dose within recommended cumulative limit for treatment				

Use the following tables to select a dose size where the Desired Dose (above) is at a suitable treatment time.

Dose Size Selected (GBq): **6 GBq** Optional field for Medical Professional to document treatment dose selected
 Date & Time for Administration: **2nd Week Tuesday** Optional field for Medical Professional to document treatment window selected

Tables below show the dose to perfused target tissue, accounting for target mass, time zone variance, lung shunt fraction and residual waste.

Dose Delivered (Gy) for: **3 GBq dose size** Week 2 treatment

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM		624	482	372	287	221	171	132	102	78	60	47	36
12:00 PM	Calibration Day @ 12:00 Eastern Time	598	461	356	275	212	163	126	97	75	58	45	34
4:00 PM		573	442	341	263	203	156	121	93	72	55	43	33
8:00 PM		548	423	326	252	194	150	116	89	69	53	41	32

Dose Delivered (Gy) for: **5 GBq dose size** Week 2 treatment

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM		1041	803	619	478	369	284	219	169	131	101	78	60
12:00 PM	Calibration Day @ 12:00 Eastern Time	997	769	593	458	353	272	210	162	125	96	74	57
4:00 PM		954	736	568	438	338	261	201	155	120	92	71	55
8:00 PM		914	705	544	420	324	250	193	149	115	88	68	53

Dose Delivered (Gy) for: **7 GBq dose size** Week 2 treatment

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM		1457	1124	867	669	516	398	307	237	183	141	109	84
12:00 PM	Calibration Day @ 12:00 Eastern Time	1395	1076	830	641	494	381	294	227	175	135	104	80
4:00 PM		1336	1031	795	613	473	365	282	217	168	129	100	77
8:00 PM		1280	987	762	587	453	350	270	208	160	124	96	74

Dose Delivered (Gy) for: **10 GBq dose size** Week 2 treatment

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM		2081	1606	1239	956	737	569	439	338	261	201	155	120
12:00 PM	Calibration Day @ 12:00 Eastern Time	1993	1538	1186	915	706	545	420	324	250	193	149	115
4:00 PM		1909	1473	1136	876	676	521	402	310	239	185	142	110
8:00 PM		1828	1410	1088	839	647	499	385	297	229	177	136	105

Dose Delivered (Gy) for: **15 GBq dose size** Week 2 treatment

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM		3122	2409	1858	1433	1106	853	658	508	392	302	233	180
12:00 PM	Calibration Day @ 12:00 Eastern Time	2990	2307	1779	1373	1059	817	630	486	375	289	223	172
4:00 PM		2863	2209	1704	1314	1014	782	603	466	359	277	214	165
8:00 PM		2742	2115	1632	1259	971	749	578	446	344	265	205	158

Dose Delivered (Gy) for: **20 GBq dose size** Week 2 treatment

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM		4163	3211	2477	1911	1474	1137	877	677	522	403	311	240
12:00 PM	Calibration Day @ 12:00 Eastern Time	3987	3075	2372	1830	1412	1089	840	648	500	386	298	230
4:00 PM		3818	2945	2272	1753	1352	1043	805	621	479	369	285	220
8:00 PM		3656	2821	2176	1678	1295	999	771	594	459	354	273	210

Dose Delivered (Gy) for a Custom Dose size: **6 GBq dose size** Week 2 treatment

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM		1249	963	743	573	442	341	263	203	157	121	93	72
12:00 PM	Calibration Day @ 12:00 Eastern Time	1196	923	712	549	424	327	252	194	150	116	89	69
4:00 PM		1145	884	682	526	406	313	241	186	144	111	85	66
8:00 PM		1097	846	653	504	388	300	231	178	138	106	82	63

All dose vials will have Sunday calibration at 12:00 Eastern Time.
 Standard dose vial sizes (3, 5, 7, 10, 15, 20 GBq) are available from inventory for next-day shipping. Order as required.
 Custom dose vial sizes should be ordered by end of business Tuesday prior to Sunday calibration to ensure availability.

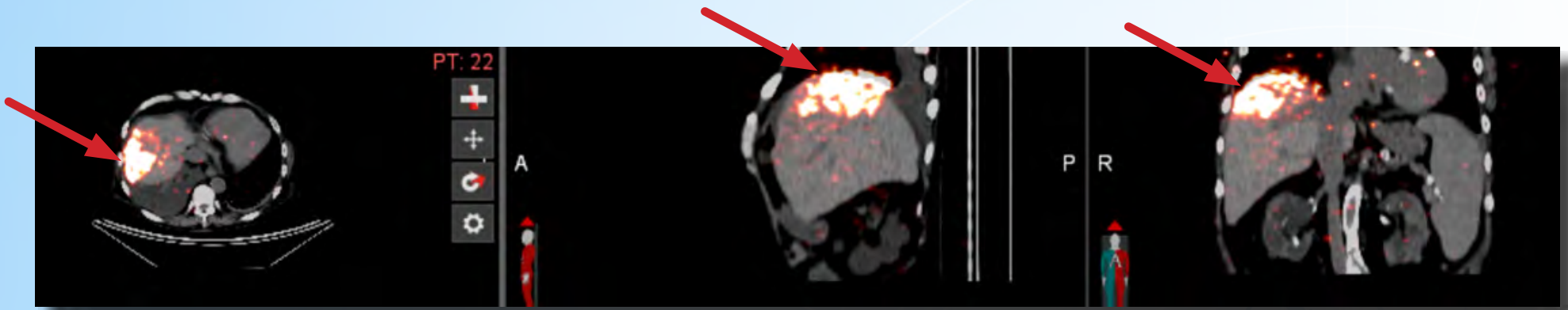


Fig 6. Nuclear Medicine Radioembolization with Y90 Glass Microspheres posttherapy PET imaging demonstrates expected particle deposition in the right hepatic lobe. The calculated dose to the liver is 148.4 Gy and the dose to the lungs is 2.1 Gy.

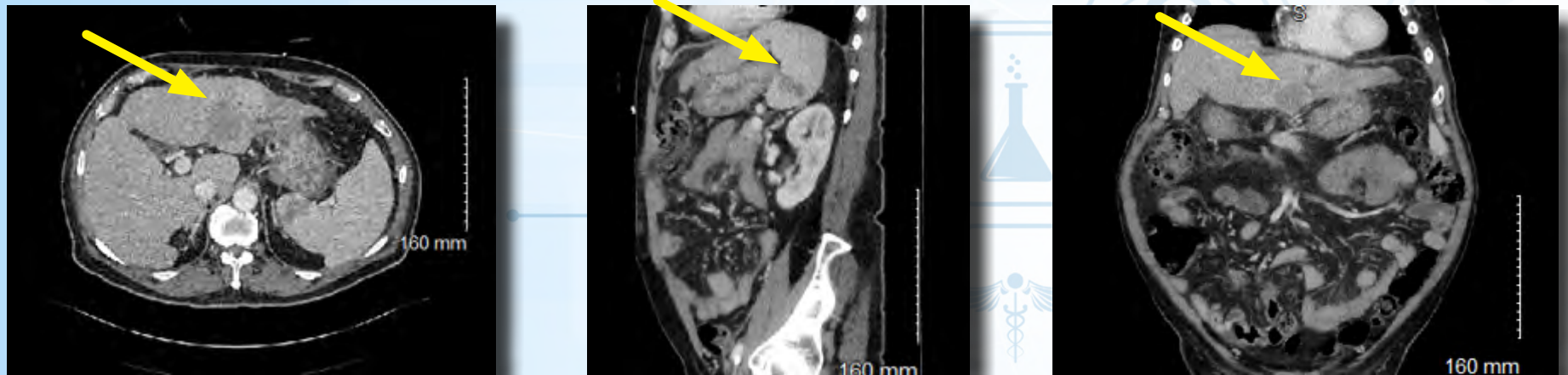


Fig 8. 71 yo male with abdominal pain has large hypodense lesion in the left hepatic lobe on contrast enhanced CT (arrow) compatible with cholangiocarcinoma.

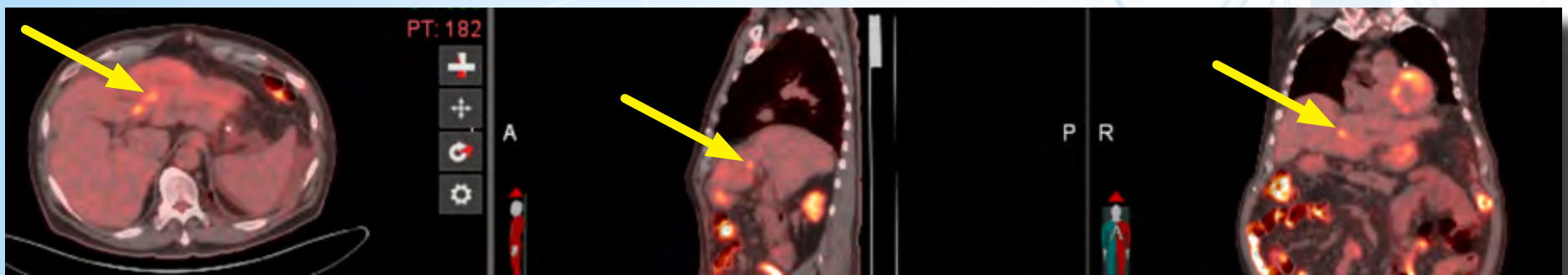


Fig 9. Subsequent FDG PET/CT imaging demonstrates diffusely increased tracer accumulation in the left hepatic lobe with more focal areas centrally with maximum standardized uptake value of 6.4.

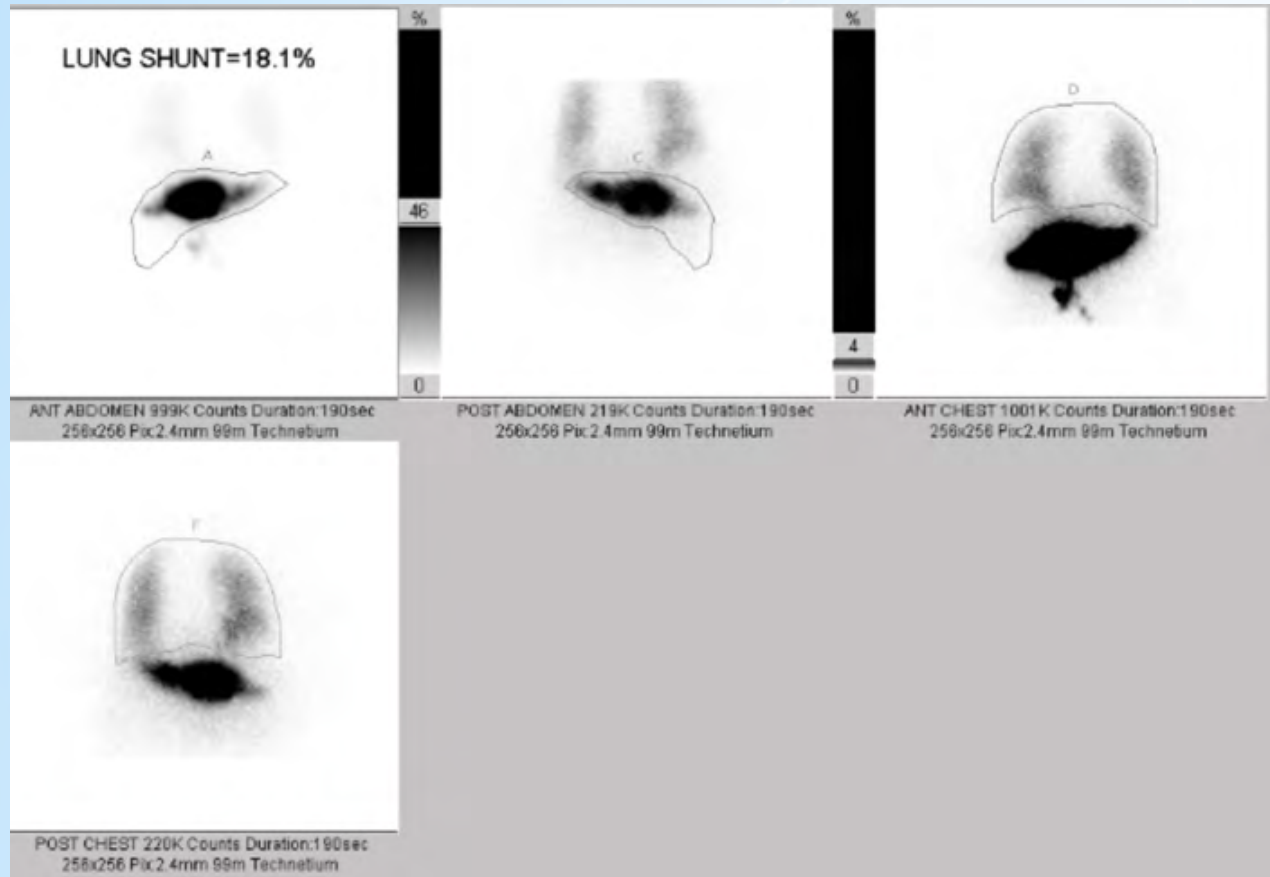


Fig 10. The patient was referred for Y90 Resin Microsphere Therapy. Nuclear Medicine MAA Shunt Study demonstrates expected left hepatic lobe deposition of radioactive particles with a Lung Shunt Fraction of 18.1%.

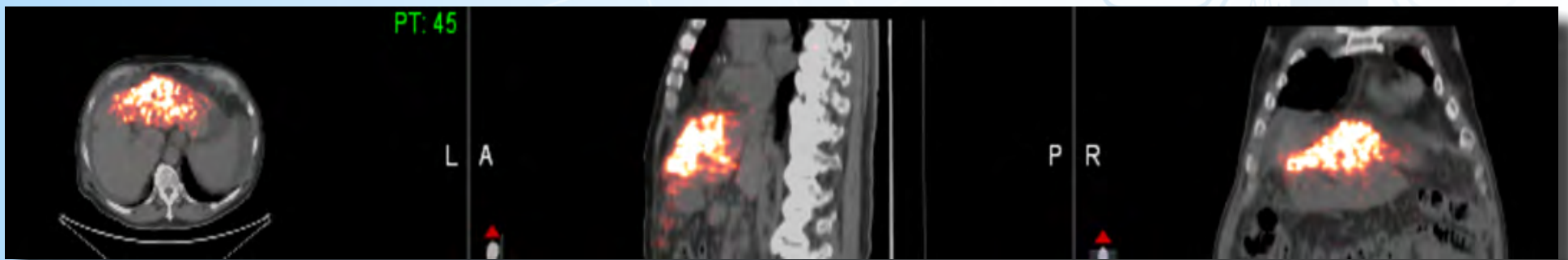


Fig 11. Nuclear Medicine Radioembolization with Y90 Resin Microspheres posttherapy PET imaging demonstrates expected particle deposition in the left hepatic lobe. The calculated dose to liver was 129.2 Gy and dose to the lungs was 14.2 Gy.

**Parameters:**

Height: 178 cm

Weight: 89 kg

Total Liver Volume: 1950 mL

Total Treatment Area Volume: 625 mL

Total Tumour Volume in Treatment Area: 300 mL

Lung Shunt %: 18.0 %

Lung Parameter: 2625 mL

T:N Ratio: 3.9

Target Dose (MIRD): 150 Gy

Target Tumour Dose (Partition): 130 Gy

Estimated Liver/Tumor MIRD dose assuming uniform distribution:

MIRD 123.0 Gy

BSA 47.7 Gy

Partition 79.7 Gy

