Understanding Dosimetry in Y-90

David Liu, MD



Disclosures

David Liu: Consultant – Sirtex Medical, Ethicon Endocare/Neuwave Medical; Grant/Research Support – BTG Medical; Speakers' Bureau – Servier Pharmaceuticals; Other Financial or Material Support – Merit Medical: Independent Director

David Liu has disclosed that the off-label use of SIR-Spheres Y-90 microspheres; TheraSphere Y-90 microspheres will be discussed.

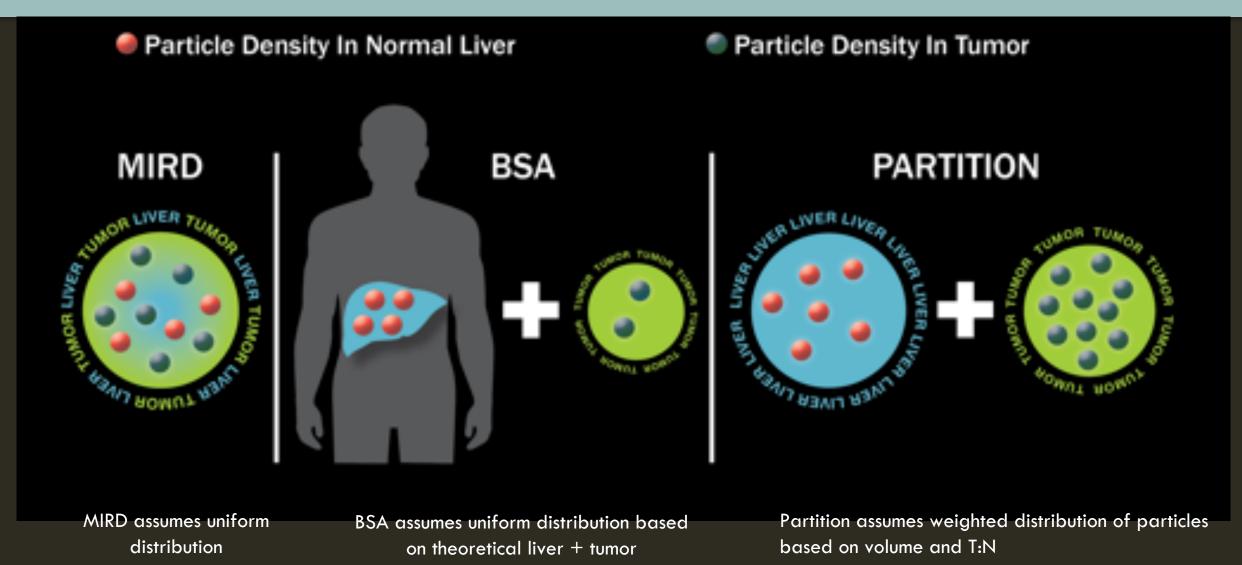
Brand names are included in this presentation for participant clarification purposes only. No product promotion should be inferred.



Spectrum of Response

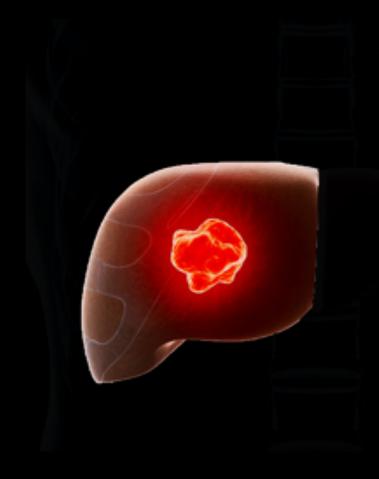
Contralateral Lobectomy **Tumor Target** Segmentectomy Hypertrophy **Increasing Liver Volume** Increasing Liver Dose **Increasing Overall Activity**

ACTIVITY CALCULATIONS AND PRESUMED RADIATION/PARTICLE DISTRIBUTION/DOSE





CONVENTIONAL APPROACH



Target the tumor dose

Confirm safe margin for lung

Confirm safe margin for liver

Conventional Approach

- Targeting the tumor
- Liver exposure is collateral damage

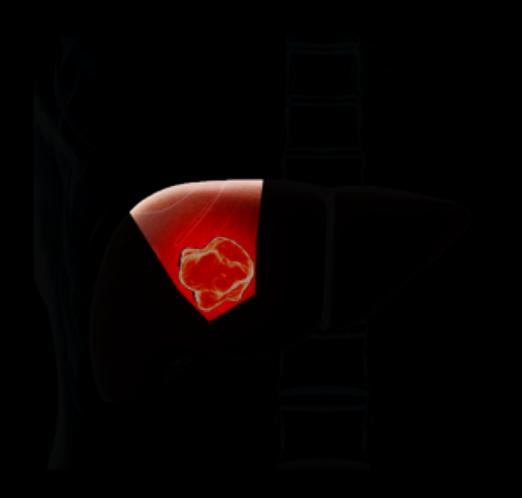
Segmentectomy Approach

- Targeting liver parenchyma
- Tumor sumps activity

Lobectomy Approach

- Targeting the liver parenchyma
- Tumor sumps activity

RADIATION SEGMENTECTOMY APPROACH



Target the dose to liver (<70 Gy)

Confirm safe margin for lung

Calculate sump to tumor

Conventional Approach

- Targeting the tumor
- Liver exposure is collateral damage

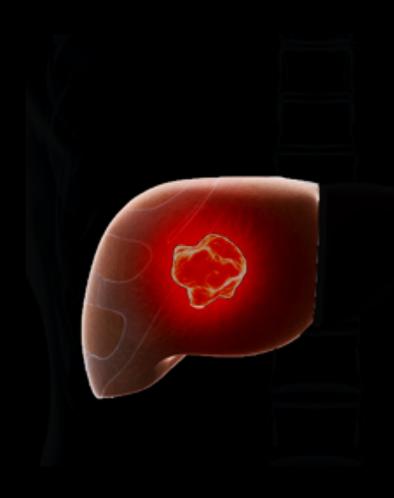
Segmentectomy Approach

- Targeting liver parenchyma
- Tumor sumps activity

Lobectomy Approach

- Targeting the liver parenchyma
- Tumor sumps activity

RADIATION LOBECTOMY APPROACH



Target the dose to liver (<70 Gy)

Confirm safe margin for lung

Calculate sump to tumor

Conventional Approach

- Targeting the tumor
- Liver exposure is collateral damage

Segmentectomy Approach

- Targeting liver parenchyma
- Tumor sumps activity

Lobectomy Approach

- Targeting the liver parenchyma
- Tumor sumps activity

PARTITION AS A LAUNCH POINT

Specific Activity	Conventional	Segmentectomy Lobectomy
Glass 'Like'	Tumor >190 Gy	MIRD 190 Gy
Resin 'Like'	Tumor >100 Gy	Liver >70 Gy



ONE SPHERE TO RULE THEM ALL

EDITORIAL COMMENTARY

The dosimetric importance of the number of ⁹⁰Y microspheres in liver transarterial radioembolization (TARE)

Carlo Spreafico • Marco Maccauro • Vincenzo Mazzaferro • Carlo Chiesa

"...reported calculations [should] emphasize the importance of the number of microspheres per GBq [and] this should be considered a crucial variable in clinical trials..."

3 GBQ OF ACTIVITY FLEX & EX

SIR-Spheres[®]
16.5-40 million
Day -3 to day 0 from 'calibration'

16.5-27 million overlap

TheraSphere®
1.2-27 million
Day 0 to day 12 from 'calibration'

NOW THAT I HAVE SO MANY WAYS TO GIVE THE SAME ACTIVITY, HOW DO I CHOOSE?

Hypovascular

Radiation segmentectomy

Radiation lobectomy

Larger tumor distribution

Poor vascularity in target

Liver parenchymal preservation in lobar infusion



PRE-CALIBRATION

				Calc	ulation from	Calibration	(18:00 E)	actions Tim	re) to Assa	y Time				
DAY THREE PRE-CALIBRATION						DAY TWO PRE-CALIBRATION			DAY ONE PRE-CALIBRATION					
	Rours Sefure Cal	Decay Factor	Activity (GBq)	Activity (mC0		Rours Before Cal	Gecay Factor	Activity (Site)	Activity (mC2		Seles Cal	Secay Factor	Activity (Silve)	Activity (mG)
8.00 AM	82	2,427	7.291	196.79	6:00 PM	72	2.178	6.535	176.62	6:00 PM	48	1.680	5.041	136.25
	818	2,414	7.242	196.73		71.5	2.167	6.500	175.67		42.5	1,671	5.014	135.52
9:00 AM	81	2.401	7.203	194.68	7:00 PM	71	2.155	6.465	174.72	7:00 PM	47	1.662	4.967	134.79
	2.00	2.398	7.166	193.63		70.5	2.143	E-430	173.76		46.5	1.850	4.960	134.06
10:00 AM	80	2.375	7.126	192.58	8:00 PM	70	2.102	6.395	122.04	8:00 PM	46	1.644	4.900	133.34
	79.5	2.362	7,087	191.55		60.5	2,120	6.361	171.91		45.5	1.606	4.907	132.62
11:00 AM	79	2.350	7.049	190.51	9:00 PM	69	2.109	6.326	170.99	9:00 PM	45	1,027	4.300	131.90
	78.5	2.337	7,0tt	189.49		68.5	2.097	6.292	170.06		44.5	1,618	4.864	131.19
NOON	78	2,324	6.973	188.45	10:00 PM	68	2.086	6.258	169.15	10:00 PM	86	1,609	4.829	130.48
	77.5	2.312	6.936	187.45		67.5	2.075	6.225	168.23		43.5	1.601	4.802	129.76
1:00 PM	77	2,299	6,898	186.44	11:00 PM	67	2.064	6.191	167.33	11:00 PM	40	1.682	4.776	129.08
	76.5	2.297	6.861	186,43		66.5	2.063	6.158	166.43		42.5	1,583	4.790	128,38
2:00 PM	76	2.275	6.824	184.43	MIDAKKHT	66	2.042	6.125	166.63	BEDARCHT	42	1.575	4.725	127.69
	75.5	2.262	6.787	180.44		65.5	2.001	6.002	164.64		ALL	1,566	4.000	127.00
3:00 PM	75	2.250	6.751	182.45	1:00 AM	65	2.020	6.059	163.75	1:00 AM	41	1,558	4.674	126.32
	74.5	2.238	6.714	181.46		64.5	2.009	6.03	162.86		405	1,550	4.649	125.64
4:00 PM	74	2.226	6.678	180.49	2:00 AM	64	1.900	5.994	161.99	2:00 AM	40	1.541	4.624	124.96
	73.5	2.214	6.642	179.51		63.5	1.967	5.901	161.11		28.5	1,533	4.500	124.29
5:00 PM	73	2.202	6.606	178.54	3:00 AM	63	1.976	6.929	160.24	3:00 AM	39	1,525	4.574	123.62
	72.5	2.190	6,671	177.58		62.5	1,966	S.807	159.38		28.5	1,516	4.549	122.96
					4:00 AM	62	1.955	5.865	158.52	4:00 AM	38	1.508	4.525	122.29
						61.5	1,945	E.804	167.67		27.5	1.500	4.500	121.63
To calc	ulate the per	contagé	of riphers	s drown -	5:00 AM	61	1,934	5.802	156.82	5:00 AM	37	1.492	4.476	129.97
from	the vial, plea	ne divide	the GBq	drawn		40.5	1,924	5.771	155.97		365	1.484	4.452	120,02
-	activity at 8				6:00 AM	60	1.913	5.740	155.13	6:00 AM	36	1.476	4.428	119.67
in f	in Radioacti	ve Decay	Dooring D	hart.		69.5	1.903	5.709	154.29		35.5	1.468	4.404	119.02
					7:50 AM	59	1.893	5.678	153.46	7:00 AM	35	1.460	4.380	115.38
						58.5	1,882	5.647	152.63		34.5	1,452	4307	117.74
					8:00 AM	58	1.872	5,617	151.01	8:00 AM	34	1,444	4.333	117.21
						57.6	1.862	5.507	160.99		33.5	1,437	4.310	116.48
					9:00 AM	67	1.852	5.517	150.18	9:00 AM	33	1.429	4.296	115.85
						56.5	1.042	6.527	149.37		32.5	1.421	4.263	115.23
					10:00 AM	56	1.832	5.497	148.56	10:00 AM	32	1,413	4.240	114.60
						85.5	1.822	5.407	147.76		21.5	1.400	4.217	113.99
					11:00 AM	55	1.813	5.438	146.96	11:00-AM	31	1.398	4.196	113.37
						54.5	1.903	5,408	146.17		30.5	1.391	4.072	112.76
					NOON	54	1.793	5.379	145.38	NOON	30	1.383	4.150	112.15
						53.5	1.793	5.350	144,60		29.5	1,376	4.127	111.86
					1.00 PM	.63	1.774	5.321	143.82	1:00 PM	29	1.368	4.106	110.96
						52.5	1.764	5.293	143,04		28.5	1.361	4.083	110.36
					2:00 PM	52	1.756	5.264	142.27	2:00 PM	29	1.354	4.067	109.75
						61.5	1,765	5.256	141.51		27.5	1.540	4.038	100.16
					2:00 PM	51	1.736	5.208	140.74	3:00 PM	27	1.339	4.017	108.67
						50.5	1.726	6.179	139.98		26.5	1.332	1996	107.99
					4:00 PM	.50	1.717	5.191	139.23	4:00 PMI	26	1.325	3.974	107.40
						49.5	1,708	6.124	139,48		25.5	1,318	1963	106.83
					5:00 PM	49	1,400	5.000	137.73	5:00 PMI	25	1.210	3.931	106.25
						48.5	1,690	5.069	136.99		245	1,303	3.910	105.68

DAY OF CALIBRATION

Calculation from Calibration (18:00 Eastern Time) to Assay Time

		AY OF CALIBRA	TION	coay Issue
	House Cal	Decay Factor	Activity (GBq)	Activity (mG)
6:00 PM	24	1.296	3.889	105.11
	20.5	1.299	1.868	104.54
7:00 PM	23	1.292	3.847	103.98
	22.5	1.275	3.626	100.42
8.00 PM	22	1.369	3.806	102.86
	21.5	1,362	3.796	102.30
9.00 PM	21	1.255	3.766	101.76
	20.5	1.248	3.746	101.20
10:00 PM	20	1.281	3.724	100.66
	19.5	1.2%	3.794	100.11
11:00 PM	19	1,228	3.684	99.57
	18.5	1.221	3.664	99.04
MIDNECKT	18	1.215	3.646	98.50
	17.6	1,308	3.625	97,97
1:00 AM	17	1.302	3.006	87.44
	16.5	1.196	3.586	96.92
2:00 AM	16	1.199	2.647	96.40
	15.6	1.182	3.547	95.88
3.00 AM	15	1.176	3.528	95.34
1000	14.5	1,170	3,500	94.85
6.00 AM	14	1,163	3.490	94.33
	135	1.167	3.472	91.00
5-00 AM	13	1.151	2.452	90.32
	12.5	1,145	3.434	92.82
0:00 AM	12	1,139	3.616	82.32
	11.5	1.132	3.597	91.82
7:00 AM	11	1.126	3,279	91.32
	10.5	1.120	3.361	90.80
SIDE AMI	10	1.114	3.343	90.54
	9.5	1,106	1.125	89.86
9.00 AM	9	1,102	3.307	89.37
	1.5	1.096	3.299	80.00
10:00 AM		1.000	3.271	86.41
	75	1.004	3.253	87.90
11:00 AM	7	1,079	3.236	87.46
	65	1,079	3.218	86.99
N004	6	1.067	3.201	86.52
	5.5	1.001	3.184	86.05
1:00 PM		1.066	3.167	86.68
	45	1.060	2.190	85.12
2.00 PM	4	1.064	2.123	14.67
	25	1.000	3,1%	8421
200 PM	1	1.003	3.099	83.75
	2.5	1.027	3.082	83.30
4:00 PM	1	1.022	3.066	82.85
	1.5	1.016	3.049	82.41
5.00 PM	1	1,011	3.033	81.96
		2000		57.00
6:00 PM	0	1	3.000	81.08

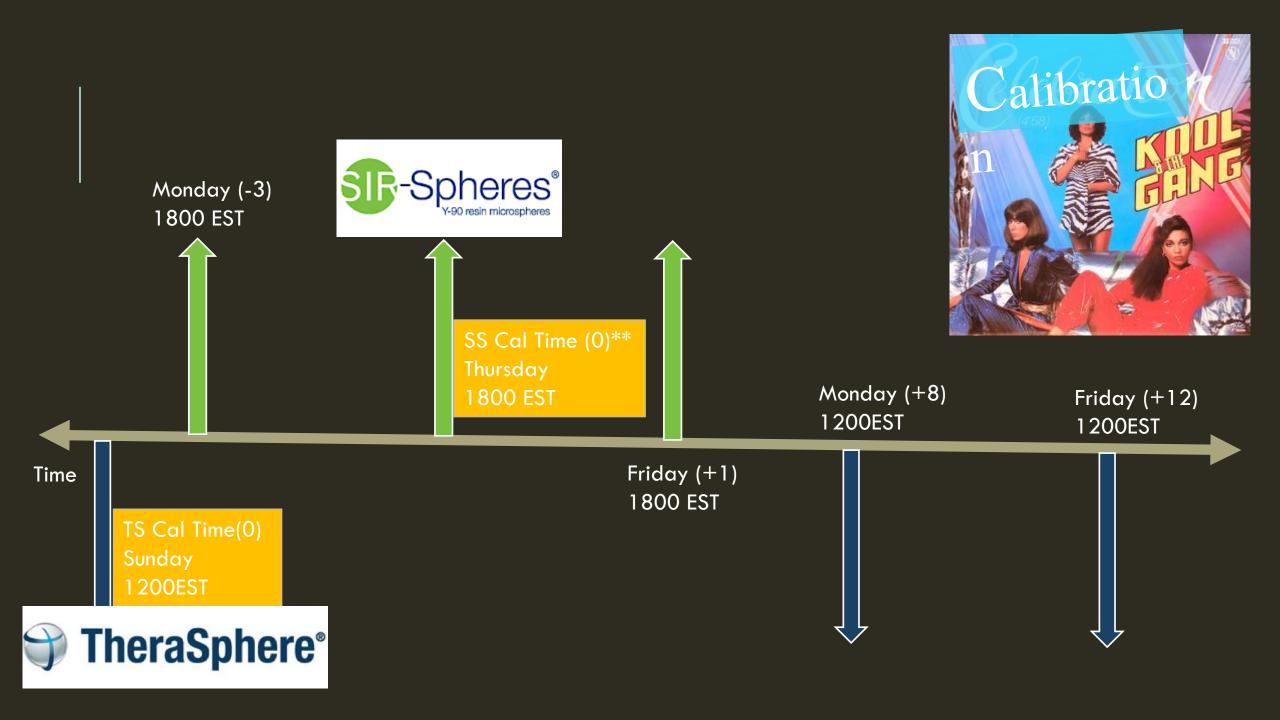
POST-CALIBRATION

Calculation from Calibration (18:00 Eastern Time) to Avery Time

_		POST-CALIBRATIO	N.	
	Room Allow Coll	Seese	Activity	Activity
		factor.	Days.	(mile)
6:00 PM	0.5		3.000	81.08
T-00 DM		5.99460794 5.999244756	2.984	80.64
7:00 PM	15	0.90091069	2.962	79.78
8:00 PM	2	£979605:92	2.806	79.35
80074	25	8.973328391	2,820	78.92
9:00 PM	1	0.968080049	2.904	78.49
and the	15	0.962960007	2.000	79.07
10:00 PM	4	6.967688111	2.673	77.65
SOUTH THE	45	6.962504212	2.868	77.23
11:00 PM	6	0.947368167	2.842	76.81
110074	5.5	0.942250796	2.827	76.40
MEDANCHT	4	8.937178981	2.812	75.00
-	65	0.932135562	2.796	75.58
1:00 AM	1	0.907090090	2.781	75.17
1.00.00	7.5	0.002100024	2766	74.76
2:00 AM	1	0.917120212	2.751	74.36
2.04.700	45	6.91218291	2,737	73.96
2:00 AM	1	0.907264274	2,722	73.56
DOM:	15	0.90237216	2,707	73.17
4:00 AM	10	1.897506425	2,693	72.77
SCHOOL STREET	3.00	0.892006827	2.678	72.38
5-90 AM	11	0.867853524	2.664	71.90
00000	11.5	0.80006676	2,649	71.60
6:50 AM	12	0.670004443	2.636	71.21
	12.5	8.873588485	2,621	70.83
7:00 AM	13	0.000050004	2.007	20.45
	13.5	0.864173042	2.593	70.07
B:00 AM	14	0.869613283	2,579	69.69
	54.5	0.85407065	2.665	69.21
9:00 AM	15	0.862399008	2.551	68.94
	15.5	6.945694221	2.537	GEST
19:00.AM	16	8.841124157	2.523	68.20
	16.5	0.830586001	2510	67.83
11:00 AM	17	9.832077661	2.496	67.47
	17.5	0.827580965	2.483	67.10
NOON	10	0.822129462	2.469	66.74
	18.5	0.818690022	2.456	66.38
1:00 PM	19	0.814275515	2.443	66.02
	18.5	0.00004811	2.400	65.67
2:00 PM	20	0.905517783	2.45T	65.31
	20.5	0.801174002	2.404	64.96
2:00 PM	21	0.796864242	2.391	64.61
	21.5	6.790557477	2.376	64.26
4:00 PM	22	0.78626368	2.365	63.91
	22.5	0.784033327	2.362	61.67
5:00 PM	23	0.779005694	2.339	63.23
	20.5	0.775600858	2,325	62.89
6:00 PM	34	0.271419094	2.356	62.55
-			1,000	

THERASPHERE EX

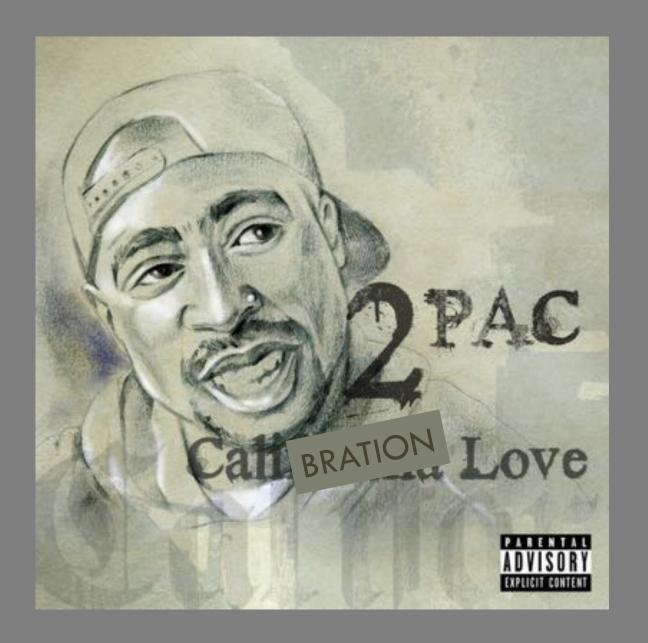
		The state of the s	ysical Decay Table e 64.1 Hours		
Hours	Fraction Remaining	Hours	Fraction Remaining	Hours	Fraction Remaining
-4	1.044	30 32 34 36 38 40 42 44	0.723 0.707	64 66	0.501 0.490
0.	1.000	34	0.692	68	0.479
4	0.958	36	0.678 0.663	70 72 (Day 3)	0.469
4 6 8 10 12	0.937	40	0.649	96 (Day 4)	0.354
8	0.917	42	0.635	120 (Day 5)	0.273
10	0.898 0.878	46	0.621 0.608	144 (Day 6) 168 (Day 7)	0.211 0.163
14	0.860	48 (Day 2)	0.595	192 (Day 8)	0.125
16 18 20	0.841	50	0.582	216 (Day 9)	0.097
18	0.823	50 52 54	0.570	240 (Day 10)	0.075
20	0.806 0.788	54	0.558 0.546	264 (Day 11)	0.058
24 (Day 1)	0.771	58	0.534	288 (Day 12)	0.044
26	0.755	56 58 60	0.523		
28	0.739	62	0.511		



SO WHAT IS CALIBRATION?

Therasphere:
Sunday 1200 EST
(concept: made once a week)

Sirsphere:
Day of Admin 1800
(concept: made to order)





CONTRALATERAL HYPERTROPHY

REVIEW ARTICLE

systematic review of contralateral liver lobe hypertrophy after unilobar selective internal radiation therapy with Y90

Jin-Yao Teo¹, John C. Allen Jr.², David C. Ng³, Su-Pin Choo⁴, David W.M. Tai⁴, Jason P.E. Chang⁵, Foong-Khoon Cheah⁶, Pierce K.H. Chow^{1,2} & Brian K.P. Goh^{1,2}

Paper	Number of patients	Age	Pathology treated	SIRT modality	Site of Y90 delivery	Number of treatment sessions	Method of volume measurement	Time to measurement	Percentage hypertrophy (mean/median (range))
Ahmadzadehfar et al. 2013 Germany ¹³	24	Median 53 (range 44-78)	Metastatic disease (mixed) 17 - bi-lobar	Resin microspheres	Right lobe	Single	FDG PET/CT	Mean 44 days, median 36 days	Mean 47%, median 34% Only right lobe disease – mean 57%, median 70%
Edeline et al, 2013 France ¹⁴	34	Not stated	Primary - HCC	30 Glass, 4 resin microspheres	23 right, 11 left	Single	СТ	3 months Not stated	Mean 29% Mean 42% (maximal)
Vouche et al. 2013 USA ¹⁵	83	Median 68 (range 36–89)	67 HCC, 8 IHC, 8 CRC mets	Glass microspheres	Right lobe	Single	MRI/CT	1- >9 months	Median overall 26% (-14-86) Median 45% at 9 months (5-186)
Theysohn et al. 2013 Germany ¹⁸	45	Mean 71.9	HCC	Glass microspheres	Right lobe	Single	СТ	6 Months	Mean 30.8%
Fernandez-Ros et al. 2013 Spain ¹⁷	83	Median 66	52 HCC, 4 IHC, 13 CRC mets, 14 others	Resin microspheres	66 right, 17 left	Single	CT/MRI	26 weeks	Mean 45%
Garlipp et al, 2013 Germany, France ¹⁸	26	Mean 59.2	Metastatic disease (mixed)	Resin microspheres	Right lobe	Single	MRI	Median 46 days (27-79 days)	Mean 29%, median 25.3%
Teo et al. 2014 Singapore 19	17	Median 72 (range 42-78)	HCC	Resin microspheres	Right lobe	Single	СТ	Median 5 months	Mean 34.2%

CONTRALATERAL HYPERTROPHY:

Hypertrophy is identified retrospectively

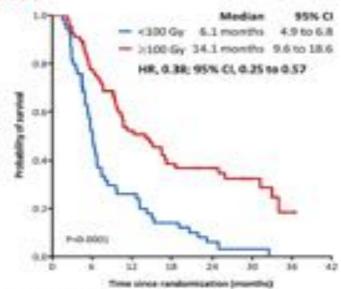
Activity determination method not formalized

Intent to treat has not been done

Dose modulation studies not performed

SARAH





Number of risk (number consumed)

*180 Gy 34 (8) 28 (8) 24 (8) 7 (3) 3 (3) 1 (3) 0 (2) 1 (30) 6 (2) 1 (30) 6 (2) 1 (30) 6 (2) 1 (30) 6 (2) 1 (30) 6 (2) 1 (30) 6 (2) 1 (30) 6 (2) 1 (30) 7 (30

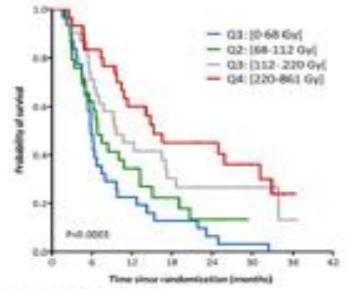
Median OS

6.1 months [95%CI 4.9-6.8] < 100 Gy

14.1 months [95%CI 9.6-18.6] ≥ 100 Gy







Number at risk (number consorred)

100	10 (0)	85-90	P40	400	Jr 101	0.000	0.00
-00	39 (0)	\$8-50	30.00	9-121	0 [3]	9 (1)	
93	30 (0)	22:10	33-(3)	#(2)	5 (4)	3 (44)	3,075 (0.00)
04	30-101	25.00	21/0	12 (2)	21-(3)	8 (6)	1/91/1/201

Median OS

5.8 months [95% CI 4.9–7.4] Q1: < 68 Gy 15.2 months [95% CI 10.4–31.2] Q4: ≥ 220 Gy



DOSIMETRY: THE NEXT GENERATION





medical



1 Oncorpy 1 Products 1 Software

SHARE TO CO STARRED



solutions company news worldwide contact Book a demo

PLANET® Dose

DOSI & soft

Personalized 3D dosimetry for Targeted Radionuclide Therapy using 90Y-microspheres or

PLANET® Dose provides pre & post-implementation dosimetry, estimation of time-integrated activity, allows the possibility of comparing between treatment planning and validation control dose maps, and the consolidation of multitreatment stages.

It offers a complete integration of oncology features (PLANET Onco), with versatile and high performance solutions for the whole clinical workflow.



90Yttrium

- Pre-implantation dosimetry based on 99Tcm-MAA-SPECT exam (MacroAggregate Albumin)
- Liver-lung shunt assessment
- Post-implantation dosimetry based on 90Y-microspheres-PET (or SPECT Bremsstrahlung) exam
 Voxel S-Values dose kernel convolution algorithm/Local Deposition Method
- Dose map comparison: treatment planning vs. in vivo control
 Consolidation of multi-treatment stages

177Lutetium

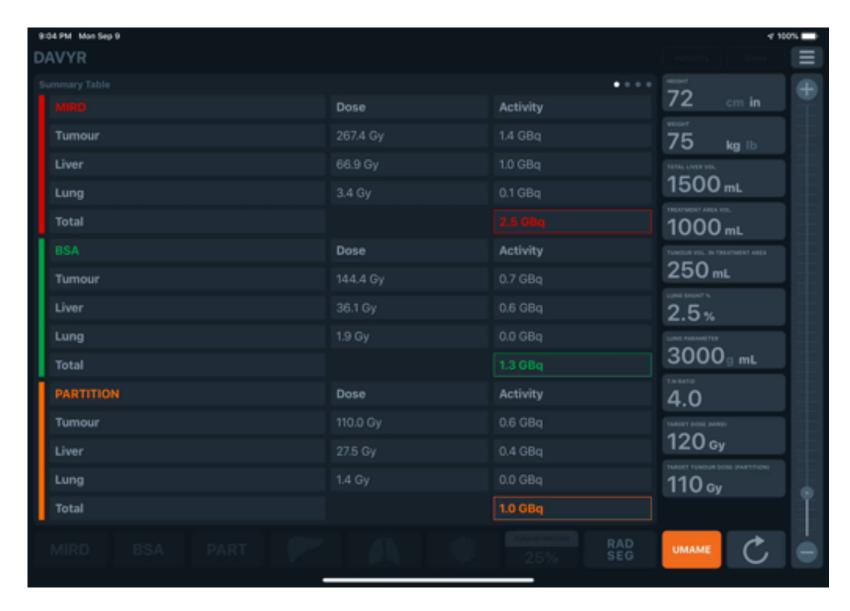
- Multi-time points elastic registration
- Automatic deformable propagation of VOI across times
- Residence time calculation
- Dose computation based on voxel-level analysis
 Voxel 5-Values dose kernel convolution algorithm/Local Deposition Method
 Dosimetry comparison and consolidation of multi-treatment stages

DOSIMETR' ACTIVITY VISUALIZER FOR YTTRIUM-90 RADIOEMBOLIZATION

Now With Radiation Segmentectomy



DAVYR Workflow Demo



BSA, MIRD, and partition

Dose estimation

Exportable to PDF and CSV

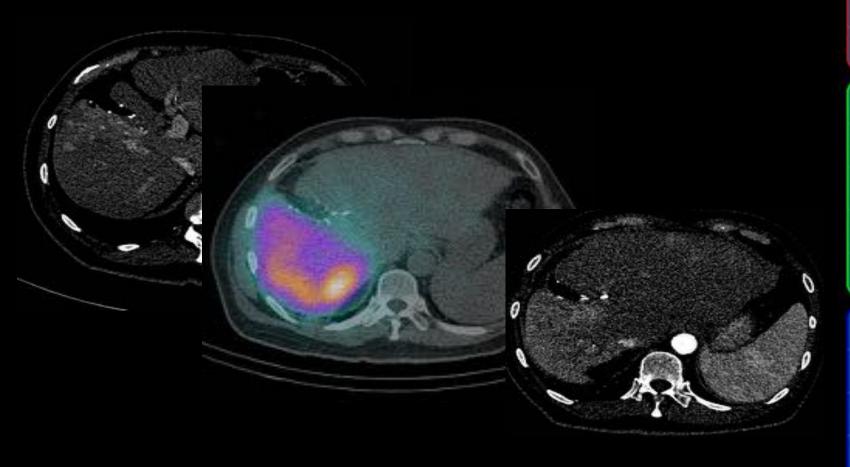
Built-in tutorials

For iOS and Android

Graphical functions available on iPad



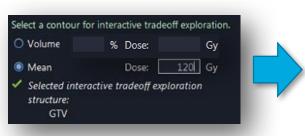
PARTITION MODEL RADIATION LOBECTOMY & HYPERTROPHY



?	DAVYR	Û
MIRD	DOSE	ACTIVI
TUMO	365.1	0.9 GBq
LIVER	81.1 Gy	1.4 GBq
LUNG	2.2 Gy	0.1 GBq
TOTAL		2.4 GBq
BSA	DOSE	ACTIVI
TUMO	149.1 Gy	0.4 GBq
LIVER	33.1 Gy	0.6 GBq
LUNG	0.9 Gy	0.0 GBq
TOTAL		1.0 GBq
Partition	DOSE	ACTIVI
TUMO	315.0	0.8 GBq
LIVER	70.0 Gy	1.2 GBq
LUNG	1.9 Gy	0.1 GBq
TOTAL		2.0 GBq

RapidSphere[™] Exploration (Varian)

Interactive dosimetry of Y-90 activity



Retrospectively optimize activity to desired dose

Explore injected activity effects on dose distribution

Understand dose response to drive research



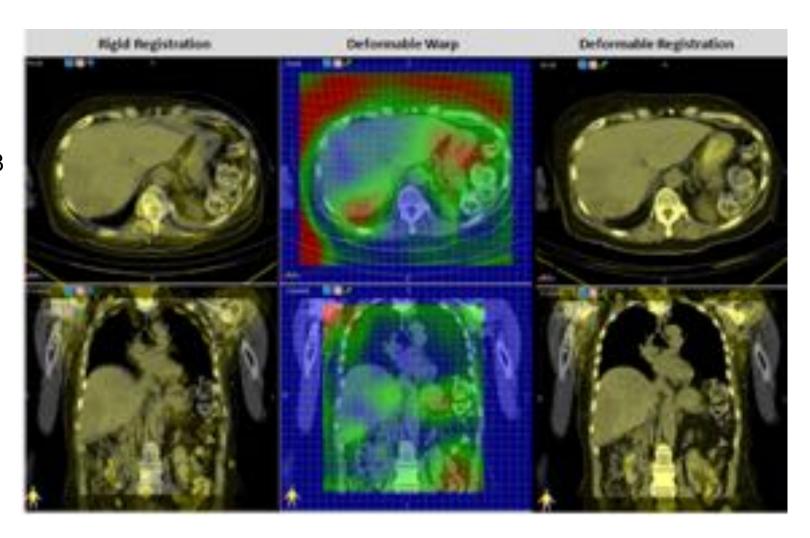
VARIAN CONFIDENTIAL/ PROPRIETARY: DISCLOSED SOLELY FOR IMMEDIATE RECIPIENT ONLY

Work in progress: not available for sale or guarantee of commercialization.

Deformable Dose Mapping and Dose Summation

Typically 4 procedures to treat whole liver, which requires deformable dose summation

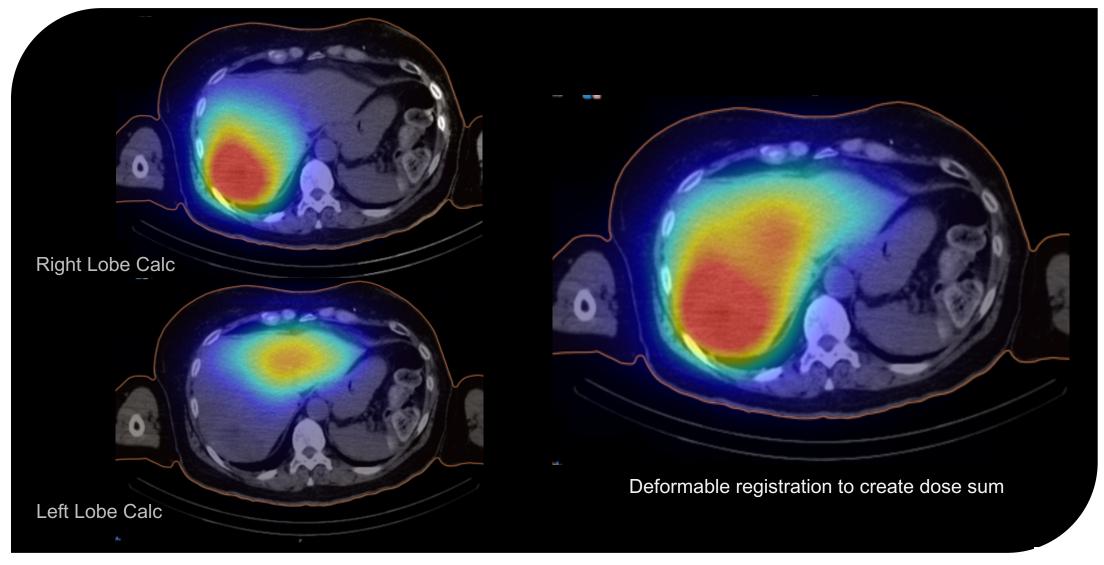
- Can treat unilobar (left or right), whole liver, or focal lesion
- Goal of completing treatment in 6-8 weeks (often 4 procedures to treat whole liver)
- Registration of the 2 independent SPECT-CT-Dose datasets will be implemented using non-rigid BSpline technique with mutual information metric



RapidSphere Workflow Demo

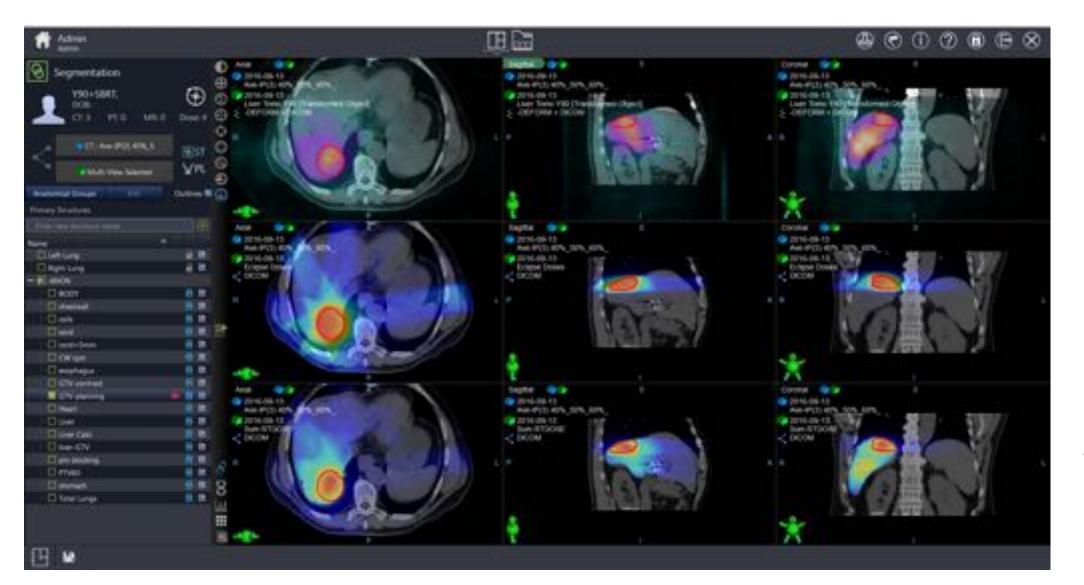
Treatment Delivery: RapidSphere

Example of composite dose distribution of Y-90 microsphere therapy



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Y-90 Dose + SBRT Dose Deformable Summation: RapidSphere



Y90 dose

SBRT dose

Summed Y90 & SBRT dose

SUMMARY

- 1. Activity calculators based on safety
- 2. Partition based on segmentation
- 3. DVH and voxel based on personalized DOSIMETRY

Empiric BSA MIRD

Partition

DVH
Voxel
Based

