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Multidisciplinary Approaches to Cancer Symposium

Debate: When to Do What? Locoregional Therapies for Hepatocellular Carcinoma

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Panel & Disclosures

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- *No relevant financial relationships*

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This presentation and/or comments will be free of any bias toward or promotion of the above referenced company or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Cultural Linguistic Competency (CLC) & Implicit Bias

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- *We will discuss the heterogeneity of patients with HCC that we treat and how to tailor our treatment plan to each individual patient.*
- *We can discuss disparities in care delivery for patients with HCC and rectal cancer.*

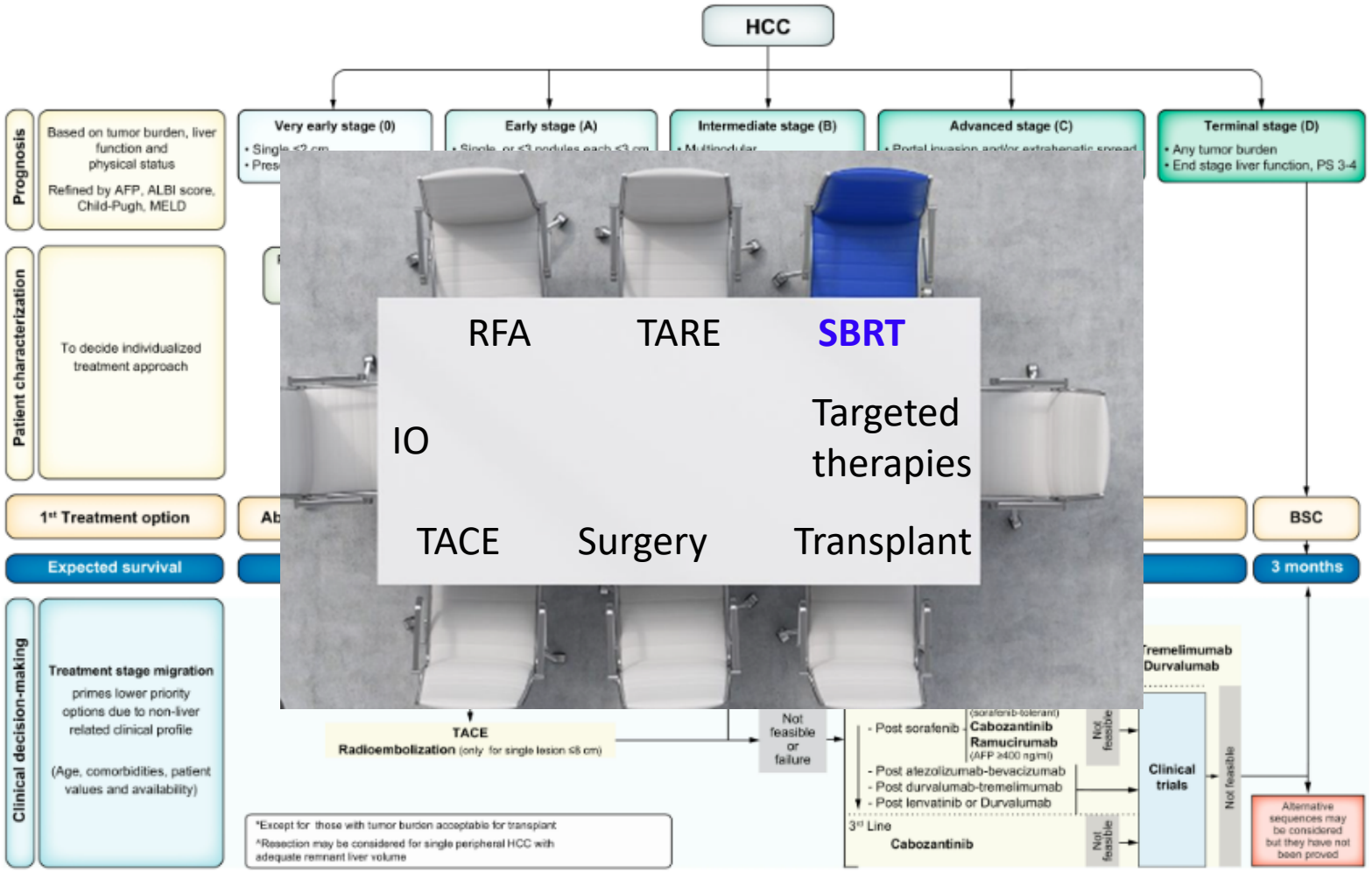
DEBATE:

Which Locoregional Therapy is Best for treating HCC?

Resolution:

SBRT is the Ideal Locoregional Therapy for Treating HCC

Advocating for SBRT to have a seat at the Table



Reig, et al. *Journal of Hepatology*. 2022.

Stereotactic Body Radiation Therapy for HCC

- SBRT is a safe and effective locoregional therapy for inoperable patients with localized or recurrent HCC.
- SBRT leads to superior local control compared to radiofrequency ablation (RFA), especially for large (>3cm) tumors or subphrenic HCC.
- SBRT has similar OS and PFS as locoregional therapies like RFA and TARE.
- SBRT can be used as a bridging therapy before liver transplant.
- SBRT to the liver can be safely and effectively combined with systemic therapies like sorafenib and trials with immunotherapy are underway.
- SBRT is endorsed by clinical practice guidelines from American Association for the Study of Liver Diseases (AASLD) and the American Society for Radiation Oncology (ASTRO).
- **Compared to RFA, transarterial chemoembolization (TACE), and Y-90 trans-radioembolization (TARE), SBRT is unique in that it allows for risk-adapted prescription of ablative dosing to the entire tumor target across a range of tumor sizes and peritumoral vascularity.**

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SBRT as a Definitive Treatment Option for HCC

Prospective studies of SBRT for small HCC

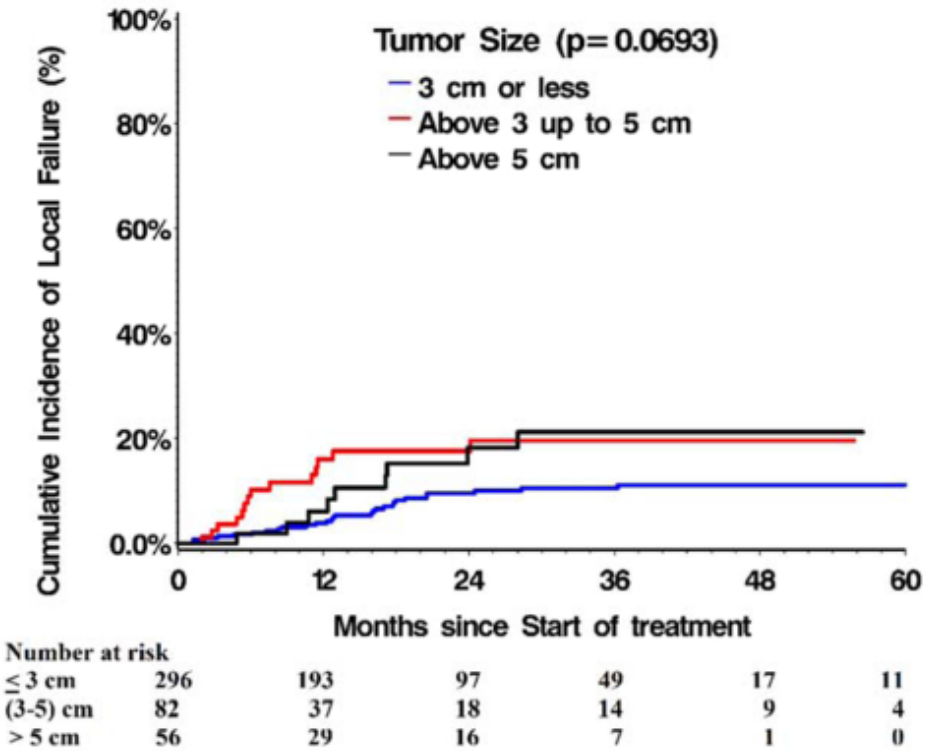
	Study design	N	Median tumor size	BCLC stage C	Previous treatment	Dose/fraction (Gy/fr)	Prescription	LC	OS	Toxicity G3≧
Andolino, 2011 USA	Phase I/II	60	31 mm	17%	100%	42-60Gy/3fr	70-80% isodose	94.6% (2y)	68.7% (2y)	10.7%
Kang, 2012 Korea	Phase II	47	29 mm	N.A	N.A.	24-48Gy/3fr	80% isodose	90% (2y)	67% (2y)	25%
Bujold, 2013 Canada	Phase I/II	102	72 mm	65.7%	52%	24- 54Gy/6fr	N.A.	87.0% (1y)	34% (2y)	30%
Lasley, 2015 USA	Phase II	CPC-A: 38	N.A.	N.A.	N.A.	48Gy/3fr	80-90% isodose	91% (3y)	61% (3y)	11%
		CPC-B: 21	N.A.	N.A.	N.A.	40Gy/5fr	80-90% isodose	82% (3y)	26% (3y)	38%
Takeda, 2016 Japan	Phase II	90	23 mm	16%	64%	40 or 35Gy/5fr	60-80% isodose	96.3% (3y)	66.7% (3y)	15%
Jang, 2020 Korea	Phase II	65	24 mm	6.2%	100%	42-60Gy/3fr	90% isodose	95% (3y)	76% (3y)	2%
Durand-Labrunie, 2020, France	Phase II	43	28 mm	0%	0%	45Gy/3fr	80% isodose	94% (2y)	69% (2y)	31%
Kimura, 2021 Japan	Phase II	36	23 mm	0%	0%	40Gy/5fr	70% isodose	90% (3y)	78% (3y)	11%

- Patients with small tumors (<3cm), 1-5 lesions, Child Pugh A-B7
- 2-3 year local control rates ≥ 90%
- 2-3 year OS = 61-78% for CP A

Aoyama and Dawson, ASTRO/JASTRO Joint Session: Advances in Liver Cancer Radiation Therapy, 2024 ASTRO Annual Meeting

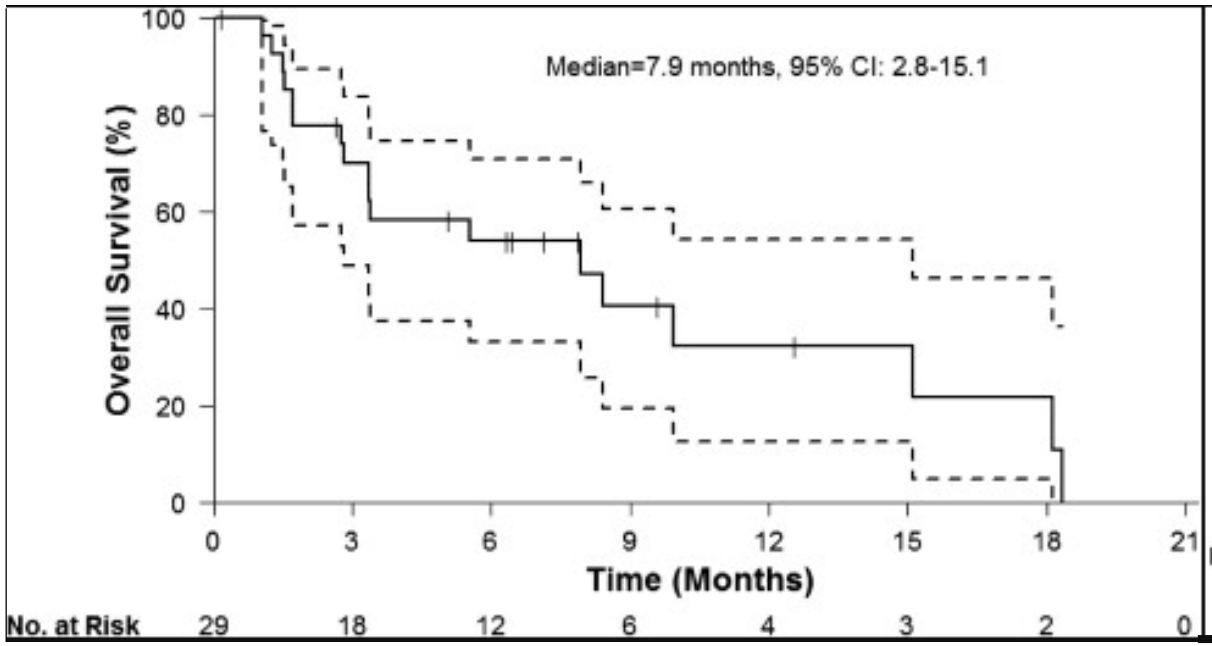
SBRT for HCC - U Michigan/ Princess Margaret

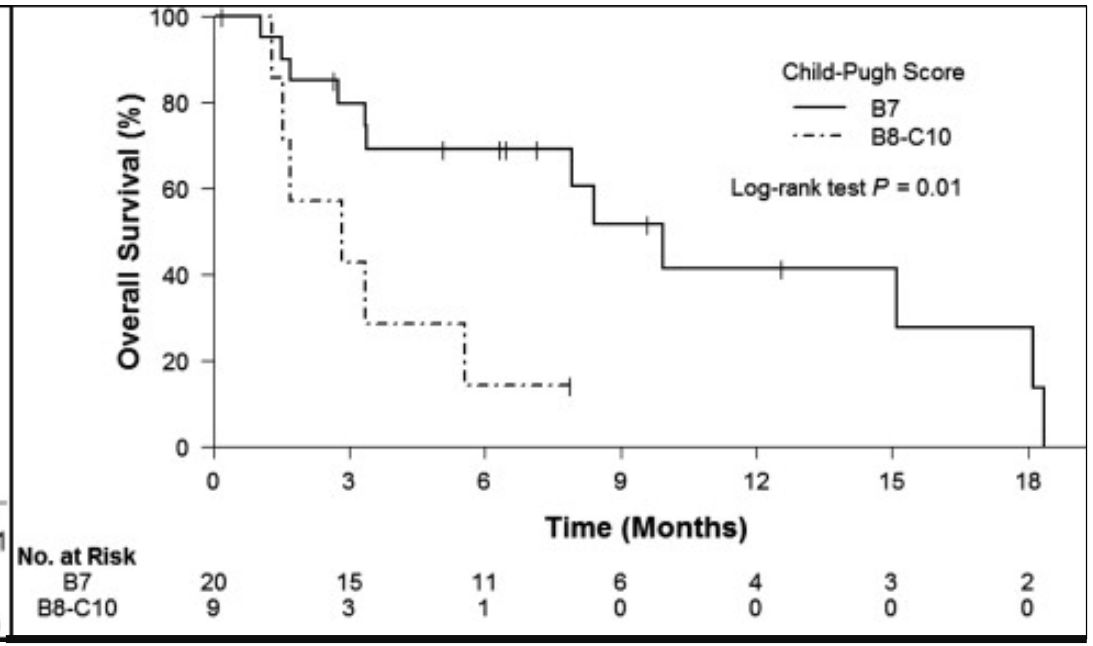
- 310 patients with early or intermediate stage HCC treated using SBRT
  - No vascular invasion, no extrahepatic HCC, < 5 tumors
  - Median size 2.7cm (0.5cm, 18cm); 23% > 5cm
  - Unsuitable for standard loco-regional therapies (60% recurrent/post-liver-directed treatment)
  - Not suitable for liver transplant upfront
  - Child Pugh A5-C10
- Doses = median 40 Gy (30-60 Gy) in 3-5 fractions
- Median OS = 24.6 months
- Median PFS = 10.6 months
- 5-year LC = 86%
- Slightly lower local control for large tumors > 5cm, but there was also sustained local control (about 80%) for large tumors



Matthew A, et al. *European Journal of Cancer*. 2020.

SBRT can be used to treat Child Pugh B HCC





Median survival = 7.9 months (95% CI 2.8-15.1)

Factors associated with better OS:

- AFP < 4500 mg/mL
- Child Pugh B7 vs. B8/B9

Culleton S, et al. *Radiotherapy and Oncology*. 2014.

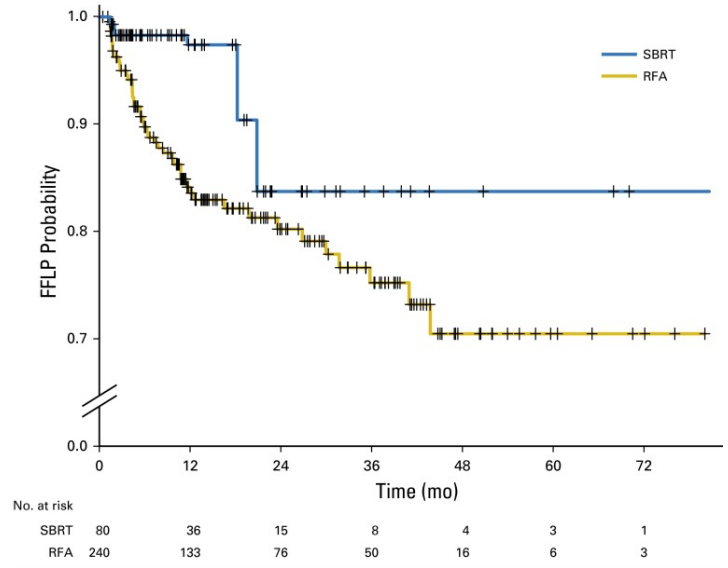
Comparison of SBRT & other Locoregional Therapies

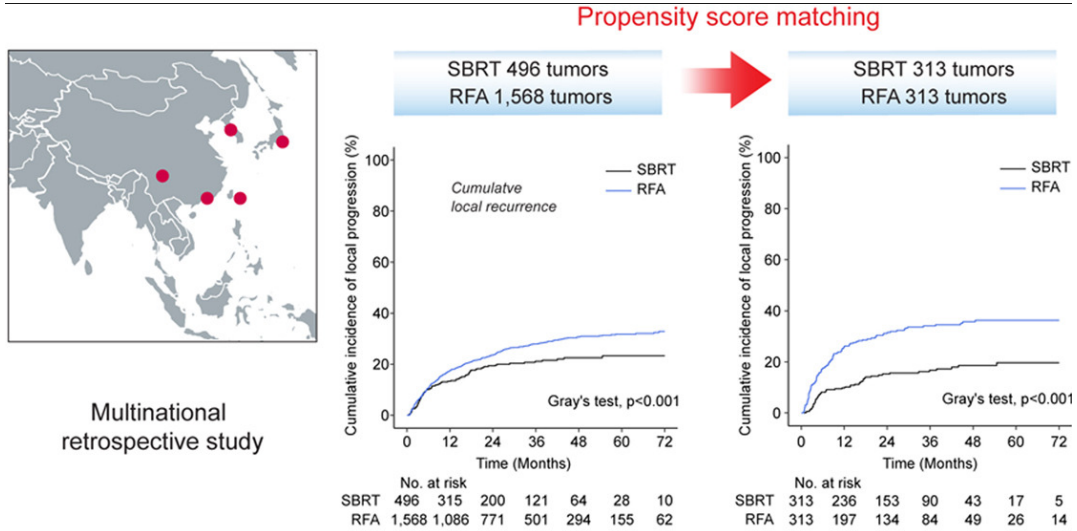
Author/year	Study design	Modality	N (matched)	Median tumor Size (mm)	LC (%)	P	PFS (%)	P	OS (%)	P	Toxicity (%)	P
Spair, 2018 USA	IPTW	SBRT	125	23	91 (2y)	0.008	26.9 (2y)	<0.001	55 (2y)	0.21	8	0.05
		TACE	84	29	23 (2y)		10.7 (2y)		35 (2y)		13	
Su, 2017 China	PSM	SBRT	82 (33)	33	N.A.	-	43.9% (5y)	0.945	74 (5y)	0.45	N.A.	-
		Surgery	35 (33)	35	N.A.		35.9% (5y)		69 (5y)		N.A.	
Sun, 2020 China	PSM	SBRT	122 (104)	26	N.A.	-	49% (5y)	0.350	71 (5y)	0.673	0	N.A.
		Surgery	195 (104)	27	N.A.		47.3% (5y)		71 (5y)		21.5	
Nakano, 2018 Japan	PSM	SBRT	27 (27)	18	N.A.	-	16.4% (5y)	0.051	48 (5y)	0.015	3.7	N.A.
		Surgery	254 (54)	18	N.A.		33.8% (5y)		75 (5y)		9.1	
Wahl, 2016 USA	IPTW	SBRT	63	22	84 (2y)	N.S.	N.A.	-	53 (2y)	N.S.	5	0.31
		RFA	161	18	80 (2y)		N.A.		46 (2y)		11	
Rajyaguru, 2018 USA	PSM	SBRT	296 (275)	N.A.	N.A.	-	N.A.	-	19 (5y)	<0.001	N.A.	-
		RFA	3684(521)	N.A.	N.A.		N.A.		30 (5y)		N.A.	
Hara, 2019 Japan	PSM	SBRT	143 (106)	18	94 (3y)	<0.001	N.A.	-	70 (3y)	0.86	0	N.A.
		RFA	231 (106)	17	80 (3y)		N.A.		69 (3y)		2	
Kim, 2020 Korea	PSM	SBRT	496 (313)	21	81 (2y)	<0.001	N.A.	-	78 (2y)	0.308	1.6	0.27
		RFA	1568(313)	22	76 (2y)		N.A.		71 (2y)		2.6	

Aoyama and Dawson, ASTRO/JASTRO Joint Session: Advances in Liver Cancer Radiation Therapy, 2024 ASTRO Annual Meeting

Superior Local Control after SBRT vs. RFA

- SBRT provides superior local control compared to RFA in large retrospective studies.
  - **Higher freedom from local progression (FFLP) for SBRT** at 1 year (97.4% vs 83.6%) and 2 years (83.8% vs 80.2%).
  - Subgroup analyses showed **tumors >= 2cm favored SBRT.**
- In a propensity score analysis of a large multi-national study (>2000 patients), SBRT resulted in **higher local control for large (>3cm) subphrenic tumors and after TACE.**
  - 3-year local recurrence rates for SBRT (21.2%) vs. 27.9% (RFA).
- Phase 3 RCT comparing FFLP following SBRT and RFA for small (<3cm) unresectable HCC (NCT05433701).

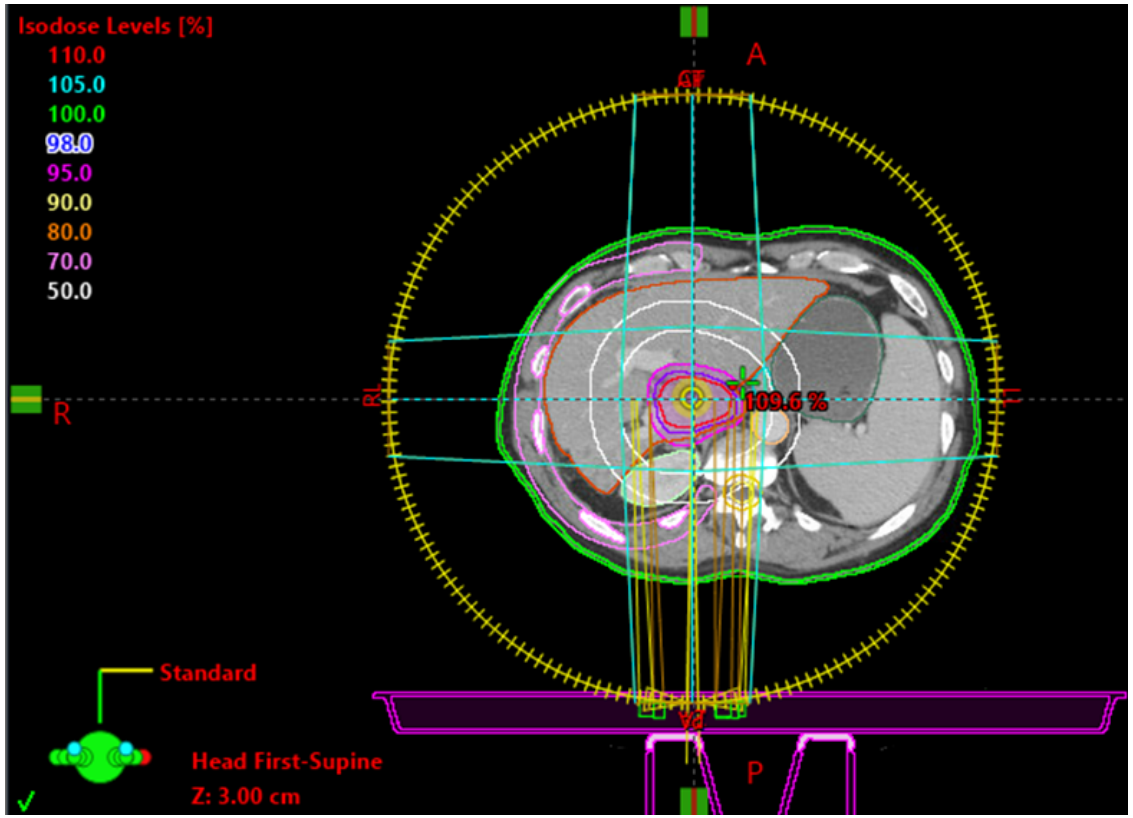




Wahl DR, et al. *Journal of Clinical Oncology*. 2016. Kim N, et al. *J Hepatol.* 2020.

Dosimetric Advantage of SBRT vs. RFA

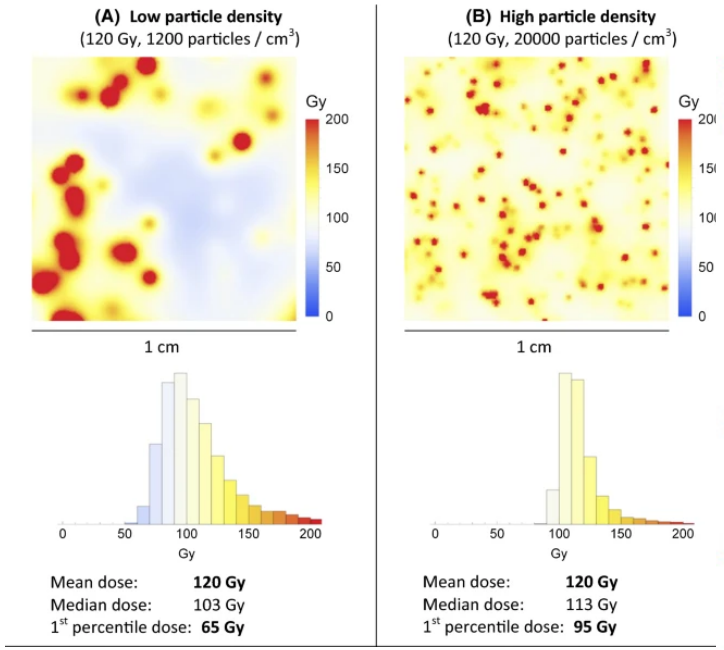
- Local control of **RFA is limited by:**
  - **"Heat sink" effect** (convection cooling from large vessels may result in incomplete ablation of perivascular disease)
  - Large tumor size
  - Distance from the ablation zone to tumor edge
- **SBRT allows for prescription of ablative dose to the entire tumor.**
- SBRT is better than RFA for:
  - Larger tumors
  - Tumors w/ peri-vascular disease
  - Tumors in a Subphrenic location (i.e. segment 8)
  - Tumors in the caudate lobe (close proximity to the IVC makes needle placement challenging and increases the risk of complications)
  - Tumors with a poor response to TACE or progression after TACE

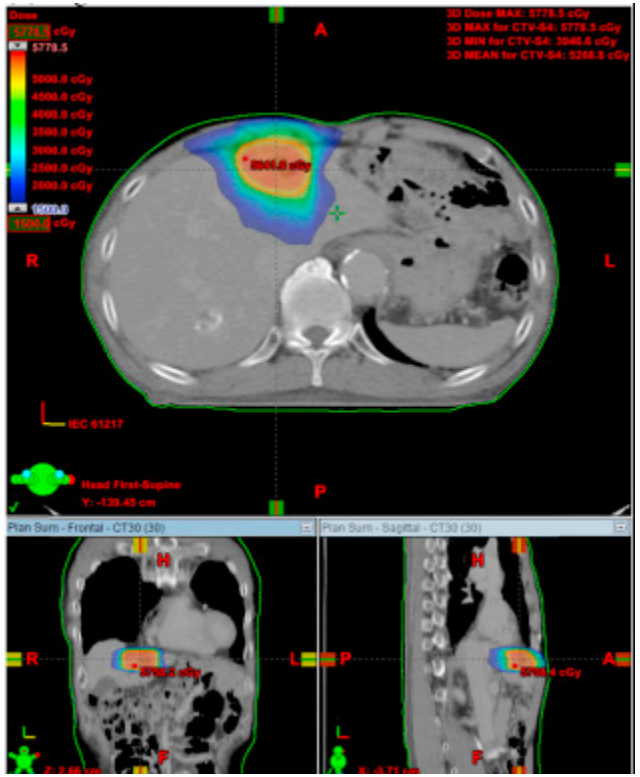


Lin Z, et al. *J Caner Res Ther.* 2016. Rhim, et al. *Gut Liver*. 2021.

SBRT is Superior to TARE (Y-90) for HCC

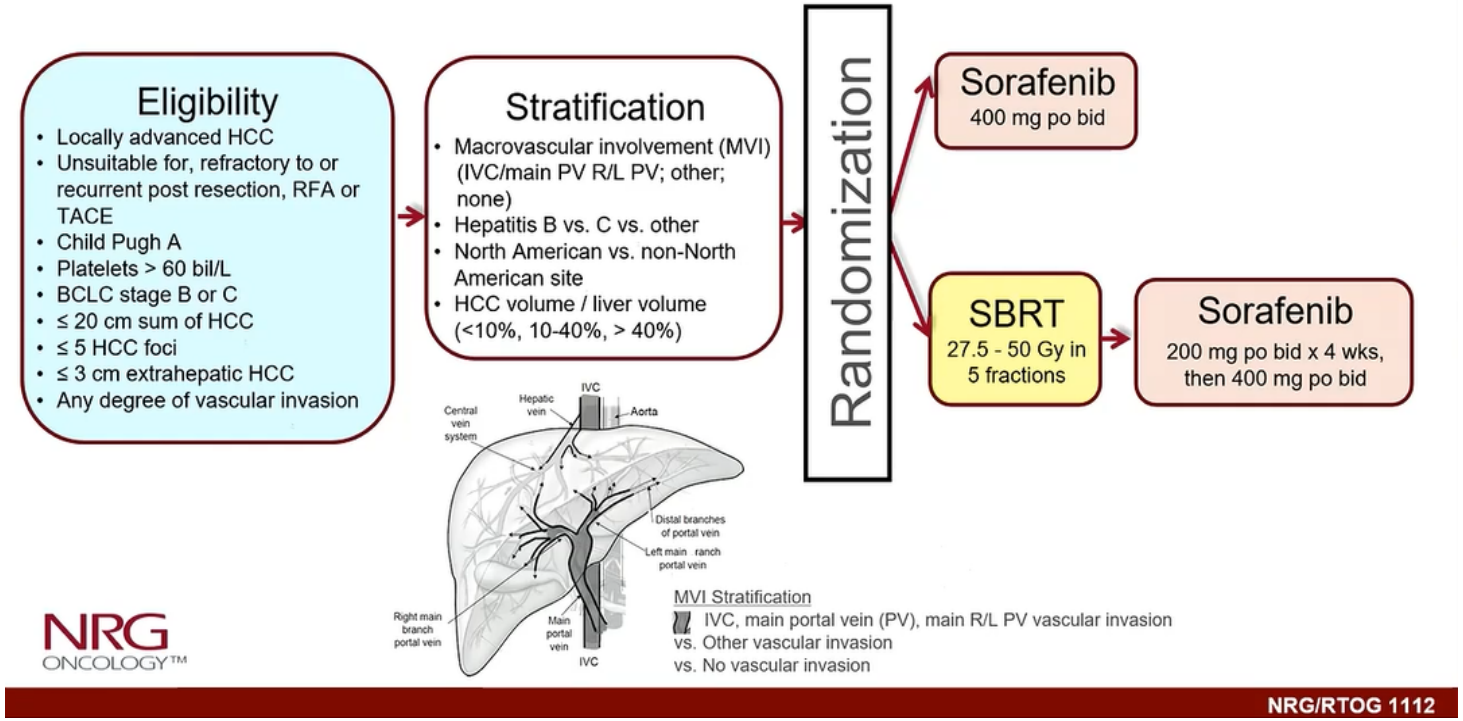
- Comparable local control after SBRT vs. TARE with Y-90
  - Median FFLP is similar (9 months vs 8 months) for lesions < 10cm or 10000 cc (Liang et al).
  - 1 year LC is similar between SBRT and Y-90 TARE (87% vs. 89%) (deBettencourt M et al).
- TARE w/ Y-90 leads to greater extremes of intra-tumoral hot and non-ablative cold spots, due to radioembolization of neovasculature heterogeneously distributed within tumors.
- SBRT generates a <u>homogenous distribution of ablative dose throughout tumors</u>. Coverage of the gross tumor volume with ablative dose, rather than aggressive escalation of median/partial doses, leads to better treatment response for HCC.





Maxwell, et al. *Cardiovascular and Interventional Radiology.* 2022.

NRG/RTOG 1112

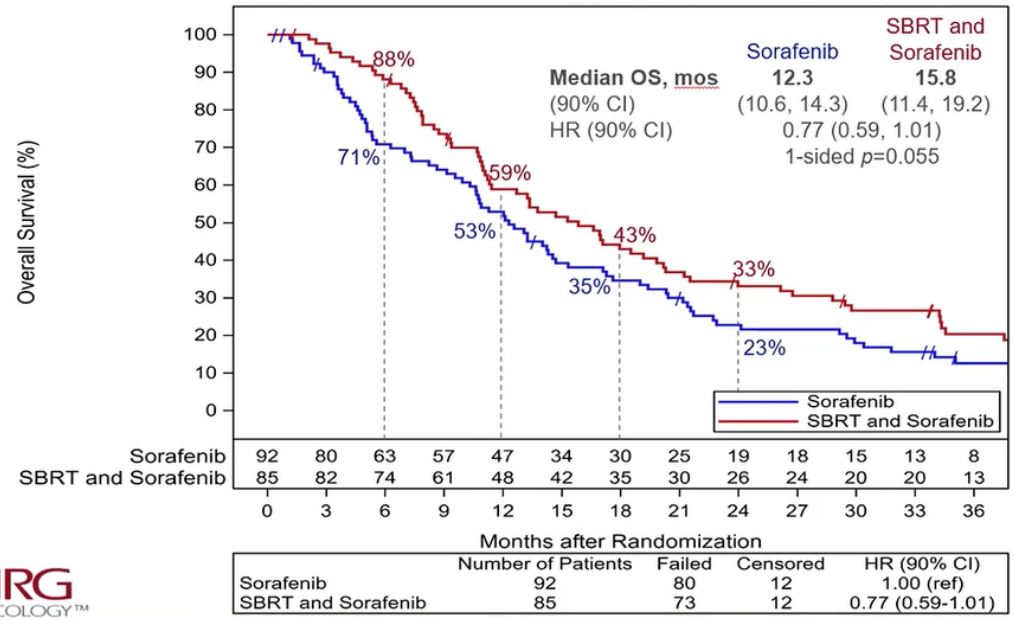


- Multi-center phase III RCT of sorafenib vs SBRT followed by sorafenib in patients with HCC unsuitable for resection, transplant, RFA or TACE.
- 193 patients with new or recurrent locally advanced HCC who were ineligible for surgical resection or other locoregional therapies due to underlying clinical factors or due to refractory or recurrent cancer.
- Patients on this trial had very advanced disease (82% were BCLC-C, 74% had Macrovascular invasion (MVI))
- Up to 5 lesions and large tumors were permitted (medium sum of maximum diameter was 6.7cm in the SBRT arm) w/ a maximum sum of diameters up to 20cm allowed)

Dawson, LA et al. *Journal of Clinical Oncology.* 2023.

SBRT + Systemic Therapy Improves OS and PFS

Overall Survival



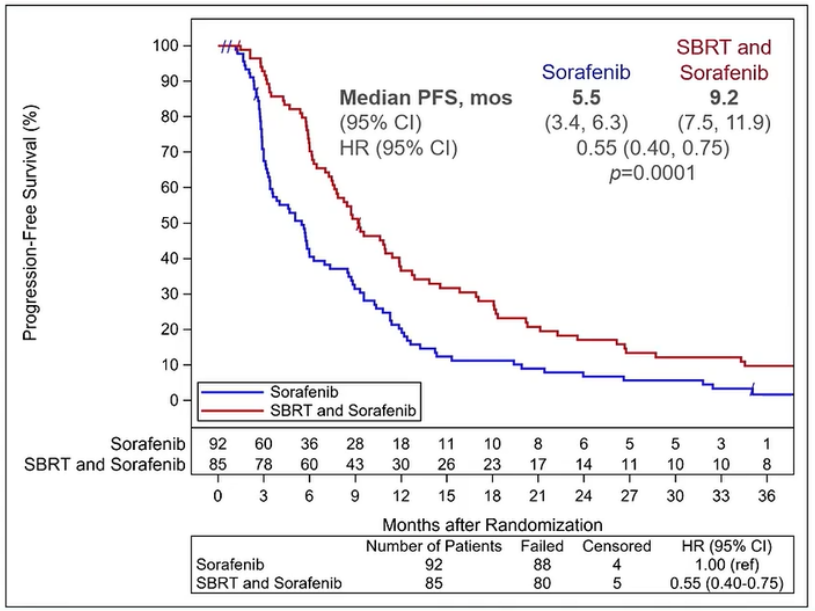
NRG ONCOLOGY™

Median follow: all patients – 13.2 months; alive patients – 33.7 months

NRG/RTOG 1112

Progression-Free Survival

Estimate (95% CI)	Sorafenib (n=92)	SBRT and Sorafenib (n=85)
6-month	41% (30%, 51%)	71% (62%, 81%)
12-month	20% (12%, 29%)	37% (26%, 47%)
18-month	11% (5%, 18%)	28% (18%, 38%)
24-month	7% (2%, 12%)	17% (9%, 25%)



NRG ONCOLOGY™

NRG/RTOG 1112

- Overall survival was longer for patients receiving SBRT and sorafenib, compared to sorafenib alone (15.8 vs. 12.3 months; one-sided p = 0.055).
- This was statistically significant after controlling for clinical prognostic factors such as performance status and the degree of vascular invasion (p=0.042).
- **Adding SBRT to systemic therapy improved progression-free survival from 5.5 months to 9.2 months (HR = 0.92, p<0.001).**

Dawson, LA et al. *Journal of Clinical Oncology*. 2023.

SBRT has Low Toxicity Rates

- SBRT and RFA have equally low toxicity rates (0-11%) with no statistical differences across propensity score analyses of single- and multi-institutional trials.

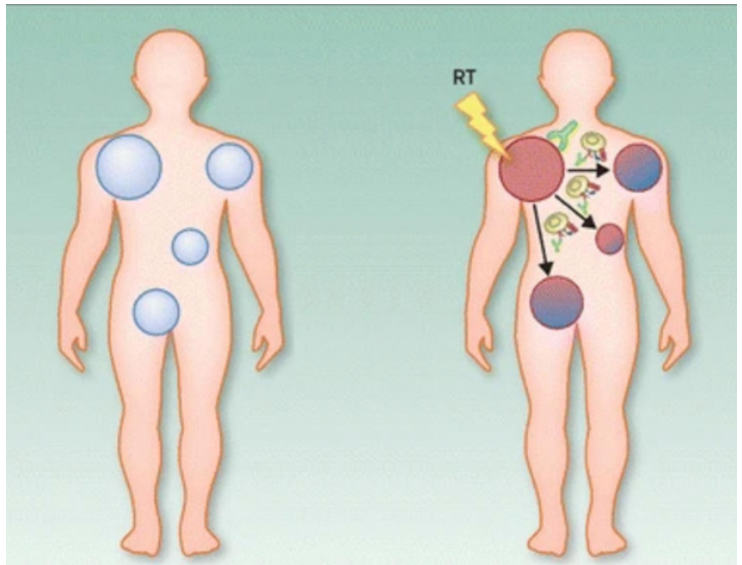
- RTOG 1112 reported no difference in treatment-related grade 3+ toxicity rates between SBRT + Sorafenib (47%) and sorafenib alone (42%).

Liver Veff	Planned Prescription Dose (Gy)	If the allowed Veff is exceeded at this planned dose
< 25%	50	Reduce to 45 Gy and re-evaluate
25 - 29%	45	Reduce to 40 Gy and re-evaluate
30 - 34%	40	Reduce to 35 Gy and re-evaluate
35 - 44%	35	Reduce to 30 Gy and re-evaluate
45 - 54%	30	Reduce to 27.5 Gy and re-evaluate
55 - 64%	27.5	Ineligible

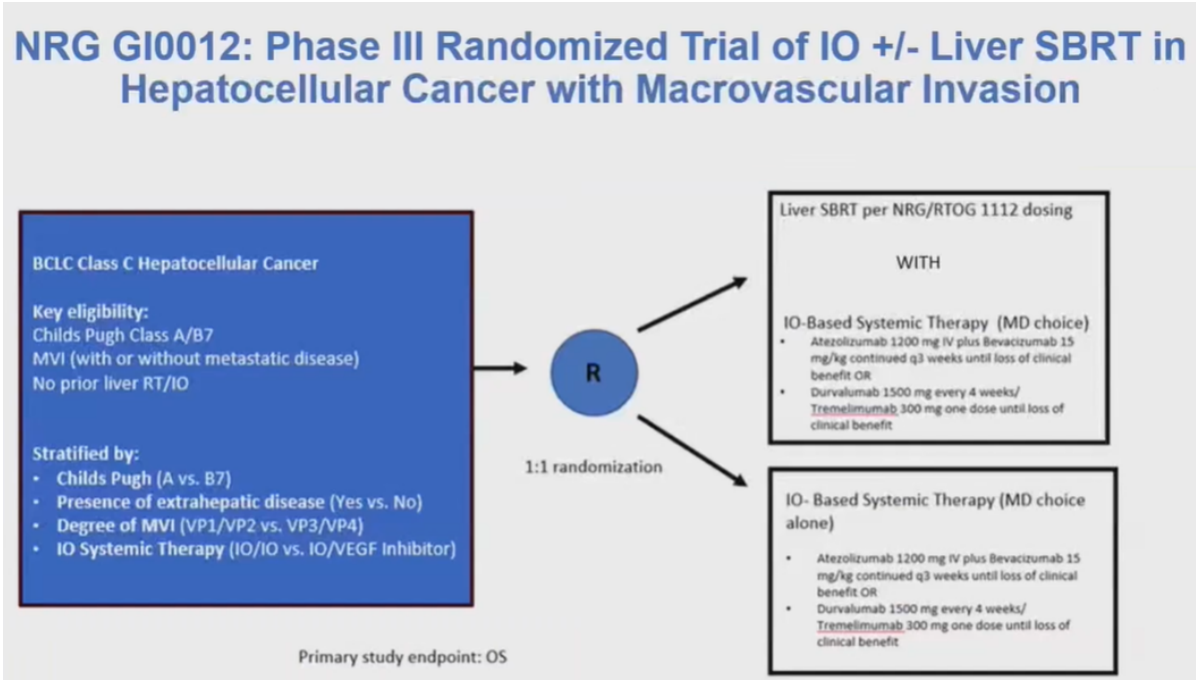
Dawson, et al. RTOG 1112.

Enhancing Immuno-Modulatory Effect of SBRT + IO

- Adding IO to SBRT improved 12-month OS (92% vs 74%) and ORR (88% vs 50%) compared to SBRT alone in a retrospective multi-institution cohort with <=3 unresectable tumors (Chiang et al).

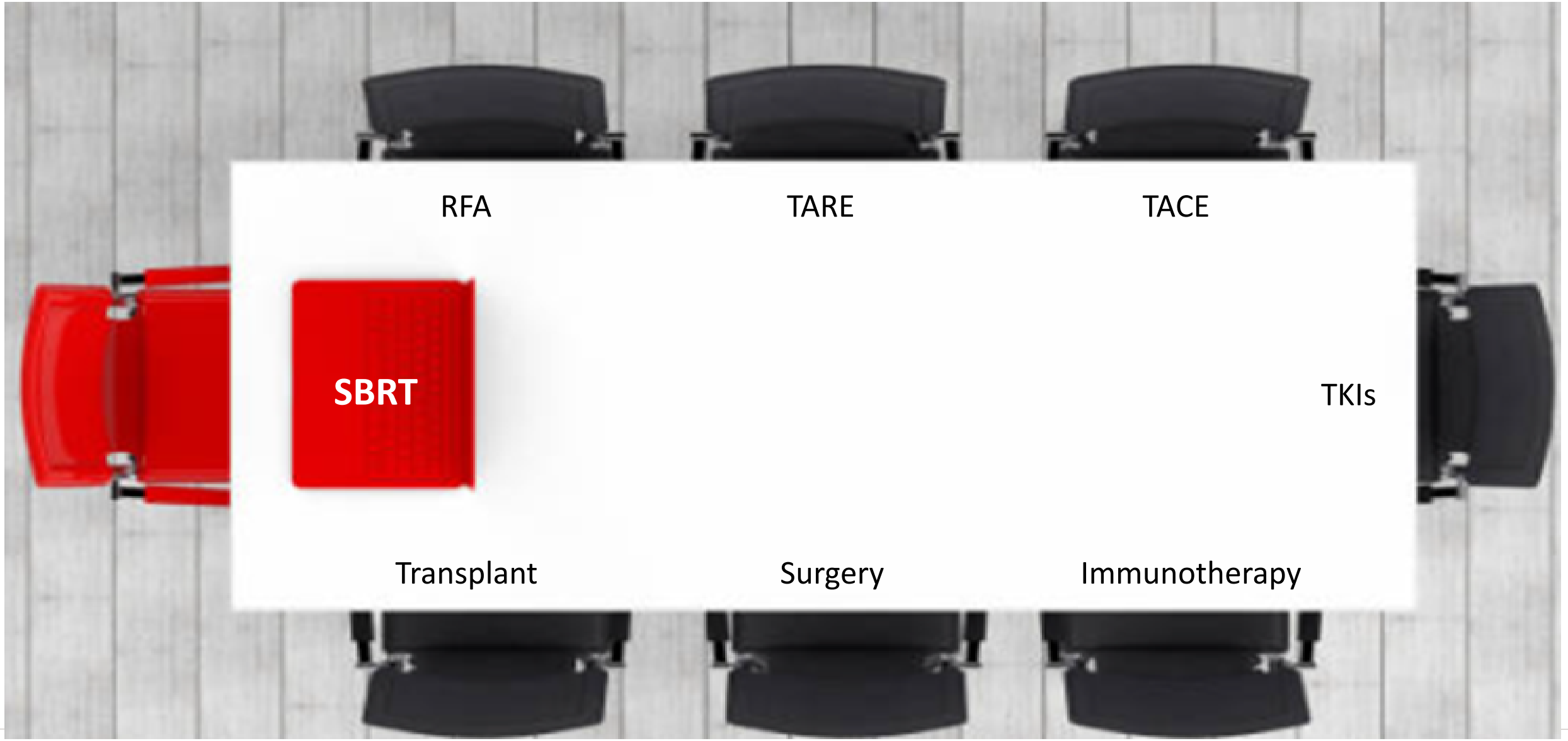


- Pre-clinical studies are needed to better understand the synergies of SBRT and immunotherapy and the role of HCC tumor microenvironment in modulating this response.



Chiang, et al. *Liver Cancer.* 2023.

SBRT Deserves a Seat at the Table



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Matthew, A.S, et al. European Journal of Cancer. 2020.

Counter Resolution:

Thermal Ablation and Trans-Arterial Radioembolization are the best locoregional therapies for treating HCC

What do we mean by "locoregional therapy"

- Is this palliative or curative?
- How big is the tumor we are trying to treat?
- How much liver are we trying to spare?

I'm a simple man

Don’t take my word for it…

Team Jon

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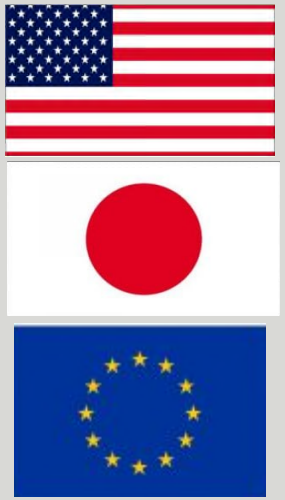

Team Heather

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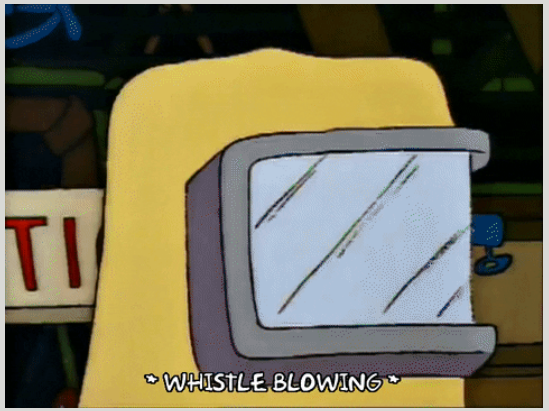
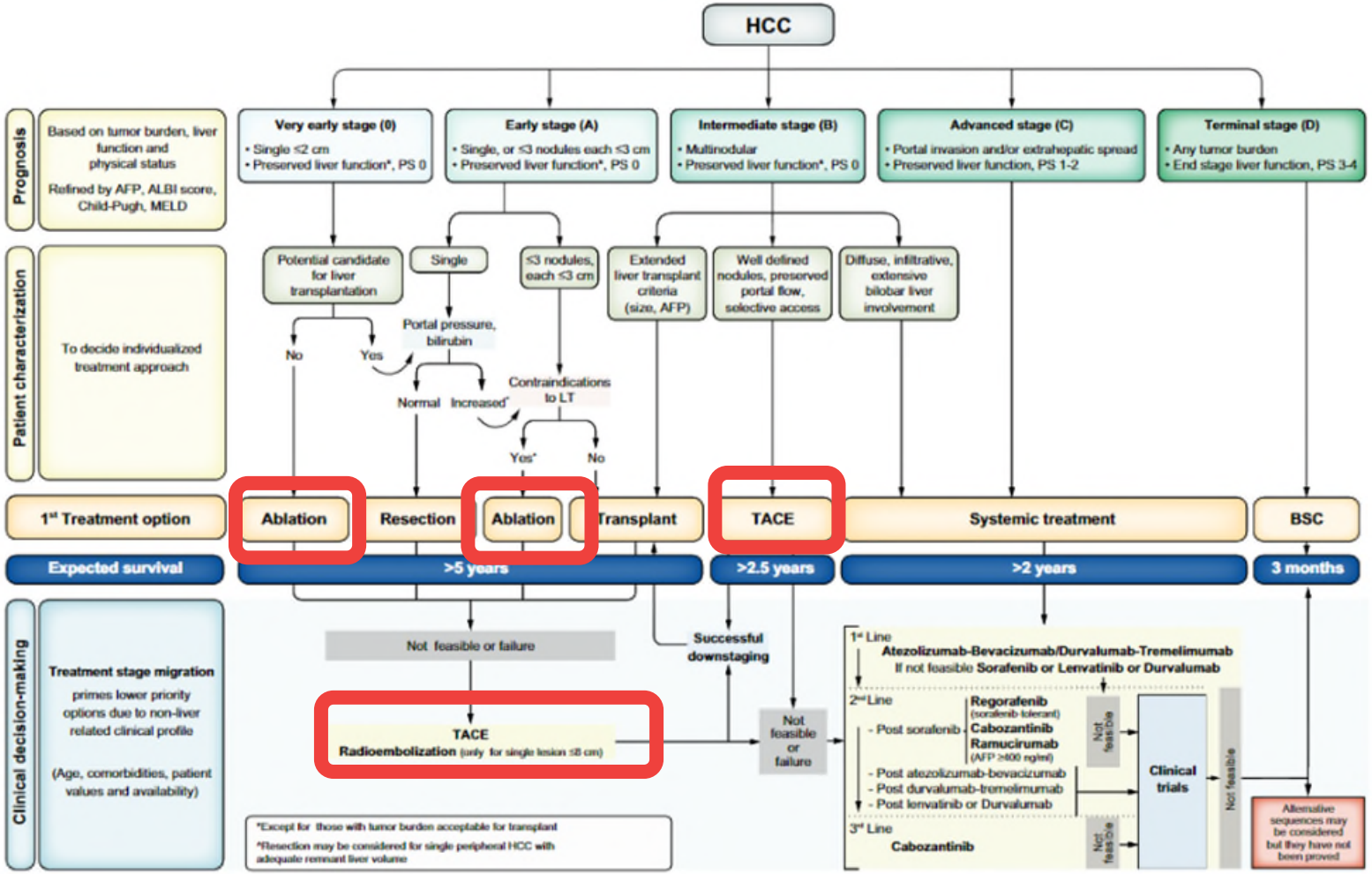


BCLC (Barcelona Clinic Liver Cancer)



"Stereotactic body radiation bears antitumoral activity but further prospective studies are needed to define its role."

Reig. BCLC strategy for prognosis prediction and treatment recommendations:The 2022 update. J Hepatology 2022 March; 76:681-693

What's the data!

- 2019 meta-analysis of studies of SBRT for HCC
  - 29/33 single center retrospective
  - Median tumor size 3.3 cm
  - Nonrandom prospective studies OS 1,2,3 yr
    - Feng - 63%, 36%, 22%
    - Bujold - 55%, 34%, 23.8%
    - Moon - 36%
    - Weiner – 38%
  - Prospective studies Local Control
    - NR, 53%, 71%, 95%

Author/year		Study type	n	Male (%)	Age (median, range)	CPC A (%)	Viral etiology (%)	TVI (%)	EHM	Tumor size (median [in cm], range)
Shiozawa K	2015	R	35	68.6	m75.2 (55–89)	80	77.1		0	m2.86 (1.2–5)
Huertas A	2015	R	77	75.3	71 (44–91)	85.7				2.4 (0.7–6.3)
Yoon SM	2013	R	93	80.6	62 (42–86)	74.2	87.1	0.0	0	2.0 (1.0–6.0)
Jeong Y	2018	R	119	81.5	60 (36–90)	90.8	87.4	0.0	0	1.7 (0.8–6.0)
Bibault JE	2013	R	75	84.0	70 (44–86)	88	14.9		0	3.7
Kubo K	2018	R	65	67.7	73 (49–90)	86.2	90.8			1.6 (0.5–4.7)
Sanuki N	2014	R	48	67.0	73 (40–86)	47.9	77.0			2.7 (1.0–5.0)
Sanuki N-2	2014	R	137	64.0	74 (48–89)	98.5	84.0			2.4 (0.8–5.0)
Andolino DL	2011	R	37	81.1	63 (24–85)	64.9	51.3		0	3.5 (1–6.5)
Jang WI	2013	R	82	73.0	60 (39–79)	90.2	76.0	10.0		3.0 (1.0–7.0)
Yamashita H	2014	R	79	75.9	73 (38–95)	84.8				2.7 (0.6–7.0)
Kwon JH	2010	R	42	76.2	m60.1	90.5	85.7			3.1*, 15.4cc
Ibarra RA	2012	R	21	76.2	72 (47–88)				9.5%	8.6*, 334.2cc
Feng M	2018	P	69	70	62 (34–85)		40.0	18		3 (0.5–13)
Bujold A	2013	P	102	78.4	69.4 (40.4–90.3)	100	76.4	54.9	11.8	7.2 (1.4–23.1)
Lo C.-H.	2017	R	89	73	68 (36–87)	77.5	83.2	49.4	0	6.2 (1.2–18.5)
Scorsetti M	2015	R	43	72.1	m72 (46–87)	53	69.8	20.0		4.8 (10–12.5)
Kim JW	1905	P	18	77.8	59.5 (42–83)	94.4	83.3	0.0	0	1.95 (1.0–3.3)
Hasan S	2017	R	40	82			68.0			3.5 (1.5–8.9)
Madhavan R	2017	R	10		61.5 (52–69)	80		50		5.1, 69.3cc
Zhang T	2018	R	28	75	49 (22–65)	85.7	100.0	0	0	2.1 (1.1–3.0)
Que J	2016	R	115	76.5		90.4	87.8	29.6		(1.8–18)
Hijazi H	2016	R	23			52				5 (2–9)
Gkika E	2018	R	40	83	69 (29–84)	55	30.0	28		7 (1.7–22)
Kim M	2017	R	72	79.2	62 (37–81)	72.2	75.0	31.9	0	7 (5–10)
Uemoto K	2018	R	121	57.9	75 (44–91)	78.8		7		4.4*, 45.3cc
Lam MHC	2017	R	39	79.5	72 (54–90)	89.7	89.7			1.9 (0.6–5.0)
Sapir E	2018	R	125	81	60.8 (46.2–83.2)		50.9	7	0	2.9 (0.7–15.0)
Moon DH	2018	P	11		65.5 (23–86)					3.5 (1.7–6.5)
Guarneri A	2016	R	29	79	70 (55–88)	66	65.0			4.7 (3.1–12)
Weiner AA	2016	P	12	46	72 (51–95)					5 (1.6–12.3)
Baumann BC	2018	R	37	84	65 (41–88)	70	68.0		0	2.7 (1.1–5.6)
Hanazawa H	2017	R	17	76.5	77 (63–75)	82.3			0	4.7*, 54.6cc

Abbreviations: CPC, Child-Pugh class; TVI, tumor vascular invasion; EHM, extrahepatic metastases; R, retrospective; P, prospective.
m' heading indicates mean value.
* Diameter is calculated from volume, assuming tumor is spherical.

Rim et al. Radiotherapy and Oncology Feb 2019

What's the data!

- 2023 met-analysis
  - RFA vs MWA/SBRT/Y90
  - Both MWA and Y90 showed improvement
  - NS SBRT

Table 1 Local control rate, regional progression rate and distant progression rate

Groups	Cohorts (n)	Patients (n)	Events (95%)	I^2	Relative risk (95%)	*p*
Local control rate						
RFA	7	651	0.823 (0.733–0.887)	19.626	1	–
MWA	5	569	0.926 (0.867–0.960)	0.000	0.889 (0.852–0.927)	< 0.001
SABR	7	424	0.848 (0.765–0.906)	38.215	0.971 (0.920–1.024)	0.276
Particle	4	165	0.915 (0.826–0.961)	0.000	0.899 (0.848–0.954)	< 0.001
Regional progression rate						
RFA	3	156	0.298 (0.231–0.375)	0.000	1	–
MWA	2	125	0.136 (0.086–0.208)	0.000	0.456 (0.276–0.755)	0.002
SABR	4	194	0.317 (0.255–0.387)	10.563	1.064 (0.775–1.461)	0.703
Particle	2	71	0.437 (0.327–0.553)	0.000	1.466 (1.026–2.096)	0.036
Distant progression rate						
RFA	4	260	0.064 (0.030–0.132)	9.812	1	–
MWA	2	164	0.024 (0.007–0.083)	0.000	0.375 (0.127–1.105)	0.075
SABR	3	188	0.201 (0.103–0.353)	55.123	3.141 (1.821–5.418)	< 0.001
Particle	2	71	0.187 (0.079–0.379)	0.000	2.922 (1.492–5.720)	0.002

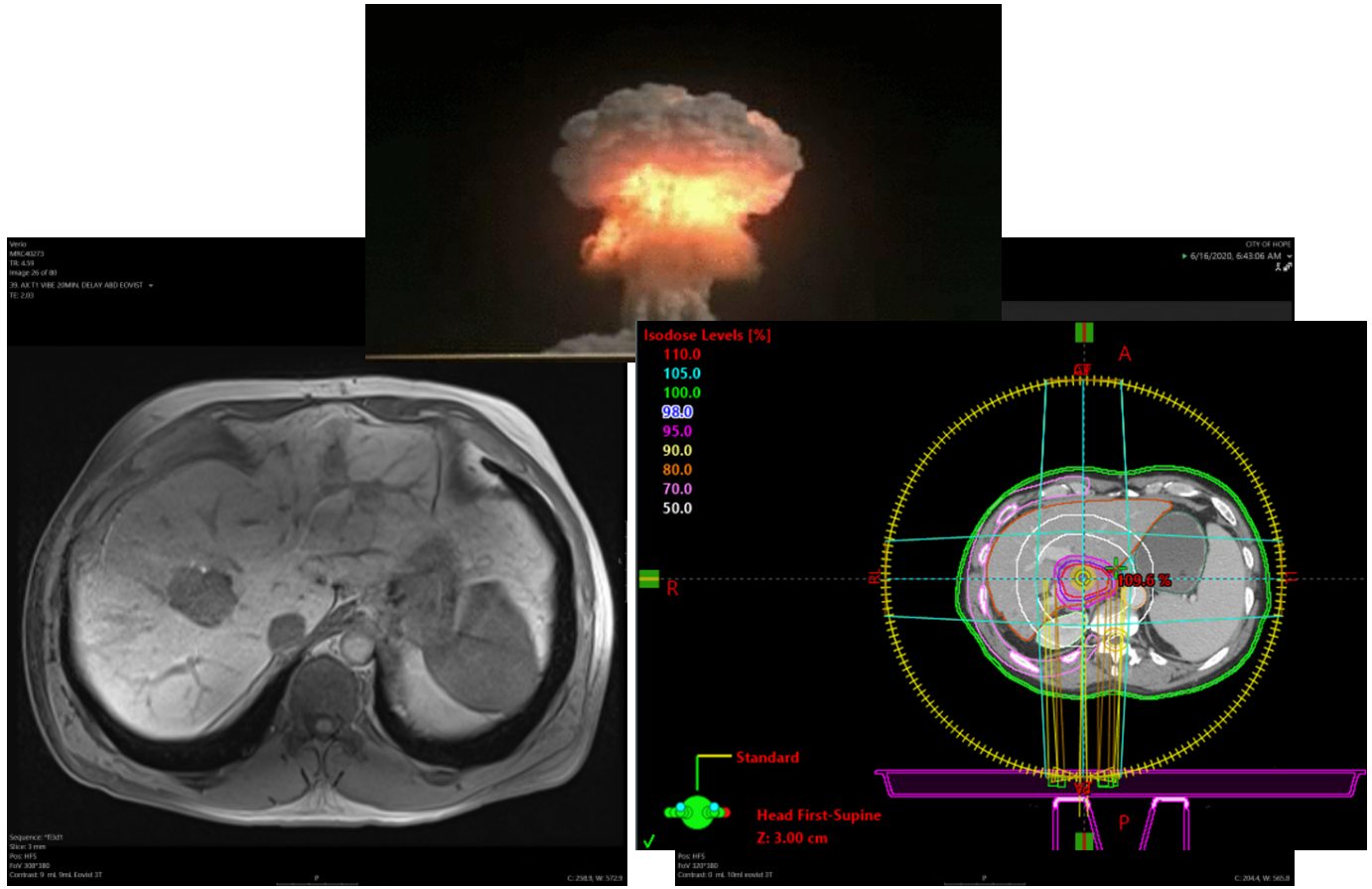
MWA: Microwave ablation; RFA: radiofrequency ablation; SABR: stereotactic ablative radiotherapy

Cheng et al Exper Heme Oncol 12:37 2023

Safer?

Phase I/II SBRT for hepatic malignancy

- 26 pts, 32 lesions
- 9 pts with >2 point decline CPS
- 2 deaths from hepatic failure
  - Early study closure



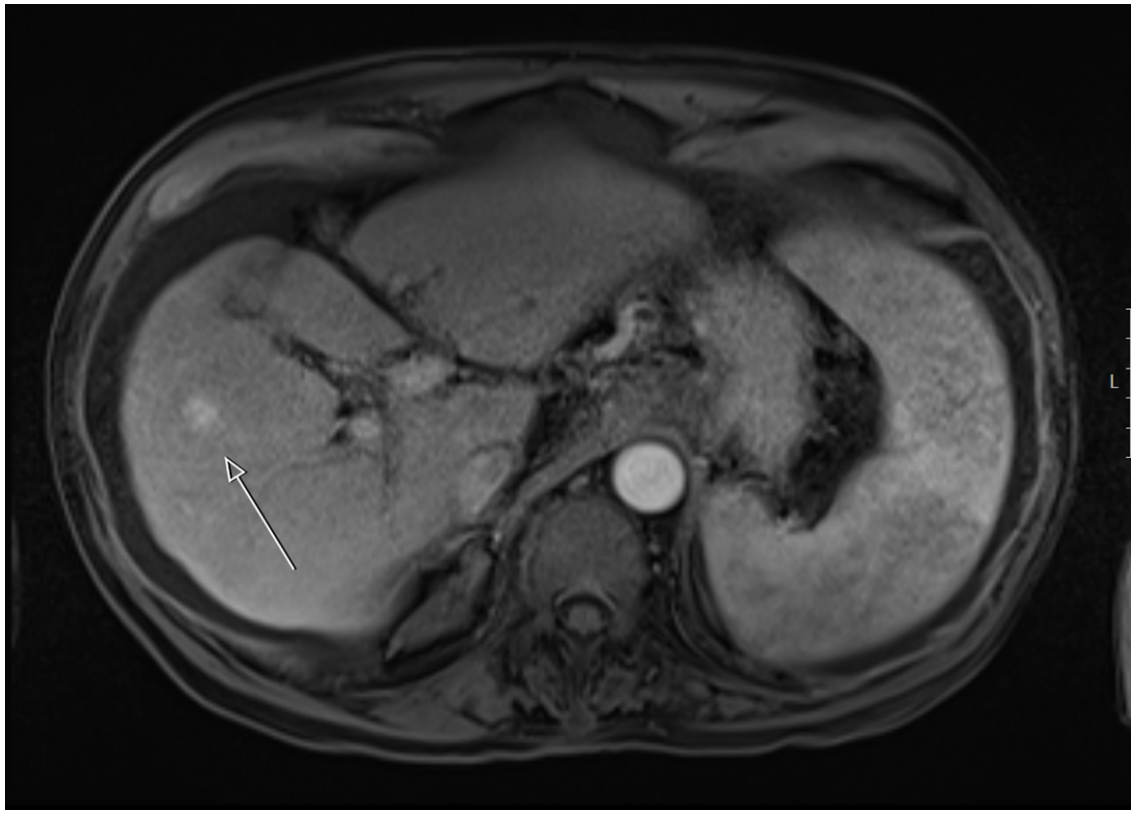
Pre and post SBRT to liver lesions

Curative treatment for HCC

Surgery is the gold standard

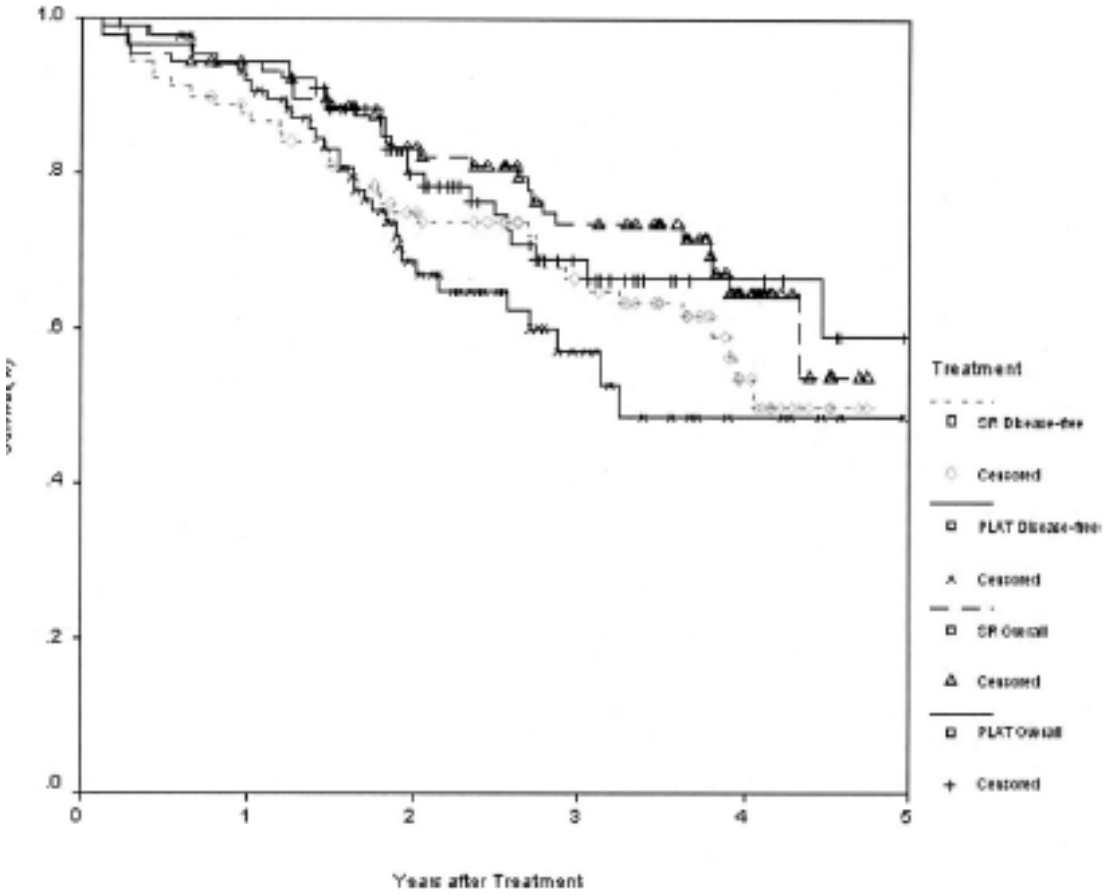
Ablation VS Resection

- What do we need to replace the gold standard?
  - Equivalent or superior outcomes
  - Lower morbidity/complications
  - Shorter hospital stay
  - Lower cost



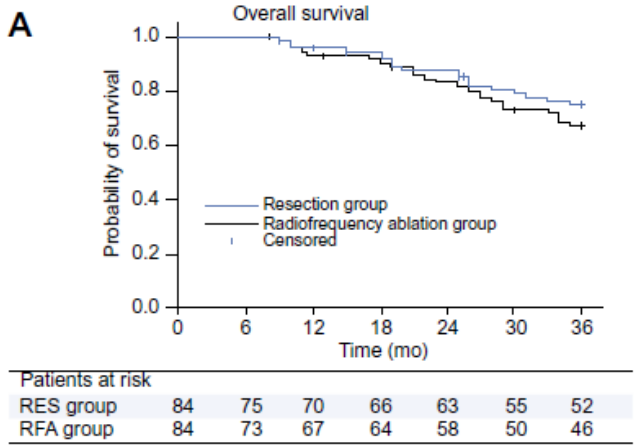
What's the gold standard for HCC

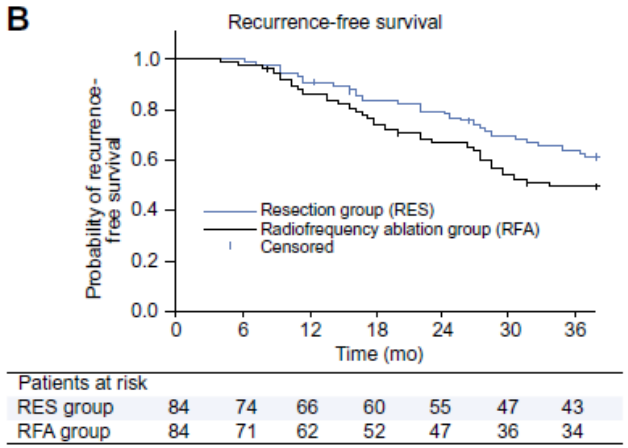
- Chen et al Annals of Surgery 2006
  - RCC 180 pts with HCC<5cm
  - Compared RFA to Rxn
  - No statistical difference
    - Overall survival
    - Disease free survival



What's the gold standard for HCC

- **Feng et al.** Journal of Hepatology 2012
  - RCC 168 pts with HCC <4cm
    - Resection vs Ablation
    - No difference in overall survival
    - No difference in recurrence free survival





Gold Standard

Ng KKC et al. Br J Surg 2017

- RCT resection vs. RFA for early HCC
  - Shorter hospital stay
  - Less blood loss
  - No difference in
    - OS
    - DFS
    - Recurrence rate

OS

DFS

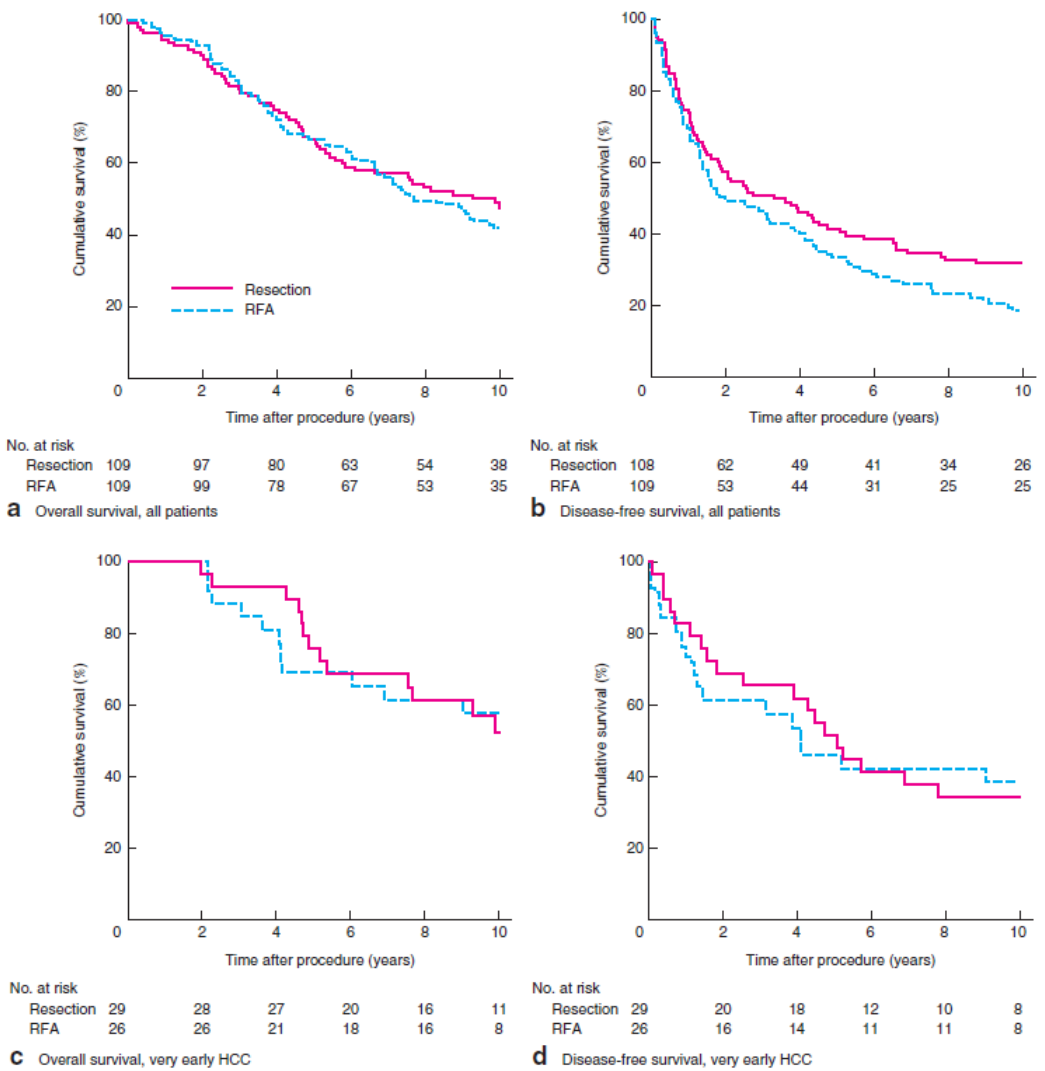
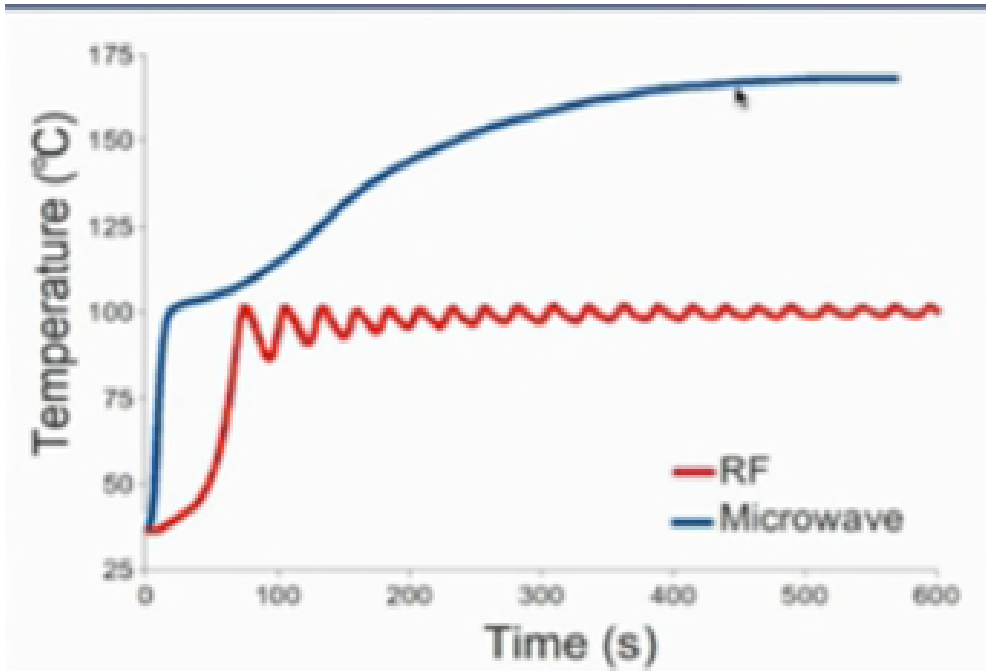


Fig. 2 **a** Overall and **b** disease-free survival rates in the hepatic resection and radiofrequency ablation (RFA) groups by intention-to-treat analysis. **c** Overall and **d** disease-free survival rates among patients with very early hepatocellular carcinoma (HCC) in the resection and RFA groups. **a** $P = 0{\cdot}531$, **b** $P = 0{\cdot}072$, **c** $P = 0{\cdot}950$, **d** $P = 0{\cdot}896$ (log rank test)

RFA vs MWA

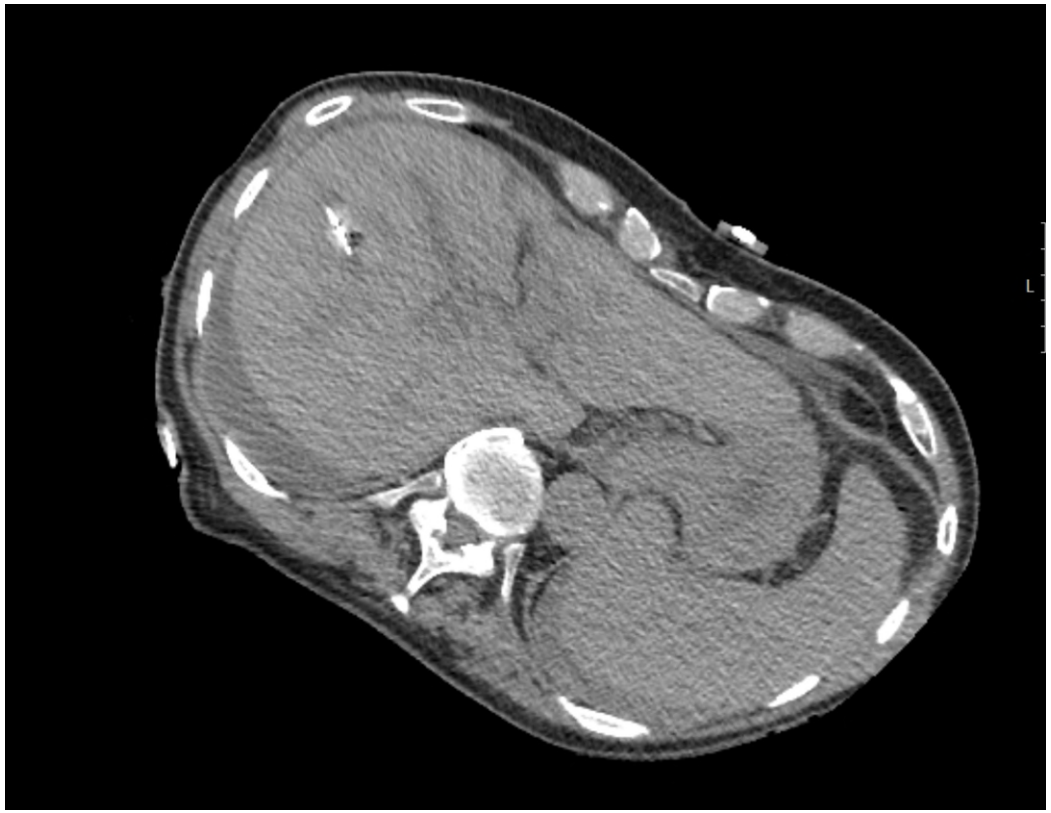


- Electromagnetic waves→ rotation of water molecules→ tissue agitation and heating
  - Minimal Heat Sink
- Does not rely on local tissue conduction, so may achieve larger ablation zones

Dong B. Percutaneous sonographically guided microwave coagulation therapy for hepatocellular carcinoma: results in 234 patients. AJR Am J Roentgeno 2003; 180:1547–1555
Liang P Prognostic factors for survival in patients with hepatocellular carcinoma after percutaneous microwave ablation. Radiology 2005; 235:299–307
Lu MD Hepatocellular carcinoma: US-guided percutaneous microwave coagulation therapy. Radiology 2001; 221:167–172 Laeseke JVIR 2009

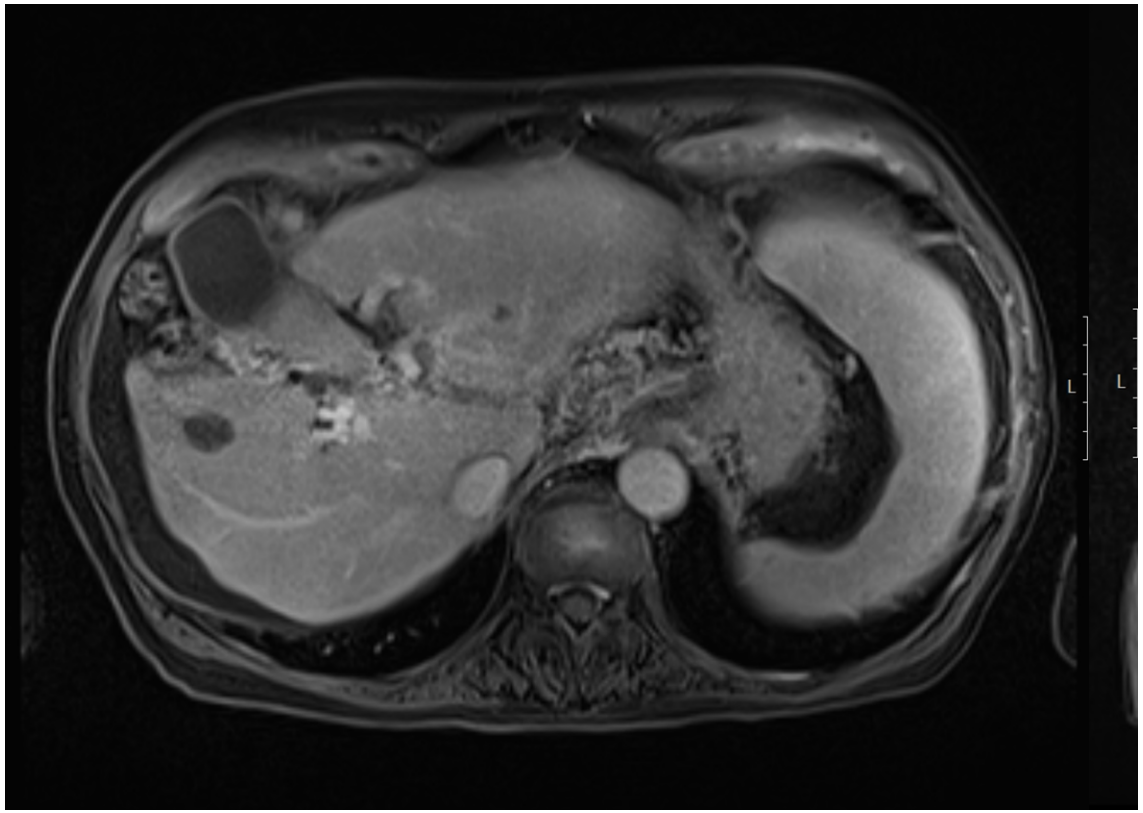
Collision trial

- Phase 3 randomized study metastatic CRC ablation VS surgery- presented ASCO 2024
  - 341 patients enrolled
    - Fewer than 10 tumors
    - Under 3 cm in size
  - No difference DFS or OS
  - Mortality
    - 2.1% surgery vs 0% ablation
  - Ablation favored
    - Adverse events
    - Length of stay
    - Local control



Ablation VS Resection

- What do we need to replace the gold standard?
  - ✓ Equivalent or superior outcomes
  - ✓ Lower morbidity/complications
  - ✓ Shorter hospital stay
  - ✓ Lower cost



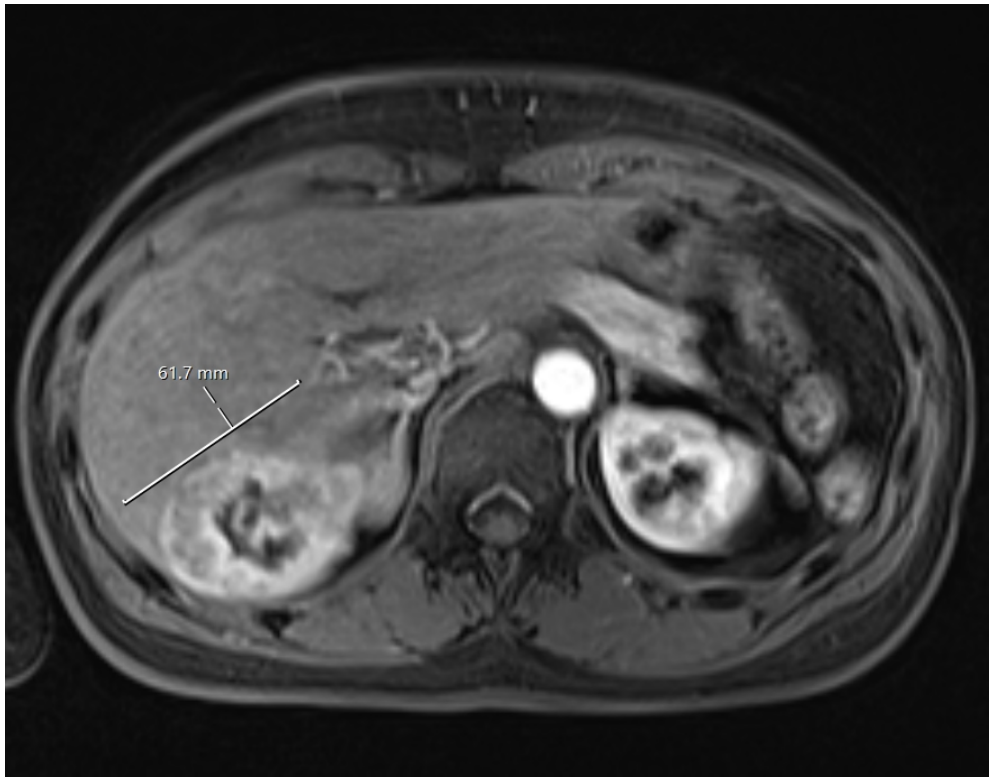
6 years later

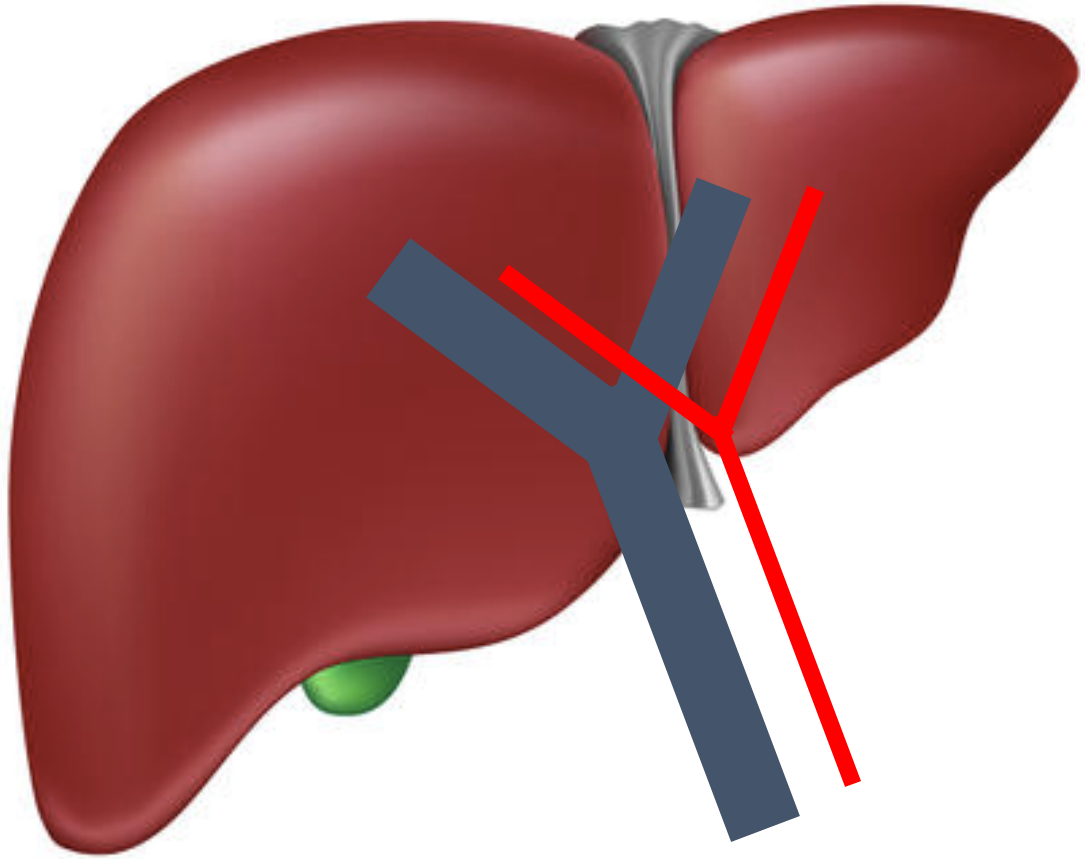
What happens when they get HUUUUGE!

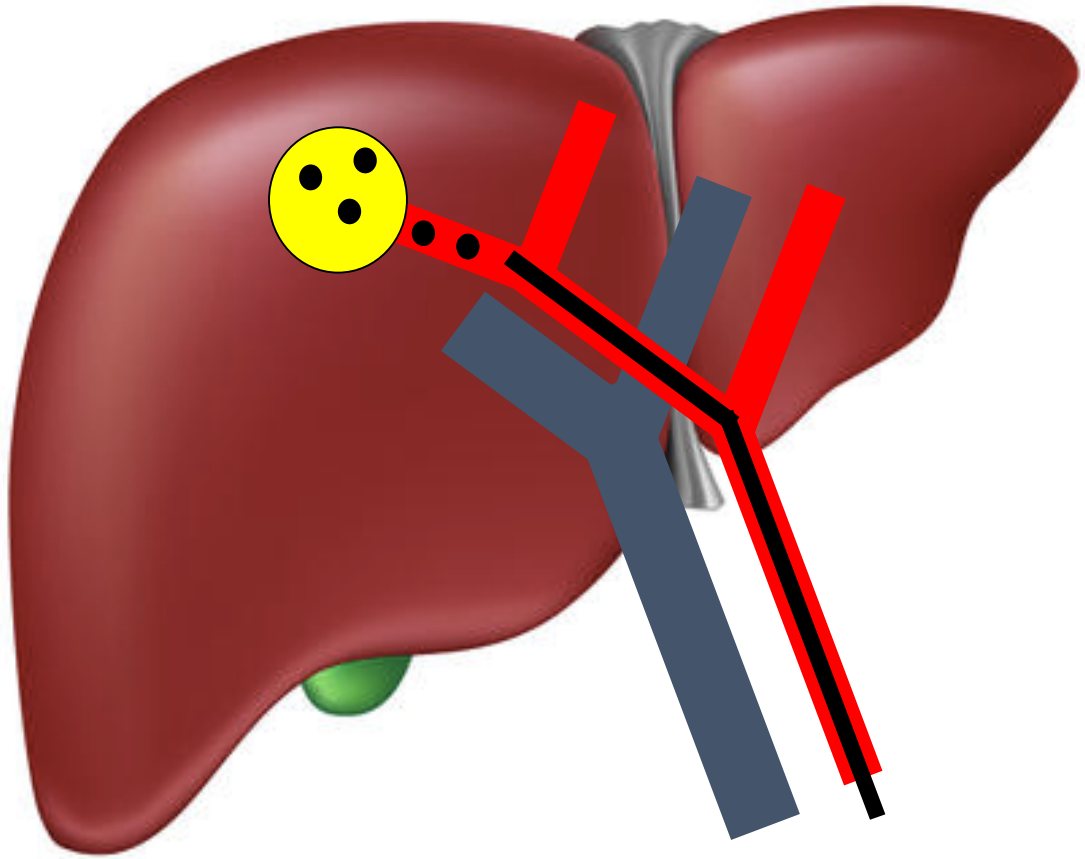
- How big is too big to treat?
- Is cure still possible?

Tumors >3cm

- Thermal ablation becomes less effective as tumors get larger
- Standard minimally invasive treatments
  - TACE
  - TACE + ablation (3-5 cm)
  - TAE
  - TARE (y-90)

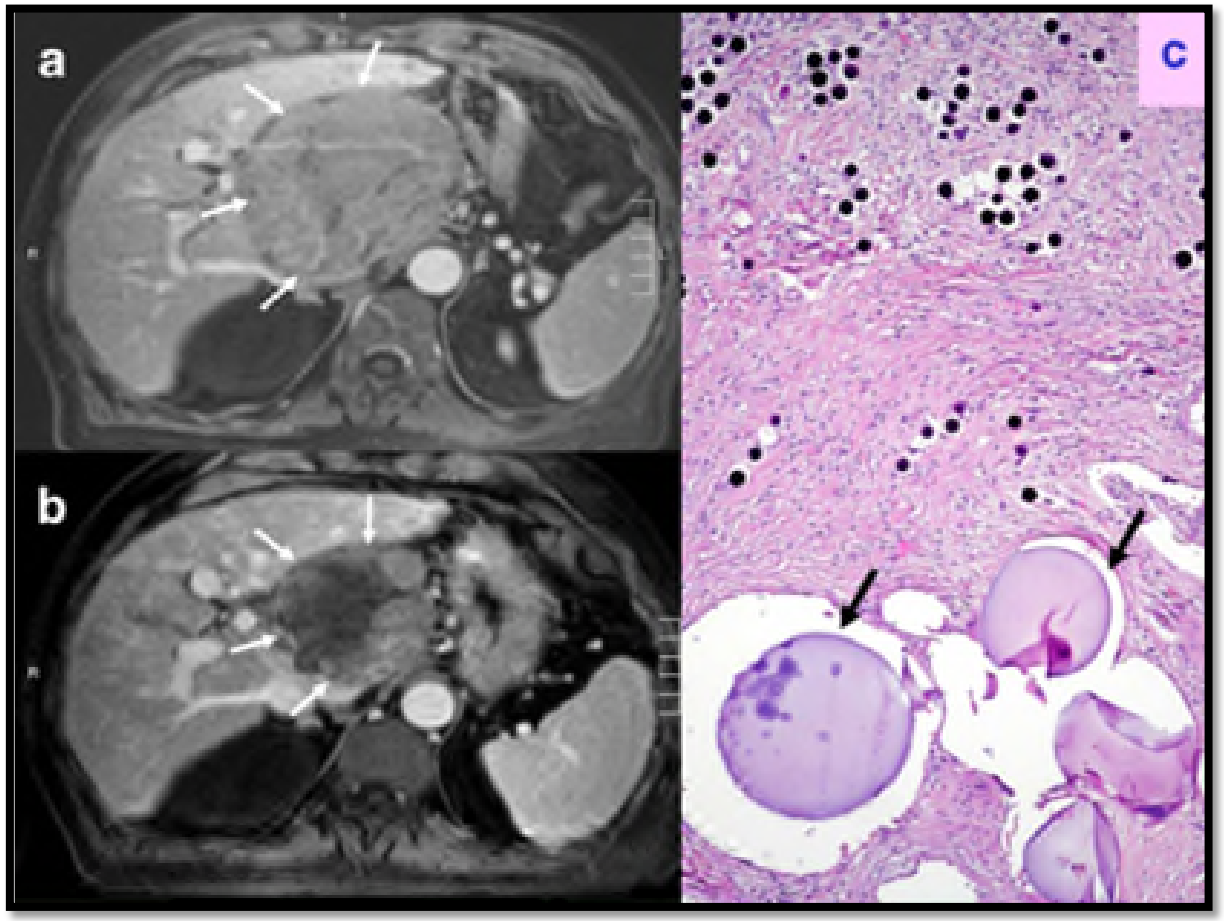






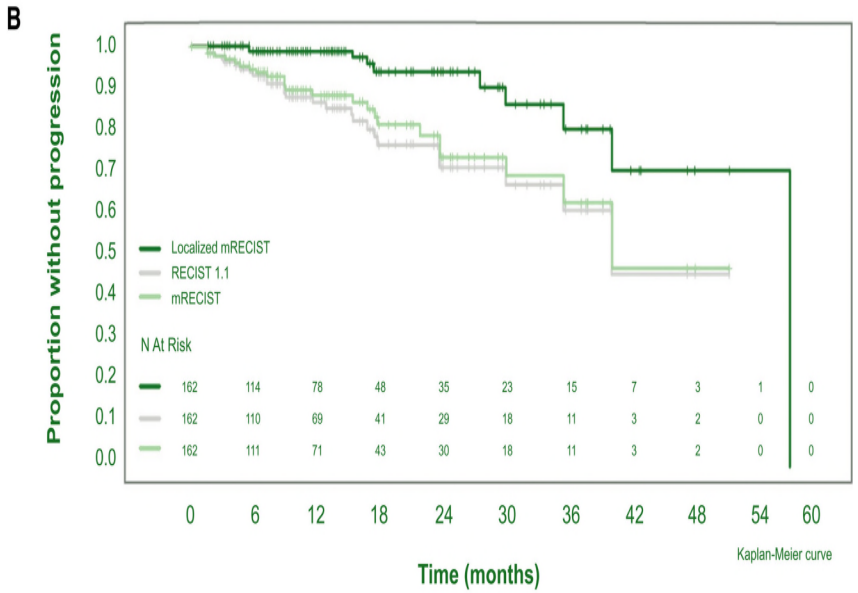
Radioembolization

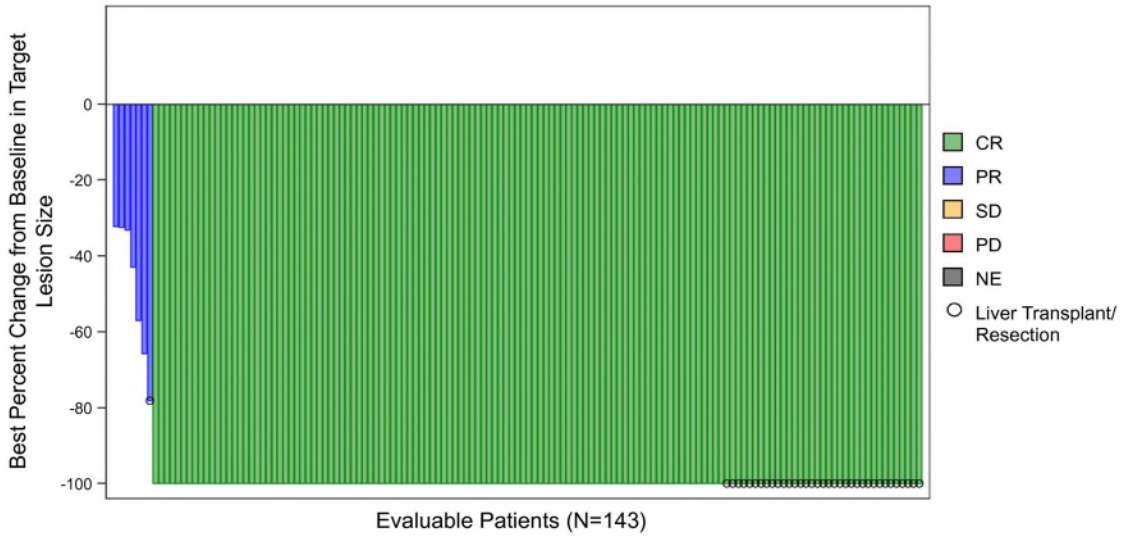
- Yttrium 90
  - pure beta-emitter with a half-life of 64.2 hours.
  - Tissue penetration of the emissions is 2.5 to 11 mm
  - Emits local high dose of radiation to tumor with little embolic effect.
  - Treatment done as outpatient procedure
  - May deliver 200- 1000Gy to tumor!!!



Legacy Study

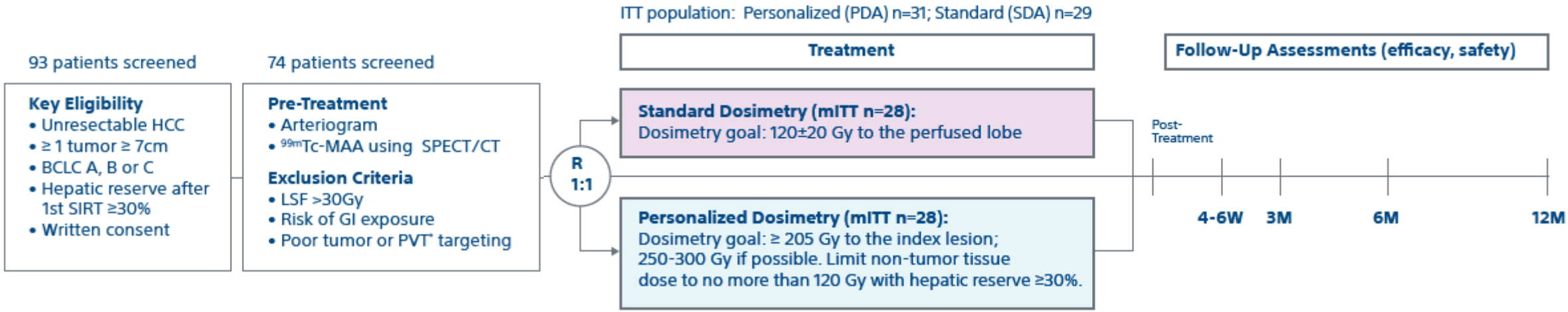
- Can we cure large tumors?
  - o Multicenter single arm 162 pts
    - Solitary Tumor up to 8 cm
    - ORR 88.3%
    - PFS 93.9% at 24 months
    - 84% 3 yr OS without surgery
    - 93% 3yr OS when downstaged to surgery/txplt





Salem et al **Yttrium-90 Radioembolization for the Treatment of Solitary, Unresectable HCC: The LEGACY Study Hepatology 2021**

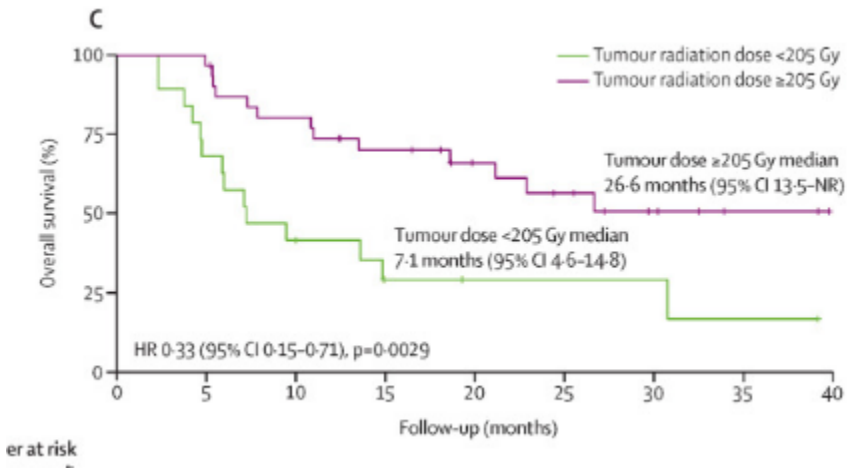
DOSISPHERE-01 trial



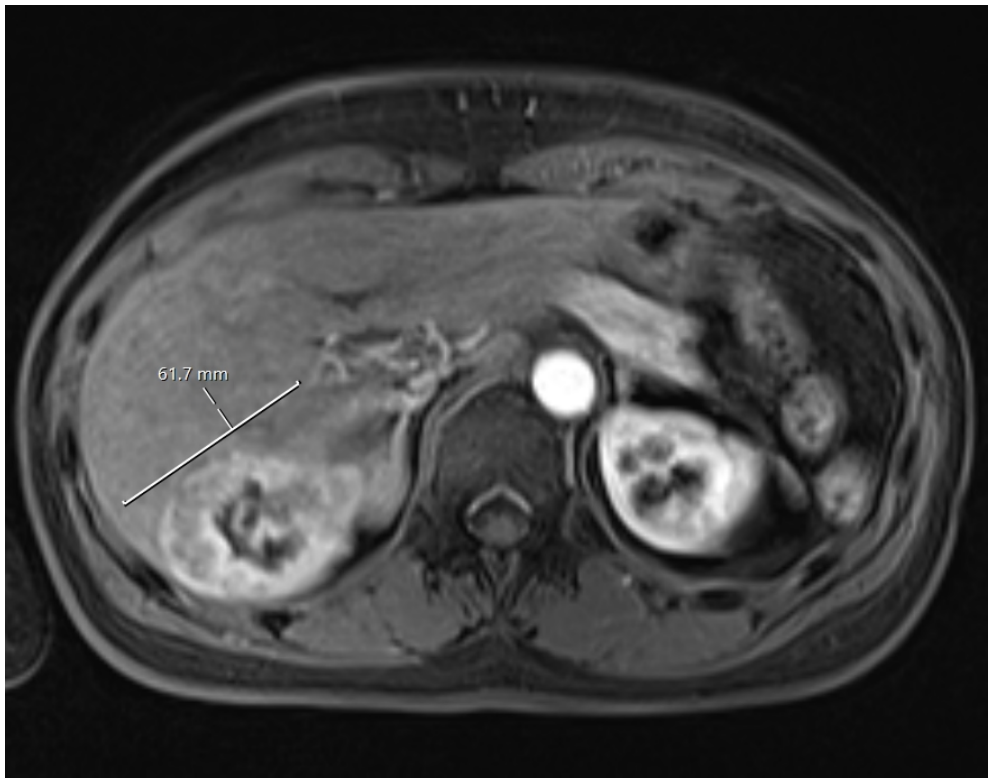
Majority of patients BCLC- C with PVT!

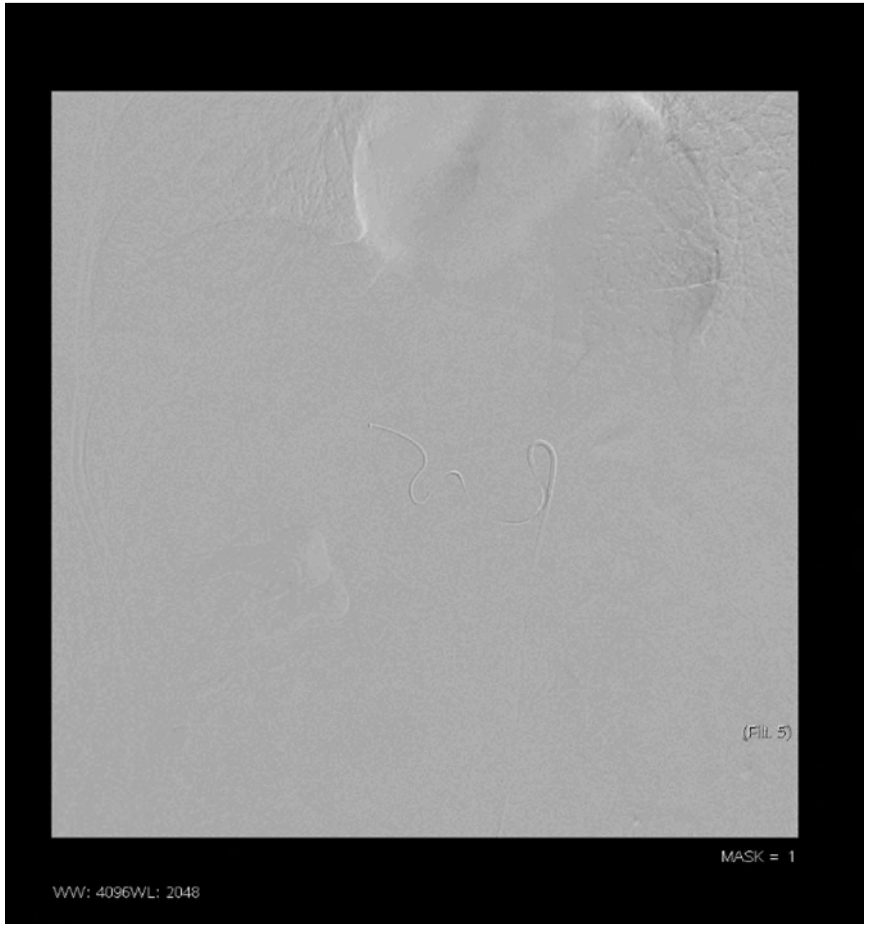
DOSISPHERE-01 trial

- 71% Objective response
- Median Overall Survival 26.6 months

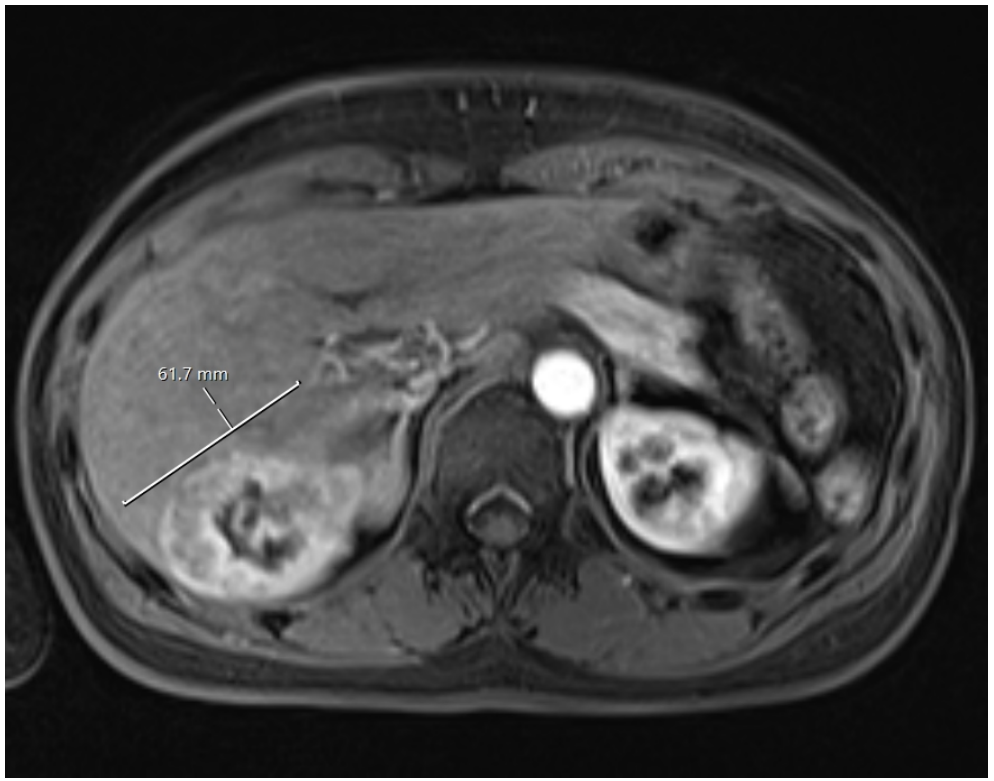


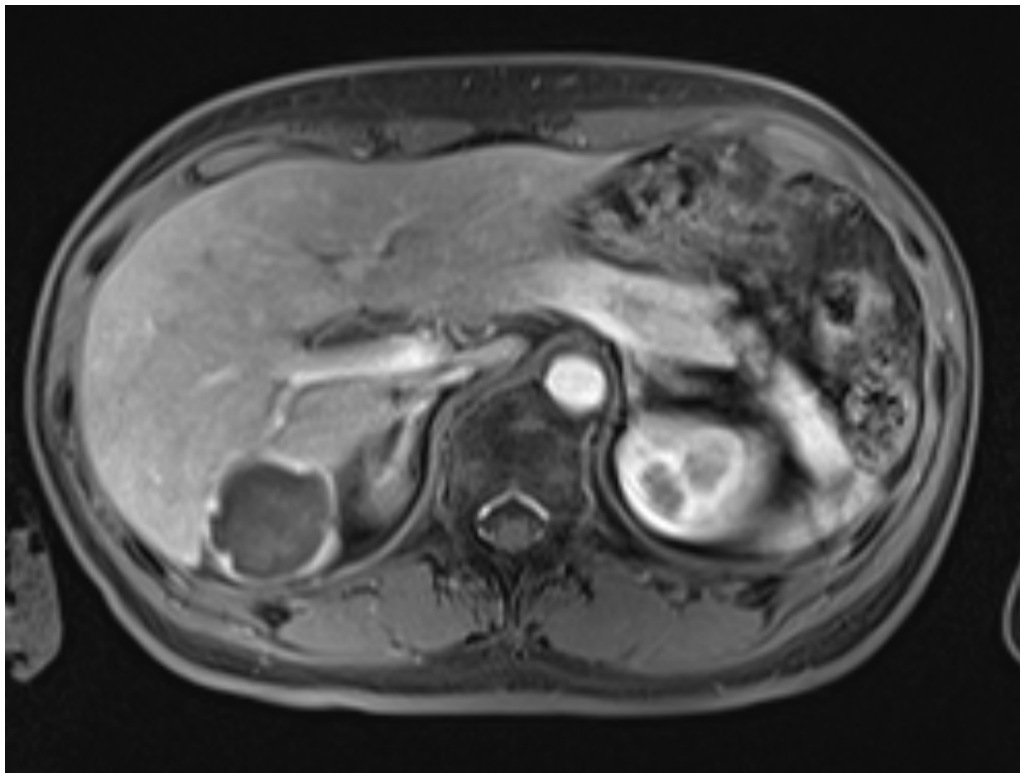
Curative Y90





Curative Y90



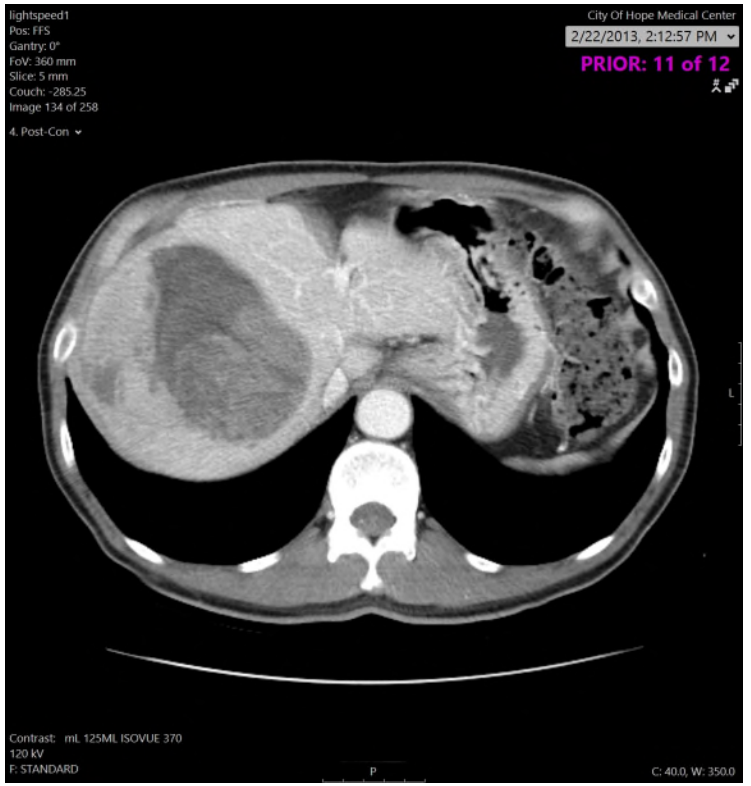


1 yr later


yes i win

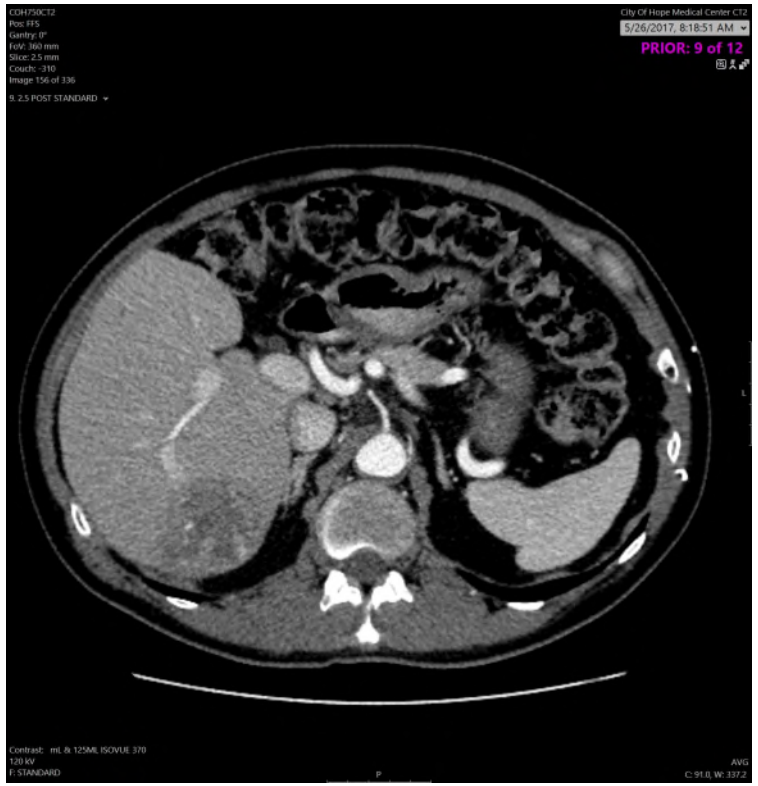
Multidisciplinary Dream Team

- 57 yo man with right liver HCC



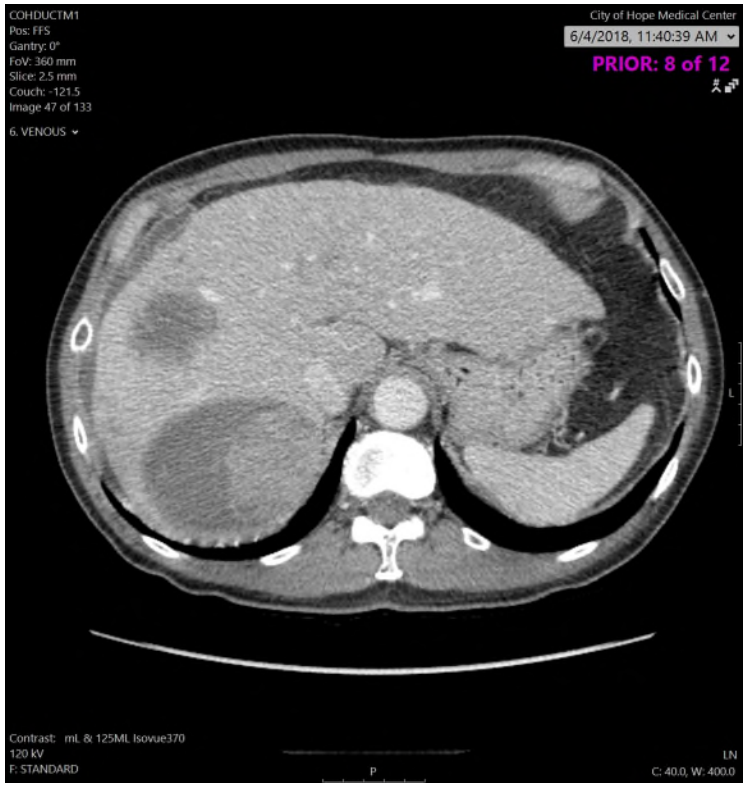
2/2013

- 57 yo man with right liver HCC
  - Embolization
    - 3/2013
    - 5/2013
  - Bone LN mets
    - Radiation -3/2014
  - Recurrence 5/2017
    - Embolization x3 2017



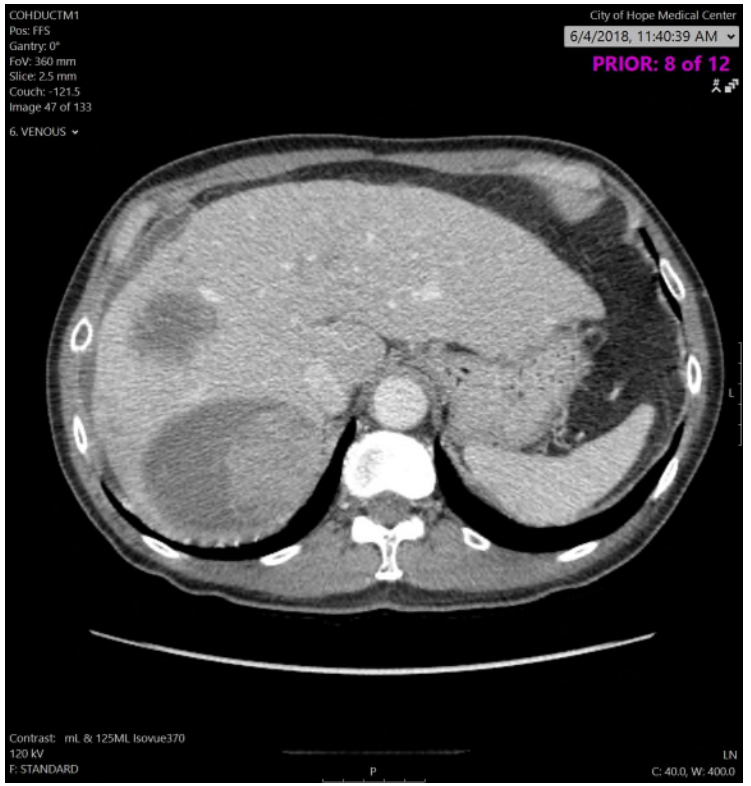
5/2017

- 57 yo man with right liver HCC
  - Embolization
    - 3/2013
    - 5/2013
  - Bone LN mets
    - Radiation -3/2014
  - Recurrence 5/2017
    - Embolization x3 2017
  - Recurrence 6/2018



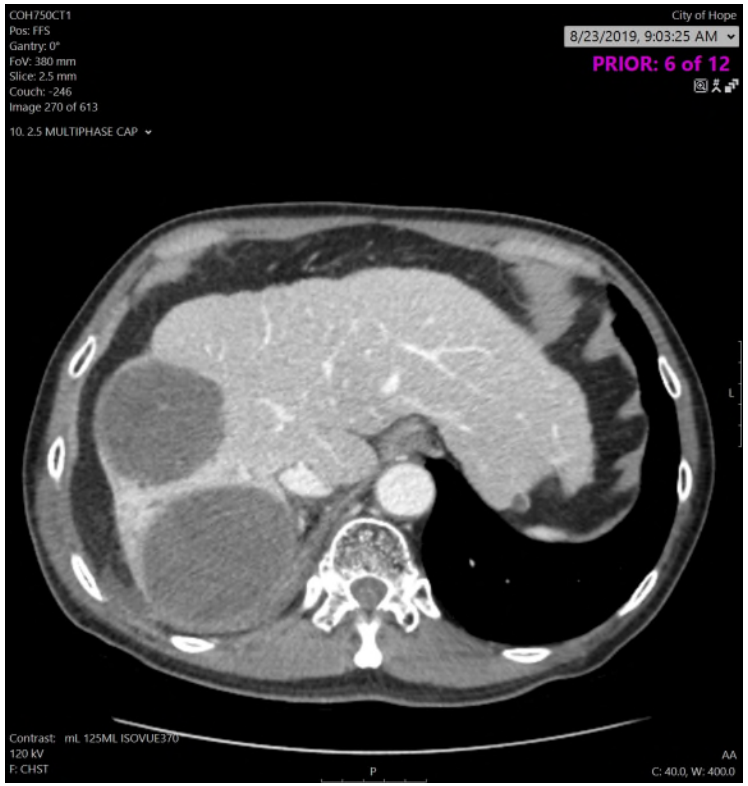
6/2018

- 57 yo man with right liver HCC
  - Embolization
    - 3/2013
    - 5/2013
  - Bone LN mets
    - Radiation -3/2014
  - Recurrence 5/2017
    - Embolization x3 2017
  - Recurrence 6/2018
    - SBRT 7/2018



6/2018

- 57 yo man with right liver HCC
  - Embolization
    - 3/2013
    - 5/2013
  - Bone LN mets
    - Radiation -3/2014
  - Recurrence 5/2017
    - Embolization x3 2017
  - Recurrence 6/2018
    - SBRT 7/2018
  - Deceased 1/2023



8/2019

57 yo man diagnosed with unresectable HCC in 2013

Embolization

3/2013

5/2013

6/2017

8/2017

11/2017

2/2018

3/2018

Radiation

Bone and LN 3/2014

Liver 7/2018

Lung 4/2020

Systemic

7/2014 clinical trial

2017 Pembrolizumab

12/12/18 regorafenib

4/17/19 cabozantinib

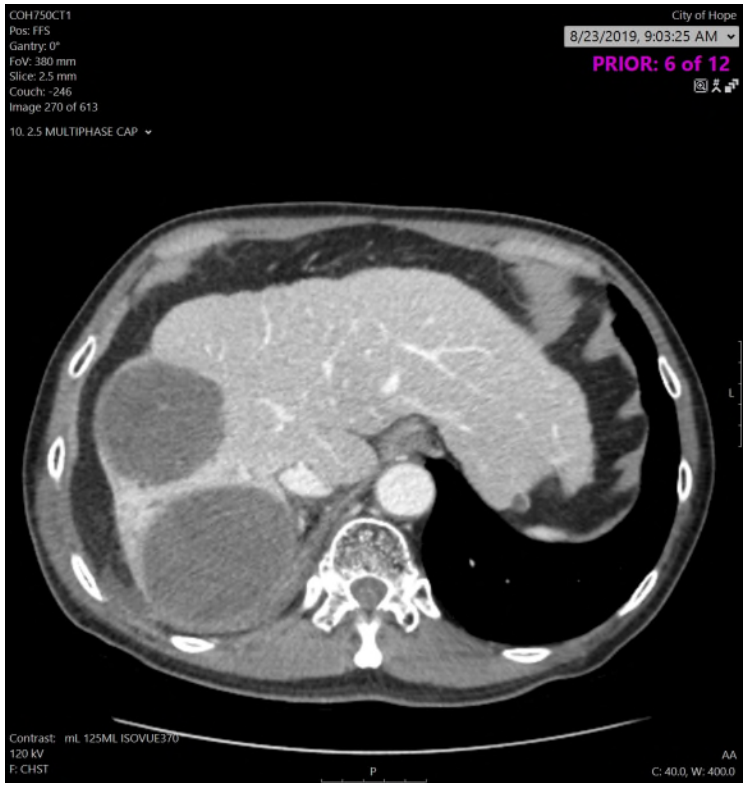
8/31/19 lenvatinib

2/16/21 nivolumab + ipilimumab

5/4/21 FOLFOX

4/22 atezo+bev

7/2022 CAR-T clinical trial



10 year survival post diagnosis with unresectable HCC