

Emerging Role of Precision Radiation – SBRT in Liver Tumors

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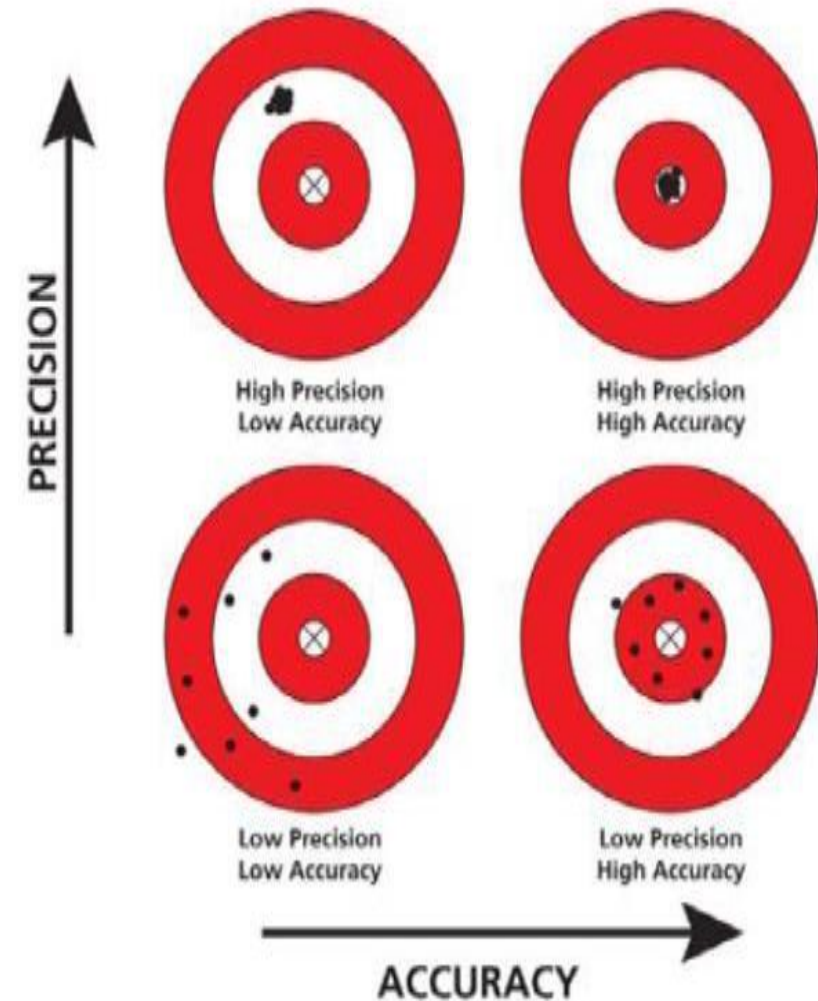
General Basic Concepts

What is Stereotactic Body Radiotherapy?

**ASTRO – ACR CARO AAPM National Radiotherapy
Implementation** group UK all agree that SBRT is:

1. A method of **external beam radiotherapy**
2. **Accurately** delivers a
3. **High dose** of radiation
4. **One or few** treatment fractions
5. To an **extracranial target** using **tumor site specific imaging modalities**

- The major feature that separates SBRT from conventional radiation treatment is the **delivery of large doses in a few fractions**, which results in a high biological effective dose BED.
- **In order to minimize the normal tissue toxicity**, conformation of high doses to the target and rapid fall-off doses away from the target is critical.
- **The practice of SBRT therefore requires a high level of confidence in the accuracy of the entire treatment delivery process.**



The term “accurate” covers

- **Disease staging**
- **Multidisciplinary discussion of the indications for SBRT**
- **Tumor site adjusted imaging with appropriate spatial and temporal resolution for target and organ at risk (OAR) definition**
- **Highly conformal treatment**
- **Image-guided patient setup**
- **Active or passive intrafraction motion management and**
- **Follow-up**

TARGET DEFINITION THE WEAKEST LINK

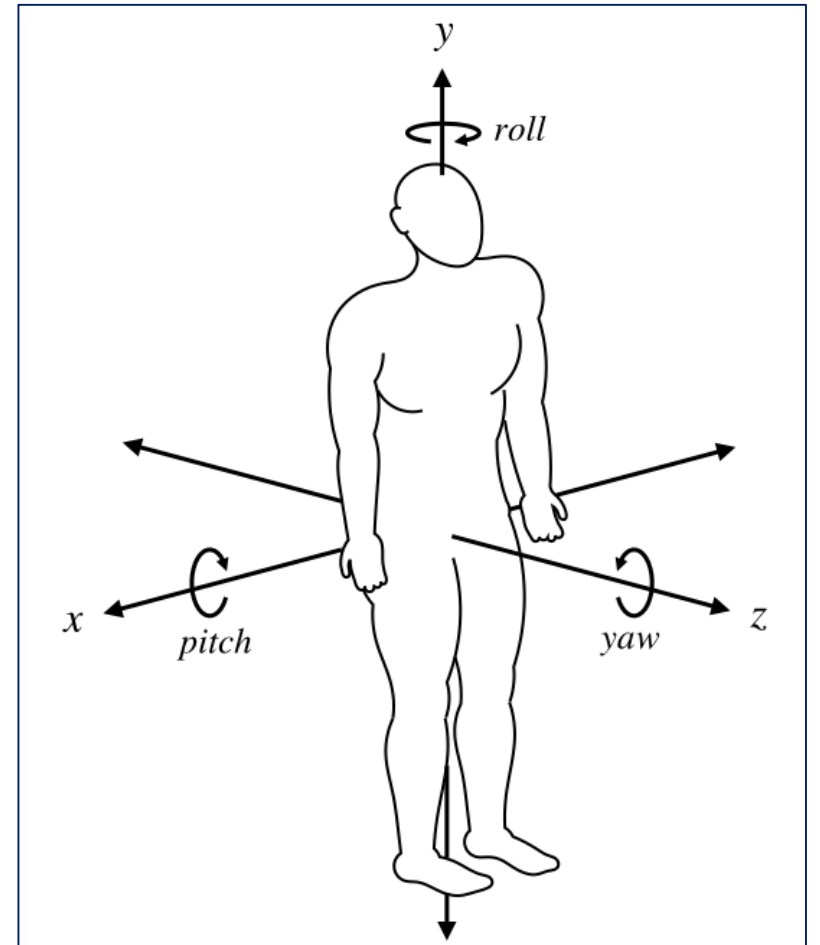
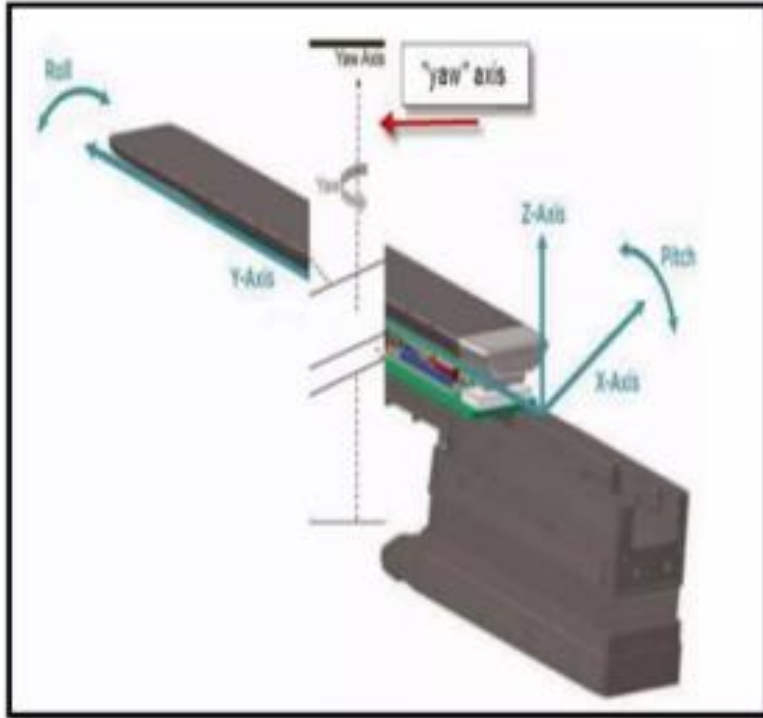
SUPERIMPOSITION OF DIFFERENT IMAGING MODALITIES HELP

STEREOTAXY IS A DYNAMIC PROCESS

STEREOTAXY IS NOT 3D CRT

Why is SBRT so complex in terms of degree of freedom of movement/motion?

Understanding **Yaw / Pitch / Roll**



Orange Peel Effect



$$V = \frac{4}{3}\pi r^3$$

Orange and its peel representing a target volume and its margin.

A 6.5 mm thick margin (peel) consists of the same volume as a 5 cm diameter target (orange)

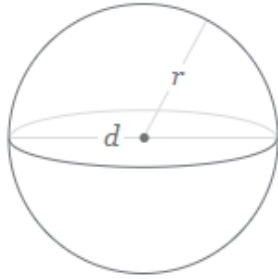
SPHERE VOLUME EFFECT

Sphere

Solve for volume ▾

$$V \approx 0.52$$

r Radius

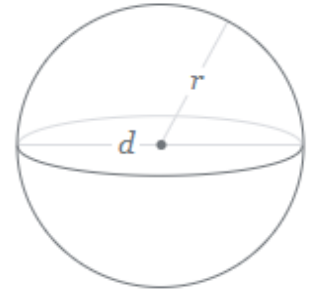


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Solve for volume ▾

$$V \approx 4.19$$

r Radius

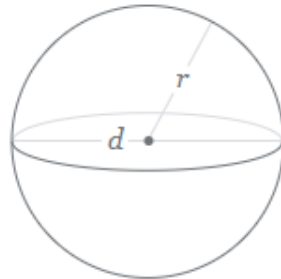


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Solve for volume ▾

$$V \approx 14.14$$

r Radius

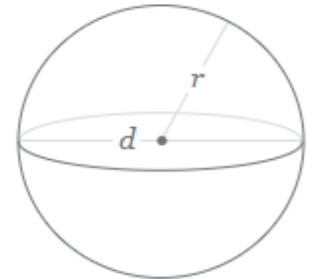


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Solve for volume ▾

$$V \approx 33.51$$

r Radius



REDUCTION IN PLANNING TARGET VOLUME

- Custom Immobilization
- Respiratory Management
- Image Guidance

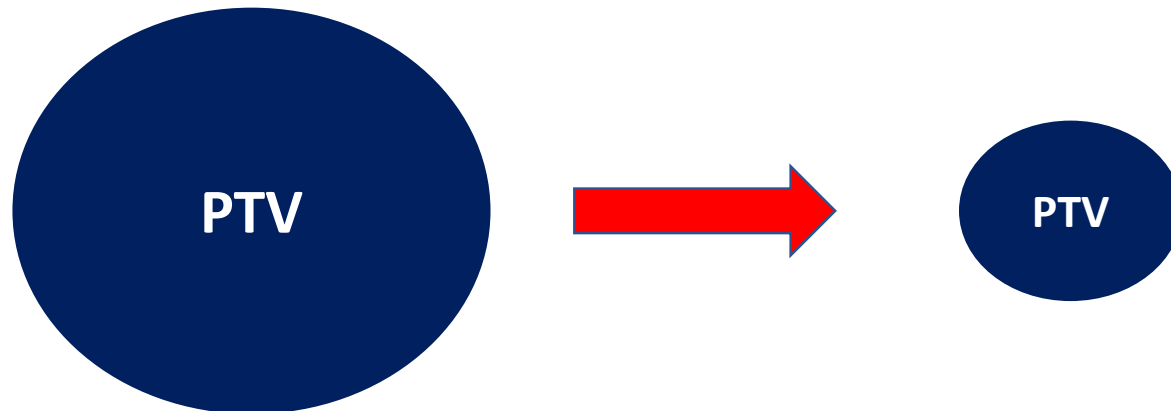
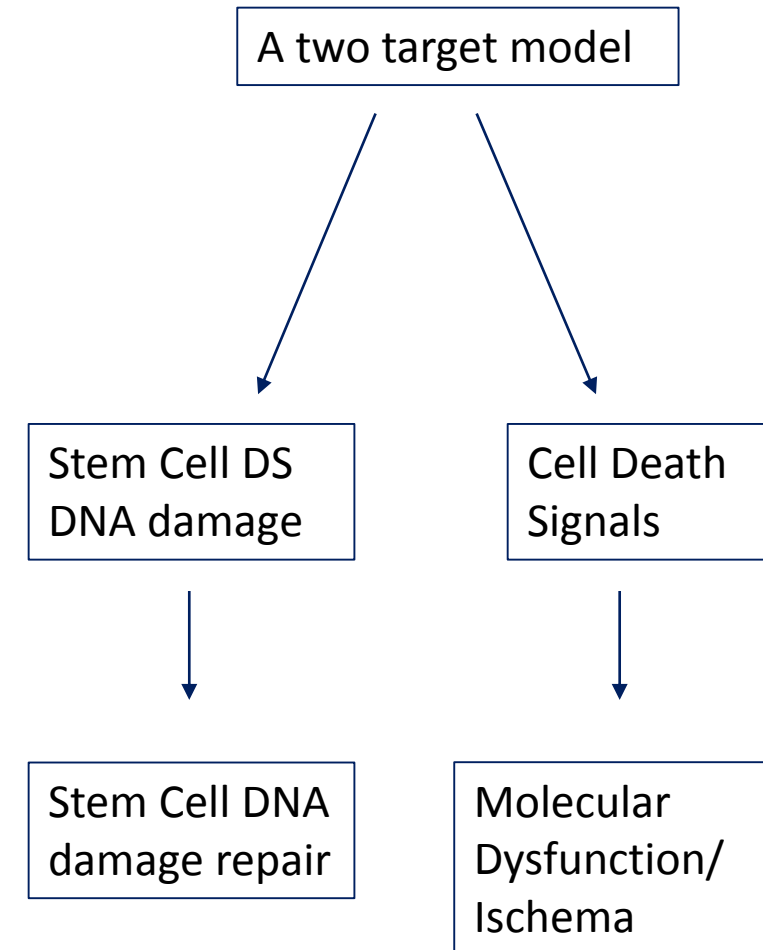




IMAGE GUIDED ABLATIVE STEREOTACTIC RADIOSURGERY

THE GAMET OF STEREOTAXY

- **Understanding biology** of hypofractionation and extreme hypofractionationapoptosis /vascular changes / DNA damage and repair / immune
- **Identification**- Physical and biological imaging
- **Precise delivery and safety** / individualised delivery and verification
 - CT / MRI? Pet correlaration
 - 4 D radiotherapy
- **Spatial integration** Stereotaxy and immunotherapy
- **Outcome measures** Survival / controls / QOL



SBRT IN HEPATOCELLULAR CARCINOMA

- BACKGROUND
- INCLUSION AND EXCLUSION
- EVIDENCE
- SIMULATION AND PLANNING
- DOSES
- CONSTRAINTS AND TOXICITIES
- TAKE HOME MESSAGE

Background

- Hepatocellular carcinoma (HCC) is the **most common malignant liver tumour**.
- As per **GLOBOCAN 2020**, HCC is the **6th most** common cancer worldwide and **the third leading cause of cancer-related mortality**.
- **Cirrhosis is the primary underlying aetiology** and is commonly caused by **viral hepatitis (hepatitis B and C), alcohol and non-alcoholic fatty liver disease secondary to obesity or diabetes mellitus**.
- The global burden of HCC **increased by 75% from 1990 to 2015**, and it is expected that the **annual increase by 2030 will be 35% greater than that in 2005**.

Background

The treatment of HCC is challenging and requires a multidisciplinary approach to decision making.

Various treatment modalities are available, such as:

- Liver transplant
- Hepatectomy
- Radiofrequency ablation (RFA)
- Microwave ablation
- Percutaneous ethanol injection
- Transarterial chemoembolisation (TACE)
- Transarterial radioembolization (TARE)
- Radiation therapy
- Targeted therapy and Immunotherapy

Surgical resection or liver transplant are considered curative options for early-stage HCC, most patients are not suitable for these therapies either due to:

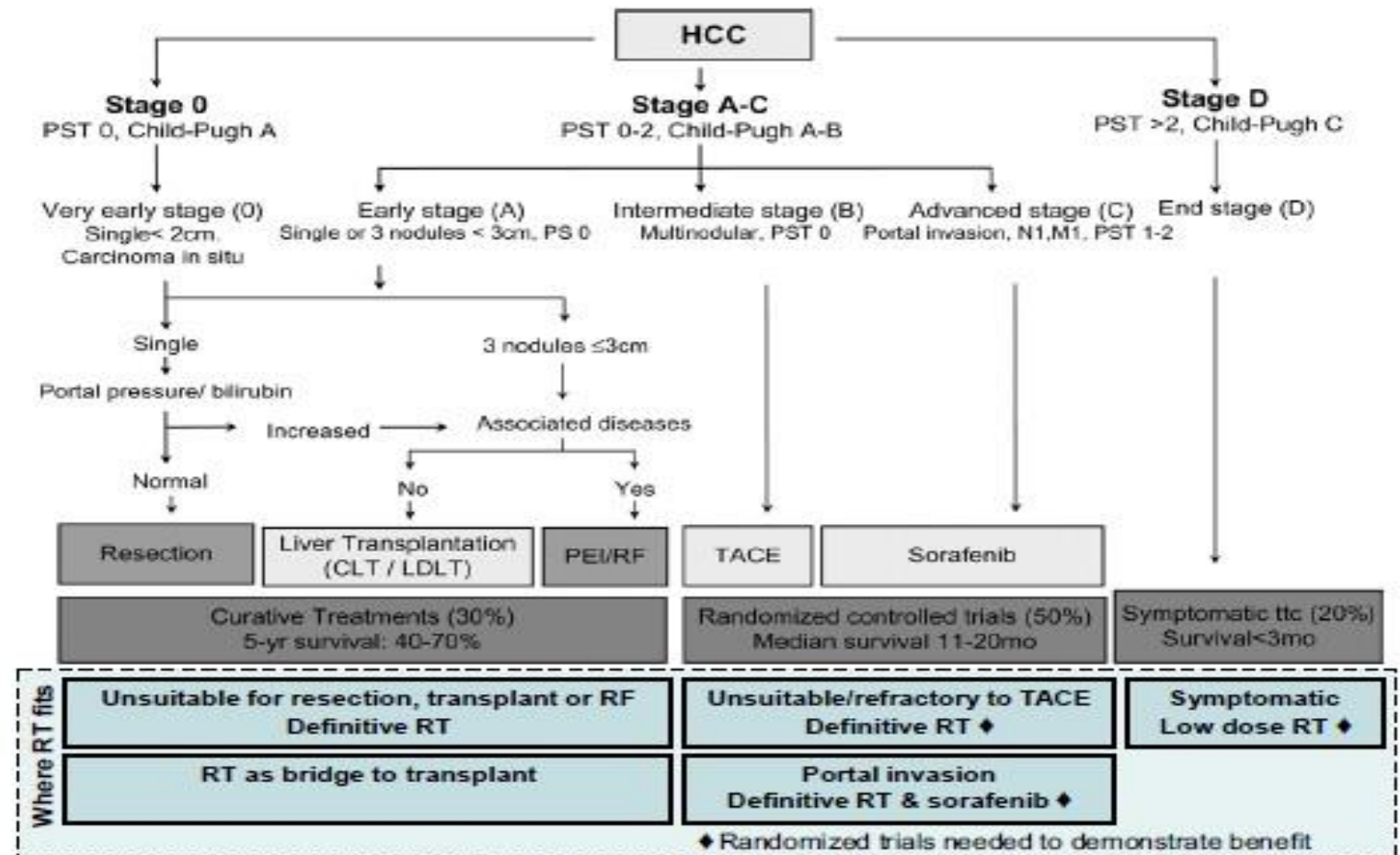
- **Medical contraindications**
- **Excessive burden of hepatic HCC**
- **Insufficient liver functional reserve**
- **Waiting list for transplants**
- **Advanced stage at presentation**
- **Unlike liver transplantation, resection does not treat the underlying cirrhosis present in the liver.**
- **Tumour recurrence is also more frequent after resection, with development of new lesions requiring further salvage treatments in the limited stage**

Local treatments for unresectable HCCs without portal vein thrombosis, include radiofrequency ablation (RFA) or other ablative approaches, which are associated with excellent local control (80-90%) for tumors away from large vessels and less than 3 cm, with reduced local control for larger tumors.

- Historically, external beam radiation therapy (RT) has not been used to treat HCC, primarily because **beyond whole liver doses of 28 Gy in 2Gy fractions**, the risk of radiation induced liver disease (RILD) increases
- Technological advances in radiation treatment planning, breathing motion management and image guided radiation therapy (IGRT), have made it possible for ablative doses of radiation to be delivered safely to focal unresectable HCC, using conformal RT, SBRT or protons.
- With focal radiotherapy the **incidence of RILD** has significantly reduced
- A high dose per fraction has several **effects at the molecular level, including initiation of various signal transduction pathways, modulating target cell phenotypes and initiating immune response, where there is a pro-inflammatory environment (activation of tumor-specific T cells, or increasing immune modulator molecules) that is triggered with radiotherapy allowing immunotherapies to be more effective.**

INDICATION, INCLUSIONS AND EXCLUSIONS

BARCELONA CLINIC LIVER CANCER STAGING



Shirley.et.al
JHEP Reports 2022

- In recent years, the use of Stereotactic Body Radiotherapy (SBRT) has increased as a result of its favourable therapeutic ratio. The use of SBRT either as stand-alone or adjuvant consolidative treatment after partial response to TACE (BCLC A-B) is associated with median overall survival of 13-45 months.
- SBRT is also associated with up to 10 months survival in patients with vascular invasion (BCLC C)

Indications

1. Patients with BCLC-A who are **not eligible for Surgery / TACE / RFA or failed TACE / RFA**, should be considered for liver **SABR**.
2. **In cases of Portal Vein Tumour Thrombus** - An effective option
3. SABR may be considered as a **bridge to transplant** if discussed within a transplant MDT
4. Emerging role in **oligometastatic** extrahepatic disease
5. Recurrent Tumors as salvage therapy

INCLUSION CRITERIA FOR SABR IN HCC

- CHILD PUGH A5-A 6, Select B7
- ECOG PS 0-2
- BCLC stage A - C (only for Portal invasion)
- Maximum single tumour size ≤ 10 cm, including any associated thrombus.
- No more than three intra-hepatic foci of radiologically confirmed active HCC
- Adequate normal functional liver reserve (Liver – GTV = 700 cc or higher)
- No extra-hepatic or abdominal nodal metastases
- No history of abdominal radiotherapy
- No concomitant Chemotherapy
- Distance from bowel , stomach , duoden - 1cm

EXCLUSION CRITERIA FOR SABR IN HCC

- Patients with CHILD > B7
- Intractable ascites
- Patients with active viral hepatitis (transaminases > 2.5 times ULN)
- History of hepatic decompensation
- Patients with platelet count < 50,000
- < 5mm distance from luminal gastrointestinal structures

EVIDENCE

Evidence: BCLC Stage 0/A.

RFA is the recommended first-line treatment for HCC less than 3 cm, if unresectable or not suitable for transplant, with 3-year local control rates of over 90%.

The application of RFA is challenging in situations where:

1. The tumour is **near vessels (heat sink effect)**
2. the **hilum or dome of the diaphragm** (risk of complications),
3. the **tumour is large** (resulting in incomplete ablation [2-60%] and poor outcomes).

SBRT in the definitive setting Early-stage HCC (BCLC 0/A)

Retrospective Matthew et.al

N=297

High risk (not suitable for RFA/TACE or had residual disease)

3-year OS:39% despite large tumors

Toxicity acceptable

Korean Study

Small HCC 1-3 cms

Treatment naïve

Retrospective

5-year LC and OS: 91% and 45%

SBRT in the definitive setting Early-stage HCC (BCLC 0/A)

No phase III randomized trials compared SBRT with RFA, TACE or surgery for early-stage primary HCC.

Meta-analysis by Pan et al.

10 studies

Comparing SBRT with RFA for treatment naïve HCC

Superior 1- and 3-year local control with SBRT.

The 2-year OS was possibly lower with SBRT due to variation in baseline liver function and tumour size.

After eliminating reporting bias, the secondary analysis showed equivalent 2-, 3- and 5-year OS rates between the 2 modalities.

Kim.et.al

phase III randomised non-inferiority trial

compared Proton Beam Therapy with RFA in recurrent HCC

(n = 144)

2-year local progression-free survival with PBT was non-inferior to RFA (92.8% for PBT vs. 83.2% for RFA).

The 4-year survival was similar between the 2 arms

Two ongoing randomized trials are comparing SBRT with RFA in small HCC in a definitive and recurrent setting (NCT03898921, NCT04047173).

Intermediate and advanced stage HCC (BCLC B/C)

TACE is a preferred treatment modality for patients with BCLC B HCC

Few studies have compared TACE with SBRT

Sapir et al.

Propensity score analysis of 209 patients with 1-2 tumours

TACE (n = 84) vs SBRT (n = 125).

The 2-year local control rate:

- SBRT 91%
 - TACE 23%
- (p<0.001)**

Bettinger et al.

TACE Vs SBRT in HCC BCLC B/C

1 year LC:

- TACE: 82.9 %
- SBRT: 84.8 %

1 year OS

- TACE: 52.9%
- SBRT: 53.1%

Ongoing studies are comparing TACE with SBRT:

NCT02470533

NCT03338647

Suggest SBRT is an alternative approach to TACE in patients with BCLC B HCC

The recent prospective and retrospective studies have shown **the safety and efficacy of SBRT with 2-year local control ranging from 68-95%**

Table 1. Select prospective and retrospective series showing outcome with stereotactic body radiotherapy.

Study	Patient number	Quality/type of study	Indication/ stage (BCLC)	Dose and fractionation	Follow up	Outcomes (LC/OS)	Toxicity (Grade 3 liver/GI)	Study conclusion	Level of Evidence ^a
Kim <i>et al.</i> , 2021 ³⁰	72	Phase III randomised trial- Proton vs RFA	0-C	66Gy/10Fr (Protons)	51.6m	2y LC: 92.8% 2y OS: 91.7%	none	Proton beam therapy was non-inferior to RFA and was tolerable.	II
Yoon <i>et al.</i> , 2020 ³¹	50	Prospective Phase II trial	0 and A (small HCC)	45 Gy/3#	47.8 m	5y LC: 97.1% 5y OS: 77.6%	4%	SBRT showed good results for ablation of small HCC with minimal toxicity.	IV
Labrunie <i>et al.</i> , 2020 ³²	43	Prospective Phase II trial	A-C	45 Gy/3#	4 y	2y LC: 94% 2y OS: 69%	5%	LC and OS was promising in HCC treated with SBRT.	IV
Jang <i>et al.</i> , 2020 ³³	65	Prospective Phase II trial	0-C	60 Gy/3#	41m	2y LC:97% 2y OS: 84%	2%	SBRT for HCC was well tolerated.	IV
Park <i>et al.</i> , 2020 ³⁴	290	Prospective Phase II trial	0-A	30-60Gy/3#	38.2m	5y LC: 91.3% 5y OS: 44.9%	8.8%	SBRT is an ablative option for small HCC.	IV
Mathew <i>et al.</i> , 2020 ³⁵	297	Retrospective	0-D	27-60Gy/3-6#	19.9m	3y LC: 87% 3y OS: 39%	16%	SBRT provides good LC and OS in HCC when it is unsuitable or refractory to other locoregional treatment.	VI
Kim <i>et al.</i> , 2019 ³⁶	32	Prospective Phase I/II trial	A-B	36-60 Gy/4#	27m	2y LC: 87% 2y OS: 81.3%	None	SBRT is a safe treatment for HCC.	IV
Hara <i>et al.</i> , 2019 ³⁷	143	Retrospective	0-C	35-40Gy/5#	30.2m	3y LC: 95.6% 3y OS: 63.6%	8.2%	SBRT for HCC provides results comparable to RFA and acceptable alternative to RFA.	VI
Feng <i>et al.</i> , 2018 ³⁸	90	Prospective Phase II trial	A-C	23-60Gy/5#	37m	2y LC:95%	7%	Individualized adaptive RT was safe and provided good LC.	IV
Takeda <i>et al.</i> , 2016 ³⁹	90	Prospective Phase II trial	0-C	35-40 Gy/5#	41.7m	3y LC: 96.3% 3y OS: 66.7%	6%	SBRT achieved high LC with acceptable toxicity in solitary HCC.	IV
Lasley <i>et al.</i> , 2015 ⁴⁰	59	Prospective Phase I/II trial	A-C	48 Gy/3# in CPA 40 Gy/5# in CPB	33.3m	3y LC: 82-91% 3y OS: 26.1- 61.3%	20%	SBRT is a safe treatment for HCC.	IV
Scorsetti <i>et al.</i> , 2015 ⁴¹	43	Prospective observational	A-C	48-75 Gy/3# to 36 Gy/6#	8m	2y LC: 64% 2y OS: 45%	16%	SBRT is safe with acceptable LC and toxicity.	IV
Bujold <i>et al.</i> , 2013 ⁴²	102	Prospective Phase I and II trials	A-C	24-56 Gy/6#	31.4m	1y LC: 87% Med OS: 17m	30%	Results provide strong rationale for studying SBRT as local treatment option in randomised phase III trials.	IV
Kang <i>et al.</i> , 2012 ⁴⁷	47	Prospective Phase II trial	A-C	42-60 Gy/3#	17m	2y LC: 94.6% 2y OS: 68.7%	6.4%	SBRT after incomplete TACE provides promising response and LC.	IV
Andolino <i>et al.</i> , 2011 ⁴³	60	Prospective observational	A-C	40-44 Gy/3-5#	27m	2y LC: 90% 2y OS: 67%	20%	SBRT is safe non-invasive option for HCC <6cm.	IV

Role of SBRT in HCC with PVT

Meta-Analysis > [Radiother Oncol](#). 2018 Oct;129(1):112-122. doi: 10.1016/j.radonc.2017.11.013.

Epub 2017 Dec 9.

Comparison of radiation therapy modalities for hepatocellular carcinoma with portal vein thrombosis: A meta-analysis and systematic review

Chai Hong Rim¹, Chul Yong Kim², Dae Sik Yang³, Won Sup Yoon⁴

The data from prospective and retrospective studies of 2513 patients who received 3D CRT, transarterial radioembolization (TARE), or SBRT for HCC with PVT to analyze overall survival, response rate, local control, and toxicity.

- The 1-year overall survival for the three modalities was similar (~ 44–48%). meta-analysis pooled
- Local control rate associated with SBRT (86.9%) and 3D CRT (82.8%) was higher than TARE (57.5%), and the overall response rate was higher from SBRT (70.7%) than 3D CRT (51.3%) or TARE (33.3%).
- More than two-thirds of the patients treated with SBRT experienced improved abdominal distention and/or discomfort.

[JAMA Oncol](#). 2018 May; 4(5): 661–669.

PMCID: PMC5885246

Published online 2018 Mar 15. doi: [10.1001/jamaoncol.2017.5847](#)

PMID: [29543938](#)

Efficacy and Safety of Transarterial Chemoembolization Plus External Beam Radiotherapy vs Sorafenib in Hepatocellular Carcinoma With Macroscopic Vascular Invasion

A Randomized Clinical Trial

[Sang Min Yoon](#), MD, PhD,¹ [Baek-Yeol Ryoo](#), MD, PhD,² [So Jung Lee](#), MD, PhD,³ [Jong Hoon Kim](#), MD, PhD,¹ [Ji Hoon Shin](#), MD, PhD,³ [Ji Hyun An](#), MD,⁴ [Han Chu Lee](#), MD, PhD,⁴ and [Young-Suk Lim](#), MD, PhD^{3,4}

A recent randomized trial compared local therapy with TACE and 3D CRT versus sorafenib in treatment-naïve patients with liver-confined HCC with macroscopic vascular invasion.

Patients treated with TACE-RT had a significantly higher radiologic response rate (15% vs. 1%) at 24 weeks and progression-free survival (86.7% vs. 34.3%) at 12 weeks and a longer median overall survival (55 vs. 43 weeks) and time to progress (31 vs. 11.7 weeks).

Bridge to Transplant –When?

- American Association for the Study of Liver Diseases recommends bridging therapy when waiting time is ≥ 6 months, and patients are often considered for the same when listed.
- The aim of local therapy in this setting is to prevent progression and downsize the tumour to maintain the eligibility for transplant

Bridge to Transplant - Evidence

University of Toronto Study

Demonstrated safety of conformal RT (8.5 – 33 Gy in 1-6 fractions)

5/10 patients had successful transplant without complications

Connor et al.

N= 10

SBRT (median 51 Gy in 3 fractions)

CR: 27 %

PR: 73%

Median time to transplant: 113 days

No increase in post-op complications

5-year OS and DFS: 100%

Mohammed et al.

Compared the pathological complete response rates (pCR) among the bridging treatments (SBRT, RFA, TACE and TARE)

lower pathological complete response rates with SBRT than other modalities (28.5% vs. 40-75%).

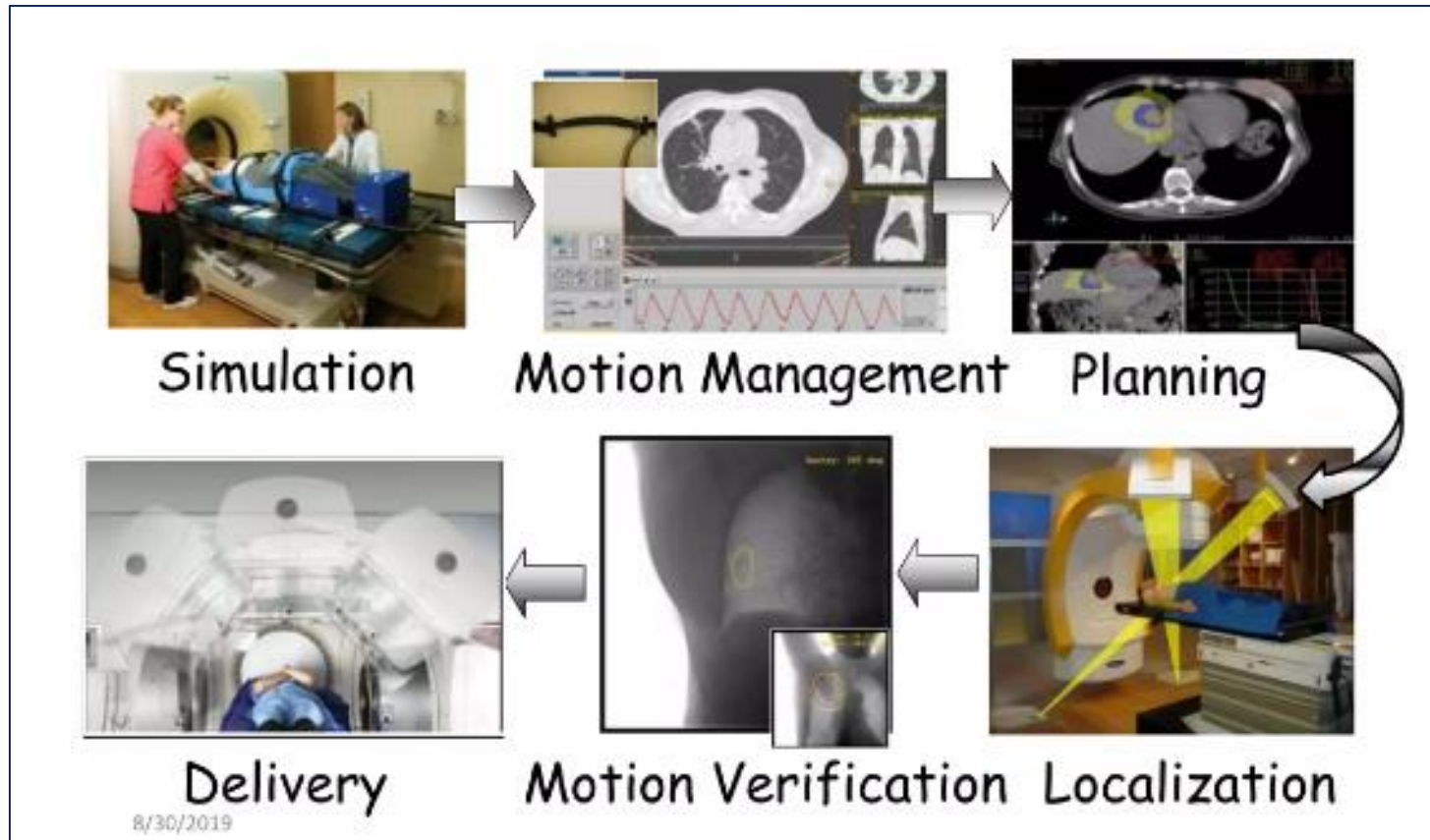
No prospective studies examining the efficacy and safety of SBRT in this setting, in direct comparison to more conventional treatments of RFA and TACE, based on retrospective data, SBRT appears to be a safe and effective alternative

Author	RT technique	Median dose (Gy)/fractions	Patients treated with SBRT or BT Total/ transplanted	Endpoints	Pathology	≥G3 toxicity	Liver constraints
Andolino et al. (21)	SBRT	40–44/3–5	60/23	LC, TTP, PFS, and OS	NA	21 × hematologic/ hepatic toxicity G3 of these 17 had preexisting G2 toxicities None	CPS A: 1/3 uninvolved liver ≤10 Gy V7 Gy≤500 cc CPS B: 1/3 uninvolved liver ≤18 Gy V12 Gy≤500 cc V27 Gy <70%
Katz et al. (22)	SBRT	50 (80%-iso)/10	18/12	Histological response	2 lesions had 100% necrosis 3 lesions had >50% necrosis 4 lesions had <50% necrosis 2 lesions had no necrosis		
O'Connor et al. (23)	SBRT	51 (50–66%- iso)/3	10/10	OS, DFS, acute toxicities, pathological response	3 lesions had no viable tumor 3 lesions had millimetric foci of viable tumor 5 lesions had residual tumor	None	Liver-PTV V15 Gy < 35% V15 < 700c cm
Mohamed et al. (24)	SBRT, yttrium-90 radio- embolization, TACE, RFA	50 (80%-iso)/5	24/14	Radiological and pathological response and DFS after LT, acute toxicity	4 lesions had 100% necrosis 6 lesions had >50% necrosis 2 lesions had <50% necrosis 2 lesions had no necrosis	None	V27 Gy < 70%
Guarneri et al. (25)	SBRT	40 (80%-iso)/5 or 48 (80%-iso)/ 3	8/8	Radiological response, pathological response, acute and late toxicities	8 lesions had CR 2 lesions had minimal pathological response 2 lesions had SD	1× non-classic RILD	Liver volume -PTV mean dose 15 Gy (> or < 700 ccm)
Moore et al. (26)	SBRT	54 (95%-iso)/3-5	23/11	OS, PFS, pathological response	3 patients had CR 6 patients had PR 2 patients had SD	1× RILD	V5 Gy <50%, V7 Gy <30%, V15 Gy <700 ccm for Child B mean liver dose <10 Gy
Sapisochin et al. (27)	SBRT, TACE, RFA	Not specified	36/30	Survival, pathological response	26 patients had some degree of tumor necrosis 4 patients had complete necrosis	None	Not specified
Rubinstein et al. (28)	SBRT, TACE, ETOH, RFA, MWA, SIRT	Not specified	2/2	Radiological response, pathological response	2× <80% pathological response	Not specified	Not specified
Uemura et al. (29)	SBRT	45/5	22/19	Pathological response	5 cases had CR 2 cases had PR 3 cases had minor necrosis 8 cases had no necrosis	None	Predicted functional liver volume (pFLV) V16 Gy <35% (4 fractions) V18 Gy <35% (5–6 fractions)
Gresswell et al. (30)	SBRT	40 (90%-iso)/5	12/11	Clinical outcome and toxicity	5 patients had CR 2 patients had extensive necrosis 1 patient had residual disease	None	Predicted functional liver volume (pFLV) V16 Gy <35% (4 fractions) V18 Gy <35% (5–6 fractions)
Denecke et al. (12)	BT, TACE	18.9/1	12/12	Matched-pair analysis	4 patients had complete/near total necrosis 7 patients had partial necrosis 1 patient had no necrosis	None	Not specified

LC, local control; TTP, time to progression; PFS, progression-free survival; OS, overall survival; CR, complete response; SD, stable disease; PR, partial response; NA, not applicable.

Walter F, Fuchs F, Gerum S, Rottler MC, Erdelkamp R, Neumann J, et al. HDR Brachytherapy and SBRT as Bridging Therapy to Liver Transplantation in HCC Patients: A Single-Center Experience. Frontiers in Oncology [Internet]. 2021;11. Available from: <https://www.frontiersin.org/articles/10.3389/fonc.2021.717792>

SBRT - Workflow



SIMULATION AND PLANNING

Patient Preparation

- Medical gastroenterology evaluation of functional liver reserve (FLR)
- Patients with oesophageal varices should be considered for prophylactic banding
- Patients with raised HBV antigen or viral titres should be started on anti-viral therapy at least 2 weeks before SABR
- SBRT should be planned 4-6 weeks after last TACE and 7-10 days after stopping oral Sorafenib (Restarted after 4 weeks)

Patient Preparation

- High-quality tri-phasic CT scan and/or a dynamic Magnetic Resonance Imaging (MRI)
- CBC, LFTs, AFP, Hepatitis B, C antigens and their viral titres
- Anti-emetics and PPIs before, during and 2 weeks after SABR
- Fasting 4 hours before simulation

CT Simulation

Immobilization: Vac Loc with arms above head (Abdominal compression as meritted)

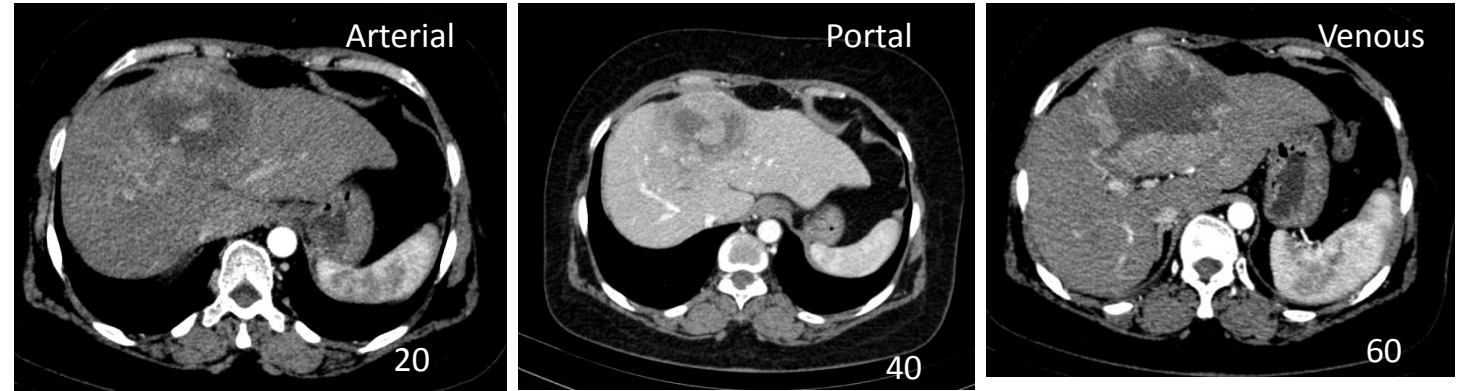
CT protocol:

- Triphasic scan in DIBH or with abdominal compression
- 4 D CT to identify motion. Motion management if > 1 cm motion. i.v contrast 1 mL/ kg at 2 mL/s; A multi-phase contrast enhanced planning CT scan
- Arterial phase and/or portal phase ima imaging recommended for GTV delineation, and venous phase for portal vein thrombosis delineation is ideal.

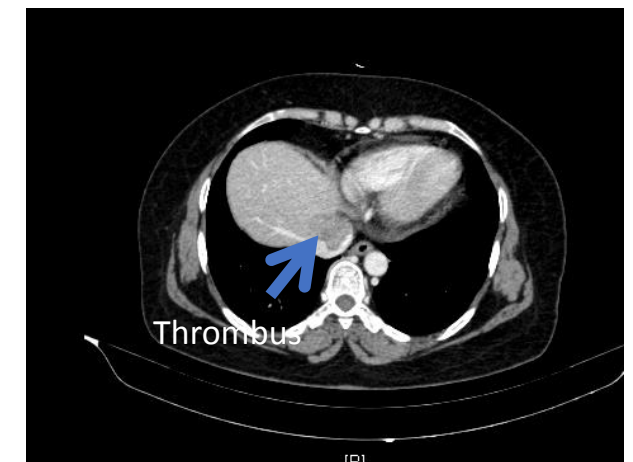
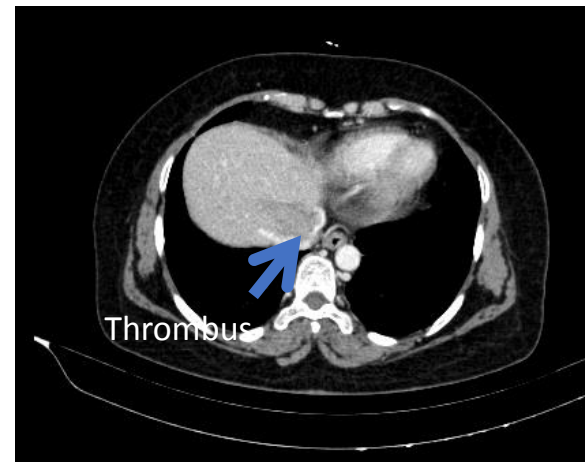
Scan delay:

- late arterial phase: 25-35 seconds post contrast injection
- portal venous phase: 55-70 seconds post contrast injection
- delayed phase: 2-5 minutes

High Quality Triphasic Scan with IV Contrast



Extremely crucial to coordinate contrast injection with deep inspiratory breath hold



IMAGING FOR TREATMENT PLANNING



**REVIEW IMAGING
WITH DIAGNOSTIC
RADIOLOGIST**



**TRIPHASIC CECT
IDEAL/ DYNAMIC MRI
COMPLIMENTARY**



**NO NEED FOR PET
FOR HCC**



**BACKGROUND OF
CIRRHOSIS TUMOUR
VS REGENERATIVE
NODULES**



**AREAS OF PREVIOUS
TREATMENT
(RFA/LIPIDIOL/
SURGICAL CLIPS)**



**VASCULAR
THROMBOSIS**

MOTION MANAGEMENT STRATEGIES

1. Active Breathing Coordinator

2. Marker based matching or tracking

3. RPM based gating

4. Calypso based gating

5. Tracking the tumour - Fiducials

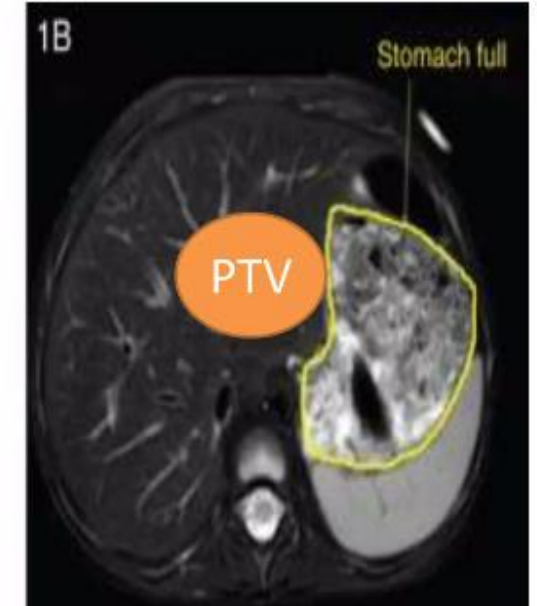
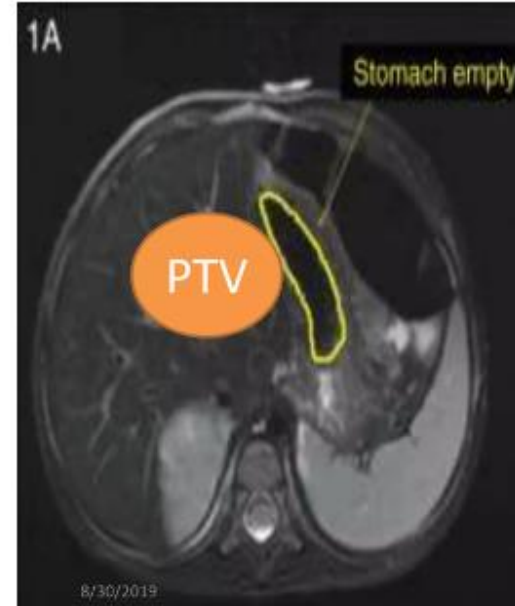
6. Abdominal compression

- Treat on Internal Target Volume (ITV), which is the tumor volume on all respiratory phases plus additional set-up margins (4DCT)
- To achieve a reduction in the volume treated is with breath-hold or abdominal compression. Abdominal compression is widely used in liver SBRT.
- Another way to reduce ITV is to identify all respiratory phases like in ITV basis treatment, but to choose the phases for treatment, either the most reproducible or the ones with the minimal movement.
- Respiratory management may use a variety of methods, including [respiratory gating](#), tumor tracking with fiducial implants etc
- If present, surgical clips of [previous surgery](#), [bile duct prosthesis](#), chemotherapy [catheters](#), lipiodol injected into the tumour during TACE might play the same role as fiducials

Handling Stomach Filling

1. Variation in gastric filling may lead to significant intra-fraction differences in dose to normal stomach
2. To mitigate this most clinicians recommend keeping patients fasting for 4 hour before simulation and each treatment fraction
3. However, treating patients at a consistent interval after meals also appears to result in reproducible gastric positioning and may be more comfortable for some patients.

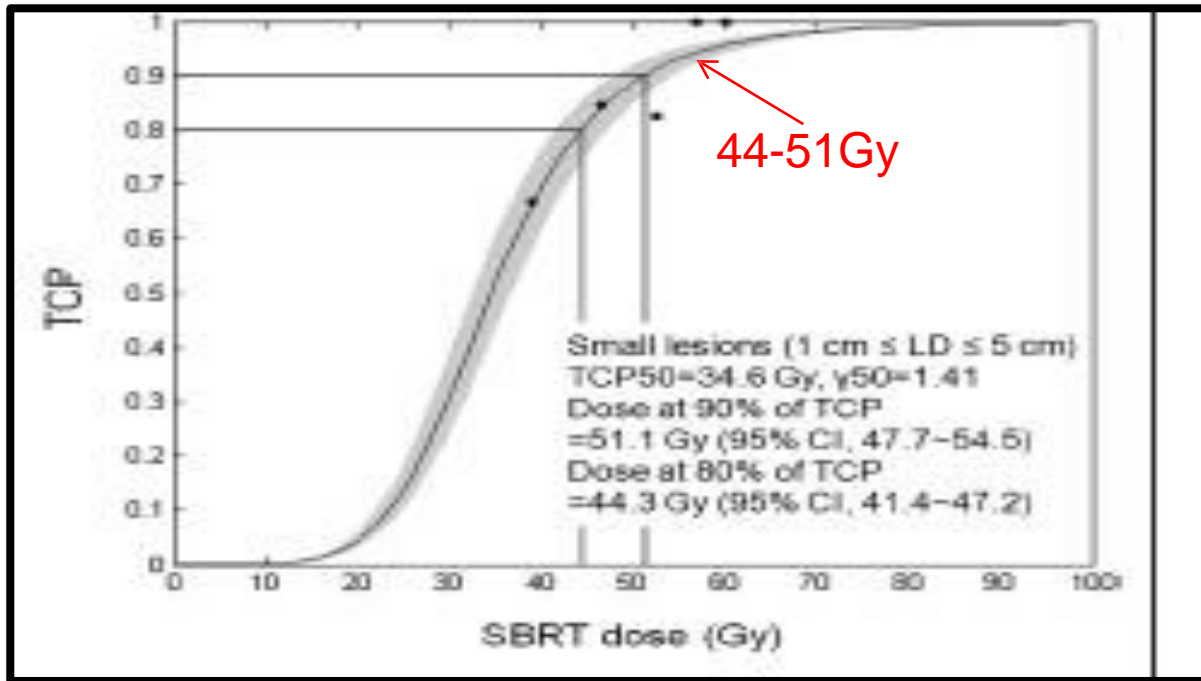
FULL VS EMPTY STOMACH



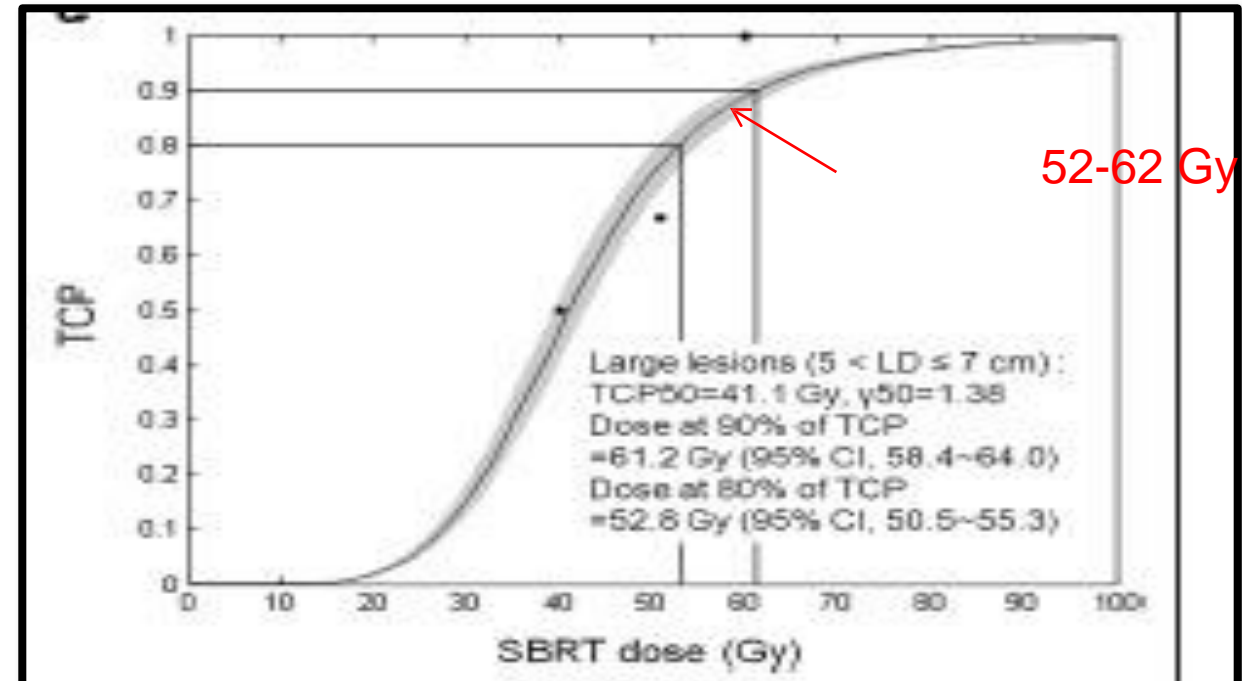
Contouring

Dose

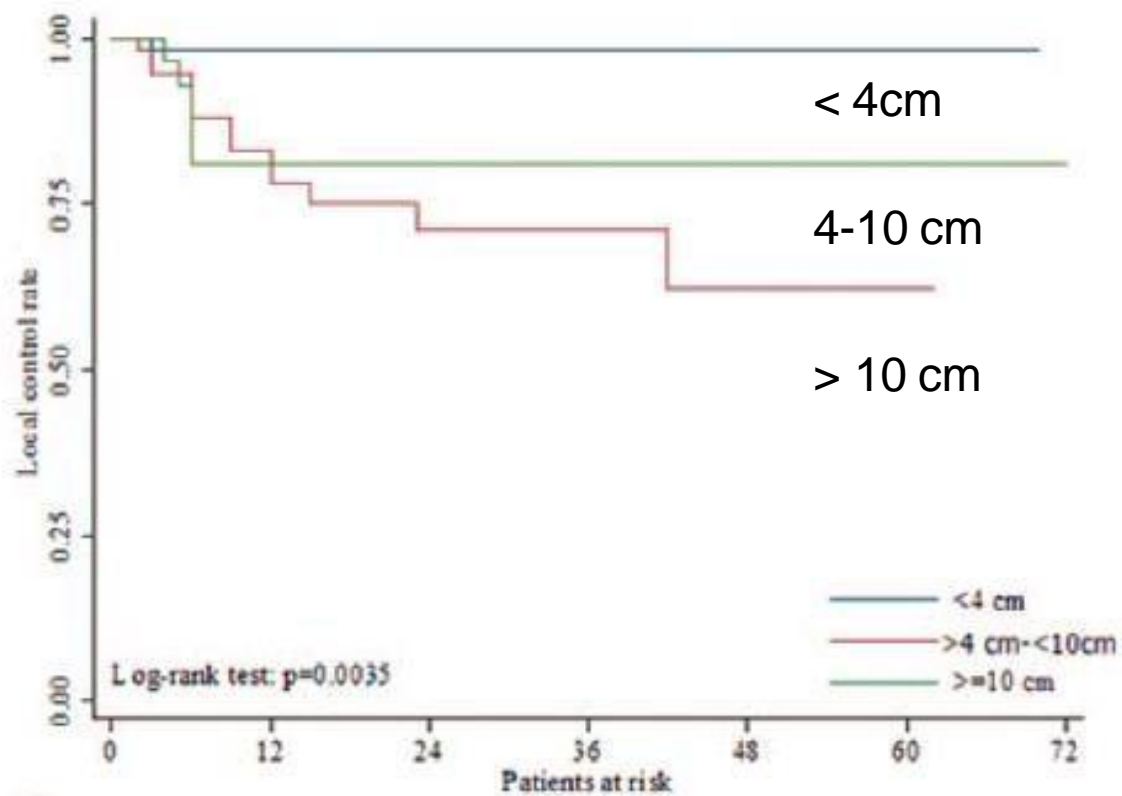
Dose Response Relationship: SBRT



1-5 cm Lesions

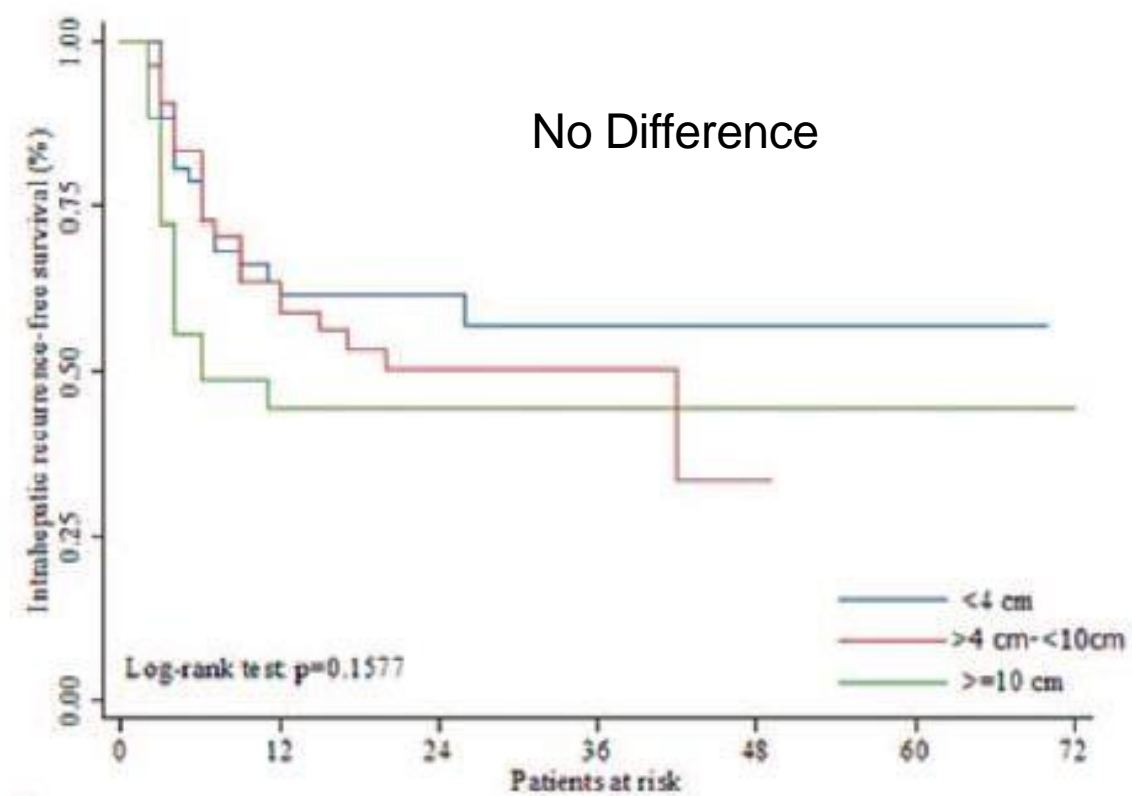


5-7 cm Lesions



A

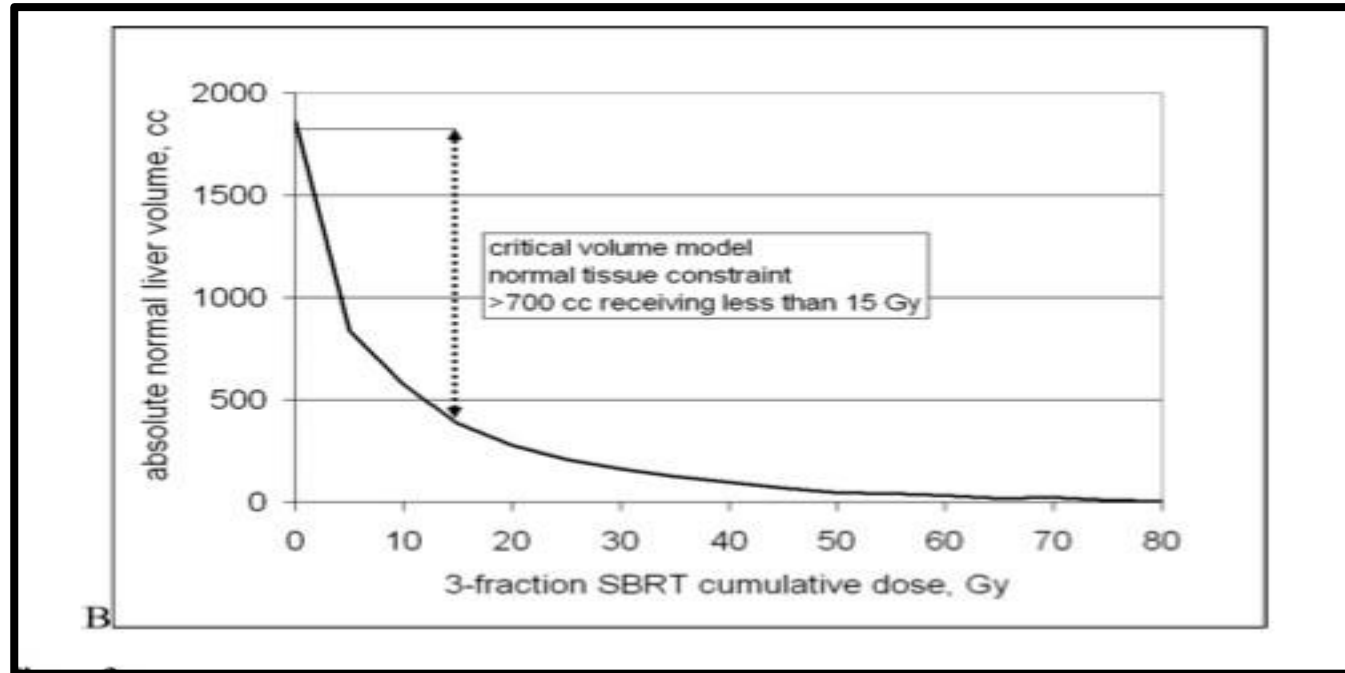
Local Control



B

Intrahepatic Recurrence free Survival

How Much Liver Will you Spare?



Partial Small Volumes could Tolerate Doses > 90 Gy

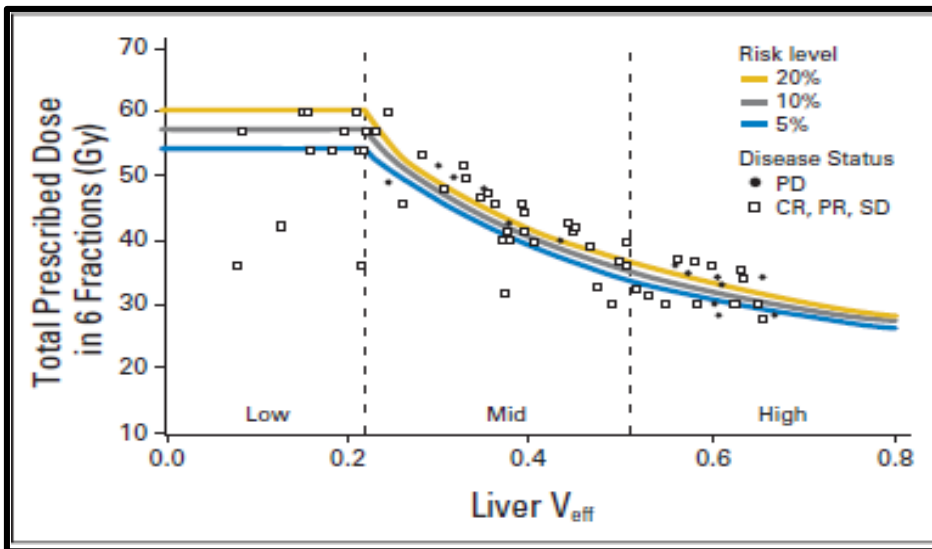
Child A

Mean Liver Dose important

Pan, Kavanagh, Dawson IJROBP 2010

Risk Adapted Liver SBRT

Akin to FLR assessment for Major Hepatic Resection



V eff	SBRT Dose Feasible	Biological Equivalence (Gy ₁₀)
0.20	54Gy/6Fractions	102
0.30	48 Gy/6 fractions	86.4
0.40	42 Gy/6 fractions	71.4
0.50	36 Gy/6 fractions	57.6
0.60	30 Gy/6 fractions	45

This is for patients with Intact Liver Function (Child A)

Dose Constraints

Table 2. Dose constraints for stereotactic body radiation therapy planning.

Organ at risk	Constraint for 3 fractions	Constraint for 5 fractions
Uninvolved liver (non-cirrhotic) ¹³⁷		
Mean dose	<12-15 Gy	<15-18 Gy
Dose to $\geq 700 \text{ cm}^3$	<19 Gy	<21 Gy
Uninvolved liver (Child-Pugh class A) ^{40,85,138}		
Mean dose	<10-12 Gy	<13-15 Gy
Dose to $\geq 700 \text{ cm}^3$	—	<15 Gy
Uninvolved liver (Child-Pugh class B) ^{40,85,138}		
Mean dose	None	<8-10 Gy
Dose to $\geq 500 \text{ cm}^3$		<10 Gy
Stomach ¹³⁷		
D 0.03 cm^3	<22 Gy	<32 Gy
D 10 cm^3	<16.5 Gy	<18 Gy
Duodenum ^{137,139}		
D 0.03 cm^3	<22 Gy	<32 Gy
D 5 cm^3	<16.5 Gy	<18 Gy
Small bowel ^{137,139}		
D 0.03 cm^3	<22 Gy	<32 Gy
D 5 cm^3	<18 Gy	<19.5 Gy
Large bowel ^{137,139}		
D 0.03 cm^3	<28 Gy	<34 Gy
D 20 cm^3	<24 Gy	<25 Gy
Common bile duct ⁸⁸		
D 0.5 cm^3	40 Gy	40 Gy

SBRT for Central Lesions

Central Biliary Structures:

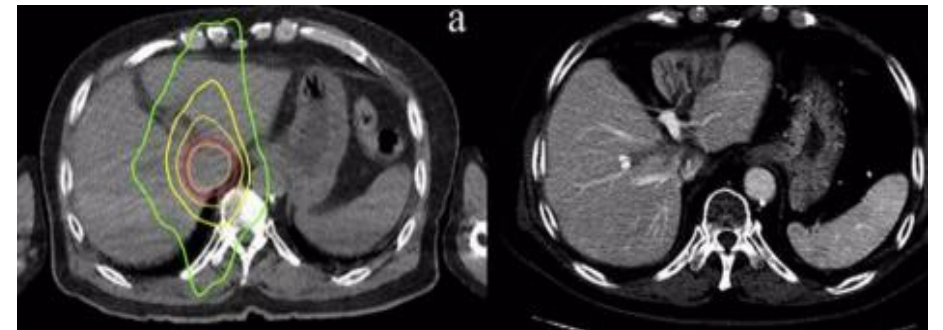
1. Gall Bladder
2. Common Bile Duct
3. Right Hepatic Duct
4. Left Hepatic Duct
5. Cystic Duct

For Liver tumors adjacent to the central biliary structures without other effective treatment options, SBRT to a dose of 40 Gy in 5# is a safe treatment with regard to biliary toxicity

Clinical Investigation

Acceptable Toxicity After Stereotactic Body Radiation Therapy for Liver Tumors Adjacent to the Central Biliary System

Takahisa Eriguchi MD *, Atsuya Takeda MD, PhD *, Naoko Sanuki MD *, Yohei Oku PhD *, Yousuke Aoki RTT, BMSc *, Naoyuki Shigematsu MD, PhD †, Etsuo Kunieda MD, PhD ‡, ☒



SBRT and Targeted Therapy in HCC

NRG Oncology clinical trial NRG-RTOG 1112

From April 2013 to March 2021, the Phase III NRG/RTOG 1112 trial accrued 193 patients from 23 sites, and 177 eligible patients were randomized to Sorafenib (n=92) vs. SBRT followed by Sorafenib (n=85).

At a median follow-up for all and alive patients of 13.2 and 33.7 months, respectively, with a total of 153 OS events, **the median OS was improved from 12.3 months with Sorafenib to 15.8 months with SBRT followed by Sorafenib (p=0.0554).**

Median PFS was improved from 5.5 months with Sorafenib to 9.2 months with SBRT followed by Sorafenib (p=0.0001)

Time to Progression was also improved with SBRT followed by Sorafenib p=0.034).

Treatment-related grade 3+ AEs were not significantly different (Sorafenib – 42%, SBRT followed by Sorafenib – 47%; p=0.52).

Toxicity

Liver toxicity RILD

Is the most dreaded toxicity of SBRT. 2 types:

- **Classic RILD**
- **Non-classic RILD.**

Classic RILD is a triad:

- **Anicteric hepatomegaly,**
- **Ascites**
- **Elevated liver enzymes and alkaline phosphatase (2 times the normal) occurring 2 weeks to 3 months after radiation.**

Pathological hallmark is veno-occlusive disease.

The non-classic RILD occurs in existing liver disease and manifests as jaundice and raised transaminases (5x the upper limit of normal).

In the modern HCC series, the incidence of classic RILD is less than 5%

Luminal gastrointestinal structure toxicity

The luminal gastrointestinal structures are vulnerable to injury because of their proximity to liver tumours and changes linked to portal hypertension-related gastroduodenopathy.

This common toxicity manifests as:

- **Ulcers**
- **Fistulas**
- **Bleeding,**

Rate of grade 3 toxicity was reported to be 5-10%.

Selection of tumours >1 cm away from the gastrointestinal structures is recommended.

Often the dose to the tumour may have to be compromised to meet the organs-at-risk constraints

Toxicity

Biliary tract toxicity

The common forms of central hepatobiliary toxicity (HBT) **are biliary stricture, biliary obstruction, hepatobiliary infection, or sepsis.**

The structures in the central hilum of the liver, such as the hepatobiliary tract and portal vein, behave as serial structures.

Toesca et al. reported grade 3 HBT in 17.5% of patients with HCC, while none had strictures.

HBT was highly correlated with the dose to the central structures.

The volumes receiving 40 Gy (>37 cm³) and 30 Gy (>45 cm³) were predictors of grade 3 HBT.

Eriguchi et al. suggest that 40 Gy in 5 fractions is safe for the biliary tract, with only 2 of the 50 treated patients having asymptomatic biliary stenosis (both treated at a dose >40 Gy)

Chest wall toxicity

Chest wall toxicity manifests as rib pain and rib fractures associated with peripherally located HCC.

Chest wall pain has been reported in up to 21% and rib fracture in about 7-8% of patients.

Chest wall toxicity is commonly self-limiting with analgesics.

The high dose (Dmax < 50 Gy and 40 Gy < 5 cm³) should be limited when treating close to the chest wall

SBRT for Liver Metastases

Background

- The liver is a common site of metastases for **gastrointestinal, lung and breast cancers**
- In **colorectal cancer** 30% to 70% of patients will develop liver metastases, often isolated or associated with **limited metastatic foci of disease**.
- In recent years, the **management** of metastatic colorectal cancer has become **more aggressive** and **more multidisciplinary**

Surgery of liver metastases: limits

- Only 10-60% of patients were suitable for surgical resection because of
 - technical difficulties
 - unfavourable tumour factors
 - patients co-morbidities

Adam, de Gramont (2012) The Oncologist.
Fong Y. et al. (1995) CA Cancer J.Clin.
Simmonds P.C. et al. (2006) Br.J.Cancer
Lam VW et al., (2013) J Gastrointest Surg.

Table 2. Contraindications to hepatic resection in patients with colorectal cancer liver metastases

Category	Contraindication
Technical (A)	
1. Absolute	Impossibility of R0 resection with $\geq 25\%$ –30% liver remnant Presence of unresectable extrahepatic disease
2. Relative	R0 resection possible only with complex procedure (portal vein embolization, two-stage hepatectomy, hepatectomy combined with ablation ^a) R1 resection
Oncological (B)	
1.	Concomitant extrahepatic disease (resectable)
2.	Number of lesions ≥ 5
3.	Tumor progression

Any patient should be categorized as A1 or A2/B1, B2, or B3. This classification may help to clearly define the type of unresectable patients included in all clinical trials.

^aIncludes all methods, including radiofrequency ablation.

RFA and MWA : limits

- **lesions higher than 3-4 cm of diameter**
- **lesions located in proximity of major blood vessels, main biliary tract, gallbladder or just beneath the diaphragm**

Liver metastases treatment: RT could be an alternative?

The **liver tissue low tolerance to irradiation** involves the risk of the radiation-induced liver disease



RILD (2 weeks to 4 months after RT)

- anicteric ascites
- elevation of alkaline phosphatase and liver transaminases
- liver failure
- death

According to the radiobiological model and the liver **parallel architecture**....



... The risk of RILD is proportional to the **mean radiation dose** delivered to normal liver tissue

...It should be possible the safely liver irradiation with adequate dose constraints for normal liver (**minimum volume of 700mL should receive a total dose less than 15 Gy**)

Patient Selection

Several factors need to be considered to ensure safety such as:

- Presence of enough reserve of non-irradiated liver (more than 1000cc)
- Good liver function
- Tumor location being far from luminal gastrointestinal (GI) tissues (>10 mm ideally)

so that ablative doses of SBRT can be delivered while avoiding potential toxicity.

Better outcomes are noted in patients with:

- Limited extrahepatic disease,
- Smaller size lesions (<3 cm vs. >3 cm)
- Limited number of hepatic lesions (< 3 vs. >3 lesions)
- High doses are delivered.

Patients should be appropriately selected taking patient comorbidities, tumor type and planning factors into consideration.

Table 2 Selection criteria for SBRT

Selection criteria	Patients categories		
	Suitable	Cautionary	Unsuitable
Lesion number	<3	4	>4
Lesion diameter (cm)	1-3	>3 and ≤6	>6
Distance from OARs (mm)	>8	5-8	<5
Liver function	Child A	Child B	Child C
Free liver volume (cc)	>1,000	<1,000 and ≥700	<700

SBRT, stereotactic body radiation therapy; OARs, organs at risk.

Evidence

Meta-Analysis > Radiother Oncol. 2018 Dec;129(3):427-434. doi: 10.1016/j.radonc.2018.06.035.
Epub 2018 Jul 9.

Stereotactic body radiotherapy for colorectal cancer liver metastases: A systematic review

Fausto Petrelli ¹, Tiziana Comito ², Sandro Barni ³, Gianfranco Pancera ⁴, Marta Scorsetti ², Antonio Ghidini ⁴, SBRT for CRC liver metastases

A systematic review published in 2018 reported that 1- and 2-year overall survival (OS) rates were 67.18% and 56.5%, respectively.

Median progression-free survival (PFS) was 11.5 months and median OS was 31.5 months.

Higher SBRT dose was associated with better LC and OS.

Mild moderate and severe liver toxicities were 30.7% and 8.7%, respectively.

RETROSPECTIVE STUDIES

Summary of some selected retrospective stereotactic body radiotherapy series.

Study	Design	Case and lesions	Dose (Gy) /fractions	Follow-up	Local control	Overall survival	PFS	Toxicity
Chang D 2011	Retrospective	65 patients 102 lesions	22-60/1-6	1.2 (0.3-5.2) years	1-year: 67% 2-year: 55%	1-year: 72% 2-year: 38%	NA	Grade 2 GI: 17% Grade 3 liver disease: 3% No Grade 3 NA
Cazic D 2020	Retrospective	16 patients	60/8	12 Mo	1- year: 62.5%	1-year: 87.5%	Median: 11 Mo	No Grade 3
Nicosia L 2020	Retrospective	61 patients 97 lesions	NA	24 Mo	NA	Median: 23 Mo 1-year: 68.6% 2-year: 42.7%	Median: 7 Mo	NA
de la Pena C 2020	Retrospective	24 patients 32 lesions	NA	22 (1-65) Mo	1-year: 82% 2-year: 76.2%	Median: 35 Mo 1-year: 85.83% 2- year: 68%	NA	No grade 3 No radiation- induced liver disease
Coffman A 2021	Retrospective	46 patients 81 lesions	36-60/3	15 (1-54) Mo	1-year: 92.5%	NA	NA	Grade 1: 37% Grade 2: 6.5% Grade ≥ 3: 3%
Py J.F. 2021	Retrospective	67 patients 99 lesions	37.5-54/3-5	47 (28-59) Mo	1-year: 86.6% 2-year: 72.4%	Median: 53Mo 1-year: 95.5% 5-year: 43.5%	2-year: 54%	0
Yu J 2021	Retrospective	44 patients 62 lesions	36-60/3-5	31.8 (3.2-122.9) Mo	NA	1-year: 91%	NA	NA
Stera S 2021	Retrospective	135 patients 227 lesions	NA	12.5 (0.5-84.3) Mo	1-year: 90% 5-year: 68.7%	1-year: 67% 2-year: 37%	NA	NA
Voglhuber T 2021	Retrospective	115 patients 150 lesions	35/5	11.4 Mo	Median: 35.1 Mo 1-year: 82% 2-year: 77%	Median: 20.4 Mo 1-year: 72% 2-year: 45%	Median: 4.3 Mo 1-year: 20% 2-year: 10%	Grade 3: 8.7%

Abbreviations: GI, Gastrointestinal; Mo, months; NA, not available; PFS, progression-free survival.

PROSPECTIVE STUDIES

Summary of some selected stereotactic body radiotherapy series.

Study	Design	Case and lesions	Dose (Gy) /fractions	Follow-up	Local control	Overall survival	PFS	Toxicity
Hoyer M 2006	Phase II	64 patients 141 lesions	45/3	4.3 (0.2-6.3) years	1-year: 86%	1-year: 67% 5-year: 13%	Median: 6.5 Mo 2-year: 19%	Grade 2: 48%
Kavanagh B 2006	Phase I-II	21 patients	60/3	19 (6-29) Mo	Median: 18 Mo 1-year: 93%	NA	NA	Grade 3: 1
Rusthoven K 2009	Phase I/II	47 patients 63 lesions	36-60/3	16 (6-54) Mo	1-year: 95% 2-year: 92%	Median: 20.5 Mo 2-year: 30%	NA	Grade 3: 2%
Lee M 2009	Phase I	68 patients	54-60/6	10.8 Mo	1-year: 71%	Median: 17.6 Mo 1-year: 63%	NA	Grade 3: 10%
Rule W 2011	Phase I	27 patients 37 lesions	30-60/5	20 (4-53) Mo	1-year: 72%	Median: 37 Mo 2-year: 57.6%	NA	Grade 3: 1
Scorsetti M 2012	Phase II	61 patients 76 lesions	75/3	6.1 years	1-year: 95%	Median: 27.6 Mo 1-year: 85% 5-year: 18%	Median: 12 Mo	No grade 3
Hong T 2017	Phase II	89 patients 143 lesions	40 GyE/5	30.1 (14.7-53.8) Mo	1-year: 71.9% 3-year: 61.2%	1-year: 66.3% 2-year: 35.9% 3-year: 20.8%	NA	No Grade \geq 3
Folkert M 2021	Phase I	33 patients 39 lesions	35-40/1	25.9 Mo	4-year: 96.6%	2-year: 82%	NA	No Grade \geq 3

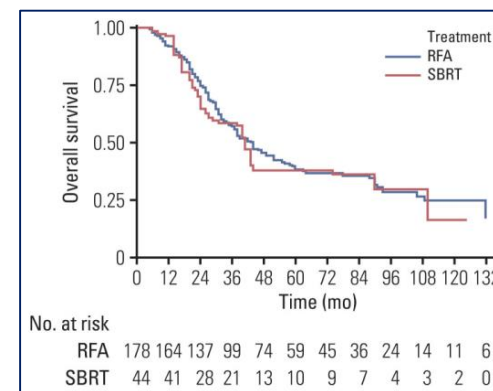
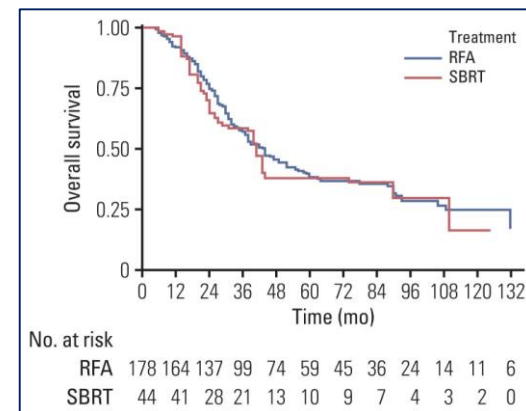
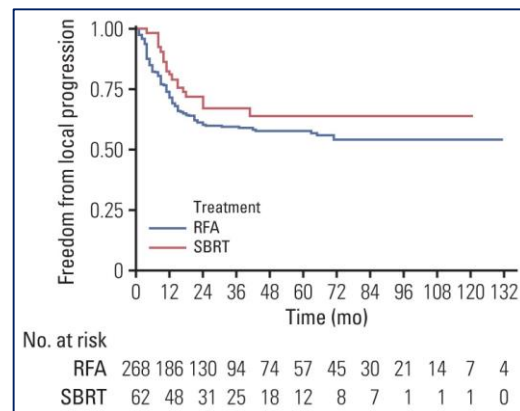
Abbreviations: Mo, months; NA, not available; PFS, progression-free survival.

RFA Vs SBRT (liver mets)

> Cancer Res Treat. 2022 Jul;54(3):850-859. doi: 10.4143/crt.2021.674. Epub 2021 Oct 13.

Radiofrequency Ablation versus Stereotactic Body Radiation Therapy in the Treatment of Colorectal Cancer Liver Metastases

Jesang Yu ¹, Dong Hwan Kim ², Jungbok Lee ³, Yong Moon Shin ⁴, Jong Hoon Kim ⁵, Sang Min Yoon ⁵, Jinhong Jung ⁵, Jin Cheon Kim ⁶, Chang Sik Yu ⁶, Seok-Byung Lim ⁶, In Ja Park ⁶, Tae Won Kim ⁷, Yong Sang Hong ⁷, Sun Young Kim ⁷, Jeong Eun Kim ⁷, Jin-Hong Park ⁵, So Yeon Kim ⁴



Analysis of 222 patients with 330 liver lesions of metastatic colorectal cancer who were treated with SBRT or RFA.

The median follow-up was 30.5 months.

The median tumor size was significantly larger in the SBRT group than in the RFA group (2.3 cm vs. 1.5 cm; $P < 0.001$).

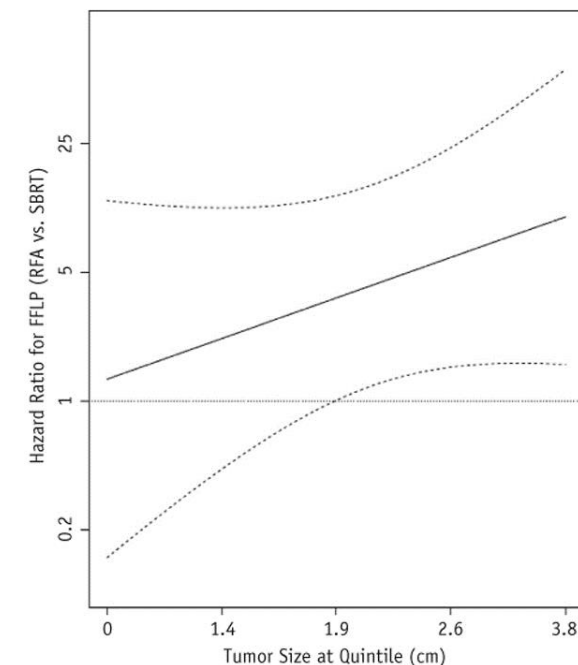
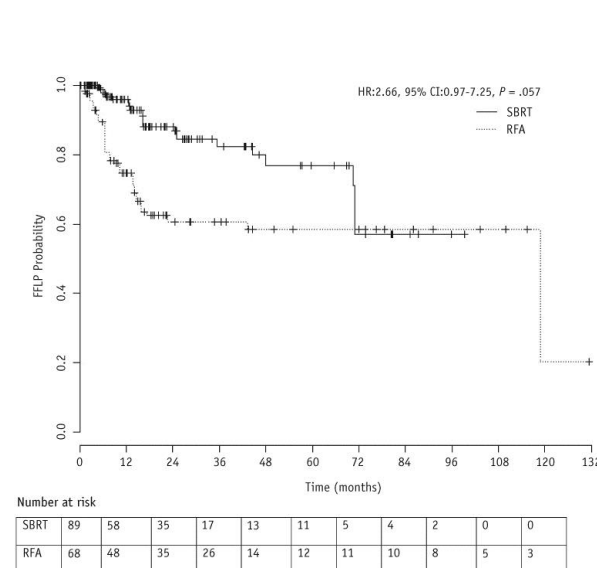
By adjusting with inverse probability of treatment weighing adjusted analysis, the two groups showed no significant difference in 1-year and 3-year recurrence-free survival, OS, and freedom from local progression.

SBRT showed higher freedom from local progression compared with the RFA group ($P < 0.001$) in **treated tumor sizes of more than 2 cm**

RFA Vs SBRT (liver mets)

Comparison of Stereotactic Body Radiation Therapy and Radiofrequency Ablation in the Treatment of Intrahepatic Metastases

William C Jackson¹, Yebin Tao¹, Mishal Mendiratta-Lala², Latifa Bazzi¹, Dan R Wahl¹, Matthew J Schipper¹, Mary Feng³, Kyle C Cuneo¹, Theodore S Lawrence¹, Dawn Owen⁴



In 2017, a study from Jackson et al. evaluated 161 patients with liver metastases.

Most of those patients had limited disease (< 5 cm) or stable extra hepatic disease.

There were 69 patients with 112 lesions treated with RFA and 92 patients with 170 lesions were treated with SBRT. The two approaches were similar with regards to local control in treated lesions of less than 2 cm in diameter.

SBRT improved LC in lesions that were larger than 2 cm compared to those treated with RFA.

In particular, 1- and 2- year LC rates were 96% and 88.2% in patients treated with SBRT and 74.7% and 60.6% for those treated with RFA, respectively, though such differences were not statistically significant

RFA Vs SBRT (liver mets)

Review > [Radiother Oncol. 2020 Apr;145:63-70. doi: 10.1016/j.radonc.2019.12.004.](#)

Epub 2020 Jan 7.

Comparisons between radiofrequency ablation and stereotactic body radiotherapy for liver malignancies: Meta-analyses and a systematic review

Jeongshim Lee¹, In-Soo Shin², Won Sup Yoon³, Woong Sub Koom⁴, Chai Hong Rim⁵

In a recent meta-analysis that included three studies comparing the efficacy of SBRT and RFA for treatment of liver metastases, the reported 2-year LC rate was higher in the SBRT group compared to that of the RFA group (83.6% vs. 60.0%, $P < 0.001$), and OS was not significantly different between the two approaches

Molecular Biomarkers for SBRT Planning

Treatment of liver metastasis should consider the biology nature of the primary tumors.

Molecular biomarkers should be considered when planning SBRT for oligo-metastatic diseases.

This includes but not limited to the lung and colorectal cancers.

Patients with an immune genotype of NRAS, CDK12, and EBF1 mutations have lower local recurrence rates compared to those with wild type who have lower survival rates.

Association of tumor genomic factors and efficacy for metastasis-directed stereotactic body radiotherapy for oligometastatic colorectal cancer

Phase II Study of Proton-Based Stereotactic Body Radiation Therapy for Liver Metastases: Importance of Tumor Genotype

Superior outcomes of nodal metastases compared to visceral sites in oligometastatic colorectal cancer treated with stereotactic ablative radiotherapy

Krishan et al. reported results of 85 patients with 109 metastatic lesions treated with SBRT.

Patients with KRAS mutation had lower OS compared to those patients with KRAS wild type.

The median OS in patients with combined KRAS and TP53 mutation was 14 months, and for patients with either KRAS or TP53 mutation, the median survival was 38 months.

Moreover, patients with TP53 mutation had a higher rate of local recurrence compared to patients with TP53 wild type

The importance of mutations in the treatment of liver metastases with SBRT has also been shown by a group from Harvard:

KRAS and TP53 mutations correlated with LC more than primary tumor type.

The results demonstrated superior LC for lesions without KRAS mutation (1-year LC of 73% vs. 42% with KRAS mutation)

Better LC for those without KRAS and TP53 mutations (1-year LC of 69% vs. 20% with mutant KRAS and TP53).

UK group that showed patients with wild type KRAS had a superior PFS compared to those with KRAS mutation.

Moreover, OS was reported to be better in patients who have KRAS-wild type compared to the KRAS-mutant type.

Molecular Biomarkers for SBRT Planning

Conclusion and future directions:

In the future, radiotherapy sensitivity signatures (KRAS wild, oligophenotype, immune molecular subtype) may help in treating patients who are likely to benefit more from SBRT treatment.

Limitations of SBRT for Liver Mets

Treatment with SBRT does come with some limitations.

- **SBRT has less chance of sustained ablation for larger tumors (> 6 cm).**
- **In tumors that are less sensitive to radiotherapy (i.e. colorectal cancer with KRAS and/or TP53 mutations), higher doses are needed for better LC.**
- One should pay attention to dose limiting factors including surrounding luminal structures so that SBRT may be delivered safely.
- **Systemic therapies may need to be held prior to, during and after SBRT.**

Take Home Message

SBRT for HCC

Current Evidence:

- **Feasibility: Non Invasive and acceptable toxicity**
- **Efficacy: Encouraging local control rate**

Future directions:

- **Randomized Controlled Trials with other local procedures**
- **Integration Therapy**

SBRT in Liver Metastasis

- In conclusion, there is an expanding role of SBRT for treatment of liver metastases.
- Indications include non-surgical candidates with large lesions (3 to 6 cm), and patients who are not suitable for or refractory to RFA (i.e. in central dome, or adjacent to large vessels).
- It is also an excellent treatment for metastases near portal structures, but one needs to be considerate of the organs at risk, and avoid hot spots on the biliary track.
- Single fraction SBRT should not be recommended for lesions around the porta-hepatis.
- As there is a degree of clinical equipoise about some topics of SBRT related to liver metastases (i.e. maximum number of treated metastases, dose fractionation), more prospective, and ideally randomized clinical trials are encouraged.

Thank You

Extra Slides

Clinical Investigation

Long-Term Results of a Phase 1 Dose-Escalation Trial and Subsequent Institutional Experience of Single-Fraction Stereotactic Ablative Radiation Therapy for Liver Metastases

Michael R. Folkert MD, PhD ^{*}, Jeffrey J. Meyer MD, MS [†], Todd A. Aguilera MD, PhD ^{*}, Takeshi Yokoo MD, PhD [‡], Nina N. Sanford MD ^{*}, William G. Rule MD [§], John Mansour MD ^{||}, Adam Yopp MD ^{||}, Patricio Polanco MD ^{||}, Raquibul Hannan MD, PhD ^{*}, Lucien A. Nedzi MD ^{*}, Robert D. Timmerman MD ^{*}

Normal tissue dose constraints on and per protocol according to previous studies

Structure	Maximum point dose	Volume constraint
		constraint [*]
Uninvolved liver	14 Gy	700 ml receives < 9.1 Gy
Spinal cord		< 0.35 ml exceeds 10 Gy
		< 1.2 ml exceeds 7 Gy
Stomach	12.4 Gy	< 10 ml exceeds 11.2 Gy
Duodenum	12.4 Gy	< 5 ml exceeds 11.2 Gy
Jejunum/Ileum	15.4 Gy	< 5 ml exceeds 11.9 Gy
Colon	18.4 Gy	< 20 ml exceeds 14.3 Gy
Skin	26 Gy	< 10 ml exceeds 23 Gy

^{*} Point dose volume = 0.035 ml

More recent studies have been looking at single fraction liver SBRT.

A report from UT Southwestern Texas included 33 patients with 39 metastases located at peripheral liver who received a dose of 35-40 Gy in one fraction.

LC was reported to be 96.6% at 4 years. Two and four-year OS rates were 82% and 50%, respectively. No grade 3-5 toxicities were reported.

- This high dose SBRT must be delivered with highly conformal techniques.
- Risk of unpredictable toxicities, including biliary toxicity, should be taken into consideration.
- Using highly accurate and precise radiotherapy delivery techniques, single fraction SBRT can be used for the treatment of small liver metastases (less than 5 cm).

The critical steps for initiating and implementing a clinical SBRT program involve:

- 1. Establish the scope of the SBRT program including a selection of treatment sites and the clinical goals for each site.(Well thought out program ,not an afterthought –ASTRO white paper)**
- 2. Determine a treatment modality, dose-fractionation scheme, and treatment planning goals target definition, target coverage, conformity index, etc. that support the clinical goals for each treatment site.**
- 3. For each treatment modality and treatment scheme, determine the equipment requirements for patient positioning, treatment delivery, and verification.**
- 4. Determine personnel needs for SBRT implementation and maintenance.**
- 5. Establish and perform acceptance and commissioning test procedures for the SBRT equipment.**
- 6. Establishing SBRT simulation, treatment planning, delivery and verification guidelines, reporting methodology and routine QA procedures, and action levels**
- 7. Conducting personnel training.**