Radiotherapy Indications and Techniques. Role Of SBRT In Early Hepatic Malignancies and Hepatic Metastasis

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Radiotherapy For Liver Tumors

- Radiosensitive organ
- Toxicity easily achieved – radiation induced liver disease **(RILD)**
- Complications of liver failure can make treatment planning difficult
- Stomach, kidney & duodenum at risk of injury
- Initially, RT was used cautiously due to the narrow therapeutic window when balancing tumor control against RILD

Radiation Induced Liver Disease (RILD)

- Occurs 4–8 weeks after termination of RT
- Has been reported to appear as early as 2 weeks or as late as 7 months after RT
- 6–66% of patients present significant RILD
- Mean dose of 30 Gy is usually considered as safe but radiation tolerance of the liver is lesser in patients with deranged liver function
- **Two types of RILD:**
  - **Classical -** patients without underlying liver disease
  - **Non-classical -** patients with underlying liver disease

RILD contd…

Classical

- **Clinical syndrome -** fatigue, abdominal pain, increased abdominal girth, hepatomegaly, anicteric ascites
- Isolated elevation of alkaline phosphatase out of proportion to other liver enzymes
- Levels of transaminase and bilirubin remain normal
- **Pathological changes –** Characteristic hallmark is hepatic veno-occlusive disease (VOD)

Non - Classical

- **Clinical syndrome –** jaundice
- Have underlying chronic hepatic diseases, such as cirrhosis and viral hepatitis
- Show more dysregulated hepatic functions
- Remarkably elevated serum transaminases (a more than fivefold increase compared to normal levels) rather than ALP
- **Pathological changes -** hepatic sinusoidal endothelial death and HSC activation leading to irreversible hepatic failure

Grading System For Cirrhosis

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criteria	**Points***		
	1	2	3
Encephalopathy	None	Grade 1 or 2	Grade 3 or 4
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
or			
International normalized ratio	<1.7	1.7-2.3	>2.3
***Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)**			
Class A = 5 to 6 points			
Class B = 7 to 9 points			
Class C = 10 to 15 points			

Treatment Options

Operable	Non – Operable
Partial Hepatectomy	Radiofrequency Ablation
Liver Transplant	Percutaneous Ethanol Ablation
	Transarterial Chemoembolization
	Cryoablation
	Systemic Chemotherapy
	Radiation Therapy
	Radioembolization

Indications of RT

HCC

Unresectable
Transplant ineligible
Ineligible for RFA, TACE
Incomplete response to TACE
Portal vein invasion
As bridge to transplant

Intrahepatic cholangiocarcinoma

Adjuvant - Margin positive, lymph node metastasis
Unresectable
Medically inoperable

Metastatic

Oligometastasis with controlled primary disease
Number of hepatic lesions ≤3, size lesions ≤3 cm, lesion distance from OARs >8 mm, good liver function and free liver volume>1000 cm3.

RT – Constraints

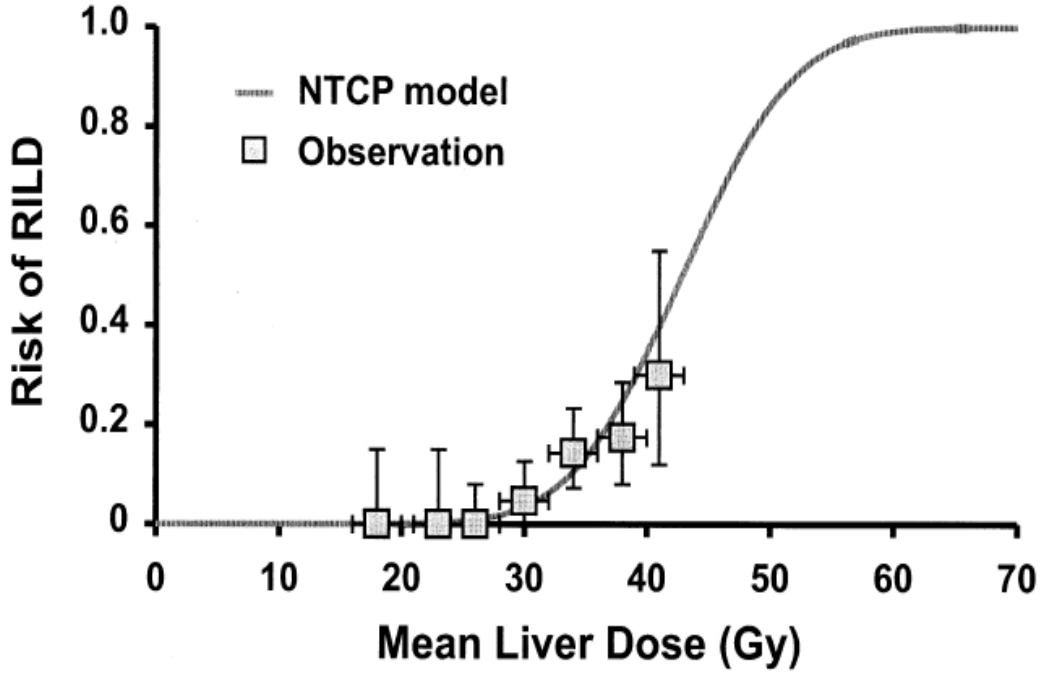


Fig. 3. Observed and predicted NTCP, according to the LKB NTCP model vs. mean liver dose (in 1.5 Gy b.i.d.). Observed NTCP calculated from patients grouped in 4-Gy bins, with 80% confidence intervals displayed. Predicted NTCP based on the LKB NTCP model, with n = 1.1, m = 0.18, and $TD_{50}(1)$ = 43.3 Gy.

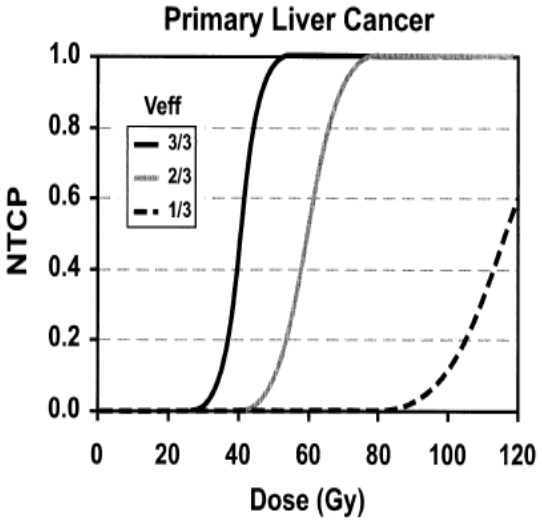
- Threshold mean liver dose was 30Gy
- NTCP increased by approx 4% per Gy increase in the mean dose
- There is a 5% chance of RILD with a mean liver dose of 31Gy
- There is a 50% chance of RILD with a mean liver dose of 43Gy
- At 2Gy /#, 5% chance of RILD corresponds to 28Gy

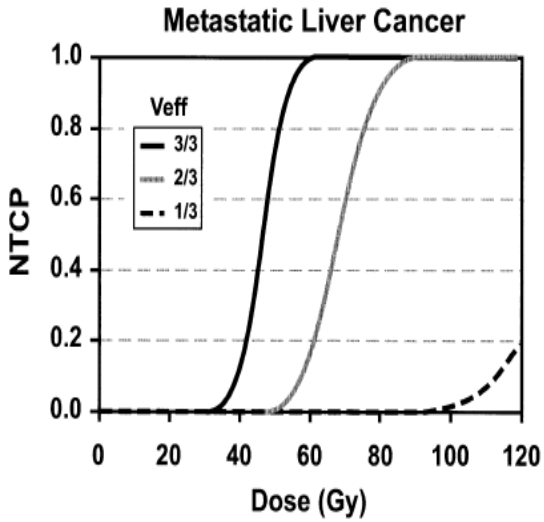
Dawson IJROBP,33,2002

RT – Constraints

Whole liver
<5%, <32Gy

TD(50) , 39.8 Gy

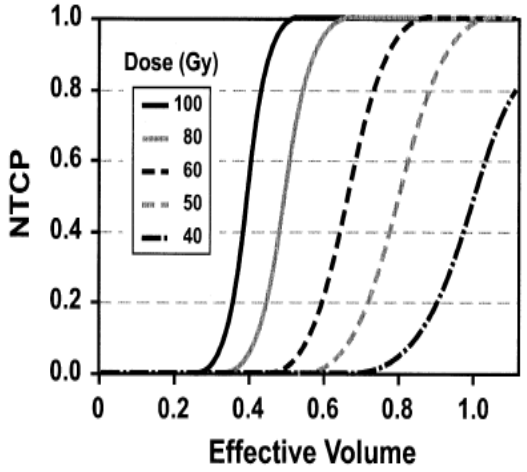


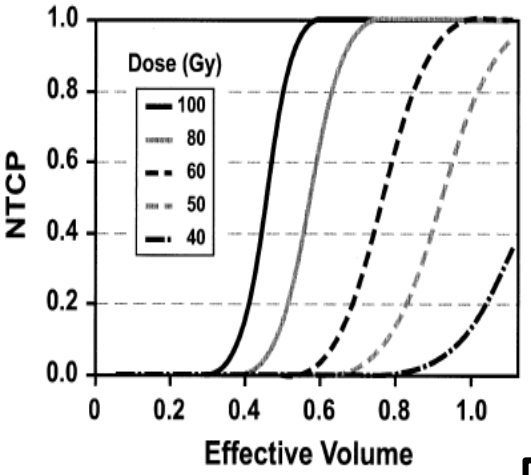


Whole liver
<5%, 36Gy

TD(50), 45.8Gy

2/3 liver
5%, 46Gy





2/3 liver
5%, 54Gy

Dawson IJROBP,33,2002

Challenges In Treatment

Challenges	Opportunities
HCC is an **aggressive** disease	**Multi-disciplinary collaboration** is essential
Normal liver is **radiosensitive**. Liver is a vital organ, and we only have 1	**Highly conformal RT** techniques (high dose cloud around liver, spare rest of the normal liver) • IMRT/VMAT, SBRT, proton **Image guidance** strategies • Conebeam CT • MRI Linac
Liver **moves** a lot during respiration (1 – 4cm)	Respiratory **motion management** and **immobilization** strategies
Hard to visualise the target	Multi-phasic and functional imaging integrated into RT planning
Tolerance of **nearby organs** (gut, stomach, chestwall, kidneys)	**Appropriate dose selection** Use of tissue spacers
1 cause 2 diseases : Uninvolved liver may be dysfunctional from the same underlying cause – **double trouble**	**Patient selection** is important.

Radiotherapy In Liver Tumors

- Techniques of Radiation:
  - Conventional radiation
  - 3-D Conformal Radiation /IMRT
  - Stereotactic body radiotherapy
  - Protons & heavy ion therapy

Radiotherapy In Liver Tumors

- Modern radiotherapy and imaging, however, permit ablative doses to be delivered to HCC without excessive dose to normal liver
- Robust target delineation, highly conformal planning, online image guidance, and methods to minimize respiratory motion are required for optimal delivery.

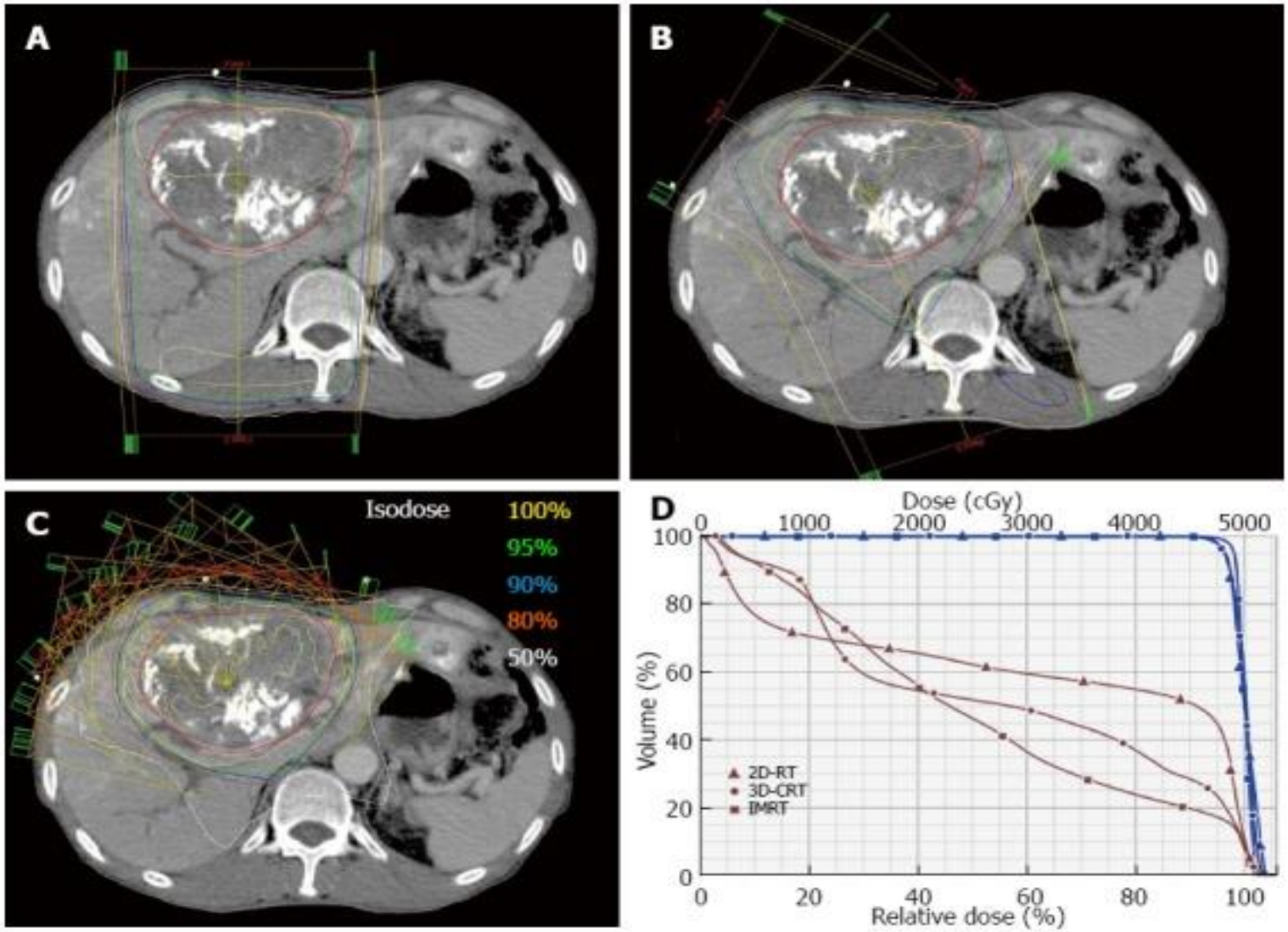
3D-CRT

- 3D-CRT uses multiple coplanar or non-coplanar fields in order to reduce the high-dose exposure of normal tissues including the liver and bowels and to increase the tumor dose coverage
- With the use of computed tomography (CT) images for RT planning and a computerized treatment planning system:
- The tumor and surrounding normal liver can be delineated accurately
- The delivered dose and irradiated volume of the tumor and normal liver can be precisely evaluated
- **More suitable for larger tumors**

IMRT

- Facilitates the delivery of a higher radiation dose
- Inverse treatment planning, modulates the intensity of each beam to gain the desired target coverage while minimizing the dose to the normal organs
- Various forms of IMRT - volumetric-modulated arc therapy (VMAT) and helical tomotherapy (HT)
- High dose region of the normal liver is smaller in IMRT than 3DCRT, the low dose region is increased in IMRT, and this increase is remarkable in h-IMRT or VMAT.
- Sparing effect of non-liver OARs is beneficial in h-IMRT or VMAT.

Different Radiotherapy Techniques For Hepatocellular Carcinoma



Strength & Weakness Of IMRT Techniques

	s-IMRT	h-IMRT	VMAT
Strength	*Compared with 3DCRT* - Improving target coverage - Sparing OARs	-	-
	Compared with h-IMRT and VMAT - Sparing the normal liver	*Compared with s-IMRT* - Same or better homogeneous dose distribution within target - Sparing non-liver OARs	*Compared with s-IMRT* - Same or better homogeneous dose distribution within target - Sparing non-liver OARs - Lower MUs - Shorter treatment time: reduction of intra-fractional movement; improvement of patient's comfort; higher patient throughput
Weakness	*Compared with 3DCRT* - Higher MUs - Longer treatment time - Larger low dose region of OARs - Less sparing the normal liver in case of large tumor > 6–8 cm	-	-
	Compared with h-IMRT or VMAT - More dependent on the beam angle and the experience of the physicist	*Compared with s-IMRT* - Larger low dose region of the normal liver (consider a directional block)	*Compared with s-IMRT* - Larger low dose region of the normal liver (consider use of non-coplanar arc) - Limitation of non-coplanar arc: availability of only asymmetric partial arc; Decrease of advantage duo to increased treatment time by couch rotation and increased MUs

Comparison of 3DCRT vs IMRT

Studies	RT technique	No. of patients	CP class	Tumor size	VI	RT dose	Combined Treatment	Median f/u (mo)	LCR	OS	Toxicity
Yoon 2014 [49]	3DCRT	122	A	Median 10 cm (1–18.6)	PVTT in 79%	1.8–5 Gy/fx, 36–60 Gy	CCRT with HAIC in 95.2%	21	28% at 3 yrs	14% at 3 yrs	RILD in 5%
	h-IMRT	65		Median 9 cm (2.2–18.8)	PVTT in 82%	2.5–3.5 Gy/fx, 47.5–60 Gy			47% at 3 yrs ($P = 0.007$)	33% at 3 yrs ($P < 0.001$)	RILD in 3% (NS)
Hou 2016 [50]	3DCRT	64	A: 50 B: 14	Mean 8.6 cm	PVTT in 88%; IVCTT in 12%	1.8–2 Gy/fx, 40–60 Gy	None	11.8	43%*	36% at 1 yr	Gr 3 toxicity* in 5%
	h-IMRT	54	A: 46 B: 8	Mean 7.5 cm	PVTT in 89%; IVCTT in 11%	2.5–4 Gy/fx, 40–66 Gy			70%*	59% at 1 yr ($P = 0.005$)	Gr 3 toxicity* in 2% (NS)

Ways To Address Motion

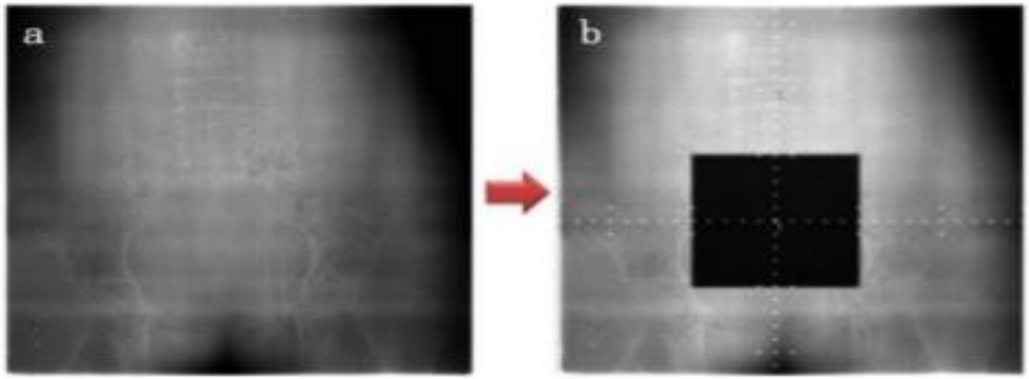
- Image guidance (IGRT)
- Limit motion
- Quantify actual motion
- Track motion
- Treat at certain phases of respiration

IGRT

- Image guidance ensures that relative positions of isocenter and target are the same during treatment and in treatment plan
- Potentially allows:
  - ✓ **Reduced treatment margins**
  - ✓ **Increased dose**
  - ✓ **Reduced complications**
  - ✓ **Avoid misses**

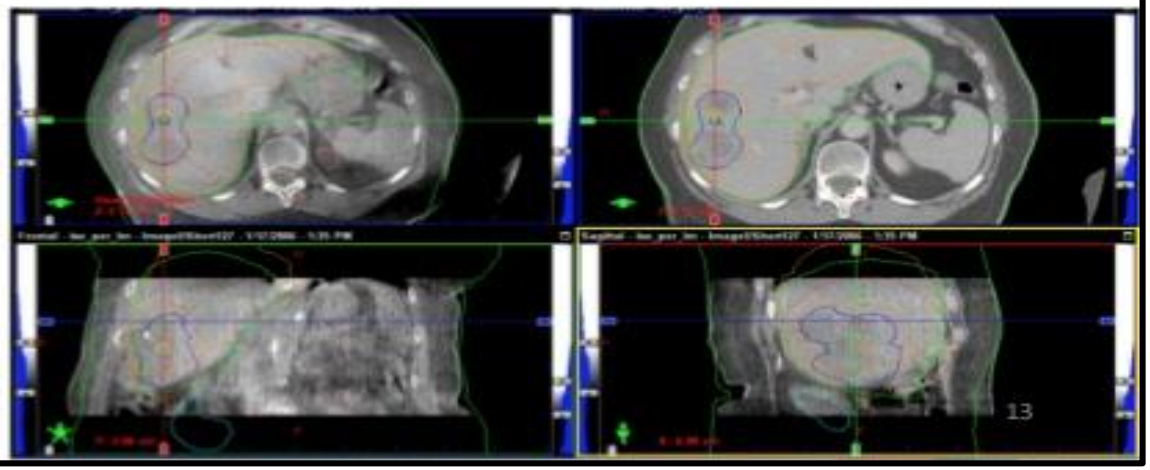
Image Guidance Then And Now…

Image guidance then and now…



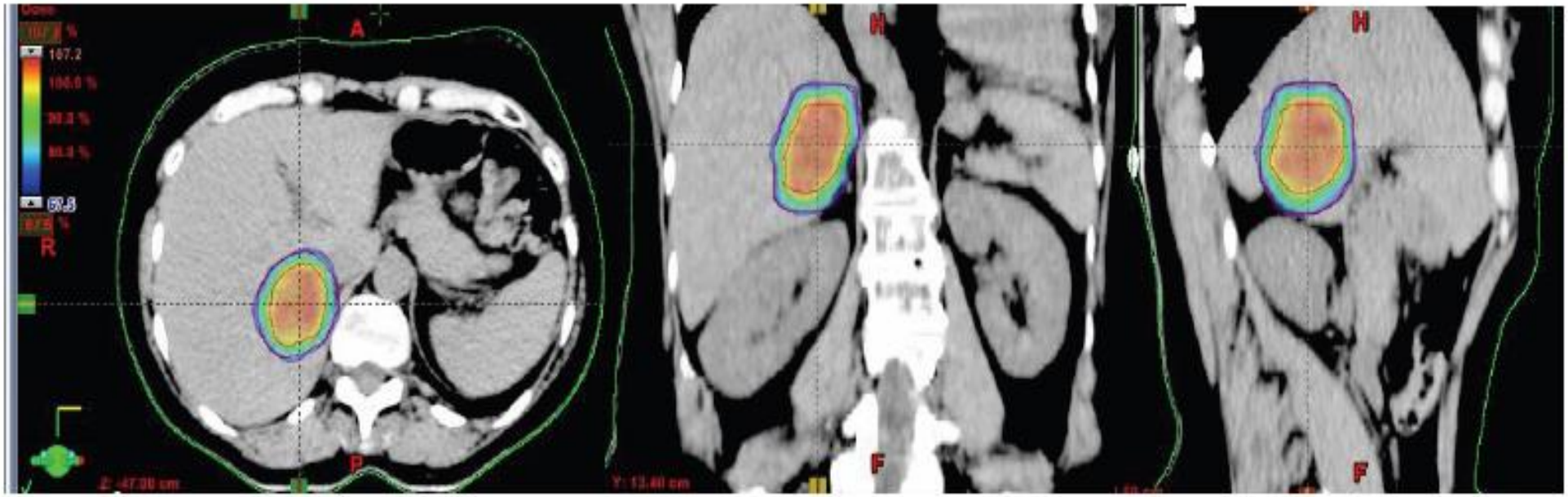
Positional verification based on bony contours

More accurate alignment using on-board cone beam CT



SBRT

- *Delivery of high precision, image guided, high dose radiotherapy.*
- *Tumor ablative intent, short course, steep dose gradient delivery.*
- *Results in a high biologically effective dose (BED)*



Is There A Biological Edge In SBRT

- Postulated mechanisms:
  1. Ablative treatment
  2. Endothelial damage
  3. Immune mediated
     - RT increases tumor antigen specific immune response
  4. Abscopal effects
     - Local therapy causes systemic response (cytokine mediated)

Positioning & Immobilization

- Usually a vac lock is used to immobilize the body from head to pelvis, arms are moved away from the field using a T- bar
- Abdominal orfit cast may also be used
- Immobilization with abdominal compression devices should be used to reduce tumor motion

Simulation Along With Motion Management

- **Aim:** To provide accurate details of the patients anatomy for target delineation and dose calculations
- To achieve a precise and reproducible position for treatment
- Different techniques of CT scanning
- Most commonly a 4DCT is used to acquire images since it give a good estimate of tumor or organ motion along with anatomical details
- A slice thickness of “1-3” mm is recommended in most clinical cases

Simulation

- Scan length should extend 5-10 cm superior and inferior of the treatment border to enable the placement of non co-planar beams
- RPM™ (Respiratory position management) system (Varian Medical Systems, Palo Alto, USA) with infrared marker used to track the breathing pattern of the patient
- To enhance the visibility of tumors on 4D-CT, 100 ml of contrast at a concentration of 300 mgI/ml was injected along with 4D-CT image acquisition
- After initiating contrast injection, the liver scanned with a 45 s time delay so as to image the liver in the portal venous phase.

Target Volume Contouring

- According to ICRU 50 and 62, GTV, PTV and OARS are contoured on each slice of the CT
- The GTV included the hypodense areas visible in the liver on the planning CT images
- GTV contoured on all the respiratory phases
- GTV expanded by 5mm in all directions to create PTV

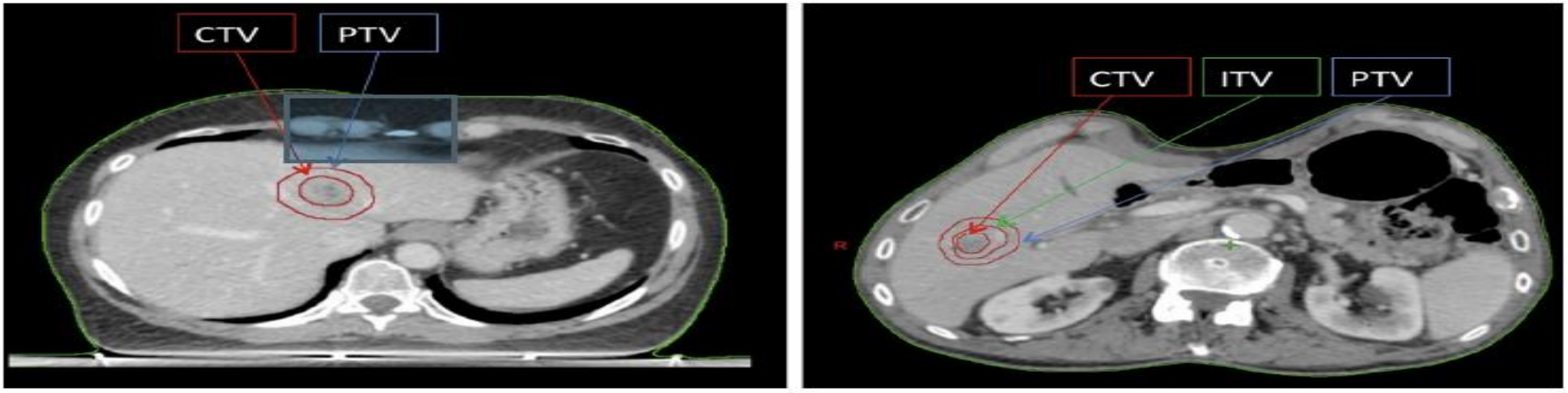
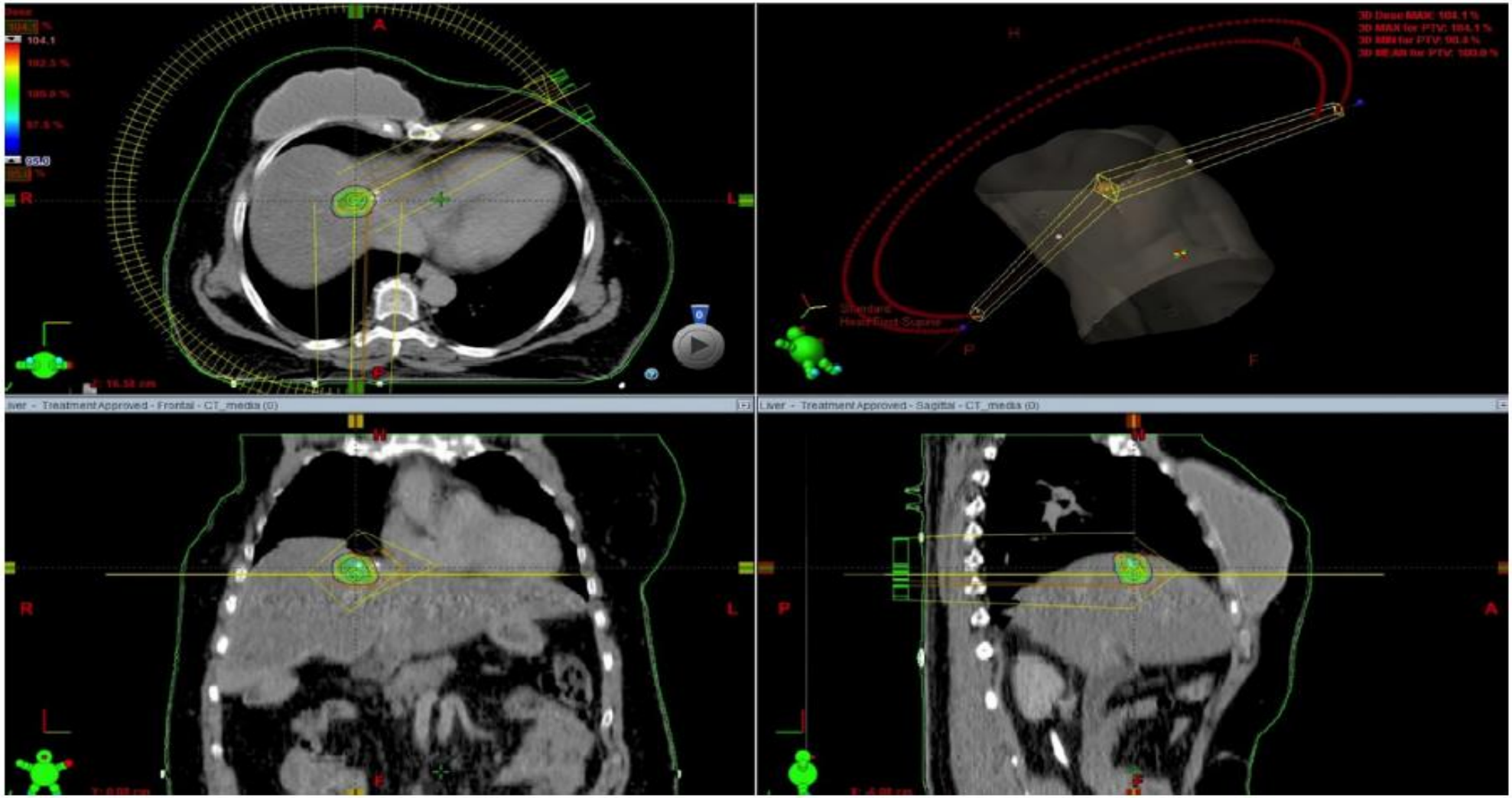


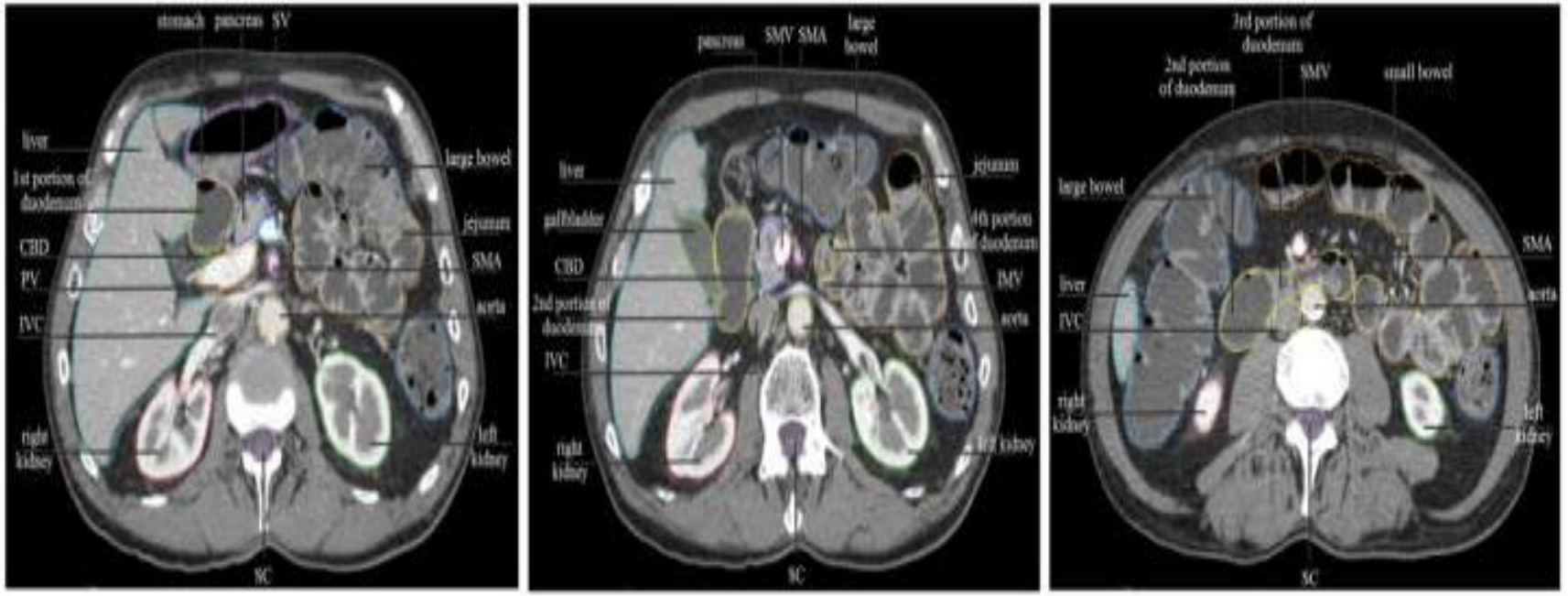
Fig. 1 – Examples of target volumes delineation for liver SBRT.

VMAT Technique (SBRT)



OAR Contouring

- At minimum, these structures are required to be contoured at the level of the PTV and over any region received > 10 Gy
- All portions of the duodenum are recommended to be contoured



Recommendations

Dose prescription for SBRT in 3 fractions according to lesion size

Lesion size	Prescription dose
≤3 cm	48–60 Gy
>3–6 cm	60–75 Gy

Recommended OAR dose constraints

OAR	Dose-volume limits
Healthy liver (total liver volume minus cumulative GTV)	>700 cm^3 at <15 Gy[a]
Stomach, duodenum, small intestine	D 3 cm^3 at <21 Gy[b]
Both kidneys	V 15 Gy at <35%
Spinal cord	D 1 cm^3 at <18 Gy
Heart	D 1 cm^3 at <30 Gy
Rib	D 30 cm^3 at <30 Gy

[a] Volume of healthy liver >1000 cm^3.
[b] Distance by GTV >8 mm.

Comito et al. Pract Oncol Radiother. 2015

Dose

- Excellent local control rates are also seen after SBRT for liver metastases when BEDs of >100 Gy_{10} are utilized
- Local control rate exceeding 90% was achieved when doses of 46–52 Gy in 3 fractions are delivered,
- Doses of 48 Gy or higher in 3 fractions should be offered if feasible

Mahadevan et al. Radiat Oncol. 2018

Potential Toxicities

Clinical

•Radiation Induced Liver disease (RILD)

1. Classic : Anicteric hepatomegaly, ascites, elevated liver enzymes (ALP>AST/ALT)

–2 weeks to 3 months

2. Non-classic : Elevation of transaminases, reactivation of Hep B, Liver function decline/ worsening of CP

–1 week to 3 months

Biliary obstruction, stricture

GI : stomach, intestinal bleeding, obstruction, fistula

Chest wall pain , rib fracture

SBRT related, site dependent.

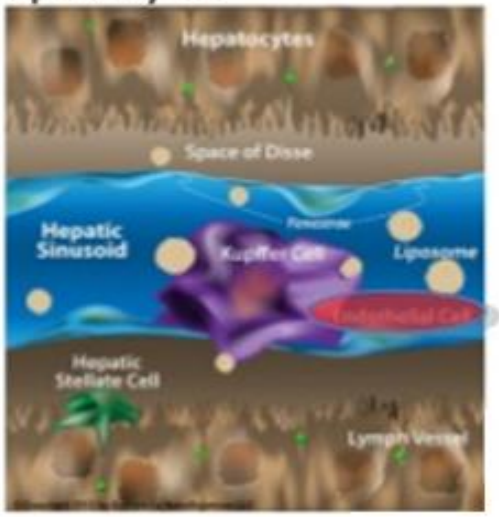
Pathological changes

Hyperemia

Veno-occlusive disease

Central venous congestion

Atrophy of adjacent hepatocytes



Definitive RT in those not suitable for Surgery & RFA

Role of definitive RT in those not suited for surgery, RFA

Selected Early HCC SBRT Series

	No. pts	Dose/Fraction	Tumor size	Med FU (mo	Response Rate/ Local control	Survival
Blomgren, 98	9	5-15 Gy/1-3#	NR	NR	70%	NR
Choi, 06	20	50 Gy / 5-10#	3.8 cm (2-6.5cm)	23	80%	1 yr: 70% 2 yr: 43.1%
Mendez, 06	11 CP A + B	25 Gy / 5 # 30 -37.5 Gy / 3#	< 7 cm	NR	LC 1 yr: 82%	1 yr: 75%
Tse, 08	31	36 Gy / 6 # (24-54 Gy)	173 cc (3 – 1913 cc)	18	LC 1 yr: 65%	1 yr: 48%
Louis, 10	25 CP A + B	45 Gy / 3#	150 cc	13	86%	1 yr: 79% 2 yr: 52%
Kwon, 10	42 CP A 90%	30 – 39 Gy/ #	15.4 cc (3-82 cc)	29	86% LC 3 yr: 68%	3 yr: 59%
Facciuto, 11	27	24-36/ 2-4#	2.0 cm +/- 0.8 cm	22	37%	2 yr: 82%
Andolino, 11	60 CP A/B: 36/24	44 Gy /3# CP A 40 Gy /5# CP B	3 cm	27	90%	2 yr: 67%
Seo, '10	38	33-57Gy/ 3	<10cm		79%	68%

Dawson, ASTRO

Summary of Prospective Studies of SBRT for HCC

Study, Year, Type of Data	Median f/u, months	n	Lesion #	CP-B %	PVTT	Prior LDT	Median GTV Diameter (Range), cm	Median Dose Gy/ fx, (Range)	LC	OS	G ≥ 3 Toxicity, %
Mendez-Romero, 2006, phase I/II[12]	13	8	11	25%	25%	NR	3.5 (0.5-7.2)	<4 cm, no cirrhosis: 37.5/3 ≥4 cm and cirrhosis: 25/5	75%	75%	13%
Kang, 2012, phase II[11]	17										– 4% GI ulcer perforation – 6% G3 GI toxicity – 9% ascites – 11% G3 thrombocytopenia – 4% G3 hyperbilirubinemia
Bujold, 2013, phase I/II[7]	31		in 61%								30%
Culleton, 2014, phase I/II[10]	NR	29	Median 2 lesions	97% (69% B7) 3% C10)	76%	14%	Sum of all lesions: 8.6 (4.1-26.6)	30/6 (19.7-46.8)	65%	32.3%	63% had decline in CP score by ≥2 at 3 months
Lasley, 2015, phase I/II[9]	CP-A: 33 CP-B: 46	59	65	36% B7/8+: 81/19	20%	15%	Volume: 33.6 cc (2-107)	CP-A: 48/5 (36-48) CP-B: 40/5	CP-A: 91% CP-B: 82%	CP-A: 94% CP-B: 57%	CP-A: 11% CP-B: 38%

Prospective clinical trials of liver SBRT have demonstrated high rates of local control (LC), typically defined as no progression of disease per RECIST criteria, ranging from 87% to 100% at 1 to 3 years

Comparison of SBRT with other Liver Directed Therapies

Study, Year	Study Type	n	Modalities Compared	Inclusion Criteria	SBRT Details	Tumor Control	OS	Comments
Wahl, 2016[73]	Single-center retrospective	224	SBRT vs RFA	Inoperable, nonmetastatic	30 Gy/3 or 50 Gy/5	Freedom from local progression 1-year 97 vs 84%	1-year 74 vs 70% 2-year 46 vs 53%	SBRT associated with better local control for tumors ≥ 2 cm
Rajyaguru, 2018[74]	NCDB							ined
Sapir, 2018[75]	Single-ce retrosp							l to have
Su, 2016[76]	Single-ce retrosp			0-1		No significant difference		Gy oved OS, PFS, LRFS, and DMFS
Su, 2017[77]	Single-center retrospective	117	SBRT vs Resection	1-2 tumors ≤ 5 cm; No prior LDT; CP-A; N0 M0; WHO PS 0-2; No PVT	42-48 Gy/3-5	Intrahepatic progression free survival	5-year 47 vs 33%[a] 1-year 100 vs 98%	SBRT recommended for patients with comorbidities who could not tolerate surgery or were medically inoperable.
						1-year 84 vs 69% 3-year 59 vs 62% 5-year 44 vs 36%	3-year 92 vs 89% 5-year 74 vs 62%	No incidence of hepatic hemorrhage or pain in SBRT group, but more acute nausea and weight loss[a]

Despite the challenges with comparing SBRT to other treatment modalities in the absence of randomized data, SBRT appears to be an effective LDT for local control with a safe toxicity profile in well-selected patients, and further work is ongoing regarding the role of SBRT in the setting of combined modality treatments

Table 2. Comparison of overall survival for small-sized hepatocellular carcinoma treated with locoregional therapies

Treatment modality	3-year survival	5-year survival
Surgical resection	75–90% [9, 52]	40–75% [10, 52]
Laparoscopic resection	70–93% [54]	50–71% [54]
Radiofrequency ablation	54–67.2% [53]	40–67.9% [10, 55]
Liver transplantation	65–85% [59]	65–80% [59]
Stereotactic body radiation therapy	54–70% [4, 5]	64% [6]

Reference 4: the hepatocellular carcinoma was <6 cm across its longest diameter, and ≤3 lesions were presented. Reference 5: a single (either solitary or recurrent) hepatocellular carcinoma lesion; unfeasible, difficult, or refusal to undergo other surgery or percutaneous ablative therapies, tumor ≤5 cm. Reference 6: maximum diameter ≤5 cm. Reference 10: intrahepatic tumor with single nodule ≤5 cm or up to 3 nodules <3 cm. Reference 53: up to 2 nodules <4 cm. Reference 55: up to 3 nodules with a maximum diameter of 5 cm.

Stereotactic body radiotherapy versus TACE or RFA as a bridge to transplant in patients with hepatocellular carcinoma. An intention-to-treat analysis

- 379 patients
- SBRT (n=36)
- TACE (n=99)
- RFA (n=244)
- The 1-, 3- and 5-year actuarial patient survival from the time of listing was 83%, 61% and 61% in the SBRT group vs. 86%, 61% and 56% in the TACE group, and 86%, 72% and 61% in the RFA group, p=0.4

- **Conclusion:** SBRT can be safely utilized as a bridge to LT in patients with HCC, as an alternative to conventional bridging therapies

Sapisochan et al. J Hepatol. 2017

LC at 2 years in relation to dose in HCC

Study, Year	n	CP-B %	Median Tumor Diameter, cm	Dose (Range) /fx	BED Gy_{10}	EQD2	Dose-Prescription Point	1-Year OS	2-Year LC
Yamashita, 2015[24]	79	11%	2.7	48 Gy/4-10	71-106	59-88	D95% PTV	78%	64%
Bujold, 2013[7]	102	0%	9.9	24-54 Gy/6	34-103	28-86	D95% PTV modified based on effective liver volume irradiated	75%	74%
Bibault, 2013[25]	75	11%	3.7	40-45 Gy/3	72-85	60-71	80% IDL	79%	90%
Andolino, 2011[26]	60	40%						82%[b]	90%
Jung, 2013[27]	92	26%						87%	92% (3 years)
Sanuki, 2013[28]	185	15%	2.7	40 Gy/5	72	60	70-80% IDL	95%	93%
Yoon, 2013[29]	93	26%	2.0	45 Gy/3-4	96-113	80-94	D100% PTV	86%	95%[b]
Takeda, 2014[30]	63	16%	2.6	35-40 Gy/5	60-72	50-60	70-80% IDL	100%	95%
Huertas, 2015[31]	77	14%	2.4	45 Gy/3	113	94	80% IDL	82%	99%
Kimura, 2015[32]	65	14%	1.6	48 Gy/4	106	88	Isocenter	NR	100%
Jang, 2013[22]	108	10%	3.0	51 Gy/3	138	115	70-80% IDL D97% PTV	83%[b]	100%

2-year LC rates of 90% can be achieved with common dose regimens such as 40 to 48 Gy in 3 fractions and 35 to 40 Gy in 5 fractions

SBRT for Liver Metastasis

Study	Number of lesions	Number of patients	Primary	Dose/ fractionation	Toxicity	Median follow Up (Months)	Local control	Survival
Blomgren et al. [24]	Variable	31	Mixed	8-66Gy/1–4	2 Hemorrhagic Gastritis	1.5–3.8	80%	NR
Herfarth et al. [25]	1–3	37	NR	14–26 Gy/1	NR	Mean 14.9	18 m:67%	1 yr.:76% 2 yr.:55%
Hoyer et al. [26]	1–6 (<6 cm)	44	Mixed Majority CRC	45Gy/3	1 Liver Failure 2 severe late GI	52	2 yr.: 86%	1 yr.:67 2 yr.:38
Mendez Romero et al. [27]	1–3 < 7 cm)	25	Mixed Majority CRC	37.5Gy/3	4 acute Grade ≥ 3 1 late Grade 3	12.9	2 yr.: 86%	1 yr.:85% 2 yr.:62%
Rusthoven et al. [29]	1–3 (<6 cm)	47	Mixed Majority CRC	60Gy/3	< 2% Late Grade ≥ 3	16	2 yr. 92% < 3 cm:100%	Median 17.6
Lee et al. [30]	Variable	68	Mixed Majority CRC	28-60Gy/3	8 acute Grade 3 1 Grade 4	10.8	1 yr.: 71%	18 m:47%
Ambrosino et al. [37]	1–3 (<6 cm)	27	Mixed Majority CRC	25-60Gy/3	NR	13	74%	NR
Goodman et al. [23]	1–5 (<5 cm)	26	Mixed Majority CRC	18-30Gy/1	4 late Grade 2	17.3	1 yr.:77%	1 yr.:62% 2 yr.:49%
Rule et al. [31]	1–5	27	Mixed Majority CRC	30Gy/3 50-60Gy/5	No ≥ Grade 2	20	30Gy56% 50Gy:89% 60Gy:100%	30Gy56% 2 yr. 50Gy:67% 2 yr. 60Gy:50% 2 yr
Scorsetti et al. [39]	1–3 (<6 cm)	61	Mixed Majority CRC	52.5–75/3	No ≥ Grade 3	24	91%	1 yr.: 80% 2 yr.:70%

RESEARCH Open Access

Stereotactic Body Radiotherapy (SBRT) for liver metastasis – clinical outcomes from the international multi-institutional RSSearch® Patient Registry

Anand Mahadevan[1*], Oliver Blanck[2,3], Rachelle Lanciano[4], Anuj Peddada[5], Srinath Sundararaman[6], David D'Ambrosio[7], Sanjeev Sharma[8], David Perry[9], James Kolker[10] and Joanne Davis[11]

- 427 patients with 568 liver metastases from 25 academic and community-based centers
- Colorectal adenocarcinoma (CRC) was the most common primary cancer
- Median SBRT dose was 45 Gy (12–60 Gy) delivered in a median of 3 fractions
- Median overall survival (OS) was 22 months
- BED10 ≥ 100 Gy was also associated with improved OS
- Two-year LC rates was better for BED10 ≥ 100 Gy (77.2% vs 59.6%) and the median LC was better for tumors < 40 cm3 (52 vs 39 months)

Mahadevan et al. Radiat Oncol. 2018

SBRT for Cholangiocarcinoma

Authors	Study	Localization	Nr. of Lesions	Nr. of Fractions	Total Dose (Gy)	LC @ 1 year	Median OS (months)	Late Toxicity
Tse [34]	P	IHCC EHCC	10 0	6	28-48	65%	15	1 biliary obstruction 1 bowel obstruction
Goodman [29]	P	IHCC EHCC	5 0	1	18-30	77%	28.6	None
Polistina [28]	R	IHCC EHCC	0 10	3	30[a]	80%[b]	35.5	1 ulceration 2 stenosis
Ibarra [35]	R	IHCC EHCC	11 0	3	22-50	55.5%	11	3 Grad 3
Barney [36]	R	IHCC EHCC	6 4	3-5	45-60	100%	15.5	1 Grade 3 biliary stenosis, 1 Grade 5 liver failure
Momm [22]	R	IHCC EHCC	0 13	10-12	32-56	78%	33.5	1 Grade 3 5 cholangitis
Weiner [37]	P	IHCC EHCC	12 0	5	40-55	91%§	13.2	1 hepatic failure§ 1 biliary stricture
Kopek [27]	R	IHCC EHCC	26 1	3	45	85%	10.6	6 ulcerations 3 stenosis
Mahadevan [30]	R	IHCC EHCC	31 11	3-5	24-45	88%	17	4 Grade 3 (ulceration, cholangitis, abscess)
Sandler [26]	R	IHCC EHCC	6 25	5	40	78%	15.7	5 Grade ≥ 3

PGI Results

Role of stereotactic body radiation therapy in liver metastasis: A pilot study from tertiary cancer institute in India

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ABSTRACT

Purpose: This trial studies the feasibility and potential utility of stereotactic body radiation therapy in patients with unresectable liver metastasis.

Aims: (1) The aim of this study is to assess the local response of the liver lesions poststereotactic body radiation therapy regarding number and size of lesions and (2) to evaluate the toxicity to organ (s) at risk.

Materials and Methods: A total of 15 patients were enrolled in this study from November 2014 to October 2015. The inclusion criteria for this study were patients having 1–3 liver metastasis from any solid tumor except germ cell tumor or lymphoma with no evidence of progressive disease (PD) outside the liver. A planning four dimensional-computed tomography (CT) scan was taken. Planning target volume was generated by giving margin of 5 mm. Dose prescribed was 36 Gy in 3#. Response was defined by CT abdomen done at 3 and 6 months poststereotactic body radiation therapy as per RECIST guideline (v1.1).

Results: At 3 months poststereotactic body radiation therapy, five patients had partial response, five patients had stable disease, and five patients had PD as per RECIST criteria. Out of 20 assessable lesions, 16 were controlled at 3 months poststereotactic body radiation therapy. The actuarial local control rate was 86% at 3 months and 77% at 6 months poststereotactic body radiation therapy. The median progression free survival was 7 months. Two patients experienced Grade 2 gastric toxicity and one patient experienced Grade 2 small bowel toxicity. No cases of radiation-induced liver disease were observed.

Conclusions: This trial examines the feasibility of stereotactic body radiotherapy to liver metastasis in the Indian scenario. It shows excellent tolerability and is a safe therapeutic option for inoperable patients, showing good local control.

- 22 patients with unresectable primary and metastatic liver tumors treated in 2016 and 2017
- Fifty four percent received prior liver directed therapies
- Dose fractionation schedules followed in patients were
  - 54 Gy in 3 fractions (n=4)
  - 48 Gy in 4 fractions (n=5)
  - 36 Gy in 3 fractions (n=12)
- Median follow-up was 11 months
- Out of 22 patients:
  - Three were lost to follow up
  - Eight had partial response
  - Four had stable disease
  - Seven had progressive disease.

Conclusion

- For Primary/ metastatic liver tumors, SBRT is safe and effective, with excellent local control achieved with few challenges:
- Is there a radiation dose-response relationship with HCC.
- What are the optimal dosimetric predictors of RILD and do they differ for patients with varying liver functions.
- How do we assess treatment response on imaging.
- How does SBRT compare to other liver-directed therapy modalities.

Thank You