Proton therapy in Liver: HPSP experiences

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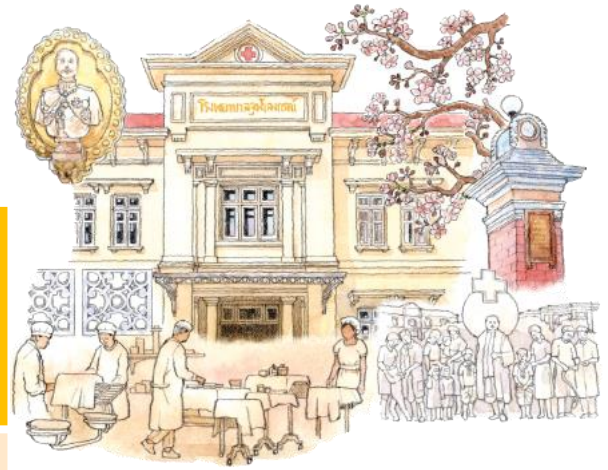
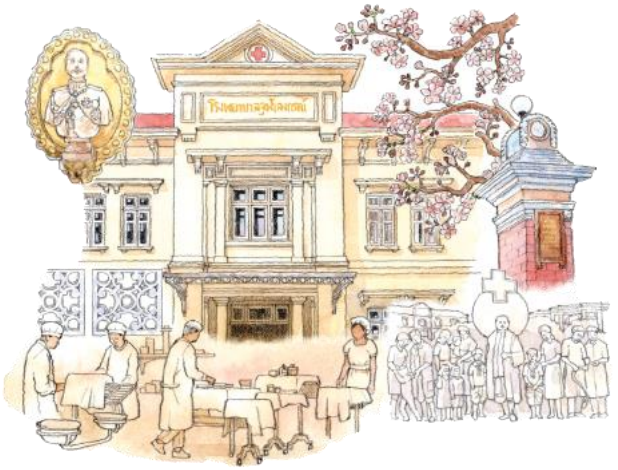
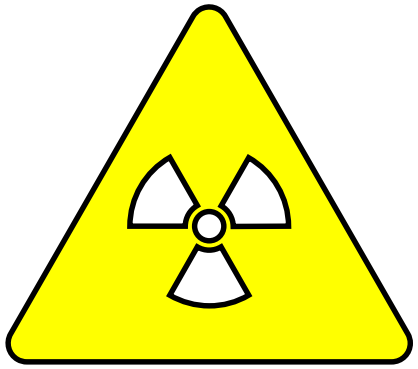
โรงพยาบาลจุฬาลงกรณ์
สภากาชาดไทย

Year	N	Percent
2022	74	21.20
2023	74	21.63



Liver tumor is the NUMBER ONE disease treated with proton therapy





INDICATIONS

RT in clinical practice guidelines (Localized HCC)

Affiliation	Country	Year	Evidence of RT	Recommendation of RT	Potential role of RT in clinical situations
APASL	Multinational (Asia)	2017	Low/very low	Weak	• SBRT for small HCC • Particle therapy for large HCC or PVTT
KLCA-NCC	Korea	2018	Low/moderate	Weak/strong	• RT for HCC ineligible for surgery, LT, other LRTs • RT for incomplete response to TACE • RT for HCC with PVTT (combined with TACE) • Palliative RT for metastases
JSH	Japan	2017	-	Weak	• SBRT for HCCs not indications for other LRTs • Particle therapy for HCCs not eligible for other LRTs • 3D-CRT when SBRT and particle therapy are not eligible (PVTT, unresectable HCC)
TLCA	Taiwan	2015	Level 2	Recommended	• Medically inoperable, refusal of standard treatment, bridge to transplant, unsuitable/refractory to TACE, localized HCC with symptoms, PVTT, symptomatic metastasis or oligo-metastasis in all BCLC stages
NHFPC	China	2017	Level 3	-	• RT for PVTT, IVCTT or extrahepatic metastases, bridge to LT, relieving symptoms • Adjuvant RT for centrally located tumors with narrow surgical margins
	Hong Kong	2015	Level 4/5	-	• RT for effective local control, a viable portion for unresectable HCC, combined with TACE for unresectable HCC • SBRT as an alternative to ablation and a bridging therapy before LT
AASLD	United States	2018	Level 2	-	• SBRT as an alternative to thermal ablation
EASL	Multinational (Europe)	2018	Low	Weak	• RT in combination with TACE • SBRT as a bridge to LT • RT for PVTT • Palliative RT for pain, impending fracture
ESMO	Multinational (Europe)	2018	Level 3	B/C	• SBRT as alternatives for the ablation • Palliative RT for bone metastases

RT, radiotherapy; APASL, Asia-Pacific Association for the Study of the Liver; SBRT, stereotactic body radiotherapy; HCC, hepatocellular carcinoma; PVTT, portal vein tumor thrombus; KLCA-NCC, Korean Liver Cancer Association-National Cancer Center; LT, liver transplantation; LRT, locoregional therapy; TACE, transarterial chemoembolization; JSH, Japan Society of Hepatology; 3D-CRT, 3-dimensional conformal radiotherapy; TLCA, Taiwan Liver Cancer Association; BCLC, Barcelona Clinic Liver Cancer; NHFPC, National Health and Family Planning Commission; IVCTT, inferior vena cava tumor thrombus; AASLD, American Association for the Study of Liver Diseases; EASL, European Association for the Study of the Liver; ESMO, European Society for Medical Oncology.

Low/weak evidence

Technique

SBRT, Particle therapy, (3DCRT)

Indication

Small HCC, ineligible to another local Tx

Combined with TACE (refractory)

Unsuitable for TACE

PVTT

Bridging therapy before liver transplant

Positive margin after Sx

More recommended in Asian countries

Yoon SM. J Liver Cancer. 2021;21(1):25-33.

Practical Radiation Oncology® (2022) 12, 28–51

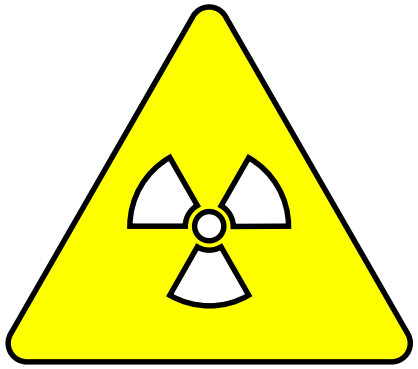
GUIDELINE

www.practicalradonc.org

Clinical Practice Guideline

External Beam Radiation Therapy for Primary Liver Cancers: An ASTRO Clinical Practice Guideline

Smith Apisarnthanarax, MD,[a,*] Aisling Barry, MD,[b] Minsong Cao, PhD,[c] Brian Czito, MD,[d] Ronald DeMatteo, MD,[e] Mary Drinane, MD,[f] Christopher L. Hallemeier, MD,[g] Eugene J. Koay, MD, PhD,[h] Foster Lasley, MD,[i] Jeffrey Meyer, MD, MS,[j] Dawn Owen, MD, PhD,[g] Jennifer Pursley, PhD,[k] Stephanie K. Schaub, MD,[a] Grace Smith, MD, PhD, MPH,[h] Neeta K. Venepalli, MD, MBA,[l] Gazi Zibari, MD,[m] and Higinia Cardenes, MD, PhD[n]

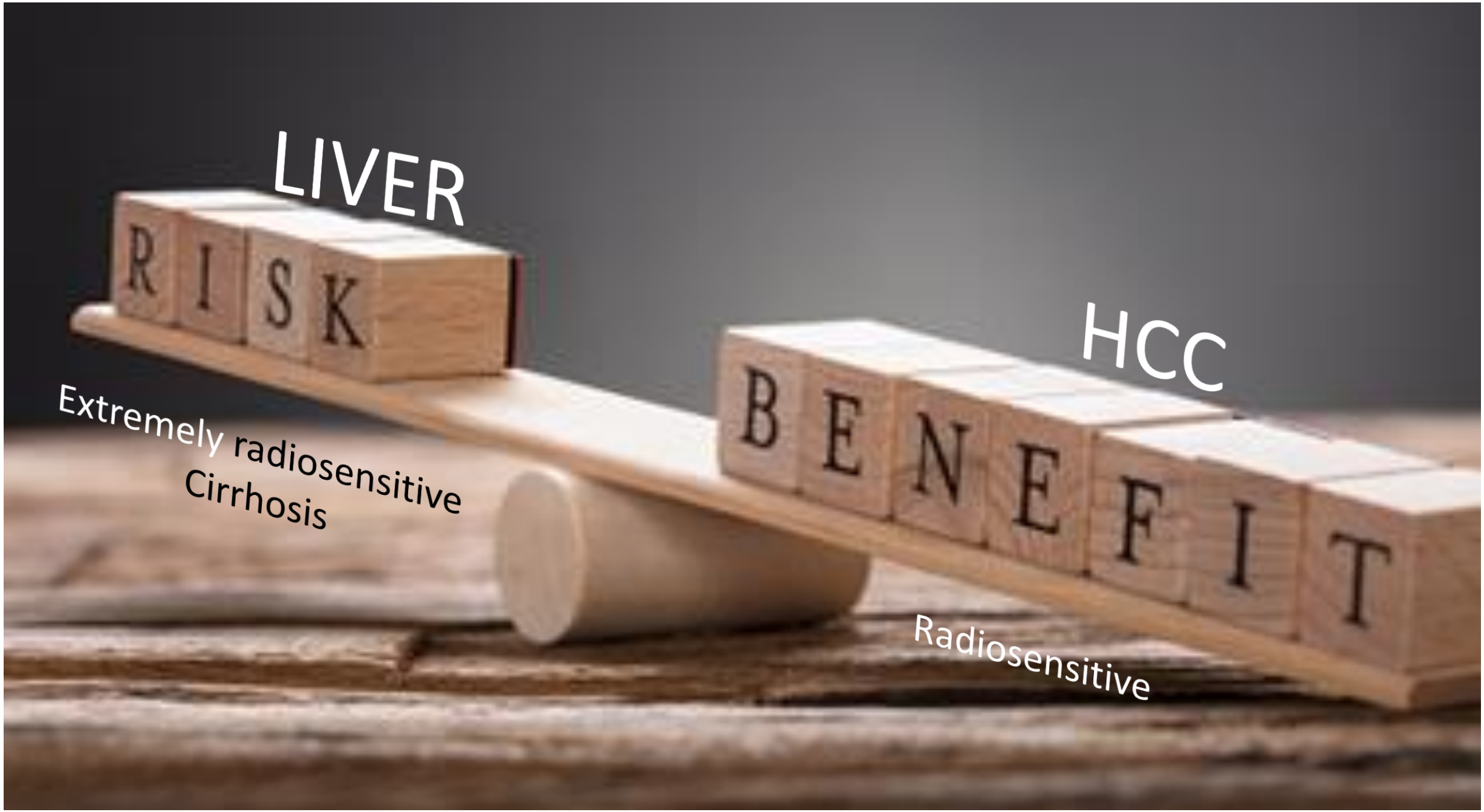


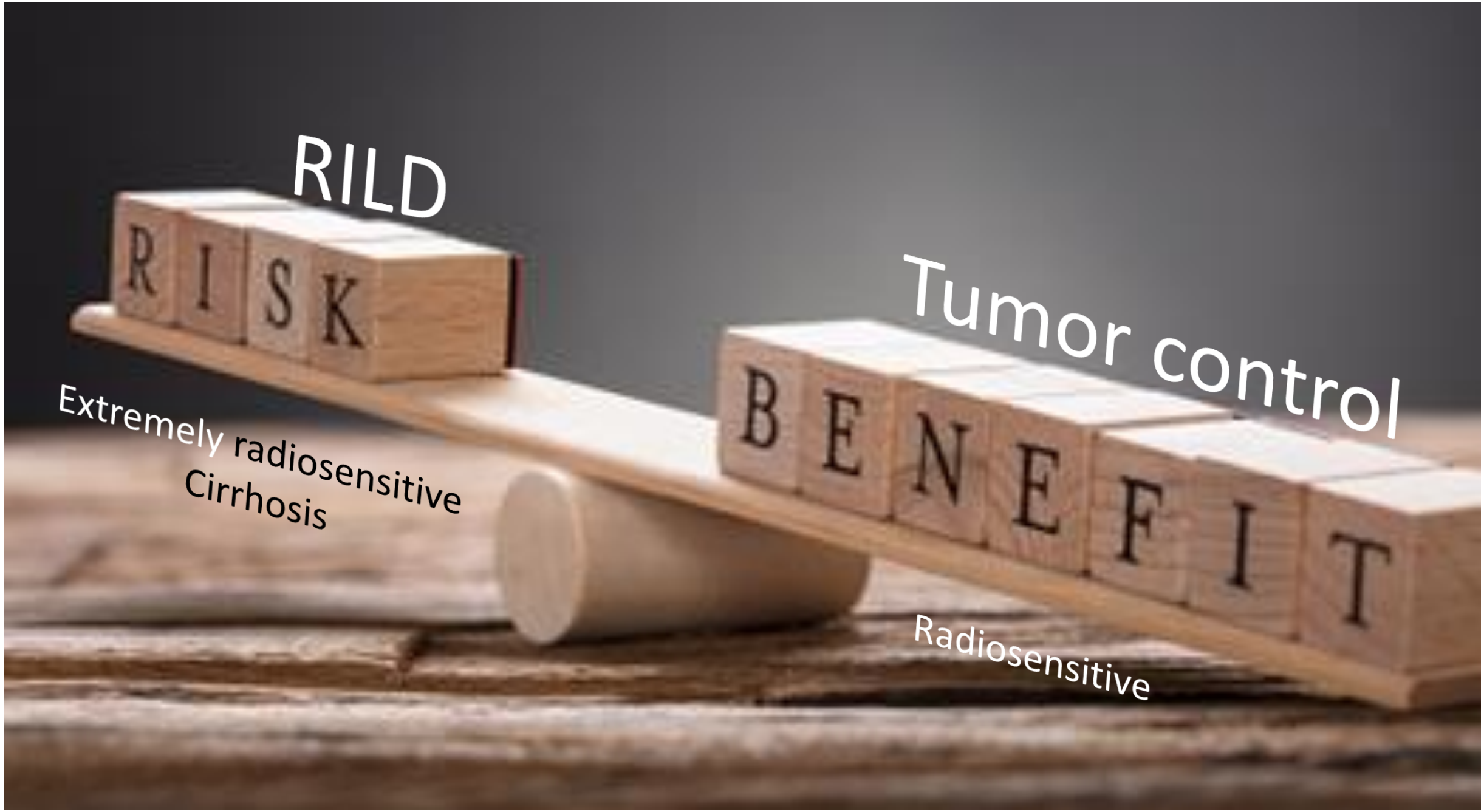
TECHNIQUE and FRACTIONATION regimen

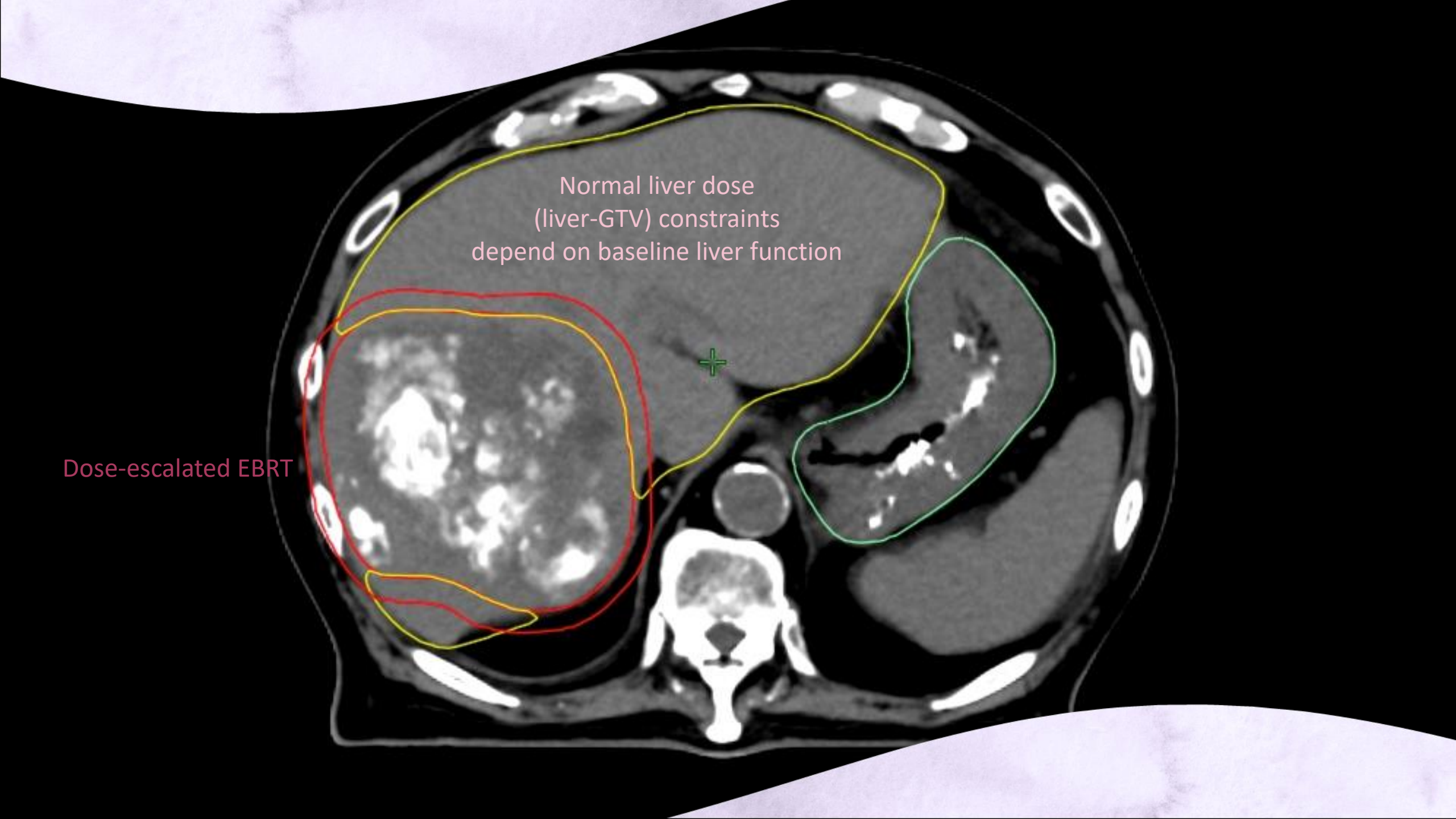
TECHNIQUE and FRACTIONATION regimen

- For patients with liver-confined HCC +/- macrovascular invasion, *dose-escalated ultra- or moderately hypofractionation* EBRT is recommended.
- Key to determining dose/fractionation and radiation technique depends on
  - Tumor location and size
  - Underlying liver function
  - Available technology

Apisarnthanarax S et al. Pract Radiat Oncol 2022;12:28-51.


LIVER
RISK
Extremely radiosensitive
Cirrhosis
HCC
BENEFIT
Radiosensitive


RILD
RISK
Extremely radiosensitive
Cirrhosis
Tumor control
BENEFIT
Radiosensitive


Normal liver dose
(liver-GTV) constraints
depend on baseline liver function
Dose-escalated EBRT

TECHNIQUE and FRACTIONATION

Regimen: Required dose escalation

- The optimal dose-response relationship is not clearly defined. (potentially had dose-response relationship)
- Using **dose escalation (minimum BED_{10} 65 – 100 Gy)** has potential benefit in term of **improved LC and OS**.

Apisarnthanarax S et al. Pract Radiat Oncol 2022;12:28-51.

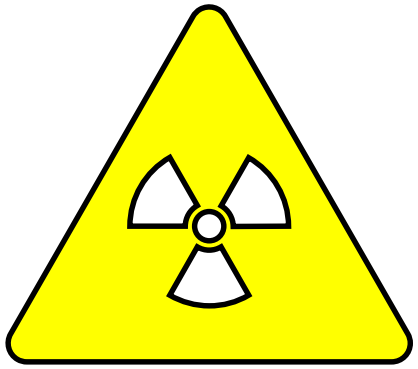
TECHNIQUE and FRACTIONATION

Regimen: ASTRO 2022

Most common 30-50GyE in 5F

Fractionation Regimen	Total dose/fractionation	BED10
Ultra hypofractionation	**CP class A: 4000-5000 cGy/3-5 fx**	7200-12,500 cGy
	CP class B7: 3000-4000 cGy/5 fx	4800-7200 cGy
	4000-5400 cGy/6 fx	6700-10,300 cGy
	5000-6600 cGy/10 fx	7500-11,000 cGy
Moderate hypofractionation	4800 cGy/12 fx	6720 cGy
	4500-6750 cGy/15 fx	5900-9800 cGy
	6000 cGy/20 fx	7800 cGy
	6600-7200 cGy/22 fx	8600-9600 cGy
Standard fractionation	**5040 cGy/28 fx‡**	5947 cGy
	6000 cGy/30 fx‡	7200 cGy
	7700 cGy/35 fx	9400 cGy

Apisarnthanarax S et al. Pract Radiat Oncol 2022;12:28-51.



DOSE CONSTRAINTS for OARs

DOSE CONSTRAINTS FOR UNINVOLVED LIVER: ASTRO 2022

Mean Liver Dose (Liver-GTV)	Ultrahypofx 3 fx	Ultrahypofx 5 fx	Toxicity endpoint
noncirrhotic	Mean <12-15 Gy ≥700 cc <19 Gy	Mean <15-18 cGy ≥700 cc <21 Gy	RILD
CP class A	Mean <10-12 Gy	Mean <13-15 Gy ≥700 cc <15 Gy	CP increase ≥2 at 3 mo RILD
CP class B7	N/R[†]	Mean <8-10 Gy ≥500 cc <10 Gy	CP increase ≥2 at 3 mo RILD

CP class B patients are at very high risk of decompensation. The task force does not recommend 3 fraction SBRT; a 5 fraction SBRT regimen or hypofractionated approach to keep the MLD as low as possible is preferred

Apisarnthanarax S et al. Pract Radiat Oncol 2022;12:28-51.

DOSE CONSTRAINTS FOR UNINVOLVED LIVER: HyTEC 2021

OARs/ References	Ultrahypofx 3 fx	Ultrahypofx 5 fx	Toxicity endpoint	Rate
Uninvolved liver (MLD)	Mean ≤ 13 Gy	Mean ≤ 18 Gy	G ≥ 3 liver enzyme change	<20%

In patients with hepatocellular carcinoma, sparing ≥ 800 cm^3 to ≤ 18 Gy in 3 Fx has been suggested.

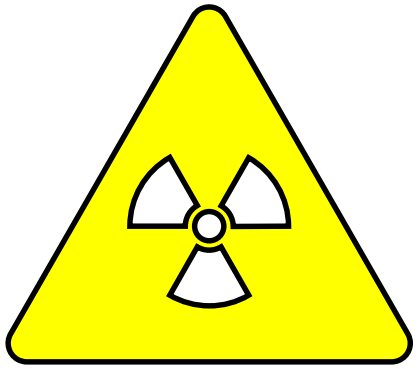
Miften M et al. Int J Radiat Oncol Biol Phys. 2021 May 1;110(1):196-205.

DOSE CONSTRAINTS FOR OARs : ASTRO 2022

CHULA CANCER
รังสีรักษาและมะเร็งวิทยา

OARs/ References	Ultrahypofx 3 fx	Ultrahypofx 5 fx	Toxicity endpoint
Central bile ducts	D0.03 cc <3570 cGy	D0.03 cc <4050 cGy	Stenosis
Stomach	D0.03 cc <2200 cGy D10 cc <1650 cGy	D0.03 cc <3200 cGy D10 cc <1800 cGy	Ulcer
Duodenum	D0.03 cc <2200 cGy D5 cc <1650 cGy	D0.03 cc <3200 cGy D5 cc <1800 cGy	Ulcer
Small bowel	D0.03 cc <2500 cGy D5 cc <1800 cGy	D0.03 cc <3200 cGy D5 cc <1950 cGy	Ulcer
Large bowel	D0.03 cc <2800 cGy D20 cc <2400 cGy	D0.03 cc <3400 cGy D20 cc <2500 cGy	Ulcer

Apisarnthanarax S et al. Pract Radiat Oncol 2022;12:28-51.

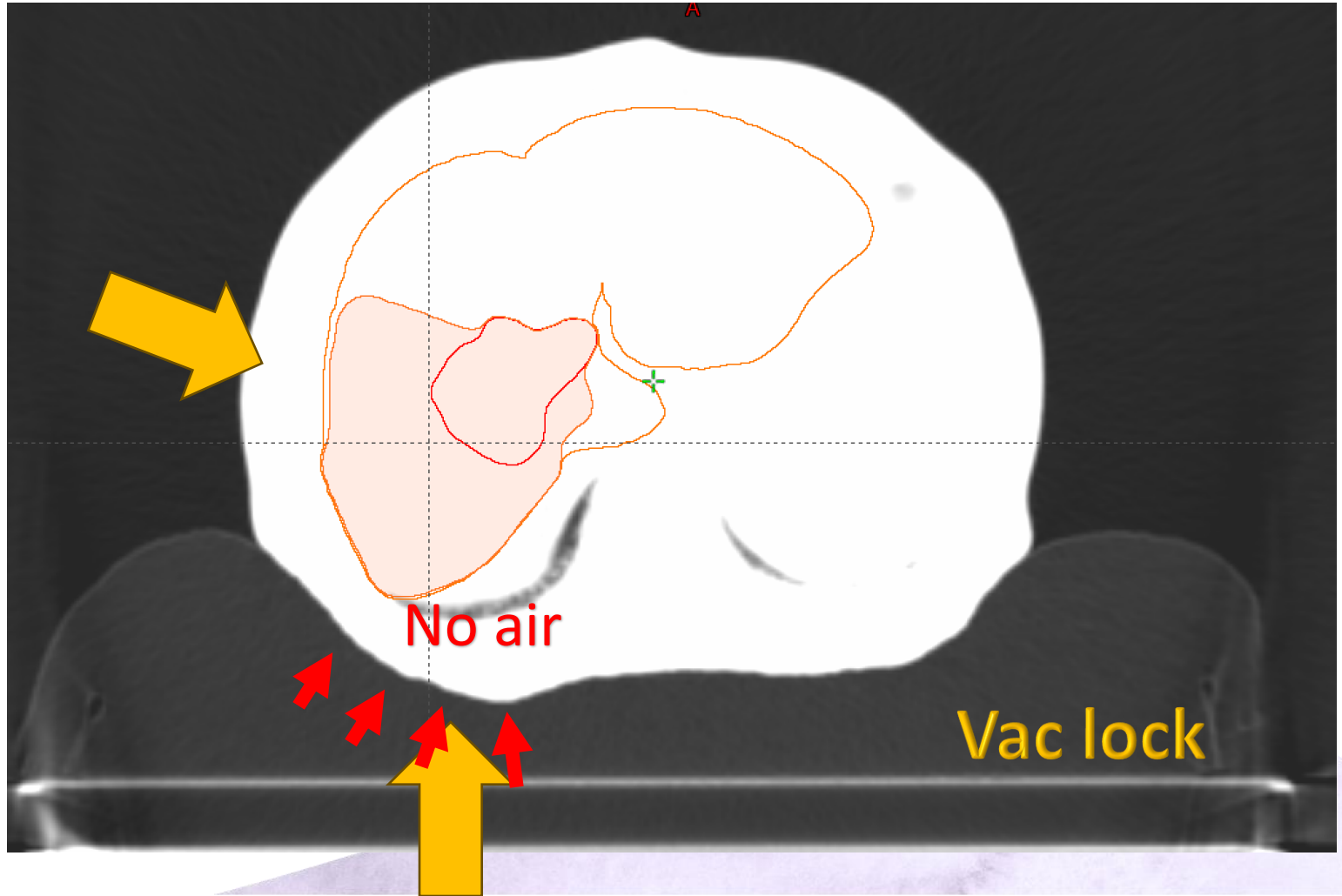


SIMULATION and CONTOURING

SIMULATION

Preparation for simulation

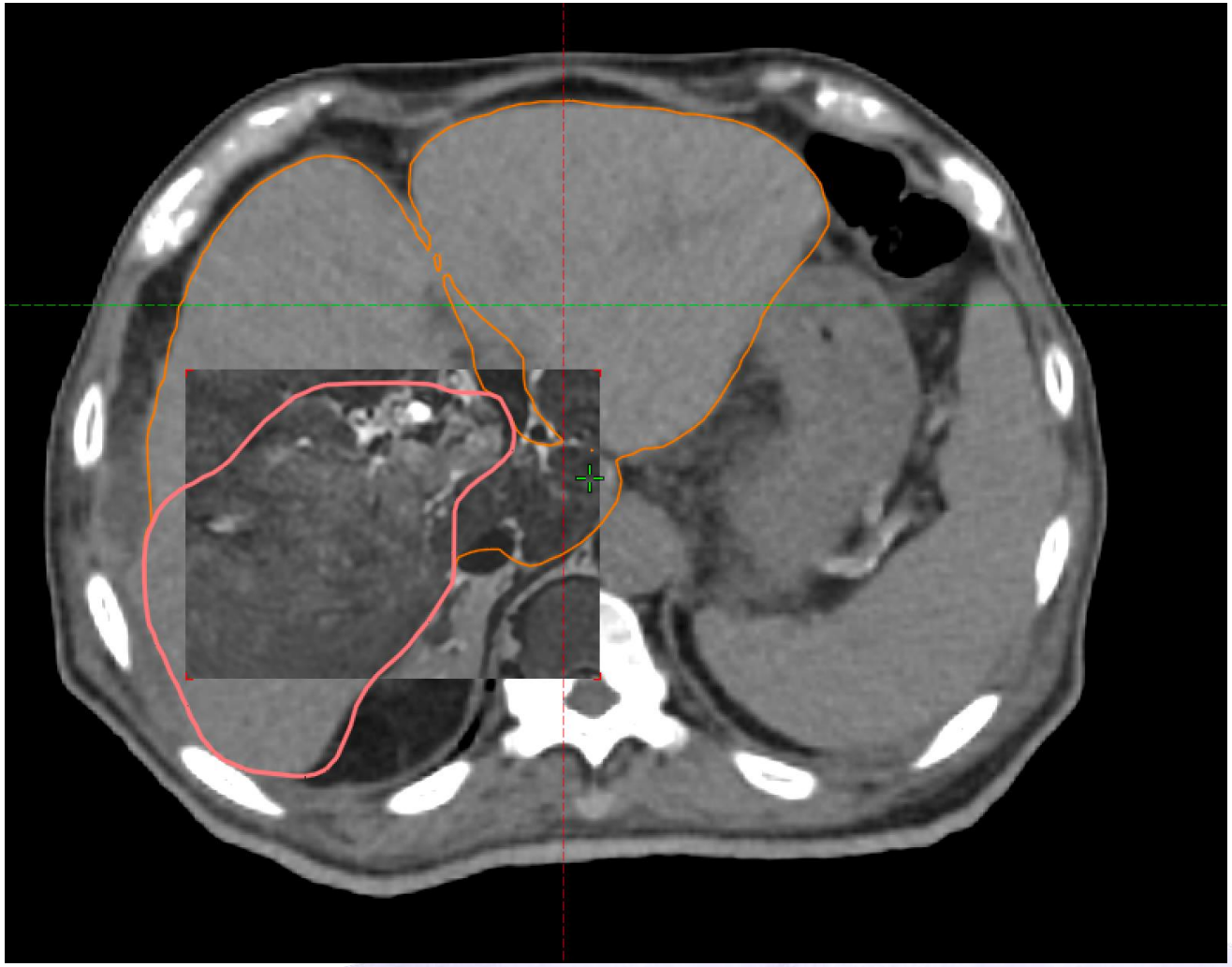
Beam directions design



SIMULATION

Simulation

- ✓ Consider **fiducial placement**
- ✓ MR sim in treatment position
- ✓ NPO prior to CT simulation
- ✓ IV contrast (triple phase) CT



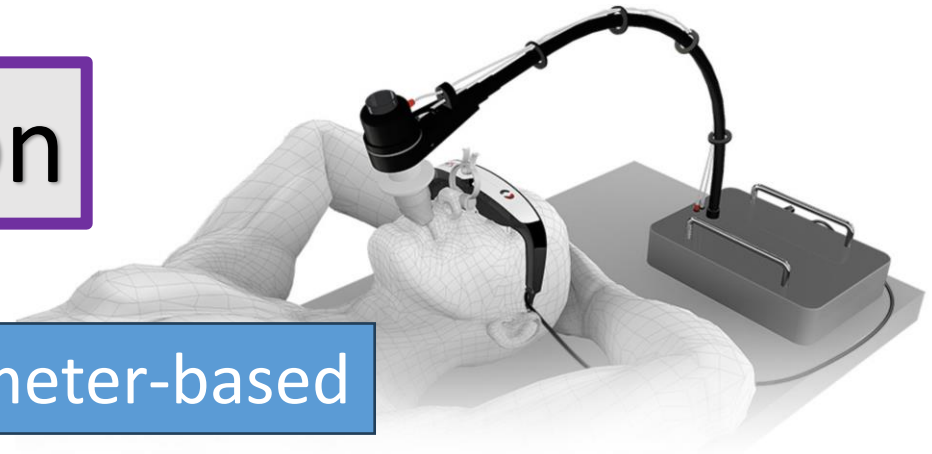
SIMULATION

Motion management

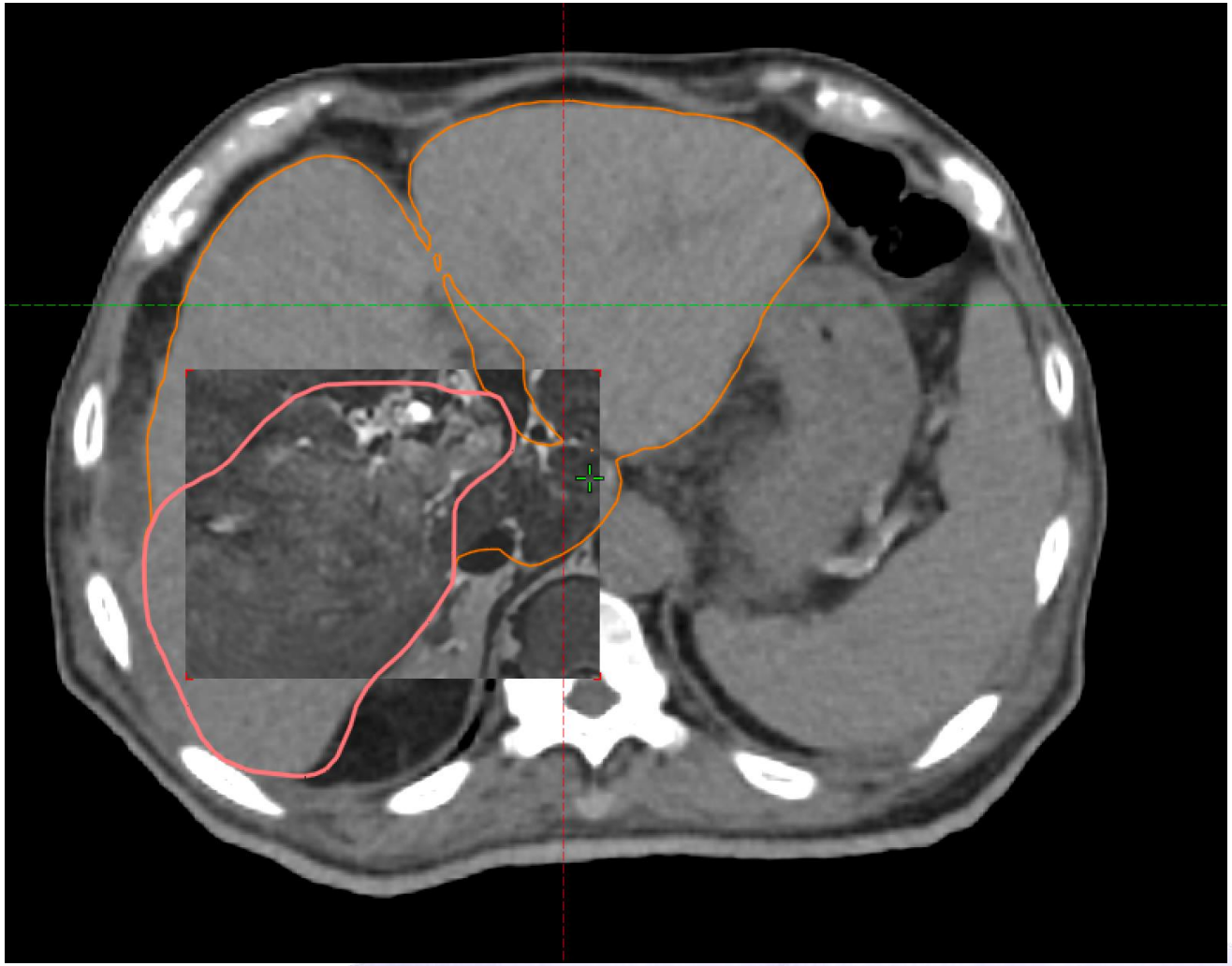
1. Deep-Expiration Breath Hold (DEBH)
2. 4D simulation +/- Gated therapy

Abdominal compression

Soon

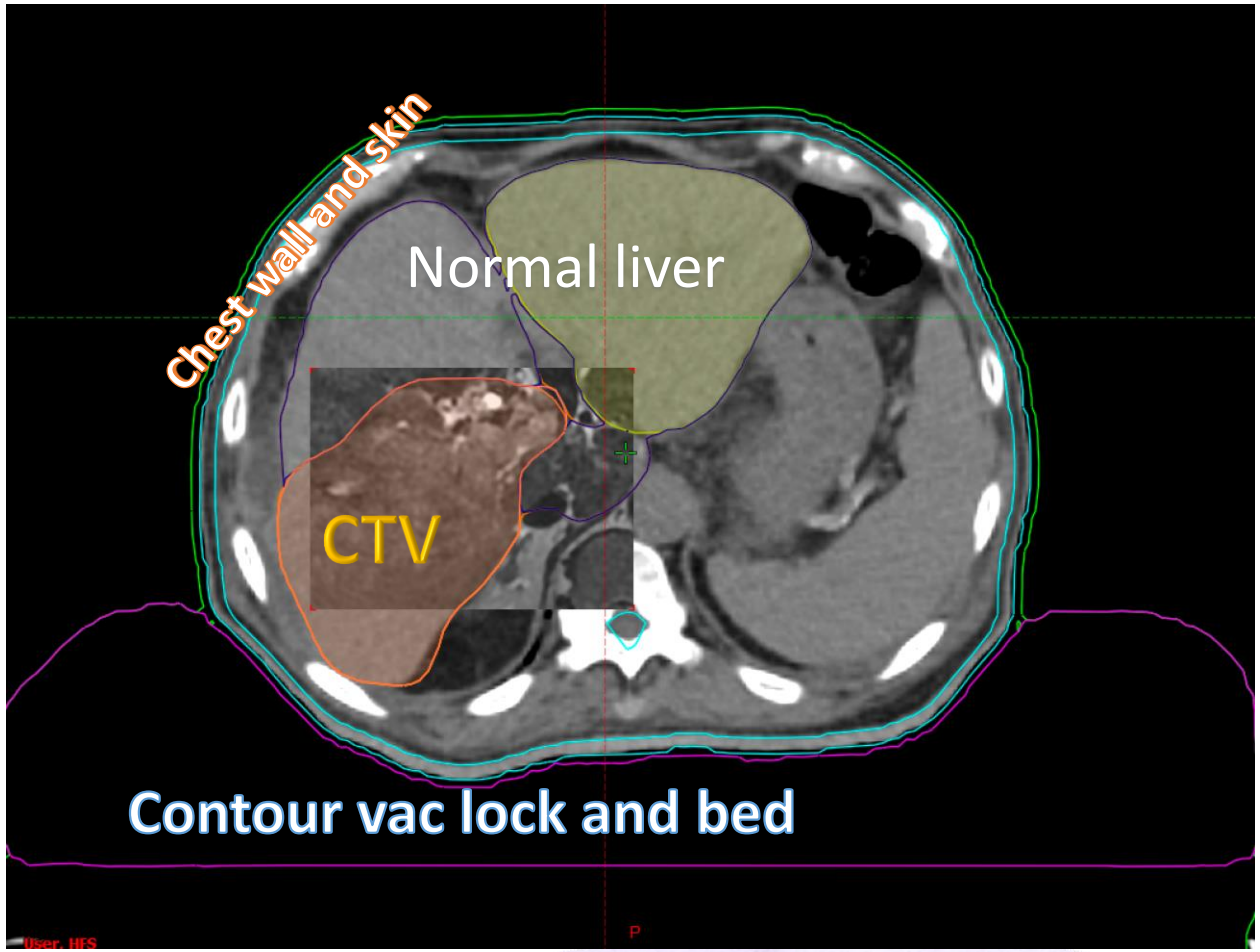


Spirometer-based



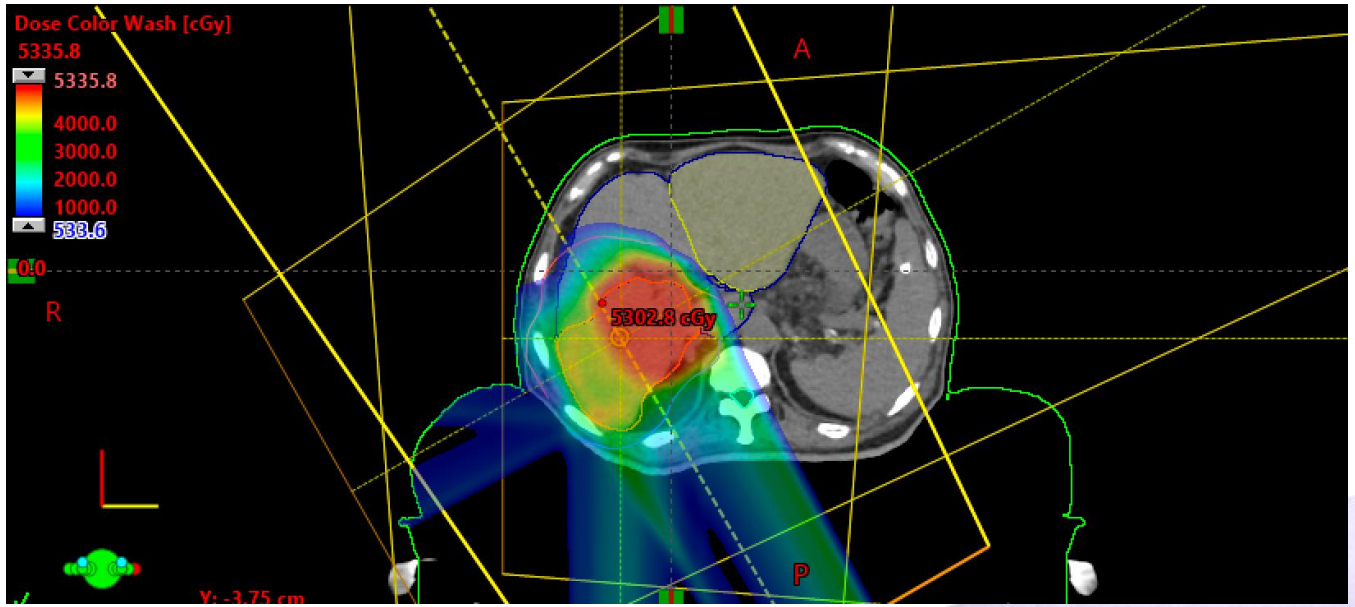
Contouring

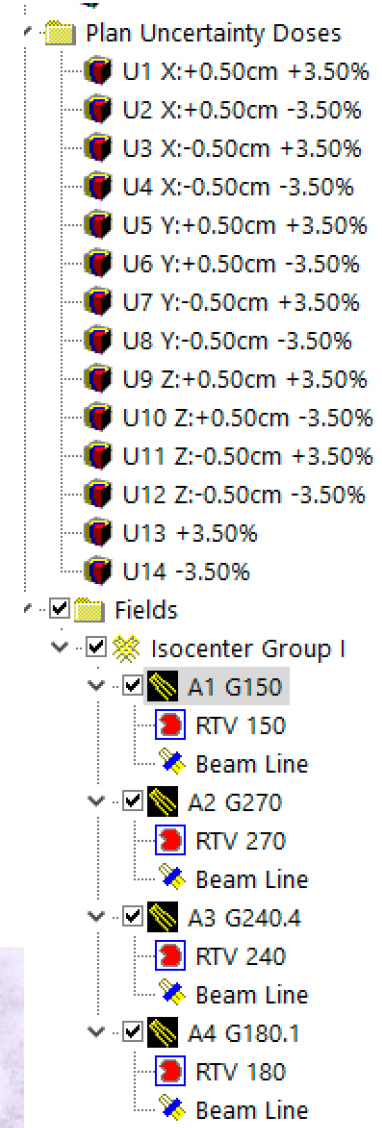
- GTV = gross tumor
- CTV = GTV + (0-10 mm)
- No PTV



Optimization

- Beam design – optimal numbers
- Robust optimization (compensated PTV)
- Dose repainting (compensated respiration)

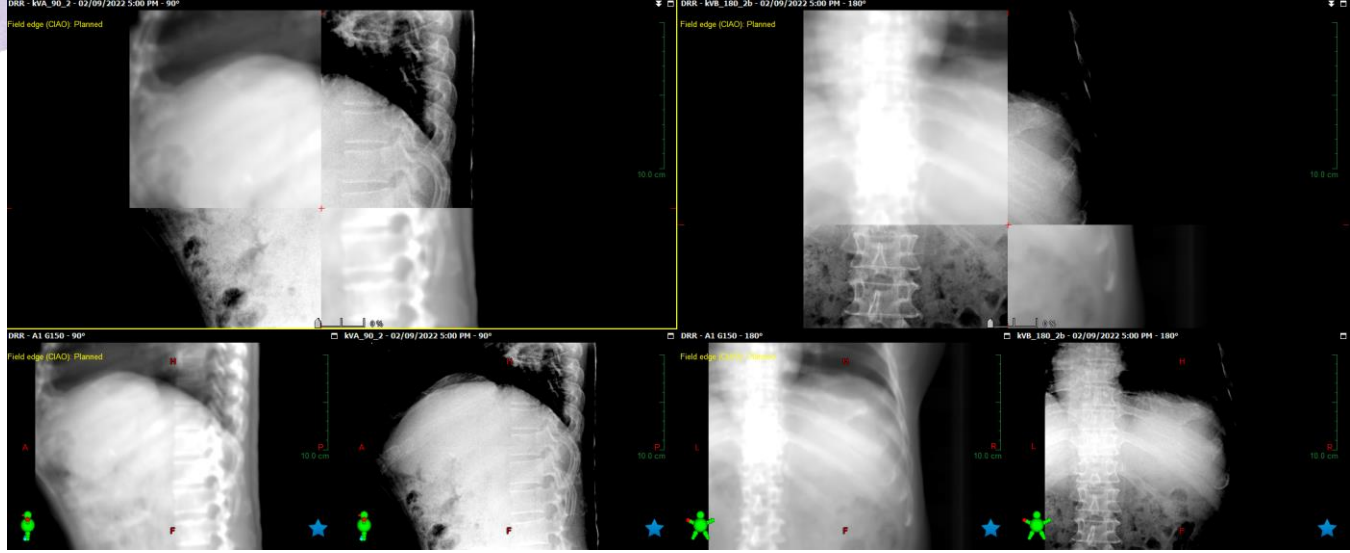


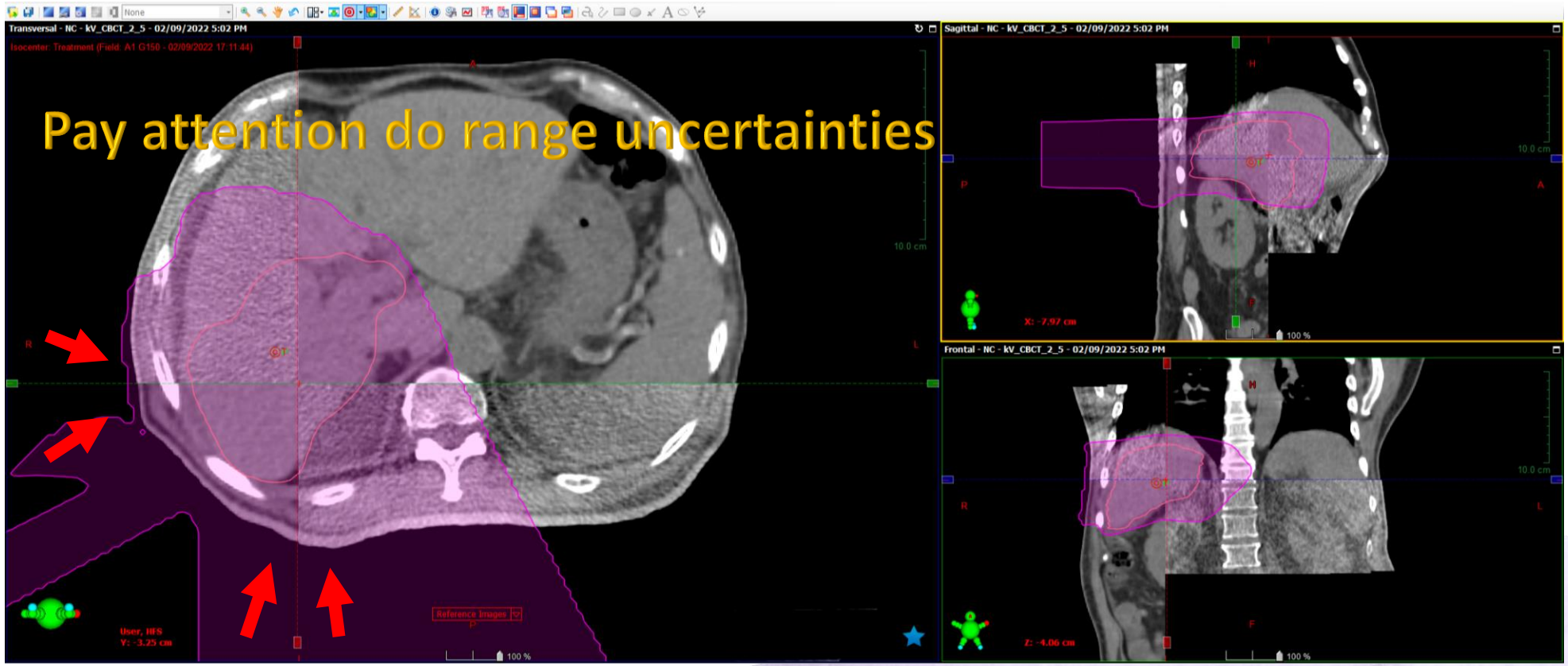


IGRT

In-room IGRT

- Orthogonal kV
- CBCT (30-60 sec)





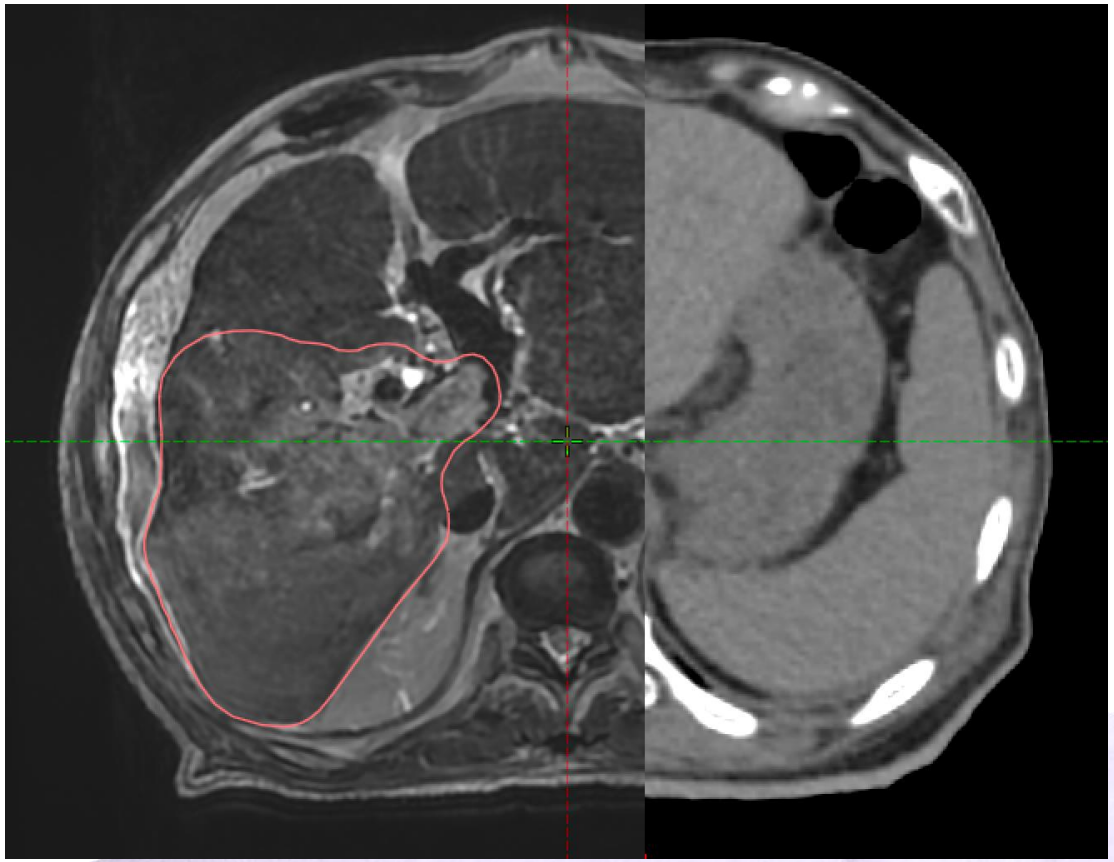
Treatment

Treatment time; depend on

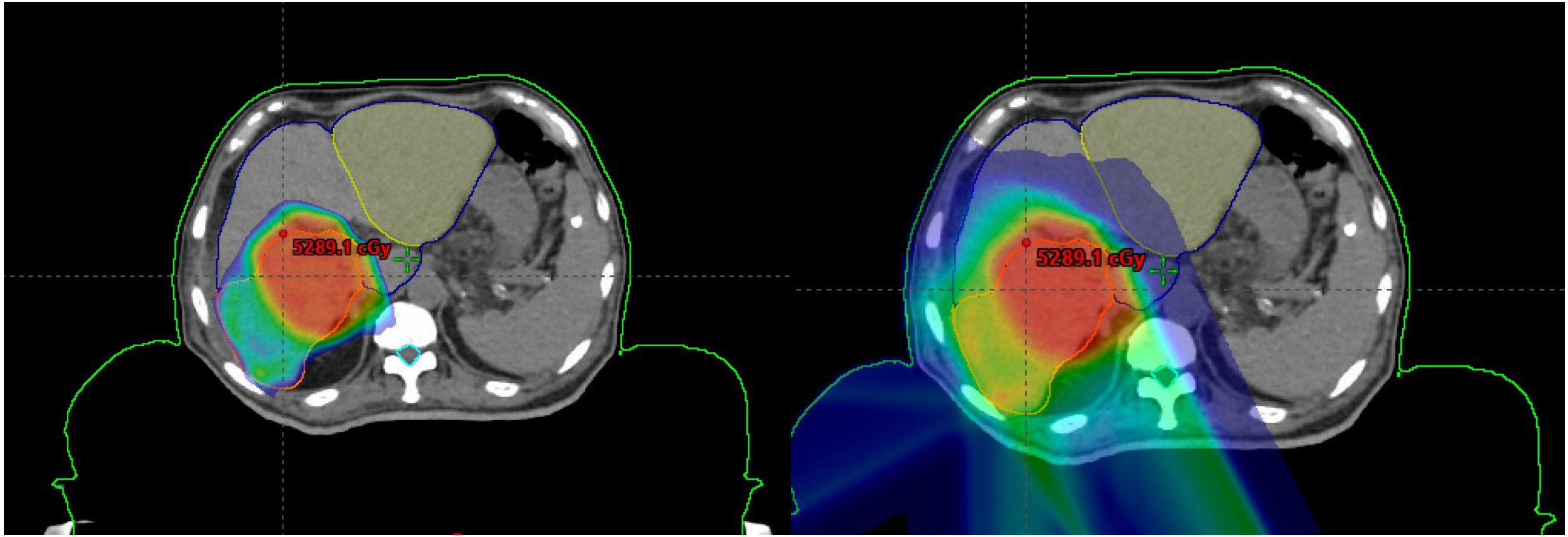
- Respiratory management
- Tumor size
- Number of fields
- 30-60 minutes

Case

- A 70 year-old male paitent
- Hepatocellular carcinoma mass at S5-6 size 6x5.5x6.5 cm extending into right hepatic vein and portal bifurcation and also invoving hilar bild ducts, other illed defined hypodense lesions at S5-6, measure 8x6.7x7.6 cm and 3.3x3.5x5 cm
- AFP 20,838 IU/mL

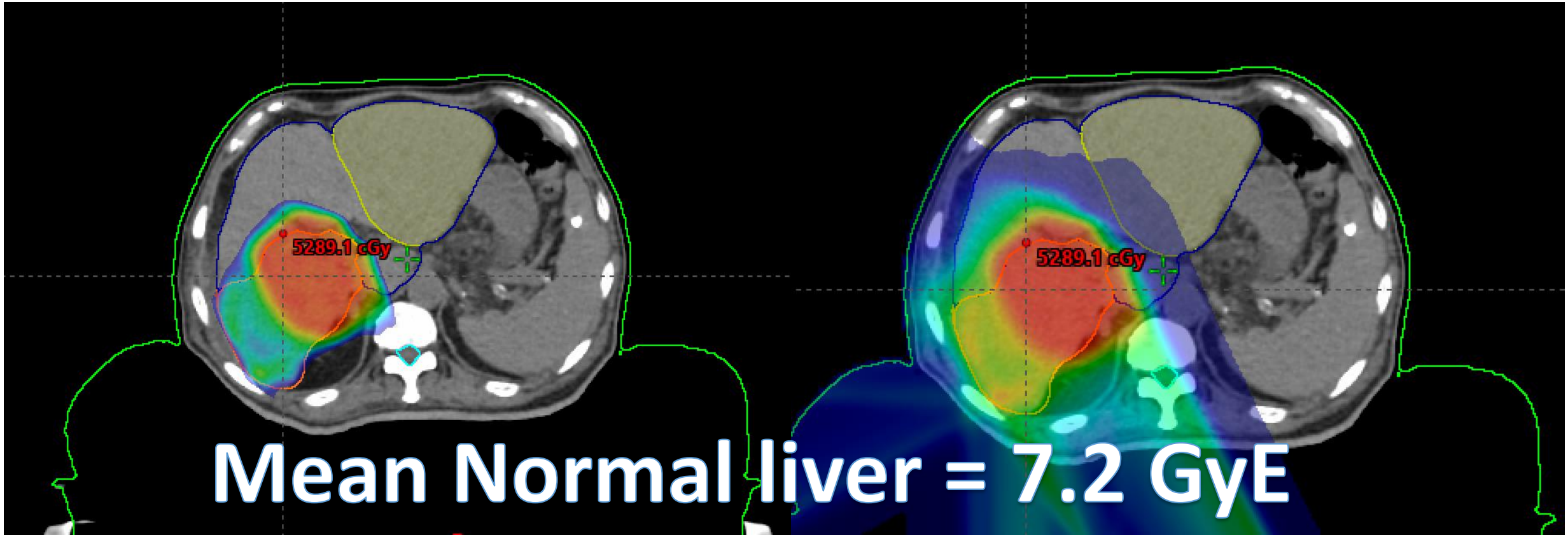


Treatment



Stereotactic proton therapy 50Gy/5F
Last 12/9/2565

Treatment



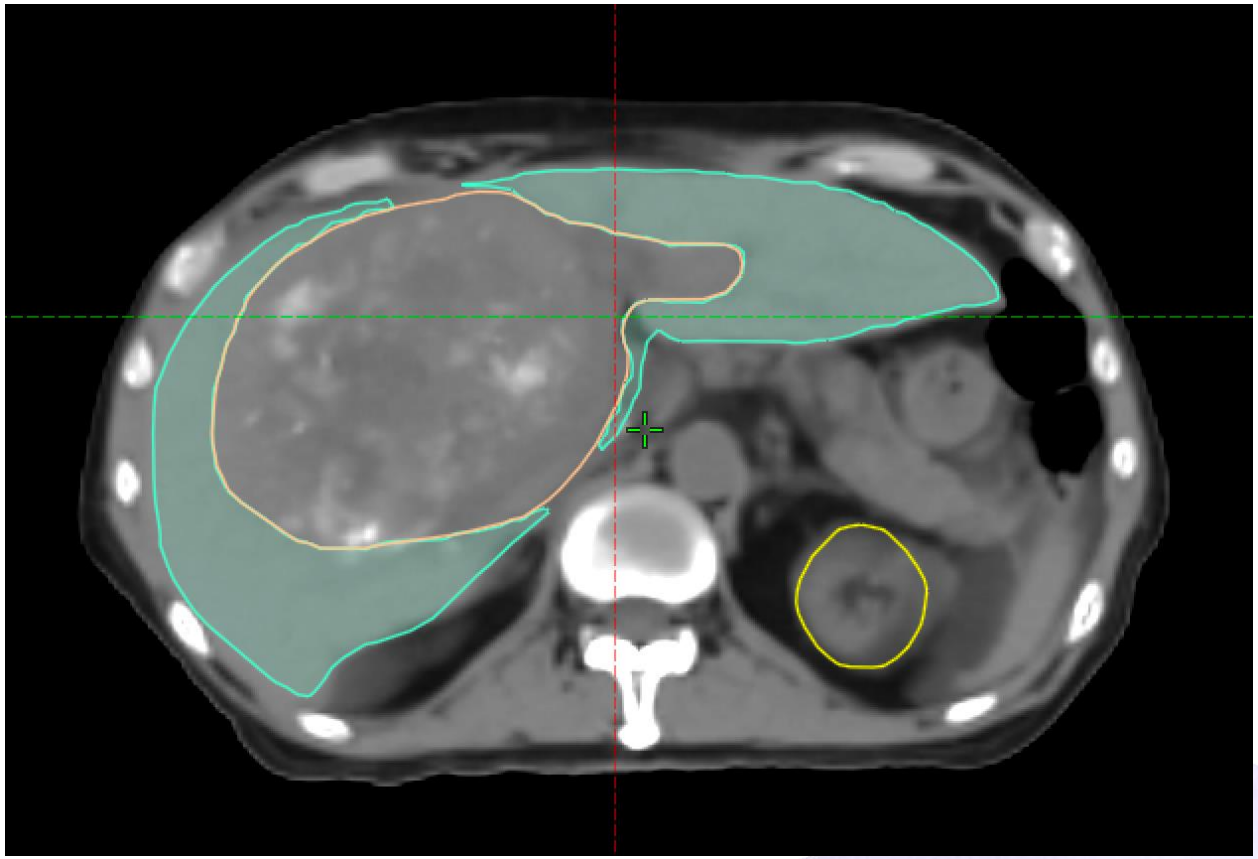
Then Atezolizumab + bevacizumab last 28/4/66

Now not ongoing treatment and CT 12/2/67 – No viable tumor

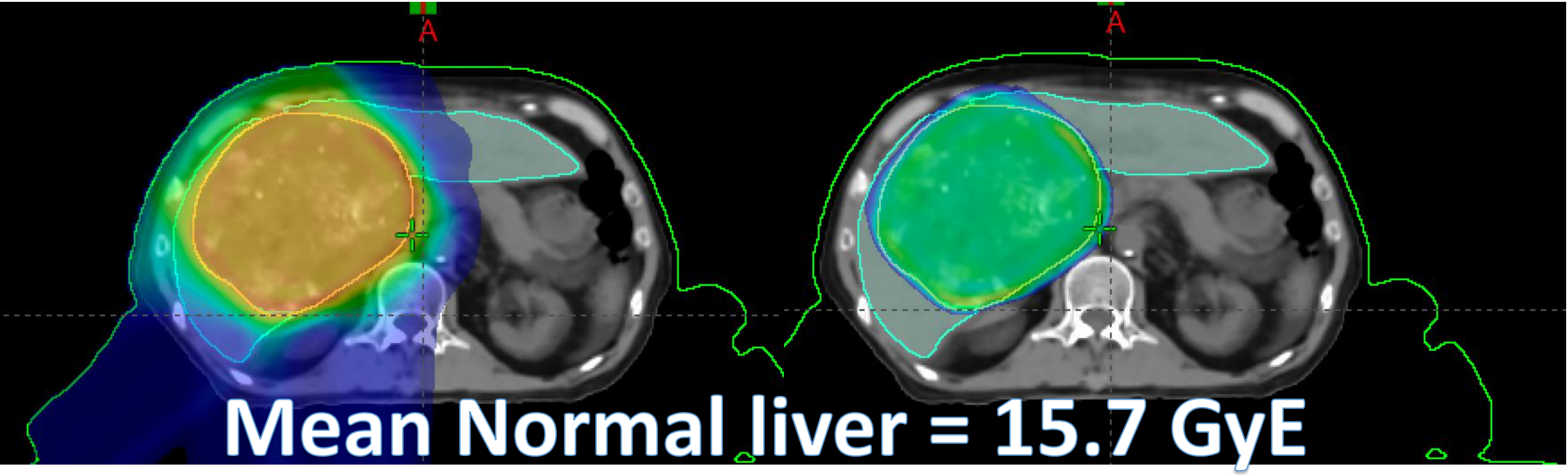
AFP < 0.75 IU/mL

Case2

- A 70 year-old male paitent with end stage renal disease
- A 10.6x13.1 cm partial lipiodol staining mass at left medial segment and right anterior segment with viable tumor
- AFP 337 IU/mL



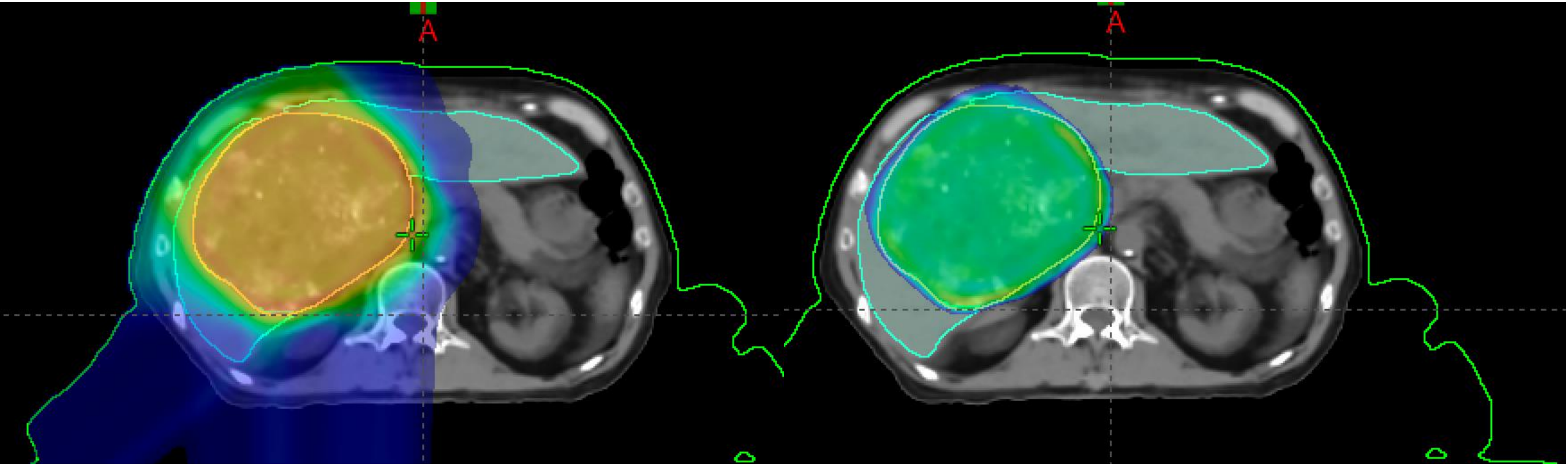
Treatment



Stereotactic proton therapy 60Gy/10F

Last 17/2/256

Treatment



Now not ongoing treatment and CT 6/2/67 – No viable tumor

AFP < 0.75 IU/mL

THANK YOU FOR YOUR ATTENTION