

Real Time Motion Synchronization and Adaptive Radiotherapy for Liver Tumors

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Objectives

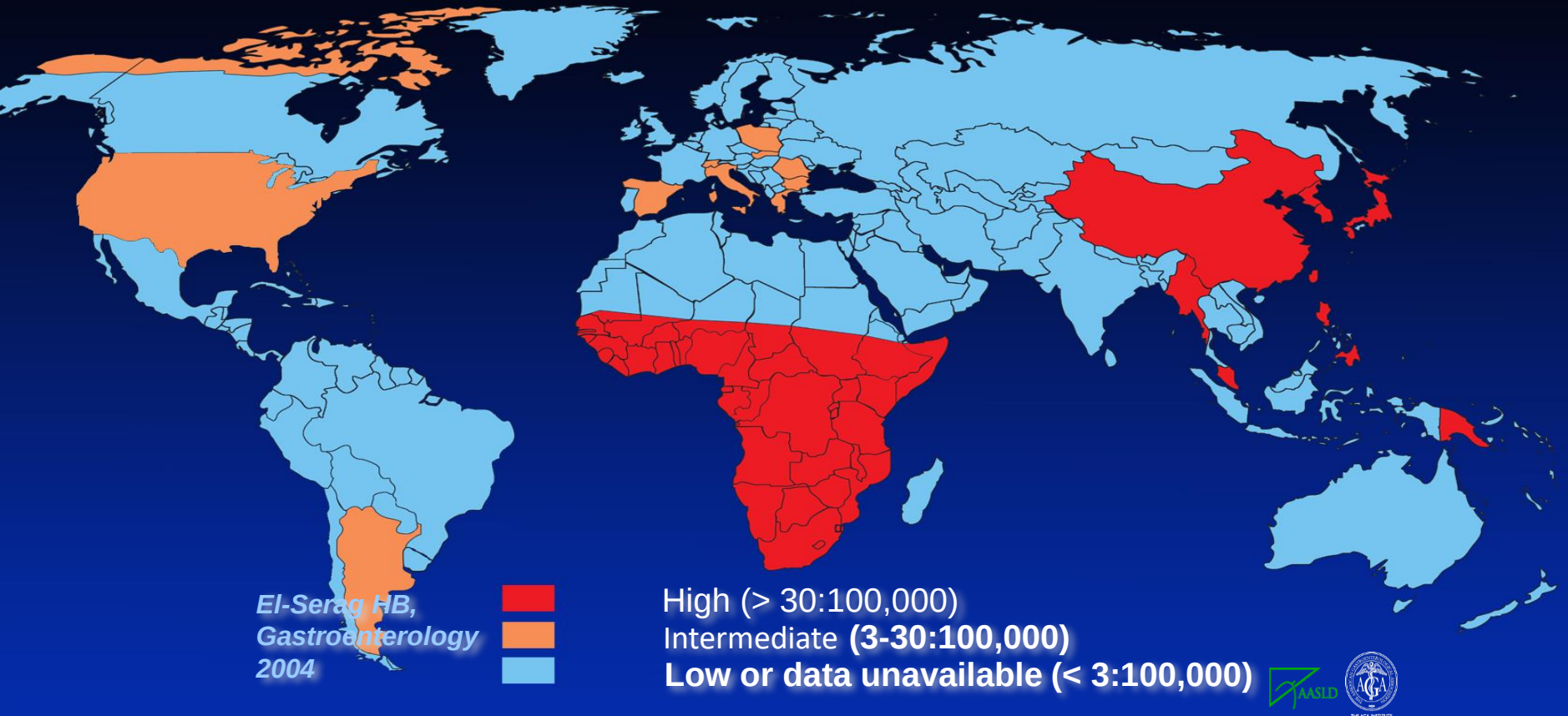
- Radiation therapy in Liver tumors
- Challenges of Radiation and SBRT for liver tumors
- Significance of Image guidance in treatment of liver tumors
- Importance of motion management
- Role of Adaptation to improve outcomes
- Future Directions

Fundamental Principles

- Surgery is the primary curative treatment for Cancer
- Systemic therapy is essential component in the multimodality management of cancer
- Radiation therapy is more about protecting normal tissue than treating cancer

HCC Epidemiology

Worldwide Incidence of Hepatocellular Carcinoma



Treatment Options – Hepatocellular carcinoma

A. Surgical resection

B. Ablation

- Cryotherapy

- Radiofrequency ablation

- Laser interstitial thermal therapy (LITT)

- Microwave coagulation therapy

C. Chemotherapy

- Intra-arterial

- Systemic

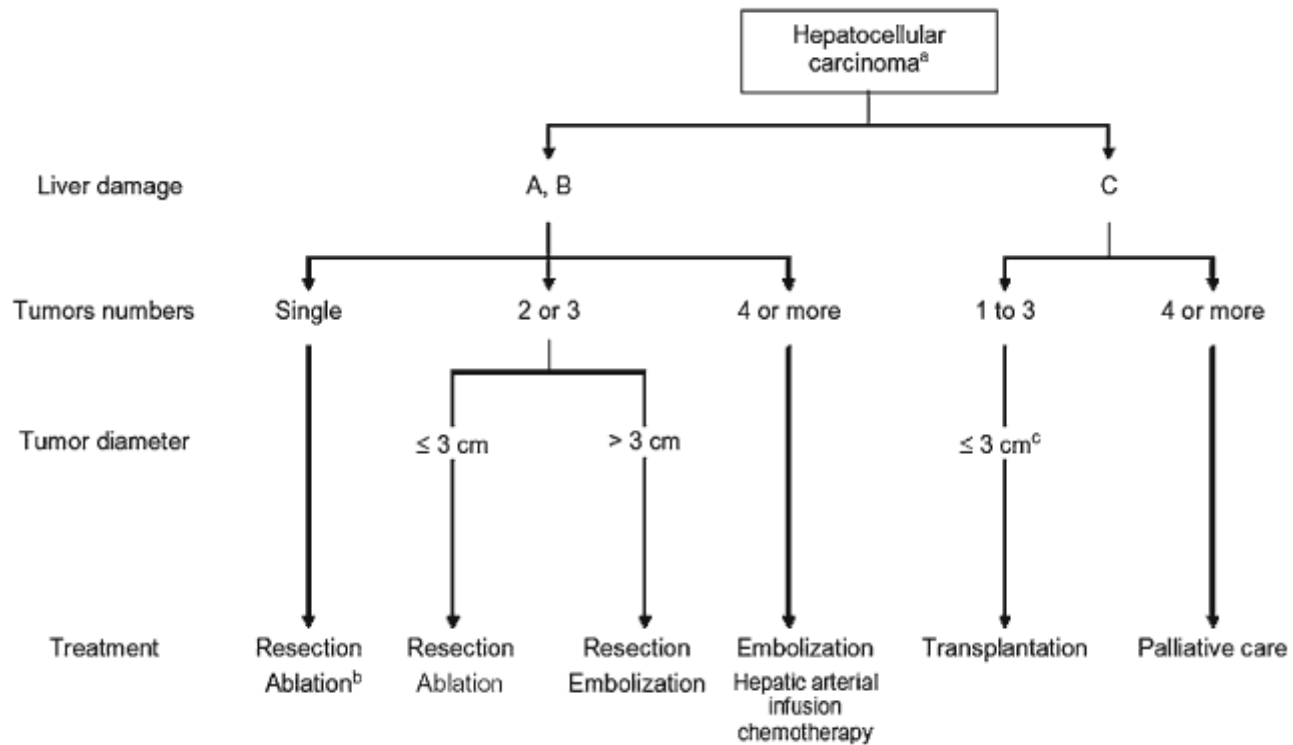
- Chemoembolisation

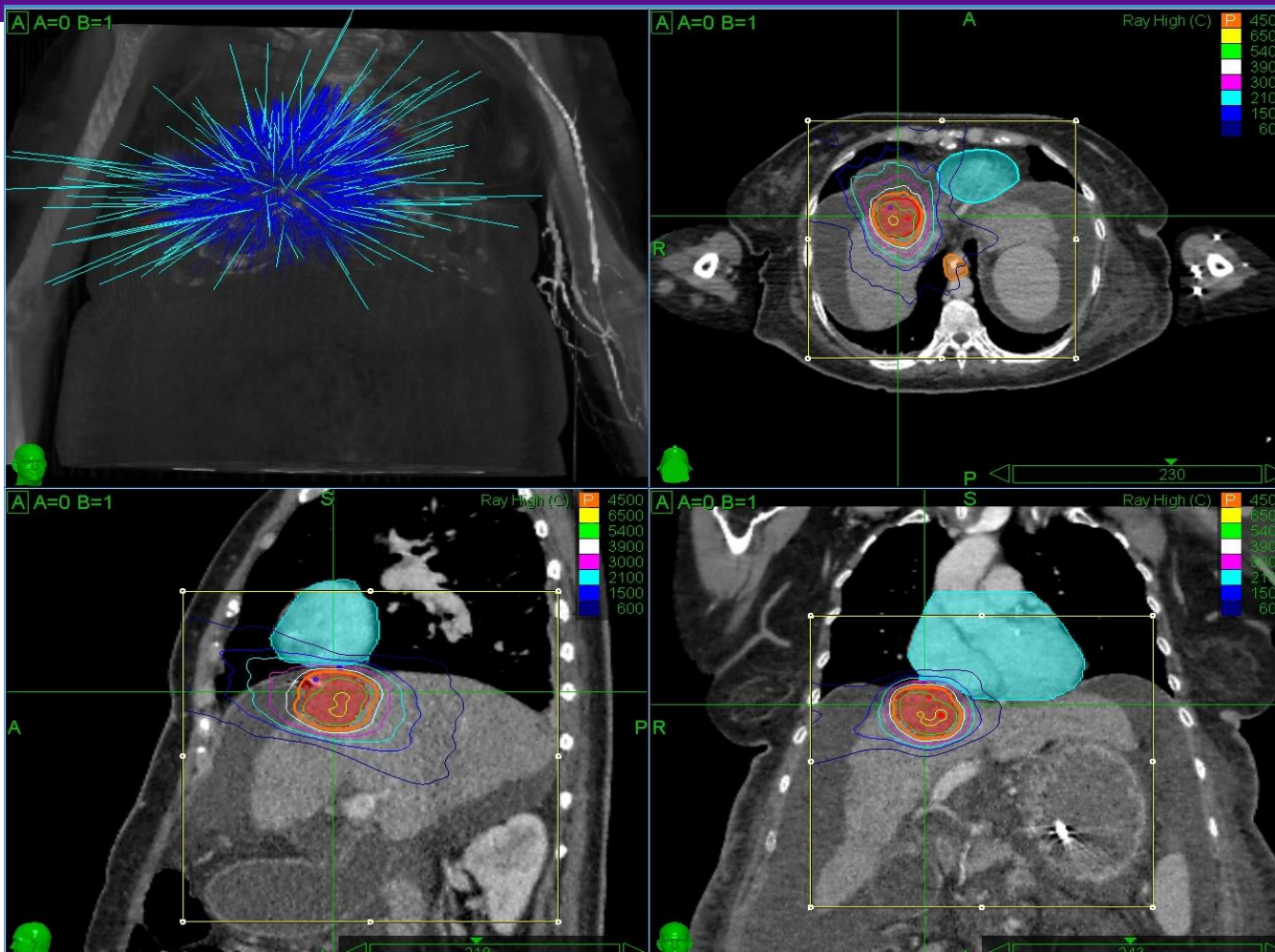
D. Radiotherapy

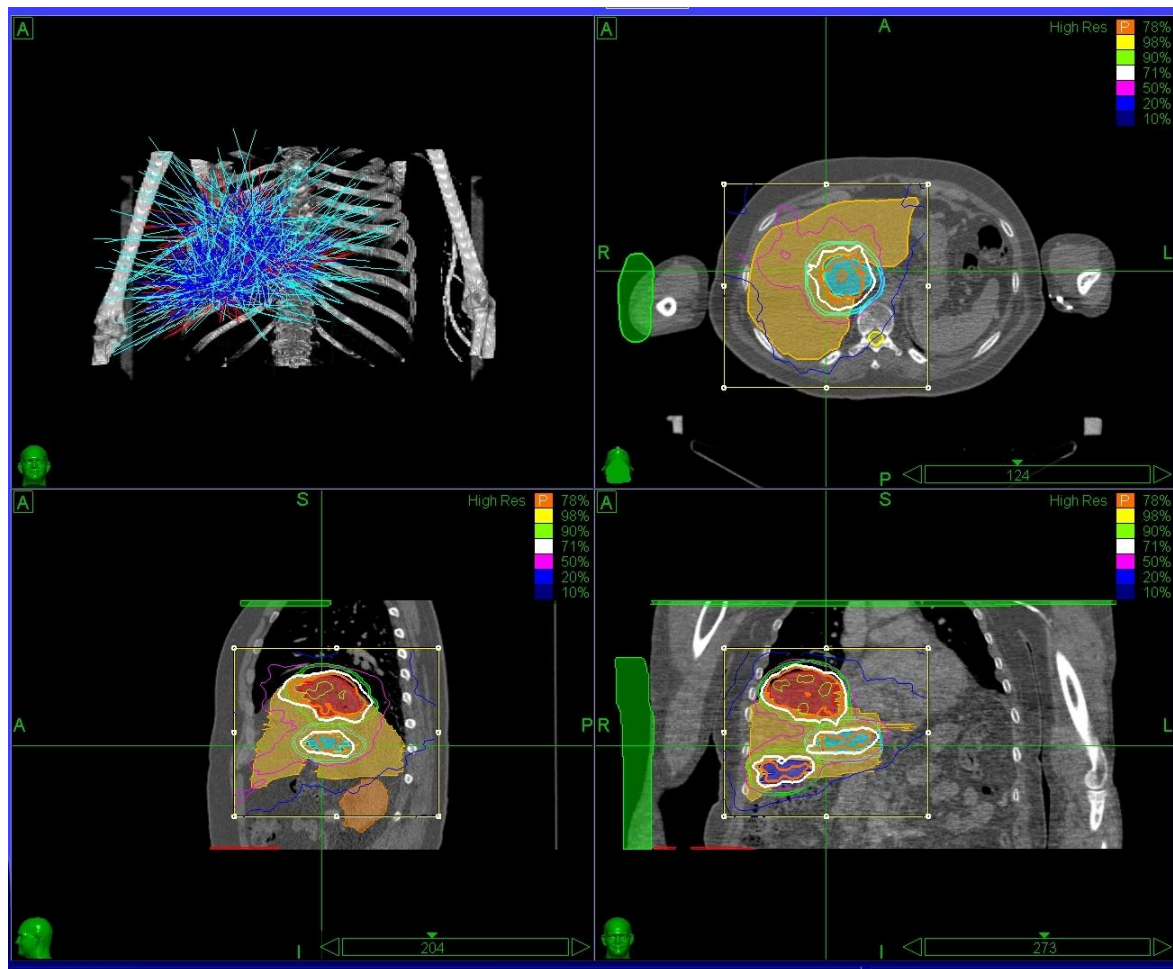
- Stereotactic body radiation

- Selective interstitial radiation therapy

E. Liver transplantation



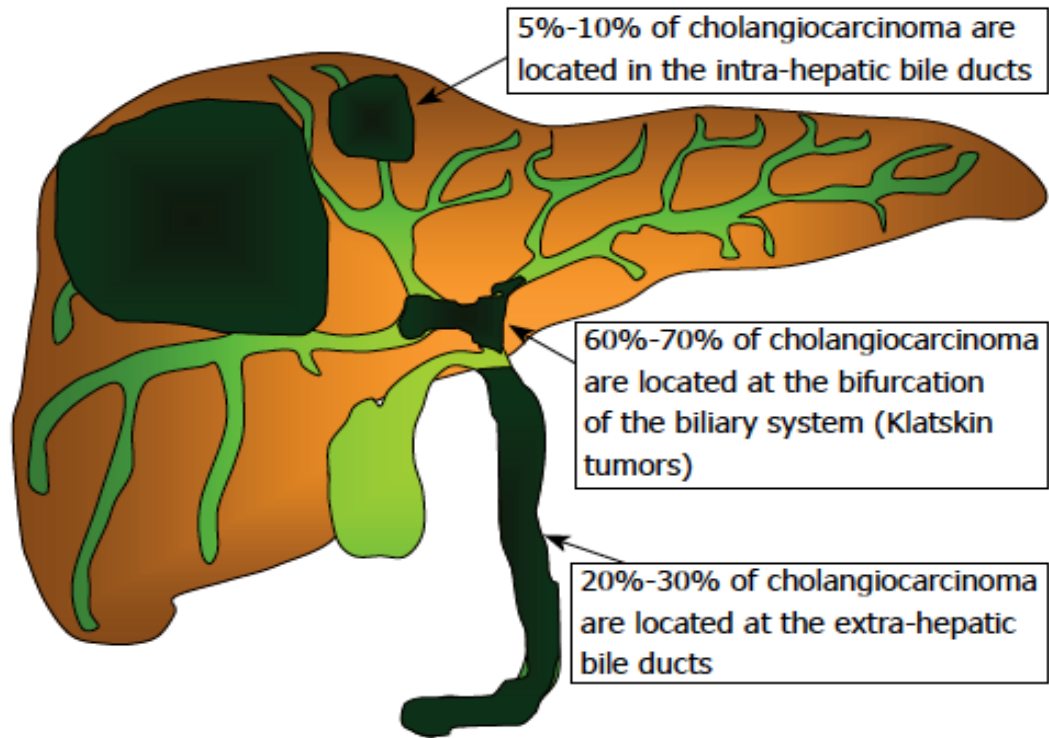




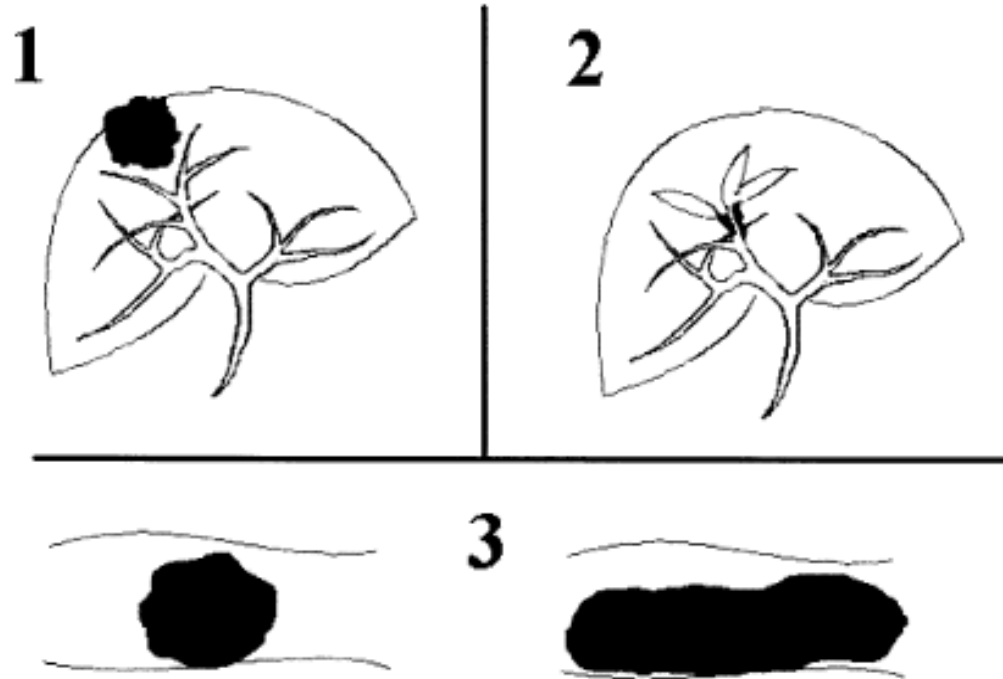
SBRT for Hepatocellular Carcinoma

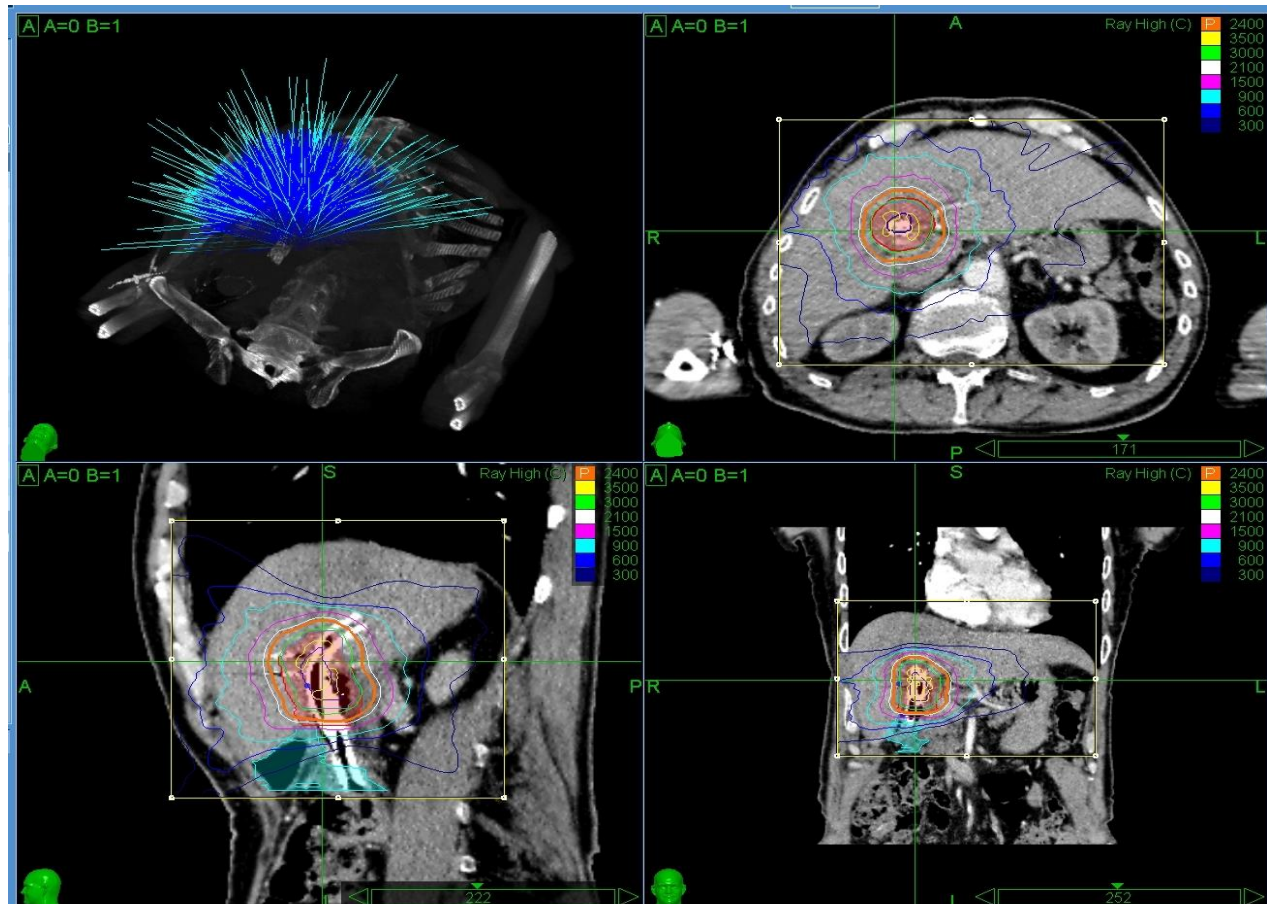
- Tumor control is good for small tumors with adequate dose
- RFA control rates are poor for intermediate (3-7cm) and large(>7cm) lesions
 - Can combination Therapy (RFA+SBRT) work
- TACE is poor for Large and multiple lesions
 - Can addition of SBRT help

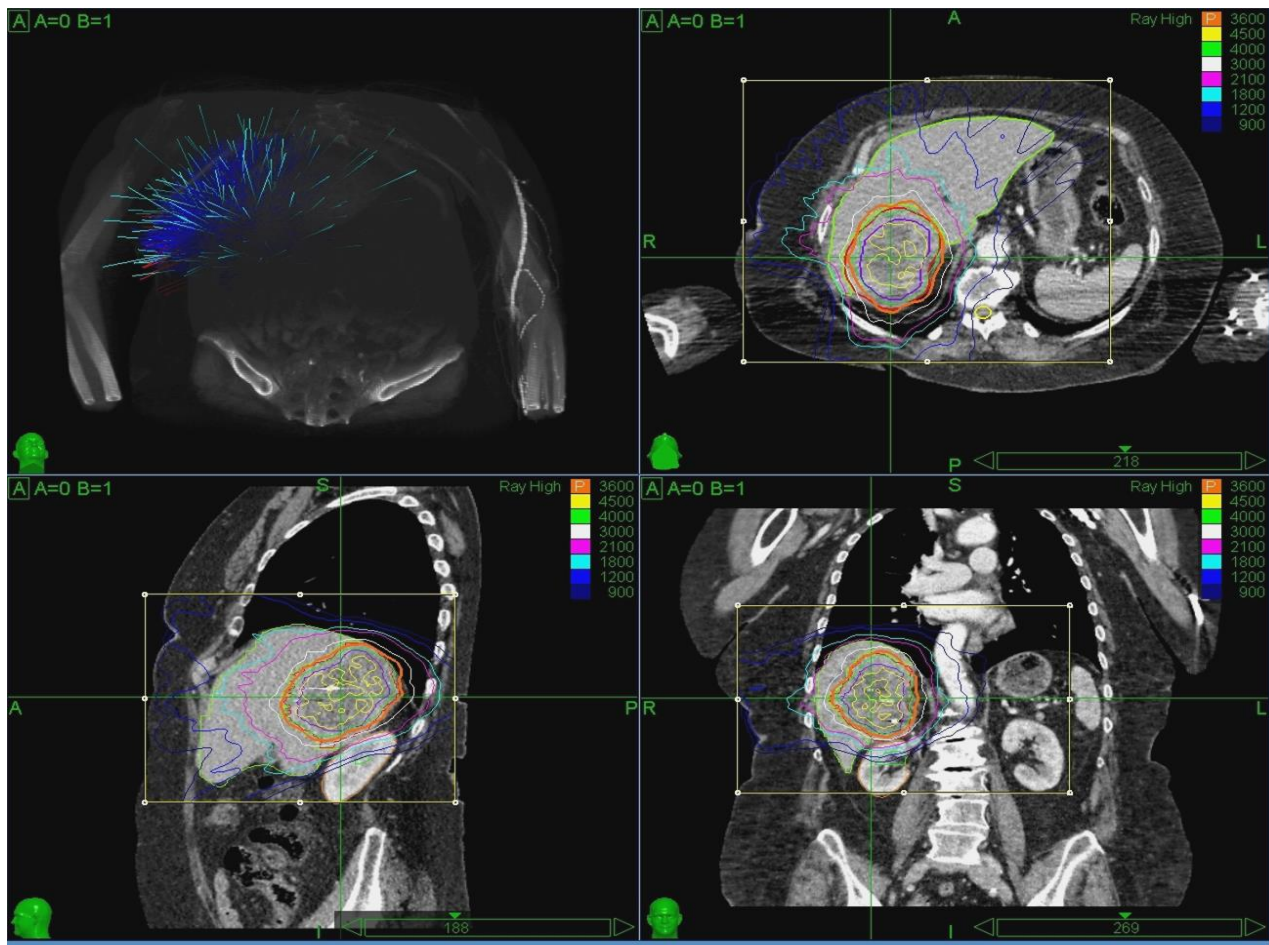
Cholangiocarcinoma



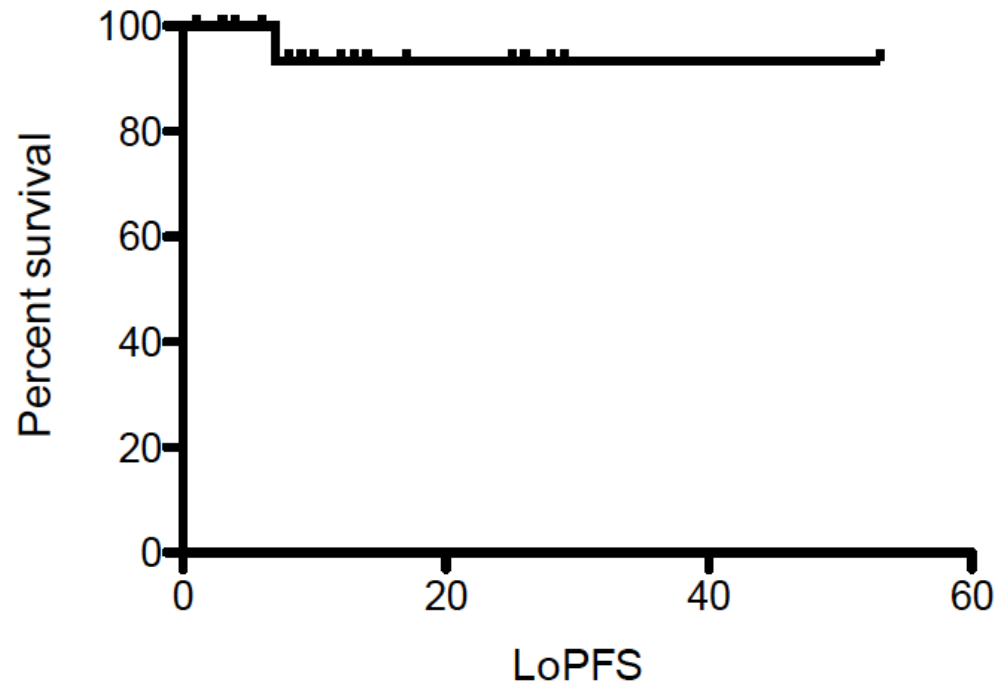
Intrahepatic Cholangiocarcinoma Morphological Types

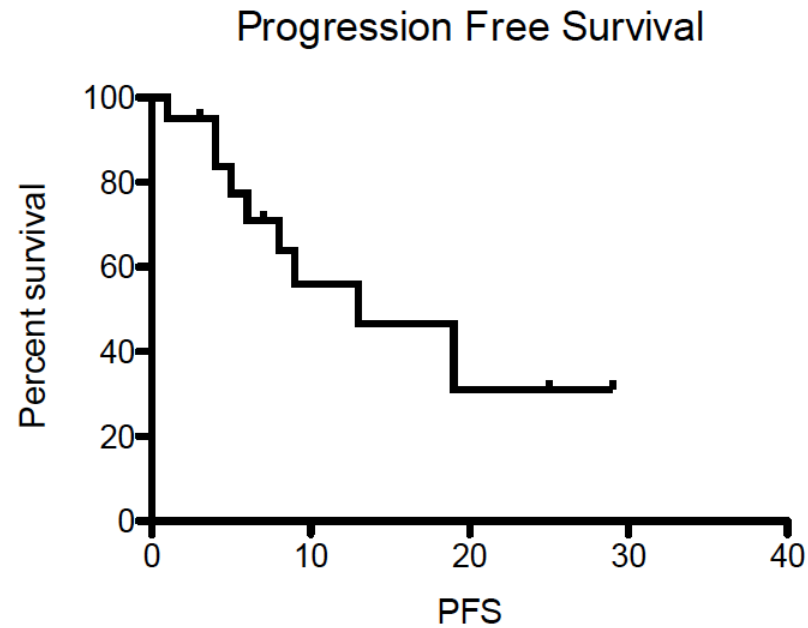






Local Progression Free Survival

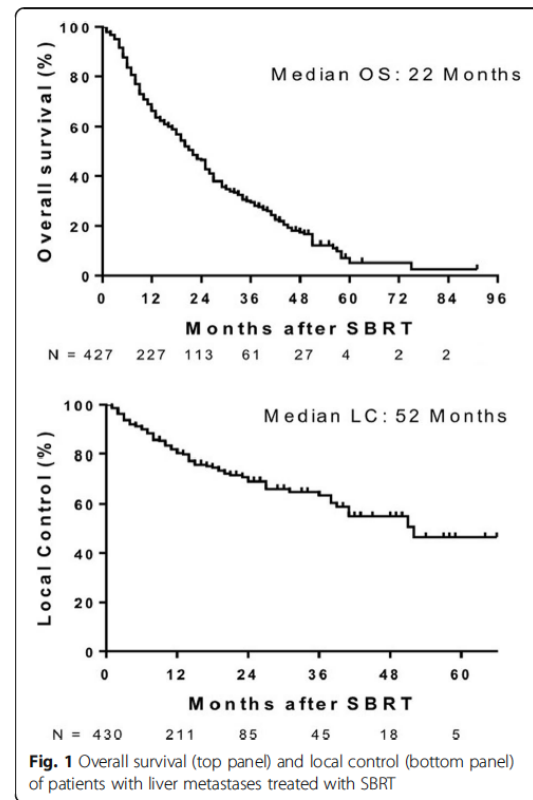
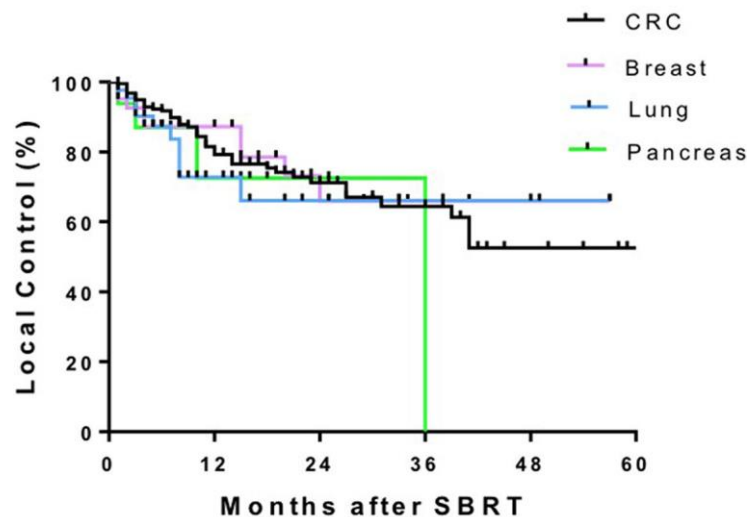




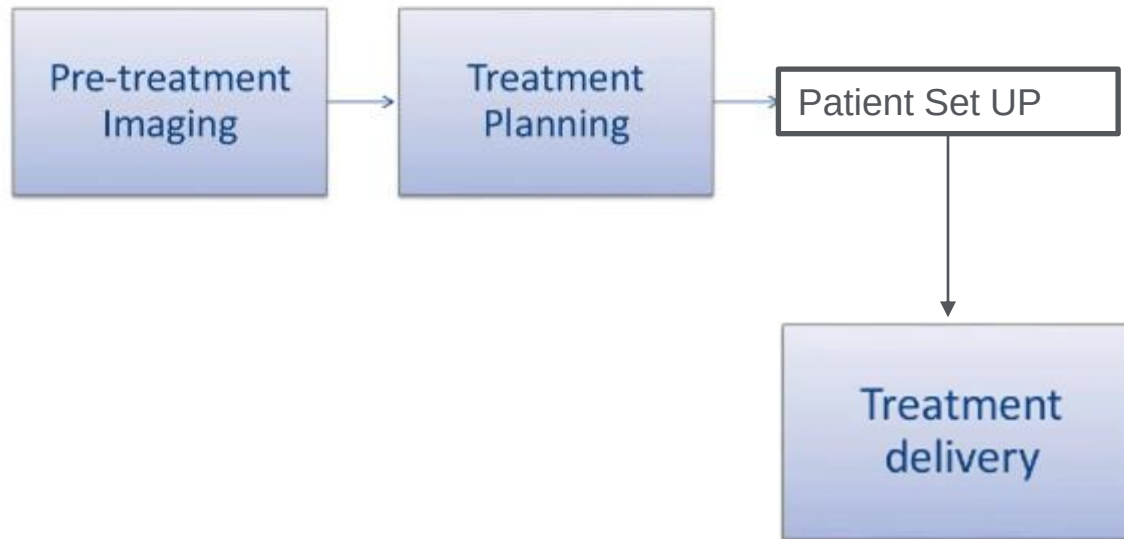
Median PFS 13m

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

Anand Mahadevan^{1*}, Oliver Blanck^{2,3}, Rachele Lanciano⁴, Anuj Peddada⁵, Srinath Sundararaman⁶,



General Radiation Therapy Workflow



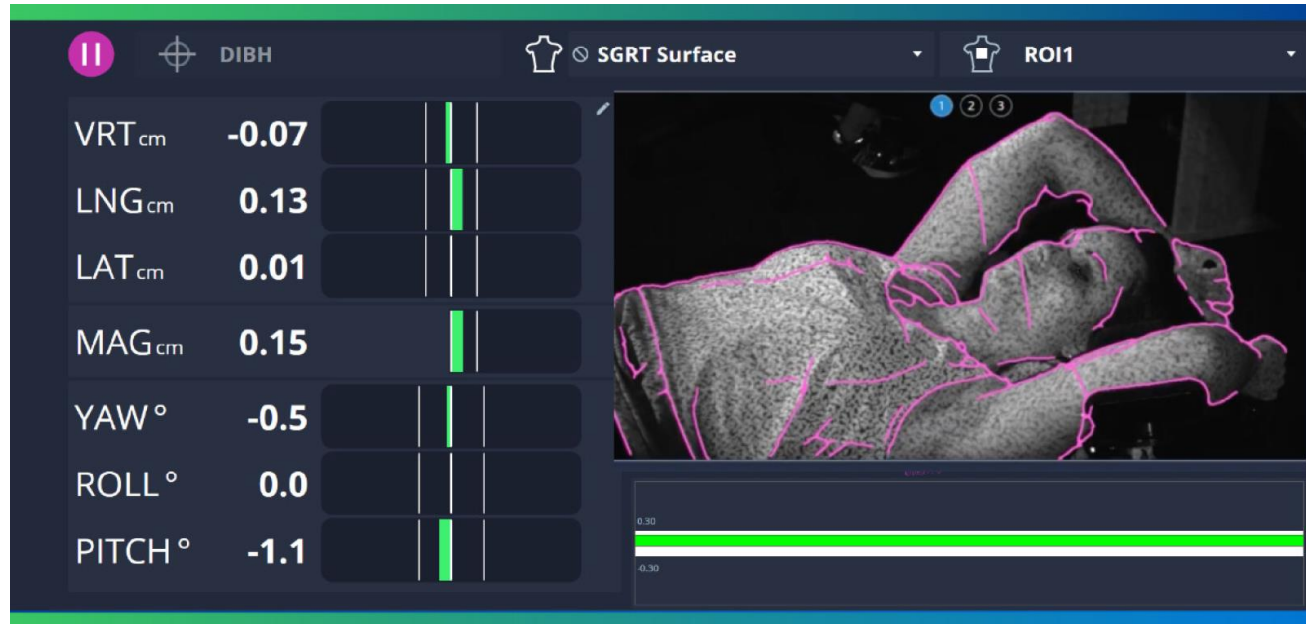
Treatment Set Up



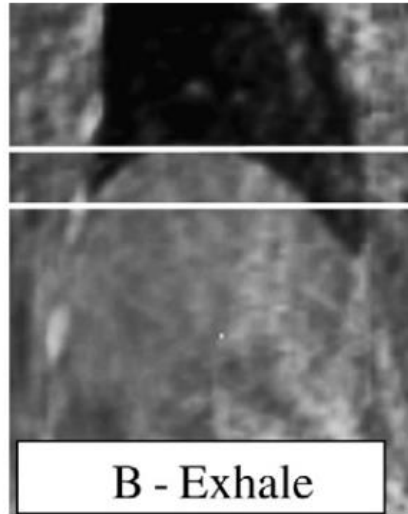
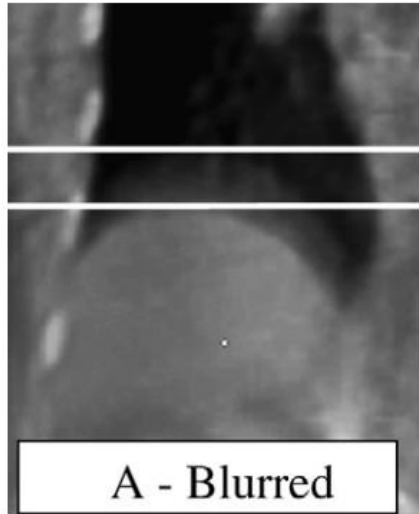
Treatment Set Up



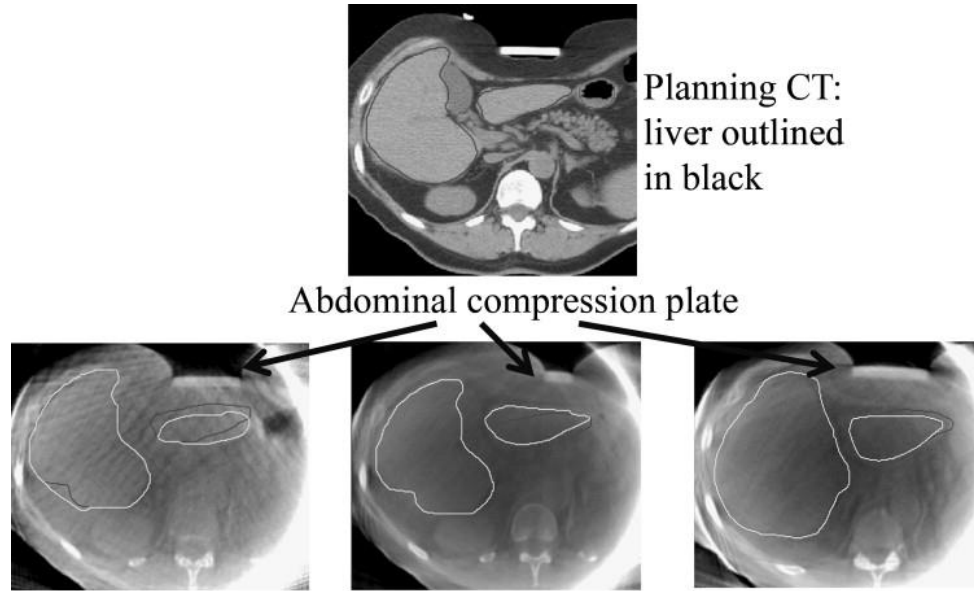
Surface Guided Radiation Therapy



Respiratory Motion



Structures Change During Treatment



CBCT from fractions 1, 5, 6 with liver from planning CT (dark contour), and liver from CBCT of each fraction (white contour).

Liver Deformation

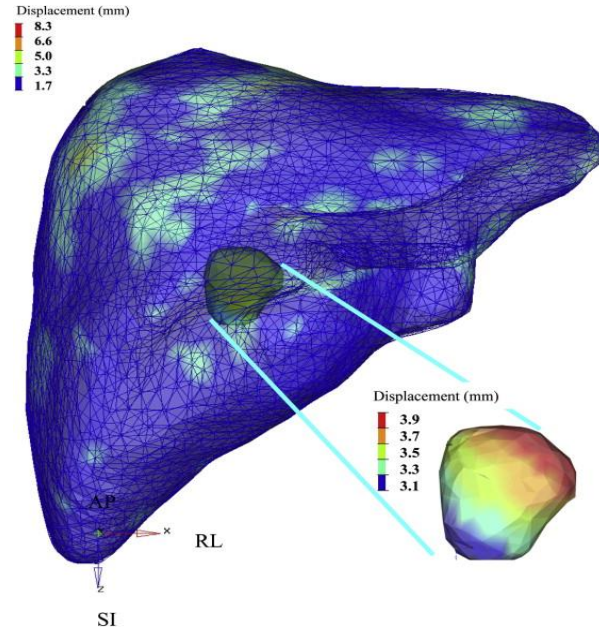
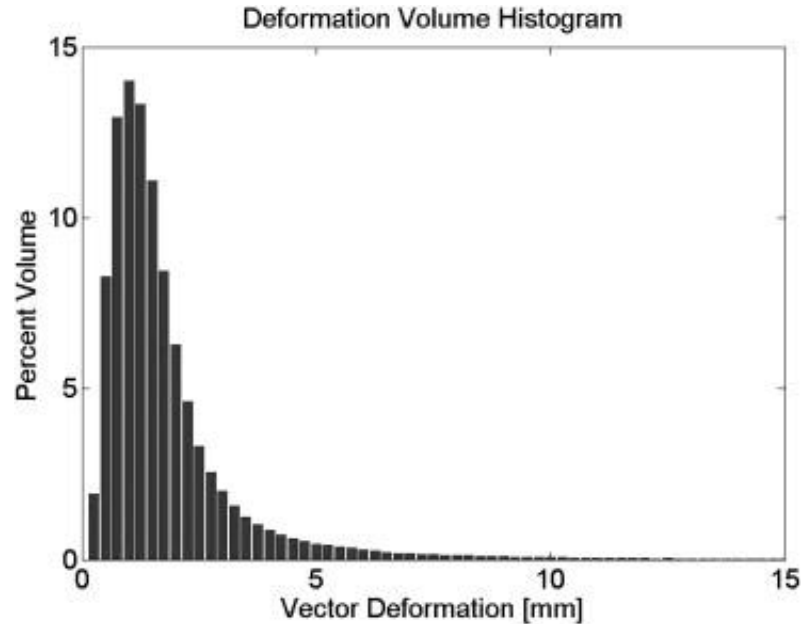
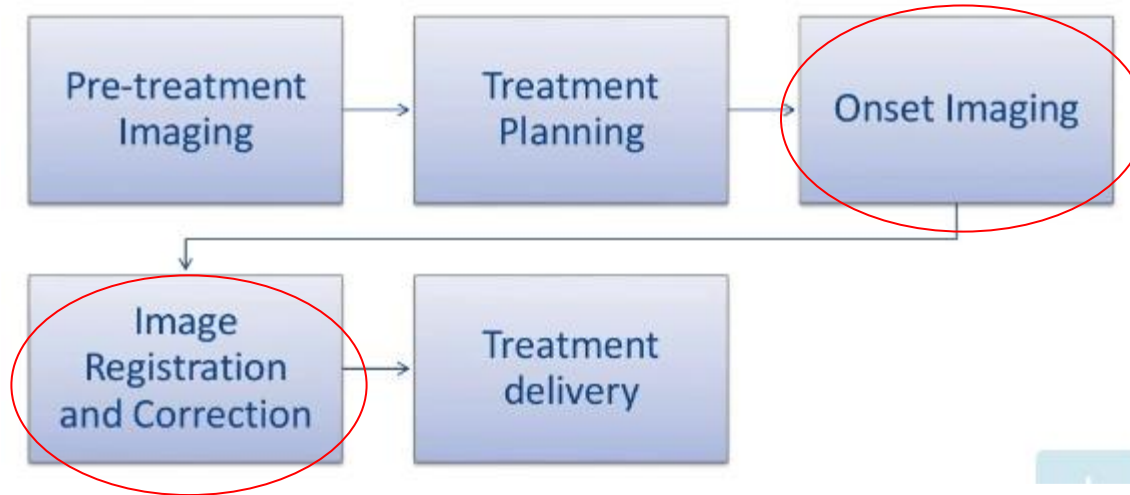
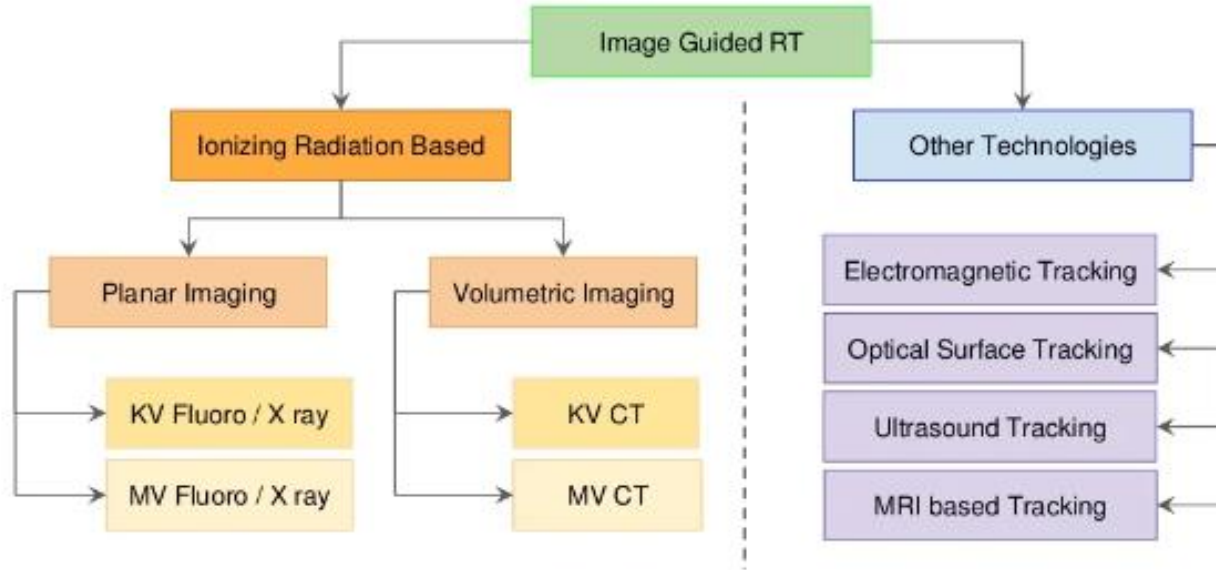


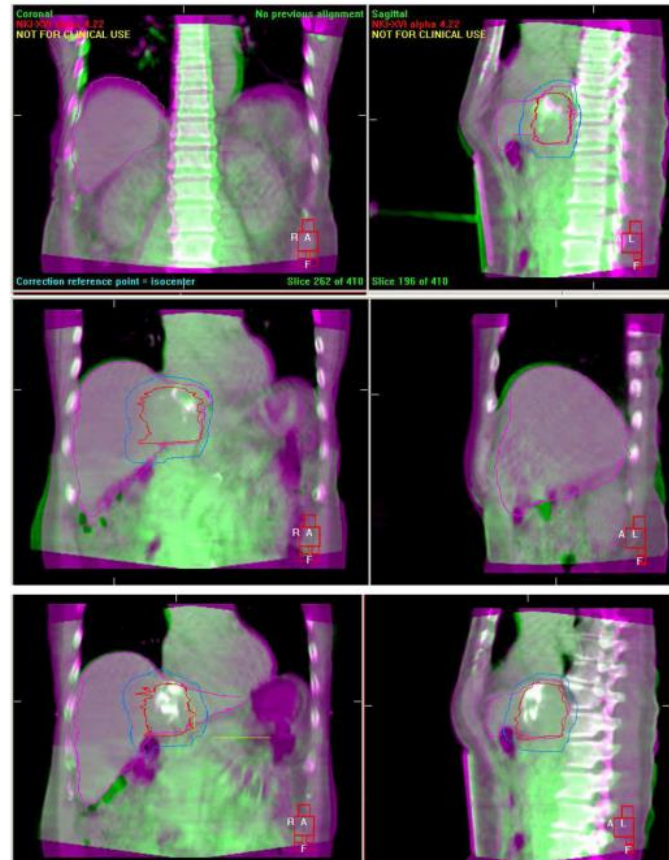
Image Guided Radiation Therapy



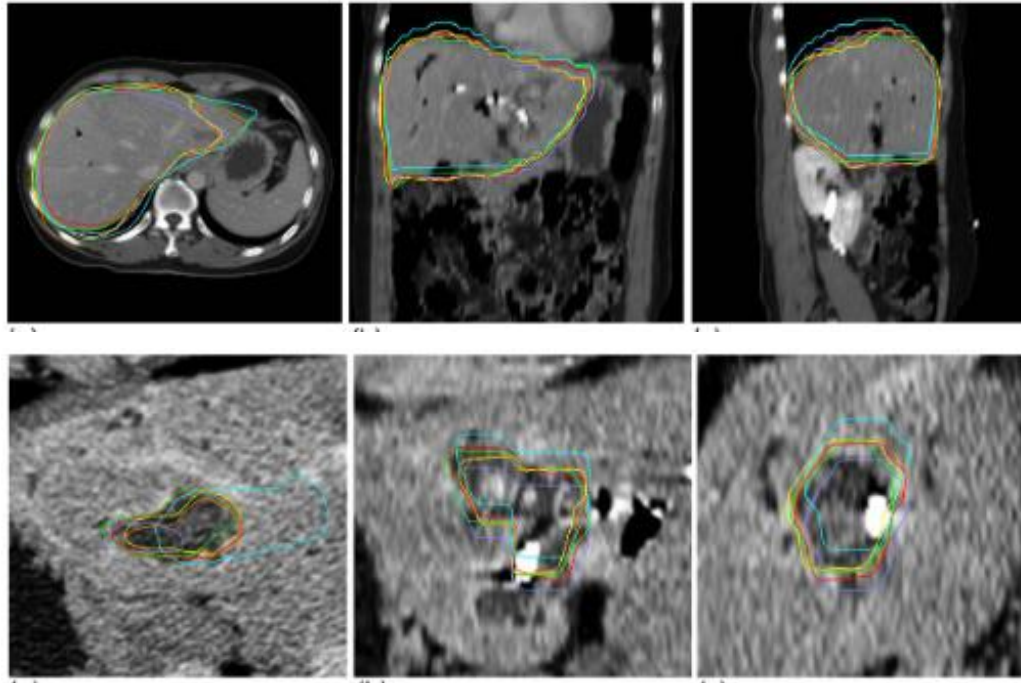
IGRT Techniques



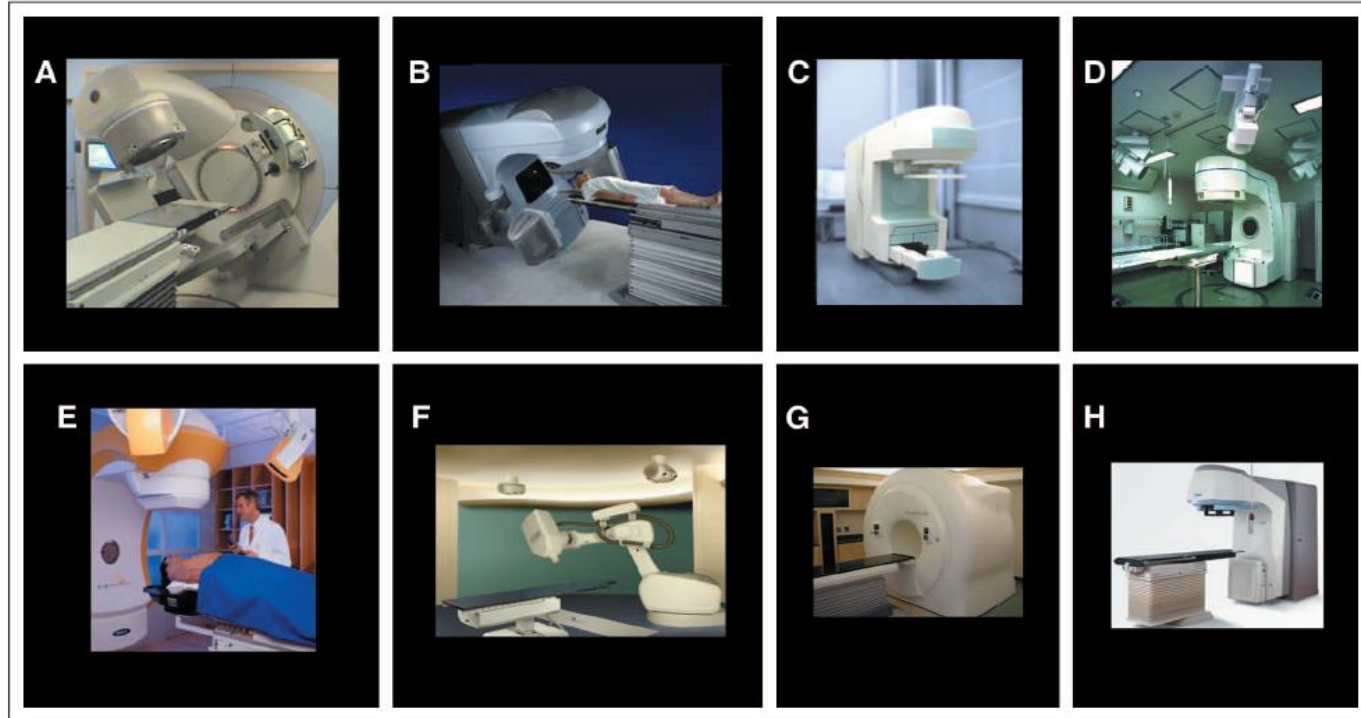
IGRT



Cross Sectional Image Guidance



Imaging Modalities



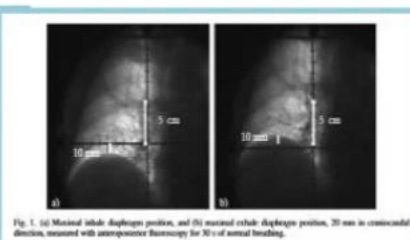
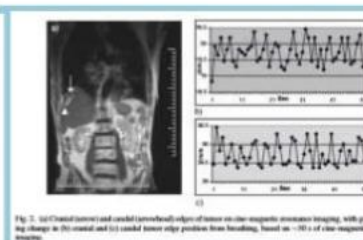
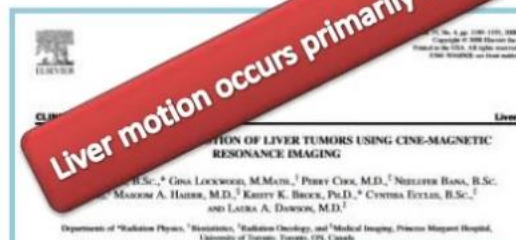
IGRT Techniques

Technology	Energy	Type	Accuracy	Comments
EPID	MV	2D	1-2 mm	Surrogate imaging of soft tissue
KV Xray	KV	2D	1-2 mm	Better resolution w.r.t. EPID
CBCT	KV	3D	< 1 mm	Volumetric “slow” scan.
MVCT	MV	3D	< 1 mm	Can be useful for adaptive radiotherapy
Stereoscopic Xray	KV	2D	< 1 mm	Useful in tumor tracking. Oblique angles.
USG	-	3D	3 mm	Main utility in prostate cancers
Surface	-	2D	1 mm	Surface based optical tracking and localization
Transponders	-	2D	-	Independent system for tumor tracking

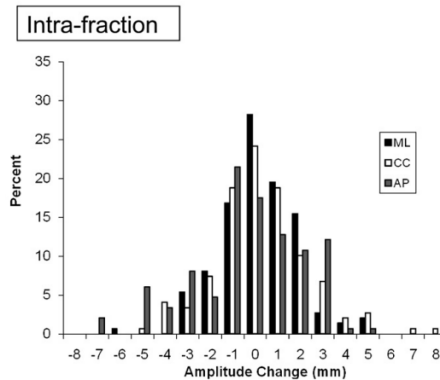
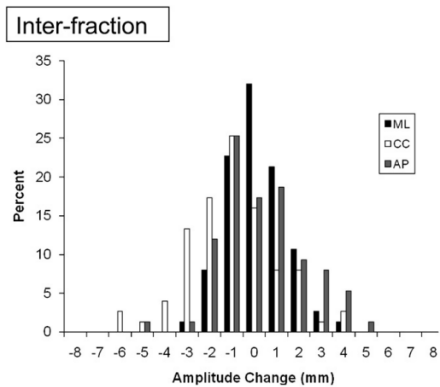
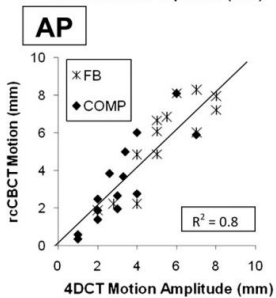
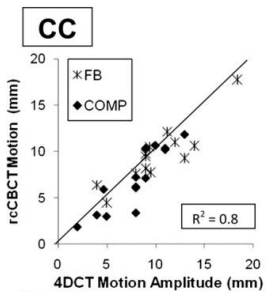
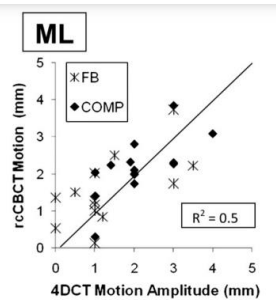
IGRT Liver Issues

- Liver tumors are difficult to visualize
- Tumors significantly move in 3 planes in addition to Hysteresis
- Tumors and OARs change during course of treatment
- Tumor and motion is independent of bone and bowel motion
- Changes in stomach and bowel filling shifts target volumes and organs at risk

SBRT in liver tumor: How much does liver move?

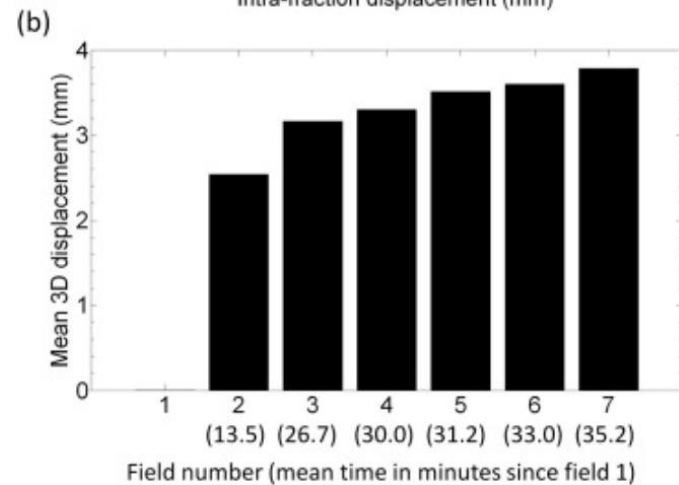
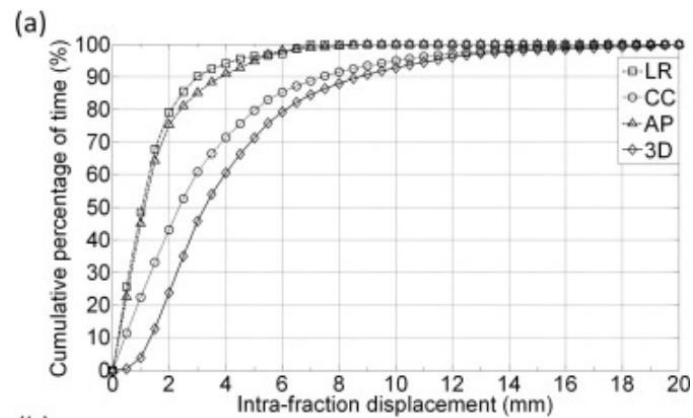


Liver motion occurs primarily in the superior-inferior (SI) direction in the range of 5 to 50 mm

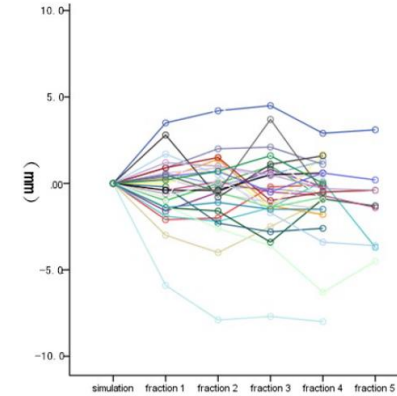
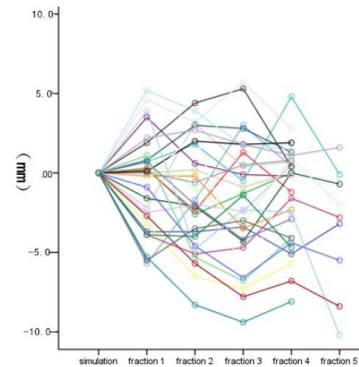
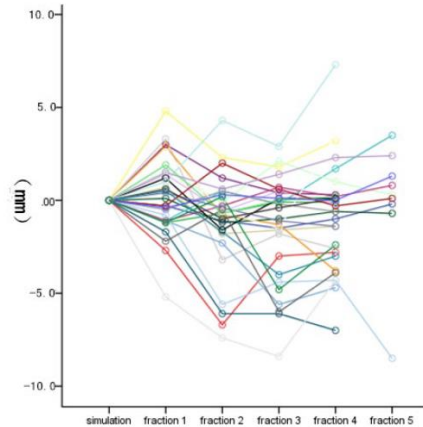
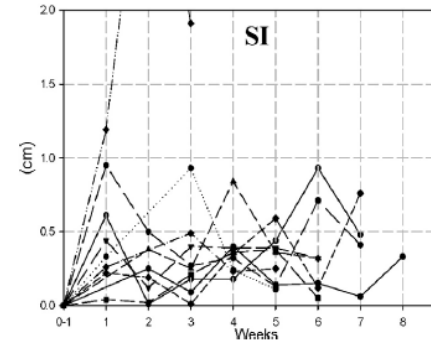
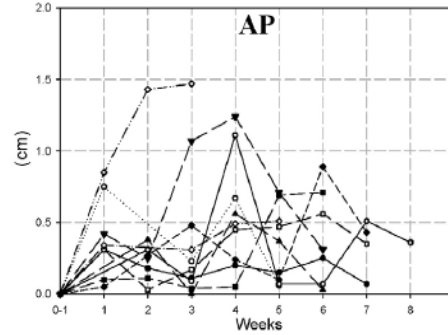
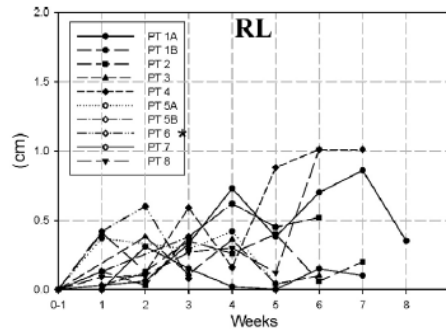


Respiratory Movement

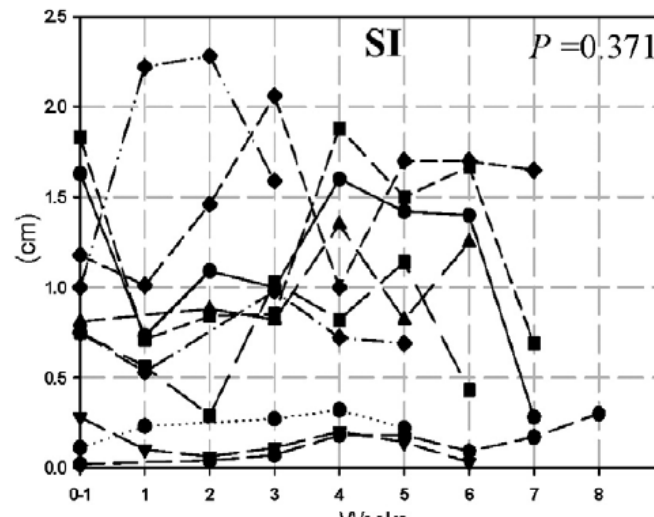
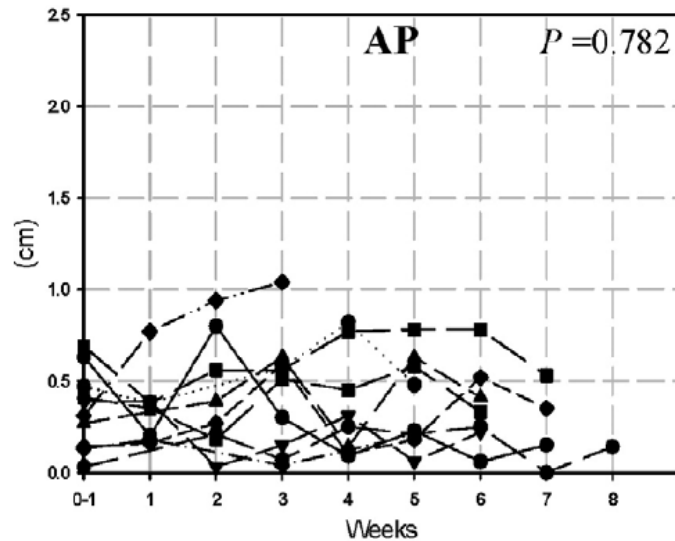
Structure	Mean excursion (mm) (range)						Number of studies	Number of patients over all studies reported
	Free breathing			Deep breathing				
	SI	AP	ML	SI	AP	ML		
Lungs	10.3 (1–31.9)	6.4 (0–24.4)	(1–10)	9.3 (0.1–70)	7.8 (0.5–18.8)	4.2 (1.1–17.6)	7	62
Diaphragm	14.9 (2.6–38.2)			44.6 (3.1–96)			10	112
Liver	12.3 (4.9–30.4)	(max. 5.2)	(max. 4.6)	38 (25–57)			6	59
Chest wall	7.3 (2–15)	2.3 (0–8)	(5–7)		16 (0.7–37.3)	11.7 (0.5–64.1)	6	88
Heart	18.1 (12–25)	2.4					2	20



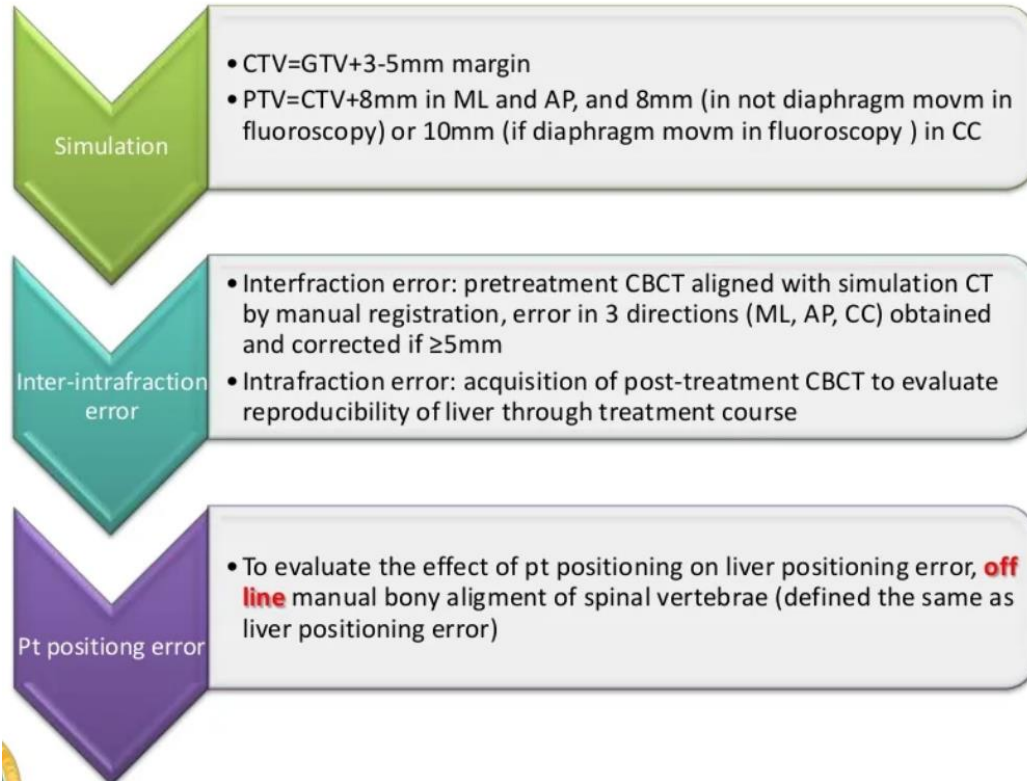
Interfraction Shift in GTV

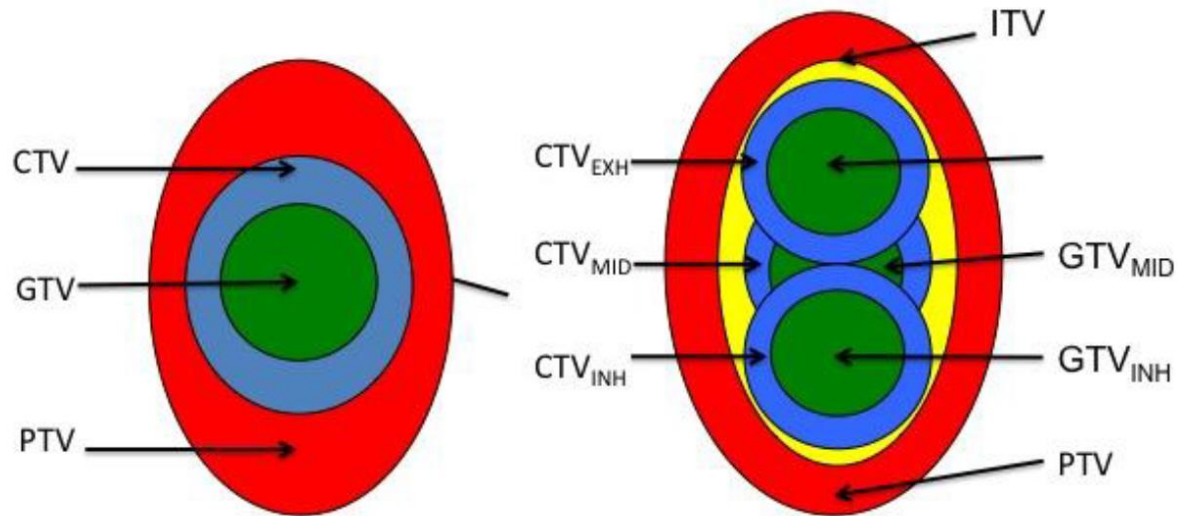


Intrafraction Movement

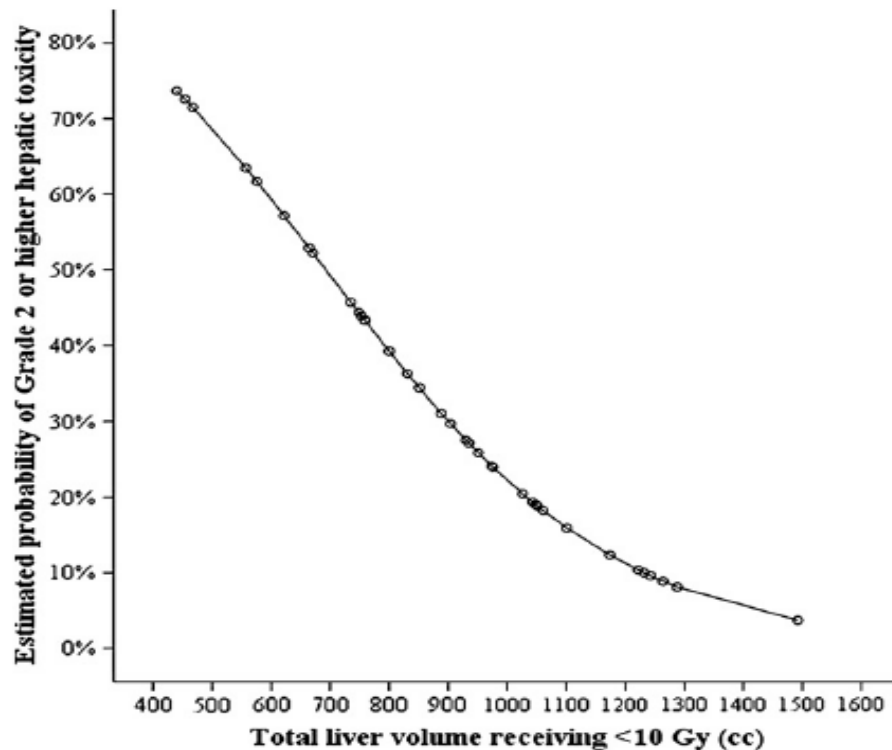


Respiratory Motion Management -Conventional

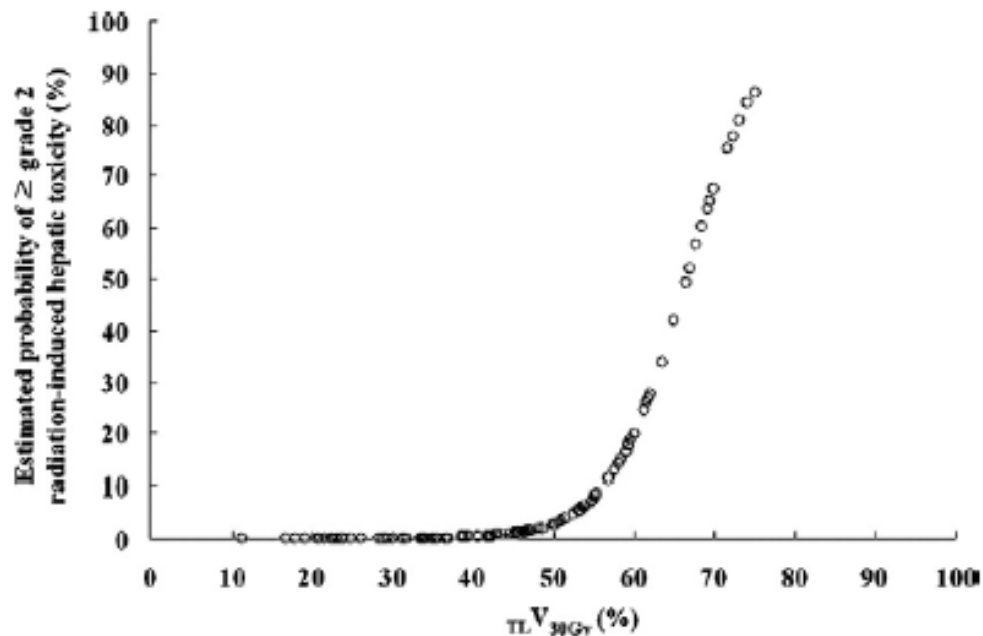




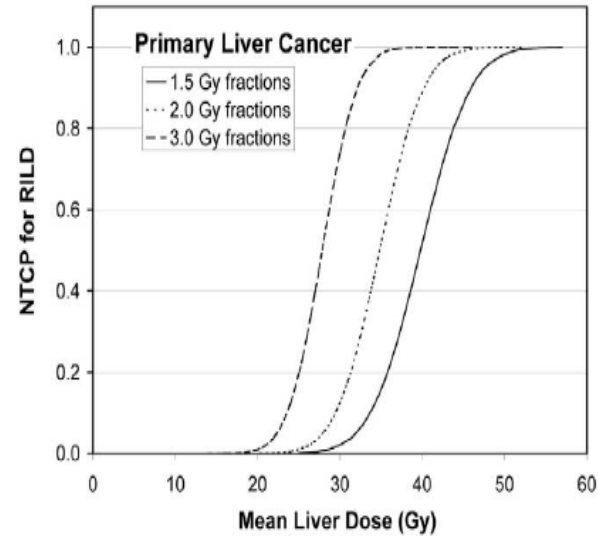
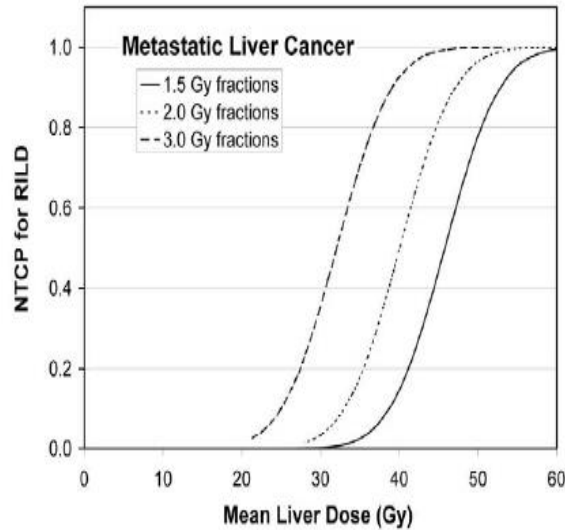
STEREOTACTIC BODY RADIOTHERAPY FOR PATIENTS WITH UNRESECTABLE PRIMARY HEPATOCELLULAR CARCINOMA: DOSE-VOLUMETRIC PARAMETERS PREDICTING THE HEPATIC COMPLICATION



**DOSE-VOLUMETRIC PARAMETERS PREDICTING RADIATION-INDUCED
HEPATIC TOXICITY IN UNRESECTABLE HEPATOCELLULAR
CARCINOMA PATIENTS TREATED WITH THREE-DIMENSIONAL
CONFORMAL RADIOTHERAPY**



Whole Liver Tolerance



Partial Volume Tolerance of the Liver to Radiation

Laura A. Dawson, MD*, and Randall K. Ten Haken, PhD[†]

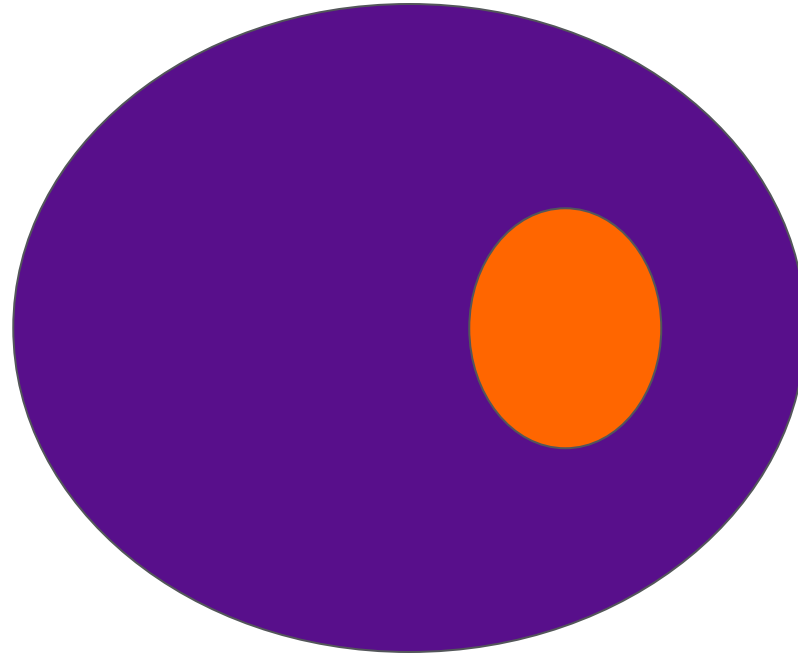


Moving Targets

- Unpredictable Fixed movements
 - Patient Movement
 - Internal Organ Movement
 - Bowel/Bladder filling/emptying
- Respiratory Movement

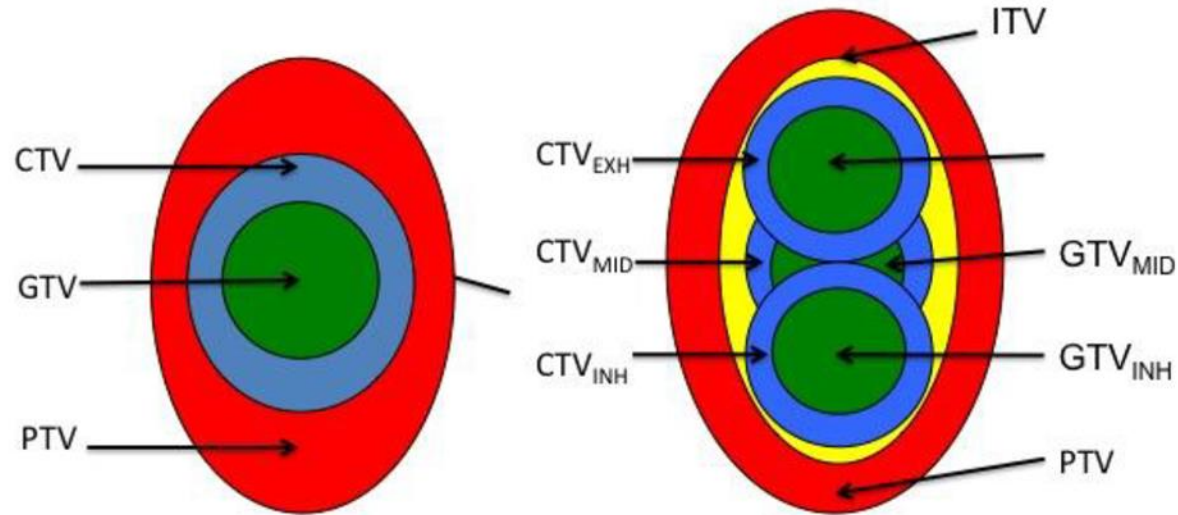
Unpredictable Movements

- Conventional Radiation



Respiratory Movements

Conventional Radiation - ITV



Respiratory Movements

Conventional Radiation- 4D Imaging



Respiratory Movements - SBRT

- Dampening
 - Active Breathing Control, Breath Hold
 - Abdominal Compression
- Gating
- Tracking

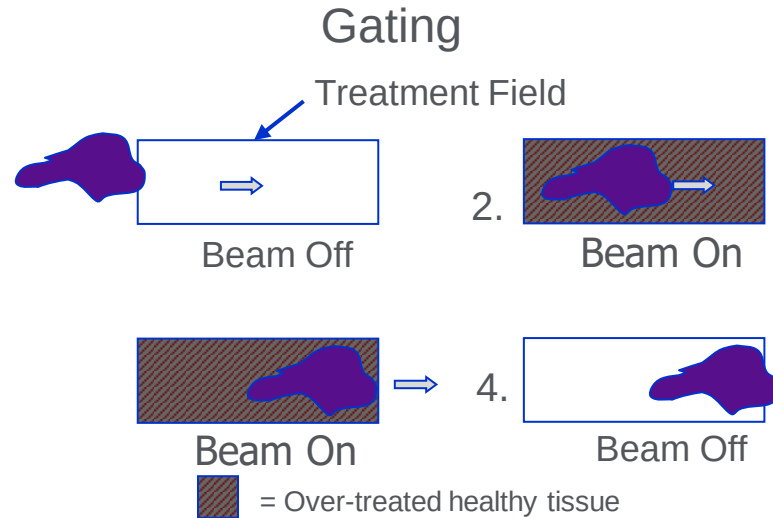
Dampening



Active Breathing Control

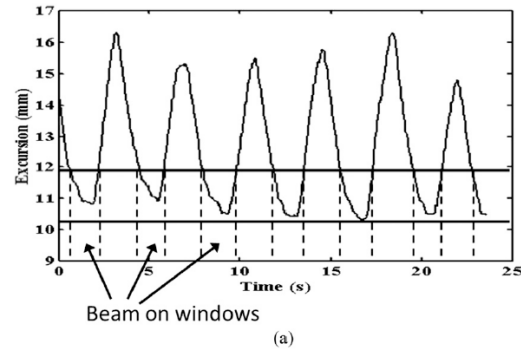


Gating

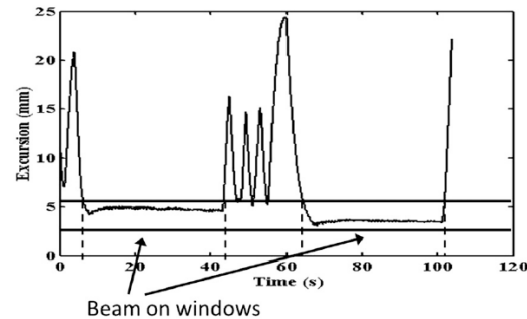


Treatment beam is turned on and off as tumor enters and exits a static treatment field

Respiratory Movement Management

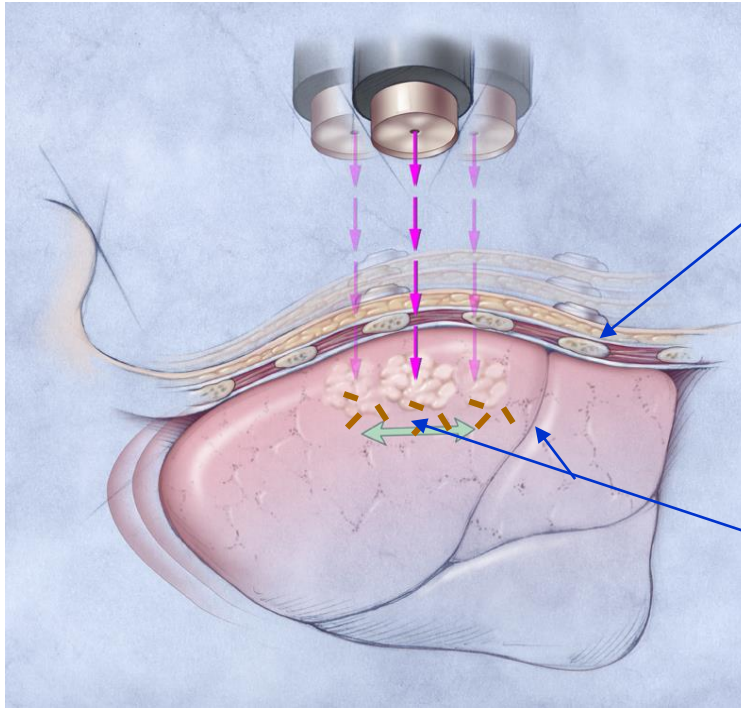


Gating



Breath Hold

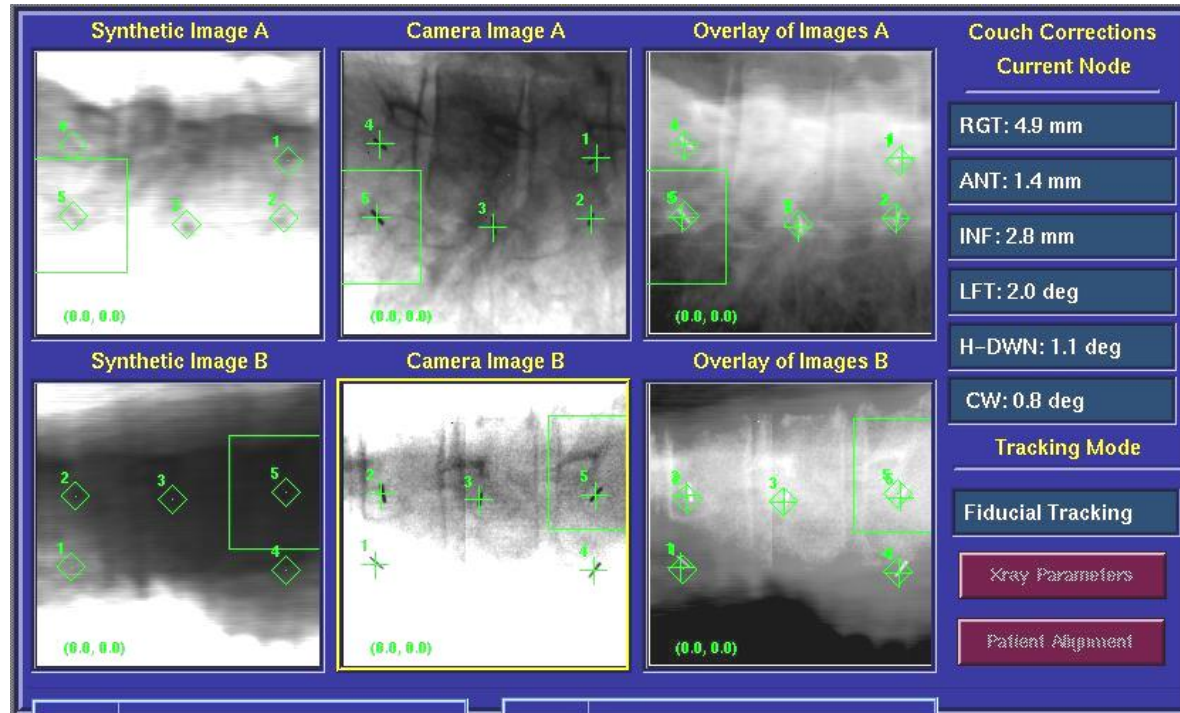
Tracking



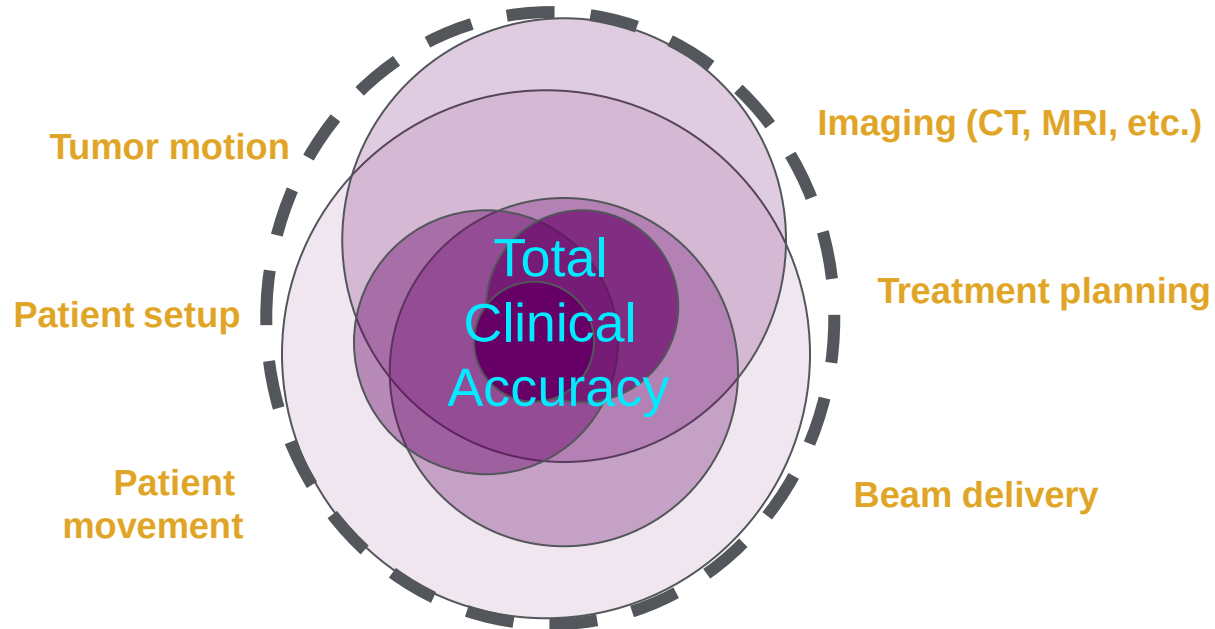
External position sensor

Internal fiducial

Fiducial Based Image Guidance



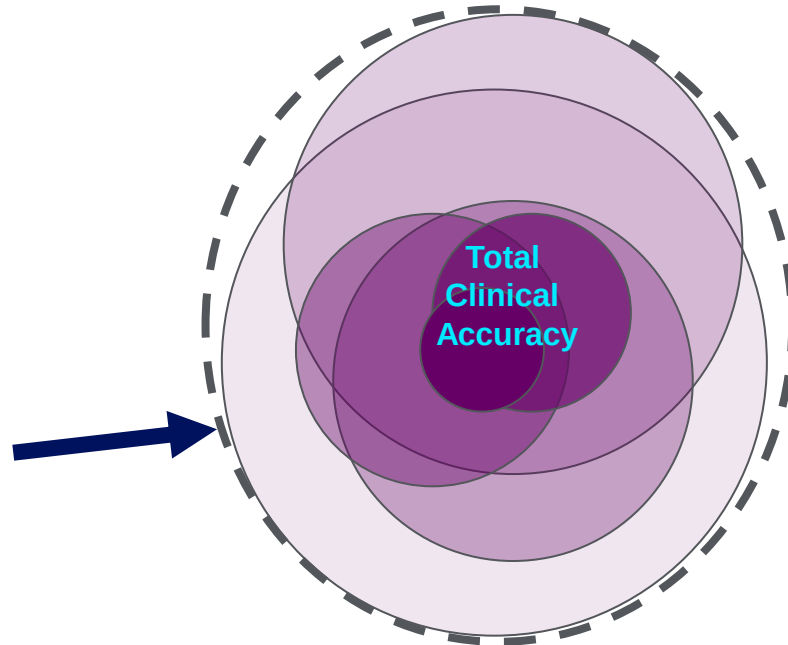
Defining Accuracy

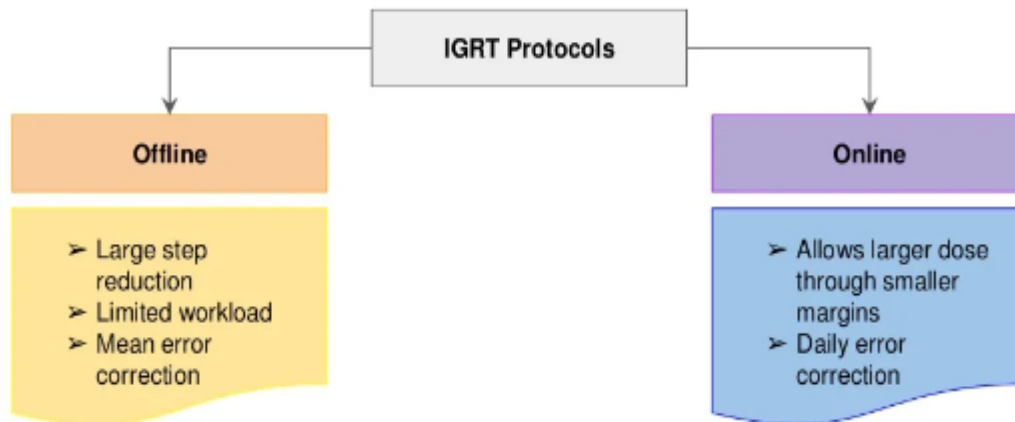


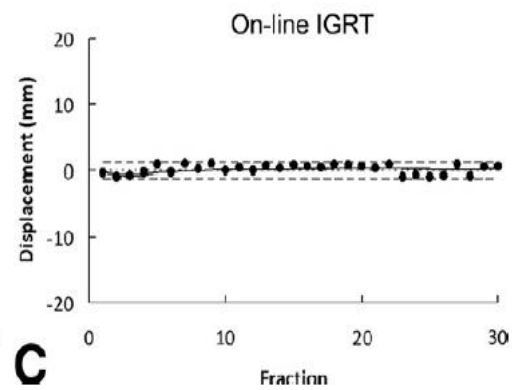
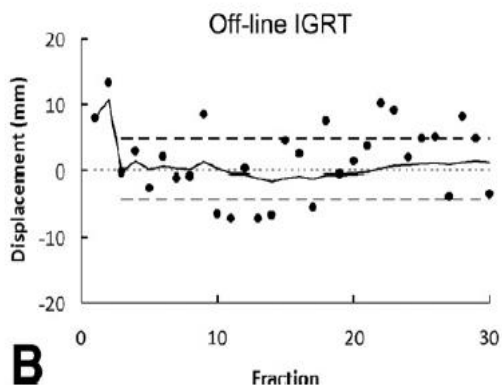
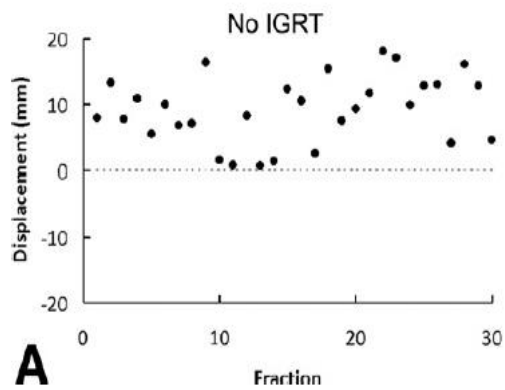
Modern SBRT Accuracy

- Mechanical Accuracy = 0.12 mm
- Total Clinical Accuracy
 - Stationary lesions: 0.95 mm
 - Moving lesions: 1 mm

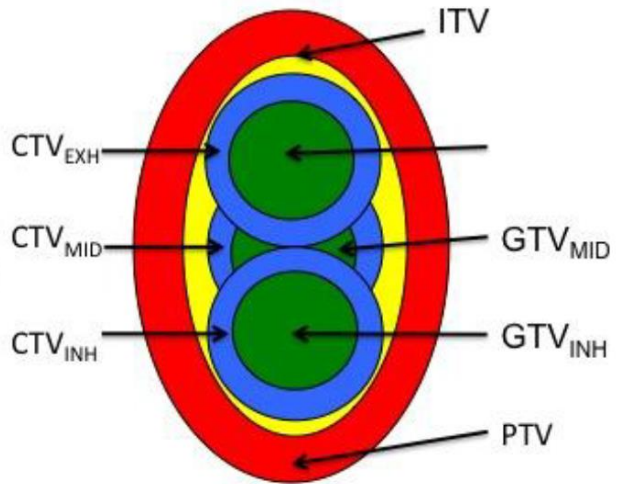
Total Clinical
Accuracy



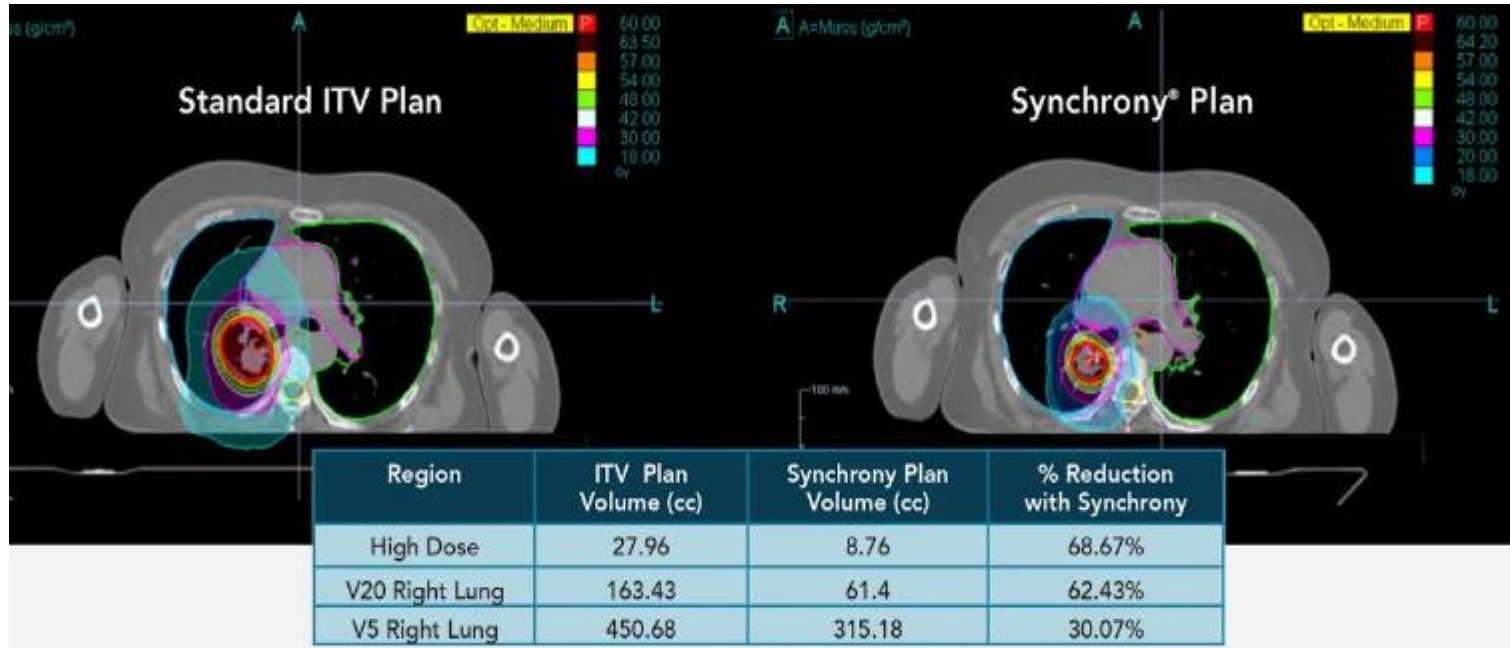


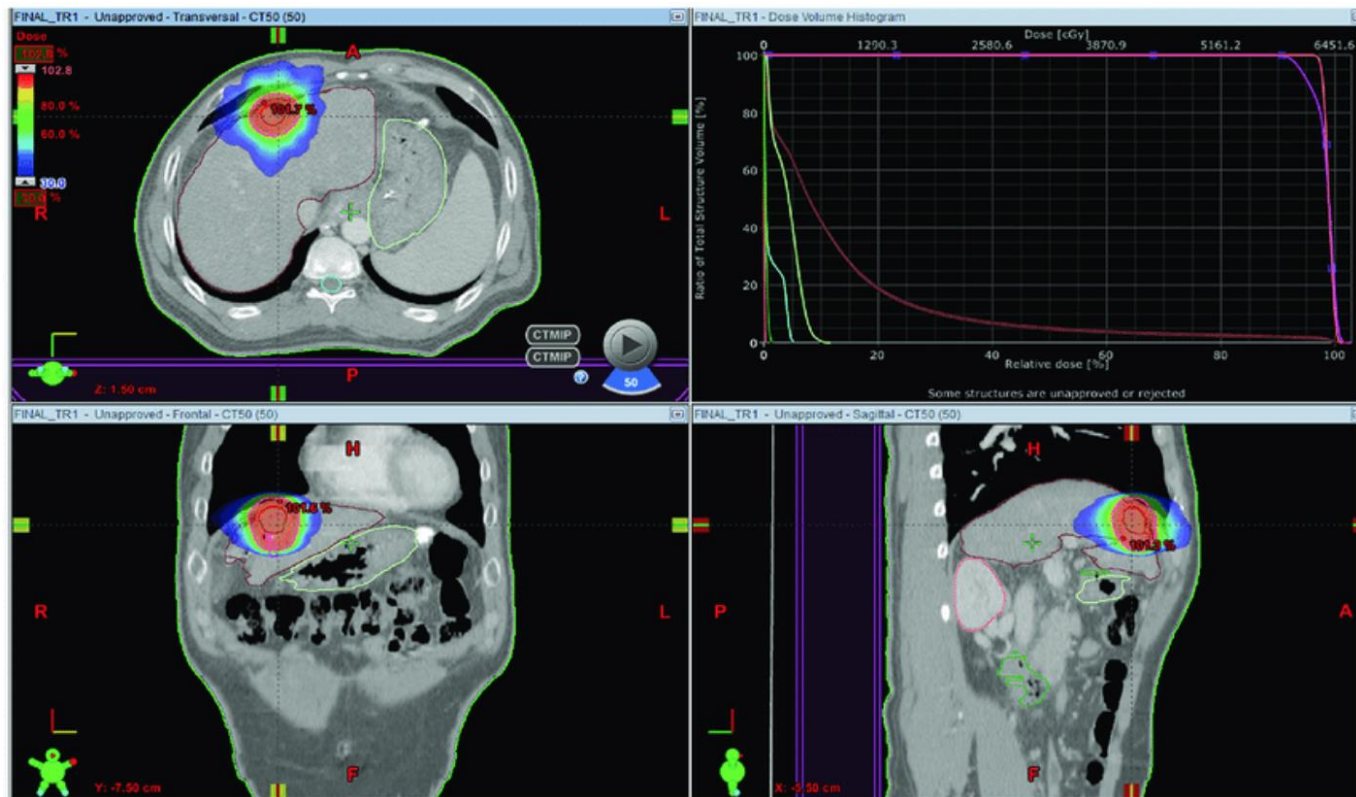


Real time on line motion synchronization

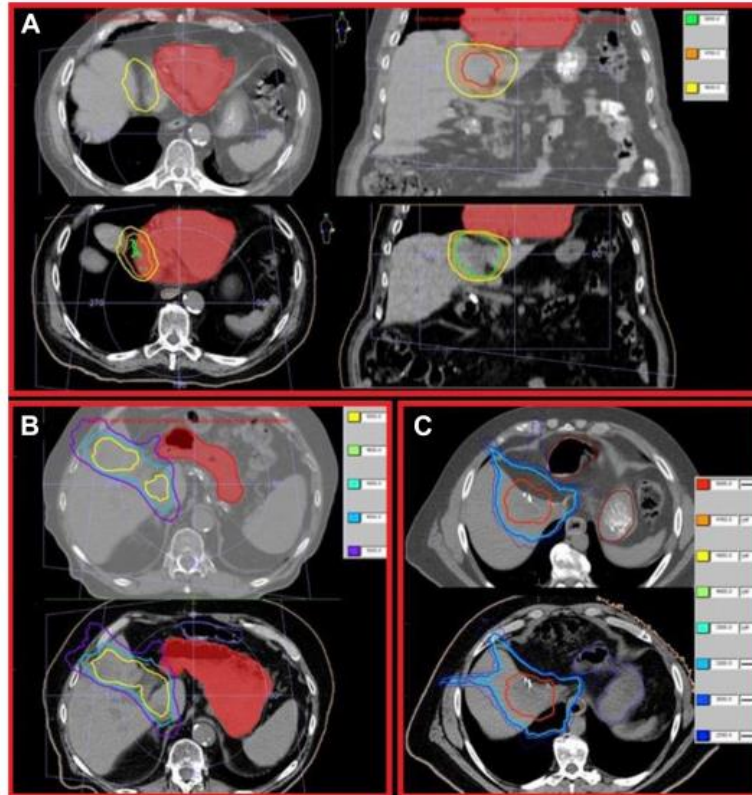


Motion Synchronization



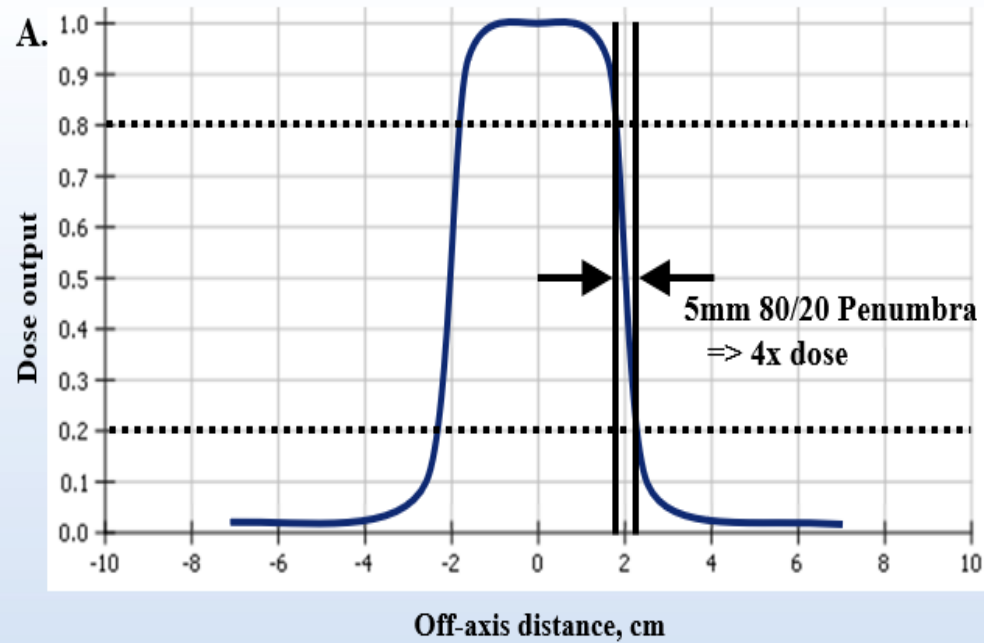


Importance of Motion Management

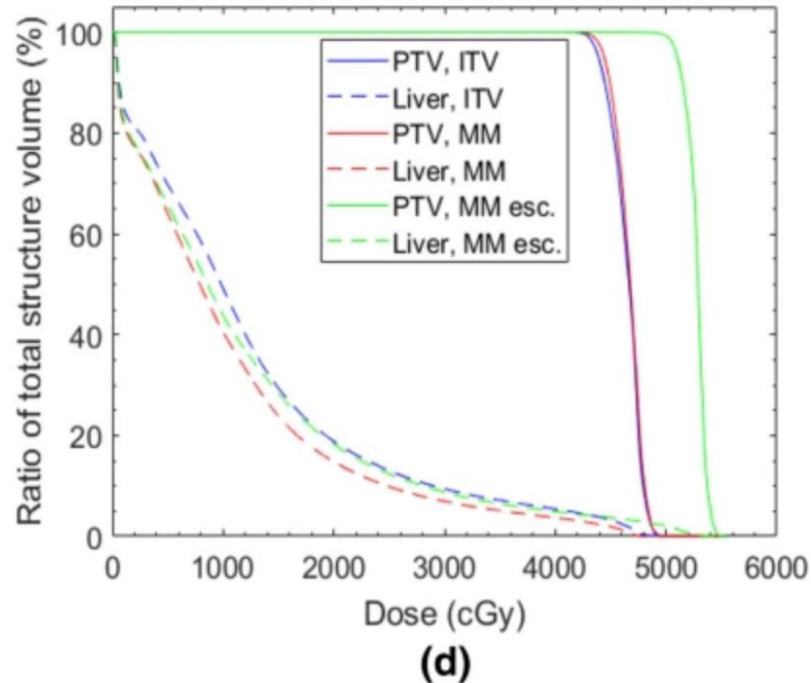
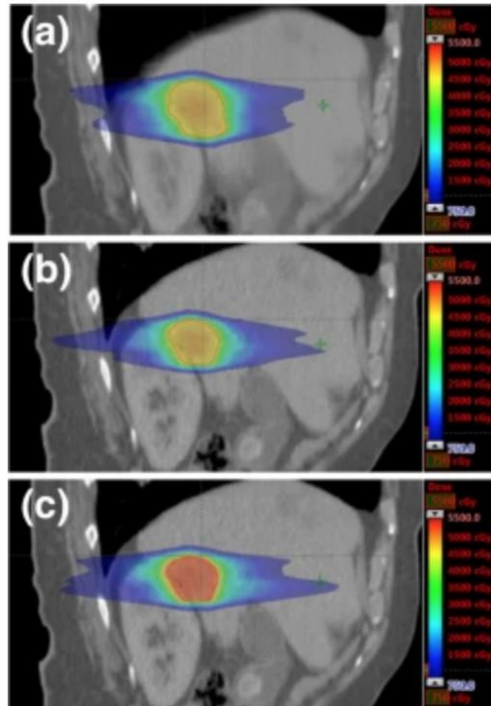


A typical Linac beam profile explains a lot:

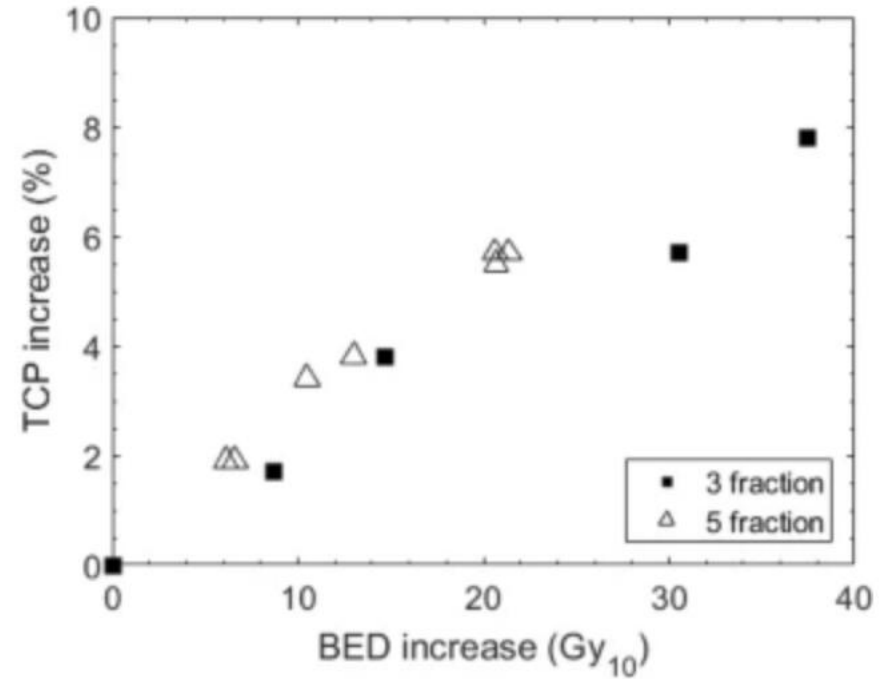
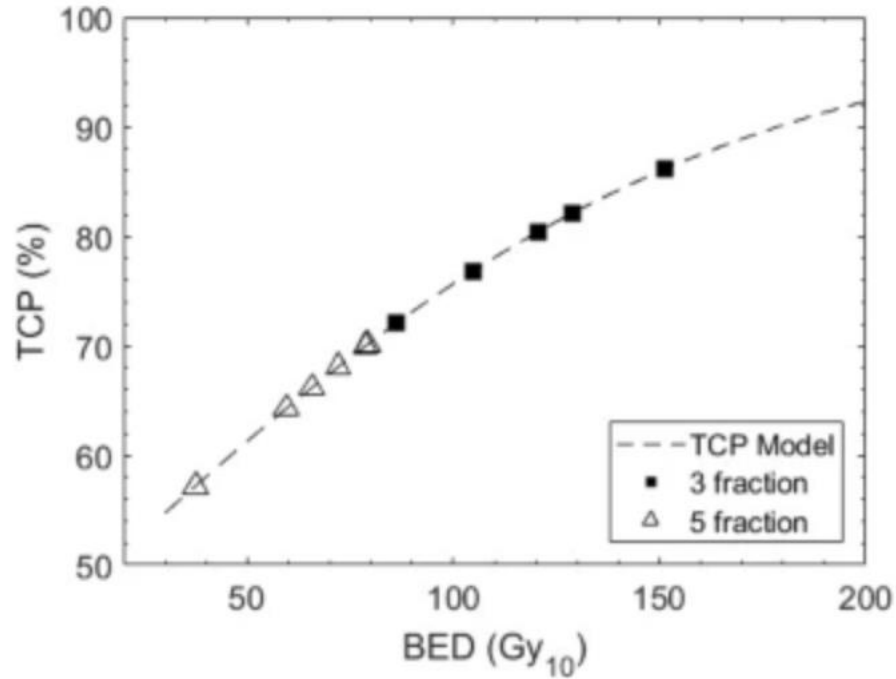
Linac 80/20 Penumbra: 5mm $\Rightarrow$ 4x dose

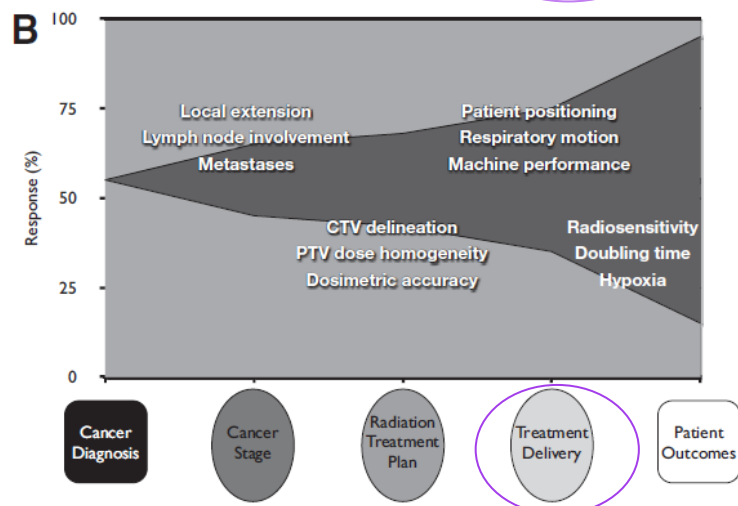
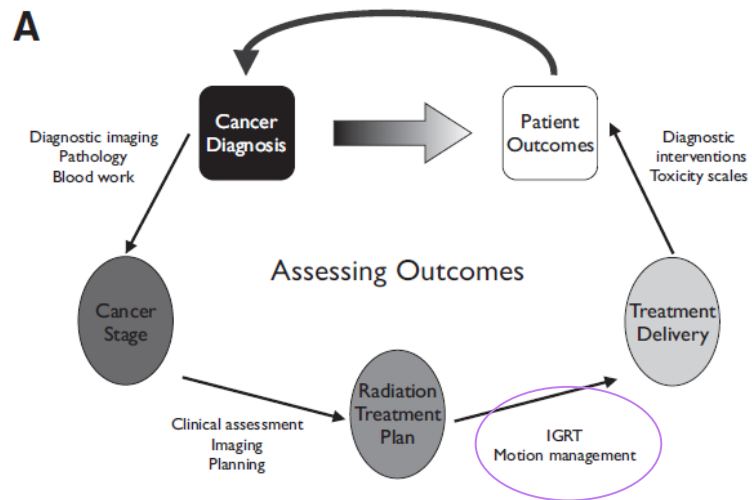


Clinical Implications of Motion Management

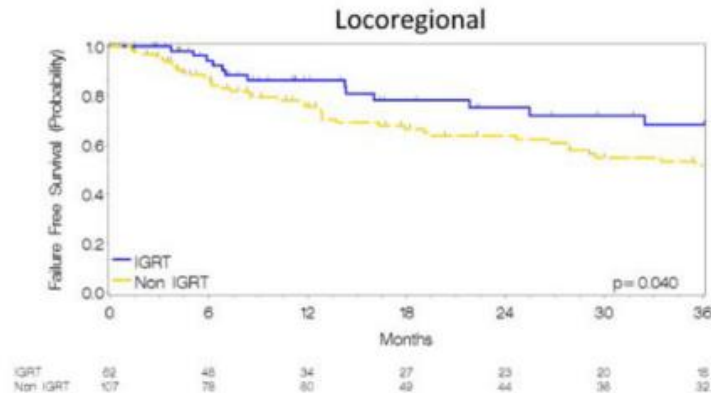
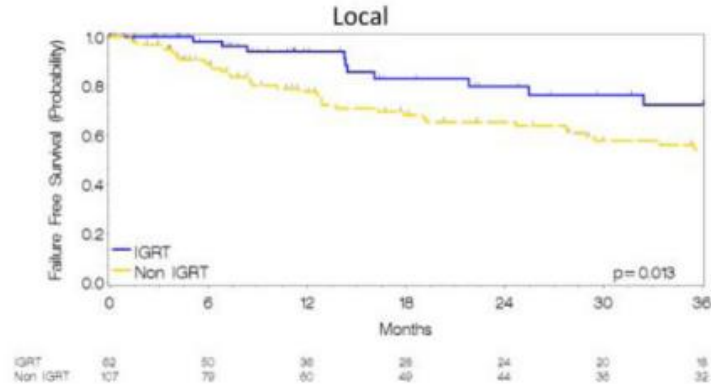


Clinical Implications of Motion Management – Increase TCP





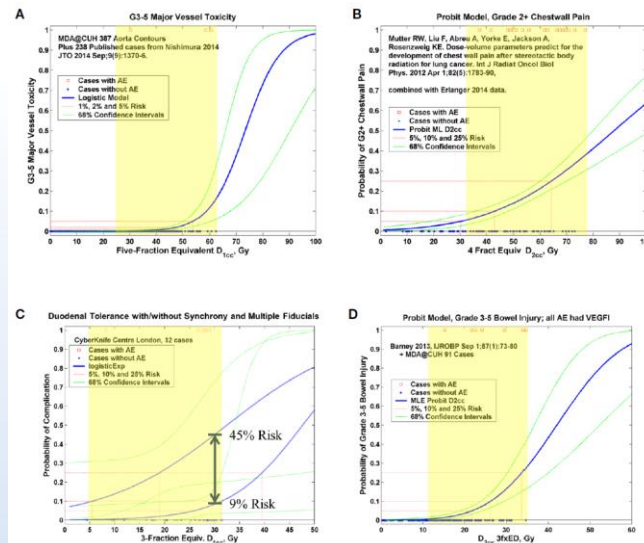
IGRT Improves outcomes



Potential Clinical Significance of Overall Targeting Accuracy and Motion Management in the Treatment of Tumors That Move With Respiration: Lessons Learnt From a Quarter Century of Stereotactic Body Radiotherapy From Dose Response Models

Anand Mahadevan¹, Bahman Emami², Jimm Grimm^{1*}, Lawrence R. Kleinberg³, Kristin J. Redmond³, James S. Welsh², Robert Rostock¹, Eric Kemmerer¹, Kenneth M. Forster¹, Jason Stanford¹, Sunjay Shah⁴, Sucha O. Asbell⁵, Tamara A. LaCouture⁵, Carla Scofield¹, Ian Butterwick¹, Jinyu Xue⁶, Alexander Muacevic⁷ and John R. Adler⁸

Front Oncol, Feb 2021, PMID: 33634020



10 Times Lower Risk

	Total number of patients in dose range		Grade 3 or higher complications		p-value
	CyberKnife with Synchrony	Linac or no Synchrony	CyberKnife with Synchrony	Linac or no Synchrony	
Aorta/Major Vessels D1cc	111	133	0	3	0.253
Chestwall D2cc	25	114	0	19	0.024
Duodenum D1cc	32	11	2	3	0.097
Small Bowel D2cc	47	65	0	7	0.021
Total	215	323	2	32	6e-6

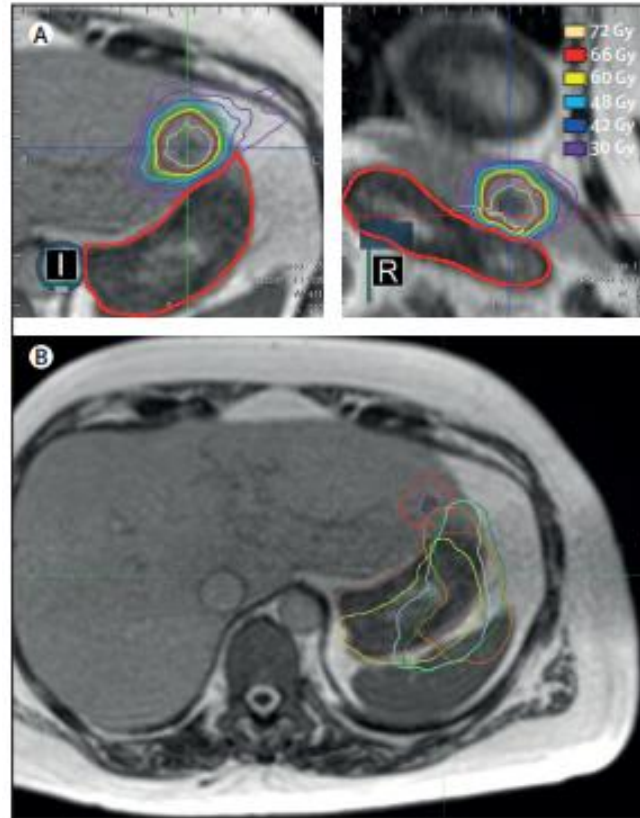
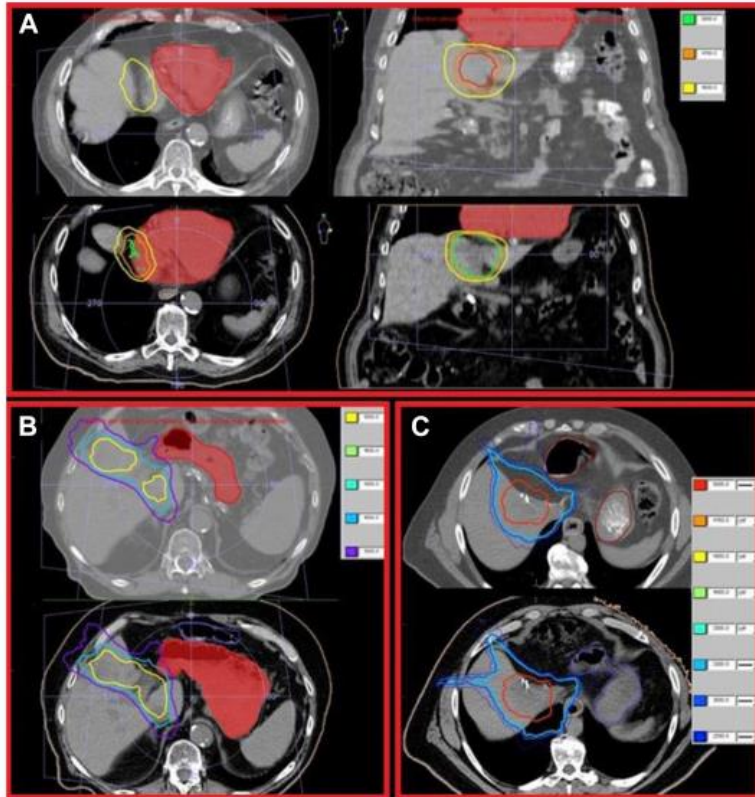
1%

10%

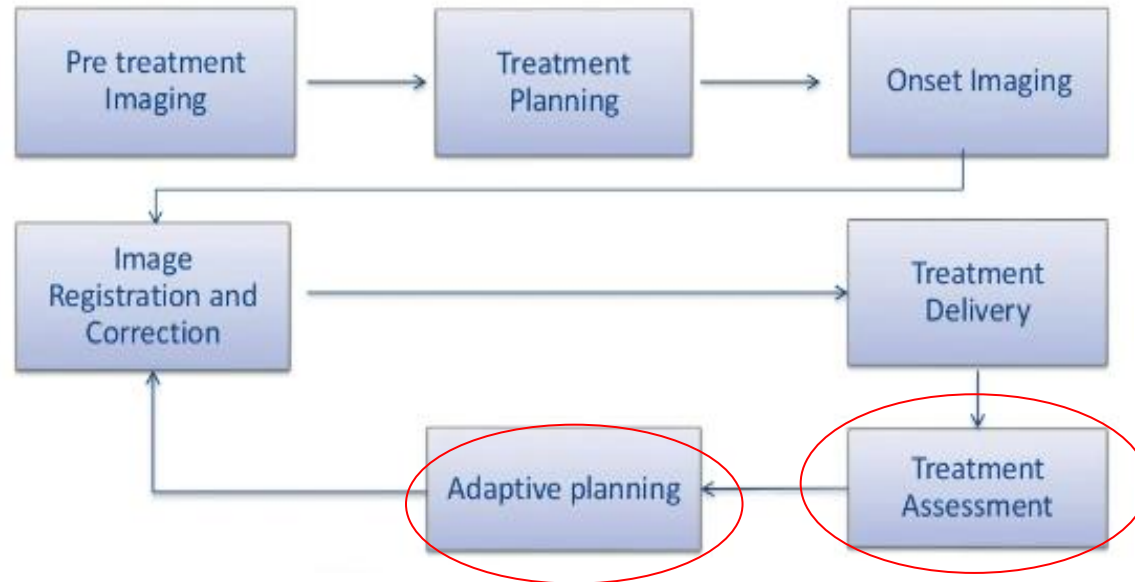
p < 0.0002

because Submillimeter End-to-End Tracking!

Significance of IGRT and Motion Management

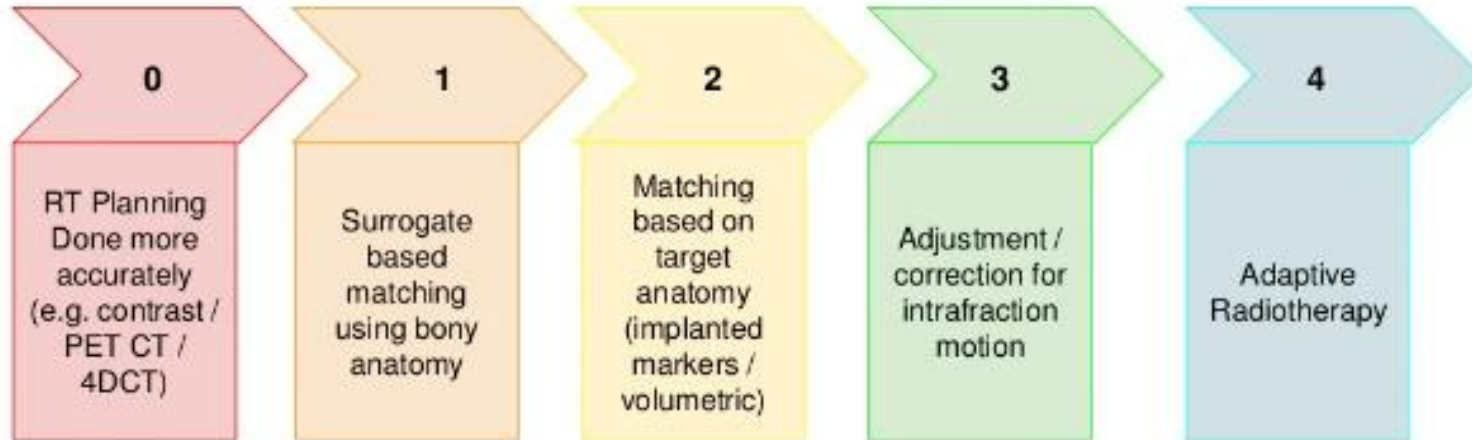


Adaptive Radiation

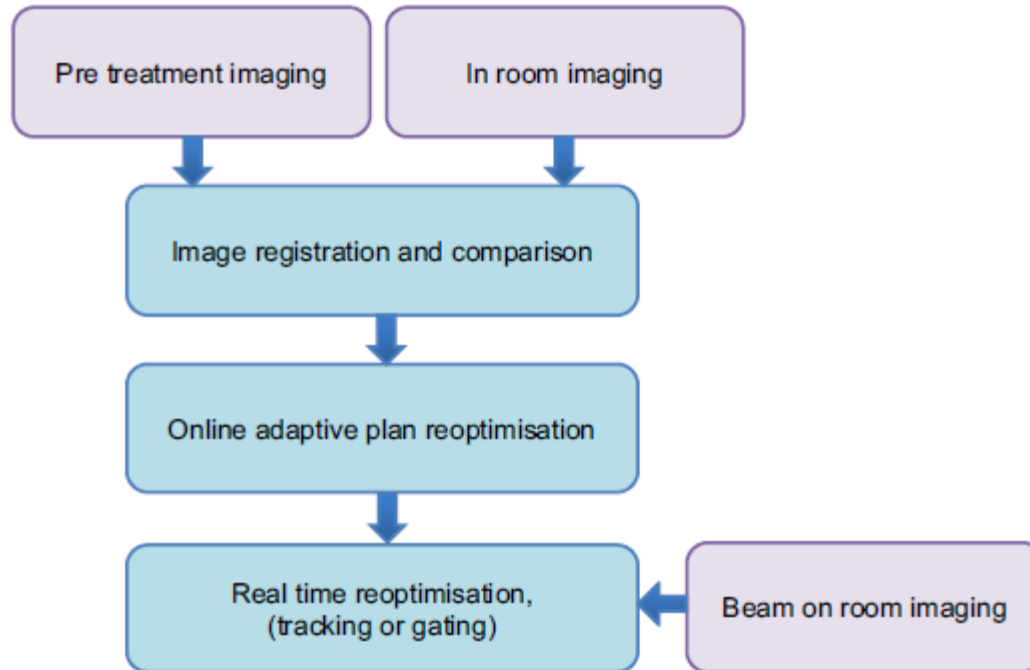


Adaptive RT

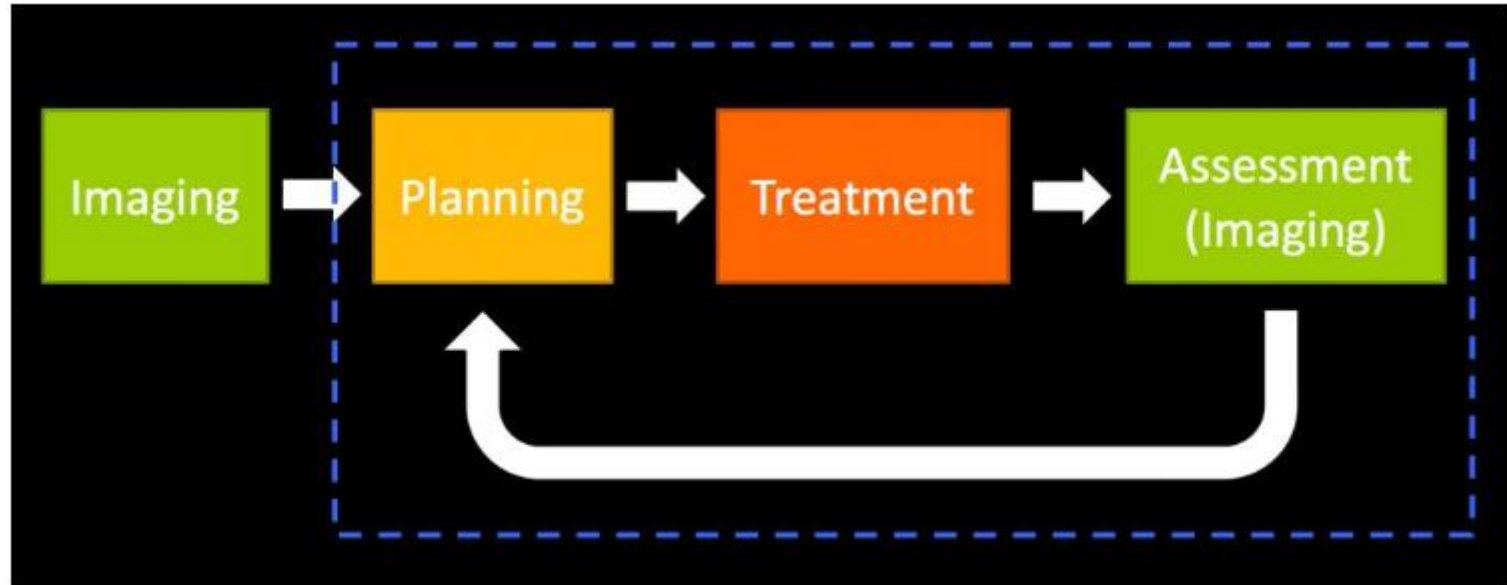
Levels of IGRT implementation

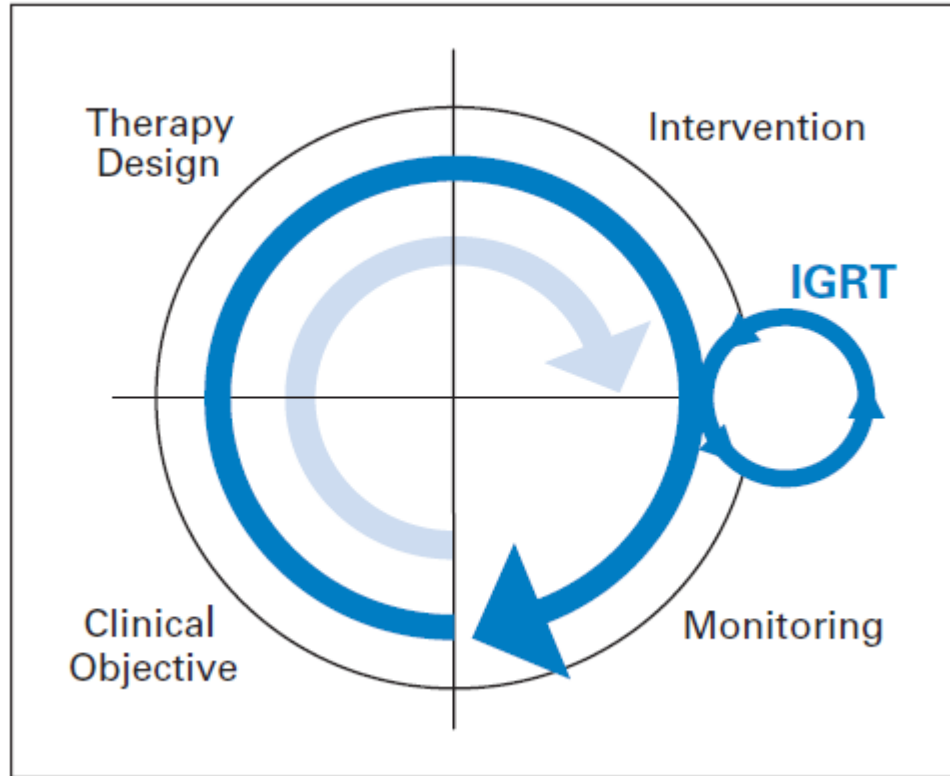


Adaptive Radiation Workflow



Adaptive Radiation Therapy





		Couch Shift	Plan Adaptation
TRANSLATIONAL ERRORS		✗ ✓	✓
ROTATIONAL ERRORS		✗ ✓	✓
DEFORMATIONAL ERRORS		✗	✓
TREATMENT RESPONSE VOLUME CHANGE		✗	✓
INDEPENDENT MOTION OF ORGANS		✗	✓

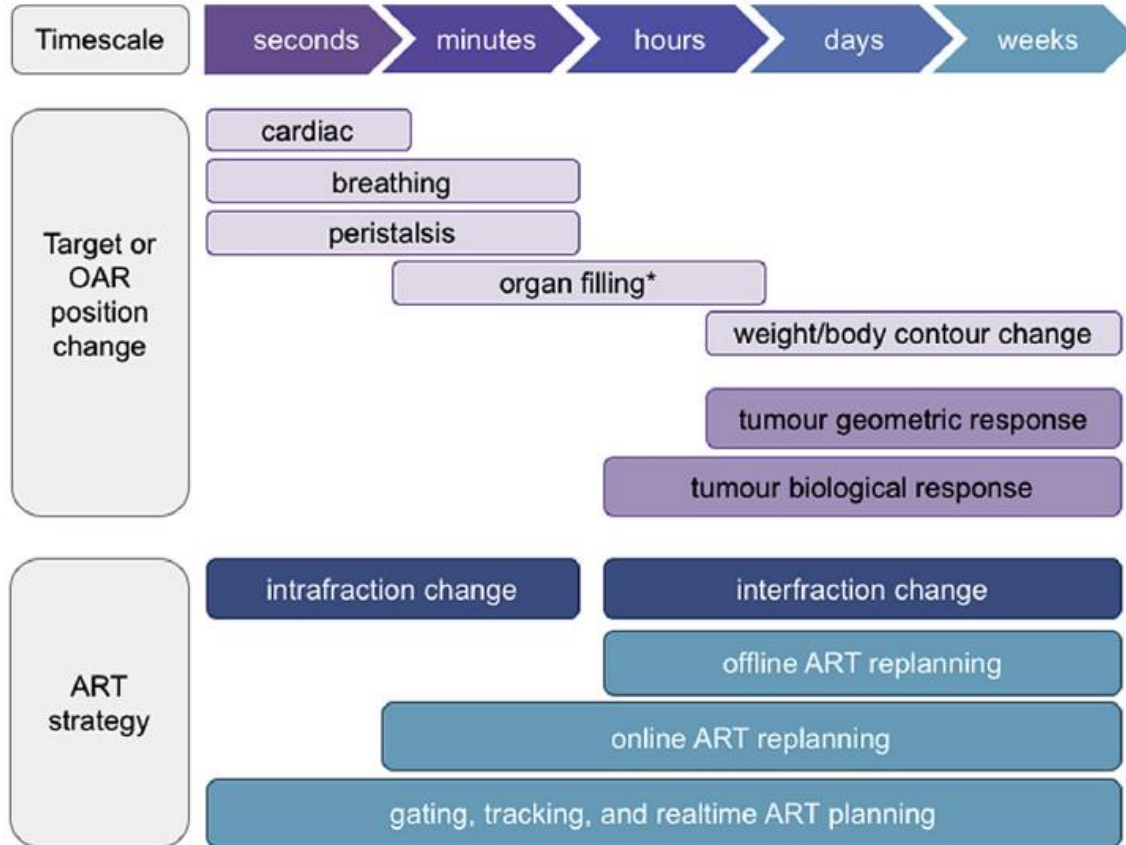
Adaptive RT Parameters

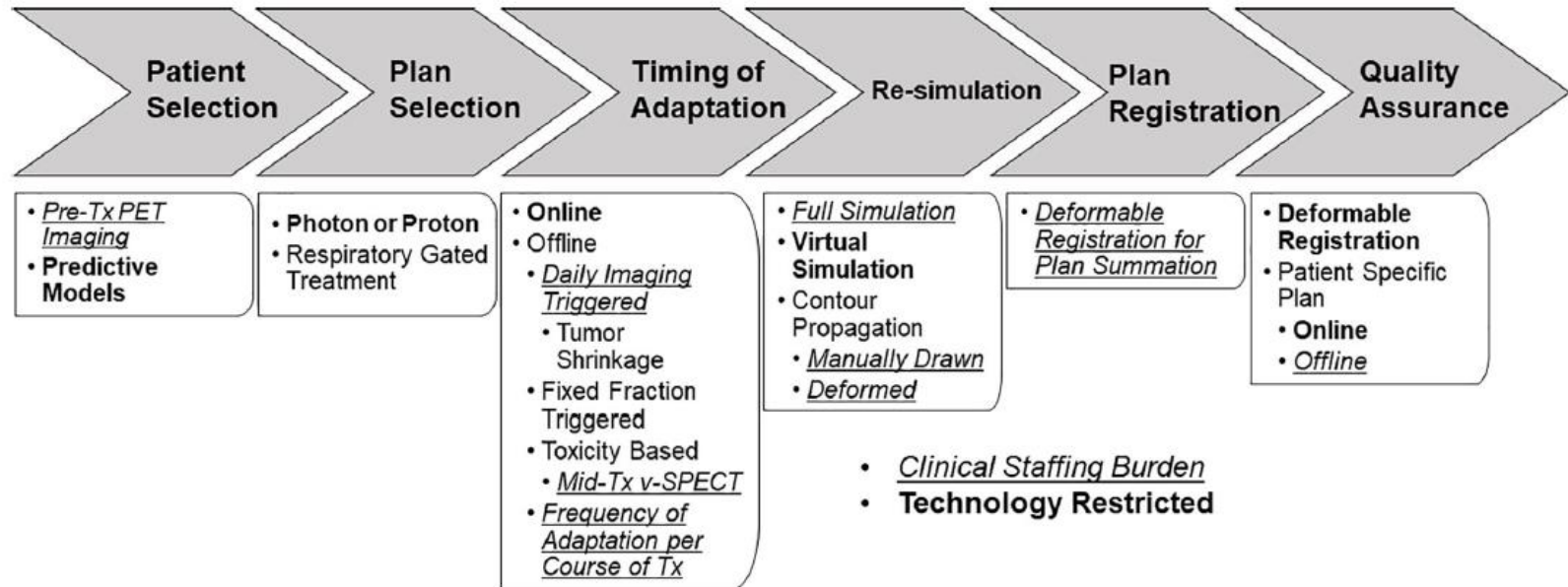
Physical

- OAR volume differences Inter and intrafractional
 - Inter – Daily IGRT
 - Intra – VMAT plans
- Target volume difference Interfractional replan
- Target position difference Inter and intrafractional
 - Inter daily IGRT and replans
 - Intra – online dose recalculation/ plan of the day

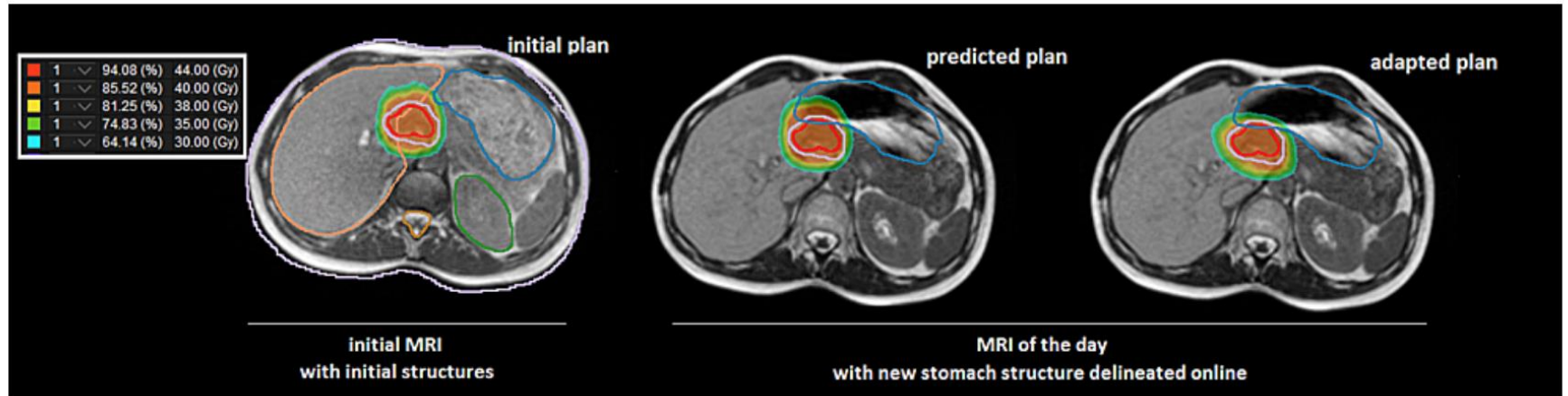
Biological

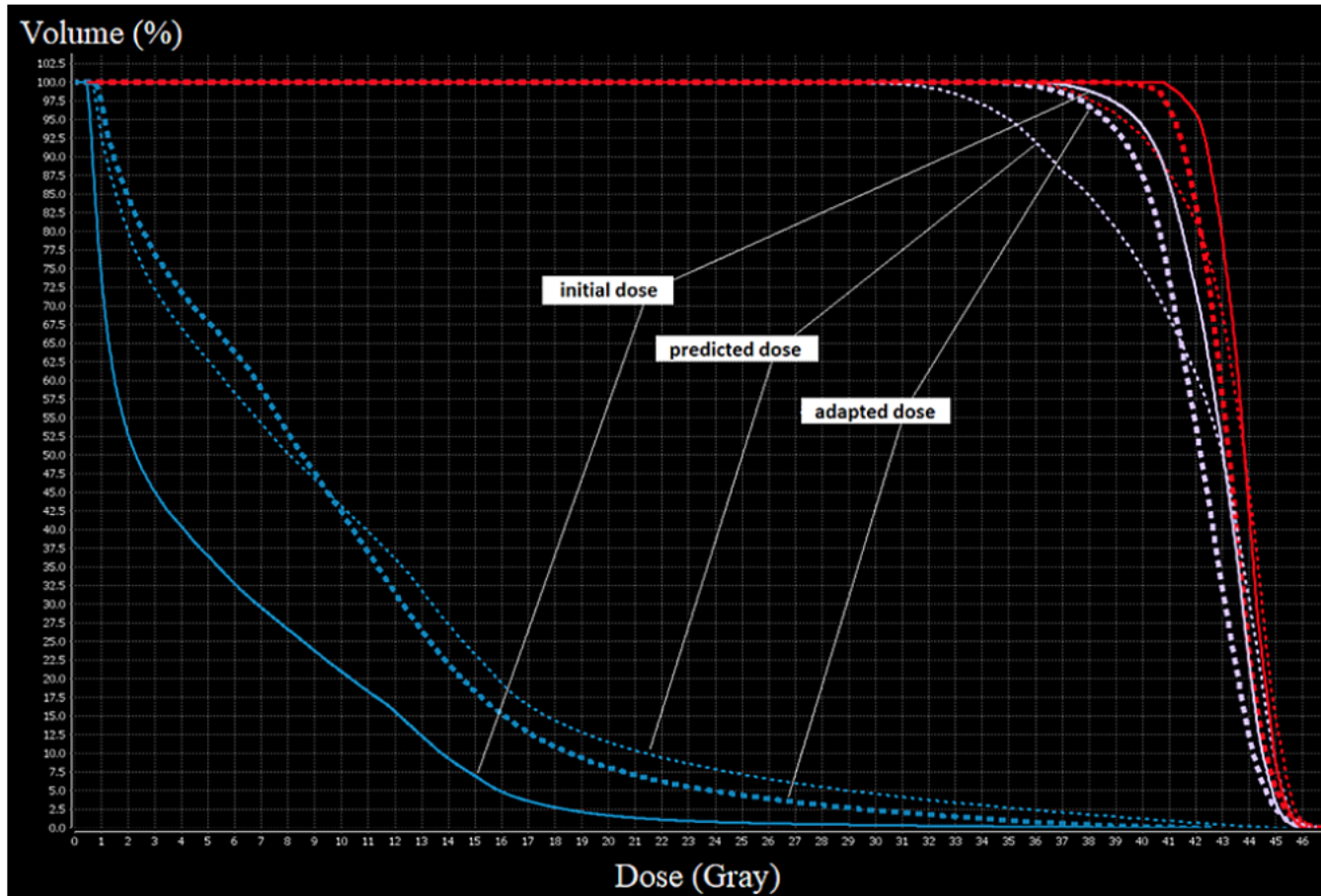
- Target Localisation
- Hypoxia Identification
- Cell Proliferation





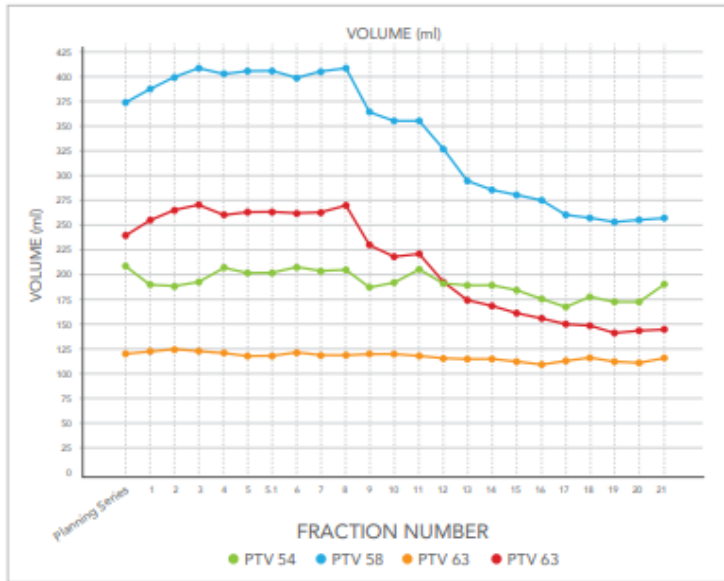
On Table Adaptive – OAR





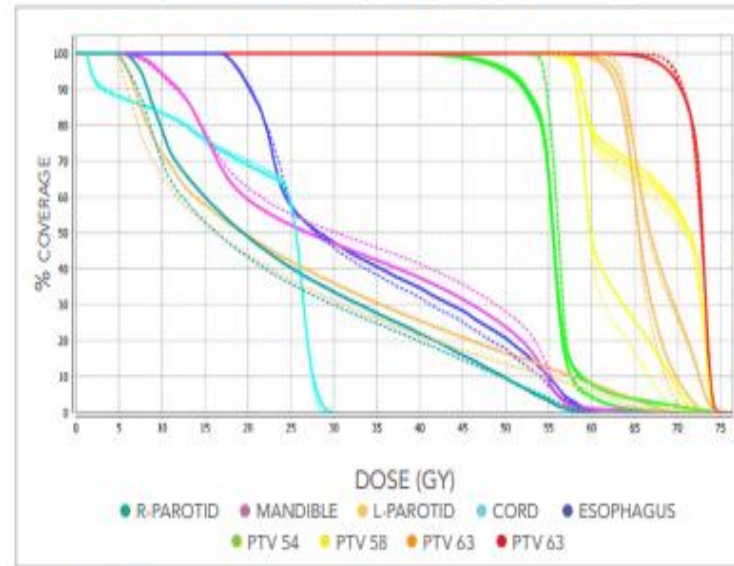
Automated Adaptation

TRENDING OF TARGET VOLUMES



Monitor automated report of trends in dose, dose-volume, target or OAR absolute volumes.

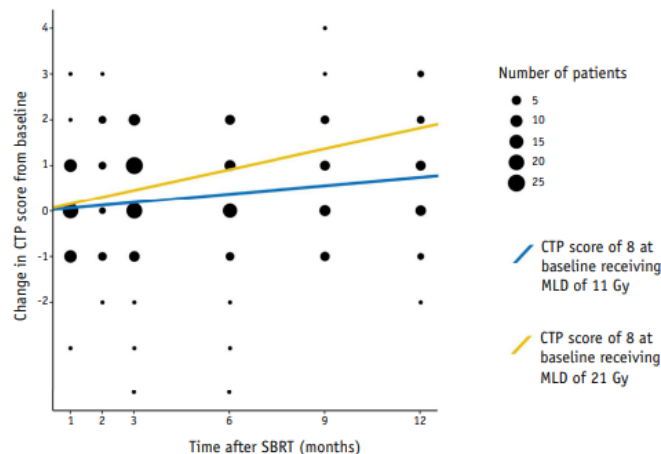
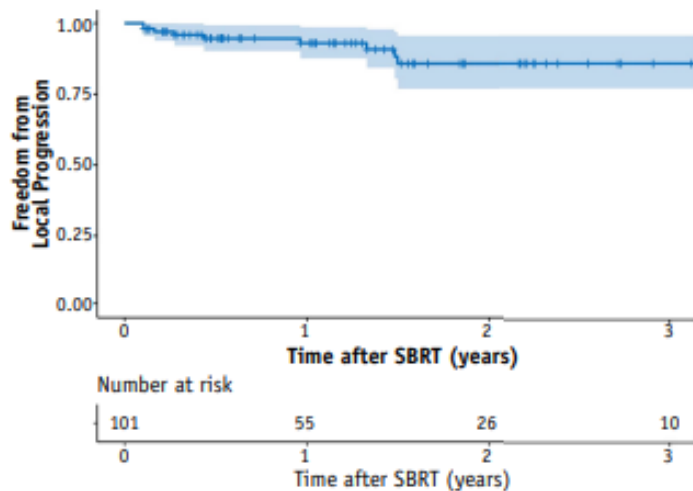
TOTAL PLANNED DOSE VS PROJECTED DOSE



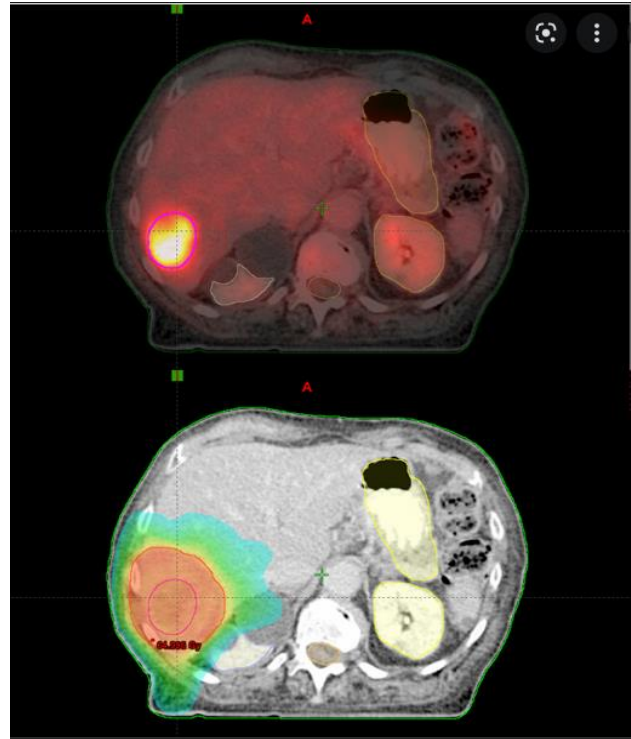
Efficiently assess the impact of anatomical changes on treatment plans.

Individualized Adaptive Radiation Therapy Allows for Safe Treatment of Hepatocellular Carcinoma in Patients With Child-Turcotte-Pugh B Liver Disease

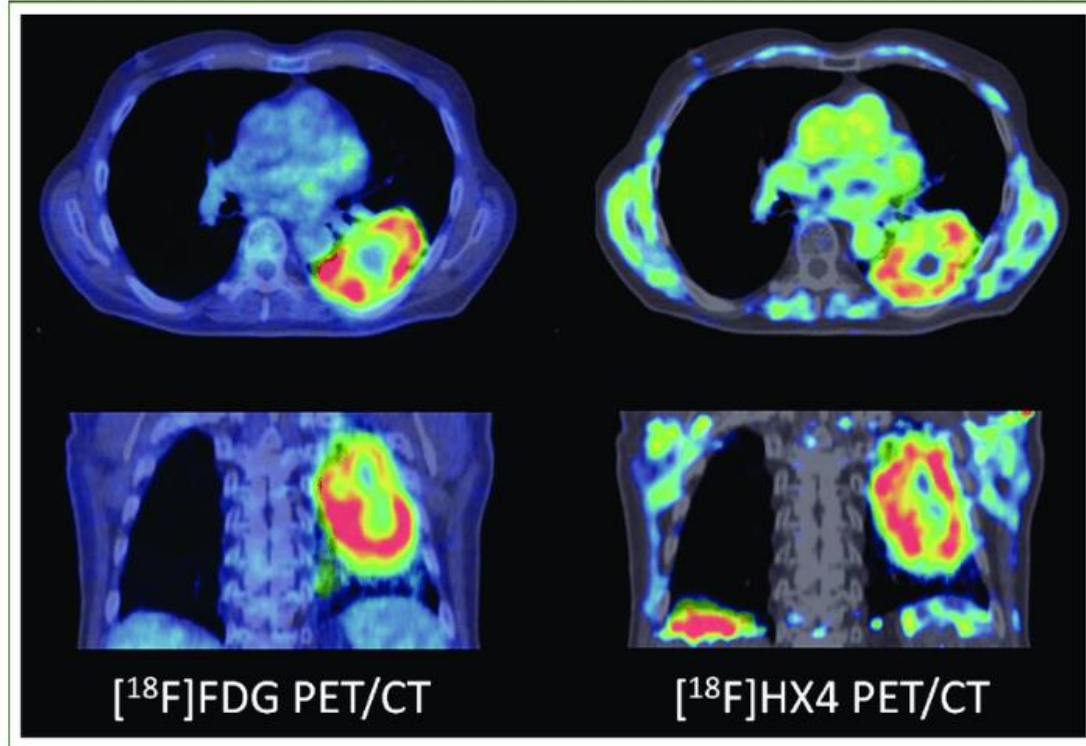
William C. Jackson, MD,* Ming Tang, MS,* Christopher Maurino, MS,*



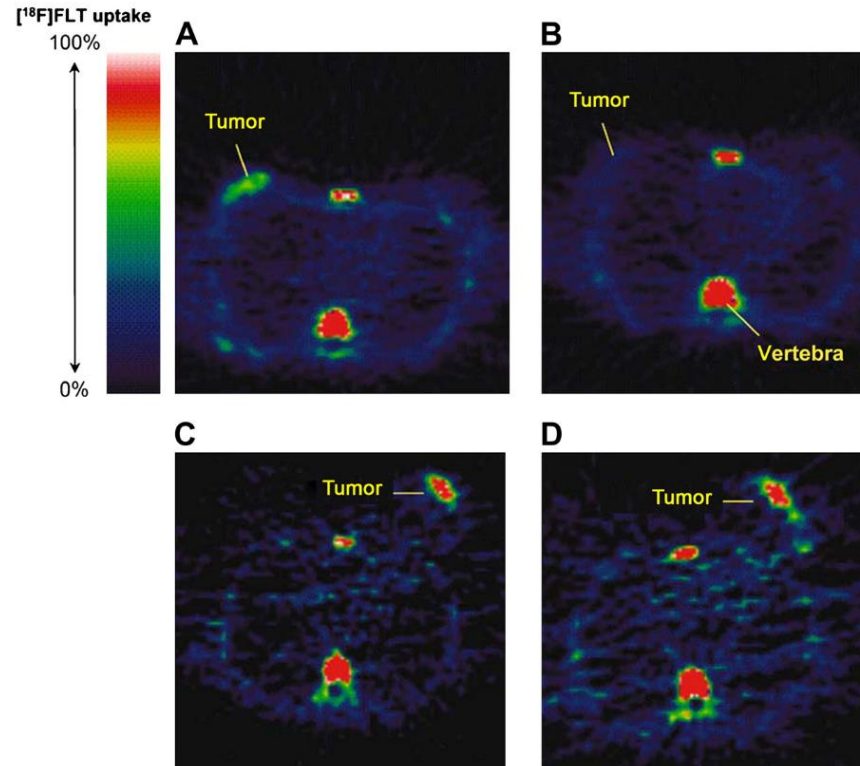
Biological Adaptation



Adapt to Hypoxia



Adapt to Proliferation



Conclusion

- Tumors can change in size, location, shape and activity from diagnosis through treatment
- Ignoring these changes can lead to incorrect treatment and poor outcomes
- Accurate image guidance and motion management is crucial in the treatment of liver cancers
- Image guided radiation therapy permits assessment and management of positional and structural changes in target volumes.
- Adaptation to changes in size, location, shape and activity improves outcomes through better local control and less toxicity



THANK YOU

