

Targeted Radiation Therapy for HCC

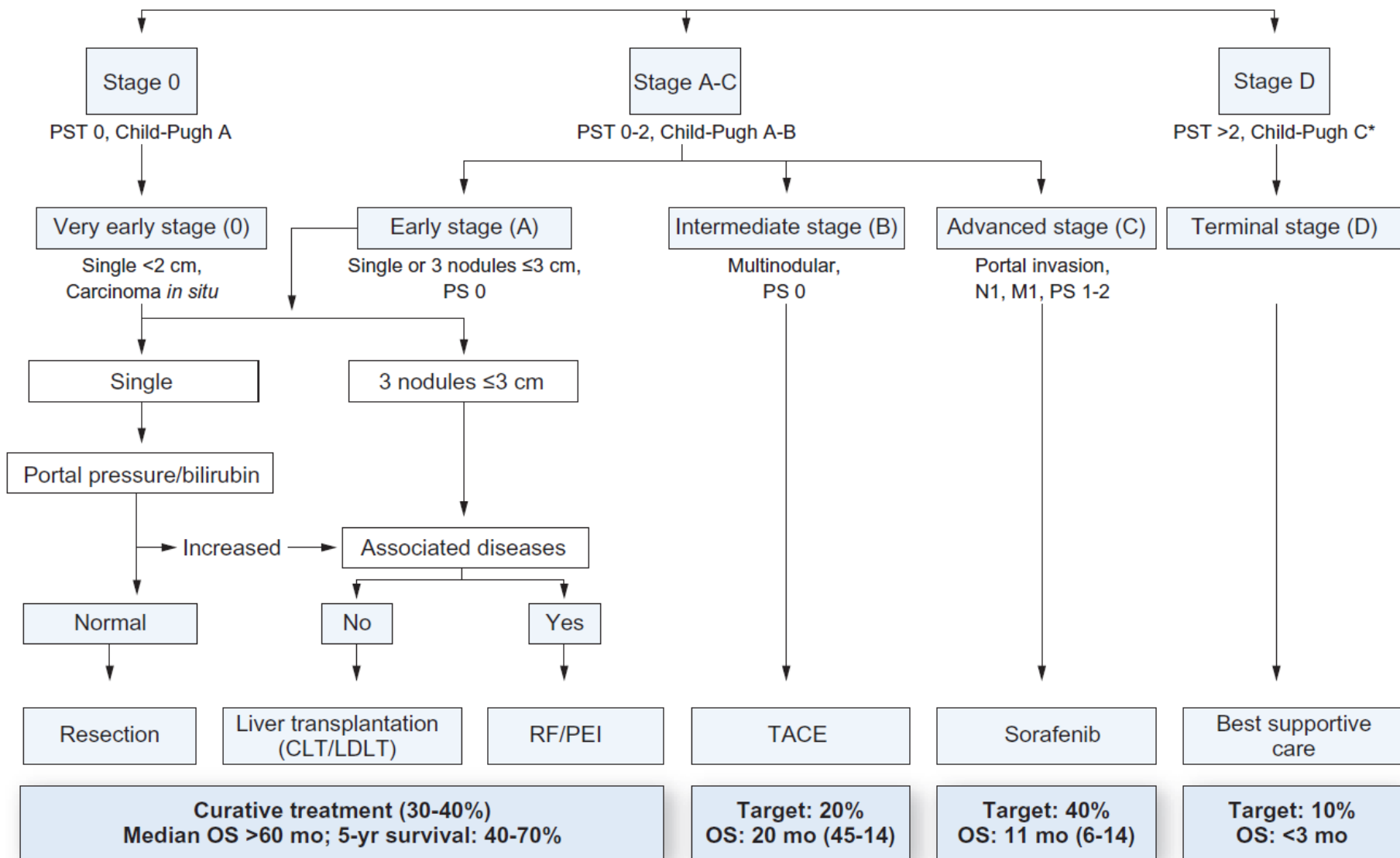
**Sungkyunkwan University
School of Medicine**

Hee Chul Park

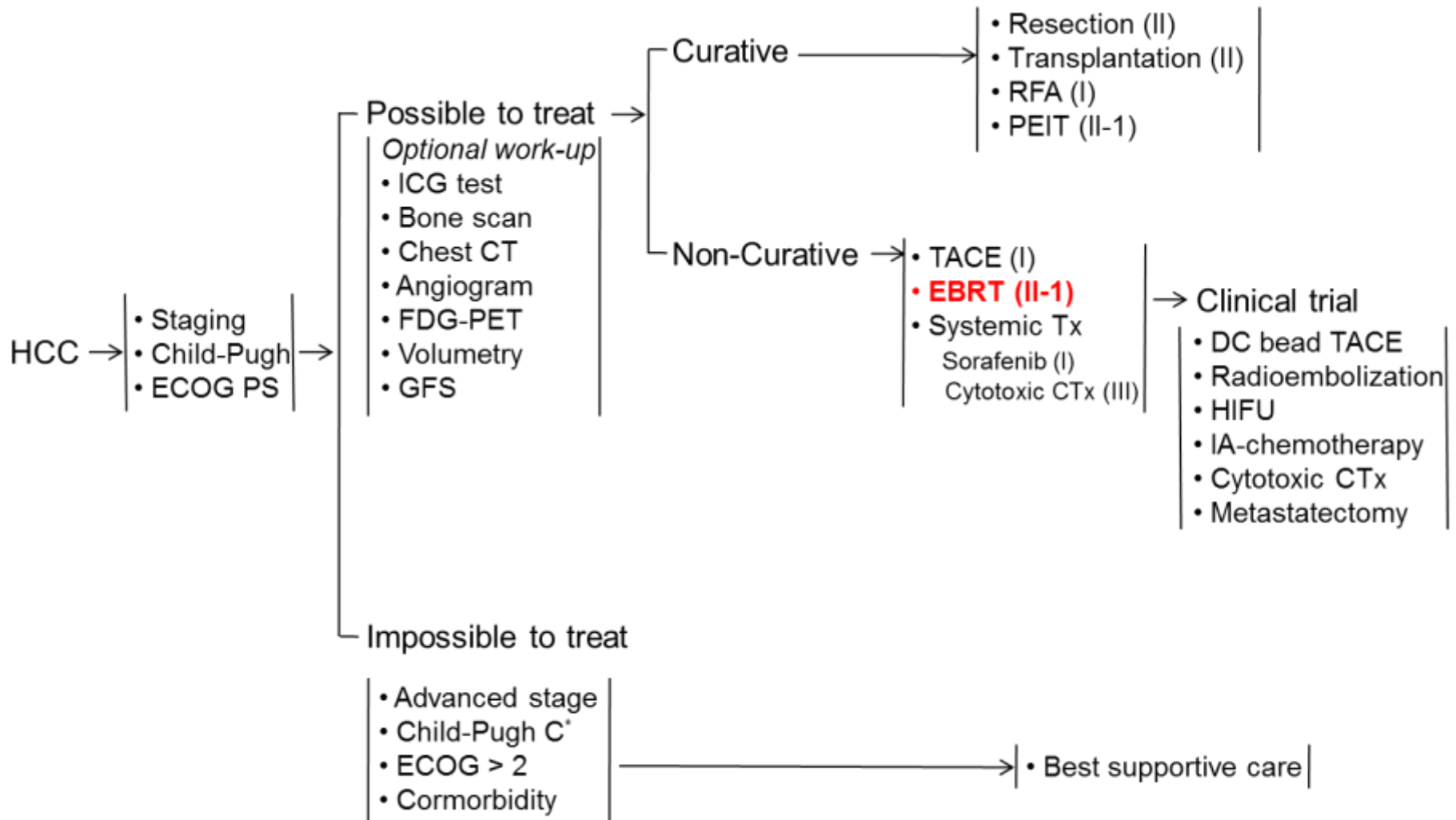


**HCC management guidelines
&
Role of RT in BCLC Staging System**

2012 EASL-EORTC (Updated BCLC Staging)



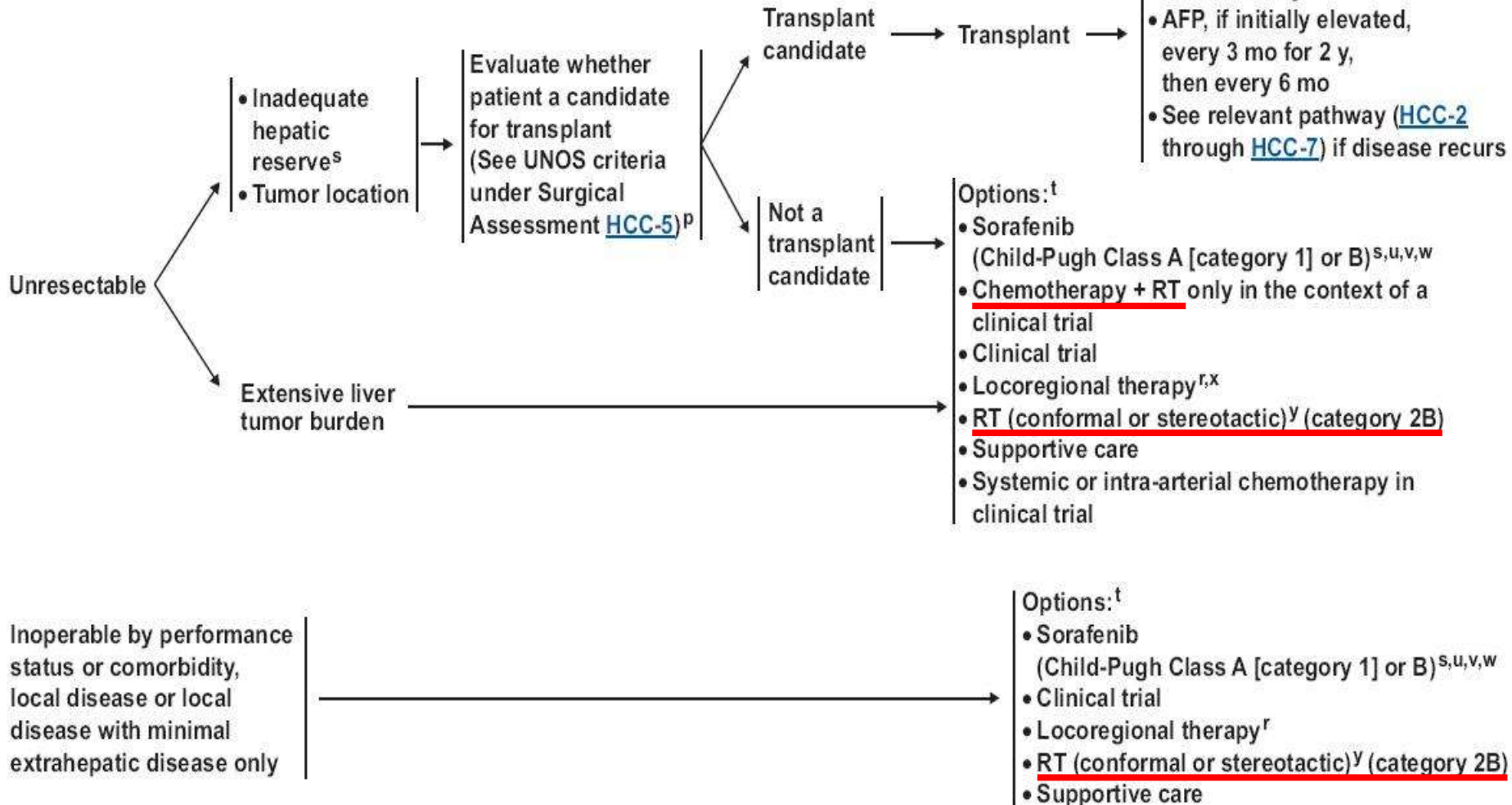
2009 Korean Liver Cancer Study Group



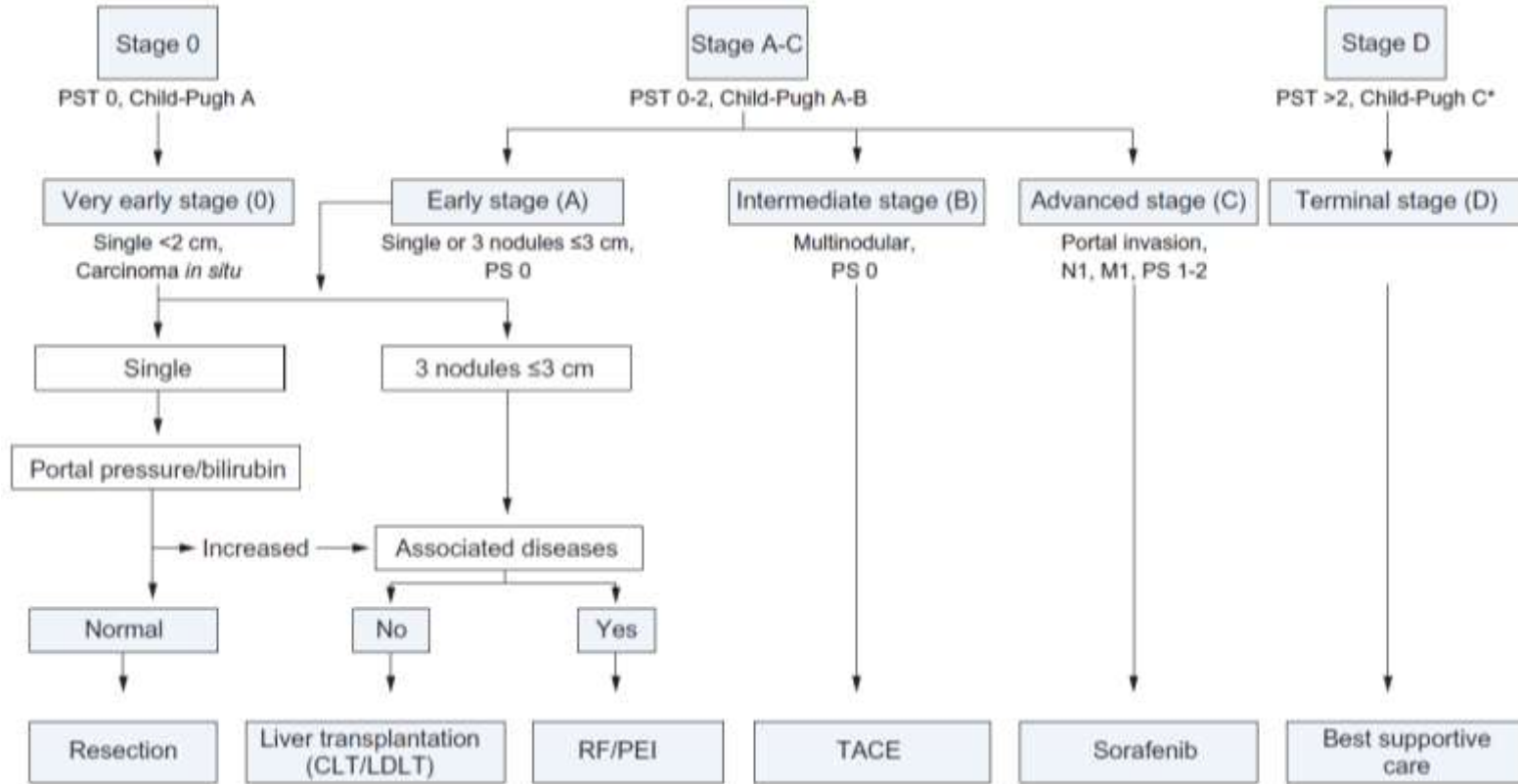
* Consider transplantation

2012 NCCN

CLINICAL PRESENTATION



RT in BCLC Staging System



Ablative RT (SABR, HypoFx)

- Inoperable
- Inaccessible
- To bridge before LT
- Salvage recurrence

TACE+RT/CCRT

- Consolidate TACE
- Salvage TACE refractoriness(SABR)
- Portal invasion

Palliative RT

- Symptom control
- Prevention of cancer related morbidity
- Oligometastasis

Support from evidence-making clinical trial efforts

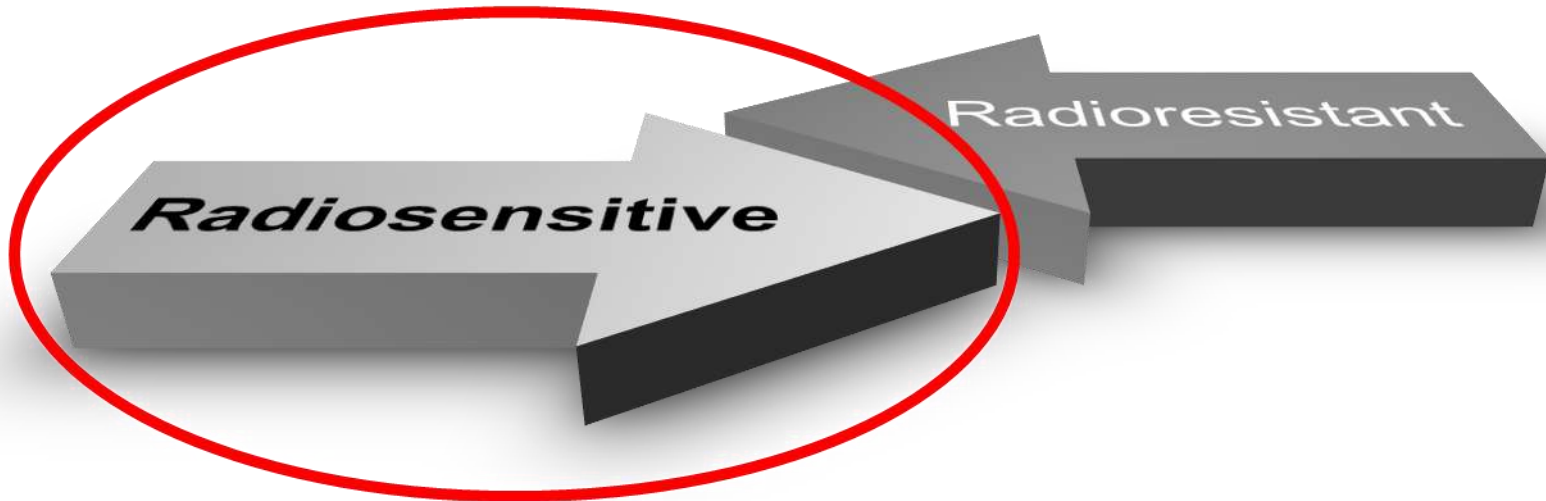
**Radiation dose response of HCC
&
Radiation tolerance of normal organs**

Skepticism versus Enthusiasm in RT for HCC

Present



Past



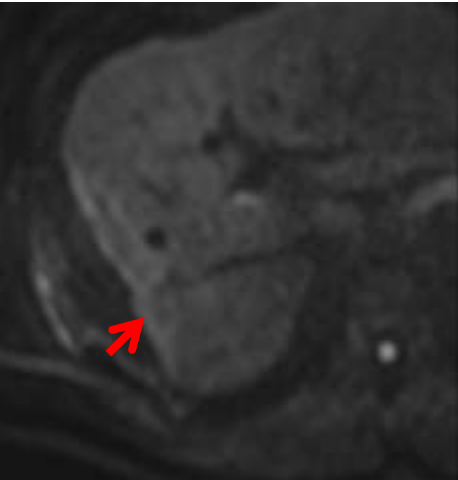
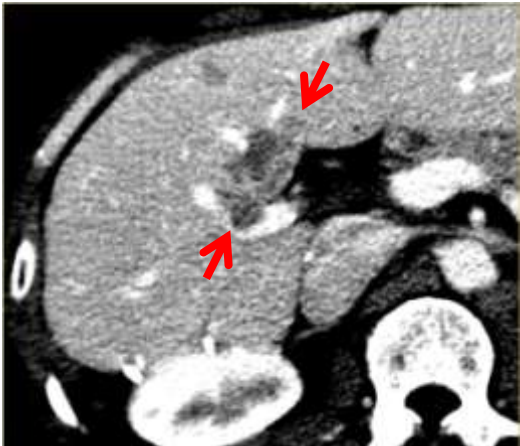
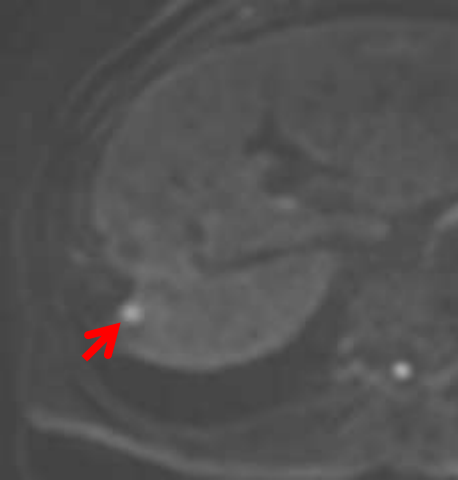
HCC is radiosensitive tumor

- From the recent clinical data (1990s ~)
- with 3-dimensional conformal technique
- Dose-response relationship (+)
- Concept of partial-volume tolerance

HCC is radioresistant tumor

- Traditional concept (~ 1990s)
- with 2-dimensional technique (old)
- Unable to give high dose RT
- No information about volumetric analysis

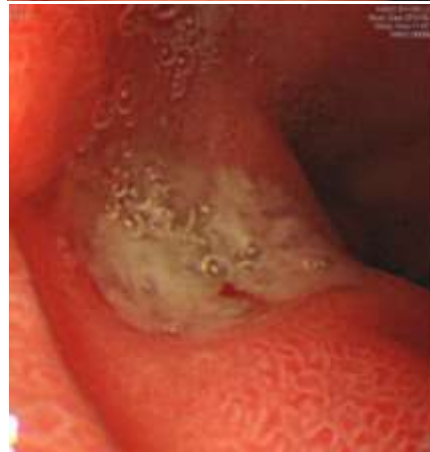
Therapeutic Effects of RT for HCC



Toxicities after Radiotherapy for HCC



Liver



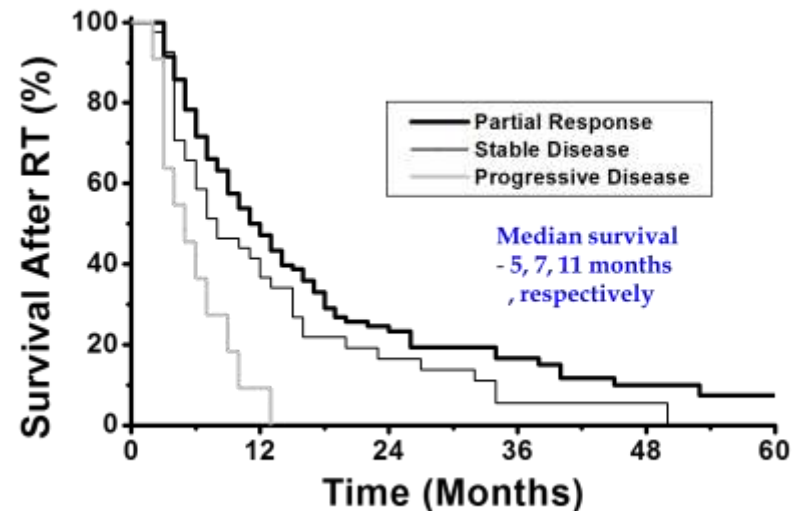
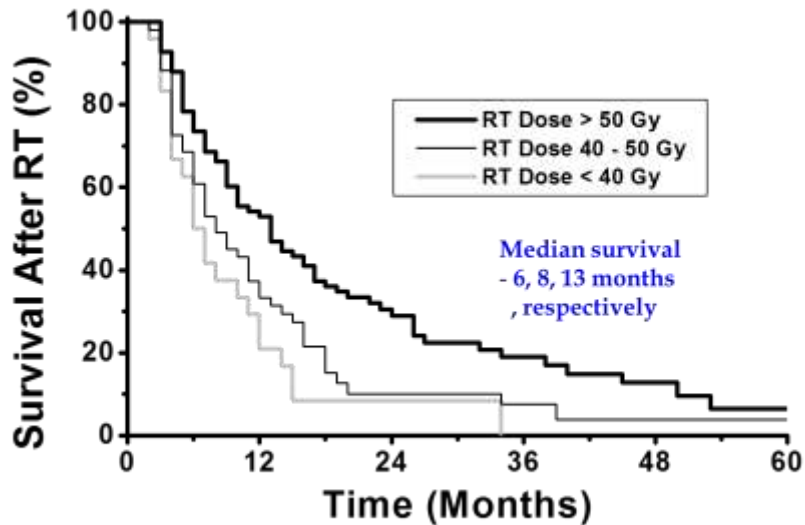
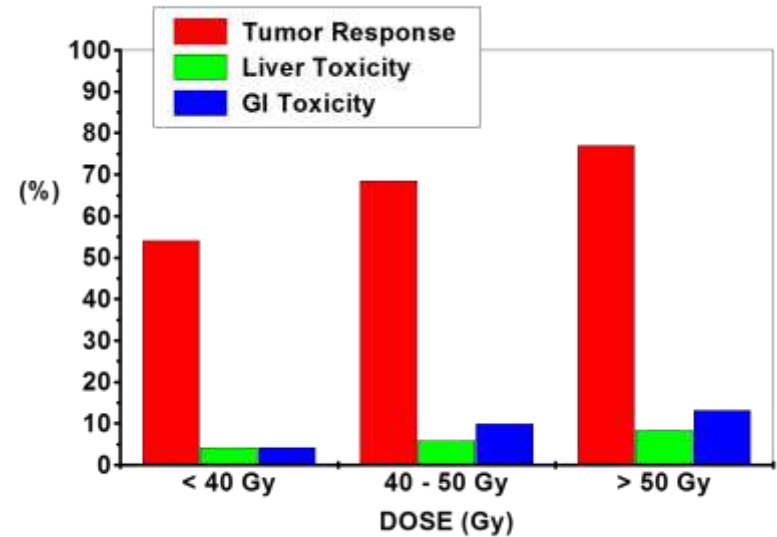
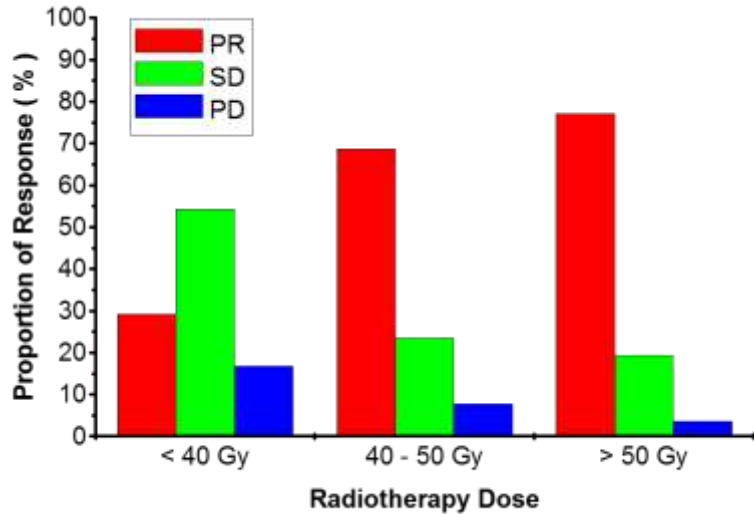
G-I



Lung

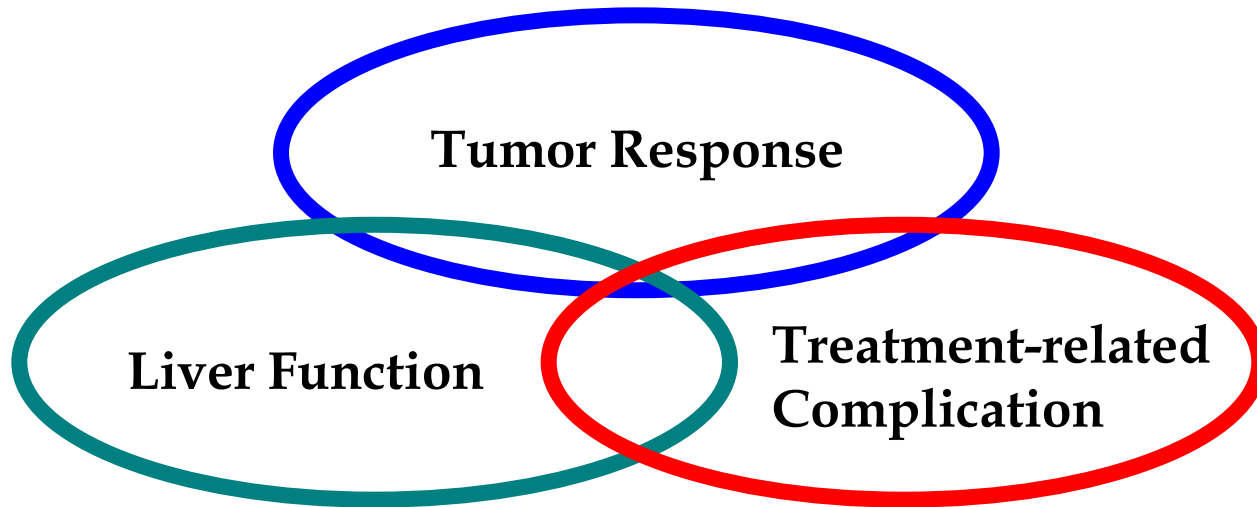
chest wall pain, rib fracture, colonopathy, skin toxicity, etc

Dose response of HCC and normal tissues



For the Better Outcome: RT perspectives

Three components affecting the outcomes of HCC patients



Radiation Oncologists' Task (RT for HCC)

→ RT dose escalation, Preserve Liver Function

→ Decrease Tx-related Toxicity

→ And one more, **not interfering further treatment**

Comparison of treatment modalities

1. Local control probability

Surgery ~ RFA > ~ TARE ~ **ERT** >>>>> sorafenib

2. Liver function preservation

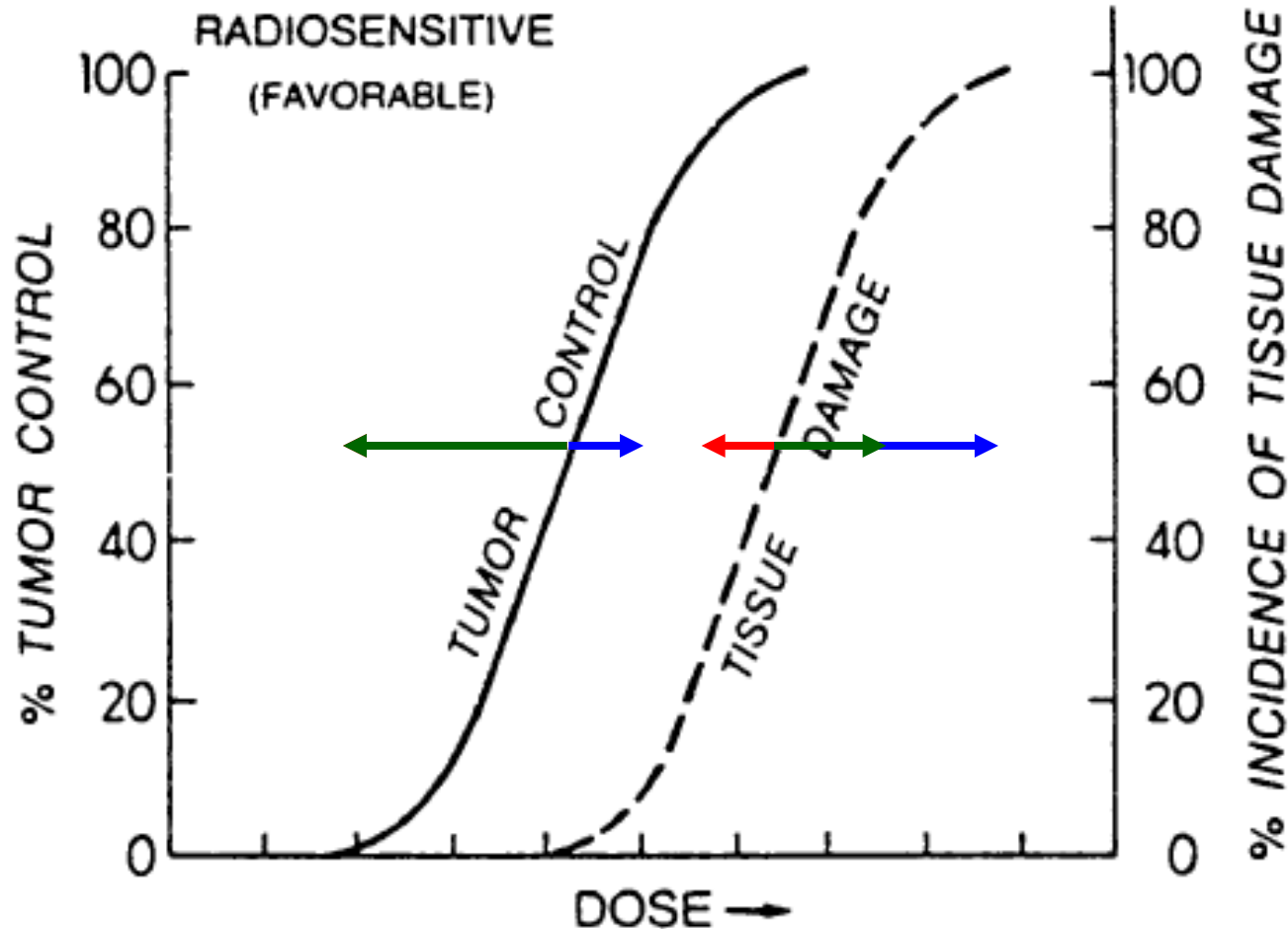
RFA >>> sorafenib ~> TARE ~> **ERT** >> Surgery

3. Treatment related toxicities

“Stigmata”

decreasing from the recent advances in ERT tech.

Therapeutic Ratio... modifying factors



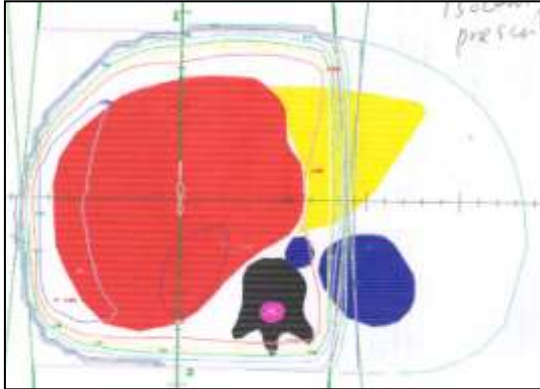
Radio-sensitizer

Radio-protector

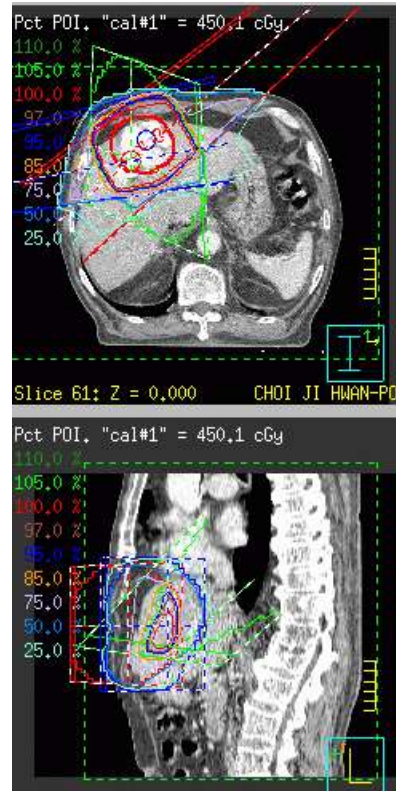
High-tech RTX

Advances in RT techniques for HCC

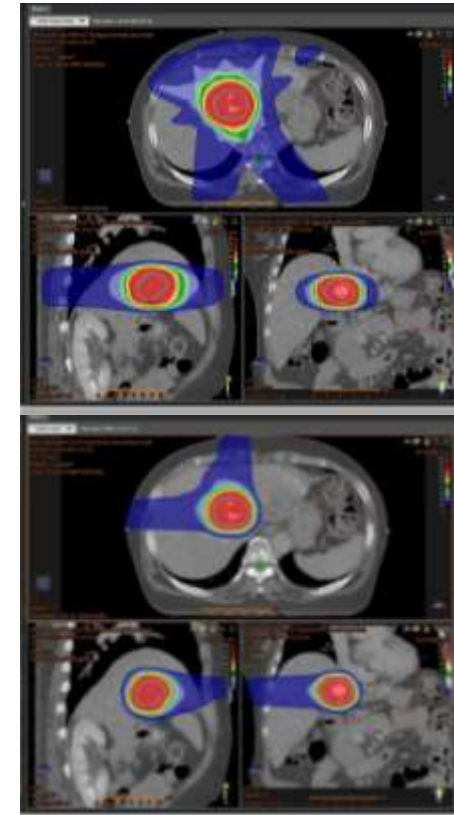
Advances in increasing conformity



2-D Radiotherapy



3D-CRT



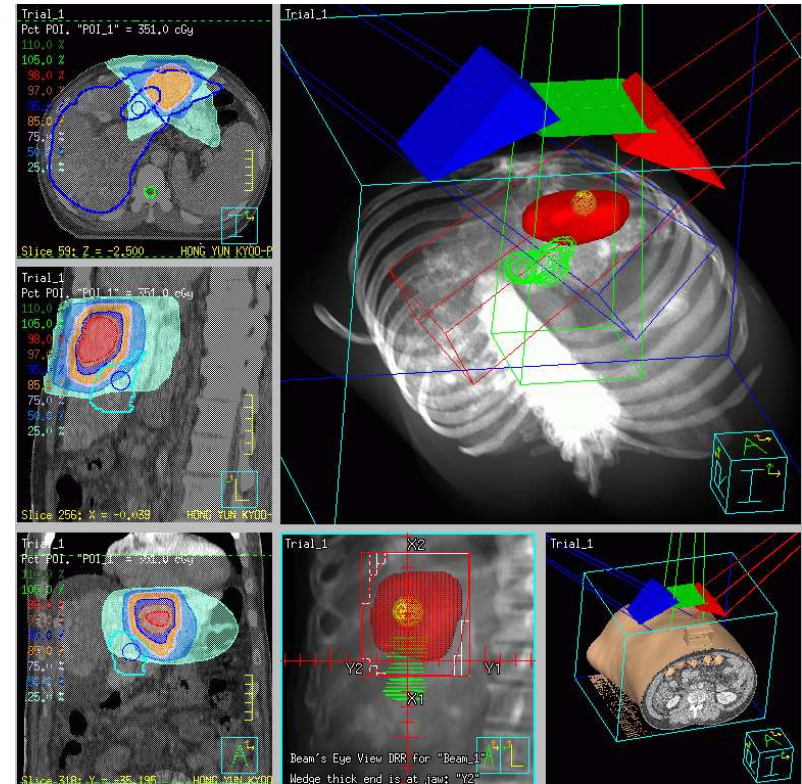
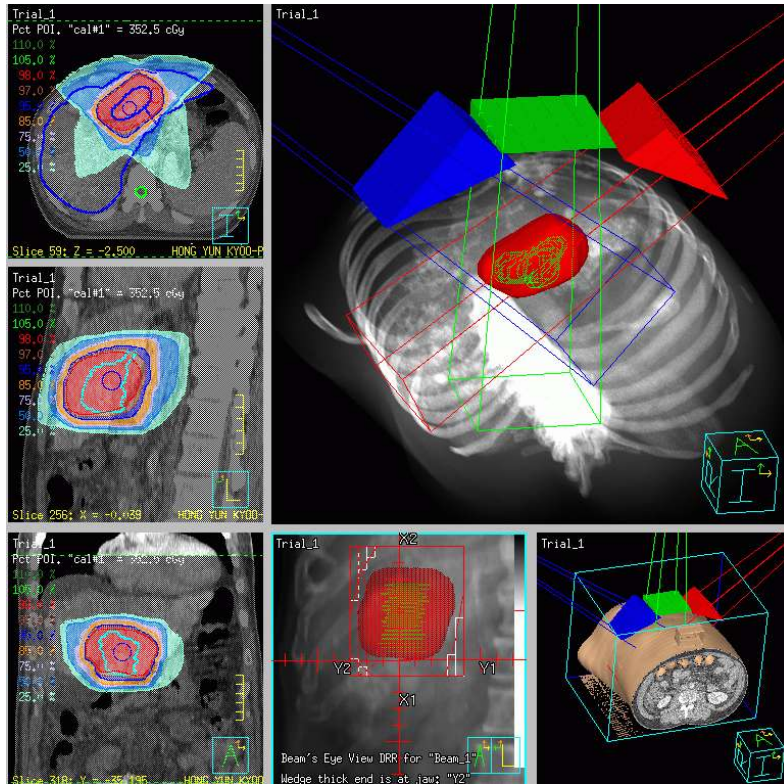
IMRT, IMPT

Efforts to improve **precision** : 2D → 3DCRT → IMRT (IMPT)

Advances in increasing accuracy

Good aiming

Bad Aiming



Internal organ motion, Volume change and deformation

Efforts to improve **accuracy** : IGRT, 4D-RT

Conventional radiotherapy for liver cancer

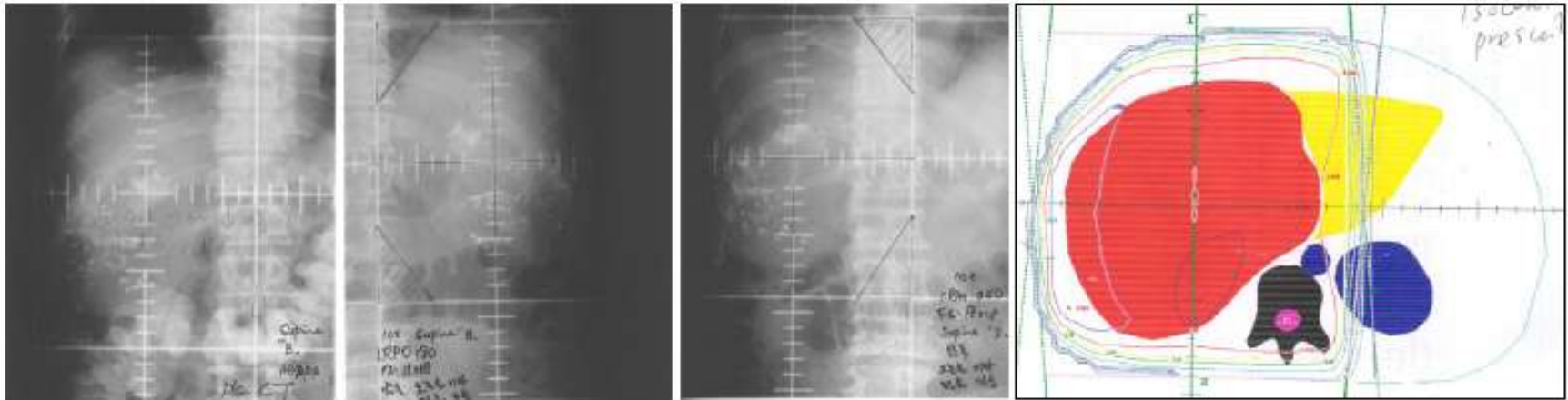
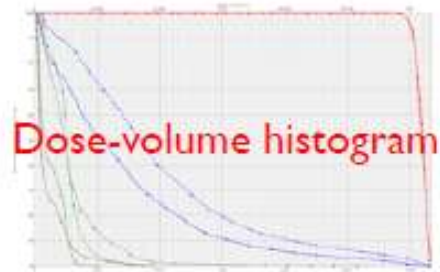
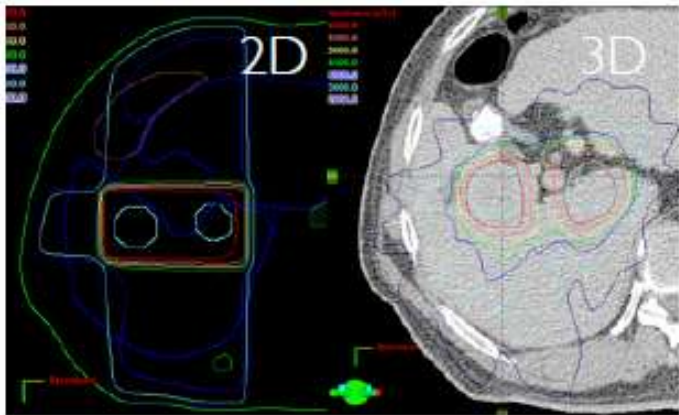
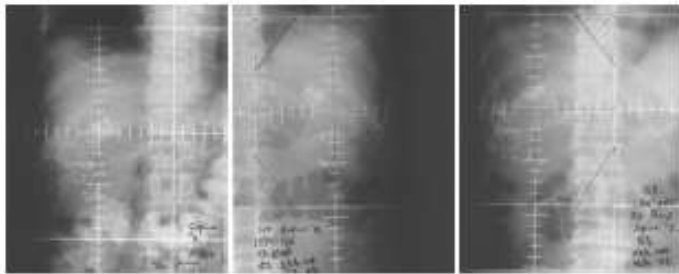


Table 2. Tolerance doses of Emami *et al.* (1) and predictions* of the 4-parameter model (Eqs. 1–4)

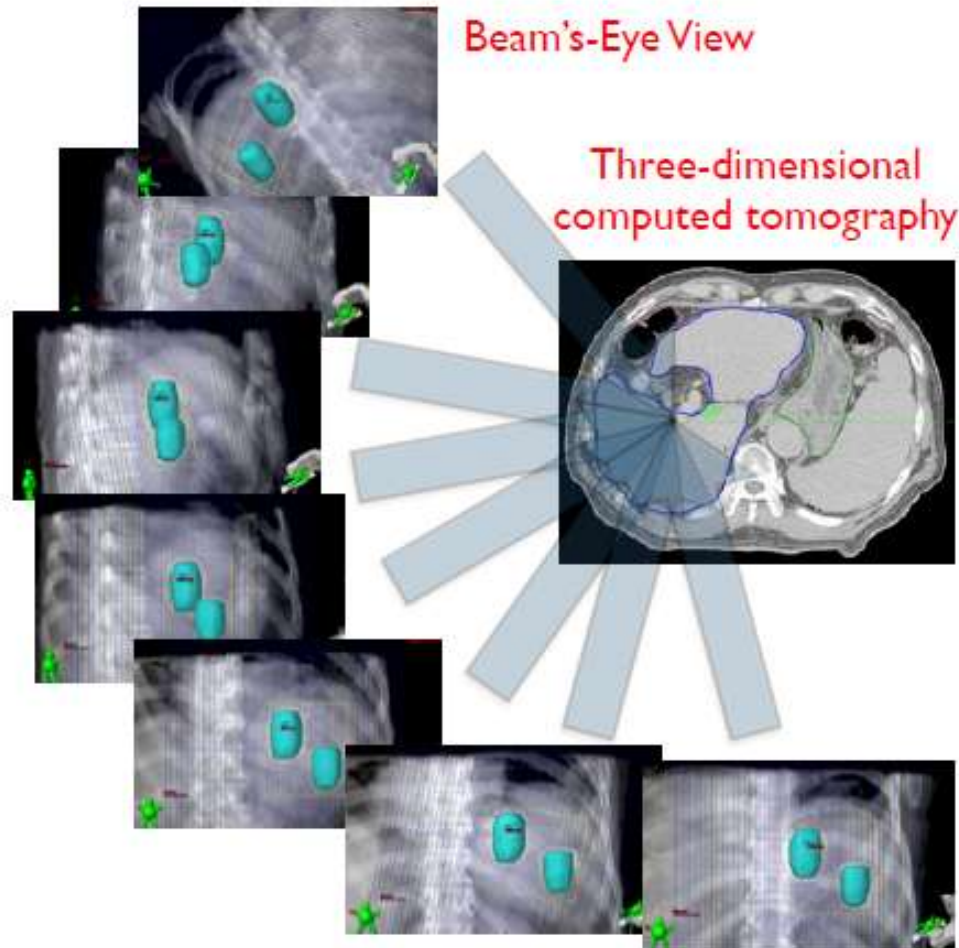
Organ	TD _{5/5} (Gy) volume			TD _{50/5} (Gy) volume			End point
	$\frac{1}{3}$	$\frac{2}{3}$	1	$\frac{1}{3}$	$\frac{2}{3}$	1	
Liver	50 (43)	35 (34)	30 (30)	55 (57)	45 (46)	40 (40)	Liver failure

Burman, C., et al., *Int J Radiat Oncol Biol Phys*, 1991, 21(1): p. 123-135.

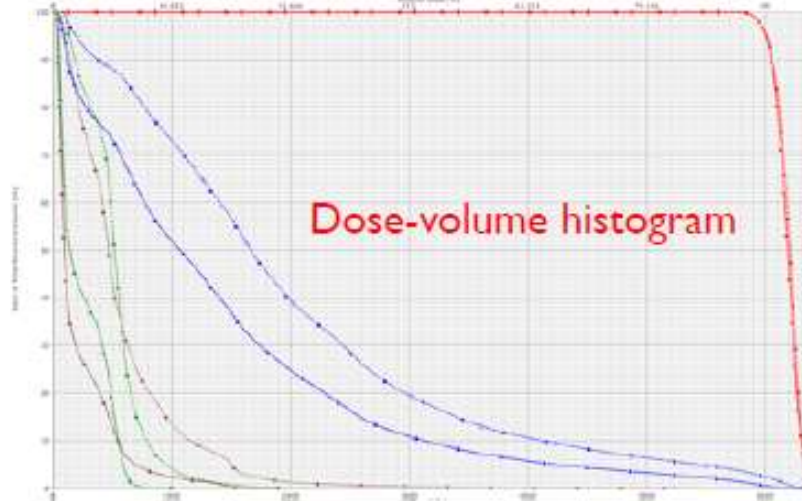
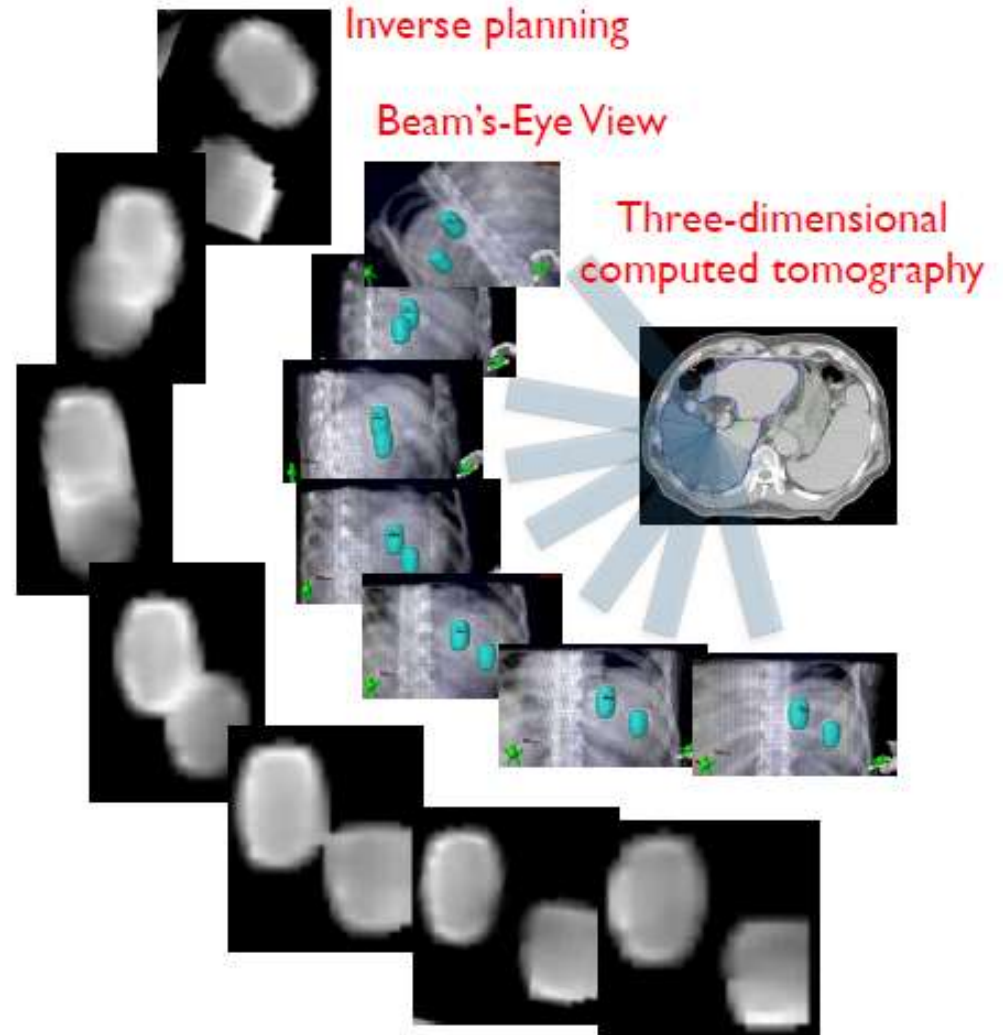
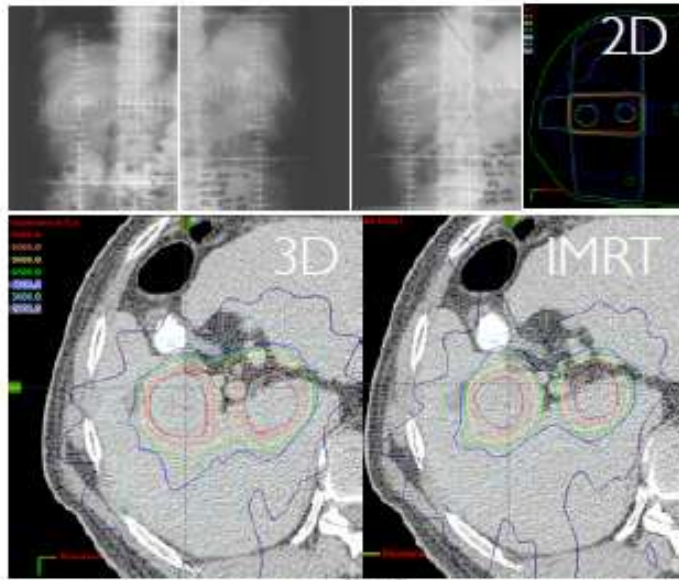
Three dimensional conformal radiotherapy for liver cancer



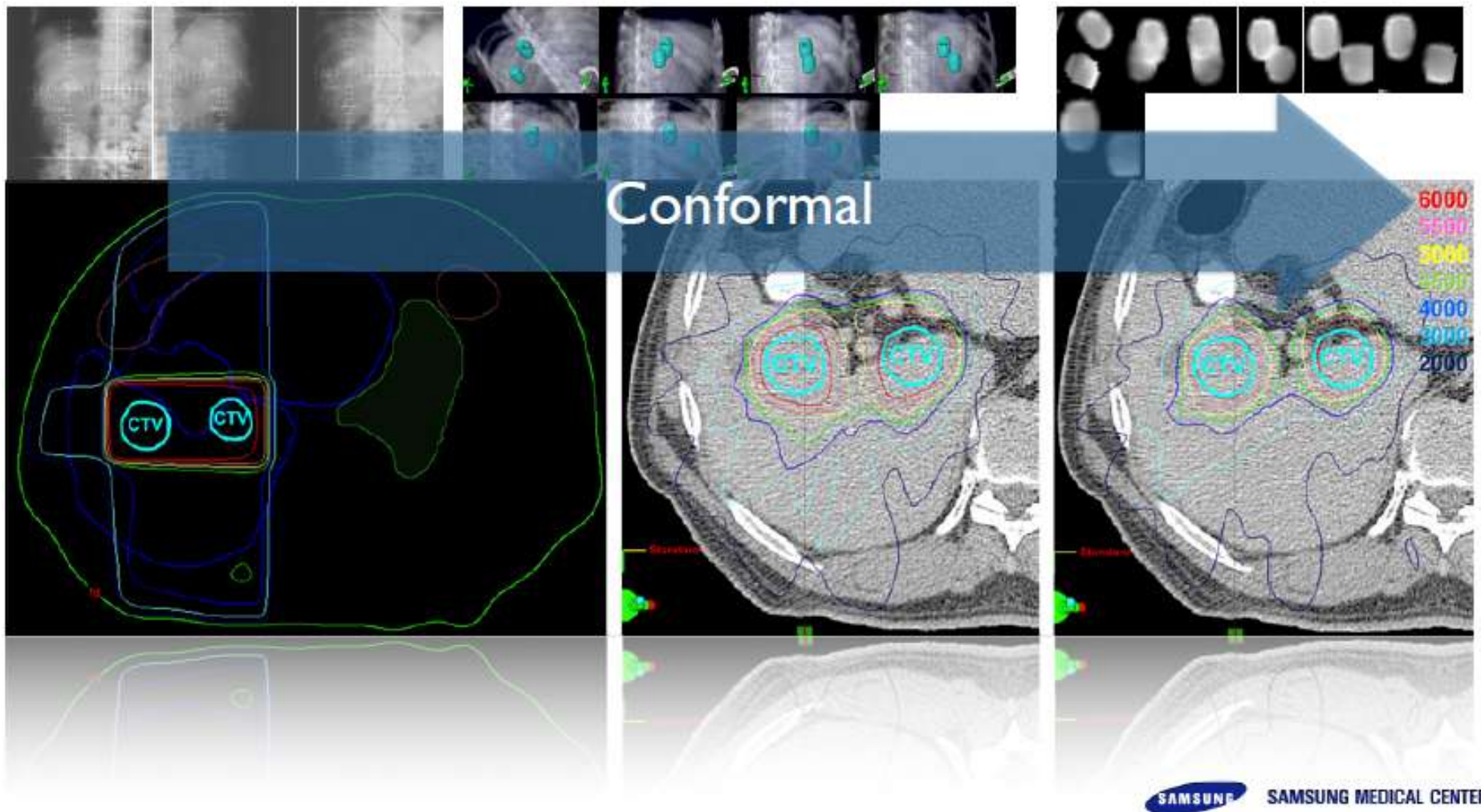
Dose-volume histogram



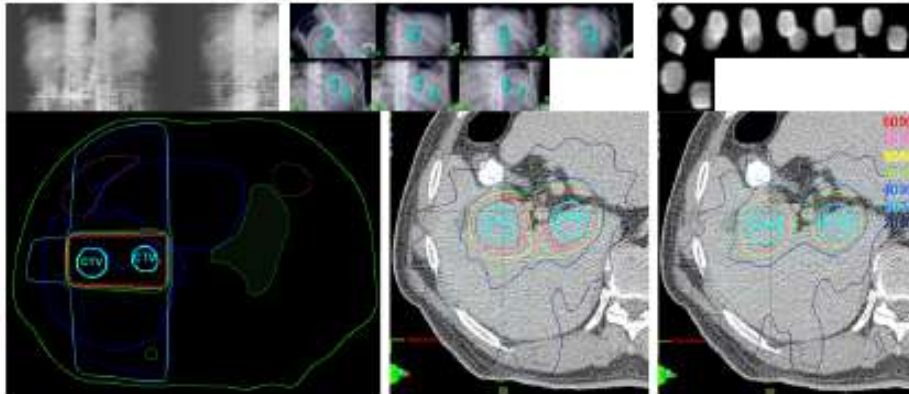
Intensity-modulated radiotherapy for liver cancer



Advanced radiotherapy for liver cancer

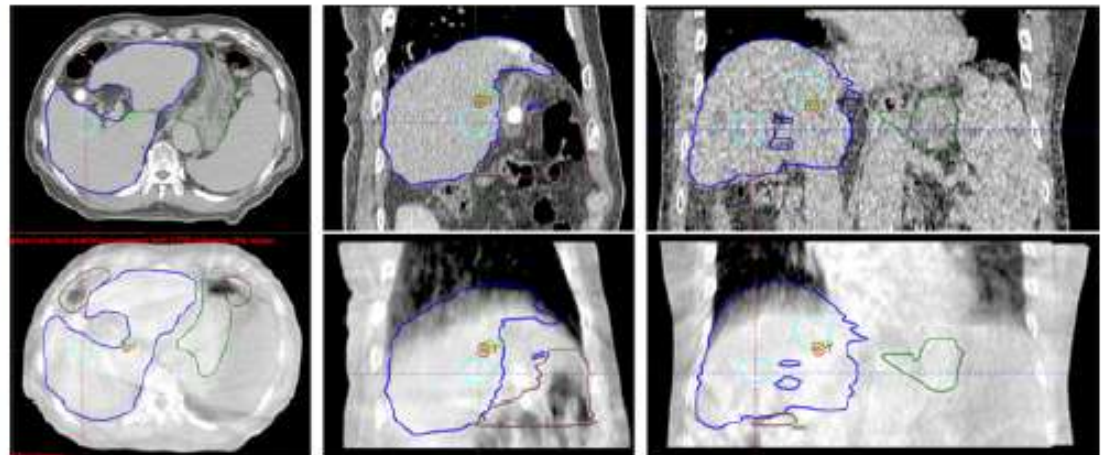
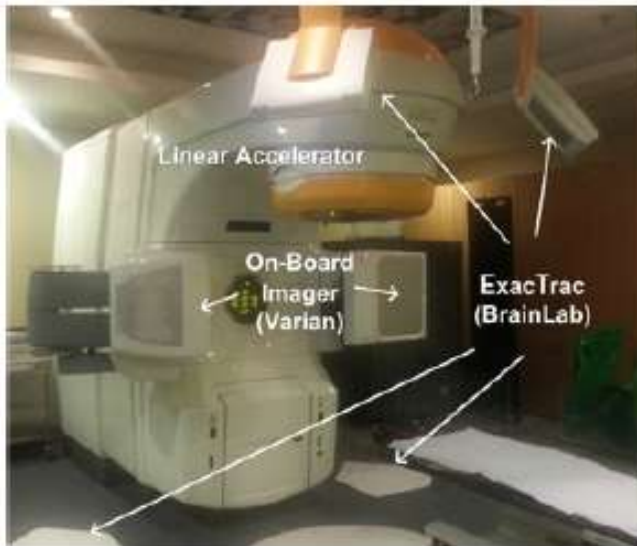
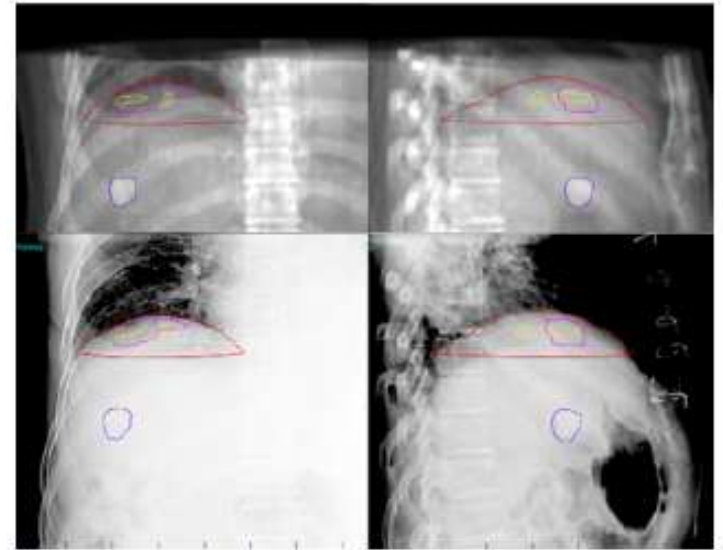


Advances in RT techniques

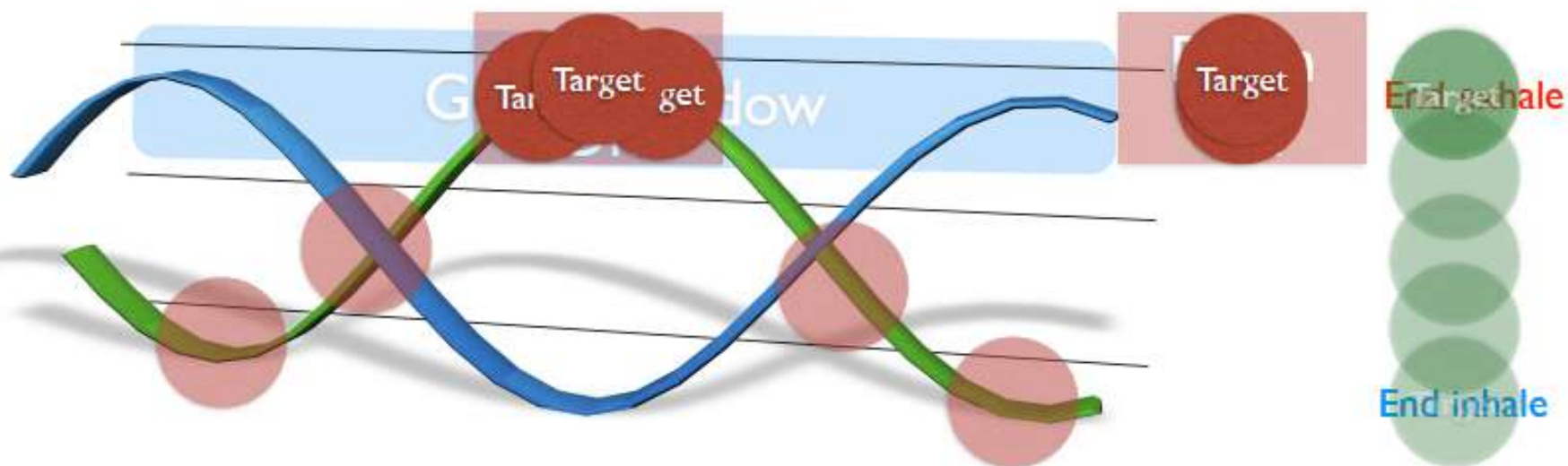
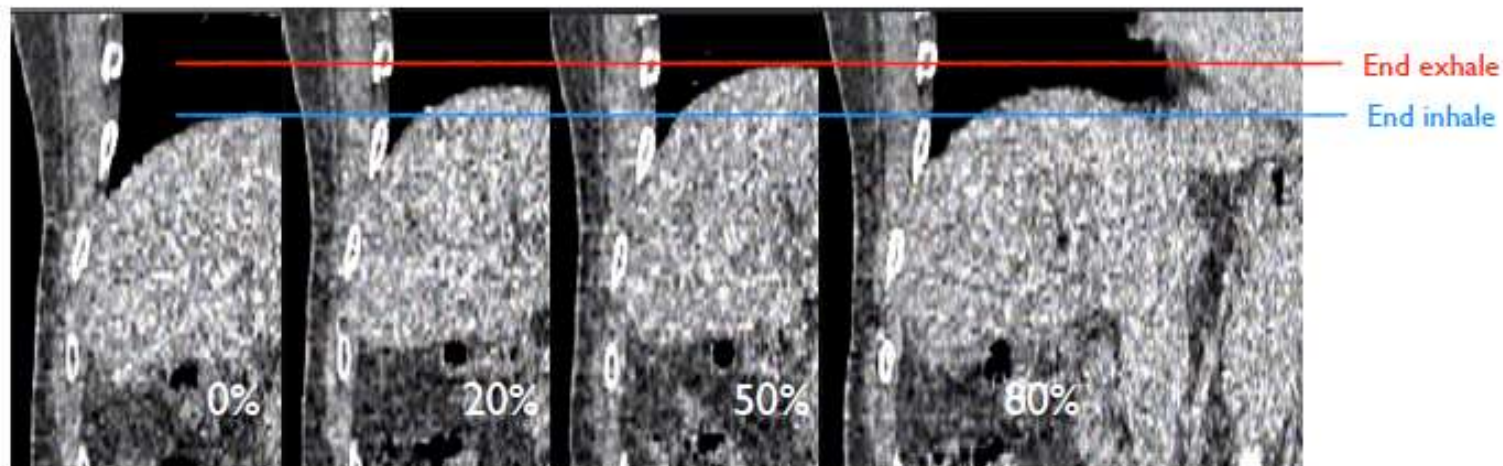


Is it enough for
SABR of liver cancer?

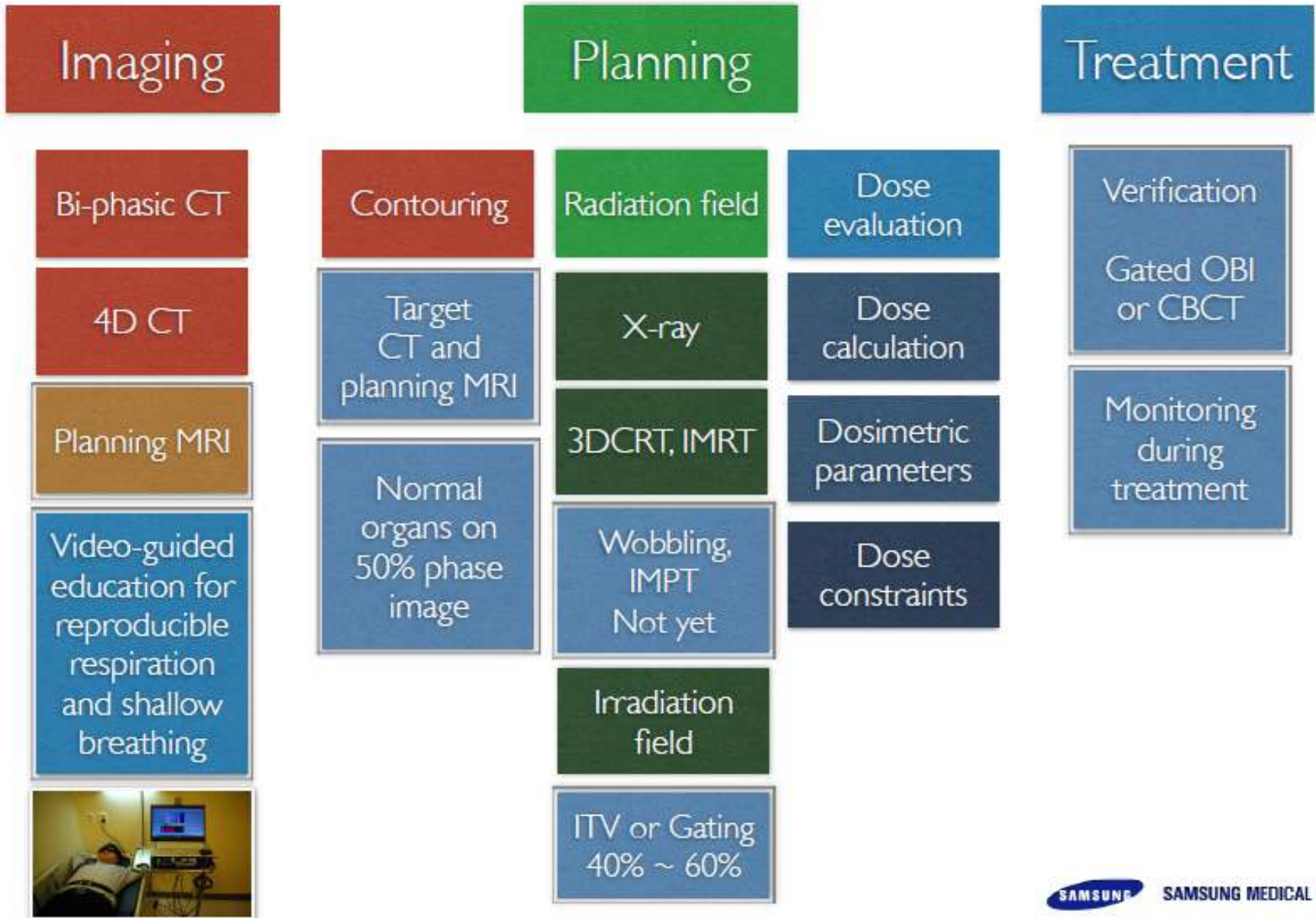
Precise
Accuracy



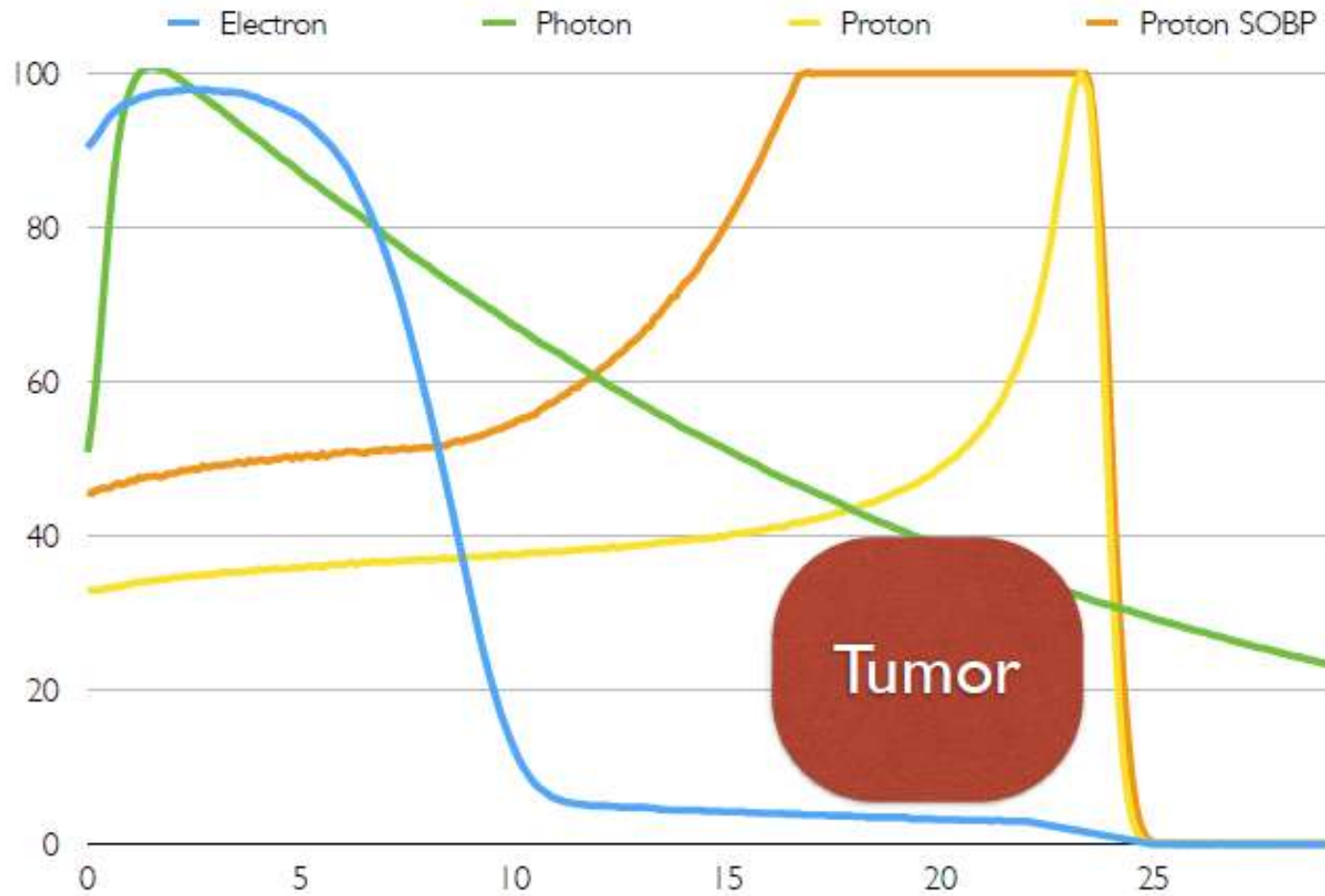
Respiratory motion management - Gating



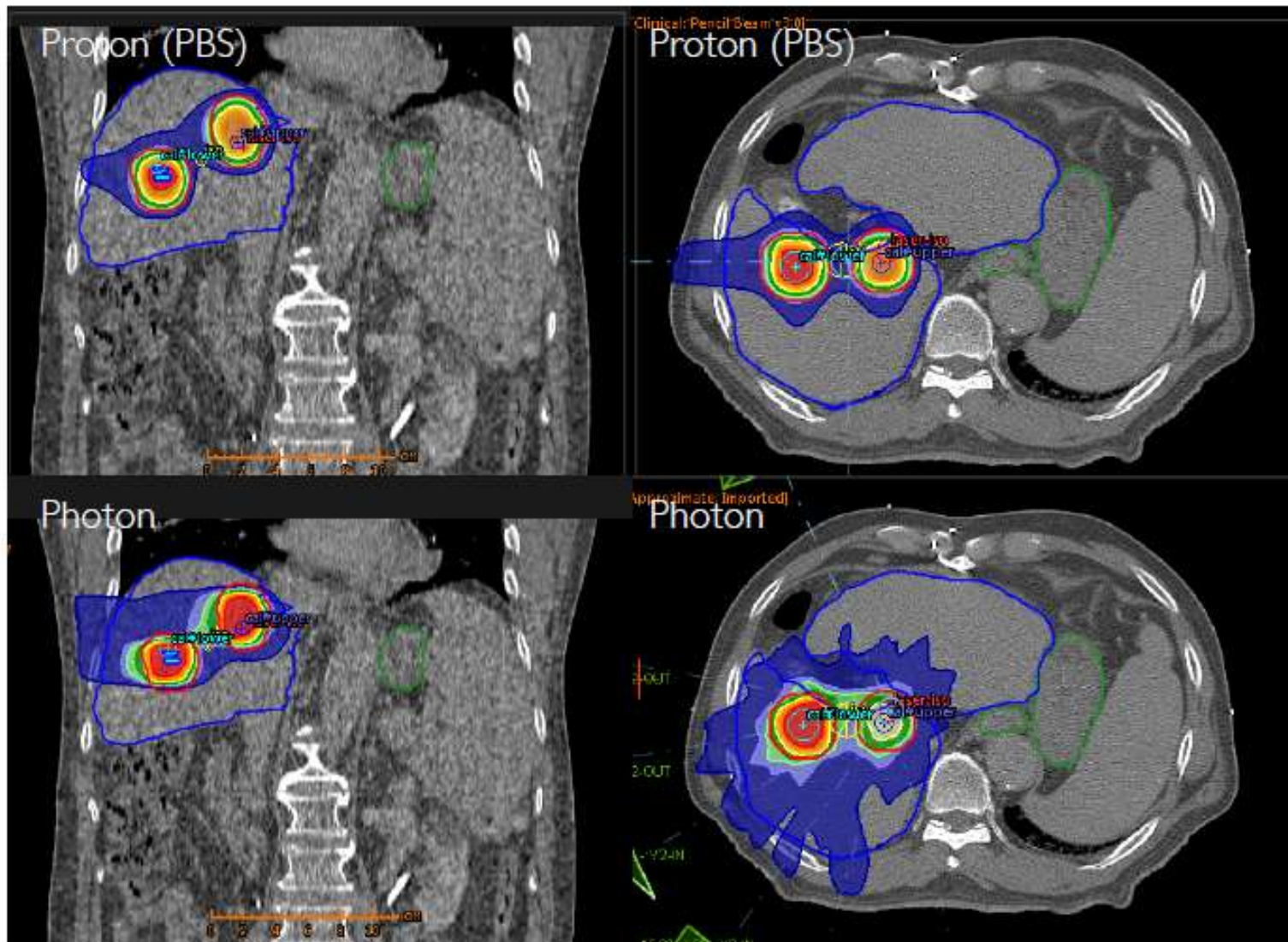
SABR of liver cancer @ SMC



Proton therapy for SABR of liver cancer



3DCRT vs. Proton

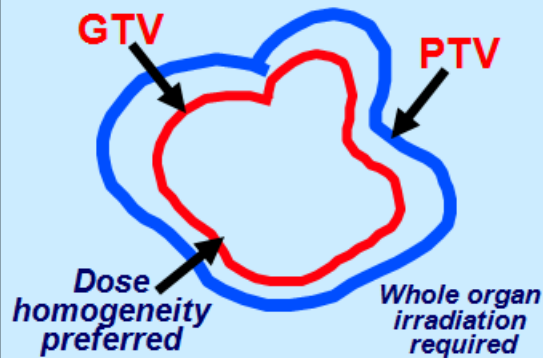


Targeted Radiation Therapy?
- In the future -

Targeted Radiation Therapy (Circa 2020?)

Biological imaging provides a basis for a paradigm change in 3D treatment planning

Classical Anatomical Planning



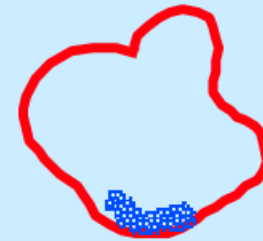
Molecular Imaging

- MRS/PET •
(choline/citrate, PSA, EGFR)



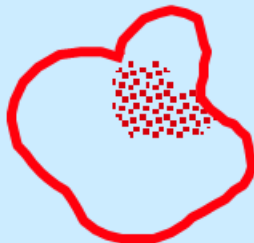
Cellular Imaging

- PET/MRS •
(IUdR, MIB1, Apoptosis)



Tissue Effects Imaging

- MRS/PET •
(Hypoxia, Angiogenesis)

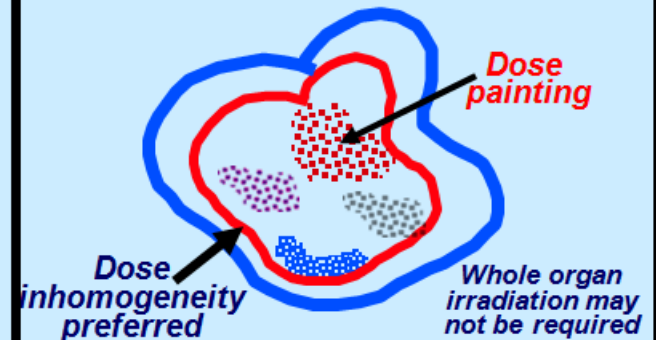


Monoclonal Antibody Imaging

- SPEC/PET •



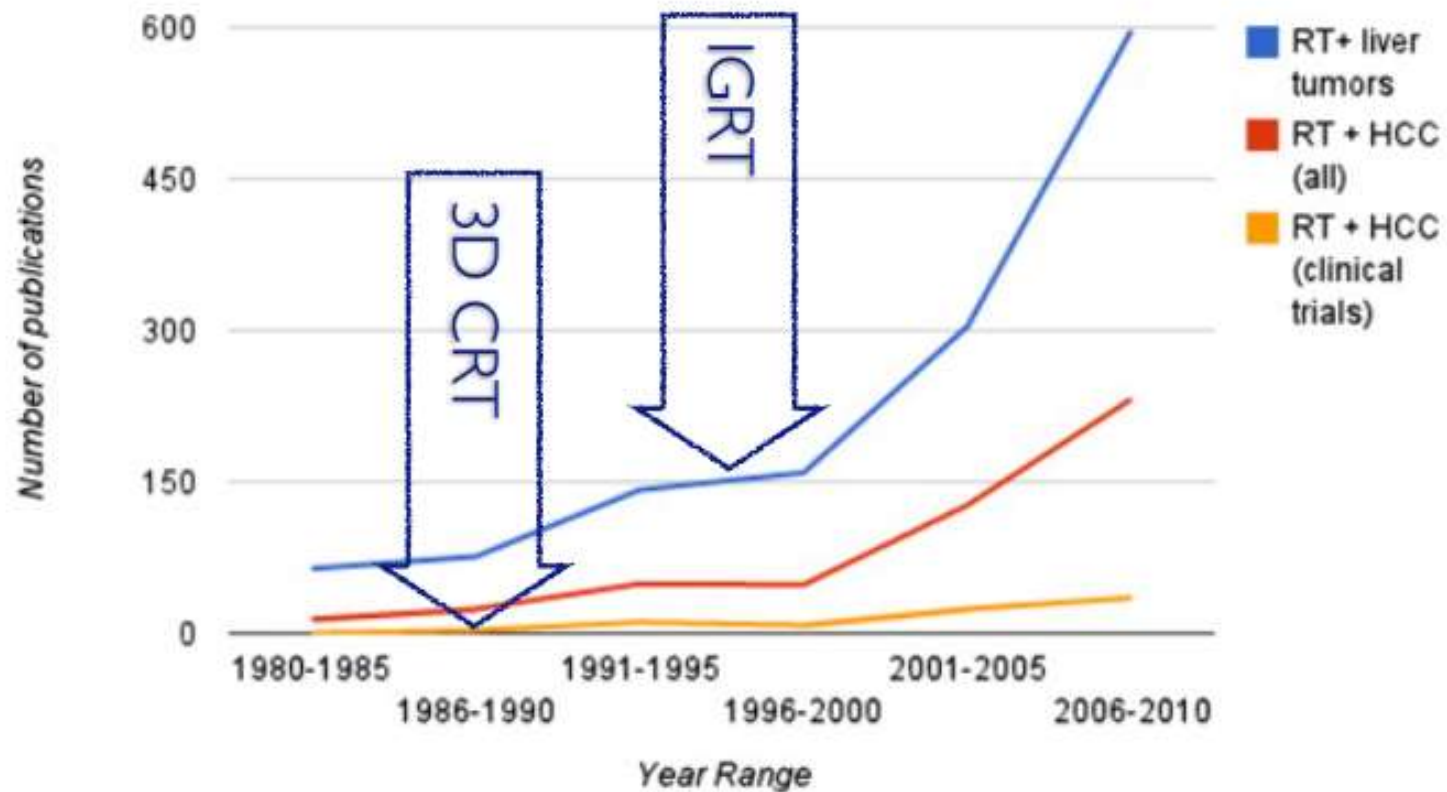
IMRT Planning Based on Biological Imaging



RT for HCC?

- The Problem is Evidence!! -

Radiation therapy for liver cancer



Klein J and Dawson L, *Int J Radiat Oncol Biol Phys*, vol. 87 (1) pp. 22-32

Clinical trials in Korea

Stereotactic Body Radiation Therapy for Hepatocellular Carcinoma

This study is currently recruiting participants.

Verified May 2013 by Korea Cancer Center Hospital

Sponsor:
Korea Cancer Center Hospital

Collaborators:
Dongnam Institute of Radiological & Medical Sciences
Soon Chun Hyang University Seoul Hospital
Inje University
Inha University Hospital
Incheon St. Mary's Hospital
Soon Chun Hyang University Cheonan Hospital

Information provided by (Responsible Party):
Mi-Book Kim, Korea Cancer Center Hospital

ClinicalTrials.gov Identifier:
NCT01850667

First received: May 7, 2013
Last updated: May 8, 2013
Last verified: May 2013
History of Changes

이 연구는 현재 참가자를 모집하고 있습니다.
확인된 날짜: 2013년 5월, 한국암센터 병원

Stereotactic Ablative Radiotherapy for Hepatocellular Carcinoma With Major Portal Vein Invasion

This study is currently recruiting participants.

Verified May 2013 by Korea Cancer Center Hospital

Sponsor:
Korea Cancer Center Hospital

Collaborators:
Seoul National University Hospital
Dongnam Institute of Radiological & Medical Sciences
Soon Chun Hyang University Seoul Hospital
Inha University Hospital
Incheon St. Mary's Hospital

Information provided by (Responsible Party):
Mi-Book Kim, Korea Cancer Center Hospital

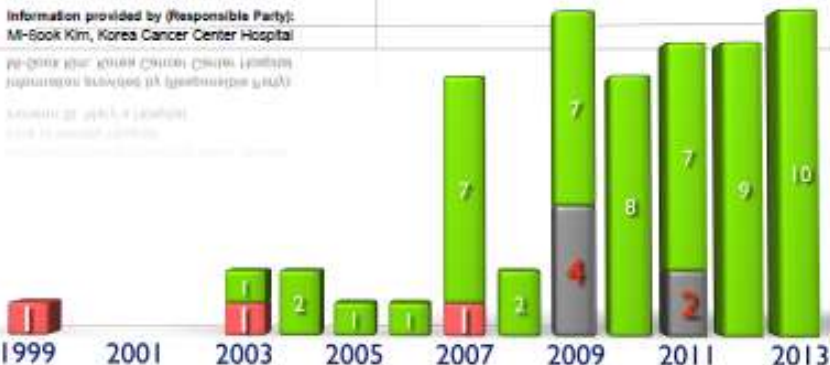
ClinicalTrials.gov Identifier:
NCT01850368

First received: May 2, 2013
Last updated: May 7, 2013
Last verified: May 2013
History of Changes

이 연구는 현재 참가자를 모집하고 있습니다.
확인된 날짜: 2013년 5월, 한국암센터 병원

이 연구는 현재 참가자를 모집하고 있습니다.
확인된 날짜: 2013년 5월, 한국암센터 병원

이 연구는 현재 참가자를 모집하고 있습니다.
확인된 날짜: 2013년 5월, 한국암센터 병원



Stereotactic Body Radiotherapy for Unresectable Hepatocellular Carcinoma (SBRT for HCC)

This study is not yet open for participant recruitment.

Verified July 2013 by Samsung Medical Center

Sponsor:
Samsung Medical Center

Information provided by (Responsible Party):
Samsung Medical Center

ClinicalTrials.gov Identifier:
NCT01910909

First received: July 17, 2013
Last updated: August 5, 2013
Last verified: July 2013
History of Changes

이 연구는 현재 참가자를 모집하지 않습니다.
확인된 날짜: 2013년 7월, 삼성의료원

Dose Escalation Study Using Proton Beam Radiotherapy for Hepatocellular Carcinoma

This study has been completed.

Sponsor:
National Cancer Center, Korea

Information provided by:
National Cancer Center, Korea

ClinicalTrials.gov Identifier:
NCT00662246

First received: April 10, 2008
Last updated: April 2, 2012
Last verified: March 2012
History of Changes

이 연구는 현재 참가자를 모집하지 않습니다.
확인된 날짜: 2012년 3월, 국립암센터

이 연구는 현재 참가자를 모집하지 않습니다.
확인된 날짜: 2012년 3월, 국립암센터

Stereotactic Ablative Radiotherapy for Hepatocellular Carcinoma ≤ 5 cm

This study is currently recruiting participants.

Verified May 2013 by Korea Cancer Center Hospital

Sponsor:
Korea Cancer Center Hospital

Collaborators:
Dongnam Institute of Radiological & Medical Sciences
Soon Chun Hyang University Seoul Hospital
Inje University
Inha University Hospital
Incheon St. Mary's Hospital
Samsung Medical Center
Soon Chun Hyang University Cheonan Hospital
Kyung Hee University Gangdong Hospital

Information provided by (Responsible Party):
Mi-Book Kim, Korea Cancer Center Hospital

ClinicalTrials.gov Identifier:
NCT01825824

First received: April 3, 2013
Last updated: May 2, 2013
Last verified: May 2013
History of Changes

이 연구는 현재 참가자를 모집하고 있습니다.
확인된 날짜: 2013년 5월, 한국암센터 병원

이 연구는 현재 참가자를 모집하고 있습니다.
확인된 날짜: 2013년 5월, 한국암센터 병원



Conclusions

Conclusions

1. Higher local control and Lower complication is important
 - as a treatment modality for HCC
2. Recent advances in RT techniques
 - enhanced the precision and accuracy
 - via conformal RT and IGRT, 4D-RT
3. For targeted RT,
 - use of multimodality imaging helps
 - awaits for more improvement of imaging for HCC
4. Clinical trial efforts are mandatory