# SABR For HPB Tumours

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Milan

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# HISTORY

## RADIUM THERAPY

The only scientific apparatus for the preparation of radio-active water in the hospital or in the patient's own home.

This apparatus gives a high and measured dosage of radio-active drinking water for the treatment of gout, rheumatism, arthritis, neuralgia, sciatica, tabes dorsalis, catarrh of the antrum and frontal sinus, arterio-sclerosis, diabetes and glycosuria, and nephritis, as described in Dr. Saubermann's lecture before the Roentgen Society, printed in this number of the "Archives."

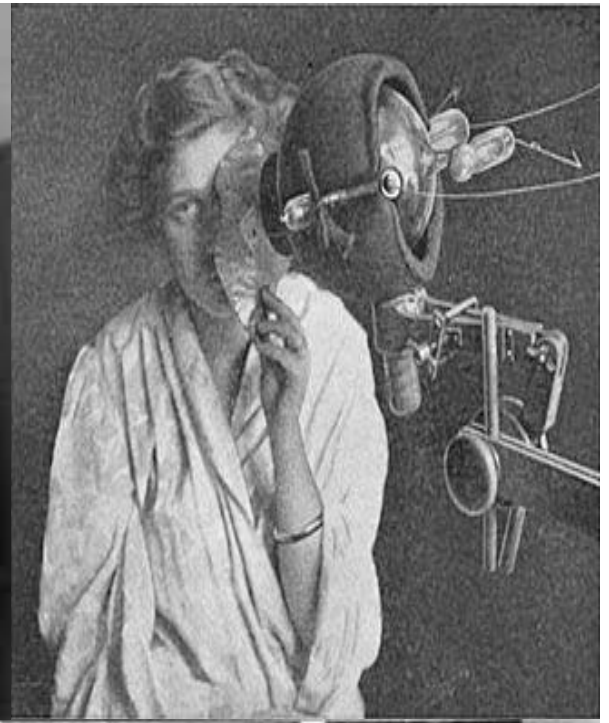
DESCRIPTION.

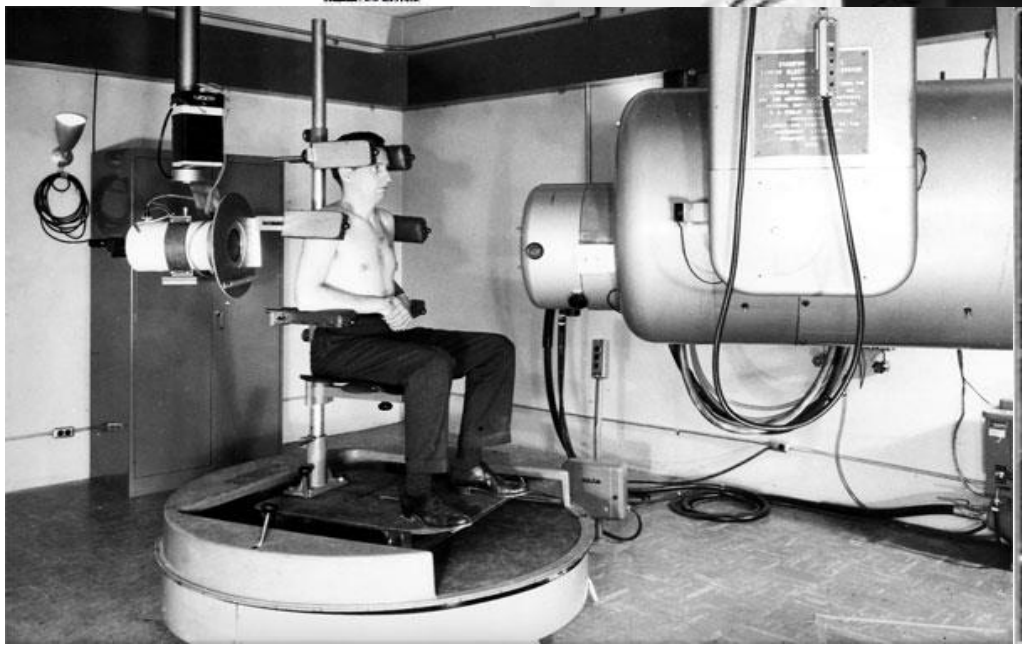
The perforated earthenware "activator" in the glass jar contains an insoluble preparation impregnated with radium. It continuously emits radium emanation at a fixed rate, and keeps the water in the jar always charged to a fixed and measureable strength, from 5,000 to 10,000 Maché units per litre per diem.

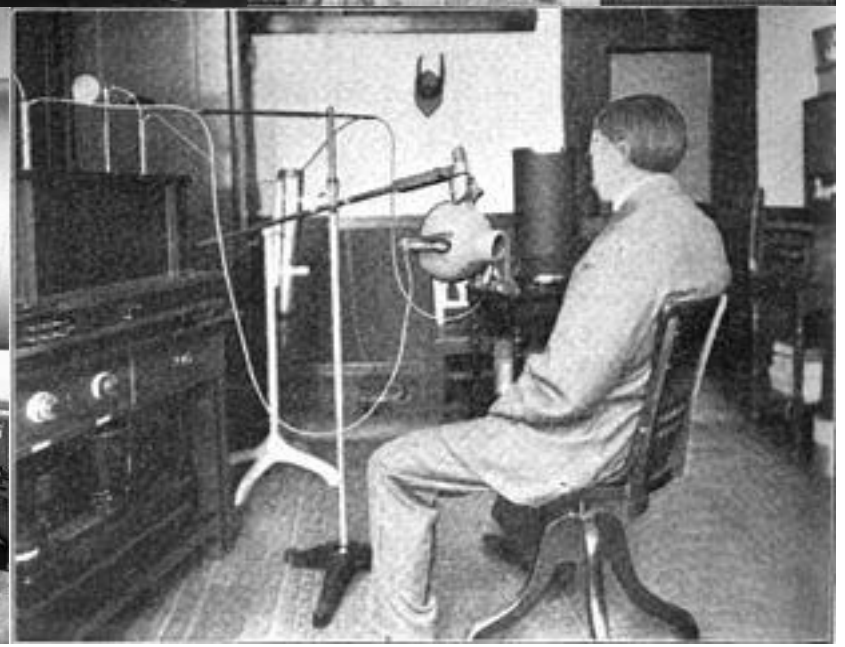
SUPPLIED BY

RADIUM LIMITED,

93, MORTIMER STREET, LONDON, W.



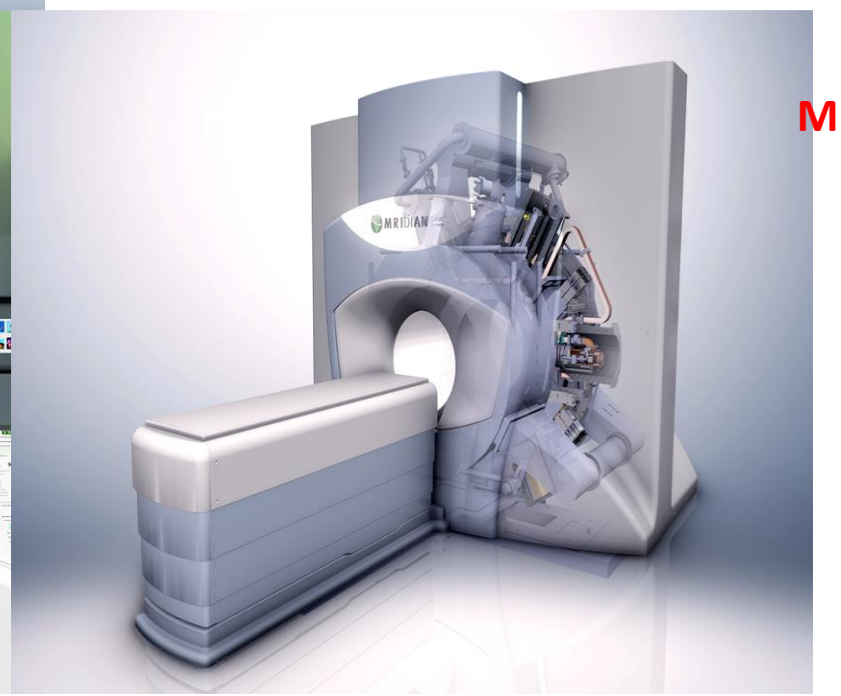




Micro MLC Linac


Cyberknife M6

Proton Therapy



MRI Linac

# What is Stereotactic Ablative Body Radiotherapy (SABR)?

- **SABR means:**

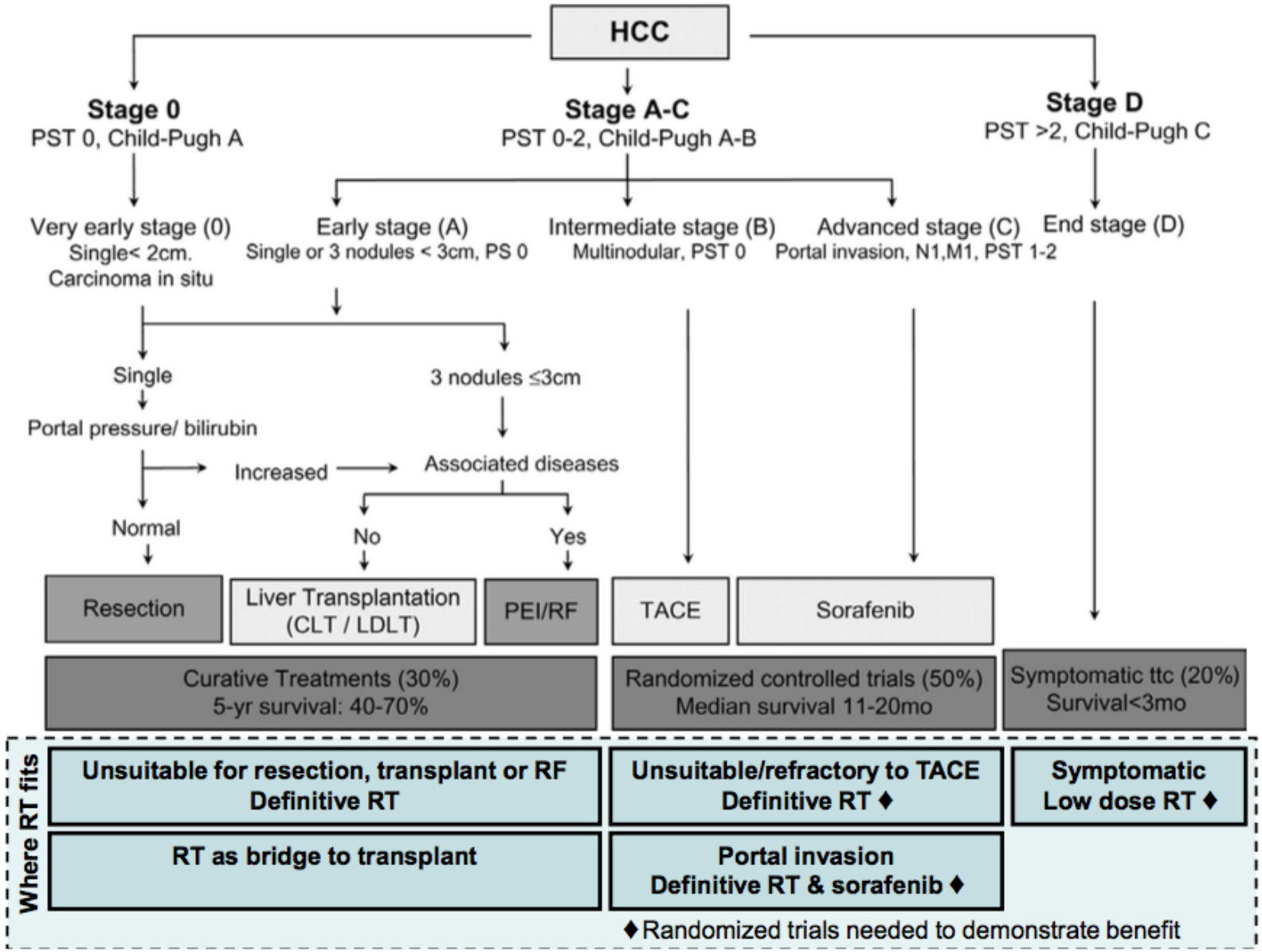
  - Highly **targeted** radiotherapy to a small volume (ideally <150cc)
  - Delivering an **ablative** radiation dose
  - (e.g. 16 – 25Gy in 1#, 45 – 60Gy in 3#, 40 – 60Gy in 5#, 60 in 8#)
  - Intratumoural dose heterogeneity
  - Steep dose gradients outside PTV
  - ***Quick***: 1 - 8 fractions over 1 - 2 weeks
  - ***Accessible***: Most RT departments in the UK have ability
  - ***Relatively cheap***: NHS tariff is £5113.55

# Ablative Options

- Surgical metastatectomy
- RFA or Microwave Ablation
- Cryotherapy
- SABR / SBRT
- Irreversible Electroporation (NanoKnife)
- Chemotherapy / Biological / Immuno Therapies

# HCC – Hepatocellular Carcinoma

- EU 1 – 13/100,000 incidence
- 6000 cases per year UK
- However 50% all HCC in the world is in China
- 47000 deaths per year in the EU (pre Brexit!)
- Risk factors – Alcohol, Hep C, PBC, NASH, (Hep B)
- Wilsons disease, haemochromatosis, autoimmune hepatitis
- 5 year OS is 30 – 50% (if resectable)


HCC
Stage 0
PST 0, Child-Pugh A
Stage A-C
PST 0-2, Child-Pugh A-B
Stage D
PST >2, Child-Pugh C
Very early stage (0)
Single< 2cm.
Carcinoma in situ
Early stage (A)
Single or 3 nodules < 3cm, PS 0
Intermediate stage (B)
Multinodular, PST 0
Advanced stage (C)
Portal invasion, N1,M1, PST 1-2
End stage (D)
Single
3 nodules ≤3cm
Portal pressure/ bilirubin
Increased
Associated diseases
Normal
No
Yes
Resection
Liver Transplantation
(CLT / LDLT)
PEI/RF
TACE
Sorafenib
Curative Treatments (30%)
5-yr survival: 40-70%
Randomized controlled trials (50%)
Median survival 11-20mo
Symptomatic ttc (20%)
Survival<3mo
Where RT fits
Unsuitable for resection, transplant or RF
Definitive RT
Unsuitable/refractory to TACE
Definitive RT ♦
Symptomatic
Low dose RT ♦
RT as bridge to transplant
Portal invasion
Definitive RT & sorafenib ♦
♦Randomized trials needed to demonstrate benefit

| Study | Design | Pts | CP class | Prior liver-directed therapies | Tumor size (range) | TVT | Multiple lesions treated | Dose (Gy) | Fx | ORR | 1-year LC | 1-year OS | Grade ≥3 Toxicity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bujold et al. [40] | Phase I/II | 102 | A | 52% | 1.4–23.1 cm | 55% | 61% | 36 (24–54) | 6 | 54% | 87% | 55% | 36% |
| Hong et al. [60] | Phase II | 44 | A,B | 45.8% | 1.0–12 cm | 29.5% | 27.3% | 58 GyE (15.1–67.5) | 15 | NR | 94.8% at 2 years | 63.2% at 2 years | 2.3% |
| Mendez-Romero et al. [41] | Phase I/II | 8 | A,B | NR | 0.5–7.2 cm | 25% | | 25–37.5 | 3–5 | NR | 75% | 75% | 12.50% |
| Kang et al. [43] | Phase II | 47 | A,B | 100% | 1.3–8 cm | 11% | 17% | 57 (42–60) | 3 | 76.6% | 95% at 2 years | 69% at 2 years | 26% |
| Cárdenes et al. [44] | Phase I | 17 | A,B | 23.5% | ≤6 cm (cumulative) | 18% | 30% | 36–48 | 3–4 | 81% | 100% | 75% | 18% |
| Tse et al. [28] | Phase I | 31 | A | 61% | 9–1913 ml | 42% | 1–3 lesions | 36 (24–54) | 6 | 49% | 65% | 48% | 26% |
| Ibarra et al. [42] | Pooled analysis | 21 | A,B | 76.2% | 9.5–1493.8 ml | NR | 23.8% | 30 (18–50) | 1–10 | 28.6% | 64% | 87% | 8% RILD only |
| Yamashita et al. [49] | Retrospective | 79 | A,B,C | 100% | 0.6–7 cm | NR | NR | 48 (40–60) | 4 | 81% | 74.1% | 52.9% at 2 years | No RILD |
| Sanuki et al. [38] | Retrospective | 185 | A,B | 60% | 0.8–5 cm | NR | No | 30–40 | 5 | NR | 99% | 95% | 13% |
| Jang et al. [45] | Retrospective | 108 | A,B | 100% | 1–7 cm | NR | 13% | 51 (33–60) | 3 | NR | 87% at 2 years | 63% at 2 years | 10%* |
| Yoon et al. [50] | Retrospective | 93 | A,B | 98.9% | 1–6 cm | 0% | 10.8% | 30–60 | 3–4 | 61.2% | 95% | 86% | 6.5% RILD only |
| Culleton et al. [53] | Retrospective | 29 | B,C | 14% | 5.1 cm (2–26 cm) | 76% | Median 2 (range 1–5) | 30 (20–46.8) | 6 | NR | NR | 31.8% | 0% |
| Huertas et al. [54] | Retrospective | 77 | A,B | 15.6% | 0.7–6.3 cm | NR | 13% | 45 (15–60) | 3 | NR | 99% | 81.8% | 5.2% |
| Bibault et al. [47] | Retrospective | 75 | A,B | 51% | 3–4.4 cm | NR | 39.6% | 45 (24–45) | 3 | NR | 90% | 79% | 16%* |
| Honda et al. [39] | Retrospective | 30 | A,B | 100% | 1–3 cm | 0% | No | 48–60 | 4–8 | 91% | 93% | 73% | 7% |
| Yuan et al. [48] | Retrospective | 22 | A,B,C | NR | 1.6–9.5 cm | NR | No | 45 (39–54) | 3–8 | 91% | 93% | 73% | 4.5% Grade ≥2 |
| Huang et al. [55] | Retrospective | 36 | A,B,C | 100% | 1.1–12.3 cm | NR | 16.7% | 37 (25–48) | 4–5 | 58.8% | 95% | 64% at 2 years | 3% |
| Andolino et al. [56] | Retrospective | 60 | A,B | 10% | 1–6.5 cm | NR | 15% | 44 (24–48) | 3–5 | 70% | 90% at 2 years | 67% at 2 years | 37% |
| Son et al. [52] | Retrospective | 47 | A,B,C | 78% | 3.0–81.3 ml | NR | NR | 30–39 | 3 | NR | NR | NR | 33% Grade ≥2 |
| Kwon et al. [58] | Retrospective | 42 | A,B | 81% | 3.0–81.8 ml | 0% | 35.7% multifocal | 30–39 | 3 | 85.8% | 72% | 93% | 2% |
| Seo et al. [57] | Retrospective | 38 | A,B | 100% | <10 cm | NR | NR | 33–57 | 3–4 | 63.1% | 79% | 69% | 3% |

Pts=number of patients; Fx=fractions; LC=local control; GyE=Gy equivalent; NR=Not reported. * Toxicities may include some redundancies.

In heavily pretreated patients…

SABR is associated with excellent local control and survival…

… with low levels of toxicity

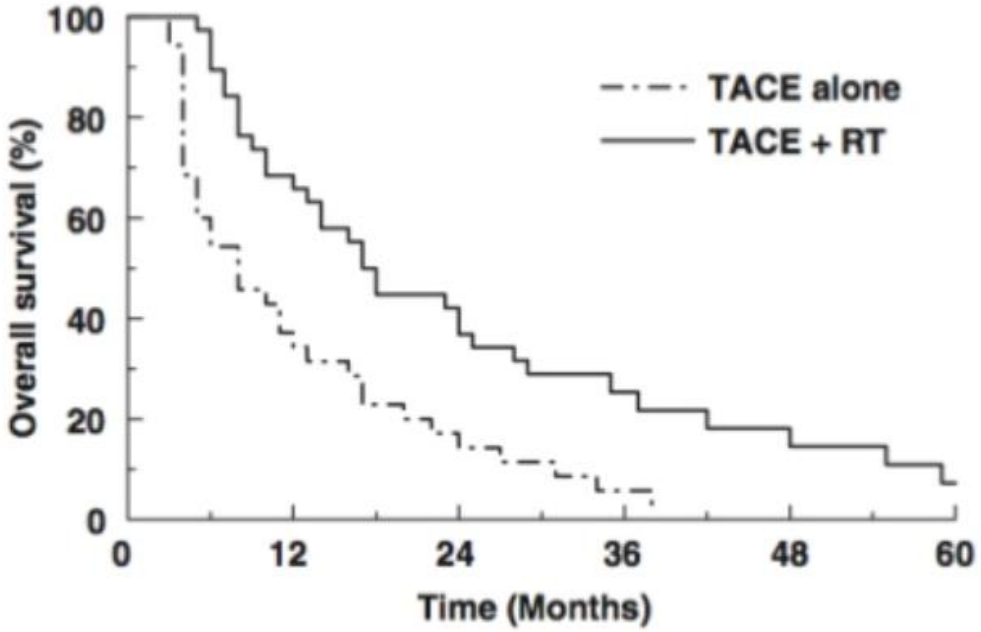
# 1. HCC - SABR vs RFA

- **Wahl et al. JCO 34: 452-59 (2016)**
  - 224 patients, retrospective cohort
  - RFA (n=161) or SABR (n=63)
  - Similar number of lesions per patient, underlying liver disease, tumour size (median 1.8 vs 2.2 cm)
  - SABR group had greater number of prior treatments ($p<0.01$)
  - One and two year LC 83.6% (SABR) vs 80.2% (RFA)
  - tumour size >2cm reduced LC in RFA but **not** SABR (HR 3.35, p=0.025)
  - Grade 3+ toxicity: 11% RFA, 5% SABR
  - OS at 1 year: 70% RFA, 74% SABR
  - OS at 2 years: 53% RFA, 46% SABR

# 2. HCC - After TACE

- **Shim et al. Liver Int 25:1189-1196 (2005)**
  - 105 patients treated with TACE
  - CP A/B, no MVI
  - 73 had an incomplete response
  - TACE alone in 35, RT in 38

| 2 year overall survival rates by tumour size | | |
|---|---|---|
| Lesion size | TACE + RT | TACE alone |
| All patients | 37% | 14% |
| 5-7 cm | 63% | 42% |
| 8-10 cm | 50% | 0% |
| >10 cm | 17% | 0% |



# 3. HCC - Bridge to transplant

- **Sapisochin G et al. J Hepatol 67:92-99 (2017)**
  - 379 patients treated 2004-2014
  - No difference in post-op complications
  - No decompensation post SABR requiring urgent transplant

| | SABR | TACE | RFA |
|---|---|---|---|
| n | 30 | 79 | 203 |
| 1y OS | 83% | 86% | 86% |
| 2y OS | 61% | 61% | 72% |
| 5y OS | 61% | 58% | 61% |

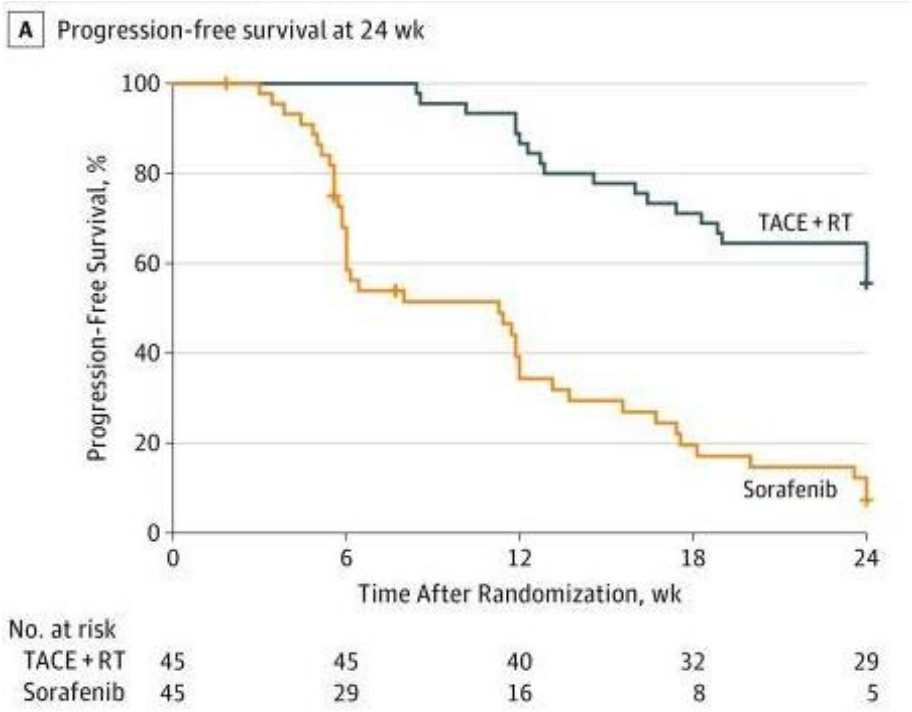
- *"In conclusion, SBRT can be safely utilized as a bridge to LT in patients with HCC, as an alternative to conventional bridging therapies."*

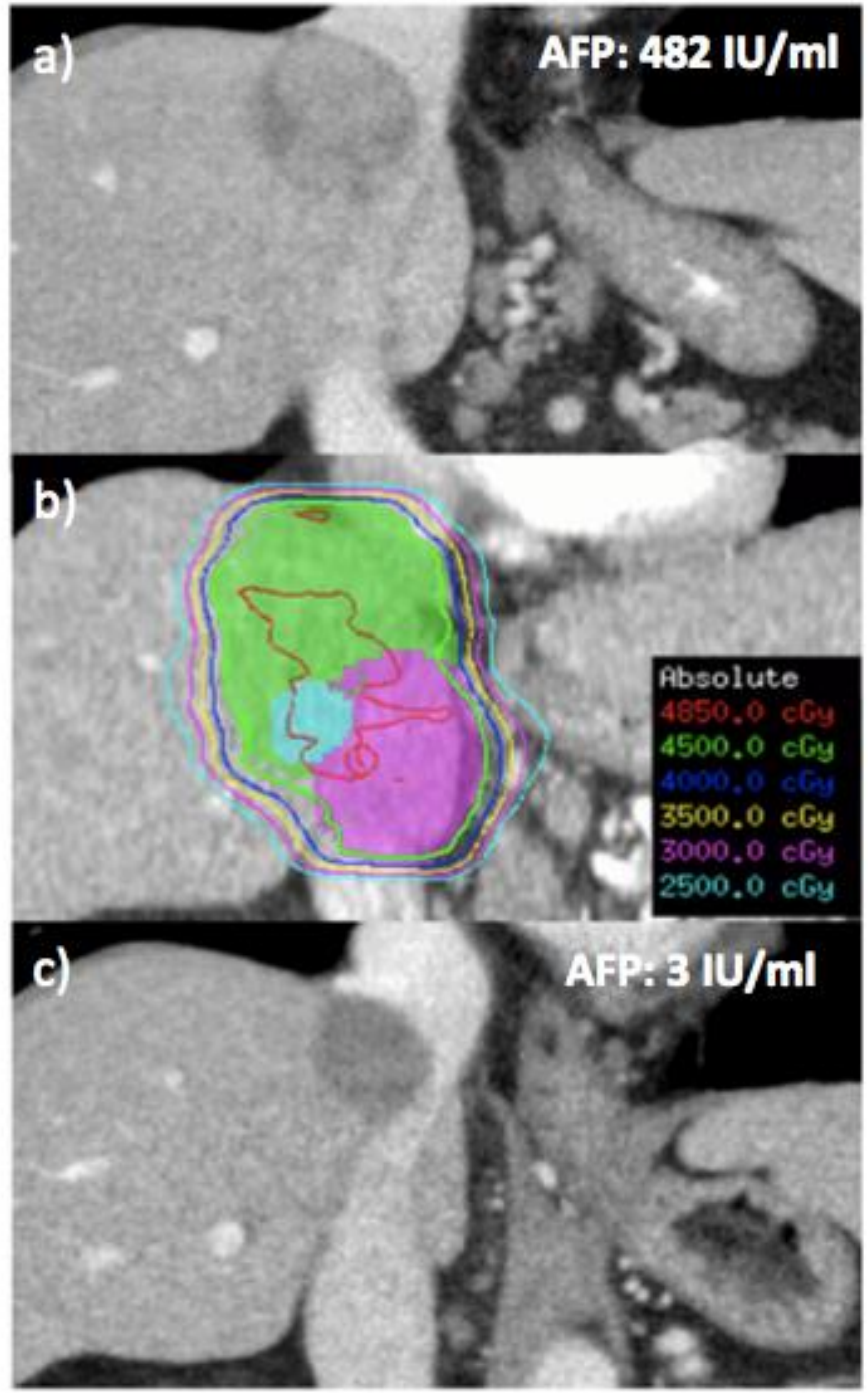
# 4. HCC - PVTT

- **Yoon et al. Efficacy and Safety of Transarterial Chemoembolization Plus External Beam Radiotherapy vs Sorafenib in Hepatocellular Carcinoma With Macroscopic Vascular Invasion: A Randomized Clinical Trial. JAMA Oncol (2018)**

- 90 patients with MVI and ChPA
- Treatment naïve
- Median size 9.7 cm
- Randomised to TACE - conformal RT vs sorafenib
- **Primary**: 12 wk ITT PFS

| Outcome | TACE + RT | Sorafenib |
|---|---|---|
| 12 week PFS | 86.7% | 34.4% |
| Median TTP | 7.3 mo | 2.5 mo |
| Median OS | 12.8 mo | 10 mo |
| SAE | 5 pts | 5 pts |




a)
AFP: 482 IU/ml
b)
Absolute
4850.0 cGy
4500.0 cGy
4000.0 cGy
3500.0 cGy
3000.0 cGy
2500.0 cGy
c)
AFP: 3 IU/ml

# SABR and SIRT (Radioembolisation) for HCC

- **Rim et al. Comparison of radiation therapy modalities for hepatocellular carcinoma with portal vein thrombosis: A meta-analysis and systematic review. Radiother Oncol (2017)**

  - 37 studies, 2513 patients
  - SIRT mainly Western, RT mainly south east Asian

| | SABR | SIRT | Conventional RT | p |
|---|---|---|---|---|
| 1y OS | 48.5%<br>(95% CI 39.4-57.8) | 46.5%<br>(95% CI 37.7-55.6) | 43.8%<br>(95% CI 37.6-50.2) | 0.635 |
| RR | **70.7%**<br>(95% CI 63.7-76.8) | 33.3%<br>(95% CI 18-53.2) | 51.3<br>(95% CI 45.7-57) | 0.001<br>0.031 |

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14th INTERNATIONAL STEREOTACTIC RADIOSURGERY SOCIETY CONGRESS
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# Liver SABR in heavily pre-treated elderly patients – a single institution experience

*Pollyanna D'Avila Leite, Asad Qureshi, Kasia Owczarczyk, Benjamin Taylor, Clare Hartill, James Barber, Mark McGovern, Vicky Goh, Andrew Gaya (andrew.gaya@gstt.nhs.uk)*

Guy's Cancer

- 32 tumours from 29 patients (15 CRC metastases, 13 HCC, 3 Cholangiocarcinomas, 1 Anal SCC metastasis)
- Median age: 71 (36-91), PS 1 (0-2)
- All HCC patients were CP A, 64% non-viral aetiology; 3 were treated as a bridge to transplant
- 90% of patients received one or more lines of treatment prior to SABR (59% ≥70 years old)

**Figure 1 - Post-SABR Survival According to Age Group**

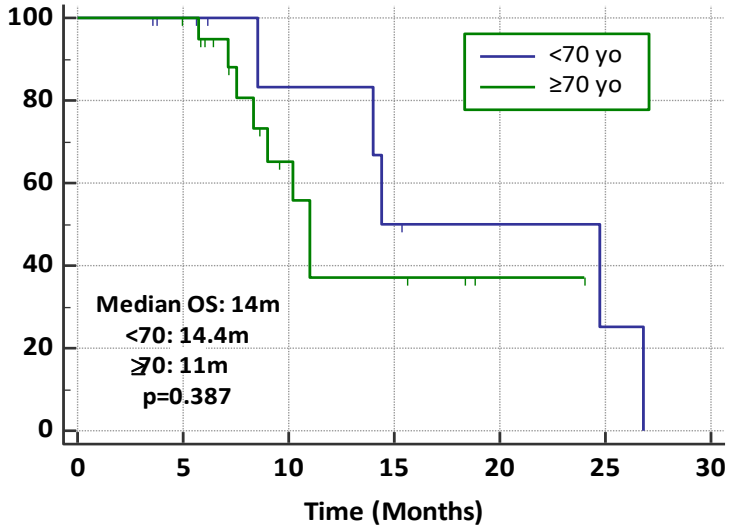



**Chart 1 – Post-SABR Acute Toxicity (N)**

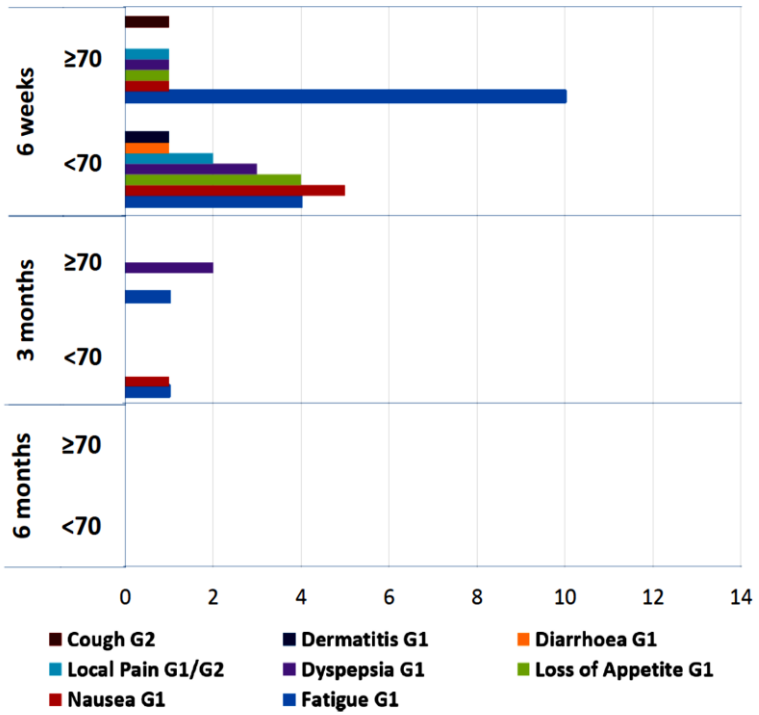
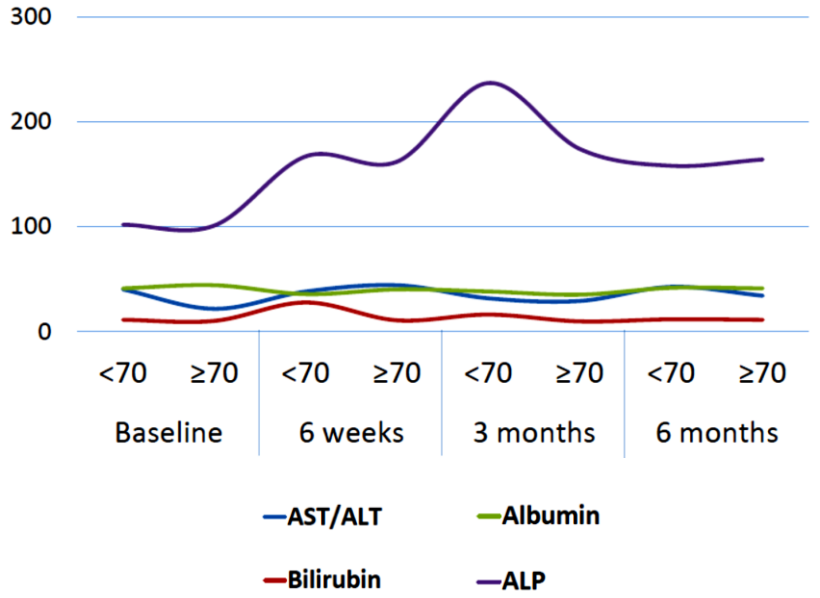



**Chart 2 - Median Acute Liver Function Tests Values**

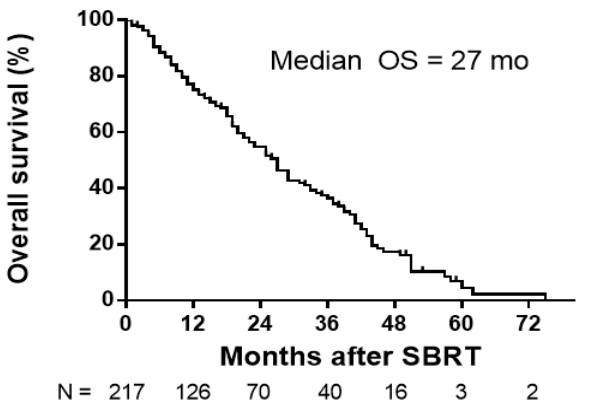


# Stereotactic body radiotherapy (SBRT) for colorectal liver metastases: Clinical outcomes from the international multi-institutional RSSearch® Patient Registry

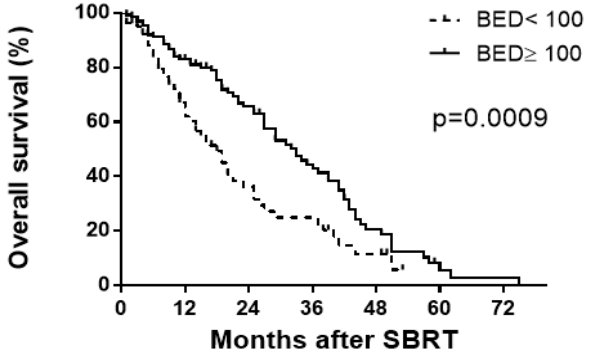
PD Leite, AM Gaya, RM Lanciano, JJ Yang, O Blanck, R Urwin, JN Davis, A Mahadevan

2019 RSS ANNUAL SCIENTIFIC MEETING MARCH 21-23, 2019 • SHERATON • SAN DIEGO
the Radiosurgery Society

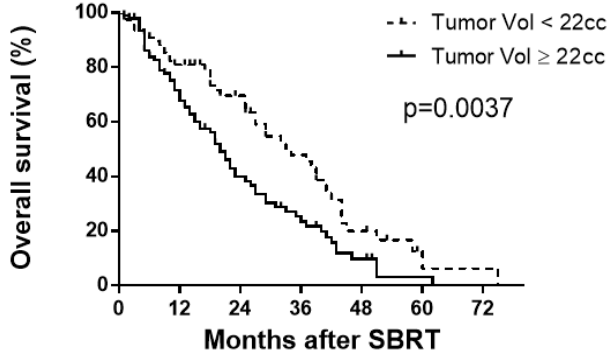
- 217 patients with 233 colorectal liver metastases treated between 2005-2017
- Median age: 67 years (31 – 90 years)
- 77% of patients received prior or concurrent chemotherapy (not associated with OS)
- Median tumor volume: 21.95 cc (0.5 – 638 cc), median dose: 45 Gy (16 – 60 Gy) in 1-5 fractions; LINAC or CK




| | |
|---|---|
| 1 year OS | 75% |
| 2 year OS | 55% |



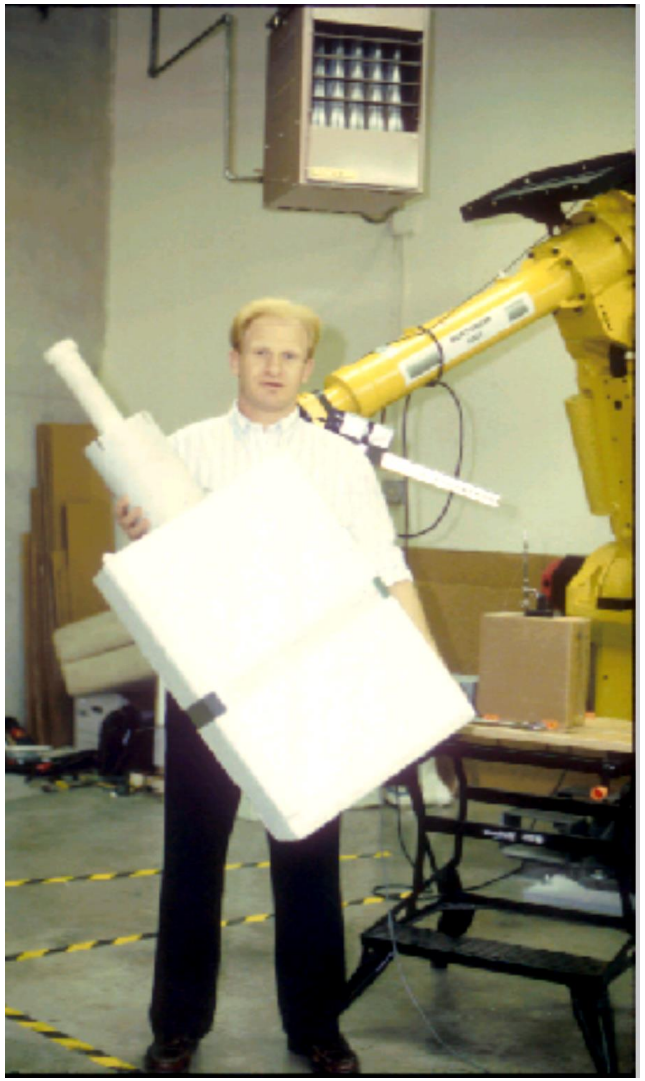

| | BED < 100 | BED ≥ 100 |
|---|---|---|
| Median OS | 18 months | 33 months |
| 1 year OS | 62% | 83% |
| 2 year OS | 36% | 66% |




| | Vol < 22 | Vol ≥ 22 |
|---|---|---|
| Median OS | 34 months | 20 months |
| 1 year OS | 81% | 68% |
| 2 year OS | 70% | 40% |

# CyberKnife

- CyberKnife 1987



**Cyberknife 2013**

# Cyberknife Tracking Types

- All < 1mm tracking spec.

- 6D Skull - Bony anatomy
- Fiducials - Directly visualised
- Synchrony - Tracks moving fiducials, predictive algorithm
- X-Sight Spine - Tracks spinal anatomy, fiducial free
- X-Sight Lung - Fiducial free lung tracking

# Planning SABR

- Fiducial insertion if needed, non coplanar, 2cm apart
- Good quality multimodality imaging
- High res scans 1-2mm slices, IV contrast
- Fusion – deformable registration
- Contouring with radiology support
- MRL or CK, no ITV, 3mm PTV margin
- Experienced dosimetrists / physics
- Steepest dose gradients around 60% prescription isodose
- Often planning to OAR tolerance, some PTV compromise

**Thoracic dose constraints**

| Description | | 3 Fractions | | 5 Fractions | | 8 Fractions | | Source | Endpoint (and magnitude of risk where quantified) |
|---|---|---|---|---|---|---|---|---|---|
| | | Optimal | Mandatory | Optimal | Mandatory | Optimal | Mandatory | | |
| Brachial Plexus | DMax (0.5 cc) | < 24Gy | < 26Gy | < 27Gy | < 29Gy | < 27Gy | < 38Gy | 3 and 5 fractions plus Optimal constraints for 8 fractions: UK SABR Consortium[2] 8 fractions Mandatory constraints from LungTECH trial[3] (excluding heart and great vessels) | Grade 3+ neuropathy |
| Heart | DMax (0.5 cc) | < 24Gy | < 26Gy | < 27Gy | < 29Gy | < 50Gy | < 60Gy | As above (8 fraction heart constraints from UK SABR Consortium[2]) | Grade 3+ pericarditis |
| Trachea and bronchus | DMax (0.5 cc) | < 30Gy | < 32Gy | < 32Gy | < 35Gy | < 32Gy | < 44Gy | As above | Grade 3+ stenosis/ fistula |
| Normal Lungs* (Lungs-GTV) | V20 Gy | - | < 10% | - | < 10% | - | < 10% | As above | Grade 3+ pneumonitis |
| Chest Wall | DMax (0.5 cc) | < 37Gy | - | < 39Gy | - | < 39Gy | - | As above | Grade 3+ fracture or pain |
| | D30 cc | < 30Gy | - | < 32Gy | - | < 35Gy | - | As above | |
| Great Vessels | DMax (0.5 cc) | - | < 45Gy | - | < 53Gy | - | - | As above (8 fractions great vessels constraints from UK SABR Consortium[2]) | Grade 3+ aneurysm |

*Normal Lung (Lungs-GTV) constraints apply for the treatment of two or three lung lesions in the same patient

**Gastro-intestinal Constraints**

| Description | Constraint | 3 fraction | | 5 fraction | | Source | End point |
|---|---|---|---|---|---|---|---|
| | | Optimal | Mandatory | Optimal | Mandatory | | |
| Duodenum | DMax (0.5 cc) | - | < 22.2Gy | - | < 35Gy | 3 fraction: AAPM[4]<br>5 fraction: ABC-07[8]/ SPARC protocols[9] | Grade 3+ ulceration |
| | D1 cc | - | - | < 33Gy | - | | |
| | D5 cc | - | < 16.5Gy | < 25Gy | - | | |
| | D9 cc | - | - | < 15Gy | - | | |
| | D10 cc | - | < 11.4Gy | - | < 25Gy | | |
| Stomach | DMax (0.5 cc) | - | < 22.2Gy | < 33Gy | < 35Gy | As above | Grade 3+ ulceration/ fistulation |
| | D5 cc | - | - | < 25Gy | - | | |
| | D10 cc | - | < 16.5Gy | - | < 25Gy | | |
| | D50 cc | - | - | < 12Gy | - | | |
| Small Bowel | DMax (0.5 cc) | - | < 25.2Gy | < 30Gy | < 35Gy | As above | Grade 3+ enteritis/ obstruction |
| | D5 cc | - | < 17.7Gy | < 25Gy | - | | |
| | D10 cc | - | - | - | < 25Gy | | |
| Common Bile Duct | DMax (0.5 cc) | < 50Gy | - | < 50Gy | - | As above | |
| Oesophagus | DMax (0.5 cc) | - | < 25.2Gy | < 32Gy | < 34Gy<br>(<40 Gy for 8 fractions) | As above plus LungTECH for 8 fraction schedules[3] | Grade 3+ stenosis/ fistula |
| Large Bowel | DMax (0.5 cc) | - | < 28.2Gy | - | < 32Gy | As above | Grade 3+ colitis/ fistula |
| Rectum | Dmax (0.5 cc) | - | <28.2Gy | - | <32Gy | AAPM[4] | Grade 3+ colitis/ fistula |

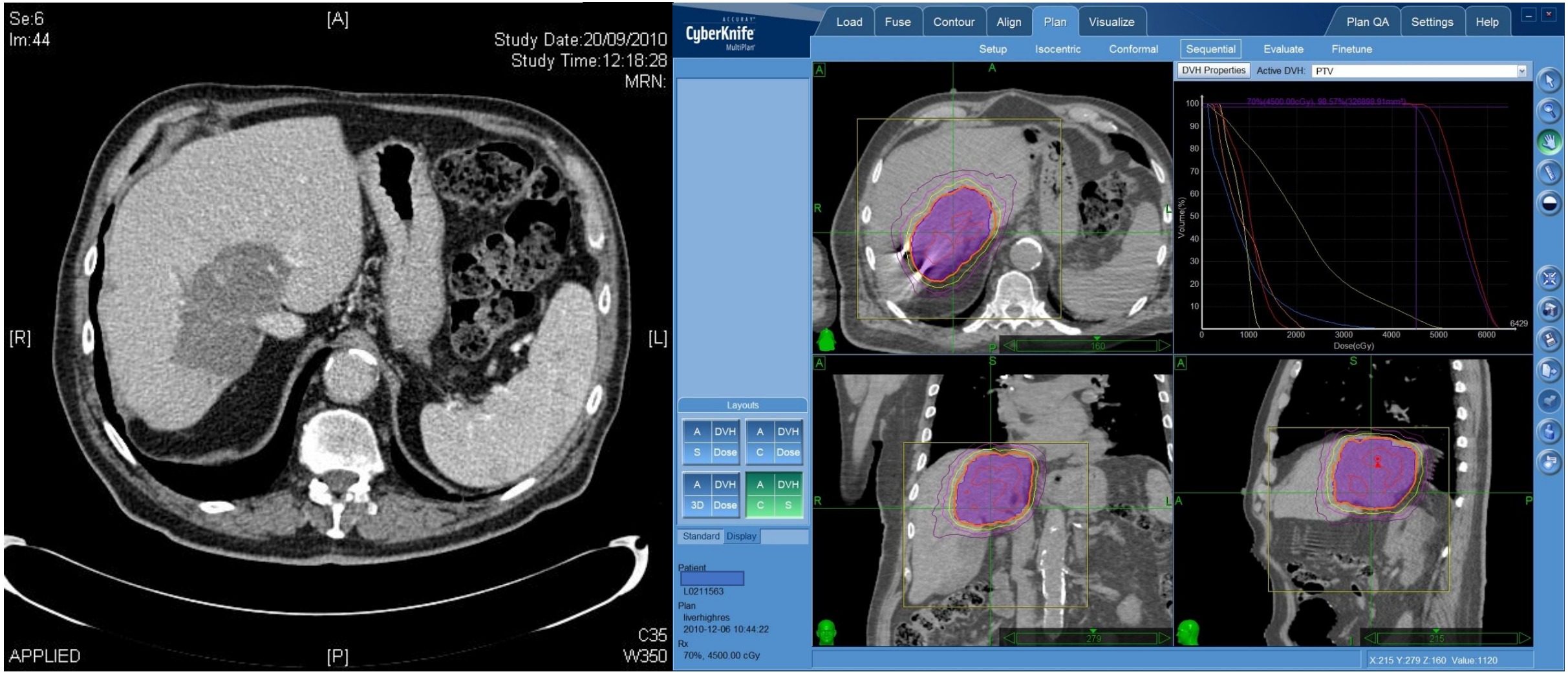
| Parallel GI organs | | | | | | | |
|---|---|---|---|---|---|---|---|
| Description | Constraint | 3 fraction | | 5 fraction | | Source | End point |
| | | Optimal | Mandatory | Optimal | Mandatory | | |
| Normal Liver (Liver minus GTV) | V10Gy | - | - | < 70% | - | 3 fraction: AAPM[4]/ Wulf et al[10,11]/ Rusthoven et al[12]<br>5 fraction: ABC-07[8]/ SPARC [9] protocols | Grade 3+ liver function dysfunction/ radiation-induced liver disease (classic or non-classic) |
| | Mean liver dose | - | - | < 13Gy | < 15.2Gy | | |
| | D50% | < 15Gy | - | - | - | | |
| | Dose to ≥700cc | < 15Gy | < 19.2Gy | - | - | | |
| Kidneys (individual and combined) | Mean kidney dose | - | - | < 10Gy | - | 3 fraction: AAPM[4]<br>5 fraction: ABC-07[8]/ SPARC [9]protocols | Grade 3+ renal function dysfunction |
| | Dose to ≥200cc* | - | < 16Gy | - | - | | |
| If solitary kidney or if one kidney mean dose >10Gy | V10Gy | - | - | < 10% | < 45% | ABC-07[8]/ SPARC[9]protocols | |

*If total kidney volume <200cc, or treating renal or adrenal lesions, then total dose to contralateral kidney should be <16Gy and minimise spillage into ipsilateral kidney if possible.

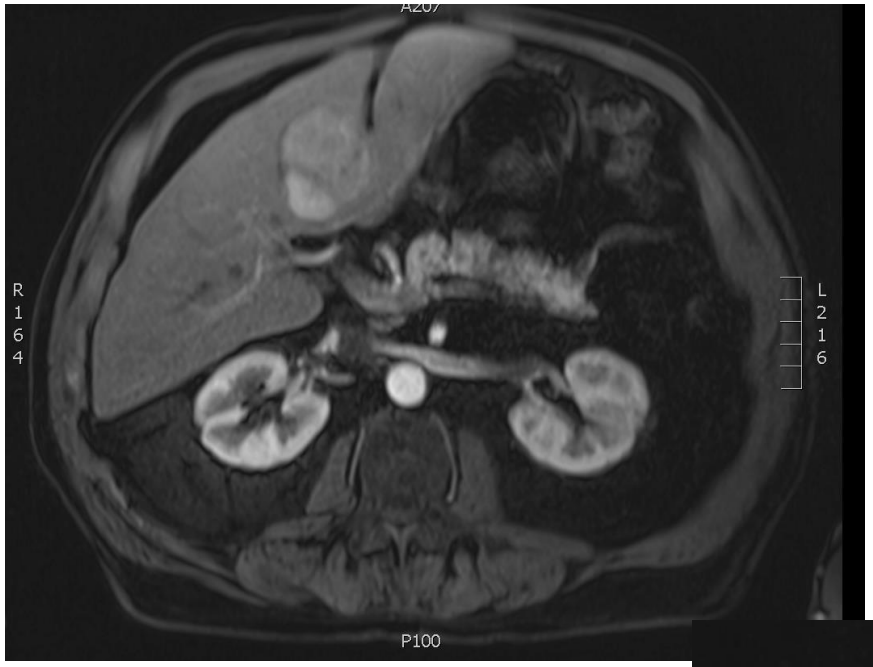
**Pelvic dose constraints (for non-prostate primary irradiation)**

| Description | Constraint | 3 Fractions | | 5 Fractions | | Source | Endpoint |
|---|---|---|---|---|---|---|---|
| | | Optimal (Gy) | Mandatory (Gy) | Optimal (Gy) | Mandatory (Gy) | | |
| Bladder | D15 cc | - | < 16.8 | - | < 18.3 | AAPM[4] | Grade 3+ cystitis/ fistula |
| | DMax (0.5cc) | - | < 28.2 | - | < 38 | | |
| Penile Bulb | D3 cc | - | < 21.9 | - | < 30 | AAPM[4] | Grade 3+ impotence |
| | DMax (0.5cc) | - | < 42 | - | < 50 | | |
| Ureter | DMax (0.5cc) | - | < 40 | - | < 45 | BR001[13] | |

# Colorectal Liver Metastasis

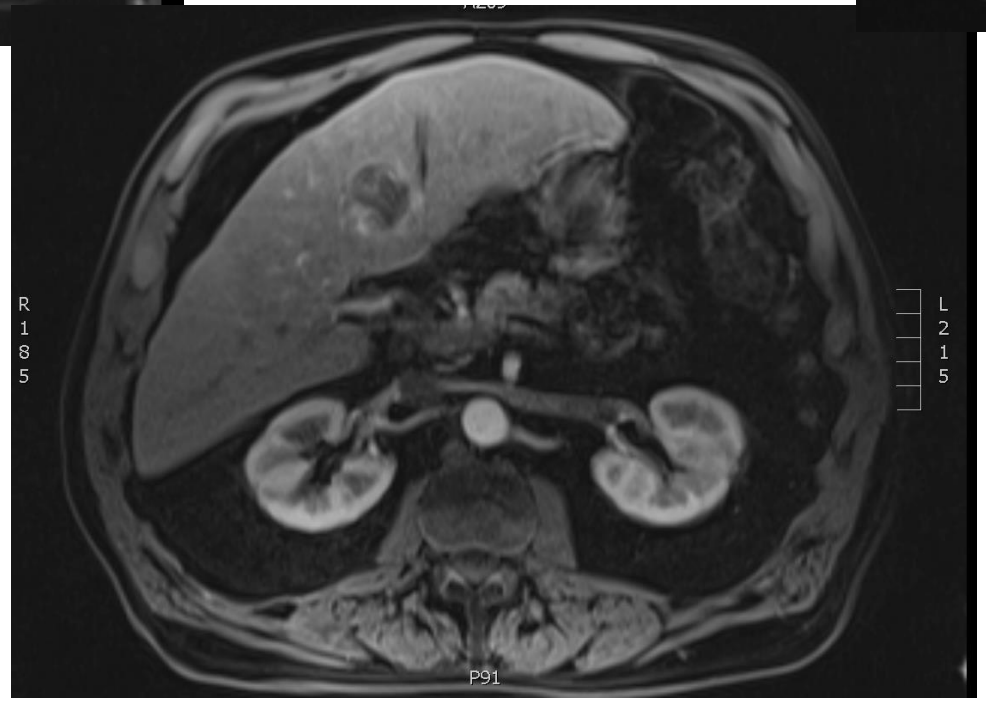


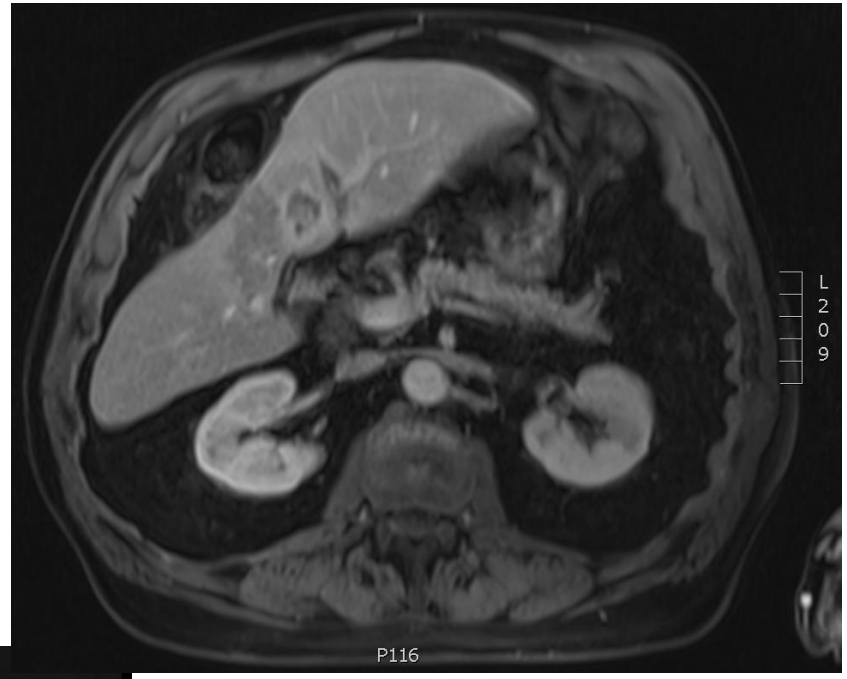
# Colorectal Liver Metastasis




HCC - Baseline

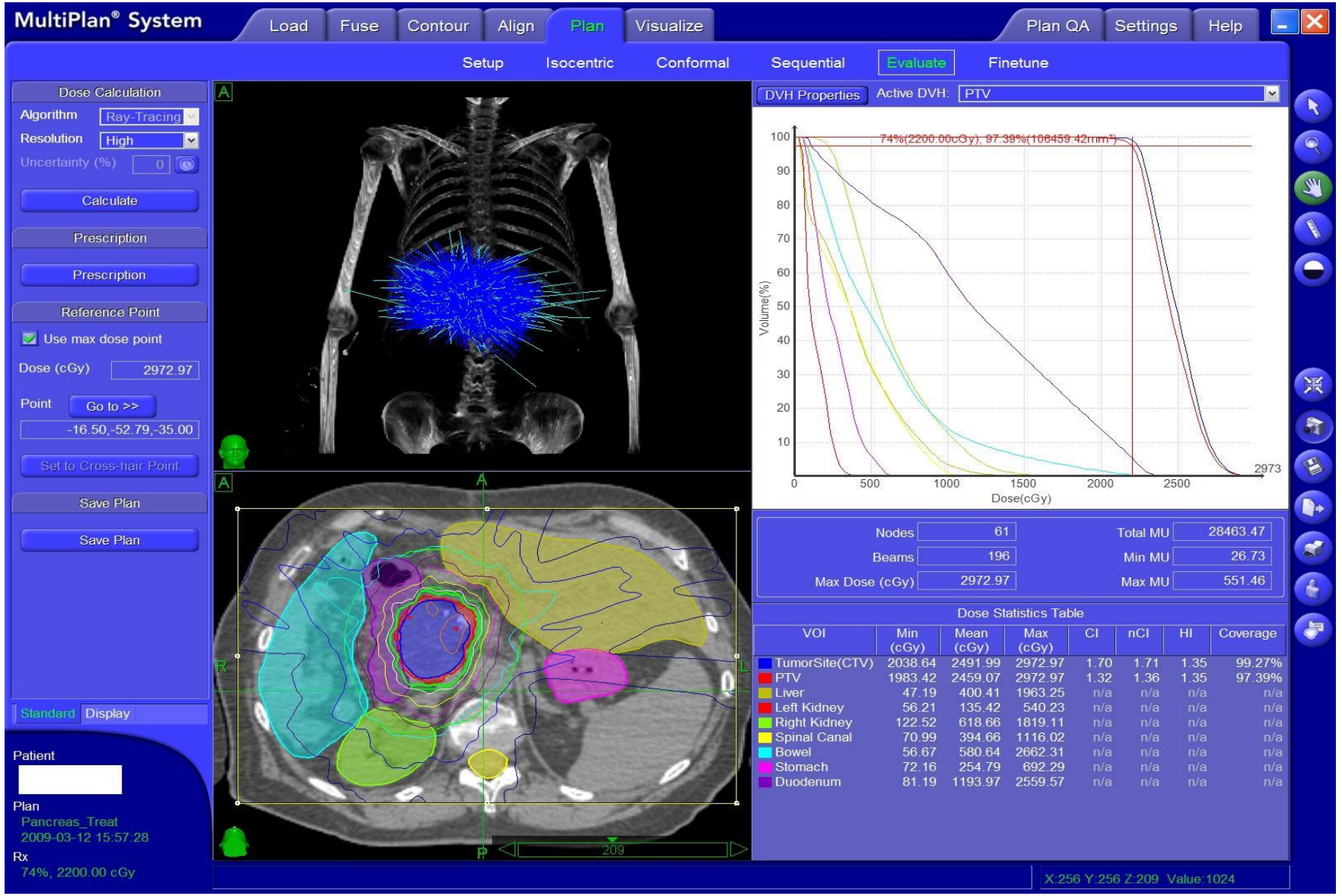
+3 months




+6 months

# Locally Advanced Pancreatic Cancer

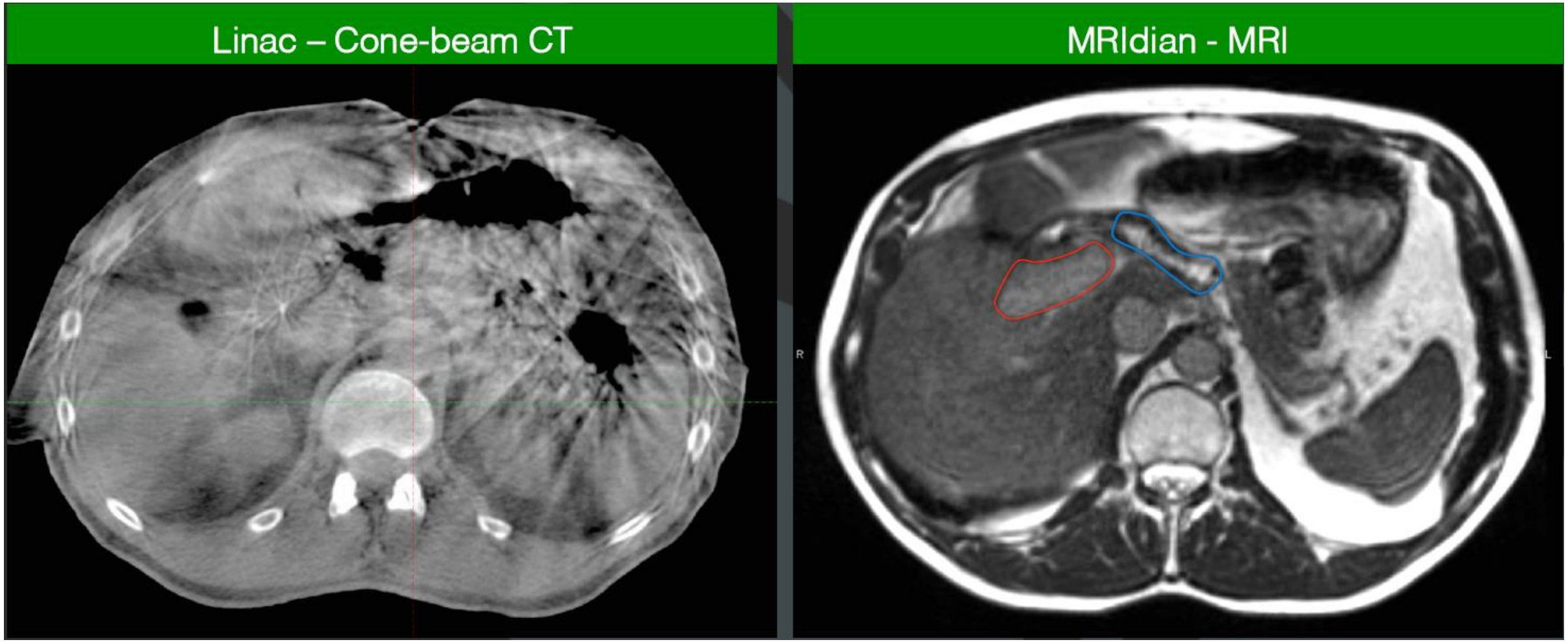


# Viewray MR Linac

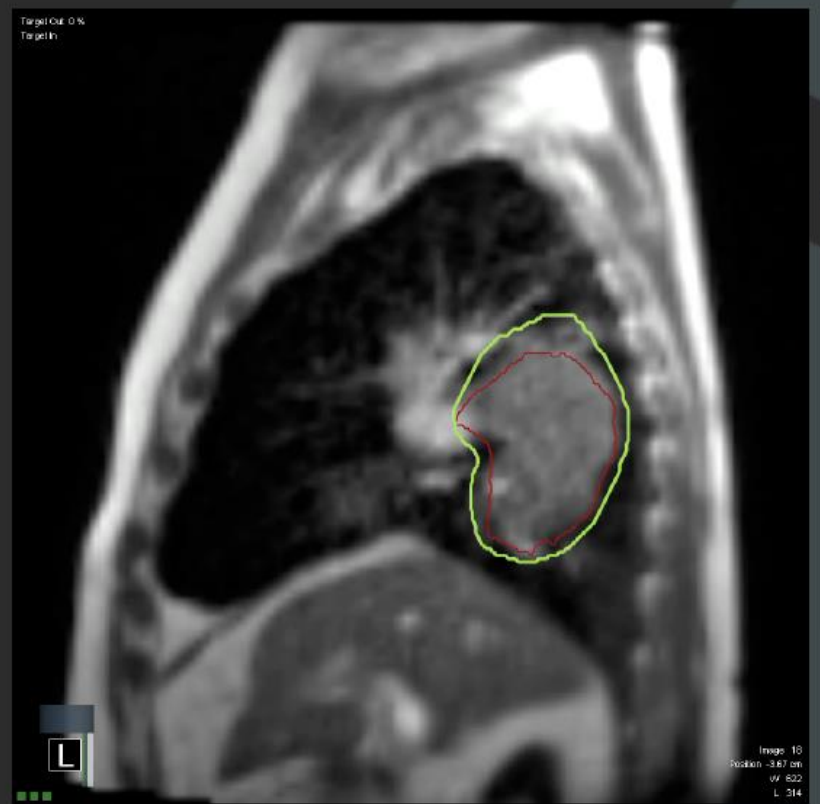
# Why MR Linac….

- SMART – Stereotactic MRI guided Adaptive RT
- ViewRay MRIdian 0.35T, Elekta Unity 1.5T
- It has numerous clinical advantages such as:
  - Real time continuous visualisation of soft tissue structures with MR
  - Sequence choice such as TruFi, DWI, T1, T2
  - Daily adaption of treatment plan – recontouring & replanning.
  - Hypofractionatated delivery
  - Active tracking and gated delivery (ViewRay)
  - Best for mobile targets and difficult to visualise targets

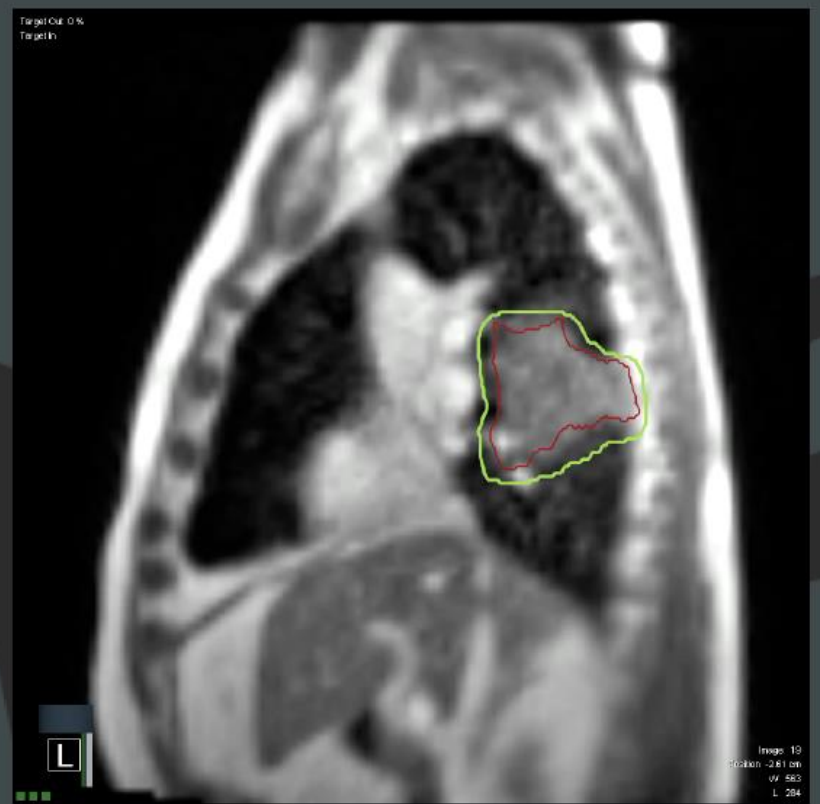
# On line Imaging



# Adapting and Tracking Optimizes Treatment



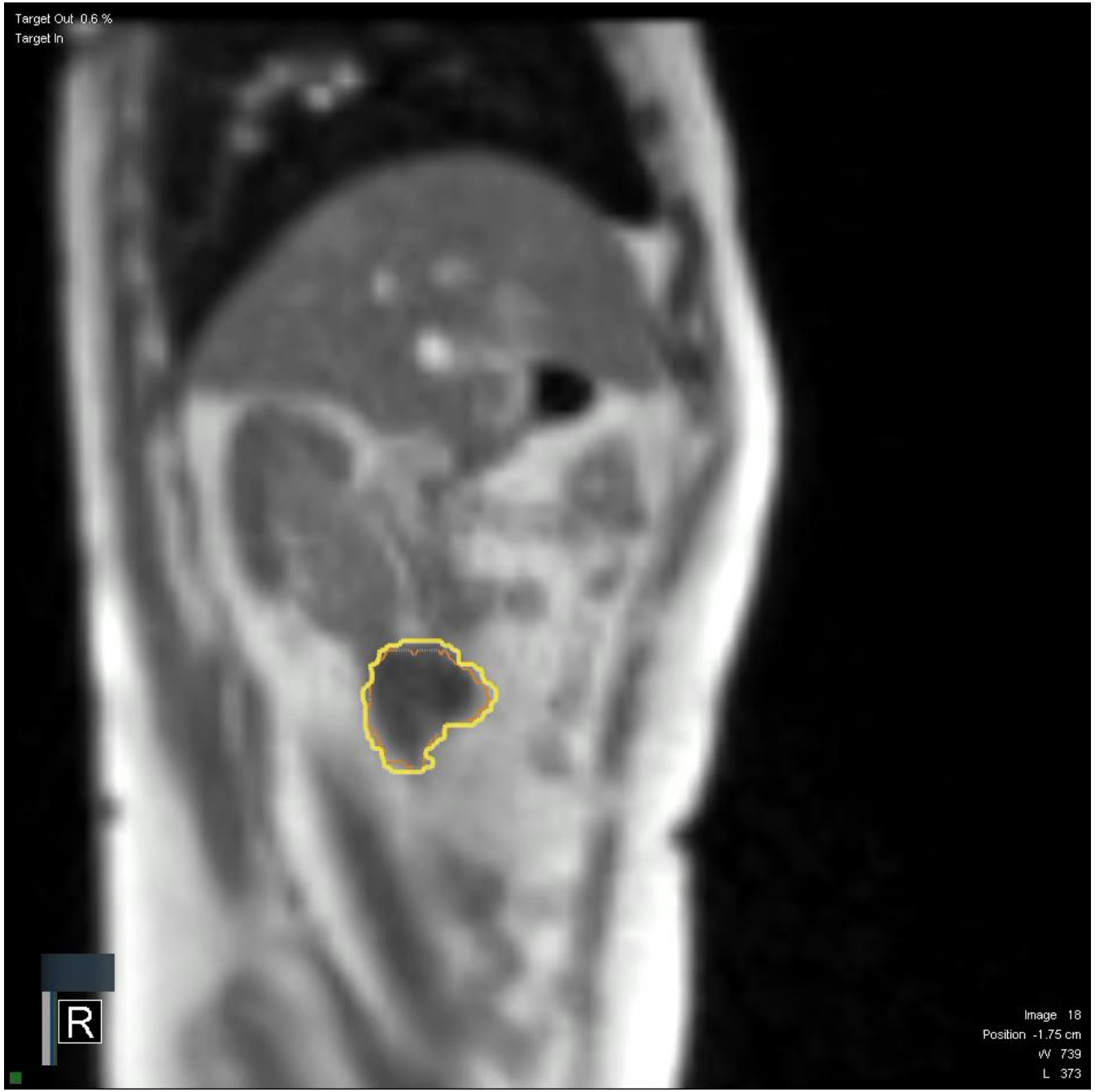
- Easily adapt for tumor response/shrinkage
- Realtime tracking ensures accurate treatment
- Reduced margins minimize complications



Fraction 1 Cine

Fraction 17 Cine

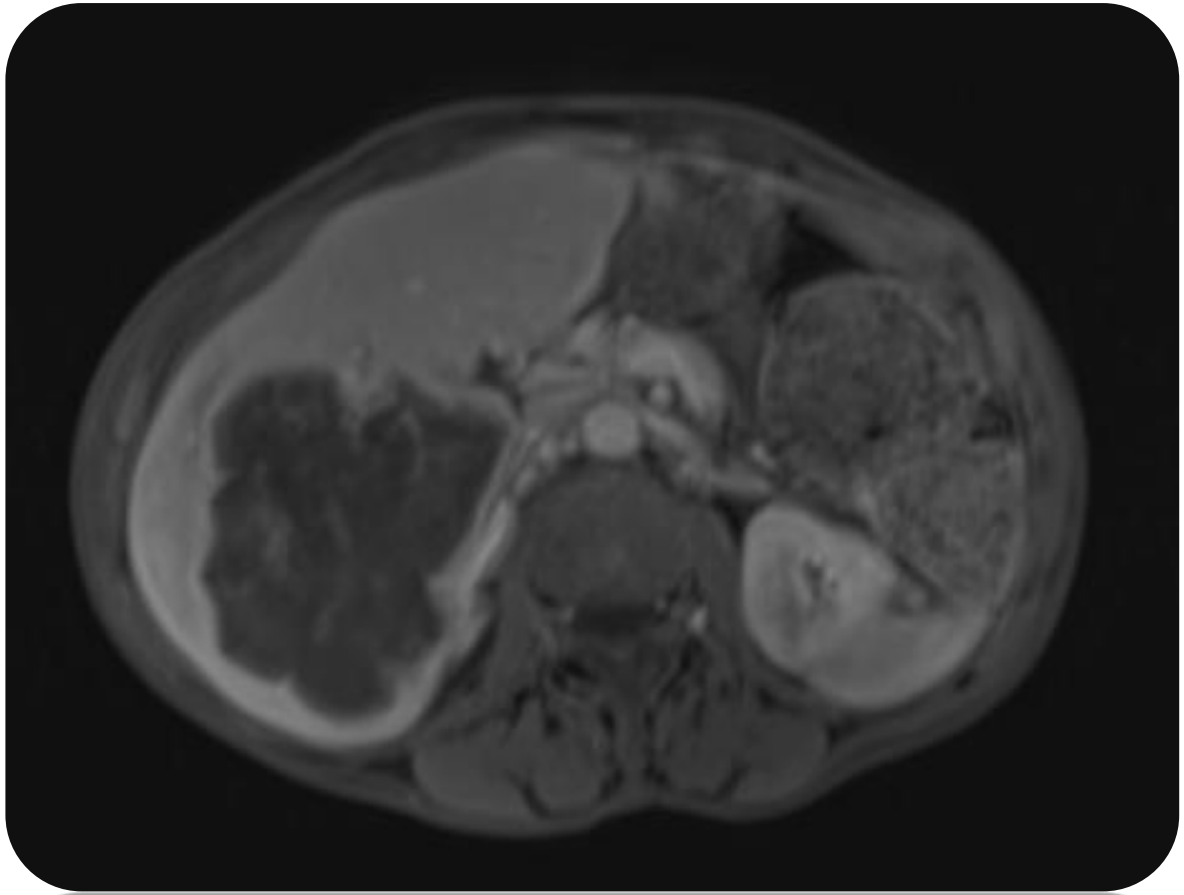
# Pancreas



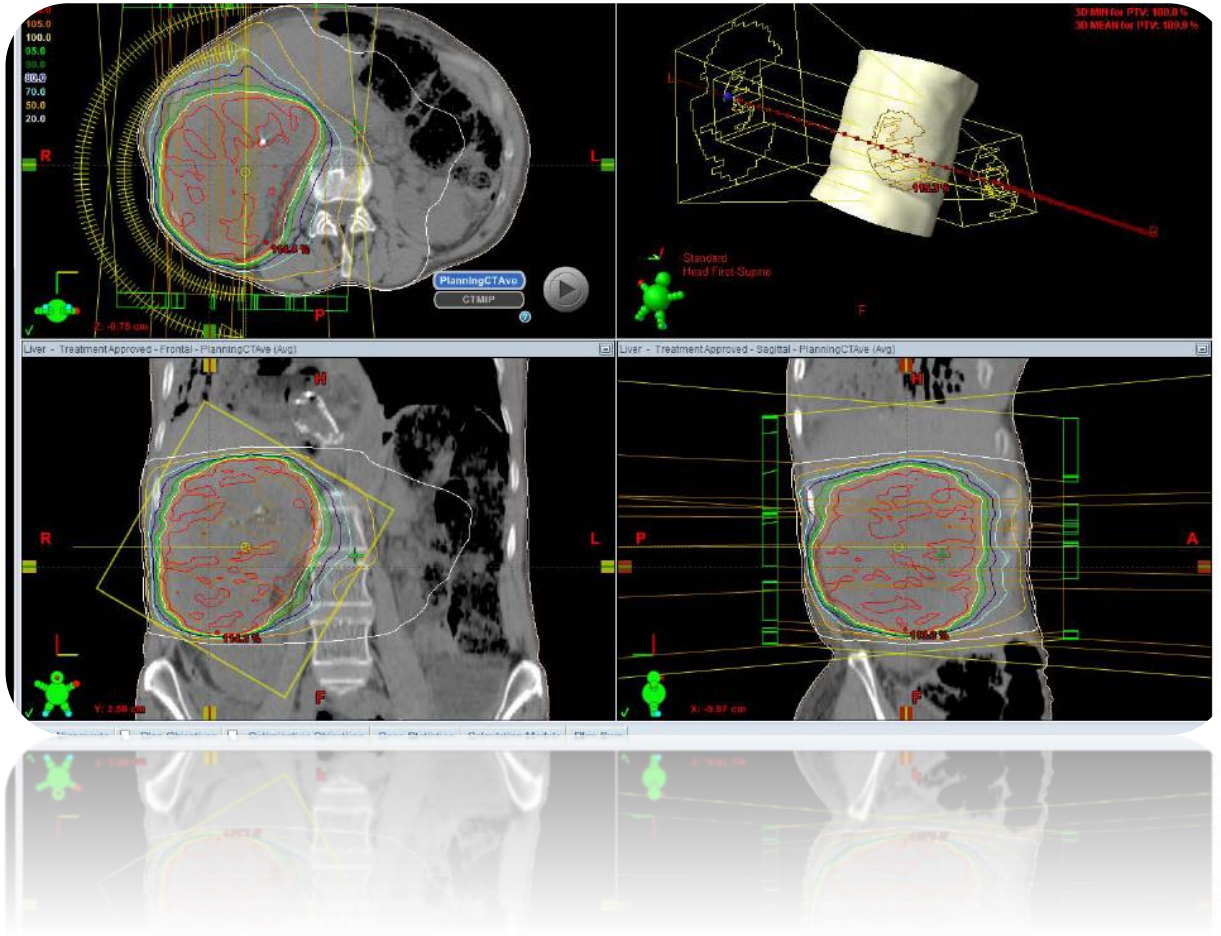
# Stereotactic Body Proton Therapy

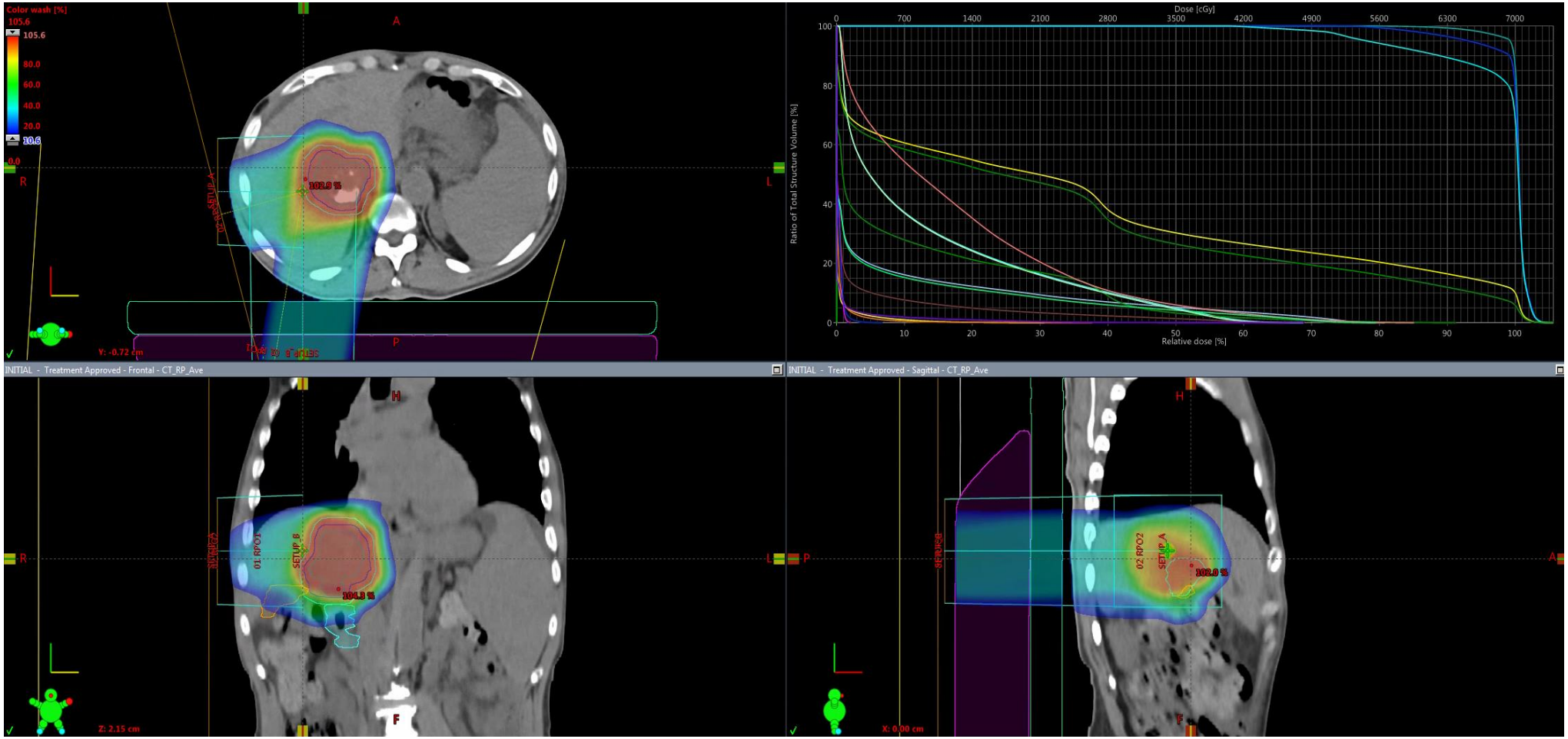
- Potential Advantages:
- Liver - Best for larger targets (>6cm) or central tumours
- Steeper exit dose gradient
- Thus normal tissue sparing
- Other sites that “may” benefit – H&N, prostate, pancreas, spine
- Retreatment Radiotherapy
- Disadvantages:
- Cost, size, IGRT, Gating

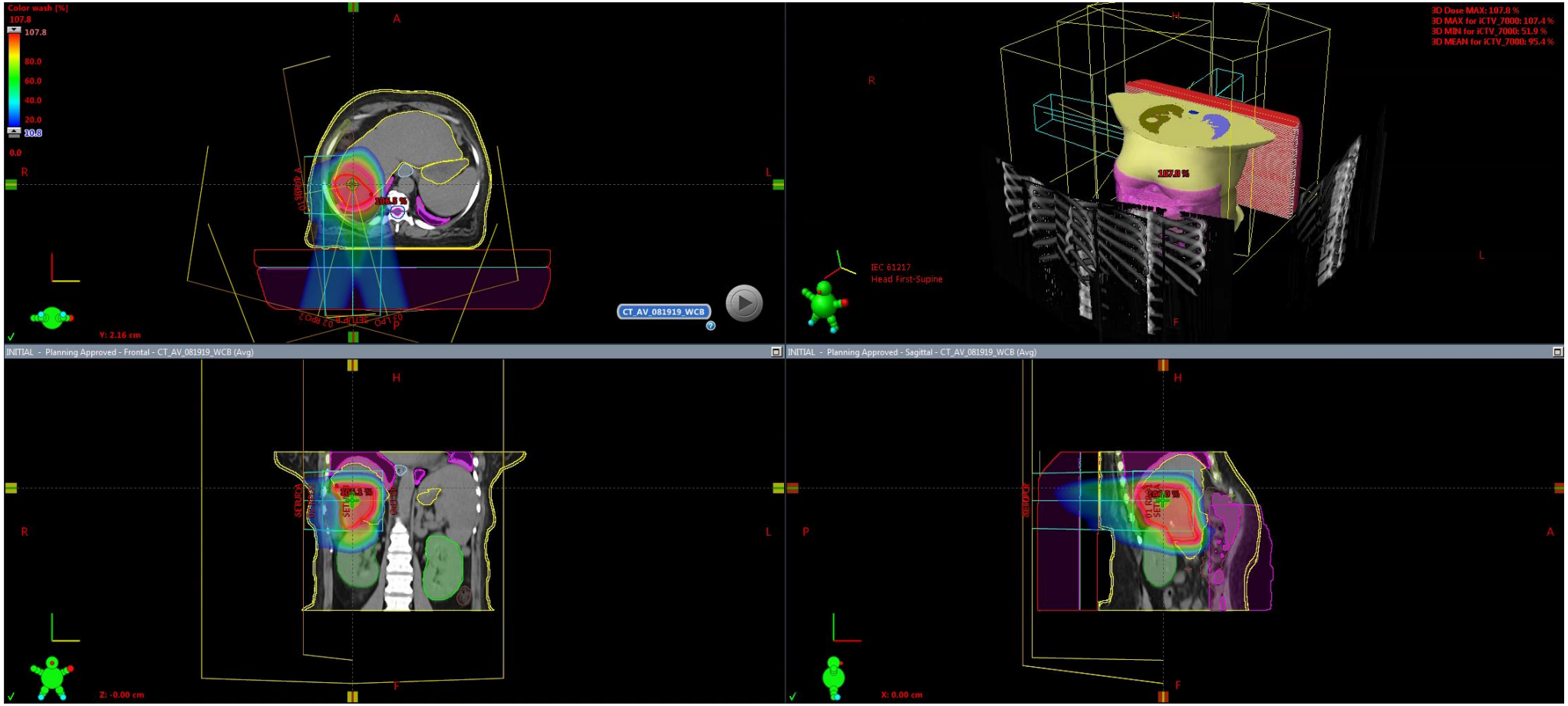
# Size Does Matter



Linac or Protons




Color wash [%]
105.6
105.6
80.0
60.0
40.0
20.0
10.6
0.0
A
R
L
P
Y: -0.72 cm
Dose [cGy]
0
700
1400
2100
2800
3500
4200
4900
5600
6300
7000
Ratio of Total Structure Volume [%]
Relative dose [%]
INITIAL - Treatment Approved - Frontal - CT_RP_Ave
INITIAL - Treatment Approved - Sagittal - CT_RP_Ave
H
F
Z: 2.15 cm
X: 0.00 cm


Color wash [%]
107.8
107.8
80.0
60.0
40.0
20.0
10.8
0.0
3D Dose MAX: 107.8 %
3D MAX for iCTV_7000: 107.4 %
3D MIN for iCTV_7000: 51.9 %
3D MEAN for iCTV_7000: 95.4 %
IEC 61217
Head First-Supine
CT_AV_081919_WCB
INITIAL - Planning Approved - Frontal - CT_AV_081919_WCB (Avg)
INITIAL - Planning Approved - Sagittal - CT_AV_081919_WCB (Avg)
Y: 2.16 cm
Z: -0.00 cm
X: 0.00 cm

# Summary

- Is SABR a replacement for surgery? No
- Is SABR a replacement for RFA ? No
- Is SABR a replacement for CF-EBRT? No
- SABR offers excellent local control, and is a well-tolerated & safe treatment
- One of many treatment options for patients
- Local expertise / Patient preference
- results of key studies are eagerly awaited

# The ph2 evidence is strong, do we need a large RCT?

## Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

**What is already known about this topic**

Parachutes are widely used to prevent death and major injury after gravitational challenge

Parachute use is associated with adverse effects due to failure of the intervention and iatrogenic injury

Studies of free fall do not show 100% mortality

**What this study adds**

No randomised controlled trials of parachute use have been undertaken

The basis for parachute use is purely observational, and its apparent efficacy could potentially be explained by a "healthy cohort" effect

Individuals who insist that all interventions need to be validated by a randomised controlled trial need to come down to earth with a bump