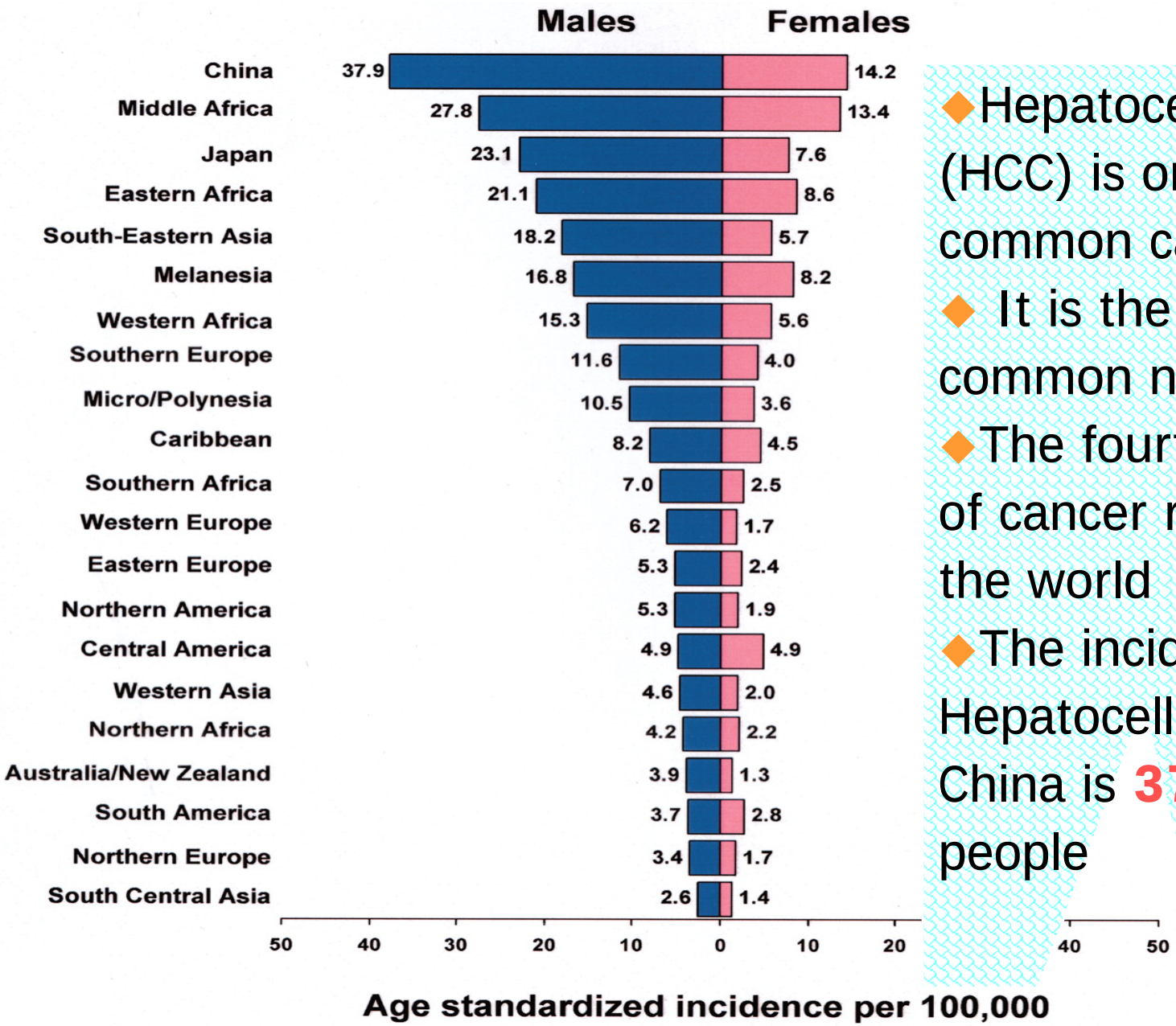
WANJIE PROTON THERAPY CENTER

Proton Beam Therapy for Hepatocellular Carcinoma

Li Jiamin, MD
Wanjie Proton Therapy Center



- Hepatocelluar carcinoma (HCC) is one of the most common cancers worldwide
- It is the eighth most common neoplasm
- The fourth leading cause of cancer related death in the world
- The incidence of Hepatocellular Carcinoma in China is **37.9** per 100,000 people

- It is the major cause of death in patients with liver cirrhosis
- Risk factors for HCC are chronic infection of hepatitis B or C, alcoholic cirrhosis, aflatoxin, hemochromatosis, and Wilson’s disease

Mortality

- Mortality is about 250,000 yearly in the world
- It is about 110,000 yearly in China

- The treatment of HCC is difficult because most patients are diagnosed when the tumor is in an advanced stage
- Good results can be achieved with surgical resection, but 80% are not eligible for surgery
- The management of technically unresectable and medically inoperable HCC remains challanging

- HCC is highly resistant to currently available chem drugs
- Transarterial chemoembolization (TACE) showed improved survival but its antitumor effect was frequently incomplete

- **Tolerance of the liver to irradiation is poor:**
  - **-The tolerance is less than 35Gy to a limited volume**
  - **-The tolerance is 30Gy to the whole liver/3 weeks**
  - **-The poor tolerance has prevented delivery of tumoricidal dosage**

- Radiation therapy has played a minor role in the treatment of HCC
- Conventional radiation therapy for HCC has resulted in unsatisfactory outcomes for the past decades

- **With**
  - -Conformal Radiation Therapy (3DCRT)
  - -Intensity Modulated Radiation Therapy Local control and survival rate improved
- **While**
  - -Massive normal liver tissue damage was found
  - -Radiation-induced liver disease (RILD) were also reported

- Proton beam therapy can give excellent dose localization to the tumor
- Normal liver tissue can be well spared
- Compared to photons, protons deliver less than half of the dose to normal tissues: therefore,
  - -reduced acute and late morbidities
  - -increased target dose

Intrinsic characteristics of proton beam

- Bragg peak
- Lower lateral scattering
- Lower entrance dose with a sharp distal dose fall-off
- Less dose to normal tissue

Cases treated at WPTC

- Between Dec. 2004 and Mar. 2007
- 39 patients with HCC were treated at Wanjie Proton Therapy Center

- Male 37 cases Female 2 cases
- Median age: 58yr
- Stage I, II: 17 cases
- Stage IIIA: 20 cases
- Stage IIIB: 2 cases
- Tumor size : 1.2 - 14.0cm (median 7.0cm)

- All of the patients were considered unsuitable for surgery for reasons such as:
  A. Poor medical condition caused by intercurrent diseases (Coronary heart disease, poor lung function, diabetes mellitus)

B. Hepatic dysfunction caused by concomitant deseases (advanced coirrhosis with high level of serum bilirubin, ascites)

C. Multiple tumors

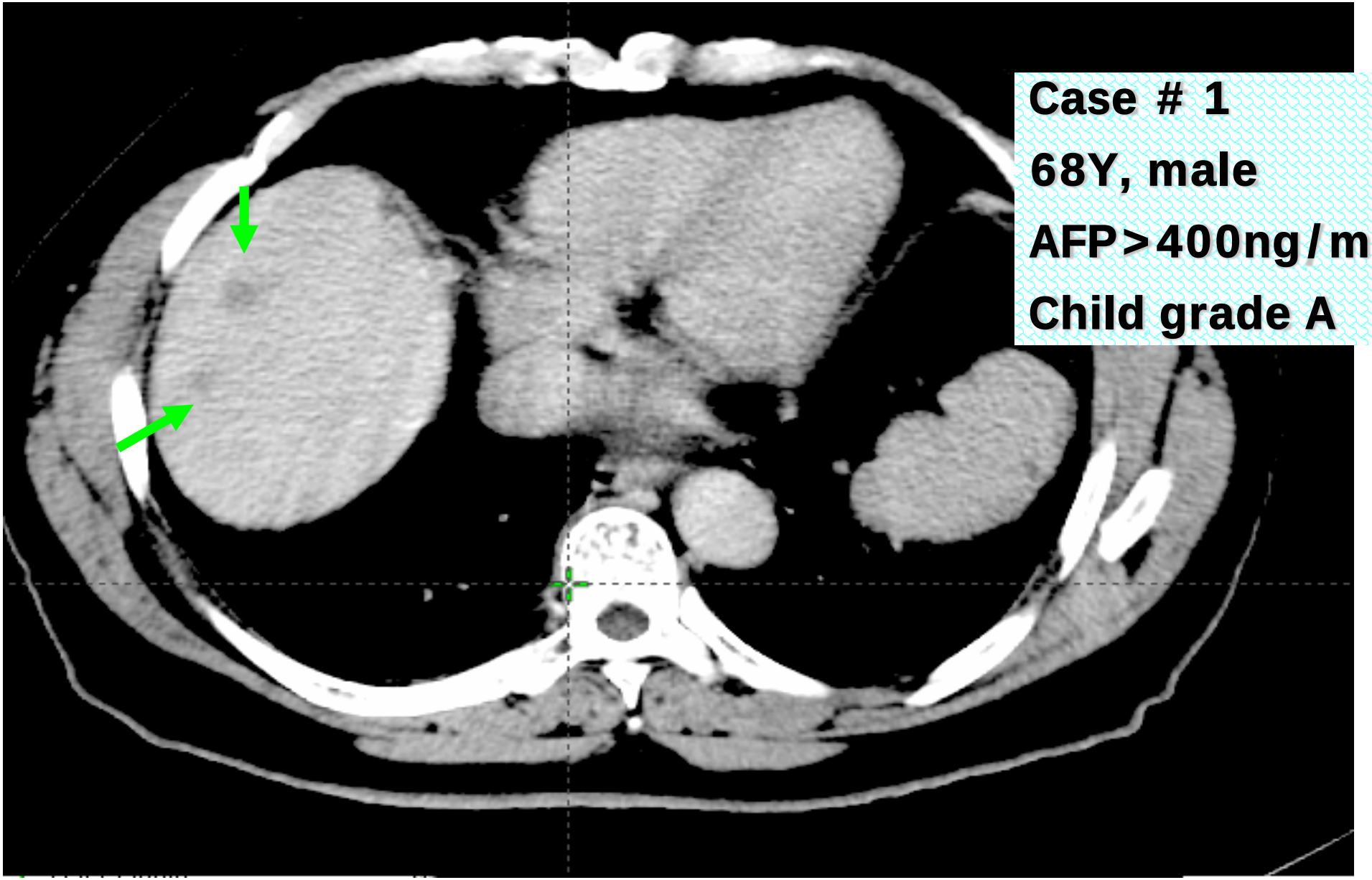
D. Advanced age

E. Patient refusal of surgery

- Solitary tumor was found in 23 patients
- Multiple tumors were found in 16 patients
- Child-Pugh Grade A in 25 patients
- Child-Pugh Grade B in 12 patients
- Child-Pugh Grade C in 2 patients

- TPS was Varian- Eclipse Proton
- PTV=GTV+0.7~2.1cm
- 2~3 proton fields were used
- Double scattering mode
- Energy range was from 70-230MeV

- 90%~95% isodose line was used to cover the PTV
- Relative biologic effectiveness 1.1 was used
- Fractionation: 2.5-4.0CGE/13-28F, 5d/w
- Total dose: from 52.0 to 72.0CGE

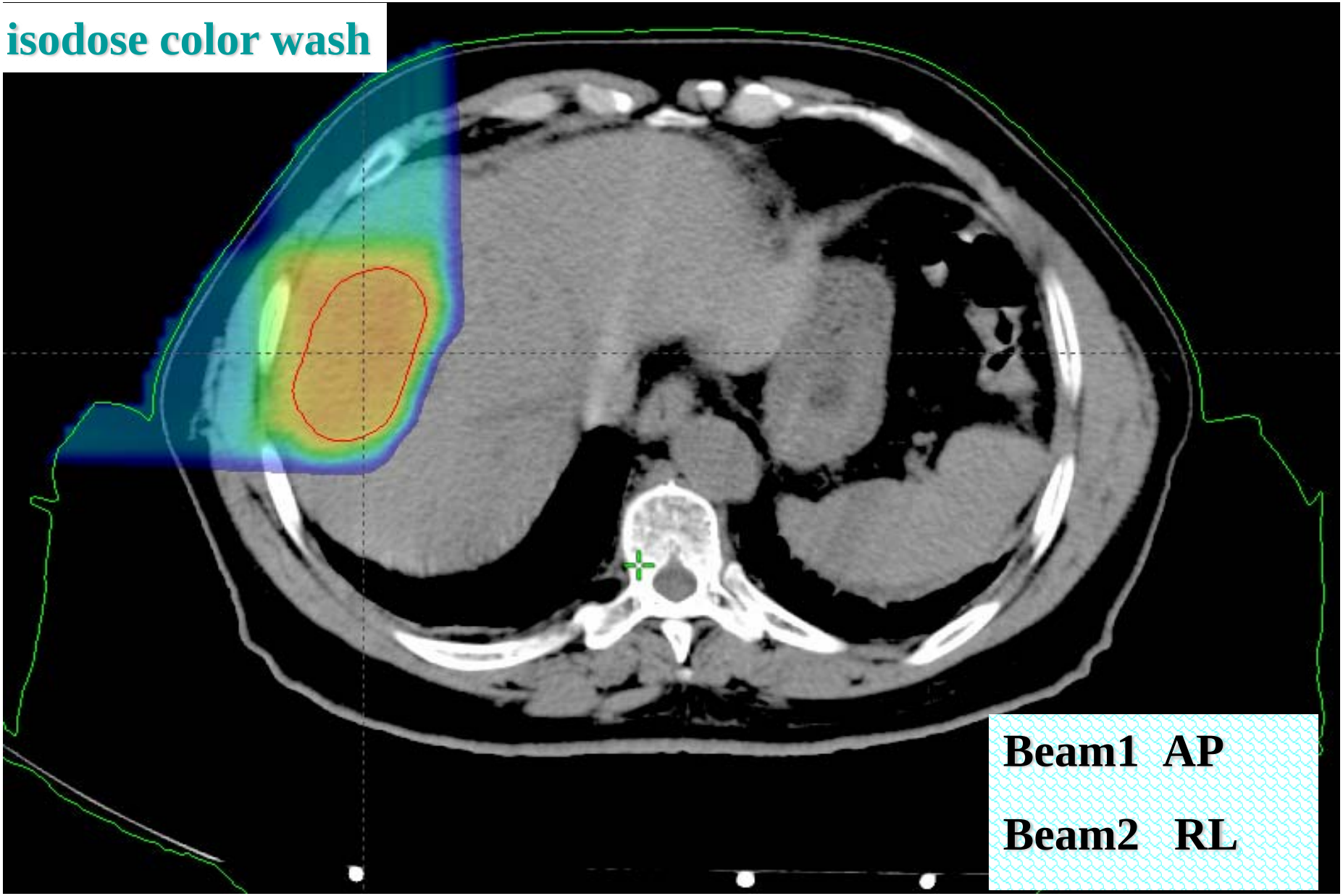


Two foci 1.8 x 1.5cm, 1.2 x 0.8cm (T2)

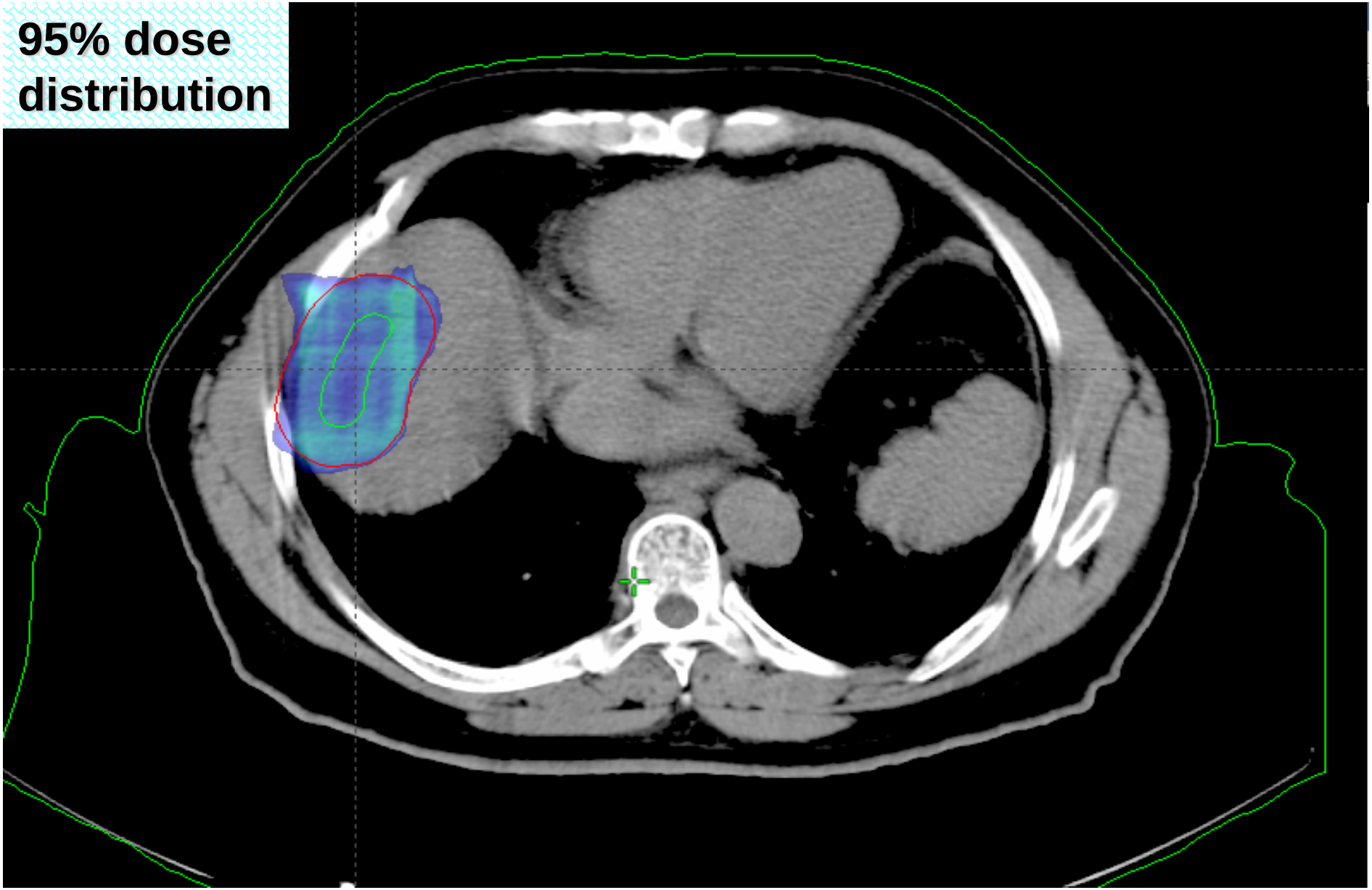
Proton treatment planning

- PTV=GTV+10~20mm (AP 10mm, CC 20mm)
- GTV 9.4cm3 , PTV 142.7 cm3
- DT 66.0CGE/22F，5d/w
- 95% isodose line to PTV
- Mean dose to liver 3.44CGE

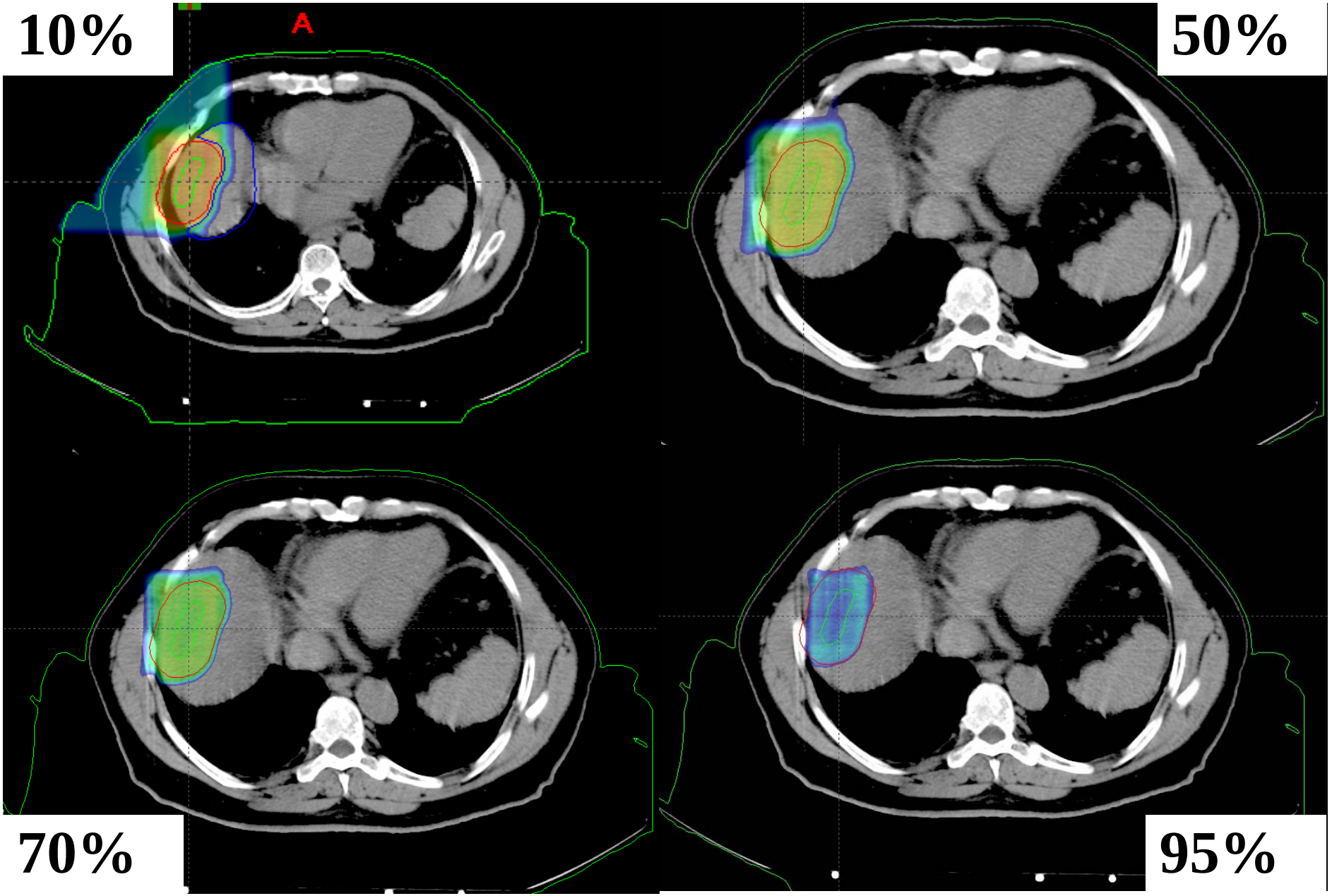
isodose color wash



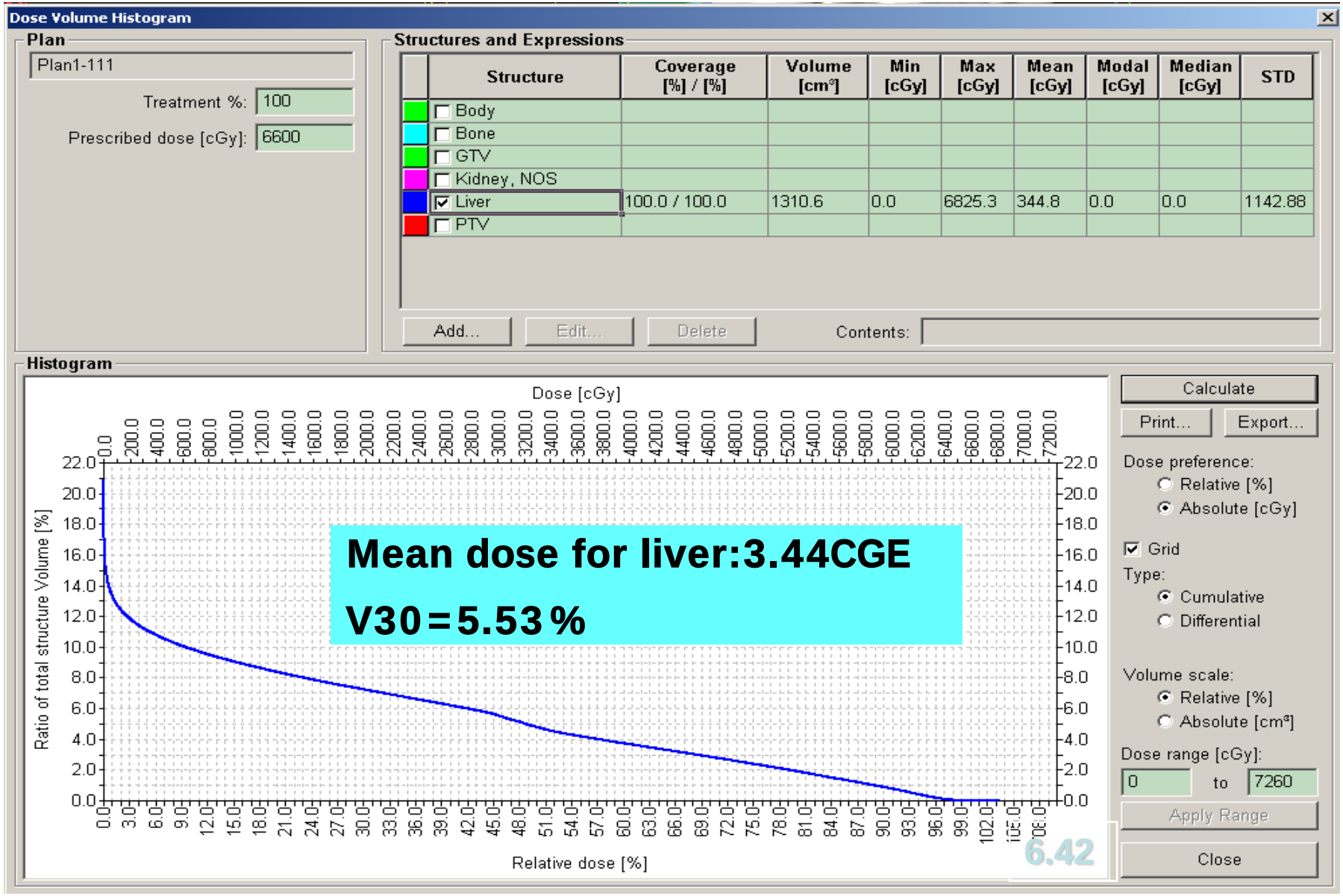
WANJIE PROTON THERAPY CENTER



WANJIE PROTON THERAPY CENTER



WANJIE PROTON THERAPY CENTER

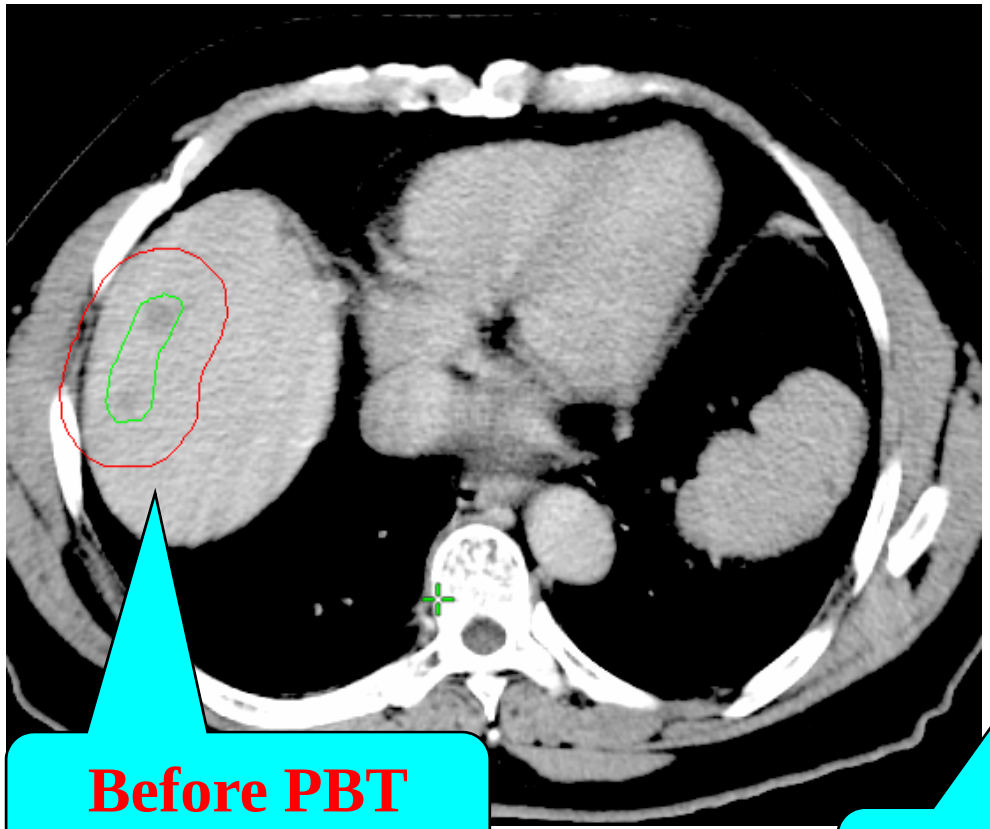


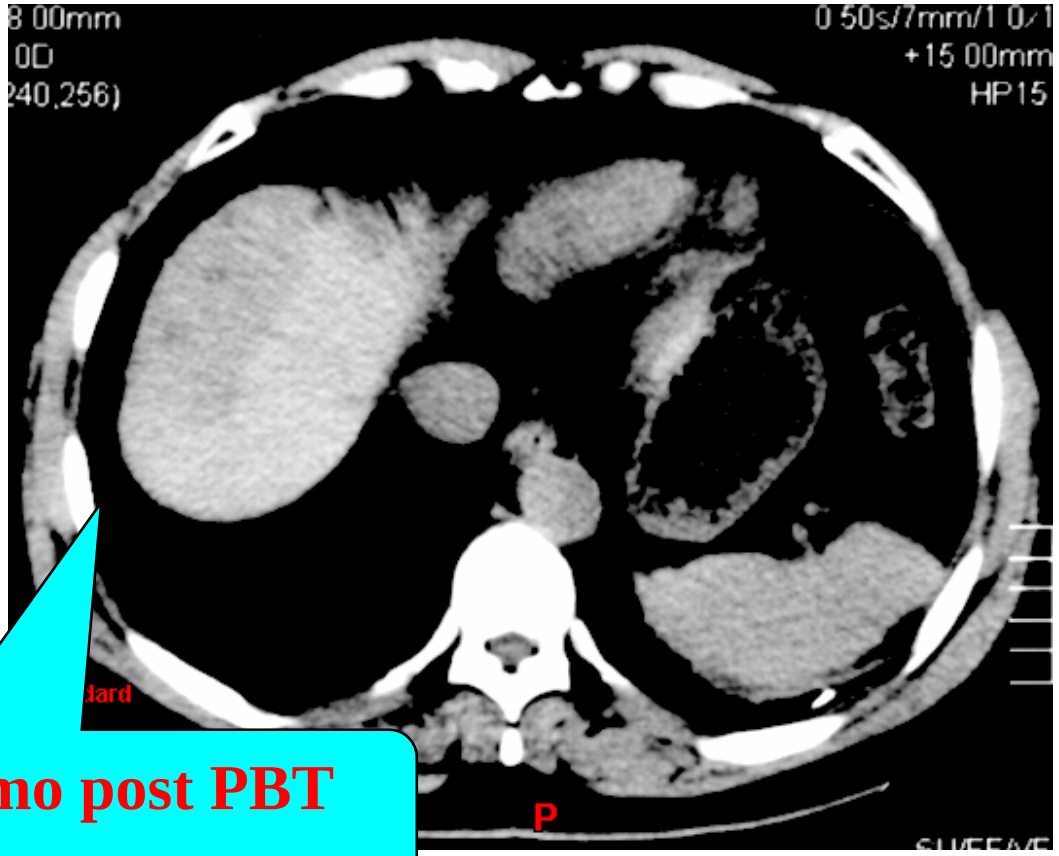
WANJIE PROTON THERAPY CENTER

- Before PBT
  - 2005-6-15 AFP 500ng/ml
- Post PBT
  - 2005-7-19 AFP 400ng/ml
  - 2005-8-03 AFP 74.02ng/ml
  - 2005-8-23 AFP 19.89ng/ml

Follow up

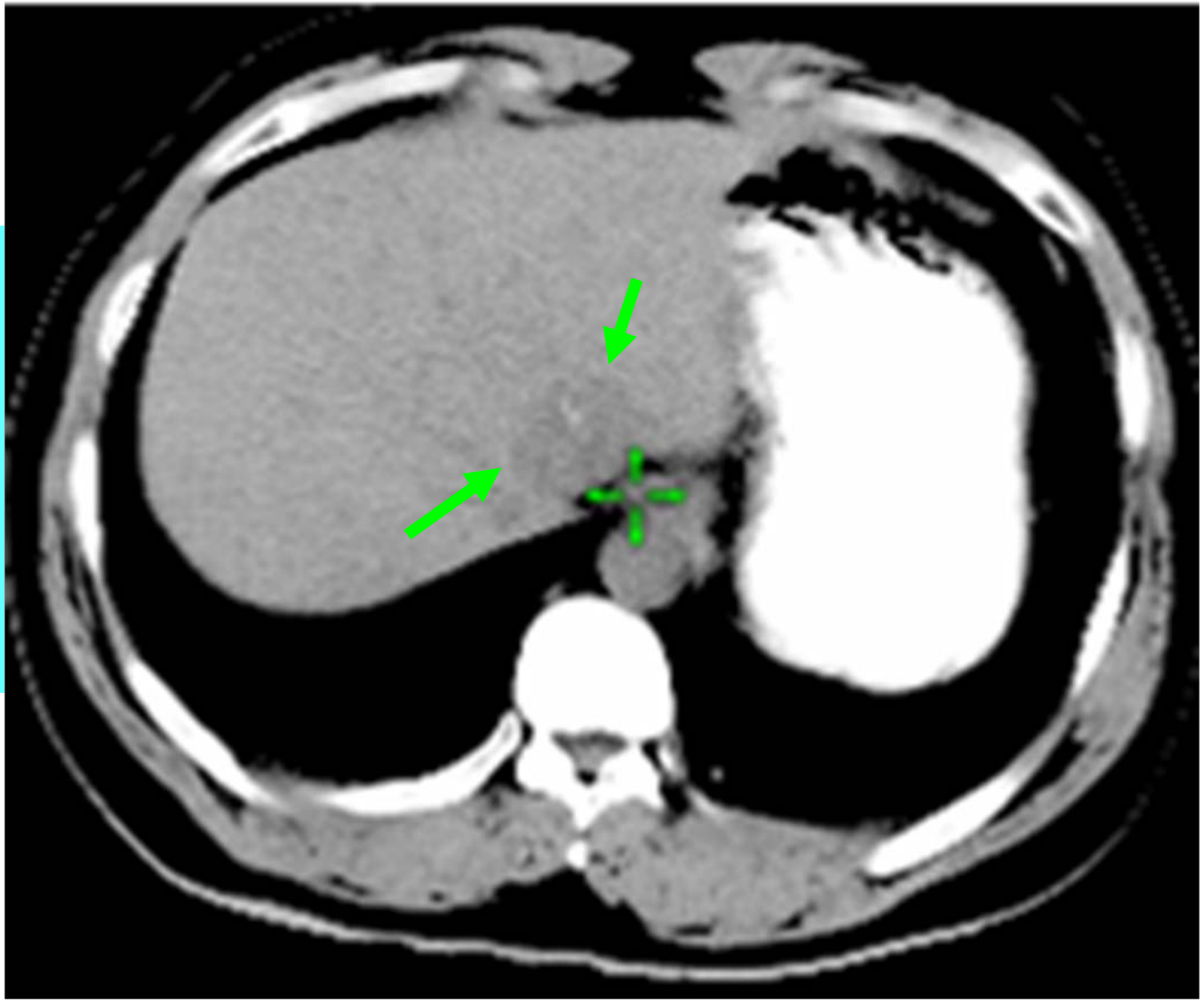
- Liver function was normal 3-mo post PBT
- CT: the two foci treated getting smaller (less than 60% in diameter)





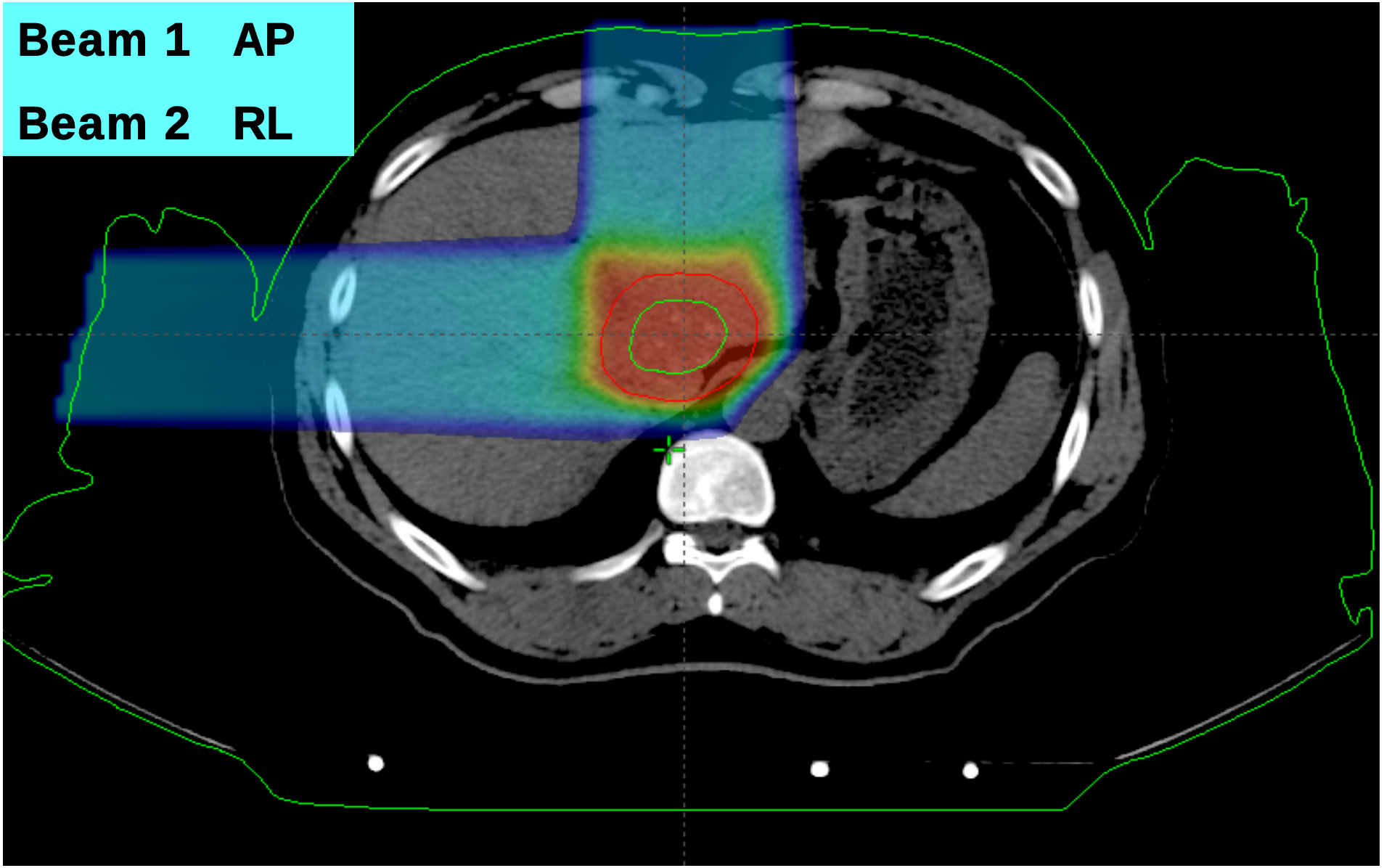
WANJIE PROTON THERAPY CENTER

Case # 2
45y, M, Child A
AFP400ng/ml
4.1x2.7cm
2-mo later
1.9x2.0cm



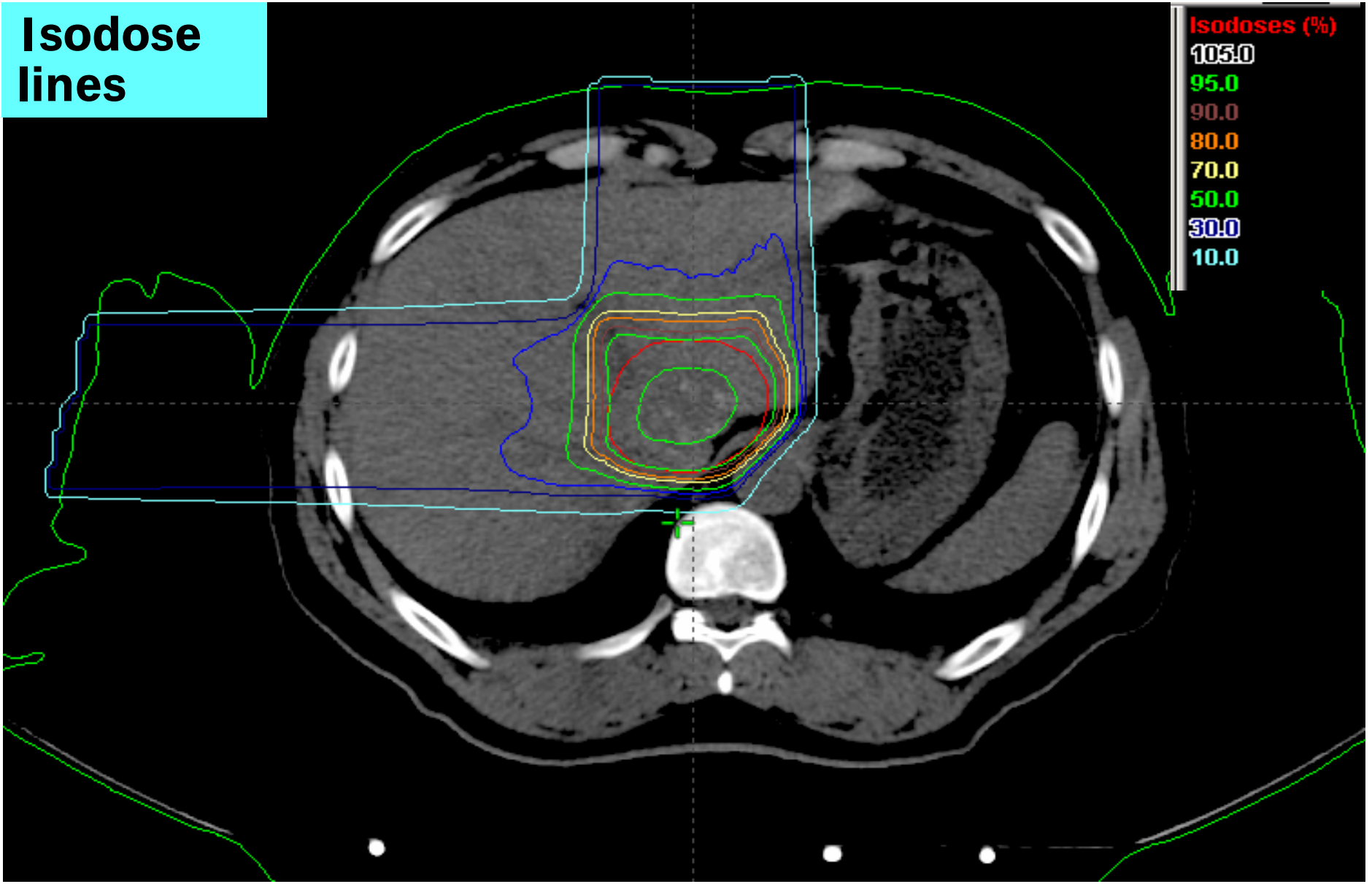
Proton treatment planning

- PTV=GTV+10~15mm(AP 10mm, CC 15mm)
- GTV16.2cm3, PTV94.4cm3
- DT60CGE/20F, RBE=1.1, 5F/W, AP、RL
- 95% isodose line to cover PTV
- Mean dose to liver 14CGE

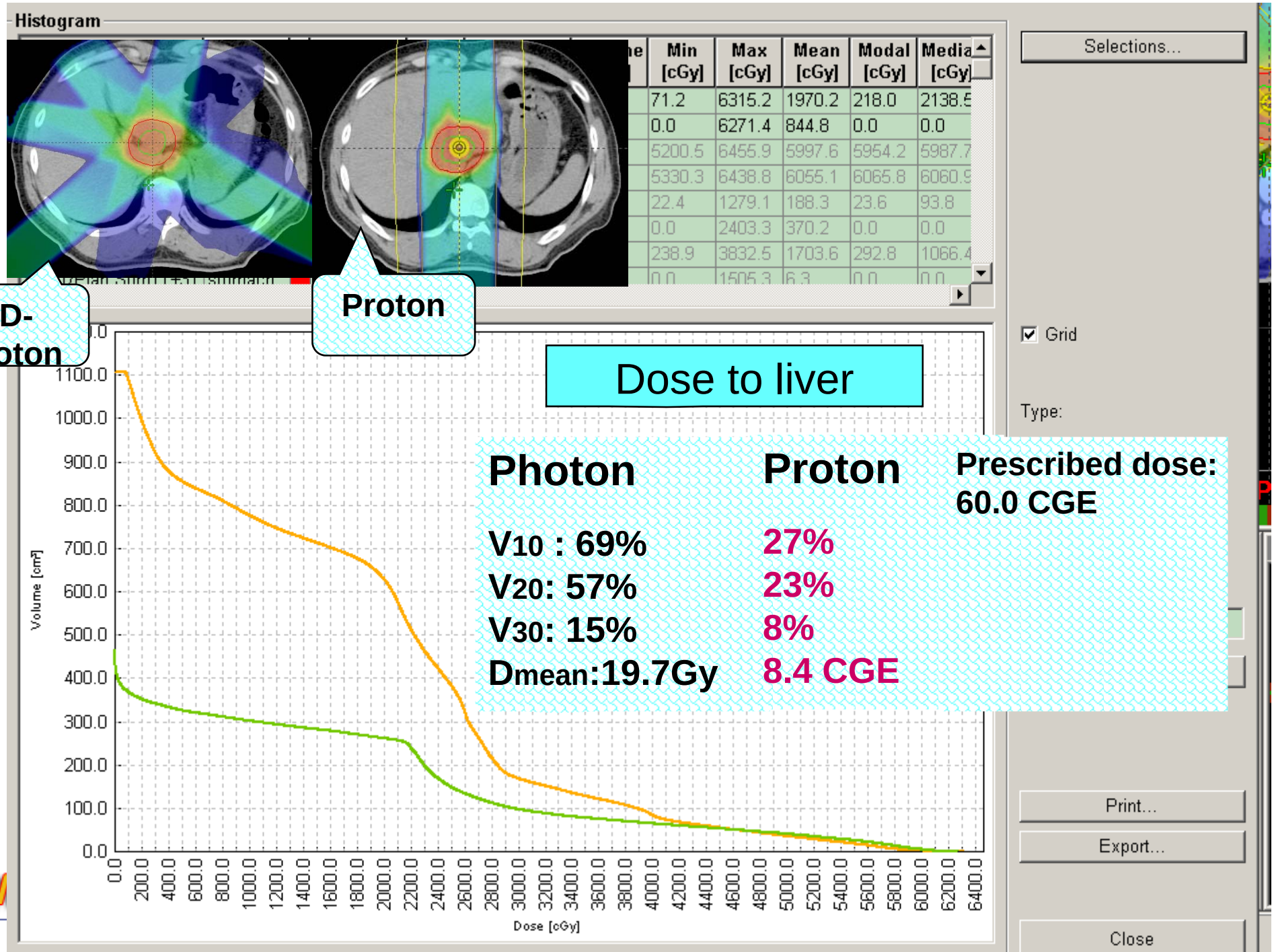


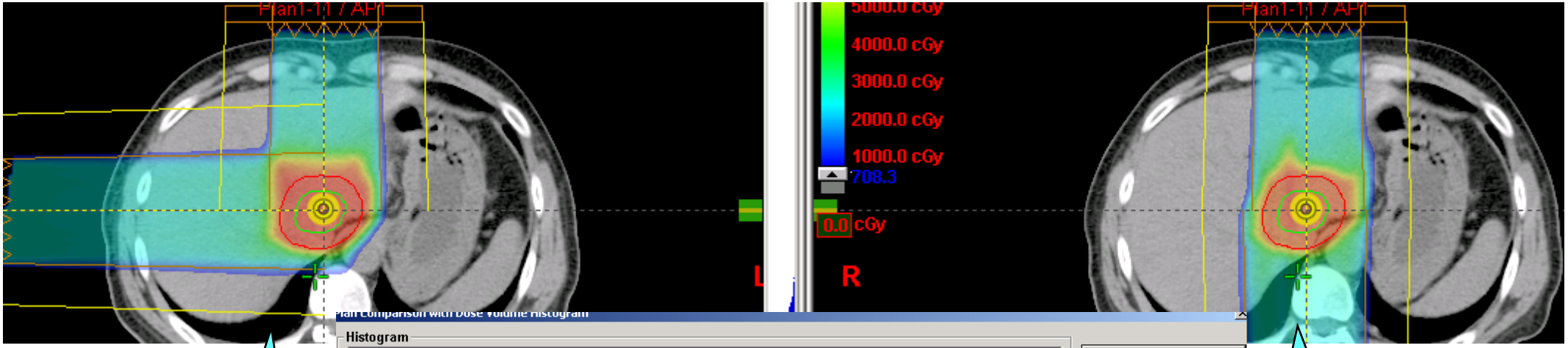
WANJIE PROTON THERAPY CENTER

Isodose lines



WANJIE PROTON THERAPY CENTER


Histogram
Min [cGy]
Max [cGy]
Mean [cGy]
Modal [cGy]
Selections...
Grid
Type:
Print...
Export...
Close
3D-Photon
Proton
Dose to liver
Volume [cm³]
Dose [cGy]
Photon
Proton
Prescribed dose: 60.0 CGE
V10 : 69%
27%
V20: 57%
23%
V30: 15%
8%
Dmean:19.7Gy
8.4 CGE

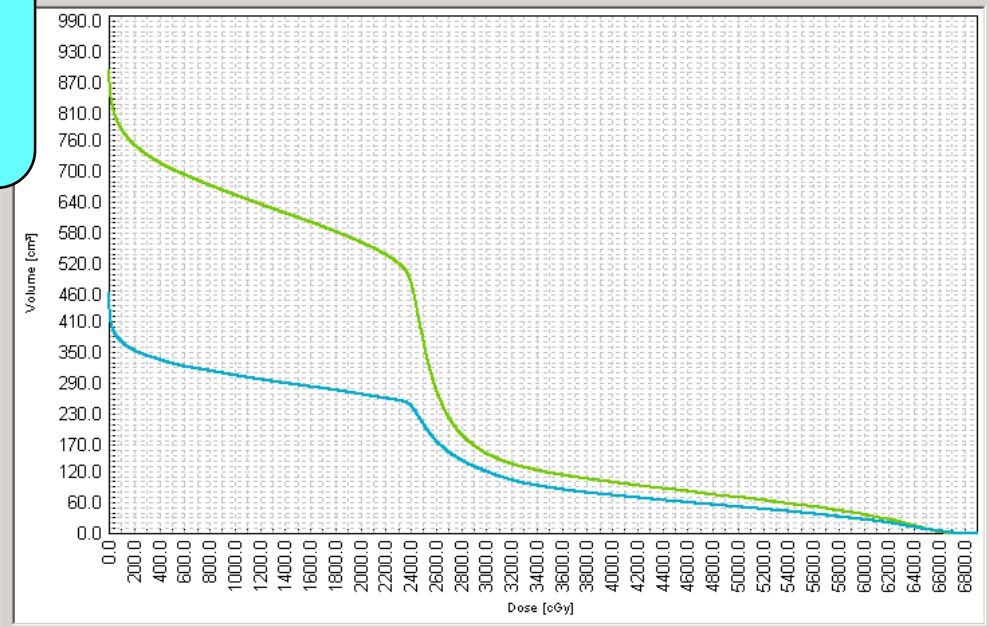


Plan Comparison with Dose Volume Histogram

Histogram

Plan	Structure		Prescr. Dose [cGy]	Treat. [%]	Cov. [%] / [%]	Volume [cm³]	Min [cGy]	Max [cGy]	Mean [cGy]	Modal [cGy]	Median [cGy]
☑ C1/Plan1 Sum11+21	Liver-PTV				100.0 / 100.0	1108.2	0.0	6750.9	1772.6	0.0	2077.8
☑ C1/Plan Sum11+31	Liver-PTV				100.0 / 100.0	1108.2	0.0	6898.6	929.3	0.0	0.0
☐ C1/Plan1 Sum11+21	Spinal Cor				100.0 / 98.3	32.3	0.0	0.0	0.0	0.0	0.0
☐ C1/Plan Sum11+31	Spinal Cor				100.0 / 98.3	32.3	0.0	2643.6	407.3	0.0	0.0

Selections...



☑ Grid

Type:
- ◉ Cumulative
- ○ Differential
- ○ Natural

Dose range [cGy]: 0 to 6900

Apply range

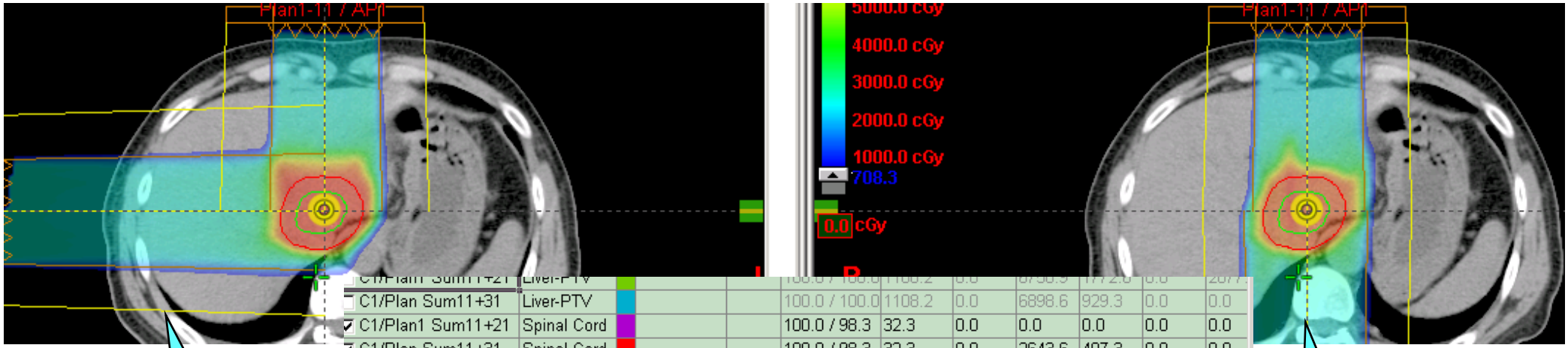
Print...

Export...

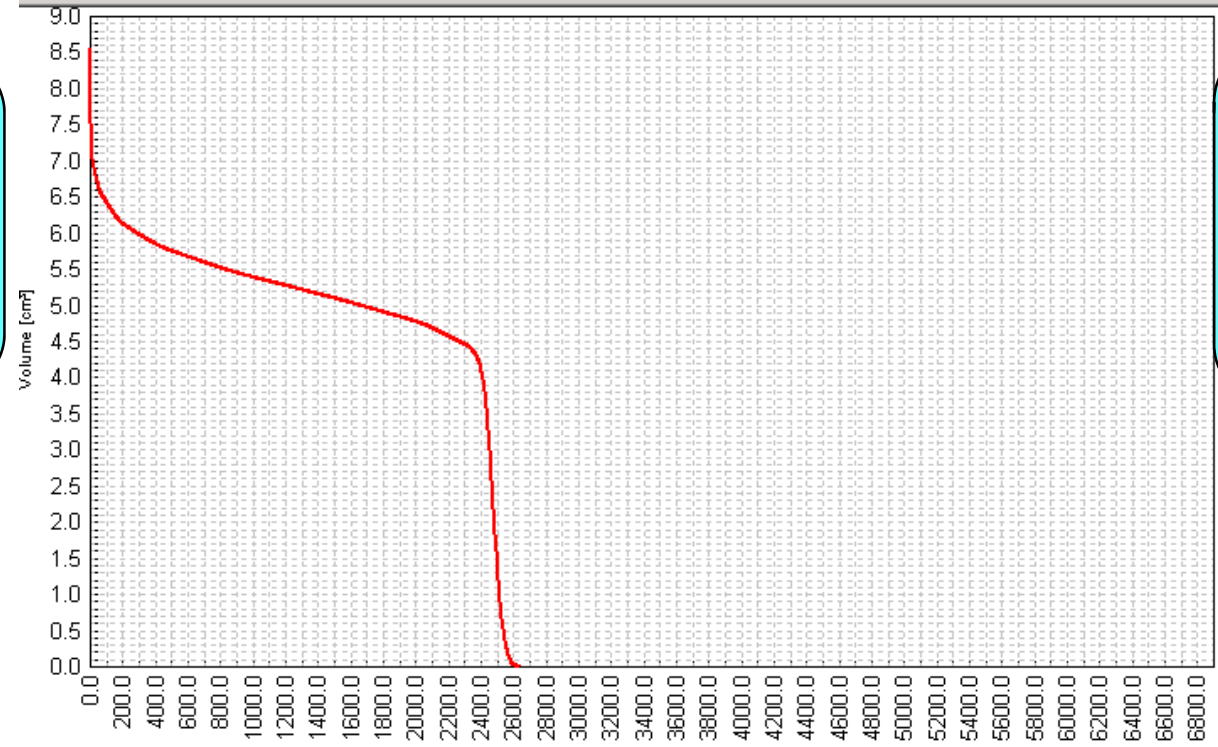
Close

Mean dose to liver: 17.7CGE

Mean dose to liver: 9.3CGE



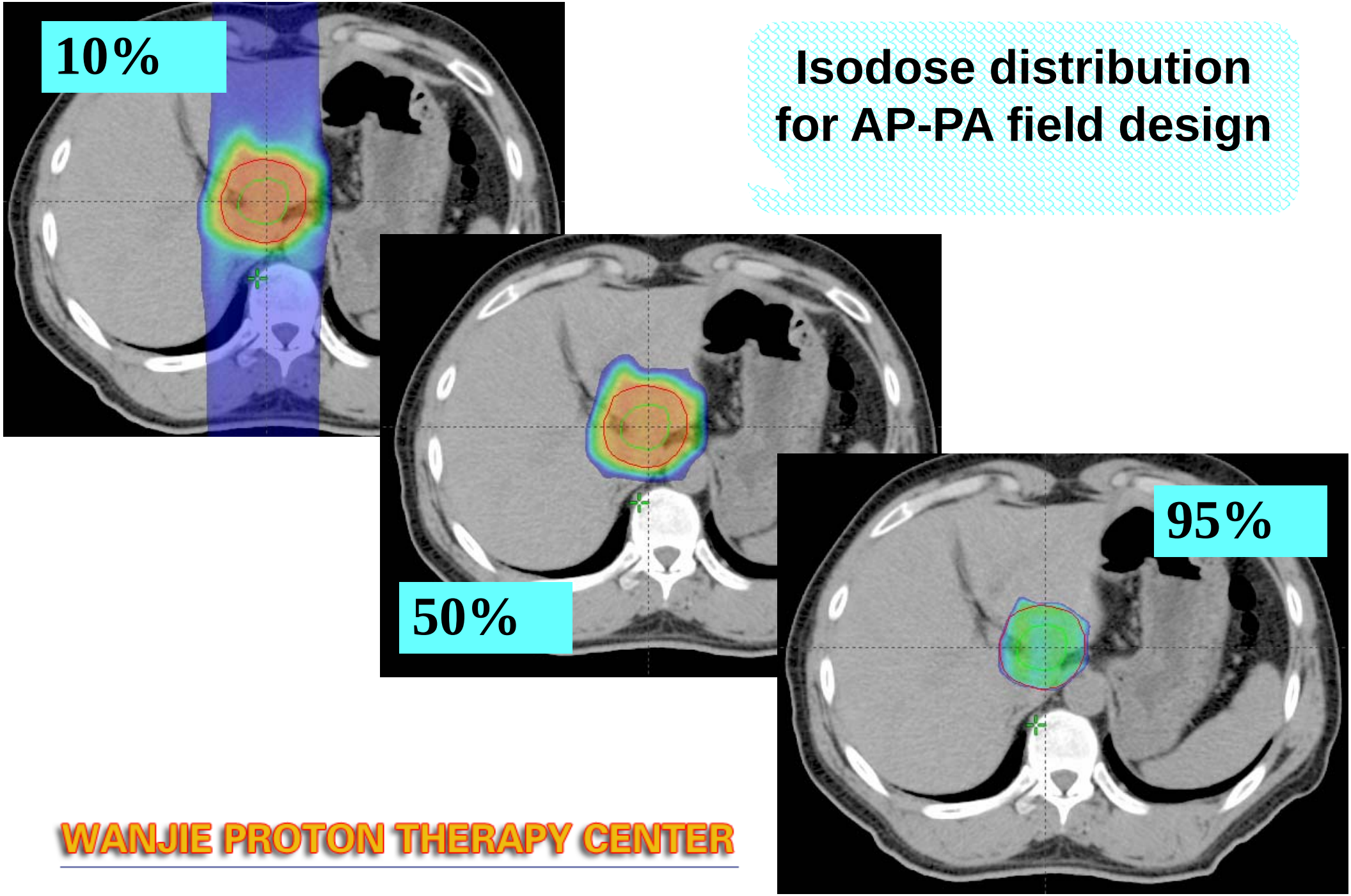
C1/Plan Sum11+31	Liver-PTV			100.0 / 100.0	1108.2	0.0	6898.6	929.3	0.0	0.0
C1/Plan1 Sum11+21	Spinal Cord			100.0 / 98.3	32.3	0.0	0.0	0.0	0.0	0.0
C1/Plan Sum11+31	Spinal Cord			100.0 / 98.3	32.3	0.0	2643.6	407.3	0.0	0.0



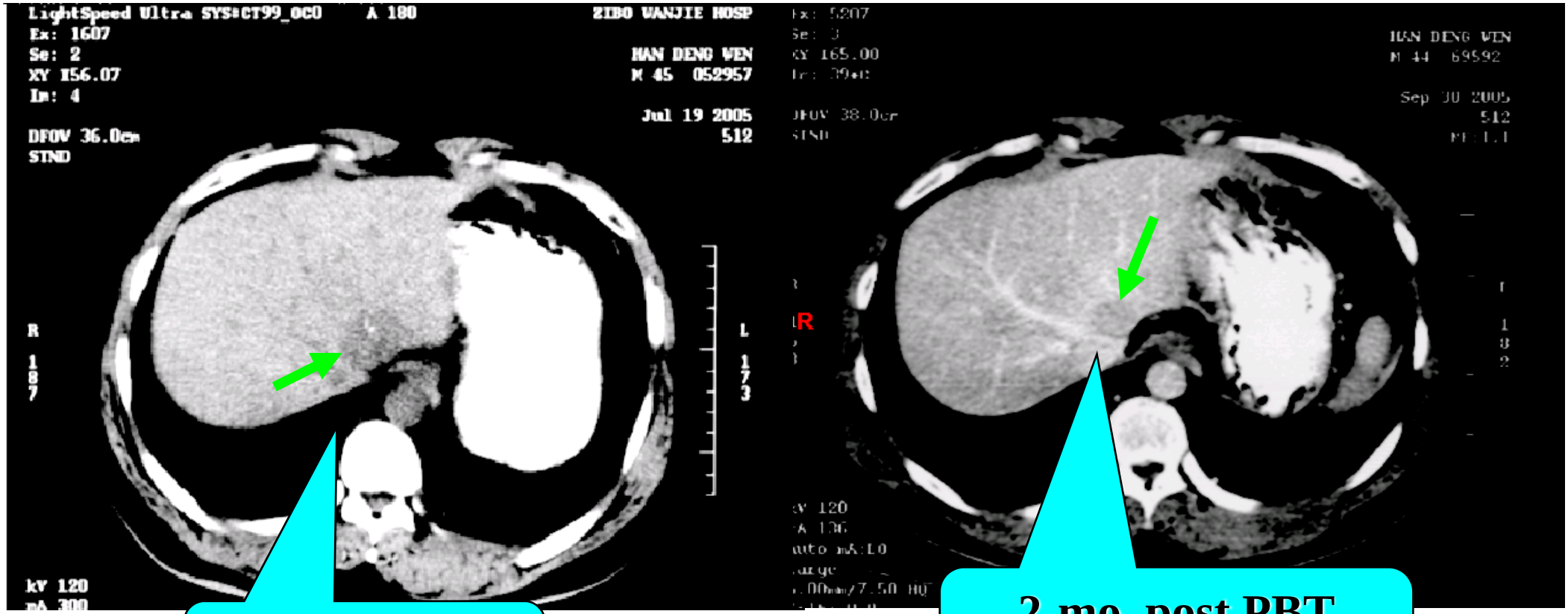
Dose to spinal cord: 0Gy

Maximum dose to spinal cord: 26.4CGE

Isodose distribution for AP-PA field design



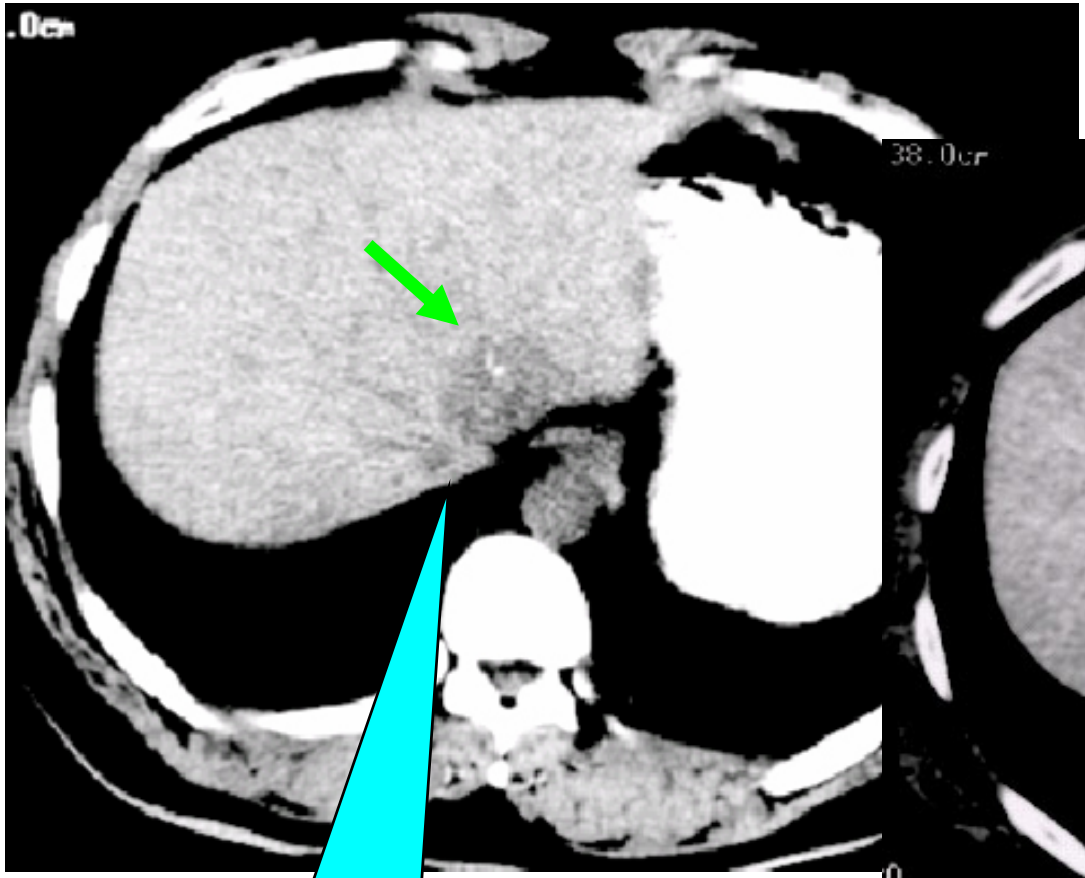
WANJIE PROTON THERAPY CENTER



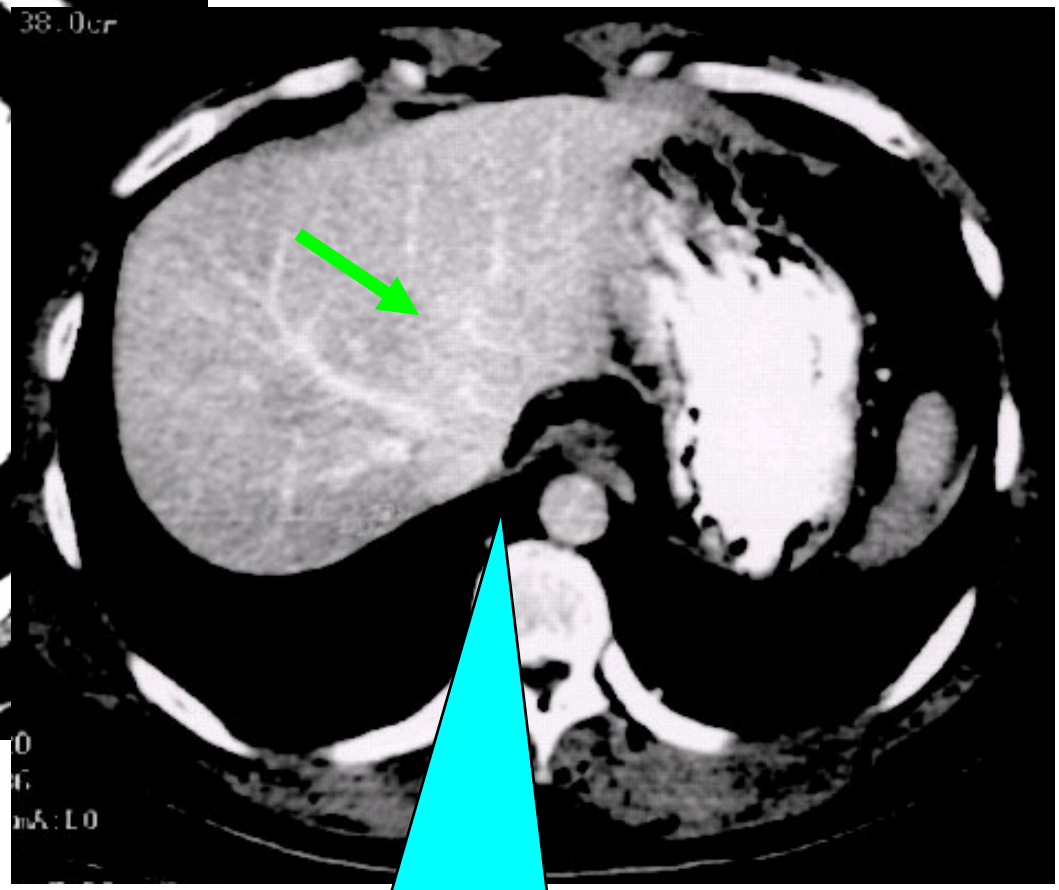
Before PBT

2-mo post PBT

WANJIE PROTON THERAPY CENTER



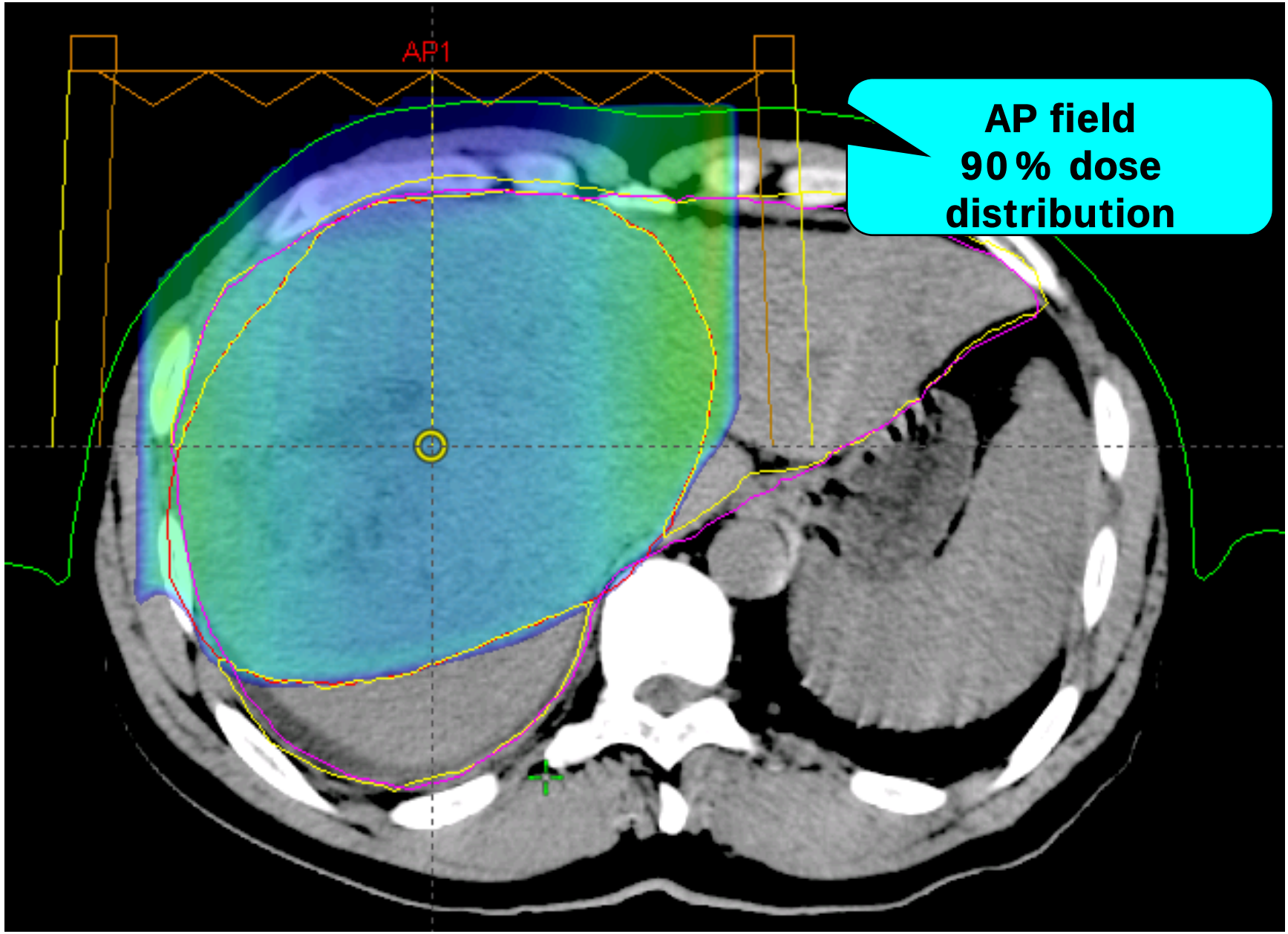
Before PBT

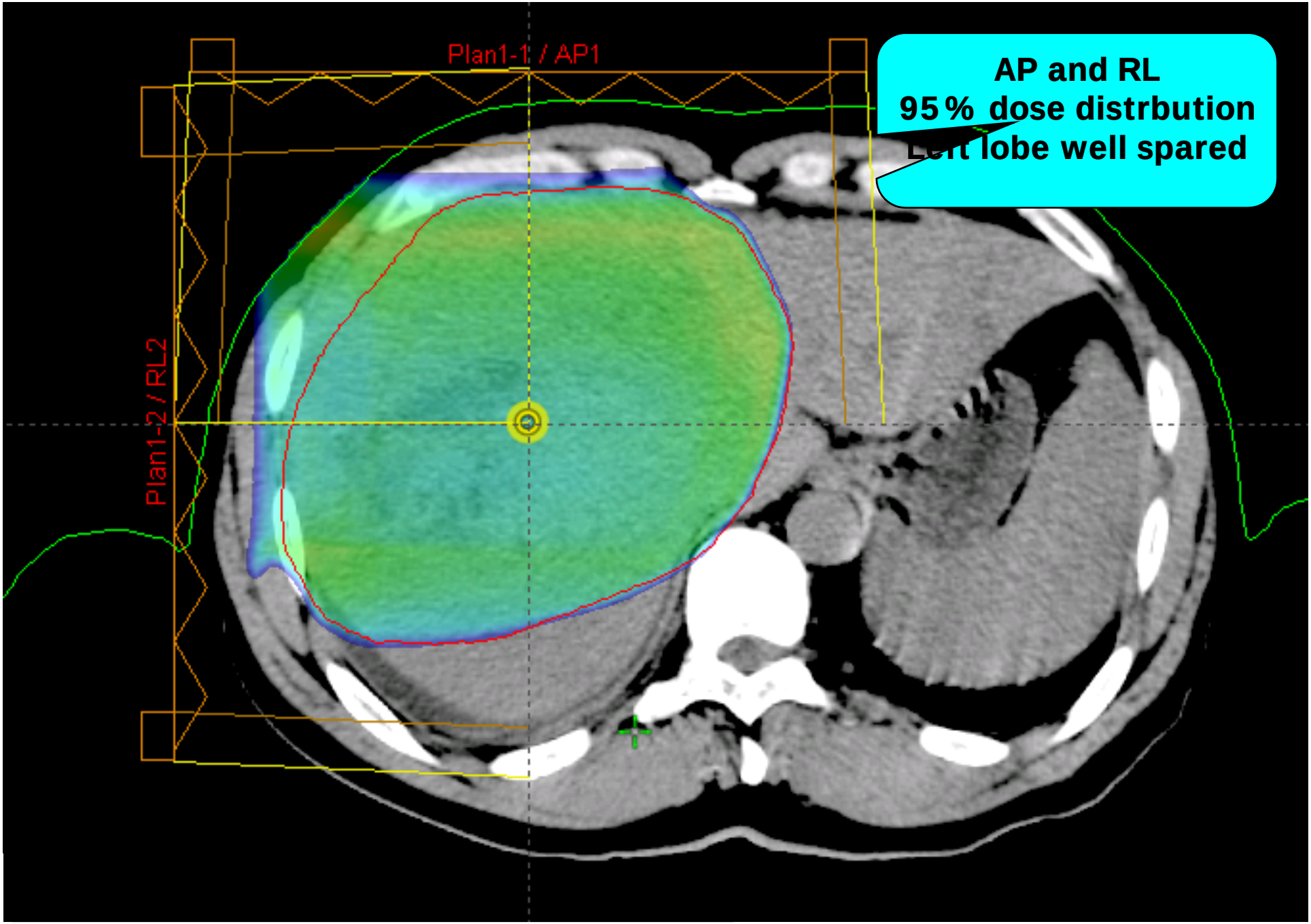


6 -mo after PBT

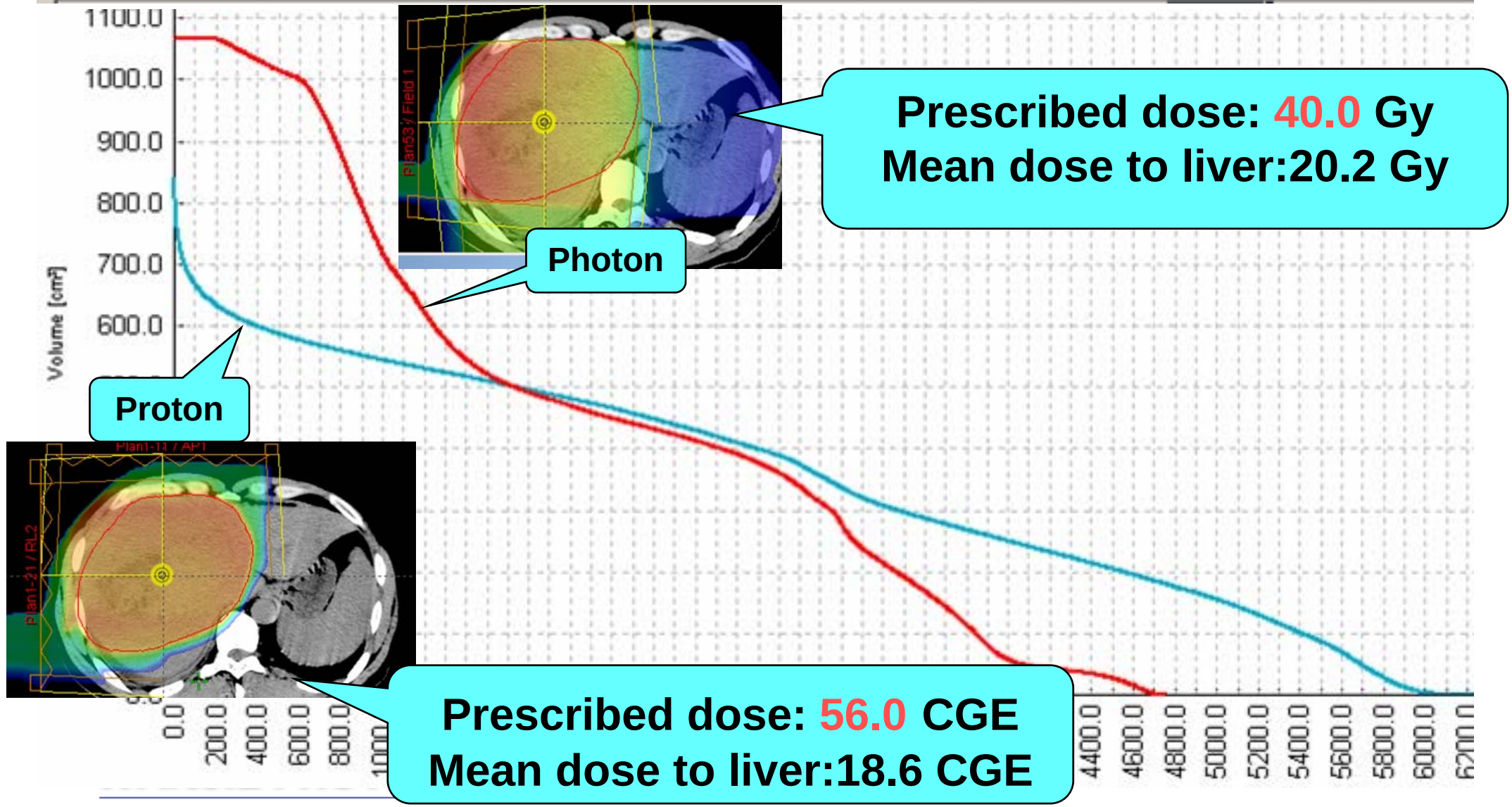
WANJIE PROTON THERAPY CENTER

Case #3, Male,42yr
locally advanced HCC,
AFP>1000ng/ml
Child A


AP1
AP field
90 % dose
distribution

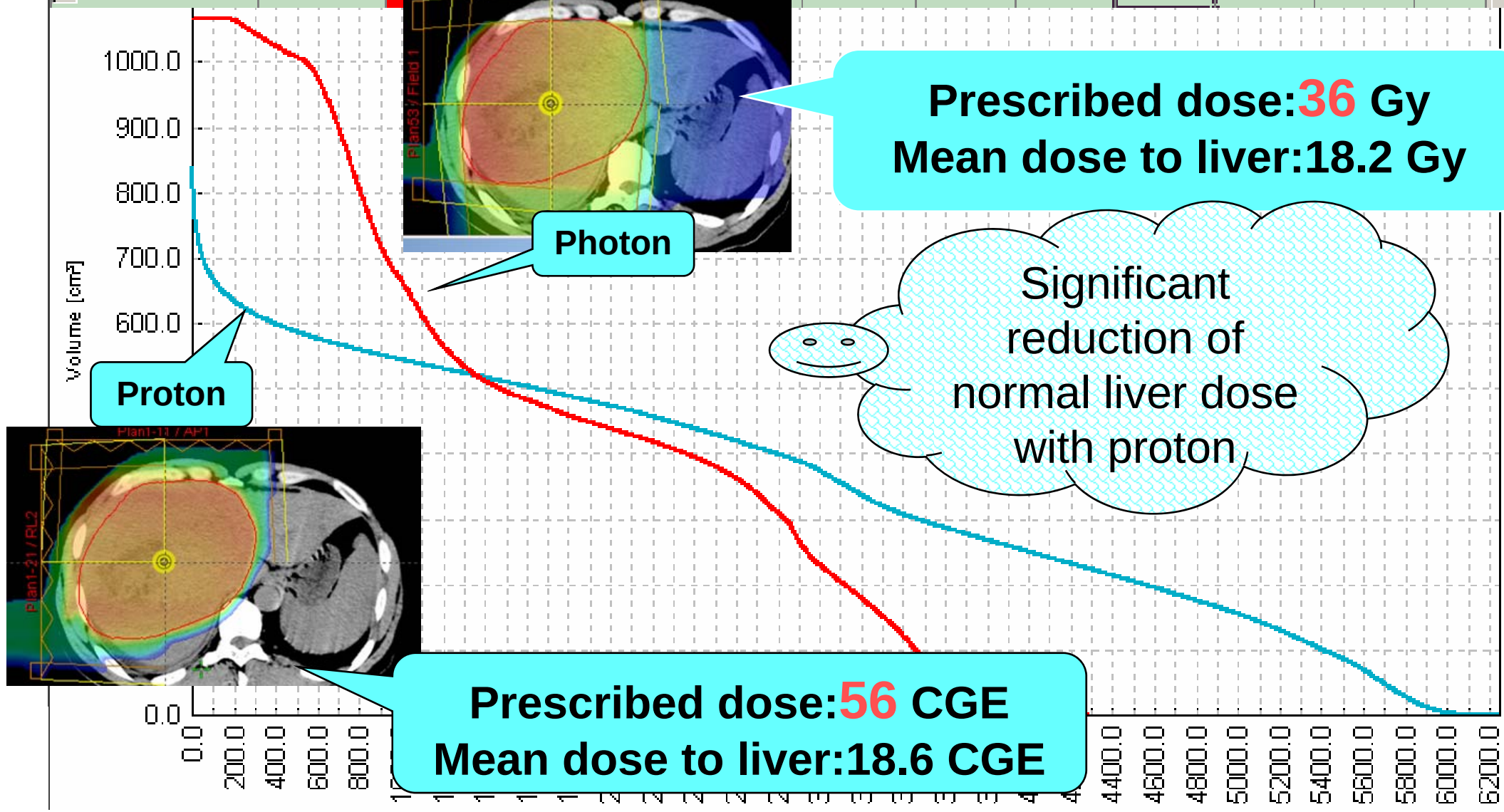

Plan1-1 / AP1
Plan1-2 / RL2
AP and RL
95% dose distrbution
Left lobe well spared

Plan	Structure		Prescr. Dose [cGy]	Treat. [%]	Cov. [%] / [%]	Volume [cm³]	Min [cGy]	Max [cGy]	Mean [cGy]	Modal [cGy]	Median [cGy]
☑ C1/Plan1 Sum	Liver-ctv				100.0 / 99.9	1139.3	0.0	6246.1	1864.4	0.0	671.1
☑ C2/Plan Sum3	Liver-ctv				93.6 / 100.5	1139.3	175.9	4754.9	2015.0	839.3	1446.8



Histogram

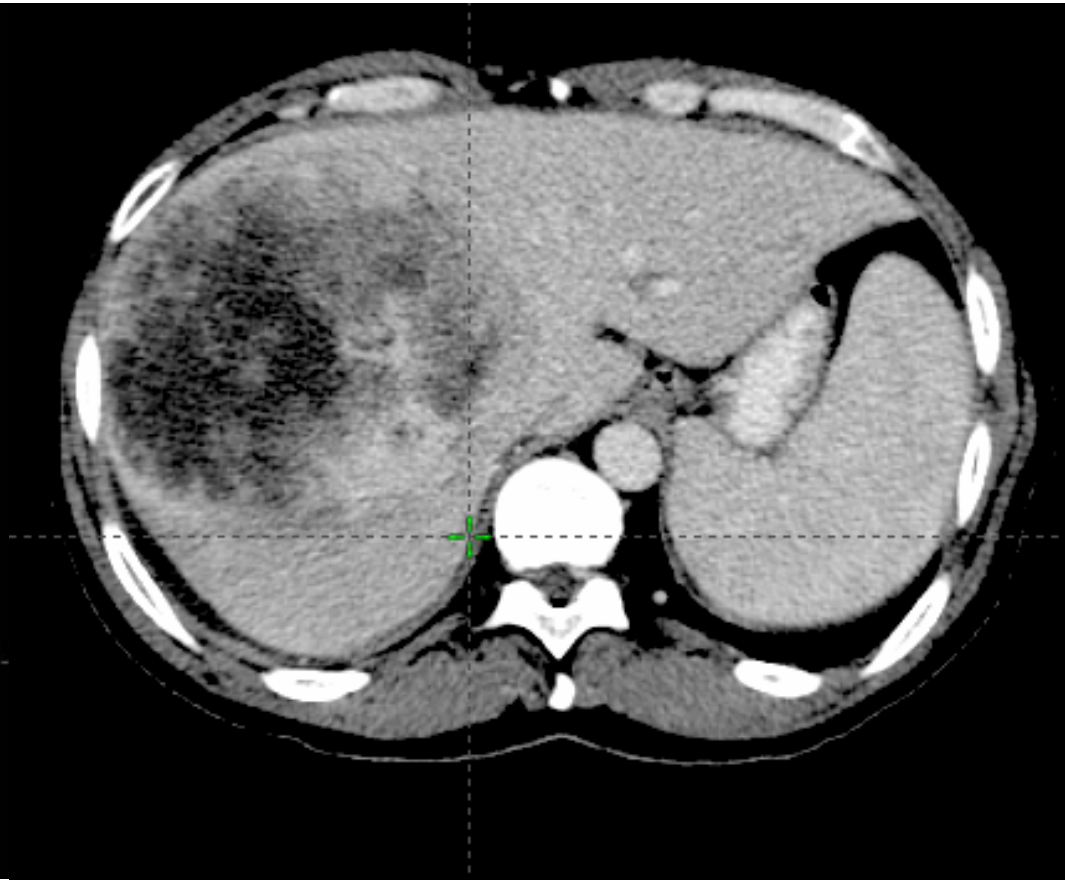
Plan	Structure		Prescr. Dose [cGy]	Treat. [%]	Cov. [%] / [%]	Volume [cm³]	Min [cGy]	Max [cGy]	Mean [cGy]	Modal [cGy]	Median [cGy]	STD
☑ C1/Plan1 Sum	Liver-ctv				100.0 / 99.9	1139.3	0.0	6246.1	1864.4	0.0	671.1	2101.
☑ C2/Plan Sum3	Liver-ctv				[illegible]	1139.3	158.3	4280.5	1813.9	597.9	1302.4	1145.



- It was reported(Park W et al) that radiation dose seems to be a significant prognostic factor in RT response for HCC
- More than 50 Gy had a significant response

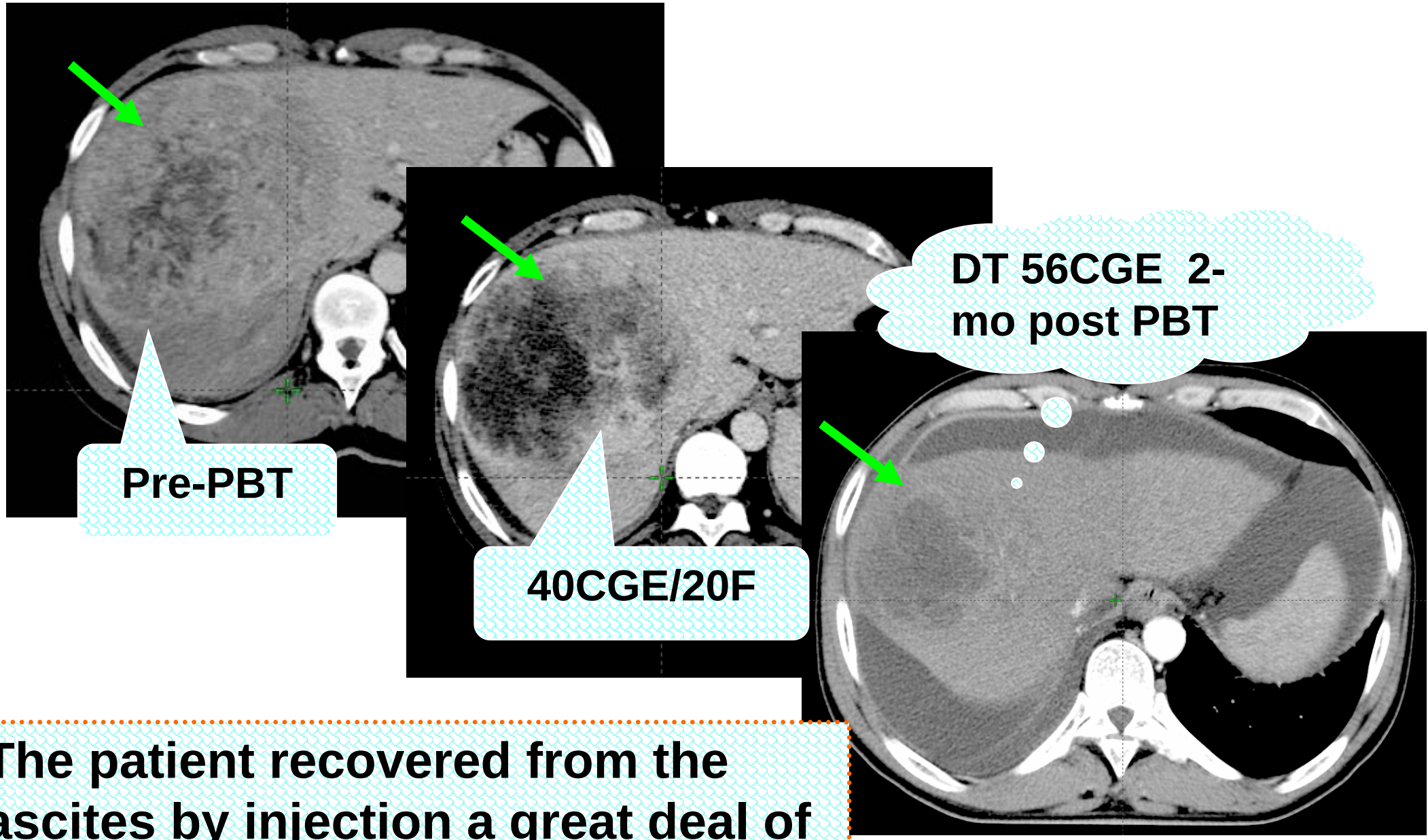
Int J Radiat Oncol Biol Phys. 2005 Mar 15;61(4):1143-50

Pre-PBT

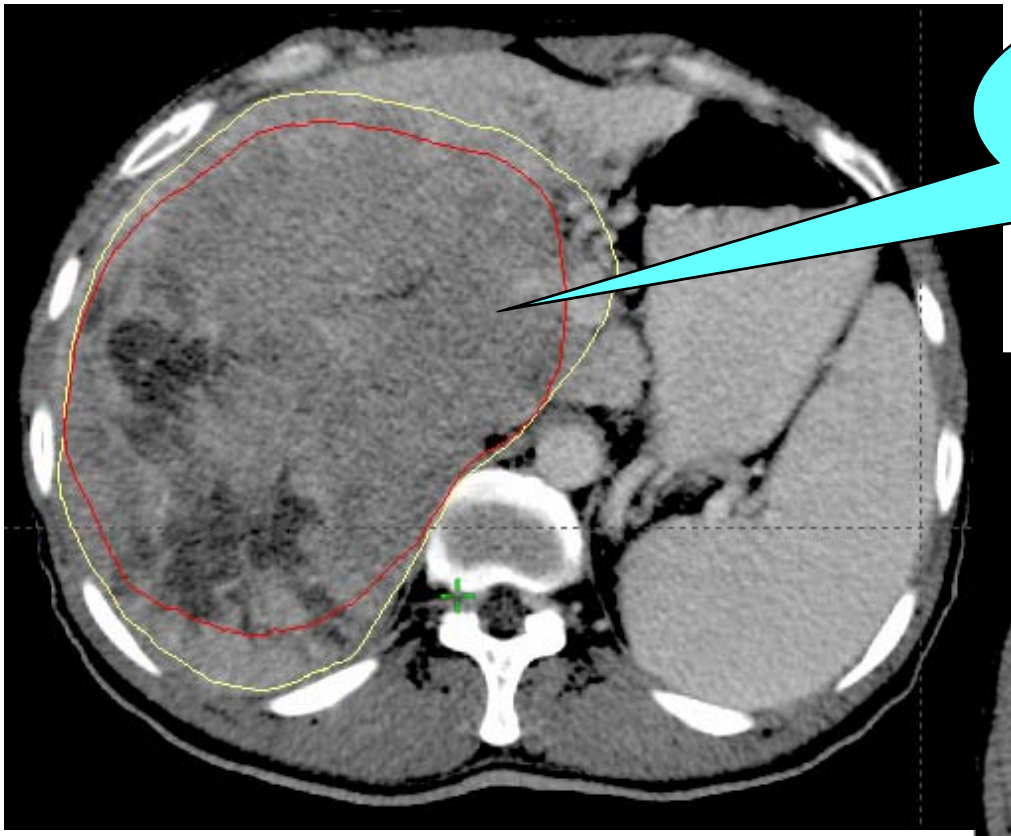


During PBT, 40CGE/20F, 5F/w

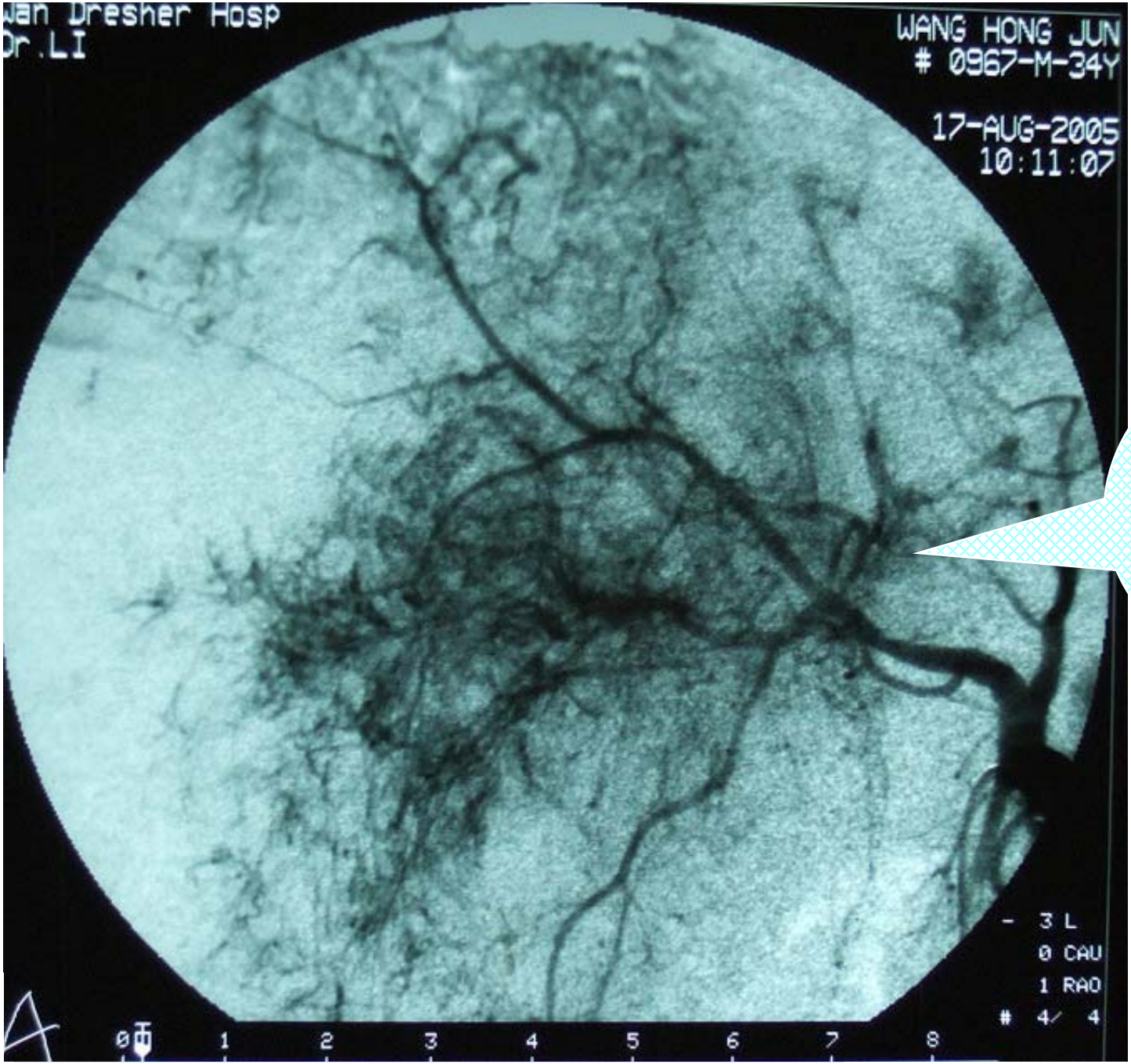
WANJIE PROTON THERAPY CENTER



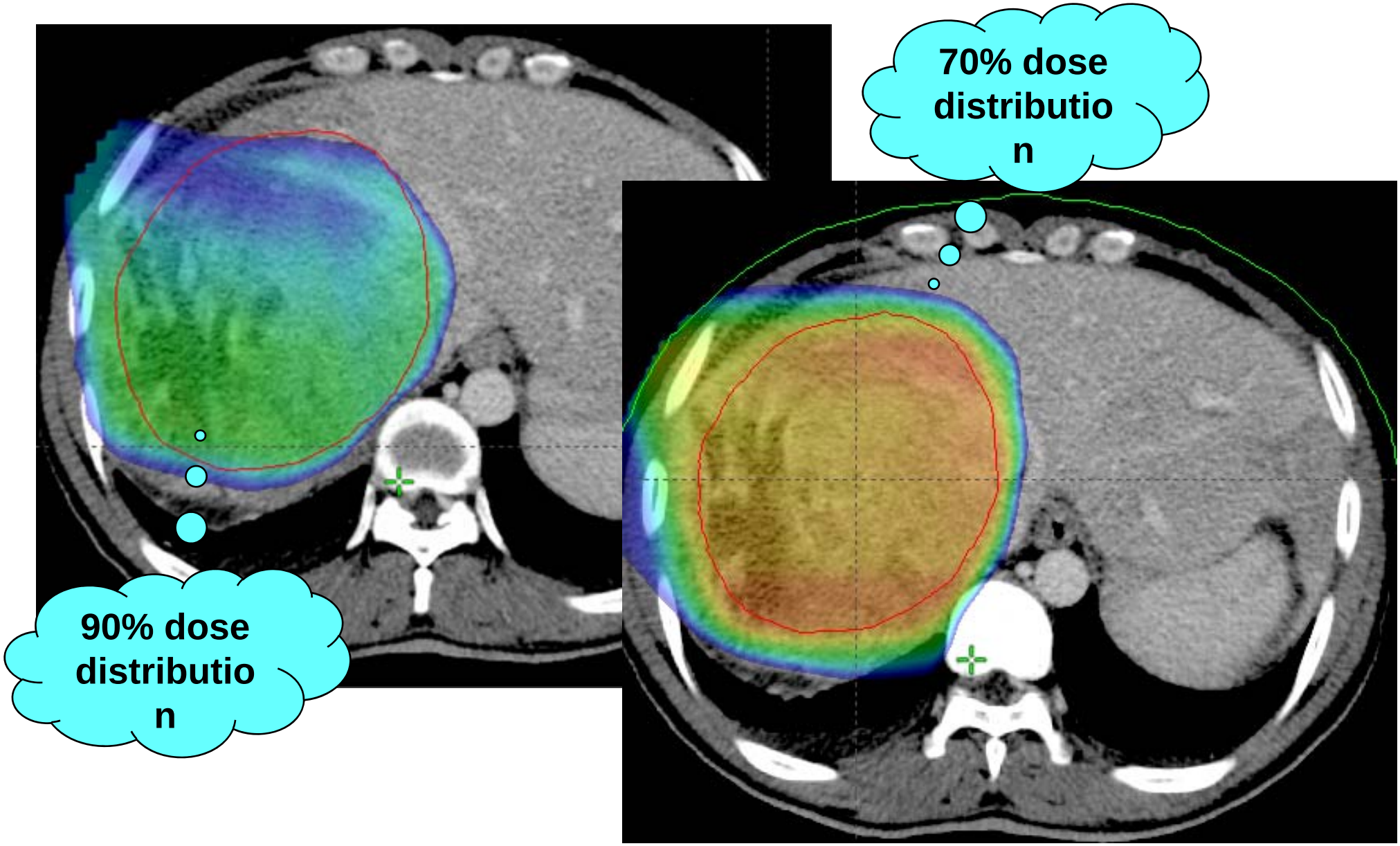
The patient recovered from the ascites by injection a great deal of albumin and other medicines .



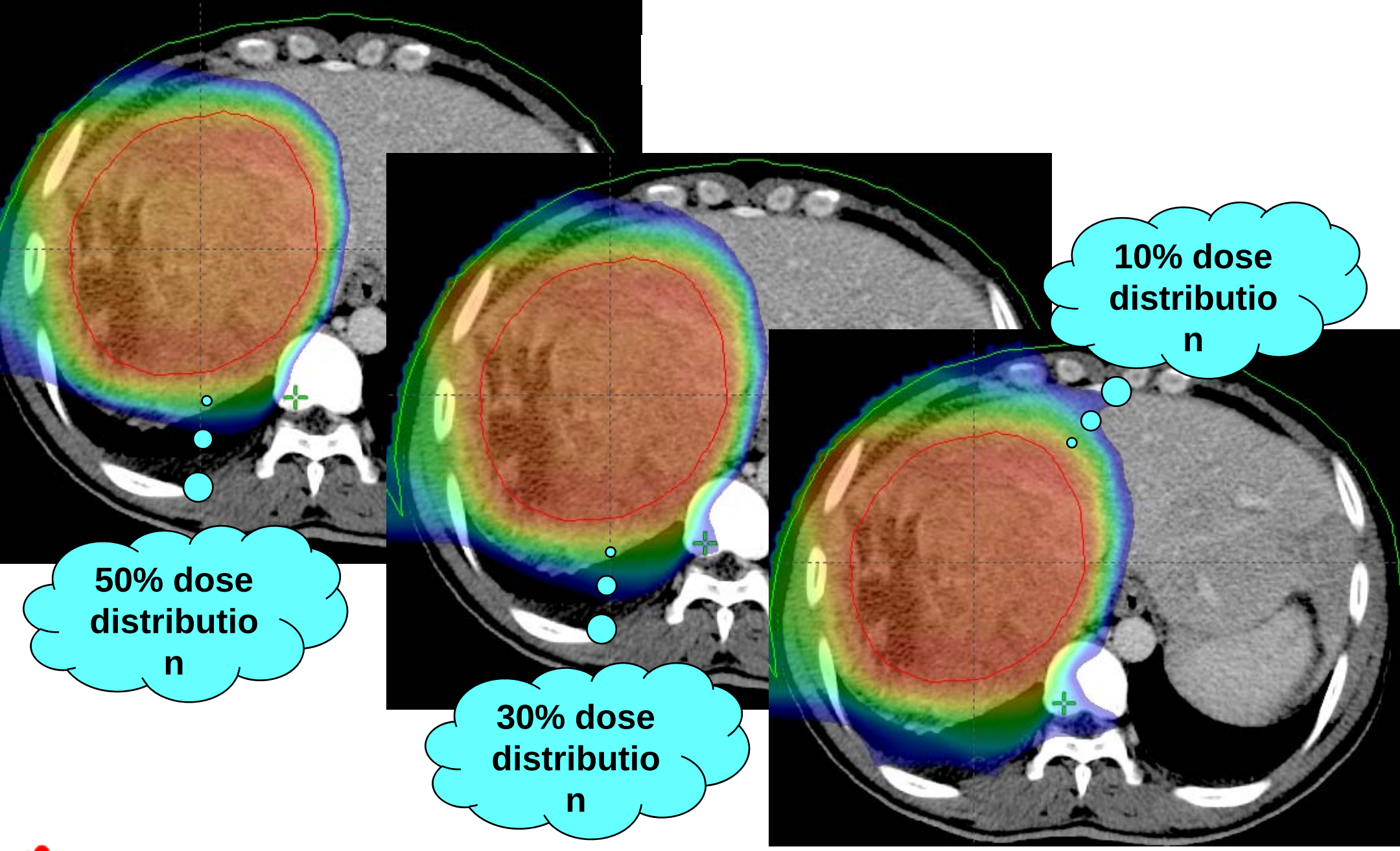
Case # 4,
34yr,M, GTV
2000cc



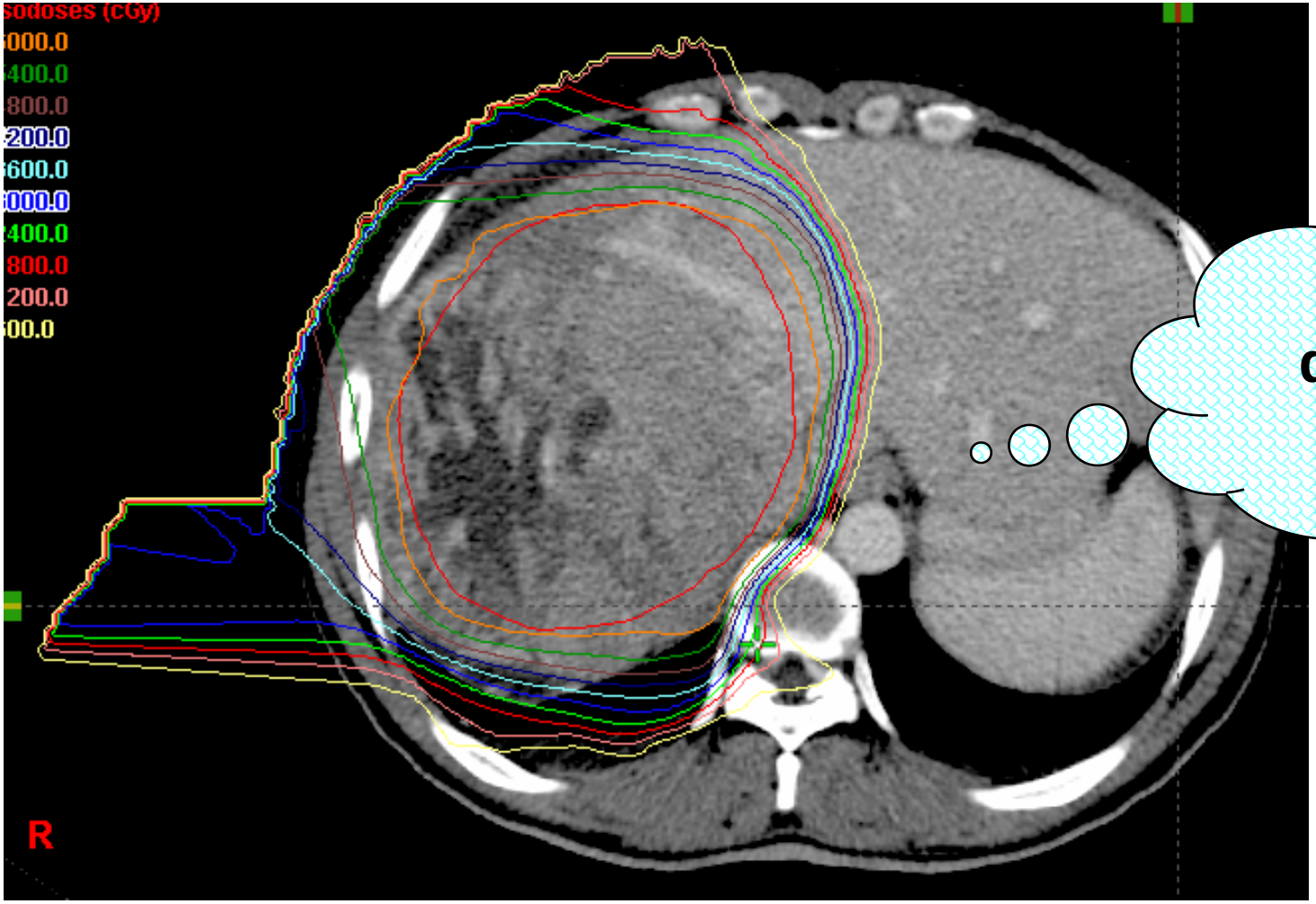
Pre- PBT Idology Showed Iodized oil retention



WANJIE PROTON THERAPY CENTER

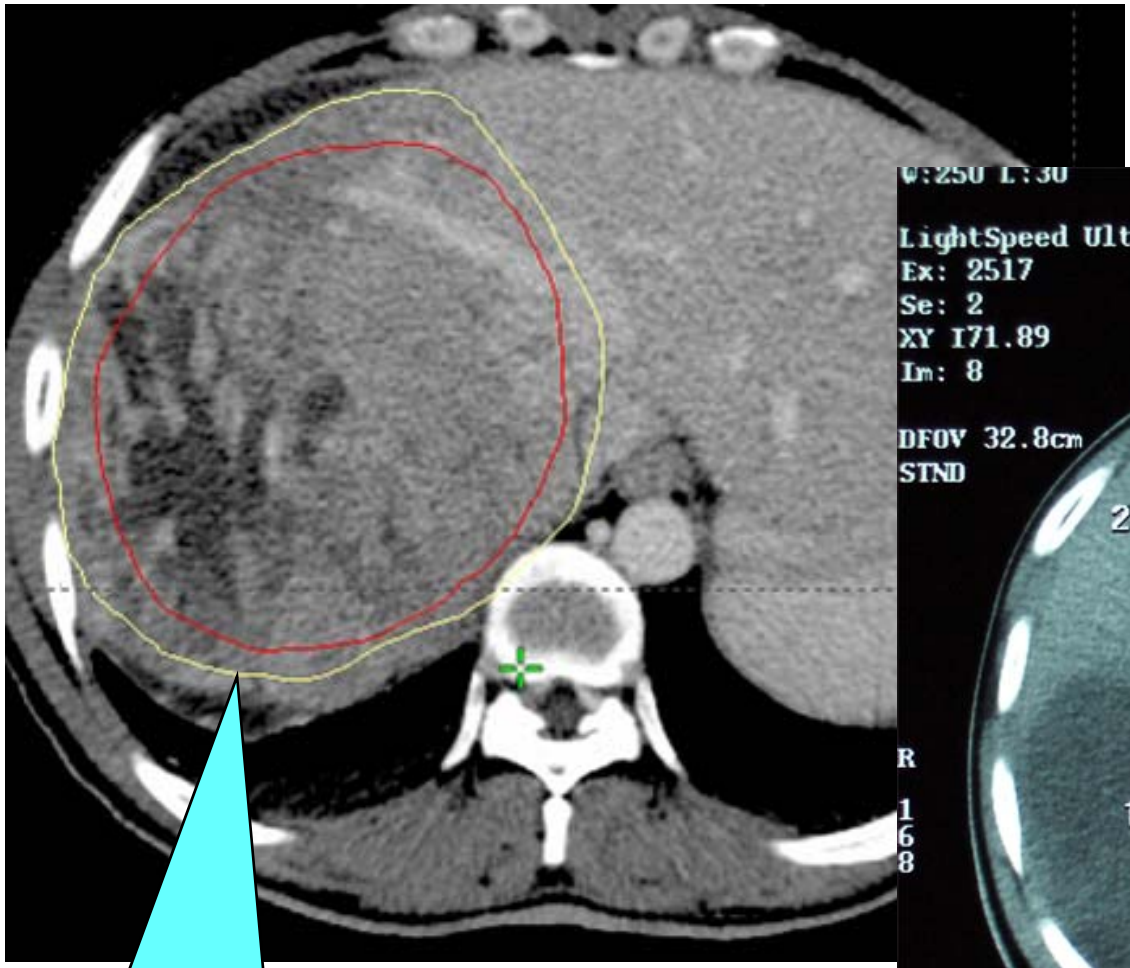


WANJIE PROTON THERAPY CENTER

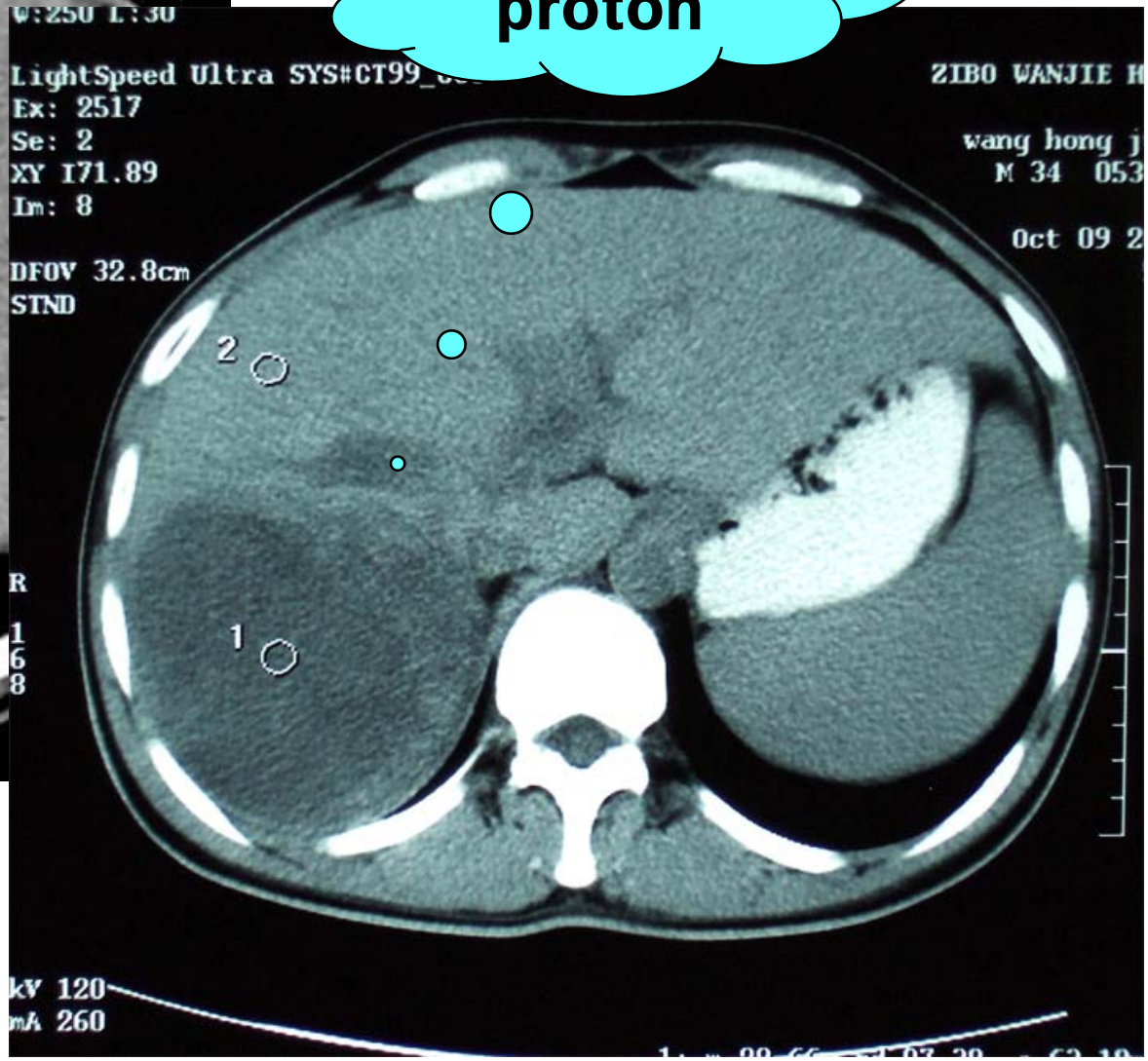


Isodose distribution
DT 44.0
CGE/22F

WANJIE PROTON THERAPY CENTER

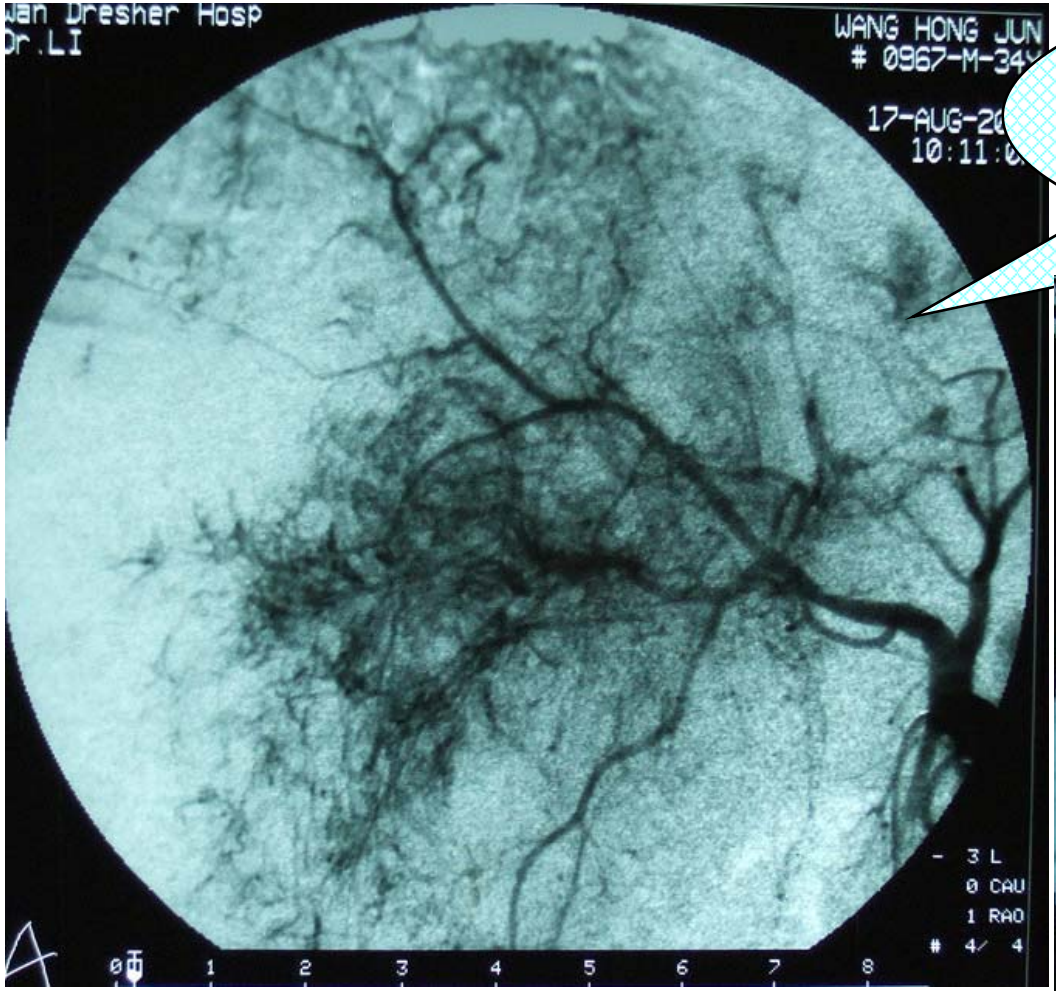


Pre-proton



2-mo Post proton

WANJIE PROTON THERAPY CENTER



Pre-PBT
Retained iodized oil

Post PBT

Results

- Median duration of follow-up :12-mo (2~23-mo)
- Stage I , II:

  CR: 35.3%(6/17) (six-mo later)

  1-yr local control rate : 94.1%(16/17)

  1-yr survival rate : 88.2%(15/17)
- Stage IIIA, IIIB:

  Response rate was 81.8%

- 2 patients with Child-Pugh Grade C died
  - - One died from liver function failure
  - - The other died from hemorrhage and distant metastasis

Side - effects

- Cutaneous reaction: grade I
- Upper gastrointestinal: grade 0~1
- No radiation induced pneumonitis was found

- Pain of thoracic wall was found in 1 patient 6-month post PBTand then released 9-month later
- Incomplete pyloric obstruction in 1 patient
  - -eat only semi liquid diet
  - -recovered after medication (dexamethasone and antibiotics)

Prognostic Factors Affecting Overall Survival

- Better prognosis
  - -early stage
  - -small GTV
  - -Child Pugh Grade A
- Poor prognosis
  - -Child-Pugh Grade B and C
  - -portal vein thrombosis
  - -lymph node metastasis

Much attention should be given

A. The patient with
   - -multiple tumors
   - -diffused

     It is difficult to encompassed in a single irradiation field

B. Ascites around the liver

C. The tumor is located near the gastrointestinal tract

D. Distant metastases are found

- Proton beam therapy plays an important role in the radical treatment of early stage HCC.
- The radiation dose is a significant factor for increasing the objective tumor response and the survival rate when treating HCC.

- As for the locally advanced HCC, proton treatment significantly reduced dose to normal liver, stomach, kidney,and spinal cord.
- Proton therapy with dose escalation may translate to better local control and survival without increasing toxicities in HCC.

Thanks for your attention
Welcome to China