Proton Beam Therapy for Hepatocellular Carcinoma

Li Jiamin, MD
Hepatocellular 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.
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 challenging.
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

May 18-23, 2007  PTCOG46, Wanjie, Zibo
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 (IMRT)

Local control and survival rate improved

While

- Massive normal liver tissue damage was found
- Radiation-induced liver disease (RILD) were also reported

May 18-23, 2007

PTCOG46, Wanjie, Zibo
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

May 18-23, 2007  PTCOG46, Wanjie, Zibo
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

- 39 patients with HCC were treated at Wanjie Proton Therapy Center

May 18-23, 2007  PTCOG46, Wanjie, Zibo
- 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 diseases (advanced cirrhosis 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: 2.0-4.0CGE/13-28F, 5d/w

Total dose: from 52.0 to 72.0CGE

May 18-23, 2007  PTCOG46, Wanjie, Zibo
Case # 1
68Y, male
AFP>400ng/ ml
Child grade A

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

May 18-23, 2007  PTCOG46, Wanjie, Zibo
isodose color wash

Beam1  AP
Beam2  RL

May 18-23, 2007  PTCOG46, Wanjie, Zibo
Isodose lines

May 18-23, 2007
PTCOG46, Wanjie, Zibo
95% dose distribution
May 18-23, 2007
PTCOG46, Wanjie, Zibo
Mean dose to liver: 3.44 CGE
V30 = 5.53%
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

May 18-23, 2007  PTCOG46, Wanjie, Zibo
Follow up

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

May 18-23, 2007  PTCOG46, Wanjie, Zibo
Case # 2
45y, M, Child A
AFP 400ng/ml
4.1x2.7cm
2-mo later
1.9x2.0cm
Proton treatment planning

- PTV = GTV + 10~15mm (AP 10mm, CC 15mm)
- GTV 16.2cm³, PTV 94.4cm³
- DT60CGE/20F, RBE = 1.1, 5F/W, AP, RL
- 95% isodose line to cover PTV
- Mean dose to liver 14CGE

May 18-23, 2007

PTCOG46, Wanjie, Zibo
Proton 3D-Photon

Dose to liver

**Photon**
- \( V_{10} : 69\% \)
- \( V_{20} : 57\% \)
- \( V_{30} : 15\% \)
- \( D_{\text{mean}} : 19.7 \text{ Gy} \)

**Proton**
- \( V_{10} : 27\% \)
- \( V_{20} : 23\% \)
- \( V_{30} : 8\% \)
- \( D_{\text{mean}} : 8.4 \text{ CGE} \)

**Prescribed dose:** 60.0 CGE
Mean dose to liver: 17.7CGE

Mean dose to liver: 9.3CGE
Dose to spinal cord: 0Gy

Maximum dose to spinal cord: 26.4CGE
Isodose distribution for AP-PA field design

10%  50%  95%
Before PBT

2-mo post PBT

May 18-23, 2007
PTCOG46, Wanjie, Zibo
Case #3, Male, 42 yr
locally advanced HCC,
AFP > 1000 ng/ml
Child A
AP field
90% dose
distribution
AP and RL
95% dose distribution
Left lobe well spared
Prescribed dose: **40.0 Gy**  
Mean dose to liver: **20.2 Gy**

Prescribed dose: **56.0 CGE**  
Mean dose to liver: **18.6 CGE**
Prescribed dose: **36 Gy**  
Mean dose to liver: **18.2 Gy**

**Significant reduction of normal liver dose with proton**

Prescribed dose: **56 CGE**  
Mean dose to liver: **18.6 CGE**
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.

Pre-PBT

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

May 18-23, 2007

PTCOG46, Wanjie, Zibo
The patient recovered from the ascites by injection a great deal of albumin and other medicines.
Case # 4, 34yr,M, GTV 2000cc
Pre-PBT Idolography showed iodized oil retention
May 18-23, 2007

PTCOG46, Wanjie, Zibo
Isodose distribution
DT 44.0
CGE/22F
Pre-proton

May 18-23, 2007

2-mo Post proton

PTCOG46, Wanjie, Zibo
Pre-PBT
Retained iodized oil

Post PBT

May 18-23, 2007  PTCOG46, Wanjie, Zibo
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

May 18-23, 2007  PTCOG46, Wanjie, Zibo
Side-effects

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

May 18-23, 2007  PTCOG46, Wanjie, Zibo
- Pain of thoracic wall was found in 1 patient 6-month post PBT and 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

May 18-23, 2007
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

May 18-23, 2007  PTCOG46, Wanjie, Zibo
The benefit from the proton beam in treating Hepatocellular Carcinoma is encouraging......

May 18-23, 2007

PTCOG46, Wanjie, Zibo
● 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.

May 18-23, 2007  PTCOG46, Wanjie, Zibo
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

May 18-23, 2007
PTCOG46, Wanjie, Zibo