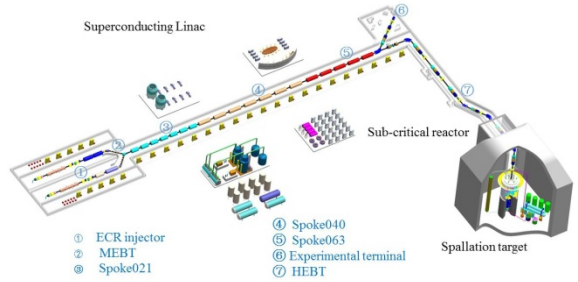
Heavy-ion Cancer Therapy in China

Institute of Modern Physics, CAS

Guoqing XIAO



Oct. 26. 2018, Lanzhou

Outlines

01 History Review and Background

02 Progress of Demon Facility

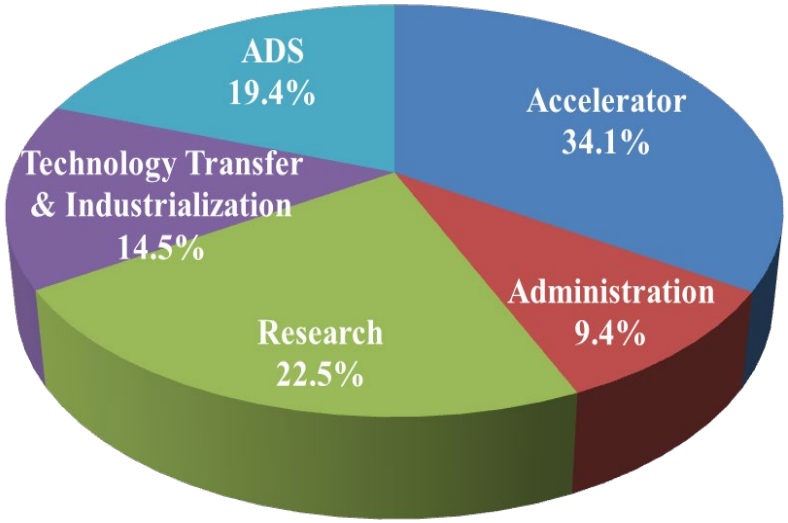
03 Future Perspectives

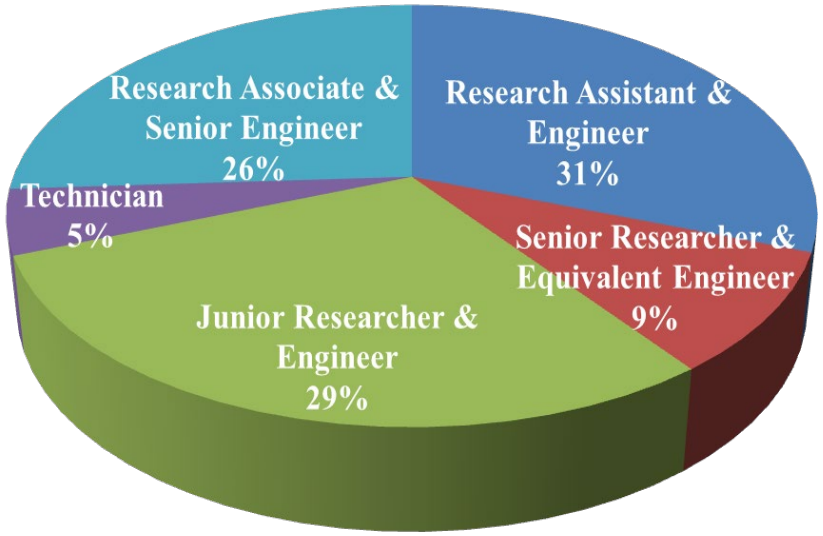
IMP and Lanzhou

IMP was founded in 1957 in Lanzhou city, which is located the banks of the yellow river with a population of ~3M.

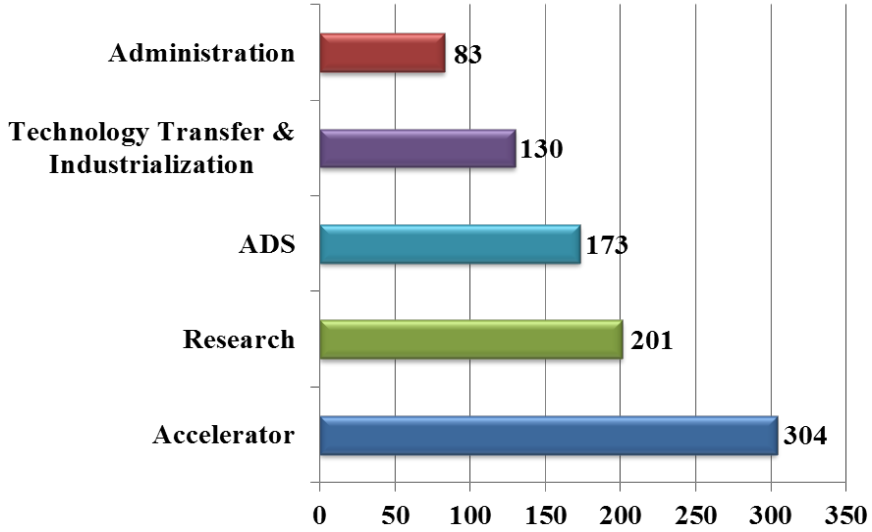
Human Resources

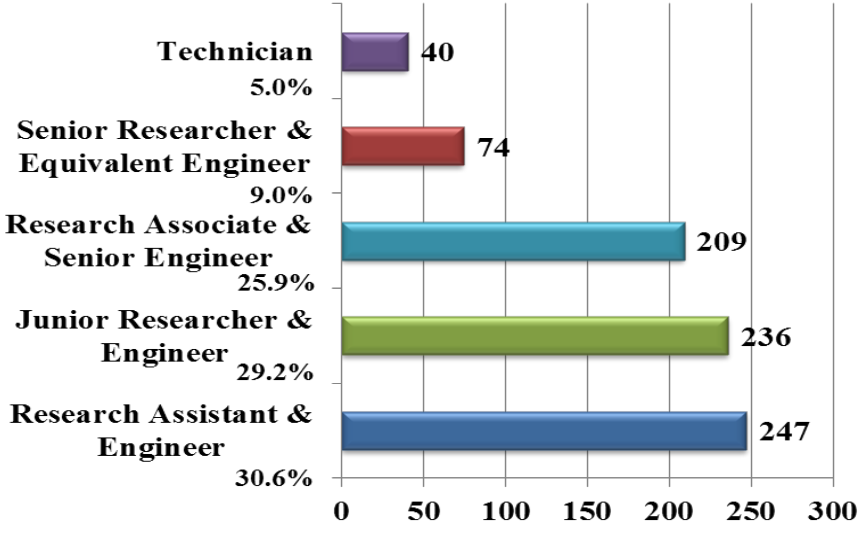
900 employees: half are under 35-years old. 350 postgraduate students





Staff distributions in the departments (left) and in academic titles (right)

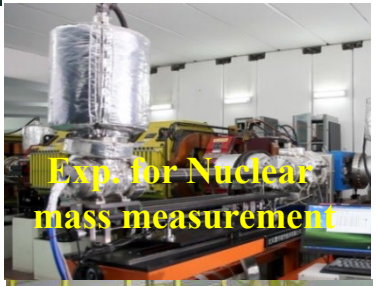


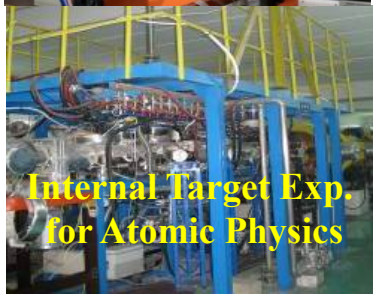


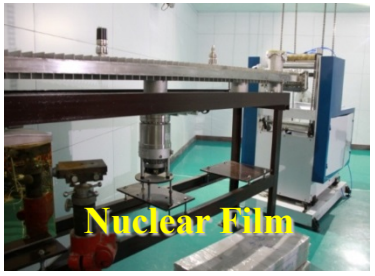
Heavy Ion Research Facility in Lanzhou (HIRFL)

National Laboratory of Heavy Ion Accelerator in Lanzhou(1991)

Main Setups







About 20 apparatuses for heavy-ion physics and applications

Scientific Activities

- **Fundamental researches on nuclear & atomic physics**
  - Reactions and structures of nuclei
  - Nuclear spectroscopy
  - Properties of asymmetric nuclear matter
  - Chemistry of super-heavy elements, and synthesis of new isotopes
  - Key reactions in stellar evolution
  - Spallation & nuclear data for ADS
  - High energy density physics
  - Hadron physics
  - HCI interaction with laser, electron, molecule, and surface
- **Applications with protons, heavy ions and micro-beams**
  - ADS, heavy-ion ICF, nanowire and membrane-tech., radiation-resistant material, …
  - Radiation medicine and biology: tumor therapy, mutation breeding, …
  - Detectors development and devices evaluation for satlite and space industry…
- **Detector and electronics development**
  - Si detectors: Si(Au), Si(Li), Si-strip
  - Scintillator detectors: CsI, LaBr3, plastic sci., liquid sci. …
  - Gaseous detectors: IC, TPC, PPAC, MWPC, MWDC, MicroMeGAS, GEM, …
- **Key technique development related to high intensity accelerators**
  - ECR, Linac, superconducting cavities and magnets,…

IMP and Related Centers

IMP main campus
National Laboratory of Heavy Ion Accelerator in Lanzhou (NLHAL)

IMP and Related Centers

IMP main campus
National Laboratory of Heavy Ion Accelerator in Lanzhou (NLHAL)

Center of Heavy Ion Therapy at Wuwei city

R&D Center of Heavy Ion Applications, New Campus in Lanzhou

Center of Heavy Ion Therapy at Lanzhou

WuWei
288km
BaiYin
76km
LanZhou

Industrialization Pilot Base at Baiyin city

Lab of Superconducting Technology at Baiyin city

Lab of Spallation Target at Baiyin city

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Center of Nuclear Energy For ADANES

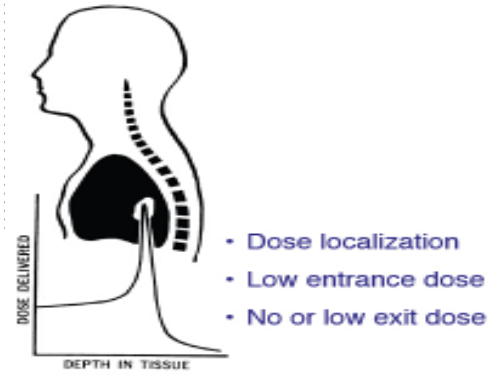
Center of Heavy Ion Science Branch of IMP at Huizhou

Research Center of Advanced Energy and materials at Huizhou

History of heavy ion cancer therapy

HISTORY

1946 — First Proposal
Robert Wilson proposed the use of Bragg Peak for radiation therapy.



1977 — First Patient
The first patient was treated with carbon ion in Phase I trials at Lawrence Berkeley National Laboratory (LBNL).

1994 — First Dedicated Facility
The National Institute of Radiol ogical Sciences (NIRS) in Japa n built the first heavy-ion accel erator for medical use in the w orld, termed HIMAC in Chiba.

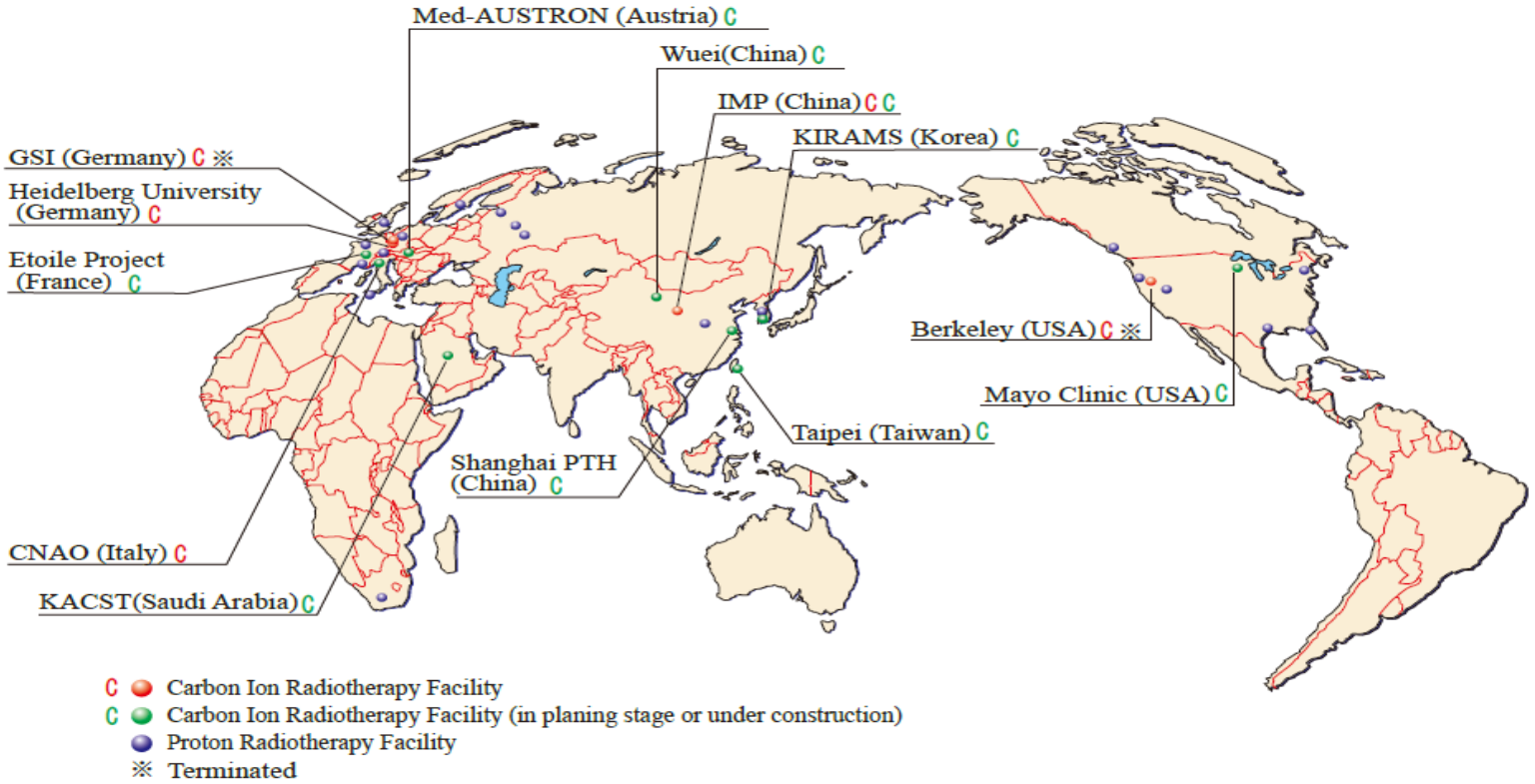
1997 — Active Scanning
GSI developed an active ion beam delivery system called raster scanning. a target volume can be painted in three dimensions with a tightly focused pencil beam.

2006 — Ion Therapy in CHINA
From November 2006 to July 2013, 213 patients were treated with carbon ions at Heavy Ion Research Facility in Lanzhou (HIRFL),China.

Up to now — Developing Prolifically
At present, more than six facilities in operation for carbon-ion radiotherapy in the world.

- Inverted depth-dose distribution
- High relative biological effectiveness (RBE)
- …

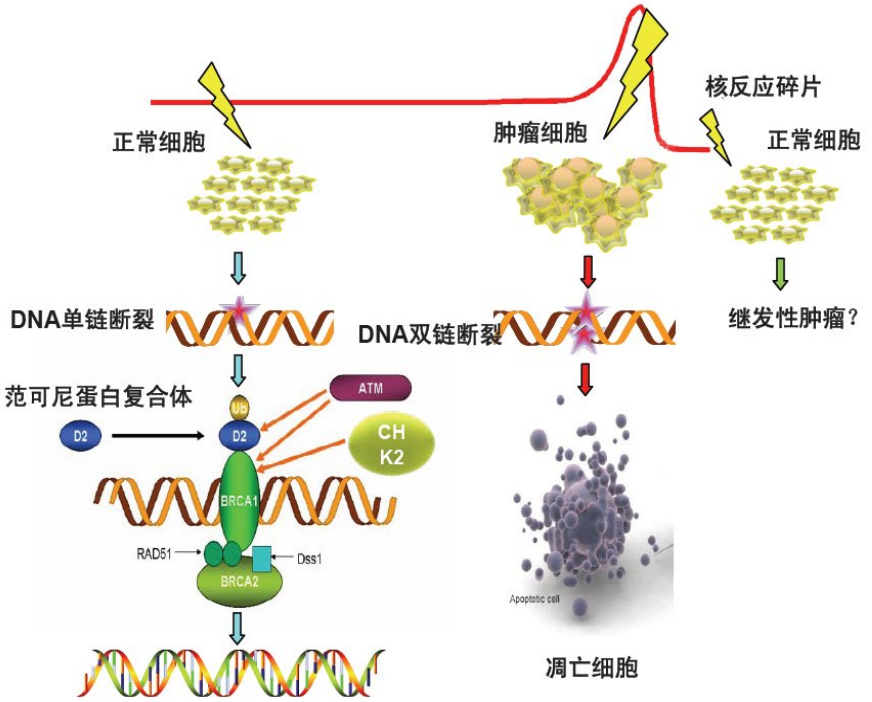
Charged Particle Therapy Facilities in the World



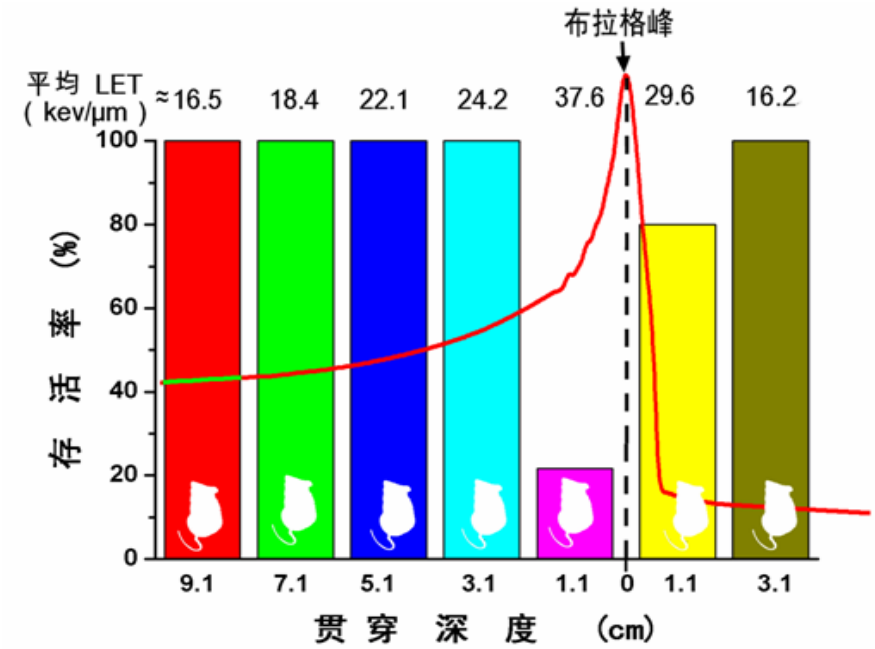
- Europe: 2 in Germany (operation)， 1 in Italy (operation), 1 in Austria (construction)
- Japan: 6 facilities in operation， 13 for recent plan， 50~60 for long-term plan
- China: Shanghai (operation), Lanzhou and Wuwei

Heavy Ion Beam: Ideal Radiation for Radiotherapy

- DNA double strand breaks: Bragg peak
- Sparing normal tissue to the most extent



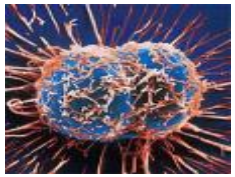
DNA double stand break

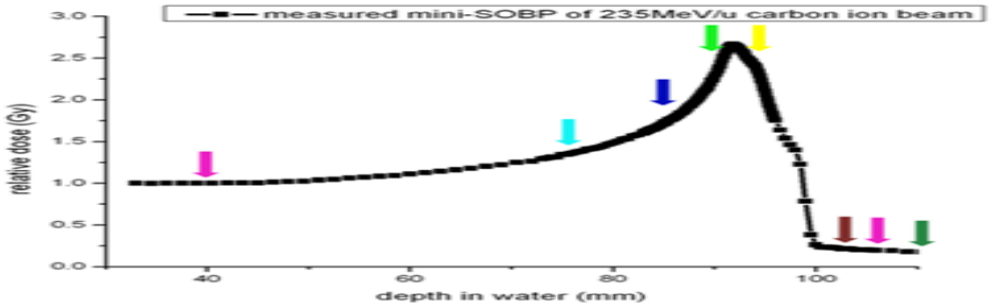


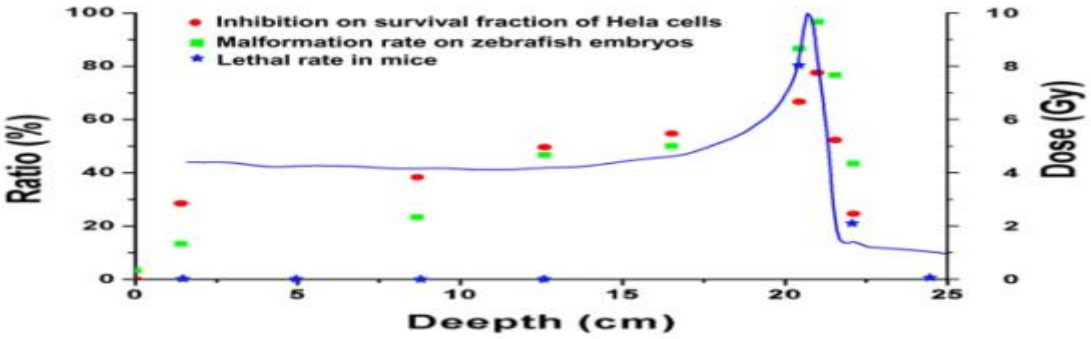
DNA double stand break

Pre-clinical Study

Biological effect along the penetration depth of carbon ion beam



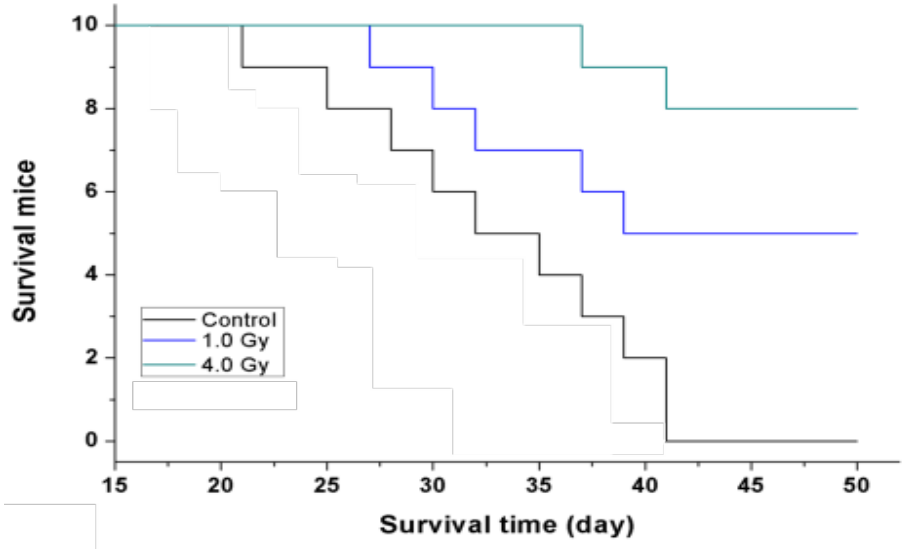


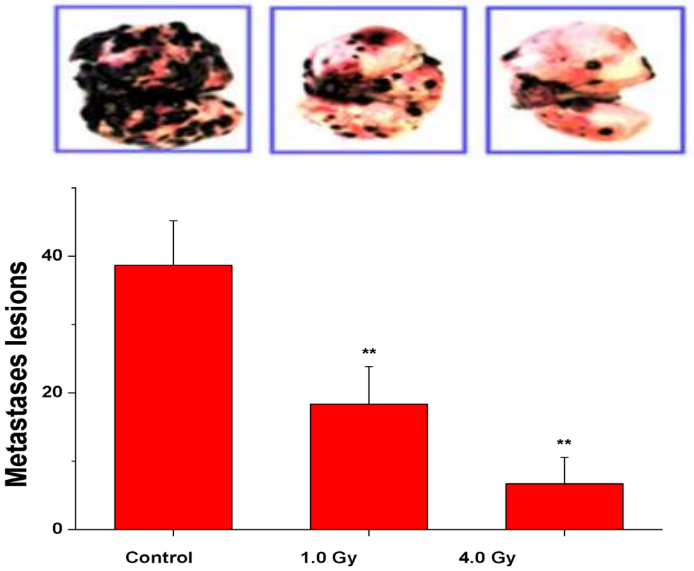


Biological effect and physical energy deposition show agreement

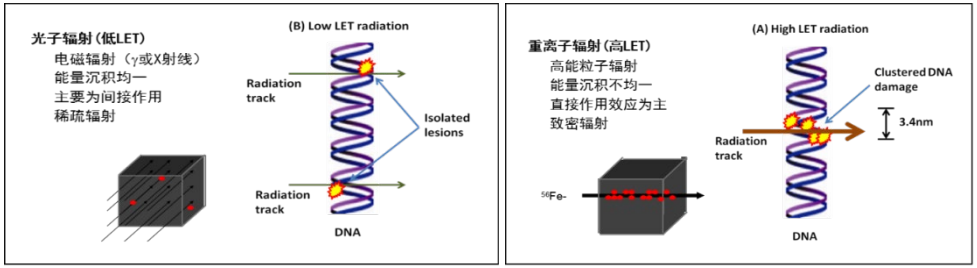
Pre-clinical Study

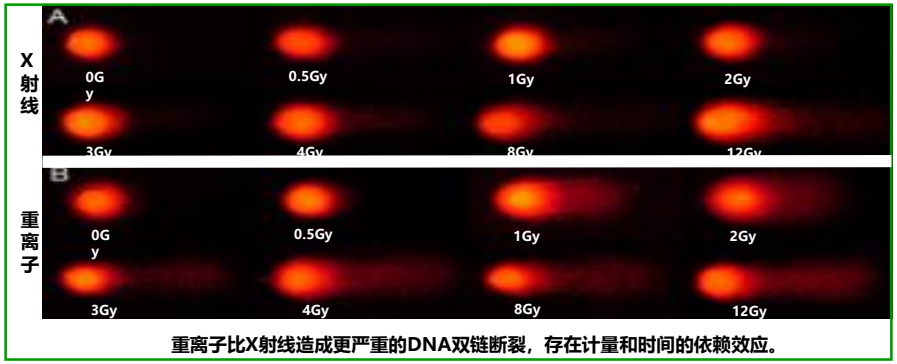
Inhibition of metastasis potential by carbon ion beam



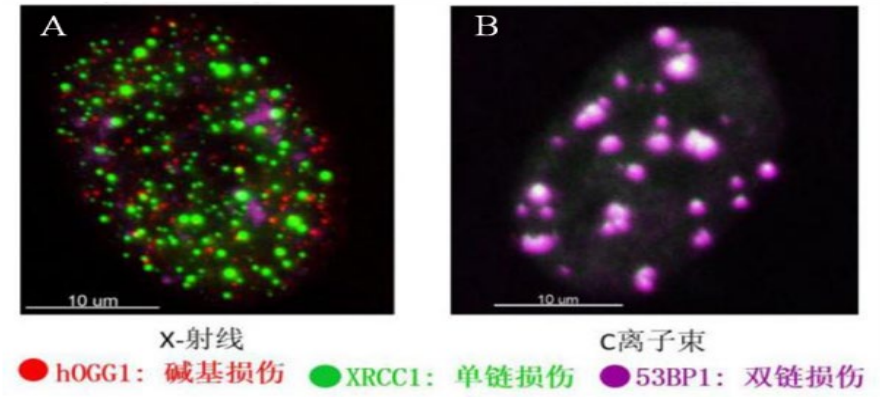


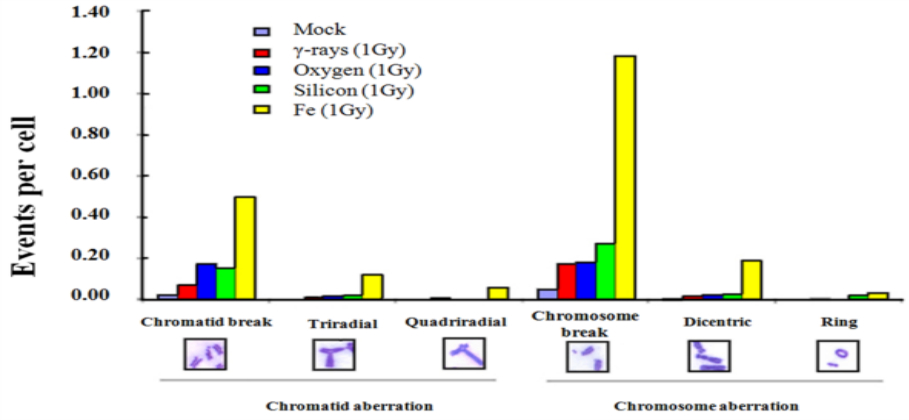
Pre-clinical Study





重离子比X射线造成更严重的DNA双链断裂，存在计量和时间的依赖效应。

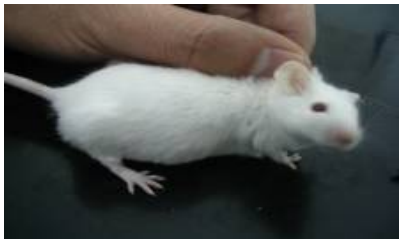




- DNA cluster damage
- Difficult to repair, strong cell-killing effect

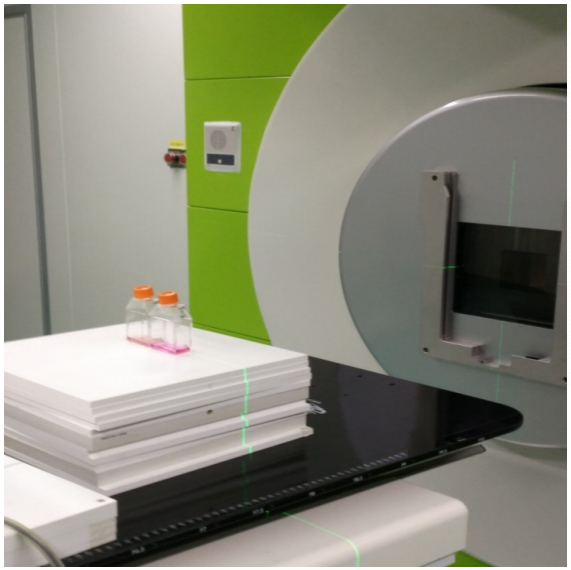
Pre-clinical Study

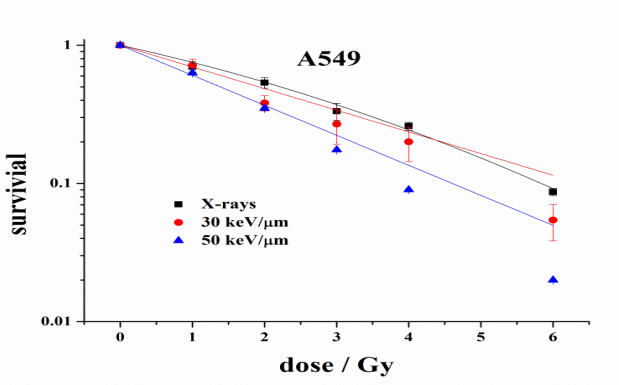
Mice experiment with 80MeV/u carbon ion beam

	control(0Gy)	10Gy	15Gy
Before irradiation			
7 days after irradiation			

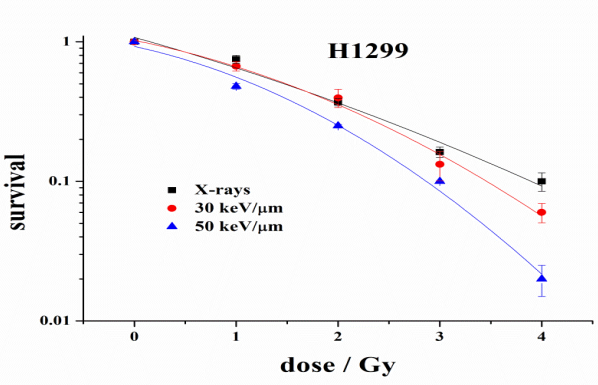
Cell experiment at HIMM RBE measurement

Lung cancer cell experiments with 30keV/um□ 50keV/um carbon ions and X-rays





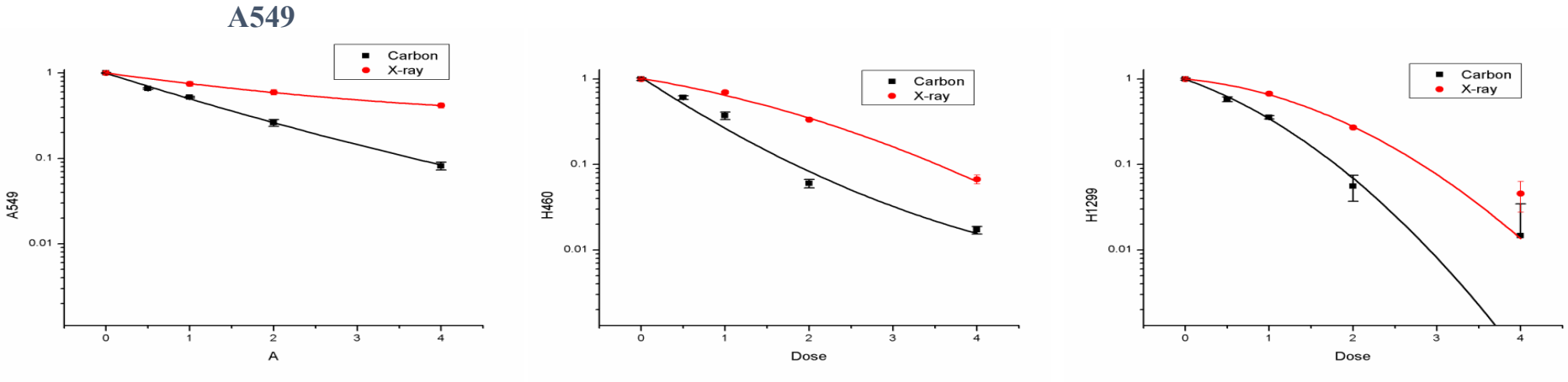
RBE (30keV/um)	0.95
RBE (50keV/um)	1.89



RBE (30keV/um)	1.13
RBE (50keV/um)	2.31

Cell experiment at HIMM RBE measurement

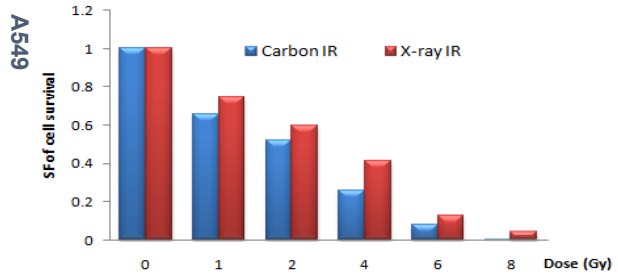
Lung cancer cells irradiated with 260MeV/u carbon ions and X-rays

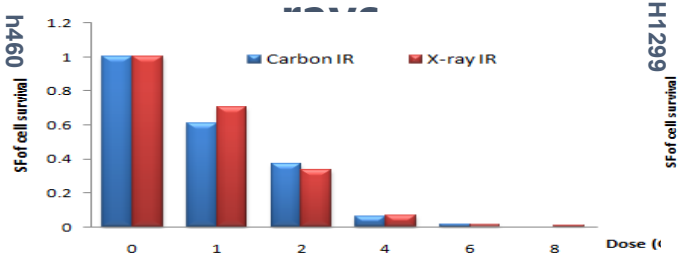


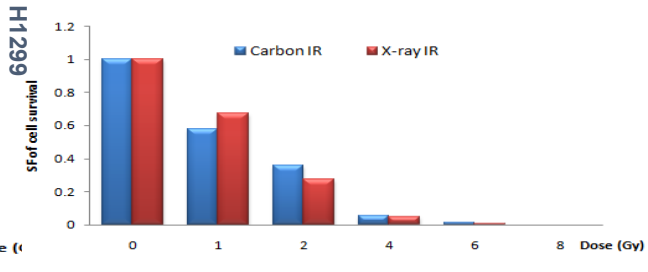
RBE>1, cell damages caused by heavy ions are more difficult to be repaired than X-rays.

Cell experiment at HIMM

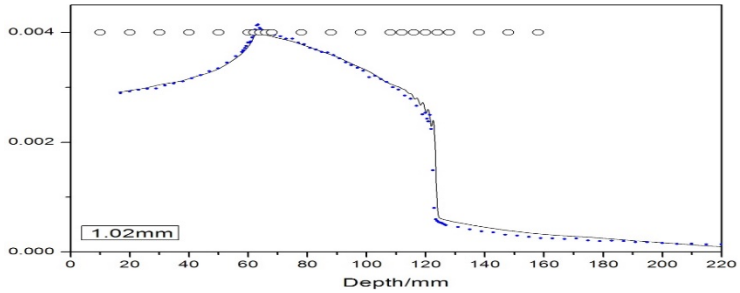
Comparison of cell survival effects by 260MeV/u carbon ions and X-



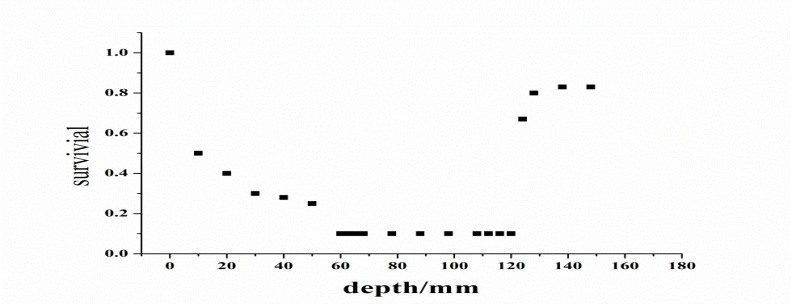




Biological verification of treatment plan

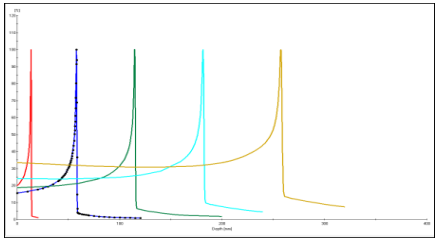


Physical dose distribution



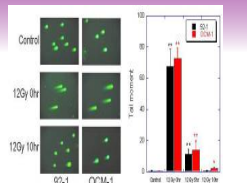
Cell survival effect

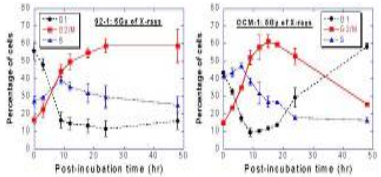
Roadmap of Heavy Ion Therapy Project



1993-

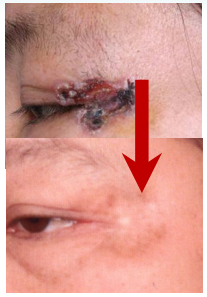
Basic research with cells and animals.





2006-2009

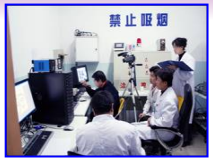
Clinical trial of superficial tumor: 103

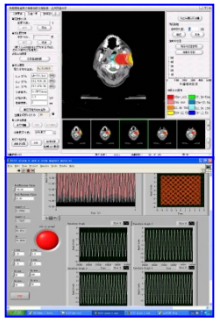


Development of treatment technology

2009-2013

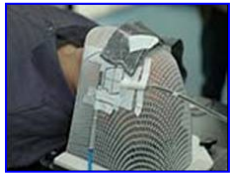
Clinical trial of deep-seated tumor: 110



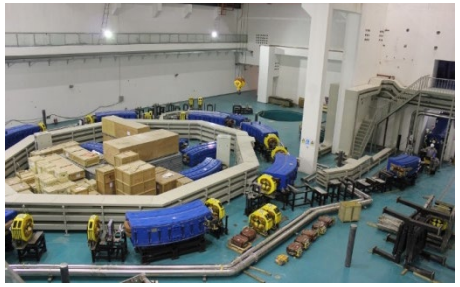


2012-

Construction of demo facilities.

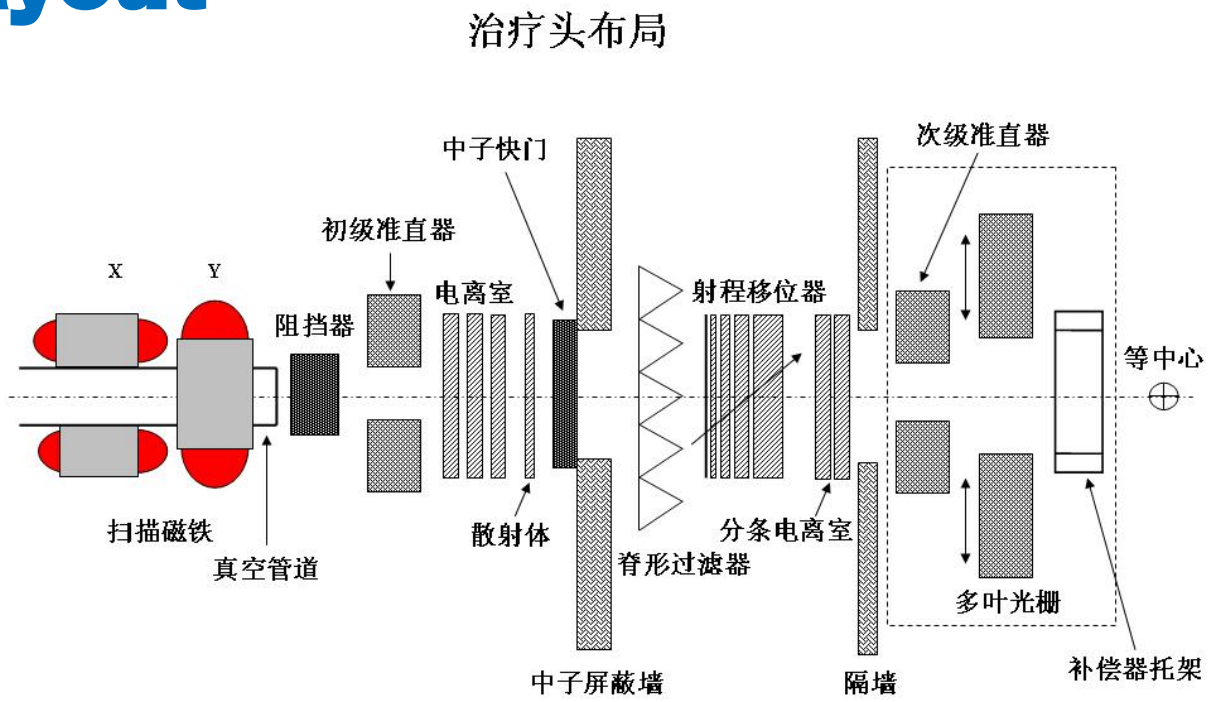


Large-scale industrialization



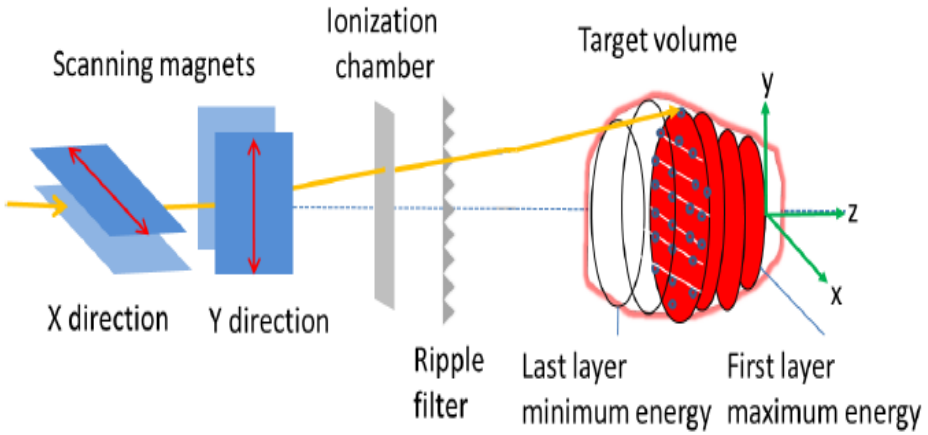
Nozzle Layout

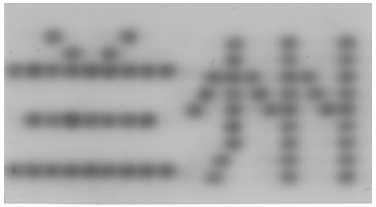
- primary collimator
- scatterer
- ridge filter
- range shifter
- secondary collimator
- multi-leaf collimator

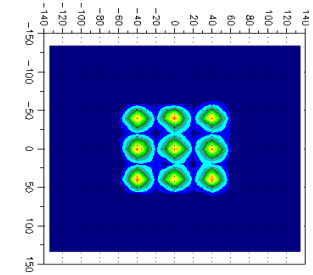


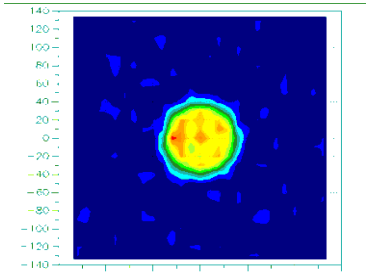
2D conformal, 2D layer-stacking conformal and 3D spot-scanning irradiations

Spot Scanning Beam Delivery

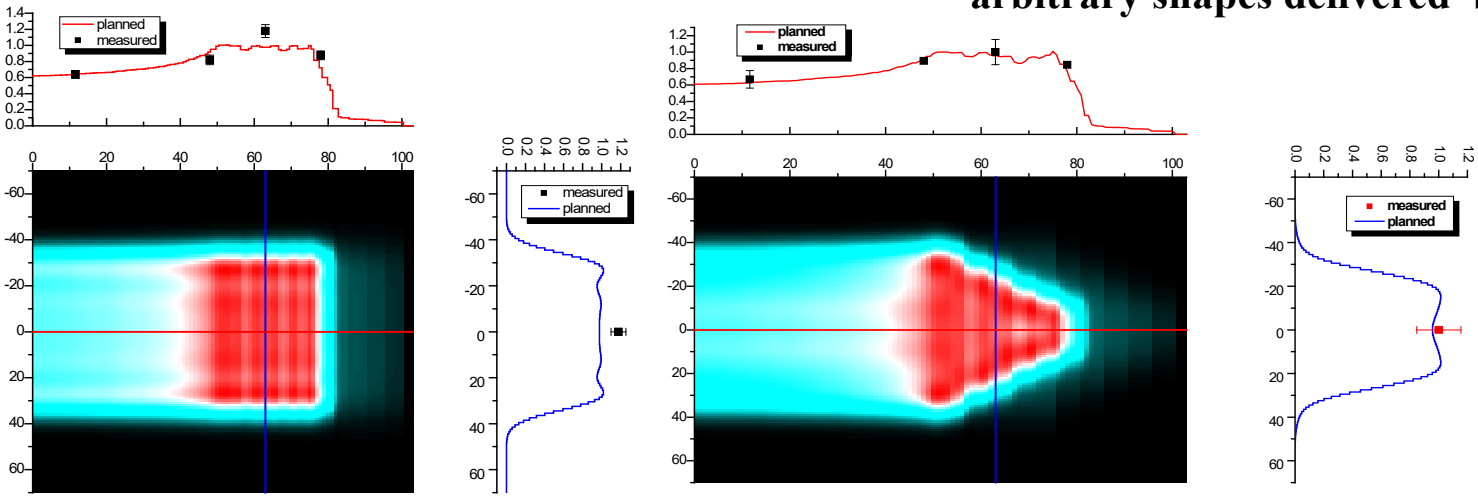








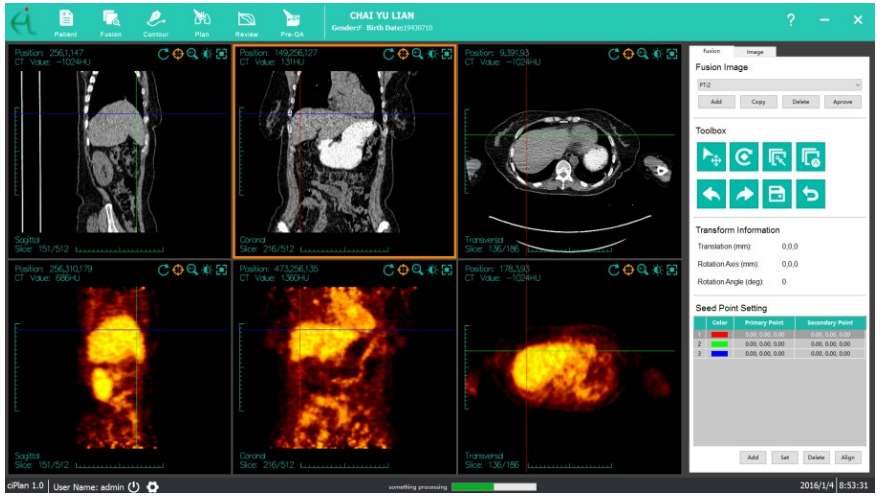
arbitrary shapes delivered by spot scanning



spot scanning beam delivery to different targets (cylinder and truncated cone)

compliance of measured and planned doses within an error of 5%

carbon ion Treatment Plan (ciPlan)



- Image preprocessing
- Organ delineation
- 3D reconstruction
- Field set-up
- Dose calculation
- Plan evaluation
- QA data preparation
- Virtual simulation
- Plan comparison
- Auxiliary positioning
- …

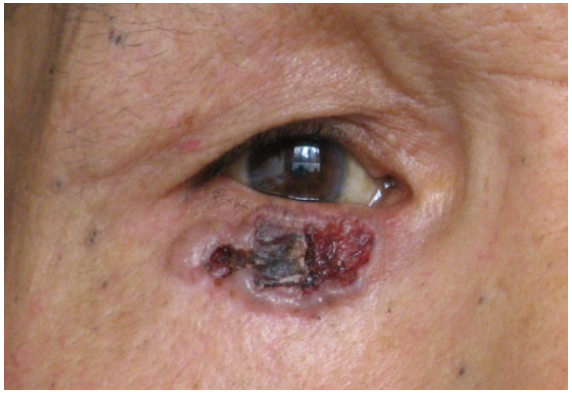
Clinical trial on 213 patients

Treatment time	Treatment depth	Number of cases
November 06-16, 2006	1.6 cm	4
January 07-15, 2007	2.1 cm	9
March 13-20, 2007	2.1 cm	14
August 11-16, 2007	2.1 cm	9
December 15-21, 2007	2.1 cm	15
March 20-25, 2008	2.1 cm	15
September 11-17, 2008	2.1 cm	16
March 02 - 07, 2009	2.1cm	21
Total		103

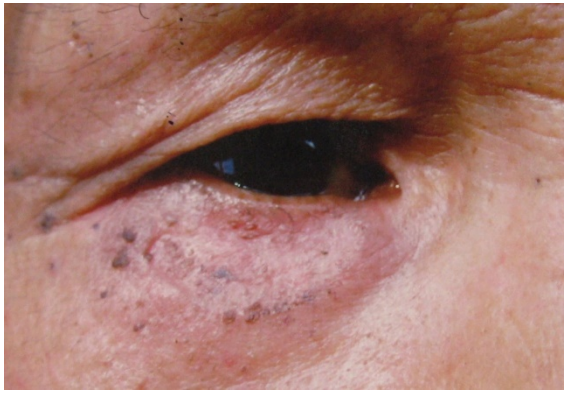
Tumor type	Number
Liver cancer	16
Lung cancer	22
Adenocarcinoma (adenosquamous carcinoma, pancreatic cancer)	3
Brain tumor (brain glioma, malignant meningioma, etc.)	18
Head and neck tumors (eyes, nose, throat, salivary gland, thyroid, etc.)	16
Bone and soft tissue sarcoma	13
Pelvic malignant tumors (rectal cancer, prostate cancer, chordoma, ovarian cancer, etc.)	9
Others	6
Total (2009-2013)	110

Examples of follow-up treatment effects

Postoperative recurrence of basal cell carcinoma



Before

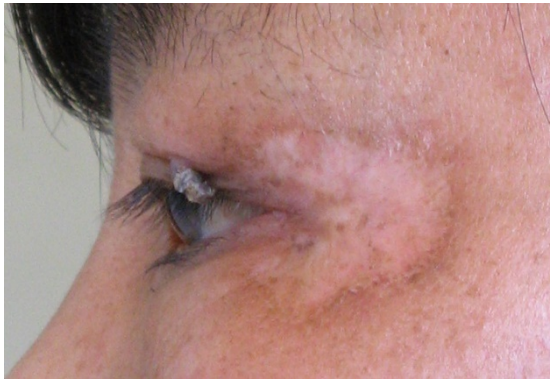


3 years later

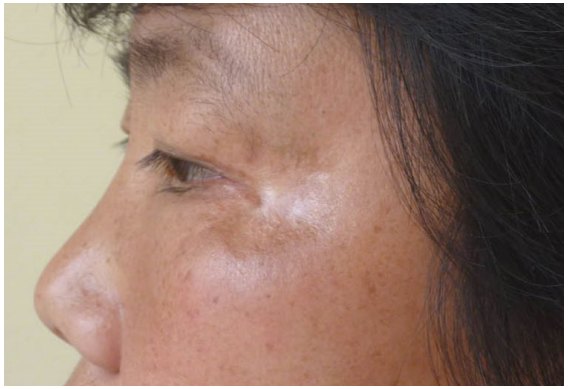
7 years later

Left outer canthus basal cell carcinoma

Before

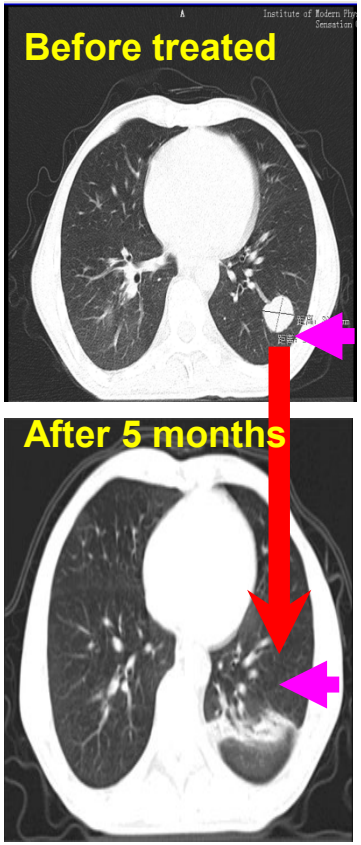


4 months later



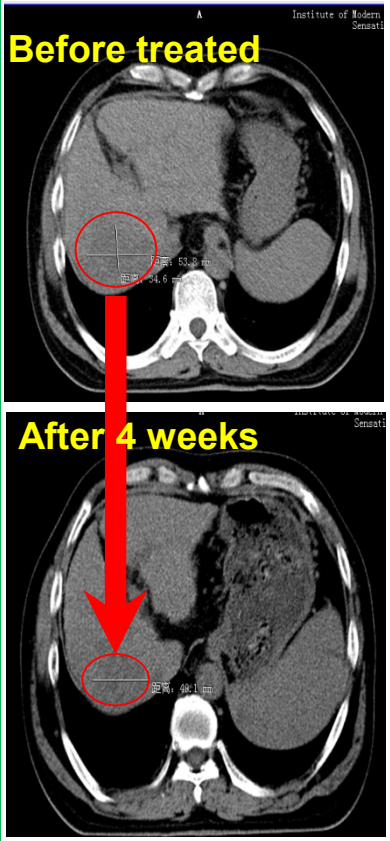
5 years later

Examples of follow-up treatment effects



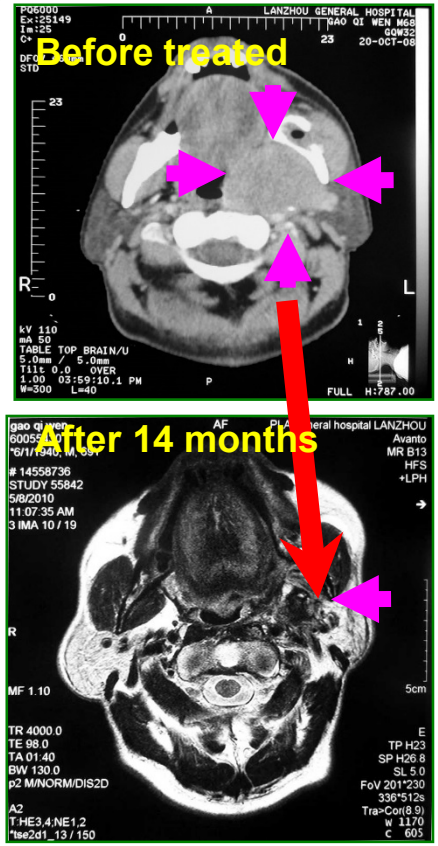
metastatic carcinoma of lung

disappears



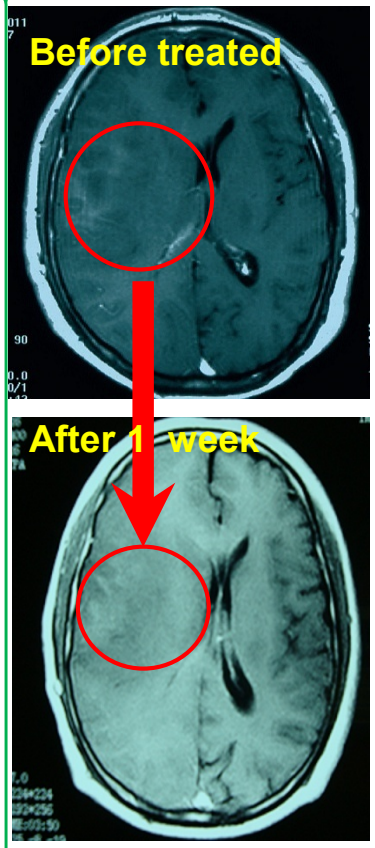
primary carcinoma of liver

reduces 30%



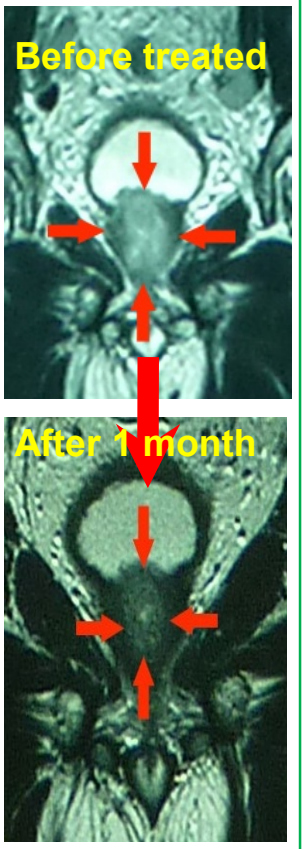
cell carcinoma of salivary gland

disappears



Brain glioma

reduces 10%



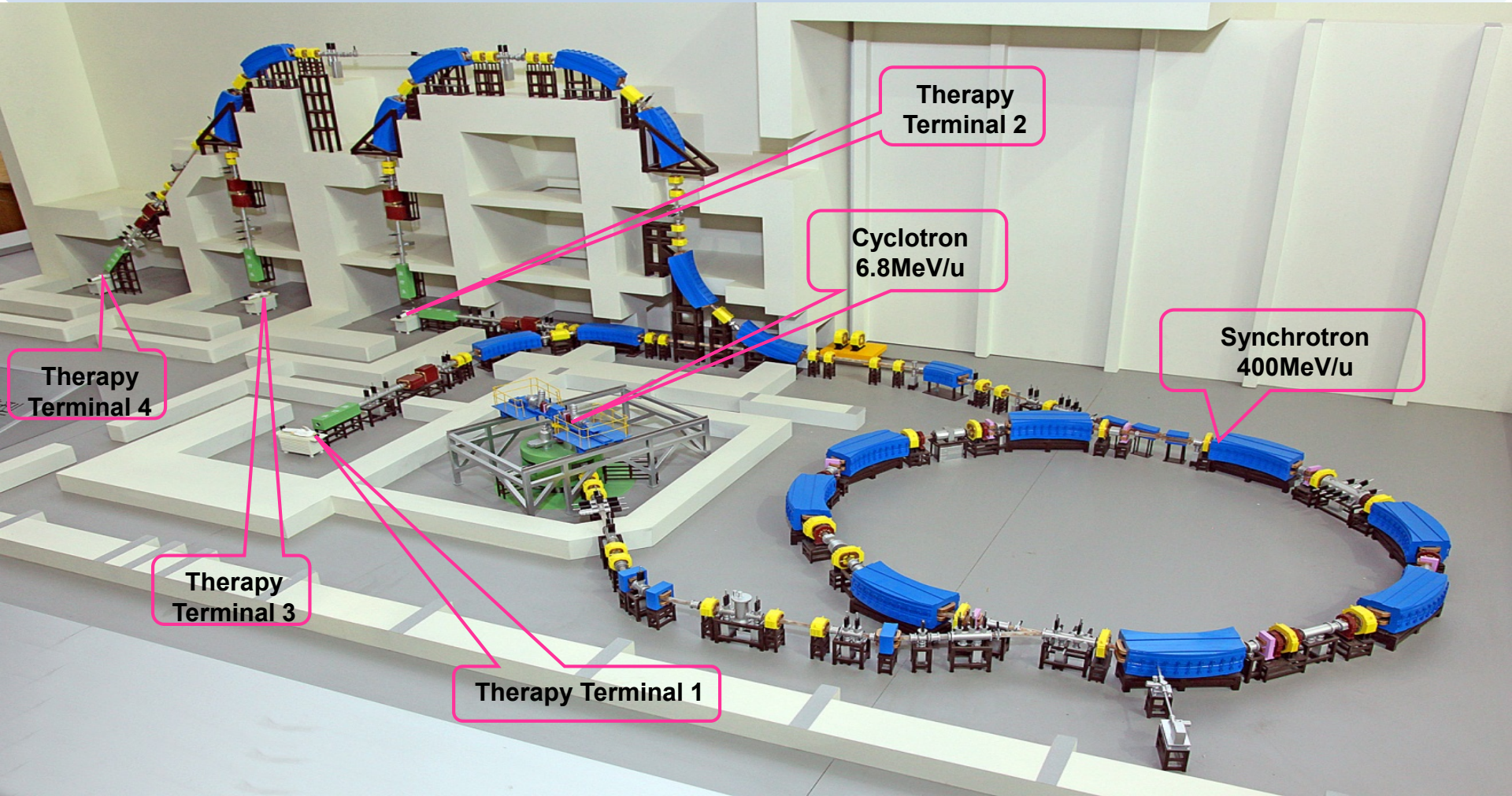
prostatic carcinoma

reduces 30%

Progress of Demon Facilities in Wuwei and Lanzhou

Demo Heavy-Ion Cancer Therapy Facility

- Combination of cyclotron injector & synchrotron
- Compact synchrotron with circumference of 56.17m
- 4 treatment terminals



Main specifications of HIMM

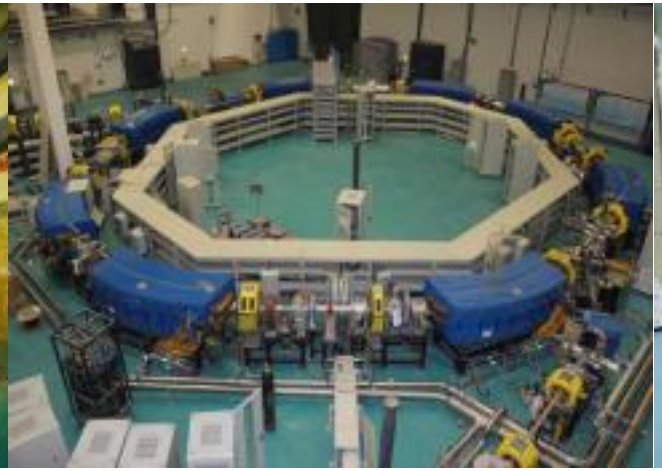
Ion	$^{12}C^{6+}$
Maximum Energy	400.0 MeV/u
Maximum Range	27.0 cm
Step Length of Range	2.0 mm
Dose Rate	1.0 Gy/l/s
Irradiation Field	200×200 mm^2
Beam Diameter	≤ 12.0 mm
Beam Intensity	1.0×10^9 pps
Cut-off Time	< 1.0 ms
Treatment Mode	Active Scanning and Passive Scanning
Treatment Terminal	One horizontal-direction terminal, one vertical-direction terminal, one terminal combined both horizontal and vertical direction, and one 45°-direction terminal.

Heavy ion therapy center in *Wuwei*

- Covering an area of 2 million square meters
- Total investment: 1.6 billion RMB, including 0.55 billion RMB for heavy ion facility
- Wuwei Tumor Hospital: ① Diagnosis and Treatment of Tumor
  ② Recovery and Recuperate

Wuwei Demo Facility

Cyclotron injector



Synchrotron

CT

Treatment Room

Treatment Control Room

TPS Room

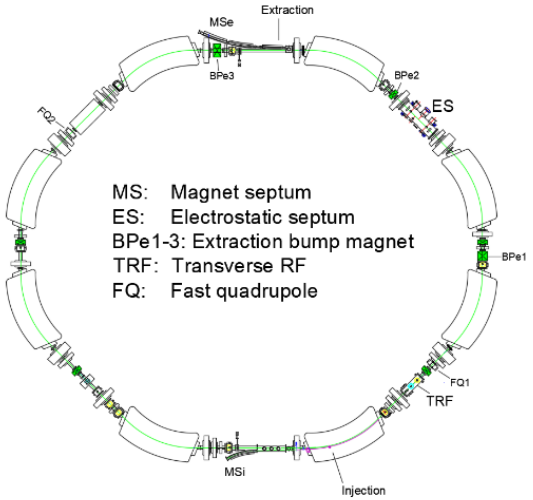
Central Control Room

Milestones of Wuwei Project

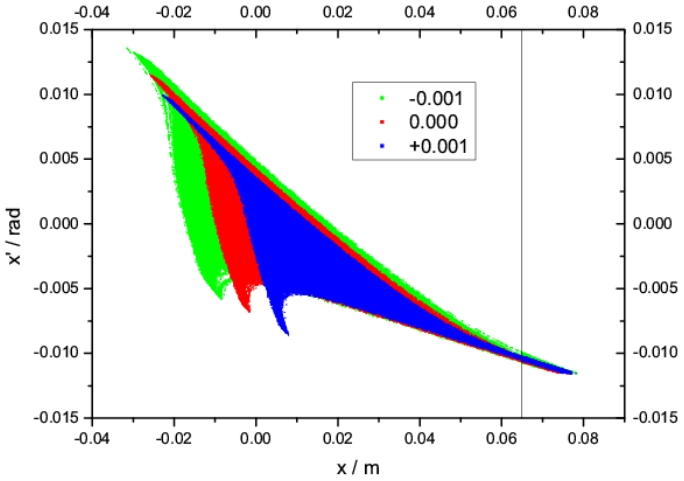
- First beam : Dec. 23, 2015
- Registration detections of national and international standards GB9706, GB4793, GB4943, YY0505, IEC60602-2-64 and so on have been finished.
- The clinical trial of 47 patients will be followed soon on October in 2018 to prove the safety performance and the validity of the facility.
- HIMM Wuwei is expected to operate in 2018.



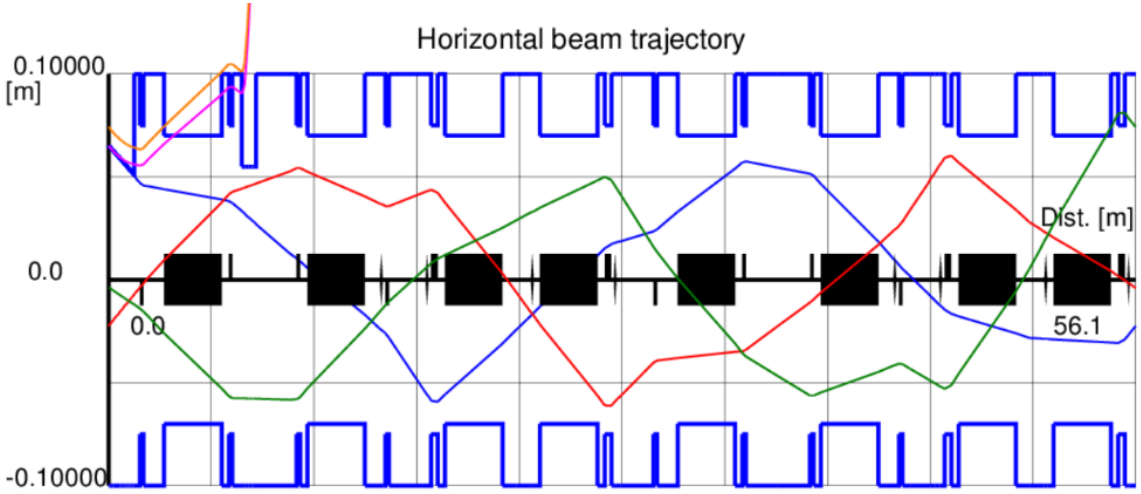

Simulation Results



Schematic layout of the HIMM synchrotron ring

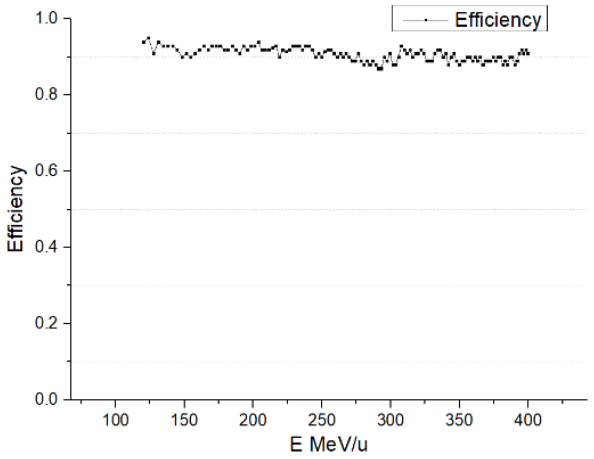


slow extraction phase space

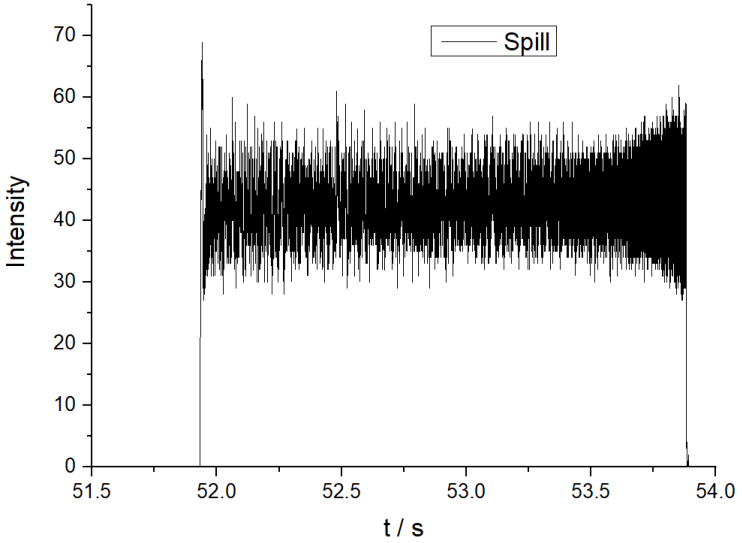


The trajectory of the last three turns and the extracted beam

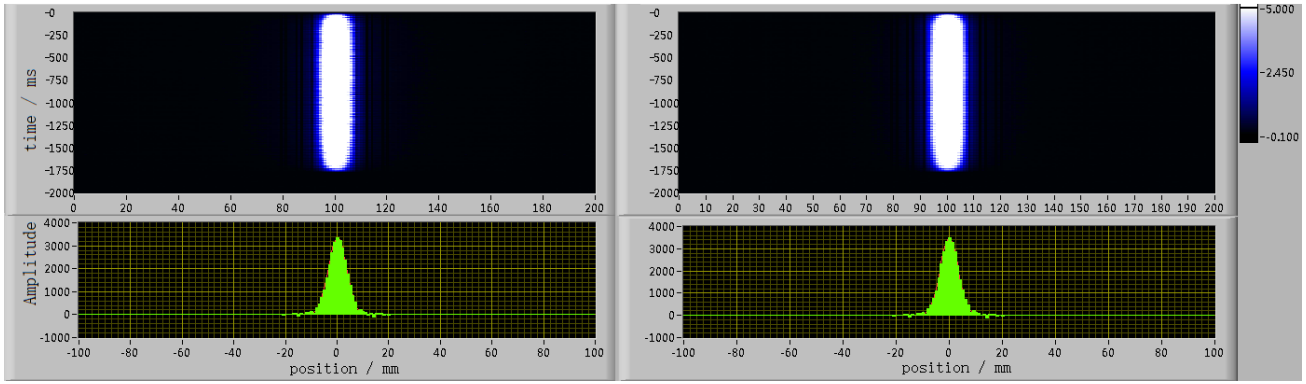
Commissioning Results



Extraction efficiency vs energies, the slow extraction efficiency was nearly 90% for all the energies.



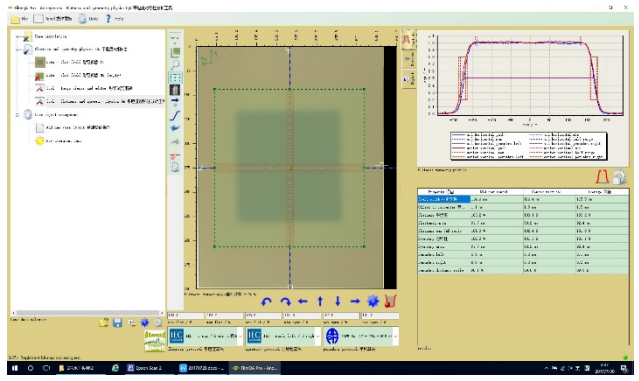
The spill duty factor exceeded 95% at a sample rate of 10 kHz



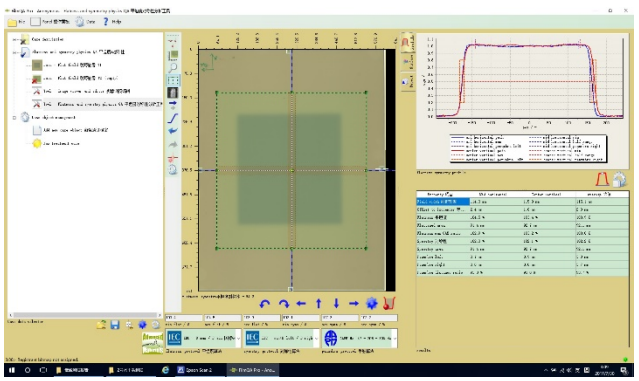
Beam signal viewed in the anode-stripped ion chamber

Field flatteness measured with radiographic films for the horizontal nozzle at the vertical+horizontal treatment terminal

120MeV/u 103.2%



190MeV/u 104.5%

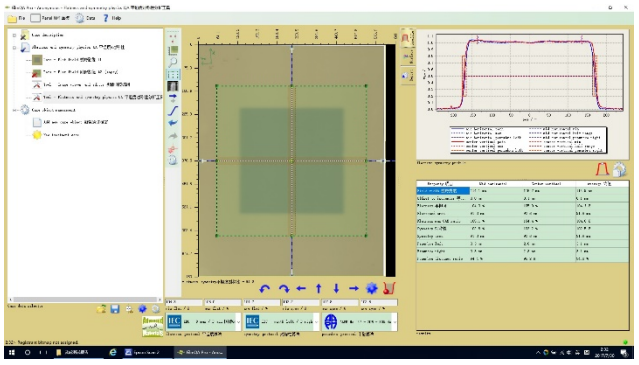


Energies
120~400MeV/u

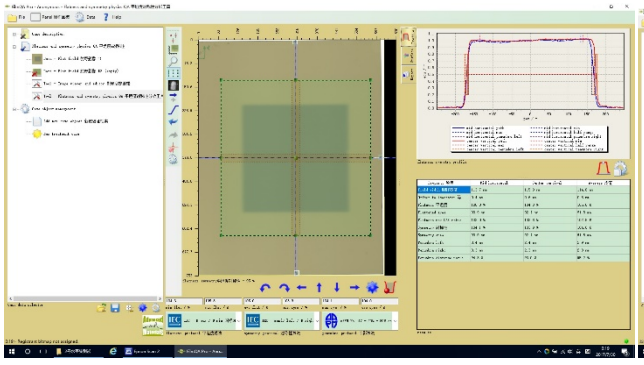
Irradiation field
15cm x 15cm

$Dose_{max}/Dose_{min}$<106%

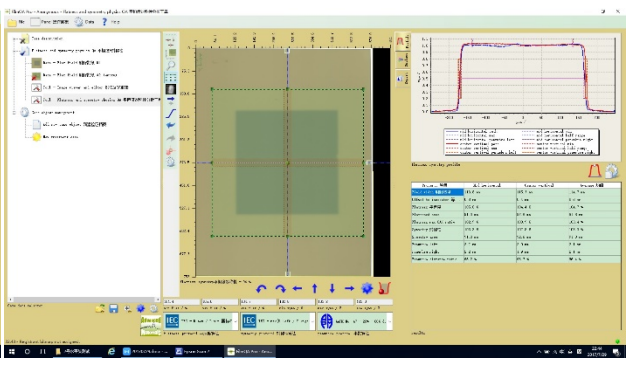
260MeV/u 105%



330MeV/u 105.8%

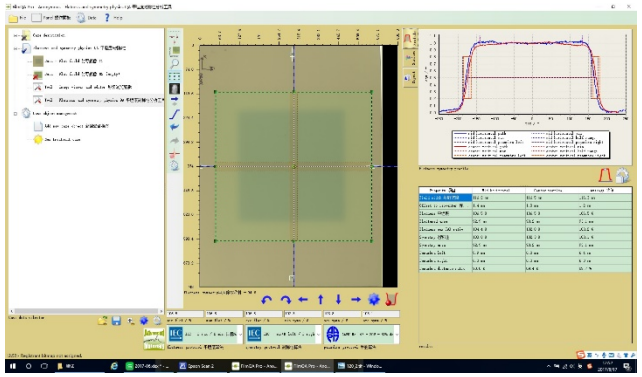


400MeV/u 105%

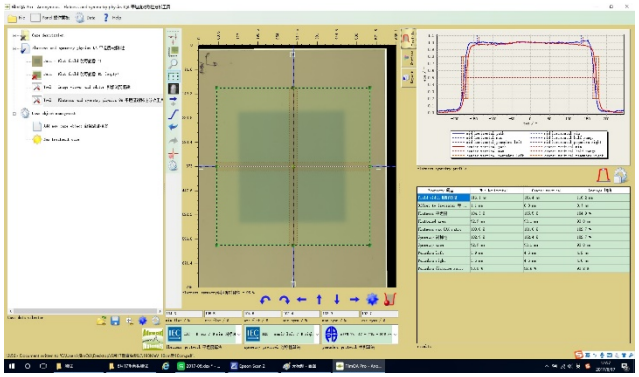


Beam flatteness of the vertical nozzle from the vertical+horizontal treatment terminal

120MeV/u 105.5%



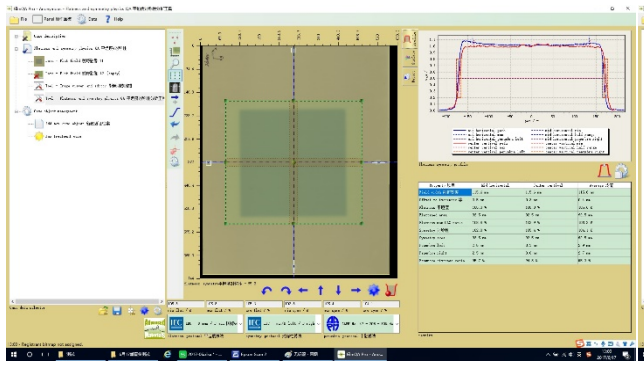
190MeV/u 105.5%



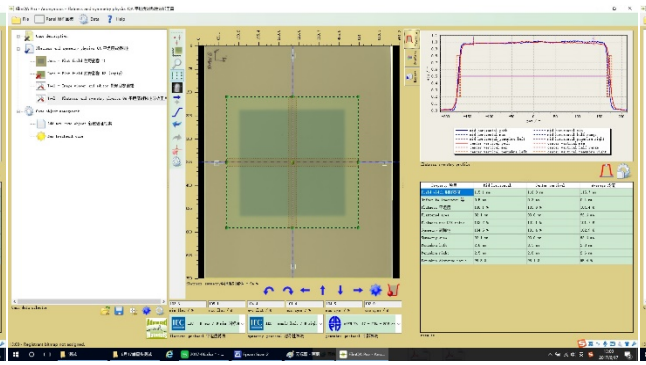
Energies
120~400MeV/u

Irradiation field
15cm x 15cm

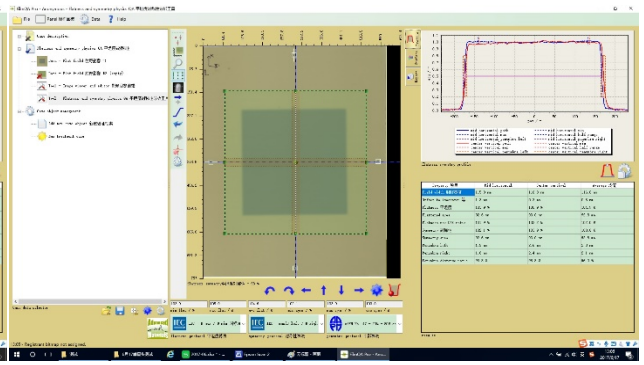
260MeV/u 105.8%



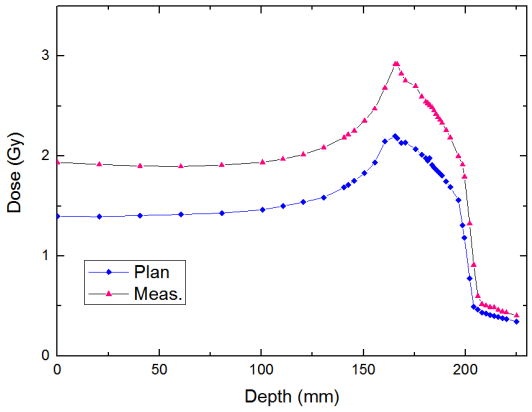
330MeV/u 105.1%

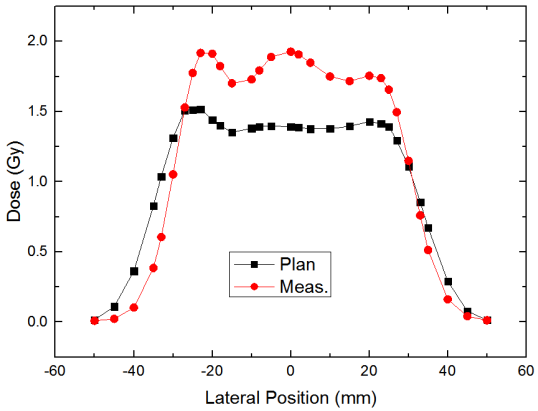


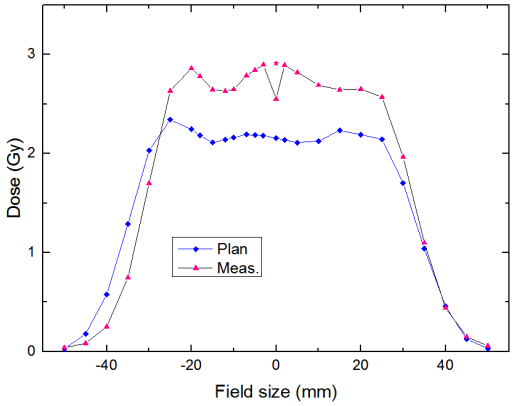
400MeV/u 105.9%



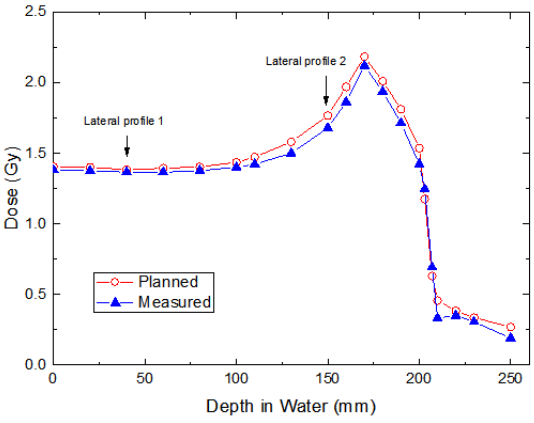
3DSS Dose Distribution

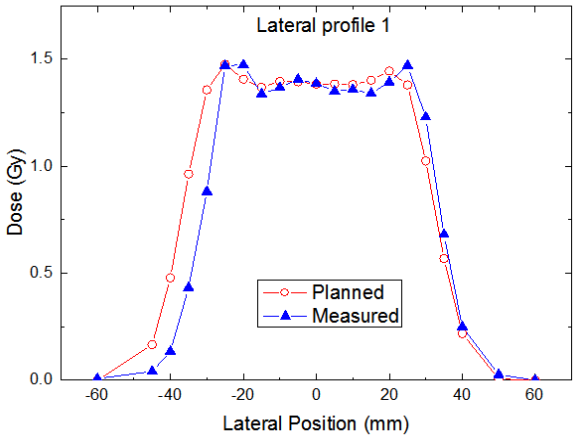


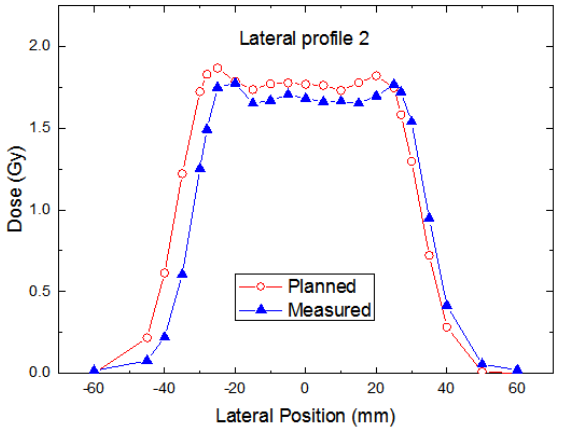




After optimization



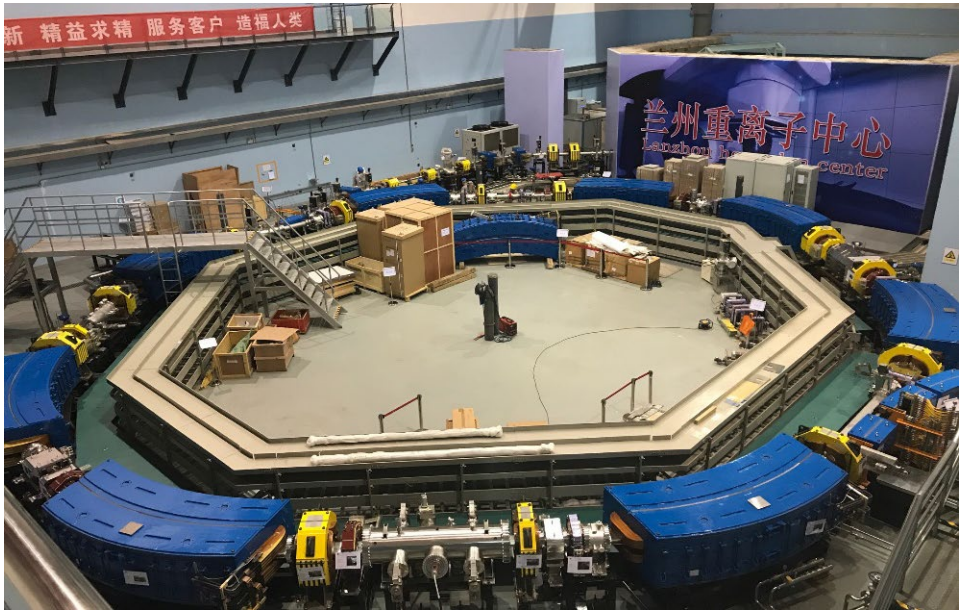




Depth distribution　　Transverse distribution at plateau　　SOBP

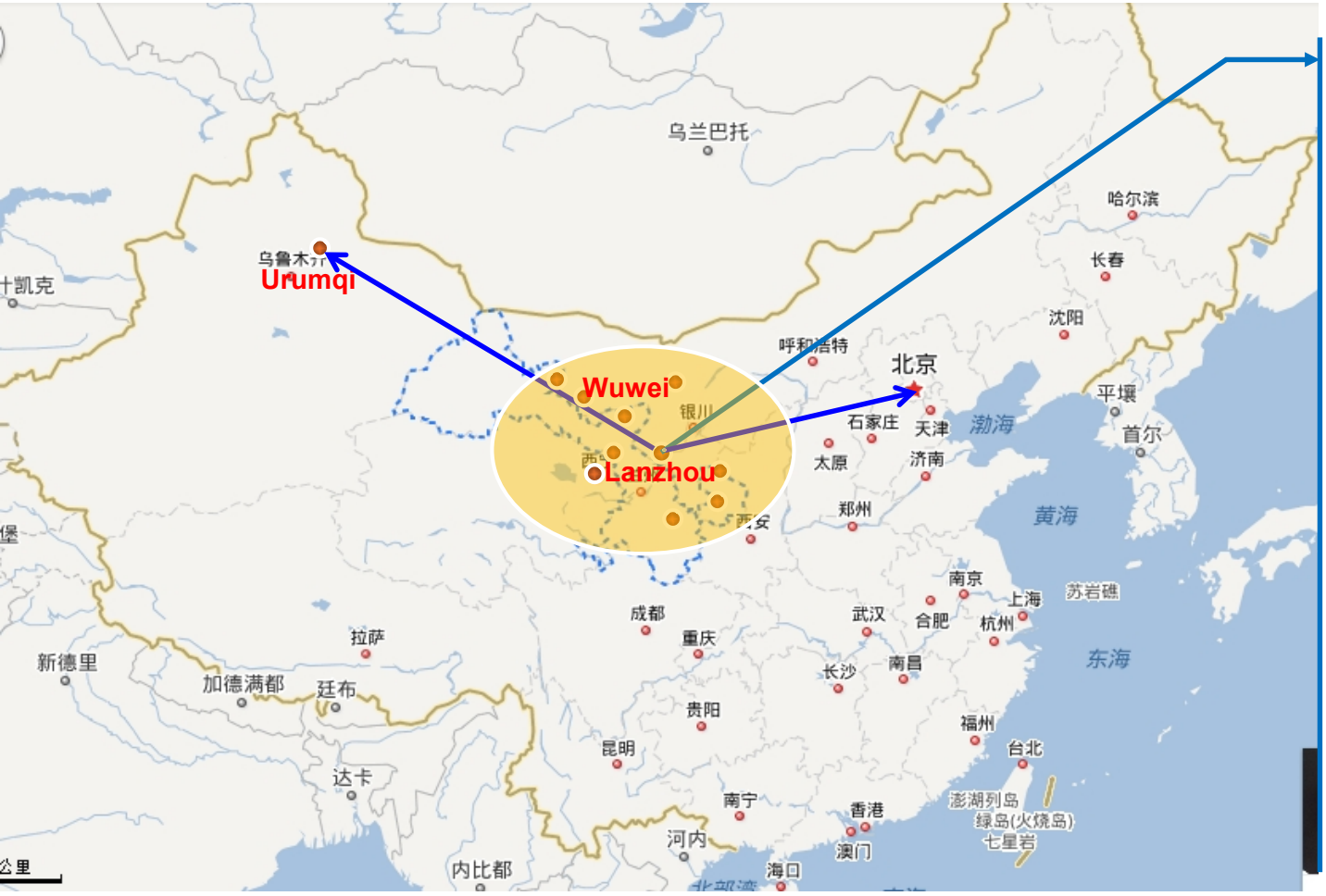
Lanzhou Heavy-Ion Tumor Therapy Center

- Covering 25 acres, a total investment of more than 400 million US dollars.
- Relying on Gansu Provincial Tumor Hospital
- Installation began in March 2016.
- The facility will be commissioned before the end of 2018.



Two provincial tumor hospitals in Gansu:

- Gansu Cancer Hospital (**Lanzhou**)
- Wuwei Cancer Hospital (**Wuwei**)



- Covers nearly 20 cities, Surrounding Population 30 million
- Cancer incidence: 2694 per 1 million people, 38% higher than the national average.
- 7.5 hours to Urumqi with Lanxin express railway

Surrounding Cities

- Lanzhou City 3.6 million people
- Wuwei City 1.8 million people
- Baiyin City 1.8 million people
- Pingliang City 2 million people
- Xining City 2.2 million people
- Tianshui City 3.7 million people
- Dingxi City 3 million people
- Zhangye City 1.2 million people
- Jiuquan City 1.1 million people
- Guyuan City 2.2 million people
- Yinchuan City 2 million people

Future Perspectives

Challenges and Perspectives

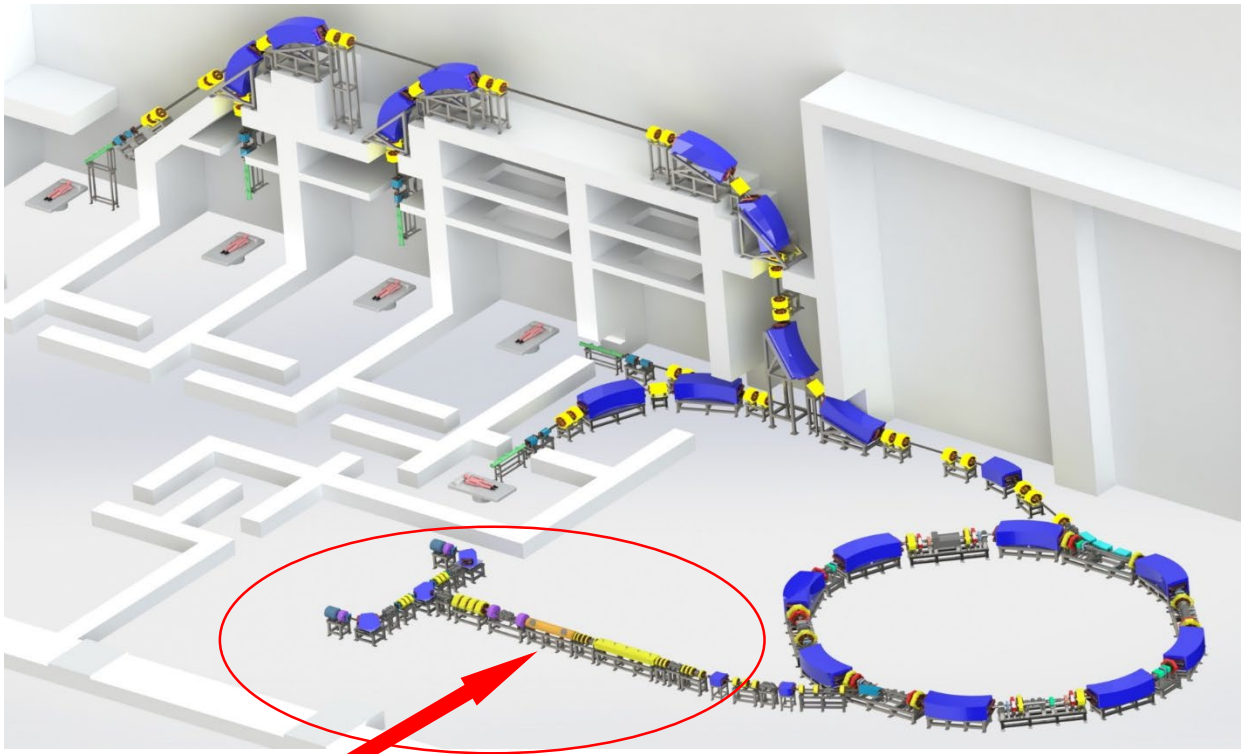
1. The application of **superconducting technology** may increase the magnetic field, minimize the size of the magnet and rotating gantry and decrease the operation cost.

2. **Linac injector** can be used to enhance the beam intensity adding a new injection mode.

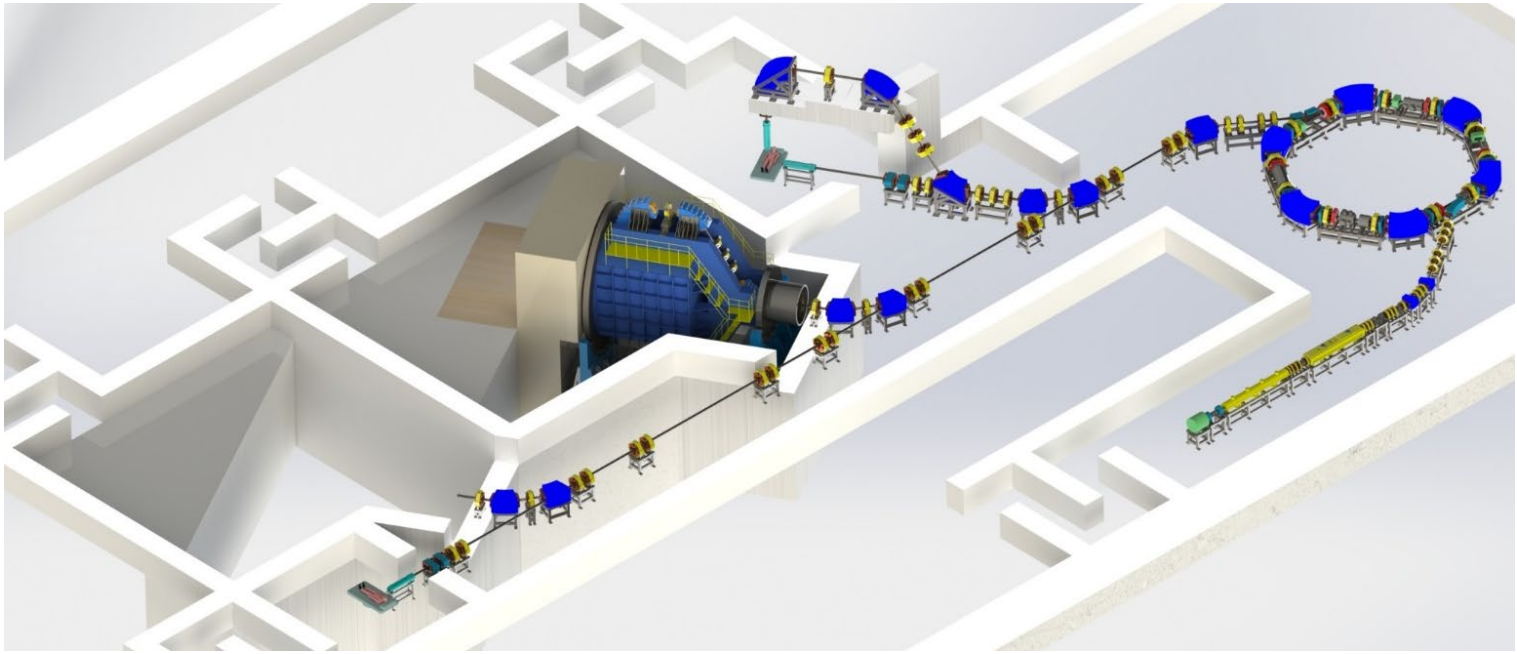
3. Different **dedicated medical facilities** may be designed and constructed for the requirements of user.

4. **New treatment technique** may be developed and used.

A new heavy-ion cancer therapy facility with a linac injector



Proton therapy machine



China Tumor Incidence & Market

- 4.3 million people were diagnosed with cancer in China in 2015 and still increased every year.

- The treatment number of each heavy ion facility: 1000~2000 patients/year. More than 100 heavy ion therapy facilities are needed in China. Each facility costs ~$100 million.

- Market Forecasting:

Equipment Manufacturing：~ $ 20 billion
Equipment operation and maintenance：$1.5 billion/ year
Medical Treatment services：~ $ 8 billion/ year

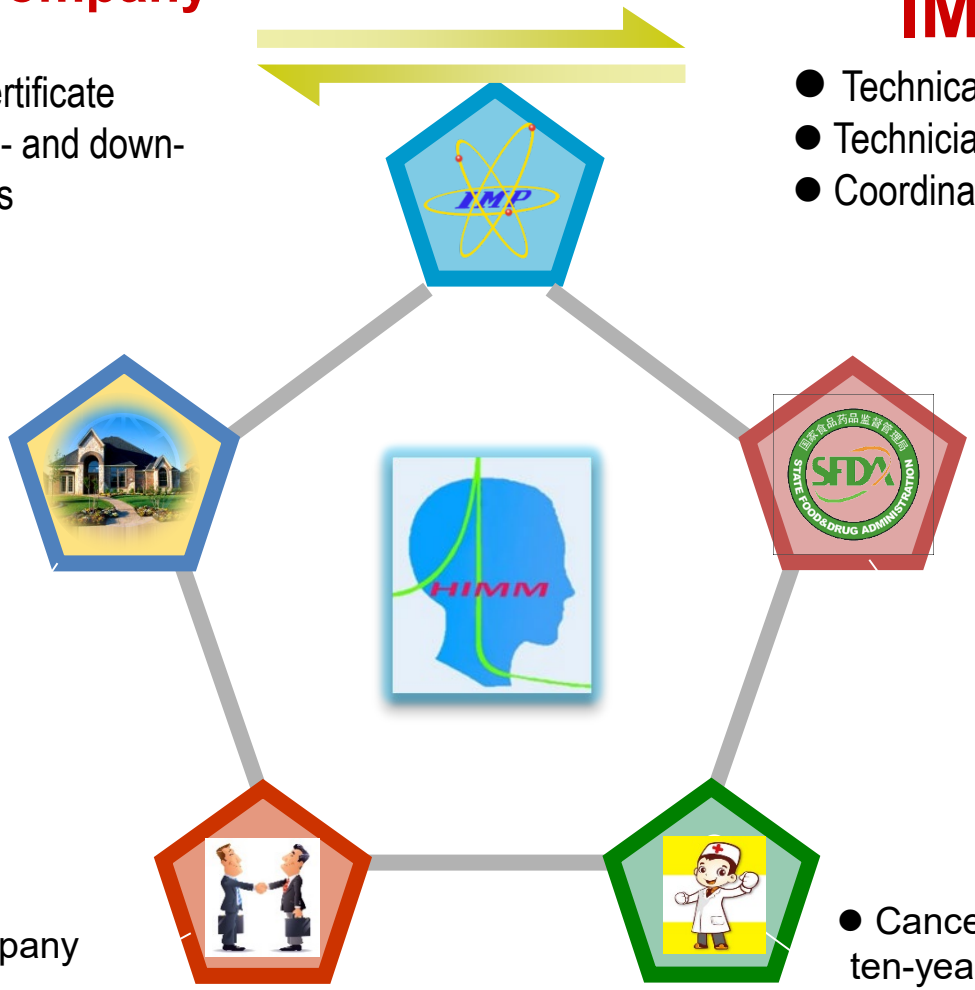
Cooperation mode of therapy Project

Kejin Taiji Company

- Product standard
- Manufacturing Certificate
- More than 400 up- and down-stream enterprises

IMP

- Technical support
- Technician support
- Coordinate



Government

- Policy support
- Coordinate
- Land and planning

CFDA

- Registration detection
- Clinical trial
- Examining
- Registration certificate

Investors

- Investment Company

Hospitals

- Cancer hospital with more than ten-year's radiation qualification

Conclusion

Heavy-ion beam has favorite characteristics such as inverted depth-dose distribution （Bragg Peak） and relative biological effectiveness (RBE).

A significant improvement for local control and survival rate has been achieved.

A huge market is forecasted for heavy-ion cancer therapy in China.

New technologies such as superconducting magnets and so on are needed in the future to reduce the size of facility and the cost.

Collaborations are welcome.

Acknowledgements

HIMM groups from IMP and Kejin Taiji company:

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Qiang Li, Xinguo Liu, Zhongying Dai, Pengbo He, Guosheng Shen, YuanYuan Ma
Guihua Li, Wuyuan Zhao, Jinzhong Ma, Fan Yang
Mingtao Sao, Guohong Li, Weiping Zhao
Xiaoqi Zhang, Guoping Sun
Xiaohong Cai

Chinese Academy of Sciences, NSFC, MOST,NDRC ,local goverments
Medical Heavy-ion Accelerator Industry Alliance
Wuwei , Lanzhou and Gansu tumor hospital and other hospitals

Thank you for your attention!