Proton Therapy in Taiwan

*Chien-Yi Yeh, Ji-Hong Hong

*葉健一　洪志宏

Chang Gung Memorial Hospital
at Lin-Kou, Taiwan
林口長庚紀念醫院

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Outline

1. The principle of proton radiotherapy

2. Introduction of the current medical environment in Taiwan

3. Preview of radiotherapy in Taiwan

4. The proton project at CGMH in Taiwan

5. Conclusion

The principle of proton radiotherapy

Clinical Rationale for Advanced Beam Modalities for Radiation Therapy

To improve local-regional control through dose escalation

to improve overall survival

To reduce normal tissue complications

to improve quality of life

To reduce treatment time/cost

Particles used in radiotherapy

Photon

Electron

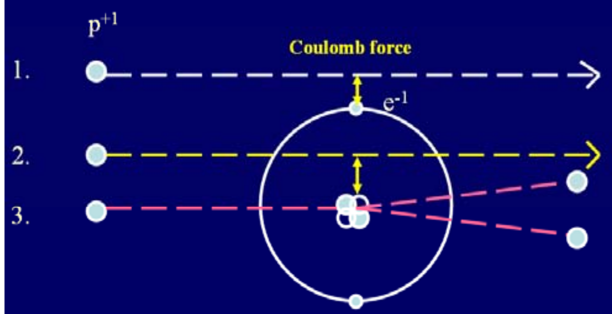
Neutron

Proton

Heavy charged particles

Type of radiation

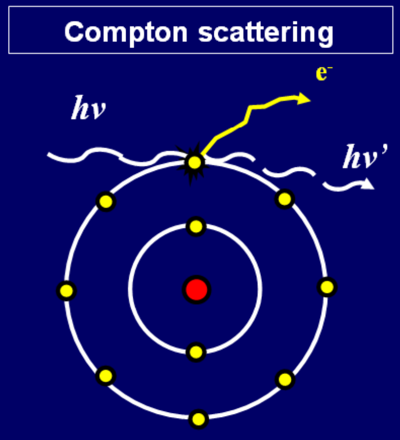
Direct ionization radiation



- electron beam
- *proton beam
- helium carbon neon
- Silicon

Charged particle

Indirect ionization radiation



- photon beam
- neutron beam

Uncharged particle

Interaction with matter in physics

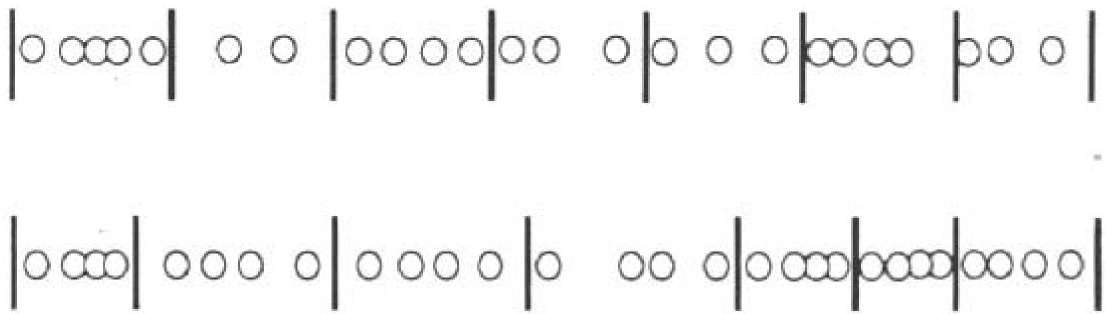
Linear Energy Transfer (LET)

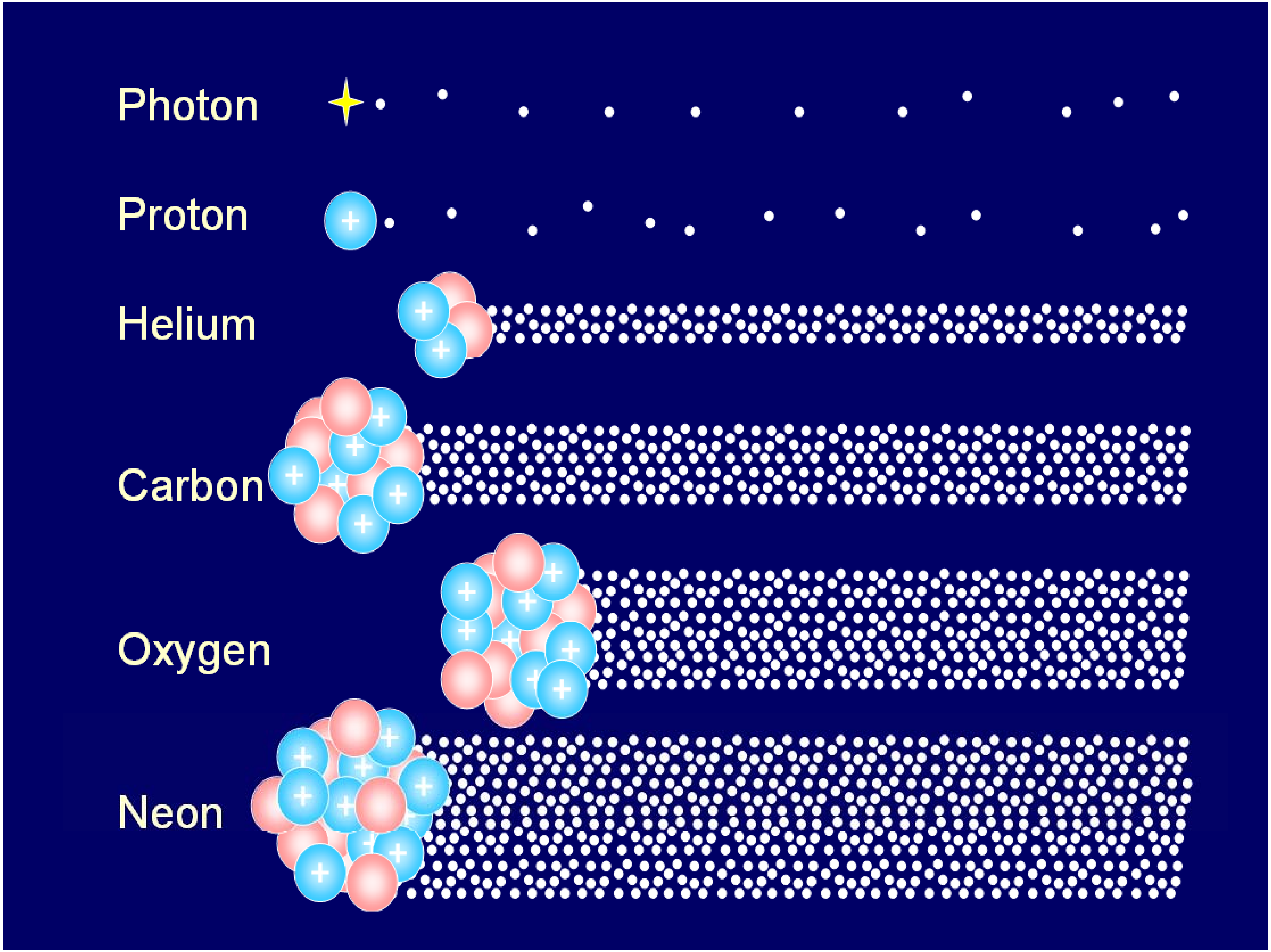
Related to mass, energy and charge of particle

LET = Average energy deposited per unit length of track (keV/μm)

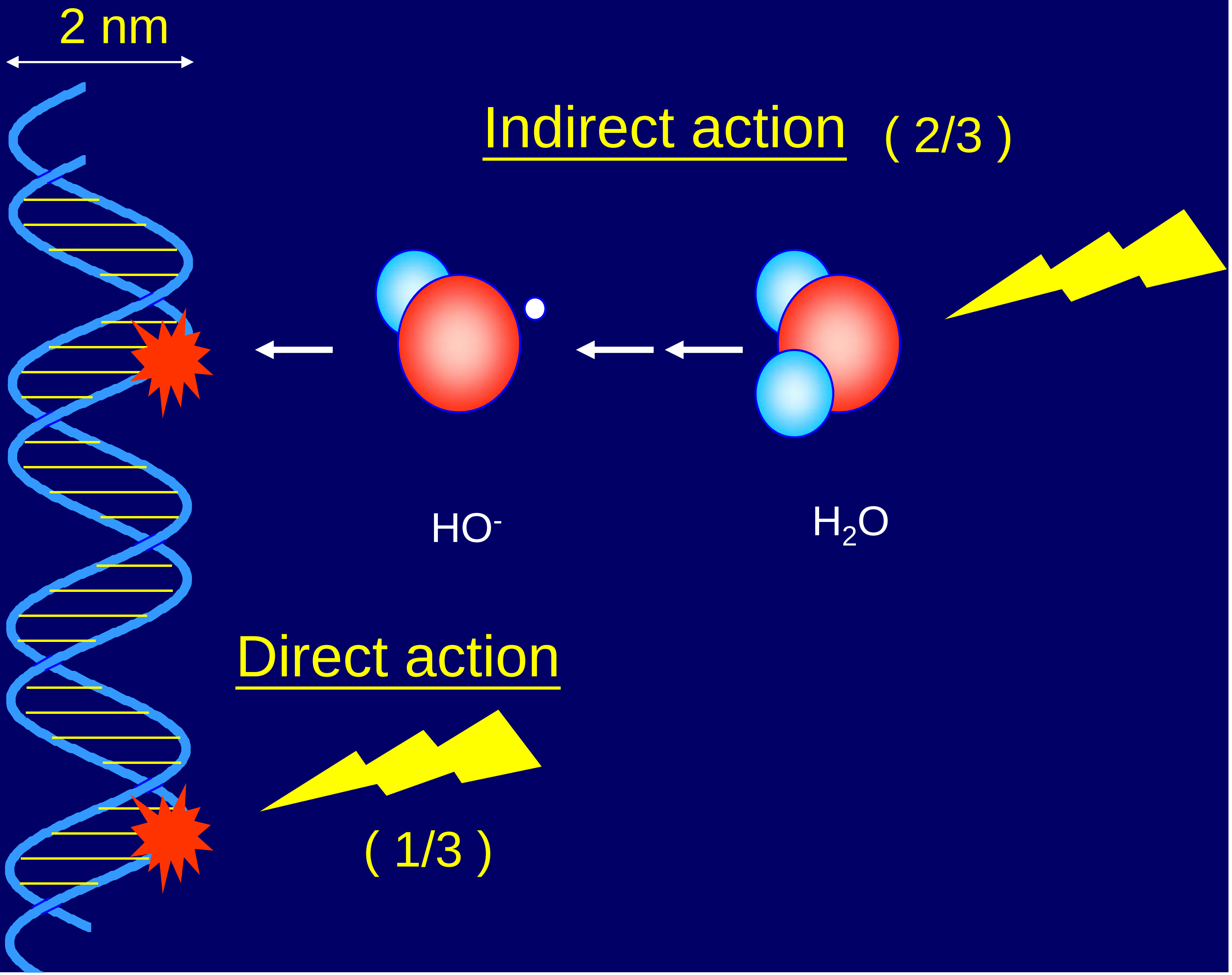
Track Average

Energy Average




Photon
Proton
Helium
Carbon
Oxygen
Neon

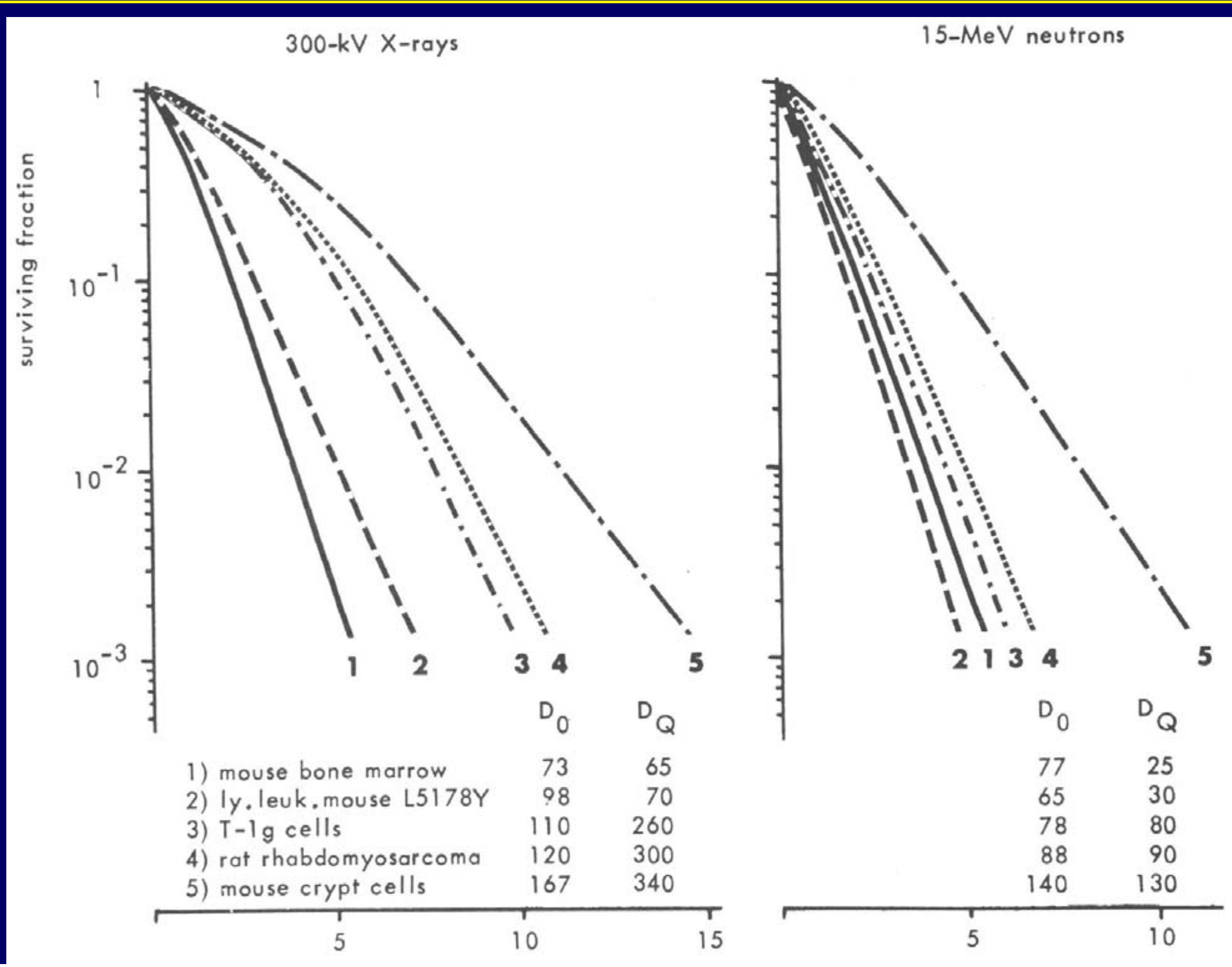
interaction with cell in biology



Relative Biological effect (RBE)

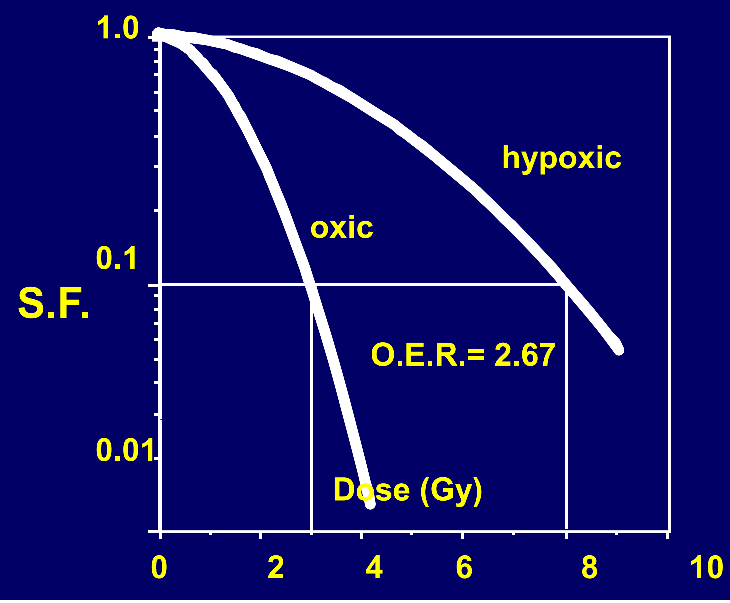
$RBE_t = D_{250}/D_t$ **(same biological end-point of 250KV X-ray)**

*RBE value related to the type of radiation, energy and cell type.

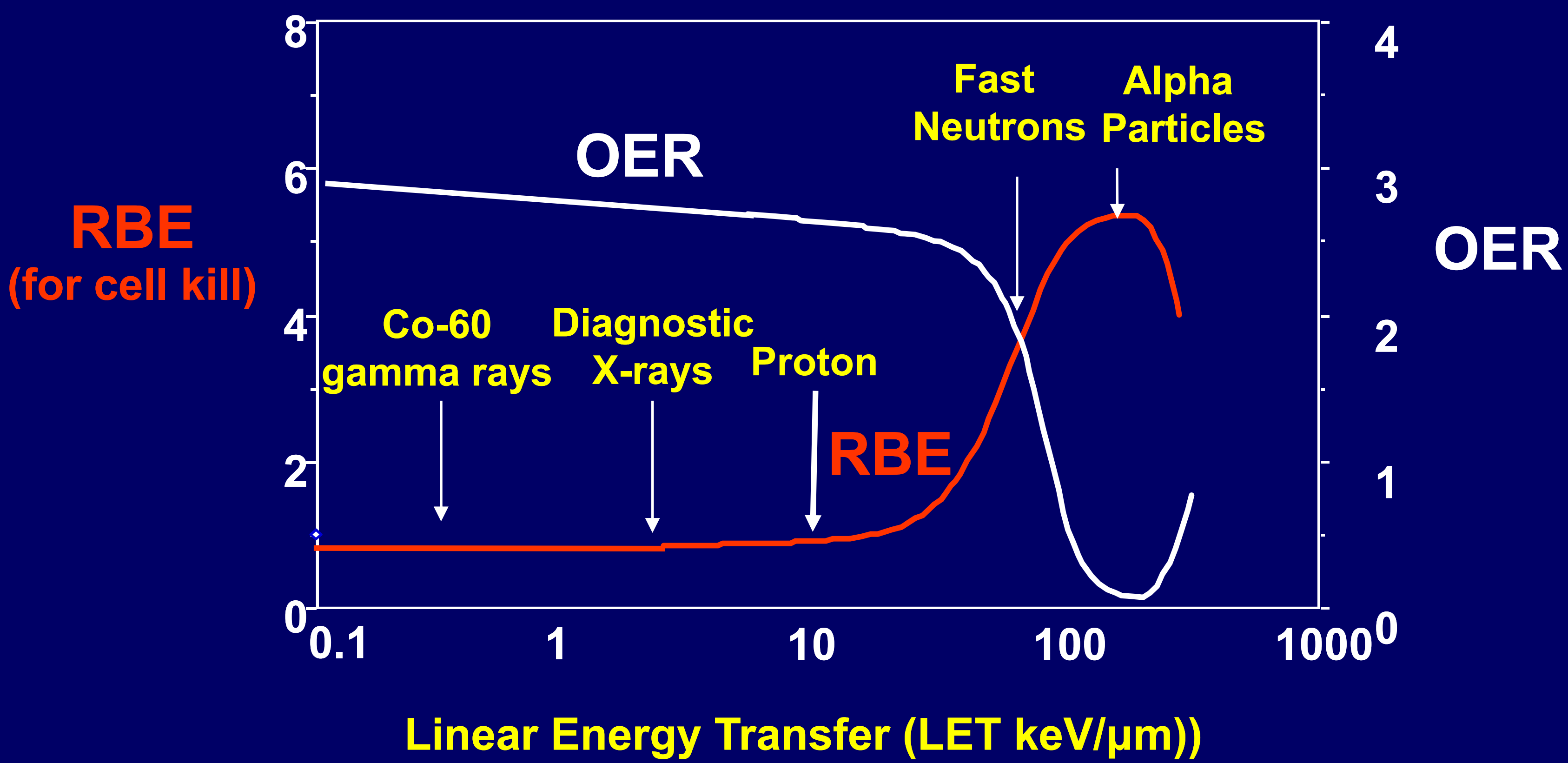


Oxygen enhancement ratio (OER)

- Oxygen is a powerful oxidizing agent and therefore acts as a radiosensitizer if it is present at the time of irradiation (within µsecs).
- Its effects are measured as the oxygen enhancement ratio (O.E.R.)
  - O.E.R. = the ratio of doses needed to obtain a given level of biological effect under anoxic and oxic conditions.
  - O.E.R. = D(anox)/D(ox)
  - For low LET the O.E.R. is 2.5-3.0
  - For neutrons, O.E.R is about 1.6

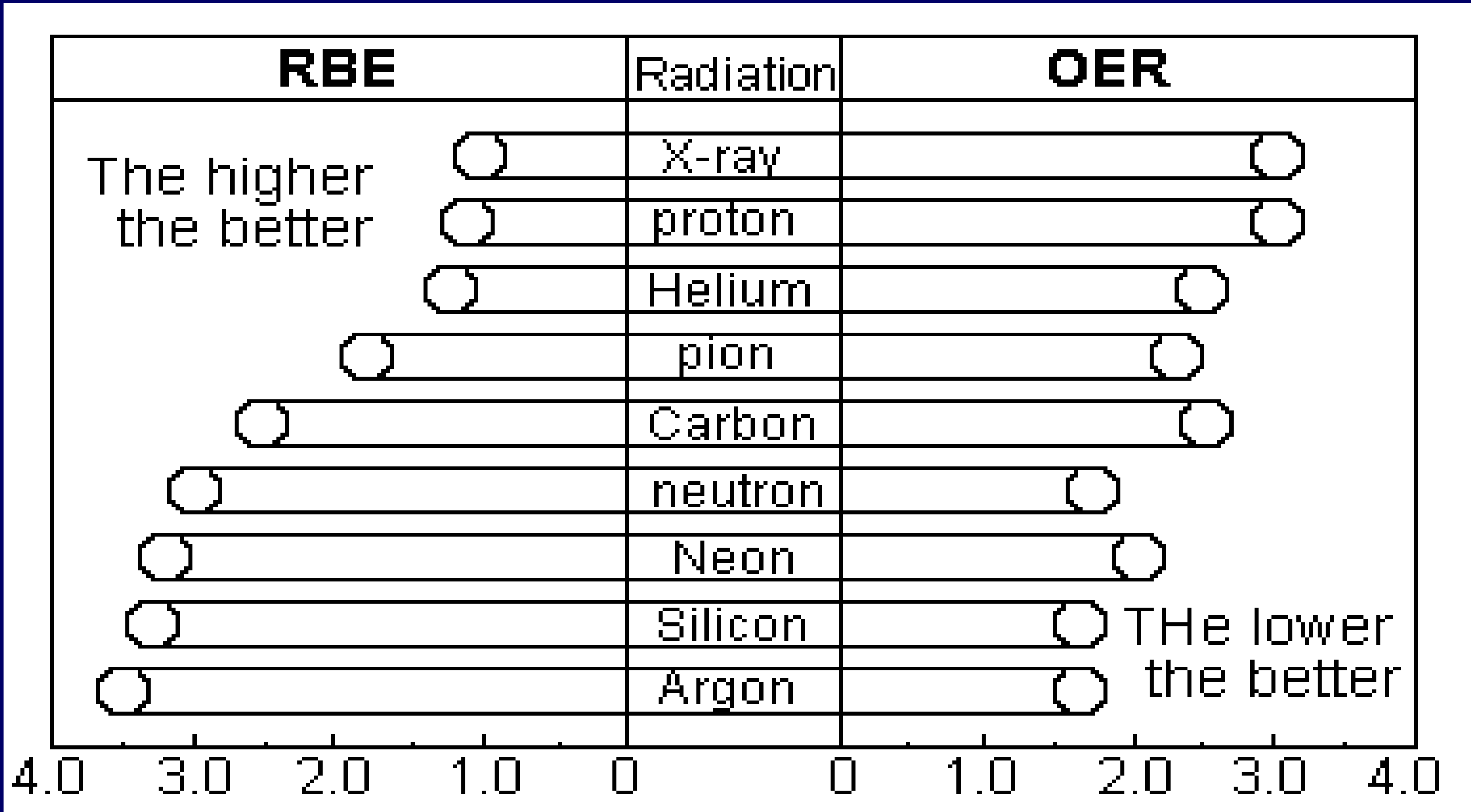


RBE and OER as a function of LET



OER is the inverse of RBE because it depends on the indirect action of ionizing radiation

RBE and OER for different beam modalities



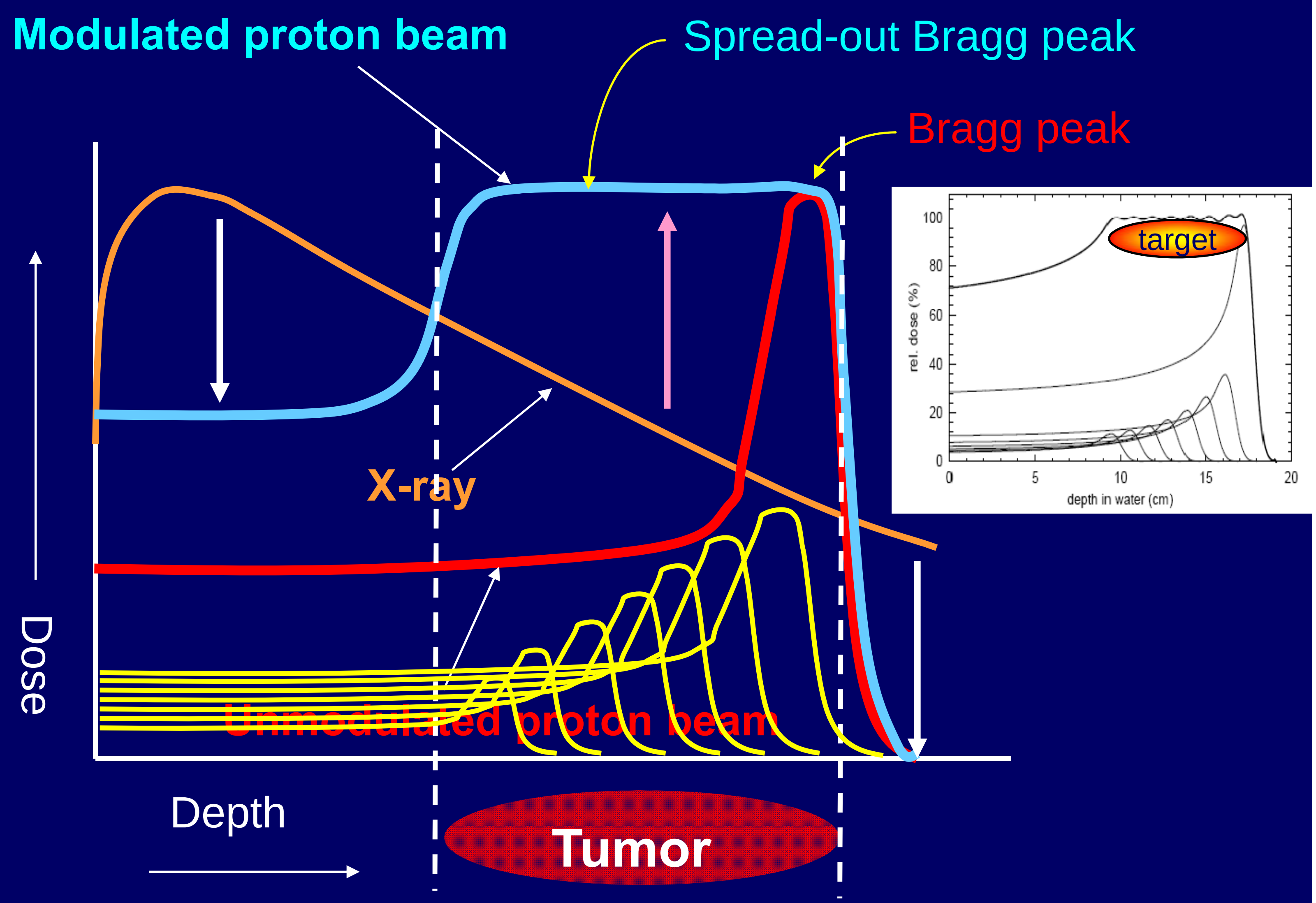
Biological Characteristics of Proton Beam

Table 2: RBE values of modulated proton beams at the Bragg peak compared to ^{60}Co[iii].

Reference	Tissue	Endpoint	Proton energy (MeV)	No. fractions	RBE
Tepper (1977)	Crypt cell	Survival	160	1	1.19
	Crypt cell	Survival	160	20	1.23
	Skin	Acute reaction	160	20	1.13
Urano (1980)	Fibrosarcoma	Survival	160	1-10	1.16
Urano (1984)	Mammary ca.	$TCD_{50/120}$	160	1	1.11
	Lens	Cataract	160	1	1.09
	Lung	$LD_{50/100}$	160	1	1.02
	Testis	Weight loss	160	1	1.23
	Tail vertebrae	Growth	160	1	1.32
Anso(1985)	Fibrosarcoma	Survival	70	1	1.06(1.01-1.12)
	Fibrosarcoma	Survival	250	1	1.06(1.03-1.09)
Tatsuzaki(1993)	Mouse	$LD_{50/30}$	250	1	1.09
	Skin	Contraction	250	10	1.03

Averaging RBE for proton =1.1

Physical Characteristics of Proton Beam



Why use proton?

No biological advantage:

RBE: 1.0-1.2

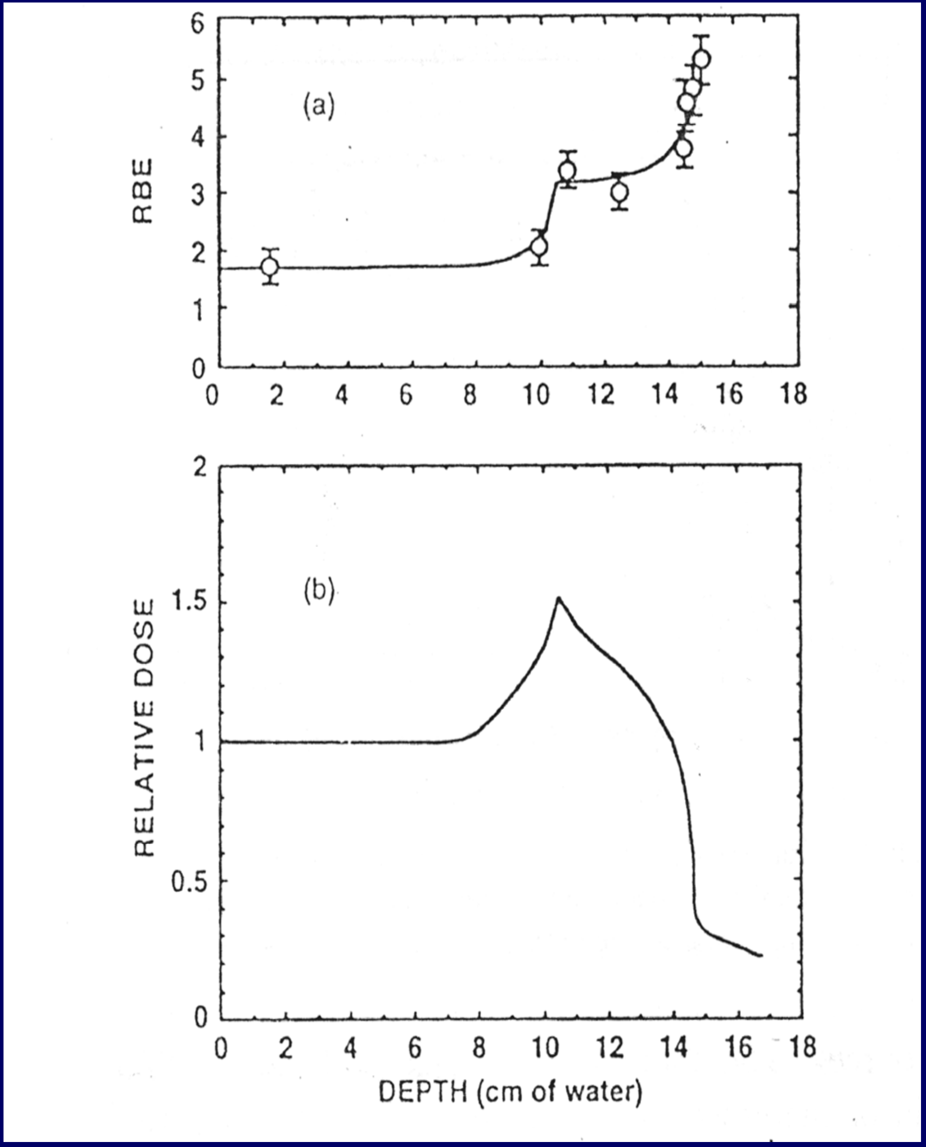
Mainly physical advantages:

Bragg Peak and Spread of Bragg peak

Abbreviated History of Protons

- 1919 Rutherford proposed existence of protons
- 1930 E. O. Lawrence built first cyclotron
- 1946 Robert Wilson proposed proton therapy
- 1955 Tobias et al treated patients at LBL
- 1961 Kjellberg et al treated patients at HCL
- 1972 MGH received first NCI grant for proton studies at HCL
- 1991 First hospital-based proton facility at LLUMC
- 2006 28 facilities worldwide treating patients; over 55,000 patients treated with protons.

How about the heavy ion?

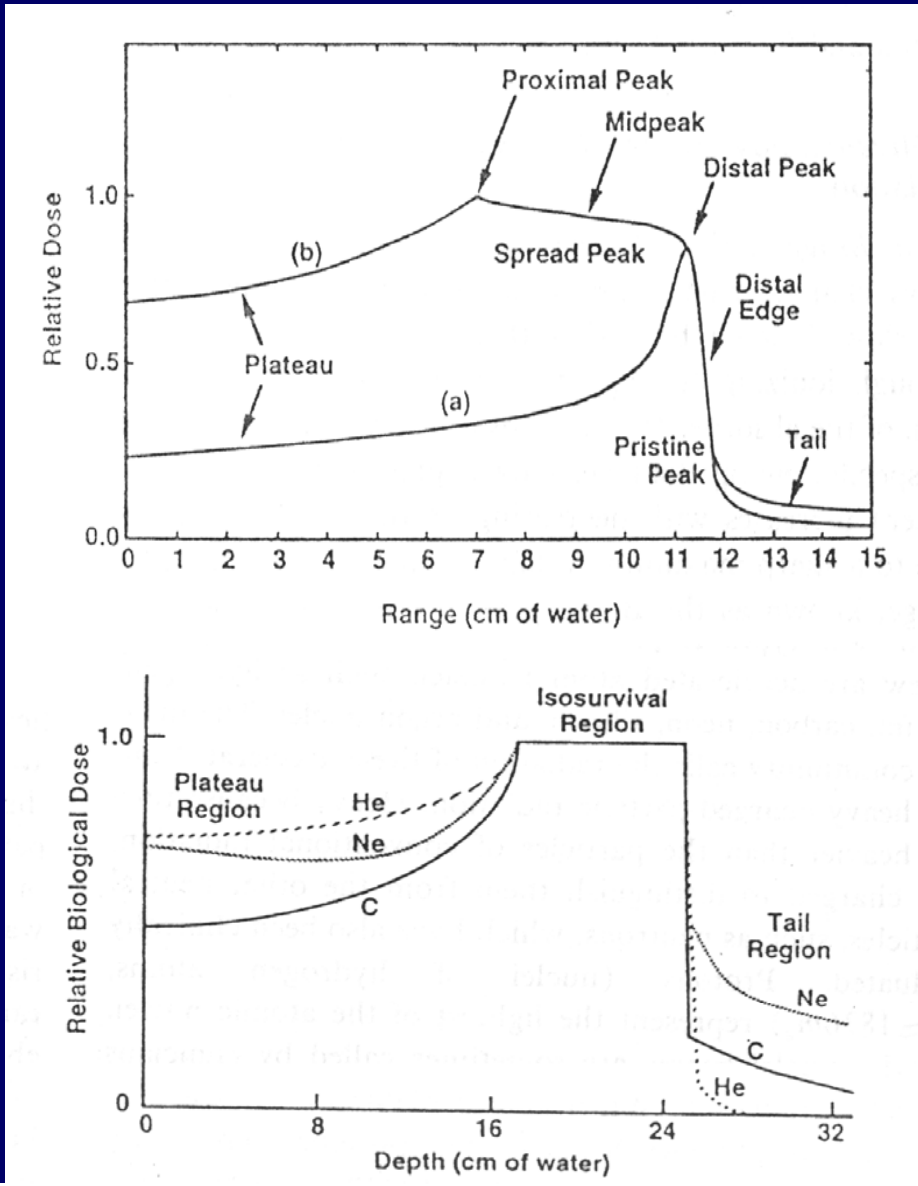


RBE significantly varied with depth.

Use physical dose to compensate the biological variation.

Biological dose as the prescribed dose

Why uses heavy ion?



1. Bragg peak & Spread of Bragg Peak (SOBP)
2. High RBE
3. Biological as well as physical advantage

But:

1. Tail dose –very high RBE
2. RBE varies with energy and depth
3. Limited facility – experimental
4. Expensive

History of heavy ions

1946 R.R. Wilson, Radiology 47,487
„potential benefits of heavy charged particles in radiotherapy“

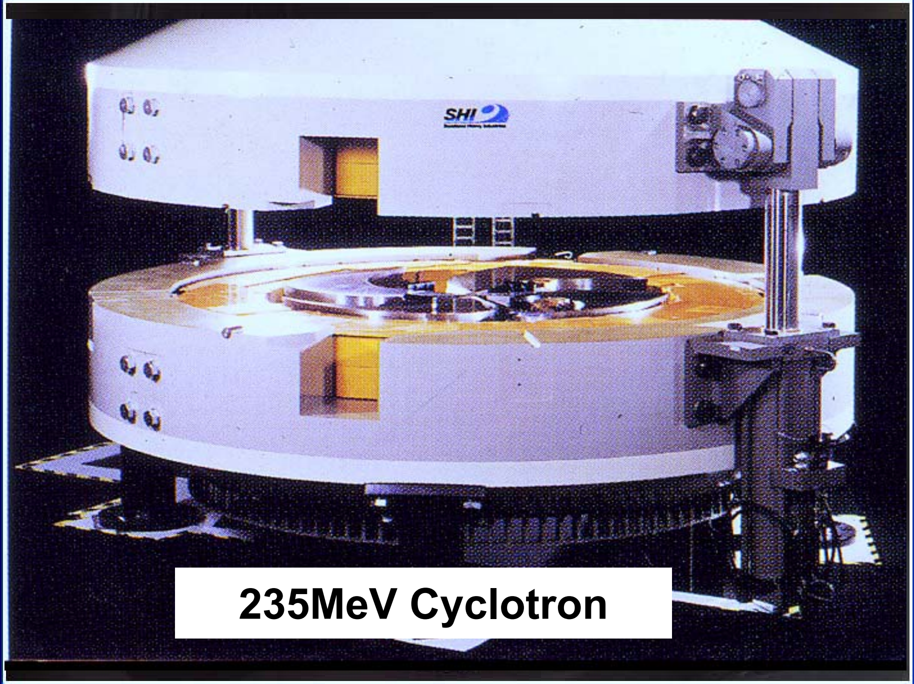
				patients
1957 - 92	^{4}He	184-inch SC	Berkeley	2054
1975 - 92	^{20}Ne	BEVALAC	Berkeley	433

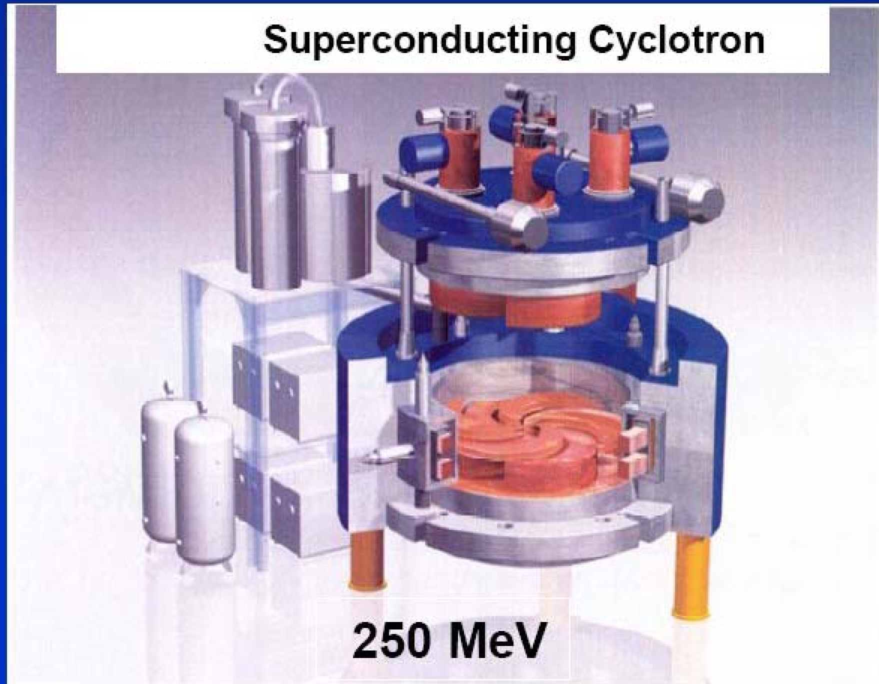
Current ion-beam facilites:

1994	^{12}C	HIMAC	Chiba	1800
1997	^{12}C	SIS-18	Darmstadt	245
2003	^{12}C	HIBMC	Hyogo	30

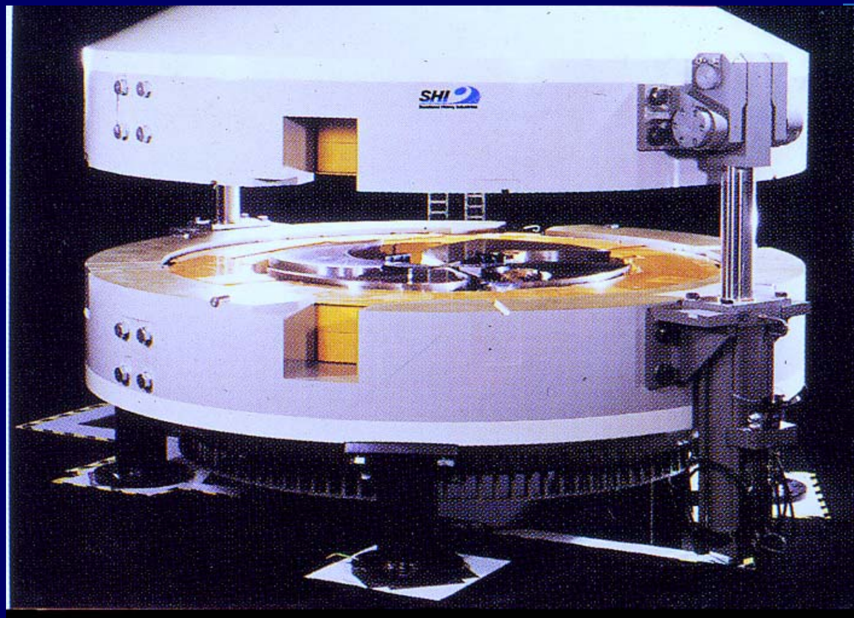
Typical Accelerators used in proton therapy facilities

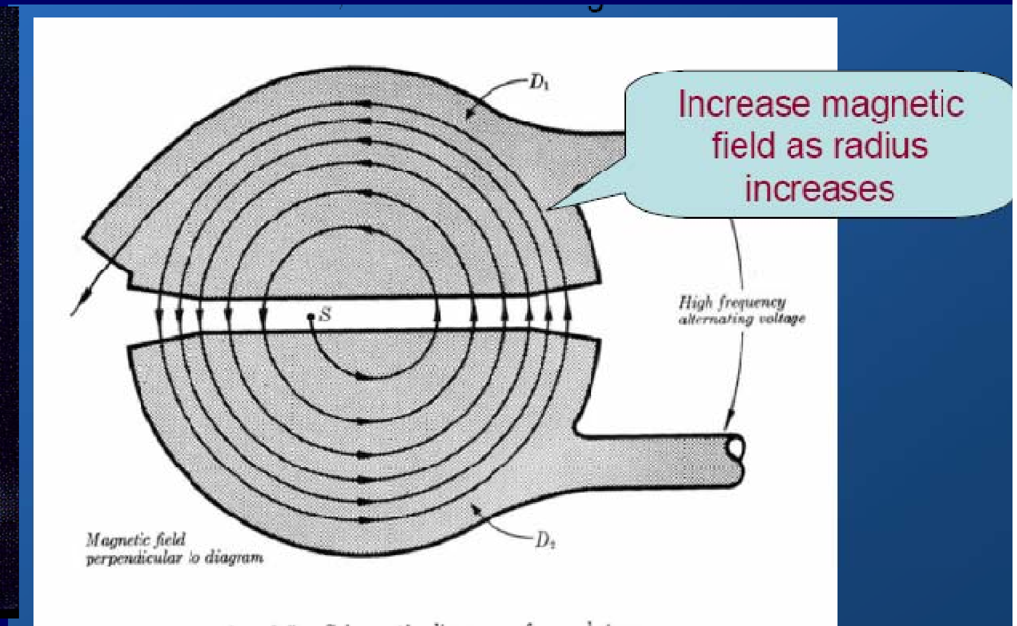
250 MeV synchrotron ring
7 MeV Linac injector





Cyclotron





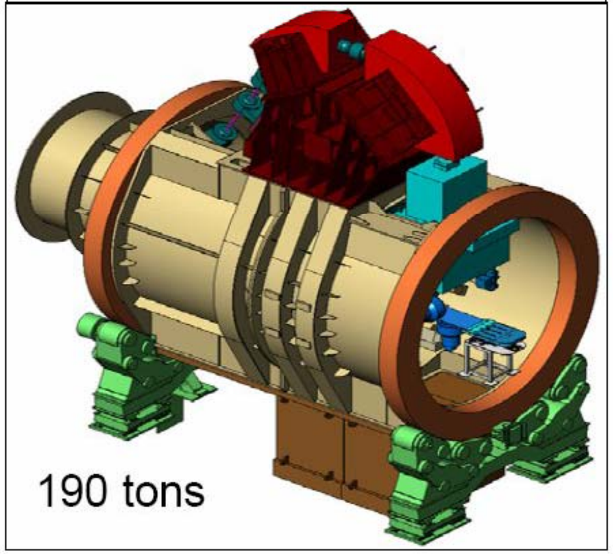
1. Fix time/per cycle, with increasing diameter to comply with the increasing speed of particle.
2. Continuous beam, not pulse. High output and dose rate.
3. Beam at the outlet: fixed energy.
4. Adjust energy by beam degrader.
5. Relatively more radioactivity of contamination.
6. Stable output, more suitable for pencil beam scanning.

Synchrotron

1. Fix diameter, with increasing the speed of changes of magnetic field to comply with the increasing speed of particle.
2. Pulse beam, not continuous. lower output and dose rate.
3. Beam at the outlet: variable energy.
4. Relatively more radioactivity of contamination.
5. Relatively not stable within a pulse, more difficult in pencil beam scan.

Proton and Carbon Ion Gantries

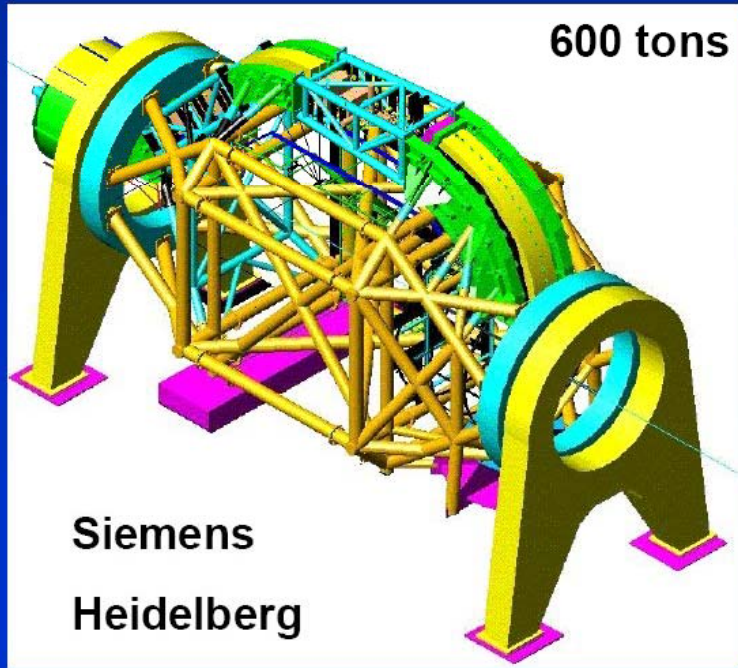
M. D. Anderson Gantry



Hitachi

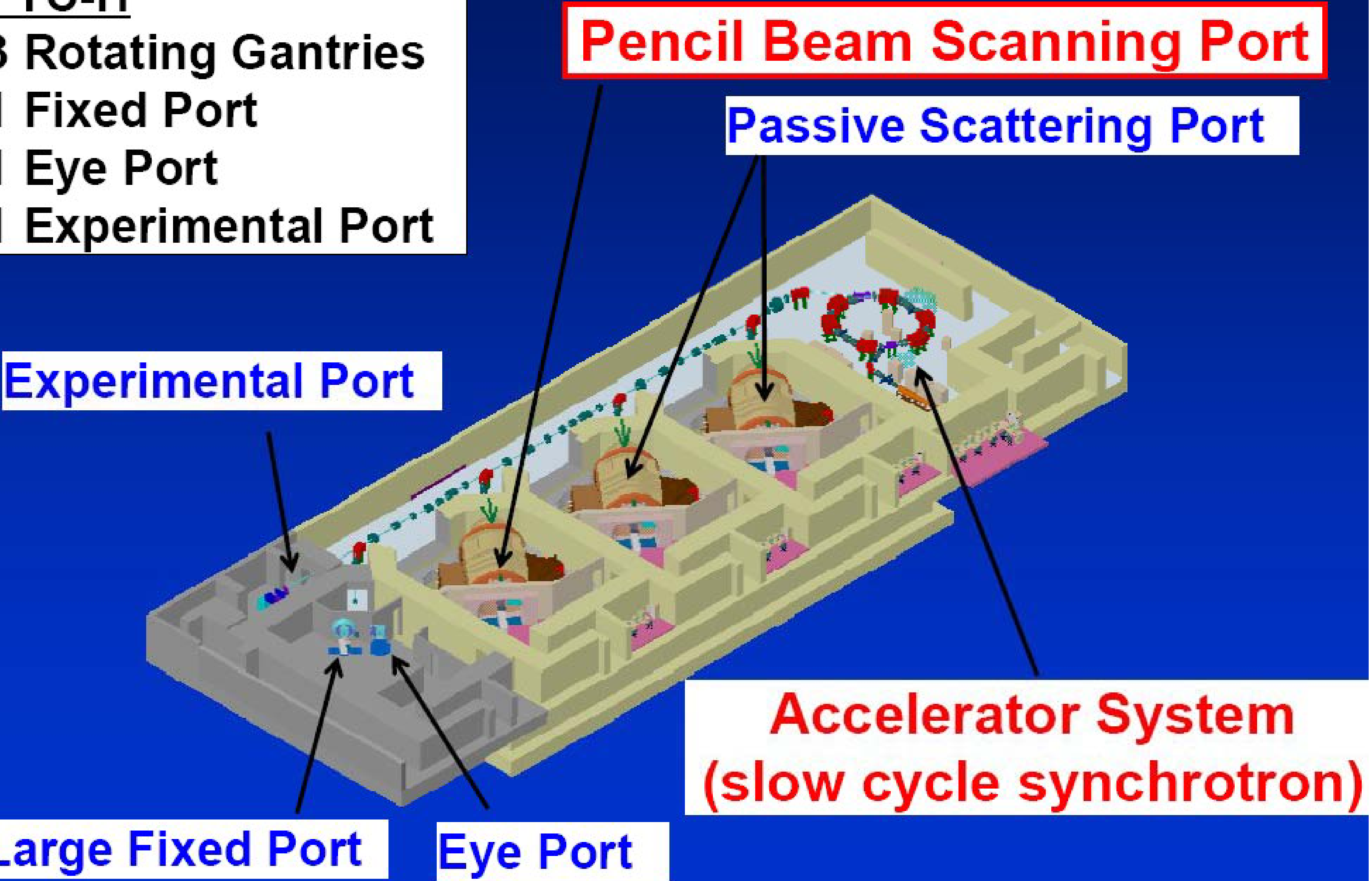
NPTC GANTRY

IBA 120 tons GENERAL ATOMICS



Proton Therapy Center - Houston

PTC-H
3 Rotating Gantries
1 Fixed Port
1 Eye Port
1 Experimental Port



Basic systems for particle facility

Accelerator system

Beam transport system

Beam delivery system

Patient positioning system

Treatment planning system

The Cost of a Proton Facility

The building/shielding – US$ 40million

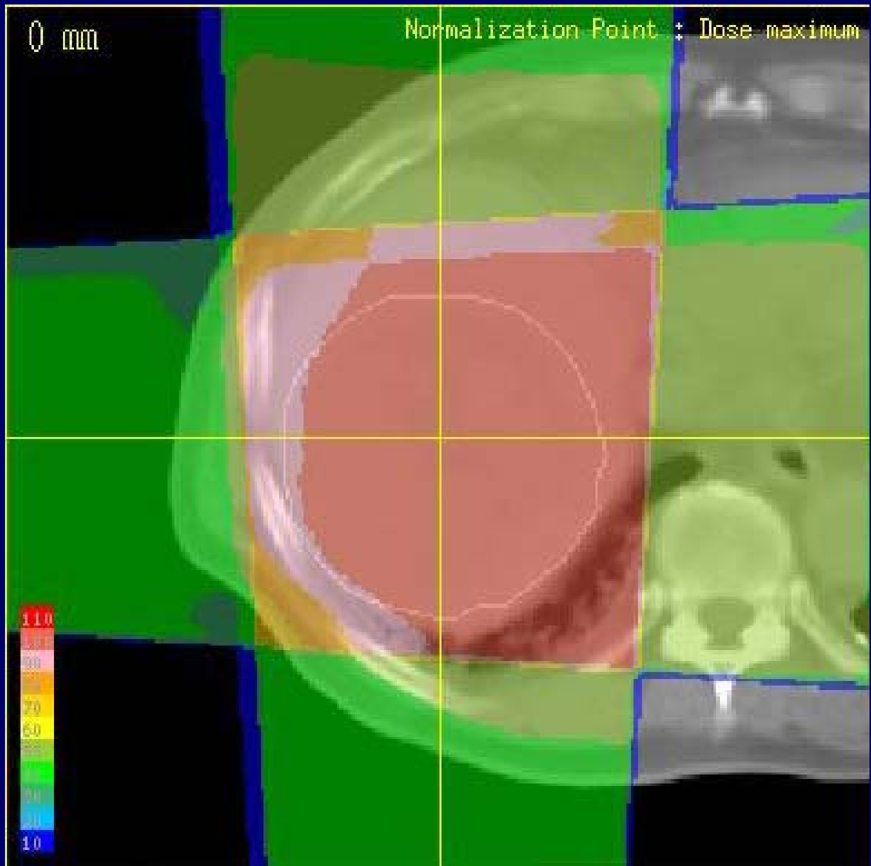
The accelerator – US$ 10-30million

The gantries/others - US$ 30million

The cost of a Carbon facility will be 2-3 times more!

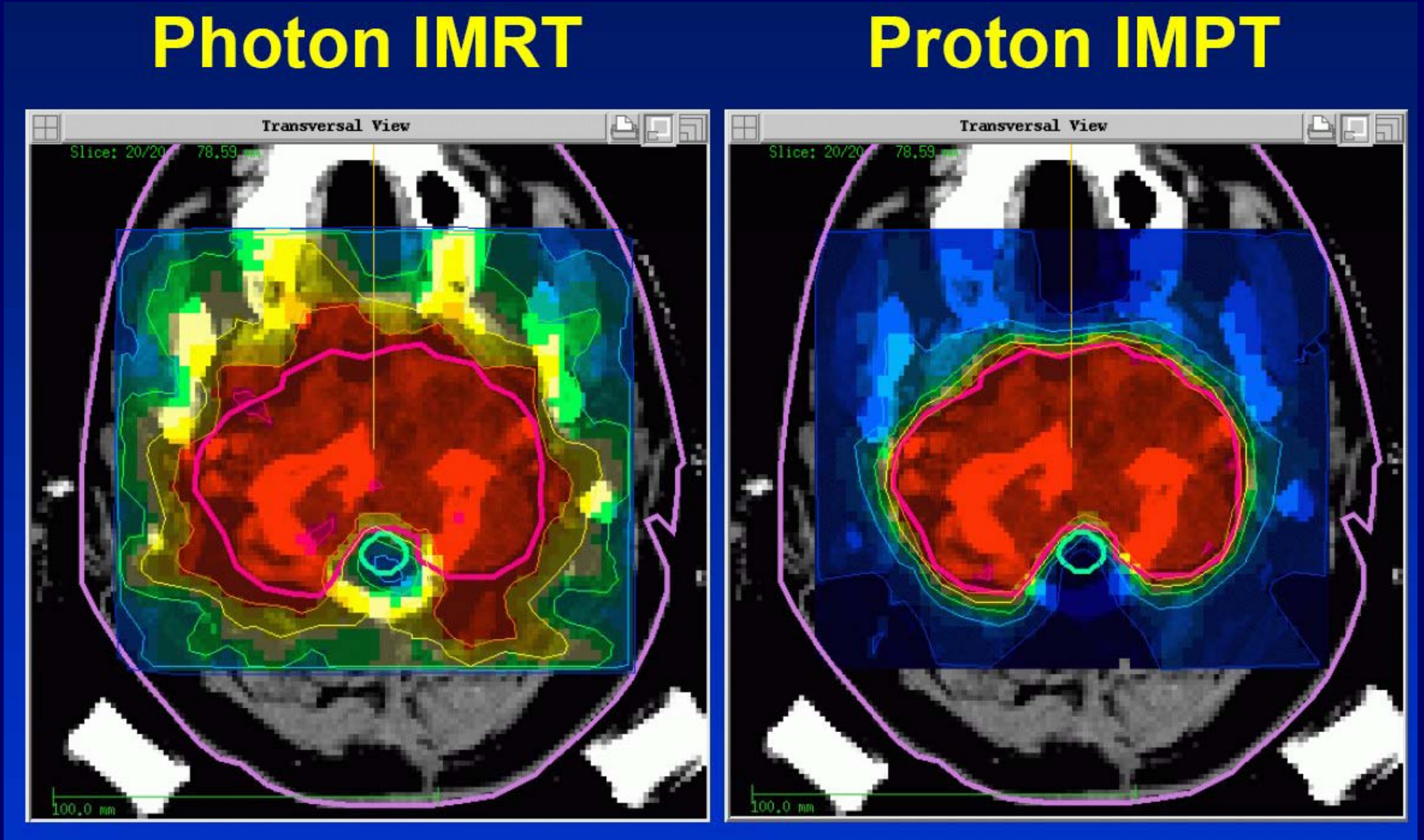
Dose comparison between photon and proton

6 MV X-rays

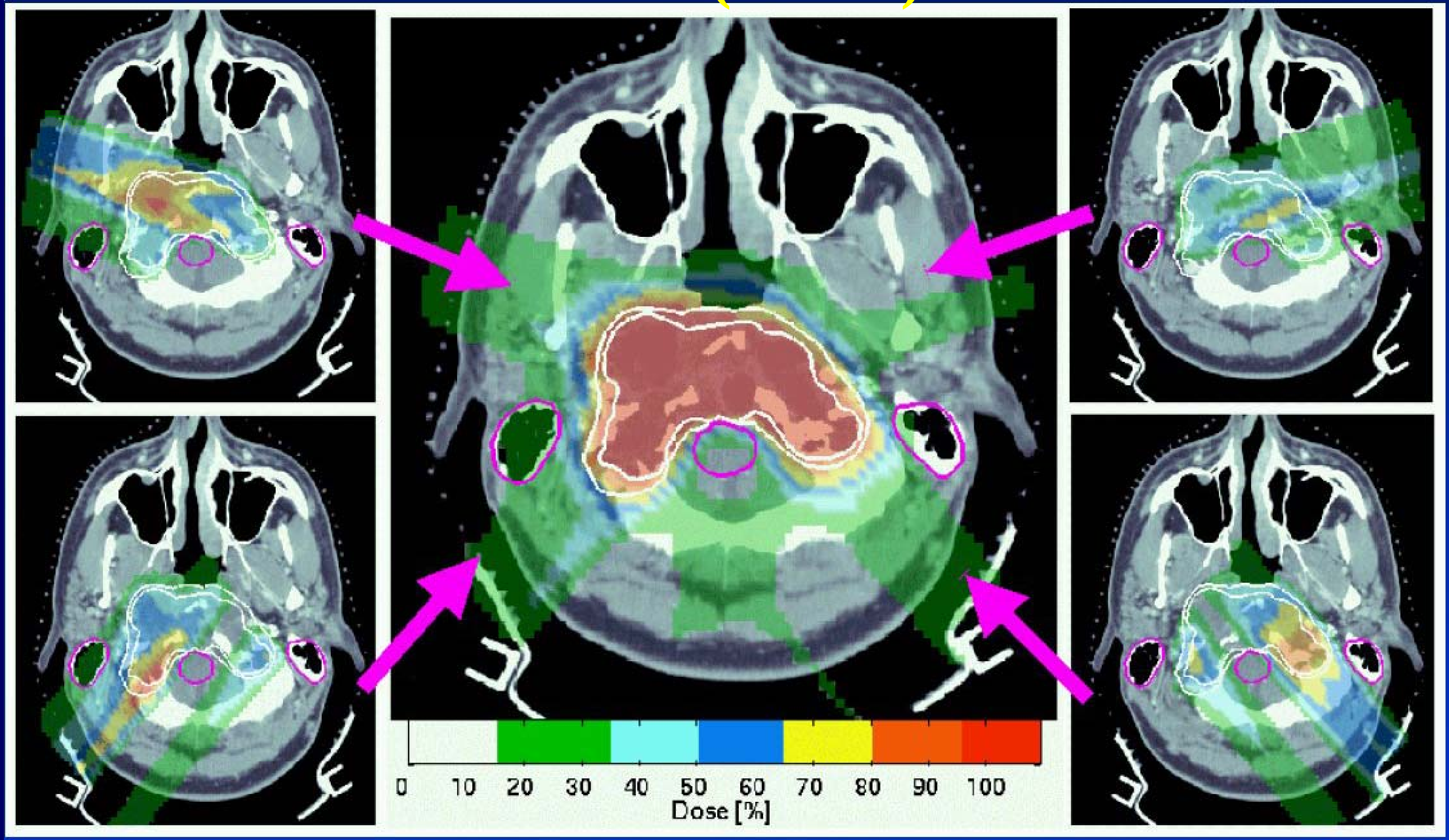


Protons

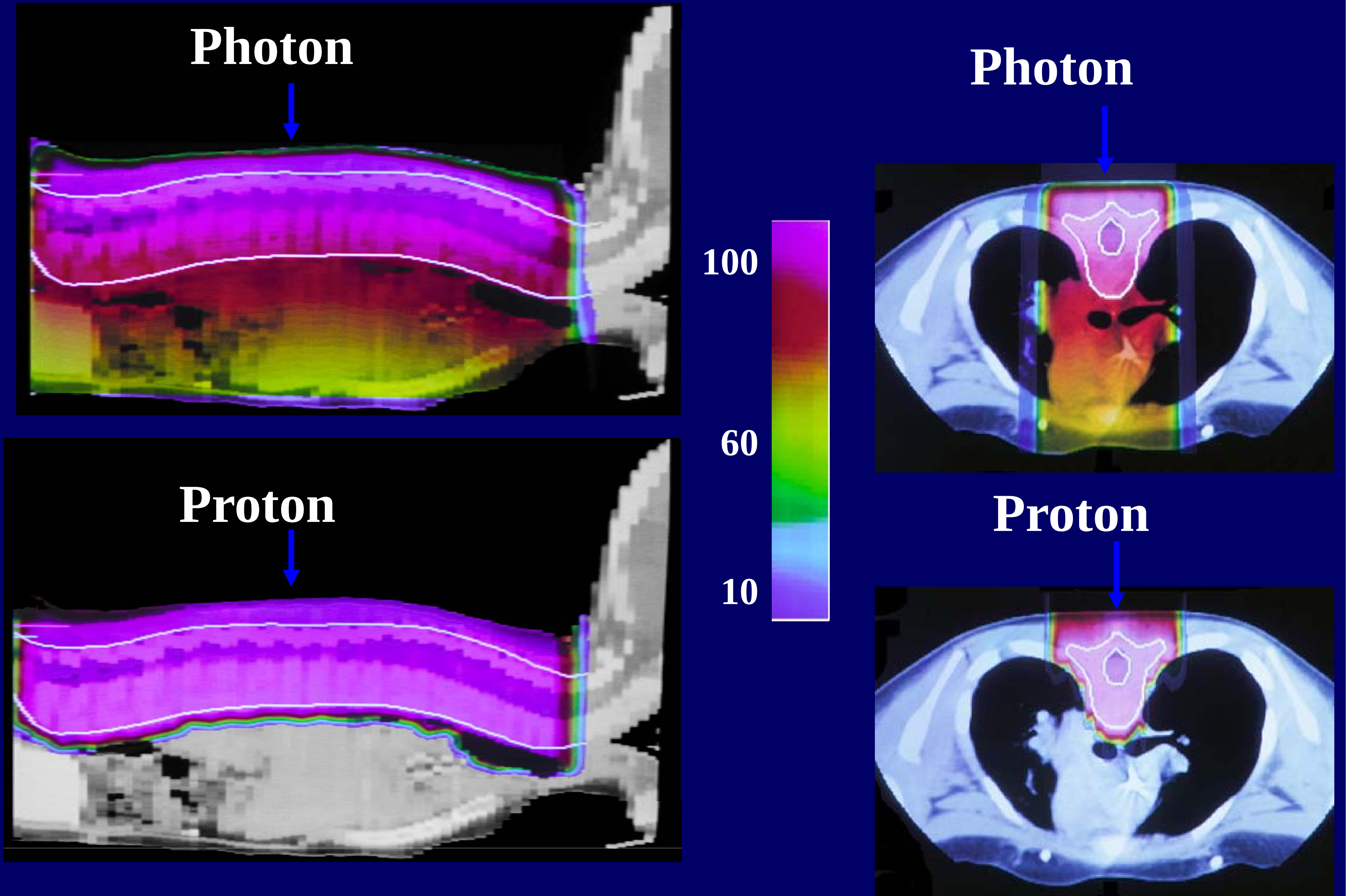
Dose comparison between photon and proton



Intensity Modulation Proton Thearpy (IMPT)



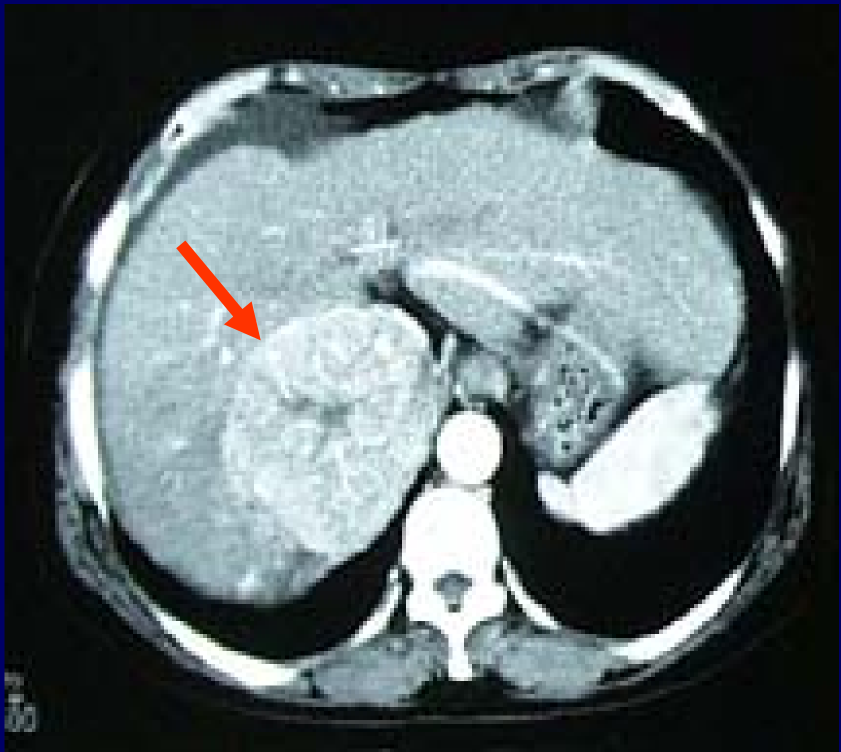
Medulloblastoma of Child



History: 1954-now Patients: > 77,000 patients

- Uveal Melanoma (眼黑色素瘤)
  - 5y Local Control Rates 96%
- Skull Base Tumor (Chordoma, Chondrosarcoma)(顱底瘤)
  - 5y Local Control Rates 65-91%
- Stage I Non-Small Cell Lung Cancer (肺癌)
  - 2y Survival Rates 75-86%
- Prostate Cancer(攝護腺癌)
  - 5y Local Control Rates 95%
- Hepatocellular Carcinoma(肝癌)
  - 3y Survival Rates 49%

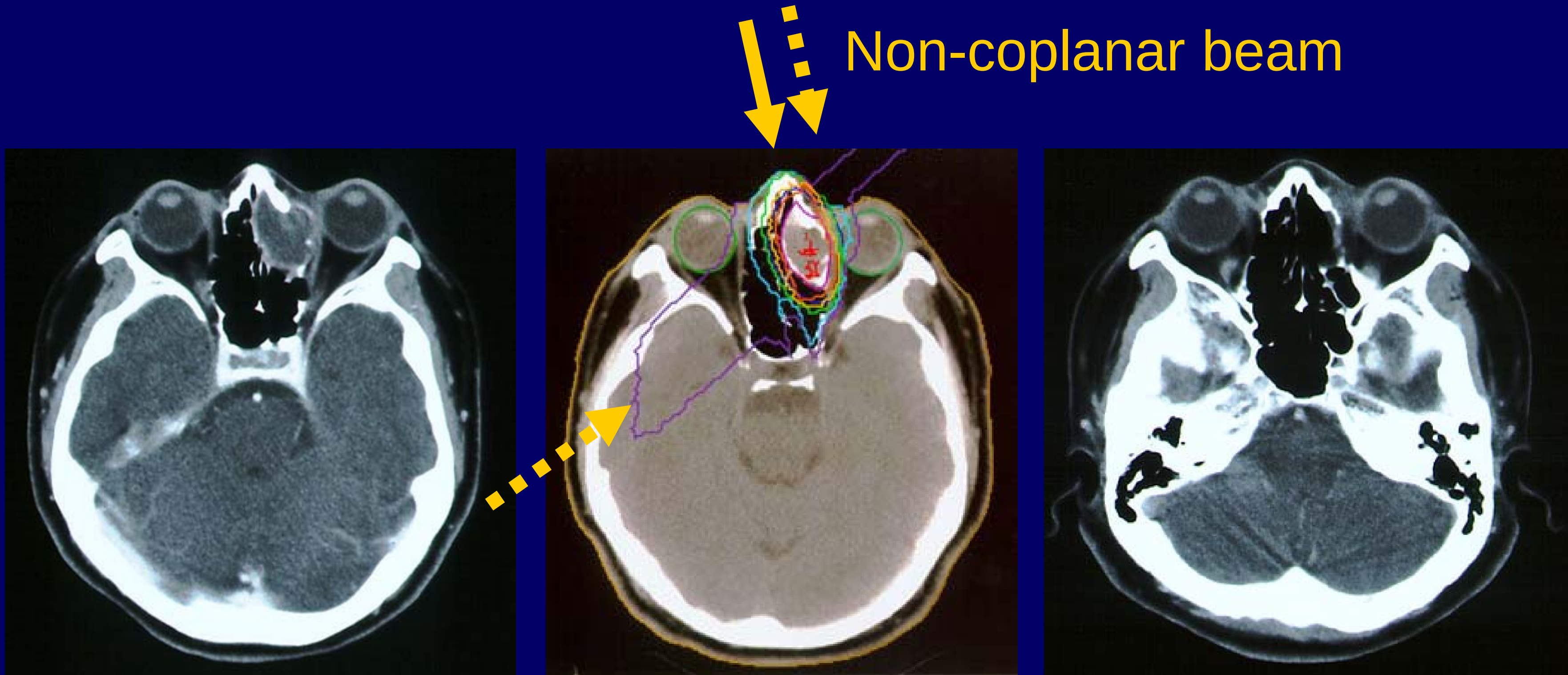
Proton Therapy



Pre-PBT **Post-76 GyE PBT**

67y F, Hepatocellular Carcinoma

Proton Therapy

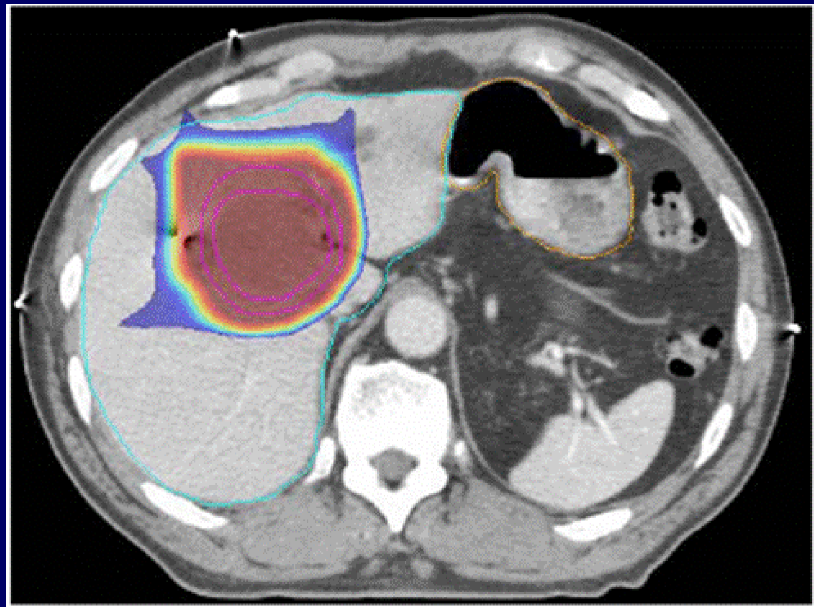


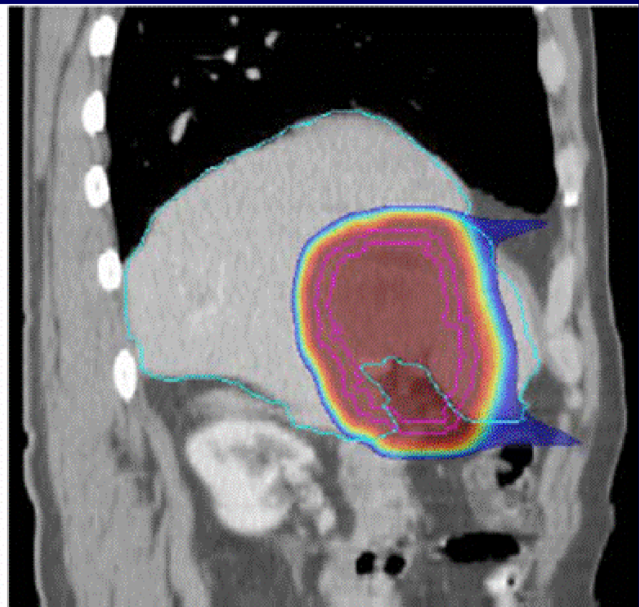
Pre-PBT | **Isodose Curve** | **Post-65 GyE PBT**

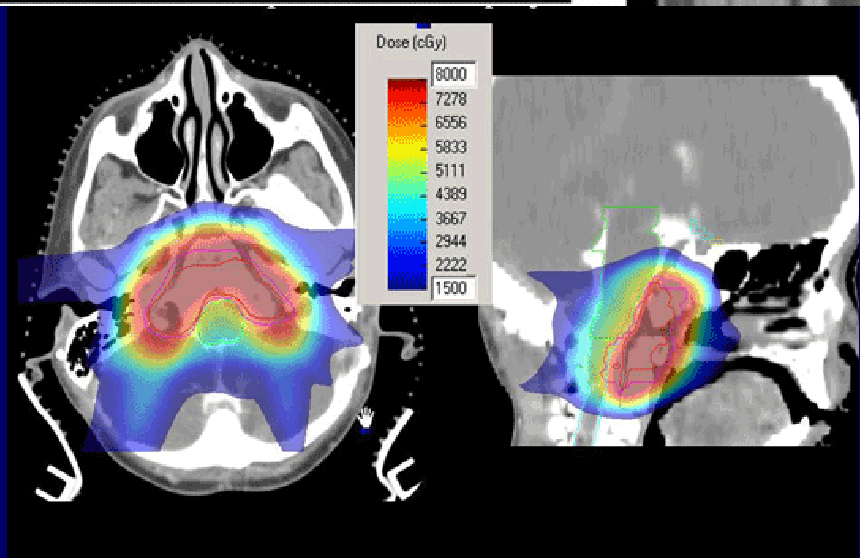
48y F, Ethmoid Sinus Cancer

No visual weakness, no brain damage

Proton Therapy







Does Taiwan need particle facility?

If need, how many is necessary?

Geography of Taiwan

Area~ 36,000 sq meter

Population~ 23,000,000

Preview of radiotherapy in Taiwan

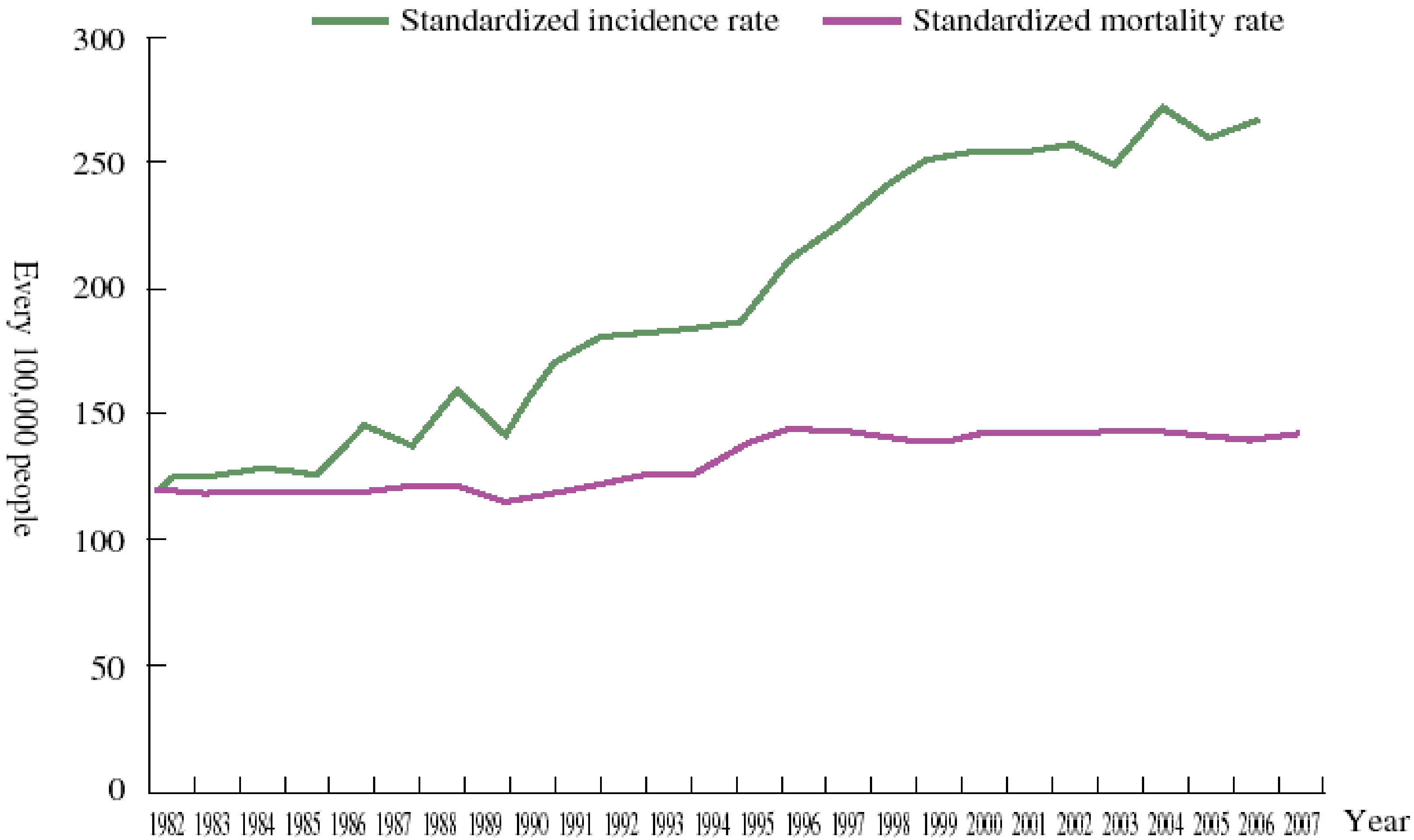
Leading Causes of Death in Taiwan, 2009

Rank	Cause of Death	No of death	Death rate per 100,000 population
1	Malignant neoplasms	39,917	173
2	Heart disease	15,058	65
3	Cerebrovascular disease	10,370	45
4	Pneumonia	8,381	36
5	Diabetes mellitus	8,239	36
6	Accidents and adverse effects	7,387	32
7	Chronic respiratory disease	4,972	22
8	Chronic liver disease and cirrhosis	4,972	22
9	Suicide	4,120	18
10	Nephritis, nephrotic syndrome and nephrosis	3,977	17
	Total	107,392	465

Leading Causes of Cancer Death in Taiwan, 2009

Rank	Cause of Death	No of death	Death rate per 100,000 population
1	lung cancer	7,943	34
2	liver cancer	7,744	34
3	colorectal cancer	4,551	20
4	female breast cancer	1,597	7
5	stomach cancer	2,275	10
6	oral cavity cancer	2,235	10
7	prostate cancer	918	4
8	esophageal cancer	1,477	6
9	pancreatic cancer	1,477	6
10	cervical cancer	639	3
	All other causes	9,061	39
	Total	39,917	173

Figure 3-10 Long-term trends of standardized incidence rates and mortality rates for all cancers in Taiwan



International Comparison of Standardized Mortality Rates Per 100,000 people Due to Cancer

	Taiwan	South Korea	Japan	Singapore	UK	USA	Australia
1992	108	117	108	132	145	132	124
1993	111	122	106	129	142	132	124
1994	112	125	106	132	139	131	126
1995	120	123	111	131	137	130	121
1996	126	119	111	128	136	128	121
1997	127	119	109	128	133	126	118
1998	123	111	109	118	132	124	117
1999	121	115	108	116	129	123	114
2000	124	118	106	114	126	121	112
2001	125	116	105	112	127	...	111
2002	126	119	102	...	126	...	...

By 1976 W.H.O. World Standard Population as the Standard

Cancer prevention and control in Taiwan

Table 3-8 Screening Results

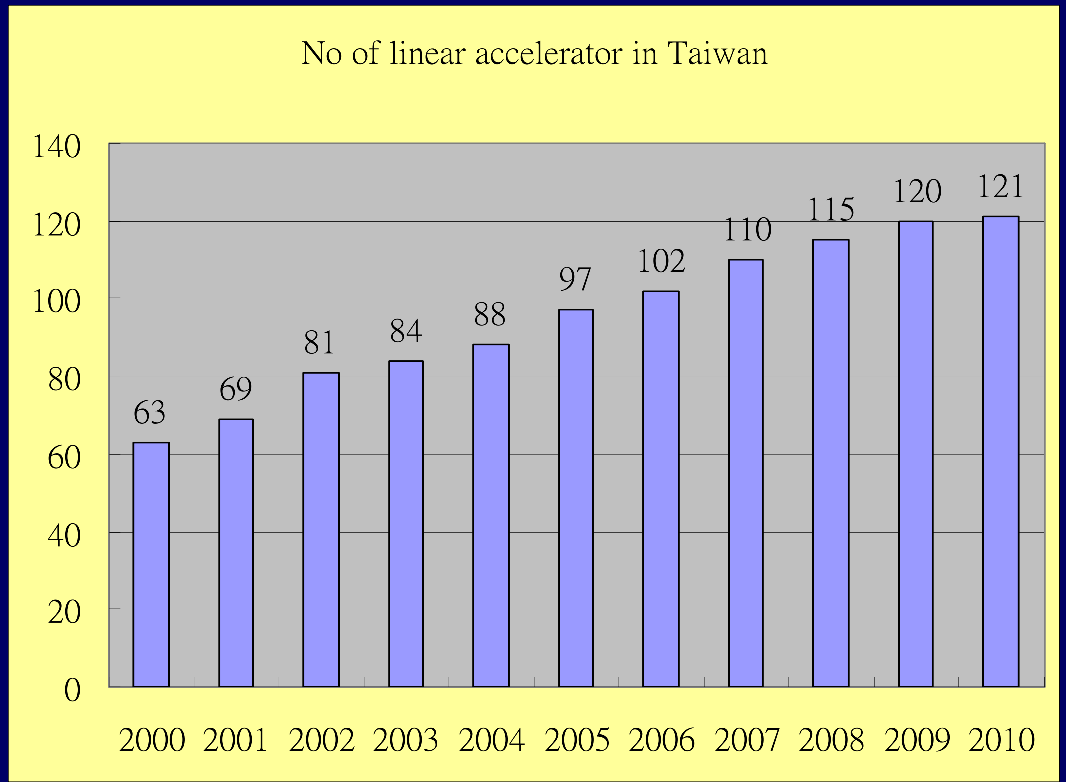
Item	Subject	Screening Policy	2008 Screening Results
Cervical cancer	Women over 30 years old	At least one Pap smear every three years	• 56% of women aged 30-69 had a Pap smear within three years • 70% of women interviewed by telephone had a Pap smear within three years
Breast cancer	Women between 50-69 years old	One mammography every two years	12% of women aged 50-69 had a mammography within two years
Oral cancer	Betel quid chewers or smokers over 18 years old	Oral visual inspection	25% of betel quid chewers or smokers over 18 years old had an oral visual checks inspection within two years
Colorectal cancer	People between 50-69 years old	One fecal occult blood test every two years	10% of people aged 50-69 had a fecal occult blood test within two years

Why need more radiotherapy facilities ?

The cancer incidence is predicted by WHO(1995) to increase to approximately 15 million new cases by the year 2015.

About 50% of cancer patients still require radiation treatment, either curative or palliative. The need for rapid worldwide expansion of radiation treatment technology demands adequate resources, including the creation of new treatment facilities, new technology, well trained medical personnel.

Preview of radiotherapy in Taiwan



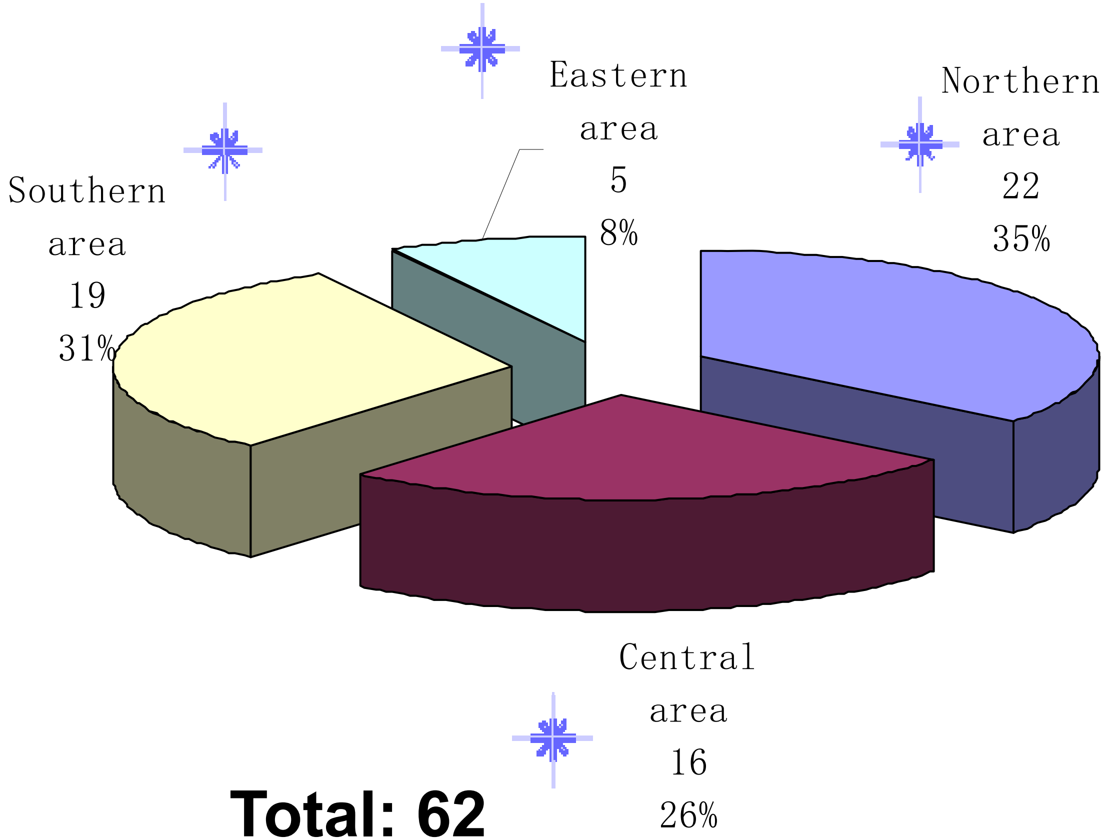
121 sets
Linear accelerator

5 sets
Cyber knife

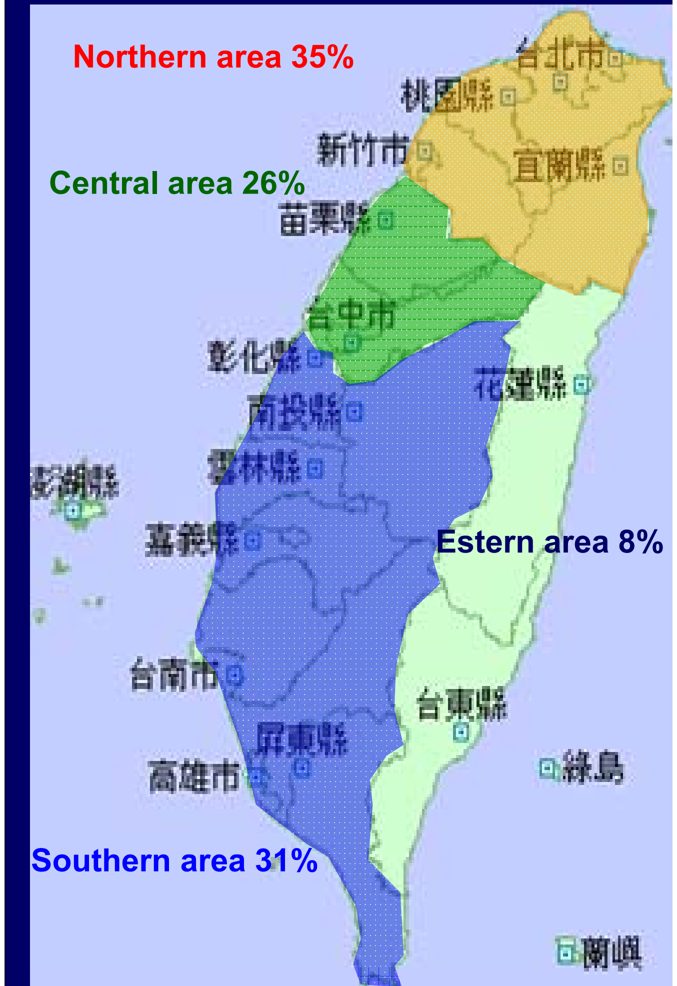
8sets
Gamma knife

10 sets
Tomotherapy

Radiotherapy facility in Taiwan



Total: 62



Preview of radiotherapy in Taiwan

210

Radiation oncology attending physicians

60

Resident doctors

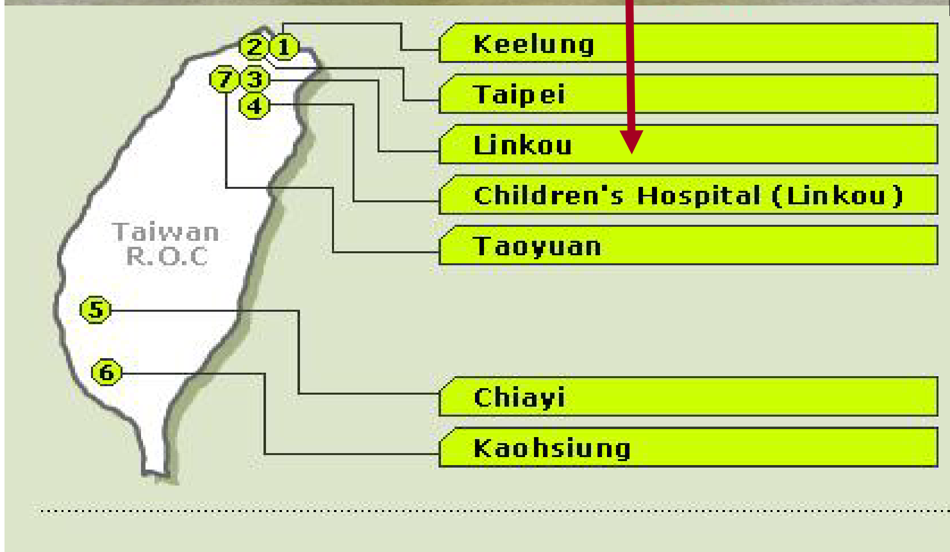
120

Medical physicists

The first proton project in Taiwan

台灣的第一步(部)

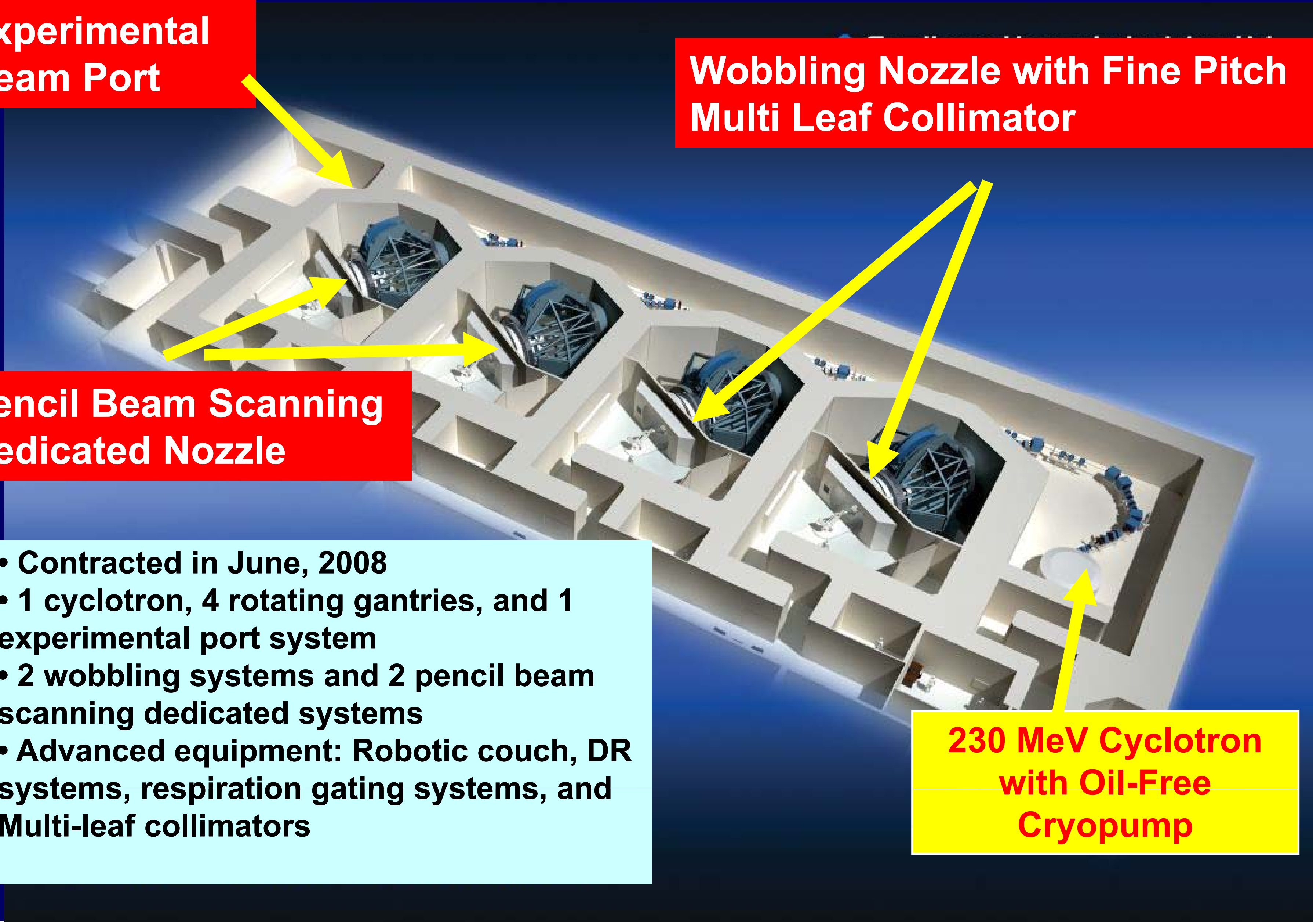
New Proton Center of Chang Gung Memorial Hospital



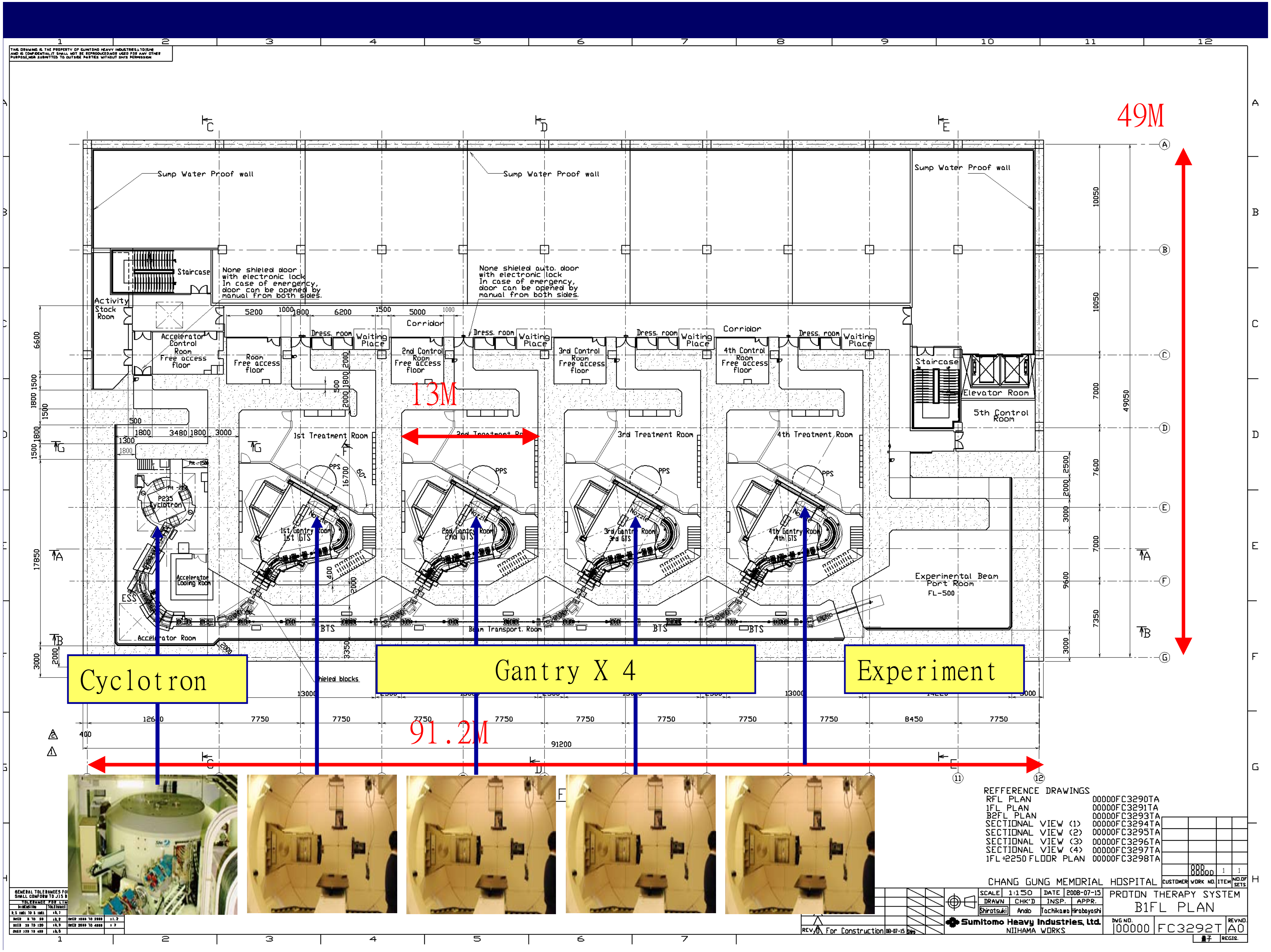
Proton Therapy in Taiwan

Chang Gung Memorial Hospital

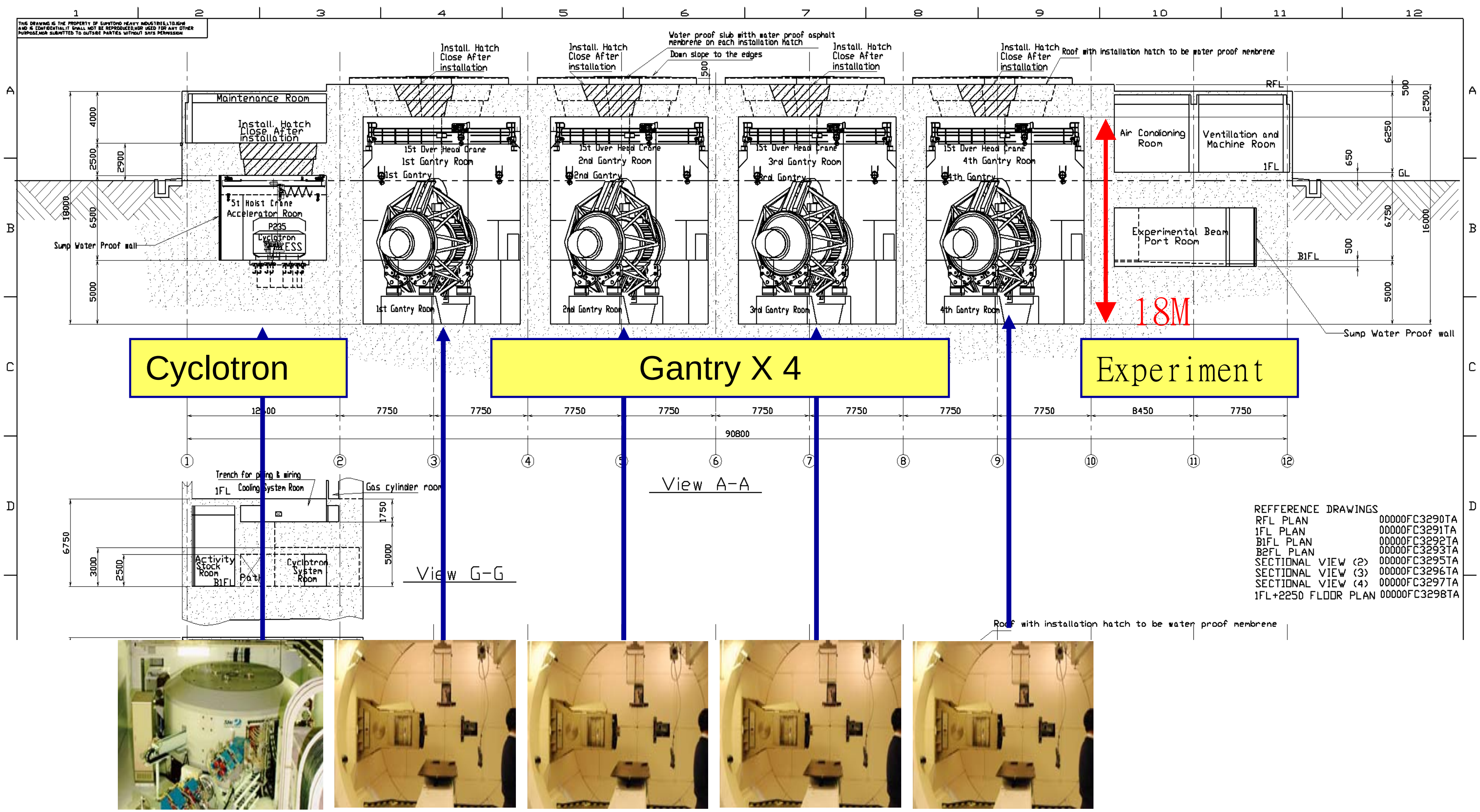
Proton Therapy System (PTS) for CGMH



- Contracted in June, 2008
- 1 cyclotron, 4 rotating gantries, and 1 experimental port system
- 2 wobbling systems and 2 pencil beam scanning dedicated systems
- Advanced equipment: Robotic couch, DR systems, respiration gating systems, and Multi-leaf collimators



49M
13M
91.2M
Cyclotron
Gantry X 4
Experiment
Sump Water Proof wall
Staircase
None shielded door with electronic lock In case of emergency, door can be opened by manual from both sides.
None shielded auto. door with electronic lock In case of emergency, door can be opened by manual from both sides.
Activity Stock Room
Accelerator Control Room Free access floor
Corridor
Dress. room
Waiting Place
2nd Control Room Free access floor
3rd Control Room Free access floor
4th Control Room Free access floor
Elevator Room
5th Control Room
1st Treatment Room
3rd Treatment Room
4th Treatment Room
PPS
P235 Cyclotron
1st Gantry Room
1st GTS
2nd Gantry Room
2nd GTS
3rd Gantry Room
3rd GTS
4th Gantry Room
4th GTS
Accelerator Cooling Room
ESS
Accelerator Room
BTS
Beam Transport Room
Experimental Beam Port Room
FL-500
Shielded blocks
91200
REFFERENCE DRAWINGS
RFL PLAN 00000FC3290TA
1FL PLAN 00000FC3291TA
B2FL PLAN 00000FC3293TA
SECTIONAL VIEW (1) 00000FC3294TA
SECTIONAL VIEW (2) 00000FC3295TA
SECTIONAL VIEW (3) 00000FC3296TA
SECTIONAL VIEW (4) 00000FC3297TA
1FL+2250 FLOOR PLAN 00000FC3298TA
CHANG GUNG MEMORIAL HOSPITAL
PROTON THERAPY SYSTEM
B1FL PLAN
SCALE 1:150
DATE 2008-07-15
Sumitomo Heavy Industries, Ltd.
NIIHAMA WORKS
For Construction
FC3292T

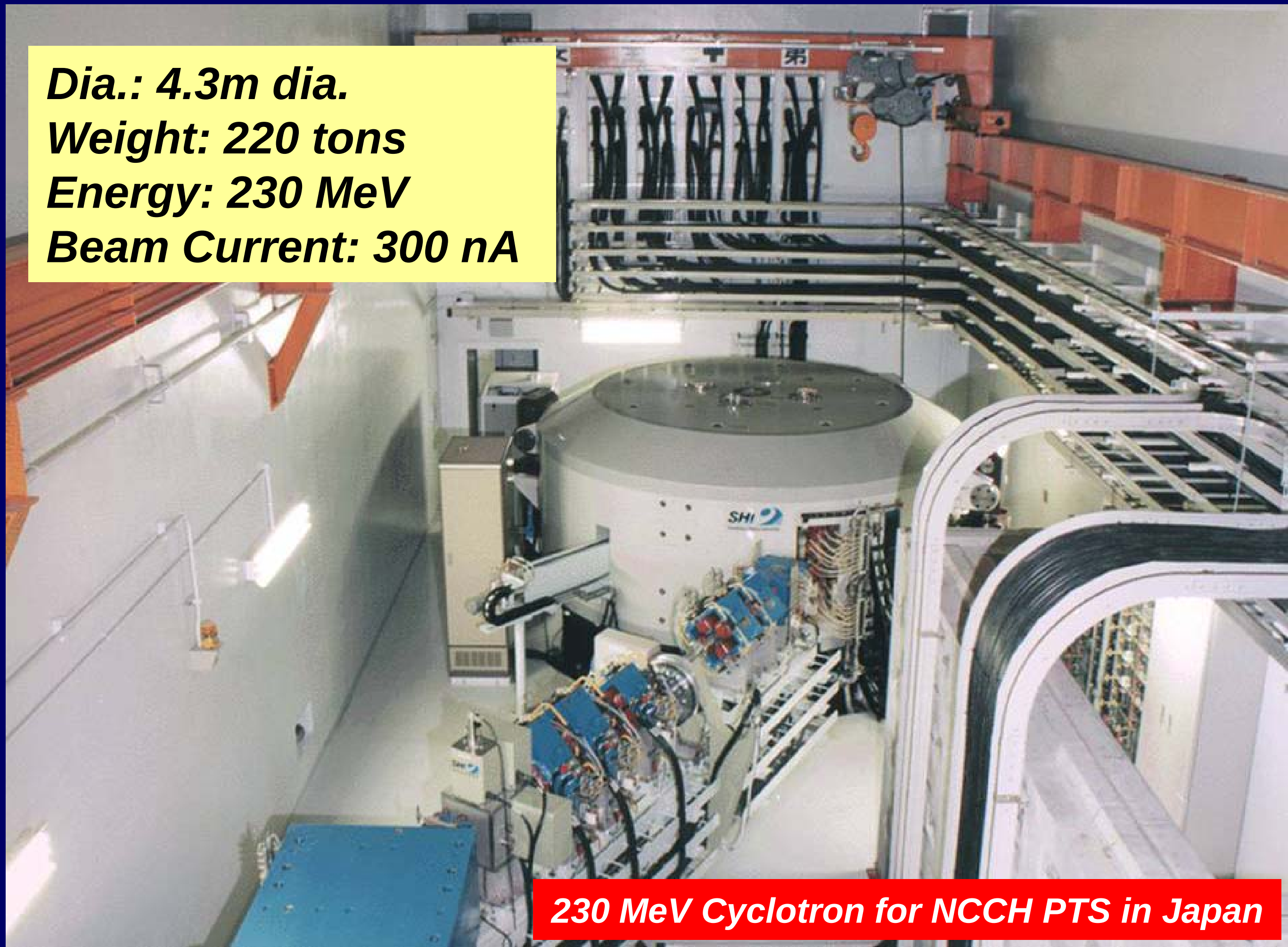


Cyclotron
Gantry X 4
Experiment
18M
Maintenance Room
Install. Hatch Close After installation
Accelerator Room
1st Gantry Room
2nd Gantry Room
3rd Gantry Room
4th Gantry Room
Air Conditioning Room
Ventillation and Machine Room
Experimental Beam Port Room
Sump Water Proof wall
RFL
GL
1FL
B1FL
12600
7750
8450
90800
View A-A
View G-G
Cooling System Room
Gas cylinder room
Activity Stock Room
Cyclotron System Room
REFFERENCE DRAWINGS
RFL PLAN 00000FC3290TA
1FL PLAN 00000FC3291TA
B1FL PLAN 00000FC3292TA
B2FL PLAN 00000FC3293TA
SECTIONAL VIEW (2) 00000FC3295TA
SECTIONAL VIEW (3) 00000FC3296TA
SECTIONAL VIEW (4) 00000FC3297TA
1FL+2250 FLOOR PLAN 00000FC3298TA
Roof with installation hatch to be water proof membrene

Clinical Specifications of Proton therapy at CGMH in Taiwan

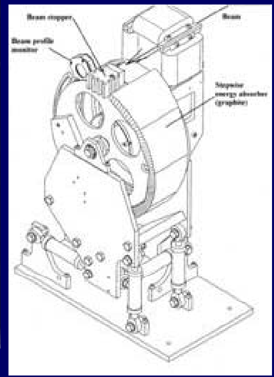
Item	Wobbling Nozzle	Pencil Beam Scanning Nozzle
Max. Field Size	25 cm x 25 cm (w/o MLC) 20 cm x 20 cm (with MLC)	40 cm x 30 cm (L x W)
Max. Range (Energy)	32 g/cm^2 (230 MeV) without scatterer	32 g/cm^2 (230 MeV)
Min. Range (Energy)	4 g/cm2 (70 MeV)	
Energy Steps	Continuous from 230 MeV to70 MeV	
Range Modulation	Steps of 1g/cm2 by ridge filters	Steps of 0.2 g/cm2
Dose Uniformity	± 2.5% over 80% of field size	± 2.5% over 40 cm x 30 cm (comformity)
Average Dose Rate	1 Gy/min/liter (regardless of depth and field size)	

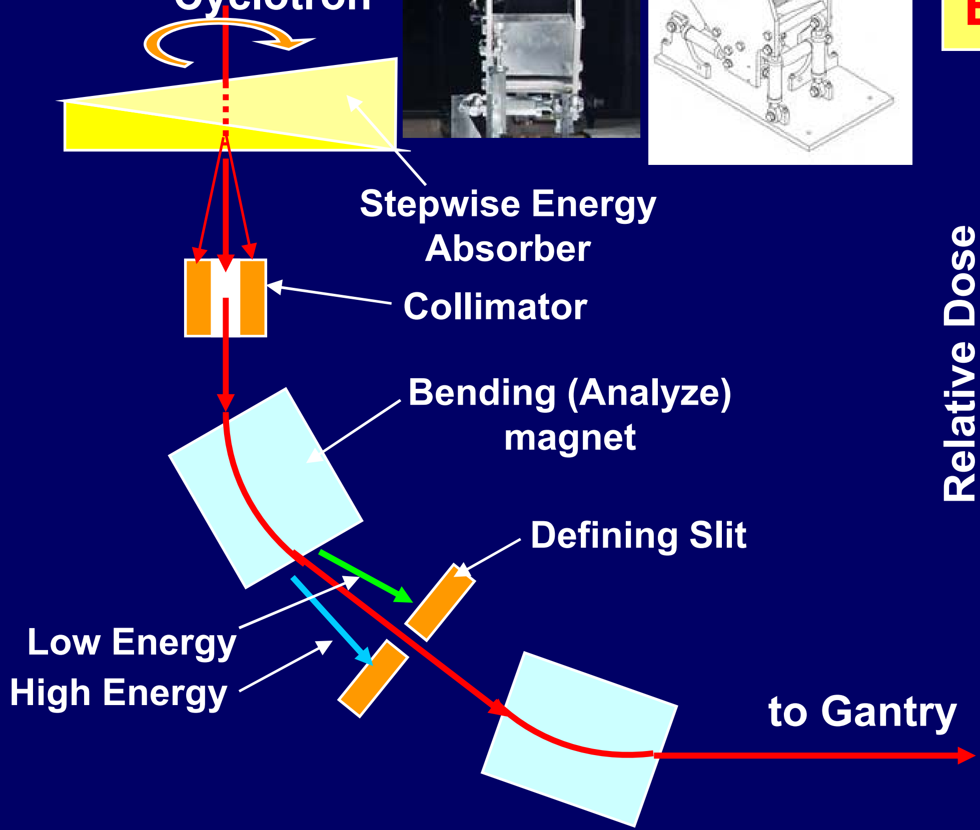
230 MeV Sumitomo Cyclotron



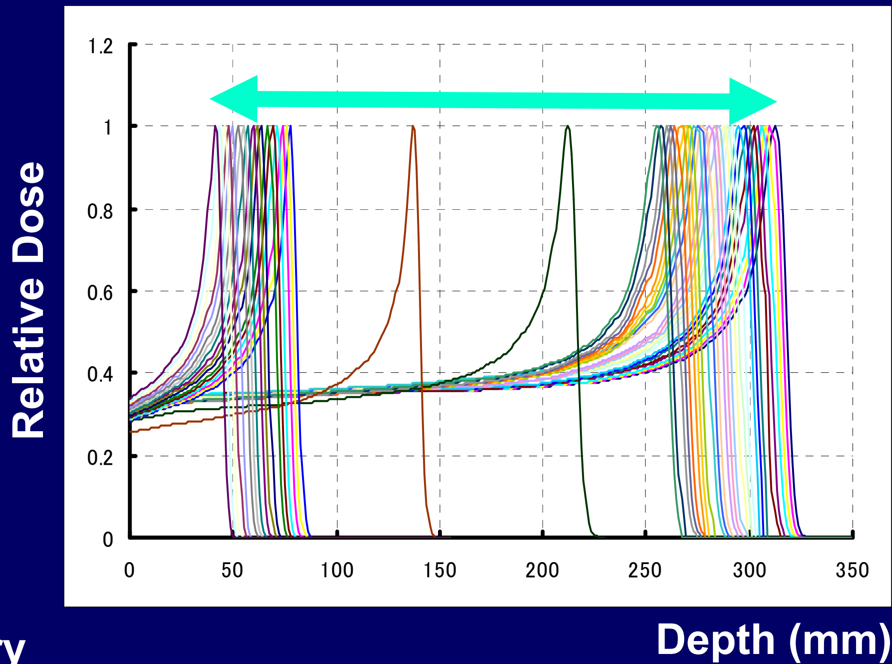
230 MeV Cyclotron for NCCH PTS in Japan

Energy Selection System (ESS)

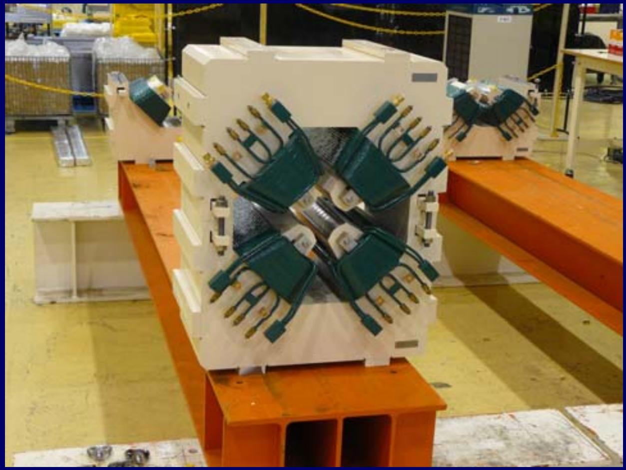




Beam Energy Range: 70 – 230MeV



Beam Transport System



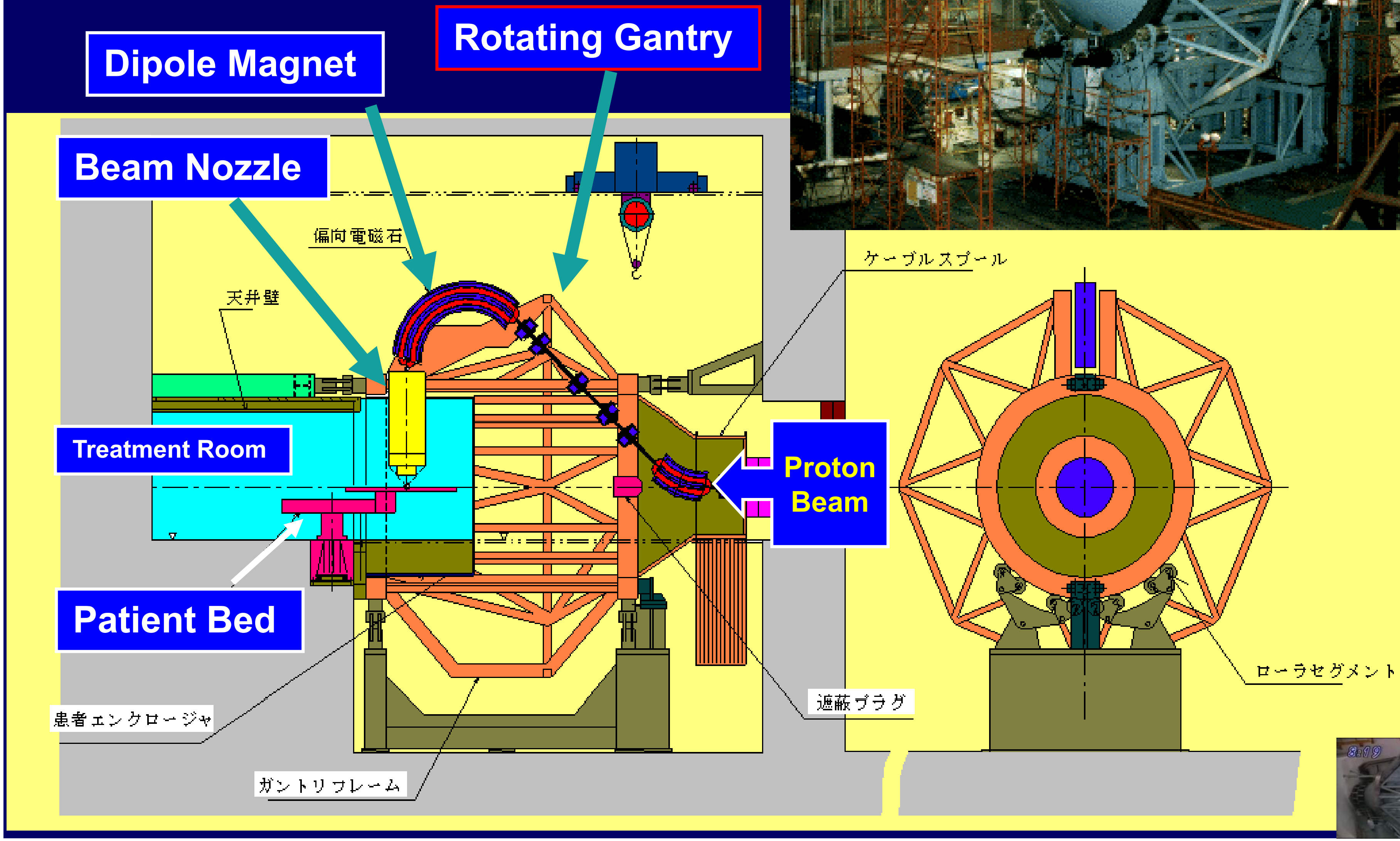
Quadrupole Magnet

Magnet Shop in SHI

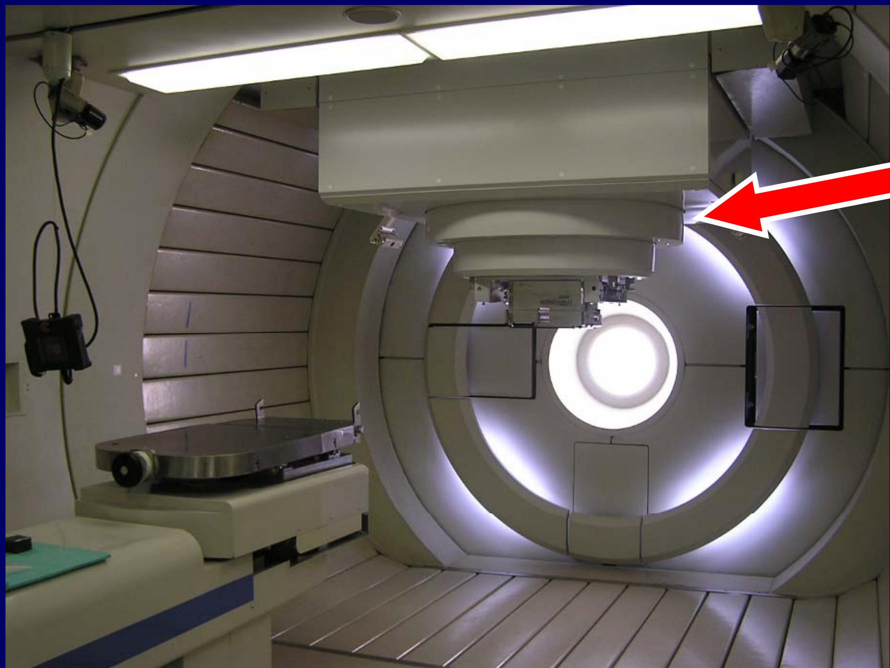
Requirement for beam delivery room switching time
< 2 sec

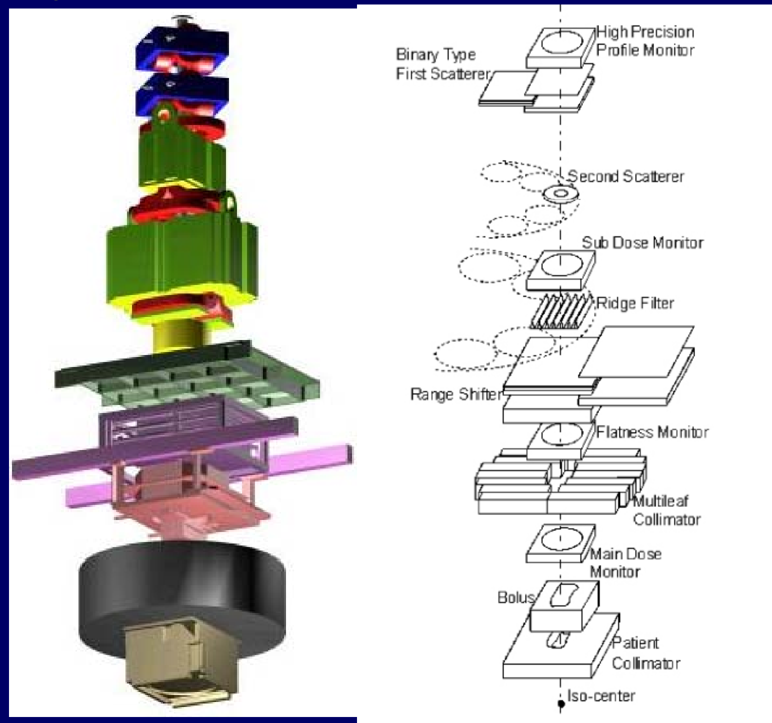
Changed Block Magnets to Laminated Magnets

Rotating Gantry



1st and 2nd Treatment Room:
Wobbling Nozzle



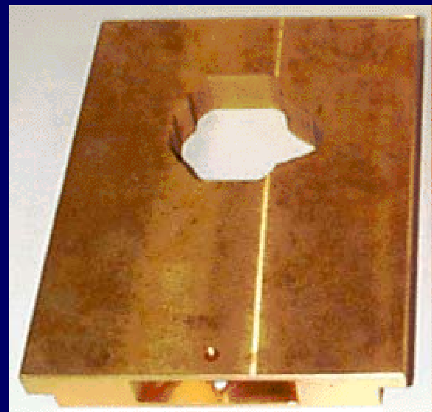


Multi Leaf Collimator

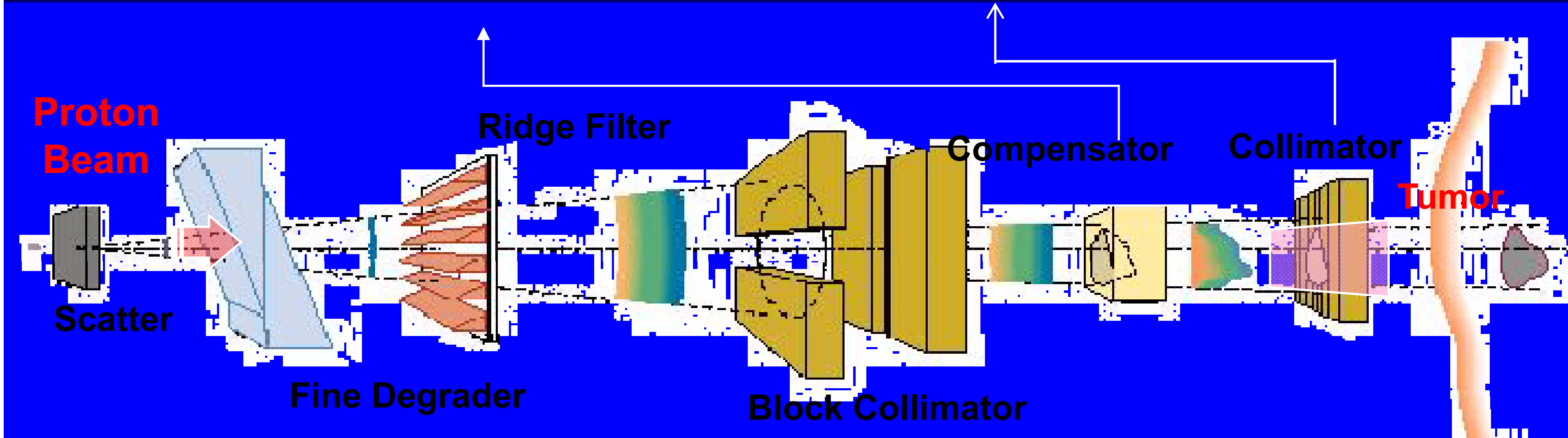
Patient Snout

Radiation Field Formation by Collimator and Compensator

Compensator
(Polyethylene)



Collimator
(Brass)

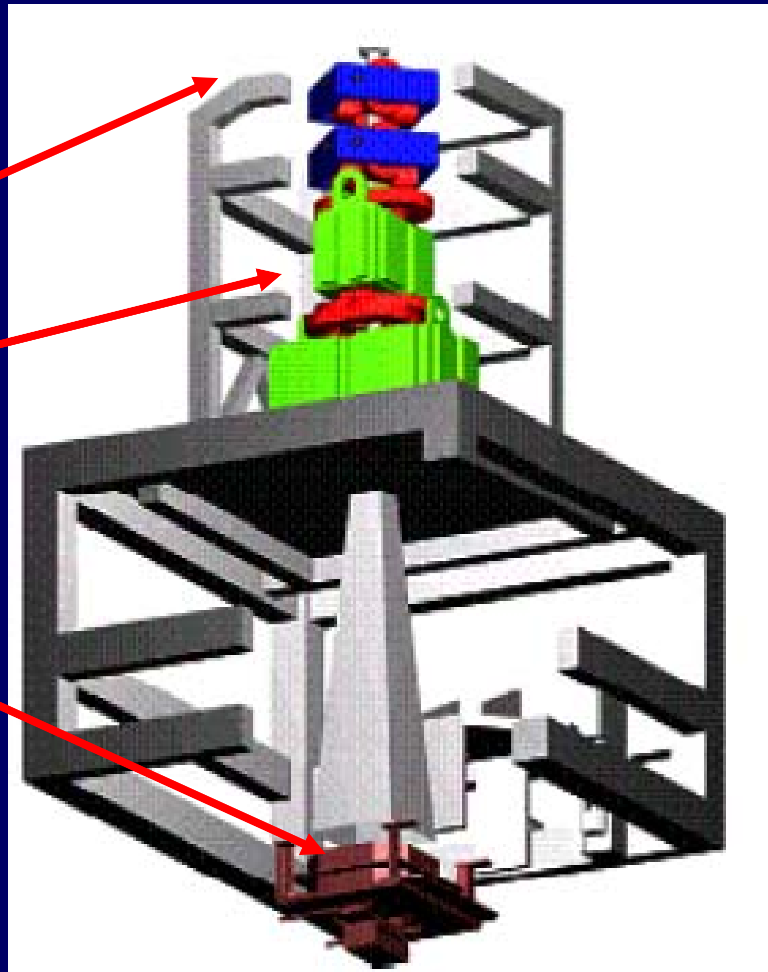


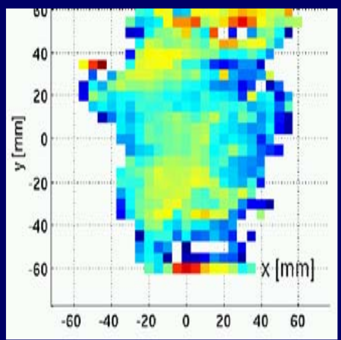
Proton Radiation Beam by Scattering Method

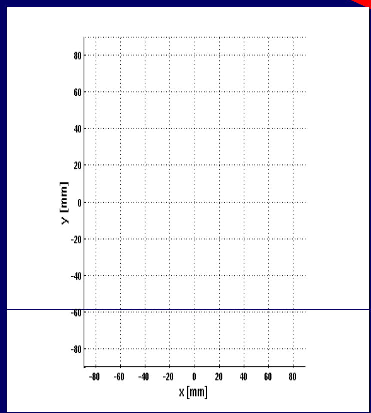
3rd and 4th Treatment Room: Pencil Beam Scanning Nozzle

For Pencil Beam Scanning

Quadrupoles
Scanning magnets
Dose monitor
2D monitor

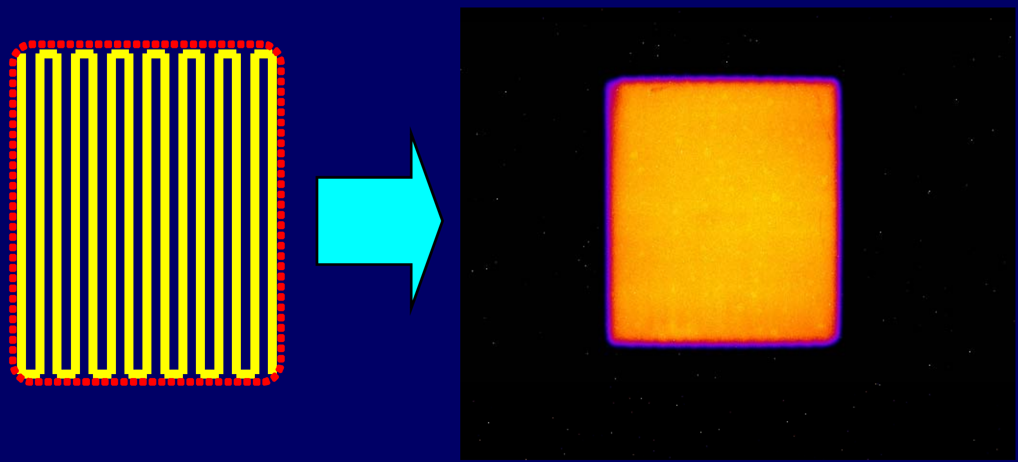






Continuous Line Scanning

- Continuous line scanning is realized by two X-Y scanning magnets. The power supplies of scanning magnets can generate output current with fast time response.
- - scanning speed : 10mm/ms
- - response of velocity change : < 1ms

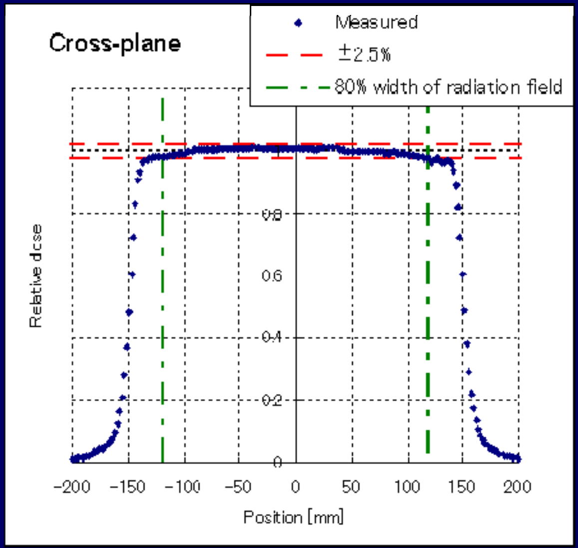


Scanning pattern for uniform field

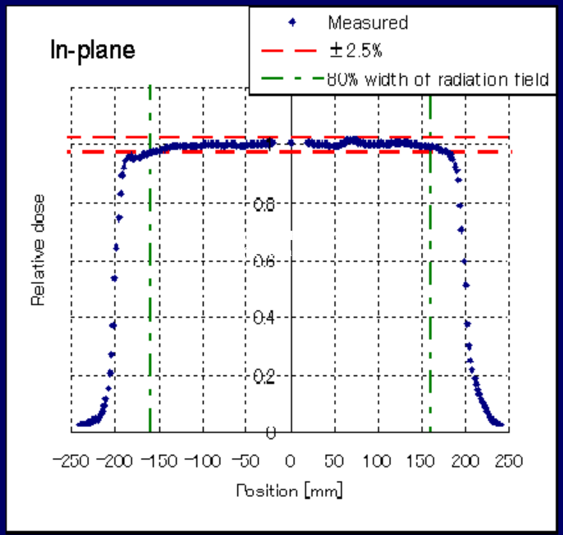
Scanned field measured with a fluorescent plane + CCD camera

Maximum Field Size

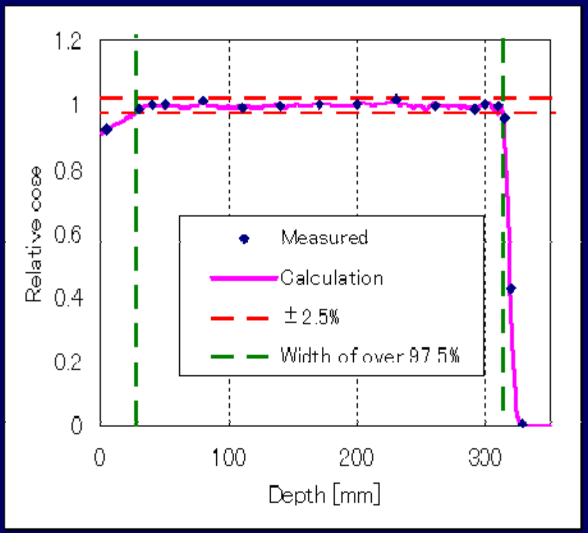
Maximum field of 30cm(X) × 40cm(Y) × 28cm(SOBP)
Field uniformity of ±2.5% was confirmed at 230 MeV



Dose at the center of SOBP (X-direction)



Dose at the center of SOBP (Y-direction)

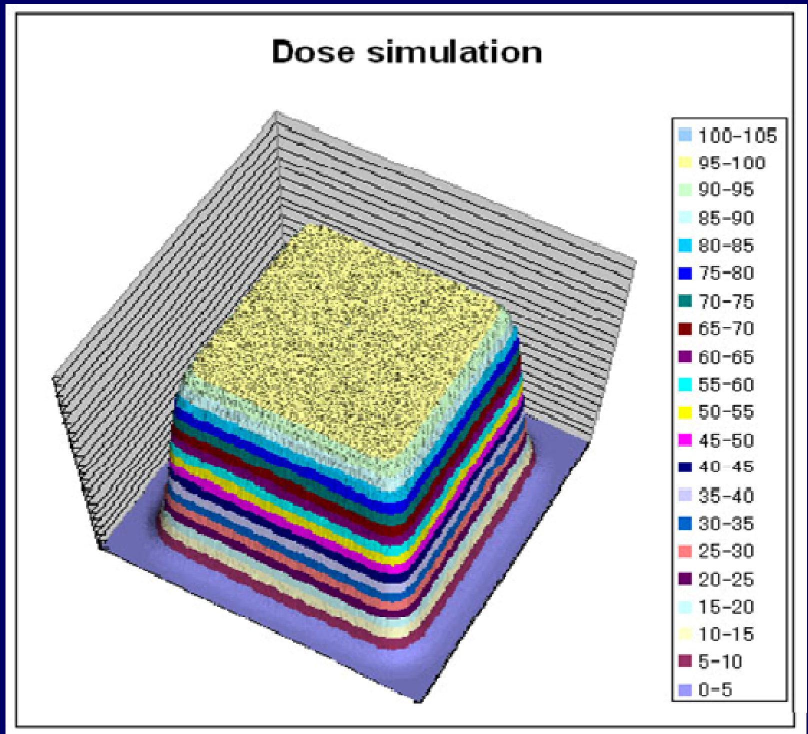


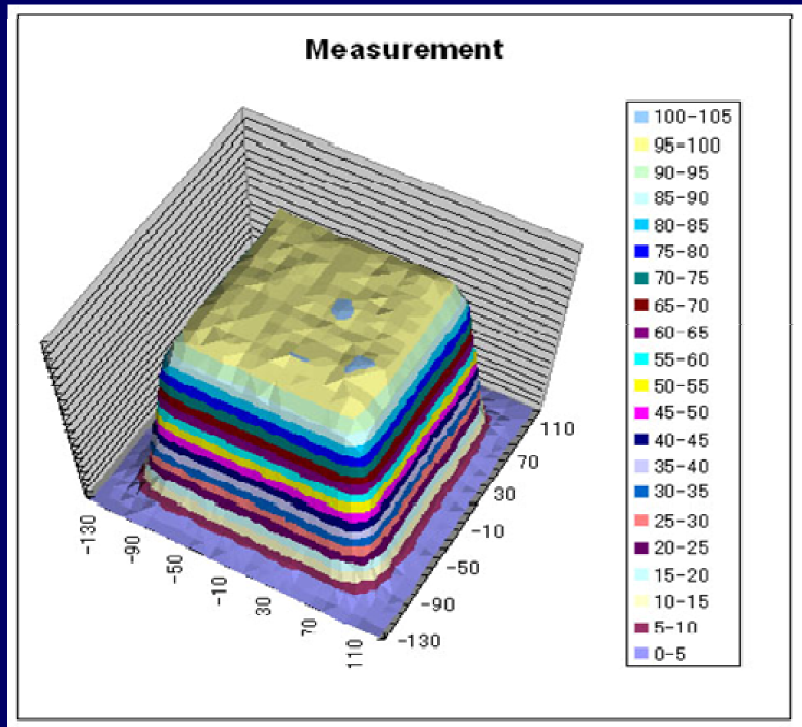
Depth dose with SOBP=28cm (at beam center)

Field Evaluation by Gamma Index

- Gamma index evaluation at 3%/3mm has been done for the uniform and intensity-modulated 2D fields, which were measured at the Bragg peak using 230MeV beam.

1) Uniform field

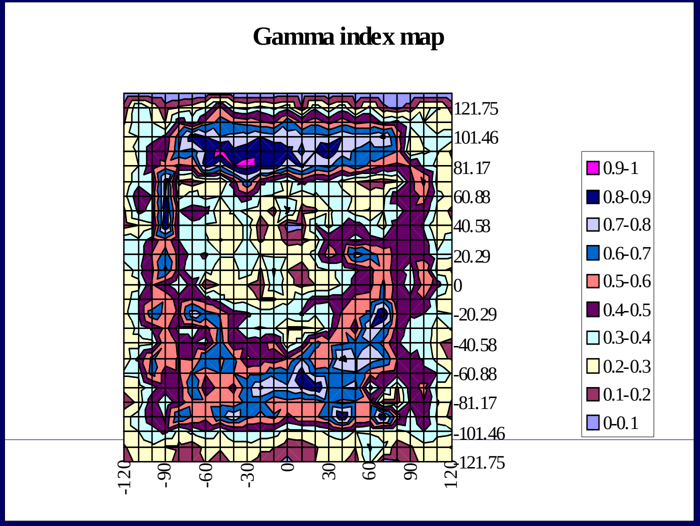


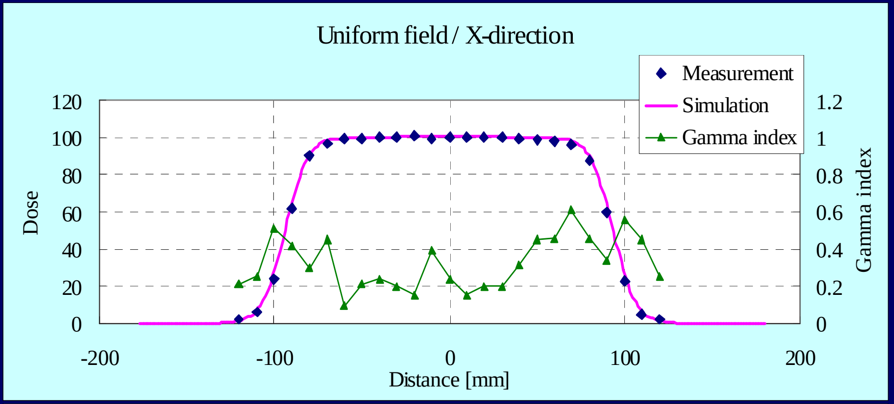


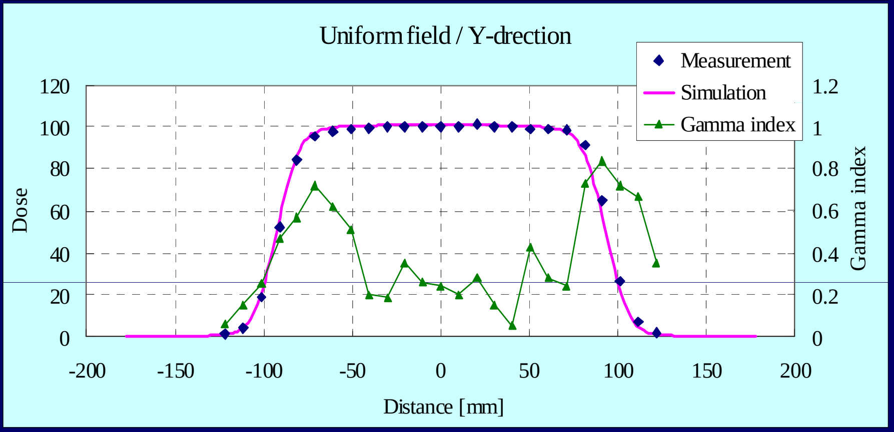
Field Evaluation by Gamma Index

1) Uniform field

100% of evaluation points have passed the criterion of gamma index <1.0.







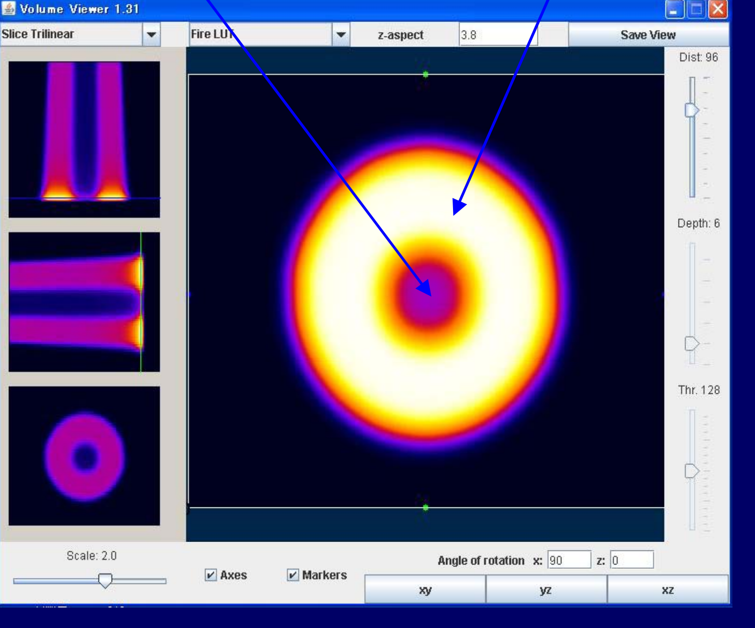
Intensity Modulation by Scanning Speed

- Intensity modulation is done by
  - changing the scanning speed (high speed for low dose)
  - keeping the beam current constant in each layer

low dose region
(high scanning speed)

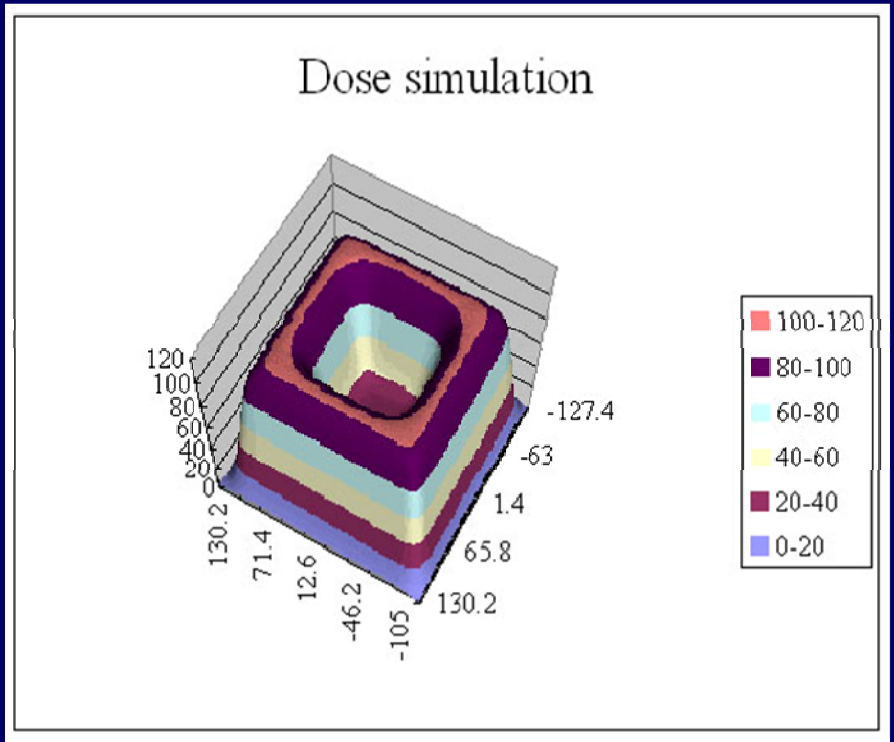
high dose region
(low scanning speed)

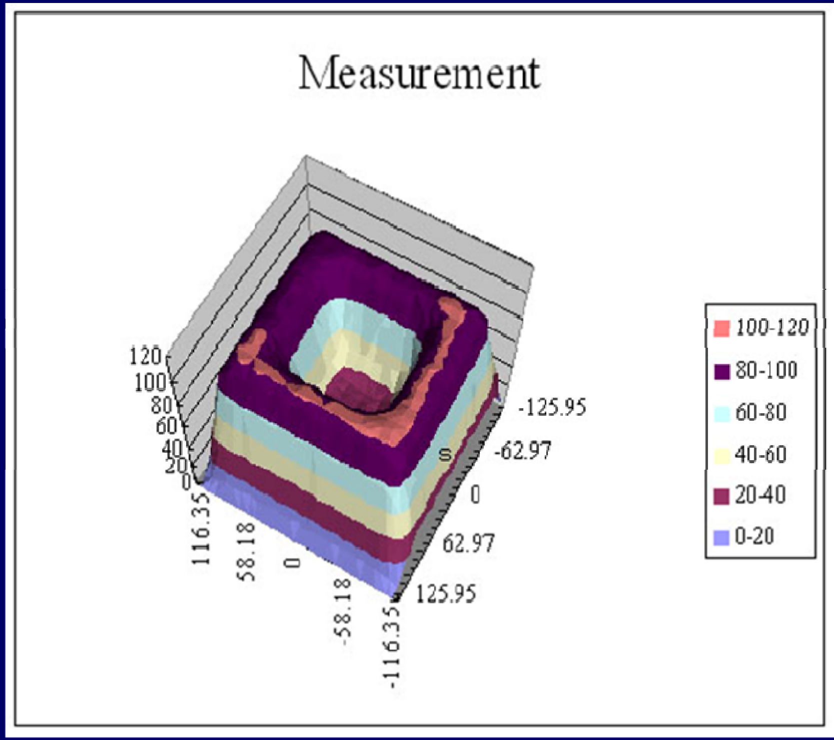
Dose simulation of
two steps pattern



Field Evaluation by Gamma Index

2) Intensity modulation field

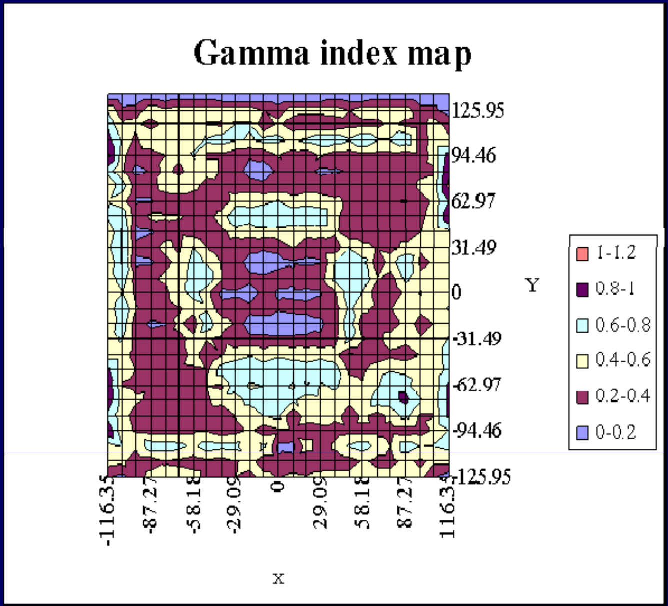


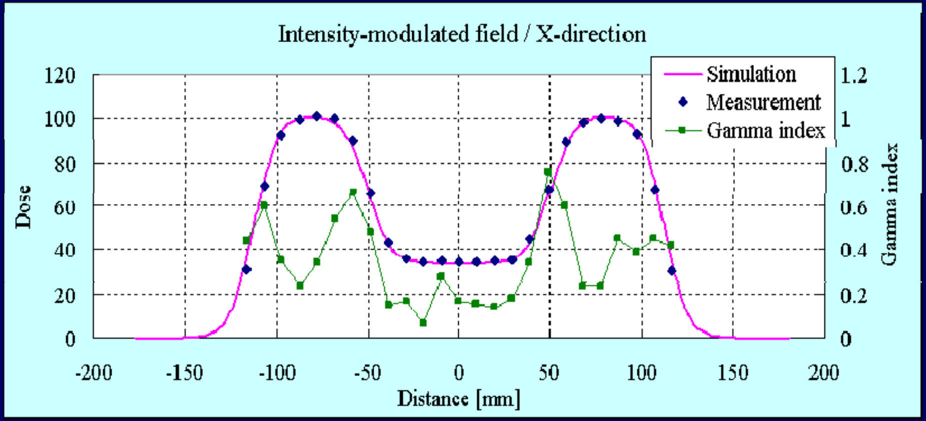


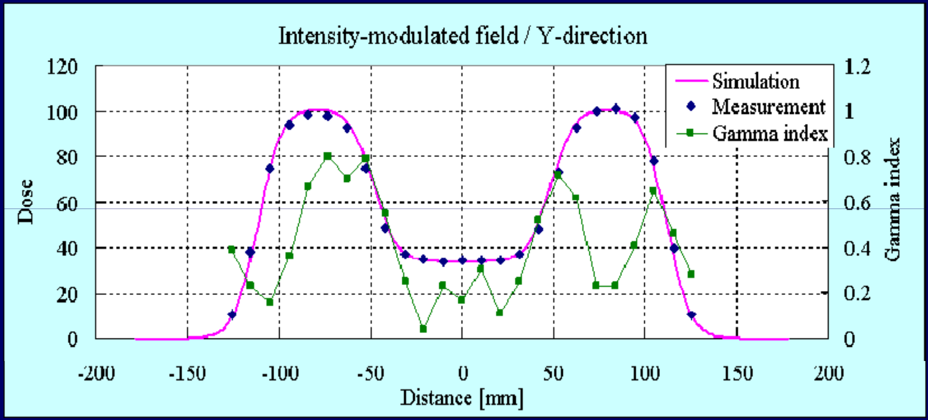
Field Evaluation by Gamma Index

2) Intensity modulation field

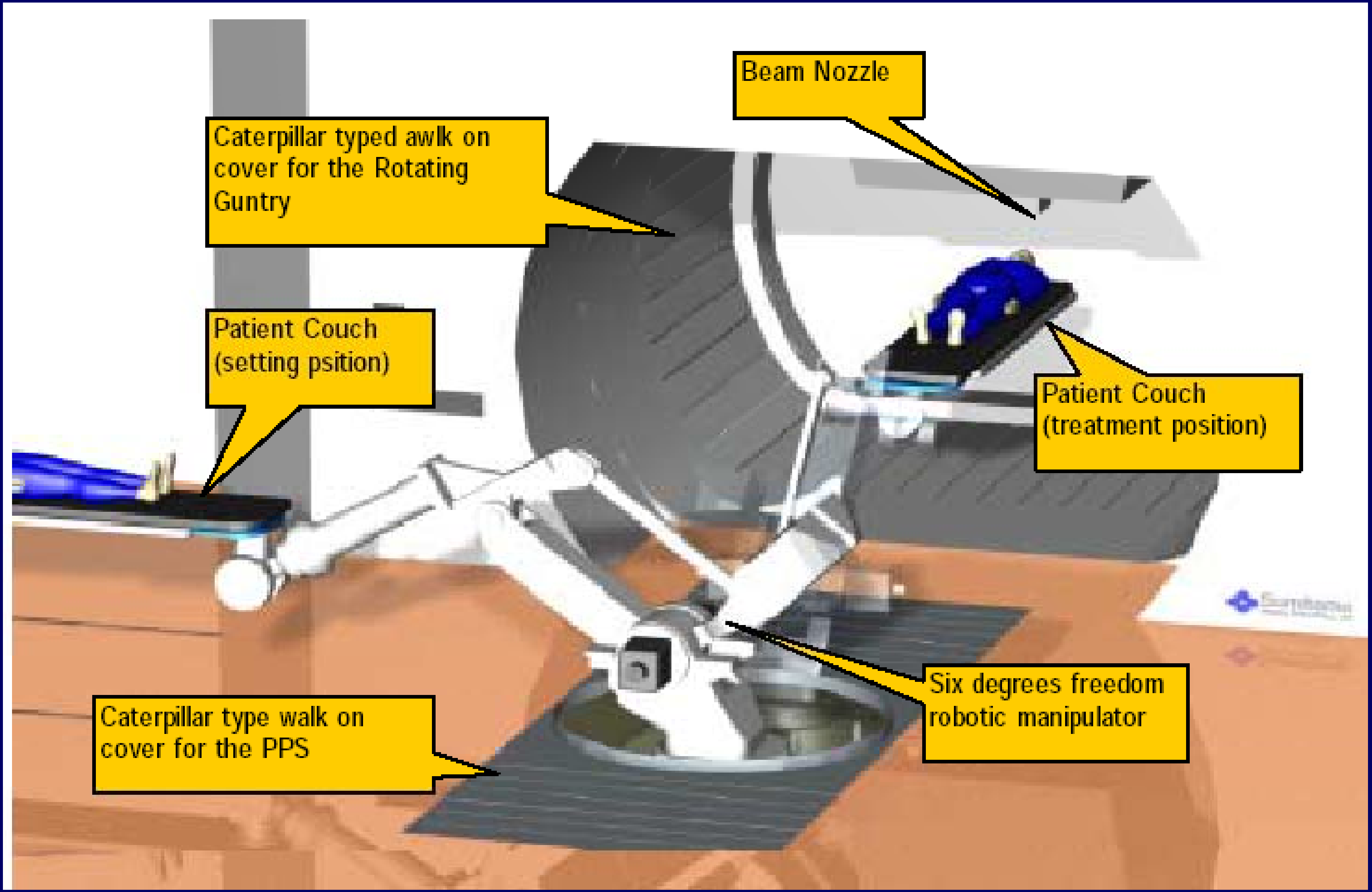
99.7% of evaluation points have passed the criterion of gamma index <1.0.



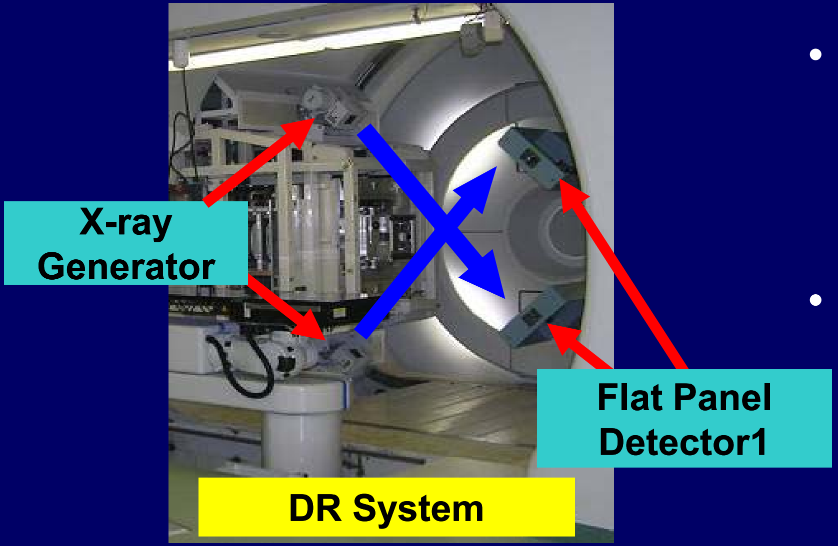




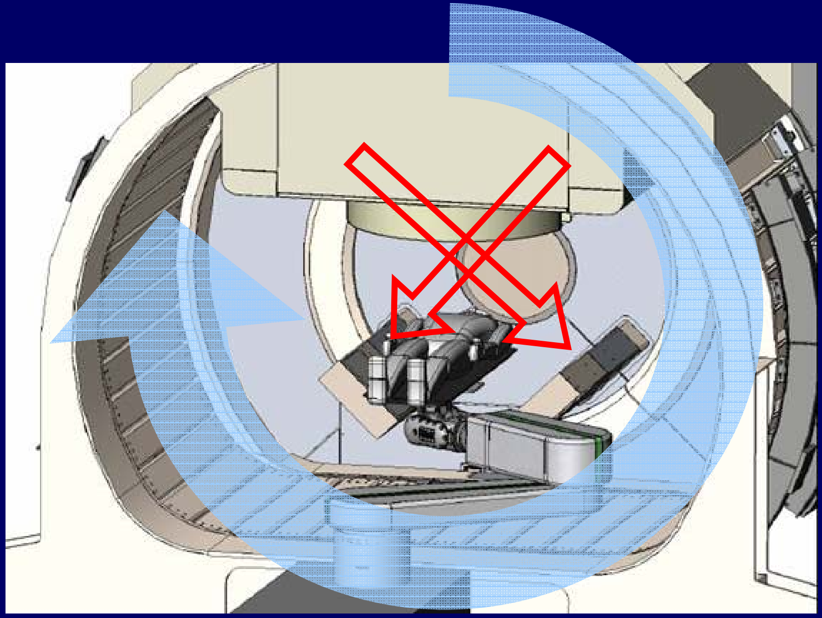
Patient Positioning Verification System

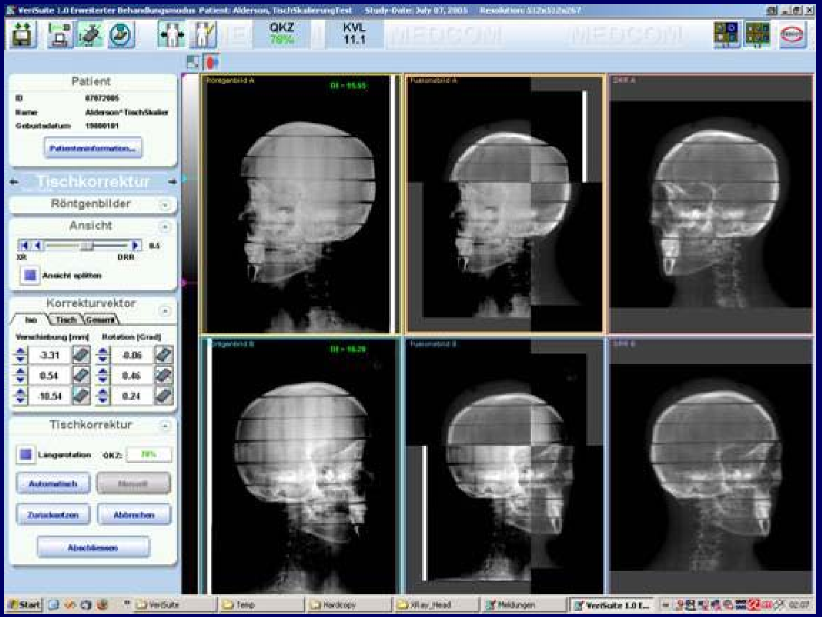


DR System with Cone Beam CT Function for Easy and Accurate Patient Positioning



- DR system and Patient Positioning Verification System (PPVS) make Cone Beam CT (CBCT) image.
- PPVS also provides high speed and high accuracy 3D-3D image matching to correct the error of patient set-up.

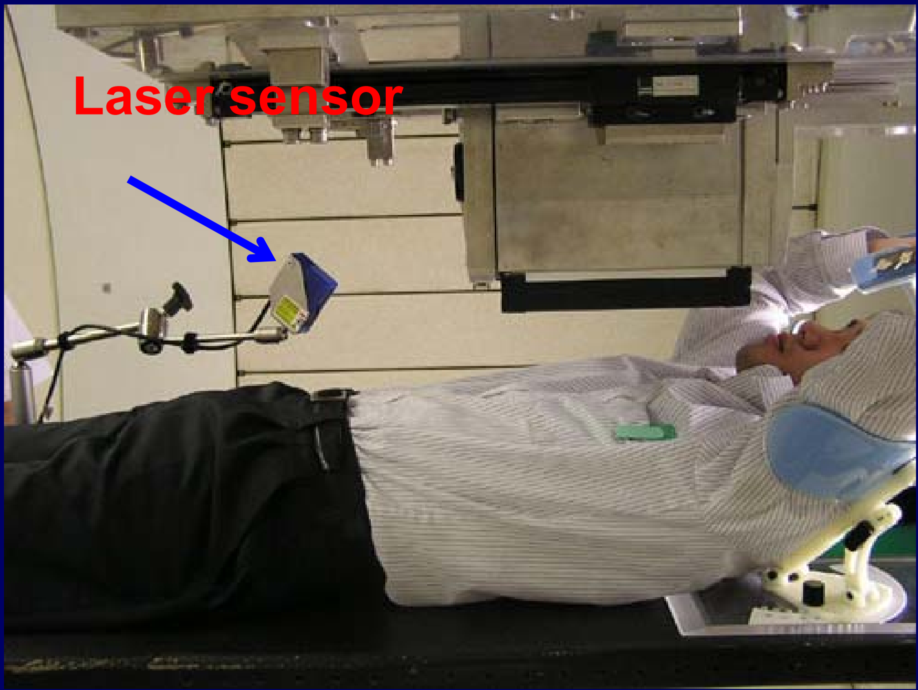




Positioning Accuracy: < 0.5 mm

Accurate Irradiation for Moving Tumor by Respiration Gating System

Respiratory-gated irradiation can be made by Respiration Gating System with laser sensor and DR system.



Example of gating display on PC

Project Schedule

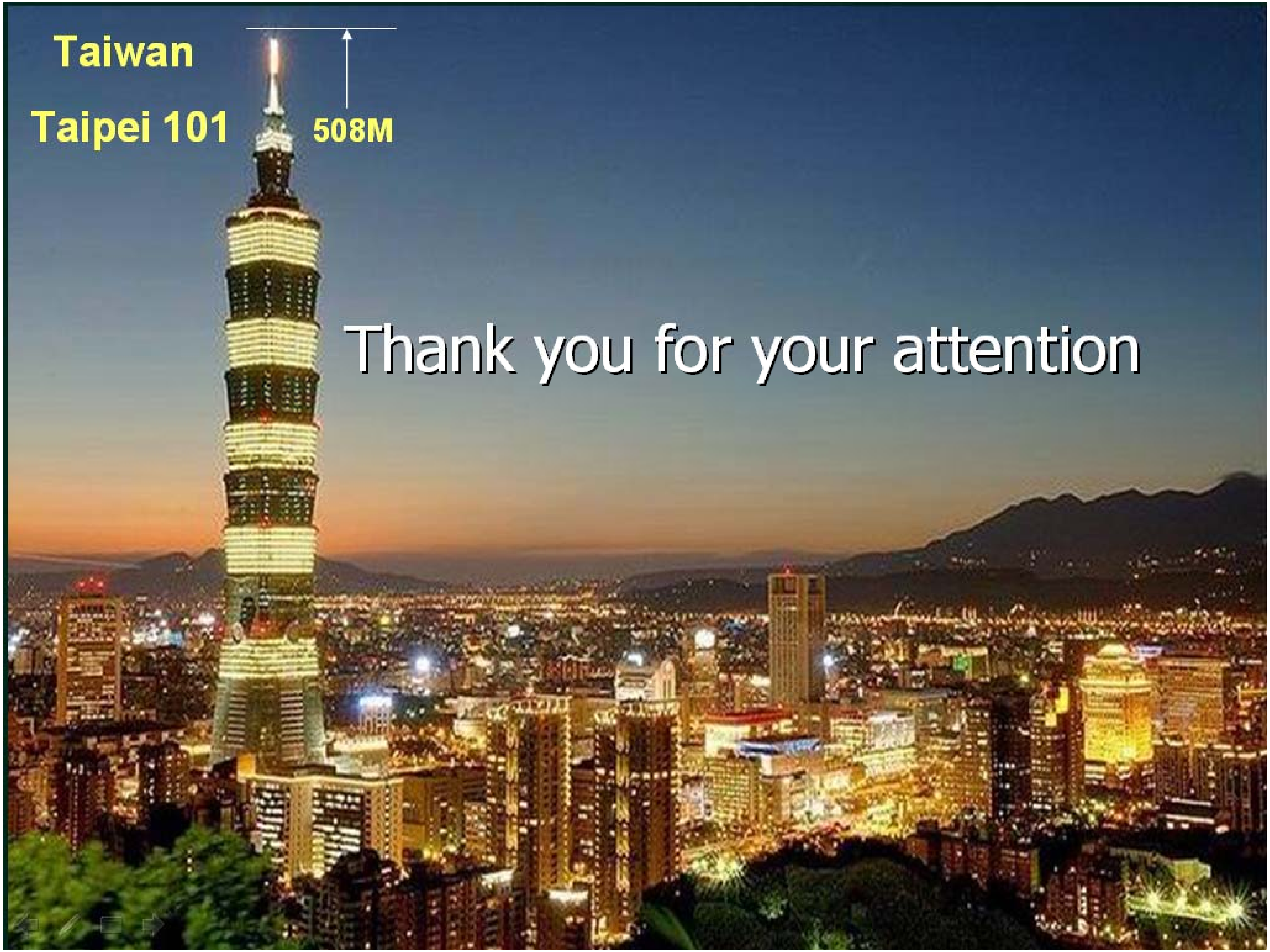
Manufacturing at Niihama Factory in Japan

230 MeV Cyclotron manufactured at Sumitomo Niihama Factory

Major and critical components are designed and manufactured in Sumitomo's own factory to maintain high quality, high reliability, high performance, low cost, and short delivery time.

Conclusion

- The therapeutic effects of proton therapy in many cancers have been well established.
- In Taiwan, liver tumors and head and neck tumors will be the tumors having greatest benefit.
- The indication covers different type of tumors, but main issue is the cost and cost/effectiveness.
- If one proton therapy treated around 1500 patients per year, Taiwan needs 2 or more proton therapy centers.


Taiwan
Taipei 101
508M
Thank you for your attention