CURRENT NATIONAL AND INTERNATIONAL STATUS ON HADRON THERAPY FOR CANCER TREATMENT

Presentation at Indo Japan School On Advanced Accelerators of Ions & Electrons, IUAC

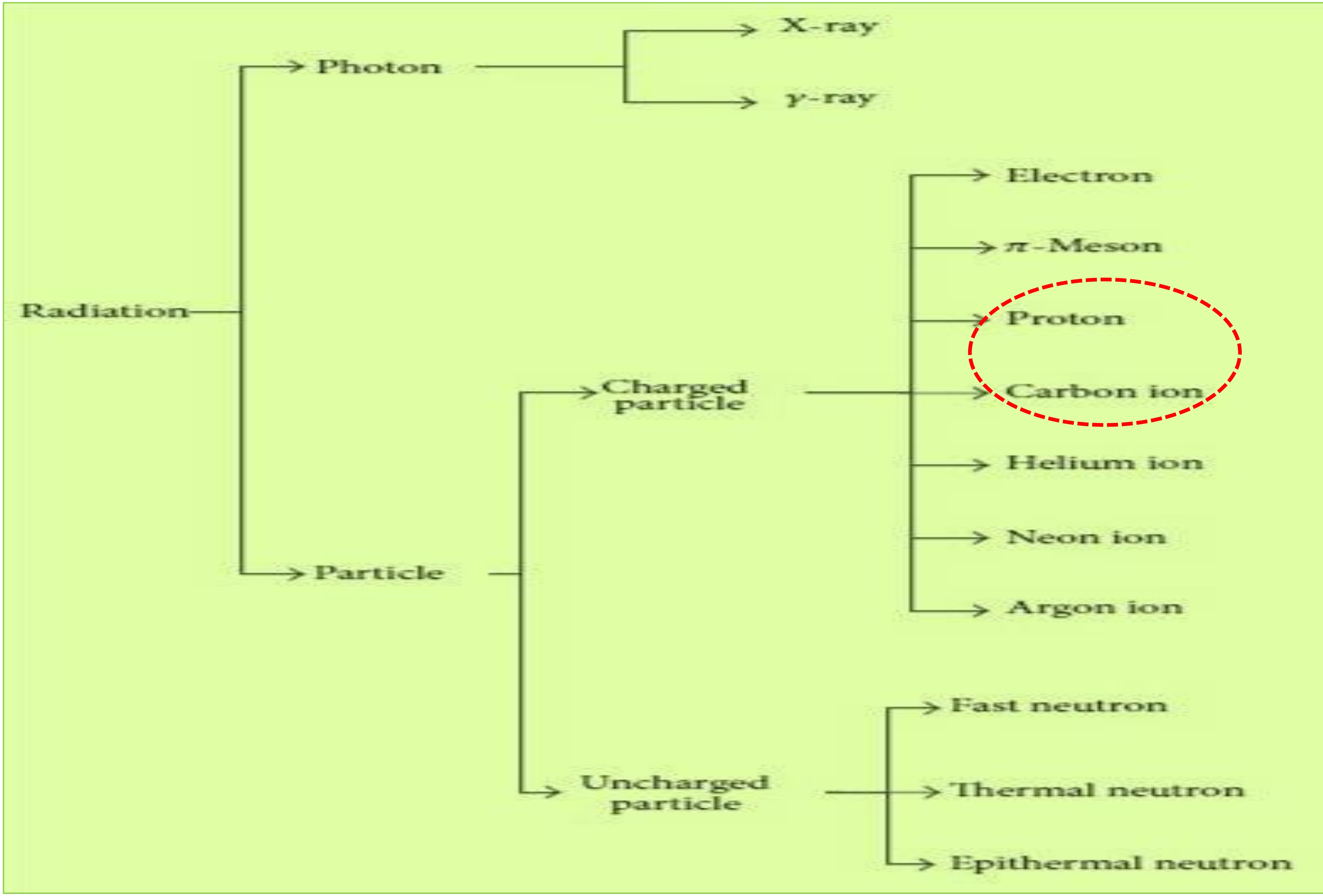
17 FEBRUARY 2015

PROF RK GROVER

DIRECTOR & CEO

DELHI STATE CANCER INSTITUTES

Particle Radiation Including Hadrons in Clinical Radiotherapy



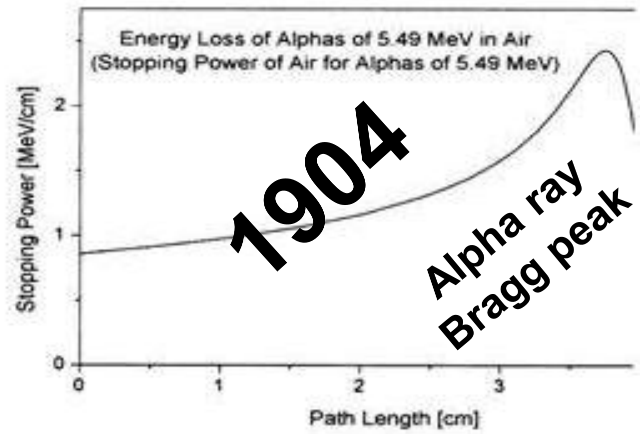
Ionizing Radiations

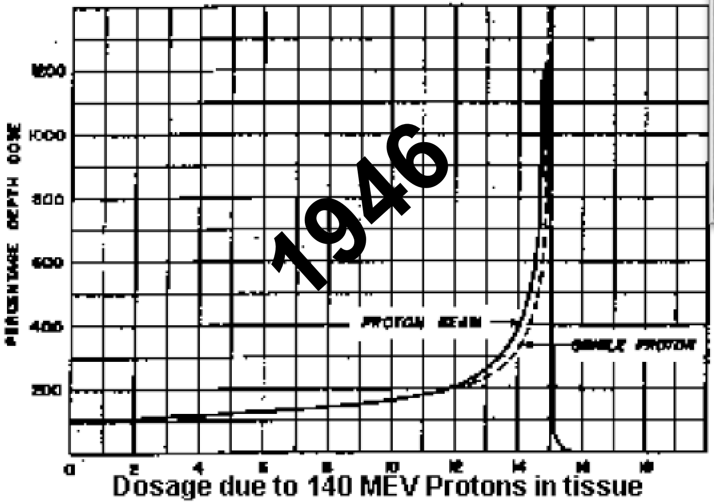
- X-rays – 1895
- Radioactivity & Radium – 1898
- Biological effects of Radioactivity – 1898
- Clinical use of Radium in Cancer – 1903
- Era of Superficial X-ray, Deep X-ray, 226-Radium, 137-Cs, Radon Gold Seed
- Discovery of Neutron, VG Generator – 1931-32
- Clinical application of Neutrons – 1938 – Poor Results
- Radium substitutes, Linear Accelerator – 1951
- Proton tt – 1954, Berkley, 1957 Uppsala
- Cyclotron – Hammersmith Hospital – 1955
- Long gap – renewed interest from 1980s onward

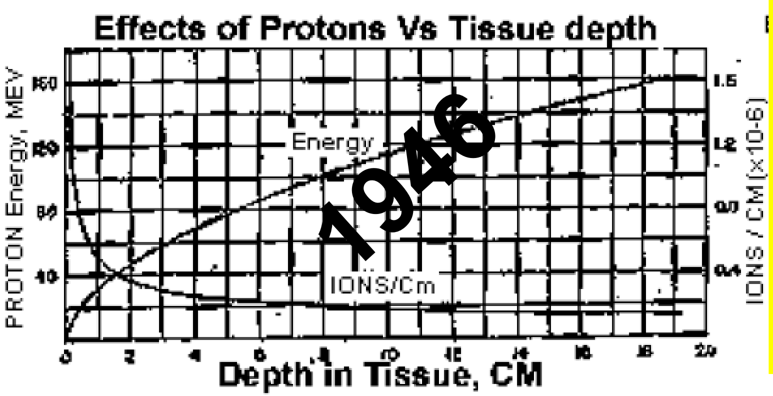
Comparison conventional RT vs Hadron RT

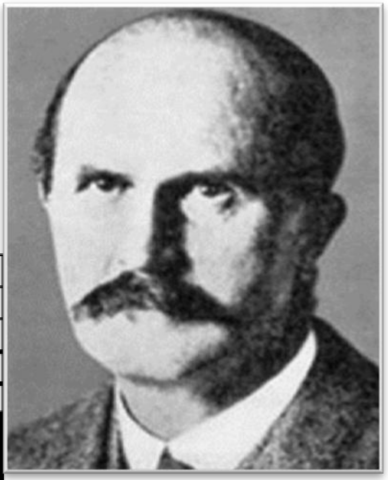
- **Conventional (X- & γ Rays):**
  - Sparsely & Indirectly ionizing
  - Infinite range
- **Hadron RT**
  - Densely & Directly Ionizing
  - Finite Range [Brag Peak (not seen in electrons)]

VISIONARIES



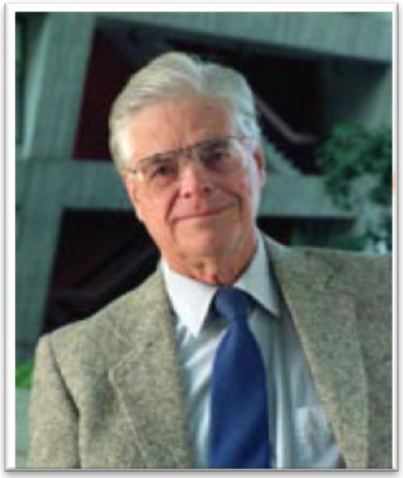






W H Bragg
(1904)

E O Lawrence
*(1939-46)**



Robert Wilson
(1914 - 2000)

1946: Harvard physicist Robert Wilson suggested:

- **Protons can be used clinically**
- **Accelerators are available (1939-1946)***
- **Maximum radiation dose can be placed into the tumor**
- **Proton therapy spares normal tissues**
- **Modulator wheels can spread narrow Bragg peak**

NOTE: **ESS, PSPT & IMPT(SPOT or LINE Scanning now a days**

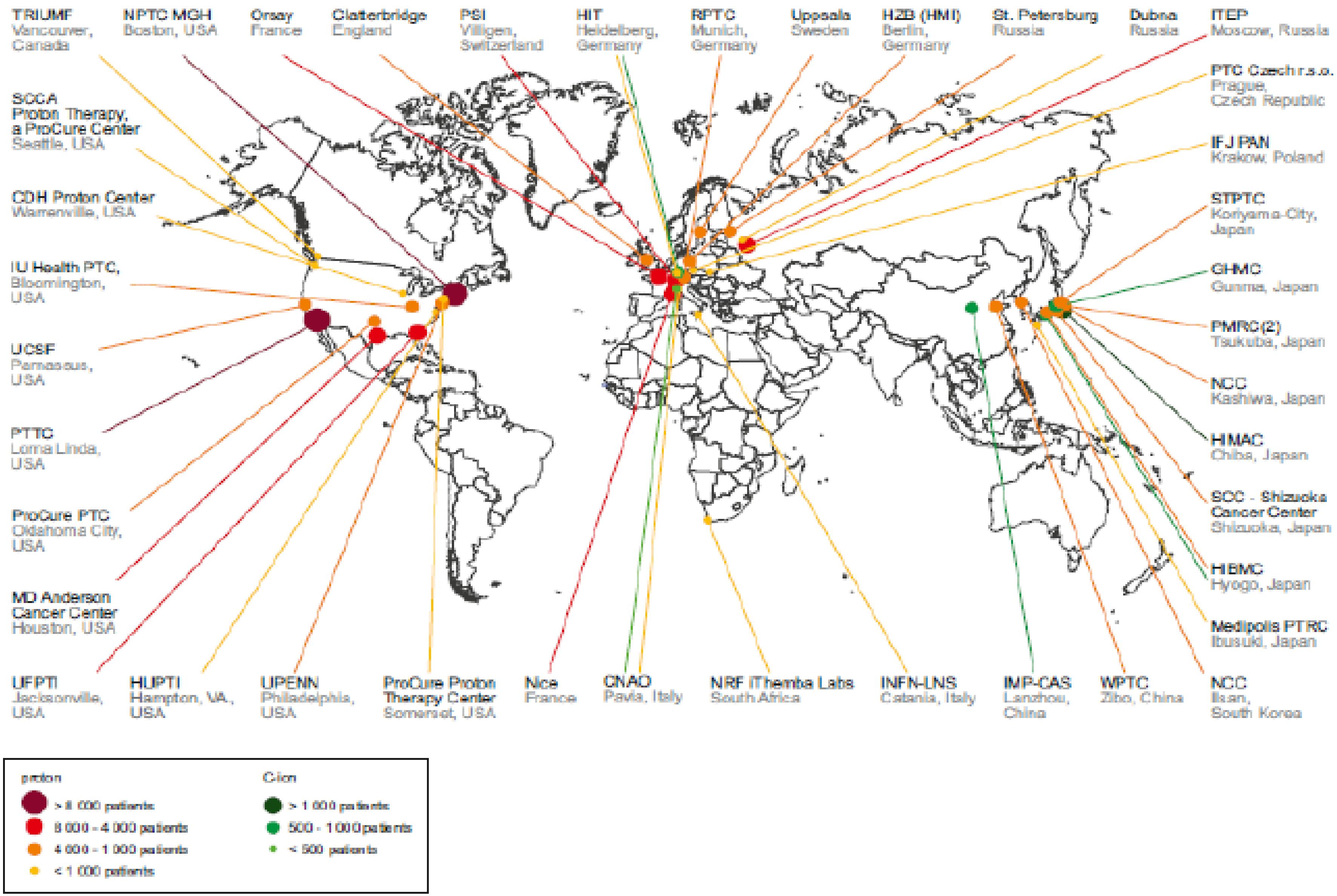
1954: John Lawrence treats first patients at Berkeley
Research centre open for clinical application

Some Earlier Hadron Therapy Projects

Particle	Location
Protons	Uppsala, Sweden
	Harvard/Massachusetts General Hospital, United States
	Harwell, United Kingdom
	Dubna, Soviet Union
	Gatchina, Soviet Union
	Moscow, Soviet Union
	Chiba, Japan
Helium	Berkeley, United States
Heavy Ions	Berkeley, United States
Negative Pions	Los Alamos, United States
	Vancouver, Canada
	Villigen, Switzerland
	Dubna, Soviet Union[a]

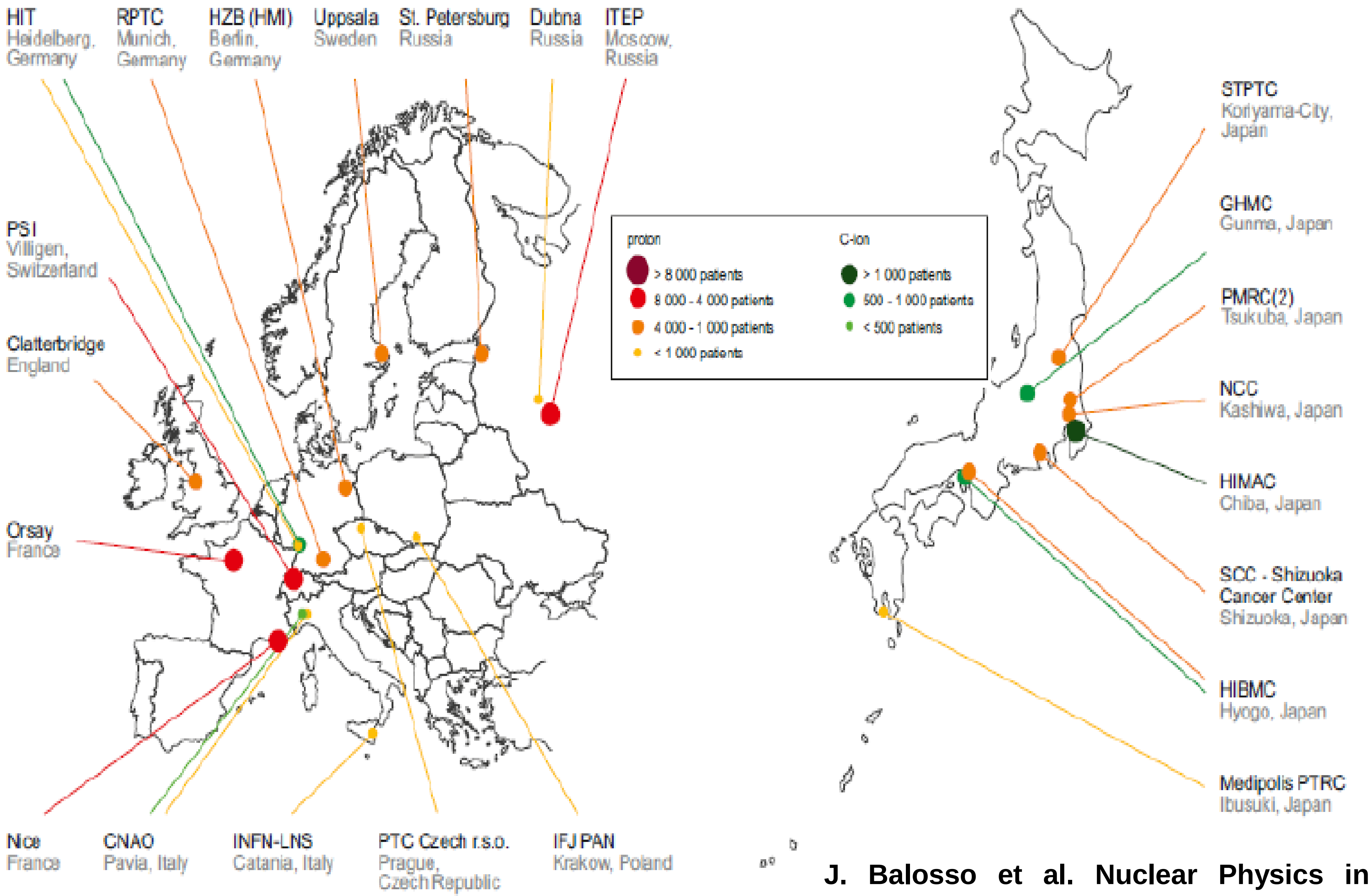
Neutrons	Location
Cyclotrons	Hammersmith, United Kingdom
	Edinburgh, United Kingdom
	Berlin-Buch, Federal Republic of Germany
	Louvain, Belgium
	Tokyo, Japan
	Chiba, Japan
	Anagawa, Japan[a]
	Tohoku, Japan[a]
	College Station/Houston, United States
	Houston, United States
	Chicago, United States
	National Accelerator Laboratory, United States (near Chicago)
	Cleveland, United States
	Seattle, United States[a]
	Los Angeles, United States[a]
D-T Generators	Manchester, United Kingdom
	Glasgow, United Kingdom
	Amsterdam, The Netherlands
	Hamburg, Federal Republic of Germany
	Heidelberg, Federal Republic of Germany
	Philadelphia, United States

*Proton & Carbon Ion therapy facilities (43) & Patient capacity end of 2013)



*J. Balosso et al. Nuclear Physics in medicine – Hadrontherapy, 2013 (http://www.nupecc.org/Nuclear Physics in medicine)

*Proton & Carbon Ion facilities & Patient capacity in Europe- 17 & Japan- 10 in the of 2013):



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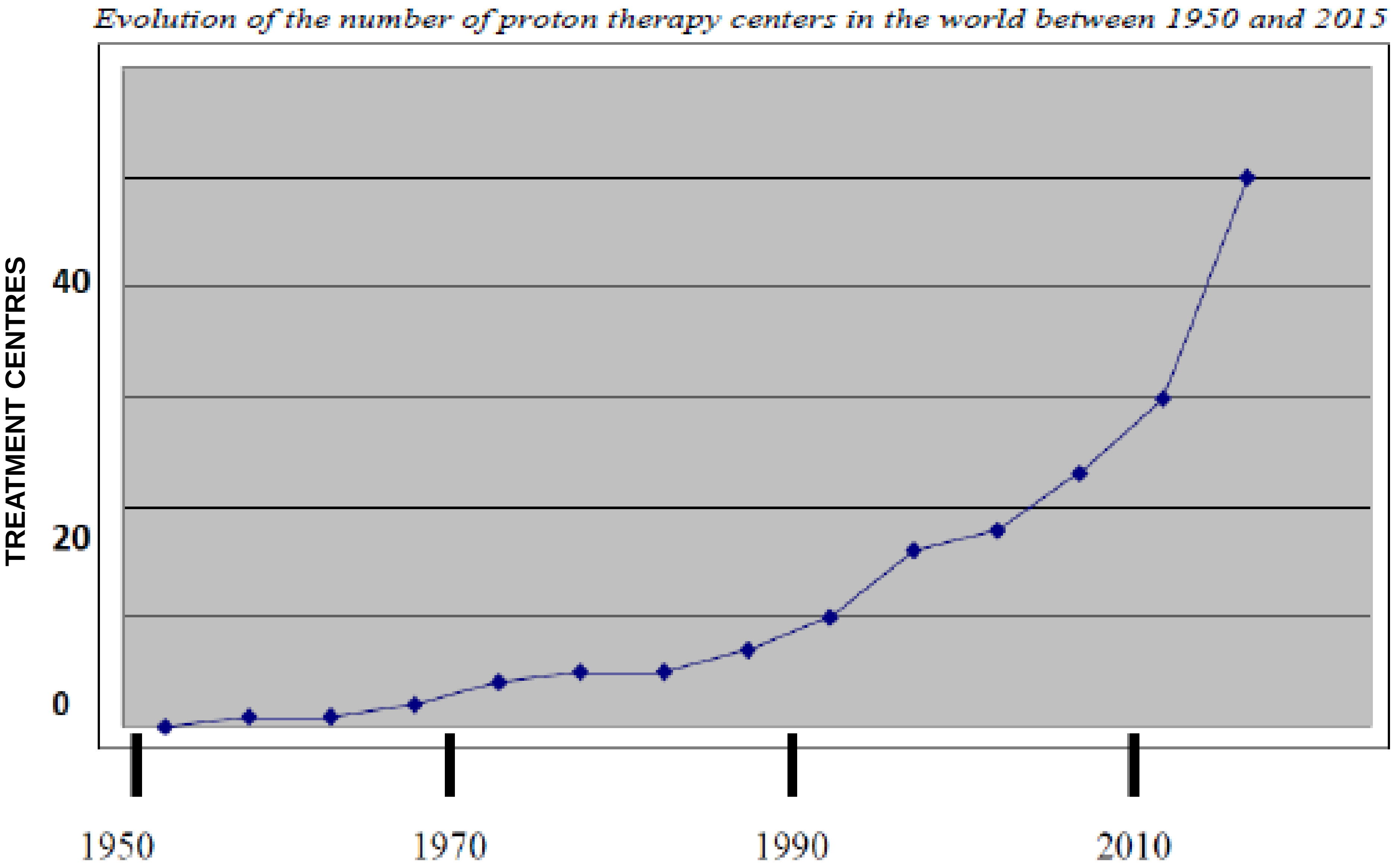
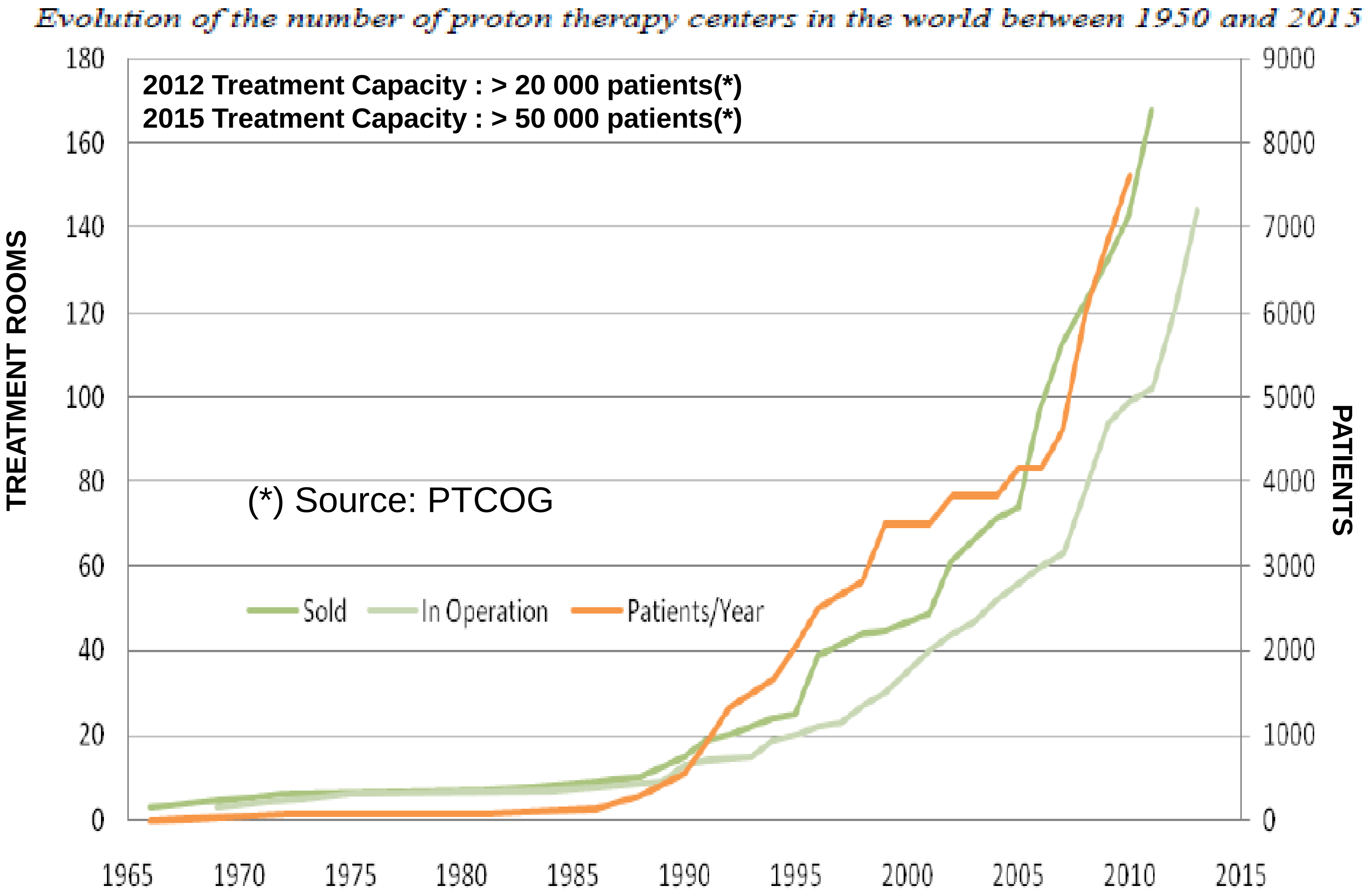


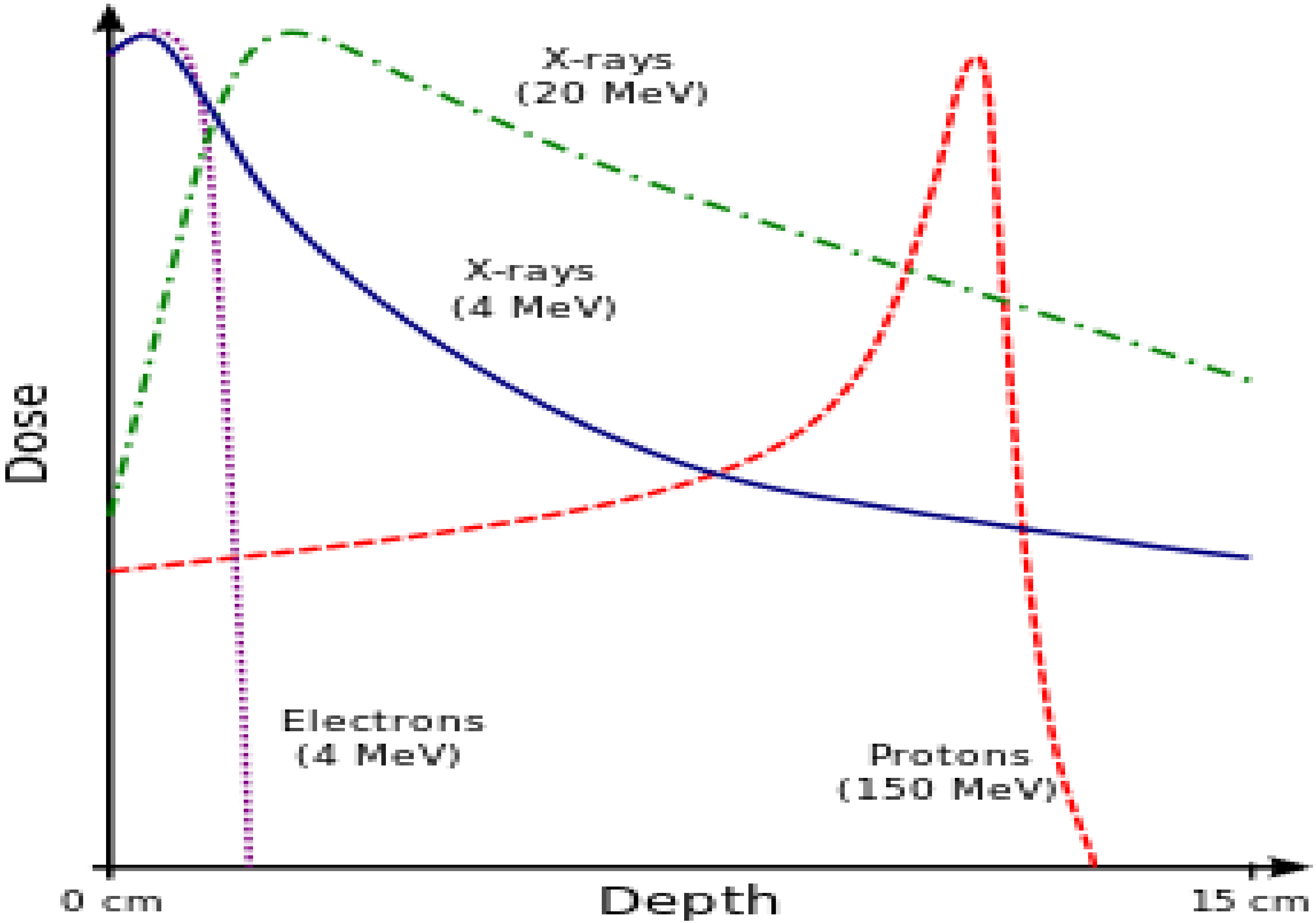
Exponential Growth of Centres, Treatments Rooms & Projected Number of Patients

Worldwide Status of Hadron Therapy Facilities

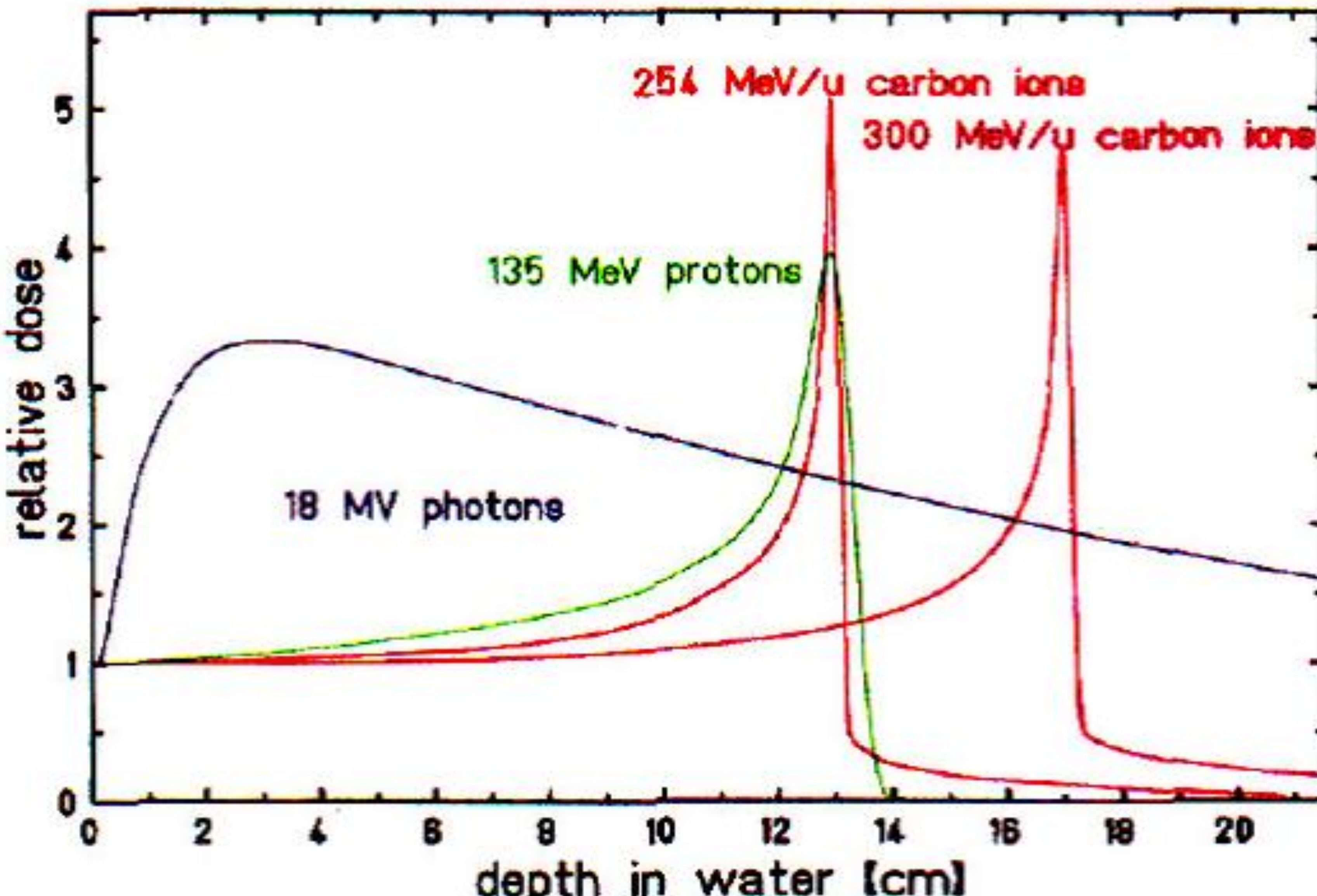
- **About 43 (end of 2013)**
- **About 27 under construction in 2013**
- **Likely Proton therapy room facilities by 2017 : 255**
- **Likely Proton therapy room facilities by 2020 : 1000**
- **No. of patients treated:**
  - **Proton : ≈ 1,00,000**
  - **Other Ions : ≈ 14,000**
- **Approx. Cost of setting up:**
  - **Cyclotron based Proton : 70 – 80 M□**
  - **Synchrocycl. Based Carbon : 200 M □**
- **Approx. Tt. Cost for patients:**
  - **Proton Treatment : ≈ 3-times of normal RT**
  - **Carbon Treatment : ≈ 7-times of normal RT**



Exponential Growth of Centres, Treatments Rooms & Projected Number of Patients

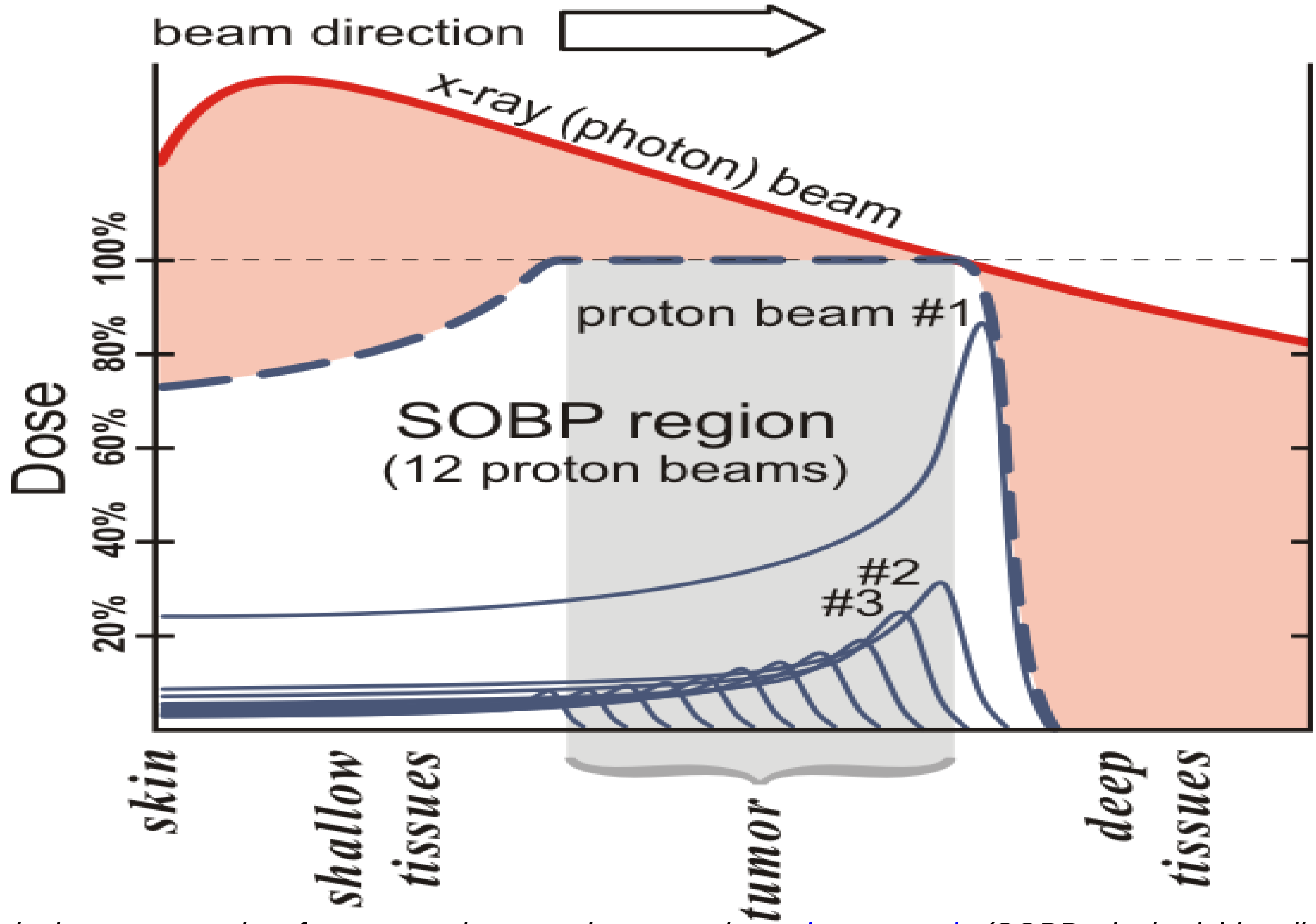


The dose from protons to tissue is maximum just over the last few millimetres of the particle's range.

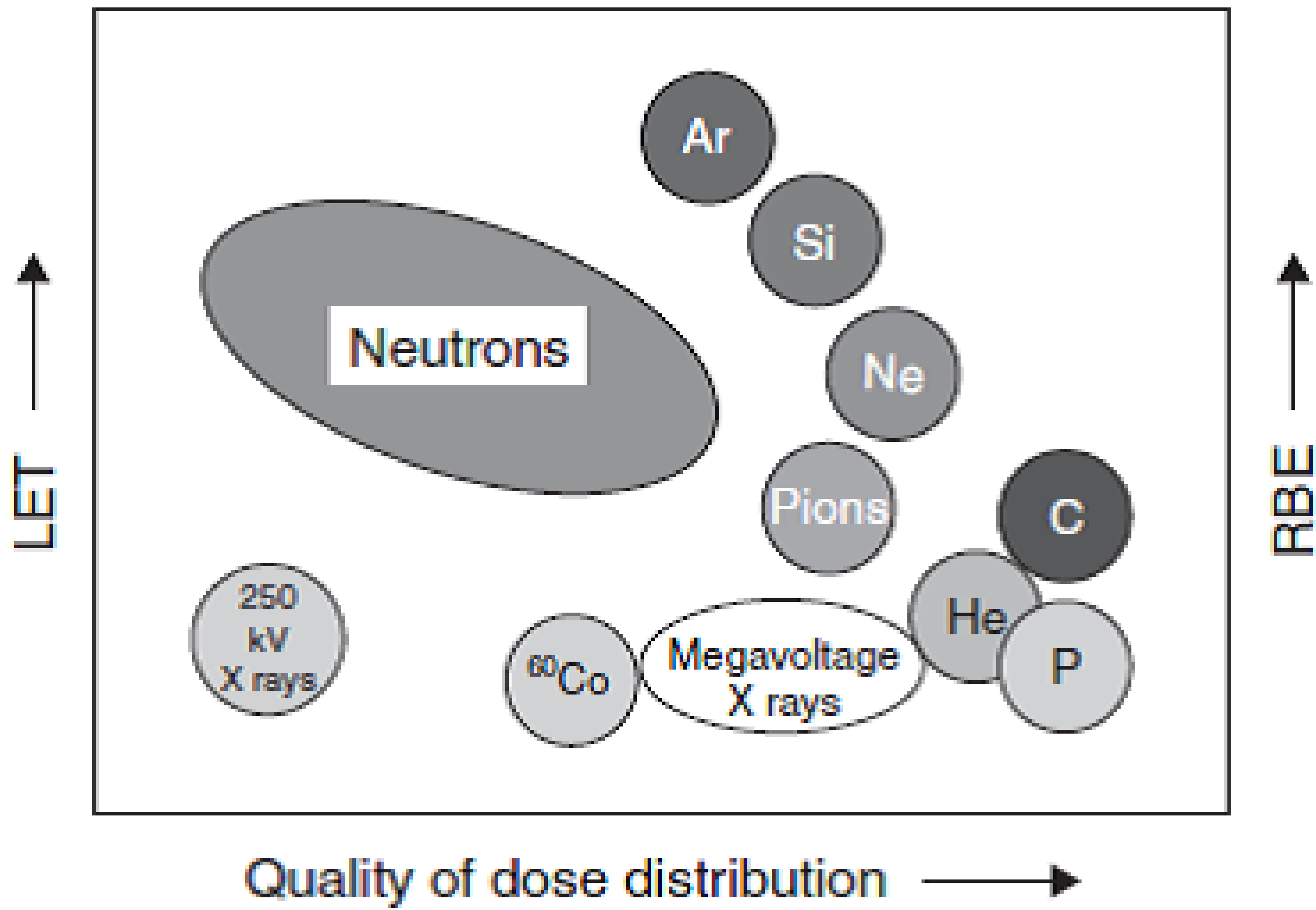


The advantageous dose profile of a charged particle beam compared to X-ray photons -

Weber U, Kraft G. Comparison of carbon ions versus protons. Cancer J. 2009 Jul-Aug;15(4):325-32.

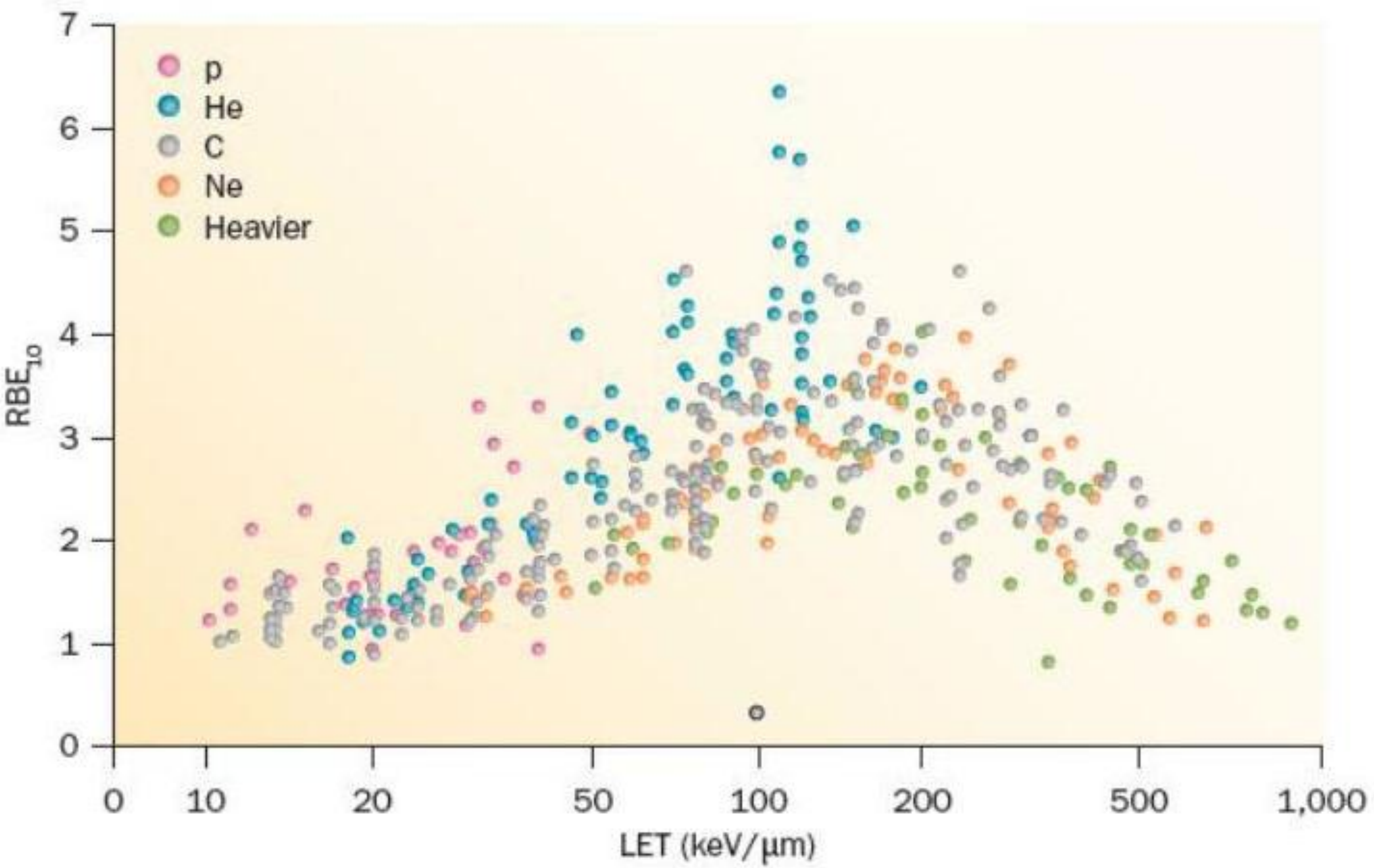


In a typical treatment plan for proton therapy, the spread out [bragg peak] (SOBP, dashed blue line), is the therapeutic radiation distribution. The SOBP is the sum of several individual Bragg peaks (thin blue lines) at staggered depths.The [depth-dose] plot of an x-ray beam (red line) is provided for comparison. The pink area represents additional doses of x-ray radiotherapy—which can damage to normal tissues and cause secondary cancers, especially of the skin - "Proton beam therapy" Levin et al British Journal of Cancer (2005) 93, 849–854



The RBE for protons is much lower than that of carbon ions or neutrons as it has a lower LET value.
Kogel AVD, Joiner M. Basic Clinical Radiobiology. 4th ed ed: Hodder Arnold; 2009.

L.E.T Related RBE of Hadron Particles



EXPANDING
PROTON FACILITIES,
PATIENT LOAD
& PATIENTS ROOMS

Patient Statistics (for Hadrontherapy facilities in operation end of 2011):

WHERE		PARTICLE	FIRST PATIENT	PATIENT TOTAL	DATE OF TOTAL
Canada	Vancouver (TRIUMF)	p	1995	161	Dec-11
China	Wanjie (WPTC)	p	2004	1078	Dec-11
China	Lanzhou	C ion	2006	159	Dec-11
England	Clatterbridge	p	1989	2151	Dec-11
France	Nice (CAL)	p	1991	4417	Dec-11
France	Orsay (CPO)	p	1991	5634	Dec-11
Germany	Berlin (HMI)	p	1998	1859	Dec-11
Germany	Munich (RPTC)	p	2009	895	Dec-11
Germany	HIT, Heidelberg	C ion	2010	568	Dec-11
Germany	HIT, Heidelberg	p	2010	94	Dec-11
Italy	Catania (INFN-LNS)	p	2002	290	Dec-11
Italy	Pavia (CNAO)	C ion	2011	5	Dec-11
Japan	Chiba (HIMAC)	C ion	1994	6569	Dec-11
Japan	Kashiwa (NCC)	p	1998	870	Dec-11
Japan	Hyogo (HIBMC)	p	2001	3198	Dec-11
Japan	Hyogo (HIBMC)	C ion	2002	1271	Dec-11
Japan	Tsukuba (PMRC, 2)	p	2001	2166	Dec-11
Japan	Shizuoka	p	2003	1175	Dec-11
Japan	Koriyama-City	p	2008	1378	Dec-11
Japan	Gunma	C ion	2010	271	Dec-11
Japan	Ibusuki (MMRI)	p	2011	180	Dec-11
Korea	Ilsan, Seoul	p	2007	810	Dec-11
Poland	Krakow	p	2011	11	Dec-11
Russia	Moscow (ITEP)	p	1969	4300	Dec-11
Russia	St. Petersburg	p	1975	1372	Dec-11
Russia	Dubna (JINR, 2)	p	1999	828	Dec-11
South Africa	iThemba LABS	p	1993	521	Dec-11
Sweden	Uppsala (2)	p	1989	1185	Dec-11
Switzerland	Villigen PSI, incl OPTIS2	p	1996	1107	Dec-11
USA, CA.	UCSF - CNL	p	1994	1391	Dec-11
USA, CA.	Loma Linda (LLUMC)	p	1990	16000	Dec-11
USA, IN.	Bloomington (IU Health PTC)	p	2004	1431	Dec-11
USA, MA.	Boston (NPTC)	p	2001	5562	Oct-11
USA, TX.	Houston (MD Anderson)	p	2006	3400	Feb-12
USA, FL	Jacksonville (UFPTI)	p	2006	3461	Dec-11
USA, OK.	Oklahoma City (ProCure PTC)	p	2009	623	Dec-11
USA, PA.	Philadelphia Upenn)	p	2010	433	Dec-11
USA, IL.	CDH Warrenville	p	2010	367	Dec-11
USA, VA.	Hampton (HUPTI)	p	2010		
				77191	Total
			thereof	8843	C-ions
				67904	protons

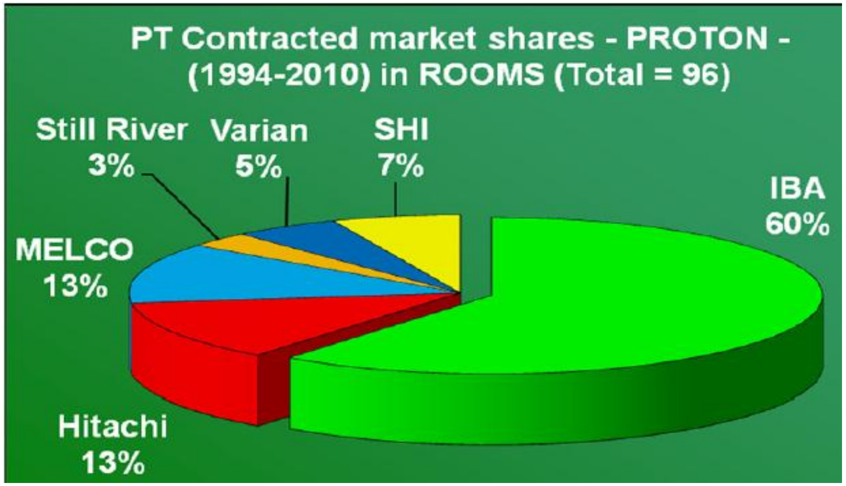
Patient Statistics as per March 2012

He-ion	P-ions	C-ions	Other-ions	Protons	Grand Total
2054 (2.13%)	1100 (1.13%)	9283 (9.62%)	433 (0.45%)	83667 (86.67%)	96537 (100%)

Worldwide Proton Therapy Facilities in Operation (43 Nos)

US-09, EUROPE-17, JAPAN-10, CHINA-02, CANADA-02, TAIWAN-01, KOREA-01 S. AFRICA-01

Facilities under planning (27)



CHALLENGES TO ADOPTION OF PROTON TO HERAPY

- Limited vendors/FDA & CE approval
- Equipment/Software maturity/ integration
- Need based facility layout planning
- 2D/3D Imaging integration/In-vivo imaging
- Cost/ Gestation for implementation Period
- New immobilization techniques
- Quality of man power support
- Dosimetery and delivery QA
- **Lack of knowledge about clinical conditions for which proton therapy provides better cancer care.**

iba

MITSUBISHI

HITACHI

Sumitomo Heavy Industries, Ltd.
QUANTUM EQUIPMENT DIVISION

VARIAN
medical systems

PROTOM
INTERNATIONAL, INC.

OPTIVUS
PROTON THERAPY

Still River
SYSTEMS
(MeVion)

SIEMENS

Proton Facilities under planning (27)

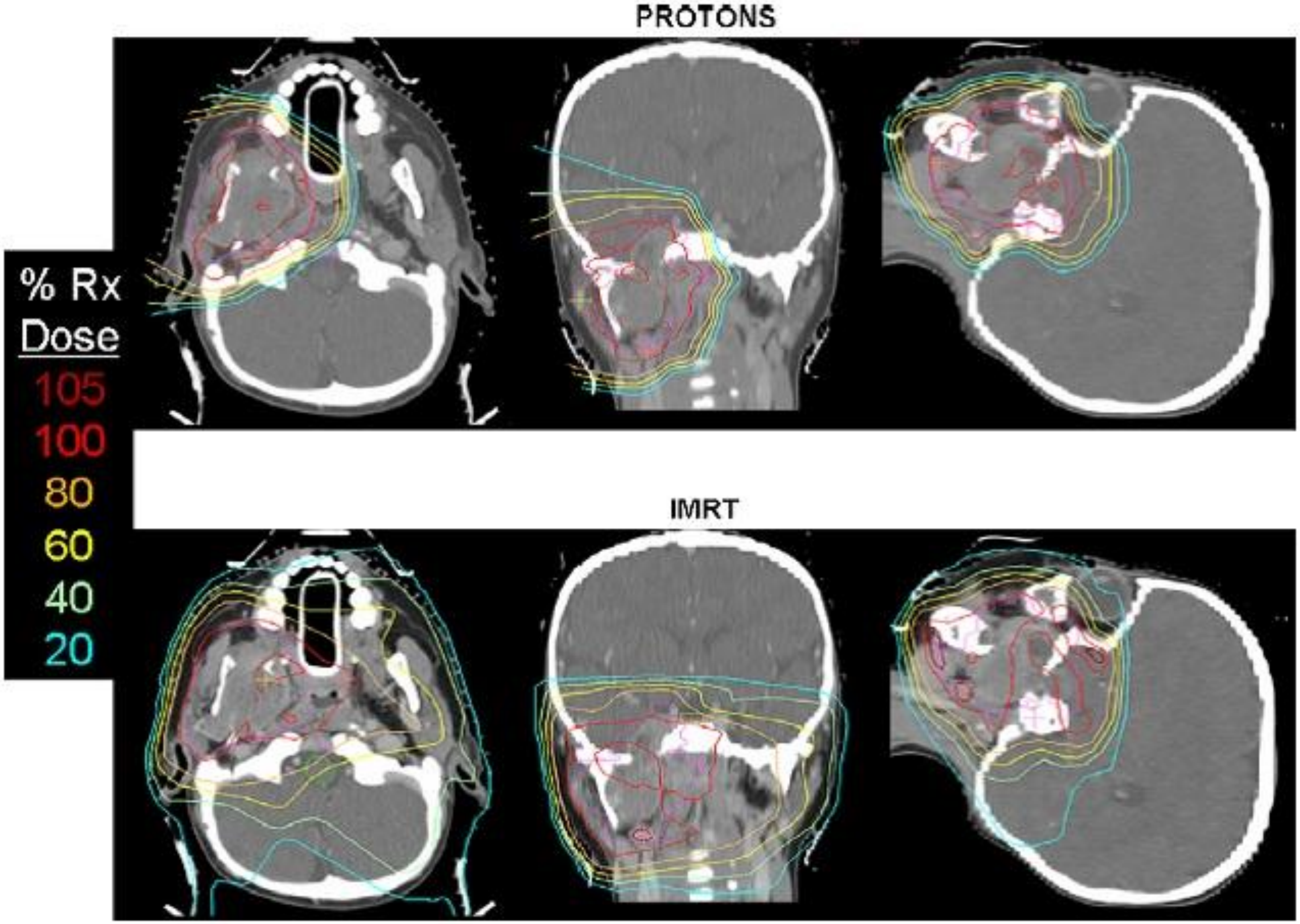
USA-09, EUROPE-11, JAPAN-01, CHINA-02, KOREA-01,

India-03*

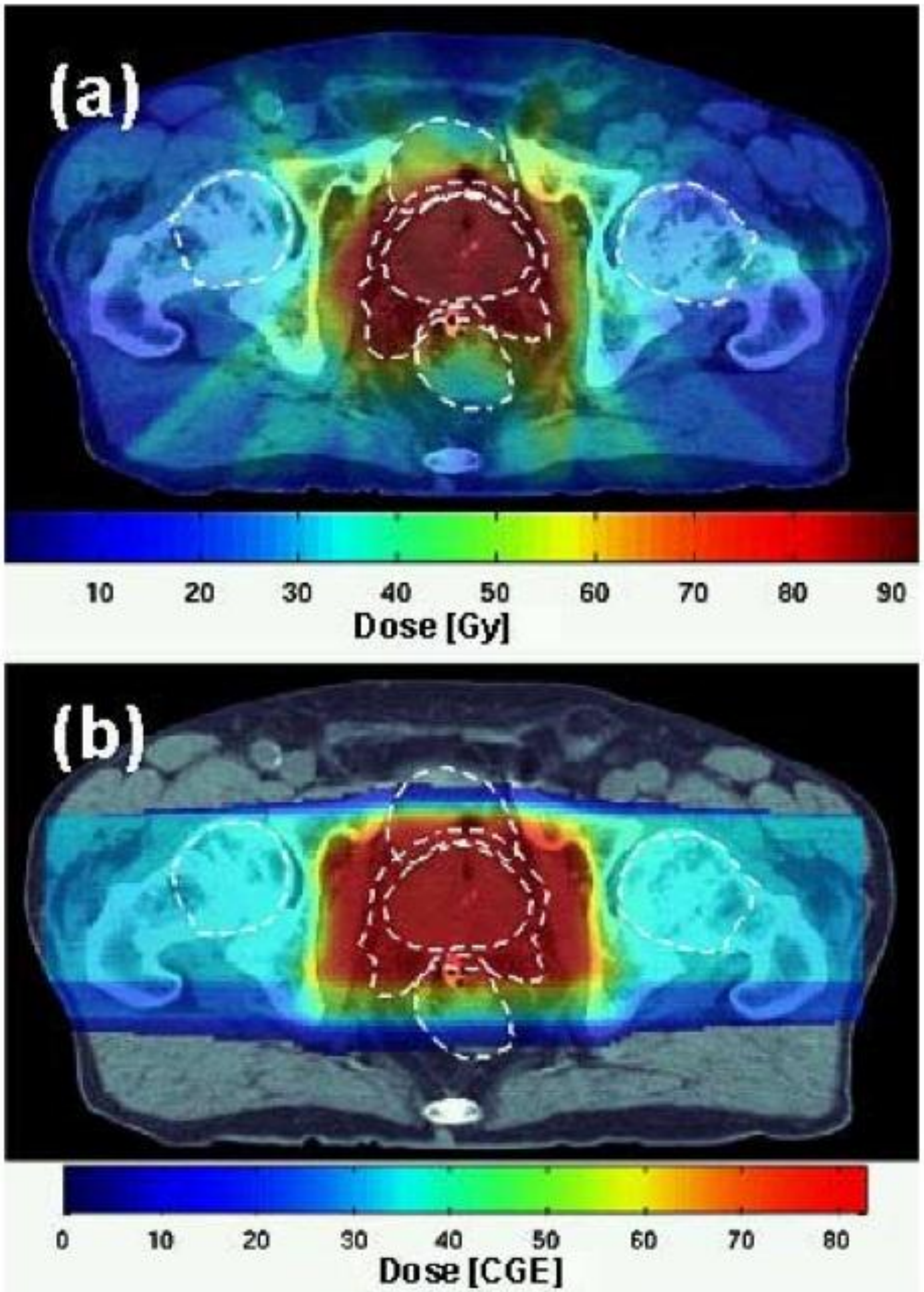
*** Apollo, TMC, DSCI**

Types of Machines: Variable Design (Specific QA and Safety)

- Home grown (Cyclotron)
  - Harvard Cyclotron
  - Indiana university
- Loma Linda (only one of its kind): (Synchrotron)
- IBA (Cyclotron)
- Hitachi (Synchrotron)
- Mitsubishi (Synchrotron)
- Sumitomo (Cyclotron)
- ProTom (Compact Synchrotron)
- Mevion (Superconducting Synchrocyclotron)



Dose distributions for IMRT versus proton plans for a paediatric rhabdomyosarcoma - *Kozak et al, IJROBP, May 2009*



The dose distribution of

(a) IMRT photons

versus

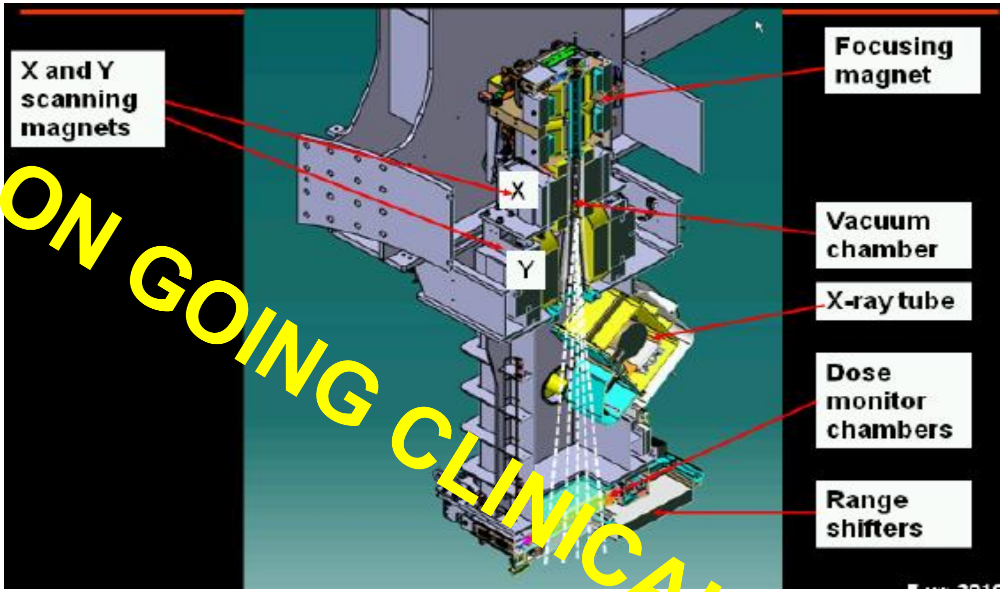
(b) 2 field protons.

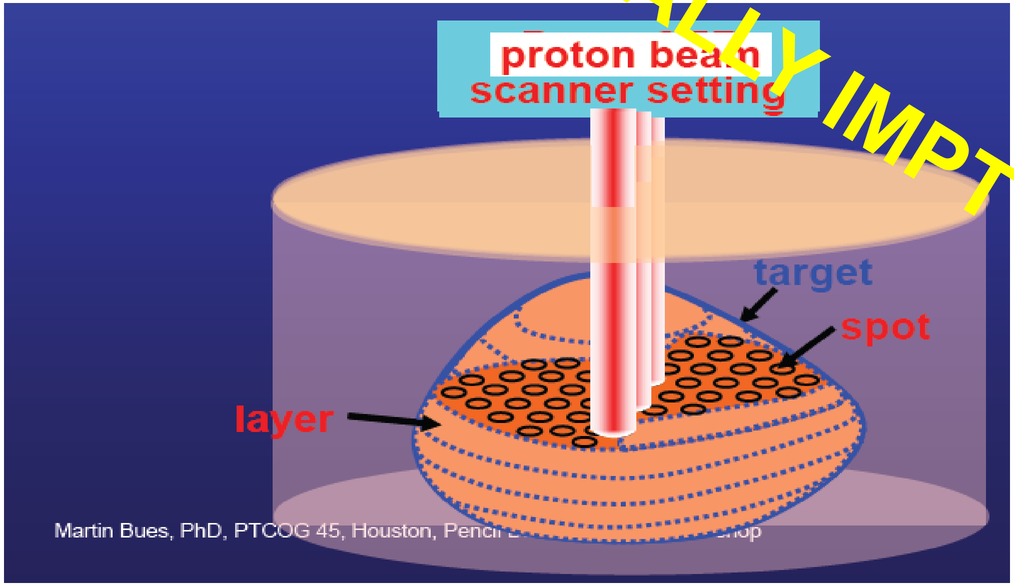
Trofimov A et al. IJROBP, Oct 2007

PENCIL BEAM SCANNING TECHNOLOGY

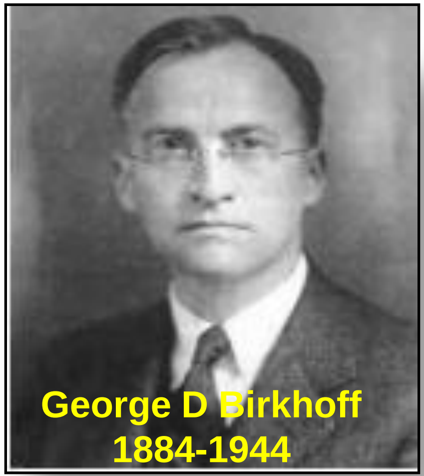
Clinically useful IMPT Technology

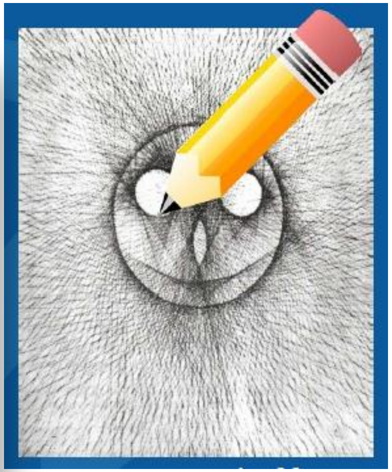
ON GOING CLINICALLY IMPT TECHNOLOGY





Pre- history of pencil beam Math

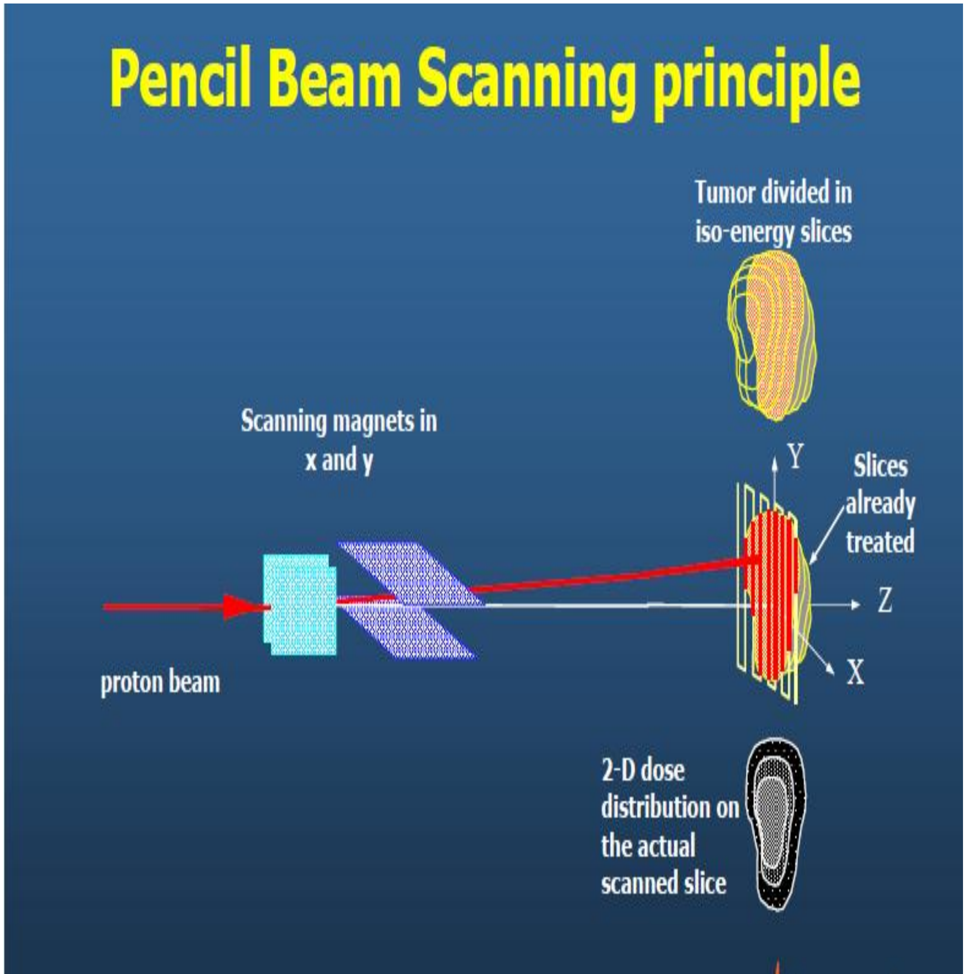




George D Birkhoff, on drawings composed of uniform straight lines Journal de Math. Pures et appl. 1940 (19), 221-36

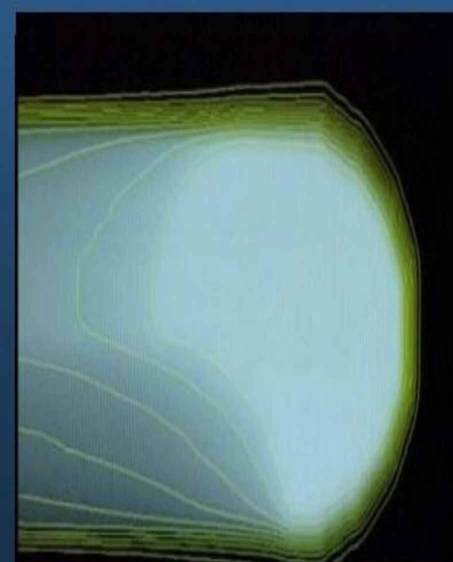
- ❖Precursor of the PENCIL BEAM concept
- ❖ Arbitrary picture with a pencil and a ruler by drawing straight lines with different 'intensities'
- ❖ Requires both ends of the pencil

Depth Related Layer Wise Energy Deposit



Layer by Layer Pencil Beam Energy Deposit

- Deliver many small beams to a tumor using magnetic beam deflection.
- Energy is changed in accelerator to scan each successive layer.



A full set, with a homogenous dose conformed distally *and* proximally

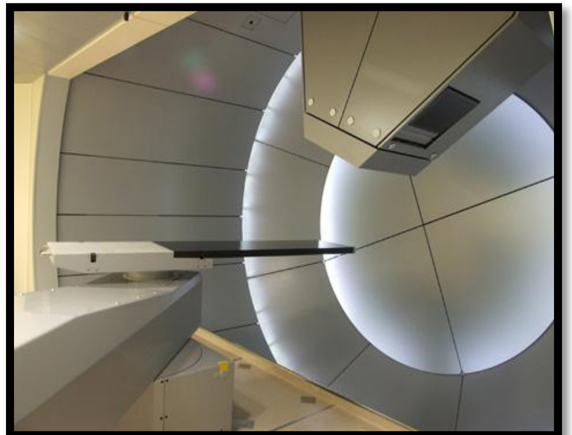
Pedroni, PSI

McLaren

Over all Uniform Dose to PTV

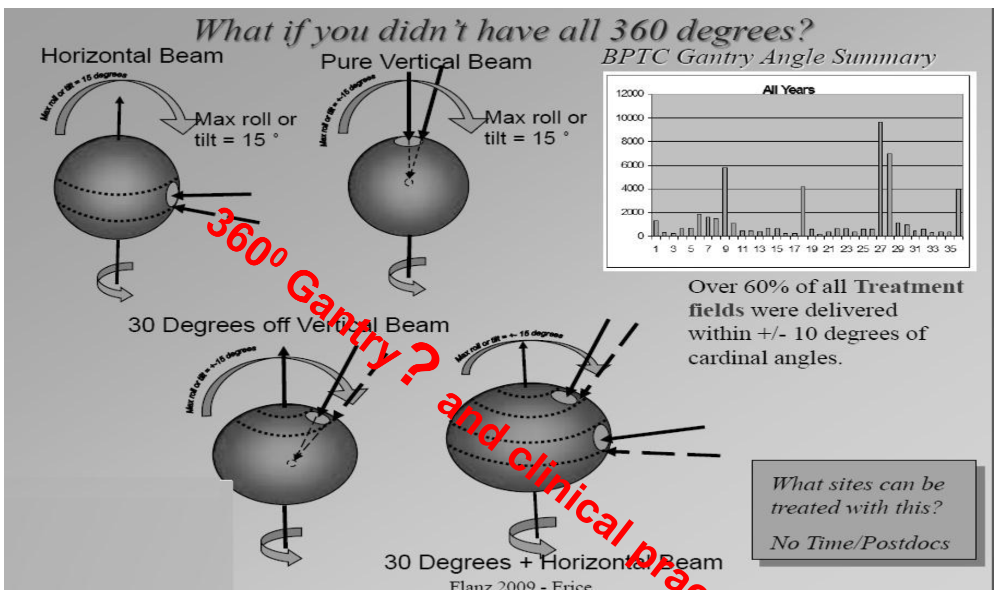
Some active scanning PTS's

IBA PTS 220⁰ Gantry

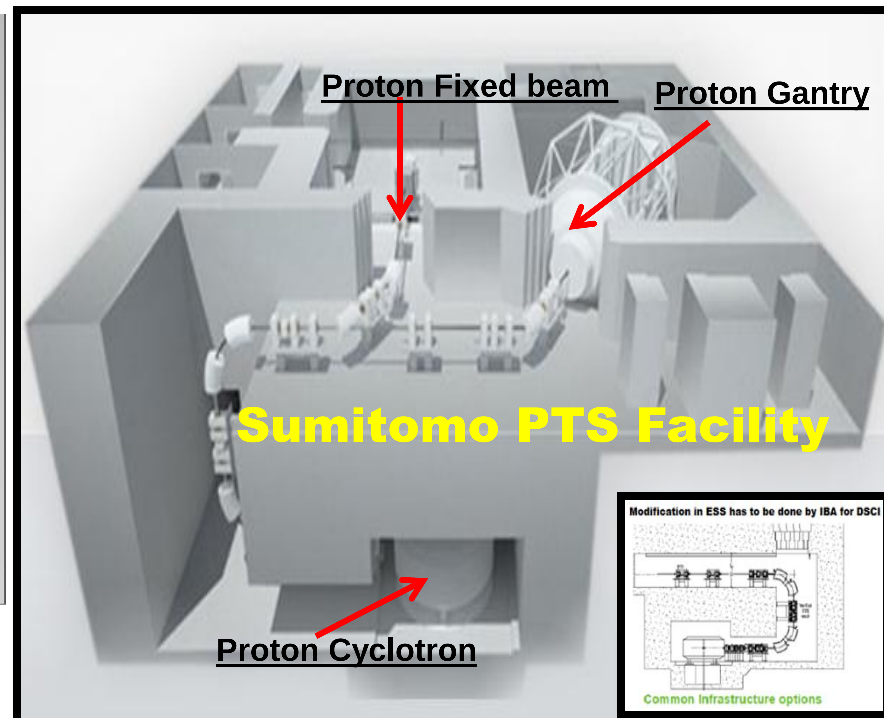


Varian PTS 360⁰ Gantry

MEVION PTS 360⁰ Gantry



Jay Flanz, *Beam Delivery Systems: Scattering, Scanning, w/wo Gantries or Cost Effective Particle Therapy?* Ion Beam Therapy Workshop; Erice, 2009



PROTON THERAPY: THE GAME CHANGER

- **Presently radiotherapy plays a major role in cancer treatment, either curative or as palliative; alone or in a multimodality plan, usually in conjunction with surgery and/or chemotherapy.**

BUT

- **Proton therapy will completely change the present scenario of multimodality cancer care**

CANCER MANAGEMENT IN THE ERA OF PROTON THERAPY: CLINICAL EVIDENCE

- **Tumours that are relatively radiation resistant and lie adjacent to critical dose-limiting normal structures. These include chordoma and chondrosarcoma of the skull base.**

- **Tumours in children, particularly where the target volume is large. Considerations of the risk of second malignancy and the detrimental effects of radiotherapy dose on growth and endocrine function are important. There is clear evidence that the use of proton beams can reduce unnecessary dose in many non-target structures .The most dramatic example of this is in medulloblastoma**

(St Clair WH, Adams JA, Bues M, Fullerton BC, La Shell S,Kooy HM, et al, 2009 & Brodin P, Radiobiological optimization including consideration of secondary cancer risk: A treatment modality comparison study for pediatric medulloblastoma, Master of Science Thesis, Copenhagen University Hospital (Rigshospitalet), Lund University, June 15, 2010).

CANCER MANAGEMENT IN THE ERA OF PROTON THERAPY

Clinical Oncologists & Surgical Oncologists treating Head and Neck cancers and pelvic malignancies need to familiarize with Proton Radiotherapy techniques as it could replace current management standards of Head/Neck, and Pelvic malignancies which are the major load of cancer in India.

Cont….

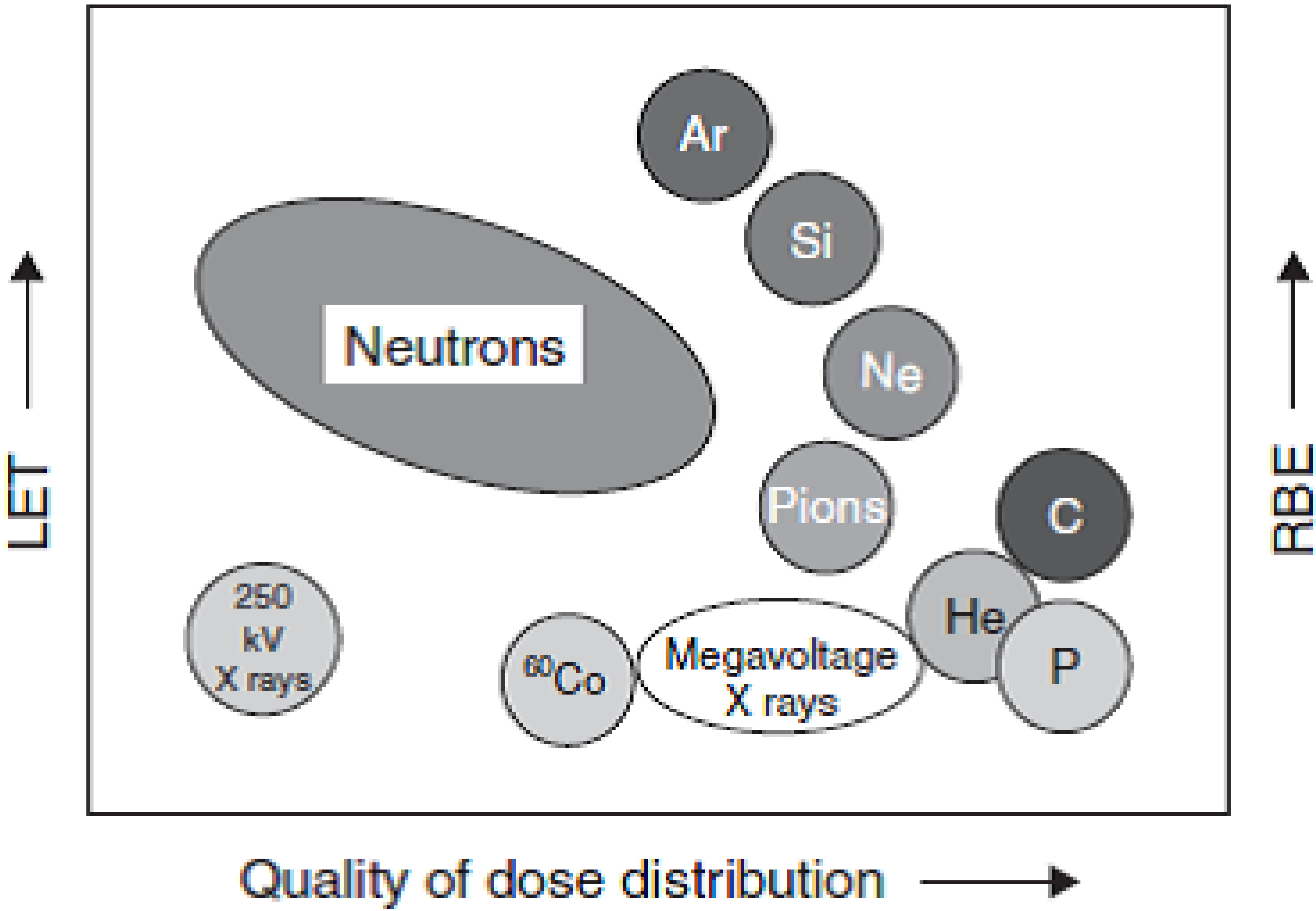
CLINICAL MANAGEMENT OF CANCER IN THE ERA OF PROTON THERAPY

- **Pediatric Malignancies (PBRT & XSBRT candidate)**
- **Sarcomas of the Base of Skull (PBRT & XSBRT candidate)**
- **Sinonasal Malignancies**
- **Nasopharyngeal Carcinoma**
- **Oropharyngeal Carcinoma**
- **Paraspinal tumours (PBRT & XSBRT candidate)**
- **NSC Lung Cancer (PBRT & XSBRT candidate)**
- **Hepatocellular Ca. (PBRT & XSBRT candidate)**
- **Prostate Cancer**

NEW PTS:PHYSICAL & CLINICAL BENEFITS

Large majority of the patients were treated by conventional passive scattering proton therapy techniques. More and more precise and sharp dose distributions by new dynamic/ scanning proton beam technology along with KVCBCT Image guidance including ONLINE PET IMAGING will give PTS a marked edge over other presently available competing photon based radiotherapy technologies resulting in significant clinical benefits to patients.

CARBON ION THERAPY: PHYSICAL & CLINICAL BENEFITS



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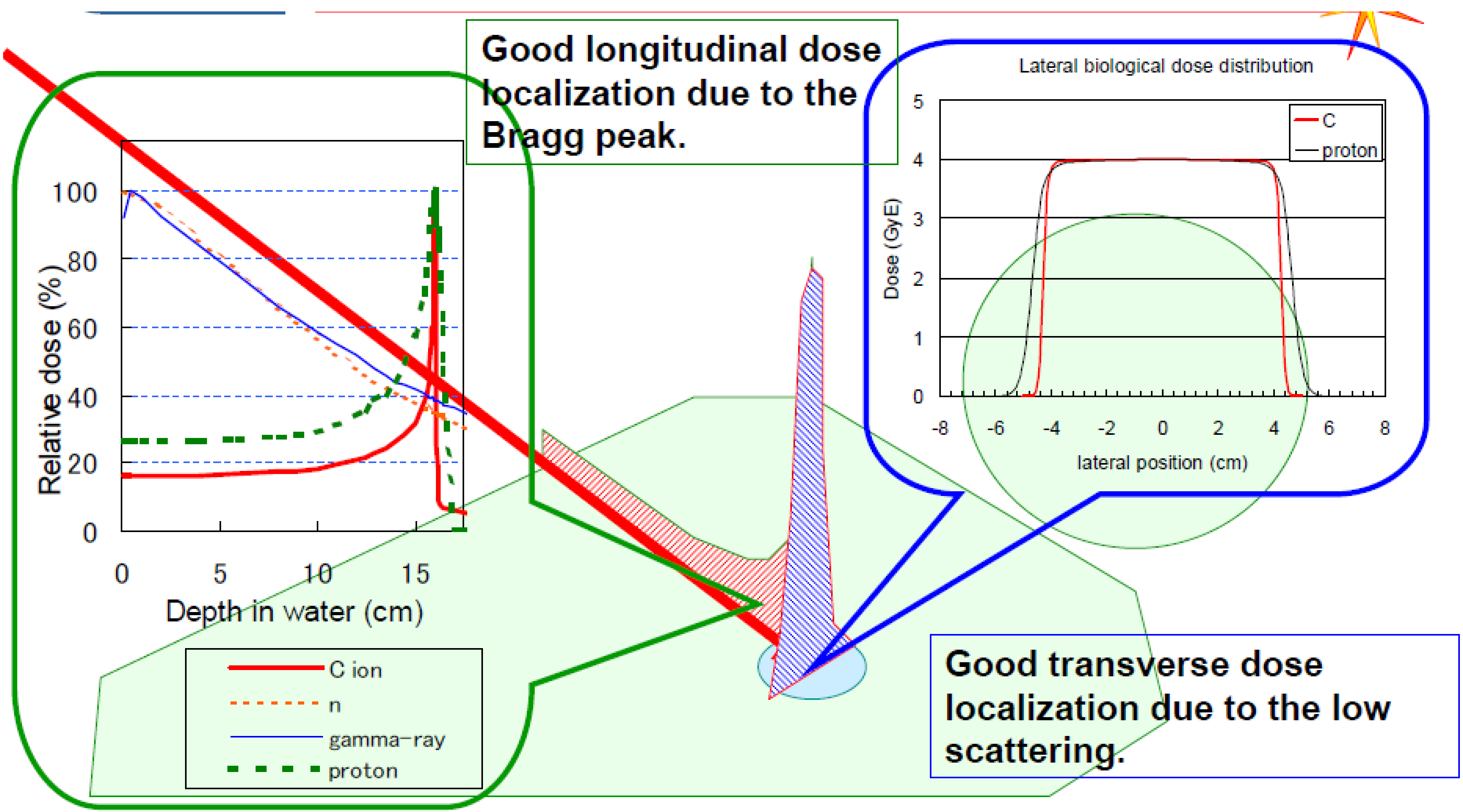
PHYSICAL ADVANTAGE OF CARBON ION THERAPY OVER PTS



COURTSEY – A KITAGAWA NIRS, HIMAC, JAPAN

Carbon Ion Therapy Operational Facilities

(October 2012 report)

Institute / Hospital	Name of facility	Location (Country)	Start year	Total patients	Treat-ment rooms	Irradiatin port			Target deseases	Irradiation method	Max. Energy	Typical beam intensity from accelerator	Type of injector	Type of ion souce	No. of ion souce	Operation schedule	Maintenance interval
						H	V	Other			MeV/u						
~~Lawrence Berkeley Laboratory~~	~~Bevalac~~	~~Berkeley (USA)~~	~~1975 – 1992~~	~~433~~	~~1~~	~~1~~	~~0~~	~~0~~	~~whole body~~	~~Scatterer / Wobbler~~	~~670 for Ne~~	~~1E10 ppp (0.25Hz)~~	~~Elec.Stat. + Alvarez~~	~~PIG~~	~~3~~		
National Institute of Radiological Sciences (NIRS)	HIMAC	Chiba (Japan)	1994 -	6512 (Feb.'12)	3	2	2	0	whole body	Wobbler / Layer stacking / Raster scanning	400	1.8E9 pps (typ. 0.3Hz)	RFQ + Alvarez	ECRIS, PIG	3	24 hours / 6 days / 10 month	2times / year
~~Gesellschaft fur Schwerionenforschung (GSI)~~	~~UNILAC + SIS~~	~~Darmstadt (Germany)~~	~~1997 – 2009~~	~~440~~	~~1~~	~~1~~	~~0~~	~~0~~	~~head & neck~~	~~Raster scanning~~	~~430~~	~~1E6 – 4E10 ppp~~	~~RFQ + IH + Alvarez~~	~~ECRIS~~	~~1~~	~~7 days / 4weeks at 5 per year~~	~~5times / year~~
Hyogo Ion Beam Medical Center (HIBMC)	HIBMC	Hyogo (Japan)	2002 -	1393 (Mar.'12)	3+	2	1	1 (fix45)	whole body	Wobbler	320	2E9 pps	RFQ + Alvarez	ECRIS	2	5days / 1week	1times (4days) / 1month
Institute of Modern Physics (IMP)	HIRFL-CSR	Lanzhou (China)	2009 -	shallow 103 deep 56 (Oct.'11)	1	1	0	0	sarcoma	Wobbler / Layer stacking	235	5E8 ppp	Cyclotron	ECRIS	1	7days / 1week	2times / year
University Hospital Heidelberg	Hidelberg Ion Therapy Facility (HIT)	Heidelberg (Germany)	2009 -	~900 (May '12)	3	2	0	1 Gantory	whole body	Raster scanning	430	1E9 ppp	RFQ + IH	ECR	2		
Gunma University	Gunma-University Heavy-Ion Medical Center (GHMC)	Maebashi (Japan)	2010 -	424 (Dec.'11)	4*	2	3*	0	whole body	Wobbler / Layer stacking	400	1.2E9pps	RFQ + APFIH	ECR	1		
Fondazione Centro Nazionale Adroterapia Oncologica	Centro Nazionale Adroterapia Oncologica (CNAO)	Pavia (Italy)	2012 -	- (Oct.'12)	3	3	1	0	whole body (start:hea	Raster scanning	400	4.5E8ppp	RFQ + IH	ECR	2		

* include research room, + exclude other rooms for proton only, pps: particle per second, ppp: particle per pulse (spill)

Carbon Ion Therapy: Indications & Clinical Benefits

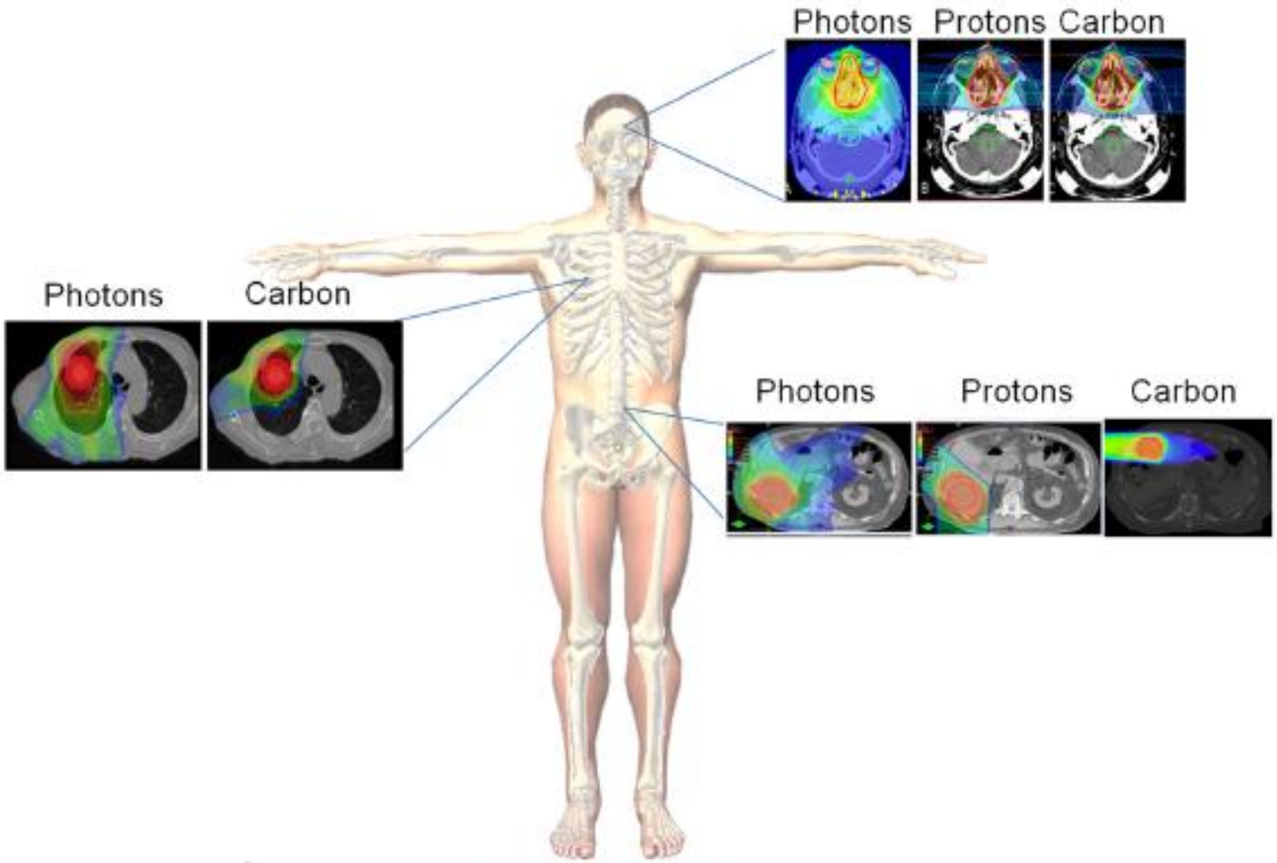


Figure 3 Anatomical constraints can be overcome with carbon ions for various histologies. Comparing the same histologies at different sites which have anatomical constraints such as glioblastoma multiforme (intracranial), lung (thoracic region), and rectal carcinoma (abdominal/ pelvic) using treatment planning software for photons, protons and carbon it is evident that implementing carbon ions gives better biological dosage to the target area (tumor) while limiting treatment to surrounding healthy tissue. Adapted with permission from [169-172].

Cont….

Carbon Ion Therapy: Indications & Clinical Benefits

Table 1 Effectiveness comparison for various histologies by anatomical location between Standard of Care (SOC) and Carbon Ions

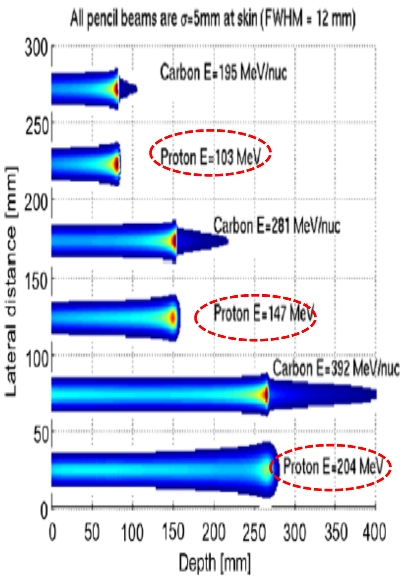
Site	No. of carbon ion studies	5-year LC range		Toxicity range (late ≥ GIII injury)		References
		SOC	Carbon	SOC	Carbon	
Intracranial						
Glioma	2	< 20%	-	Location dependent	-	Trials ongoing[§†]
Meningioma	2	80-90%	-	Location dependent	-	Trials ongoing[§‡]
Head and Neck						
Adenoid cystic	3	27-72%	26-96%	0-12.9%	0-17%	[141,142]
Bone/soft tissue sarcoma	2	43-70%	24-73%	0%	2-18.5%	[20,140,143-147]
Skull base	3	46-73%	82-88%	0-7%	0-5%	[117-121,148]
Thorax						
NSCLC	4	80-97%	90-95%	0-15%	3% (pneumonitis)	[21,149]
Abdomen and Pelvis						
HCC	4	75-96%	81-96%	7-22%	3-4%	[21,130-133,150]
Pancreas	2	10-20%	66-100%	1.8-20%	7.7%	[136,151-153]
Prostate	2	80-95%**	87-99%*	4-28%	0.1-25%	[21,24,154-159]
Rectal cancer	1	24-28%	95%	14-27%	-	[21,160-162]
Cervix cancer	1	20%	53%	0-10.6	9.6-18.2%	[163-165]
Sacral chordoma	1	55-72%	88%	17.6%	5.9%-17.9%	[166-168]
Chondrosarcoma	1	20-40%	60%	-	-	[167,168]

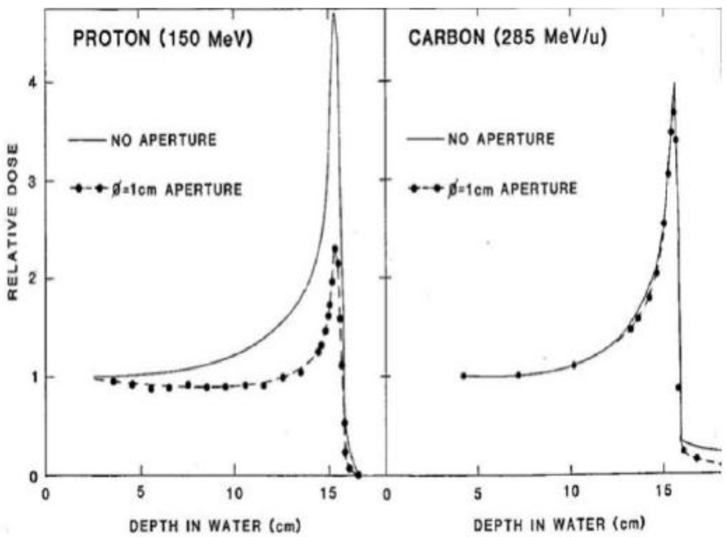
Abbreviations: SOC Standard of Care, *LC* Local Control, *HCC* Hepatocellular carcinoma, *GIII* Grade III toxicity, *OS (Overall survival); **bPFS (biochemical progression free survival); [§]CLEOPATRA (NCT01165671); [†]CINDERELLA (NCT01166308); [‡]MARCIE (NCT01166321).

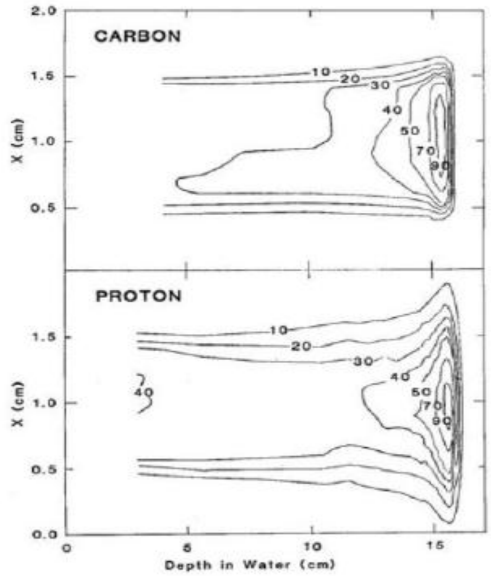
CARBON ION THERAPY BEAM DEPOSIT MORE DOSE AT THE DISTAL EDGE COMPARED TO PROTON THERAPY BEAM

Contd…

Dose Profile & Dose Issues Of Small Beam in SBPT & SBCIT







Heng Li et al. (2013) have shown that the treatment log file in a spot scanning proton beam delivery system is precise enough to serve as a quality assurance tool to monitor variation in spot position and MU value, as well as the delivered dose uncertainty from the treatment delivery system.The analysis tool developed here could be useful for assessing spot position uncertainty and thus dose uncertainty for any patient receiving spot scanning proton beam therapy. Heng Li,Narayan Sahoo et al, **Use of treatment log files in spot scanning proton therapy as part of patient-specific quality assurance, Med. Phys. 40 (2), February 2013, pp 1-11**

RCT EVIDENCE & NEW TECHNOLOGIES

Adoption of new technologies of proton & carbon ion therapy in situations of 'uncertain' clinical benefit is hotly debated. It should be understood that many innovations, including cobalt-60 units, linear accelerators, electron beams, IMRT and image-guided RT have entered into clinical practice without phase III RCT evidence.

HADRON THERAPY: PROSPECTS

I. Prospects of Proton Therapy System

- Proton therapy is booming, but the investments to build the multiroom centres are large and discouraging.
- **The future of proton therapy is in single-room facilities and companies are proposing new ‘low cost’ solutions including gantry design. If proton accelerators were ‘small’ and ‘cheap’, no radiation oncologist would use X rays** hence protontherapy is the real **game changer.**

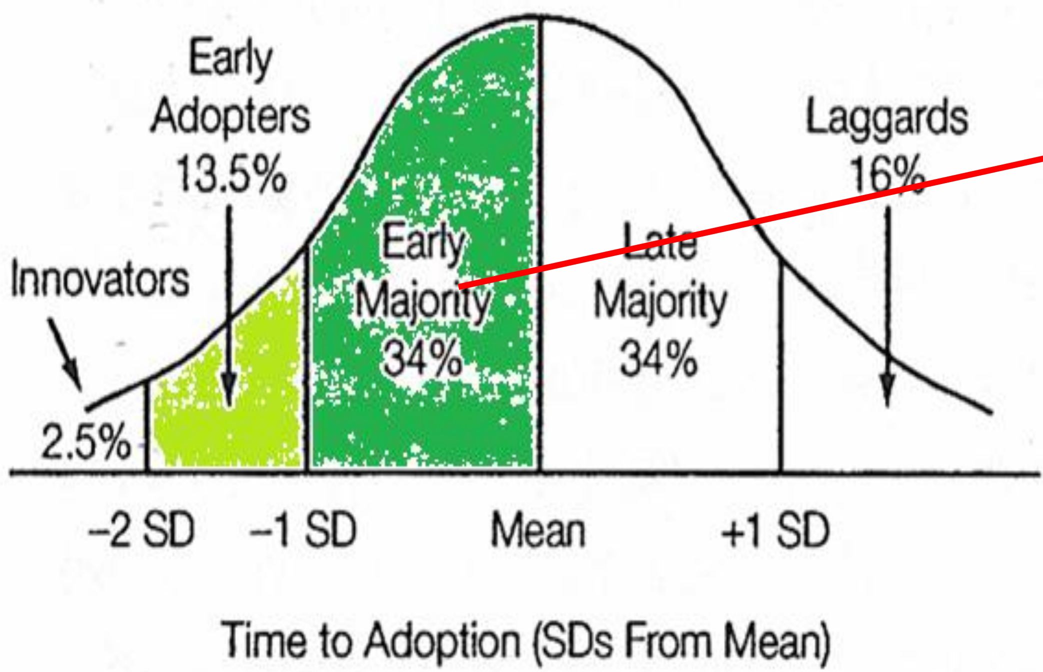
II. Prospects of Carbon Ion Therapy System

- Carbon ion therapy is developing in Japan and in Europe, but more should be built to define – with clinical phase III trials -tumour sites and the protocols in comparison with proton therapy.
- New carbon ion accelerators will become soon a reality.
- To move forward, ion gantries should be available; novel ideas are being proposed but the way is long.

Ugo Amaldi, PARTICLE ACCELERATORS IN TUMOUR THERAPY, http://dpnc.unige.ch/seminaire/talks/amaldi.pdf.,16th Oct,2013,Geneva

PROTON THERAPY IN INDIA

Figure 2. Adopter Categorization on the Basis of Innovativeness



Reprinted with permission from Rogers.[21]

D. Berwick,JAMA, April 16, 2003-Vol. 289, No. 15 (Reprinted)

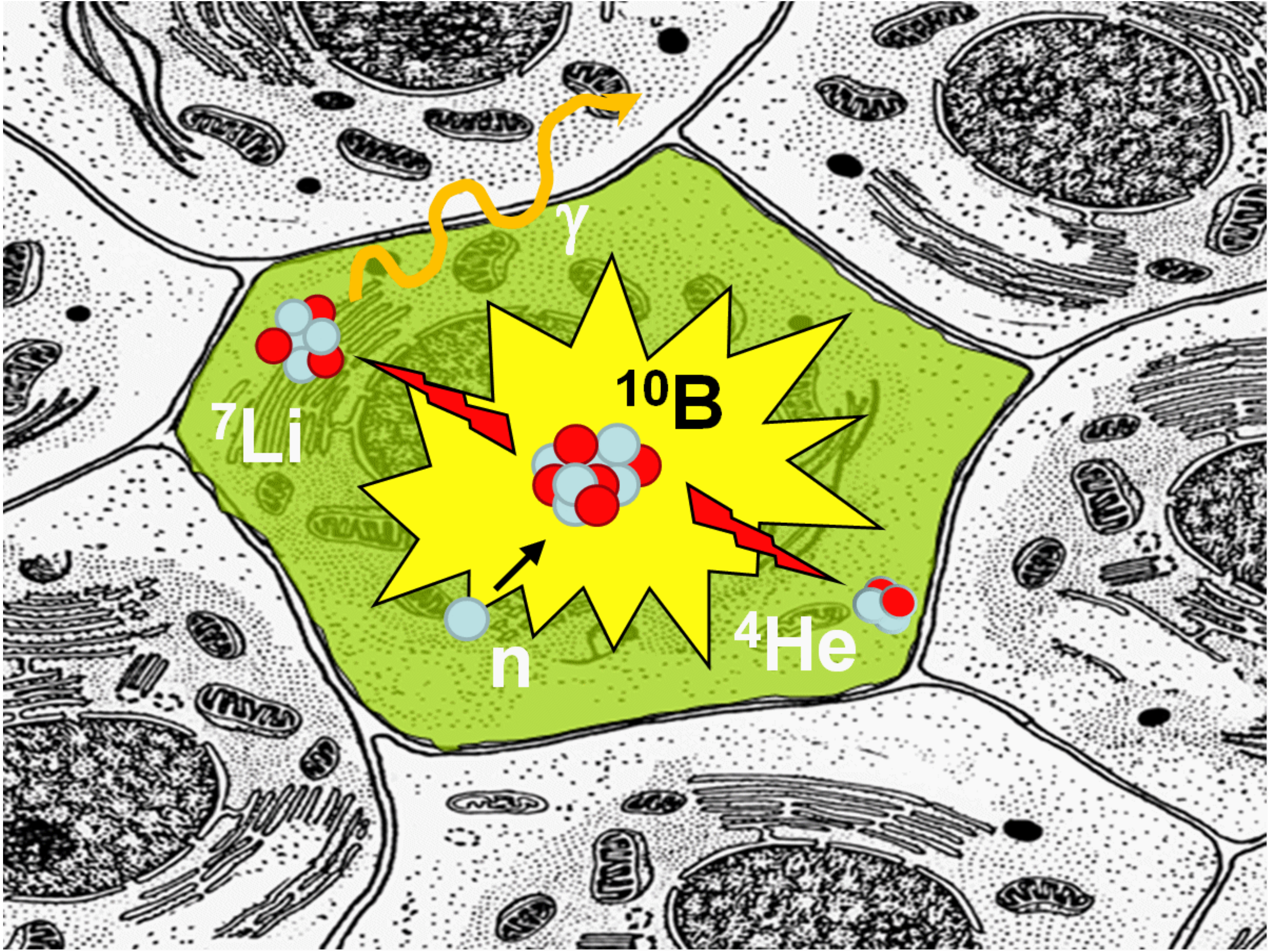
✓**Community of Radiation Oncologists & Medical Physicists in INDIA is not a "<u>Doubting Tom</u>" and has preferred to be in the "<u>early majority</u>" group for adoption of Proton Therapy initially and carbon ion therapy subsequently.**

&

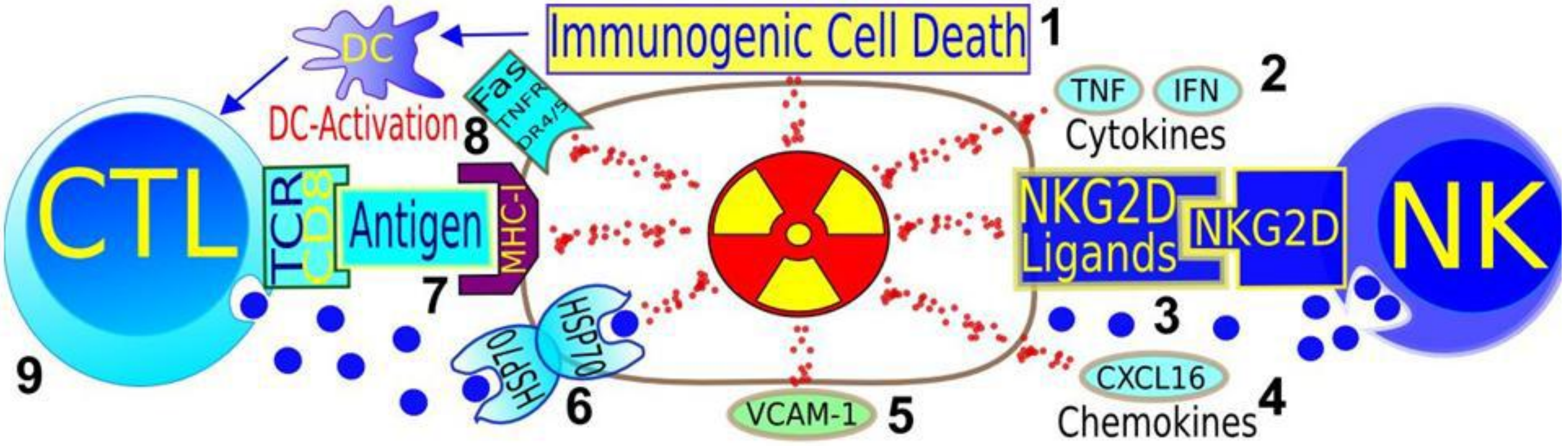
✓ **Our Technology Adoption will be consistent with our Strategic and Clinical Priorities.**

BNCT?????

BORON CAPTURE THERAPY IS ANOTHER TYPE OF HADRON THERAPY WHICH IS NOT IN WIDE CLINICAL PRACTICE THE CENTERS WHICH STILL PRACTICE ARE SHOWN IN THE NEXT SLIDE



Artistic description of BNCT. The 10B atom, previously charged into the tumour cell, undergoes nuclear reaction when it absorbs a thermal neutron. The short-range high-LET reaction fragments destroy the tumour cell.

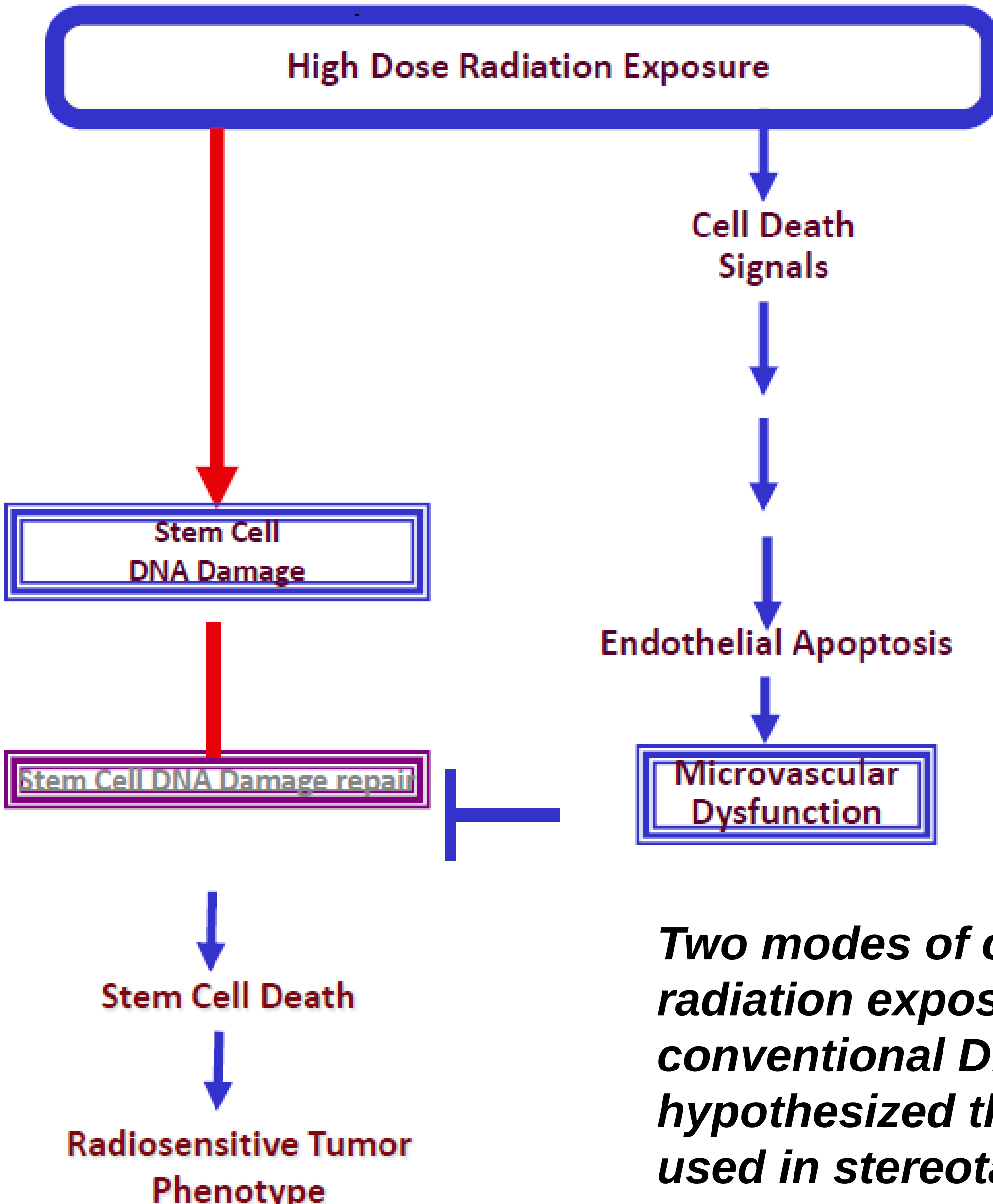


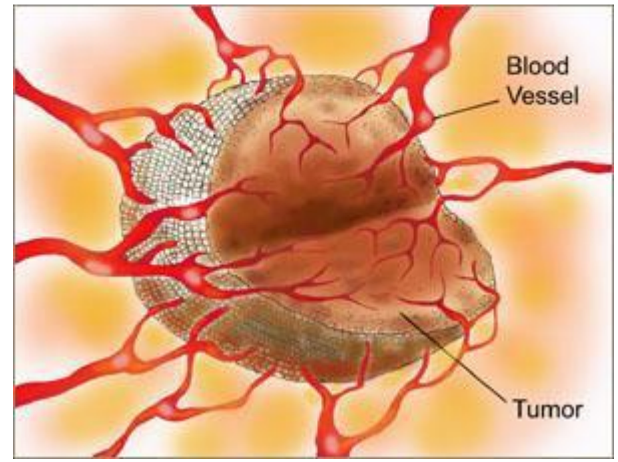
Pathways where radiation can synergize with immune adjuvant therapy for cancer*.** ***1. *Immunogenic cell death is promoted by ionizing radiation, through dendritic cell activation and consequently, T-Cell expansion.* ***2.*** *Cytokines play a role in radiation therapy success.* ***3.*** *NKG2D-Ligands, sensitizing stressed cells to Natural Killer Cells (innate immunity) are upregulated by radiation.* ***4.*** *Chemokines can be induced by radiation, attracting effector T Cells to the tumor.* ***5****. Radiation-induced interferon-gamma dependent upregulation of cell adhesion molecule also influences antitumor immunity.* ***6.*** *Heat Shock proteins sensitize to cytotoxic granzymes.* ***7.*** *Radiation can lead to enhanced expression of MHC-I and to de novo expression of neoantigens.* ***8.*** *Death receptors can be upregulated by irradiation.* ***9.*** *CD8 T Cells are essential for the success of radiotherapy.* ***Image courtesy of Norman Reppingen, TU Darmstadt.***

Boron Neutron Capture Therapy (BNCT)

^{10}B has to be carried into or close to the target cell with a drug properly designed for having a better affinity for tumour cells rather than the surrounding healthy cells. Two drugs are nowadays available for clinical investigations: BSH (*mercaptoundecahydro-cloco-dodecarborate Na2 ^{10}B12 H11 SH) and BPA (para-borophenylalanine C9 H12 ^{10}BNO4).*

CENTER	STATES	NEUTRON SOURCE	NEOPLASM	TREATED PATIENTS
Helsinki University Central Hospital, Helsinki, Finland	Europe	FIR-1, VTT Technical Reserch Centre, Espoo	GB and HN	50 GM 2 AA 31 HN
Faculty Hospital of Charles University, Prague, Czech Republic	Europe	LVR-15 Reactor, Nuclear Reserch Institute Rez	GB	5 GM
University of Tsukuba, Tsukuba City, Ibaraki	Japan	JRR-4, Japan Atomic Energy Agency, Tokai, Ibaraki	GB	20 GM 4 AA
University of Tokushima, Tokushima	Japan	JRR-4 (Kyoto University Research Reactor, Osaka)	GB	23
Osaka Medical College and Kyoto University Research Reactor, Kyoto University, Osaka and Kawasaki Medical School, Kurashiki	Japan	KURR	GB, HN, CM	30 GBM 3 AA 7 Men 124 HN
Taipei Veterans General Hospital, Taipei, Taiwan	Republic of China	THOR, National Tsing Hua University, Hsinchu, Taiwan	HN	10
Inst de Oncol. Angel H, Buenos Aires	Argentina	Bariloche Atomic Center	CM and AT	7CM 3 AT





Two modes of cell death following high-dose radiation exposure. In addition to the conventional DNA damage pathway, it is hypothesized that very high dose, such as those used in stereotactic ablative radiotherapy, elicit vascular damage, which contributes to cell death

RADIOLOGICAL PROTECTION ISSUES IN HADRON THERAPY

ICRP

DRAFT REPORT FOR CONSULTATION: DO NOT REFERENCE

ICRP ref 4851-1931-9834
17 April 2014

Annals of the ICRP

ICRP PUBLICATION 1XX

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ICRP HAS JUST RELEASED DRAFT REPORT IN APRIL 2014 WHICH IS LIKELY TO BE OFFICIALLY READY AND PUBLISHED IN 2016. IT WILL BE A DOCUMENT FOR PHYSICAL AND CLINICAL ISSUES IN HADRON THERAPY

ONLINE IMAGING IN HADRON THERAPY PRACTICE

PET FOR IN-VIVO DOSIMETRY IN PROTON THERAPY

1. OFFLINE PET
2. INLINE PET

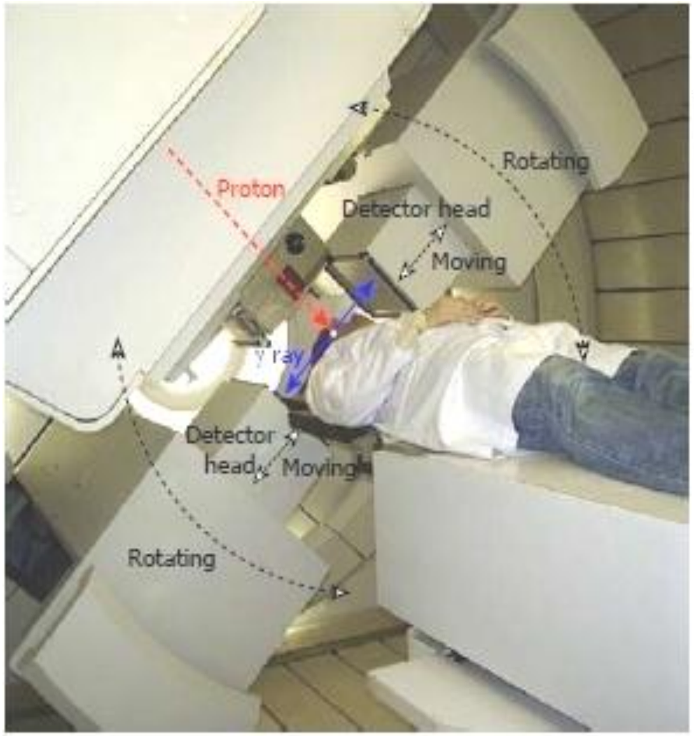
RELEVANT POSITRON EMITTER REACTIONS IN TISSUE FROM PROTON THERAPY

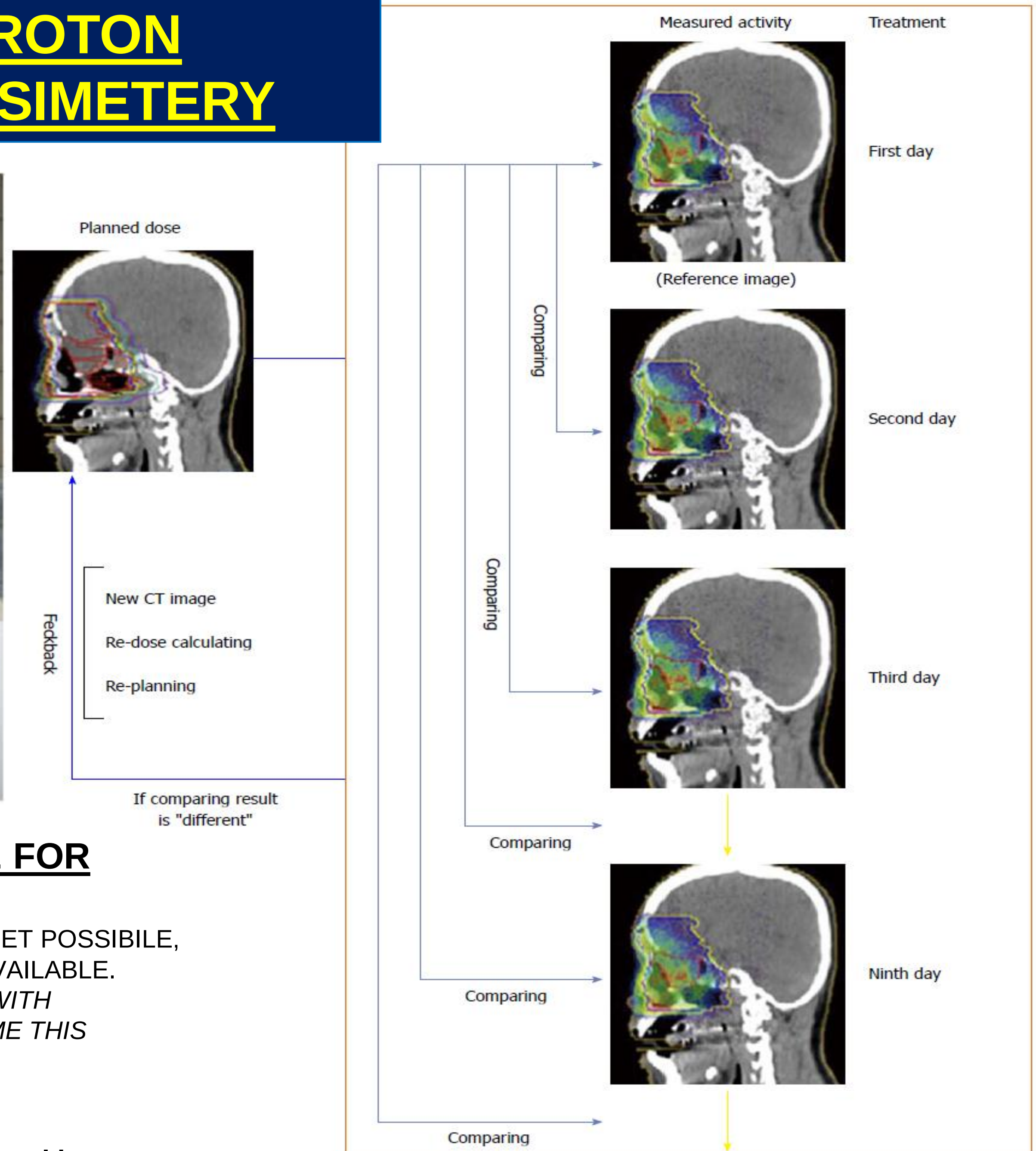
Reaction	Threshold energy (MeV)	Half life (min)	Positron energy (MeV)
$^{16}O(p, pn)^{15}O$	16.79	2.037	1.72
$^{16}O(p, \alpha)^{13}N$	5.66	9.965	1.19
$^{14}N(p, pn)^{13}N$	11.44	9.965	1.19
$^{12}C(p, pn)^{11}C$	20.61	20.390	0.96
$^{14}N(p, \alpha)^{11}C$	3.22	20.390	0.96
$^{16}O(p, \alpha pn)^{11}C$	59.64	20.390	0.96

1. OFFLINE PET IMAGING:

Daily offline PET is possible by transferring the patient to the dedicated PET CT Room which may take time more than the half life of positron emitter in the tissue from proton therapy. The problem may be over come by installing in room PET CT.

2. ONLINE PET FOR PROTON THERAPY IN-VIVO DOSIMETERY





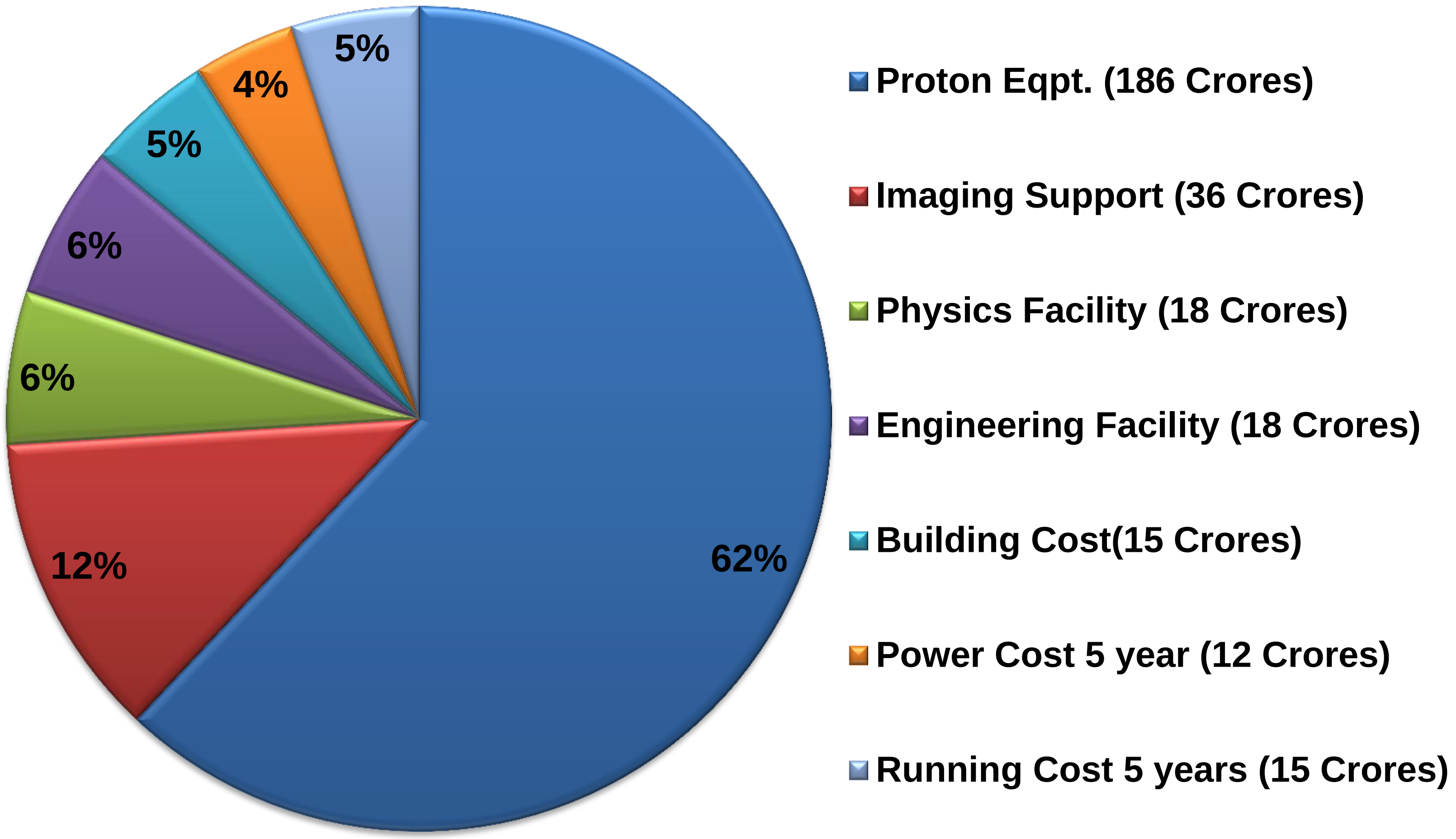
QA/ DELIVERY CHALLENGE FOR MEDICAL PHYSICS

IN-LINE OR ONLINE PET IMAGING : DAILY PET POSSIBILE, HOWEVER ANOTMICAL IMAGING STILL NOT AVAILABLE. *ADDITION OF DAILY ONLINE KVCBCT ALONG WITH DEFORMABLE IMAGE FUSION WILL OVERCOME THIS PROBLEM.*

Parodi et al (2002, 2005 & 2007), Nishio et al (2005,2006 & 2010), Lin et al (2008) and Studenski & Xiao (2010)

MITIGATION OF ORGAN AND TUMOR MOTION IN HADRON THERAPY BY PROTON AND CARBON ION IS AN ISSUE WHICH IS STILL PENDING SOLUTION IN OPTIMAL CLINICAL PRACTICE

Proton Facility Project Estimated Cost
(Rs 300 Crores)



Clinical Indications for Hadron Therapy

- **Particle therapy is effective in treating certain types of cancers as well as some non-cancerous tumors:**
  - Brain tumors
  - Prostate cancer
  - Pediatric cancers
  - Head and neck tumors
  - Base-of-skull tumors
  - Tumors near the spine
  - Lung tumors
  - Breast cancers
  - Lymphomas
  - Testicular cancers
  - Esophageal cancers


Thank you!


Felicitations on behalf of the
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MYTH 1:
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MYTH 4:
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ONE THIRD OF CANCER CASES CAN BE PREVENTED
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पंजीकरण REGISTRATION
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पूछताछ ENQUIRY
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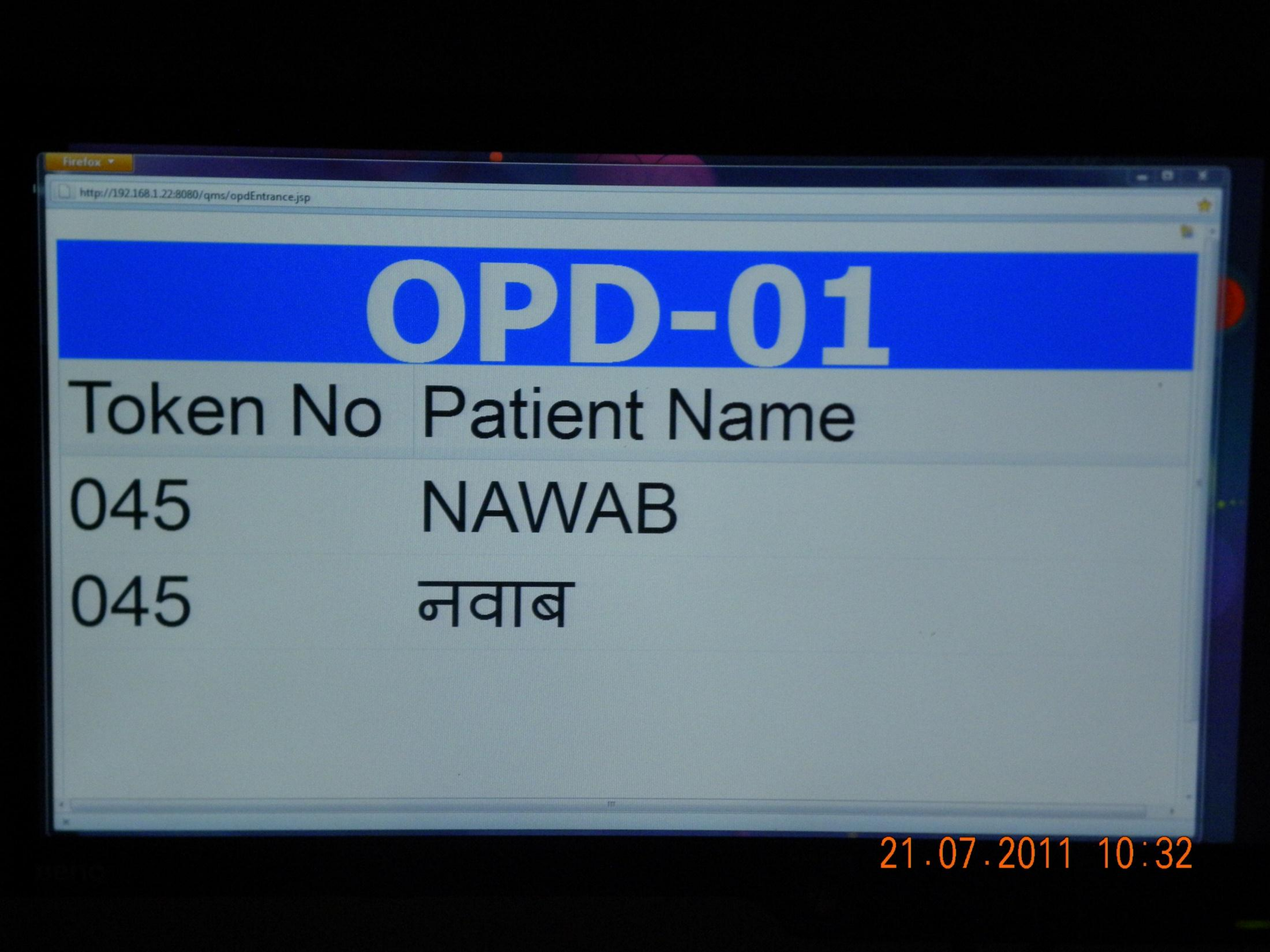
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पंजीकरण REGISTRATION
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वरिष्ठ रोगी SENIOR CITIZENS
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नये रोगी NEW PATIENTS
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आप सी.सी.टी.वी.
कैमरे की निगरानी में है।
You are under CCTV
Camera Surveillance.


1


OPD-02/Revisit
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असतो मा सत् गमय।
तमसो मा ज्योतिर्गमय।
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RADIOTHERAPY SECTION
विकिरण निदान अनुभाग
X-RAY & IMAGING SECTION
PLEASE KEEP Y
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KHALSA


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X-RAY
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X-RAY REGISTRATION & ENQUIRY
SAY NO TO TOBACCO


एक्सरे पंजीकरण एवं पूछताछ
X-RAY REGISTRATION & ENQUIRY


RADIOTHERAPY
DELHI STATE CANCER
Welcomes
UPDATE ON BREAST IMAGING
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कैमरे की
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बाह्य रोगी विभाग
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विकिरण चिकित्सा अनुभाग RADIOTHERAPY SECTION
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Happy New Year
2011
from
DSCI Family
नन्ही
KID'S
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THERAPY
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प्रतीक्षा क्षेत्र
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विकिरण चिकित्सा अनुभाग RADIOTHERAPY SECTION
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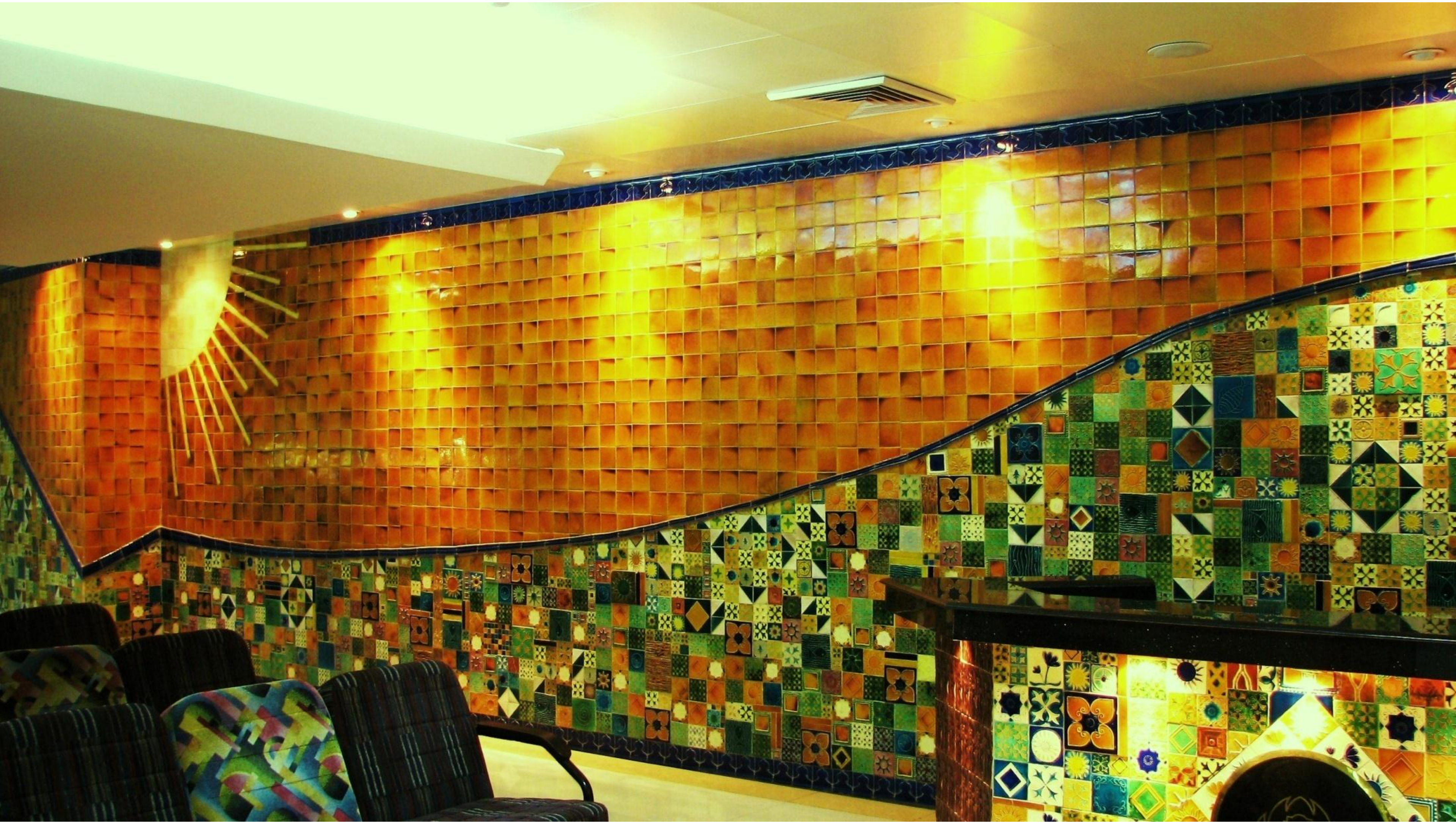


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OT & ICU

आपरेशन थियेटर परिसर OPERATION THEATRE COMPLEX


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GEORGES MATHE BMT SUITE
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EMERGENCY
CONTAINER


सर सोभा सिंह धर्मशाला
SIR SOBHA SINGH DHARMSHALA
سر سوبھا سنگھ دھرم شالہ
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धर्मशाला गेट


यह धर्मशाला
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सर सोभा सिंह पब्लिक चैरिटेबल ट्रस्ट के ट्रस्टी
SIR SOBHA SINGH DHARMSHALA
सर सोभा सिंह धर्मशाला
Built in the memory of
SIR SOBHA SINGH & LADY VEERAN BAI
Inaugurated
by
THE HON'BLE SHRIMATI SHIELA DIKSHIT,
Chief Minister
on 05-03-2005
Trustees of Sir Sobha Singh Public Charitable Trust


सर सोभा सिंह धर्मशाला
SIR SOBHA SINGH DHARMSHALA
سر سوبھا سنگھ دھرم شالہ
ਸਰ ਸੋਭਾ ਸਿੰਘ ਧਰਮਸ਼ਾਲਾ


यहाँ पर पानी ओर दूध ही गर्म कराया जाता है।
BED SHEET IS COMPULSORY FOR PER BED - RS. 5/- PER DAY
दलीया, खिचड़ी, सब्जी ओर चावल यहाँ पर गर्म नही होते है।
QUIT.
FOOD ORDER TIME


08.04.2010 11:08


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ओ पी डी व डे-केयर कीमोथैरेपी की सुविधाओं का
दिनाँक 13 मार्च 2013 को
दिल्ली की मुख्यमंत्री माननीया श्रीमती शीला दीक्षित द्वारा
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पश्चिमी दिल्ली के सांसद माननीय श्री महाबल मिश्रा
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उद्घाटन व जनता की सेवा में समर्पित किया गया।
एम स्पोलिया
सचिव, दिल्ली सरकार एवं
अध्यक्ष, प्रबंधन समिति
दिल्ली राज्य कैंसर चिकित्सा संस्थान
एस सी एल दास
सचिव (स्वास्थ्य एवं परिवार कल्याण), दिल्ली सरकार
एवं उपाध्यक्ष, प्रबंधन समिति
दिल्ली राज्य कैंसर चिकित्सा संस्थान
डा राजेश
निदेशक, मुख्य कार्य
दिल्ली राज्य कैंसर
एवं सदस्य सचिव


प्राईवेट रोगी प्रतीक्षालय
PVT. PATIENT WAITING AREA


कीमोथैरेपी
CHEMOTHERAPY
DAY CARE


STAFF ROOM
MINOR OT

OPD ROOM 3
OPD ROOM 2
1


Williams
HEMATOLOGY
WINTROBE'S
CLINICAL
HEMATOLOGY
Practical Approach to
Respiratory Diseases
CANCER
MEDICINE
SURGICAL ONCOLOGY
MEDICAL ONCOLOGY
Diagnostic
Histopathology
of Tumors


WORLD CANCER DAY 4th FEBRUARY
ਕੈਂਸਰ ਦਾ ਹੋਸਕਦਾ ਹੈ ਸਮਾਧਾਨ
ਜੇਕਰ ਸ਼ੁਰੂ 'ਚ ਹੋ ਜਾਵੇ ਇਸਦਾ ਨਿਦਾਨ
ਸਮੇਂ ਨਾਲ ਸਾਵਧਾਨੀ, ਦੂਰ ਰਖੇ ਪਰੇਸ਼ਾਨਾ
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DELHI STATE CANCER INSTITUTE
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FOR COMPREHENSIVE MANAGEMENT OF CAN
THE LATEST TECHNOLOGY EQUIPMENTS UND
-a centre par excellence in the service of huma
-Being established as a dedicated, state of the art Institute by the Govt.
दिल्ली सरकार द्वारा स्थापित किया जा रहा
No.6
Recent change in bowel or bladder habits.
No.7
No.8
No.9
No.5
Indigestion or pain/difficulty during swallowing.
No.1
No.2
No.4
FACILITIES ESTABLISHED
Outpatient services
Inpatient services-General Ward
Day Care Services
Screening Services
Chemotherapy
Latest Generation Radiation
Latest technology Digital X-ray
Ultra Modern Laboratories
उपलब्ध सुविधाएं
ओ पी डी
सामान्य वार्ड
डे-केयर वार्ड
स्क्रीनिंग सर्विसिस
कीमोथैरेपी
अत्याधुनिक रेडियोथैरेपी
अत्याधुनिक एक्स रे,
अत्याधुनिक लैबोरेटरी सुविधायें
दर्द निवारण क्लीनिक
लघु शल्य चिकित्सा
आहार क्लीनिक
धर्मशाला सुविधाएं
Private Wards
Semi-Private Wards
Most modern,
Modular Operation Theatres, ICU
Integrated HDR Brachytherapy
PET-CT with Cyclotron
Gamma Camera
Bone Marrow Transplant
Endoscopy Procedures
Naturopathy, Yoga,
Meditation, Ayurveda, Homeopathy Research
Dedicated Research Labs
Particle Therapy
Executive Health Check up
Additional Institutions


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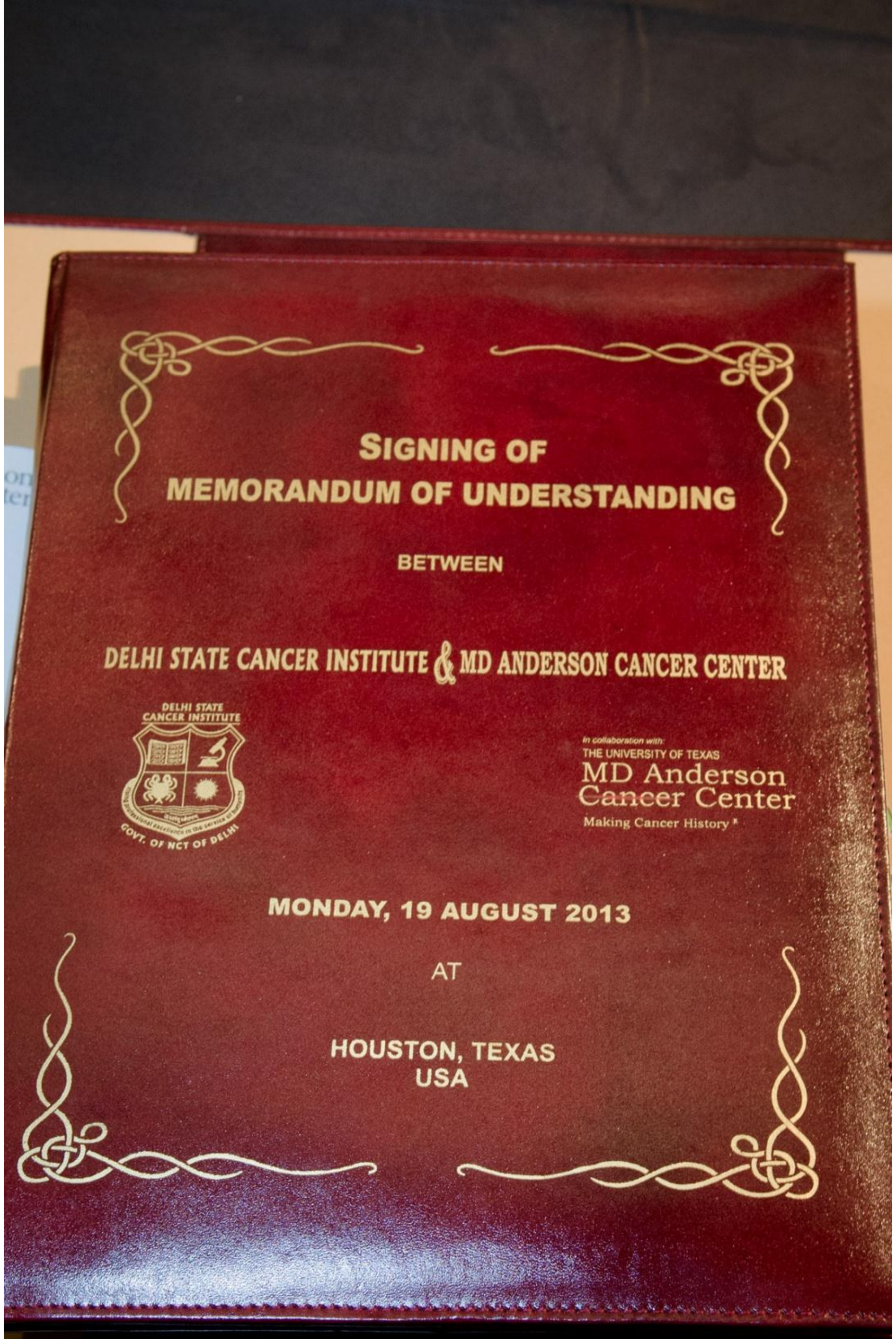
RECEPTION AND REGISTRATION


SIGNING OF
MEMORANDUM OF UNDERSTANDING
BETWEEN
DELHI STATE CANCER INSTITUTE & MD ANDERSON CANCER CENTER
DELHI STATE CANCER INSTITUTE
GOVT. OF NCT OF DELHI
in collaboration with:
THE UNIVERSITY OF TEXAS
MD Anderson
Cancer Center
Making Cancer History®
MONDAY, 19 AUGUST 2013
AT
HOUSTON, TEXAS
USA

If to DSCI:	Delhi State Cancer Institute East: Dilshad Garden, Delhi 110 095 West: C-2/B, Janak Puri, Delhi 110 058 Attention: R. K. Grover, M.D. Director and Chief Executive Officer Telephone:	+91-11-2211 0303 +91-11-2550-3333
	Facsimile:	+91-11-2211 0505 +91-11-2554 9999
	Cell:	+91-98101 70405
With a copy to:	Department of Health & FW Government of Delhi Delhi Secretariat IP Estate, New Delhi 110 002 Attention: SCL DAS, IAS Secretary (Health & FW) Telephone: +91-11-2339 2017 Facsimile: +91-11-2339 2464	

14. This MOU may be executed in two or more counterparts, each of which shall be deemed an original and all of which together shall constitute but one and the same instrument.

AGREED AND ACCEPTED:

THE UNIVERSITY OF TEXAS
M. D. ANDERSON CANCER CENTER

PLEASE &

By: [signature]
Ronald A. DePinho, M.D.
President

Date: Aug 19, 2013

Reviewed and Approved by
UTMDACC Legal Services for
UTMDACC Signature:
B Brown 8-16-13

DELHI STATE CANCER INSTITUTE

By: [signature]
Rajesh K. Grover, M.D.
Director & Chief Executive Officer

Date: Aug 19, 2013

Please Sign & Date

By: [signature]
Sudhir Kumar
Special Secretary,
Department of Health & FW
Govt. of NCT of Delhi

Please Sign & Date

Date: Aug. 19- 2013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