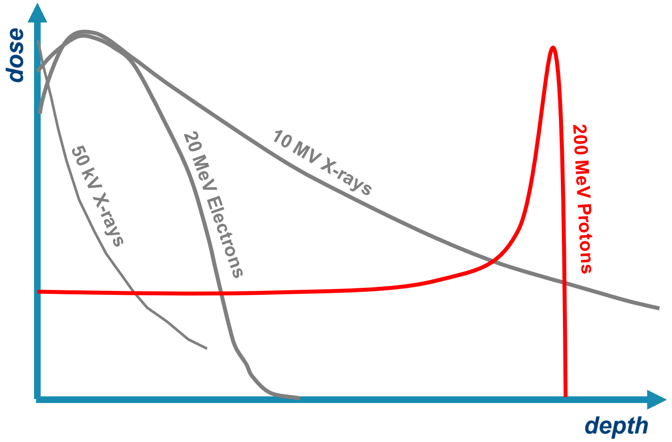
KU LEUVEN

ICRP 4TH INTERNATIONAL SYMPOSIUM ON THE SYSTEM OF RADIOLOGICAL PROTECTION
October 10-12 2017, Paris, France
ERPW 2ND EUROPEAN RADIOLOGICAL PROTECTION RESEARCH WEEK

Proton therapy technology in the clinic

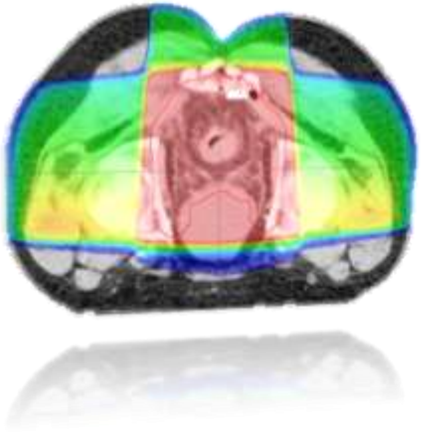
Tom Depuydt, ir, PhD
Head of Medical Physics
Radiation Oncology department UZ Leuven
and ParTICLe Proton Therapy Center
KU Leuven

Proton therapy (PT) logic step in the evolution of the last 30 years

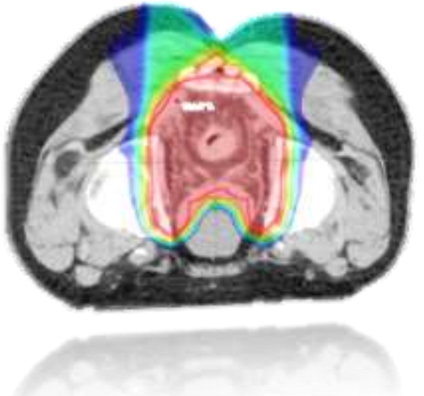


“Based on ballistics: Obvious advantage for radiation therapy”

Classic Radiotherapy

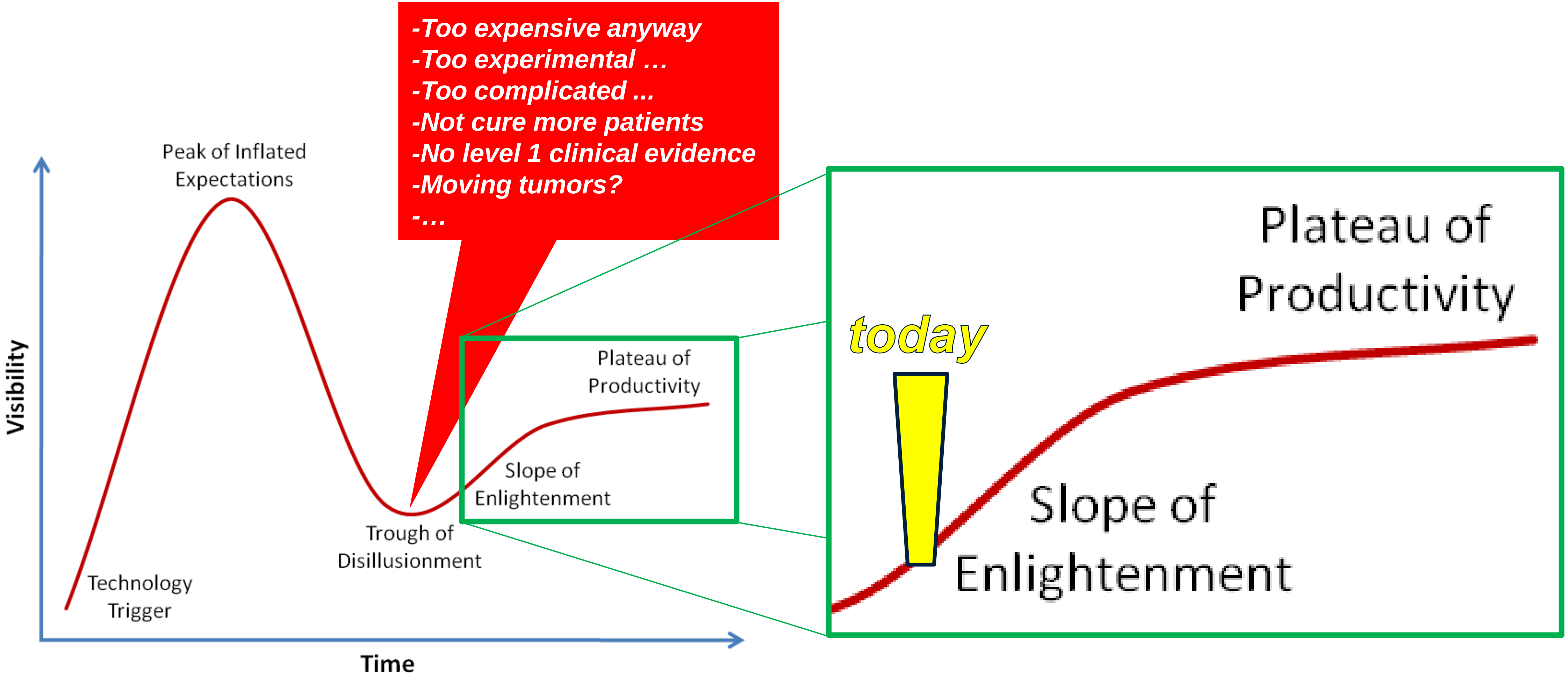


Highly conformal Radiotherapy



“Dose sculpting, hitting the target, avoiding other tissues”

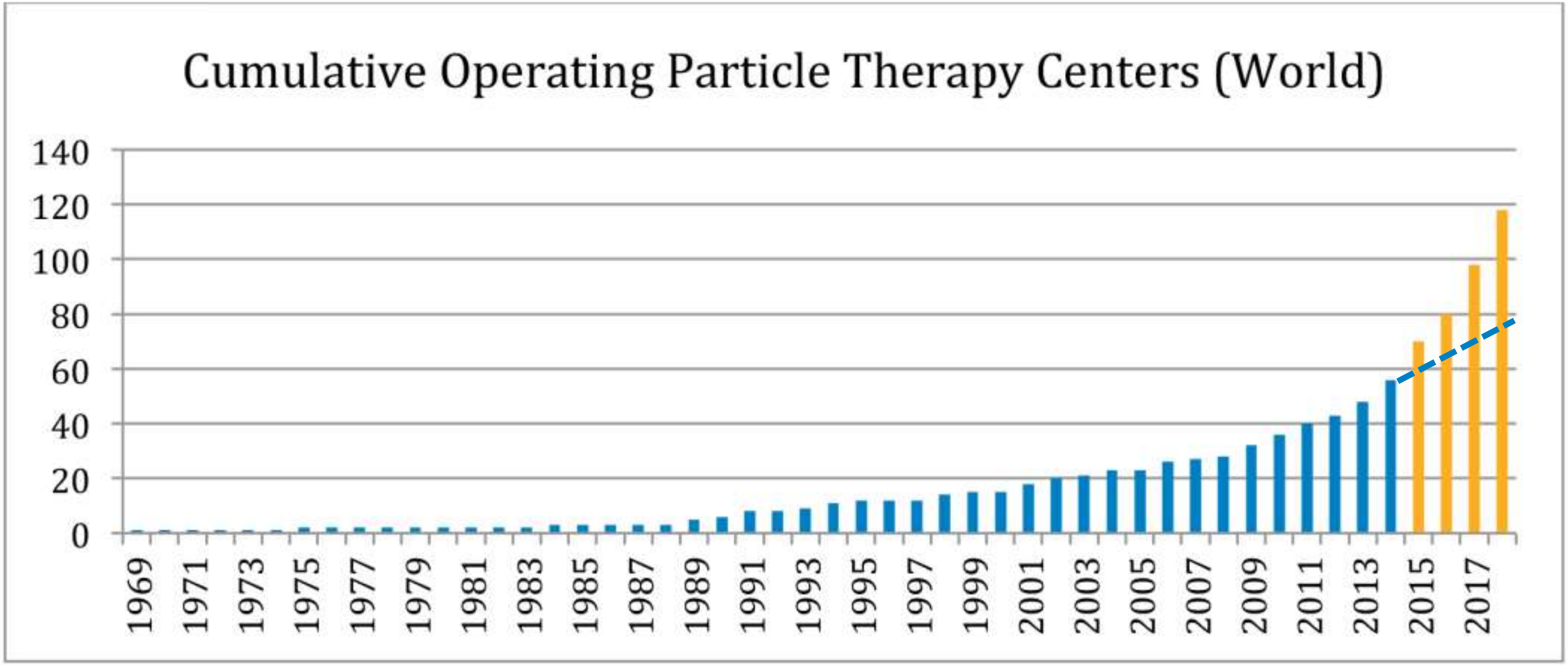
Gartner **Hype Cycle** for Proton Therapy Technology



-Too expensive anyway
-Too experimental …
-Too complicated ...
-Not cure more patients
-No level 1 clinical evidence
-Moving tumors?
-…

"Climbing the slope of enlightenment"

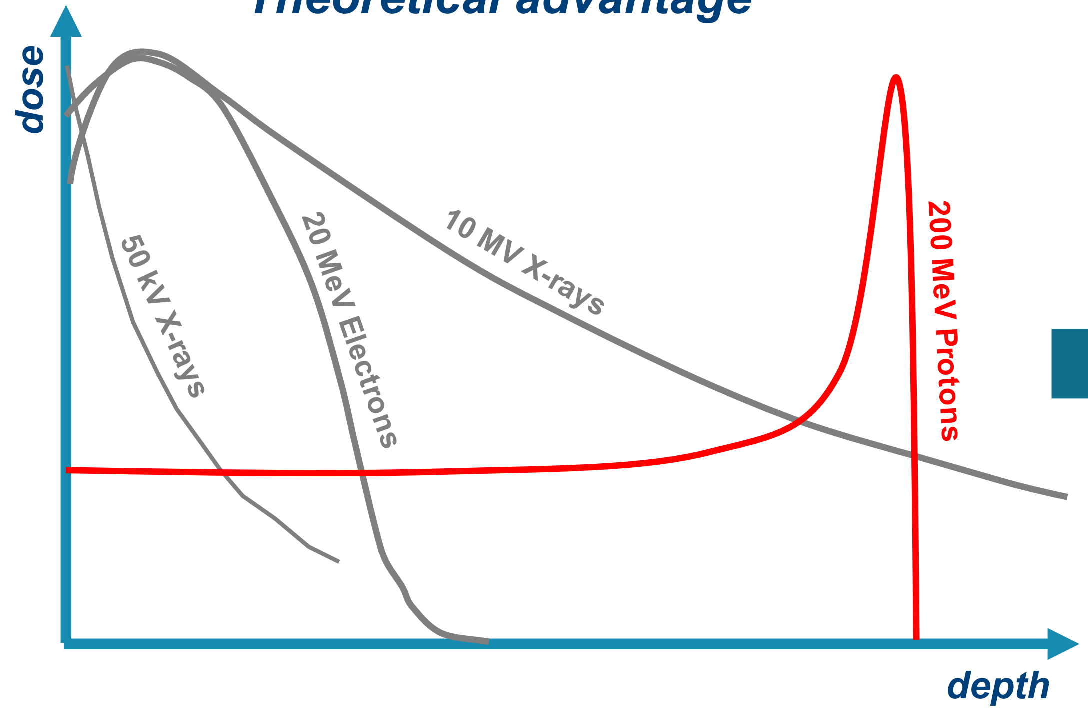
Rising numbers of PT centers in the world



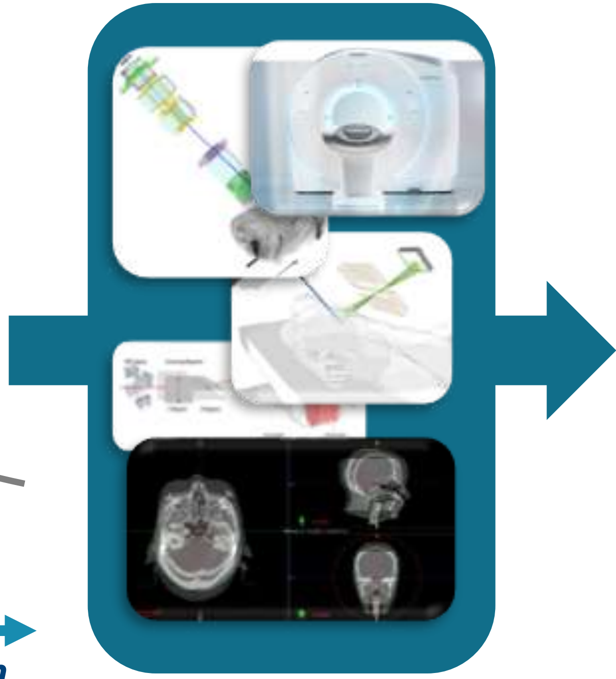
"Regained optimism reflected in the rising of number of PT centers worldwide"

From radiation **physics** to a **clinical** radiotherapy treatment modality

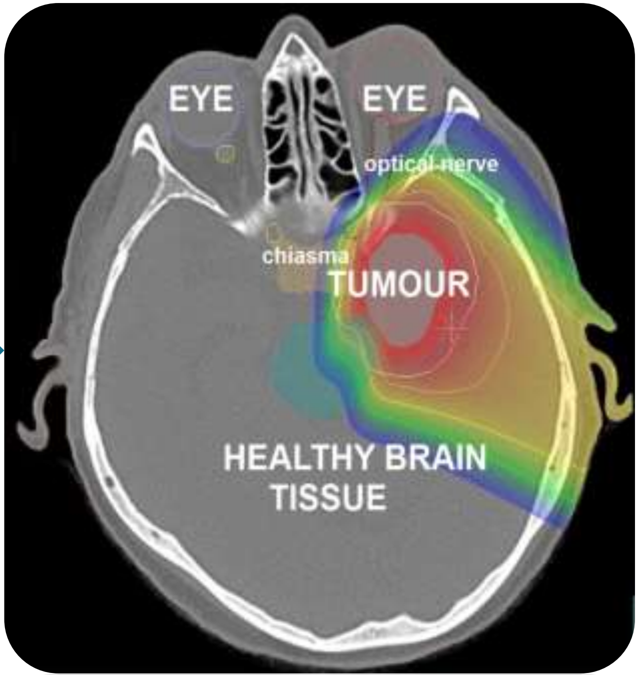
“Theoretical advantage”



“TECHNOLOGY is KEY”



“Clinical solution”



“A whole range of technologies is necessary to fully unleash the potential of proton therapy in the clinic”

Topics

- *Delivery technology*
- *Compact layout systems*
- *In-room imaging and treatment verification*
- *Concluding remarks*

Radiation protection of

patient

personnel

hospital/environment

Topics

- *Delivery technology*
- *Compact layout systems*
- *In-room imaging and treatment verification*
- *Concluding remarks*

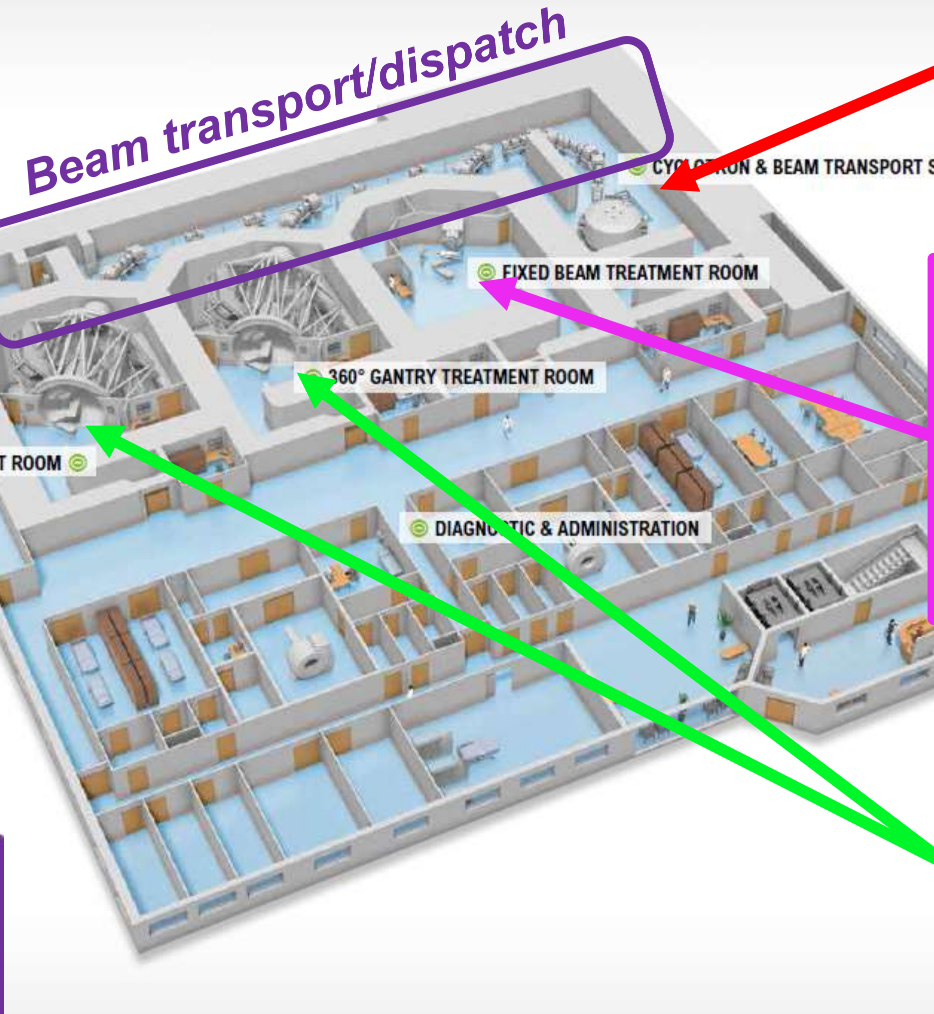
Radiation protection of

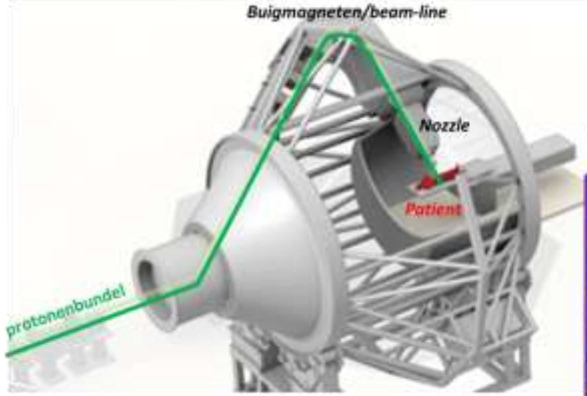
patient

personnel

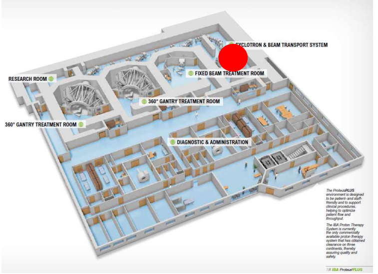
hospital/environment

Layout of a “typical” PT facility

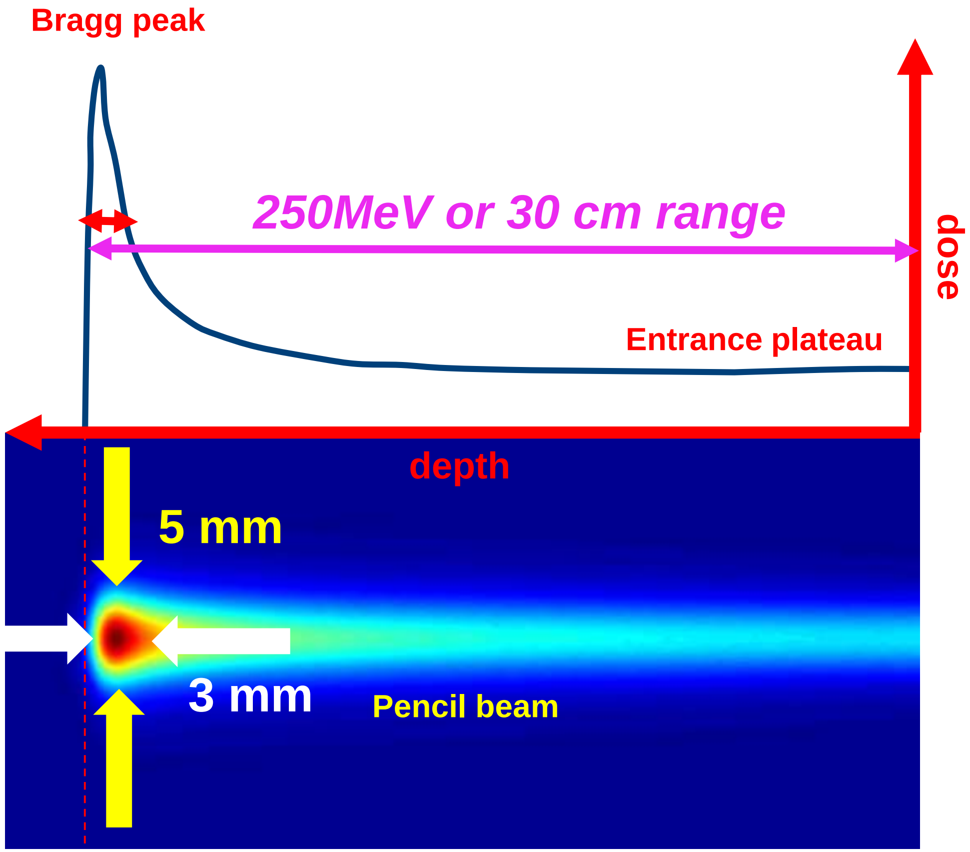




Proton therapy delivery technology

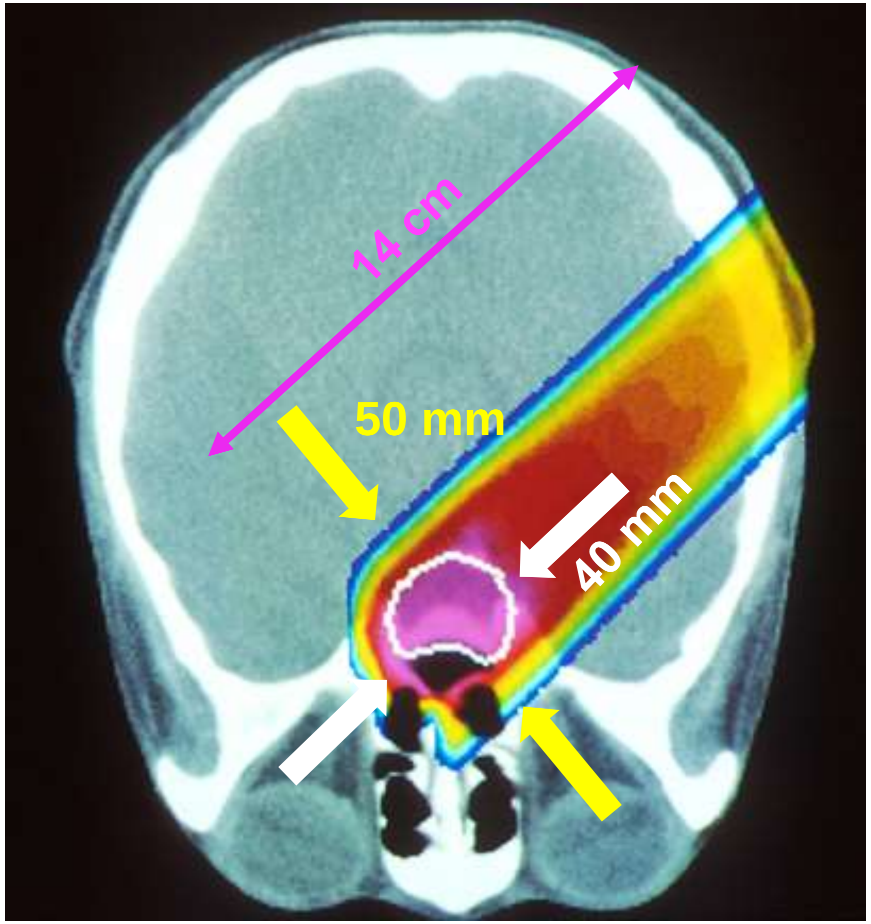


Pristine pencil beam

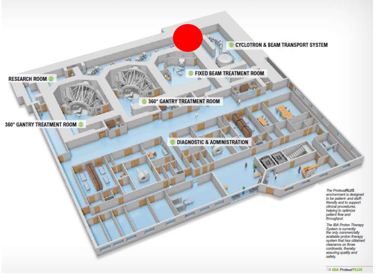


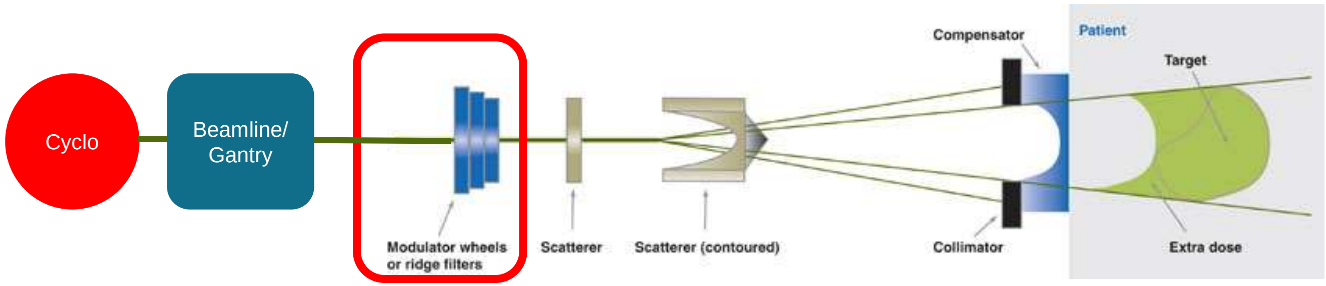
"Cyclotron produces small single high-energy proton beam of ≈250 MeV"

Therapeutic dose distribution



Passive scattering (PS) nozzle





"Generating high dose plateau in depth"

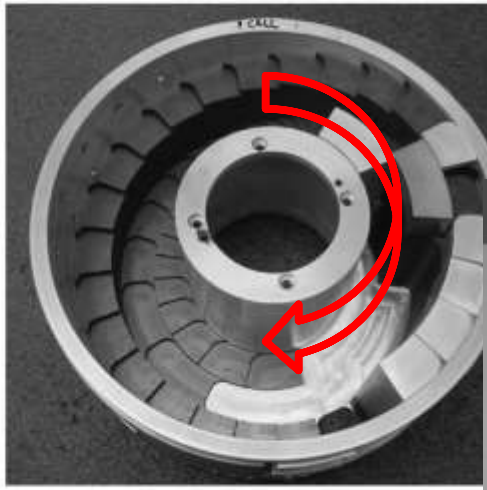
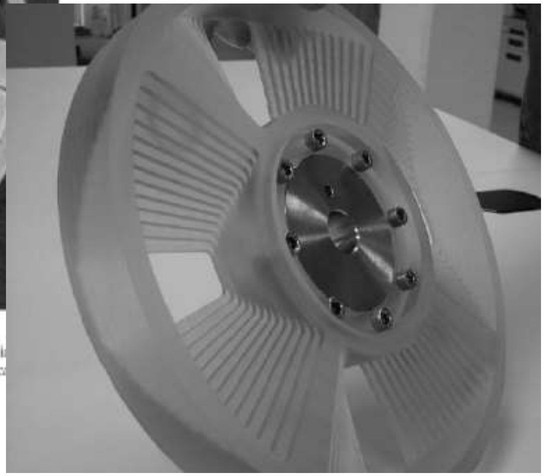


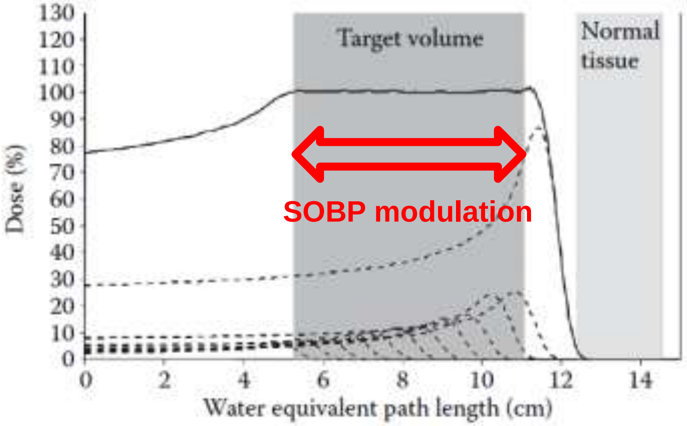
FIGURE 5.5
Range modulator wheel combining three range modulation tracks as installed i
versal nozzle. (Note that the outer track is used in range shifting for uniform sc



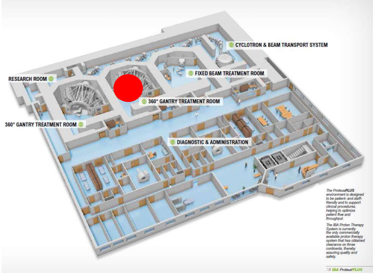
- Create from a Bragg peak single energy proton beam a **Spread Out Bragg Peak (SOBP)** covering a volume in depth
- SOBP is a weighted sum of Bragg peaks

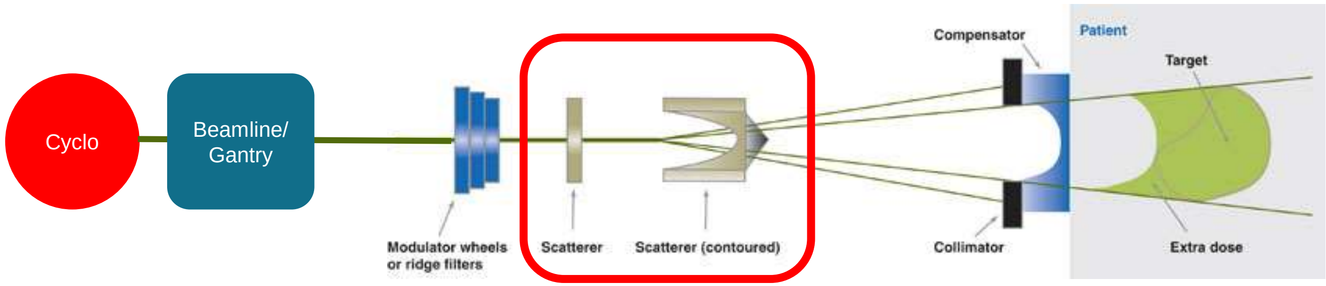
$$SOBP(R,d)=\sum_{i=1}^{N} w_i \cdot PP(R_i,d)$$

- Range modulator wheels rotate at high frequencies and "scan" the Bragg peak fast in depth to create a SOBP

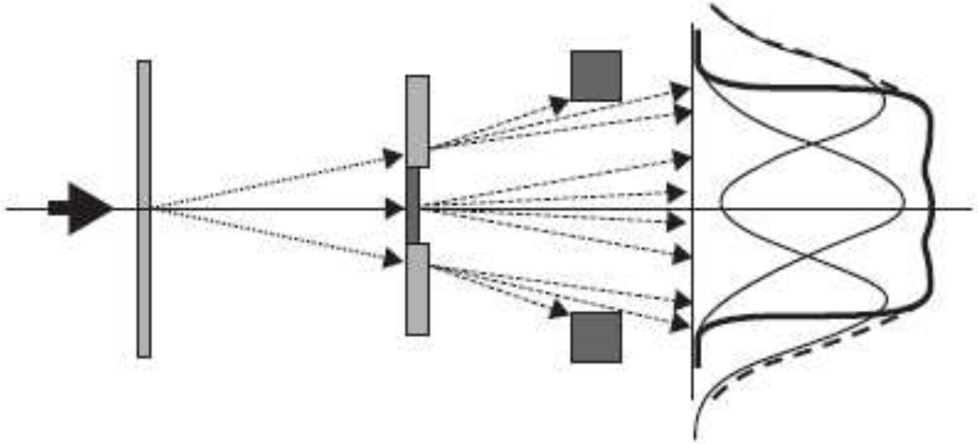


Passive scattering (PS) nozzle





"Generating wide beam"



- Create from a 3 mm diameter single energy proton beam **a wide beam with homogeneous intensity** (similar to linac system for photons)

- **Multiple scatterers in a cascade**, homogenous or constructed from a combination of **rings of high-Z and low-Z materials** to refocus as many protons as possible into the field aperture

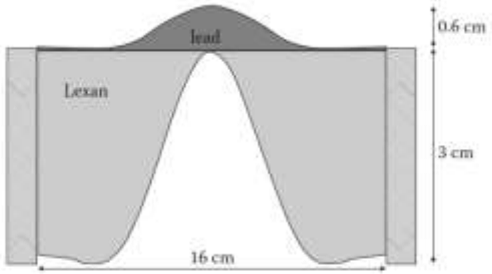
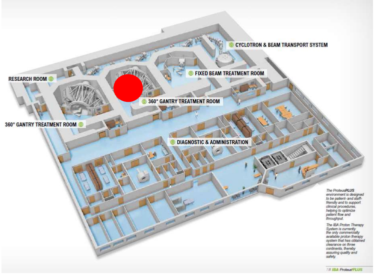
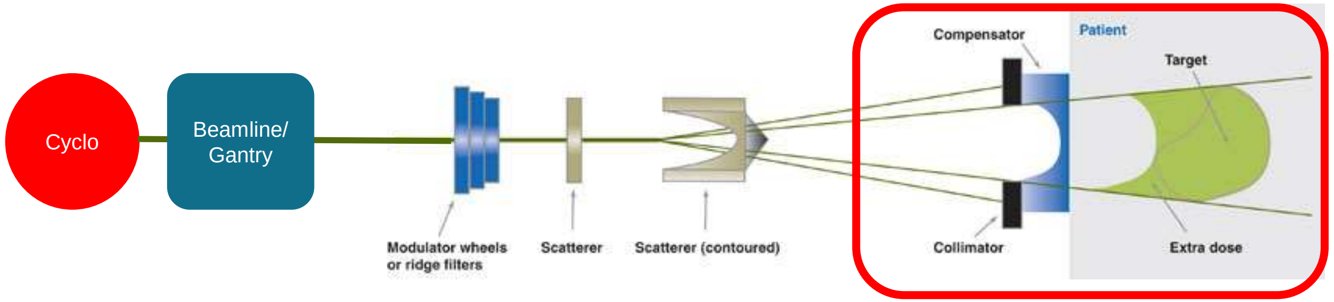


FIGURE 5.2
Schematic cross section of an energy-compensated contoured scatterer in the IBA universal nozzle.

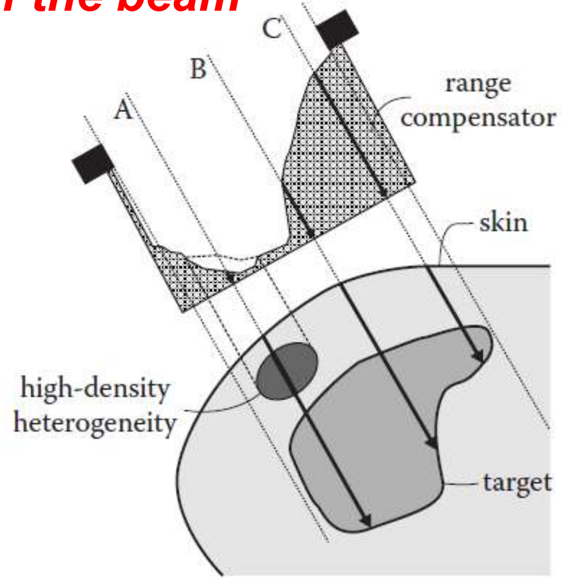
Passive scattering (PS) nozzle

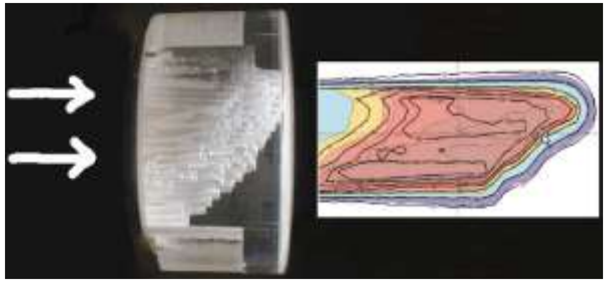


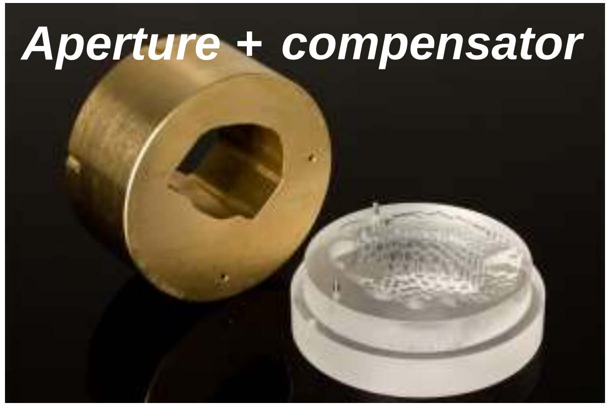


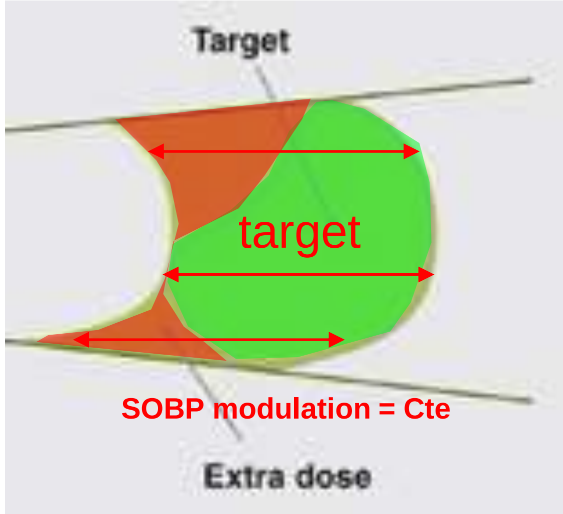
- **Patient-specific Apertures and range compensators** are used to **shape the beam and distal edge depth of the SOBP to the target volume contours**

"Customize distal edge and shape of the beam"

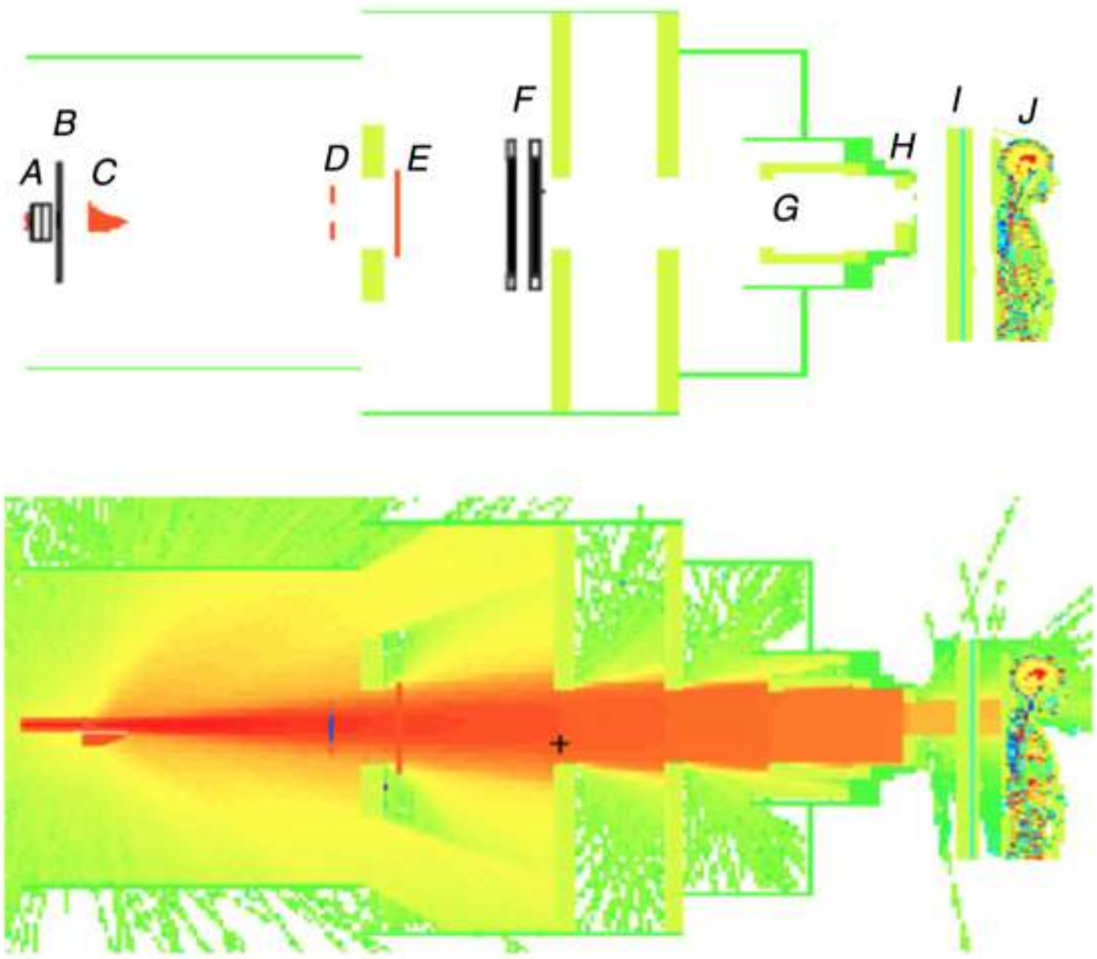








Stray radiation in PS



- Interactions of the proton beam with **components of the PS delivery system, primarily in the nozzle** generate secondary radiation
- Interactions of the proton beam **with the patient** generate secondary radiation
- **Backscatter** from treatment vault walls
- These secondary radiation sources cause a **total body neutron dose bath to patient** during PT delivery
- Some concerns about secondary cancer induction (Hall 2006): “**Passive modulation results in doses distance from the field edge that are 10 times higher than those characteristic of IMRT with X-rays**.”

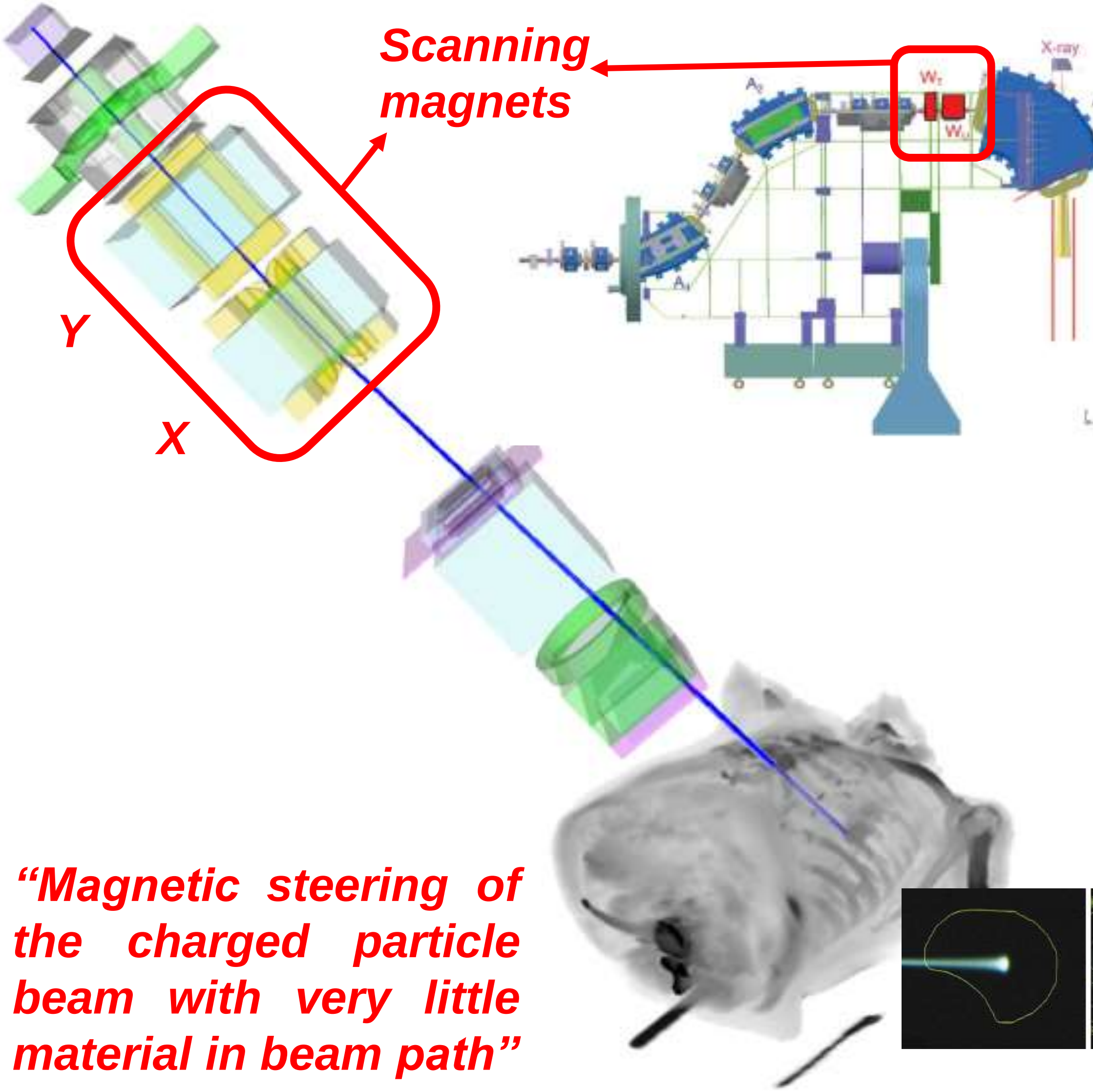
Zhang et al. Nucl Technol 2013, Newhauser et al. Phys Med Biol 2015, Hall et al. IJROBP 2006

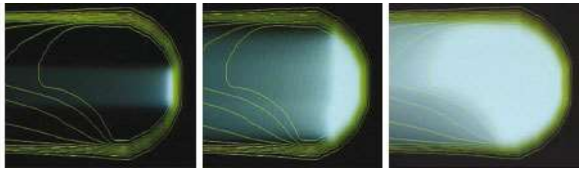
Activation of beam modifiers in PS

- Range compensators and apertures placed in the beam are **activated by nuclear interactions** of protons, scattered neutrons and gamma rays
- For **high-Z material** apertures (Brass, Cerrobend, …) it is advised to store them for **cooling down several months** before sending them for scrap
- Some **isotopes generated in low-Z materials** of range compensators (Lucite, Blue Wax, …) need **30-40 minutes to decay to background**
- Compensators and apertures are treatment field specific devices **replaced manually by the therapy personnel**
- **Data on occupational exposure** from these sources very limited

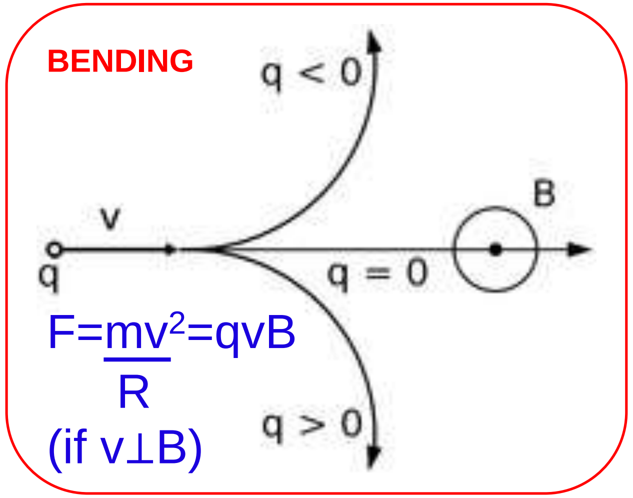
Spitznagel et al. Med Phys 2014, Moskvin et al. IJROBP 2013

Pencil Beam Scanning (PBS) nozzle





“Magnetic steering of the charged particle beam with very little material in beam path”



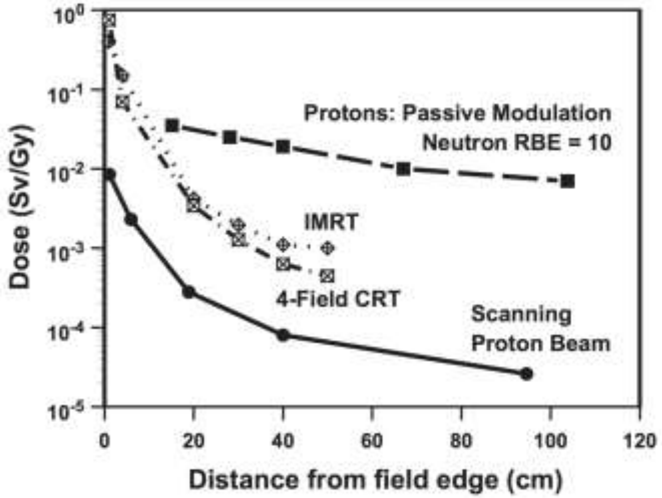
$F = \frac{mv^2}{R} = qvB$

(if v⊥B)

$$\mathbf{F} = q(\mathbf{v} \times \mathbf{B})$$

“Secondary neutrons mainly generated in the patient. Contribution of nozzle negligable”

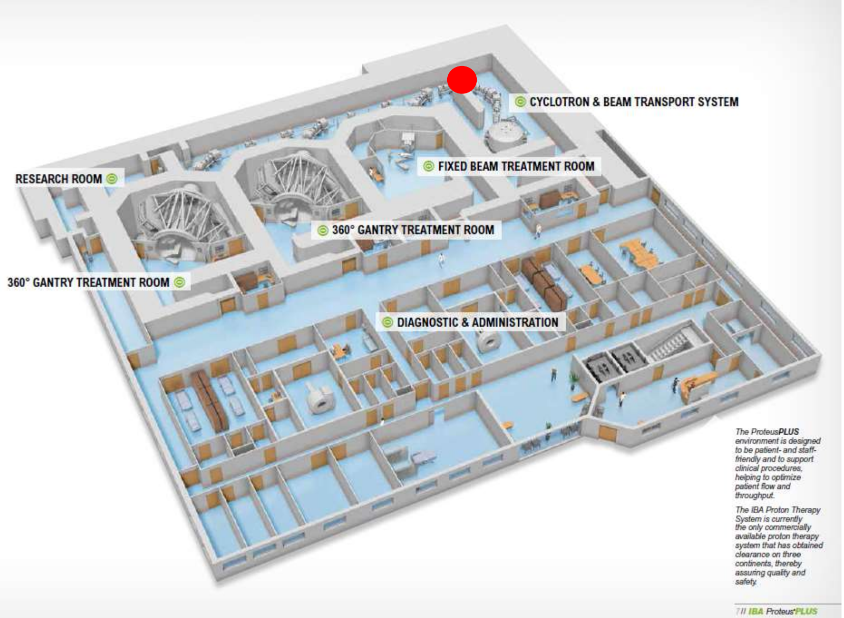
=Less out-of-field dose



Energy selection system (ESS)

Layer/Energy switching using degraders

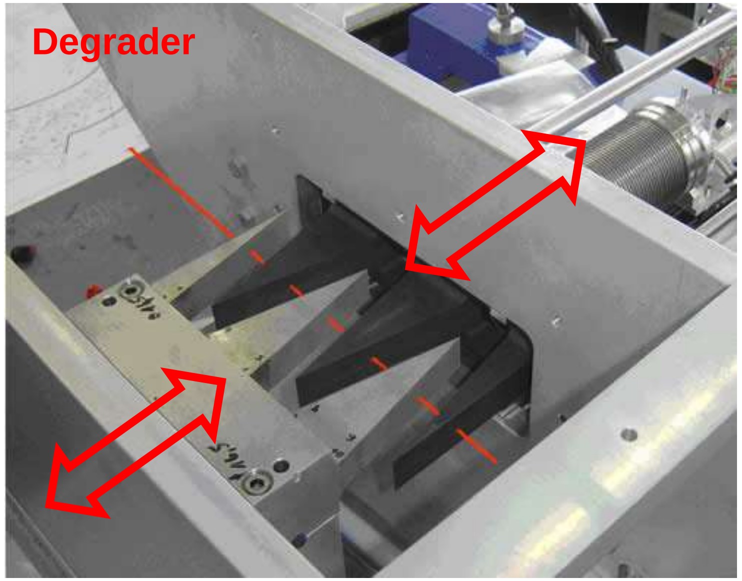
-Cyclotron produces single energy (fe. 250 MeV)
-”Degrader + Bending magnet + movable slit” to select lower proton beam energy

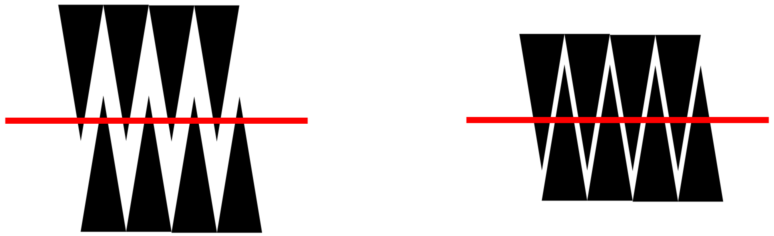


*The Proteus**PLUS** environment is designed to be patient- and staff-friendly and to support clinical procedures, helping to optimize patient flow and throughput.*

The IBA Proton Therapy System is currently the only commercially available proton therapy system that has obtained clearance on three continents, thereby assuring quality and safety.

7 // IBA Proteus PLUS





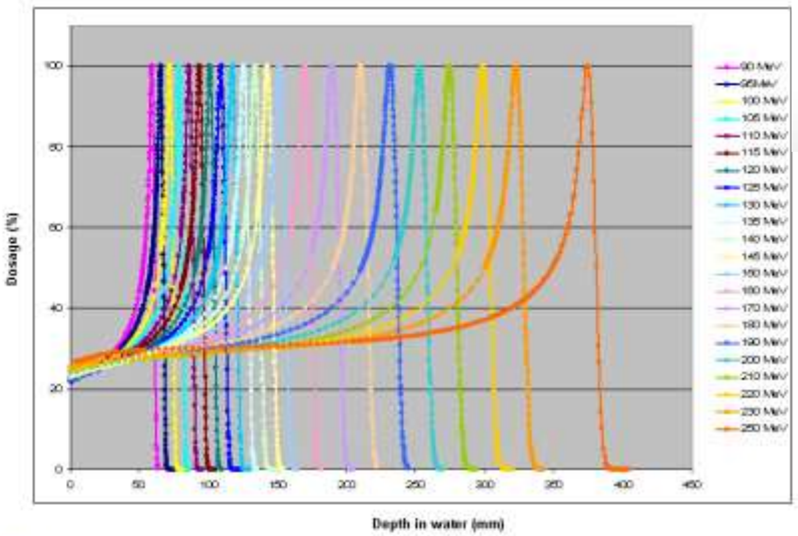


Figure 6

Measurement results of different Bragg peaks at the RPTC. For clinical applications, any intended penetration depth between 4 and 38 cm can be adjusted with sub-millimeter accuracy for scanning.

E = modified,
thus proton range is changed

Time=1-2 seconds

“ESS is an important source of secondary radiation, however usually located at large distance from the patient, behind shielding”

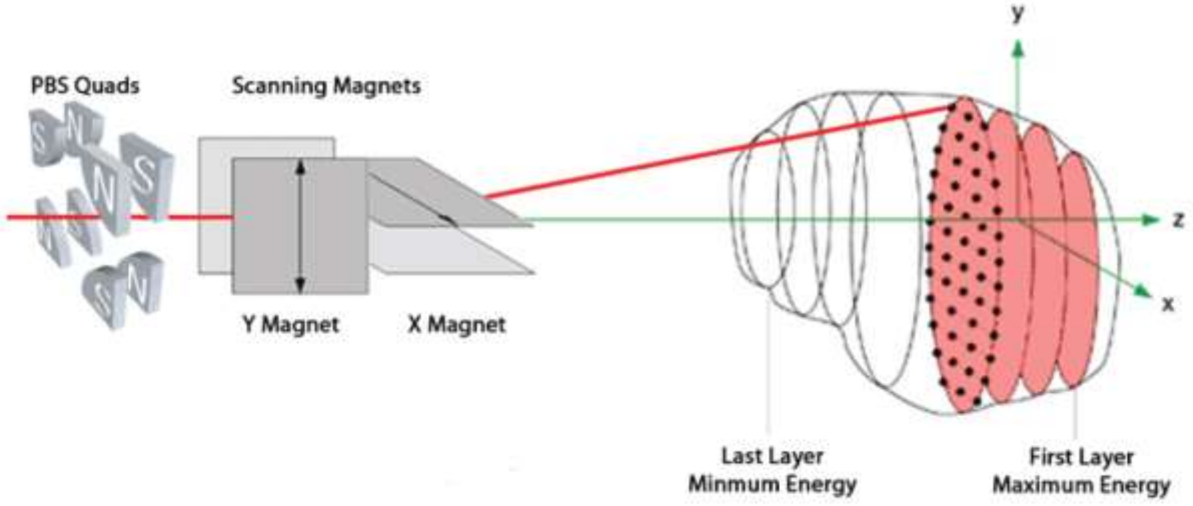
PBS **spot map** delivery

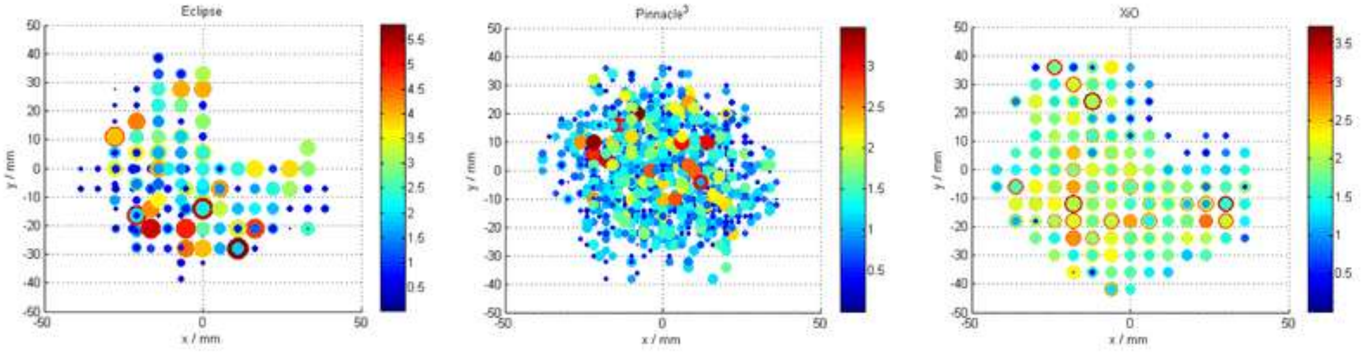
"Degrees of freedom":

Spot position (X,Y)

Energy/Layer (Z)

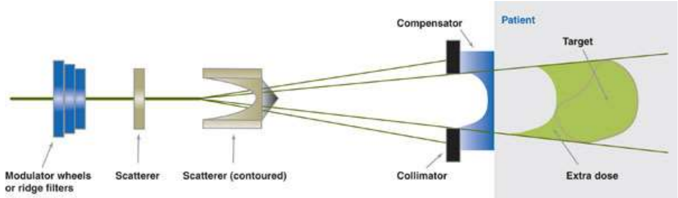
Weight (Dose)

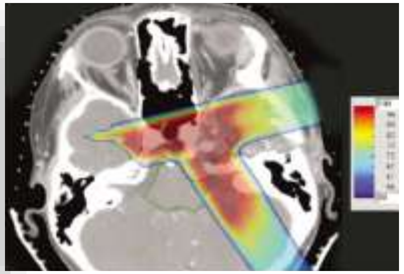




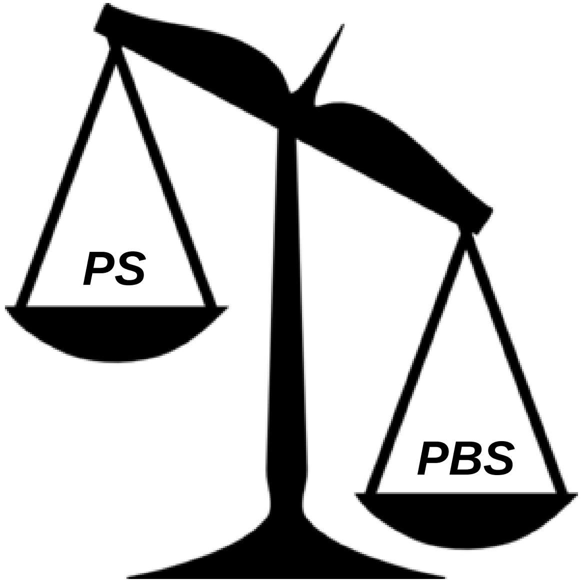
Preferred PT Delivery technology anno 2017

Passive scattering wide beam (PS)

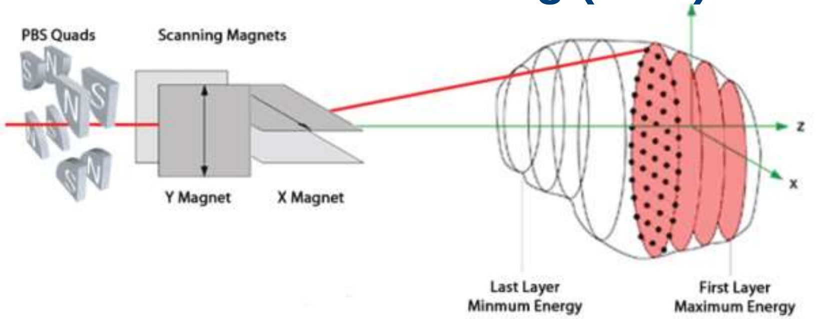


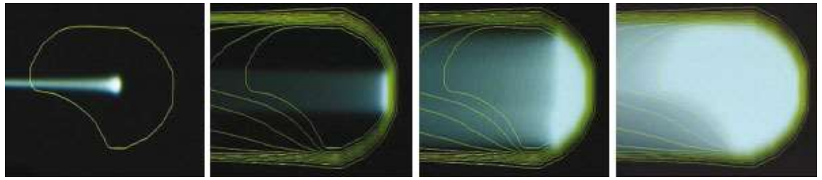


- *Proven technology (most PT patients treated today with PS)*
- *“Simple” wide beam approach*
- *Excess dose to normal tissue*
- *Patient specific collimators and compensators (labor intensive)*
- *Significant neutron dose bath?*



Pencil beam scanning (PBS)

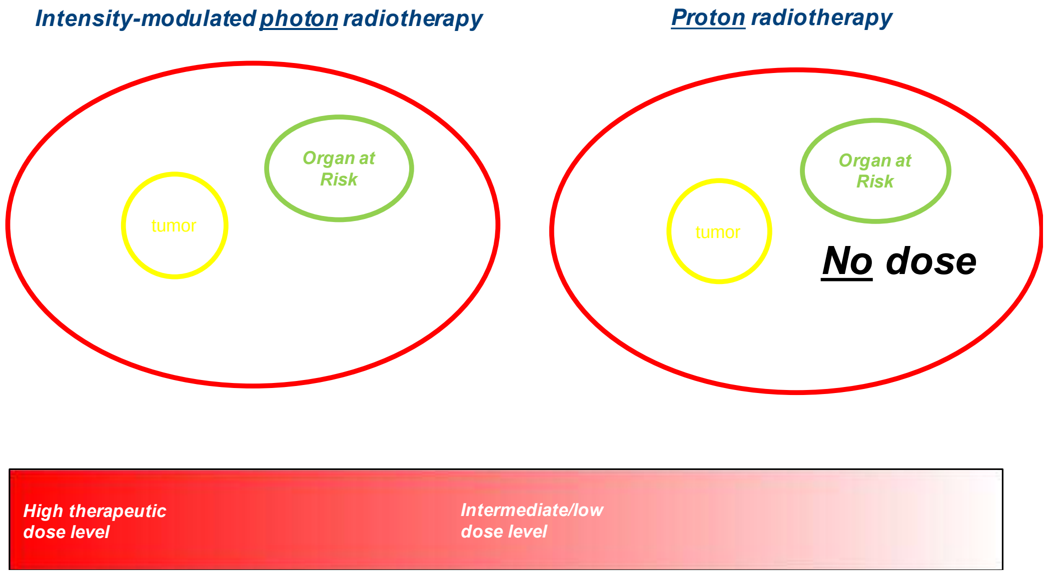


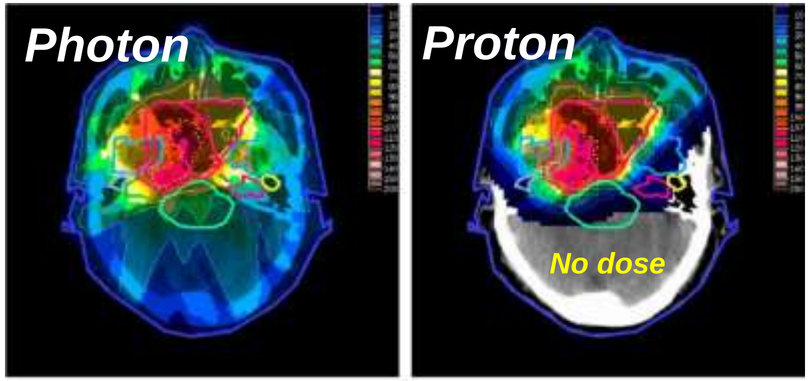


- *More flexible (IMPT)*
- *No patient/field specific collimators and compensators*
- *Interplay effects for moving targets*

Protons vs. photons, PS vs. PBS, …

"Proton beams have no exit dose"



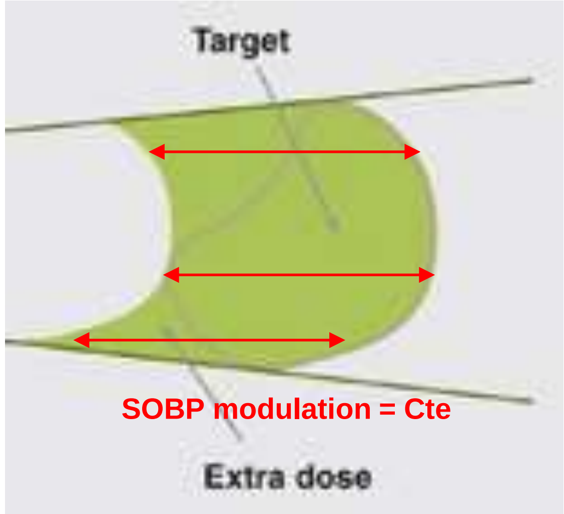


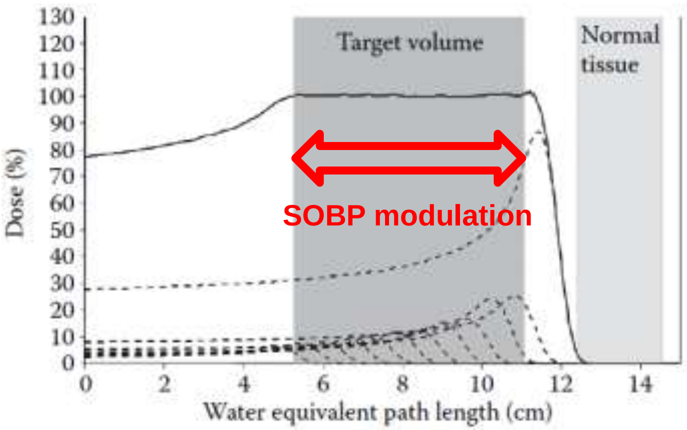
- **PBS** generates less stray radiation compared to PS, **less out-of-field dose**
- **Generally accepted** that the major component of **secondary cancer risk is from in-field radiation rather than out-of-field stray** radiation
- **Most of the gain here is thus in the transition from photon radiotherapy to PT** because of the additional healthy tissue sparing.
- The difference in total risk on secondary cancer **moving from PS to PBS is estimated to be small**.
- Nevertheless, **striving toward a reduction in secondary neutron dose to the patient remains justified** given the **still incomplete knowledge of stray neutron exposures** and **secondary cancer** induction.

Newhauser et al. Phys Med Biol 2015, NCRP 2011 Report 170

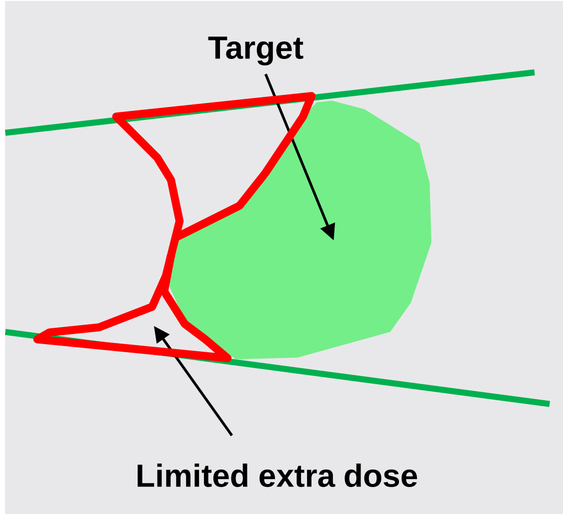
“Why move to PBS?”: more conformal

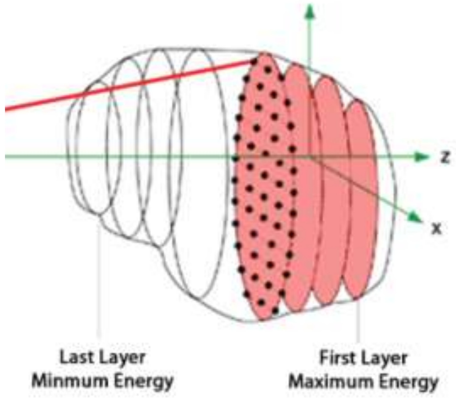
Passive scattering wide beam (PS)





Pencil beam scanning (PBS)





“Why move to PBS?”: Multi-field optimization IMPT

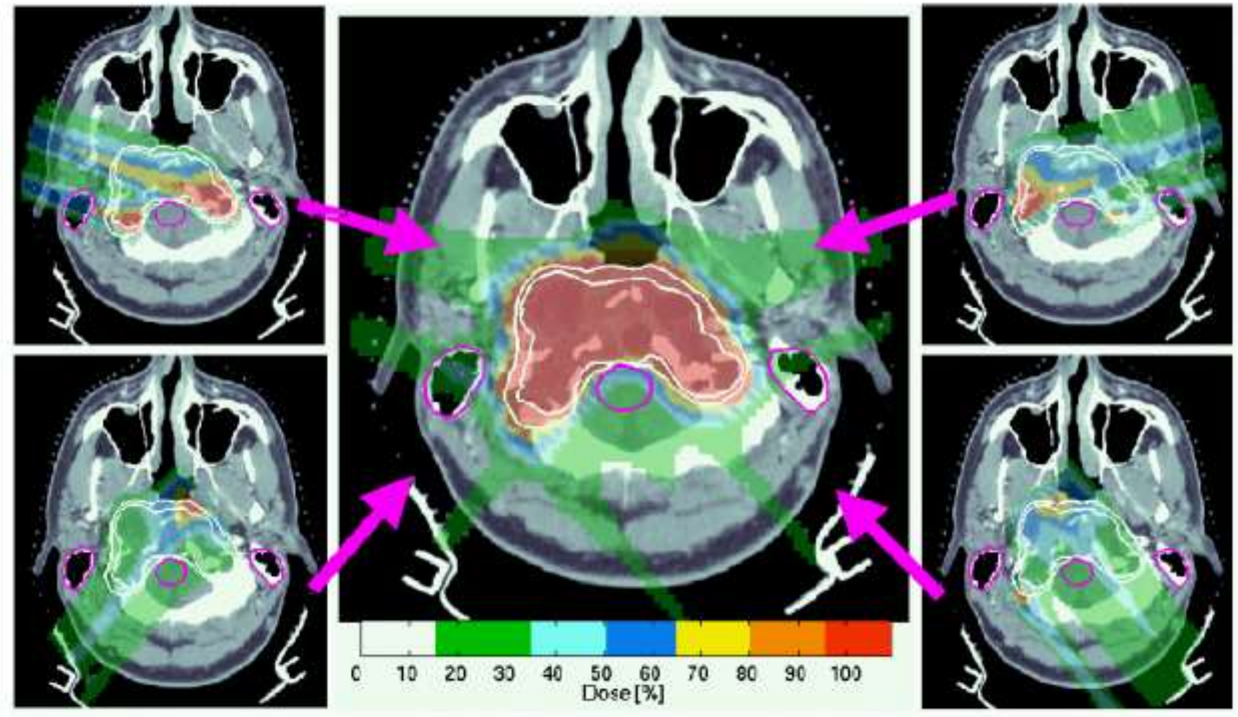
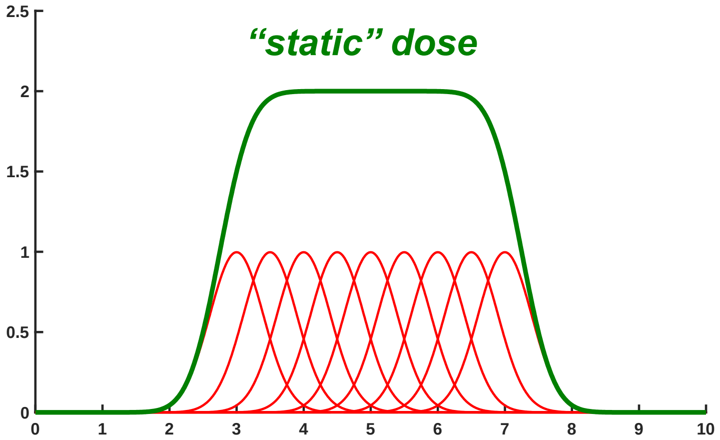


Figure 14: The principle of intensity modulated proton therapy (IMPT). Non-uniform dose distributions from a number of fields (4 in this case) yield the desired (uniform) target dose. Figure provided by Alex Trofimov (Massachusetts General Hospital).

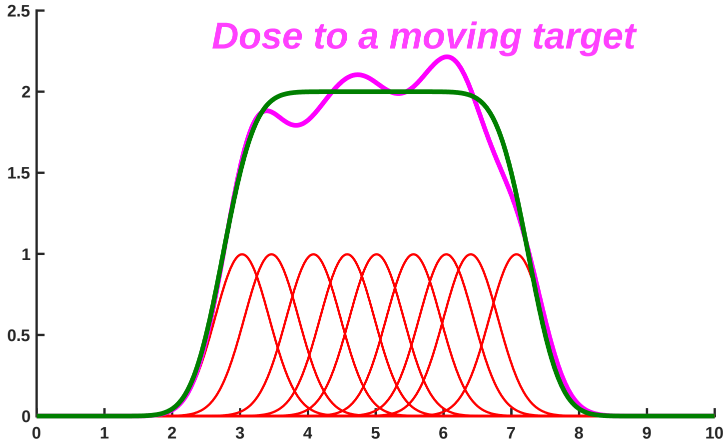
- Spot map of each treatment field generates an optimized non-uniform dose distribution in the target volume
- Only the combination of all treatment field of the IMPT plan generate the uniform dose to the target
- **Better sparing of healthy tissue** achieved with IMPT then with Passive Scattering and PBS using Single Field Optimization (SFO) IMPT
- **Strong in-field dose gradients can lead to a greater sensitivity of plans to uncertainties**, particularly to inter-field motions.

Lomax et al. Phys Med Biol 2008

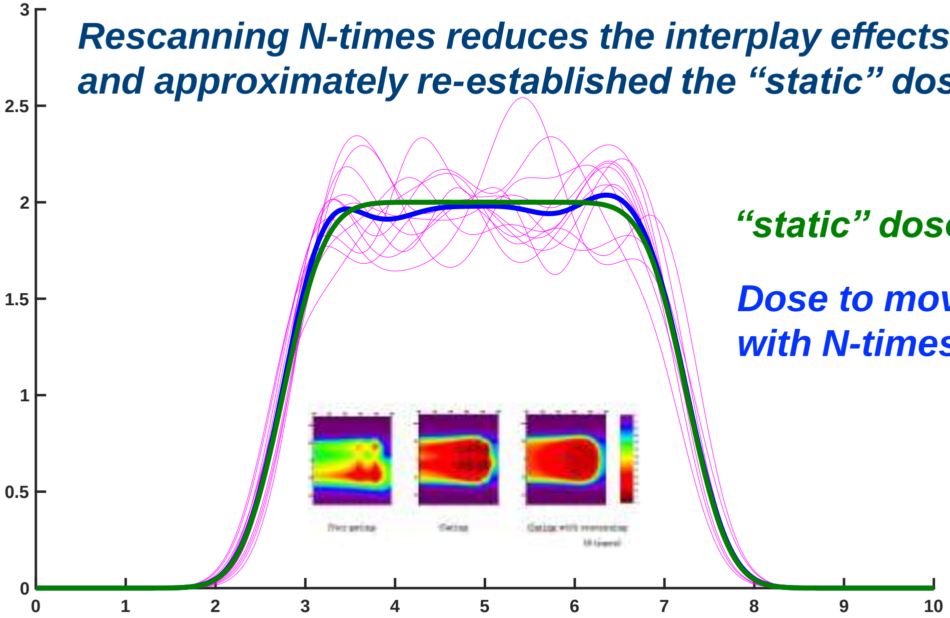
“Why move to PBS?”: Despite sensitivity to organ motion, interplay



Generating high dose region using multiple pencil beams (spots)



Organ motion can change the position of the spots relative to each other, resulting in hot/cold spots



Rescanning N-times reduces the interplay effects and approximately re-established the “static” dose

“static” dose

Dose to moving target with N-times rescanning

"Why move to PBS?": Despite lack of international guidelines

International guidelines for PBS PT ?!

> ***"The*** current activity of different guideline working groups shows that PBS is getting to maturity, but it is not there yet. It also shows that existing guidelines do not meet the current needs**."**

Publishes guidelines

- AAPM Report 16 (1986), Protocol for heavy charged-particle therapy beam dosimetry, **no PBS**
- ICRU Report 59 (1998) , Clinical Proton dosimetry, **no PBS**
- IAEA TRS-398 (2000), The current Code of Practice for proton dosimetry **no PBS**
- ICRU Report 78 (2007), **coverage PBS limited**

Guidelines in preparation

- IAEA: Update of TRS-398 (<2020?)
- AAPM TG-185: Commissioning of Proton Therapy Systems
- AAPM TG-224: Proton Machine QA
- NCS subcommittee on proton dosimetry
- EPTN ("ESTRO initiative")
- IPEM

Topics

- *Delivery technology*
- *Compact layout systems*
- *In-room imaging and treatment verification*
- *Concluding remarks*

Radioprotection of

patient

personnel

hospital/environment

History of Proton Therapy (PT) facilities

"PT facilities evolves from being …"

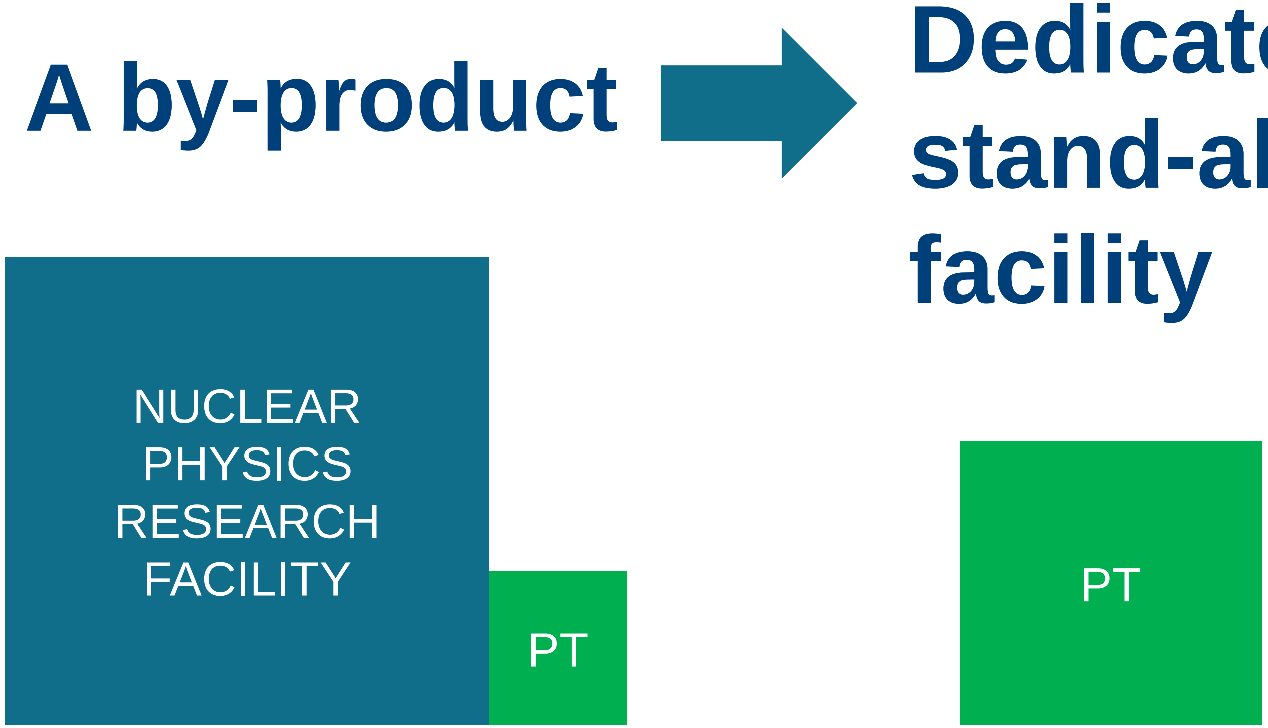
A by-product


NUCLEAR PHYSICS RESEARCH FACILITY

PT

History of Proton Therapy (PT) facilities

"PT facilities evolves from being …"



A by-product

Dedicated stand-alone facility

NUCLEAR PHYSICS RESEARCH FACILITY

PT

PT

History of Proton Therapy (PT) facilities

"PT facilities evolves from being …"

A by-product

Dedicated stand-alone facility

Embedded Facility

PT **Facility size**

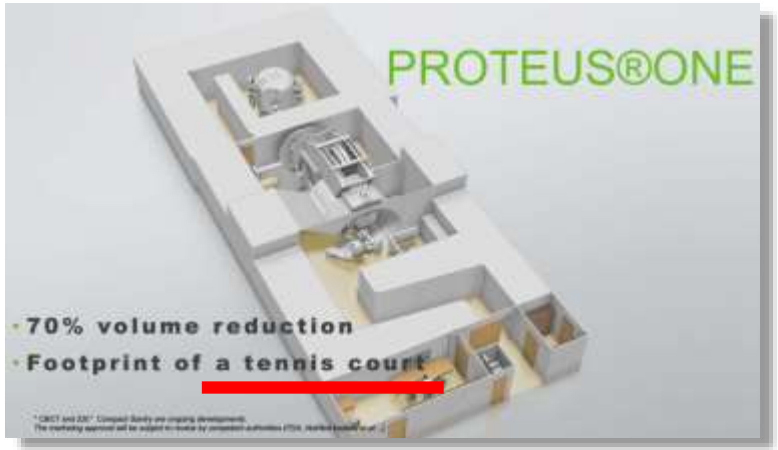
"The metaphors in PT …"

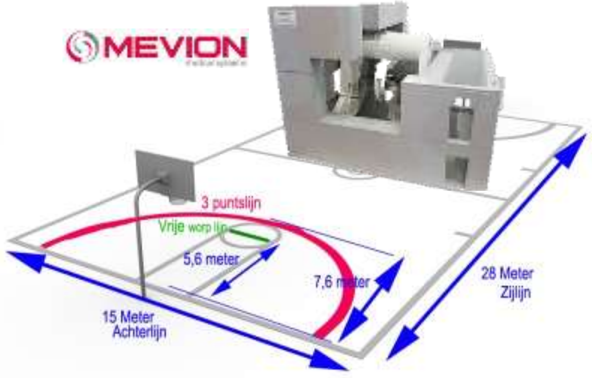
"Size measure of PT centers … sport field?"

KU LEUVEN

PT **Facility size**

"Compact systems as enabling technology for embedding PT… ?"

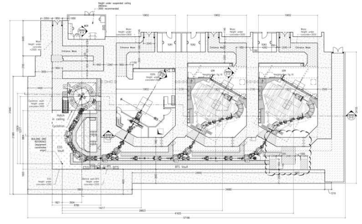




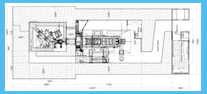
Next milestone in the history of Proton Therapy (PT)

Custom built installations

Commercial installations



Compact commercial installations



today

"First patients treated with PT at Harvard Cyclotron Lab. and Massachusetts General Hospital"

1946

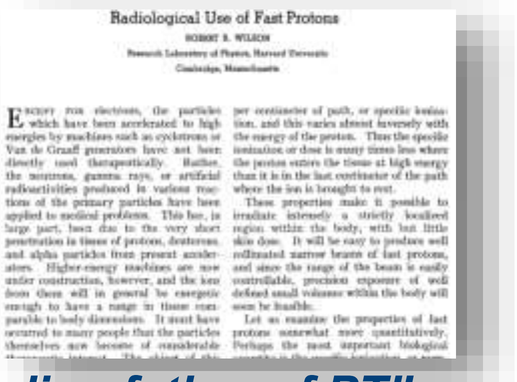
1961

1984

2000

2010

2013



Radiological Use of Fast Protons

ROBERT R. WILSON

Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

Except for electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in large part, been due to the very short penetration in tissue of protons, deuterons, and alpha particles from present accelerators. Higher-energy machines are now under construction, however, and the ions from them will in general be energetic enough to have a range in tissue comparable to body dimensions. It must have occurred to many people that the particles themselves now become of considerable

per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate intensely a strictly localized region within the body, with but little skin dose. It will be easy to produce well collimated narrow beams of fast protons, and since the range of the beam is easily controllable, precision exposure of well defined small volumes within the body will soon be feasible.

Let us examine the properties of fast protons somewhat more quantitatively. Perhaps the most important biological

"Founding father of PT"

"First patients treated with Pencil Beam Scanning "

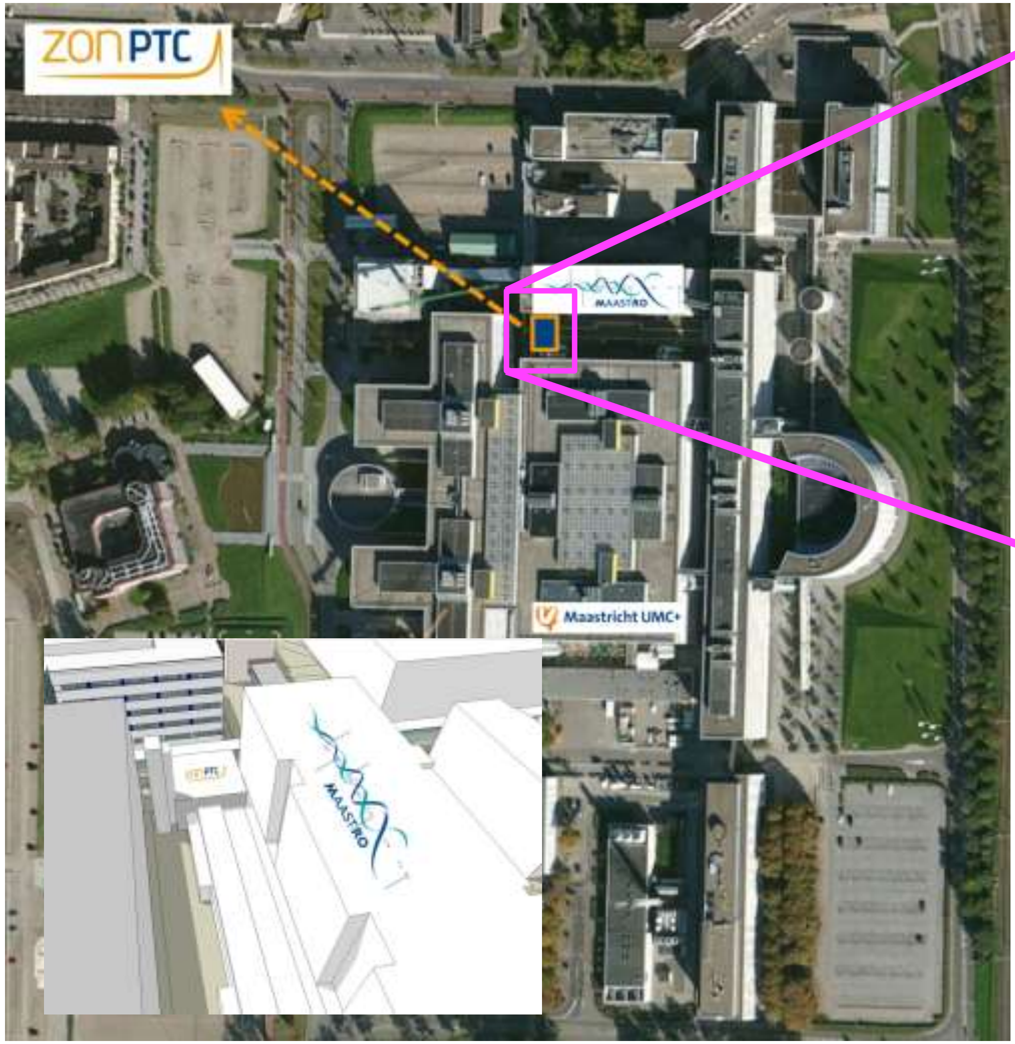
"PBS in other facilities (MGH, MDA, …)"

"First compact system clinically used"

KU LEUVEN

***PBS = Pencil Beam Scanning**

PT **embedded** in existing radiation oncology clinic




Original X-ray vault


Operating heavy machineryin small space

ZONPTC (Zuid-Oost Nederland Proton Therapie Centrum)

PT **embedded** in existing radiation oncology clinic

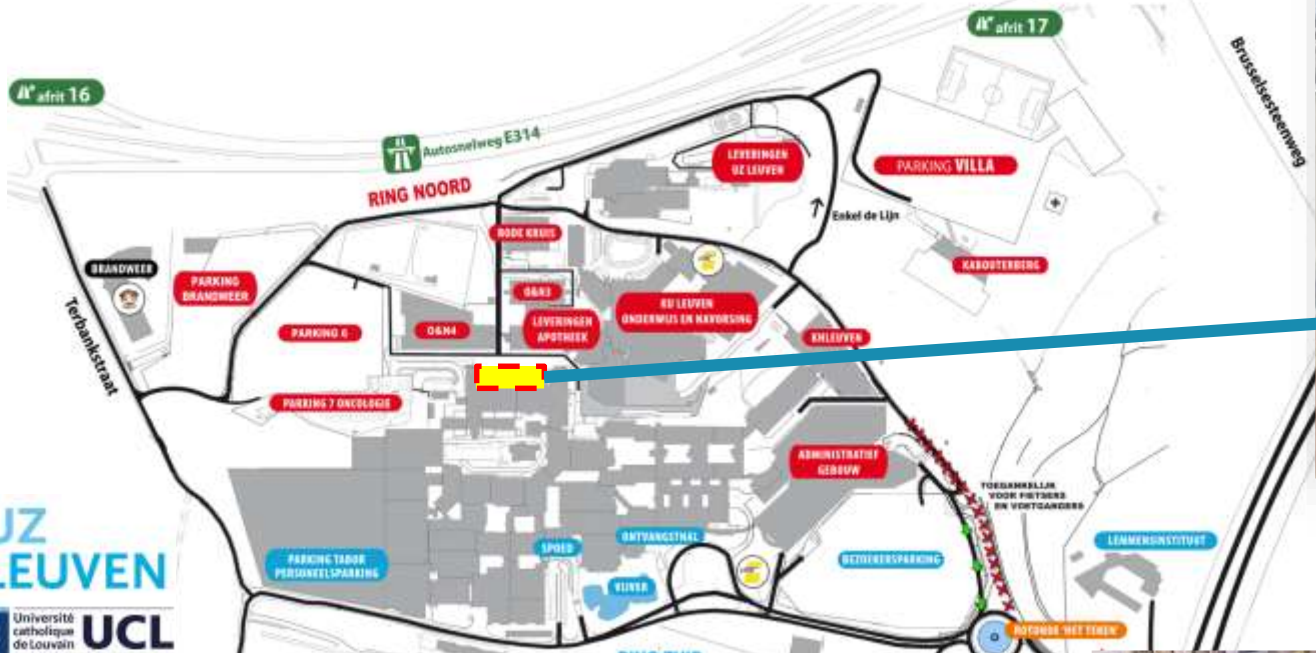
zonPTC

Zuid-Oost Nederland Protonen Therapie Centrum

KU LEUVEN

PT **embedded** in existing radiation oncology clinic

UZ Leuven Health Campus Gasthuisberg




September 20th 2017

Impression of finished facility

KU LEUVEN

ParTICLe (Particle Therapy Interuniversitary Center Leuven)

Large Multi-room vs. Compact unit: Secondary radiation source location

Cyclotron

Energy Selection System

- **Degrader**
- **Collimator**
- **Divergence slits**
- **Momentum slits**

Nozzle

Patient

Large Multi-room vs. Compact unit

- **Secondary neutron dose to patients*:**
    - **Distances/location/orientation** of some **secondary radiation sources** (f.e. the ESS) are different with respect to the patient
    - Neutron **scatter from the walls** could potentially be increased in the smaller vaults

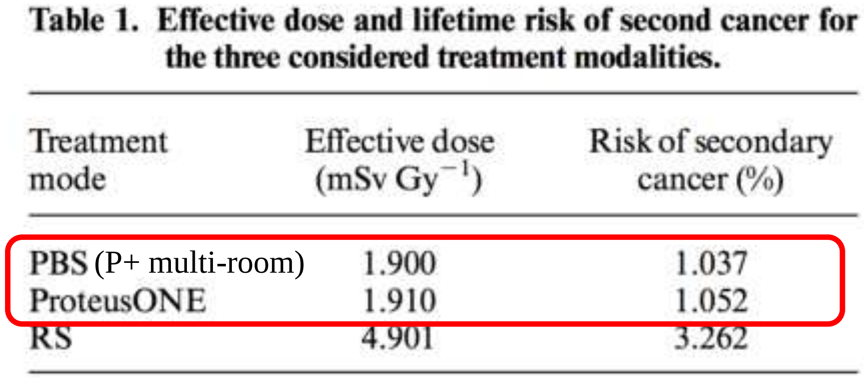


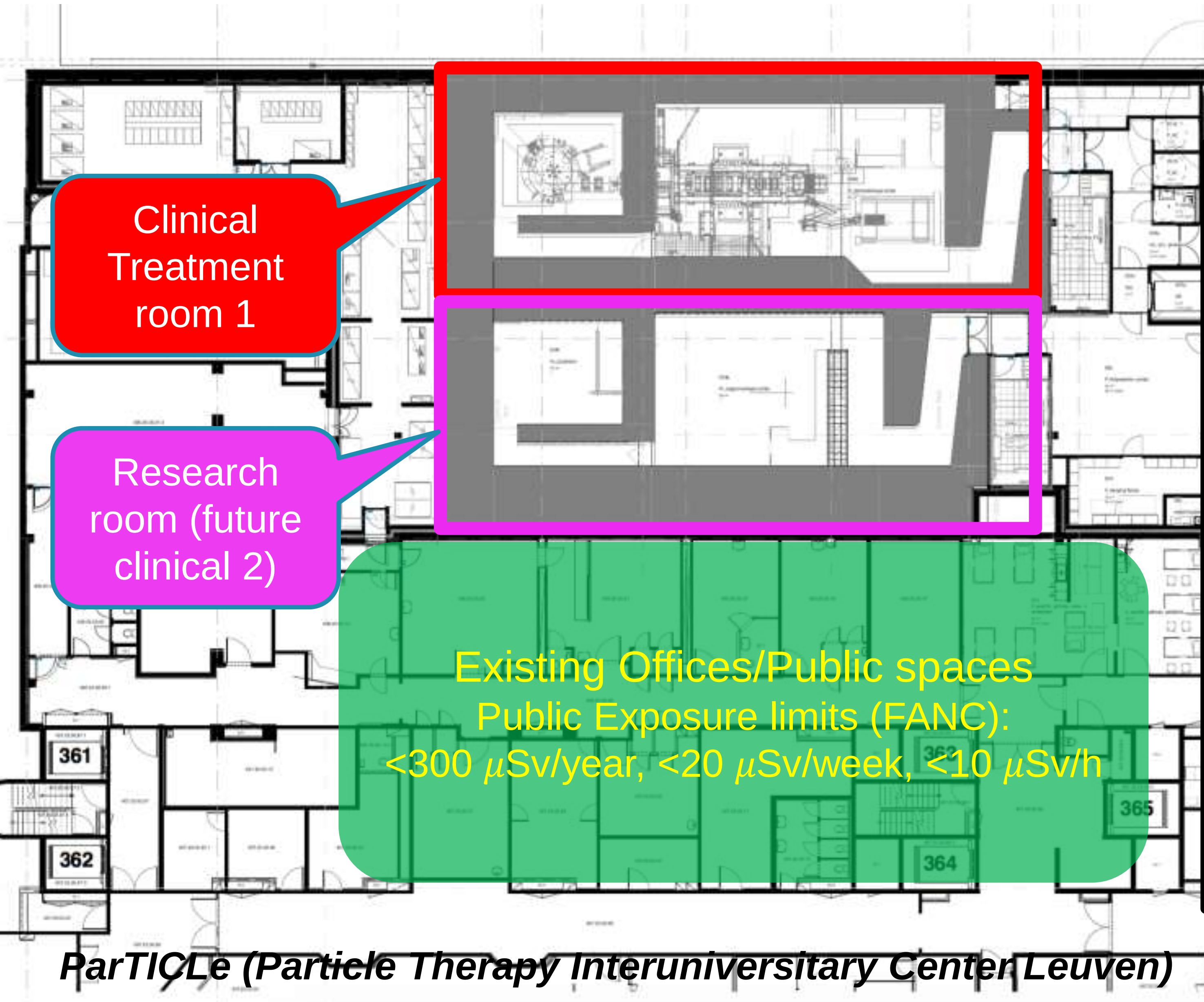
Table 1. Effective dose and lifetime risk of second cancer for the three considered treatment modalities.

Treatment mode	Effective dose (mSv Gy^{-1})	Risk of secondary cancer (%)
PBS (P+ multi-room)	1.900	1.037
ProteusONE	1.910	1.052
RS	4.901	3.262

- **Shielding:**
    - **Limited gantry rotation** of compact gantries limit the beam orientation to one side
    - **Radiation sources closer to walls** reduces the value of dose reduction with distance
    - **Embedding of a PT facility in existing hospital building** usually leads to absolute public limit requirement at outer shell, in a limited space

*Stichelbaut et al. Radiation Protection Dosimetry 2014

Achieving Public **Exposure limits** of “Embedded” facilities



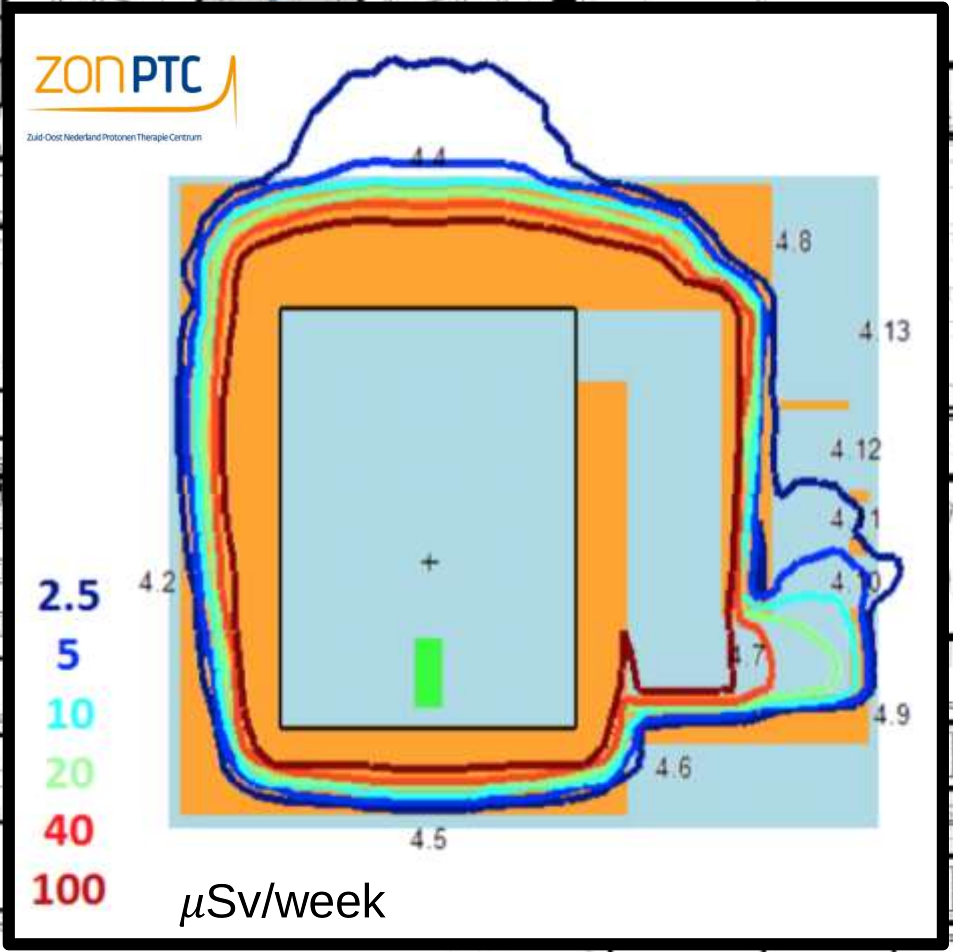
Clinical Treatment room 1

Research room (future clinical 2)

Existing Offices/Public spaces

Public Exposure limits (FANC):

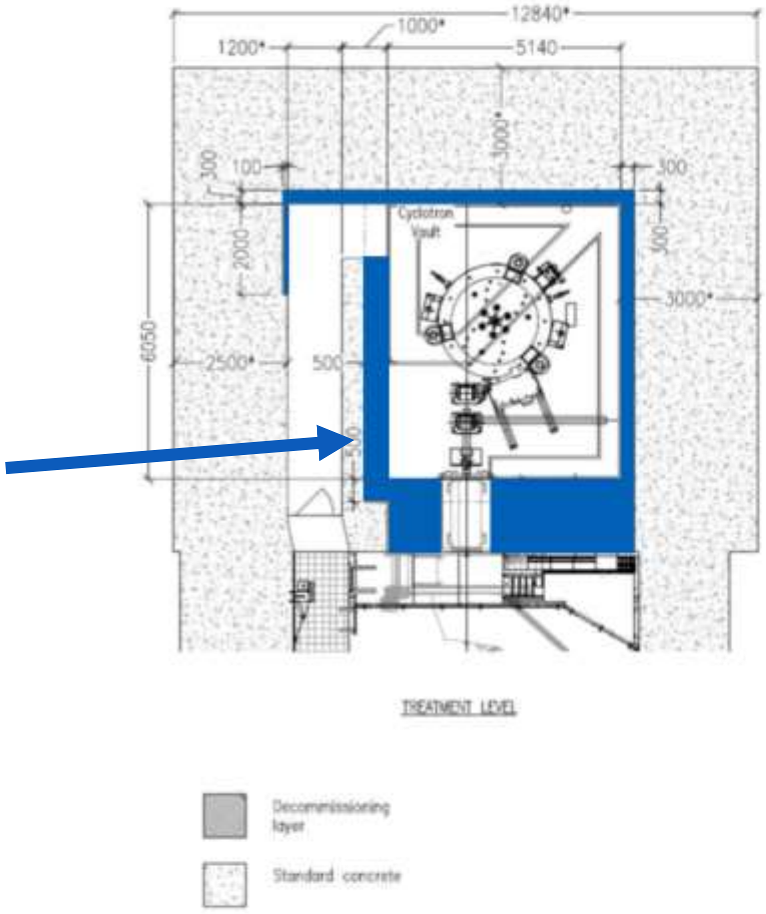
<300 μSv/year, <20 μSv/week, <10 μSv/h



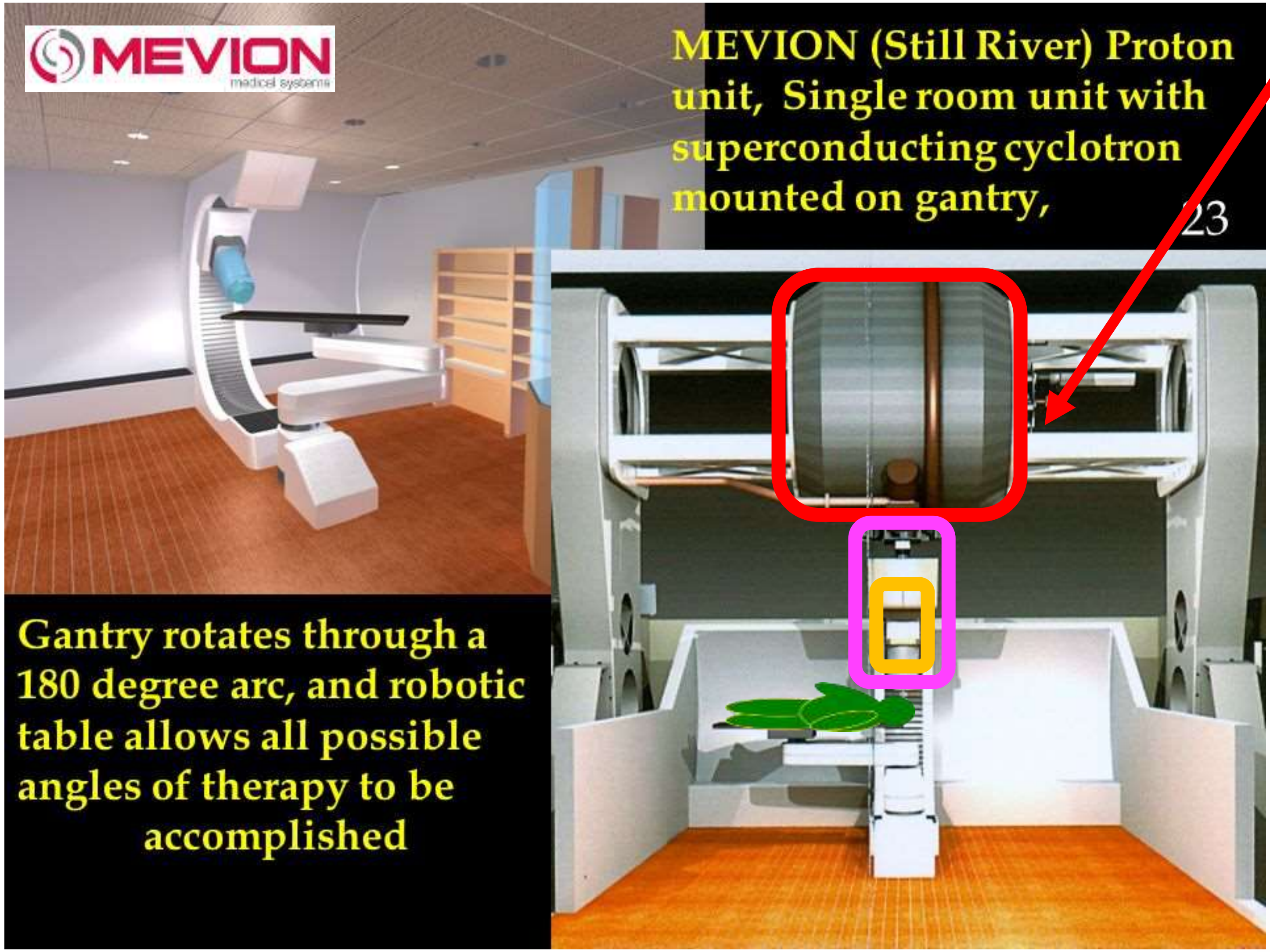
ParTICLe (Particle Therapy Interuniversitary Center Leuven)

Large Multi-room vs. Compact unit

- **Concrete activation/dismantling nuclear waste:**
    - The **walls in vaults for compact systems can be closer** to the cyclotron, resulting in **higher intensity of neutron fluence on the wall**.
    - The **specific activity after 20 years** due to long-lived isotopes (^{152}Eu, ^{60}Co) will be larger
    - Using a **decommissioning layer** of low activation concrete, Norwegian Marble aggregates with **low Eu levels <0.1ppm**



Further “*miniaturization*” of PT: Cyclotron mounted on gantry



MEVION (Still River) Proton unit, Single room unit with superconducting cyclotron mounted on gantry,

Gantry rotates through a 180 degree arc, and robotic table allows all possible angles of therapy to be accomplished

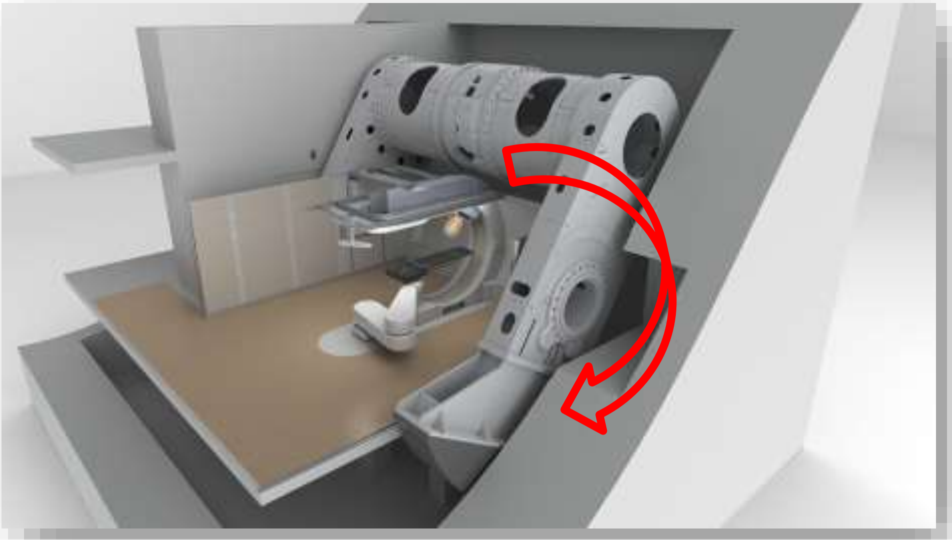
Cyclotron

Energy Selection System

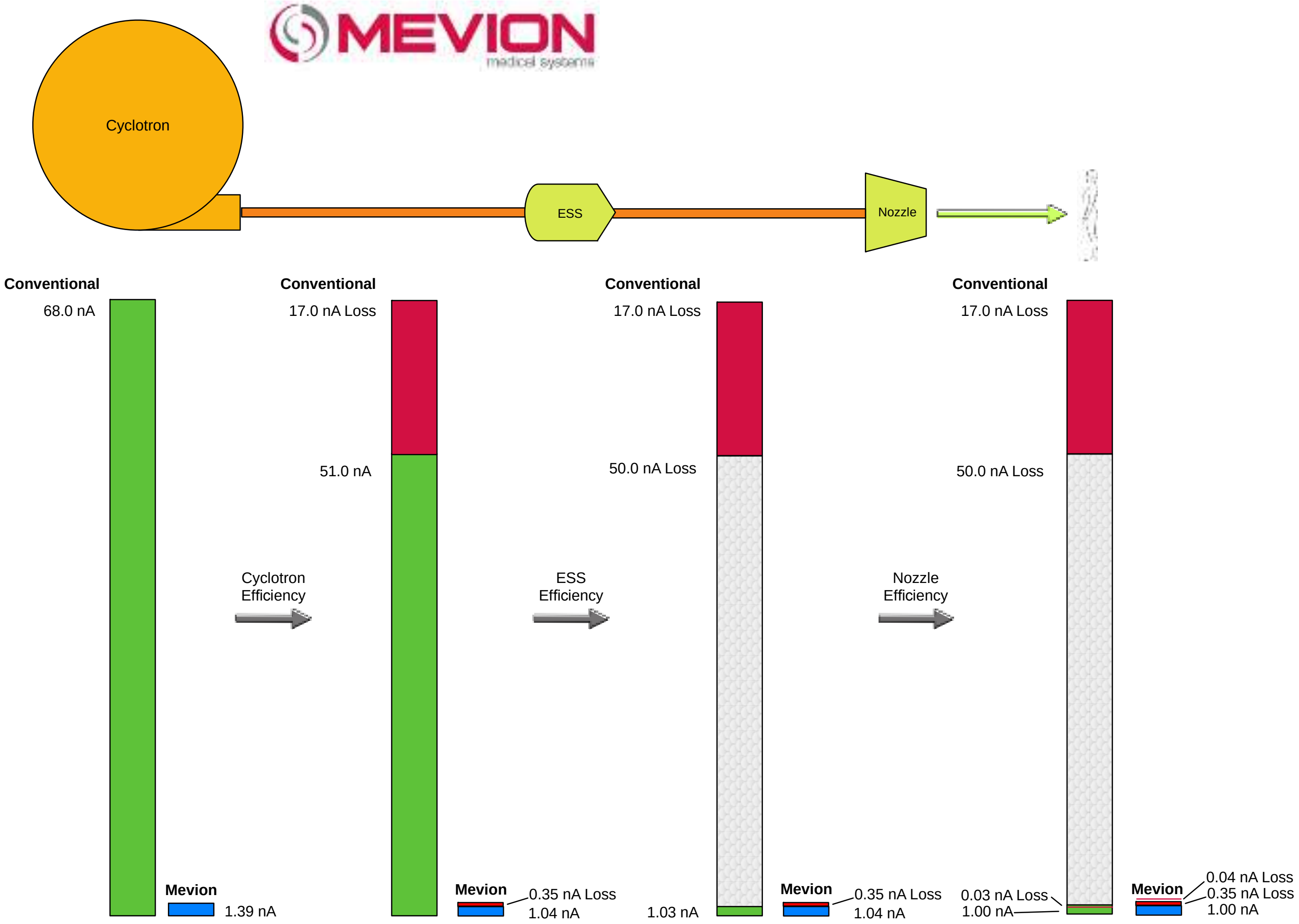
- Degrader only
- ~~Collimator~~
- ~~Divergence slits~~
- ~~Momentum slits~~

Nozzle

Patient



Further “*miniaturization*” of PT: Cyclotron mounted on gantry



-**Beam extracted** from cyclotron directly **pointing at isocenter**

-**Energy selection** only by degrading, **no bending/momentum slits**

-Higher beam current efficiency

-Secondary neutron sources close to patient, but system **operated at low proton currents**

-Less difference in out-of-field dose between PS and PBS?

-**Less “pure” energy spectrum** due to range straggling in degraded

Total Losses*
Conventional = 67.00 nA
Mevion = 0.39 nA

Total Efficiency
Conventional = 1.5%
Mevion = 71.9%

* Efficiency factors for “Conventional” systems from IBA and MGH publications.

PT **embedded** in existing radiation oncology clinic

- **Smaller facility truly integrated** in existing radiation oncology and hospital environment
- **Commercial compact systems** with **one or 2 treatment rooms**
- **Proton beam only**
- **Pencil beam scanning (PBS) only** (mostly)
- **Sharing treatment preparation imaging equipment and clinical workflow** with conventional radiation oncology and hospital

- **Clinically oriented staff, shared but PT trained staff from XT clinic,** with limited technical staff to run the facility
- **Usually only clinical treatment rooms**, no research beam-line
- PRICE: **projects of 50M€**

"PT seen as an <u>additional modality</u>, rather than an separate facility"

Topics

- *Delivery technology*
- *Compact layout systems*
- *In-room imaging and treatment verification*
- *Concluding remarks*

Radiation protection of

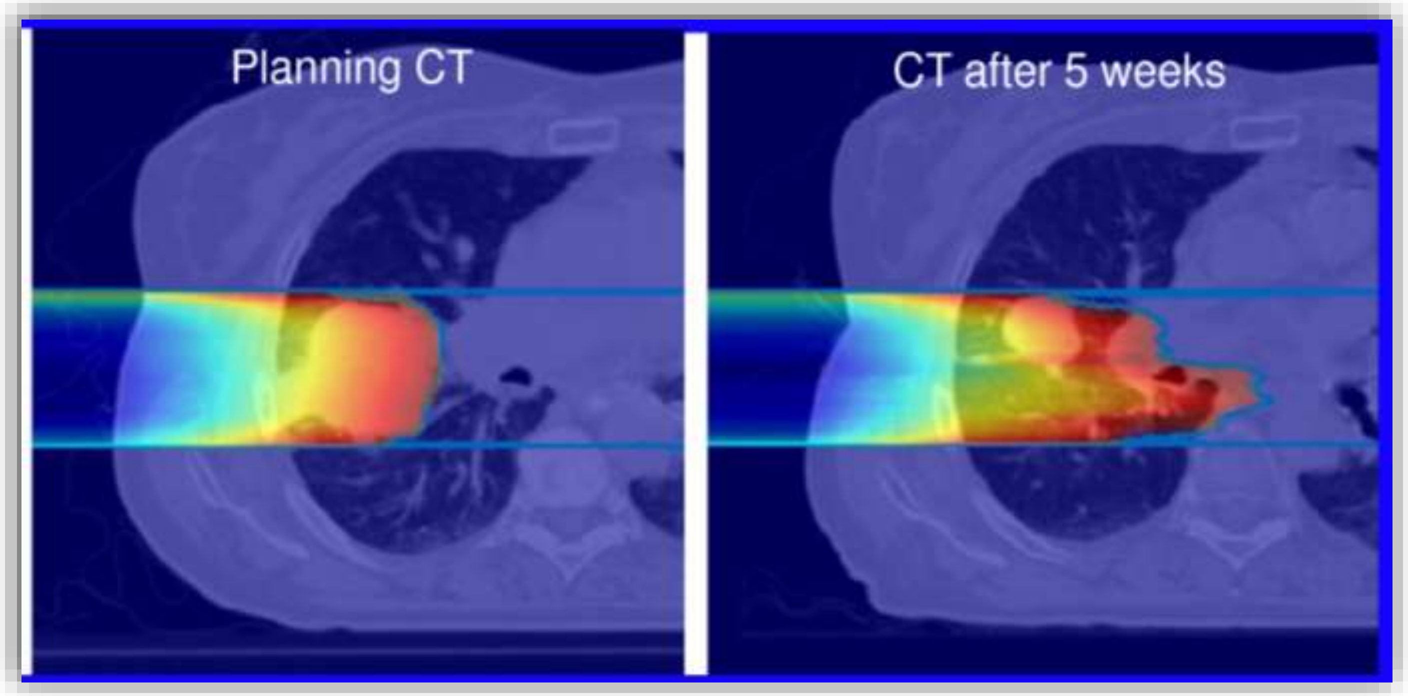

patient


personnel


hospital/environment

Range uncertainty issue in proton therapy

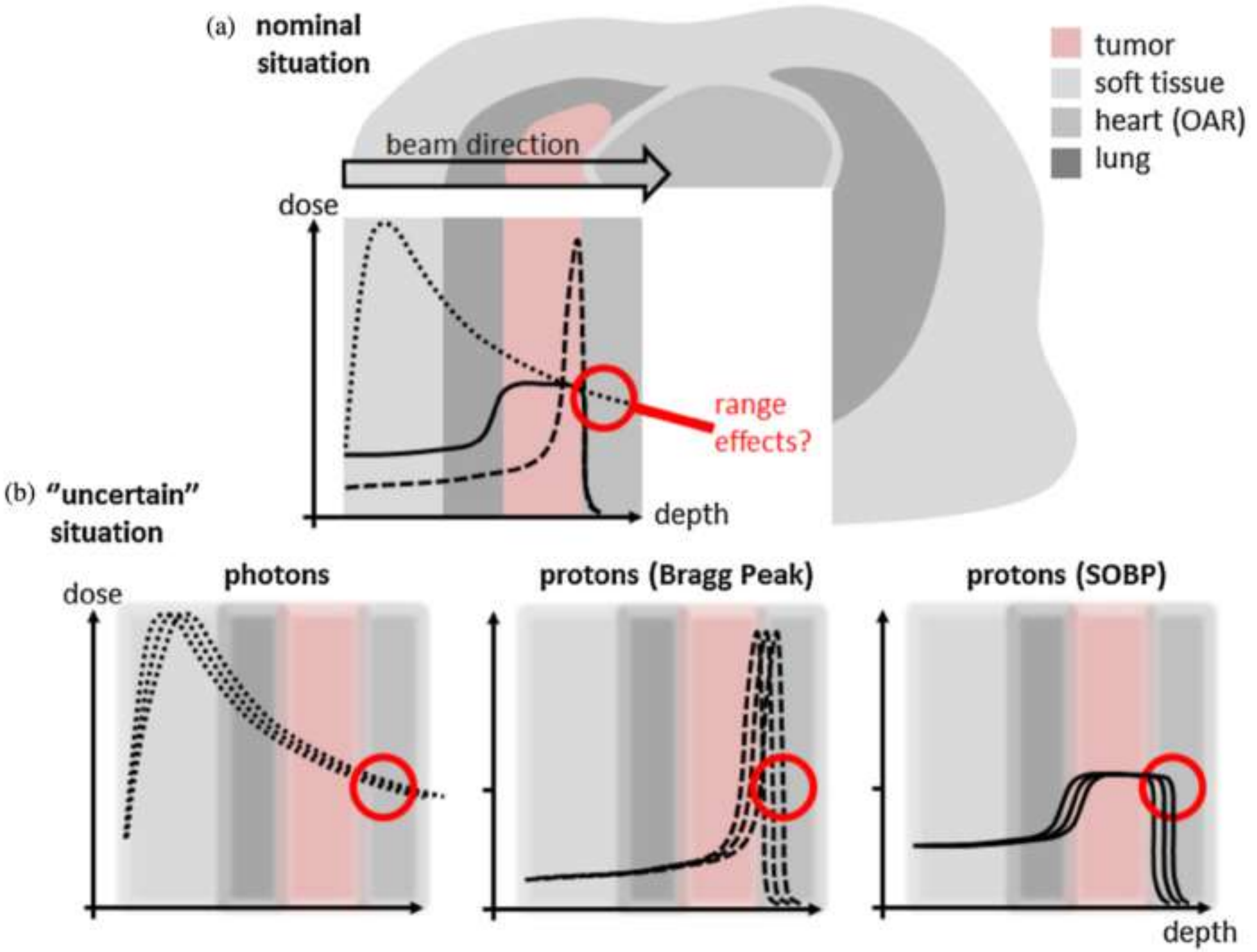
The **Gare Montparnasse** became famous for the derailment on 22 **October 1895** of the Granville–Paris Express, which overran the buffer stop. The engine careered across almost 30 metres (100 ft) of the station concourse, crashed through a 60-centimetre (2 ft) thick wall, shot across a terrace and smashed out of the station, plummeting onto the Place de Rennes 10 metres (33 ft) below, where it stood on its nose.



"Protons do stop but there is an uncertainty on where exactly"

Paganetti et al. Phys. Med. Biol. **2012** and Knopf et al. Phys. Med. Biol. **2013**

Reducing uncertainties in proton therapy



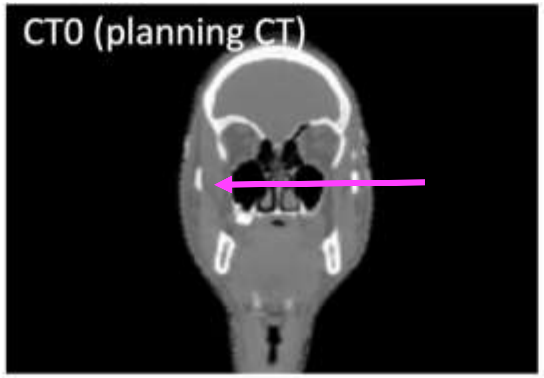
Bortfeld et al. Nature 2017

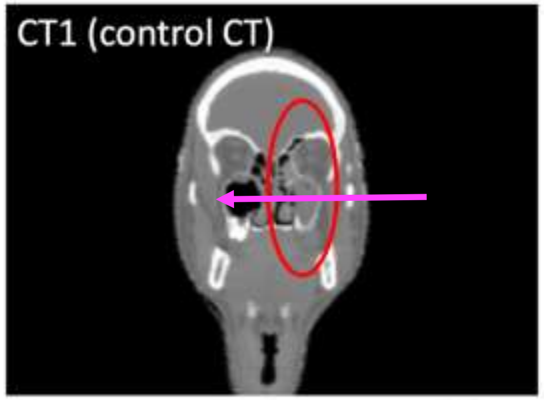
"The speed of the proton, or its kinetic energy, determines the depth at which the spot reaches below the skin. Uncertainties in this slowing process can affect whether the dose spot hits the tumour as intended, or over- shoots into healthy organs."

"Impact of range uncertainty is more severe (potentially 100%) in PT than in XT"

Knopf et al. Phys. Med. Biol. 2013, Bortfeld et al. Nature 2017

Impact of anatomical changes …

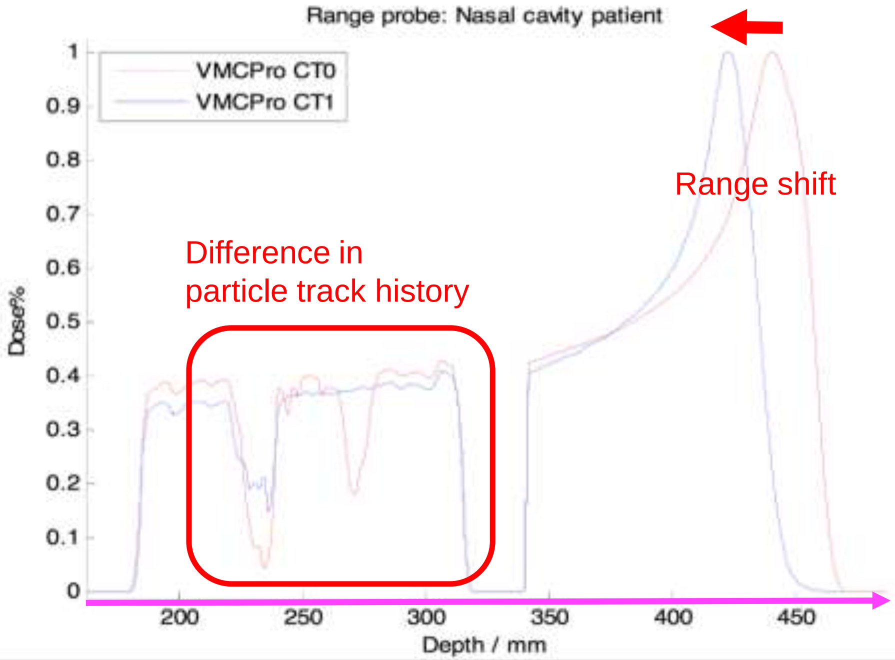




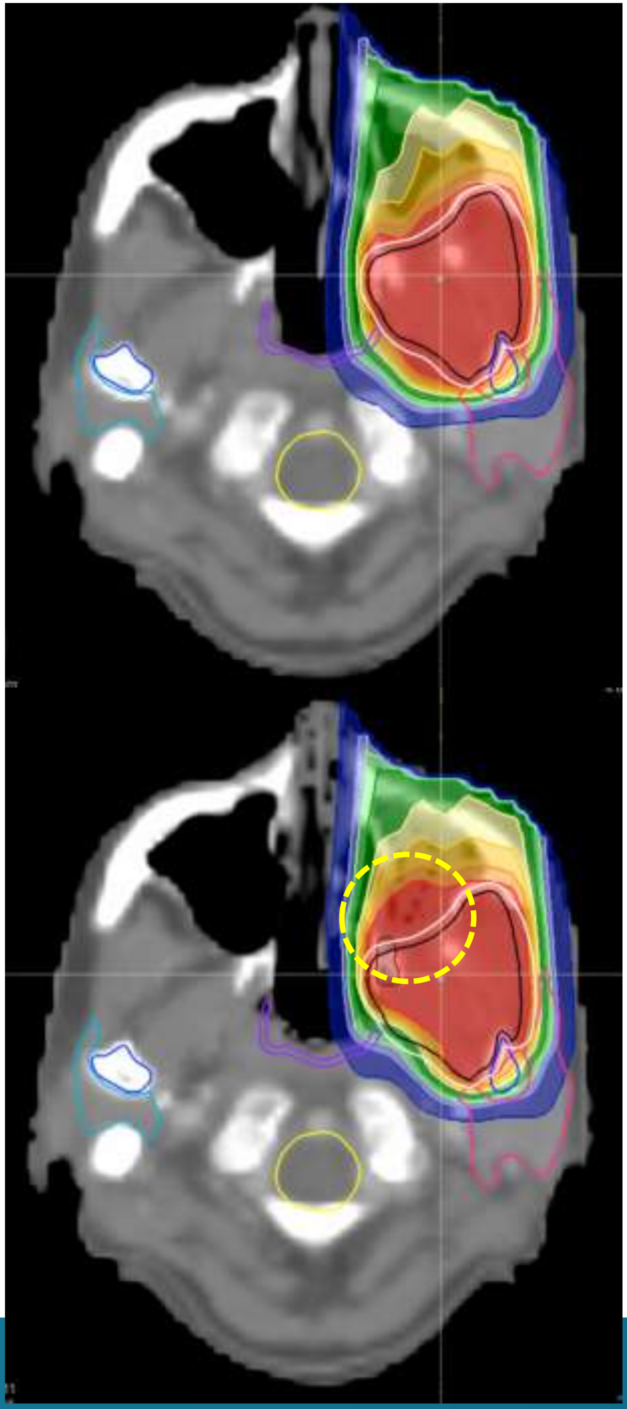
Abdel Hammi & Marta Mumot, PSI

Patient with nasal changes

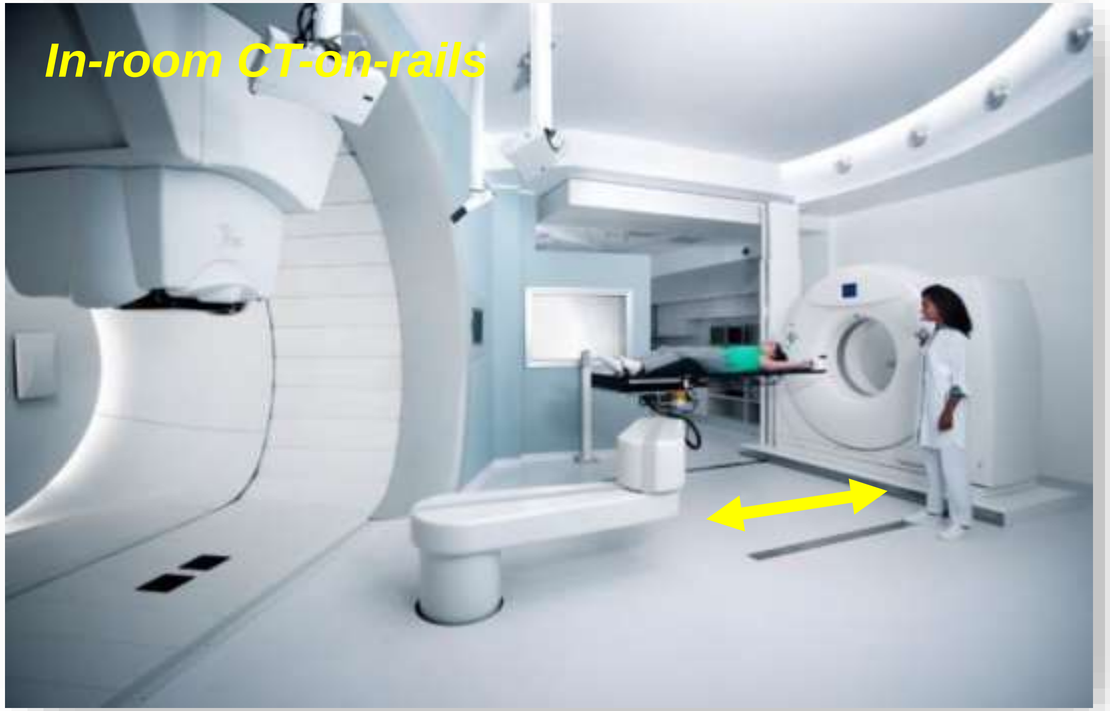
VMCPro: pencil beam energy 177MeV.
Shift between two curves = 22.5mm.



“Example: Changes in nasal cavity filling”



In-room CT-on-rails in proton therapy



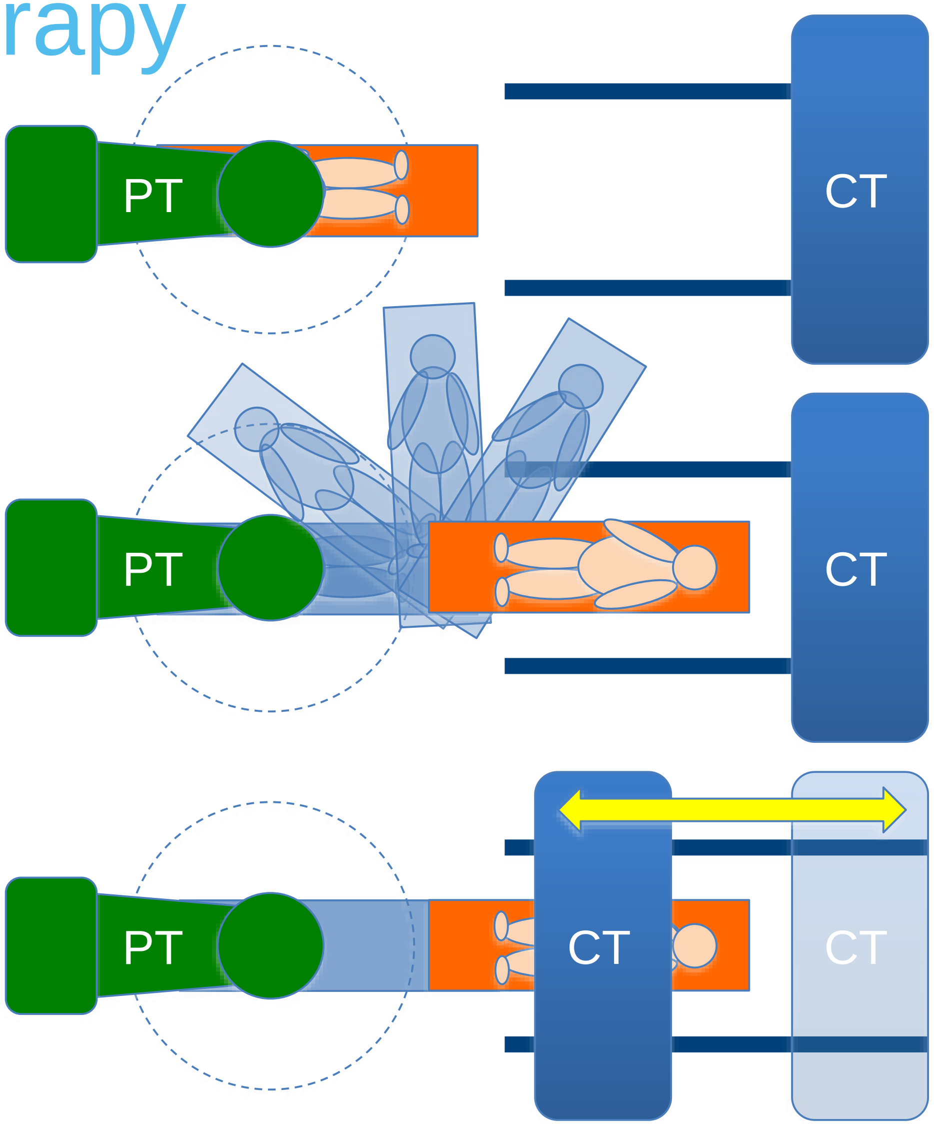
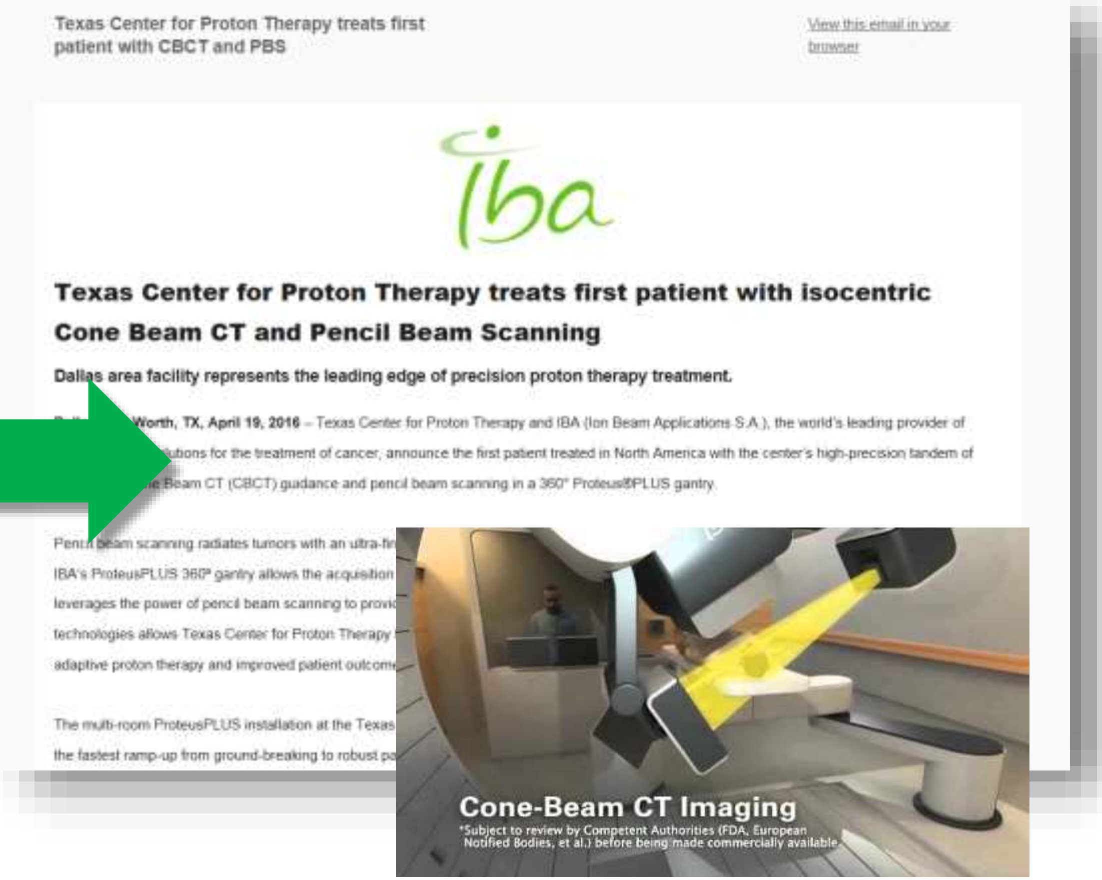


Image guidance in PT: Learning from XT !?

1999: David Jaffray and first CBCT integrated in XT linac

2016: First CBCT-guided PT



Texas Center for Proton Therapy treats first patient with CBCT and PBS

View this email in your browser

Texas Center for Proton Therapy treats first patient with isocentric Cone Beam CT and Pencil Beam Scanning

Dallas area facility represents the leading edge of precision proton therapy treatment.

Worth, TX, April 19, 2016 – Texas Center for Proton Therapy and IBA (Ion Beam Applications S.A.), the world's leading provider of

utions for the treatment of cancer, announce the first patient treated in North America with the center's high-precision tandem of

e Beam CT (CBCT) guidance and pencil beam scanning in a 360° Proteus®PLUS gantry.

Pencil beam scanning radiates tumors with an ultra-fi

IBA's ProteusPLUS 360° gantry allows the acquisition

leverages the power of pencil beam scanning to provi

technologies allows Texas Center for Proton Therapy

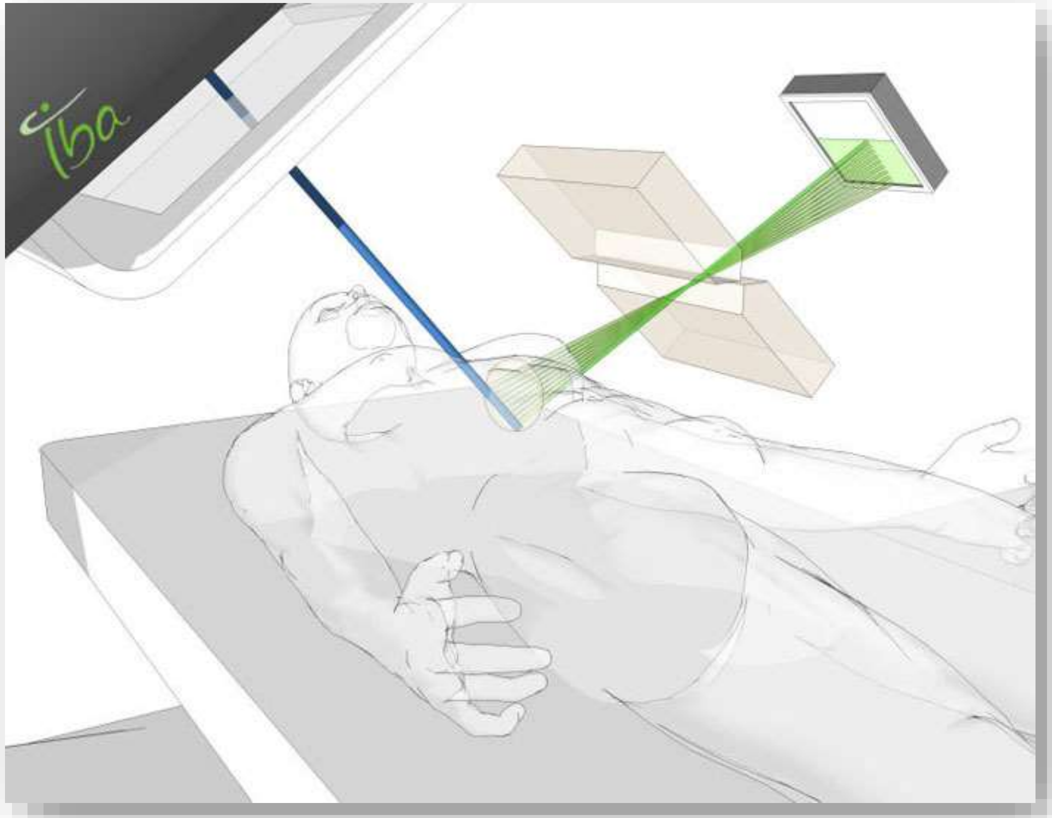
adaptive proton therapy and improved patient outcome

The multi-room ProteusPLUS installation at the Texas

the fastest ramp-up from ground-breaking to robust pa

KU LEUVEN

Range verification in PT: Prompt gamma imaging

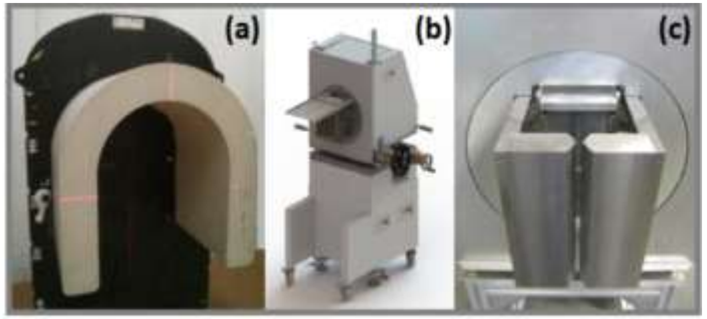


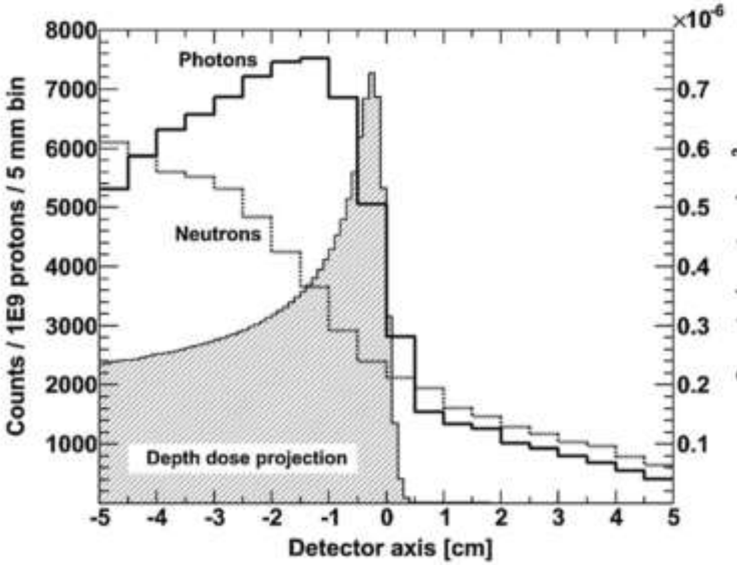
Slit-design gamma camera (IBA prototype)

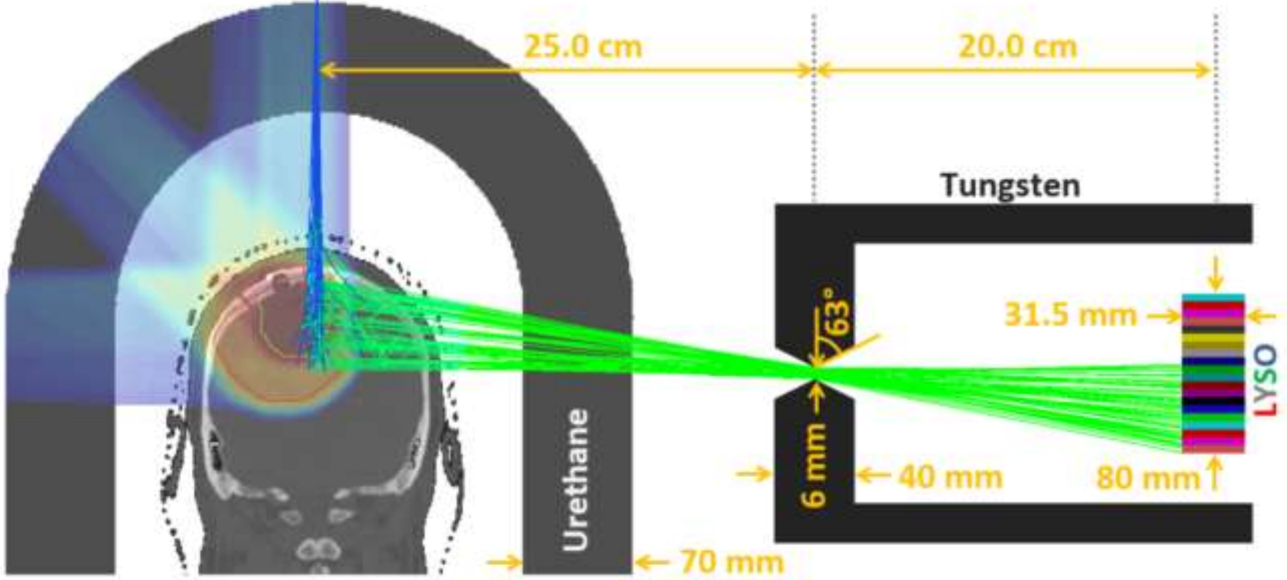
- Resulting from **inelastic interactions of incident protons and target nuclei**
- The **nucleus is excited** to a higher energy state and emits a single photon (PG) as it **returns to the ground state**
- the **isotropic PG rays** can be **detected instantaneously** (within a few nanoseconds) following the nuclear interactions
- Wide energy spectrum, between 0 and 7 MeV
- **reasonably high production rate/signal** for a typical therapeutic dose of 2 Gy min^{-1}
- PG are **produced along the proton tracks**, the path of a pencil beam within the patient could be **imaged as a line source by an adequate gamma camera.**
- **Real-time online verification method**

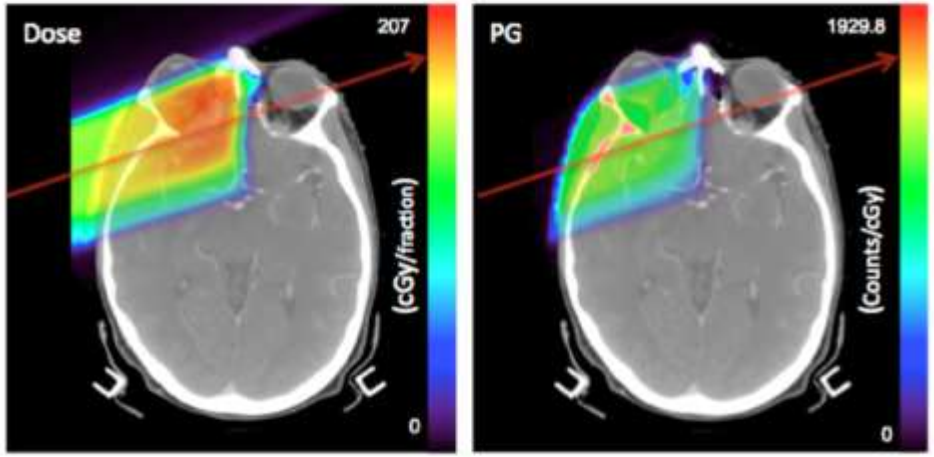
Moteabbed et al. Phys Med Biol 2011 Smeets et al. Phys Med Biol 2012

Range verification in PT: Prompt gamma imaging



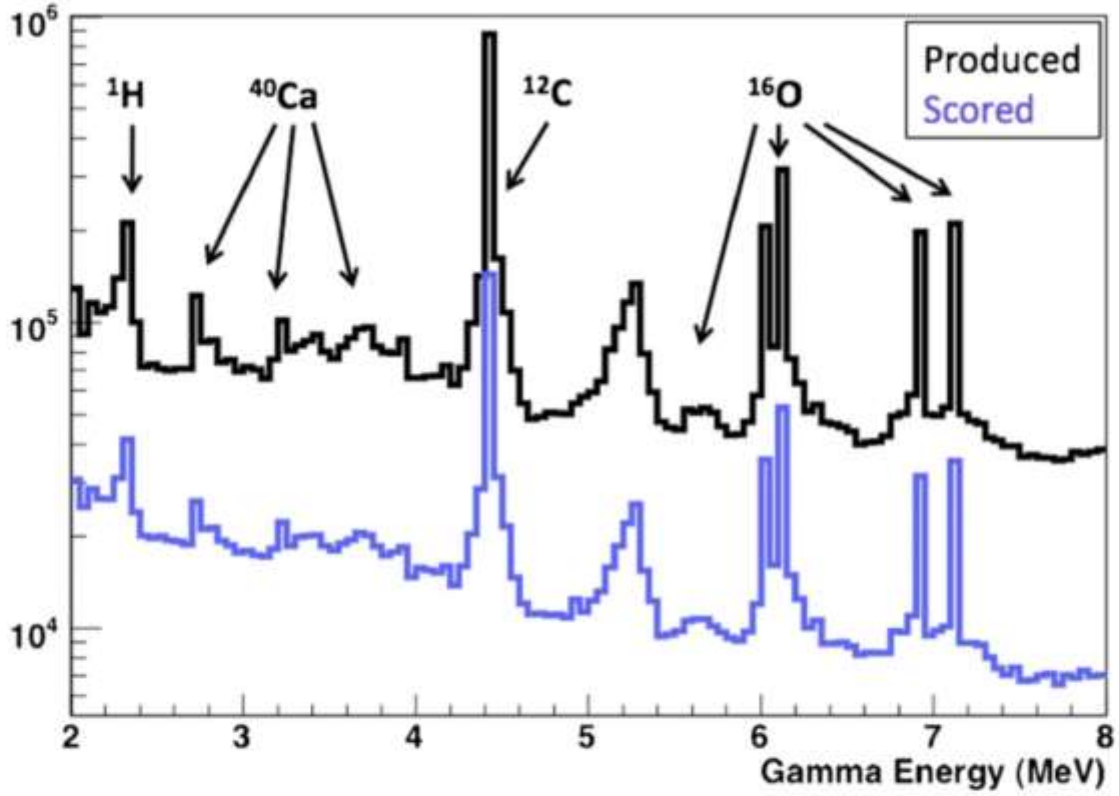






Smeets et al. Phys Med Biol 2012

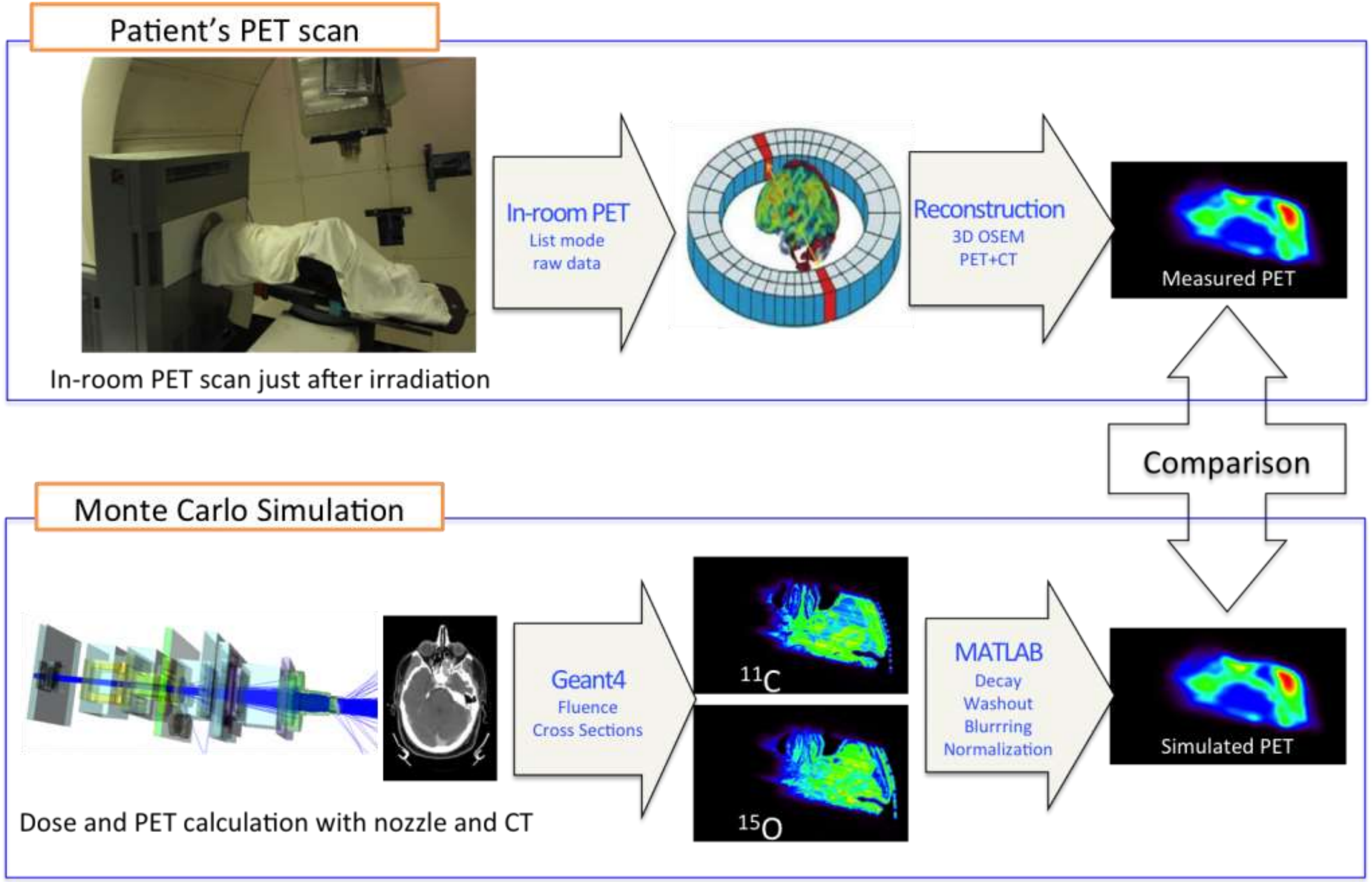
Range verification in PT: In-vivo PET imaging



- **Inelastic interaction of the proton beam with atomic nuclei** create unstable isotopes
- **Excited atomic nuclei undergo β+- decay** and emit characteristic positrons
- **^{11}C (T1/2 = 20.39 min), ^{15}O (*T*1/2 = 2.03 min),** ^{13}N (*T*1/2 = 9.97 min), ^{30}P (*T*1/2 = 2.50 min) and ^{38}K (*T*1/2 = 7.63 min)
- Annihilation of positrons create **a 511 keV gamma pair detectable by the PET scanner** coincidence measurement

Parodi et al. Phys Med Biol 2002, 2005, 2007a/b

Range verification in PT: In-vivo PET imaging



Patient's PET scan

In-room PET scan just after irradiation

In-room PET
List mode
raw data

Reconstruction
3D OSEM
PET+CT

Measured PET

Comparison

Monte Carlo Simulation

Dose and PET calculation with nozzle and CT

Geant4
Fluence
Cross Sections

^{11}C

^{15}O

MATLAB
Decay
Washout
Blurrring
Normalization

Simulated PET

Parodi et al. Phys Med Biol 2002, 2005, 2007a/b

Topics

- *Delivery technology*
- *Compact layout systems*
- *In-room imaging and treatment verification*
- *Concluding remarks*

Radiation protection of


patient


personnel


hospital/environment

History of Proton Therapy (PT) facilities

"PT facilities evolves from being …"

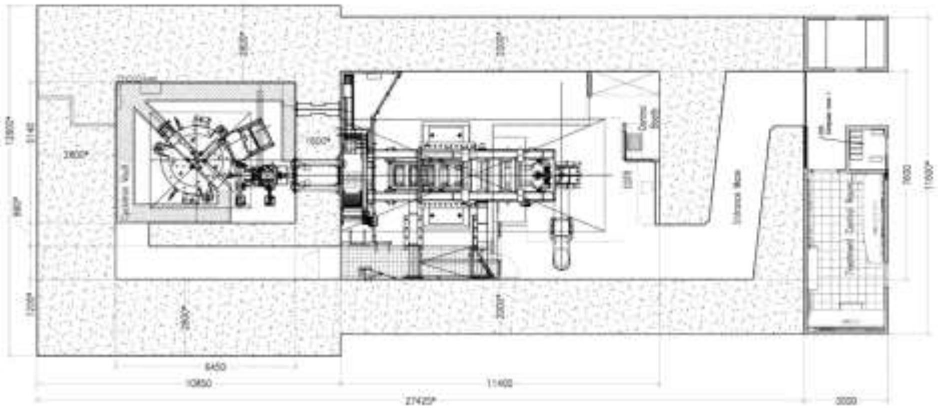
A by-product

Dedicated stand-alone facility

Embedded Facility

Standardization/commercialization of PT similar to XT

"PT sold as single room units"



Scalability of a PT facility

"IGRT technology and interface become similar"

"Standardization of PT solutions"

Varian Probeam PT

Varian Truebeam XT

Conclusions

- **“PBS has become the preferred PT technology”**
  - Advanced capabilities of Multi-field-optimization IMPT
  - Less stray radiation generated in the nozzle
  - No patient specific beam modifiers required
  - Large number of PS PT centers are upgrading their nozzles to PBS
- **“Compact systems have been succesfully introduced in PT”**
  - IBA: 62% of sold/operational compact facilities, 16% of rooms
  - First step in PT cost reduction! (Investment, resources to run, ...)
  - Compact systems can be seen as units (accelerator+gantry+PBS)
  - “Minaturization” impact on radiation protection (smaller distances, wall activation, in-nozzle degradation)
  - …

Acknowledgements: F. Stichelbaut, L. Herremans, G. Bosmans, P. Pleunis, C. Gomà

Conclusions continued

- **“Compact systems have been succesfully introduced in PT”**
  - ... (continued)
  - Enables “embedding” in existing hospital environments/infrastructure
  - Potential role in balancing justified application of PT compared to XT?
  - Standardization of PT?
- **In-room image guidance and treatment/range verification**
  - Crucial in reducing uncertainties in the PT process
  - On-board volumetric imaging IGPT has become available
  - Technologies for in-vivo range verification using PG in advanced state of development, applied in first clinical testing
  - The search for optimal use/combination of these new IGPT tools has started

Acknowledgements: F. Stichelbaut, L. Herremans, G. Bosmans, P. Pleunis, C. Gomà

Technological evolution in PT today

"Using the <u>train</u> metaphor …"

Starting up PT today ...

… feels like <u>jumping a moving train</u>

Acknowledgements: F. Stichelbaut, L. Herremans, G. Bosmans, P. Pleunis, C. Gomà