Hadrontherapy

Outline:

1. Rationale for Hadrontherapy
2. Rationale for Imaging in Hadrontherapy
3. In-beam Positron Emission Tomography
4. Prompt-Gamma Imaging

Acknowledgments

III Biomedical Engineering Summit
Coimbra, 2023-09-08

crespo@uc.pt

1. Rationale for Hadrontherapy

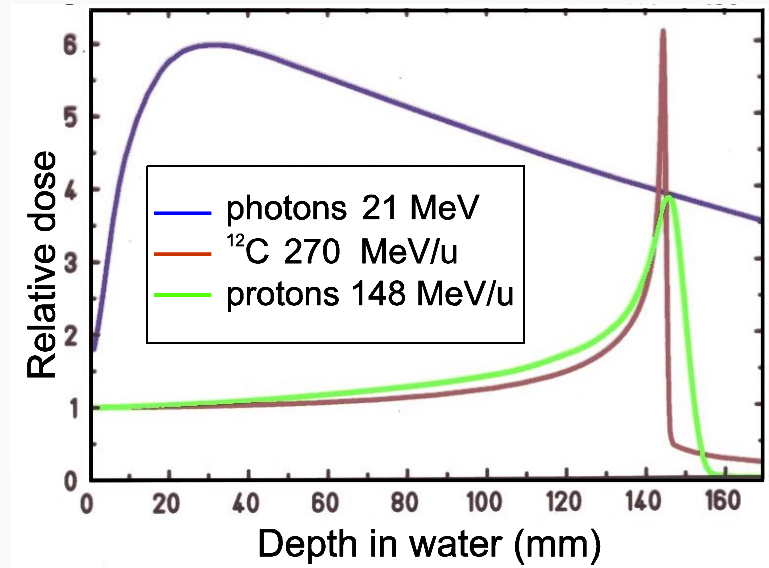
- **Physics Rationale**

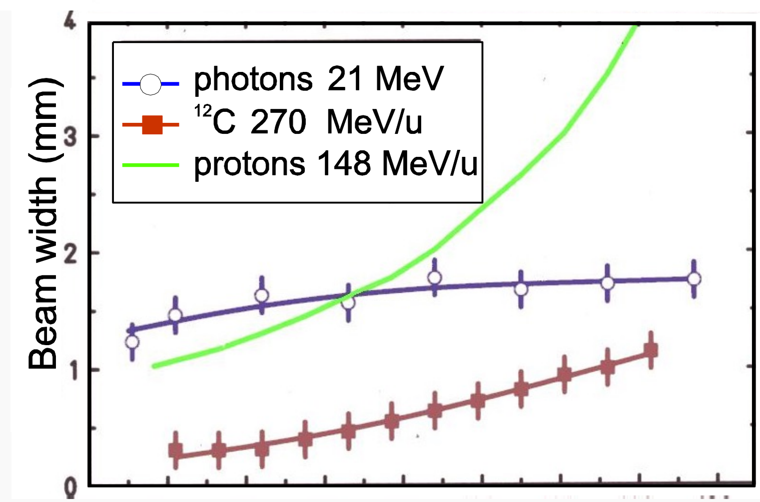
  Kraft, Prog Part Nucl Phys 45 (2000)

  Kraft, Prog Part Nucl Phys 46 (2001)

  ▶ Inverse depth-dose profile (Bragg-peak)

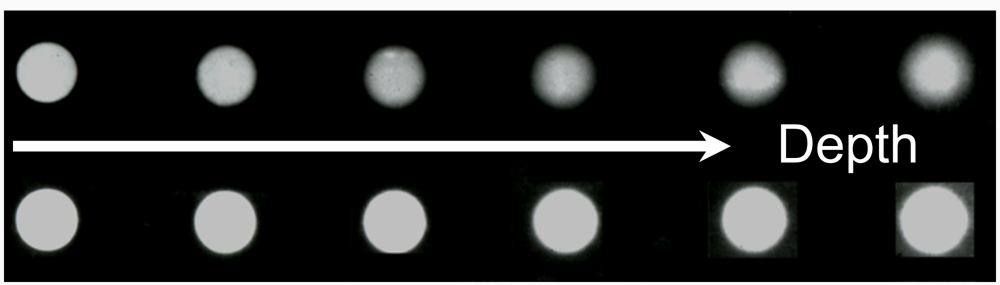
  ▶ Small lateral scattering





from U. Weber 1996, thesis

Protons



5 cm

Carbon ions

1. Rationale for hadrontherapy

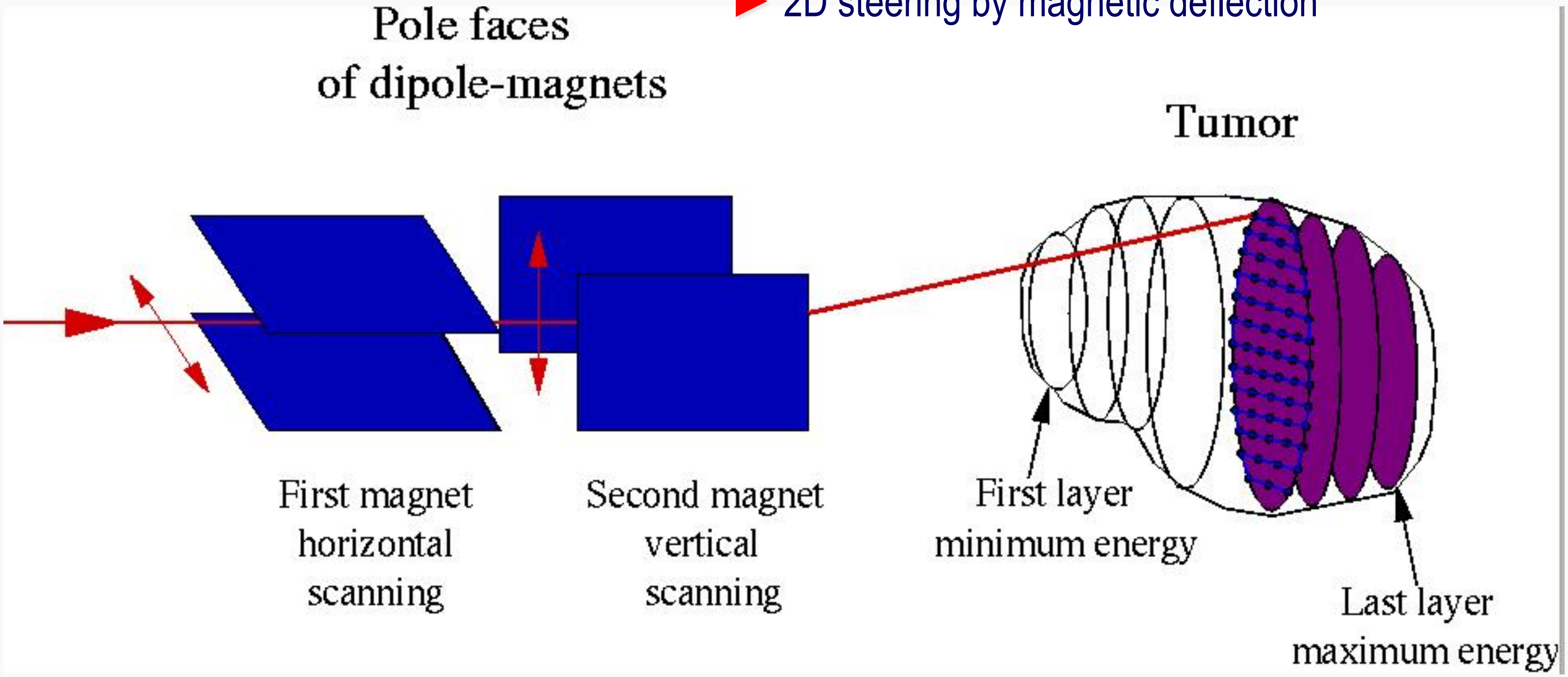
- **Physics Rationale: Active beam shaping ($^{12}C^{6+}$)**

Haberer et al., NIM A 330 (1993)

√ Inverse depth-dose profile (Bragg-peak)

√ Small lateral scattering

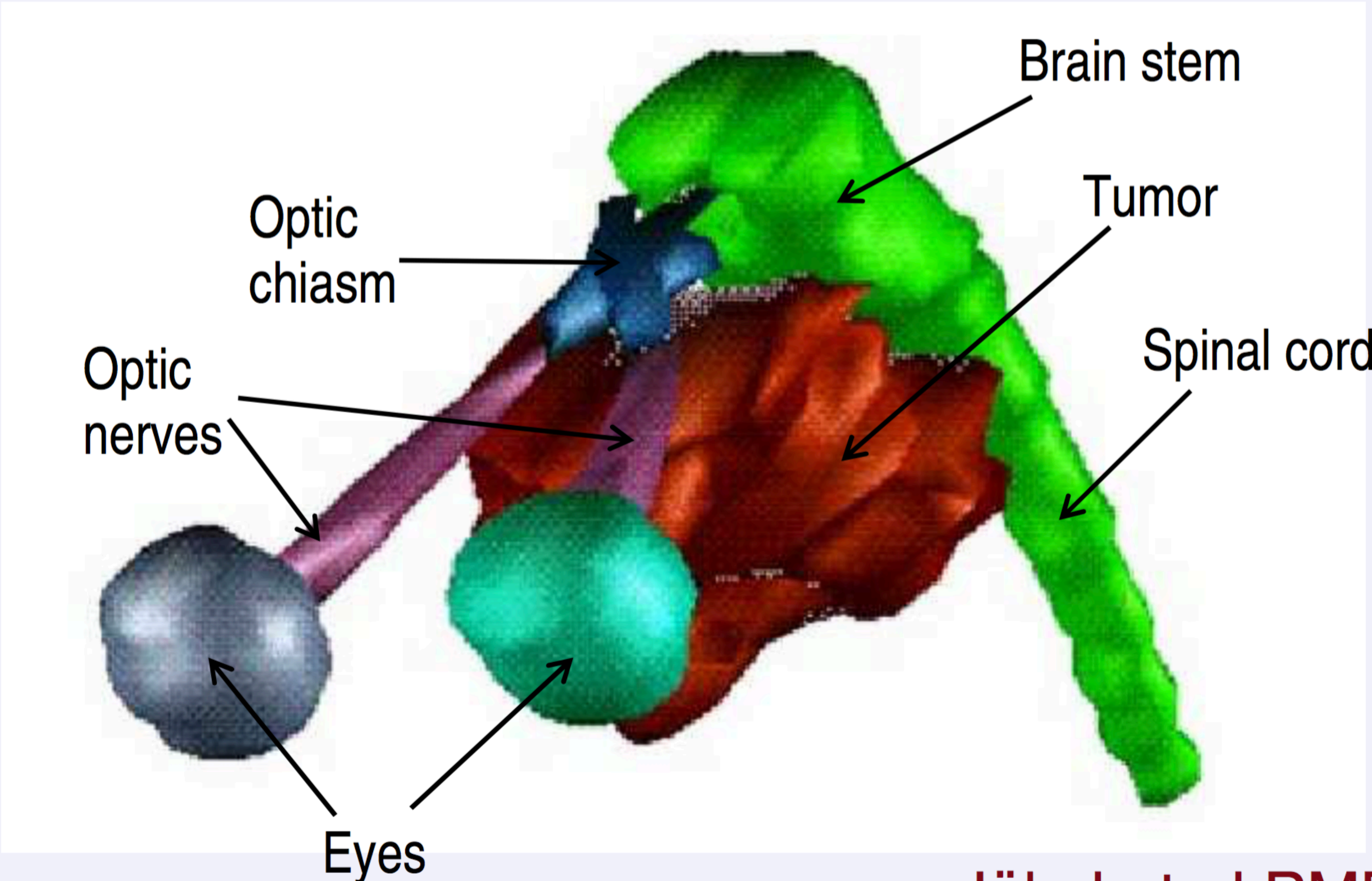
► 2D steering by magnetic deflection



1. Rationale for hadrontherapy

- **Physics Rationale**

Clivus chordoma at the base of the skull



Jäkel et al PMB 2000

1. Rationale for hadrontherapy: carbon ions

- **Localized dose = better sparing of organs at risk**
  - ► Before and 6 weeks after radiotherapy with ^{12}C

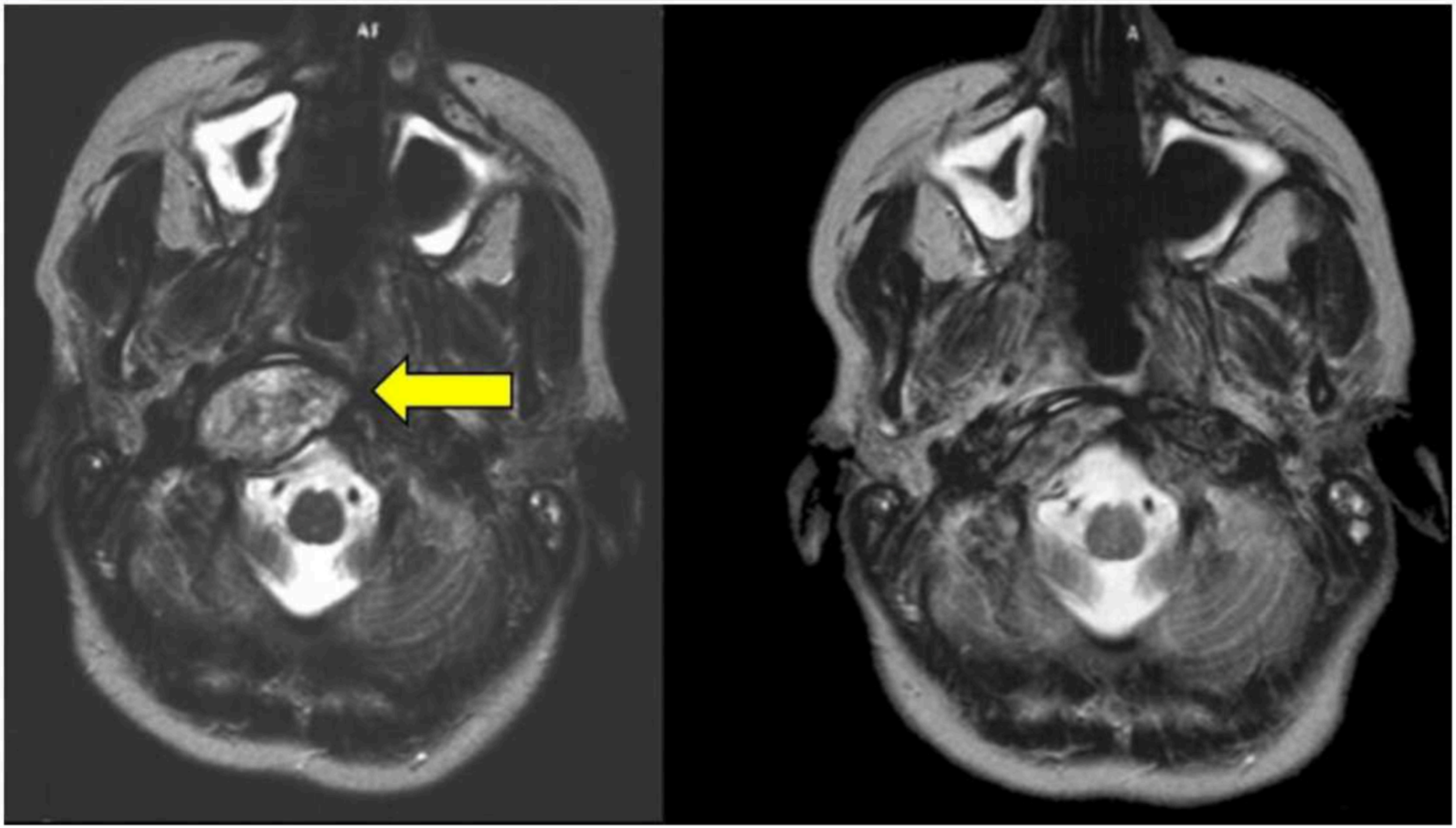
GSI Nachrichten (1999)

Before	After

1. Rationale for hadrontherapy

Regression of chordoma in the base of the skull:

- MRI before RT with ^{12}C (left) and six weeks after (right).

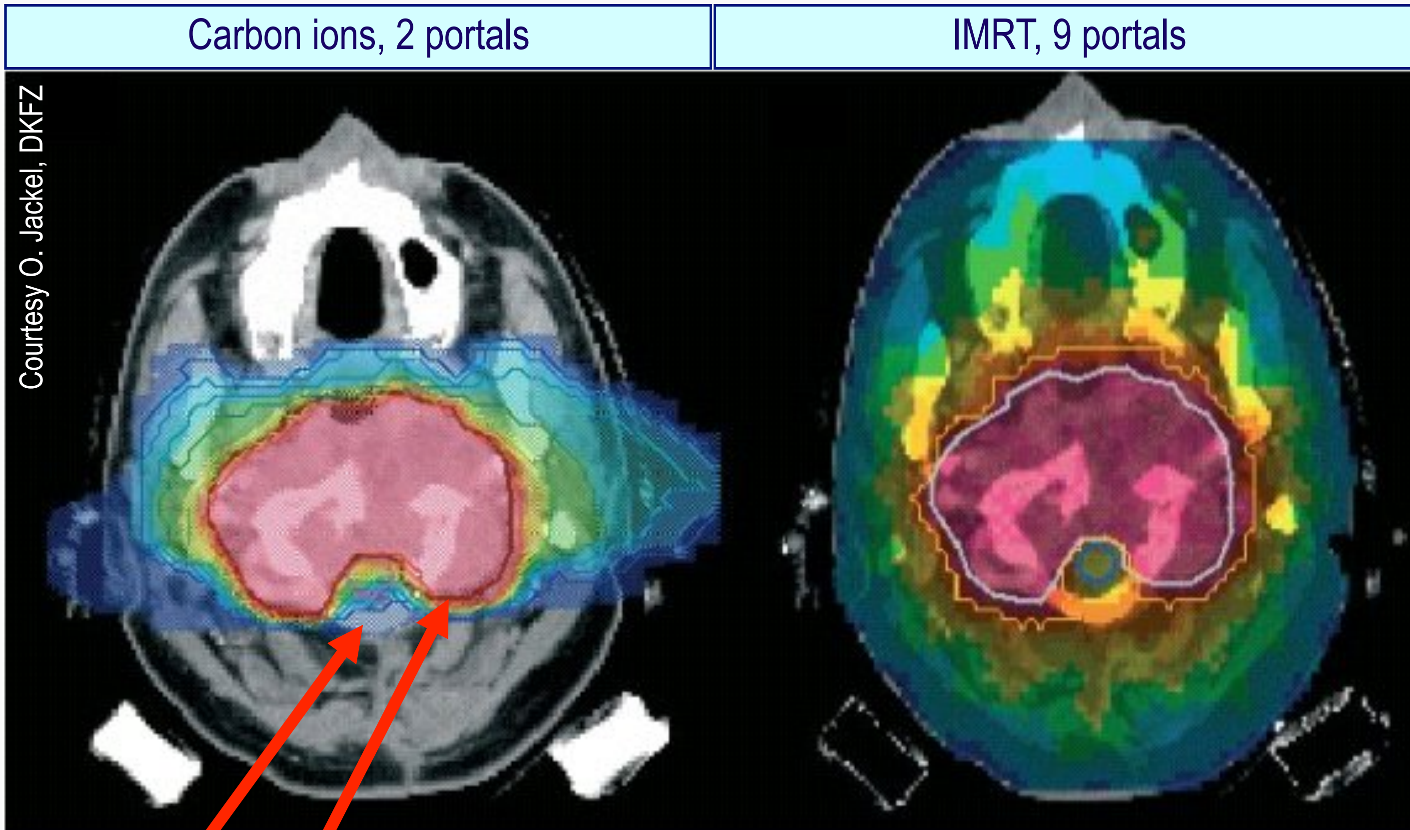


Schardt et al Rev Mod Phys 2010

1. Rationale for hadrontherapy

- **Localized dose = better sparing of organs at risk**

► Combined factors allow **very high tumor-conformation**, therefore enabling the irradiation of **inoperable tumors** growing in close vicinity to organs at risk

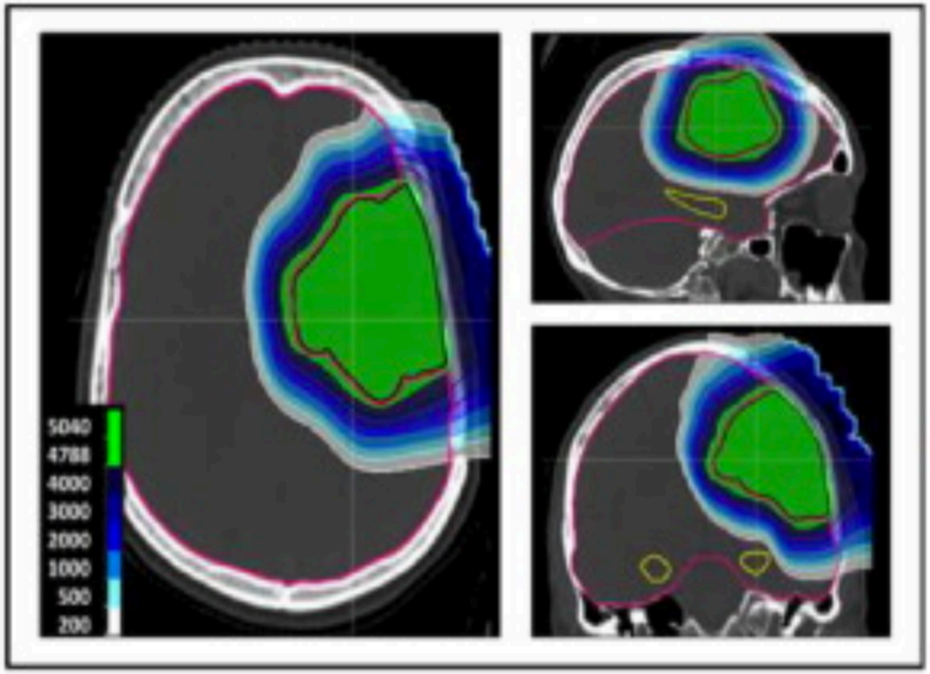


Tumor, 95 % of maximum dose
Brain stem, critical organ, very radiosensitive

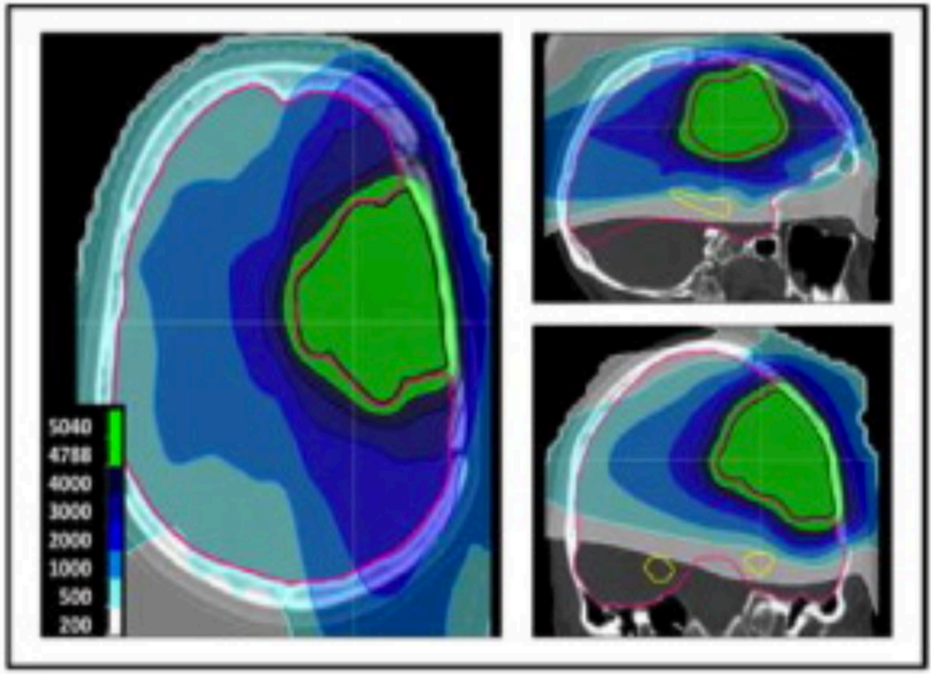
Some evidence of advantages of PT over state-of-the-art X-rays

Low-grade glioma, female, 38 y.o.: **dose reduction accepted as being clinically relevant**

Two-field intensity modulated PT



Volumetric intensity modulated arc therapy

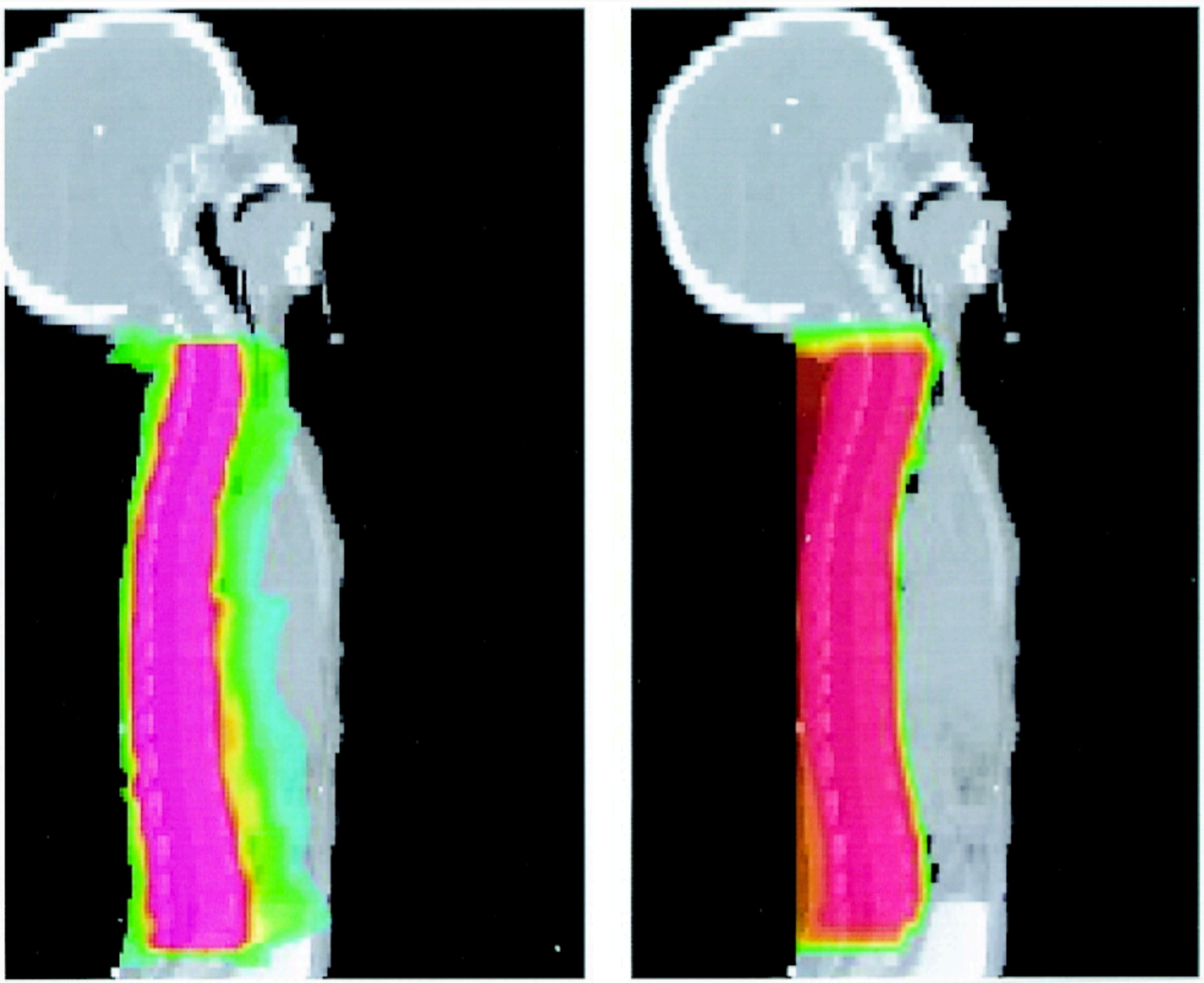


van der Weide et al., Radiother Oncol (2020)

Some evidence of advantages of PT over state-of-the-art X-rays

Pediatric medulloblastoma: **Dose to 50% of the heart volume was reduced from 29.5% for IMRT to 0.5% for protons**

IMRT – intensity modulated radiation therapy



PT

Clair et al., IJROBP (2004)

1. Rationale for hadrontherapy

- **Radiobiological Rationale: Ionization density**

Krämer and Kraft, Radiat Environ Biophys 38 (1994)

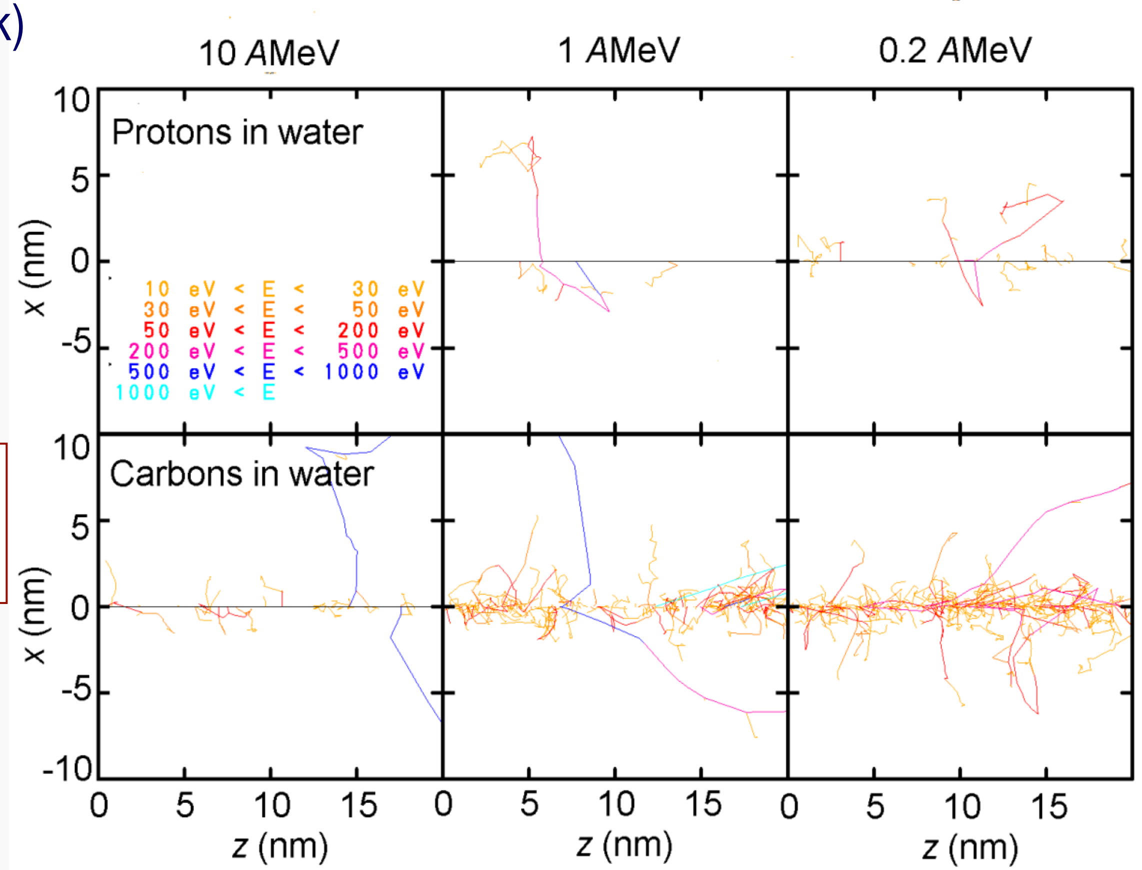
√ Inverse depth-dose profile (Bragg-peak)

√ Small lateral scattering

√ 2D steering by magnetic deflection

► Increased ionization density only at Bragg peak

$$-\frac{dE}{dx} = Kz_{eff}^2 \frac{Z}{A}\frac{1}{\beta^2}\left[\frac{1}{2}\ln\frac{2m_e c^2\beta^2\gamma^2 T_{max}}{I^2} - \beta^2 - \frac{\delta}{2}\right]$$



1. Rationale for hadrontherapy

- **Radiobiological Rationale: RBE**

K.-Weyrather and Debus, Clin Oncol 15 (2003)

√ Inverse depth-dose profile (Bragg-peak)

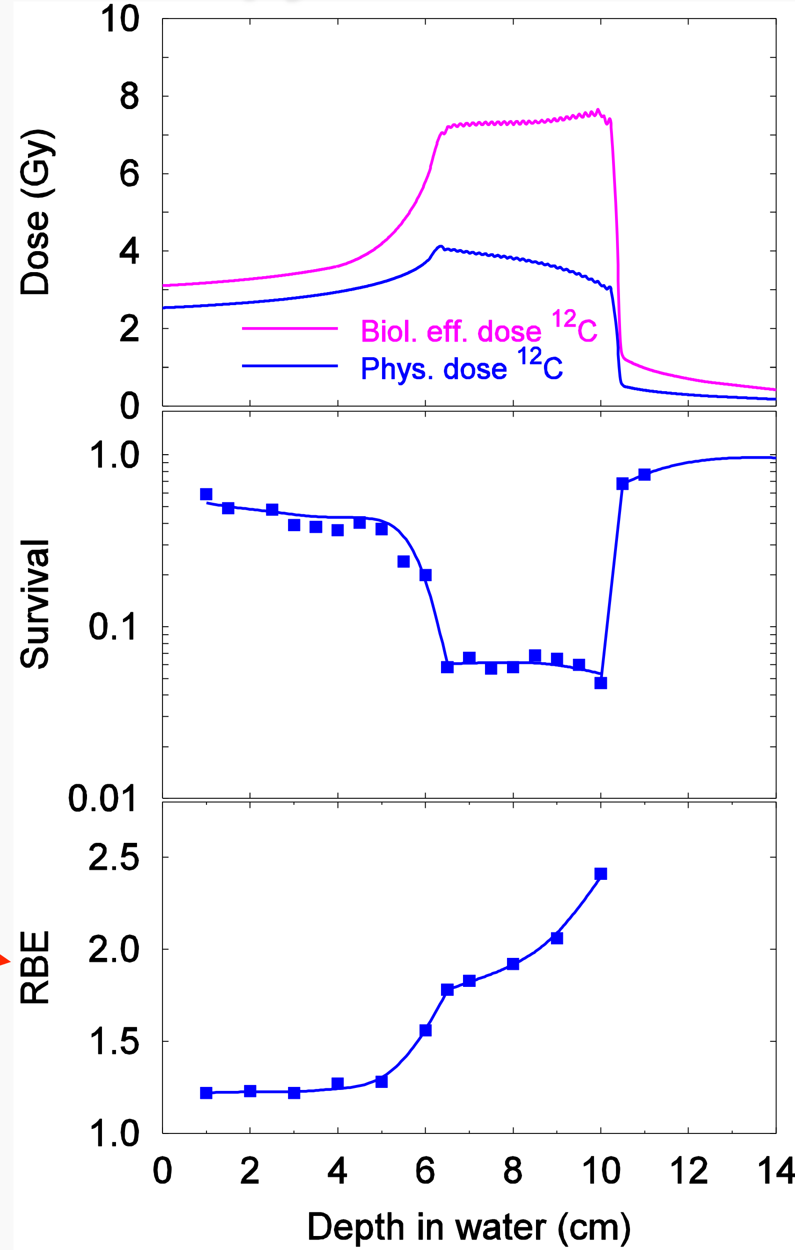
√ Small lateral scattering

√ 2D steering by magnetic deflection

► Increased ionization density only at Bragg peak

► Increased relative biological effectiveness

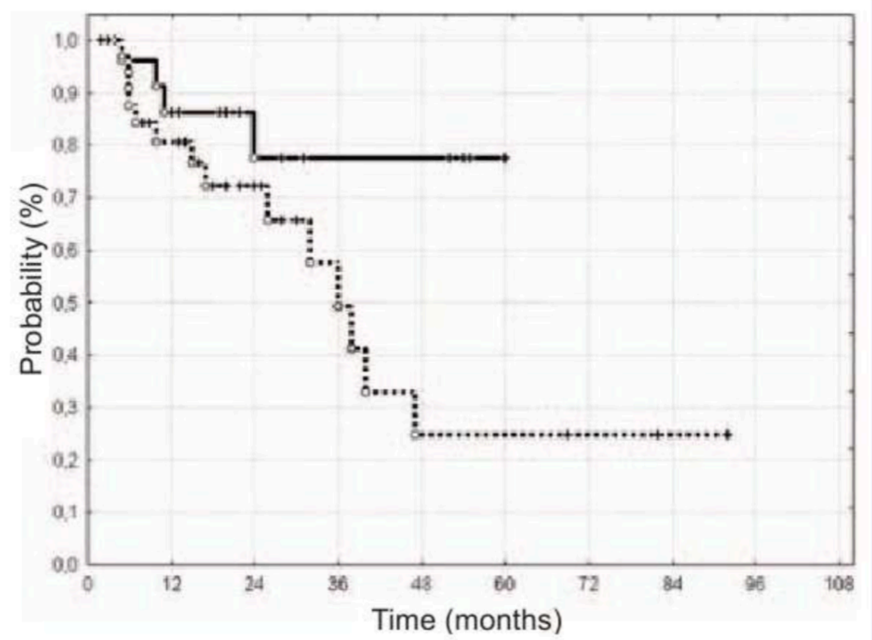
$$RBE = \left.\frac{D_\gamma}{D_{ion}}\right|_{ISOEFFECT}$$



1. Rationale for hadrontherapy

Salivary gland carcinoma in advanced stage

- Solid curve (top): local control rate for 29 patients treated with IMRT combined with carbon ions (boost).
- Dashed curve (bottom): results of 35 patients treated with IMRT only.



Kraft 2007

Irradiation with ^{12}C: local control rate at 60 months (5 years) ~75%.

IMRT alone: ~25%.

1. Rationale for hadrontherapy: X-rays vs protons vs carbon ions

Head-and-neck (left), lung (NSCLC, right)

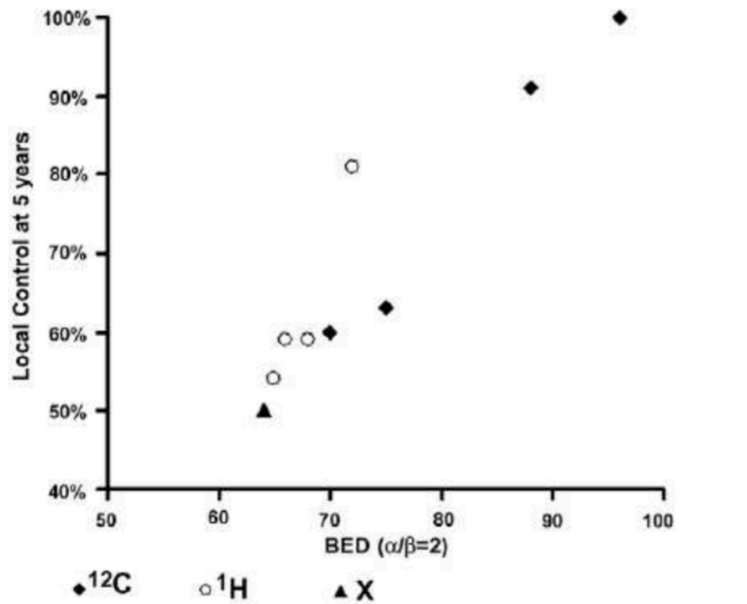


Fig. 12. Local control at 4 or 5 years for X, ^{1}H and ^{12}C ion irradiation of skull base chordomas *vs* BED, $\alpha/\beta = 2$.

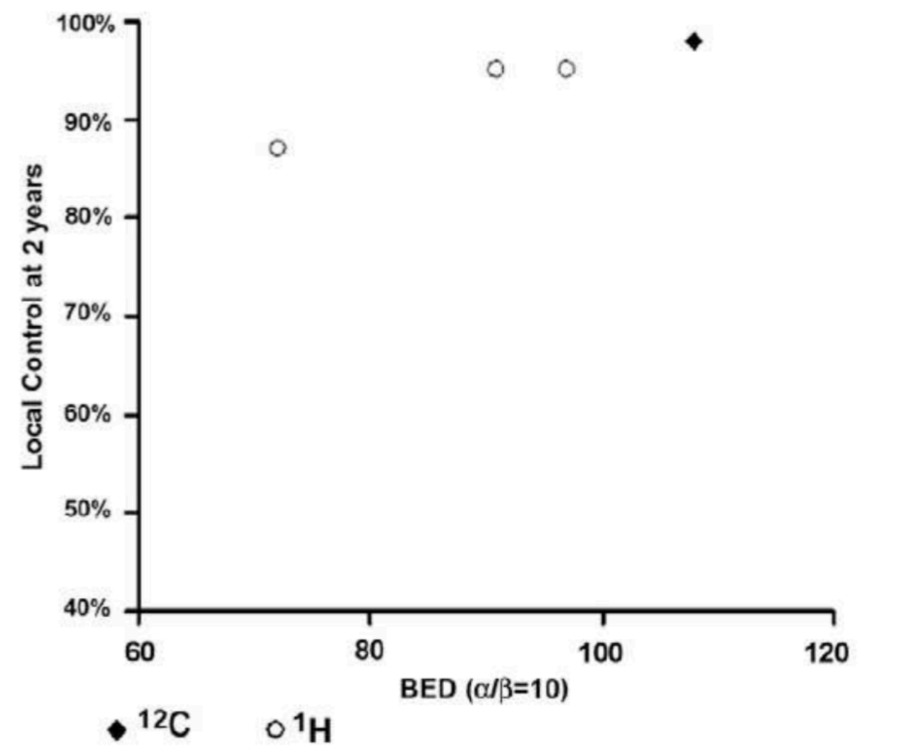


Fig. 13. Local control at 2 years for ^{1}H and ^{12}C ion irradiation of stage T1 NSCLC v BED, $\alpha/\beta = 10$.

Suit et al Radiother Oncol 2010

1. Rationale for hadrontherapy

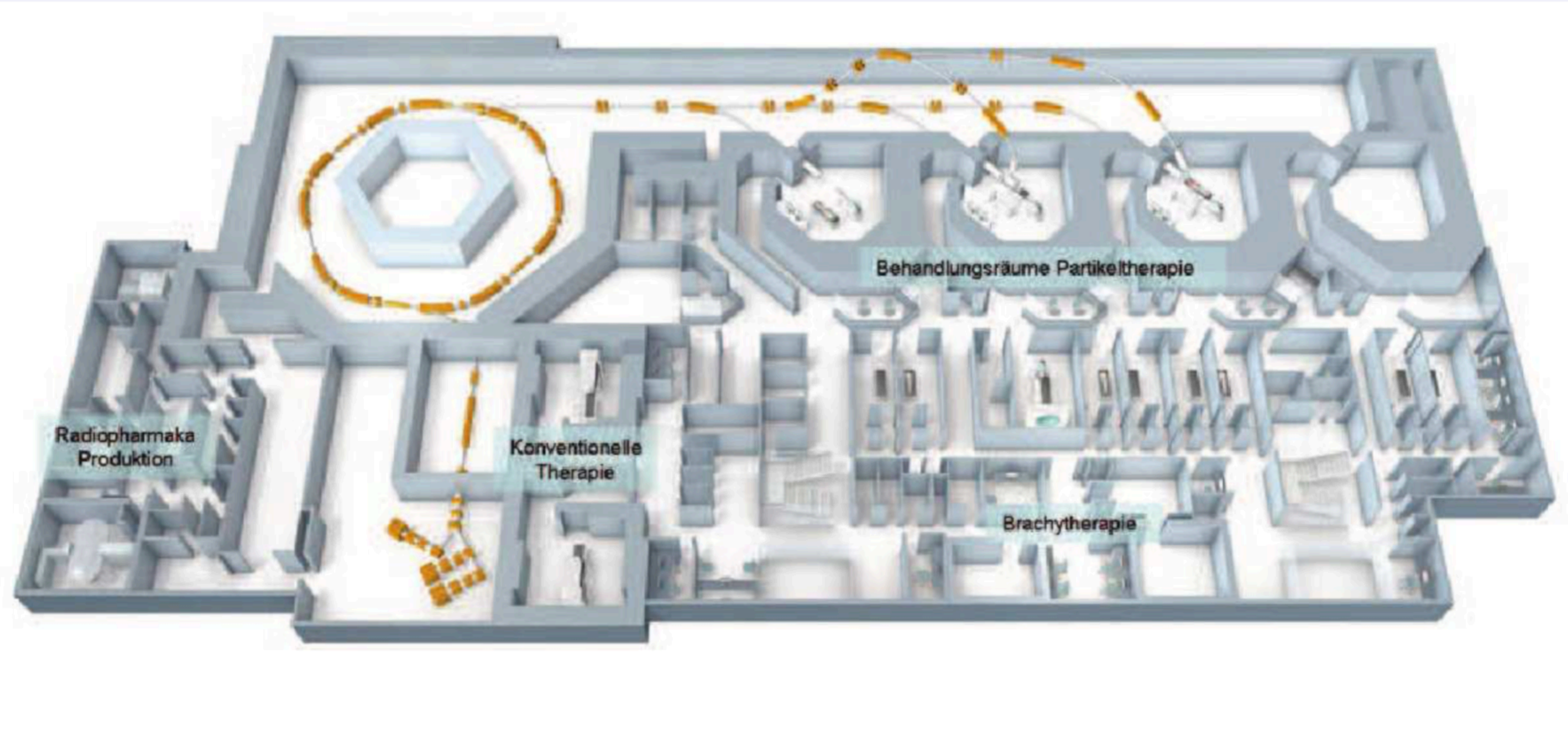
- **Better outcomes of inoperable tumors in dedicated hospital**

▶ HIT - **H**eidelberg **I**on-beam **T**herapy centre

▶ Rotating gantry in operation

▶ Dedicated hospital facility in operation

▶ Aim: 1000 patients / year

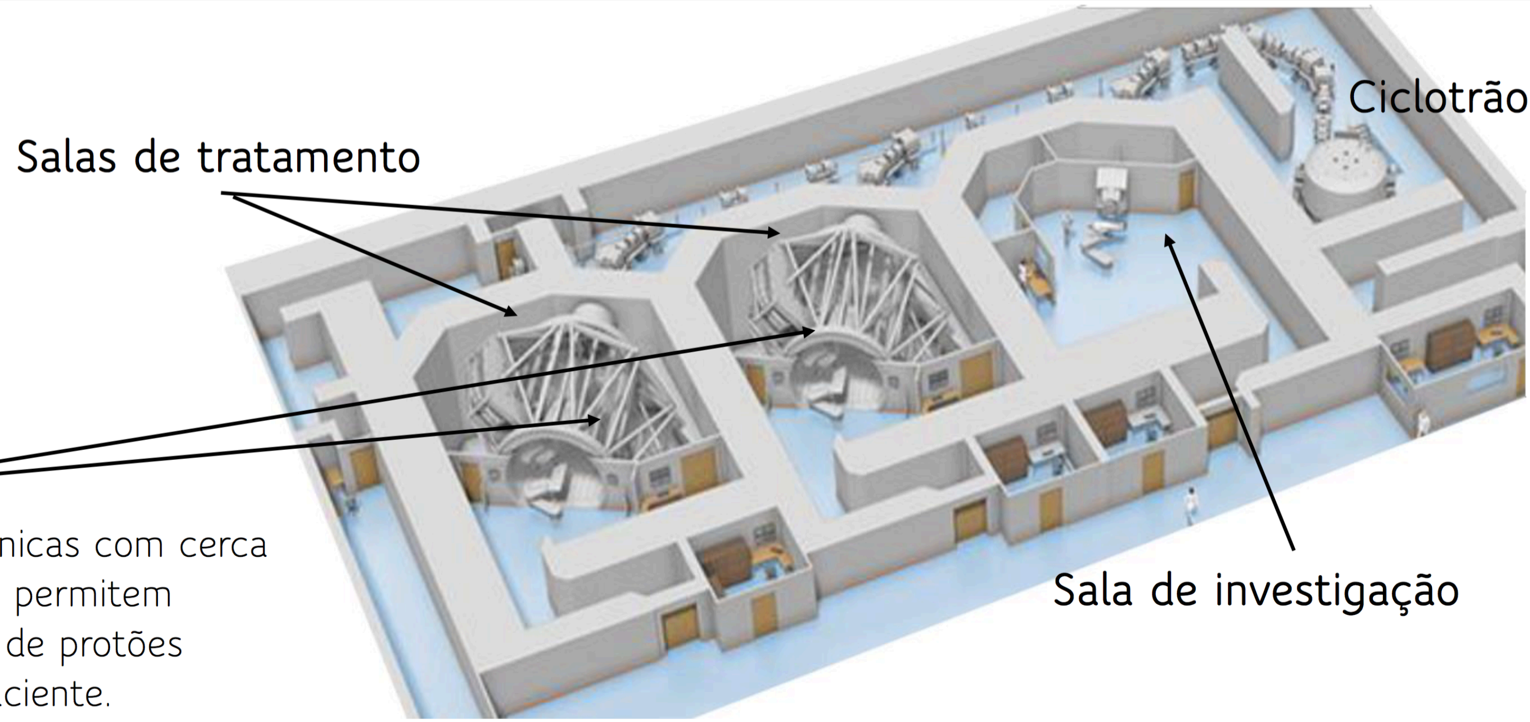


Courtesy of Prof. Dr. Thomas Haberer, HIT Heidelberg

1. Rationale for hadrontherapy

- **Better outcomes of inoperable tumors in dedicated hospital**

► Less complicated: proton therapy center (cyclotron instead of synchrotron)



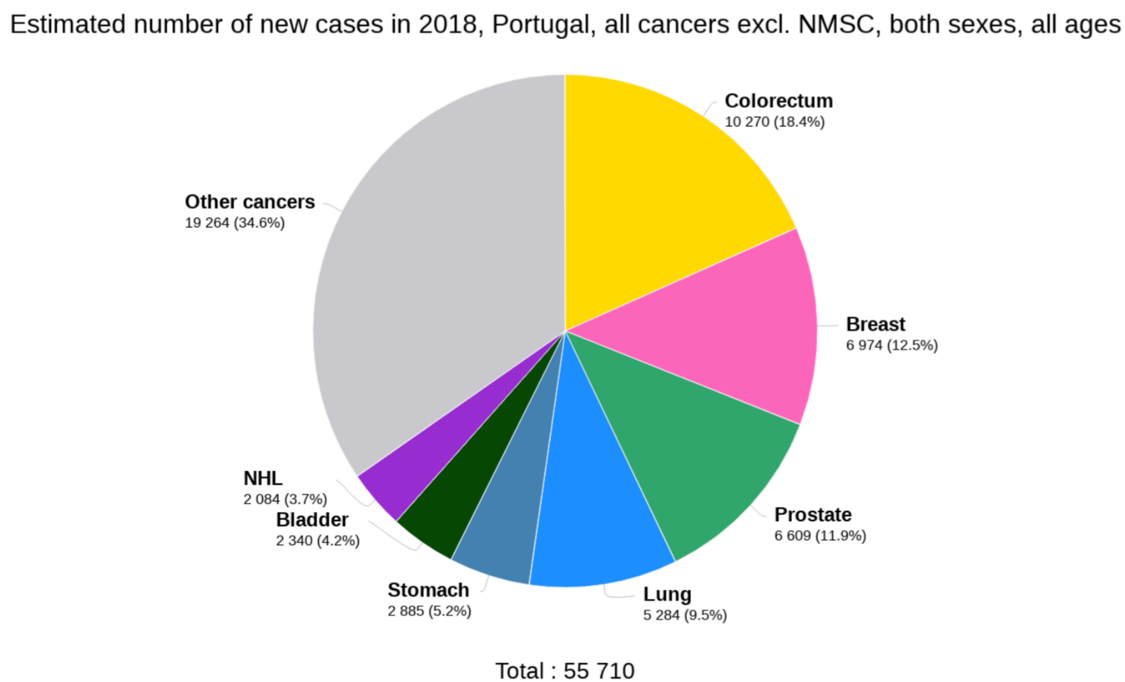
Gantries:
estruturas eletromecânicas com cerca de 3 pisos de altura e permitem curvar e rodar o feixe de protões 360º em torno do paciente.

https://iba-worldwide.com/proton-therapy/proton-therapy-solutions/proteus-plus

1. Rationale for hadrontherapy

- **A proton therapy facility in Portugal?**

Incidência de diferentes tipos de cancro em Portugal



Pacientes estimados com recomendação para terapia com protões

15% dos pacientes recomendados para radioterapia (50% of Total): **4200** pacientes/ano

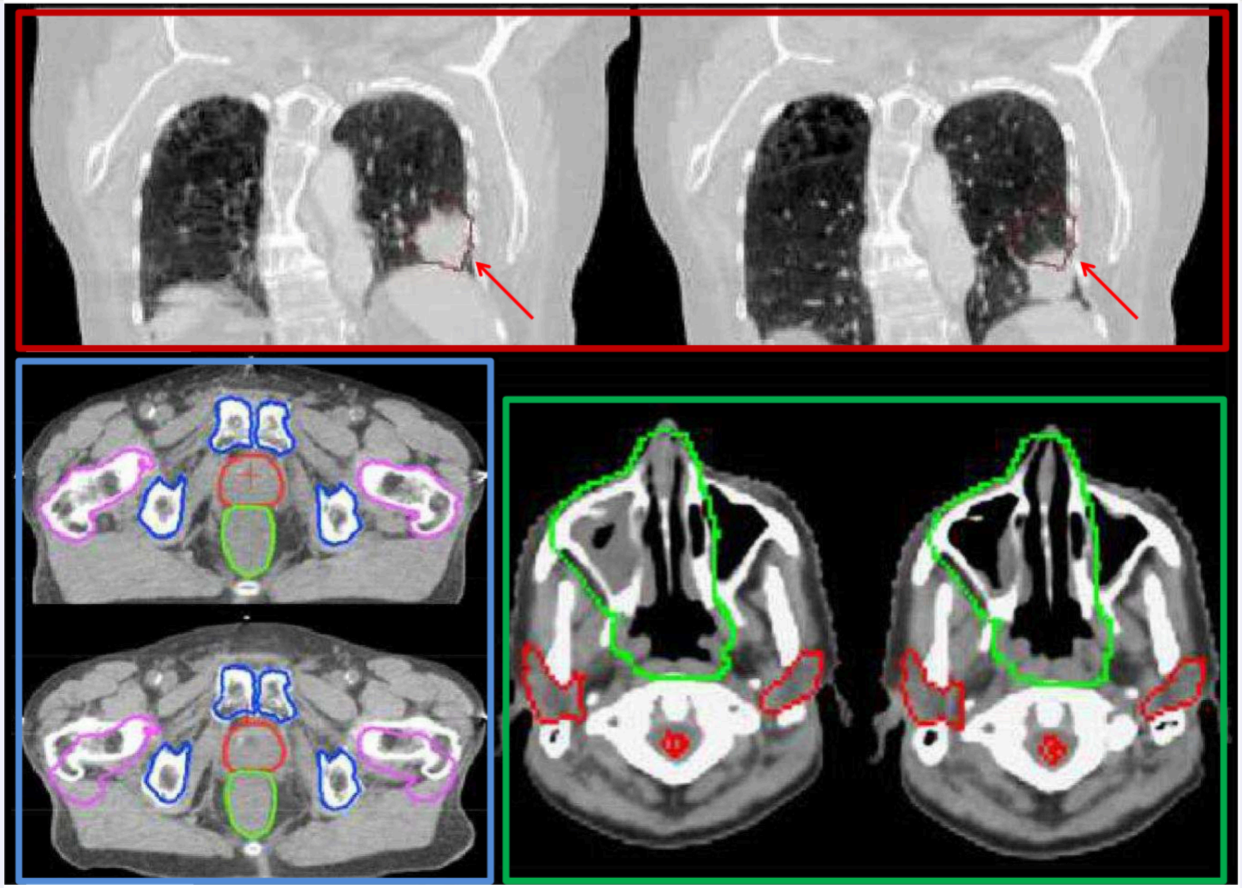
2017 Hirohiko Tsujii „Overview of Carbon-ion Radiotherapy" Journal of Physics: Conf. Series 777 (2017) 012032

1. Rationale for hadrontherapy

- **A proton therapy facility in Portugal?**

2. Rationale for imaging in hadrontherapy

Morphologic changes / patient positioning:

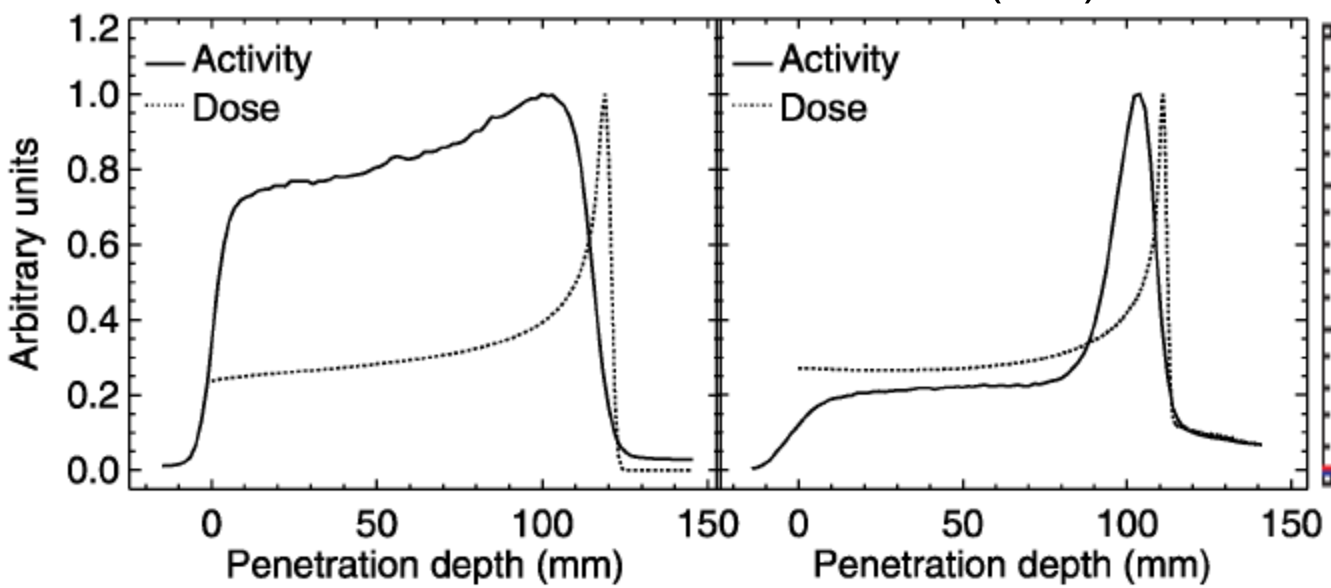


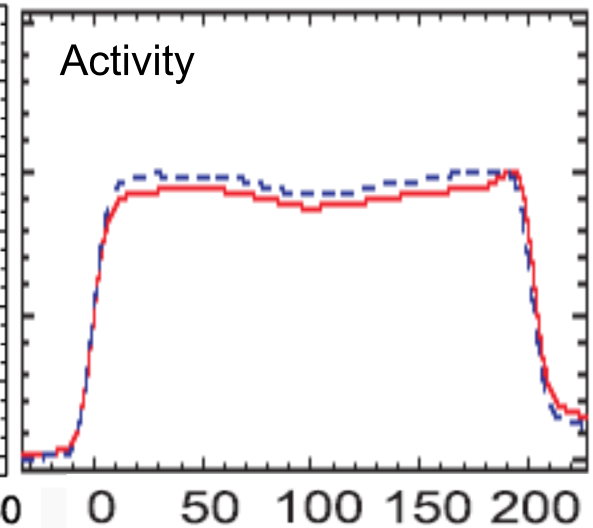
Engelsman and Bert 2011
Lüchtenborg PhD 2012

Very high conformality provides high-precision and highly accurate RT, but need for RT imaging also increases (e.g. next slide).

3. In-beam PET: Near future
Monitoring other species

- Protons (p^+):
- Carbons (C^{6+}):
- Helium-3 (He^{2+}):





- Proton and helium: only target activation

Protons: Parodi et al., IEEE Trans Nucl Sci 52 (2005)

Helium: Fiedler et al., IEEE Trans Nucl Sci 53 (2006)

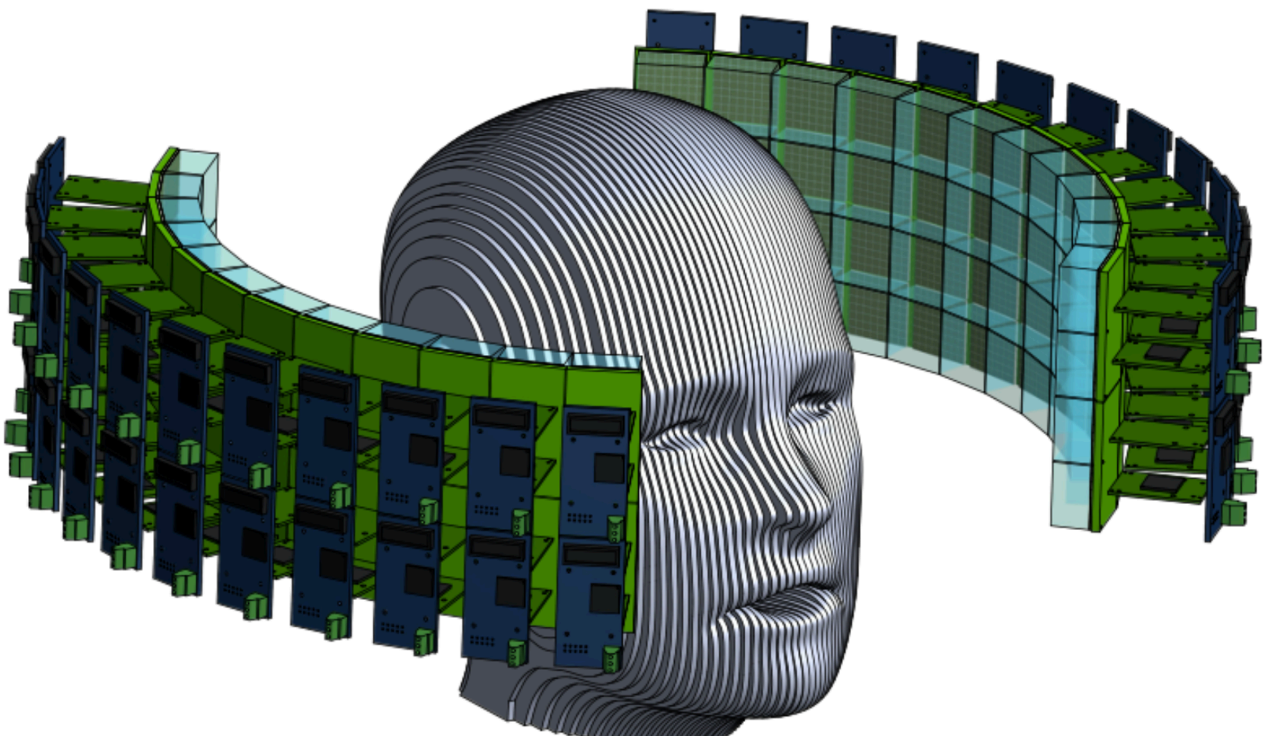
Photons: Enghardt et al., Phys Med Biol 51 (2006)

3. In-beam PET: monitoring proton therapy

- Consortium between PETsys Electronics (Lisbon), LIP (Lisbon & Coimbra), ICNAS-UC, IST, Un. Texas at Austin, USA, MDACC (Houston), USA

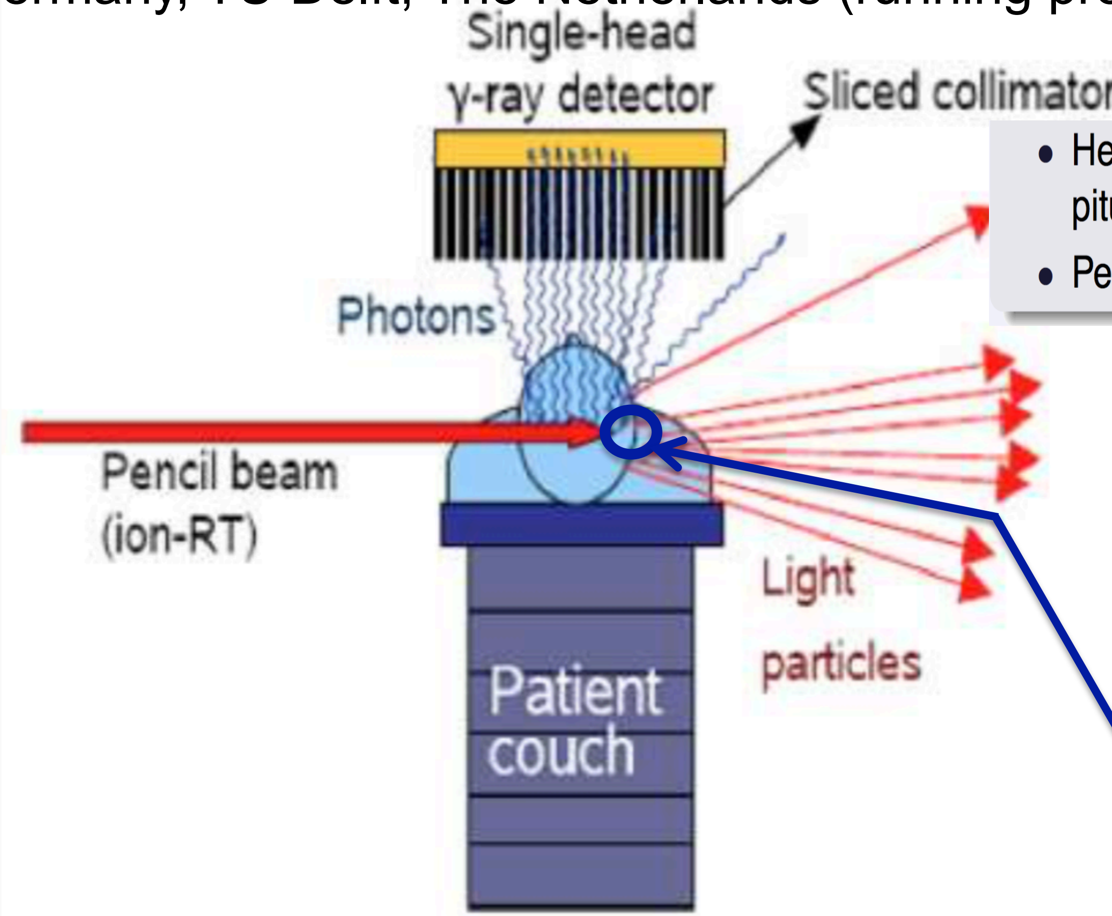
TOF-PET for Proton Therapy (TPPT) – In-beam Time-of-Flight (TOF) Positron Emission Tomography (PET) for proton radiation therapy

Coincidence time resolution of 200 ps FWHM (corresponds to Gaussian with 3 cm FWHM)



4. Prompt-gamma imaging: the concept

- Collaboration between LIP (Lisbon & Coimbra), UC, IST, FCUL, LMU Munich, Germany, TU Delft, The Netherlands (running proton therapy facility



- Head irradiation: nasal cavities (cavity filling) and pituitary (change in brain density)
- Pelvic irradiation: prostate (patient mispositioning)

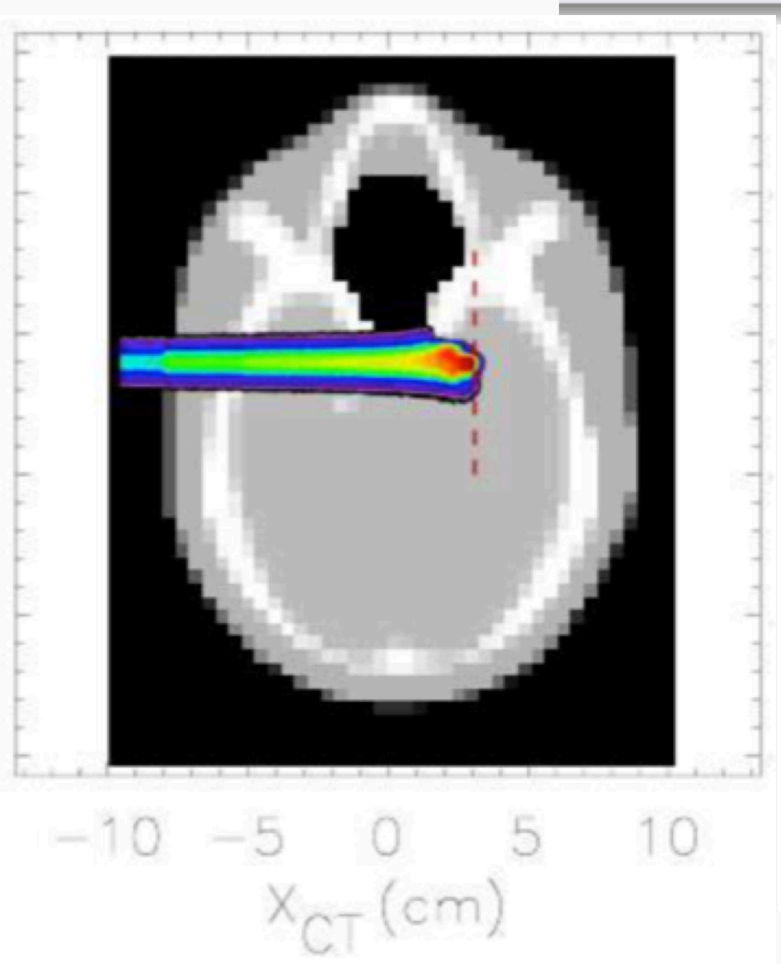
Image with prompt gammas “stops” at beam range

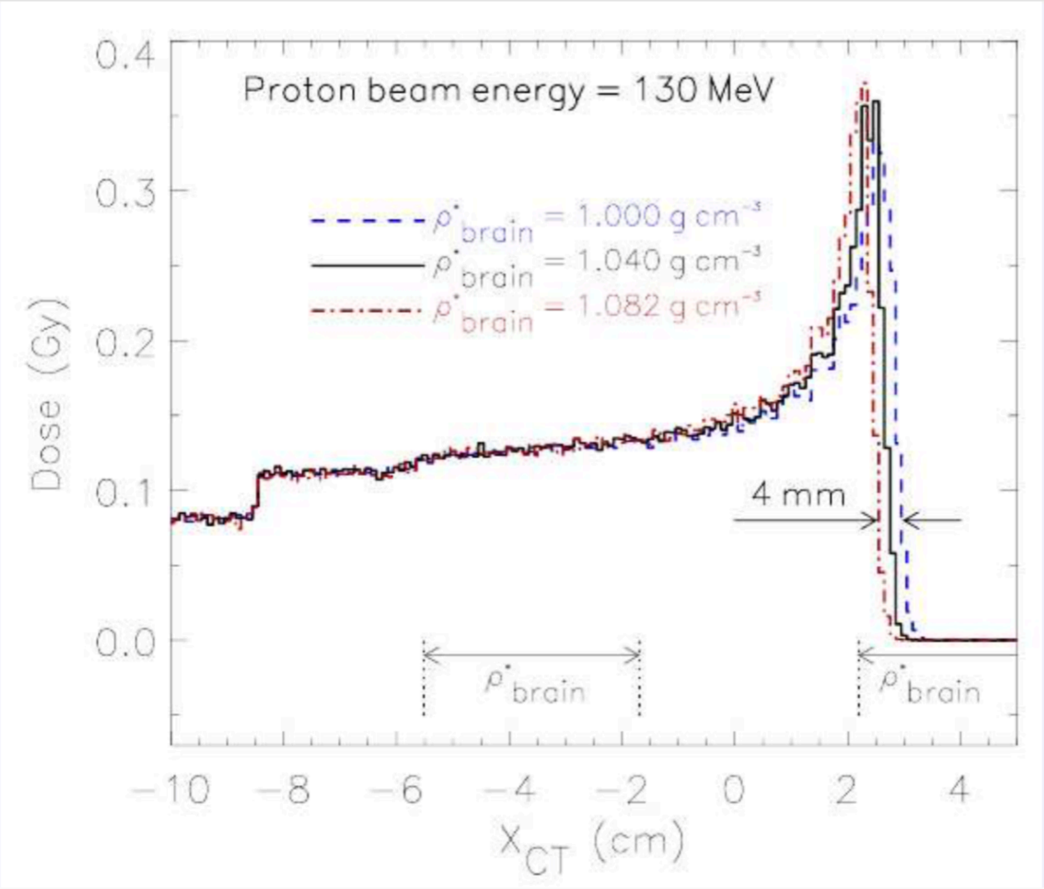
Provides real-time images of selected region without rotation of beam source.

4. Prompt-gamma imaging: feasibility study

4.1 Change of brain density due to fractionated RT

- Conjecture: brain tissue hypo/hyperdense
- Corresponding dose profiles (protons):



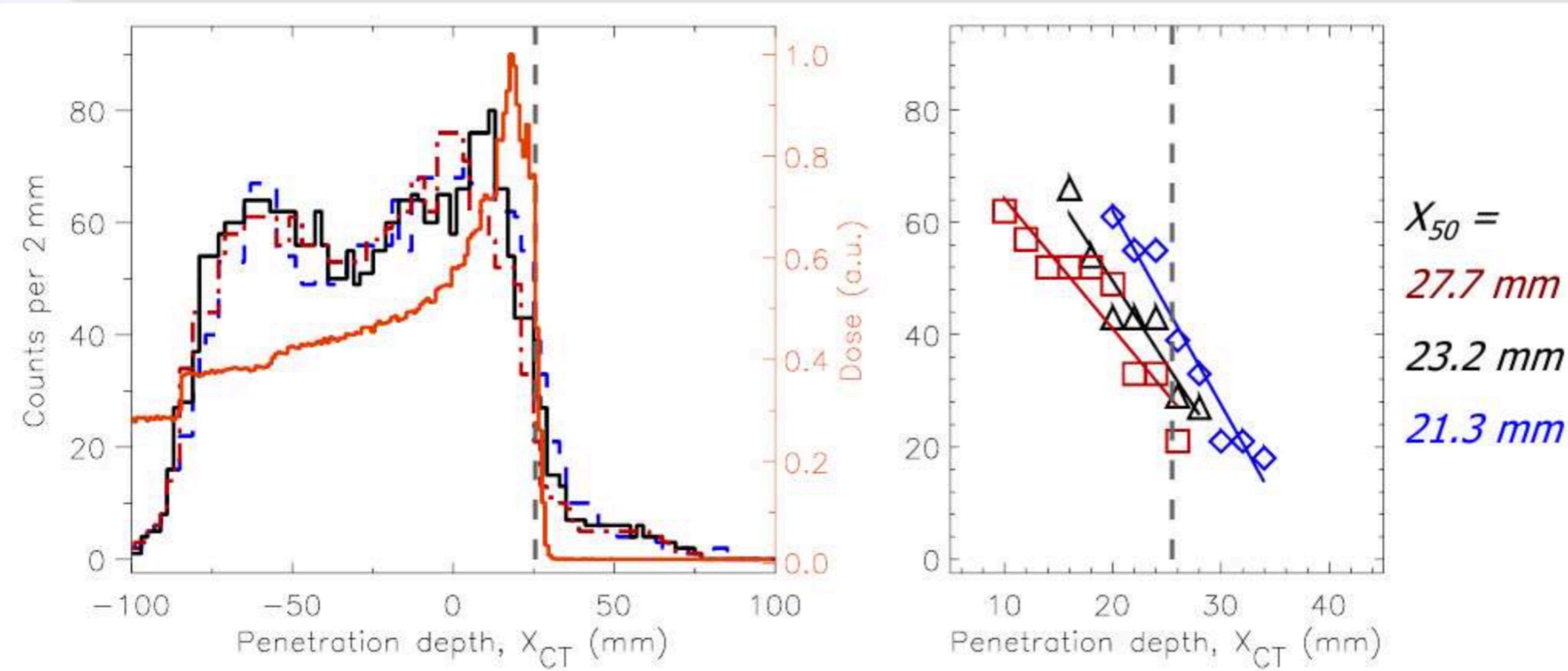


(Cambraia Lopes et al Physica Medica 2018)

4. Prompt-gamma imaging: feasibility study

4.1 Change of brain density due to fractionated RT

- Conjecture: brain tissue hypo/hyperdense
- Monte Carlo results with proposed detector (Geant4):



(Cambraia Lopes et al Physica Medica 2018)

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