MR-guided Proton Therapy: current status and beyond

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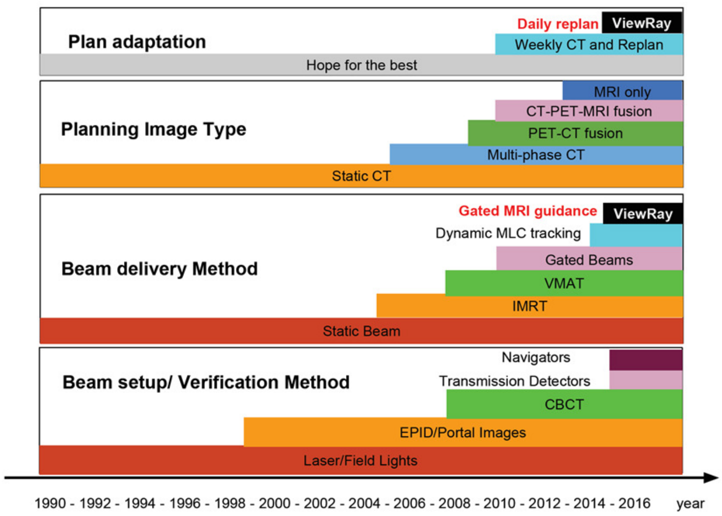
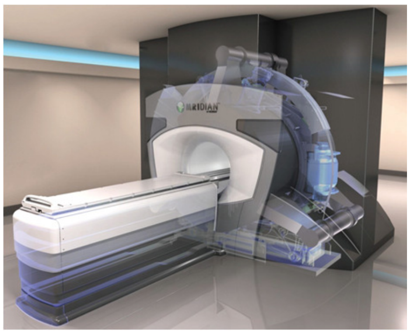
Technical developments in radiotherapy



Courtesy: dr. Brad Oborn (Univ. Wollongong)

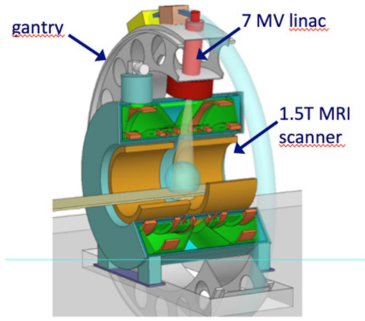
Real-time MRI-guided radiotherapy

MRIdian (ViewRay Inc.)



- Gantry with three ^{60}Co source heads
- Split-bore 0.35 T magnet

Integrated MRI-Linac



Elekta/Philips (Utrecht group)

These hybrid systems facilitate

- Beam delivery under gated MRI guidance
- Plan adaptation by daily re-planning

MR-linac opinion leaders

Future of medical physics: Real-time MRI-guided proton therapy

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First Published: 4 July 2017
DOI: 10.1002/mp.12371
Accessed: 1995 time(s)
Free

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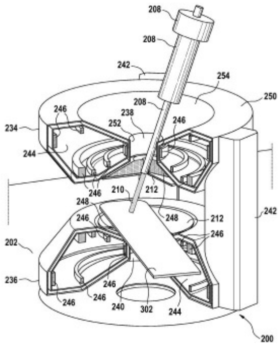
Four Dutch centres each fighting for #protontherapy. I like to retweet my 23-7'14 statement: Protons must become MRI guided or will not be.

Integration of MRI and proton therapy

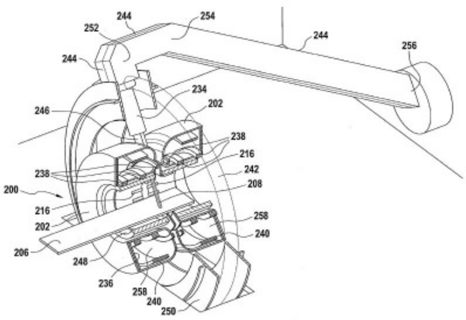
Vision: develop an ***in-beam*** **MRI scanner**

- *WYSIWYT: Treat what you See*
- *WYTIWYT: Track what you Treat*

patent EP2376195



Open MRI scanner



Split-bore MRI scanner

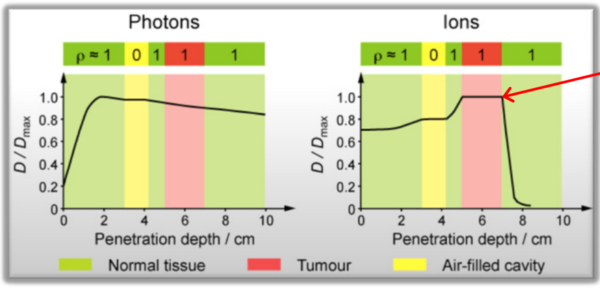
Rationale of MRiPT

1. **Image-guidance in proton therapy lags behind IGXT**
   - 2D X-ray imaging (throughout available)
   - in-room CT (only available in some centers)
   - on-board CBCT (recently released product)

   X-ray based systems:
   - limited intra-fractional imaging capabilities
   - limited soft-tissue contrast

Rationale of MRiPT

2. Protons are **more sensitive to anatomical variations** than photons
   - **material composition** in beam path determines **Bragg peak location**

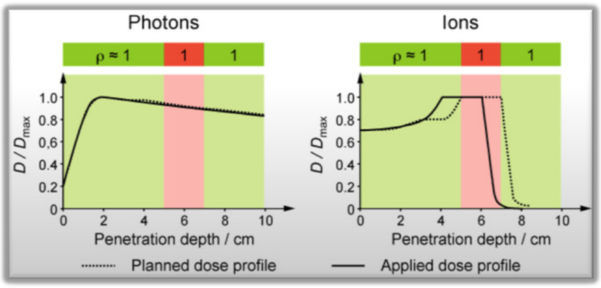


spread-out Bragg peak (SOBP) perfectly covers tumour volume and maximally spares the normal tissue at distal end

- What happens if the air-filled cavity (ρ ≈ 0) is replaced by normal tissue (ρ ≈ 1)?

Rationale of MRiPT

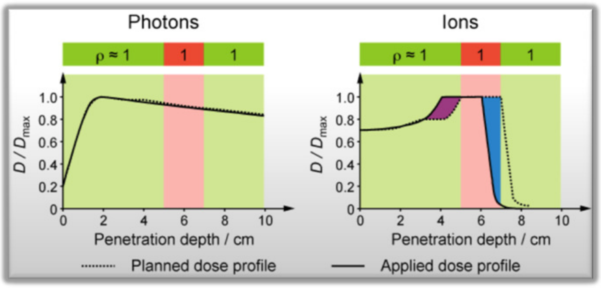
2. Protons are **more sensitive to anatomical variations** than photons
   - **material composition** in beam path determines **Bragg peak location**



- **Protons**: SOBP will shift stream upwards
- **Photons**: hardly any dosimetric effect between planned and applied dose

Rationale of MRiPT

2. Protons are **more sensitive to anatomical variations** than photons
   - **material composition** in beam path determines **Bragg peak location**



changed ion range will cause

- **overdose** in normal tissue
- **underdose** in tumour

- Because of these uncertainties, relatively **large margins** are still needed

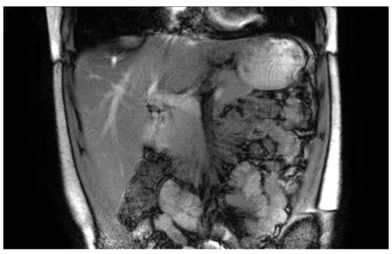
Currently the dosimetric benefit of proton therapy is **not** fully exploited !!

Motivation for MRI

- **MRI** offers
  - ✓ Fast real-time imaging
  - ✓ Superior soft tissue contrast
  - ✓ Freedom from radiation dose

- **Challenge**

Integration of MRI and PT for on-line image-guidance faces the challenge of their **mutual interaction**



2D-cine MRI scan showing intrafractional motion in the abdomen

Technical challenges in MRiPT

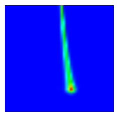
Vision: integrate MR scanner at beam isocenter

R I S K

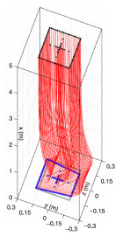
- MR image degradation from gantry and beam line magnets
- MR image degradation during irradiation
- Radiation harness of magnet
- Beam interaction with RF antenna
- Planning on MR images
- Range detection
- Dosimetry in the presence of a magnetic field
- **Beam deflection due to magnetic field of MR scanner**

Beam deflection in magnetic field

Simulation studies:



- **2008 Dose to phantom in uniform $B_\perp$ field**
  Raaymakers *et al.*, Phys Med Biol 53(20), 2008
  Wolf & Bortfeld, Phys Med Biol 57(17), 2012
- **2014 Dose to patient in uniform $B_\perp$ field**
  Moteabbed *et al.*, Med Phys 41(11), 2014
  Hartman *et al.*, Phys Med Biol 60(11), 2015
- **2015 Dosimetric effects of MRI fringe field**
  Oborn *et al.*, Med Phys 42(5), 2015
- **2017 Fast and accurate numerical model**
  Schellhammer & Hoffmann, Phys Med Phys 62(4), 2017



Experimental validation:

- **2017 First „*in magnet*" film dosimetry in slab phantom**
  Schellhammer *et al.*, arXiv 1709.00373

Measurement setup

Proton beam

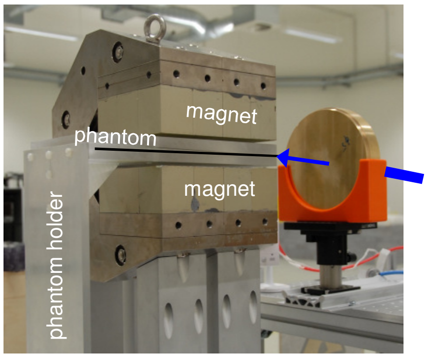
- Brass collimators with circular voids (∅10 mm)
- Pencil beams (blue arrow in figure)
- Energy: 80, 100, …, 180 MeV

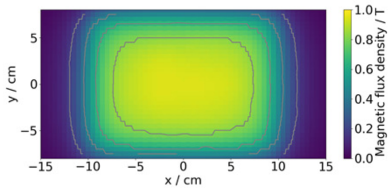
Tissue equivalent phantom

- 2 horizontal PMMA slabs
- placed between magnet poles
- 2D dose measurement with Gafchromic EBT3 film placed in central plane (1° inclination)

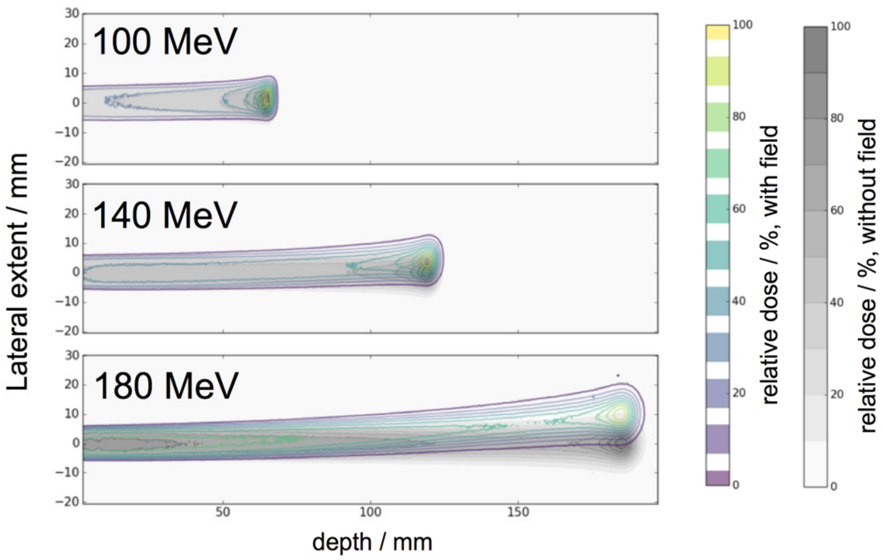
Magnetic field

- C-shaped 0.95 T permanent $Nd_2Fe_{14}B$ dipole magnet (20 × 15 cm^2)
- 3D Hall probe magnetometry used to map out the main and fringe field





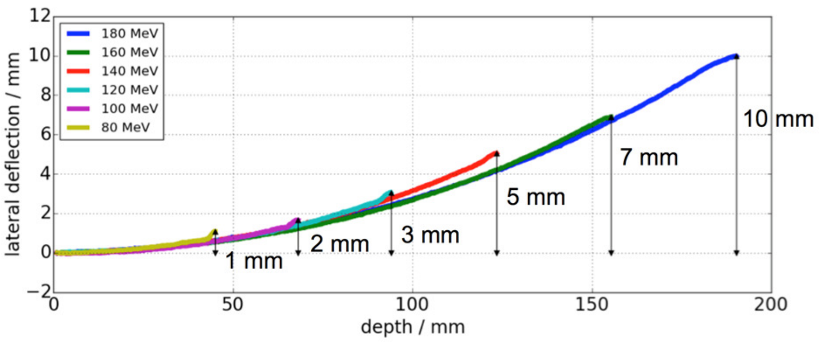
Results: 2D relative dose distributions



Results: central beam trajectory

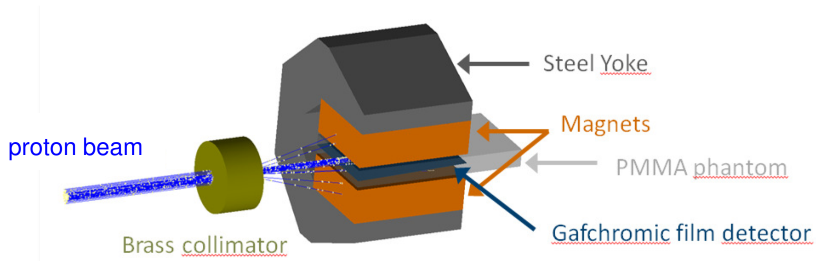
Beam deflection

- Increases with initial beam energy
- Lateral displacement of Bragg peak position increases from 1–10 mm for 80–180 MeV



Deflected beam trajectories for different initial beam energies

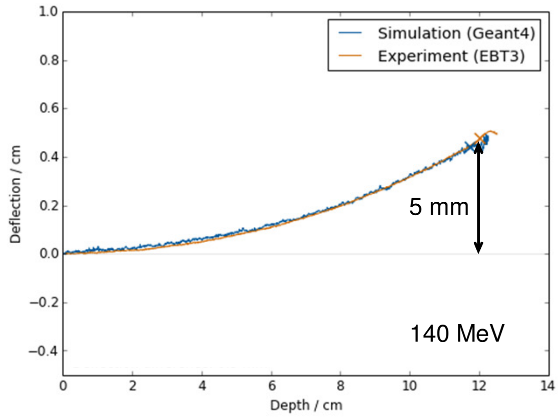
Monte Carlo simulation (Geant4)



- **Beam** : E_0 = 70–180 MeV, σ_r = 4 mm, d = 170 cm
- **Collimator** : ∅ = 5, 10 mm, r_{out} = 9 cm, l = 6.6 cm, d = 20 cm, brass
- **Phantom** : 30 × 15 × 3 cm^3
- **Film** : 20 cm × 15 cm × 28 µm, tilted by 1°
  Gafchromic® EBT3 material = polyester + LiPAD
- **Magnets** : magnetic field extension: 50 × 50 × 50 cm^3

Comparison: simulation *vs.* experiment

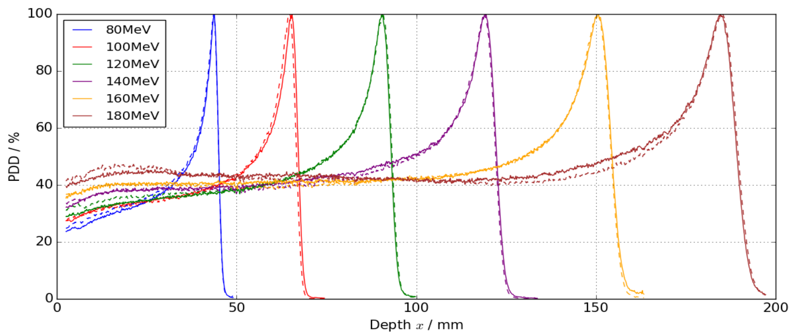
Good agreement between **predicted** and **measured beam path**



Results: depth-dose distribution

Measured percentage depth-dose curves

- Similar with and without magnetic field
- No significant beam retraction of projected range (within measurement uncertainties)



Measured PDDs in PMMA with (solid line) and without (dashed lines) magnetic field

Technical challenges in MRiPT

Vision: integrate MR scanner at beam isocenter

R I S K

- **MR image degradation from gantry and beam line magnets**
- MR image degradation during irradiation
- Radiation harness of magnet
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- Planning on MR images
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- Dosimetry in the presence of a magnetic field
- Beam deflection due to magnetic field of MR scanner

Mutual electromagnetic interference

1. Interference of PT system with MR system

*Does the presence of a static (DC) or time varying (AC) electromagnetic field of the PTS perturb the MRI scanner's magnetic field such that the **MR image quality** is degraded?*

- Gradients of external magnetic fringe fields may compromise MR scanner's **magnetic field homogeneity**

- Perturbation of B_0 field (ΔB_0) results in **frequency shift** (Δf) of MR signal
- Δf may result in **phase changes** of MR signal, leading to image **blurring** and **geometrical deformation**

- Pulse sequences have **different sensitivity** to B_0 field perturbations

Mutual electromagnetic interference

2. Interference of MR system with PT system

*Does the presence of a static (DC) or time varying (AC) electromagnetic field of the MRI system perturb the PTS's magnetic field such that the **PT beam quality** is degraded?*

- MR magnetic field induced effects on **beam control** and **monitoring**?
- Effect of **MR fringe field** on scanning magnets and ionization chambers in PBS nozzle?

Sources of EM interference

1. Proton Therapy system

- Large ferromagnetic masses: cycloton, gantry, beam stopper
- Static magnetic fringe field of cyclotron
- Dynamic magnetic field of: rotating gantry, beamline magnets, bending magnet on gantry, scanning magnets
- RF accelerating voltage operates in 10-100 MHz range

2. MRI system

- Static main magnetic (B_0) field — Only far fringe field has potential to interfere
- Dynamic gradient fields for spatial encoding — Fringe fields are negligible
- RF field for spin excitation — RF field is negligible outside Faraday cage

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Proton beam dosimetry in B-field

- **Magnetic field impacts the response of dosimetry equipment**
  - Effects of magnetic field exposure on dosimetry tools should be investigated
  - QA procedures for PT in the presence of B-fields have not been established
  - Dedicated radiation dosimetry methods for MRXT could be instrumental
  - **Radiochromic film dosimetry**:
    - B-field may affect monomer crystal orientation and polymerization [Reynoso *et al*. 2016]
    - Magnetokinetic changes may explain dose-dependent under-response in B-field
  - **Electron return effect**: will be less significant for MRPT than for MRXT
    - Simulation studies show a local dose enhancement of less than ~10% within 1 mm
    - First measurements with our 0.95 T magnet confirm these results

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MR-only based treatment planning

- **Dose calculation**
  - Electronic stopping power (ESP) is most important tissue property for PT
  - Currently based on CT-based conversion from HU into SPR
  - MR images do not contain stopping power information

- **Generation of pseudo-CT images from MR images**
  1. **Classification-based** tissue segmentation (bone, air, water, fat, muscle, ...)
     - Based on ultrashort echo time (UTE) sequences
     - For brain tumors: minor and clinically acceptable deviations from reference CT images

     Rank *et al.*, Radiother Oncol 109(3), 2013; Edmund *et al.*, Radiat Oncol 8, 2013
  2. **Transformation** of intensity values of in-phase MR images into HU
     - For brain and prostate tumors: 2D Gamma Index >91% at 1% / 1mm criterion

     Koivula *et al.*, Med Phys 43(8), 2016

MR-only based treatment planning

- **For heterogeneous tissues**
  - Large uncertainties in stopping power ratios exist for PT
  - Dedicated MR sequences to extract WEPL maps are under investigation

- **For moving targets**
  - Classification-based methods are currently too slow
  - More accurate and fast translation of MRI information into ESP is required

Conclusions

1. **Magnetic field induced beam deflection**
   - is measurable with film dosimetry and accurately predictable with MC
   - dose calculation is feasible for treatment planning in B-fields
2. **Mutual electromagnetic interference**
   - image degradation is expected from transient magnetic fringe fields of beamline magnets
   - fringe field of MR will affect ionization chambers in PBS nozzle
3. **Proton beam dosimetry in magnetic fields**
   - reference dosimetry protocols need to be established
   - local dose enhancement by ERE is small but non-negligible
4. **MR-only based treatment planning**
   - feasibility shown for homogeneous tissues (brain, prostate)
   - for heterogeneous tissues: work in progress

Acknowledgements

OncoRay (Medical Radiation Physics)

Sonja Schellhammer
Sebastian Gantz
Armin Lühr
Leonhard Karsch
Jörg Pawelke

HZDR (Institute of Radiation Physics)

Michael Bussmann
Karl Zeil

IBA (R&D Department)

Julien Smeets
Sébastien Henrotin
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