Non-clinical Research: Medical Radiation Physics

Georg D[1,2]

[1] Div. Medical Rad. Phys., Dept. of Radiation Oncology / Medical Univ. Vienna & AKH Wien

[2] Christian Doppler Laboratory for Medical Radiation Research for Radiation Oncology

[3] PEG MedAustron

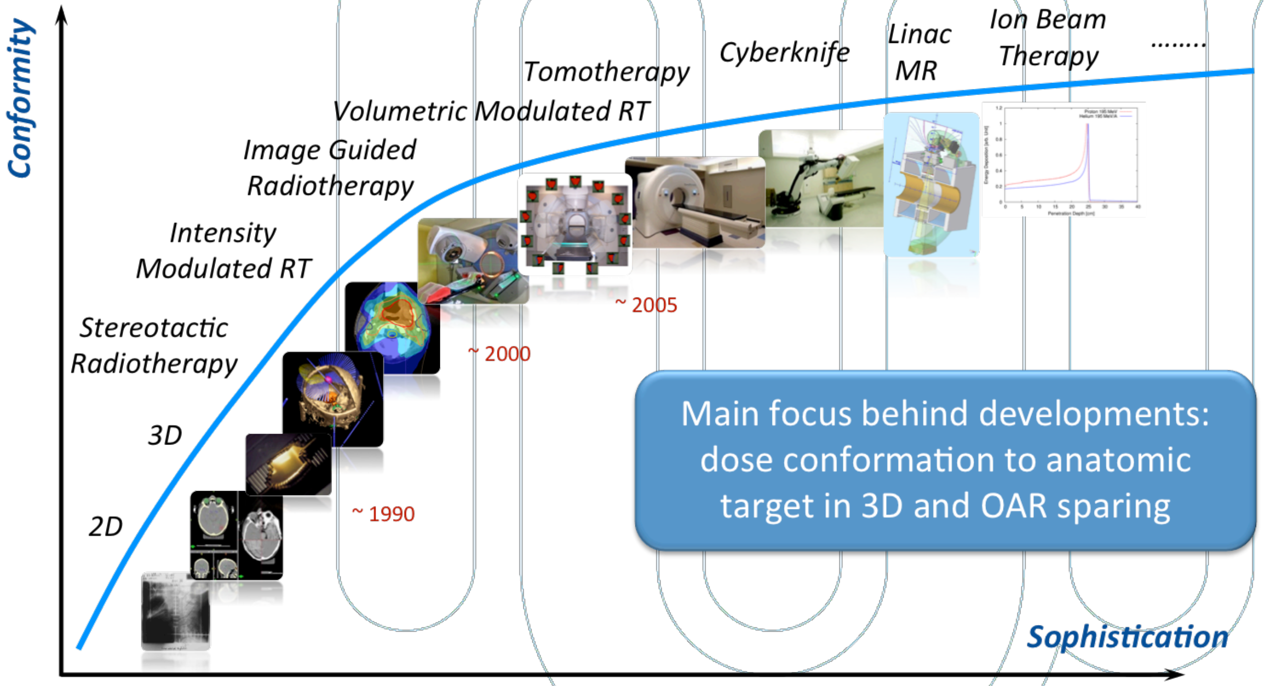
Outline of talk

- Background
- Research topics
  - → More general
- Examples
  - → **Novel ion species**
  - → **Moving organs**
  - → **Dose painting**
- Outlook

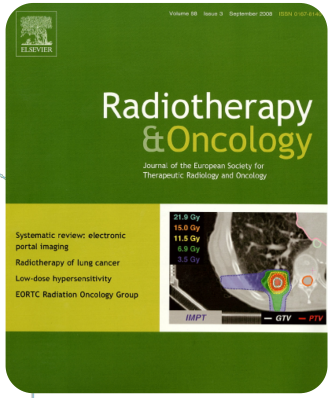
Editors: T. Schreiner & D. Georg

The “view” of advanced photon beam therapy

- Medical Univ. Vienna: active research in external beam therapy and brachtherapy



Main focus behind developments: dose conformation to anatomic target in 3D and OAR sparing



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ELSEVIER

Radiotherapy
&Oncology

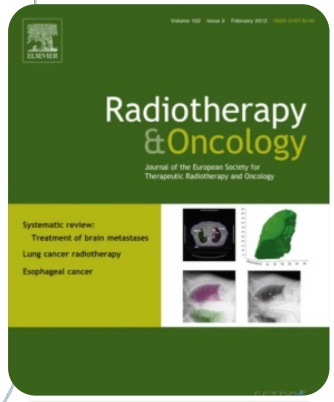
Journal of the European Society for
Therapeutic Radiology and Oncology

Systematic review: electronic portal imaging

Radiotherapy of lung cancer

Low-dose hypersensitivity

EORTC Radiation Oncology Group



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ELSEVIER

Radiotherapy
&Oncology

Journal of the European Society for
Therapeutic Radiotherapy and Oncology

Systematic review:
Treatment of brain metastases

Lung cancer radiotherapy

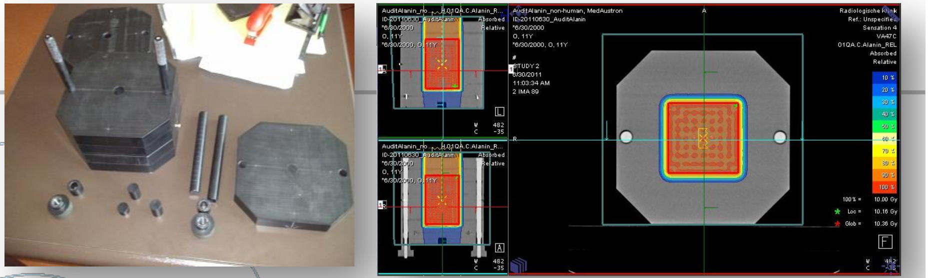
Esophageal cancer

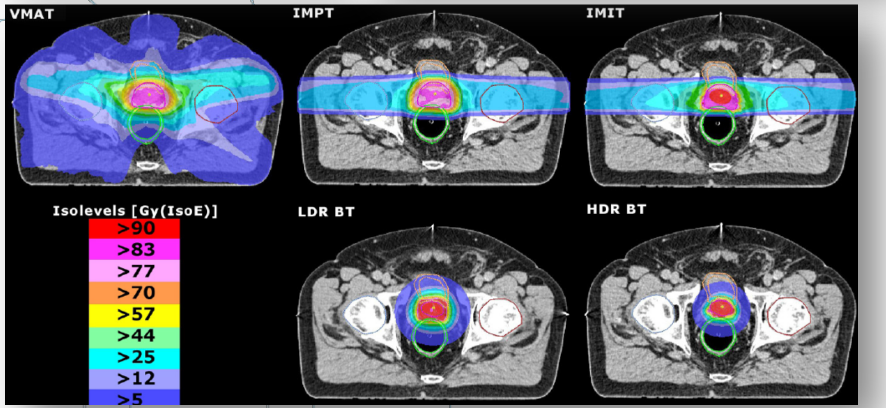
Benchmarking of photon beam innovations with particles became obvious

Ongoing projects

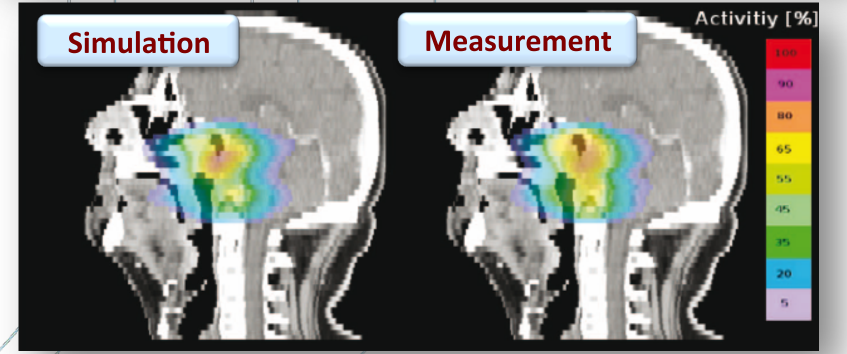
- Basic and applied dosimetry
- Dose calculation and optimization
  - ➔ Helium, Oxygen, Protons, Carbon ions
- Advanced imaging for ion beam therapy
  - ➔ Methodologies & Technology (MR, PET, kV)
- Monte Carlo simulations
  - ➔ Application driven
- **Research plan for 2015 - 2018**

Ableitinger et al





Georg et al



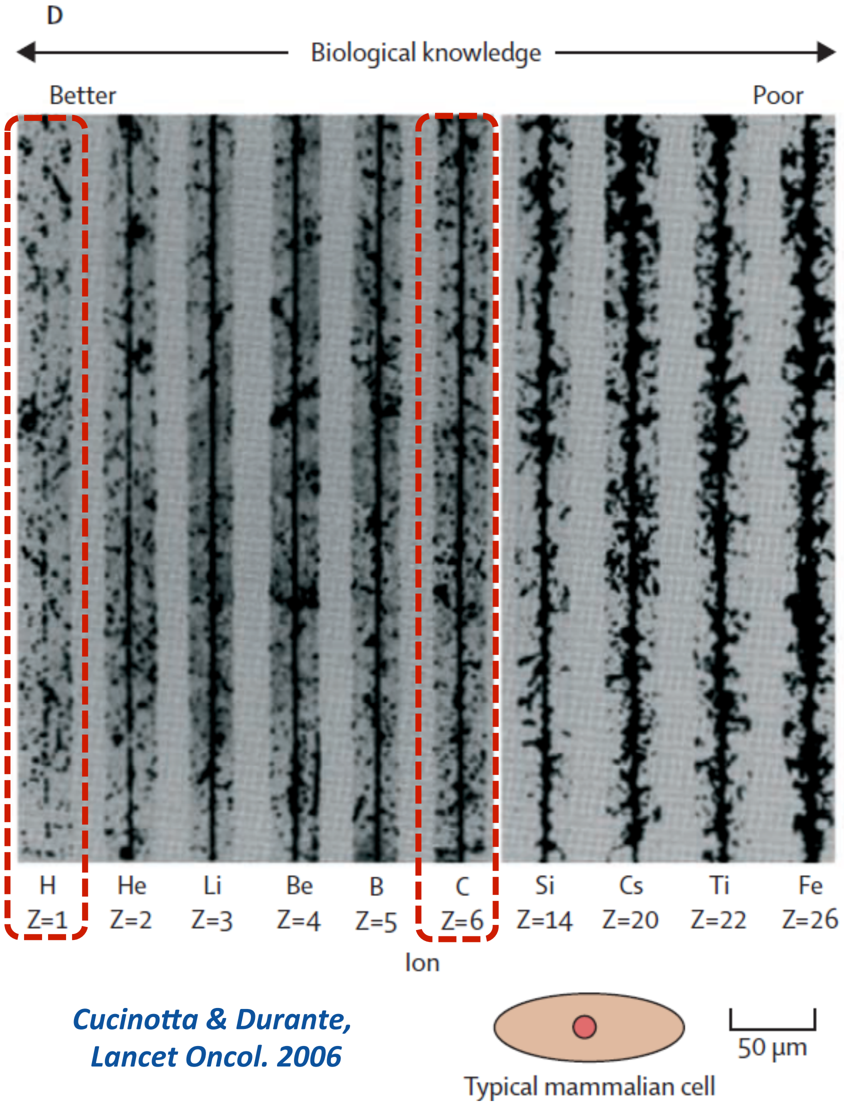
Kuess et al

Log Term Vision: Setting up multi-institutional research group

Particle beam therapy

- **Proton and Carbon ions are in clinical “focus”**
  - ➔ Many more particles in high and low LET range
- Lack of physics and radiobiological data on other ions
- Upcoming facilities offer new research opportunities

The “Future” of Particle Beam Therapy has just started



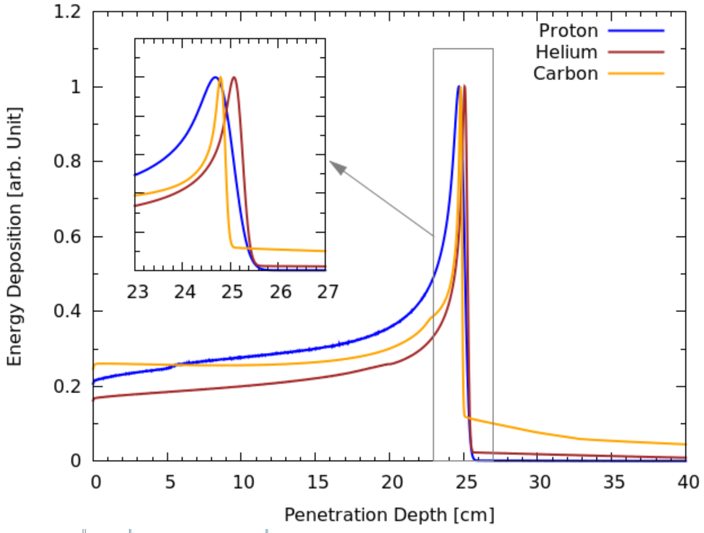
Cucinotta & Durante, Lancet Oncol. 2006

Novel Beam Qualities – e.g. Helium

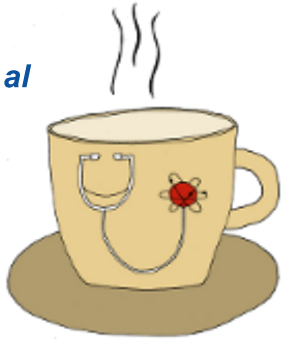
- **Helium** offers
  - ➔ Reduced scattering
  - ➔ Sharper penumbra
- Treatment planning system needed for pre-clinical assessment "in-silico"
  - ➔ In house development
- (Currently) very few experimental data
  - ➔ Both physic and radiobiology

Are Helium ions the better protons ?

Ströbele et al ZMP (2012) / Fuchs et al MP 39 (2012)



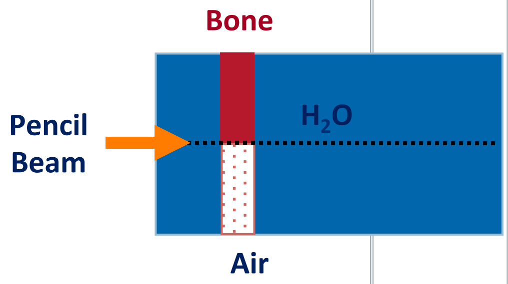
Hirtl, Fuchs et al



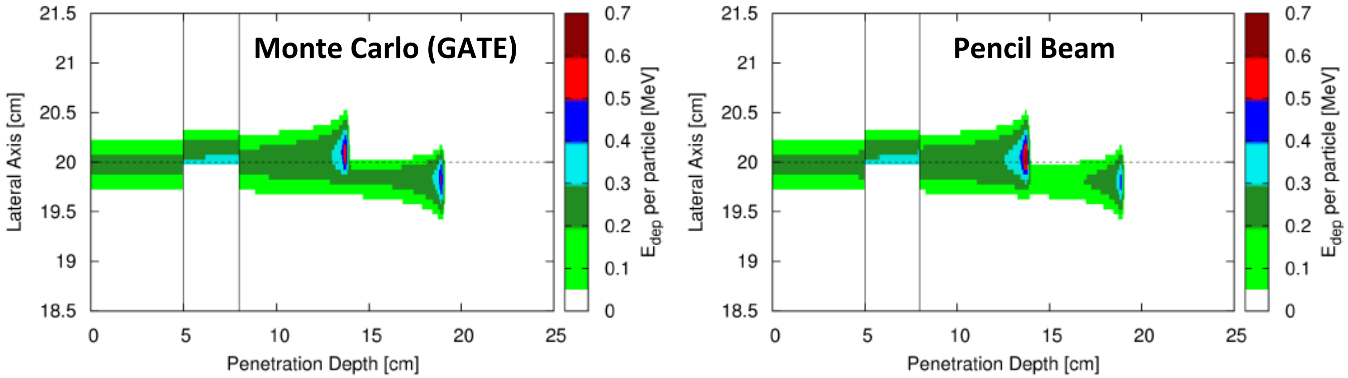
Vienna MOCCAMED Group

Helium Ion Pencil Beam Model – physical dose

- Validation Example – physical dose
  - ➔ γ - Index criteria with 2% dose and 2mm DTA criteria fulfilled



Fuchs et al Med Phys 39 (2012)



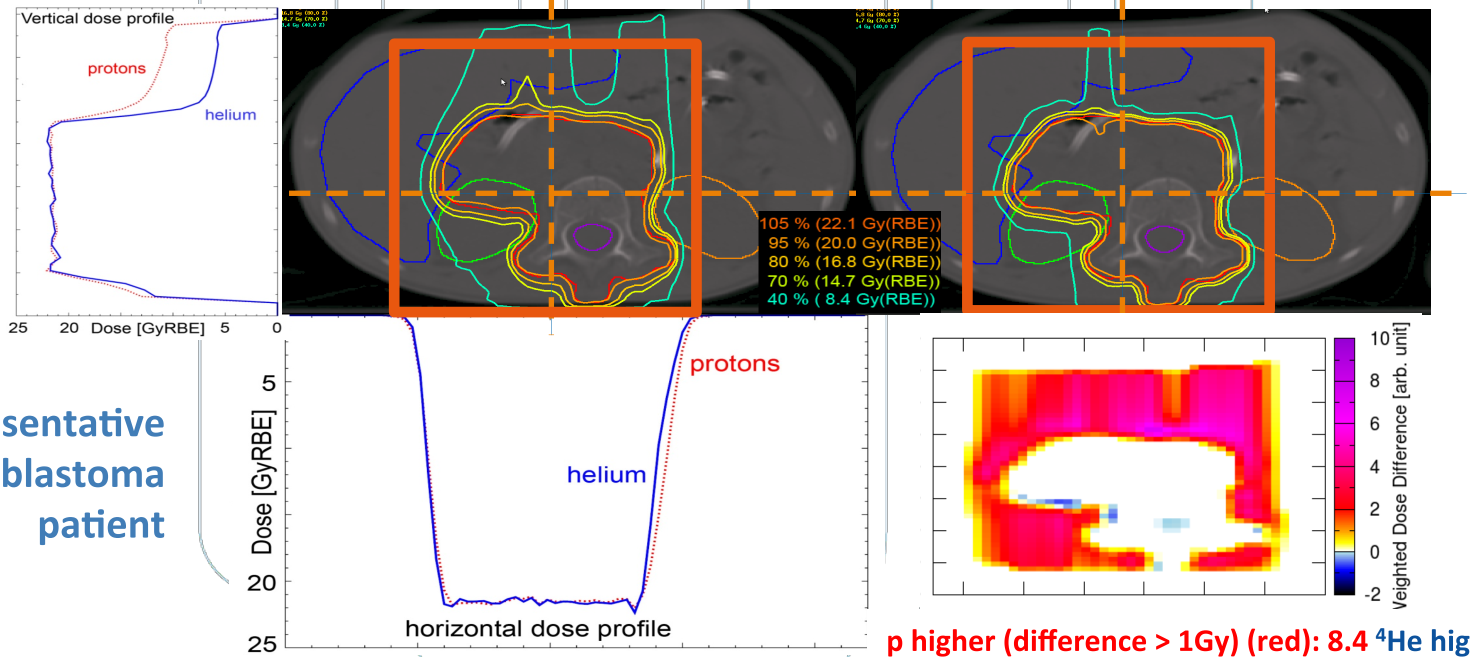
- Implemented in research treatment planning system

Research version of a He-ion TPS successfully developed

Treatment planning study using ^{4}He

- **Neuroblastoma patients:** 11 pts, 21.0 Gy(RBE)
- **Wilms tumour patients:** 5 pts, 14.4 Gy(RBE) + 10.8 Gy(RBE)
- **Hodgkin Lymphoma patients:** 9 pts, 19.8 Gy(RBE)

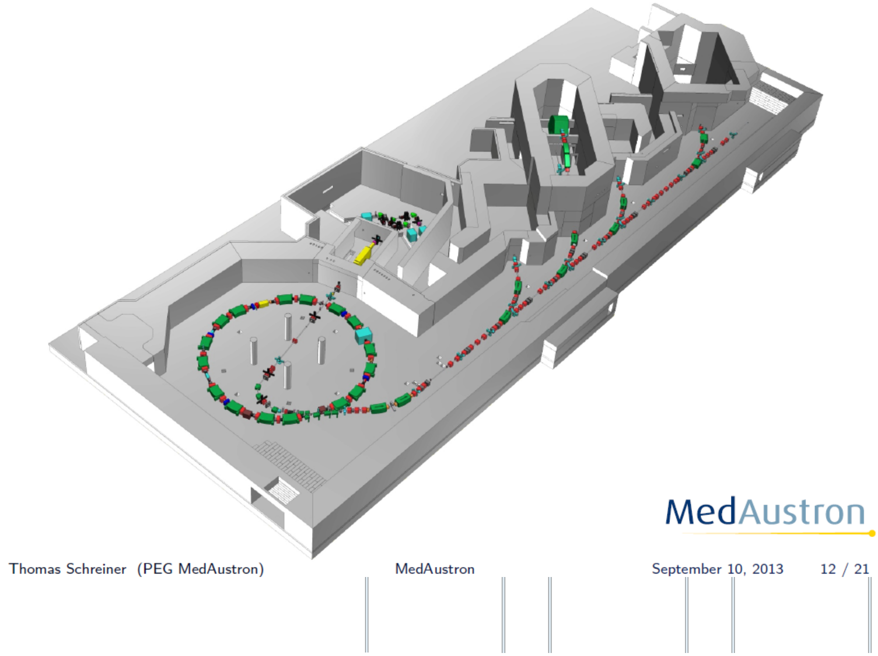
Representative Neuroblastoma patient



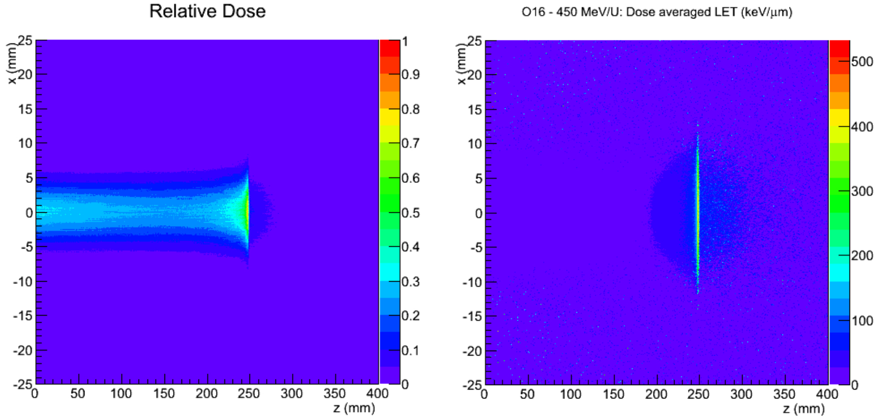
p higher (difference > 1Gy) (red): 8.4 ^{4}He higher (blue): 2.1

Next step: experimental validation of theoretical developments

Novel ion species – general aspects



Thomas Schreiner (PEG MedAustron) MedAustron September 10, 2013 12 / 21



- Multiple ion sources
- Energies to reach > 20 cm water equivalent depth
- “Flexibility” on site
- Current concepts based on dose distribution optimization
  - ➔ Non optimal for OAR

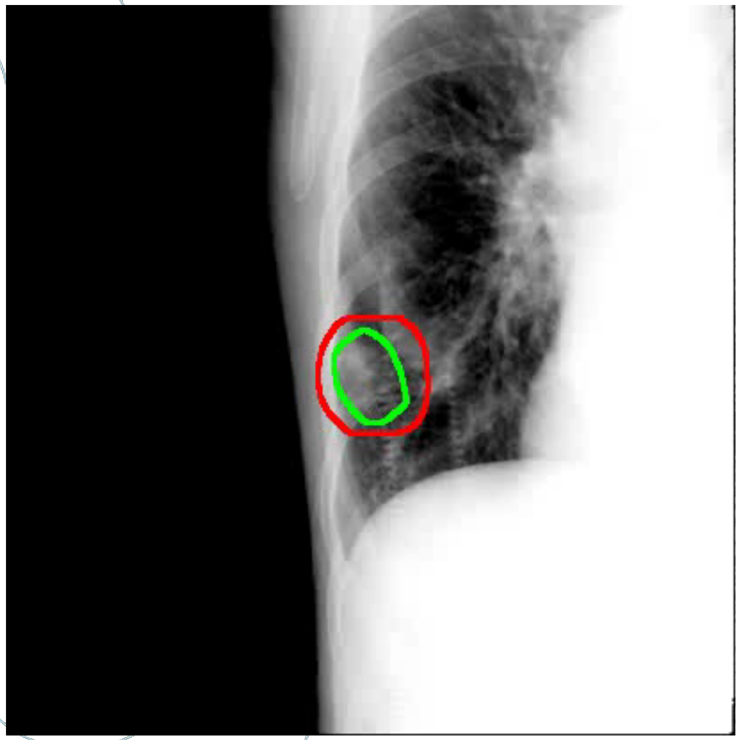
LET painting instead of dose painting is current focus of research

Lehner, Fuchs, …

Moving targets & scanning beams

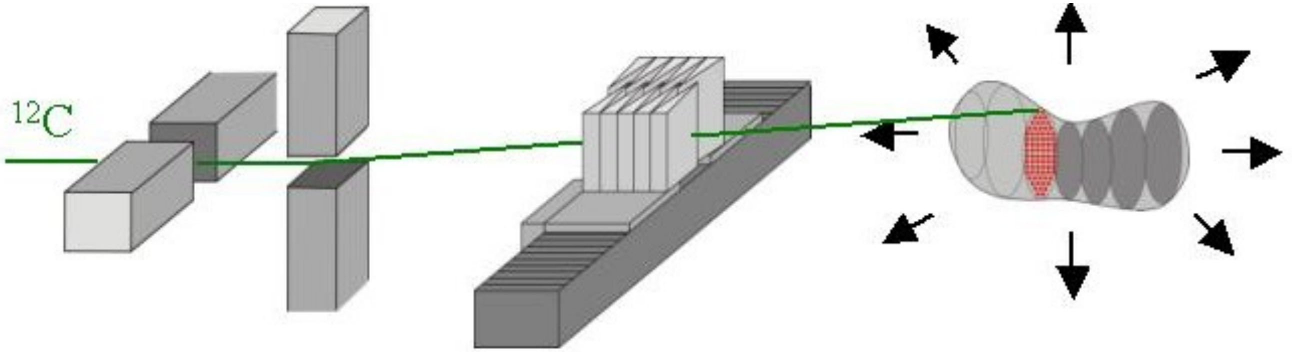
- Lung lesions treated so far with passive scattering techniques
- Respiration management techniques
  - ➔ Tracking, gating, breath hold
- Rescanning in "2D"
  - ➔ Scanning speed cm per ms
- 3rd dimension ?
  - ➔ "few" mm in "hundreds" of ms

Gendrin et al Med Phys (2011) / R & O (2012)
Furtado et al Acta Oncol (2013)



Maybe a combination of techniques is optimal solution ?

Motion compensation in particle therapy



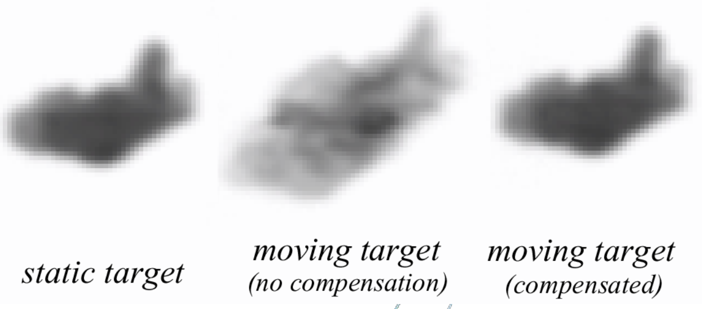
magnetic scanner system

PMMA wedge system

suitable motion tracking system

dynamic treatment plan

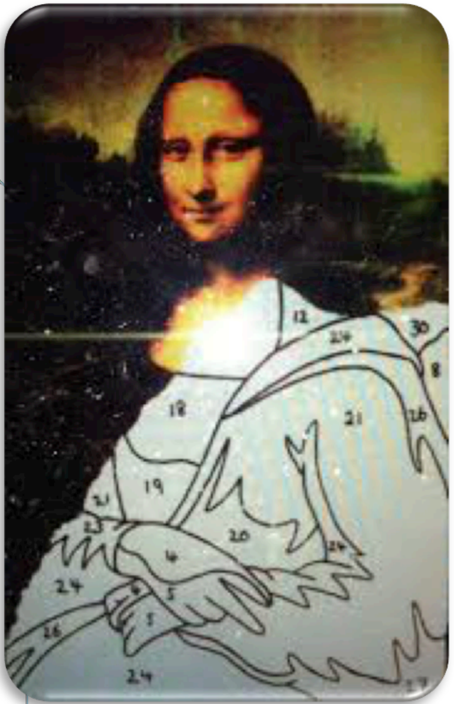
GSI / HIT developments
C. Bert et al



Work on motion compensation to premature. . .

Dose painting

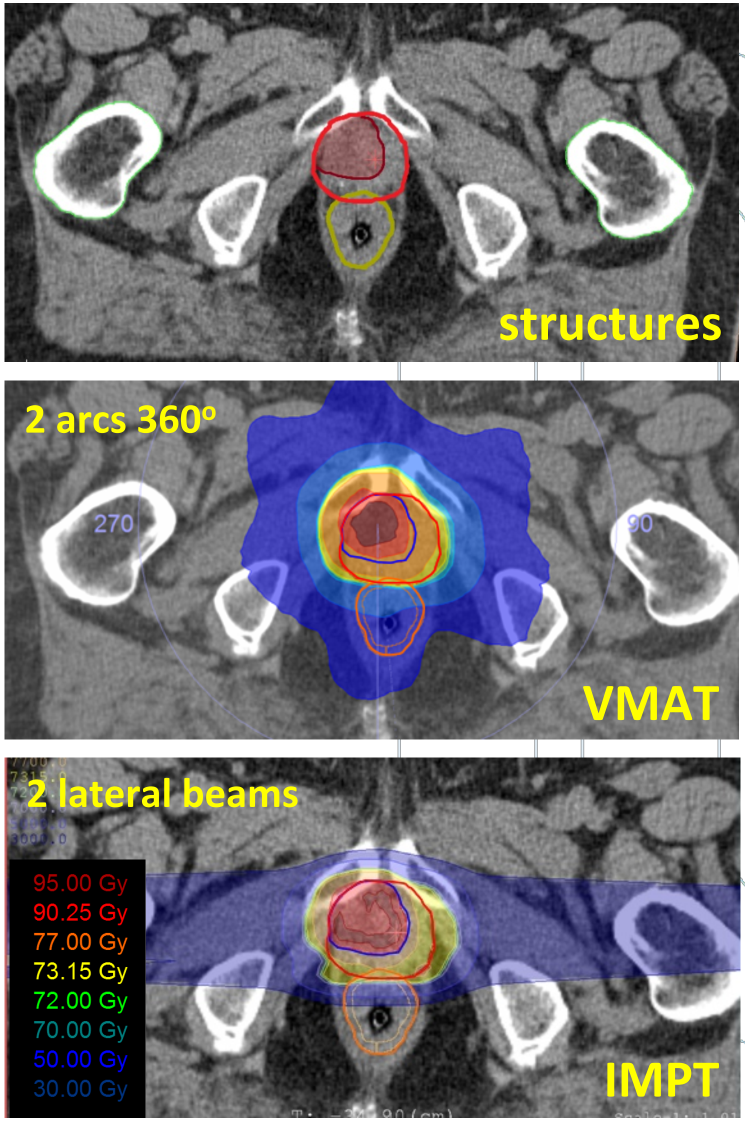
- Idea is based on sub-volume characterization of tumor tissue
- „Brushes“ for painting
  - ➔ High energy photons, **brachytherapy**, **particles**
  - ➔ Role of multimodality or mixed treatments
- Pre-requisite:
  ”Quantitative” Imaging



Ling et al IJROBP (2000)

Biological motivated adaptations open new degree of freedom in Rad Oncol

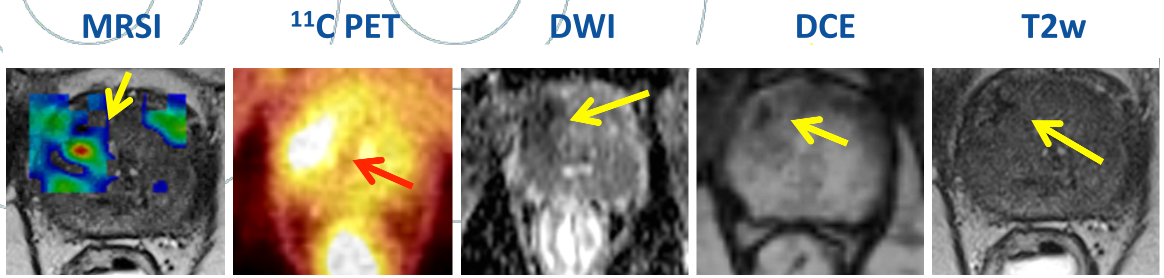
Dose painting



Requirements

- Small spot sizes
- Spot stability
    - ➔ spill to spill and intraspill
    - ➔ < 0.5 mm.
- Image guidance of patient

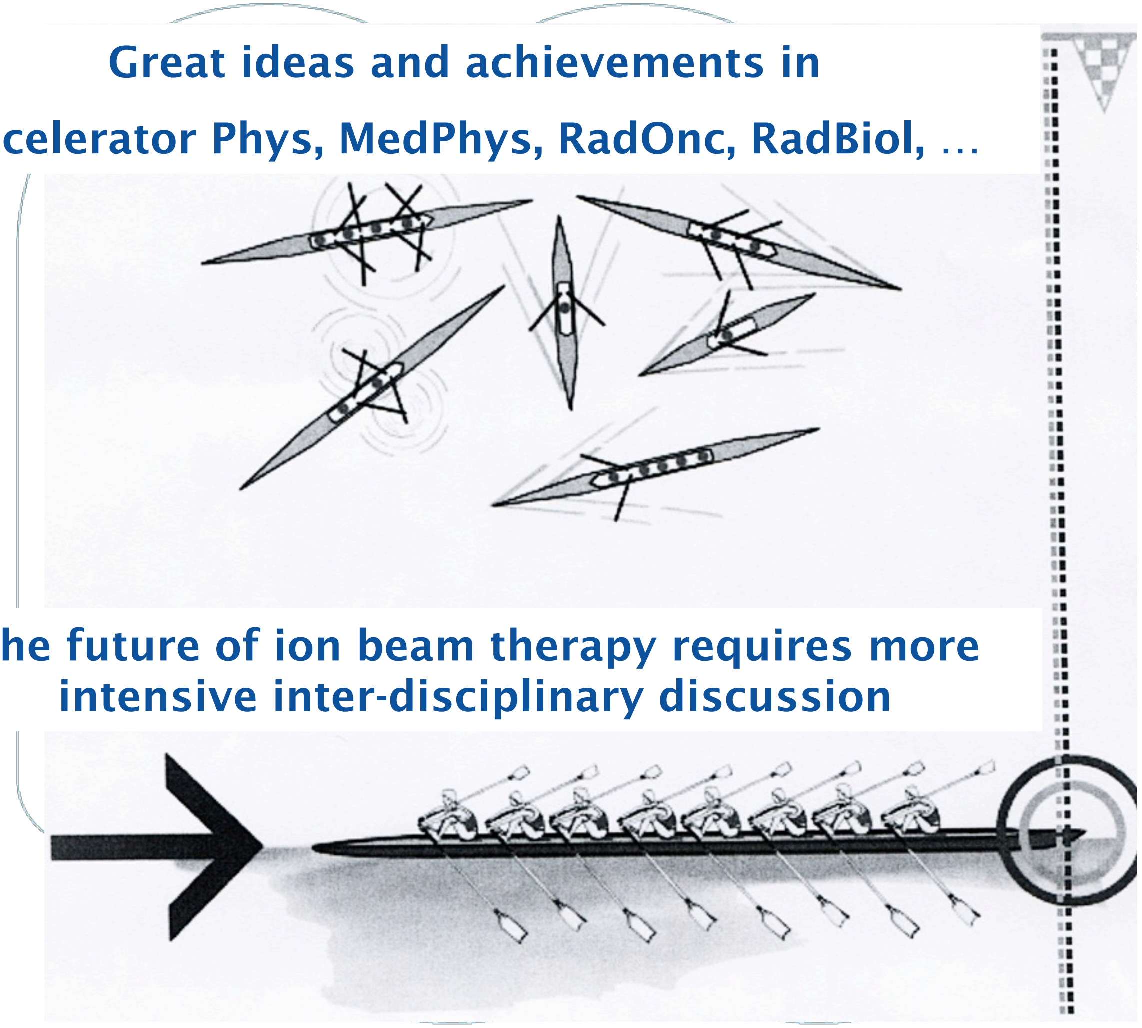
Andrzejewski et al, submitted to R&O



Concluding remark

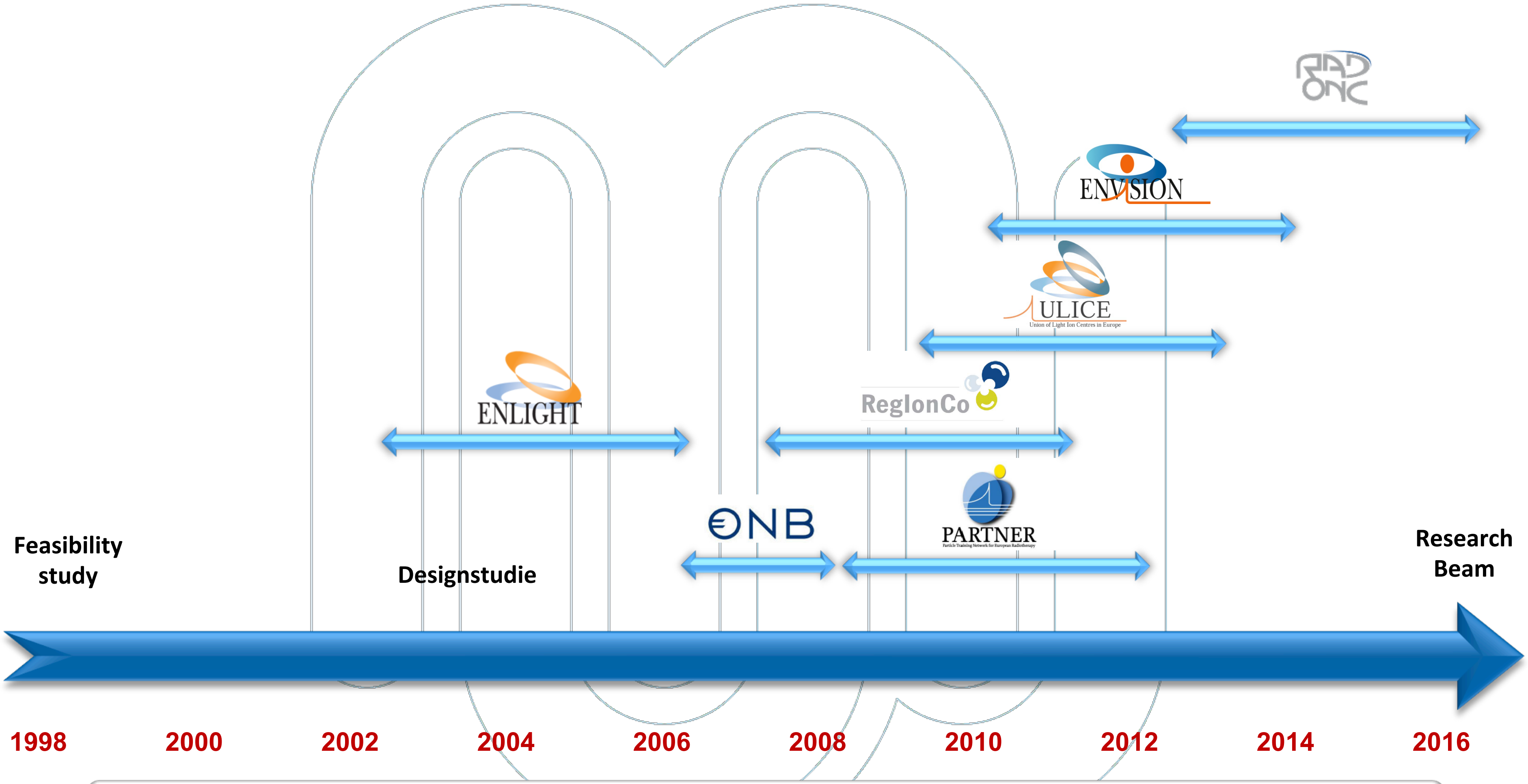
Great ideas and achievements in

Accelerator Phys, MedPhys, RadOnc, RadBiol, …



The future of ion beam therapy requires more intensive inter-disciplinary discussion

Milestones for ion beam research



Feasibility study

Designstudie

Research Beam

1998 2000 2002 2004 2006 2008 2010 2012 2014 2016

Cooperation with MedAustron throughout the years is acknowledged !

Acknowledgements

Visit http://www.meduniwien.ac.at/hp/radonc/

and many others ……

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Summary

From a (clinical) medical physics perspective

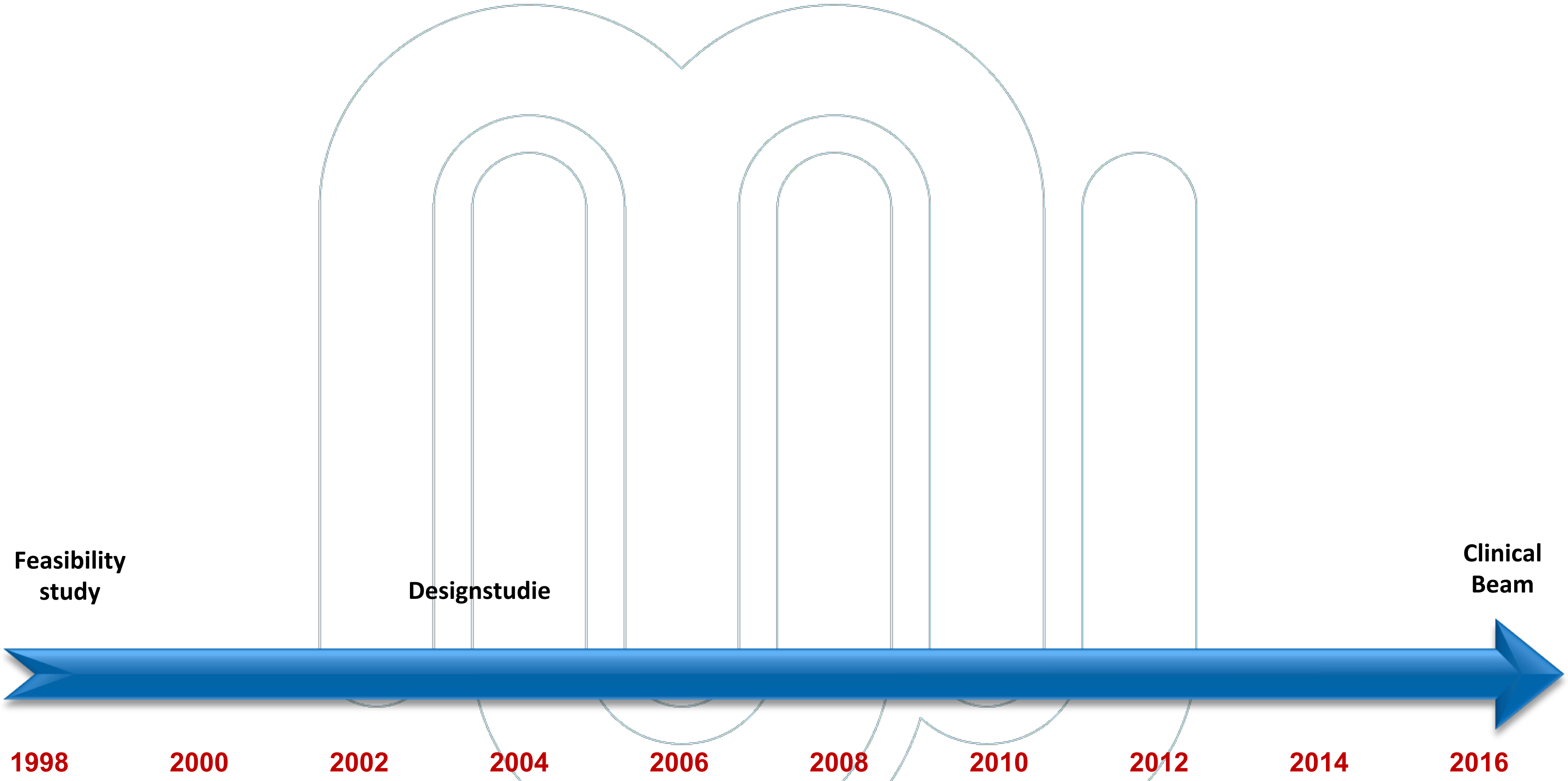
→Novel ions species

→Moving targets

→Dose painting

with impact on accelerator, control systems etc. that go beyond current standards

Milestones for the ion beam facility



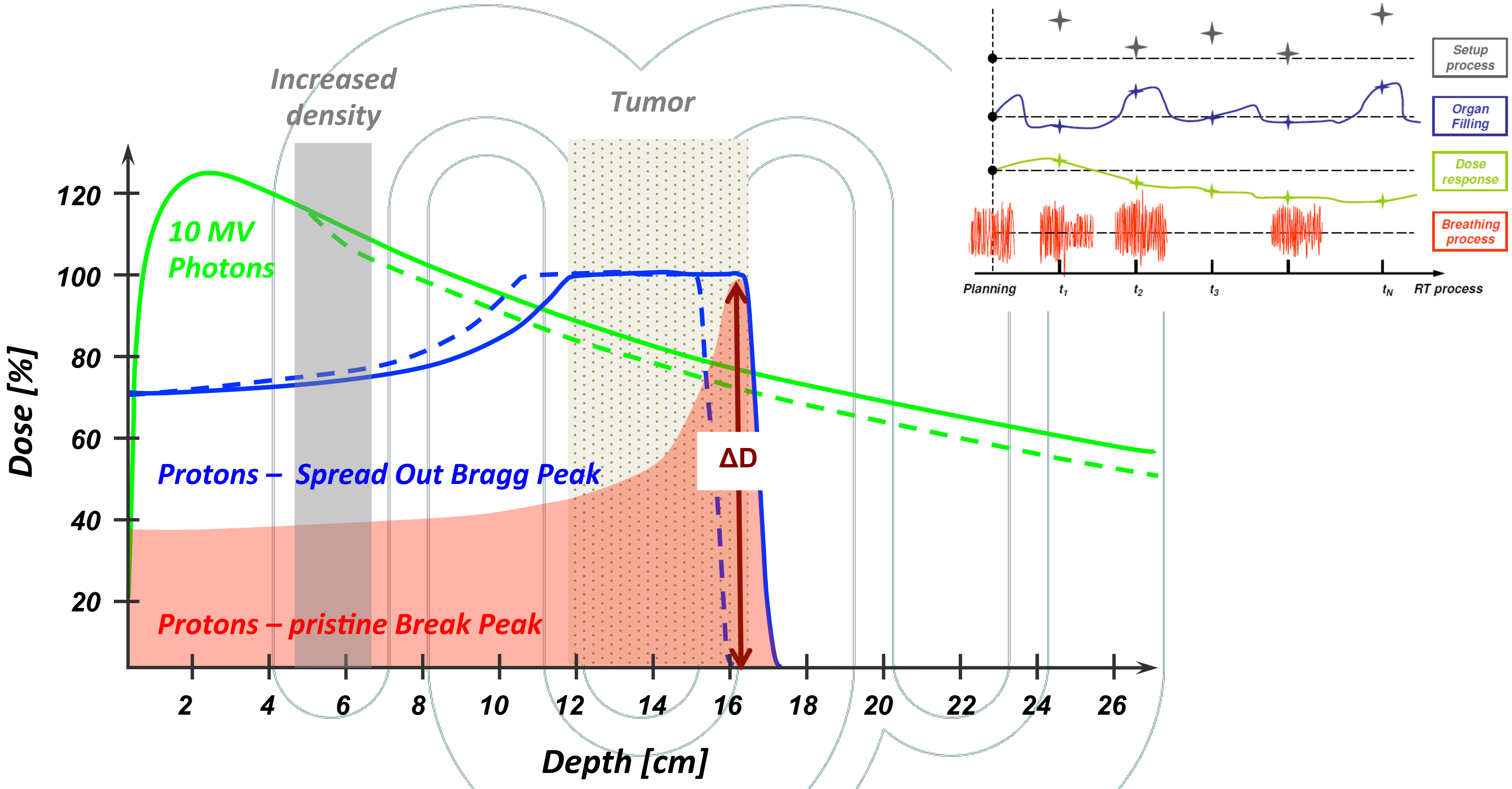
Feasibility study

Designstudie

Clinical Beam

Research activities (even without a beam) were given high priority

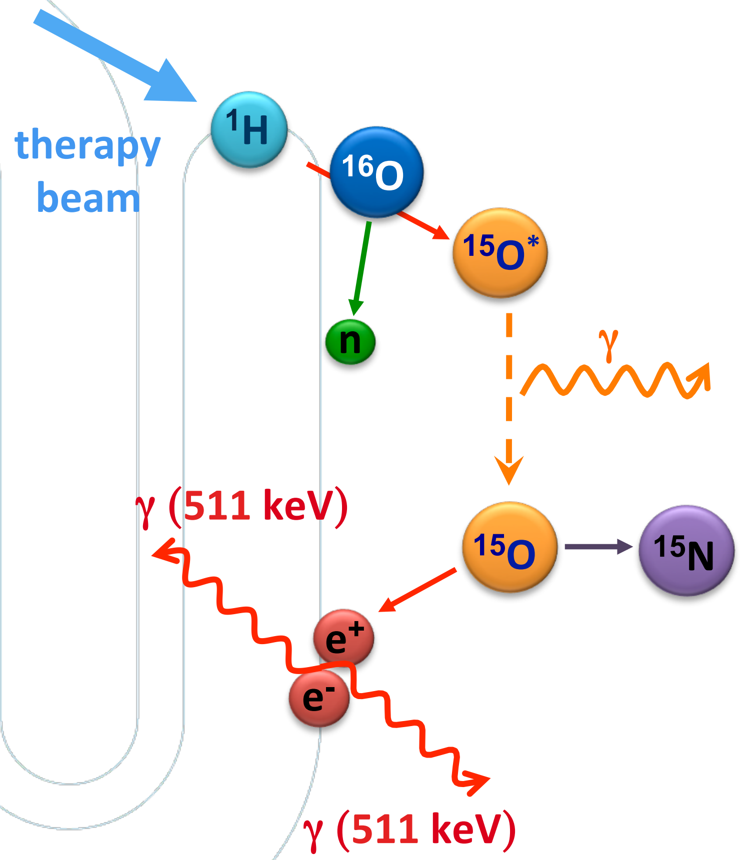
Impact of path length variations



Sensitivity of particles to path length variations motivate verification

“Imaging” of particle beam delivery

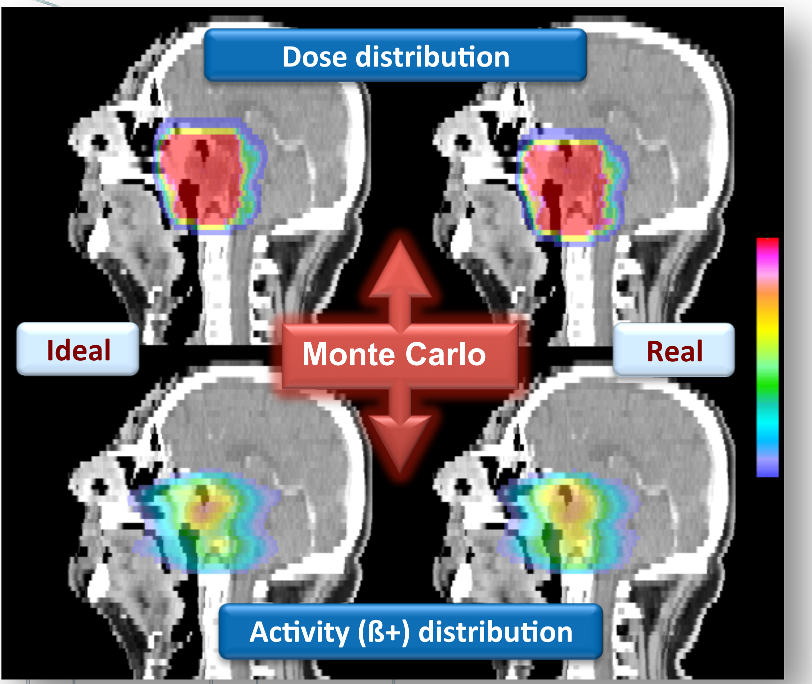
- Uncertainties in beam delivery
  - ➔ Range, inter- and intra-fraction motion, CT calibration, RBE, shrinkage, ……
- Imaging options under investigation
  - ➔ **PET, prompt gamma**, gamma spectroscopy, particle radiography,
  - ➔ **MR guidance**



In-vivo dosimetry via secondary radiation is feasible in ion beam therapy

In-vivo dosimetry (IVD)

- Activity and dose are not directly correlated
  - ➔ Challenge: low counting statistics
  - ➔ ß⁺- activity predicition model
- Visual inspections of ß⁺- activity distributions by team of experts
  - ➔ very time consuming
  - ➔ requires well trained personnel
  - ➔ not objective
- Automated comparison
  - ➔ EC Project: ENVISION



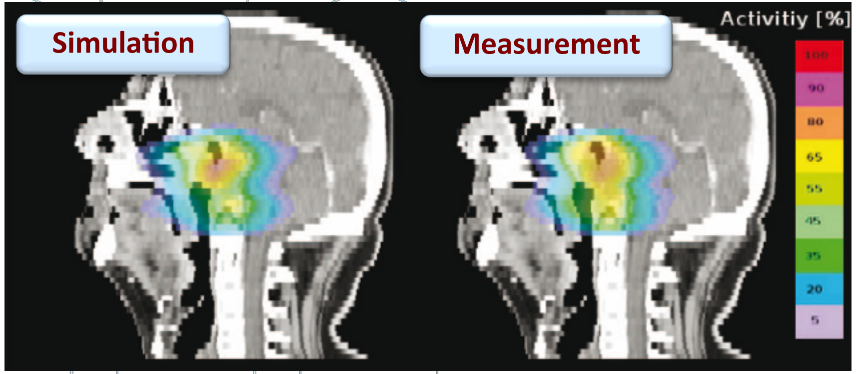
Kuess et al MP 39 (2012)
Kuess et al Med Phys 40 (2013)

Proof of principle established but no widespread implementation

Towards automated PT-PET verification

- 1st application of image comparison methods to PT-PET images
  - ➔ Pearson's correlation coefficient (in selected ROI)
    - ○ PCC=1: perfect correlation
    - ○ PCC=0: no correlation at all
  - ➔ Algorithms developed in MATLAB

$$\boxed{\mathrm{PCC} = \frac{\sum_i (x_i - \overline{x})(y_i - \overline{y})}{\sqrt{\sum_i (x_i - \overline{x})^2}\sqrt{\sum_i (y_i - \overline{y})^2}}}$$



x_i … ith voxel in reference image
y_i… ith voxel in compared image

- Detection Software tested for:
  - ➔ Beam range distributions: 4, 6 and 10 mm
  - ➔ Patients' set-up errors: -8 mm to + 8 mm cranio-caudal and rotational shifts

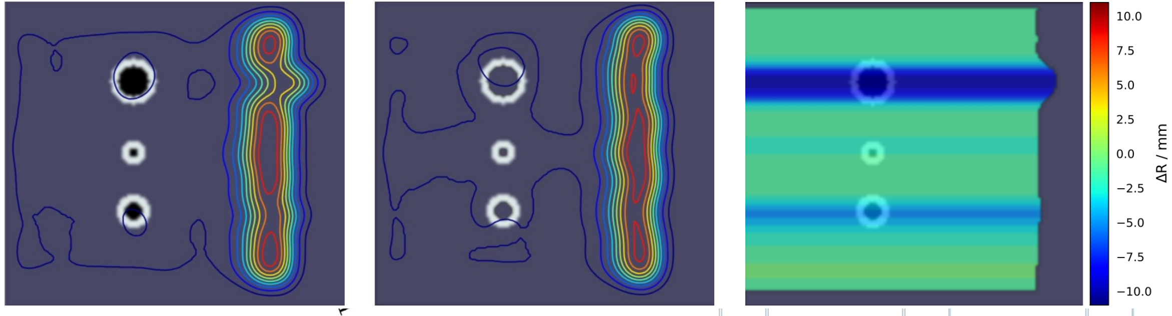
(Medical) Image Processing is becoming increasingly important

PET Verification - options

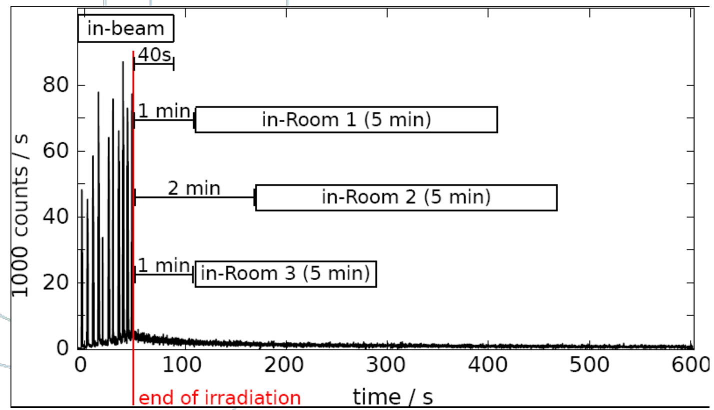
- Use of image processing methods (PCC) for comparison of measured activity distributions

Kuess et al Med Phys 39 (2012) / Helmbrecht PMB (2011)

  - ➔ Proof of principle based on in-beam PET data from GSI and synthetic data



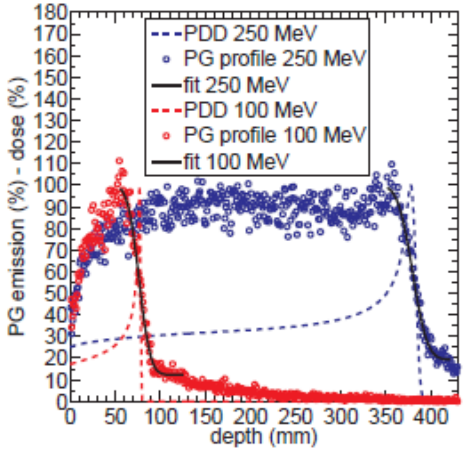
- Is the detection of setup errors possible?
  - ➔ comparison **in-beam** vs. **in-room** simulated data sets



There are limitations in PET verification for range verification . . .

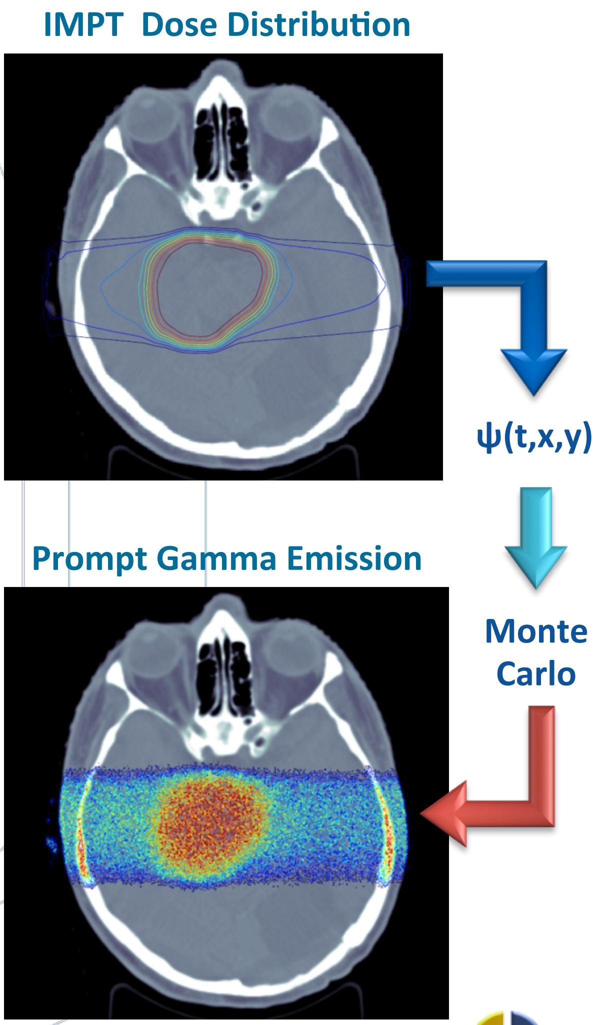
Novel QA methods: prompt gamma detection

- Not influenced by metabolic washout
- Gamma distribution can be predicted
  - ➔ Correlation between dose and gamma emission promising
- **Open issues**
  - ➔ Optimal detector
  - ➔ 3D maps realistic ?
  - ➔ Clinical validation
  - ➔ Feedback to treatment planning



Janssen et al

Prompt gamma imaging is in its infancy but promising . . .



IMPT Dose Distribution

ψ(t,x,y)

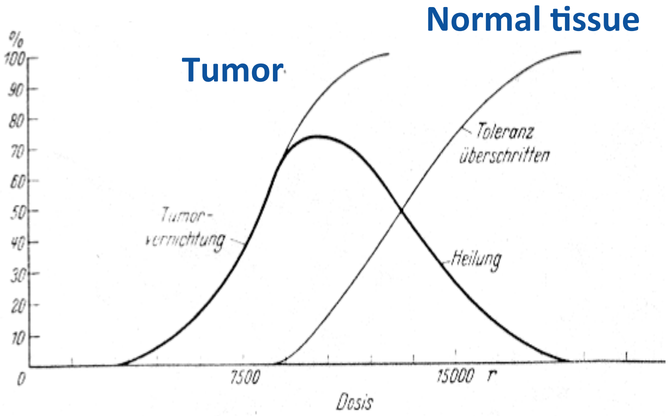
Prompt Gamma Emission

Monte Carlo

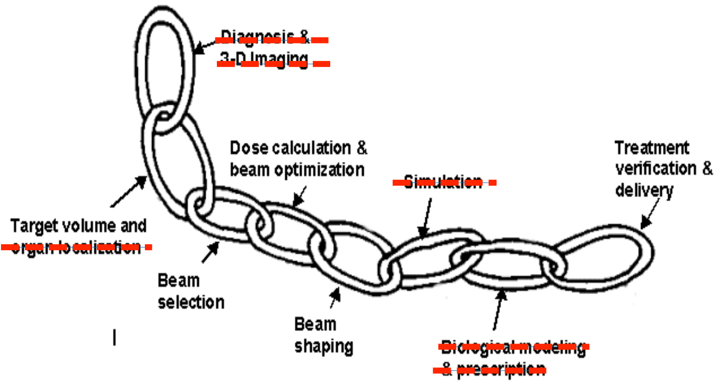
© A. Müller / Dresden

Dosimetric Audits

- High dosimetric accuracy motivated by steep dose response relation
  - ➔ Required in some EC countries by radiation protection legislation
  - ➔ Required for participation in trials
- For particle beam therapy there is no dosimetric audit (in Europe)
  - ➔ Suitable detectors and procedures?



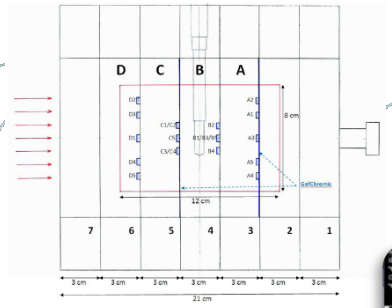
Holthusen, Strahlentherapie - 1936

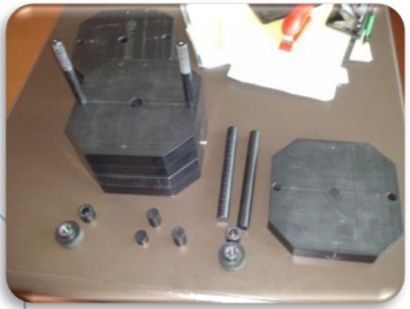


External dosimetric audits are standard in photon beam therapy

Dosimetry Audit for particle beam therapy

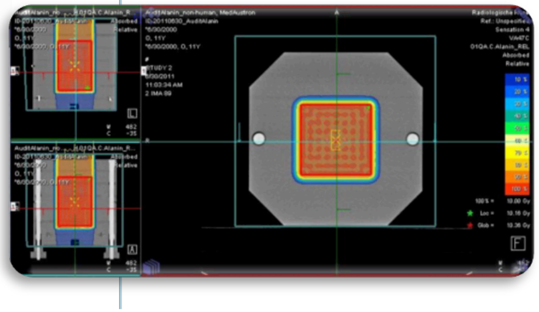
- Phantom design for end-to-end test
  - ➔ 20 Alanine pellets + 2 EBT films
  - ➔ IC (for the first tests)





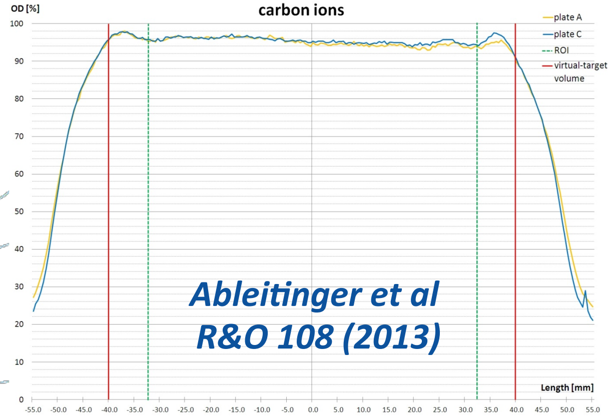
- Challenge: calibration in Co-60

$$\underbrace{D_{w,X}}_{\text{compared with TPS}} \cong \underbrace{\frac{1}{\eta}}_{\text{MC}} \cdot \underbrace{D_{w,{}^{60}Co}}_{\text{NPL reported dose}} \cdot \underbrace{\left(\mu_{en}^{{}^{60}Co}/\rho\right)_{w}^{al}}_{\approx 0.97} \cdot \underbrace{\left(S^{X}/\rho\right)_{al}^{w}}_{\text{MC}}$$



- ➔ Protons: 2.4 ± 0.9% (1σ) / C-12: 2.2 ± 1.1% (1σ)

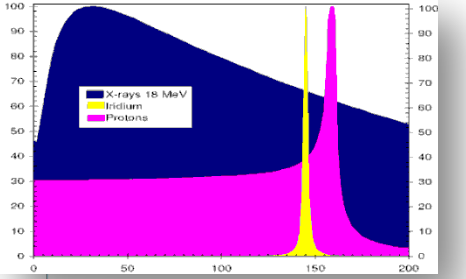
Successful pilot tests at Heidelberg facility (HIT) for protons & C-12 ions

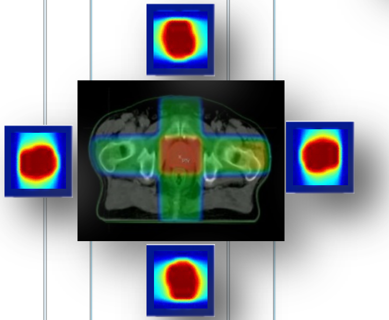


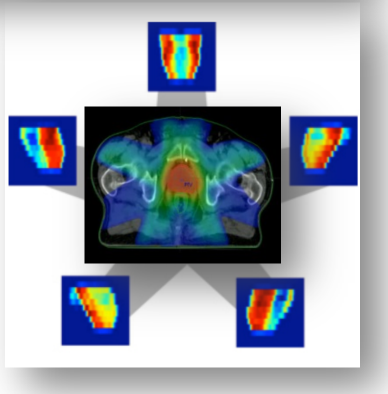
Ableitinger et al R&O 108 (2013)

Technology assessment

- **Physics Evidence**
  - ➔ radiation type & modality, energy, …
- **Technology Evidence**
  - ➔ e.g. this car has a 2.7-liter flat-six engine with direct fuel injection . . .
  - ➔ Pencil beam scanning versus passive scattering
- **Clinical Evidence**
  - ➔ e.g. this car drives faster
  - ➔ less side effects








© Verellen

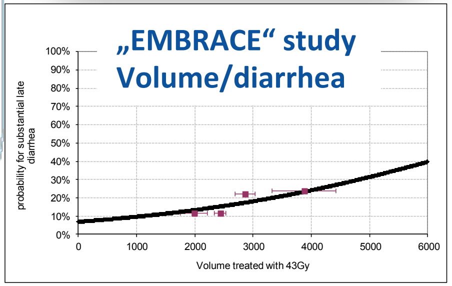
r

↓

πr^2

↓

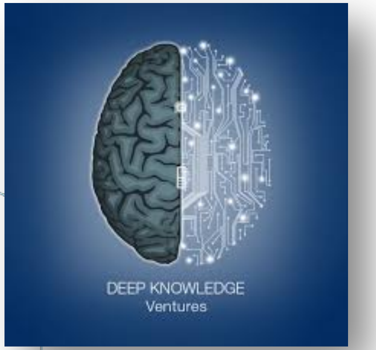
$4/3\pi r^3$


„EMBRACE“ study Volume/diarrhea

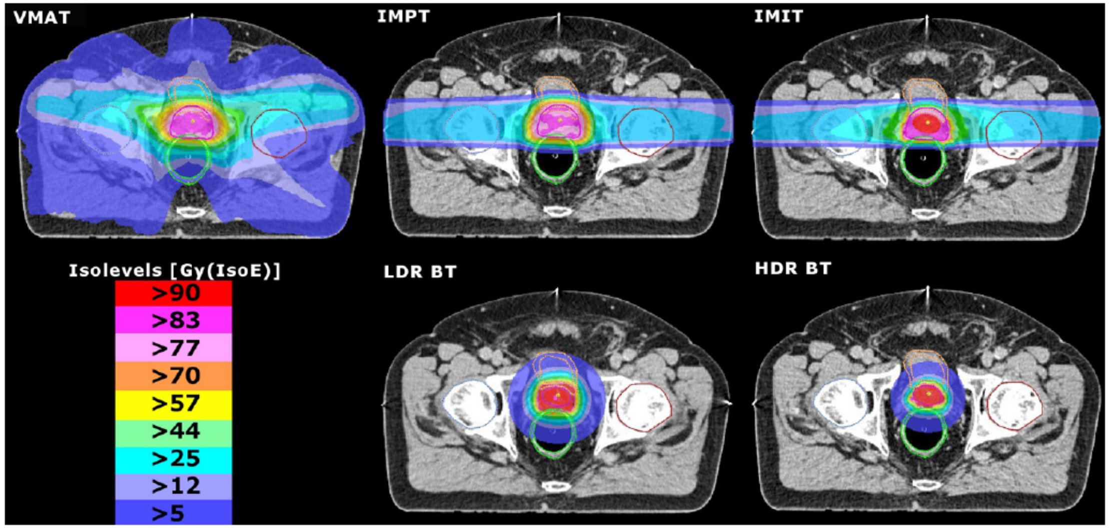
The importance of health technology assessment increases

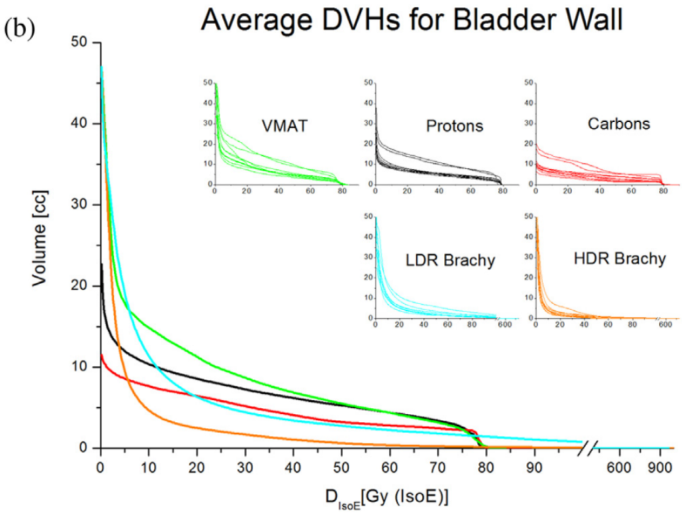
Treatment planning comparisons

- **„In-silico“ trials:** rival treatment techniques are “dosimetrically” evaluated
  - ➔ Theoretical assessment
  - ➔ Often includes radiobiologic modeling



Georg et al IJROBP (2014)



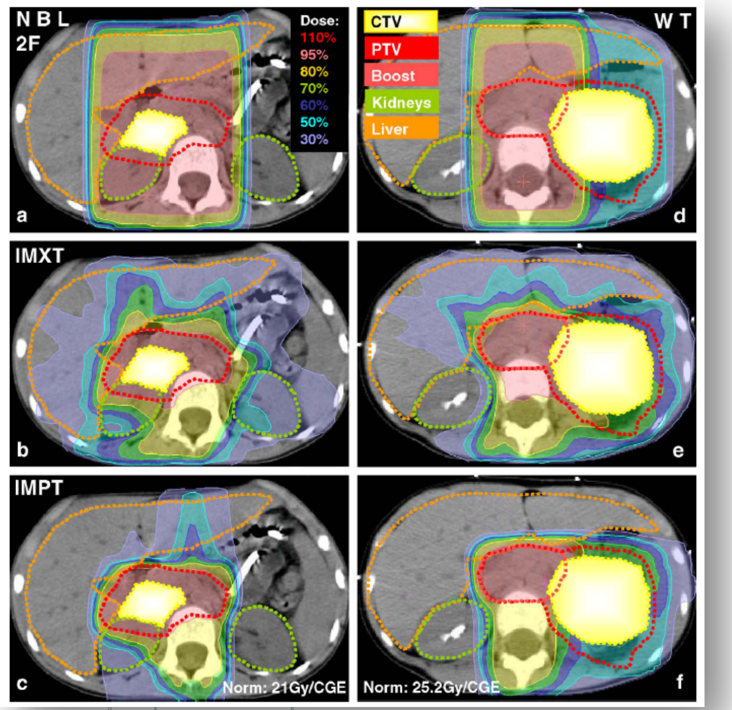


Treatment planning comparison is common first benchmarking method

Pediatric Radiation Oncology

- **E.g.: Neuroblastoma and Wilms tumour**
- Current standard - opposing photon fields (2F) vs. photon intensity modulated radiotherapy (IMXT) vs. proton techniques

Hillbrand et al R&O(2008)



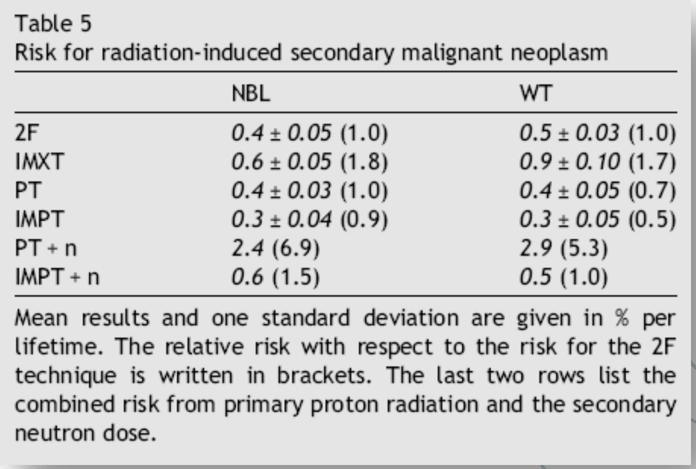


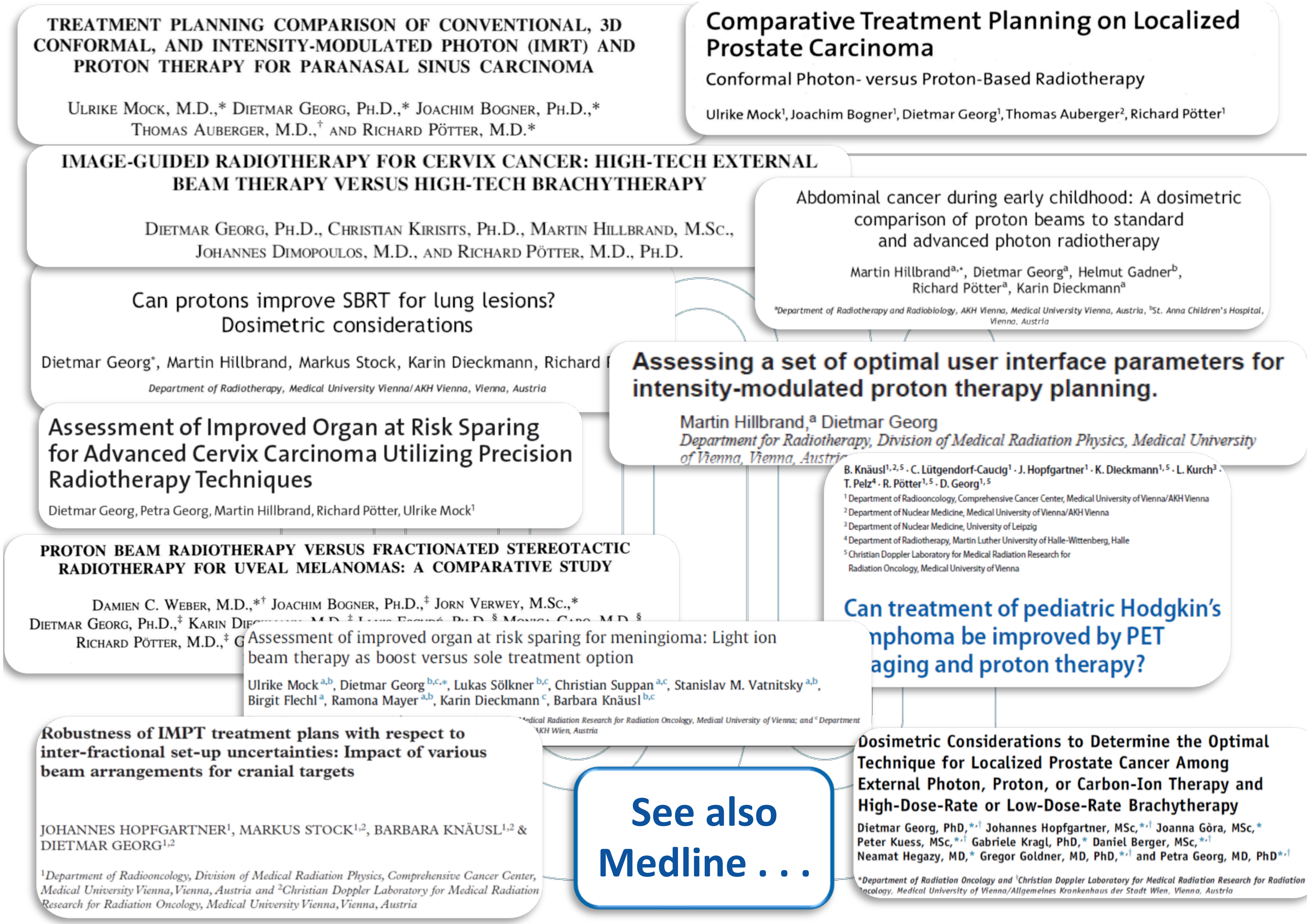
Table 5
Risk for radiation-induced secondary malignant neoplasm

	NBL	WT
2F	0.4 ± 0.05 (1.0)	0.5 ± 0.03 (1.0)
IMXT	0.6 ± 0.05 (1.8)	0.9 ± 0.10 (1.7)
PT	0.4 ± 0.03 (1.0)	0.4 ± 0.05 (0.7)
IMPT	0.3 ± 0.04 (0.9)	0.3 ± 0.05 (0.5)
PT + n	2.4 (6.9)	2.9 (5.3)
IMPT + n	0.6 (1.5)	0.5 (1.0)

Mean results and one standard deviation are given in % per lifetime. The relative risk with respect to the risk for the 2F technique is written in brackets. The last two rows list the combined risk from primary proton radiation and the secondary neutron dose.

- Relative risk for SM is valuable indicator for the ranking of treatment techniques

Pediatric patients are a main indication for particle therapy



TREATMENT PLANNING COMPARISON OF CONVENTIONAL, 3D CONFORMAL, AND INTENSITY-MODULATED PHOTON (IMRT) AND PROTON THERAPY FOR PARANASAL SINUS CARCINOMA

Ulrike Mock, M.D.,* Dietmar Georg, Ph.D.,* Joachim Bogner, Ph.D.,*
Thomas Auberger, M.D.,† and Richard Pötter, M.D.*

Comparative Treatment Planning on Localized Prostate Carcinoma

Conformal Photon- versus Proton-Based Radiotherapy

Ulrike Mock[1], Joachim Bogner[1], Dietmar Georg[1], Thomas Auberger[2], Richard Pötter[1]

IMAGE-GUIDED RADIOTHERAPY FOR CERVIX CANCER: HIGH-TECH EXTERNAL BEAM THERAPY VERSUS HIGH-TECH BRACHYTHERAPY

Dietmar Georg, Ph.D., Christian Kirisits, Ph.D., Martin Hillbrand, M.Sc.,
Johannes Dimopoulos, M.D., and Richard Pötter, M.D., Ph.D.

Abdominal cancer during early childhood: A dosimetric comparison of proton beams to standard and advanced photon radiotherapy

Martin Hillbrand[a,*], Dietmar Georg[a], Helmut Gadner[b],
Richard Pötter[a], Karin Dieckmann[a]

[a]Department of Radiotherapy and Radiobiology, AKH Vienna, Medical University Vienna, Austria, [b]St. Anna Children's Hospital, Vienna, Austria

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Can protons improve SBRT for lung lesions? Dosimetric considerations

Dietmar Georg*, Martin Hillbrand, Markus Stock, Karin Dieckmann, Richard

Department of Radiotherapy, Medical University Vienna/AKH Vienna, Vienna, Austria

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Assessing a set of optimal user interface parameters for intensity-modulated proton therapy planning.

Martin Hillbrand,[a] Dietmar Georg
Department for Radiotherapy, Division of Medical Radiation Physics, Medical University of Vienna, Vienna, Austria

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Assessment of Improved Organ at Risk Sparing for Advanced Cervix Carcinoma Utilizing Precision Radiotherapy Techniques

Dietmar Georg, Petra Georg, Martin Hillbrand, Richard Pötter, Ulrike Mock[1]

B. Knäusl[1,2,5] · C. Lütgendorf-Caucig[1] · J. Hopfgartner[1] · K. Dieckmann[1,5] · L. Kurch[3] · T. Pelz[4] · R. Pötter[1,5] · D. Georg[1,5]

[1] Department of Radiooncology, Comprehensive Cancer Center, Medical University of Vienna/AKH Vienna
[2] Department of Nuclear Medicine, Medical University of Vienna/AKH Vienna
[3] Department of Nuclear Medicine, University of Leipzig
[4] Department of Radiotherapy, Martin Luther University of Halle-Wittenberg, Halle
[5] Christian Doppler Laboratory for Medical Radiation Research for Radiation Oncology, Medical University of Vienna

Can treatment of pediatric Hodgkin's mphoma be improved by PET aging and proton therapy?

PROTON BEAM RADIOTHERAPY VERSUS FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR UVEAL MELANOMAS: A COMPARATIVE STUDY

Damien C. Weber, M.D.,*† Joachim Bogner, Ph.D.,‡ Jorn Verwey, M.Sc.,*
Dietmar Georg, Ph.D.,‡ Karin Di
Richard Pötter, M.D.,‡ G

Assessment of improved organ at risk sparing for meningioma: Light ion beam therapy as boost versus sole treatment option

Ulrike Mock[a,b], Dietmar Georg[b,c,*], Lukas Sölkner[b,c], Christian Suppan[a,c], Stanislav M. Vatnitsky[a,b], Birgit Flechl[a], Ramona Mayer[a,b], Karin Dieckmann[c], Barbara Knäusl[b,c]

edical Radiation Research for Radiation Oncology, Medical University of Vienna; and [c] Department
AKH Wien, Austria

Robustness of IMPT treatment plans with respect to inter-fractional set-up uncertainties: Impact of various beam arrangements for cranial targets

Johannes Hopfgartner[1], Markus Stock[1,2], Barbara Knäusl[1,2] & Dietmar Georg[1,2]

[1]Department of Radiooncology, Division of Medical Radiation Physics, Comprehensive Cancer Center, Medical University Vienna, Vienna, Austria and [2]Christian Doppler Laboratory for Medical Radiation Research for Radiation Oncology, Medical University Vienna, Vienna, Austria

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Dosimetric Considerations to Determine the Optimal Technique for Localized Prostate Cancer Among External Photon, Proton, or Carbon-Ion Therapy and High-Dose-Rate or Low-Dose-Rate Brachytherapy

Dietmar Georg, PhD,*,† Johannes Hopfgartner, MSc,*,† Joanna Gòra, MSc,* Peter Kuess, MSc,*,† Gabriele Kragl, PhD,* Daniel Berger, MSc,*,† Neamat Hegazy, MD,* Gregor Goldner, MD, PhD,*,† and Petra Georg, MD, PhD*,†

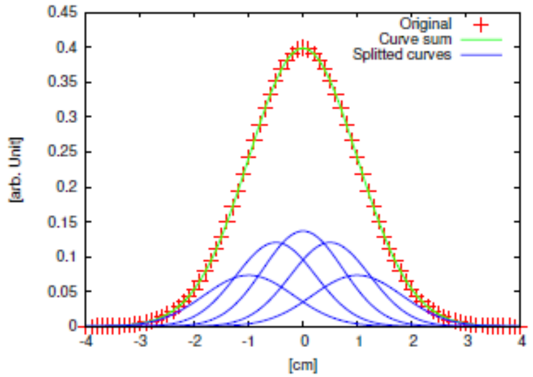
**Department of Radiation Oncology and †Christian Doppler Laboratory for Medical Radiation Research for Radiation ncology, Medical University of Vienna/Allgemeines Krankenhaus der Stadt Wien, Vienna, Austria*

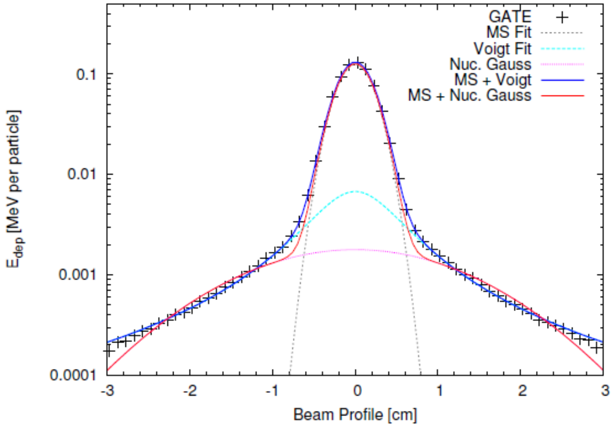
See also Medline . . .

Helium Ion Pencil Beam Model – physical dose

- Pencil beam "spot" splitting
- Longitudinal dose deposition:
  - ➔ LUT for water based on MC generated data
  - ➔ water equivalent depth scaling
- Lateral dose deposition:
  - ➔ Gaussian broadening for multiple scattering
  - ➔ Correction for nuclear interactions using Voigt-function

Fuchs et al Med Phys 39 (2012)





Pencil Beam model was validated for protons and helium ions

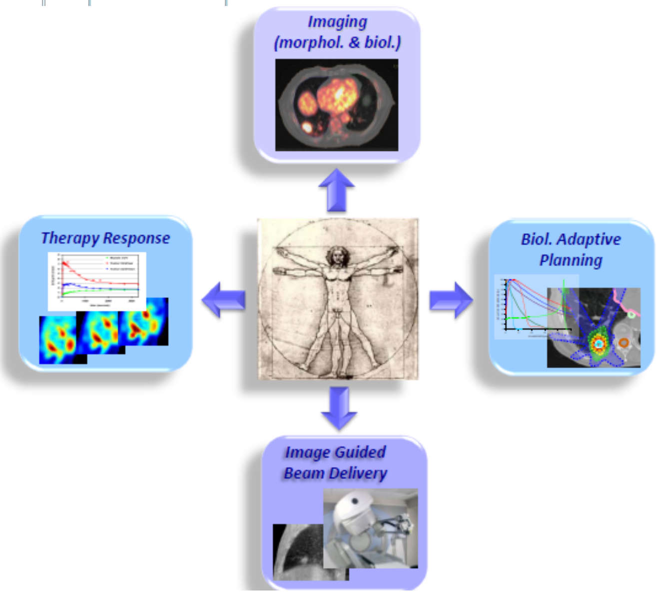
Facility Layout

- 4 Irradiation rooms
  - ➔ 2 x Horizontal BL
  - ➔ Horizontal + vertical BL
  - ➔ Proton only gantry
- Protons
  - ➔ intensity per pulse < 10^{10}
  - ➔ Energy 60 – 800 MeV
- Carbon ions
  - ➔ intensity per pulse < 4 x 10^{8}
  - ➔ Energy 120 – 400 MeV / A
- Later additional ions
  - He, O, ….

Summary

- Continuous research activities w.r.t to ion beam therapy since 2000
  - ➔ Planning, dosimetry, dose calc, QA, …
  - ➔ CD Lab opening new perspectives
- Necessity for building up research competency pointed out permanently
  - ➔ Interdisciplinary research (MP, MD, RB, IT, P, ..) is a "must" ion beam therapy
- Milestone reached in 2015: Medical Univ. Vienna investments in personnel


Opening ceremony CD Lab / March 2012



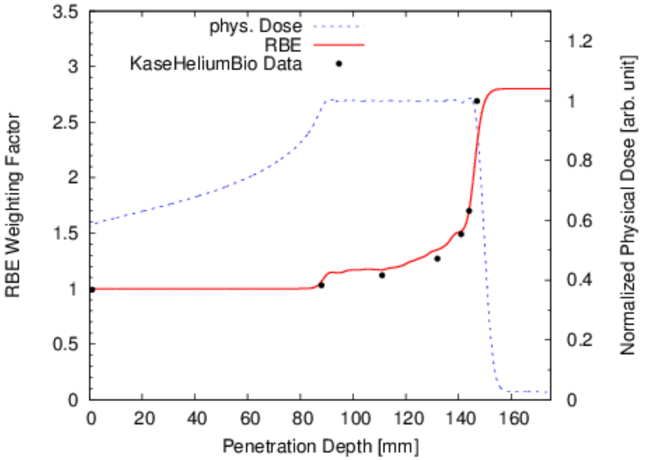
Helium Ion Pencil Beam Model – biological dose

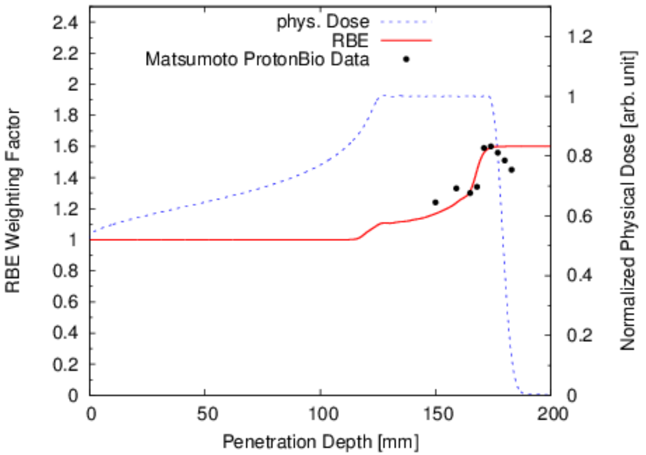
- Biological modeling employing a ‚zonal‘ model based on LET variations
  - ➔ Data from (historical) literature and LET taken into account
  - ➔ Helium ions: RBE ranging from 1.0 to 2.7

    Kase et al (2006) Radiat Res 166
  - ➔ Protons: RBE ranging from 1.0 to 1.6

    Matsumoto et al (2014) J Radiat Res 55
- Implemented in research TPS HYPERION

  Fuchs et al (2014), Submitted





Dedicated helium ion dose calculation module was developed