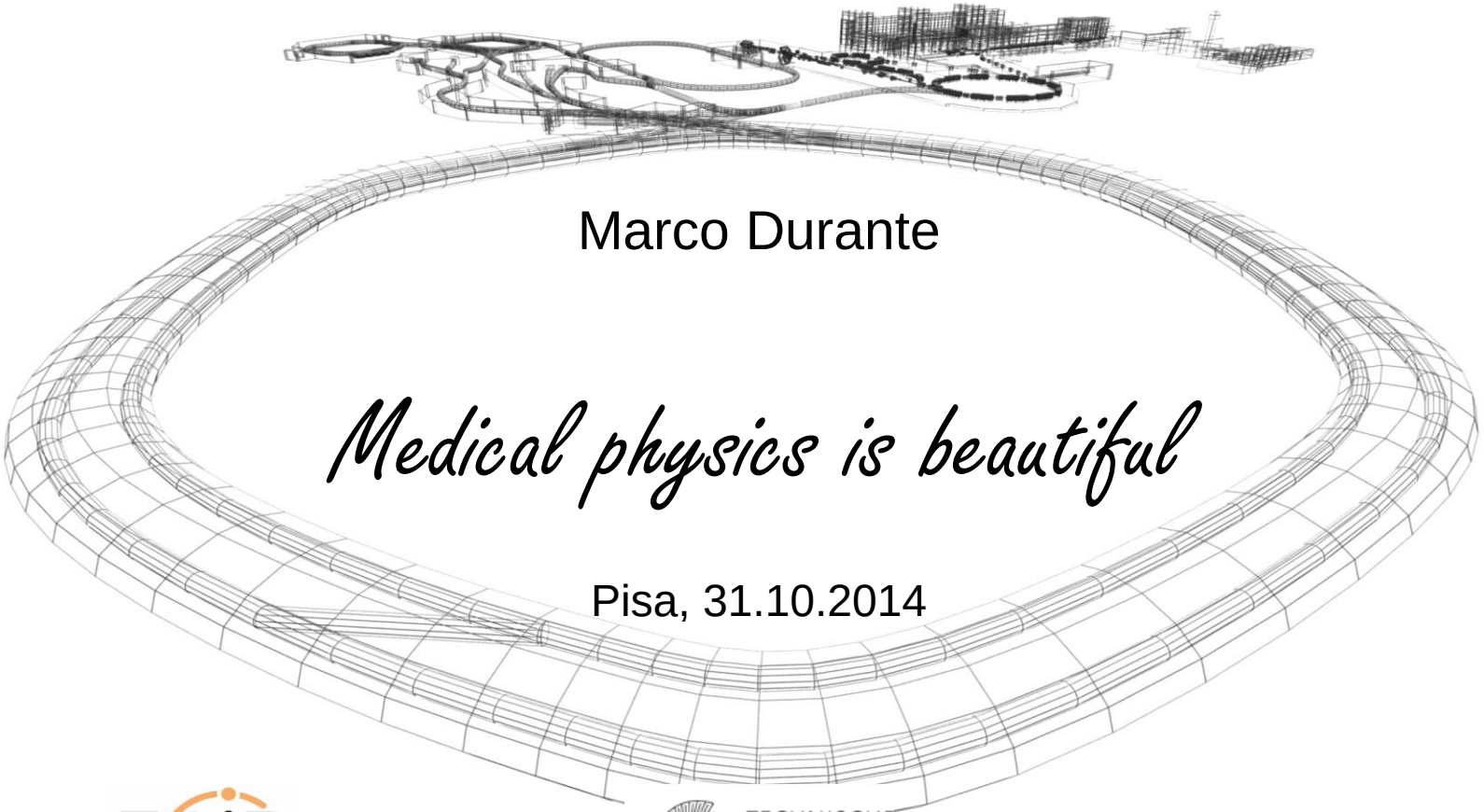
Translational research in particle therapy



Marco Durante

Medical physics is beautiful

Pisa, 31.10.2014

FAIR

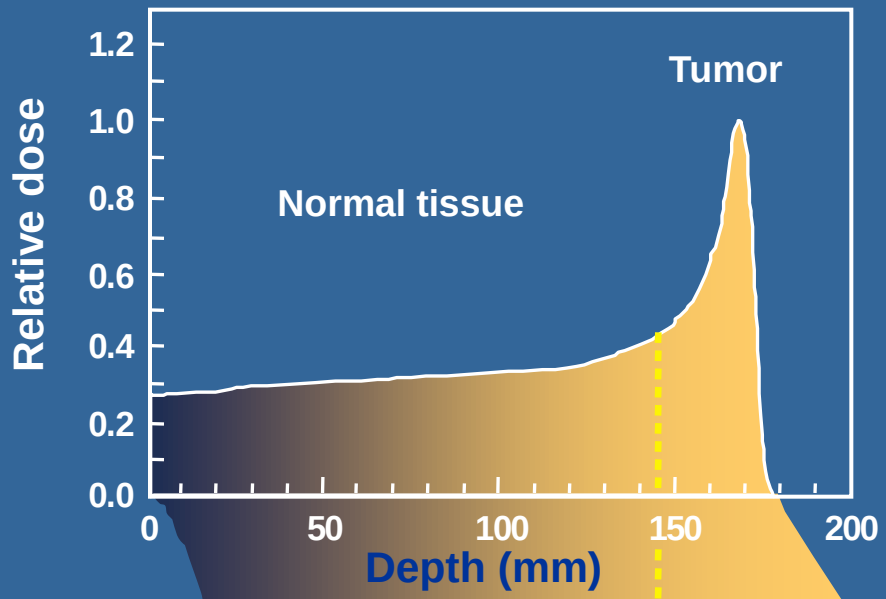
TECHNISCHE UNIVERSITÄT DARMSTADT

FIAS Frankfurt Institute for Advanced Studies

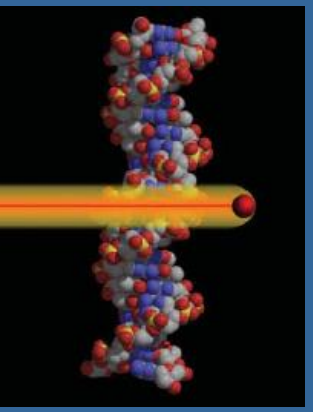
GSI

Durante & Loeffler,

Nature Rev Clin Oncol 2010



Energy	high	low
LET	low	high
Dose	low	high
RBE	≈ 1	> 1
OER	≈ 3	< 3
Cell-cycle dependence	high	low
Fractionation dependence	high	low
Angiogenesis	Increased	Decreased
Cell migration	Increased	Decreased

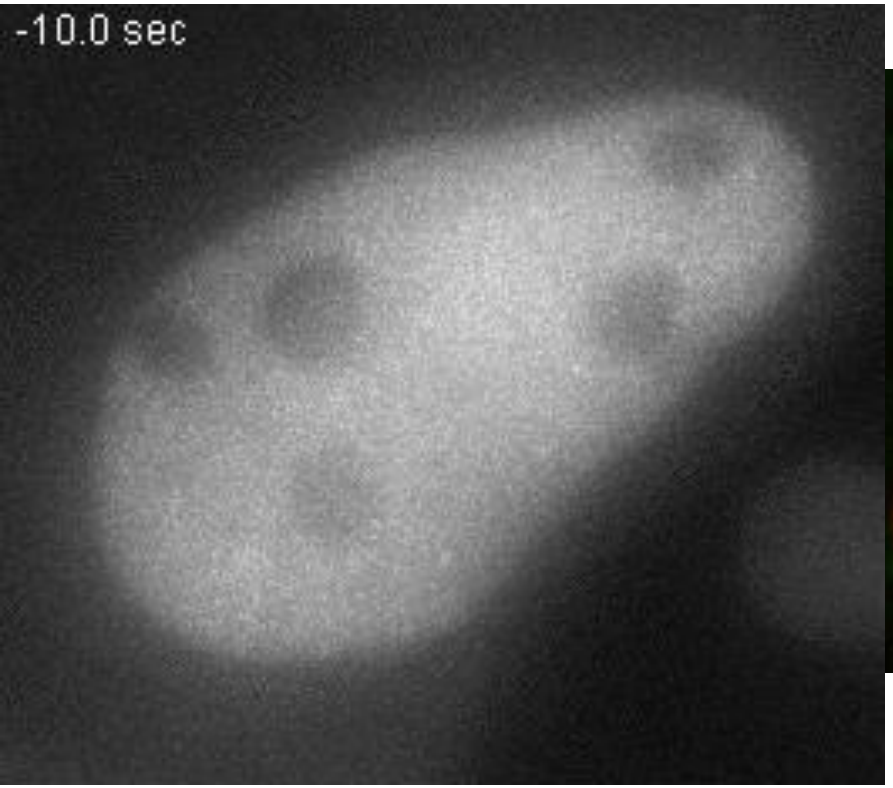


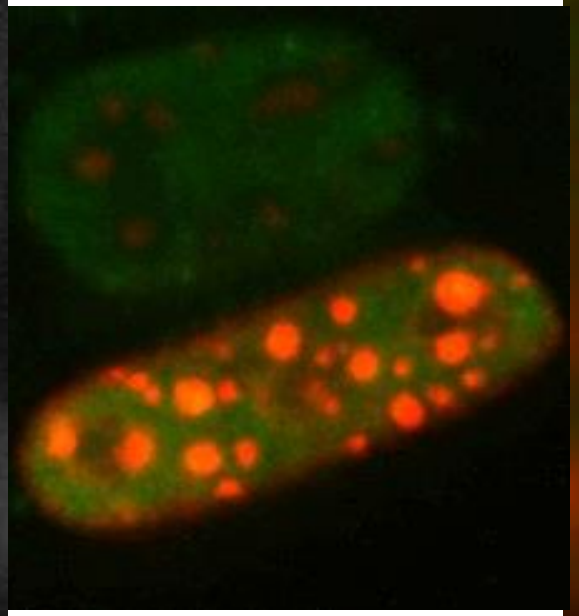
Potential advantages

- High tumor dose, normal tissue sparing
- Effective for radioresistant tumors
- Effective against hypoxic tumor cells
- Increased lethality in the target because cells in radioresistant (S) phase are sensitized
- Fractionation spares normal tissue more than tumor
- Reduced angiogenesis and metastatization

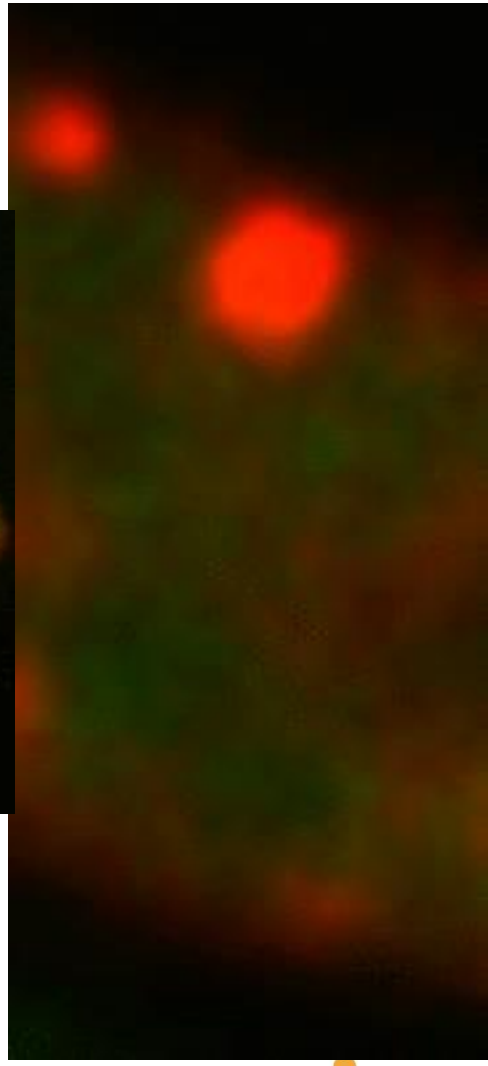
Live cell imaging of heavy ion traversals in euchromatin and heterochromatin

GFP-NSBS1



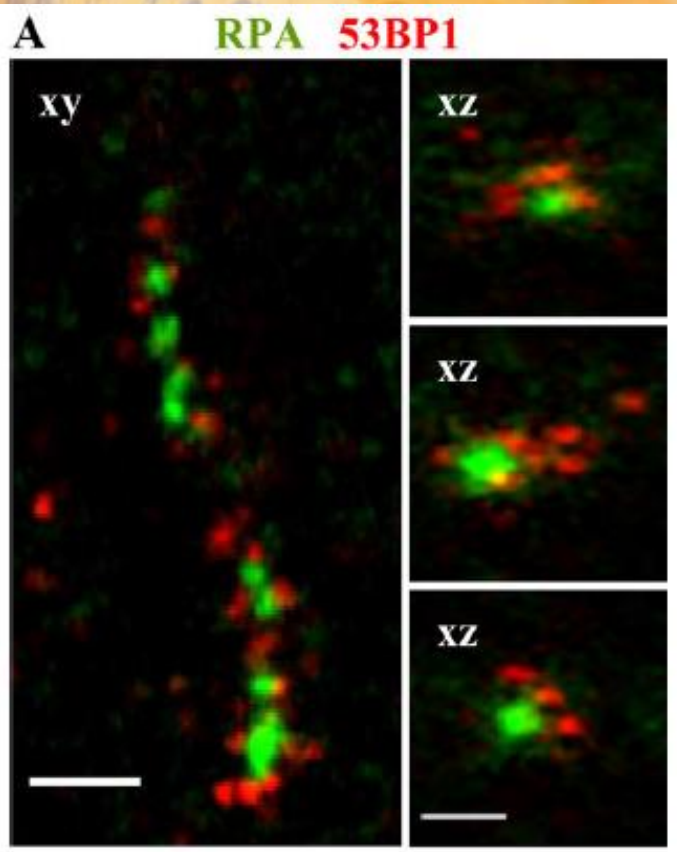


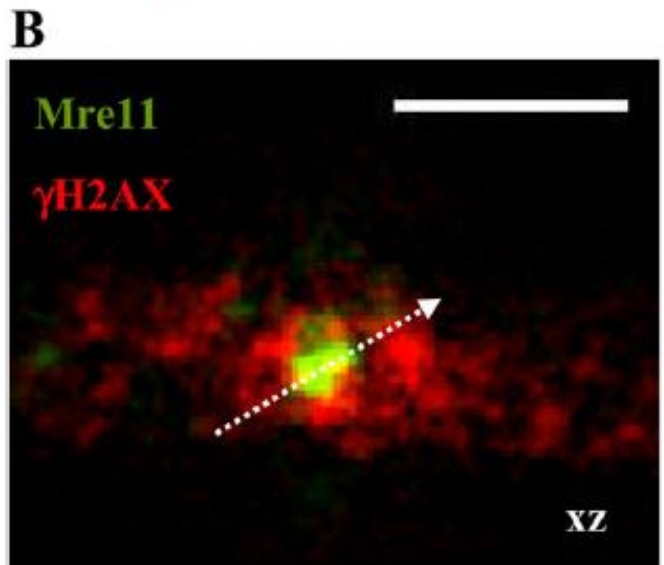
GFP-XRCC1

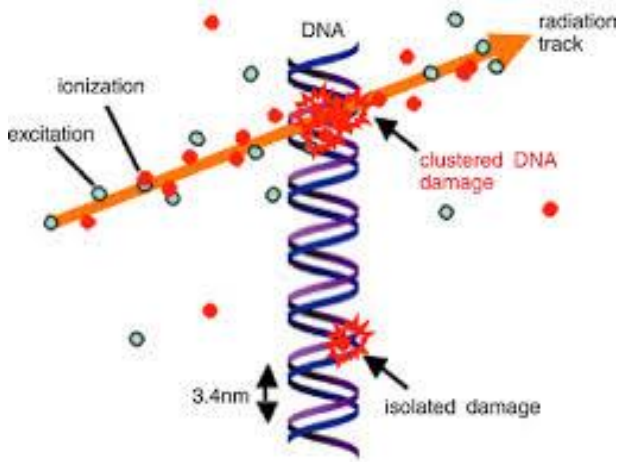


Jakob *et al., Proc. Natl. Acad. Sci. USA* 2009*; Nucl. Acids Res*. 2011

Clustered DNA breaks induced by charged particles





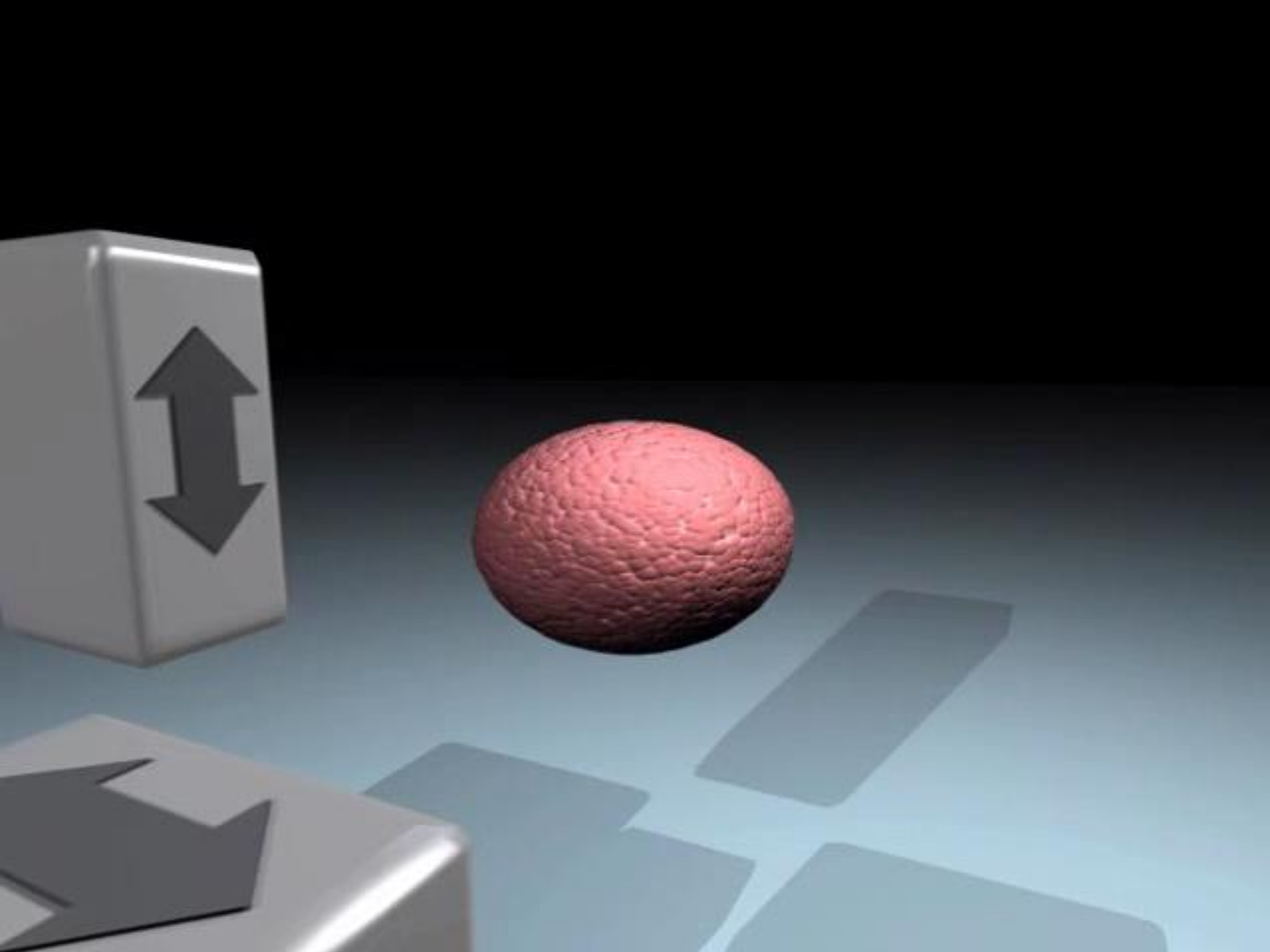


Biological dose estimation of UVA laser microirradiation utilizing charged particle-induced protein foci

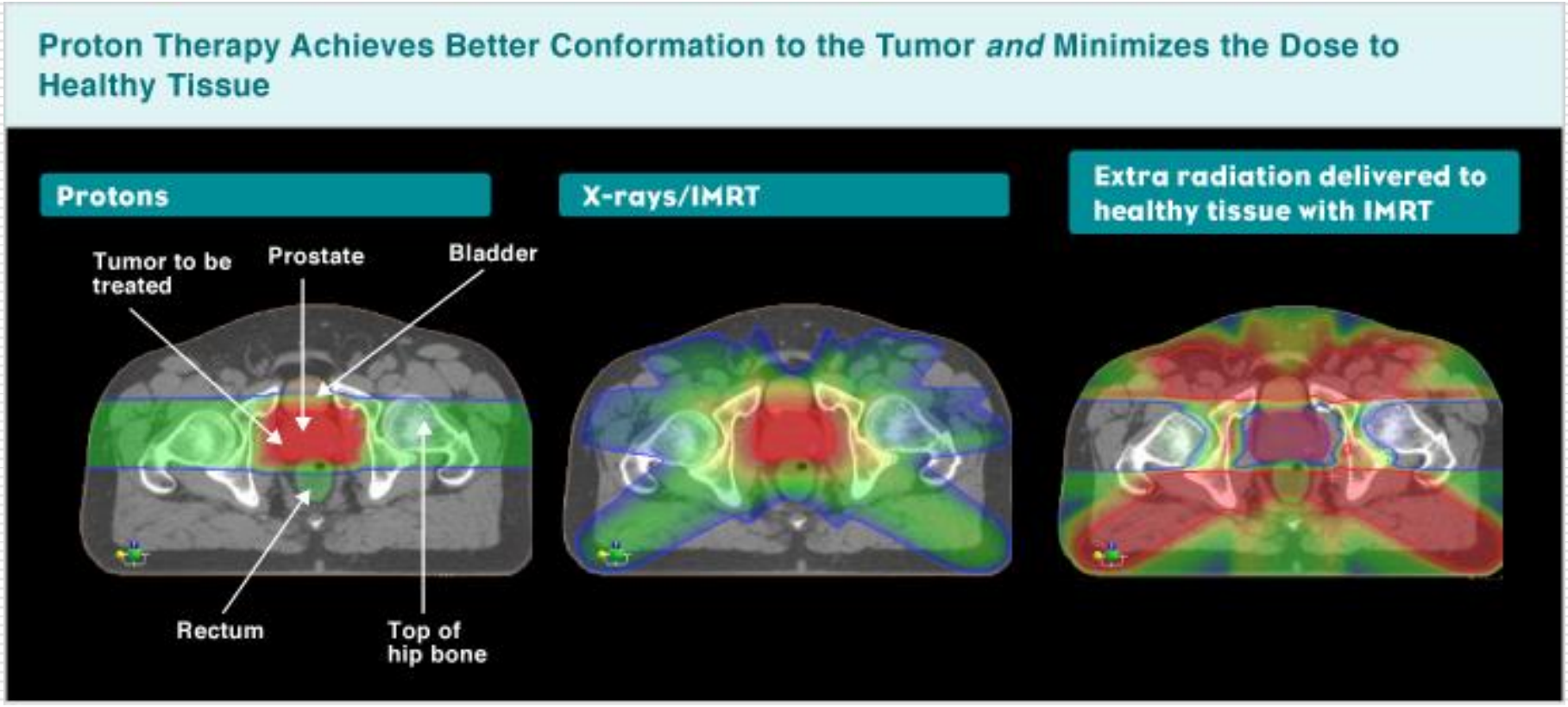
J. Splinter[1], B. Jakob[1,*], M. Lang[2], K. Yano[3], J. Engelhardt[2], S. W. Hell[2], D. J. Chen[3], M. Durante[1,4] and G. Taucher-Scholz[1]

[1]Department of Biophysics, GSI Helmholtz Center for Heavy Ion Research, Planckstrasse 1, D-64291 Darmstadt, Germany, [2]Department of High Resolution Optical Microscopy, German Cancer Research Center, D-69120 Heidelberg, Germany, [3]Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA and [4]Institute for Condensed Matter Physics, Technical University Darmstadt, D-64289 Darmstadt, Germany.

Mutagenesis pp. 1–9, 2010

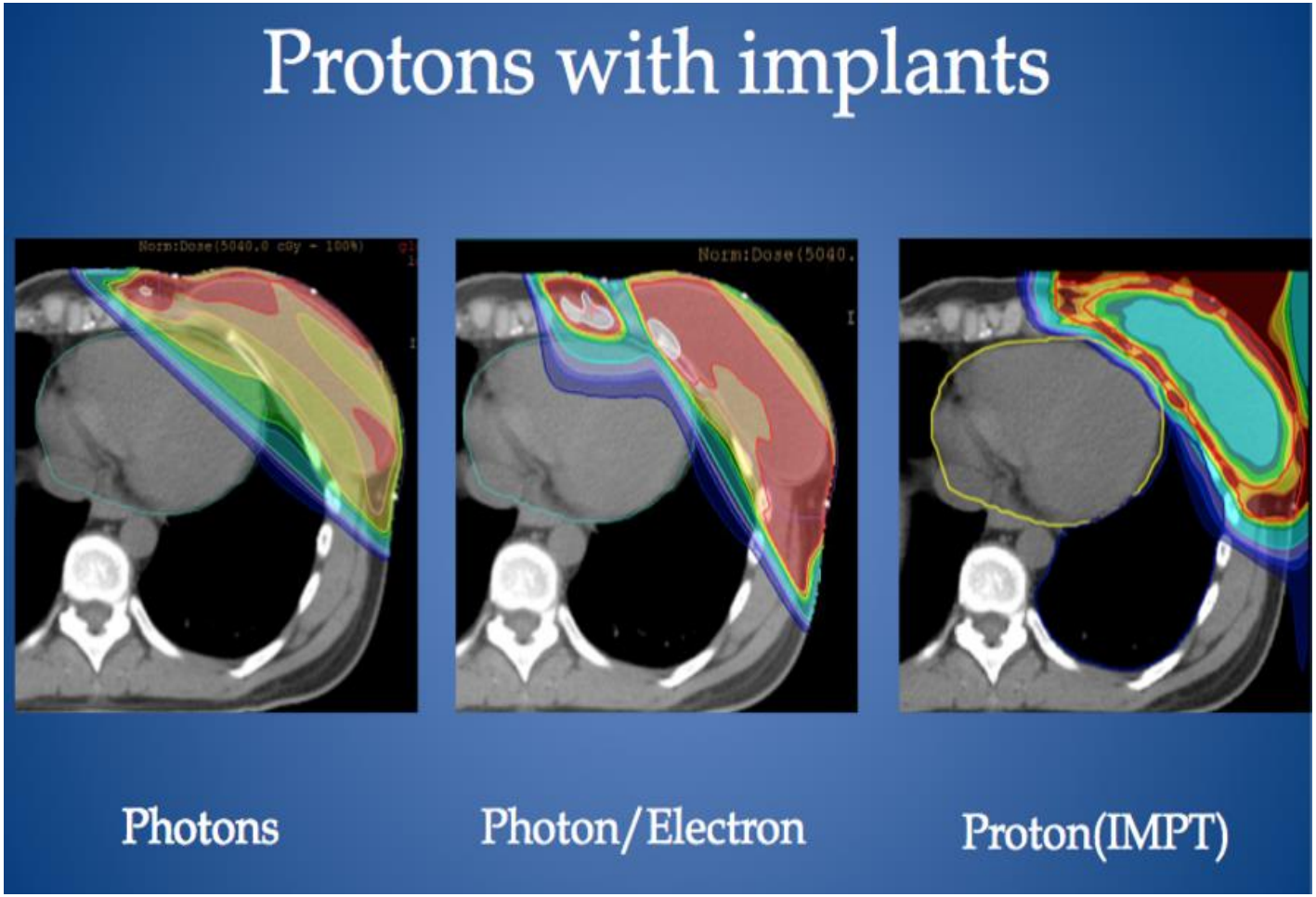


Treatment plans with protons: prostate



Courtesy of Reinhold Schulte, LLUMC

Treatment plans with protons: breast



MacDonald et al, Int J Radiat Oncol Biol Phys, 1-7, 2013

Clinical indications for particle therapy

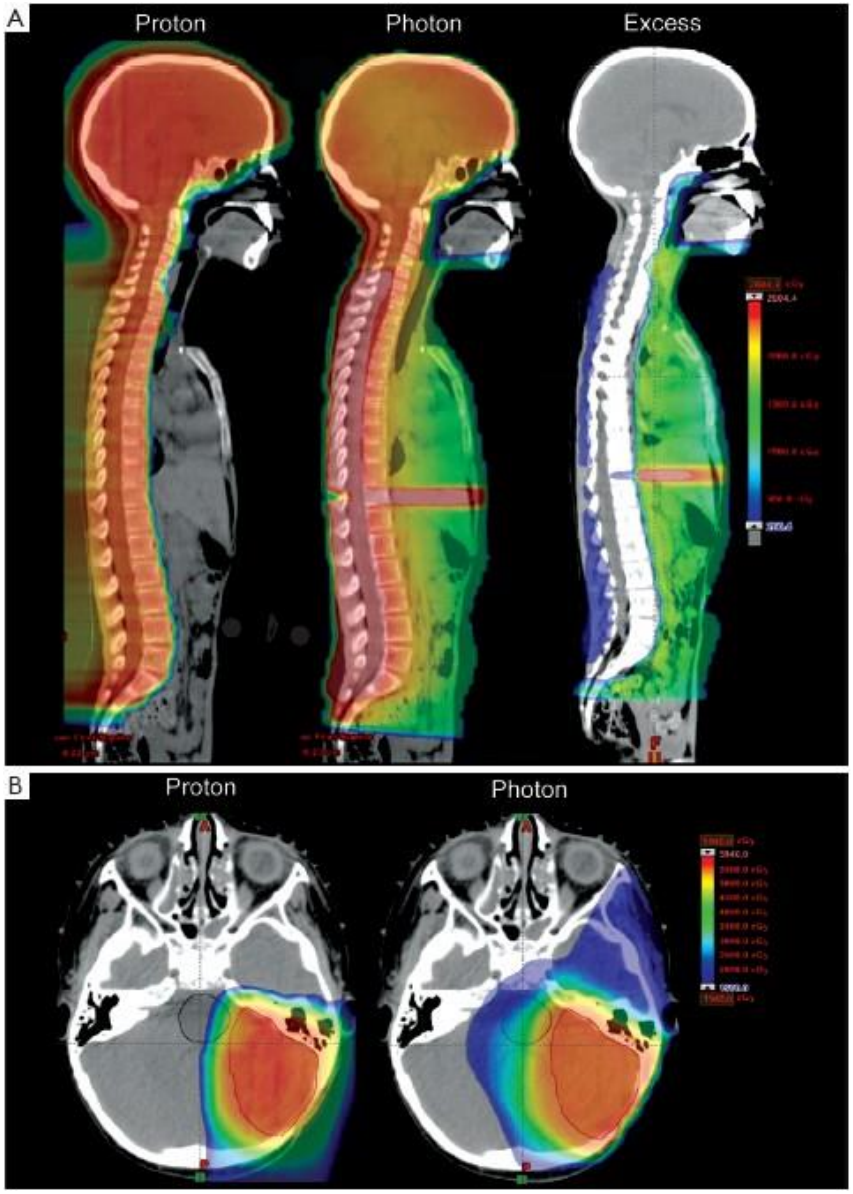
Established clinical indications

- Skull base and spine tumors
- Hepatocellular carcinoma
- Eye tumors
- Pediatric tumors

More research needed for

- Thoracic malignancies
- Head and Neck tumors
- Pelvic and abdominal sites

ASTRO Model Policy, May 2014

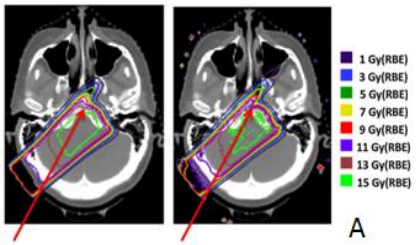


Medulloblastoma treatment, MD Anderson Cancer Center, USA

Range uncertainty

Range verification

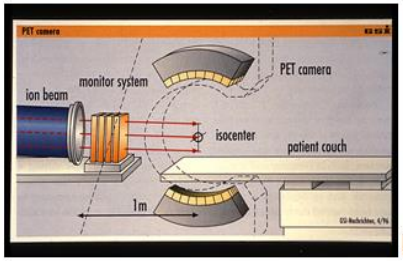
Source of range uncertainty in the patient	Range uncertainty
Independent of dose calculation:	
Measurement uncertainty in water for commissioning	± 0.3 mm
Compensator design	± 0.2 mm
Beam reproducibility	± 0.2 mm
Patient setup	± 0.7 mm
Dose calculation:	
Biology (always positive)	+ 0.8 %
CT imaging and calibration	± 0.5 %
CT conversion to tissue (excluding I-values)	± 0.5 %
CT grid size	± 0.3 %
Mean excitation energies (I-values) in tissue	± 1.5 %
Range degradation; complex inhomogeneities	- 0.7 %
Range degradation; local lateral inhomogeneities *	± 2.5 %
Total (excluding *)	**2.7% + 1.2 mm**
Total	**4.6% + 1.2 mm**



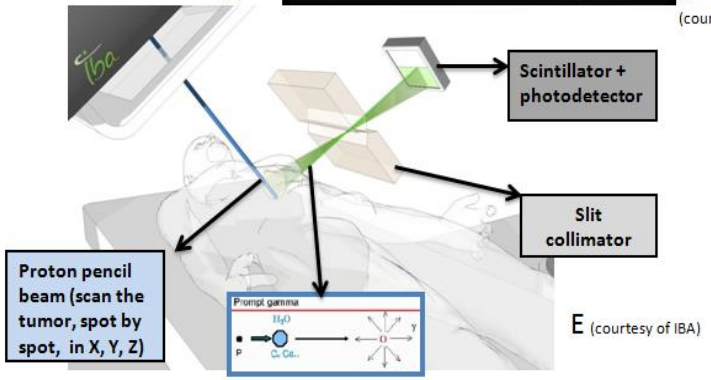
A

B

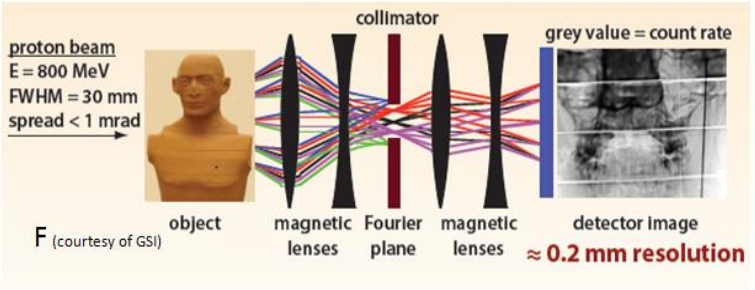
C



D (courtesy of GSI)



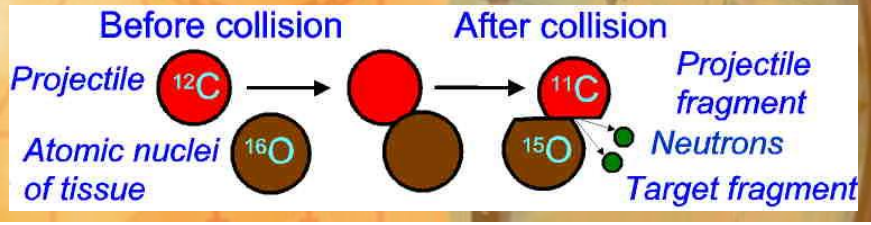
E (courtesy of IBA)

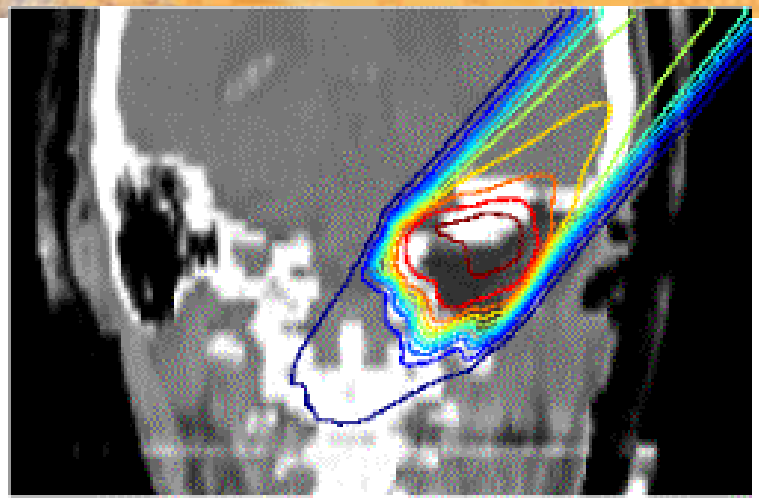


F (courtesy of GSI)

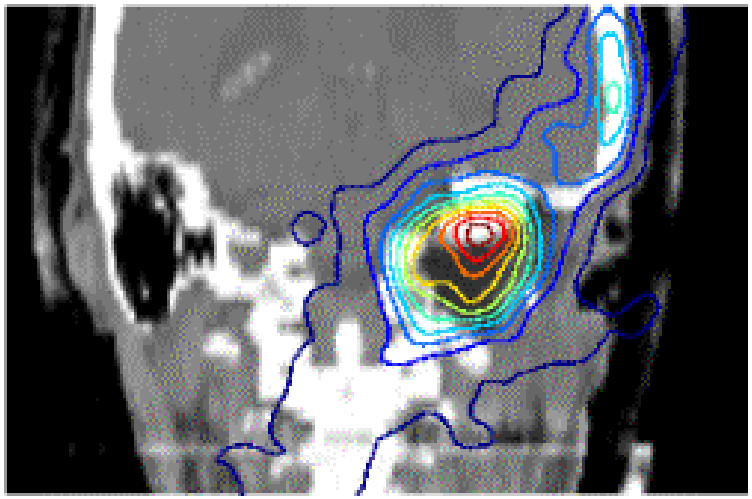
NuPECC report „Nuclear Physics in Medicine“, 2014

In situ control with PET

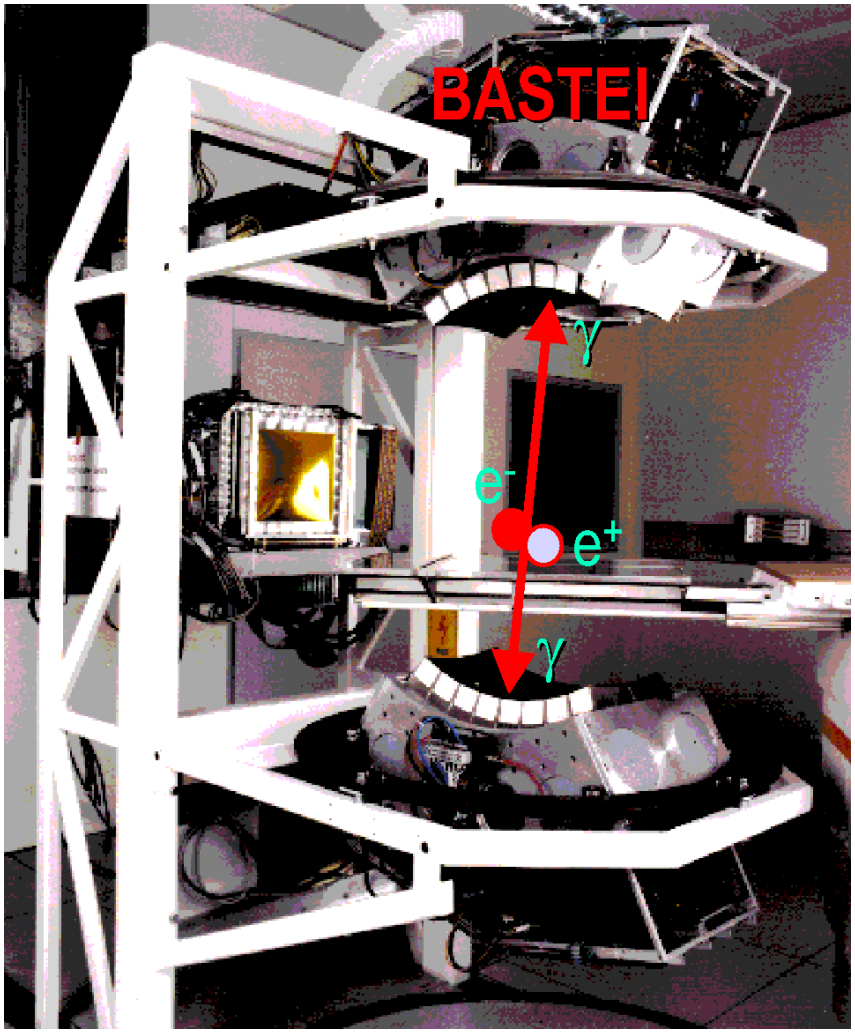




dose plan



measured



Courtesy of Wolfgang Enghardt, HZDR, Dresden

Comparison of two dedicated 'in beam' PET systems via simultaneous imaging of ^{12}C-induced β^+-activity

F Attanasi[1], N Belcari[1], A Del Guerra[1], W Enghardt[2,3], S Moehrs[1], K Parodi[4], V Rosso[1] and S Vecchio[1]

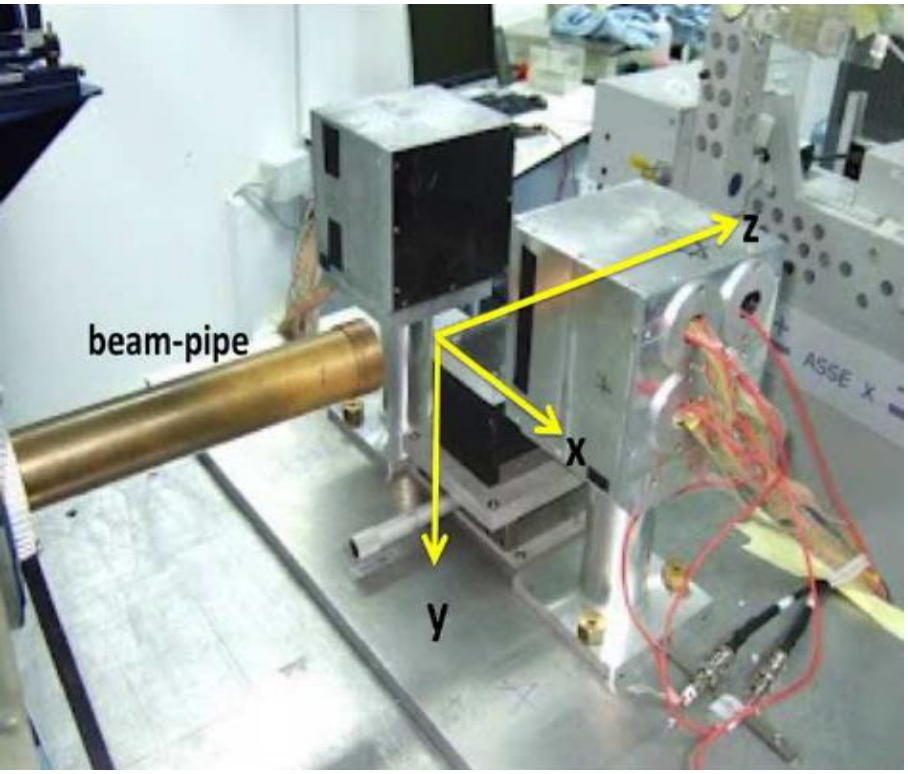
[1] Università di Pisa and Istituto Nazionale di Fisica Nucleare (INFN), Largo B. Pontecorvo 3, 56127 Pisa, Italy

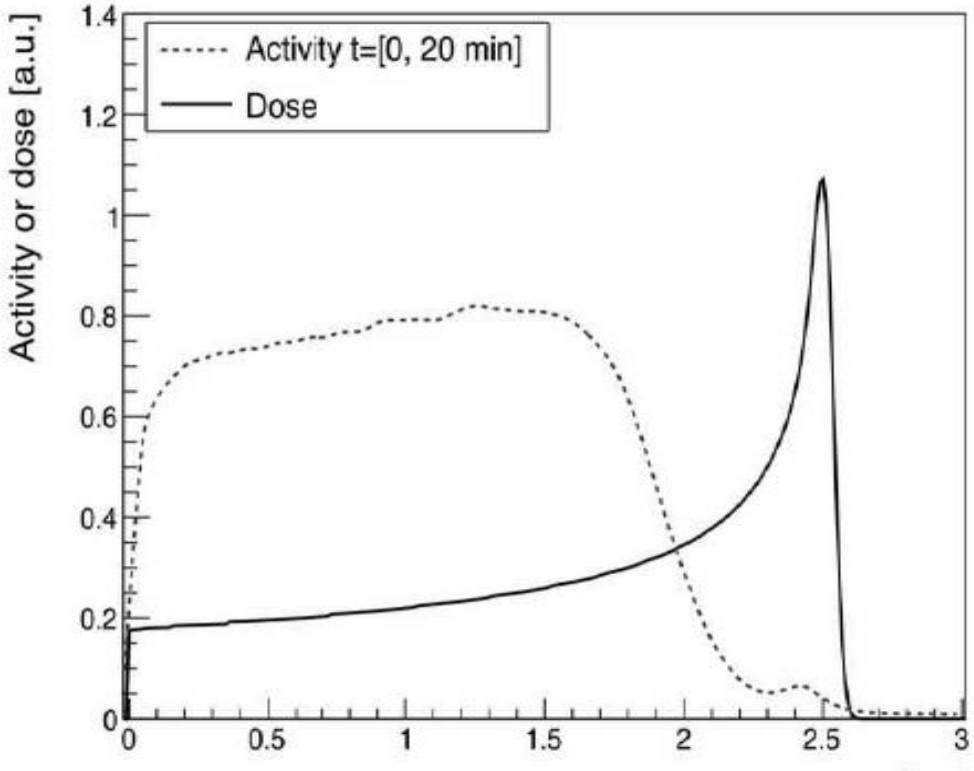
[2] Forschungszentrum Rossendorf, Institute of Nuclear and Hadron Physics, PO Box 510119, 01314 Dresden, Germany

[3] Technische Universität Dresden, Radiation Research in Oncology-Oncoray, Fetscherstr. 74, PO Box 86, 01307 Dresden, Germany

[4] Heidelberg Ion Beam Therapy Center (HIT), Im Neuenheimer Feld 450, 69120 Heidelberg, Germany

Proton range monitoring with in-beam PET: Monte Carlo activity predictions and comparison with cyclotron data



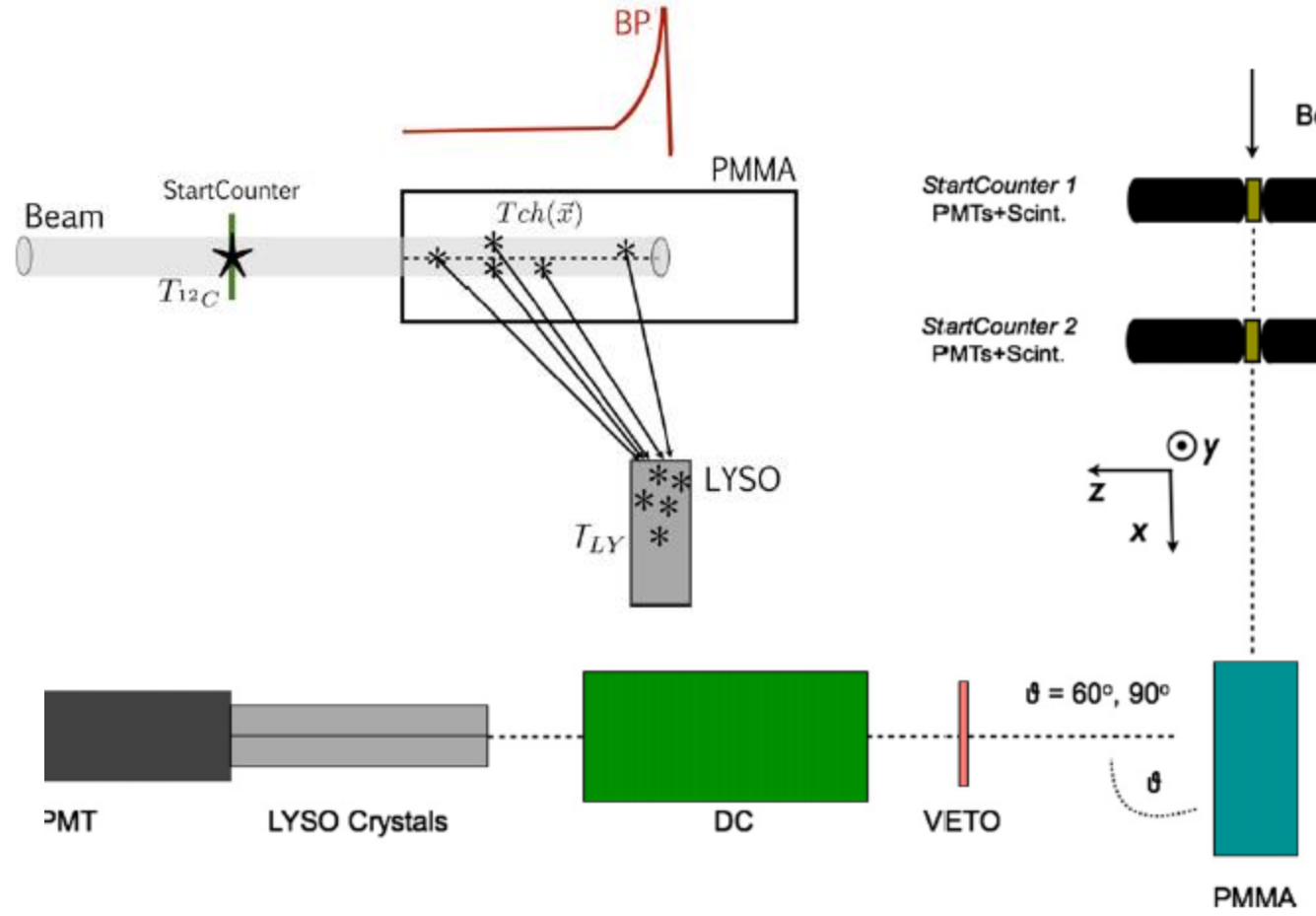


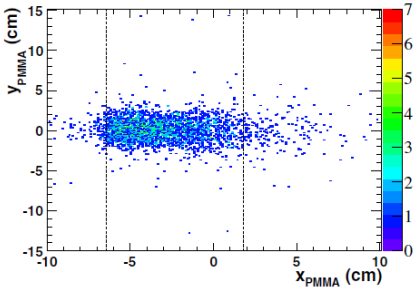
Kraan *et al., Phys. Med.* 2014

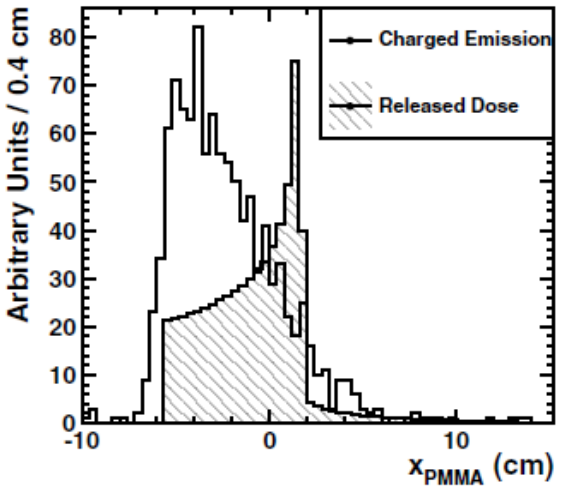
INFN Istituto Nazionale di Fisica Nucleare

UNIVERSITÀ DI PISA

Prompt charged particles







Piersanti *et al., Phys. Med. Biol*. 2014

Conclusions

- The future of particle therapy strongly depends on improvements in medical physics
- Range uncertainty is one of the main hindrance to a widespread use of particle therapy: only with a higher precision we can safely go into radiosurgery and treat moving targets
- Even if IGRT in PT is (surprisingly) not as advanced as for IMRT, charged particles offer opportunities (γ and secondary proton emission, β^+ production) not available with X-rays
- Online PET (combined with TOF) is likely to become the golden standard for beam monitor, especially for organs with high blood supply and therefore rapid washout

Biophysics Department

M. Durante (Director)

G. Kraft (Helmholtz Professor)

G. Taucher-Scholz (DNA damage)

S. Ritter (Stem cells)

C. Fournier (Late effects)

W. Tinganelli (Clinical radiobiology)

M. Scholz (Biophysical modelling)

M. Krämer (Treatment planning)

C. Graeff (Medical physics)

C. La Tessa (Dosimetry)

Thank you very much!

http://www.gsi.de/biophysik/