

# Imaging beam in patient (and patient with beam...)

Katia Parodi, Ph.D.

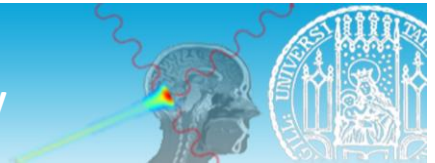
Ludwig-Maximilians-Universität München (LMU Munich)  
Department of Medical Physics, Munich, Germany

## International Conference on Medical Accelerators and Particle Therapy

Sevilla, September 4<sup>th</sup>, 2019



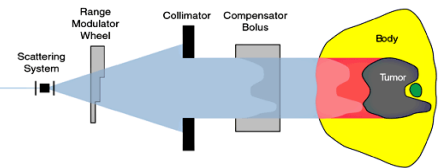
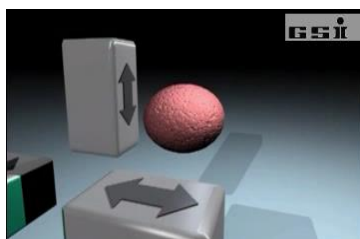
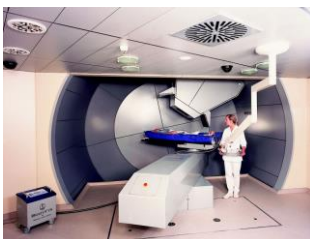
# The technological evolution of ion therapy



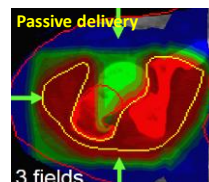
*From fixed beamlines and  
passive beam delivery ...*



*... to rotating gantries and  
active beam delivery...*



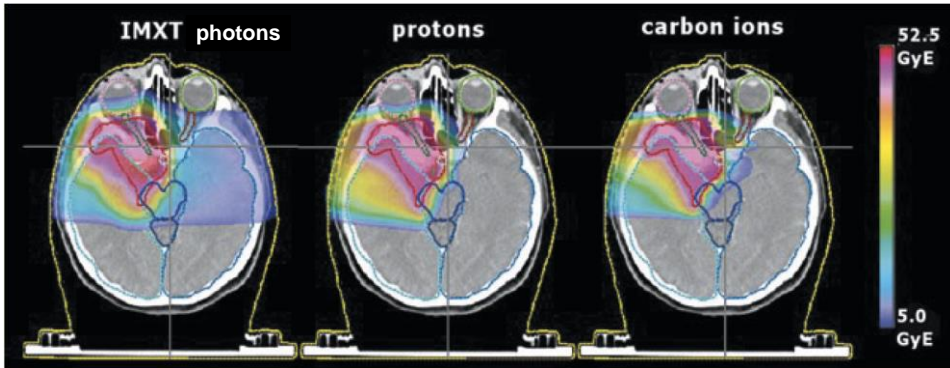
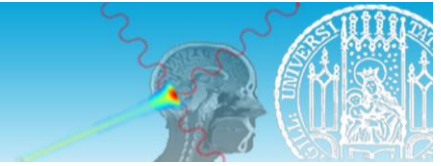
*... and intensity modulated particle  
therapy treatment planning (IMPT)*



Sources: Courtesy of Eleanor Blakeley, RPTC, GSI and Antony Lomax, PSI



# Clinical rationale of ion beam therapy

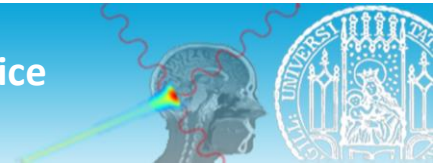


Is what we see what the patient receives?

Nuclear Physics for Medicine Report, NUPECC, 2014

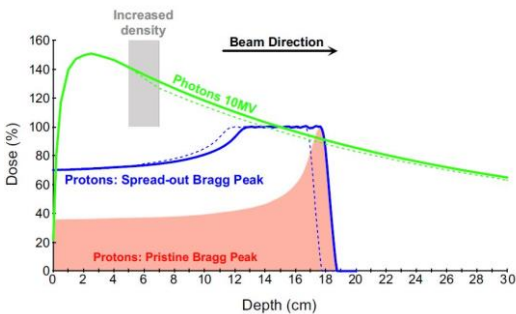
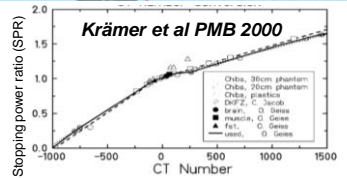


# Challenges in clinical practice

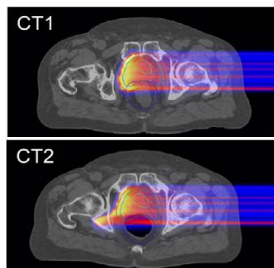


Increased sensitivity to uncertainties in beam delivery

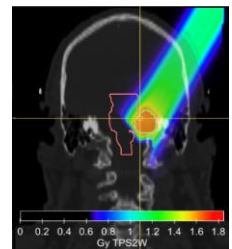
- Anatomical changes (inter- and intra-fractions)
- Tissue stopping power (relative to water, SPR)



M. Engelsman et al, Seminars Rad. Onc. 2013



S. Schmid...K. Parodi, G. Dedes, PMB 2015

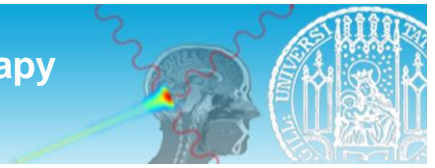


Bauer et al, HIT

In-vivo verification and adaptation?

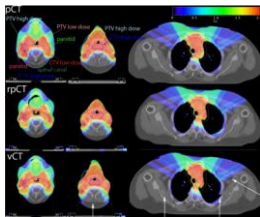


## Imaging for ion beam therapy

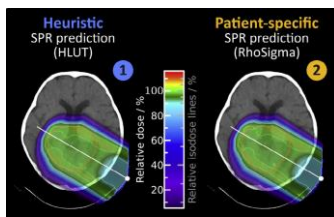


More demanding than solutions in clinical use for photon therapy  
 Enhanced in-room (ideally at isocenter) imaging with SPR information

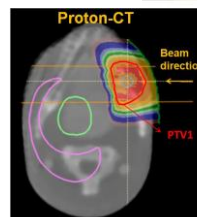
- On-board scatter-corrected CBCT
- On-rails (DE)CT
- Ion radiography/tomography
- Magnetic Resonance Imaging



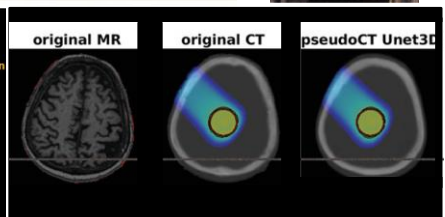
Landry ...Parodi MP 2015



Wolfahrt et al, IJROBP 2017



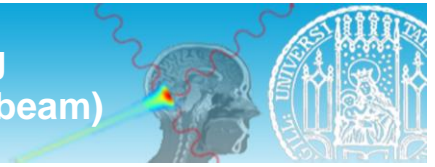
Oancea&Schulte, IEEE MIC 2018



Neppi, ...Parodi, Kamp, Acta Oncol 2019

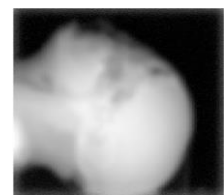
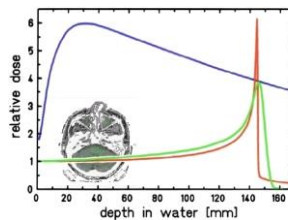


## Ion transmission imaging (imaging the patient with the beam)



### Ion radiography / tomography for:

- Direct (integral) SPR determination for patient-specific refinement of planning information (Schneider et al, Med Phys 2005, Schulte et al TANS 2012)
- Daily, low-dose image guidance for patient positioning (Cassetta et al JACMP 2019)



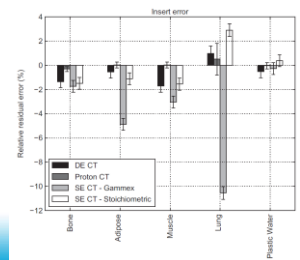
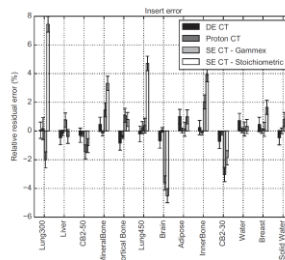
Krah et al PMB 2019

Several detector concepts under investigation worldwide and discussion about optimal ion

### Comparison of simulated (realistic) proton CT vs experimental DECT and SECT

Reduced errors (RMSE) for pCT (~0.2-0.5%) vs DECT (~0.5-0.9%) and SECT (1.6-2.7%)

Acta Oncologica, 2015; 54: 1638-1642  
 A simulation study on proton computed tomography (CT) stopping power accuracy using dual energy CT scans as benchmark  
 DAVID C. HANSEN<sup>1</sup>, JOAO SEGO<sup>2</sup>, THOMAS SANGILD SØRENSEN<sup>1</sup>, JØRGEN BREIDE BALTZER PETERSEN<sup>1</sup>, JOACHIM E. WILDBERGER<sup>3</sup>, FRANK VERHAEGEN<sup>2</sup> & GUILLAUME LANDRY<sup>2,4</sup>

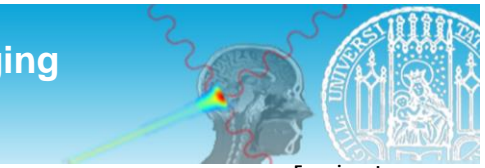
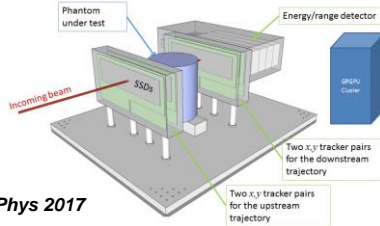




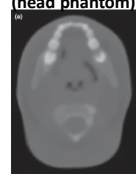
# Ion transmission imaging

Proton CT scanner  
Prototype at Loma  
Linda University

*Bashkirov et al Med Phys 2016, V.  
Giacometti...Parodi...Schulte Med Phys 2017*



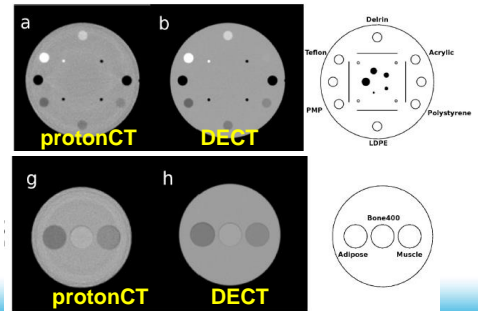
Experiment  
(head phantom)



Competitive performance of proton CT prototype vs dual-source DECT (MAPE of 0.55% vs 0.67% at ~20 reduced dose)

*Dedes, ..., Schulte, Landry, Parodi, PMB, 2019*

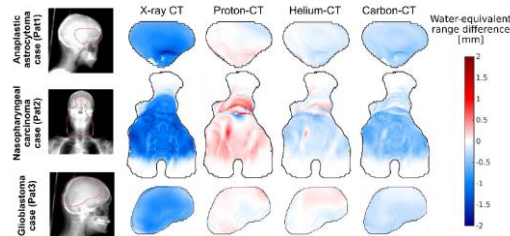
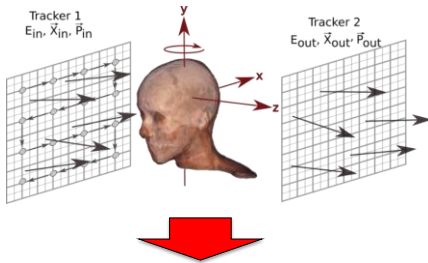
**Proton imaging promises better than 1% SPR accuracy at dose  $\leq 1-2$  mGy**



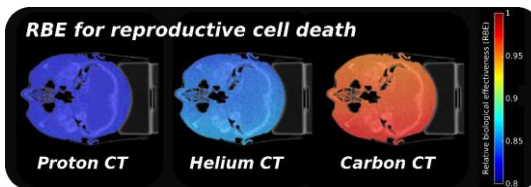
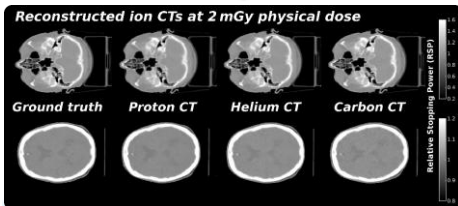
# Proton or heavier ion CT?



MC simulation of an ideal detector for proton, helium and carbon ion CT



Comparably better range accuracy than X-ray CT regardless of ion species



Reduced RBE for ion CT compared to imaging X-rays (according to RMF model\*)

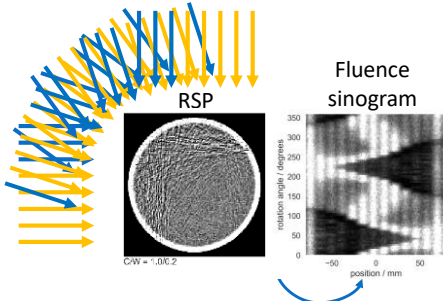
*S. Meyer, ..., K. Parodi PMB 2019, presented at AAPM 2018*

*\* Carlson et al, Radiation Research 2008*



# Fluence-modulated proton CT (FMpCT)

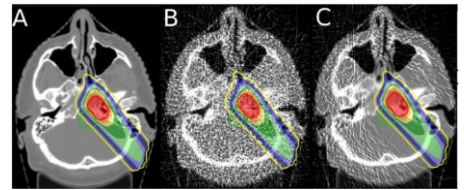
FMpCT achieves arbitrary image noise targets



Iterative optimization based on variance reconstruction and a Monte Carlo patient model

Local reduction of imaging dose

Frequent dose verification within region of good image quality



noise in beam	Low	High	Low
dose outside beam	High	Low	Low

J. Dickmann, G. Dedes...K. Parodi, G. Landry, presented at AAPM 2019; Dedes et al Med Phys 2018



# Make the invisible visible (imaging the beam in the patient)

## Imaging particle beams for cancer treatment

Jeremy C. Pohl and Kallia Parodi

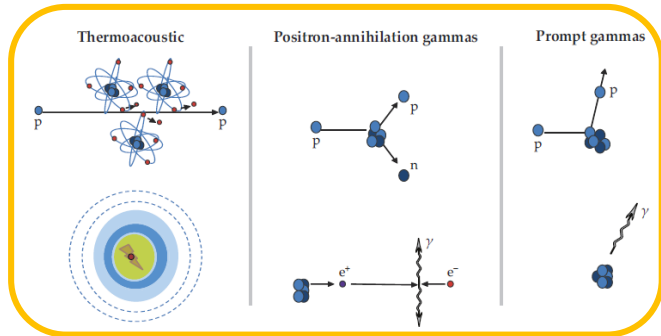
Proton and carbon-ion radiotherapy are powerful tools for killing tumor cells, but only if the particles deposit their energy where they're supposed to.

In 2014 approximately 1 to 7 deaths worldwide were due to cancer and an estimated 14 million new cases of cancer were diagnosed. Many cancer patients receive radiotherapy either on its own or in conjunction with chemotherapy or surgery. Radiotherapy works as a cancer treatment by depositing energy through atomic and nuclear interactions in patient tissues and thereby damaging tumor cells. The energy deposition, known as the Bragg peak, is maximal in units of joules per kilogram of tissue, or gray. The goal is to deliver the prescribed radiation treatment dose to the tumor while sparing healthy tissue. In the past 20 years have seen the development and deployment of sophisticated new treatment techniques designed to precisely target and deliver radiation to the tumor volume. One of these techniques is proton and carbon-ion radiotherapy. In particular, the prevalence of radiotherapy



28 October 2015 | Physics Today | www.physicstoday.org

## Different emission mechanisms





# “Ionoacoustic” range verification

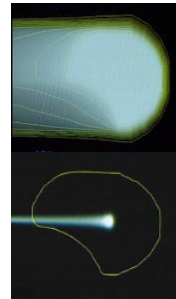
First observed in passively scattered proton therapy

- **diffuse** local dose deposition
- **small** ionoacoustic signal amplitude
- **complex** range information

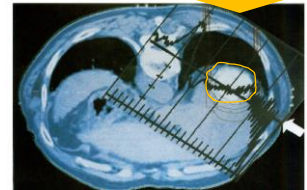
Revived interest in connection with pencil beam scanning

- highly **localized** dose deposition
- **enhanced** ionoacoustic signal amplitude
- **direct** range information

Trends of **high pulse intensity** for new accelerators like synchro-cyclotrons (e.g., 6-7  $\mu\text{s}$  FMHW, up to  $\sim 5\text{pC/pulse}$  @ 1kHz for IBA S2C2) or possibility to **pulse isochronous cyclotrons** (e.g, Jones et al Med Phys 2016)

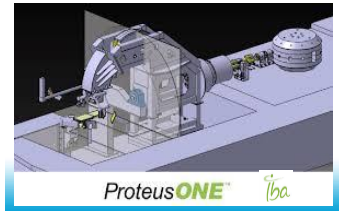
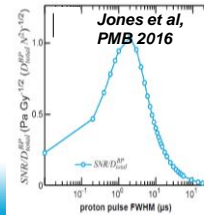


Passively scattered, pulsed proton beam



Hydrophone

Y. Hayakawa et al, Rad Onc Invest 1995

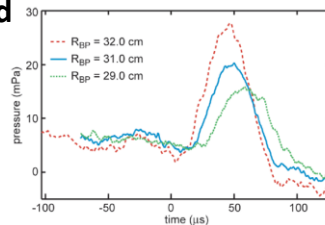


# “Ionoacoustic” range verification

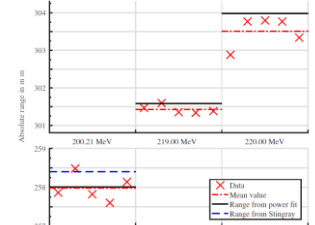
Promising experimental campaigns and MC simulations at clinical energies

Sub-mm proton range retrieval accuracy and precision in water at few Gy dose with hydrophones

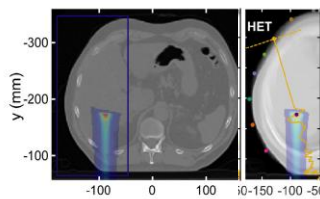
Expected (sub)millimeter range verification capabilities also in heterogenous patient anatomy, when using TOF and time reversal methods (with ideal detector properties)



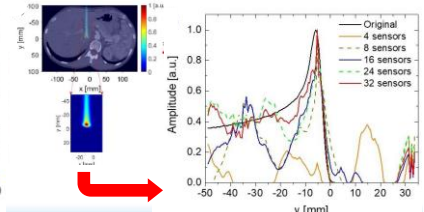
Jones et al, Med Phys 2015



Lehrack, ...Parodi, PMB Letter, 2017



Jones et al, PMB 2018



Yu et al, Med Phys 2019

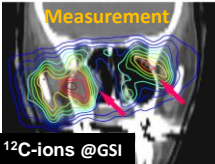
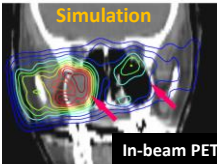


# PET range verification: The clinical implementations

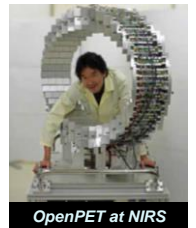
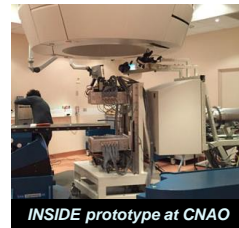


Feasibility to detect inter-fractional changes (anatomy, positioning) despite low SNR, biological washout and suboptimal instrumentation

**New dedicated detector concepts under development worldwide**



**In-beam PET <sup>12</sup>C-ions @GSI**



*K. Parodi PhD Thesis 2004  
W. Enghardt, K. Parodi et al, Radiother Oncol 2004*

*Bisogni et al, J Med Imag 2016*

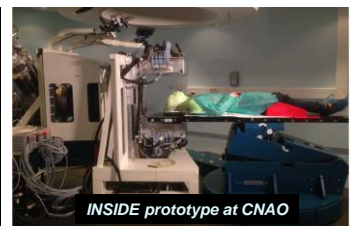
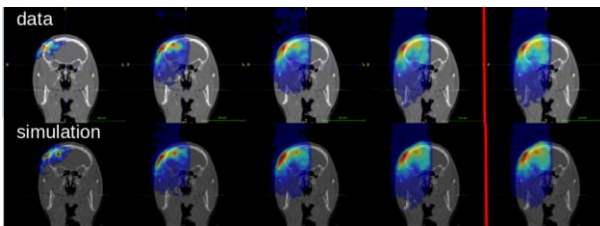
*Tashima... Yamaya, PMB 2016*



# PET range verification: Next-generation instrumentation

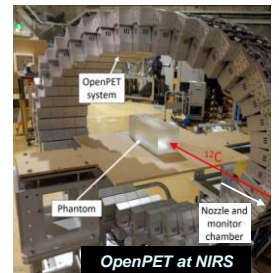
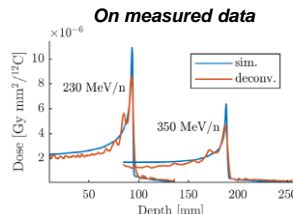
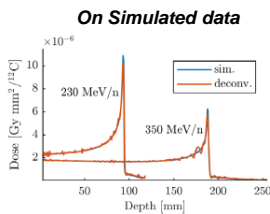


- Clinical evaluation ongoing with protons and soon also <sup>12</sup>C ions



*Fiorina...Bisogni, Phys Med 2018*

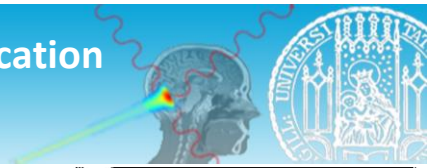
- Testing <sup>12</sup>C ion dose reconstruction algorithm



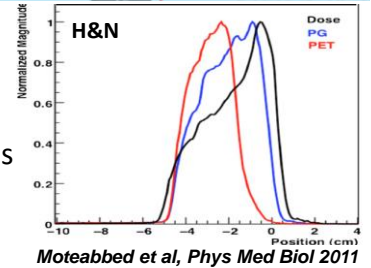
*Hofmann, Pinto... Yamaya, Parodi, PMB 2019*



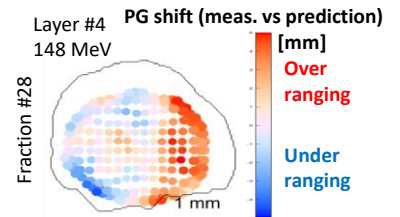
## Prompt gamma (PG) range verification First clinical implementation



Fast (sub-ns) emission eliminates issue of biological washout  
Signal fall-off is closely correlated to Bragg peak position due to lower cross section thresholds than for PET  
Dedicated developments for directional detection of high energy PGs ( $\approx 2-7$  MeV) embedded in huge neutron background



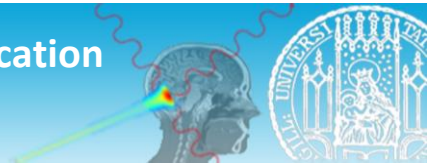
### Prototype 1D PG camera with slit collimators



Smeets et al Phys Med 2012, Xie et al IJROBP 2017, Courtesy Kevin Teo, UPENN

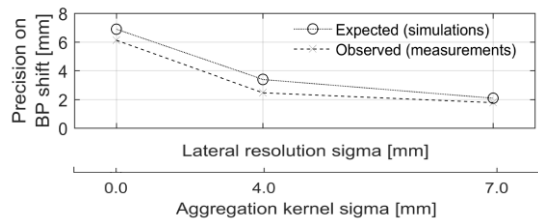
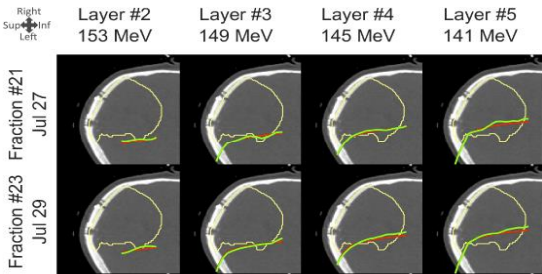


## Prompt gamma (PG) range verification First clinical implementation



First clinical study with PBS reported proton range shift retrieval accuracy of 2mm in brain with spot aggregation

Recent results for brain patient with more heterogeneities in PTV and re-planning after control CT showed ability to detect shifts, despite complex signal from range mixing



Xie et al IJROBP 2017, Courtesy Kevin Teo, UPENN

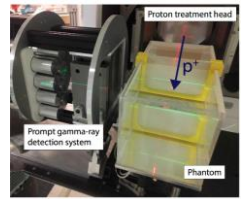
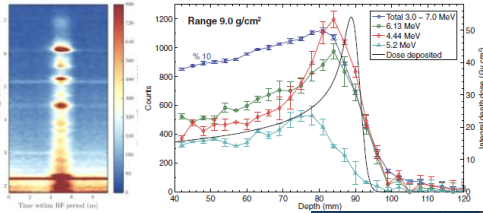




# Prompt gamma (PG) range verification Future clinical implementations

## Prompt gamma spectroscopy

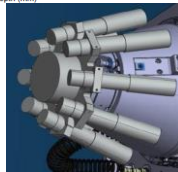
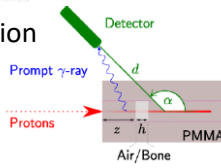
- Exploits PG energy information
  - Custom-made collimated prototype close to start pilot clinical study @ MGH
- Verburg et al, PMB 2013 Hueso-González et al, PMB 2018*



## Prompt gamma timing

- Exploits timing information, overcoming collimation
- Custom-made prototype under development for future clinical translation @ Oncoray Dresden

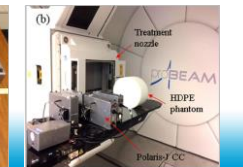
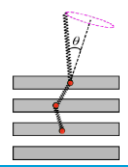
*Golnik et al PMB 2014; Pausch et al, PMB 2018; Werner...Pausch, P*



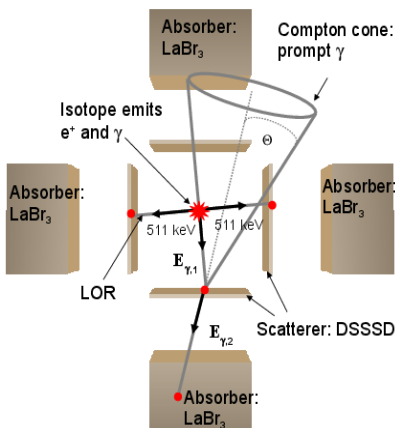
## Compton camera imaging

- Exploits Compton kinematics, overcoming collimation
- Commercial prototype under further development for future clinical translation @ Maryland

*Draeger...Polf, PMB 2018*



# Next-generation of hybrid detectors

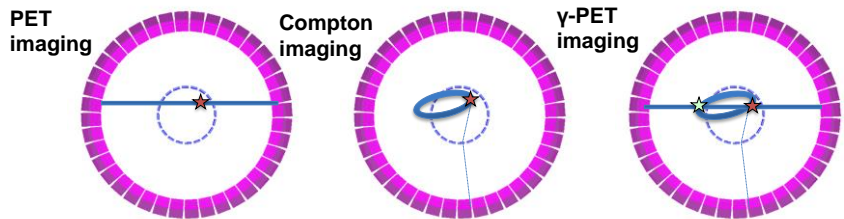


**V. Anagnostatou...K. Parodi**  
**EU Project HIPPOCRATE**  
**M. Safari, Humboldt Fellowship**



**Alexander von Humboldt**  
Stiftung / Foundation

Comparison of different detector technologies & geometries in collaboration with NIRS toward „Whole Gamma Imaging“

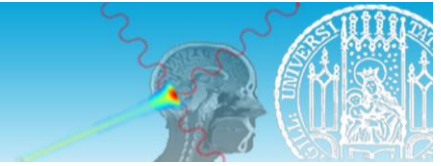


*Lang, ..., Parodi, Thirolf, JINST 2014*  
*Parodi, NIMA 2015*

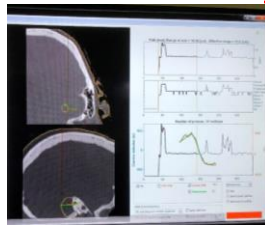
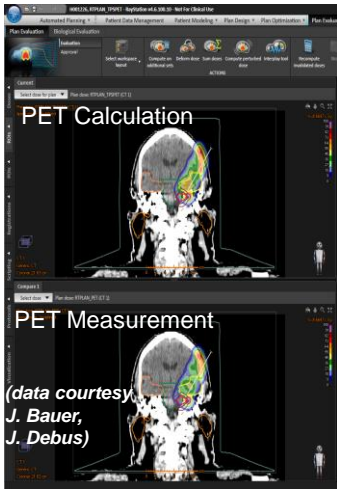




## Integration in clinical workflow



Analytical PET calculation & ongoing integration of prompt gamma in a research version of Treatment Planning System "RayStation"



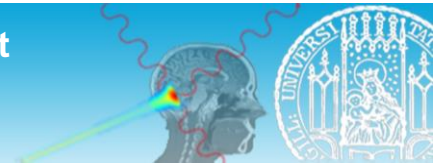
*Pinto...Parodi, to be submitted*

Pinto, Kröniger, ...E. Traneus, K. Parodi, ICCR 2016

Demo @ ASTRO 2018



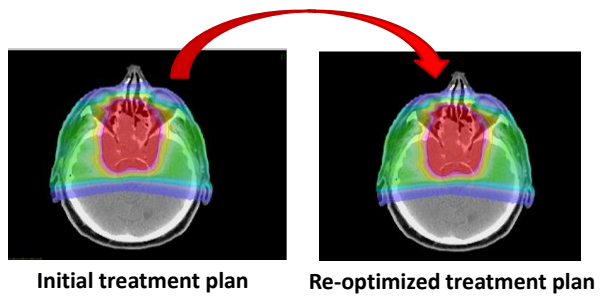
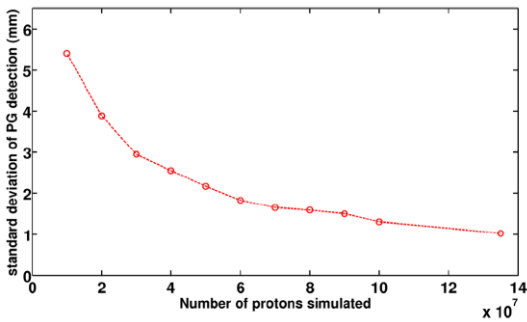
## Toward a new treatment planning strategy



Range retrieval accuracy and precision crucially depend on PB statistics and PG-dose correlation

New planning concept to account for PG statistics correlation to dose

*See talk of OMA fellow Liheng Tian*

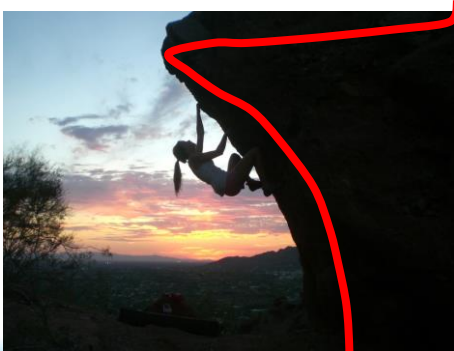


*Tian...Parodi, Phys Med Biol 2018*

## Conclusion & Outlook

Several techniques under investigation and development to enable

- Improved anatomy & SPR characterization prior to treatment
- In-vivo range verification during treatment



*...yet still a lot to do to fully exploit Bragg Peak clinically*

*Thank you*



European Research Council



## Acknowledgement

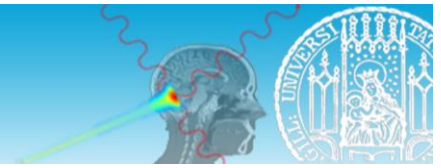


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