Advances in ion imaging and range verification

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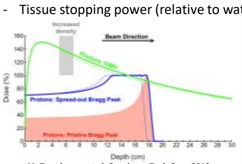
Conflict of Interest

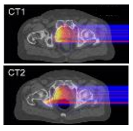
Research collaboration and two license agreements with RaySearch Laboratories AB

Challenges in clinical practice

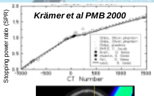
Increased sensitivity to uncertainties in beam delivery
- Anatomical changes (inter- and intra-fractions)
- Tissue stopping power (relative to water, SPR)

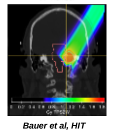


M. Engelsman et al, Seminars Rad. Onc. 2013



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





Bauer et al, HIT

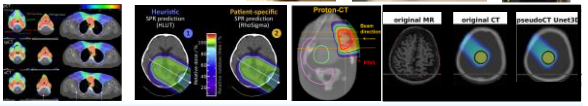
In-vivo verification and adaptation?

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

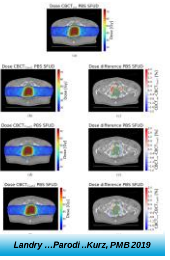


Landry …Parodi MP 2015 *Wolfahrt et al, IJROBP 2017* *Oancea&Schulte, IEEE MIC 2018* *Neppl, …Parodi, Kamp, Acta Oncol 2019*

Scatter-corrected CBCT

- Fast (< 10 s) scatter correction possible with deep learning
- Promising results for both correction methods at projection level (~ 10 ms / projection) and image level
- Space for improvement for more reliable dose calculation in ion beam therapy (e.g., connected to beam records)
- Similar results for synthetic CT generation from MRI
- However, SPR information not yet incorporated
  (enhancement with DE, pRAD, direct SPR conversion?)

See talk H. Bouchard

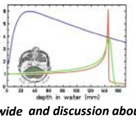


Landry …Parodi ..Kurz, PMB 2019

Ion transmission imaging

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

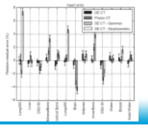
DeJongh et al SU-I330-GePD-F6-5

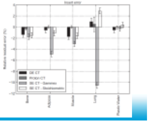
Comparison of simulated (realistic) proton CT vs experimental DECT and SECT

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

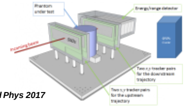
A simulation study on proton computed tomography (CT) stopping power accuracy using dual energy CT scans as benchmark



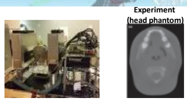


Ion transmission imaging

Proton CT scanner Prototype at Loma Linda University

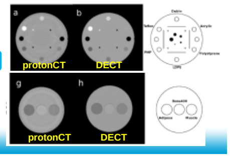


Bashkirov et al Med Phys 2016, V. Giacometti…Parodi…Schulte Med Phys 2017



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

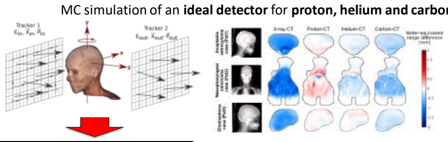
Dedes, …, Schulte, Landry, Parodi, PMB, in press **Dedes et al SU-F-221AB-5**



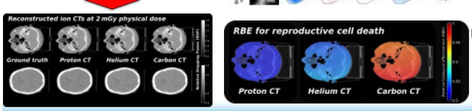
Proton imaging promises better than 1% SPR accuracy at dose ≤ 1 -2 mGy

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**



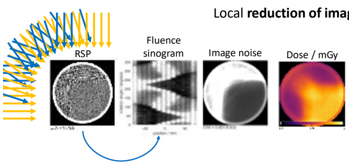
Reduced **RBE** for **ion CT** compared to imaging X-rays (according to **RMF model***)

S. Meyer, …, K. Parodi PMB 2019 (in press), presented at AAPM 2018   ** Carlson et al, Radiation Research 2008*

Fluence-modulated proton CT (FMpCT)

FMpCT achieves arbitrary **image noise targets**

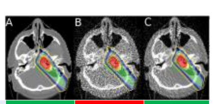
Local **reduction of imaging dose**



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

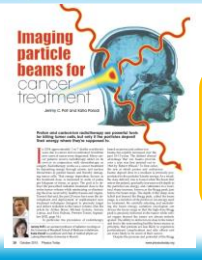
Dickmann et al WE-HI-SAN2-10

Frequent **dose verification** within region of good image quality

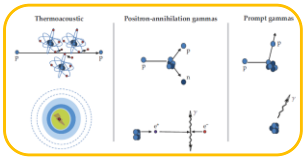


	A	B	C
noise in beam	Low	High	Low
dose outside beam	High	Low	Low

Make the invisible visible



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

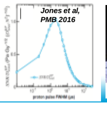
→ highly ***localized*** dose deposition
→ ***enhanced*** ionoacoustic signal amplitude
→ ***direct*** range information

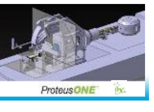
Trends of ***high pulse intensity*** for **new accelerators** like synchro-cyclotrons
(e.g., 6-7 µs FMHW, up to ~5pC/pulse @ 1kHz for IBA S2C2)

or possibility to **pulse isochronous cyclotrons**
(e.g, Jones et al Med Phys 2016)

Passively scattered, pulsed proton beam

Y. Hayakawa et al, Rad Onc Invest 1995





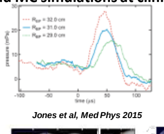
"Ionoacoustic" range verification

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

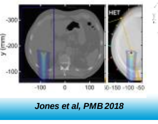
Expected (sub)millimeter range verification capabilities also in heterogenous patient anatomy, when using TOF and time reversal methods (with ideal detector properties)

MO-I345-GePD-F6-2; TU-HI-SAN4-10
SU-F-303-1; WE-C1030-GePD-F1-2
WE-C1030-GePD-F1-3; WE-C930-GePD-F7-1

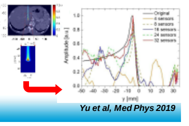


Jones et al, Med Phys 2015

Lehrack, …Parodi, PMB Letter, 2017



Jones et al, PMB 2018



Yu et al, Med Phys 2019

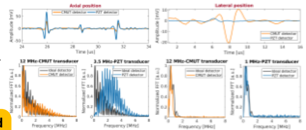
"Ionoacoustic" range verification

Investigation of high sensitivity and broadband detection systems

- Low pressure amplitudes challenging to detect (mPa vs. kPa/MPa for US imaging)
- Improvement of the signal-to-noise ratio to reduce the detection threshold (minimal dose)
- Broadband sensors: independent of the beam energy and sensor position w.r.t to the Bragg peak

Co-development of CMUT* sensors

- Collaboration with ACULAB
  Dr. Savoia - University of Roma Tre, Italy
- Dedicated CMUT design and front-end electror
- Optimization of the sensor geometry
  based on a k-Wave simulation platform



First proof-of-concept at 20 MeV compared to conventional (PZT) transducers

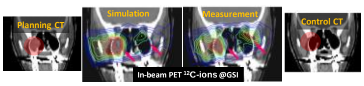
J. Lascaud …H. Wieser…Parodi, to be presented to IEEE IUS 2019

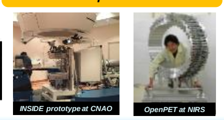
*CMUT: Capacitive Micromachined Ultrasonic Transducers

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





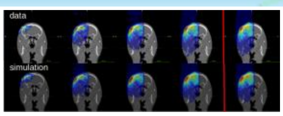
K. Parodi PhD Thesis 2004
W. Enghardt, K. Parodi et al, Radiother Oncol 2004

Bisogni et al, J Med Imag 2016

Tashima…Yamaya, PMB 2016

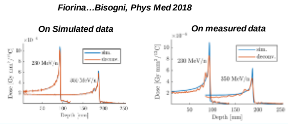
PET range verification: Next-generation instrumentation

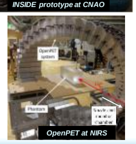
- Clinical evaluation ongoing with protons and soon also ^{12}C ions



Fiorina…Bisogni, Phys Med 2018

- Testing ^{12}C ion dose reconstruction algorithm





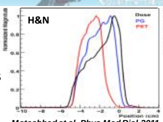
Hofmann, Pinto…Yamaya, Parodi, PMB 2019

Prompt gamma (PG) range verification
First clinical implementation

Fast (sub-ns) emission eliminates issue of biological washout

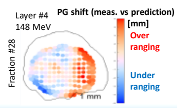
Signal fall-off is closely correlated to Bragg peak position due to lower cross section thresholds than for PET

Dedicated developments for directional detection of high energy PGs (≈ 2-7 MeV) embedded in huge neutron background



Moteabbed et al, Phys Med Biol 2011

Prototype 1D PG camera with slit collimators

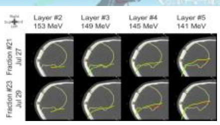


Smeets et al Phys Med 2012, Xie et al IJROBP 2017, Courtesy Kevin Teo, UPENN

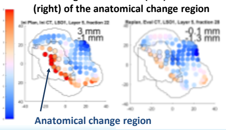
Prompt gamma (PG) range verification
First clinical implementation

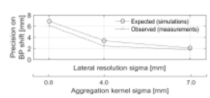
First clinical study with PBS reported proton range shift retrieval accuracy of 2mm in brain with spot aggregation

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



Shifts averaged over inside (left) and outside (right) of the anatomical change region





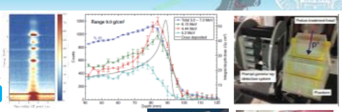
Xie et al IJROBP 2017, Courtesy Kevin Teo, UPENN

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

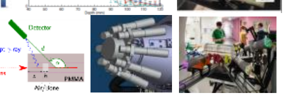
Verburg et al, PMB 2013 Hueso-González et al, PMB 2018

Verburg et al WE-HI-SAN2-6



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

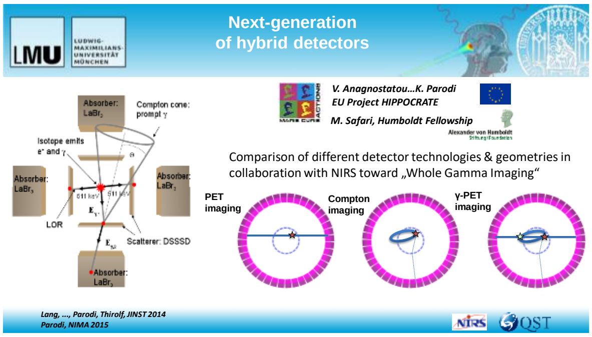
Golnik et al PMB 2014; Pausch et al, PMB 2018; Werner…Pausch, P

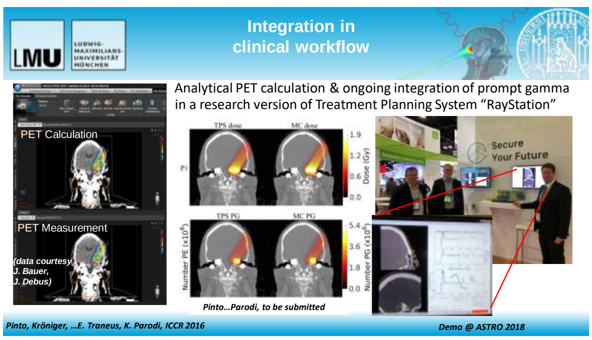


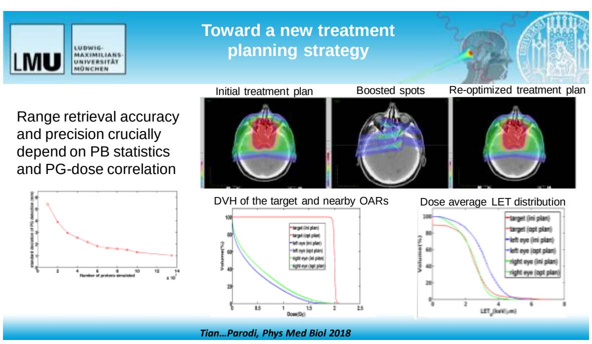
Compton camera imaging
- Exploits Compton kinematics, overcoming collimation
- Commercial prototype under further development for future clinical translation @ Maryland

Draeger…Polf, PMB 2018

Panthi et al MO-I345-GePD-F6-5

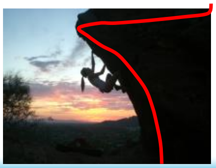

Next-generation
of hybrid detectors
V. Anagnostatou…K. Parodi
EU Project HIPPOCRATE
M. Safari, Humboldt Fellowship
Comparison of different detector technologies & geometries in collaboration with NIRS toward „Whole Gamma Imaging“
Absorber: LaBr3
Compton cone: prompt γ
Isotope emits e+ and γ
Absorber: LaBr3
Absorber: LaBr3
LOR
Scatterer: DSSSD
Absorber: LaBr3
PET imaging
Compton imaging
γ-PET 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"
PET Calculation
PET Measurement
(data courtesy J. Bauer, J. Debus)
TPS dose
MC dose
TPS PG
MC PG
Secure Your Future
Pinto…Parodi, to be submitted
Pinto, Kröniger, …E. Traneus, K. Parodi, ICCR 2016
Demo @ ASTRO 2018


Toward a new treatment
planning strategy
Initial treatment plan
Boosted spots
Re-optimized treatment plan
Range retrieval accuracy and precision crucially depend on PB statistics and PG-dose correlation
DVH of the target and nearby OARs
Dose average LET distribution
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

DFG

Acknowledgement

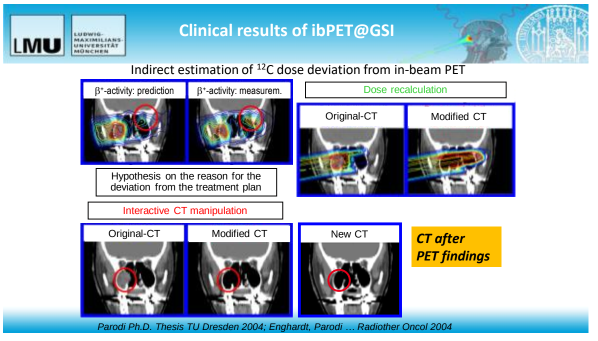
LMU Department of Experimental – Medical Physics

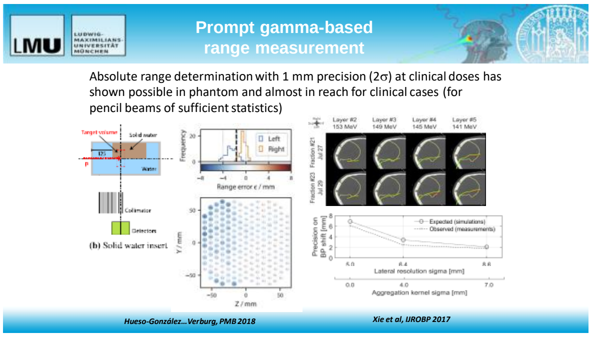
Kevin Teo
For organizing this session and providing material on PG

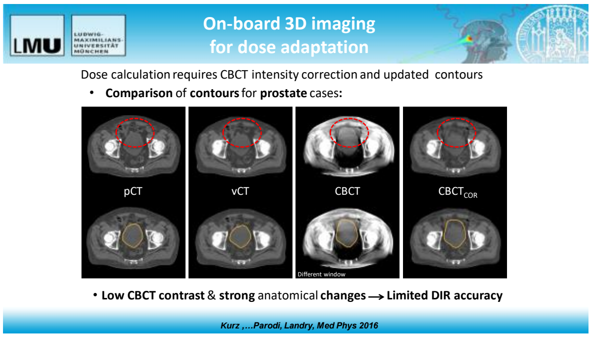
Penn Medicine
Penn Radiation Oncology

Acknowledgement

Collaborations
- C. Belka, G. Landry, C. Kurz, F. Kamp et al, LMU University Hospital
- R. Schulte et al, Loma Linda University
- A. Ferrari et al, CERN
- F. Verhaegen, MAASTRO
- T. Yamaya, NIRS
- S. Rit, CREATIS
- D. Hansen, Aarhus University Hospital
- B. Raaymakers et al, Utrecht Medical Center
- M. Vidal, J. Herault, CAL
- E. Traneus, R. Nilsson, RaySearch
- U. Weber, C. Trautmann, M. Durante, GSI


Clinical results of ibPET@GSI
Indirect estimation of 12C dose deviation from in-beam PET
β+-activity: prediction
β+-activity: measurem.
Dose recalculation
Original-CT
Modified CT
Hypothesis on the reason for the deviation from the treatment plan
Interactive CT manipulation
Original-CT
Modified CT
New CT
CT after PET findings
Parodi Ph.D. Thesis TU Dresden 2004; Enghardt, Parodi … Radiother Oncol 2004


Prompt gamma-based range measurement
Absolute range determination with 1 mm precision (2σ) at clinical doses has shown possible in phantom and almost in reach for clinical cases (for pencil beams of sufficient statistics)
(b) Solid water insert
Range error ε / mm
Lateral resolution sigma [mm]
Aggregation kernel sigma [mm]
Hueso-González…Verburg, PMB 2018
Xie et al, IJROBP 2017


On-board 3D imaging for dose adaptation
Dose calculation requires CBCT intensity correction and updated contours
• Comparison of contours for prostate cases:
pCT
vCT
CBCT
CBCTCOR
Different window
• Low CBCT contrast & strong anatomical changes → Limited DIR accuracy
Kurz ,…Parodi, Landry, Med Phys 2016