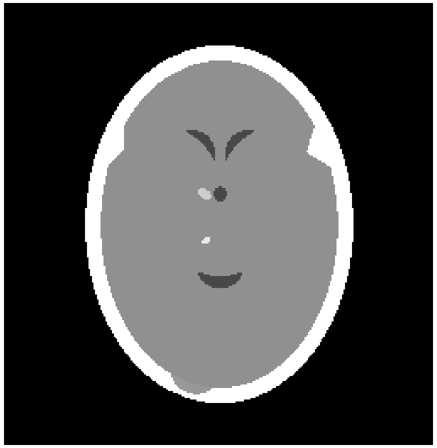
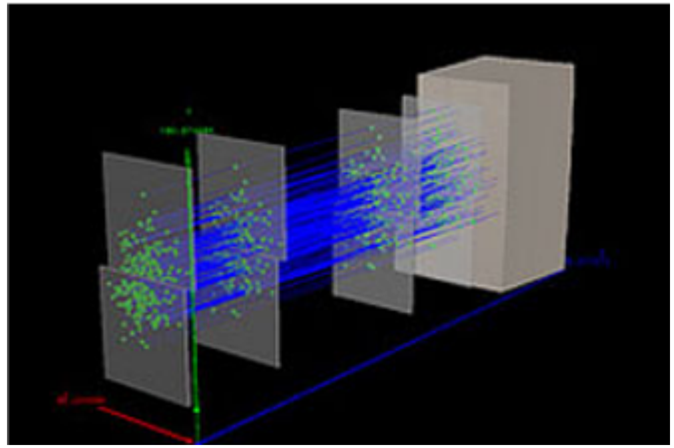
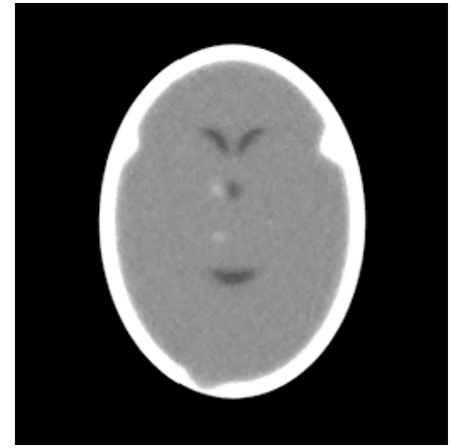






A Status Update on Proton Imaging for Applications in Medicine

Reinhard W. Schulte
Loma Linda University
pCT Collaboration
2012 NSS/MIC/RTSD Triple Joint Session

Outline

- Why should we image with protons rather than x-rays?
- A short history of charged particle CT
- Technical approaches to proton: single-particle detection, concepts and designs
- Proton CT reconstruction
- The quest for low-dose (sub-mSv) CT – is pCT the answer?

WHY SHOULD WE IMAGE WITH PROTONS?

Tomographic Imaging Modalities for Proton Therapy: **Primary** & Secondary Use

- X-ray CT: **treatment planning**, dose and range calculations, target volume delineation
- MRI: **target delineation**, alignment verification
- Positron Emission Tomography (PET)[†]: **target volume definition**, biologically weighted RT, treatment verification
- MV/kV Cone Beam CT: **alignment verification**, adaptive radiotherapy

The role of CT Imaging in Charged Particle Therapy

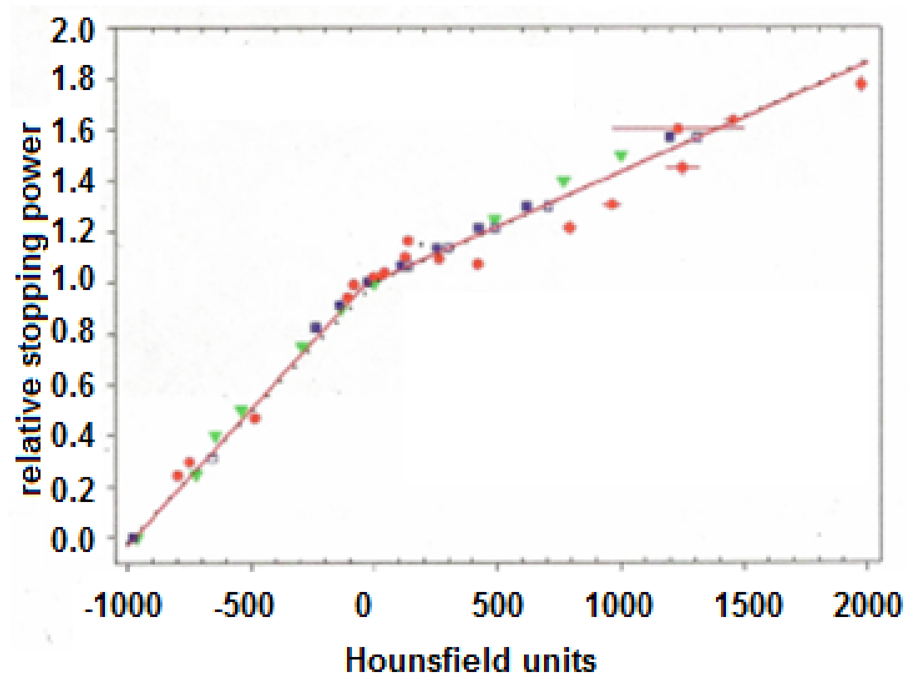
- CT imaging is needed for
  - Target volume definition (anatomical boundaries with additional information from fused MRI and PET studies
  - Dose and range calculation
  - Patient alignment verification (in-room cone beam CT, CBCT)

Pros and Cons of X-ray CT

- Pros
  - Widely available (diagnostic CT has firm industry support)
  - Thoroughly investigated and established
  - Excellent image quality (spatial and density resolution)
- Cons
  - Issues with conversion of CT units to relative proton stopping power, leading to systematic range errors of the order of 3-5% for soft tissues and higher for tissues with very low or high density (lung, bone) or in the presence of metal artifacts
  - Relatively high patient dose with CBCT when used as daily imaging modality for daily image verification
  - Reconstruction artifacts with cone beam CT -> not suitable for dose replanning

Range Accuracy of Proton/Ion Therapy when X-ray CT is used

- X-ray attenuation in the 70-120kV range is determined by photo-electric and Compton scattering
- Conversion of Hounsfield units to relative stopping power (RSP) requires careful calibration
- There is no consistent one-to-one relationship between Hounsfield units and RSP for different tissues and materials



O. Jäkel, Imaging and Tumor Localization in Ion Beam Therapy, in: Ute Linz (Ed.), Ion Beam Therapy, Springer 2012)

Process of X-ray CT to Relative Stopping Power Conversion

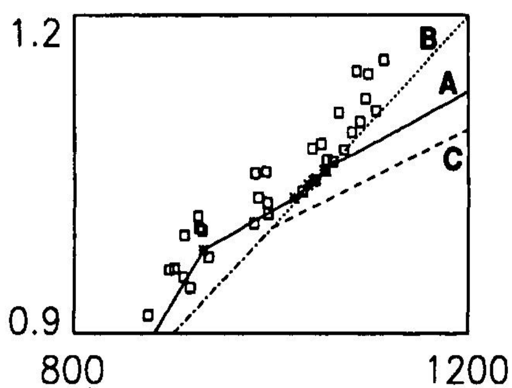
$H = 1000\ \mu^{tissue} / \mu^{water}$

$RSP = dE/dx^{tissue} / dE/dx^{water}$

CT Hounsfield values (H)

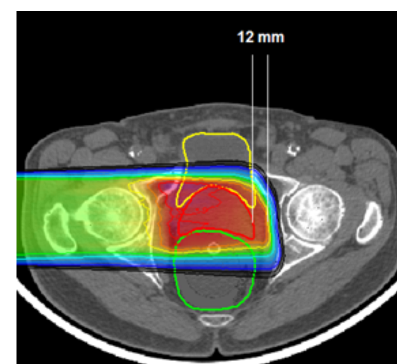
Relative proton stopping power (RSP)

Calibration curve

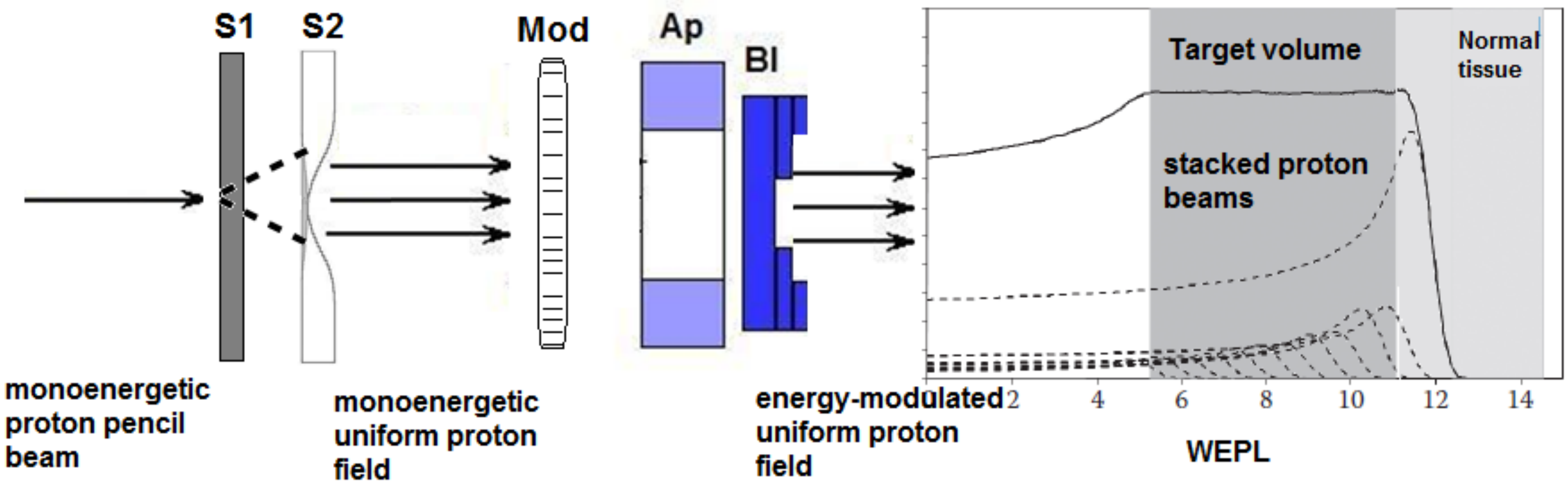


Dose & range calculation

Isodose distribution

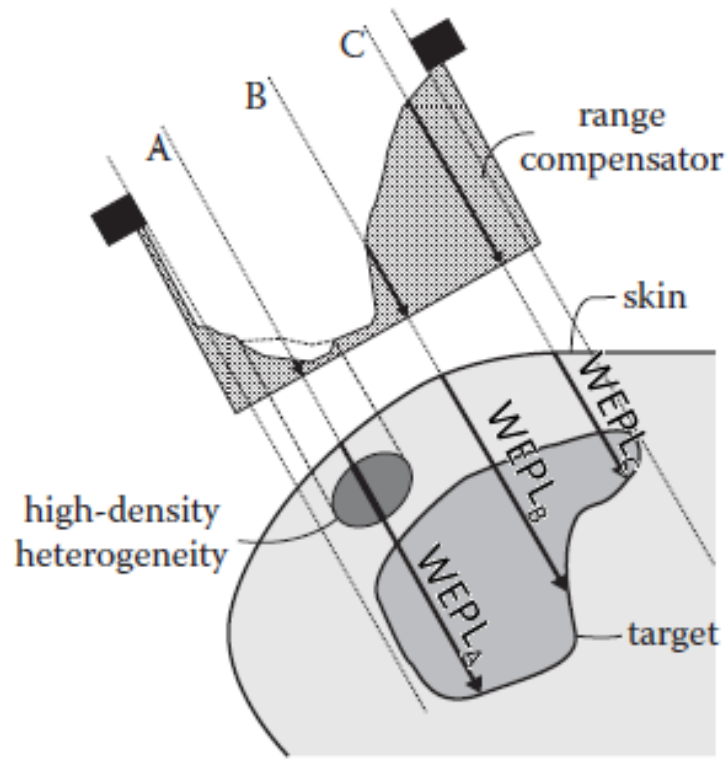


Proton Beam Delivery Technique

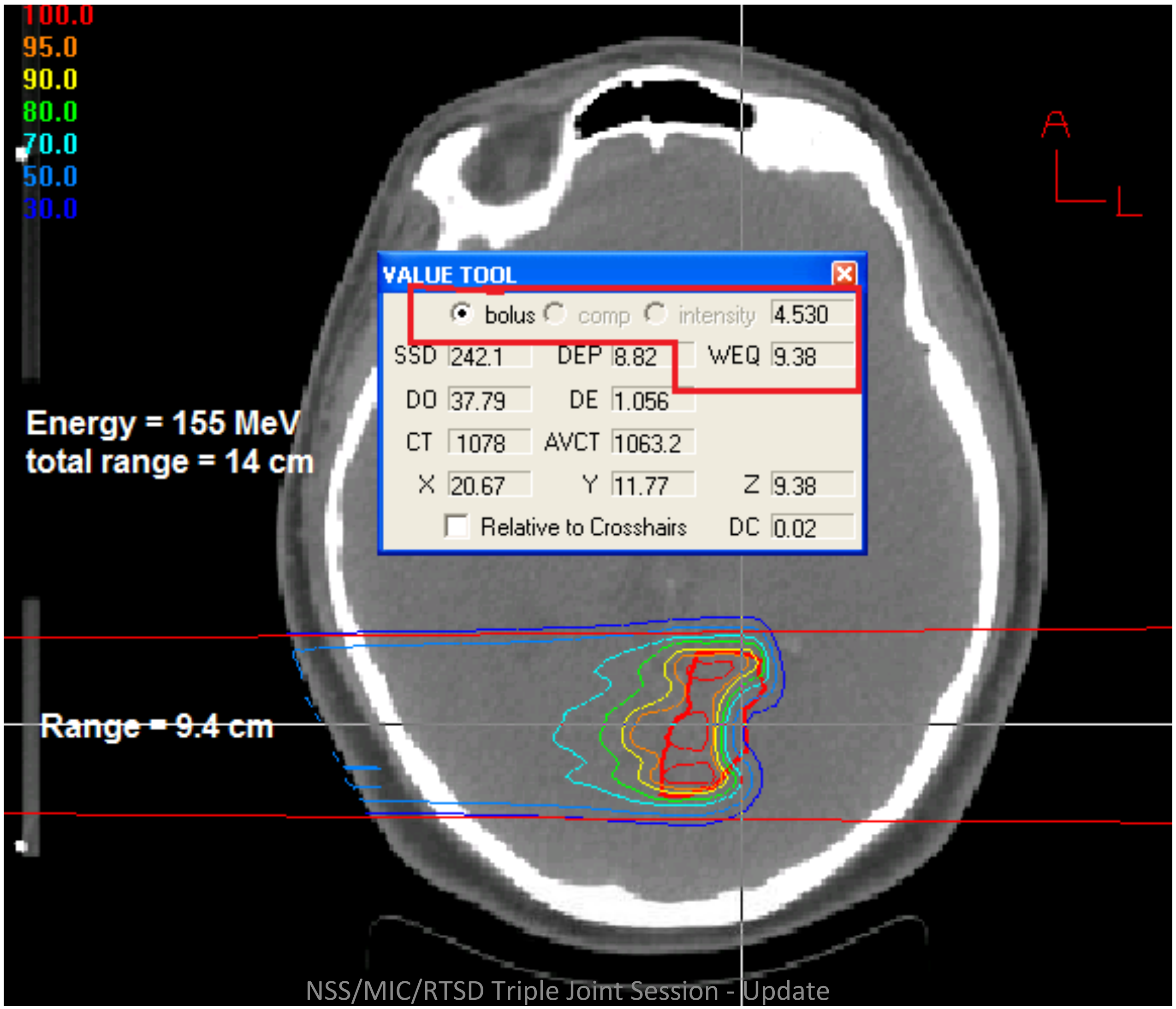


Charged Particle Treatment Planning: Proton Ray Tracing

- Protons beams are modulated in energy such that their water-equivalent pathlength in tissue places the Bragg peak at the desired location
- The most critical location is the "distal edge"
- X-ray and pCT provide the required WEPL data

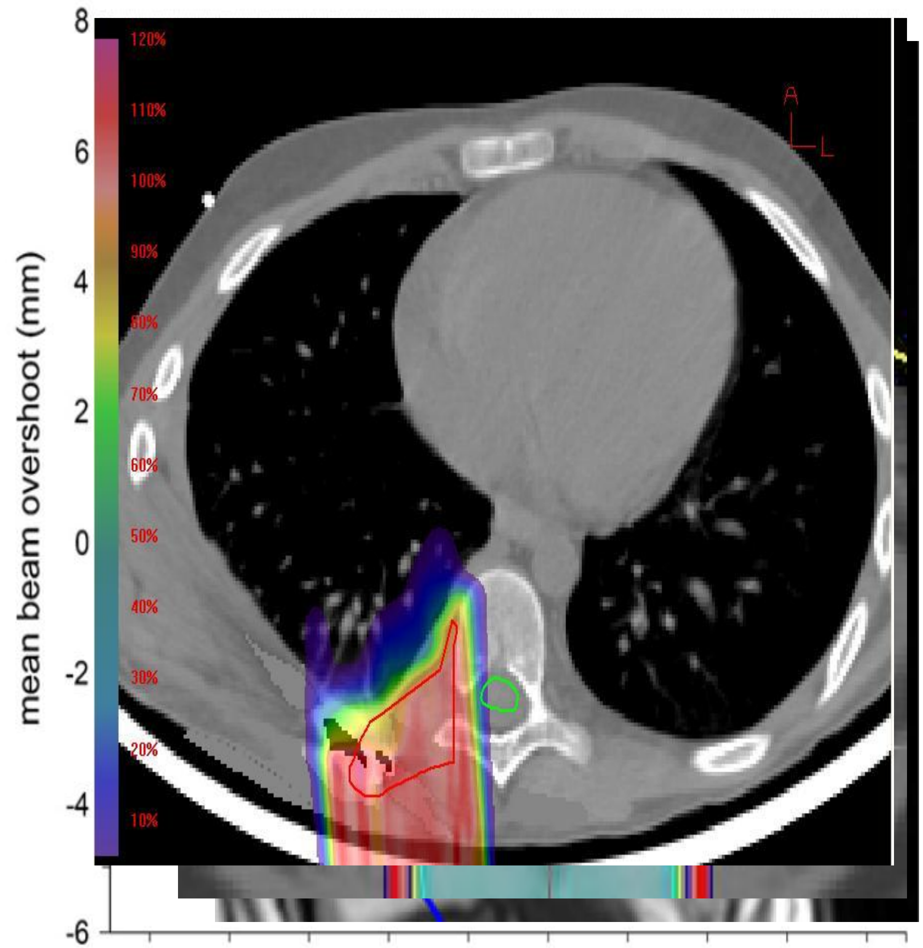


Proton Ray Tracing Example (LLUMC)



Motivation for pCT
Range Uncertainties in Proton Therapy

- Differences in the interaction of x-rays and protons with matter make proton range calculations uncertain
- Range uncertainties can range from mm to cm
- Materials of unknown stopping power and CT artifacts create additional uncertainties
- Proton CT is a potential solution to reduce this uncertainty from 3%-4% to ≤ 1% of range



Gensheimer F, et al., Int J Radiation Oncol Biol Phys 2010 (50% idosdose, red = observed, blue =

Goal: Reduction of Range Errors in Particle Therapy

- Our ultimate goal in proton and ion therapy is to use proton and carbon ion beams for tomographic imaging.
- This will allow reconstruction of the volumetric distribution of the proton ion stopping power relative to water, which is the information needed for proton and ion treatment planning.
- First systems for proton imaging have been developed by us and others in recent years

A SHORT HISTORY OF CHARGED PARTICLE RADIOGRAPHY AND CT

History of Proton Radiography (pRad)

- A. Koehler was the first to point out the potential value of pRad and to perform experiments with 160 MeV (Koehler, Science 160, 303–304, 1968)
- The higher density resolution but poorer spatial resolution than with x-ray radiography was noted by Koehler and later by Kramer et al. (Radiology, 1980)
- Medical interest in pRad as a QA tool for proton therapy was revived by U. Schneider and E. Pedroni at PSA during the 1990s
- pRad has been explored material testing at Los Alamos NL
- pRad continues to be explored for clinical use at MGH (J Seco, this meeting) and PSI
- More recently heavy ion radiography is being explored at the Heidelberg Ion Beam Therapy Center (K Parodi, this meeting)

Andy Koehler, former director of the Harvard Cyclotron)

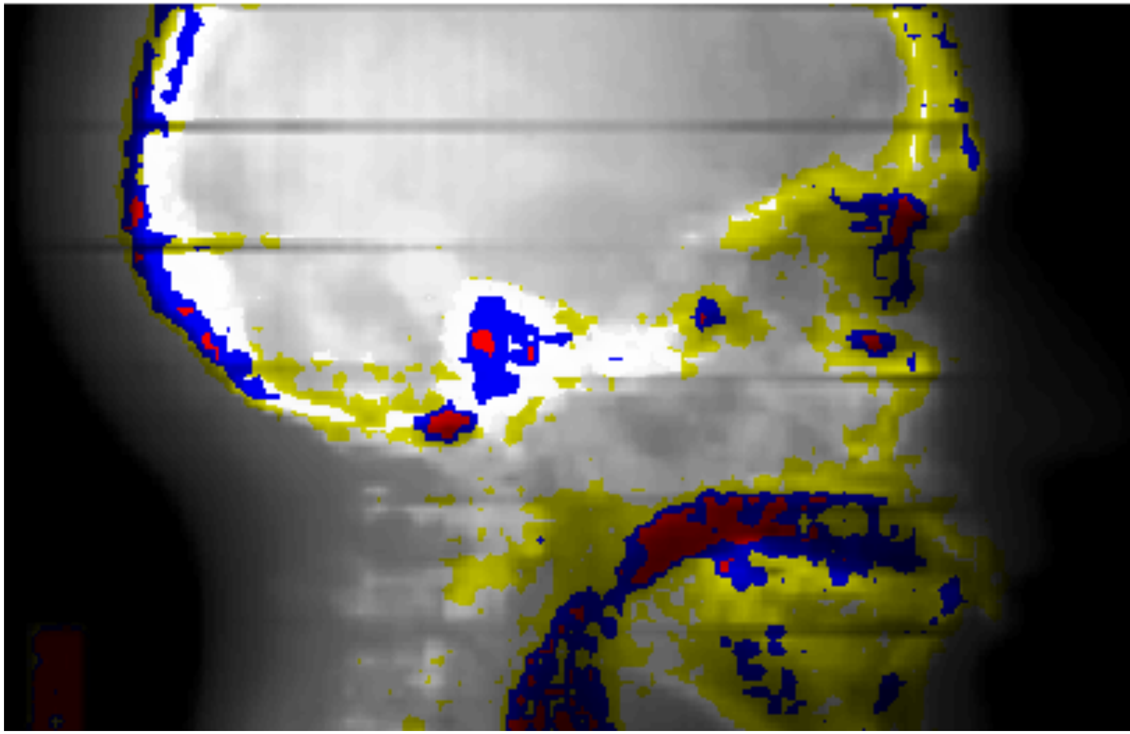
Proton Radiography as a Tool to measure Range Uncertainties

Range Uncertainties

(measured with PTR)

- > 5 mm
- > 10 mm
- > 15 mm

Schneider U. & Pedroni E. (1995), "Proton radiography as a tool for quality control in proton therapy," Med Phys. 22, 353.



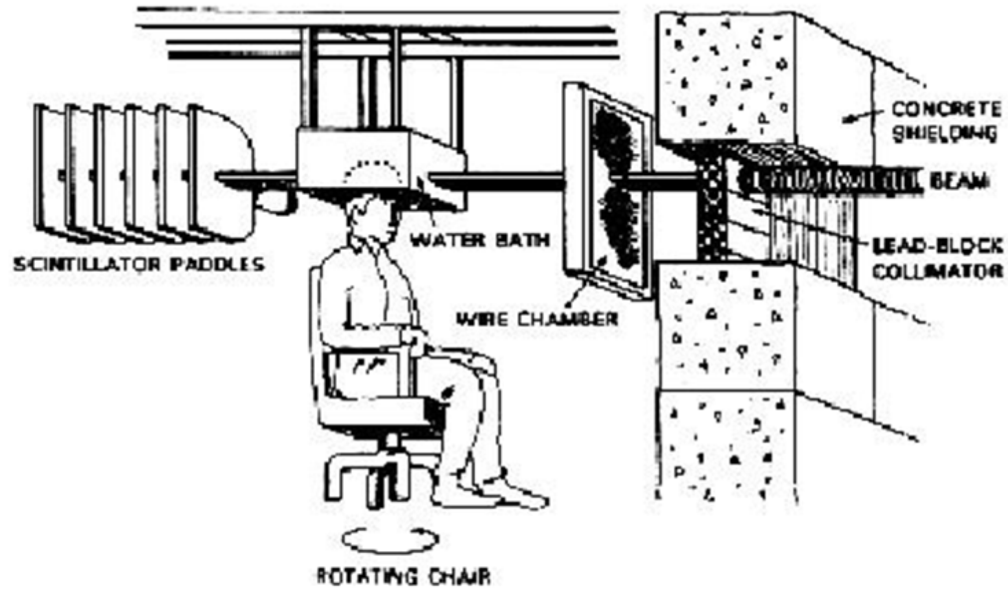
Alderson Head Phantom

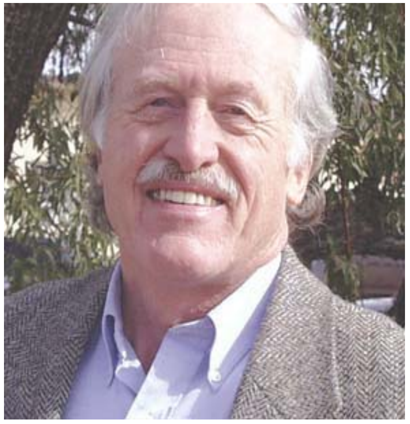
History of Proton CT (pCT)

- pCT is conceptually similar to pRad but consists of multiple pRad projections covering 360 deg followed by 3D image reconstruction
- Proton CT was originally suggested by A. Cormack in 1963
- First experiments were performed at LBL and LANL during the 1970s, and in Japan during the 1980s
- Clinical proton CT as a low-dose tomographic imaging modality was explored by R. Martin at Argonne NL during the 1990s
- A first pCT system was built by P. Zygmanski at the Harvard Cyclotron Lab in the late 1990s
- A pCT collaboration between researchers interested in pCT was formed at BNL in 2003
- pCT projects now exist at LLU/UCSC/CSUSB, NIU and FNAL, at INFN and IPHC

Particle CT in the 1970s

- Heavy ion tomography at LBNL 1972 – 1980 was explored by Cornelius Tobias and colleagues
- Proton computed tomography was investigated at LANL by Ken Hanson et al.





Proton Computed Tomography (pCT): Alan Cormack (Harvard, 1963)

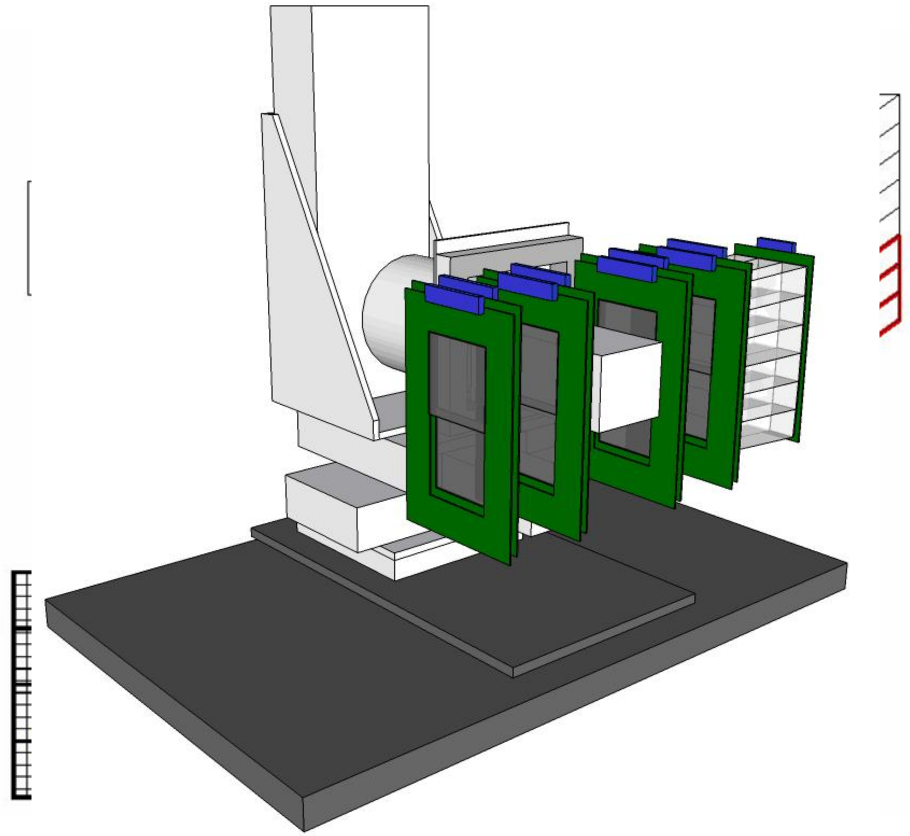
- Alan M. Cormack, physicist (1924-1998) was the first to publish a paper on the reconstruction of tomographic images based on X-ray absorption and proton degradation (J. Appl. Phys. 34, 2722, 1963)
- It took less than 10 years before his idea became reality when the first when Godfrey Hounsfield constructed the first X-ray CT scanner
- Both shared the Nobel Prize for Medicine in 1979

Alan M. Cormack, 1924-1998
Physics Nobel Laureate 1979

PRINCIPLES AND APPROACHES

Proton CT with Single Particle Detection – Evolution of Concepts

- First concepts were derived from proton radiography systems (RWS talk Brazil 2001)
- Fully developed concept of pCT (IEEE NSS/MIC 2003)
- First pCT concept realized in 2010



Single Particle Concept: Advantages and Challenges

- Single particle detection allows for
  - rejection of unsuitable events ("data cuts")
  - estimation of individual proton paths
  - use of iterative reconstruction algorithms based on single proton histories
- Challenges of single particle detection
  - Requires high data rates (fast DAQ systems)
  - Need to develop computation tools exploiting sparsity and massive parallelism

Summary of pCT Principles

- Detect location of individual primary particles, reject non related events (e.g., cosmic rays, noise)
- Reconstruct charged particle path as accurately as possible
- Measure residual energy or range of charged particle as accurately as possible
- Convert residual energy/range to water-equivalent path length (WEPL)
- Define the cpCT reconstruction problem for RSP using as much information as possible (mathematics-related)
- Solve the cpCT reconstruction problem as efficiently as possible (computing hardware related)

Current Approaches to Particle Tracking & Energy/Range Detection

Collaboration	Tracker	Energy/Range Detector
INFN	SSD	Crystal + PD
LLU/UCSC/NIU	SSD	Crystal + PD
NIU/FNAL	SciFi+SiPM	Range+WLSF+SiPM
LLU/UCSC/CSUSB	SSD	MSS (Plastic Scint) + PMT
TERA	GEM	Range+WLSF+SiPM

- SSD – Silicon strip detector
- Sci Fi – Scintillating fiber
- SiPM Silicon photo multiplier
- GEM Gaseous electron multiplier
- PD – Silicon photodiode
- WLSF – Wavelength-shifting fiber
- MSS – Multi-stage scintillator

Hartmut F. W. Sadrozinski, et al. Detector Development for pCT, IEEE NSS/MIC 2011

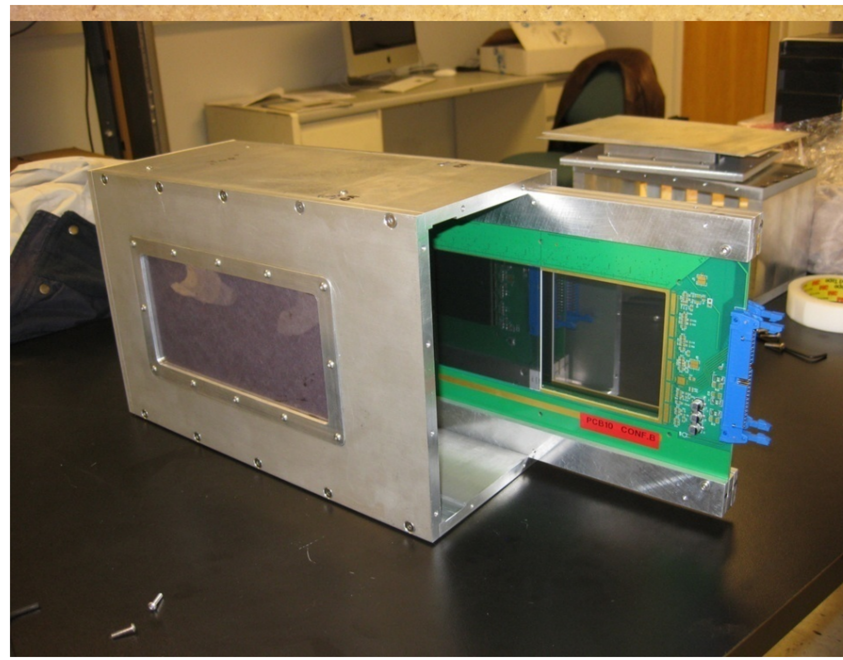
Why did we choose Silicon Strip Detectors?

- Near 100% efficiency for particle detection with essentially zero noise occupancy
- Inherently fine spatial resolution, no limitations as track estimation improves
- Simple calibration that is stable over time for period of many years
- Compact assembly using standard industry processes, with excellent mechanical stability

Robert P. Johnson, M09-78, IEEE NSS/MIC 2012

LLU/UCSC/NIU pCT Tracker

- The LLU/UCSC/NIU pCT tracker consists of front and rear module for location and direction measurements
- Modules: two detector boards measuring the X-Y position in two locations => direction
- Detector boards: 4 Si Strip Detectors (SSDs), 9 cm x 9 cm, 384 strips, 0.23 mm pitch
- Strips oriented in horizontal or vertical direction (X and Y sensitivity)
- Total sensitive area 9 cm x 18 cm
- Modified GLAST/Fermi readout chip, max rate 200 kHz
- Trackers/ASICs were developed/ modified/tested by **researchers & students from SCIPP**

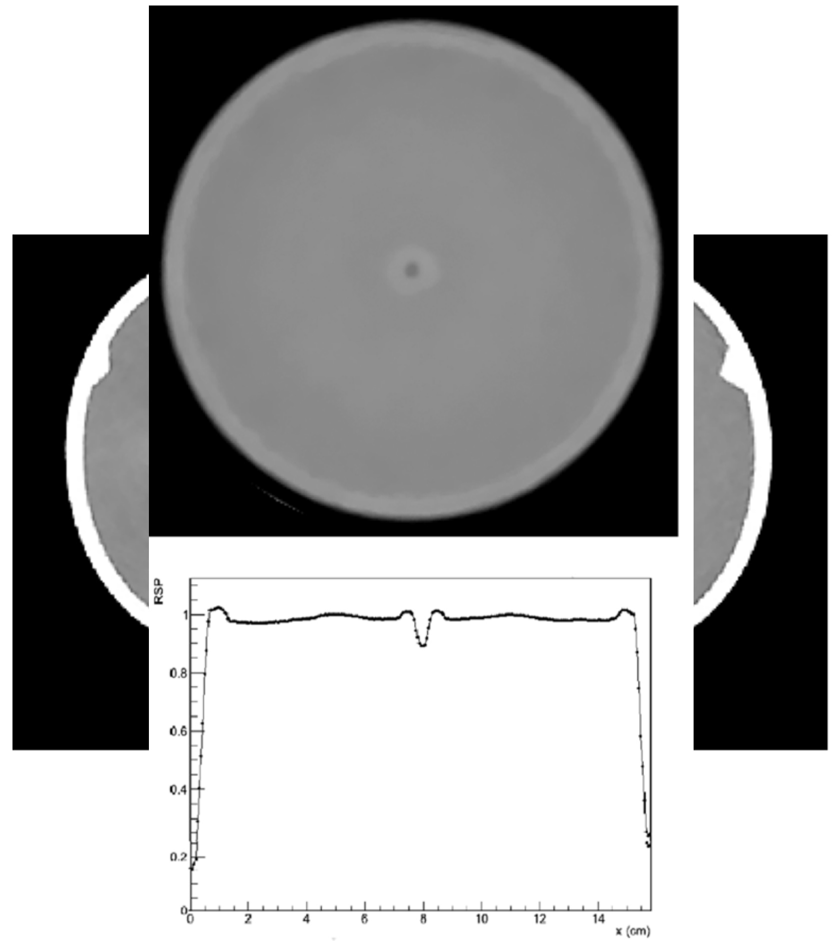


Detector board with 2 SSDs in the front (visible) and 2 SSDs in the back of the board

Phase I pCT scanner front module

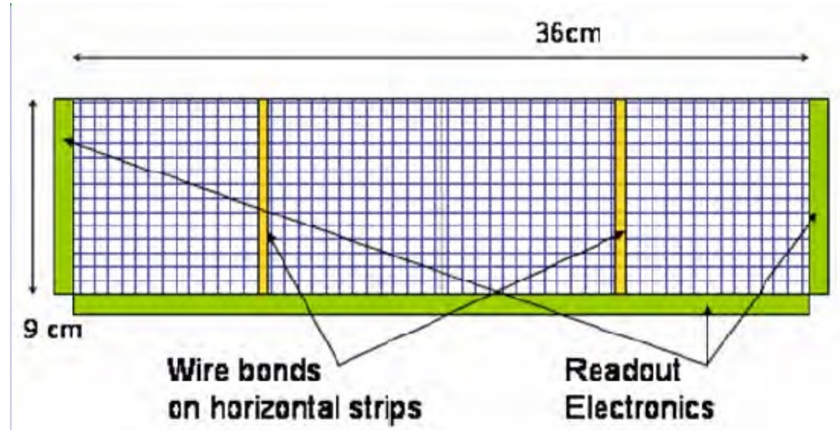
Problems with Current Tracker Design

- Tiling of SSD leads to artifacts due to gap (a) or overlap (b) between/of sensitive areas
- Confirmed by experimental scans



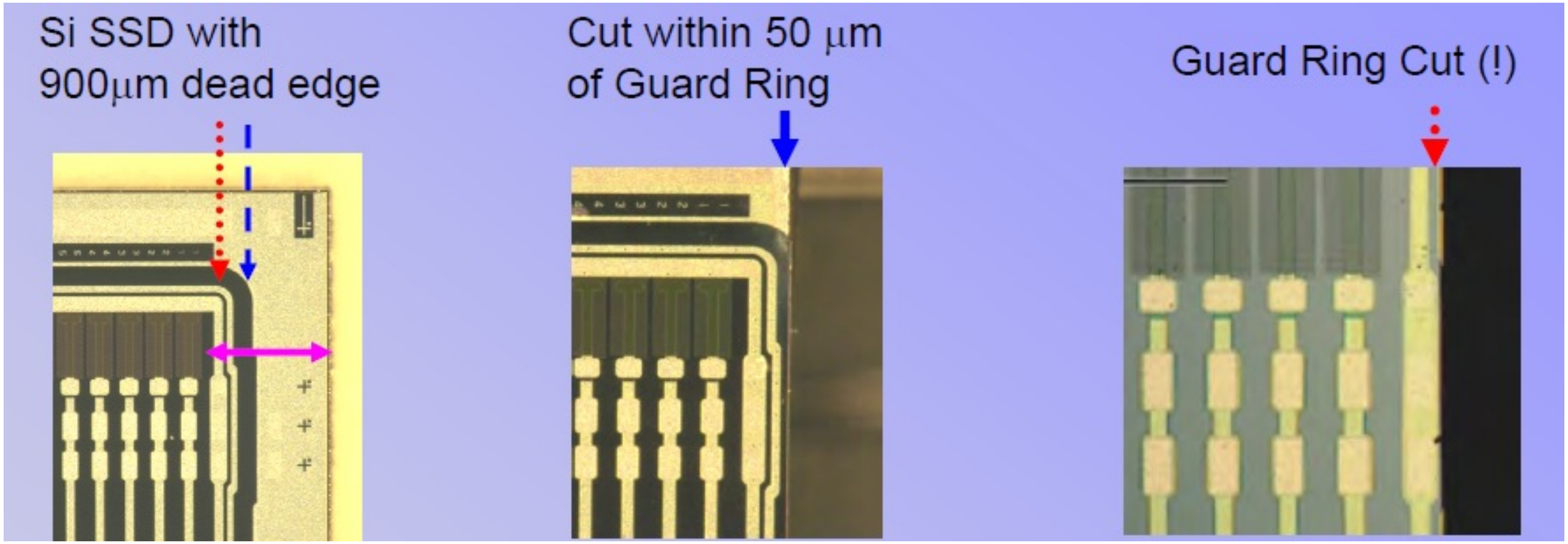
Silicon Tracker Improvements

- Large-area coverage requires tiling of Si sensors
- Larges available sensors are ~9 cm x 9 cm single-sided Si strip detectors cut from 6 inch wafers (Hamamatsu)
- Strip pitch 0.23 mm (shown not to be critical up to 1 mm by design study at NIU)
- These sensors, in their native form have ~1mm inactive edges which would create image artifacts (see next slide for solution)



Layout of one of the four x-y tracker planes using 9 cm x 9 cm single-sided silicon detectors with one side rotated by 90 degrees.

Si Sensors with "Slim" Edges

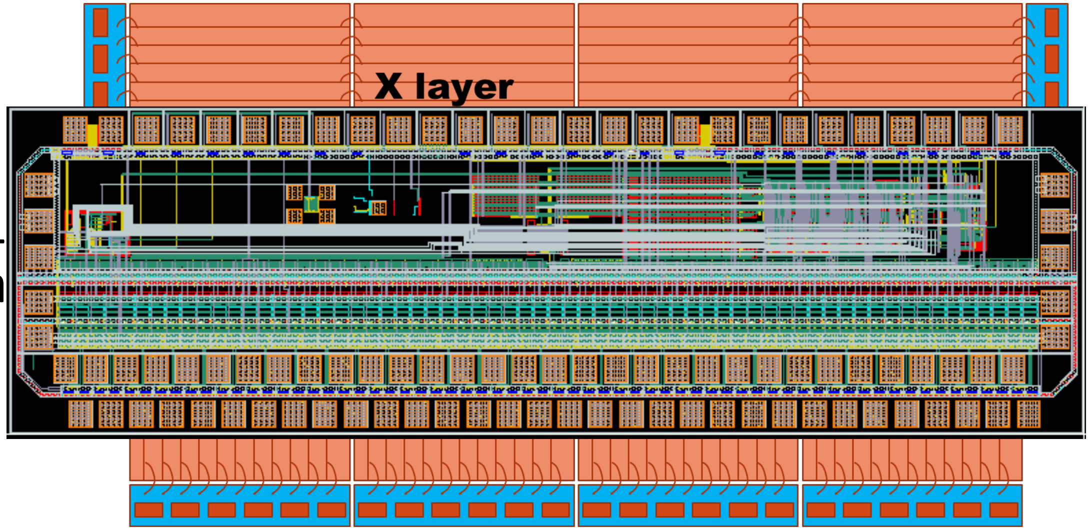


Courtesy **Hartmut F-W Sadrozinski**

- The corner of a sensor manufactured by Hamamatsu Photonics for the GLAST mission is shown on the left with the planned cut indicated by the red line
- The sensor was etch-scribed with XeF2, cleaved and passivated with nitrogen plasma-enhanced chemical vapor deposition (PECVD)
- The slim edge with strips and bias ring is shown on the right; only traces of the guard ring are visible.

Next Generation pCT Tracker/ASIC

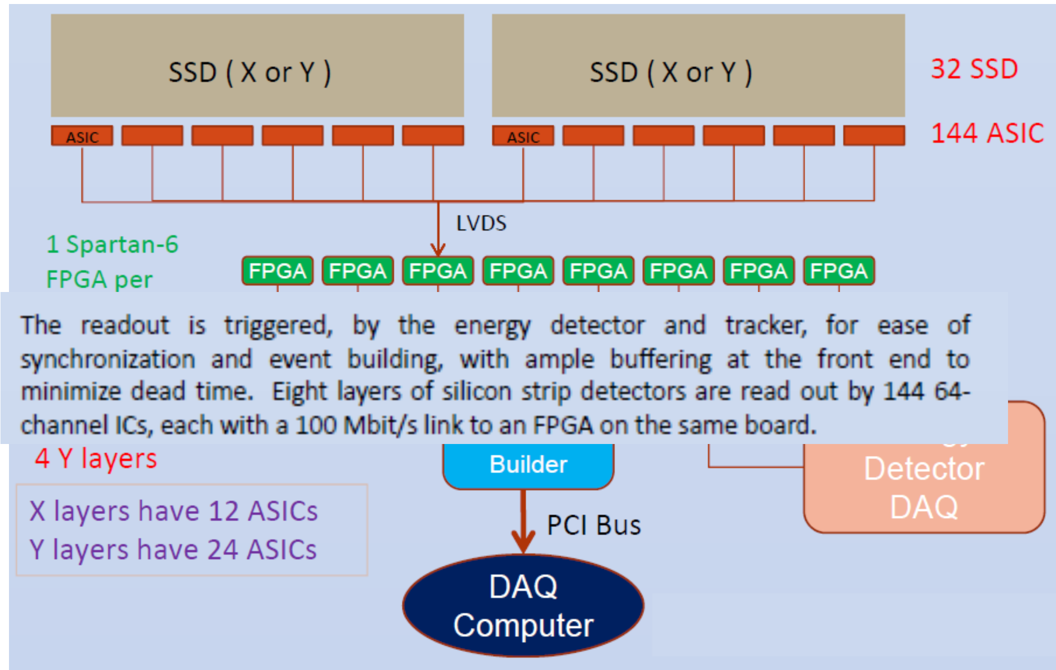
- 4 (x/y) SSDs (9 cm x 9 cm) per tracking layer cut from 6” high-resistivity n-intrinsic silicon wafers
- Eight layers of silicon strip detectors are read out by 1 64-channel ICs, each with a 100 Mbit/s link to an FPGA the same board
- Nominal data rate ~10^6 protons per sec



Poster M09-78 presented by **Robert P. Johnson**

Next Generation pCT Data Readout/ Data Flow

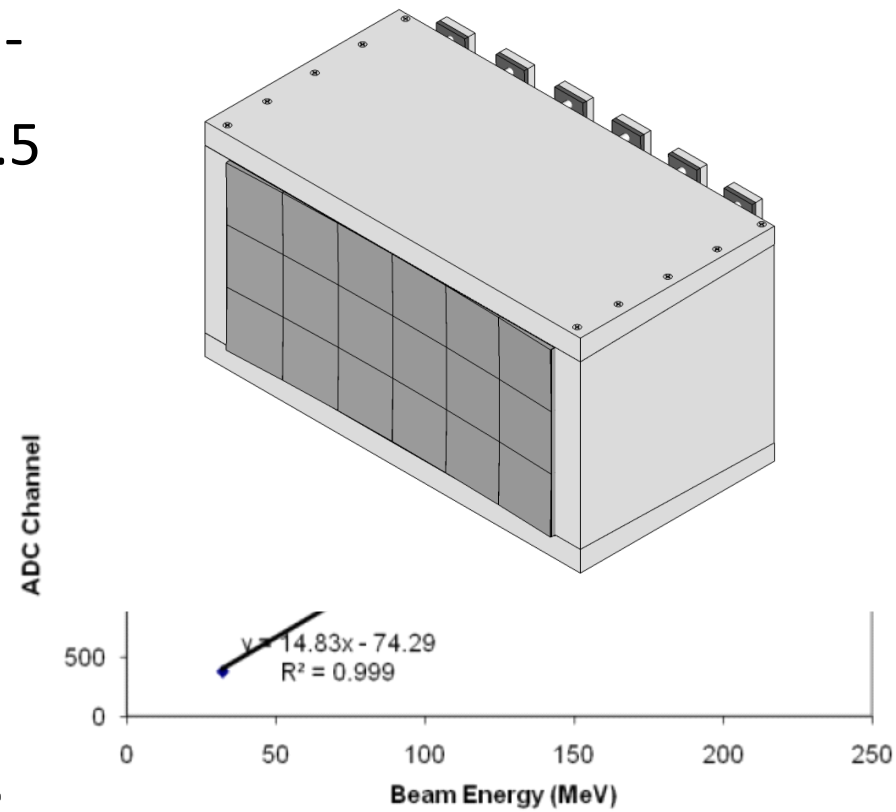
- Readout is triggered by energy detector and tracker
- Buffering at front end to minimize dead time
- Eight layers of SSDs read out by 144 ASICs and linked to an FPGA (Spartan 6, Xilinx)



Poster M09-78 presented by Robert P. Johnson

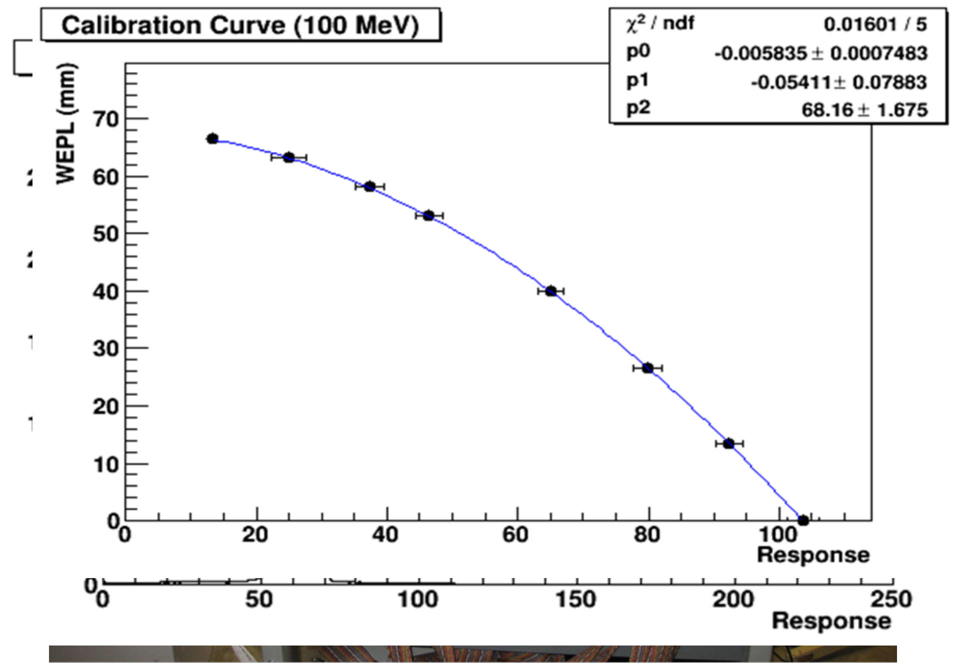
LLU/UCSC/NIU Crystal Calorimeter

- Crystal matrix with 18 thallium-doped cesium-iodide (CsI(Tl)) crystals (~3.6 cm x 3.6 cm x 12.5 cm)
- Each crystal read out by area-matched Si photodiode
- Si photodiode => preamp/ shaper => ADC
- Excellent linearity and energy resolution < 1% above 40 MeV
- Integrated with rear tracker module
- Developed by **V Bashkirov, V Rykalin** & **students from UCSC**



pCT Calorimeter Calibration

- Careful calibration to convert weighted sum of crystal responses to WEPL
- Performed prior to each pCT scan with polystyrene pates of known water-equivalent thickness (WET)
- WET vs. mean calorimeter response fitted with 2nd degree polynomial to obtain WEPL calibration curve

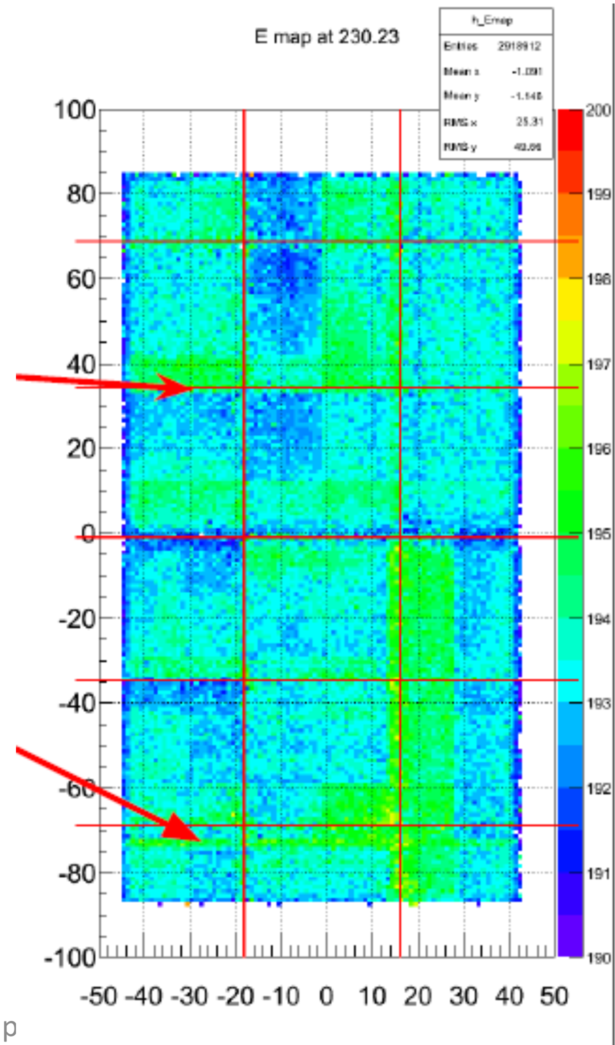


pCT scanner during WET calibration with polystyrene plates

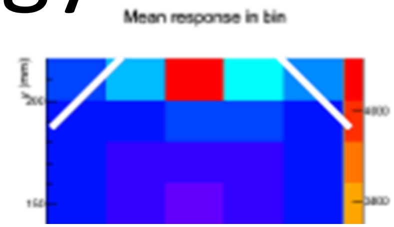
Poster N14-189 presented by **Ford Hurley**

Problems with Current Calorimeter

- Despite careful calibration, inhomogeneous response to proton histories of same residual energy (WEPL) could not be resolved
- Analysis revealed that this complicated response is due to light leakage at the level of the PDs and jitter of the timing of different front end chips

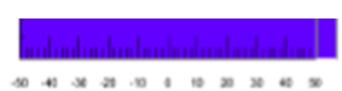


Next Generation pCT Energy Detectors



- Range counter consisting of stack of scintillator plates with SiPM readout and 3-5-stage plastic scintillator design (MSS) with PMT readout have been tested
- Range counter determines residual range by detecting most distal plate with measurable response, WEPL = max range – residual range
- MSS detects energy response of stopping scintillator, which is converted to WEPL
- Both designs have comparable WEPL resolution (~3 mm) combined with good light yield and uniformity
- MSS design preferred solution based on cost (including manpower) considerations

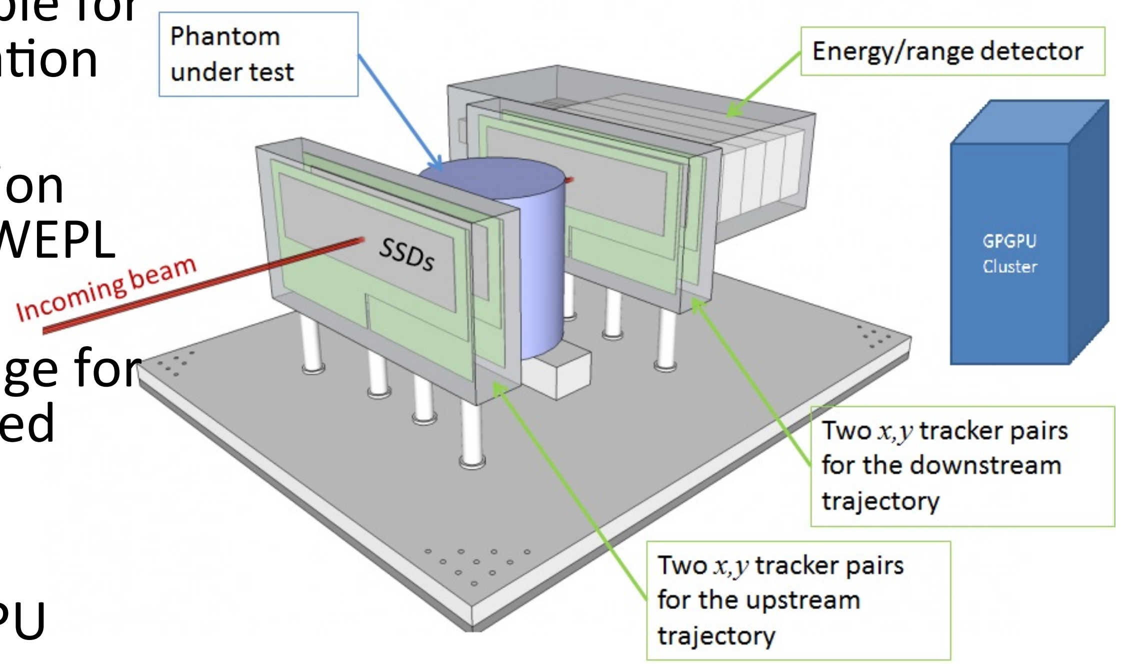
R3318 PMT



M22-21 Poster presented by **Vladimir Bashkirov**
N14-192 Poster presented by **Andriy Zatserklyaniy**

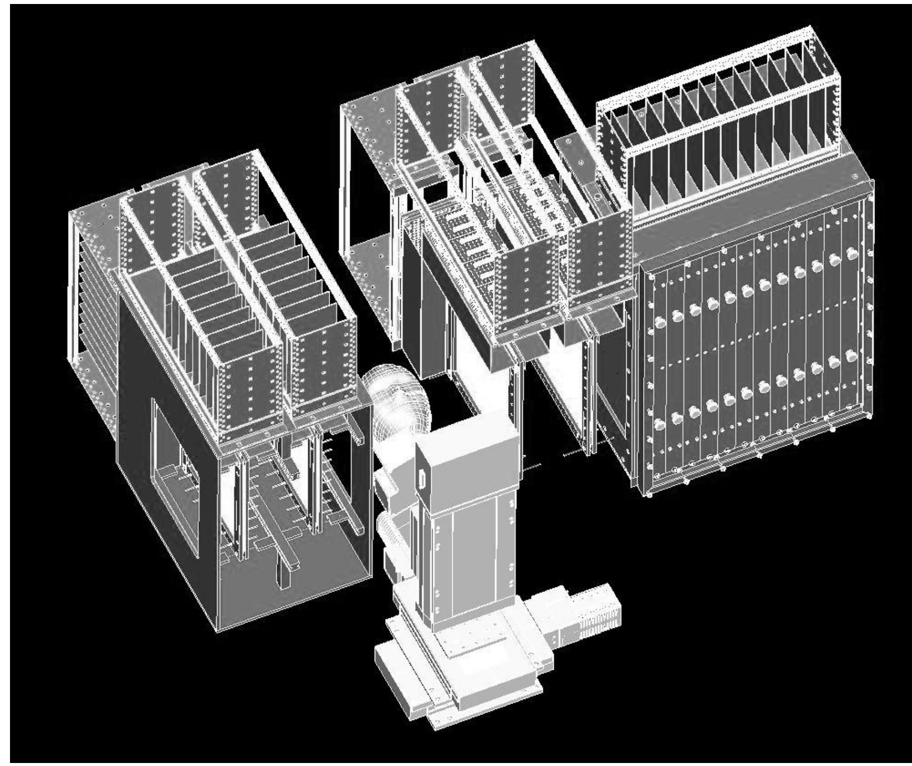
The Phase 2 LLU/UCSC/CSUSB pCT Scanner

- Large area tracker suitable for head scans + immobilization devices (36 cm x 9 cm
- Multi (5)-stage scintillation detector calibrated for WEPL measurements
- Vertical axis rotation stage for phantom rotation on fixed horizontal beam line
- FPGA-based readout
- Reconstruction on GPGPU cluster



Phase 2 NIU/FNAL pCT Scanner

- Scintillating fiber tracker
- 96-stage plastic scintillator range counter with WLSF read out by SiPMs (2 per stage)
- Reconstruction on large GPGPU cluster (reconstruction of 1 billion histories in <10 min)

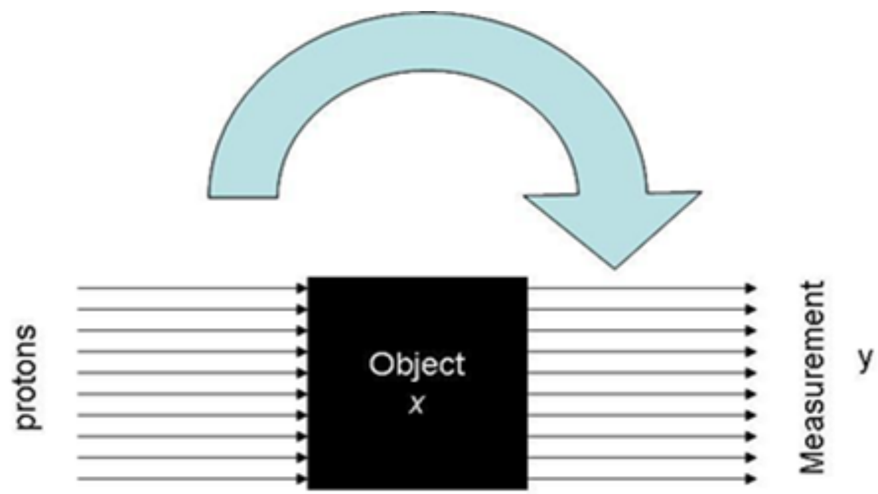


Courtesy George Coutrakon, NIU

Proton CT IMAGE RECONSTRUCTION

pCT Reconstruction Problem

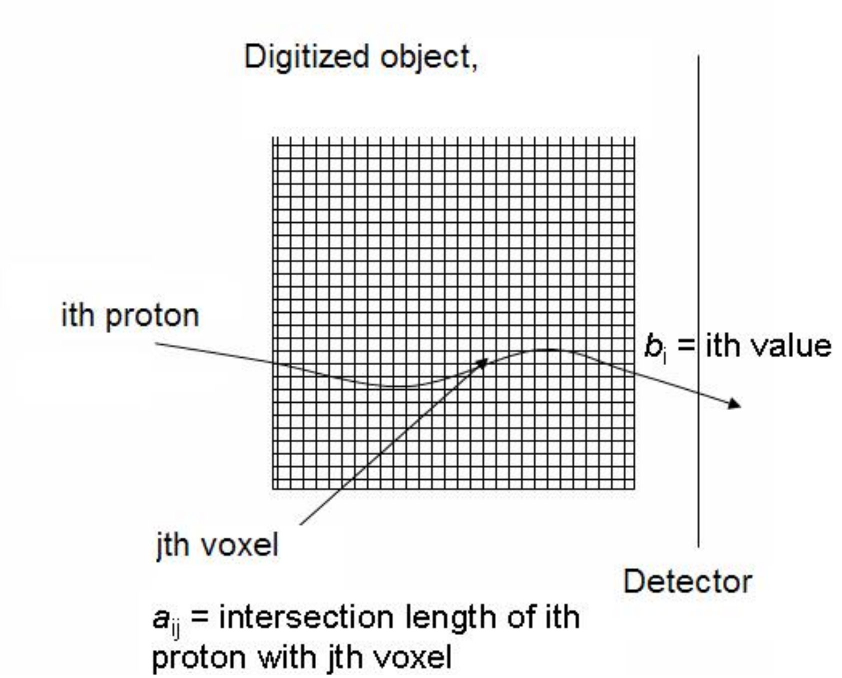
- Object is a “black box” containing a 3D distribution of target parameter (x) producing measured data y
- Recovery of object function x requires inversion of physics model operator
- Discrete linear problem approach requires x and y to be vectors and the physics operator to be represented by a matrix



$$\Im x = y \quad \text{solve} \Rightarrow x = \Im^{-1} y$$

Linear pCT System and Solution Concept

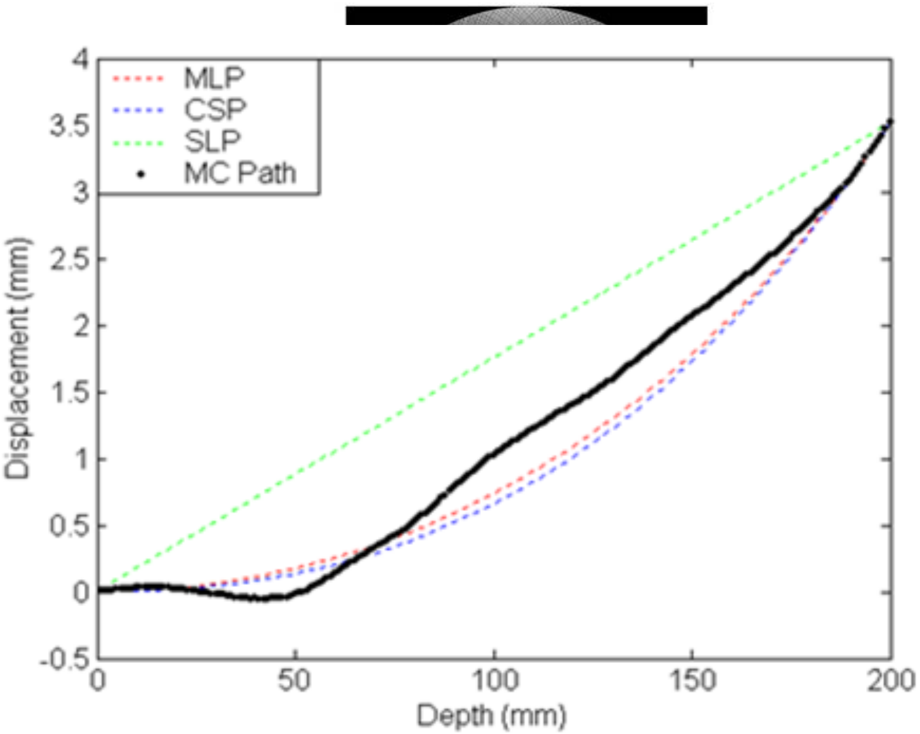
- Linear System
  - i =1…m measurements => vector b = (b_i)
  - Object vector x = (x_j), j=1…n
  - Projection matrix A = (a_{ij})
- Note: matrix A is very large & sparse, and the system is inconsistent
- Find "adequate" solution of Ax=b using iterative projection method (projection onto hyperplanes H_i)
- Parallel algorithms for pCT have been developed by **Yair Censor**, **Ran Davidi** and **Scott Penfold**



$$H_i = \{x \in \Re^n \mid \langle a^i, x \rangle = b_i, \text{ for } i = 1, 2, \ldots, m.$$

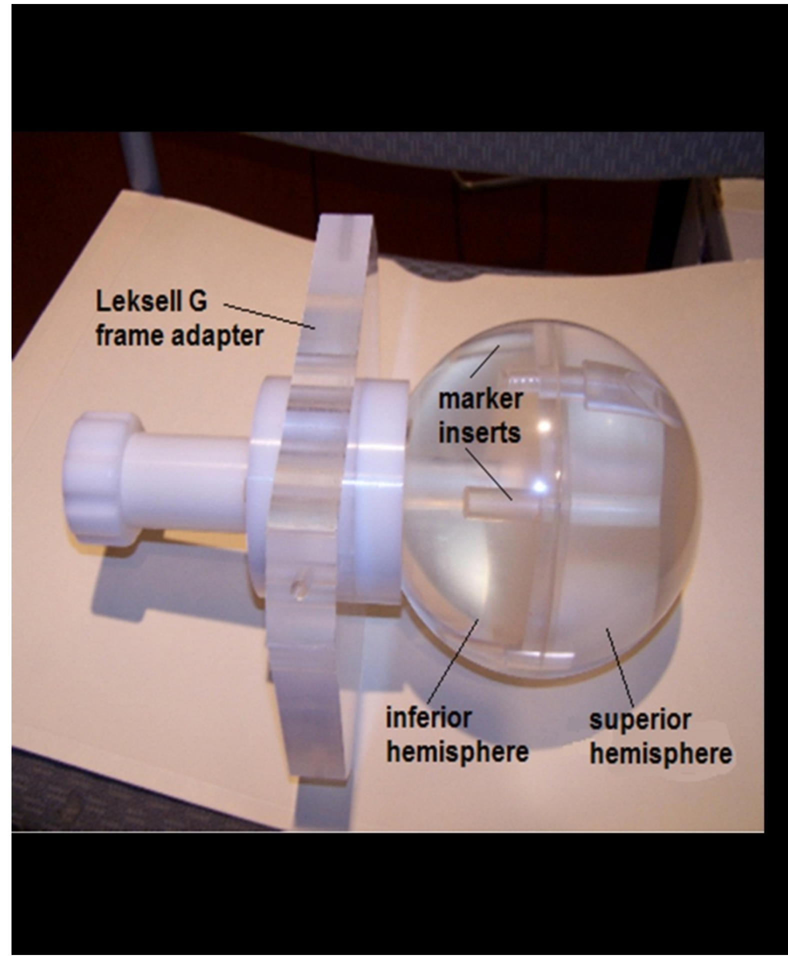
Path Reconstruction Concepts

- Different proton paths may be used in the reconstruction: MLP = Most Likely Path, SLP = straight line path, CSP = cubic spline path
- The MLP is determined by maximizing likelihood (chi square) of output parameters, given entry parameters
- MLP significantly improves spatial resolution compared to SLP, CSP reconstruction is nearly as good as MLP reconstruction
- The MLP concept was formulated by **David C Williams** (PMB 2004), & further refined by **Scott Penfold**, **John Tafas** and **Keith Schubert** (Med Phys 2008)



First pCT Scanning Results with the LLU/UCSC/NIU pCT Scanner

- A series of pCT scans of the Lucy radiosurgery phantom after completion and first calibration of the Phase I LLU-NIU-UCSC pCT scanner
- Reconstructions were done with code written by graduate student Scott Penfold

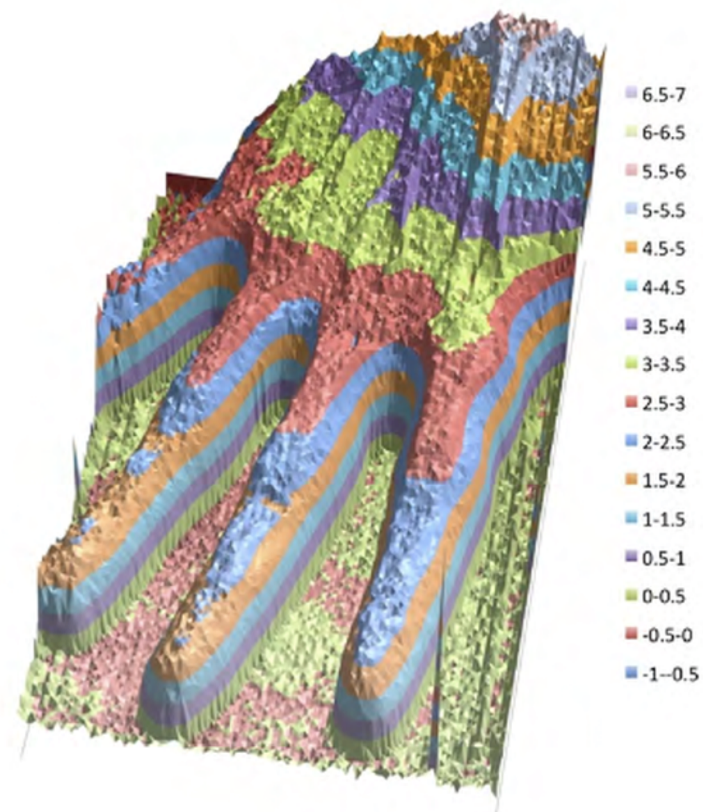


Complete Lucy Phantom Scan

Nov. 2011

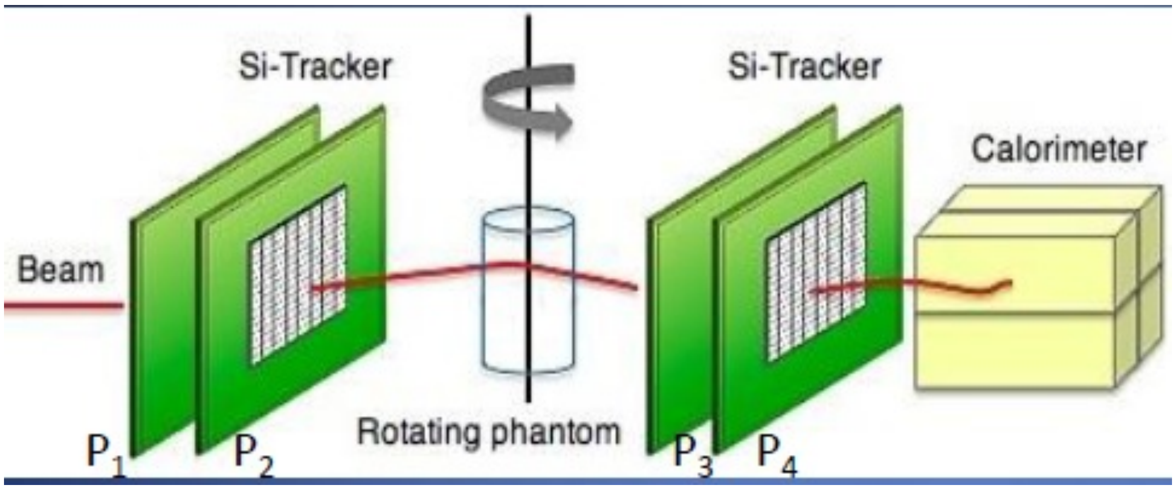
Proton Radiography

- Cp radiographs give a much more faithful representation of relative bone and soft tissue electron densities
- Experimental radiographs have been obtained with LLU/UCSC/NIU pCT prototype
- pCT radiographs have proven useful in detecting flaws in current detector designs and data processing



Poster R04-24 presented by Tia Plautz

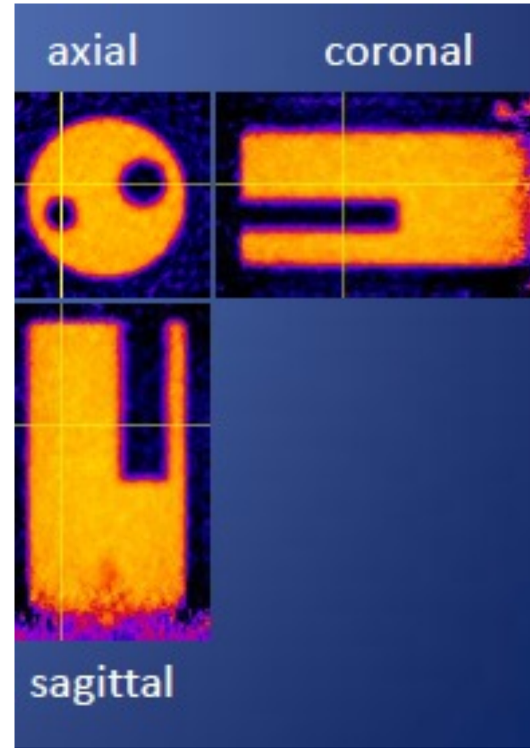
PRIMA Collaboration



INFN pCT prototype, 4 layers of Si –trackers and YAG crystal calorimeter

Courtesy E Vanzi, INFN

M06-6 PRIMA Proton Imaging for Clinical Application. Presented by Cinzia Talamonti.



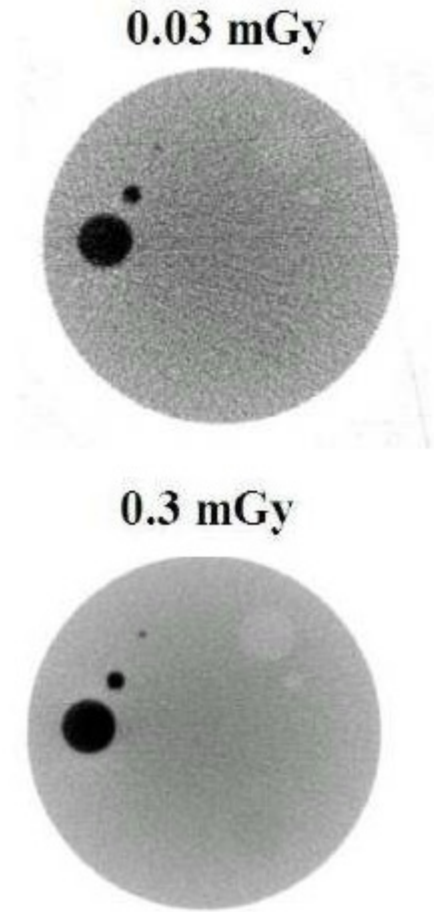
Reconstructed image of a 4 cm x 2 cm PMMA cylinder with FBP using a Butterworth filter

THE QUEST OF LOW-DOSE CT

pCT – A low-dose image modality?

- Dose per proton & image slice (180 x 180 x 1 mm^3) of unit density: 0.67 x 0.5 nGy ($\langle \Delta E \rangle$ = 100 MeV) from electronic interactions + 0.33 x 1 nGy ($\langle \Delta E \rangle$ = 200 MeV) from inelastic nuclear interactions† = 0.67 nGy per proton history
- Dimension of single slice head object vector: $180^2 = 3.6 \times 10^4$ assuming 1 x 1 x 1 mm^3 voxels
- Number of protons per slice ~ number of unknowns x10-100 ~ $3.6 \times 10^5 - 3.6 \times 10^6$
- Average dose for a given slice: ~0.04-0.45 mSv (RBE = 1)
- Comparable to 0.07 mSv from single chest X-ray

†Poster N14-186 presented by David Steinberg



R. Schulte, Med Phys. 2005

Summary and Conclusions

- pCT and radiography are evolving technologies that are driven by applications in charged particle therapy
- Fastest progress is made by continued exchange of ideas and experience between medicine, high energy & nuclear physics, applied mathematics, computer science and engineering
- Wide-spread use can be expected within the next 10 years as proton/ion therapy expands its role

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pCTlers

Vladimir Bashkirov
Ford Hurley
Andrew Wroe
Baron Black
Bob Jones
Hartmut Sadrozinski
Robert Johnson
Andriy Zatserklyaniy
Joel DeWitt
Forest Martinez-McKinney
Sergei Kashiguine
Edwin Spencer
Andrew Plumb
Cole Holcomb
David Steinberg
Vanessa Feng
Scott Macafee
Jessica Missaghian
Tia Plautz
Keith Schubert
Micah Witt
Blake Schultze
Reinhard Schulte
Scott McAllister
John Tafas
Yair Censor
Ran Davidi
Anatoly Rozenfeld
Peter Lazarakis
Valentina Giacometti
Carol Grande
Gerald Barnett

Gerald Blazey
George Coutrakon
Bela Erdelyi
Alexandre Dychkant
Eric Johnson
Sergey Uzunyan
Vishnu Zutshi
Karonis Nicholas
Kirk Duffin
Caesar Ordonez
John Winans
Andrew Gearhart
Mahmoud Yaqoub
Rick Salcido
Viktoriya Zvoda
Tony Zhang
Eric Olson
Michael Papka
Tom Uram
Peter Wilson
Greg Sellberg
John Rauch
John Krider
Paul Rubinov
Tom Fitzpatrick
Herman Cease
Michael Roman
Michael Utes
Anindya Sen
Gabor Herman
Scott Penfold

Márgio C. Loss Klock
Tianfang Li
Jerome Z. Liang
Ivan Evseev
Hugo Schelin
Olga Yevseyeva
Sergei Paschuk
Edney Milhoretto
Valeriy Denyak
David C. Williams
Todd Satogata
Steven Peggs
Klaus Mueller
Jason Heimann
Leah R. Johnson
Brian Keeney
David C. Williams,
Lan Zhang
Zheng Li
Craig Woody

Ron Martin
Ken Hansen

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Thanks for listening!