Compton Imaging for Prompt Gamma Based Verification of Particle Therapy Beams

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July 7, 2023

Disclosures

Co-Founder, Partial Ownership stake

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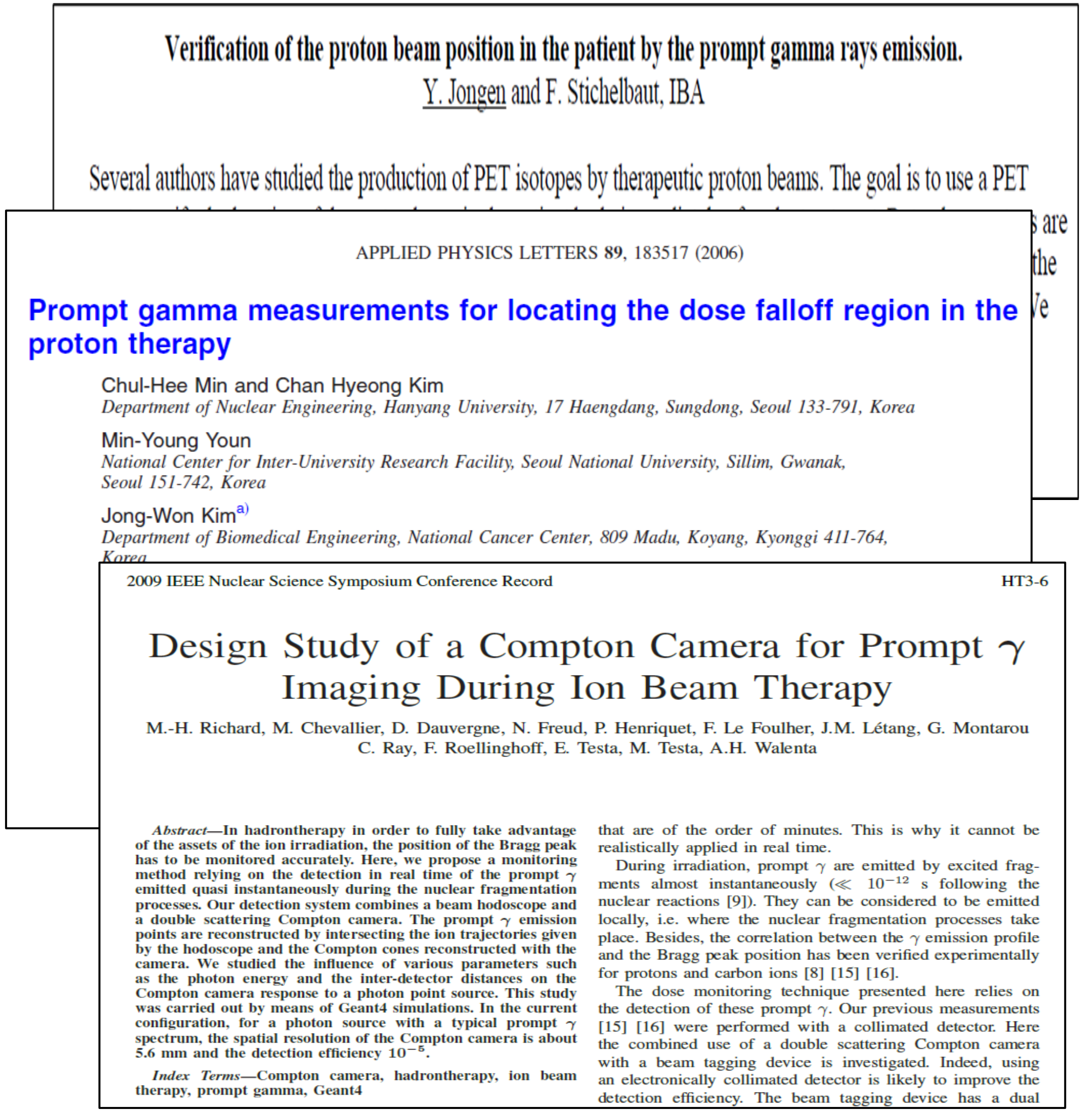
Chapter 3:3: Compton camera



Verification of the proton beam position in the patient by the prompt gamma rays emission.

Y. Jongen and F. Stichelbaut, IBA

Several authors have studied the production of PET isotopes by therapeutic proton beams. The goal is to use a PET

APPLIED PHYSICS LETTERS 89, 183517 (2006)

Prompt gamma measurements for locating the dose falloff region in the proton therapy

Chul-Hee Min and Chan Hyeong Kim
Department of Nuclear Engineering, Hanyang University, 17 Haengdang, Sungdong, Seoul 133-791, Korea

Min-Young Youn
National Center for Inter-University Research Facility, Seoul National University, Sillim, Gwanak, Seoul 151-742, Korea

Jong-Won Kim[a)]
Department of Biomedical Engineering, National Cancer Center, 809 Madu, Koyang, Kyonggi 411-764, Korea

2009 IEEE Nuclear Science Symposium Conference Record HT3-6

Design Study of a Compton Camera for Prompt γ Imaging During Ion Beam Therapy

M.-H. Richard, M. Chevallier, D. Dauvergne, N. Freud, P. Henriquet, F. Le Foulher, J.M. Létang, G. Montarou C. Ray, F. Roellinghoff, E. Testa, M. Testa, A.H. Walenta

Abstract—In hadrontherapy in order to fully take advantage of the assets of the ion irradiation, the position of the Bragg peak has to be monitored accurately. Here, we propose a monitoring method relying on the detection in real time of the prompt γ emitted quasi instantaneously during the nuclear fragmentation processes. Our detection system combines a beam hodoscope and a double scattering Compton camera. The prompt γ emission points are reconstructed by intersecting the ion trajectories given by the hodoscope and the Compton cones reconstructed with the camera. We studied the influence of various parameters such as the photon energy and the inter-detector distances on the Compton camera response to a photon point source. This study was carried out by means of Geant4 simulations. In the current configuration, for a photon source with a typical prompt γ spectrum, the spatial resolution of the Compton camera is about 5.6 mm and the detection efficiency 10^{-5}.

Index Terms—Compton camera, hadrontherapy, ion beam therapy, prompt gamma, Geant4

that are of the order of minutes. This is why it cannot be realistically applied in real time.

During irradiation, prompt γ are emitted by excited fragments almost instantaneously ($\ll 10^{-12}$ s following the nuclear reactions [9]). They can be considered to be emitted locally, i.e. where the nuclear fragmentation processes take place. Besides, the correlation between the γ emission profile and the Bragg peak position has been verified experimentally for protons and carbon ions [8] [15] [16].

The dose monitoring technique presented here relies on the detection of these prompt γ. Our previous measurements [15] [16] were performed with a collimated detector. Here the combined use of a double scattering Compton camera with a beam tagging device is investigated. Indeed, using an electronically collimated detector is likely to improve the detection efficiency. The beam tagging device has a dual

History

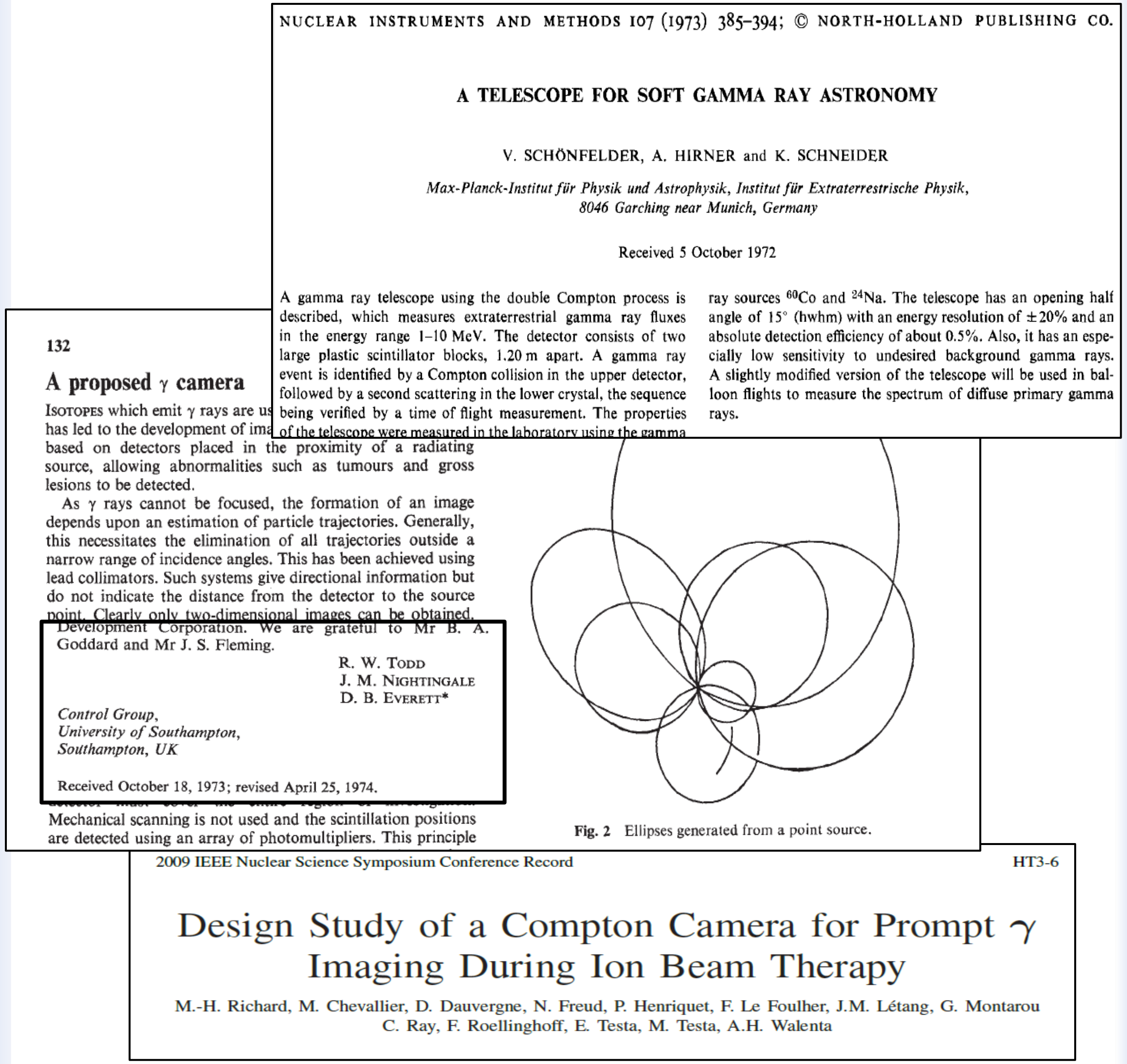
2003 — F. Stichelbaut and Y. Jongen, 39th Meeting of the Particle Therapy Co-Operative Group, San Francisco CA, October 2003).

2006 — C.-H. Min, C. H. Kim, M.-Y. Youn, J.-W. Kim, Prompt gamma measurements for locating the dose falloff region in the proton therapy, Applied Physics Letters 89 (2006).

2009 — M Richard et al, Design study of a ***Compton camera*** for prompt γ imaging during ion beam therapy, IEEE Nuclear Science Symposium Conference Record (NSS/MIC), 2009

2023 — Frontiers | Research Topics: Prompt-Gamma Imaging in Particle Therapy

Chapter 3:3: Compton camera


NUCLEAR INSTRUMENTS AND METHODS 107 (1973) 385–394; © NORTH-HOLLAND PUBLISHING CO.

A TELESCOPE FOR SOFT GAMMA RAY ASTRONOMY

V. SCHÖNFELDER, A. HIRNER and K. SCHNEIDER

Max-Planck-Institut für Physik und Astrophysik, Institut für Extraterrestrische Physik, 8046 Garching near Munich, Germany

Received 5 October 1972

A gamma ray telescope using the double Compton process is described, which measures extraterrestrial gamma ray fluxes in the energy range 1–10 MeV. The detector consists of two large plastic scintillator blocks, 1.20 m apart. A gamma ray event is identified by a Compton collision in the upper detector, followed by a second scattering in the lower crystal, the sequence being verified by a time of flight measurement. The properties of the telescope were measured in the laboratory using the gamma ray sources ^{60}Co and ^{24}Na. The telescope has an opening half angle of 15° (hwhm) with an energy resolution of ±20% and an absolute detection efficiency of about 0.5%. Also, it has an especially low sensitivity to undesired background gamma rays. A slightly modified version of the telescope will be used in balloon flights to measure the spectrum of diffuse primary gamma rays.

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A proposed γ camera

ISOTOPES which emit γ rays are us... has led to the development of ima... based on detectors placed in the proximity of a radiating source, allowing abnormalities such as tumours and gross lesions to be detected.

As γ rays cannot be focused, the formation of an image depends upon an estimation of particle trajectories. Generally, this necessitates the elimination of all trajectories outside a narrow range of incidence angles. This has been achieved using lead collimators. Such systems give directional information but do not indicate the distance from the detector to the source point. Clearly only two-dimensional images can be obtained.

Development Corporation. We are grateful to Mr B. A. Goddard and Mr J. S. Fleming.

R. W. TODD
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Control Group,
University of Southampton,
Southampton, UK

Received October 18, 1973; revised April 25, 1974.

Mechanical scanning is not used and the scintillation positions are detected using an array of photomultipliers. This principle

Fig. 2 Ellipses generated from a point source.

2009 IEEE Nuclear Science Symposium Conference Record HT3-6

Design Study of a Compton Camera for Prompt γ Imaging During Ion Beam Therapy

M.-H. Richard, M. Chevallier, D. Dauvergne, N. Freud, P. Henriquet, F. Le Foulher, J.M. Létang, G. Montarou, C. Ray, F. Roellinghoff, E. Testa, M. Testa, A.H. Walenta

History

1973 — V. Schonfelder, A. Hirner, K. Schneider, A telescope for soft gamma ray astronomy, Nucl. Instr. Methods, 107 (1973)

1974 — R.W. Todd, J.M. Nightingale, D.B. Everett, A Proposed γ camera, Nature, 251 (1974)

2009 — M Richard et al, Design study of a ***Compton camera*** for prompt γ imaging during ion beam therapy, IEEE Nuclear Science Symposium Conference Record (NSS/MIC), (2009)

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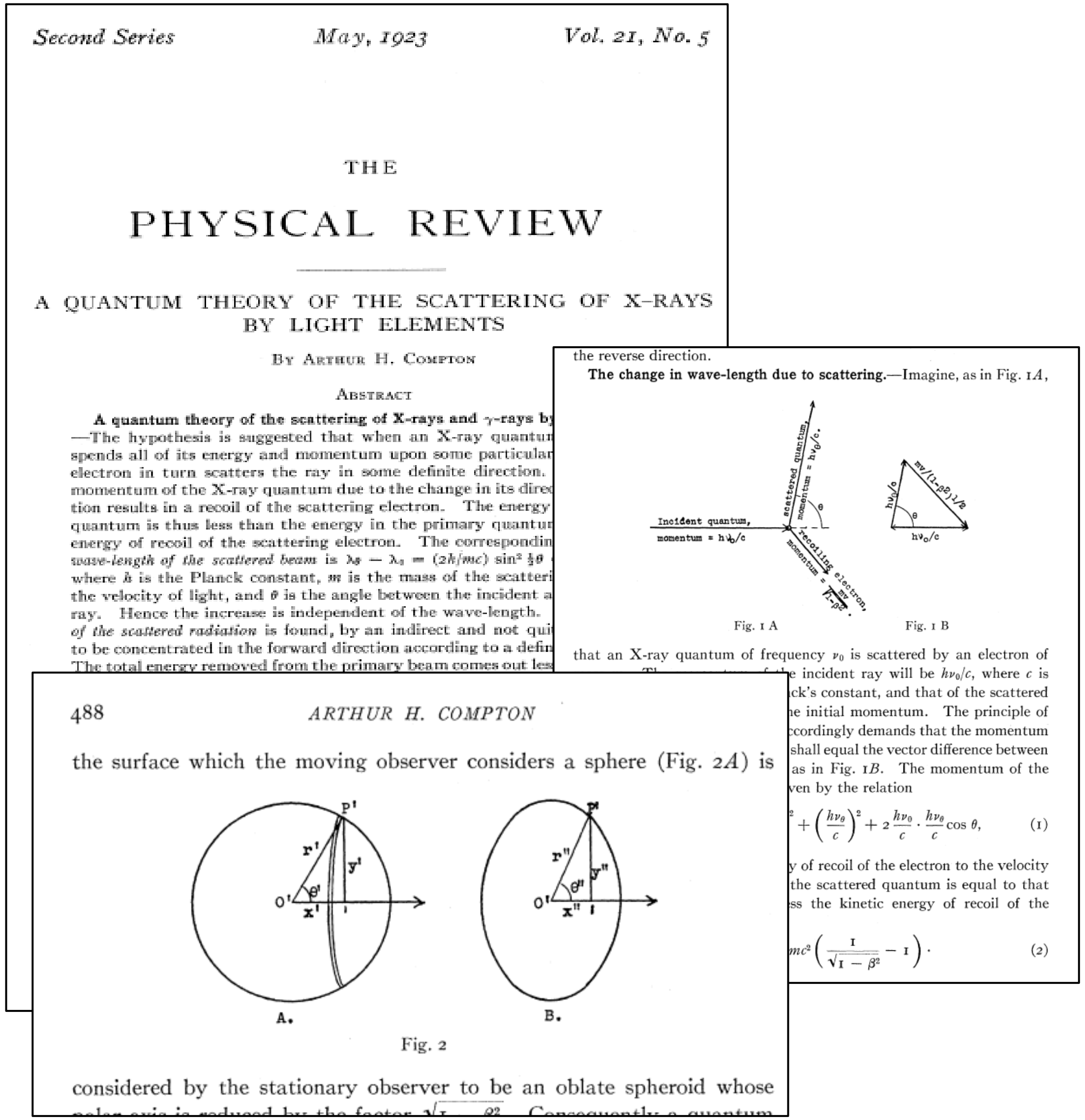
Chapter 3:3: Compton camera



Second Series May, 1923 Vol. 21, No. 5

THE

PHYSICAL REVIEW

A QUANTUM THEORY OF THE SCATTERING OF X-RAYS BY LIGHT ELEMENTS

By Arthur H. Compton

Abstract

A quantum theory of the scattering of X-rays and γ-rays by
—The hypothesis is suggested that when an X-ray quantum
spends all of its energy and momentum upon some particular
electron in turn scatters the ray in some definite direction.
momentum of the X-ray quantum due to the change in its direc
tion results in a recoil of the scattering electron. The energy
quantum is thus less than the energy in the primary quantum
energy of recoil of the scattering electron. The correspondin
wave-length of the scattered beam is $\lambda_\theta - \lambda_0 = (2h/mc)\sin^2\frac{1}{2}\theta$
where h is the Planck constant, m is the mass of the scatteri
the velocity of light, and θ is the angle between the incident a
ray. Hence the increase is independent of the wave-length.
of the scattered radiation is found, by an indirect and not quit
to be concentrated in the forward direction according to a defin
The total energy removed from the primary beam comes out les

the reverse direction.

The change in wave-length due to scattering.—Imagine, as in Fig. 1A,

Fig. 1 A Fig. 1 B

that an X-ray quantum of frequency ν_0 is scattered by an electron of
... the incident ray will be $h\nu_0/c$, where c is
...ck's constant, and that of the scattered
...e initial momentum. The principle of
...ccordingly demands that the momentum
...shall equal the vector difference between
...as in Fig. 1B. The momentum of the
...ven by the relation

$$\ldots + \left(\frac{h\nu_\theta}{c}\right)^2 + 2\frac{h\nu_0}{c}\cdot\frac{h\nu_\theta}{c}\cos\theta, \quad (1)$$

...y of recoil of the electron to the velocity
...the scattered quantum is equal to that
...ss the kinetic energy of recoil of the

$$\ldots mc^2\left(\frac{1}{\sqrt{1-\beta^2}} - 1\right). \quad (2)$$

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the surface which the moving observer considers a sphere (Fig. 2A) is

Fig. 2

considered by the stationary observer to be an oblate spheroid whose

History

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- 1973 — V. Schonfelder, A. Hirner, K. Schneider, A telescope for soft gamma ray astronomy, Nucl. Instr. Methods, 107 (1973)
- 1974 — R.W. Todd, J.M. Nightingale, D.B. Everett, A Proposed γ camera, Nature, 251 (1974)
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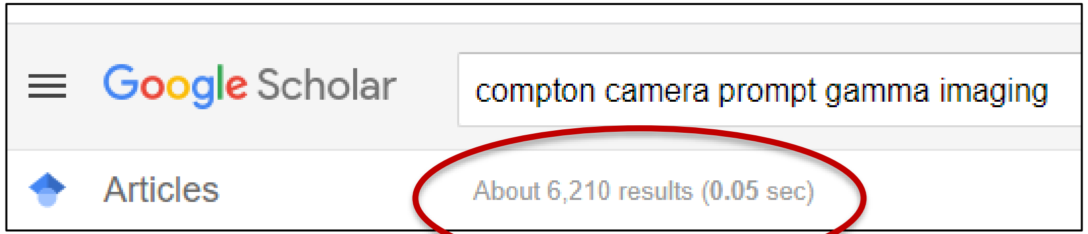
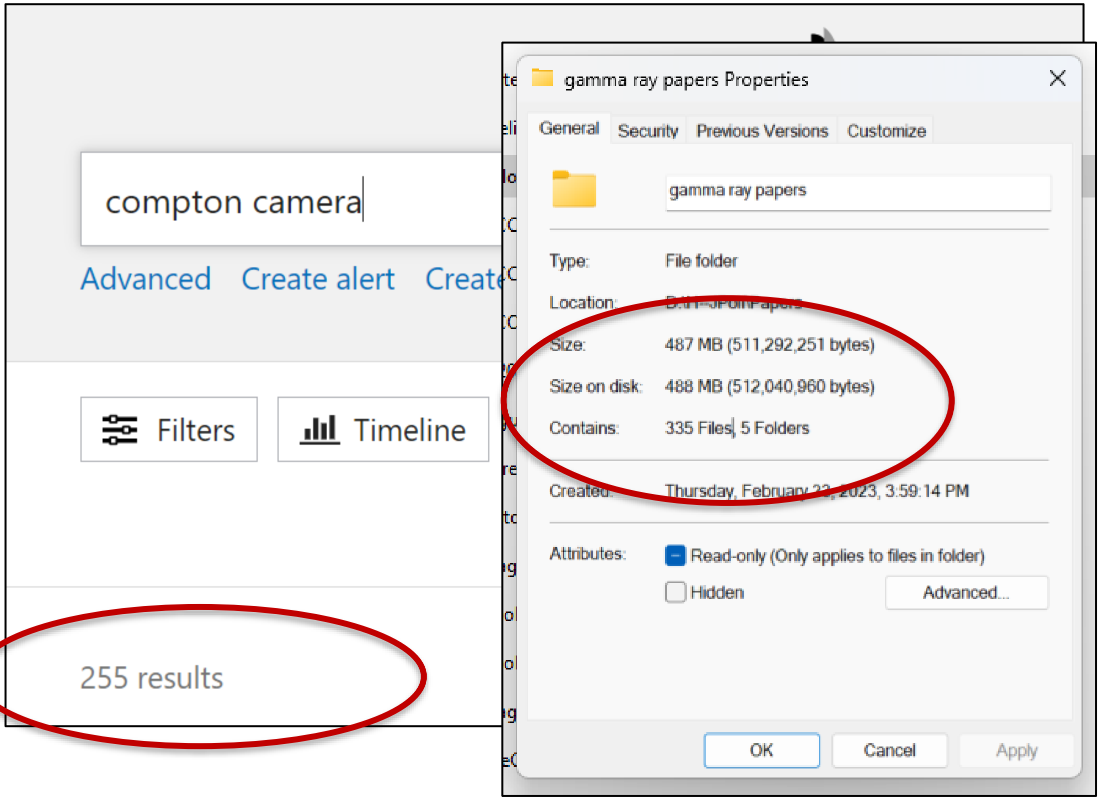
- 2023 — Frontiers | Research Topics: Prompt-Gamma Imaging in Particle Therapy

Chapter 3:3: Compton camera





History

At least 250 papers on Compton camera PG imaging!

Some reviews:

- Parajuli RK et al, Development and Applications of Compton Camera-A Review. Sensors (Basel). 2022 Sep 28;22(19):7374. doi: 10.3390/s22197374. PMID: 36236474; PMCID: PMC9573429.
- Krimmer J, et al,Prompt-gamma monitoring in hadrontherapy: A review. *Nucl Instr Methods Phys Res A* (2018) 878:58–73. doi:10.1016/j.nima.2017.07.063
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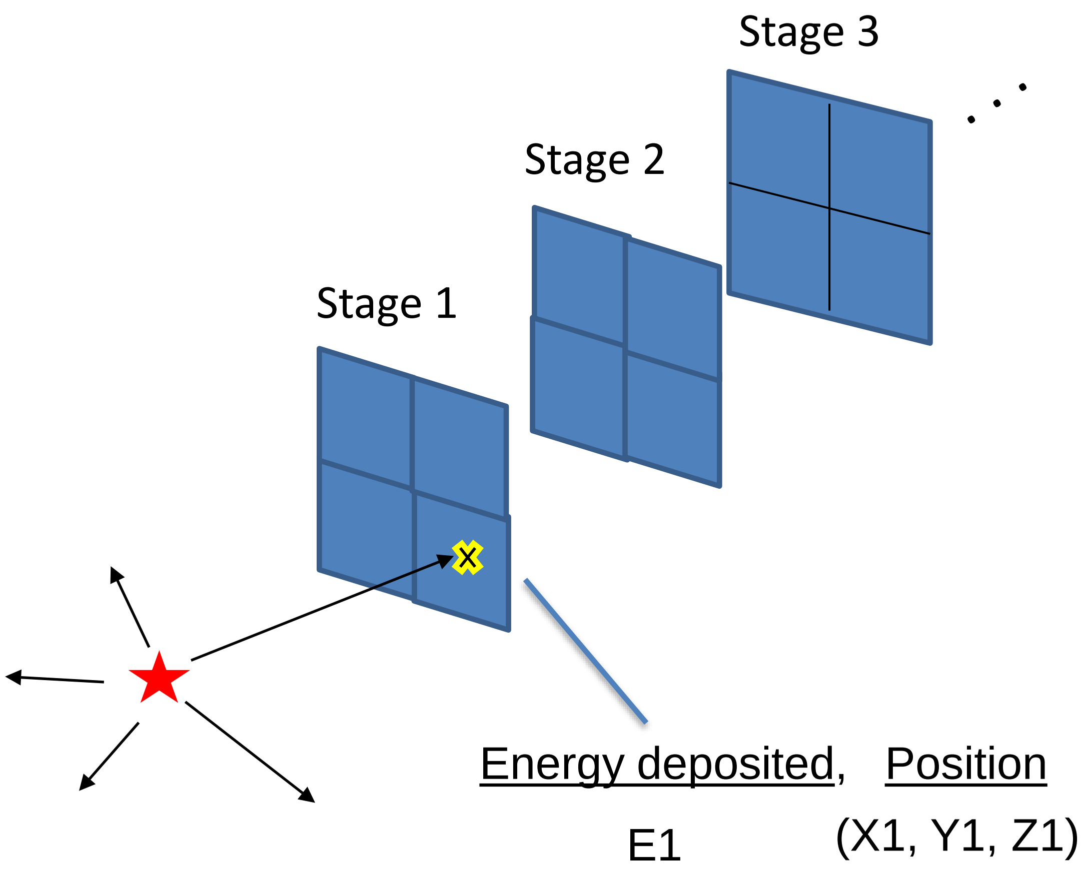
- Jerimy C. Polf, Katia Parodi; Imaging particle beams for cancer treatment. *Physics Today* 1 October 2015; 68 (10): 28–33. https://doi.org/10.1063/PT.3.2945

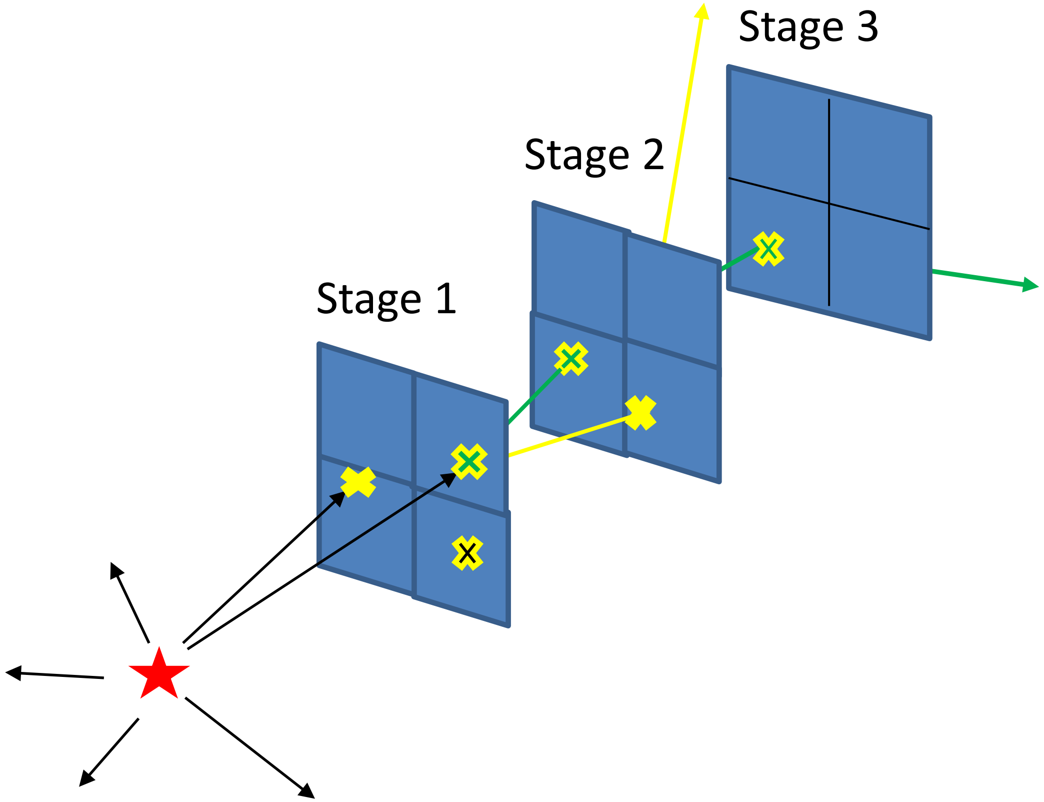
Chapter 3:3: Compton camera



Basics

- Compton Camera
  - Multi-stage detector
    - 2, 3, or more stages
  - Record energy deposited and position of a gamma interaction
  - Compton Scatter
  - Photoelectric Absorption
  - Pair Production

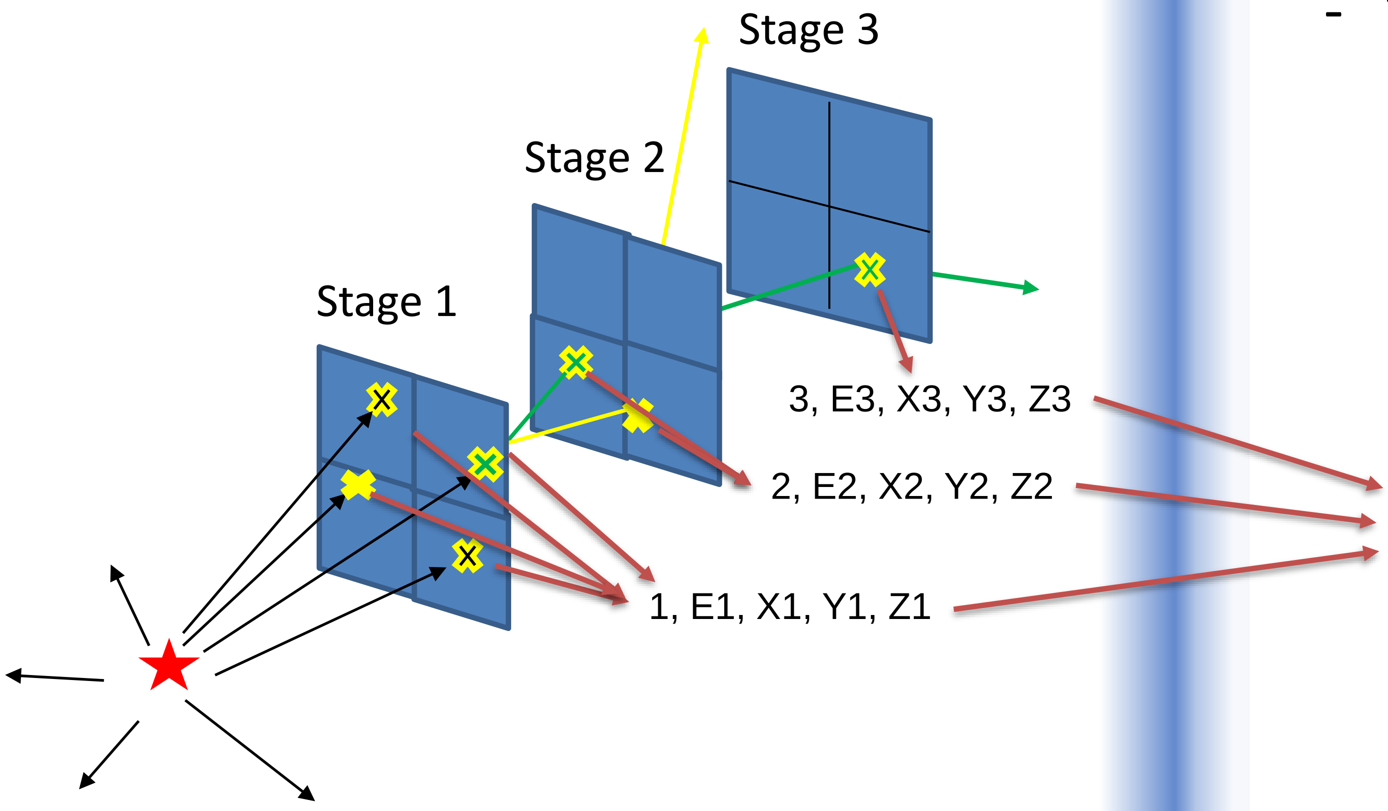
Chapter 3:3: Compton camera



Basics

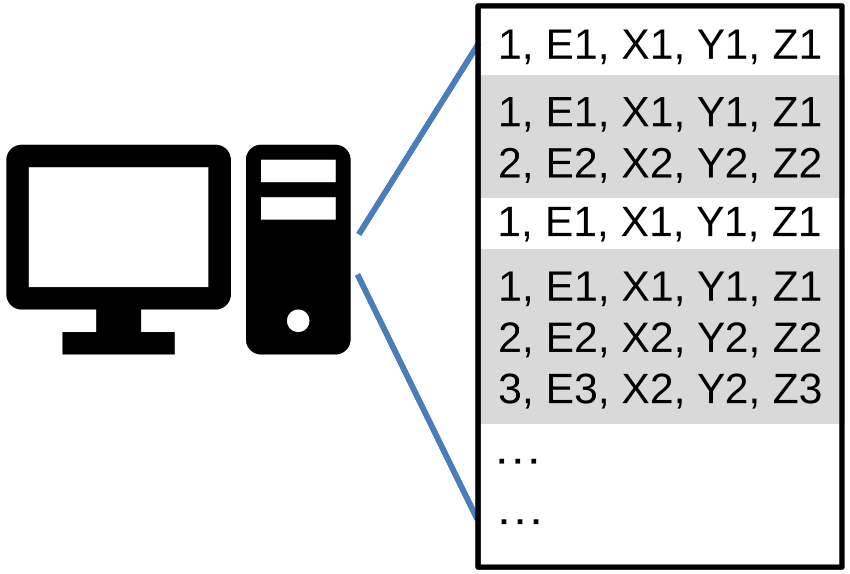
- <u>Compton Camera</u>
  - <u>Single Scatter</u> (SS)
  - <u>Double Scatter (DS)</u>
    - Compton Scatter – Photoelectric Abs.
    - Compton Scatter – Pair Production
    - Compton Scatter – Compton Scatter
  - <u>Triple Scatter (TS)</u>
    - Compton – Compton – Compton
    - Compton – Compton – Photoelectric Abs.
    - Compton – Compton – Pair Production

Chapter 3:3: Compton camera

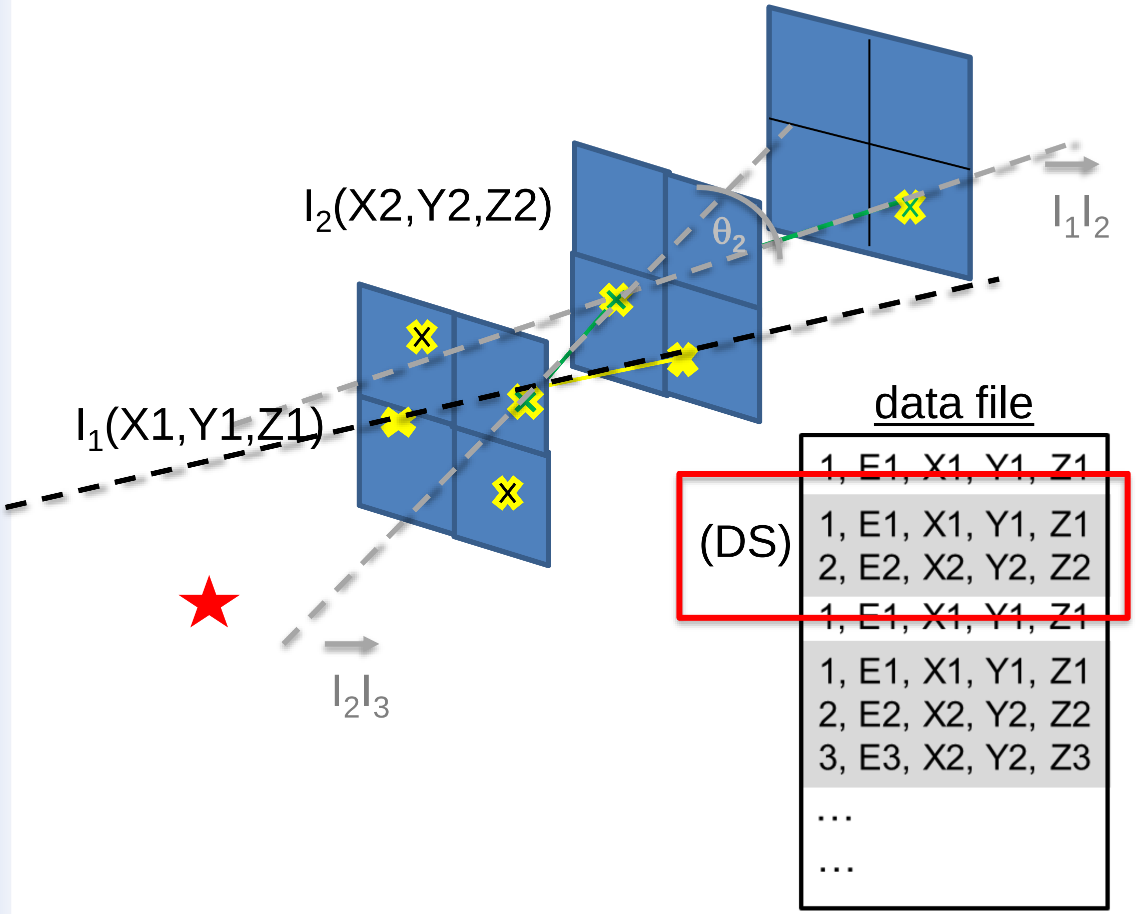


Basics

- “List-mode” data file



Chapter 3:3: Compton camera



Basics

- "Cone-of-origin"

<u>Cone central axis:</u>

$$\overrightarrow{I_1I_2} = (X2-X1)\hat{x},(Y2-Y1)\hat{y},(Z2-Z1)\hat{z}$$ "Scatter Axis"

<u>Cone half angle:</u>

$$\cos\theta_1 = 1 + m_e c^2\left(\frac{1}{E_0} - \frac{1}{E_0 - E_1}\right).$$ "Scatter Angle"

Gamma initial energy

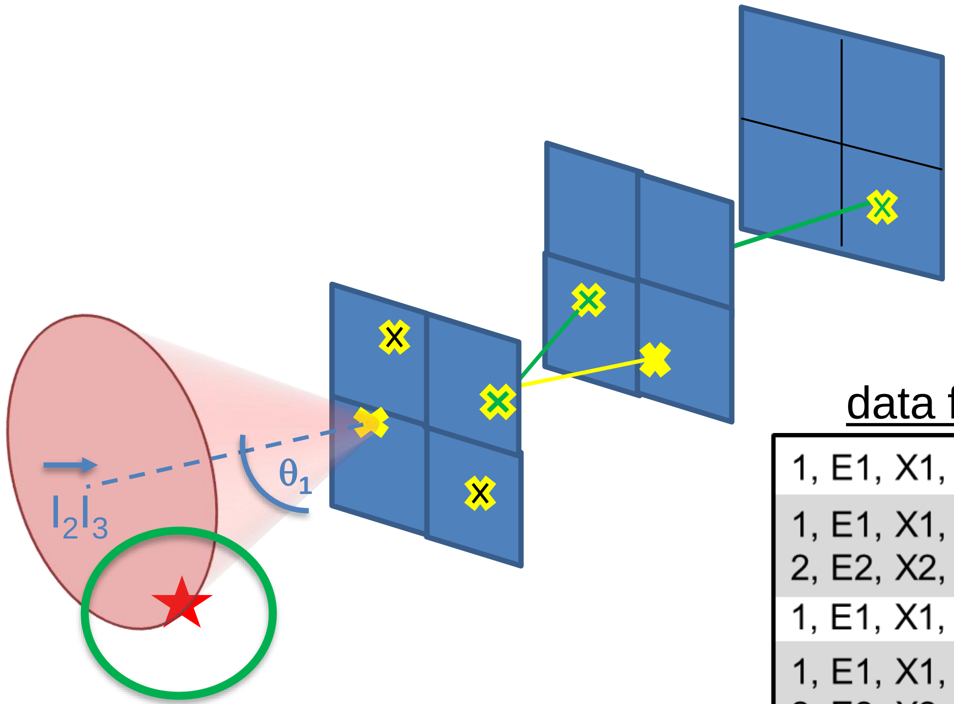
$E_0 = E_1 + E_2$ (DS)

Compton Scatter formula

$$E_0 = E_1 + 0.5\cdot\left[E_2 + \sqrt{E_2^2 + 4E_2 m_e c^2/(1 - \cos\theta_2)}\right].$$ (TS)

Second scatter angle

Chapter 3:3: Compton camera



data file

1, E1, X1, Y1, Z1
1, E1, X1, Y1, Z1 2, E2, X2, Y2, Z2
1, E1, X1, Y1, Z1
1, E1, X1, Y1, Z1 2, E2, X2, Y2, Z2 3, E3, X2, Y2, Z3
…
…

Basics

- "Cone-of-origin"

Step 1: Gamma initial energy (E_0)

$E_0 = E_1 + E_2$ (DS)

$$E_0 = E_1 + 0.5 \cdot \left[E_2 + \sqrt{E_2^2 + 4 E_2 m_e c^2 / (1 - \cos\theta_2)} \right]. \quad \text{(TS)}$$

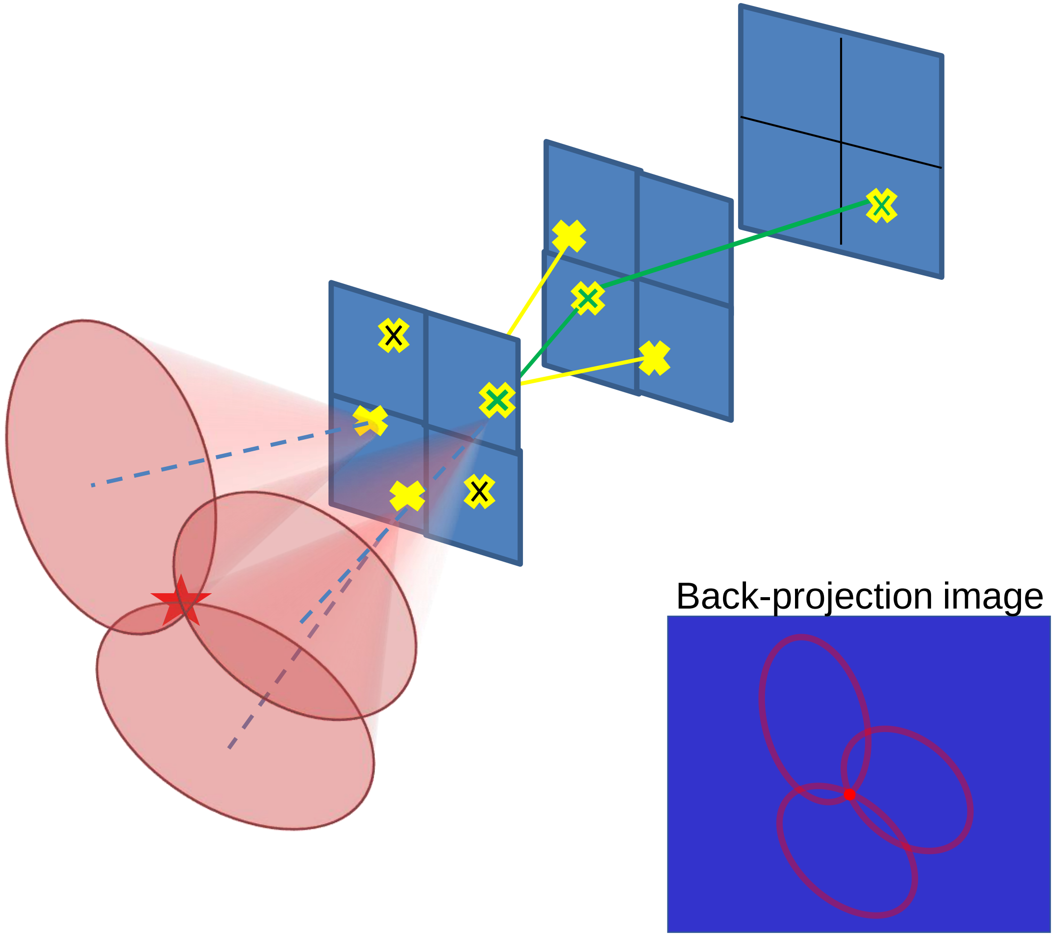
Step2: Cone half angle:

$$\cos\theta_1 = 1 + m_e c^2 \left(\frac{1}{E_0} - \frac{1}{E_0 - E_1} \right).$$ "Scatter Angle"

Step 3: Cone central axis:

$$\overrightarrow{I_1 I_2} = (X2-X1)\hat{x} + (Y2-Y1)\hat{y} + (Z2-Z1)\hat{z}$$ "Scatter Axis"

Chapter 3:3: Compton camera



Basics

- "Cone-of-origin"

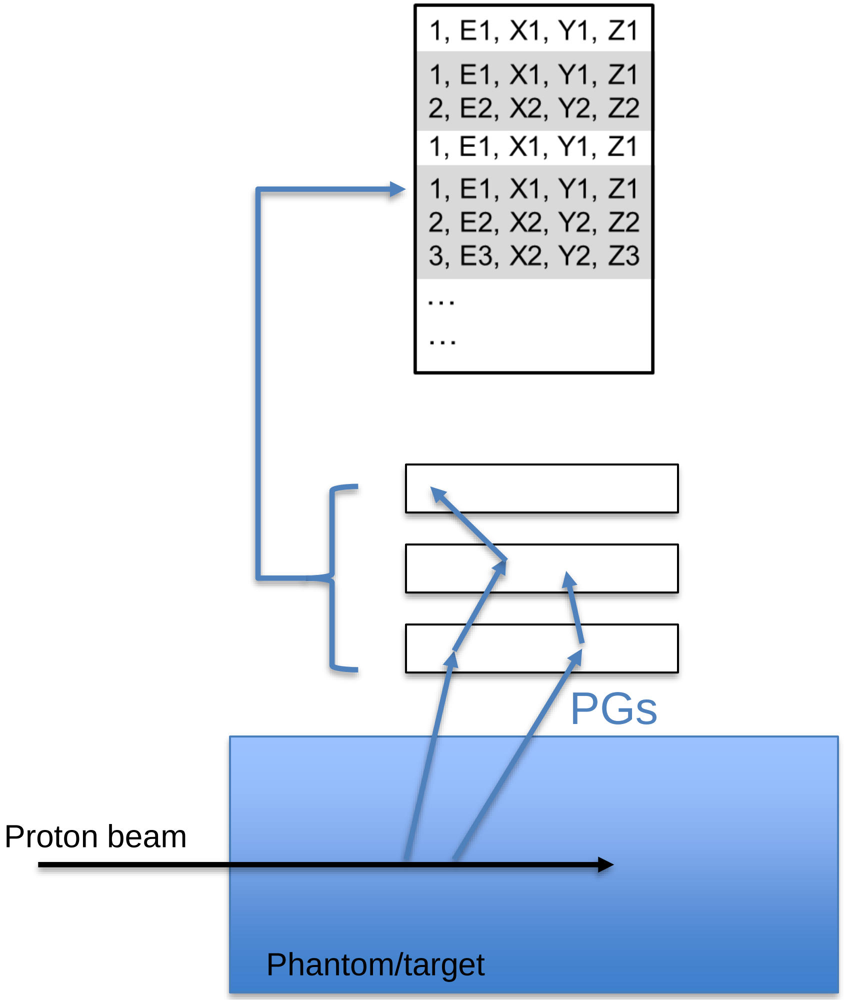
Surface of the Cone-of-origin will overlap with
The position of the gamma source.

As many cones are created, they will all overlap the source position.

Can back-project the cones onto a plane in space to form an image.

The source position: Where the most cones overlap (The brightest point in the image).

Chapter 3:3: Compton camera

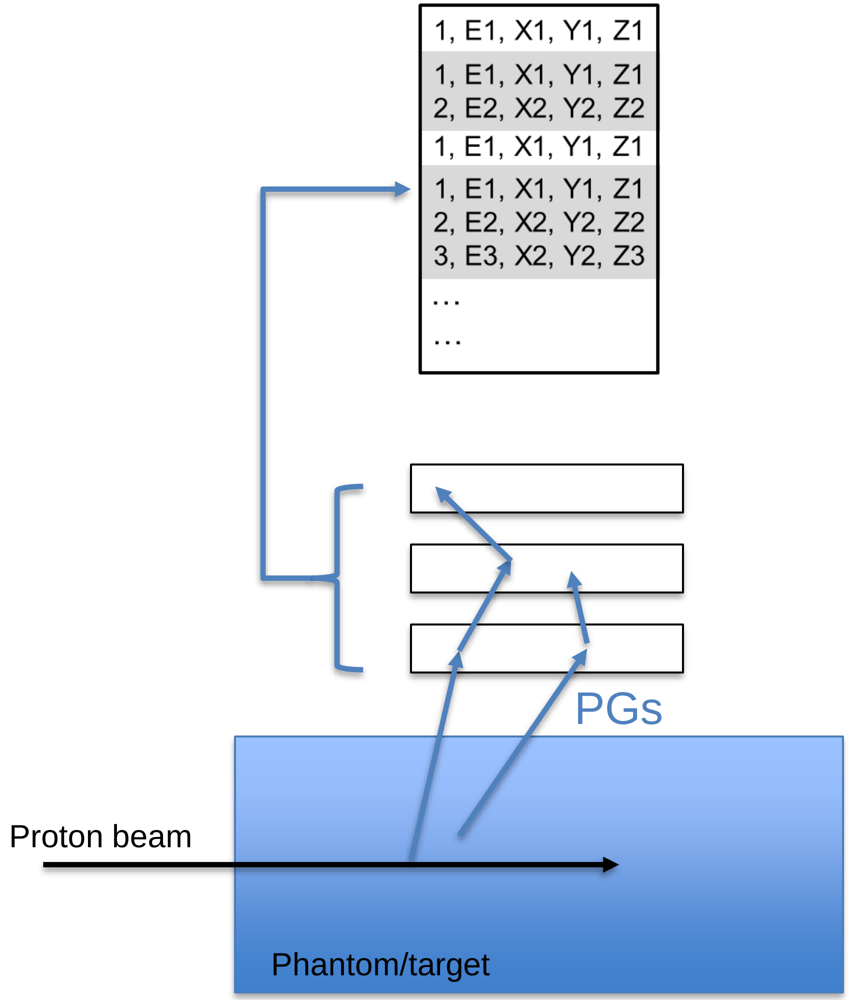


Prompt gamma imaging

A Lot of studies on using Compton cameras (CC) For prompt gamma (PG) imaging during particle Beam therapy

- Monte Carlo studies:
  - PG emission/detection characteristics
  - CC design optimization
  - Detection dynamics
  - Image reconstruction
  - Proton beam range verification

Chapter 3:3: Compton camera



Prompt gamma imaging

A Lot of studies on using Compton cameras (CC)
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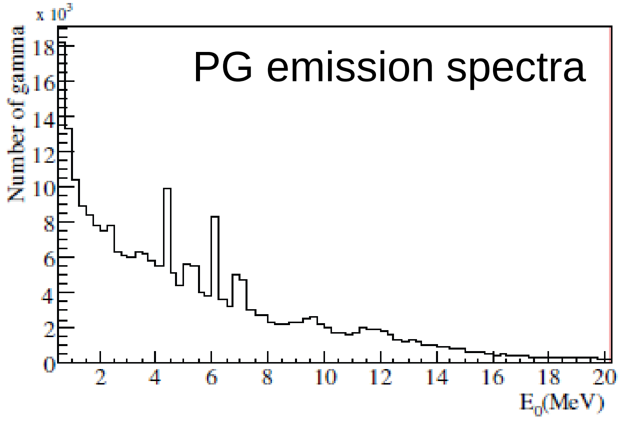
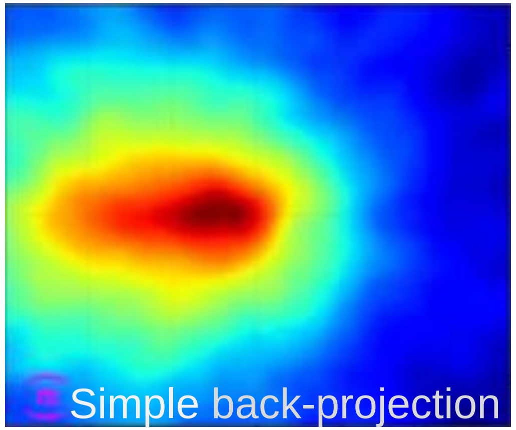
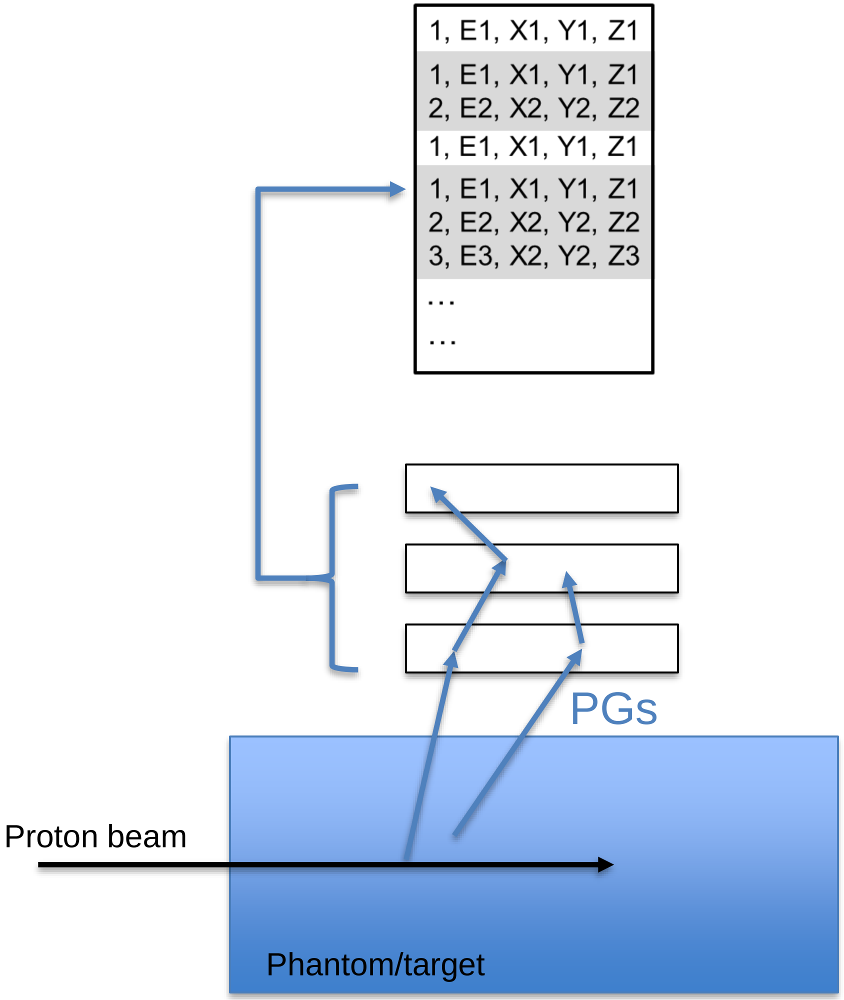
- Monte Carlo studies:





Chapter 3:3: Compton camera

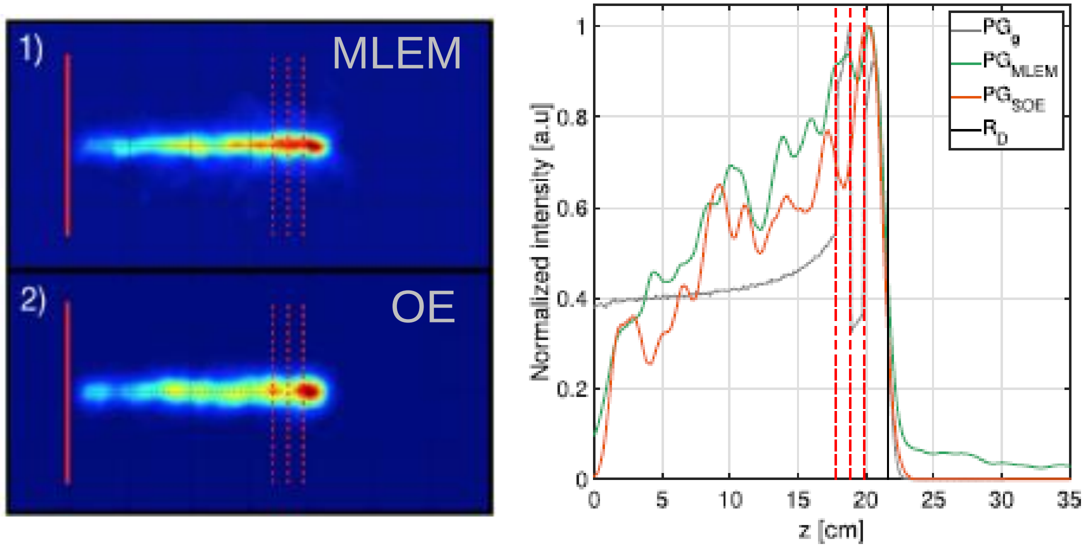


Prompt gamma imaging

A Lot of studies on using Compton cameras (CC) For prompt gamma (PG) imaging during particle Beam therapy

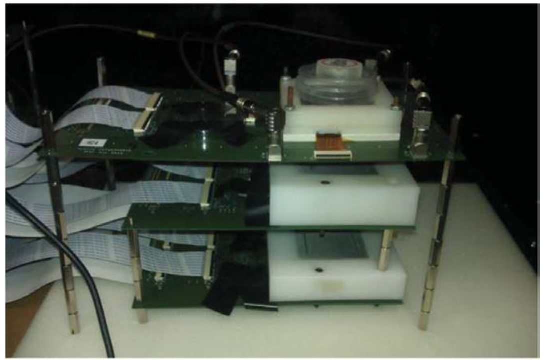
- Monte Carlo studies:

Iterative reconstruction

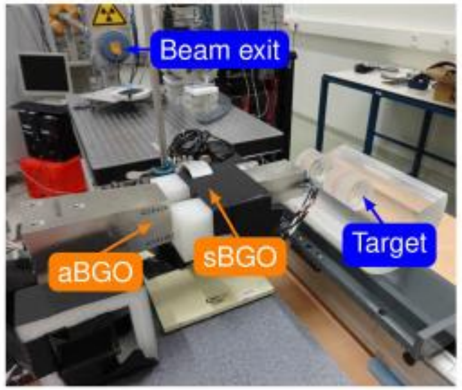


Lozano et al, Zeitschrift für Medizinische Physik, Volume 33, Issue 2, 2023,124-134,https://doi.org/10.1016/j.zemedi.2022.04.005.

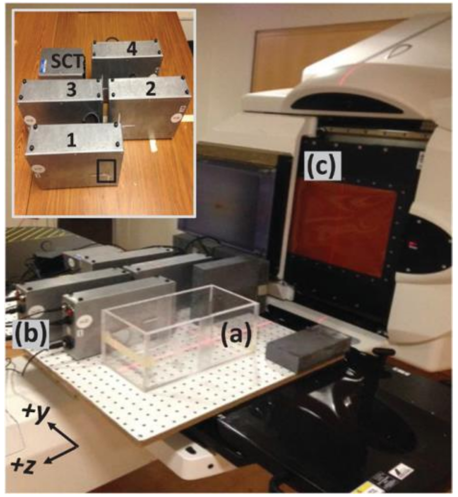
Chapter 3:3: Compton camera



Solevi et al, Phys. Med. Biol. **61** (2016) 5149



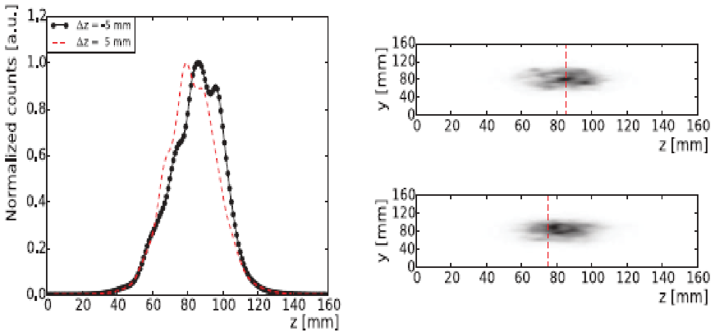
Hueso-Gonzalez et al, IEEE TRPMS, **1**(1), 2017

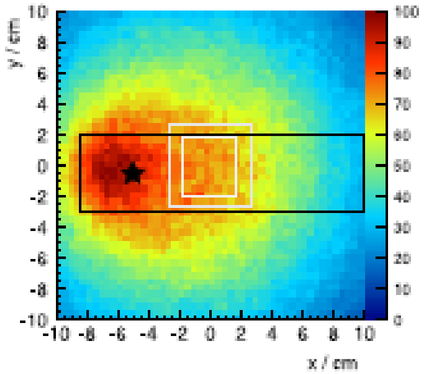


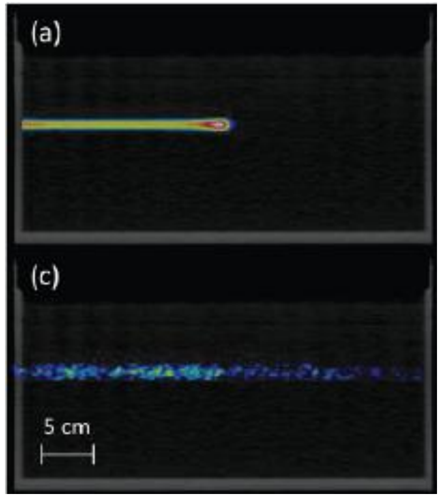
Polf et al, Phys. Med. Biol. **60** (2015) 7085

Prompt gamma imaging

- CC measurements of PG emission:

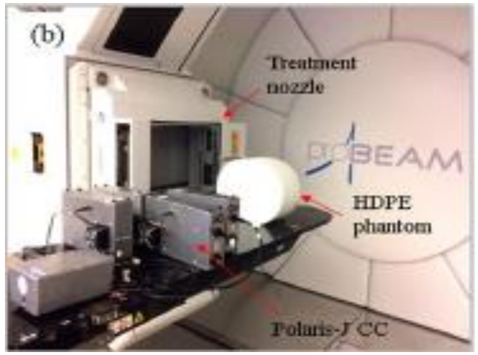




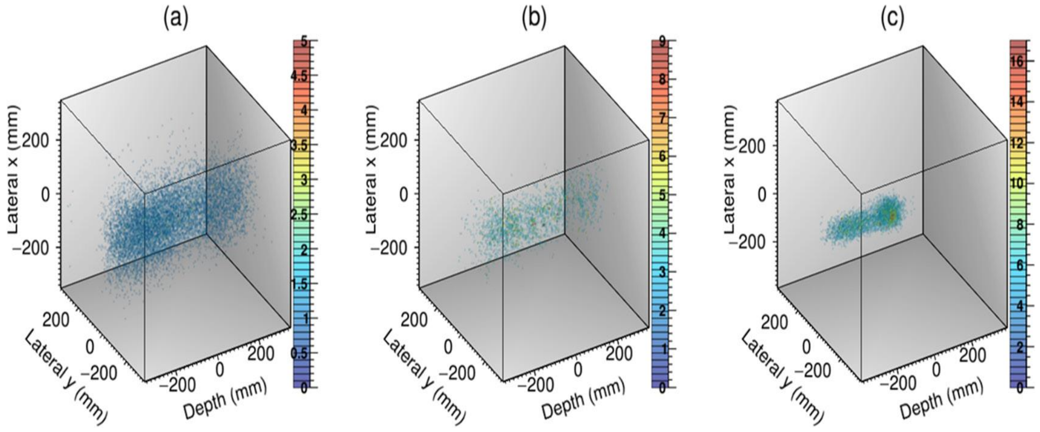


Chapter 3:3: Compton camera

Prompt gamma imaging



E Draeger *et al* 2018 *Phys. Med. Biol.* **63** 035019



- CC measurements of PG emission:

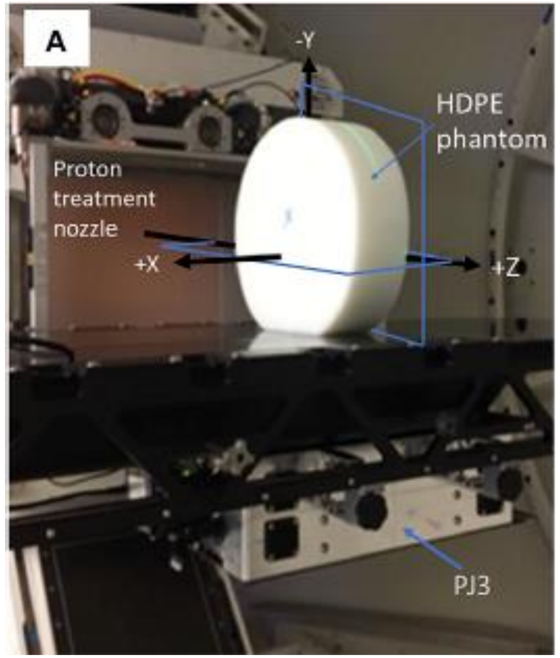
Full 3D imaging of PG emission during proton beam delivery!!!

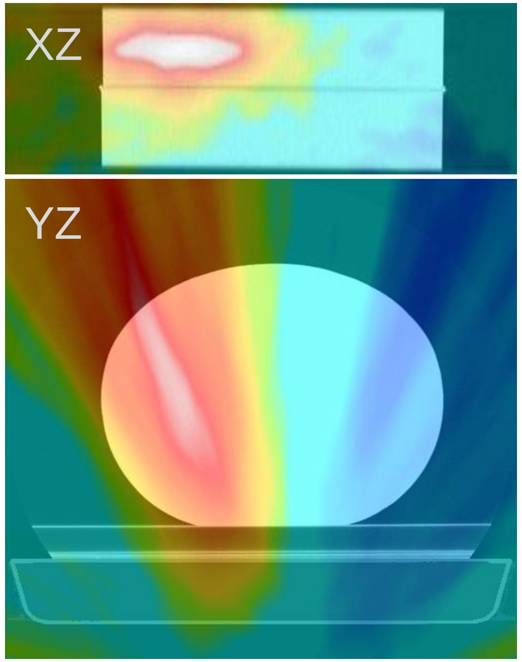
But ……

- Low intensity proton beam
- High doses delivered.

Still need to demonstrate CC imaging at clinical beam currents

Chapter 3:3: Compton camera



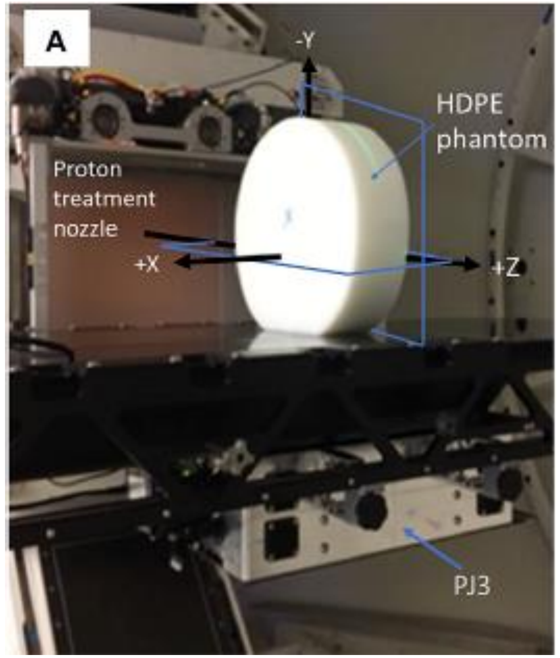


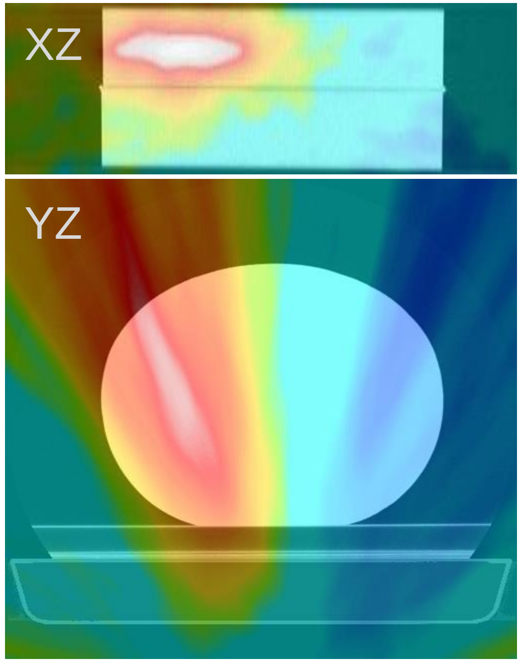
Polf et al, Front. Phys. (2022) 10:838273. doi: 10.3389/fphy.2022.838273

Prompt gamma imaging

- CC measurements of PG emission:
  - Clinical beam current: > 1 x 10^9 proton/sec
  - Total protons delivered: 3 x 10^9
  - It worked in 2D …sort of…
  - But in 3D…. …not so much…

Chapter 3:3: Compton camera





Polf et al, Front. Phys. (2022) 10:838273. doi: 10.3389/fphy.2022.838273

Prompt gamma imaging

- CC measurements of PG emission:

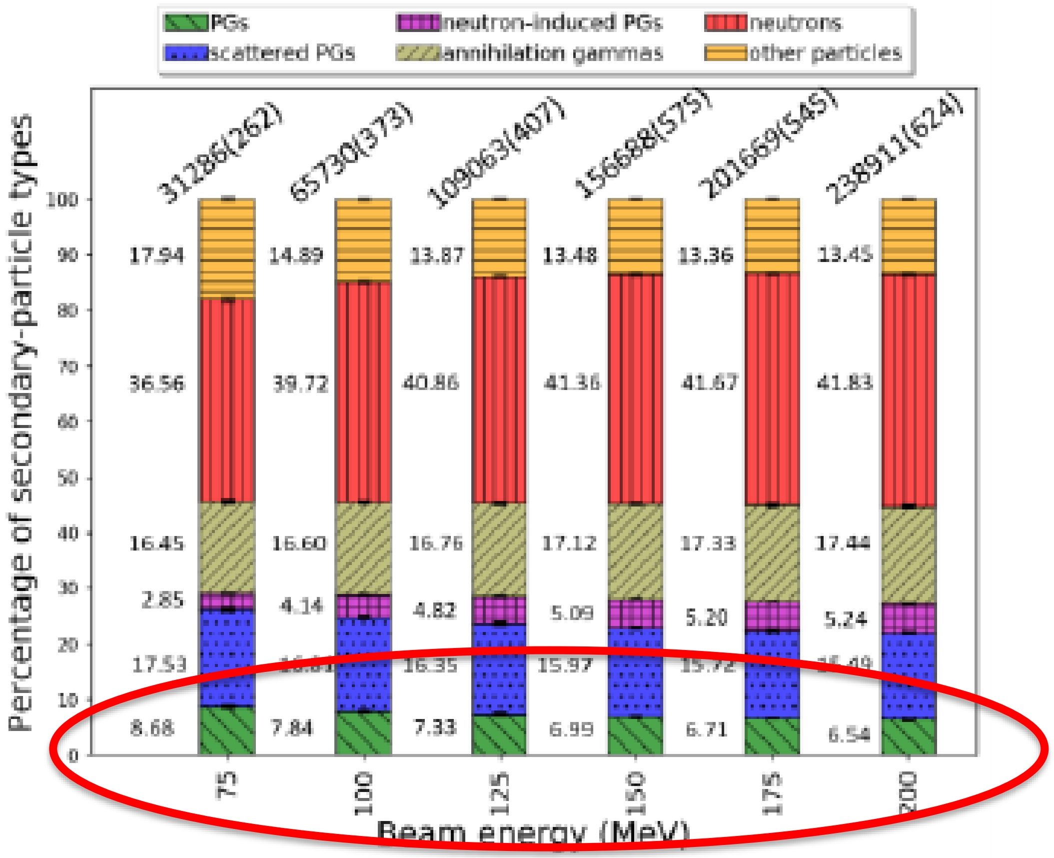
  - Clinical beam current: > 1 x 10^9 proton/sec
  - Total protons delivered: 3 x 10^9

Was possible to measure TS and DS events:
- decreased as beam current increased,

- produced noisier images, than at low current, even if we used the same number of DS/TS events.

- Could not measure small changes in proton beam range even with large number of DS/TS events.

Chapter 3:3: Compton camera



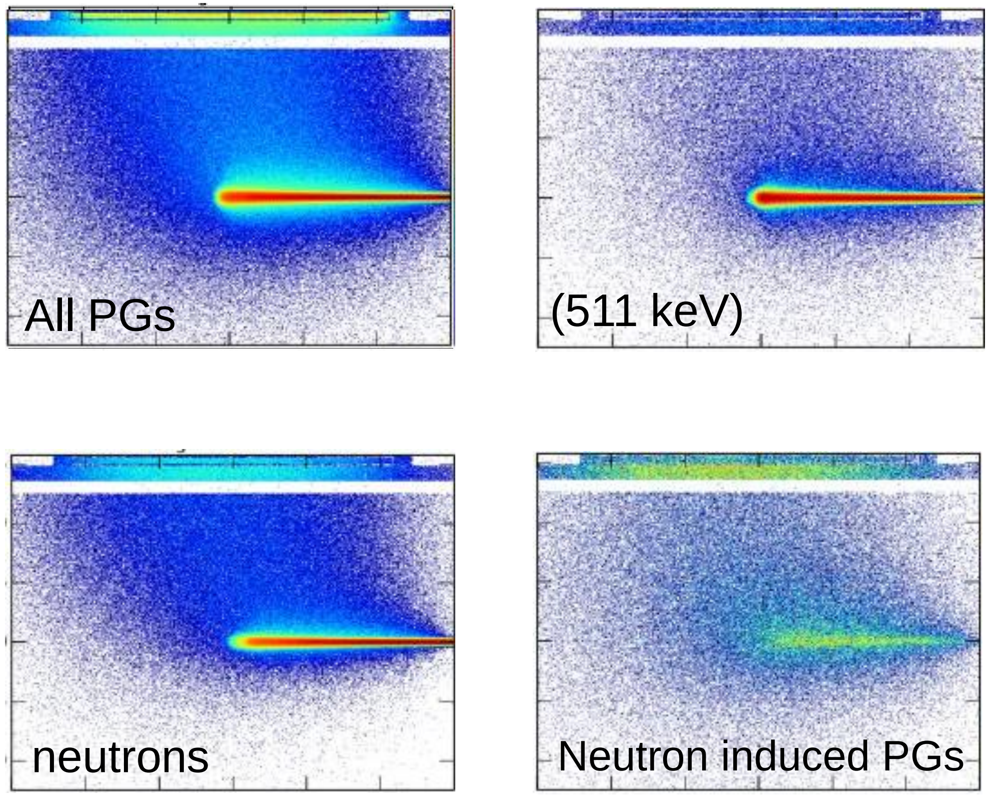
Panthi et al, IEEE TRPMS. 2021 5(3): 383–391.

What went wrong

- What is the CC measuring?
  - Everything emitted from the patient/phantom during irradiation:
    - Prompt gammas (PGs)
    - Scattered (PGs)
    - Annihilation gammas (511 keV)
    - Neutrons
    - Neutron induced PGs
    - Other particles (x-rays, scattered protons)

Chapter 3:3: Compton camera

Particle origin

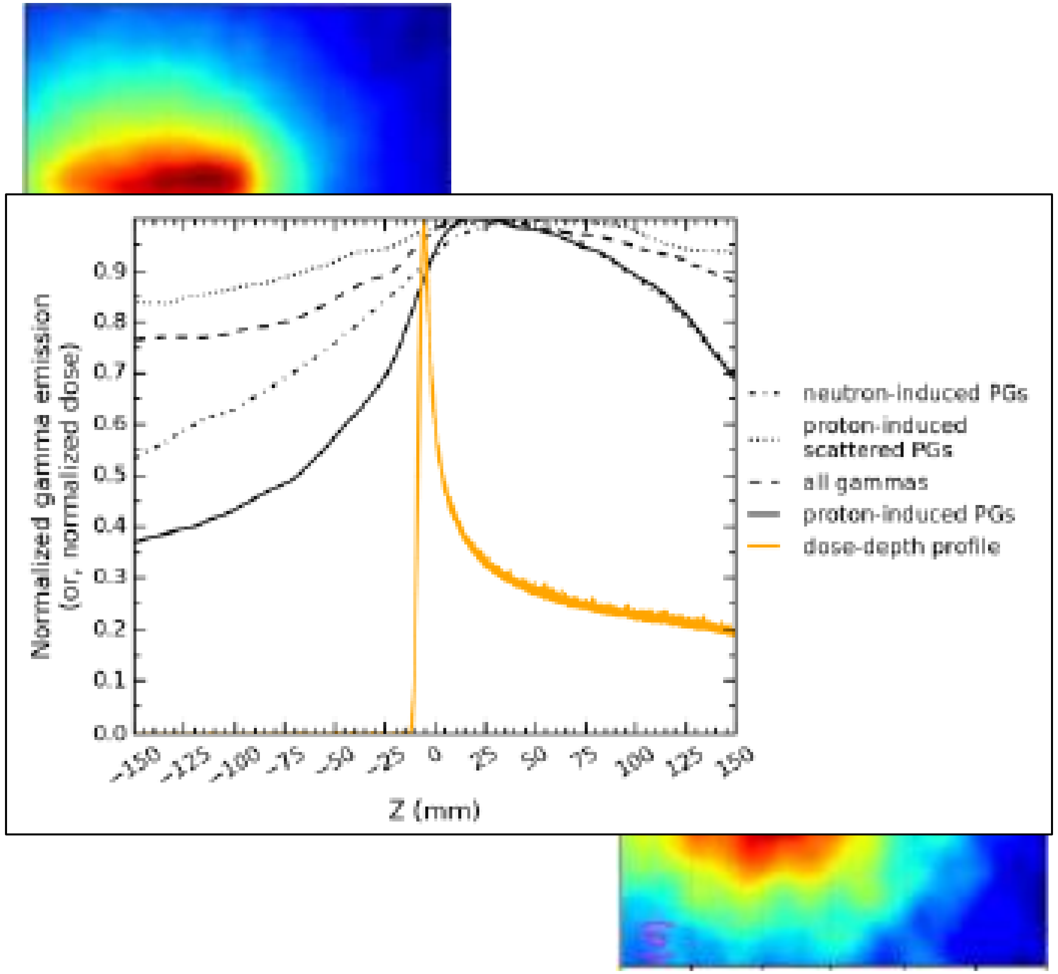


Panthi et al, IEEE TRPMS. 2021 5(3): 383–391.

What went wrong

- What is the CC measuring?
  - Everything emitted from the patient/phantom during irradiation:
    - Prompt gammas (PGs)
    - Scattered (PGs)
    - Annihilation gammas (511 keV)
    - Neutrons
    - Neutron induced PGs
    - Other particles (x-rays, scattered protons)

Chapter 3:3: Compton camera



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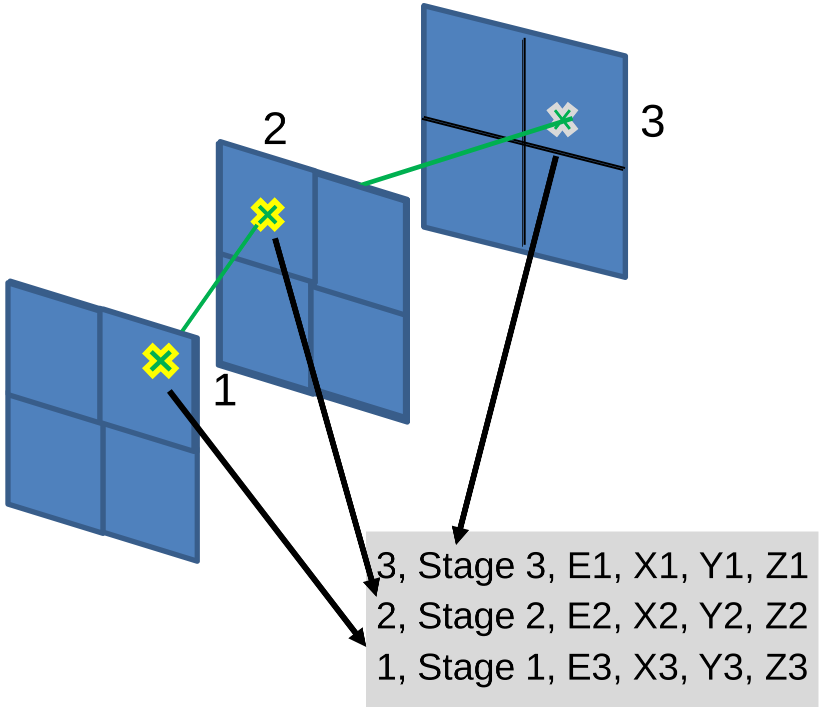


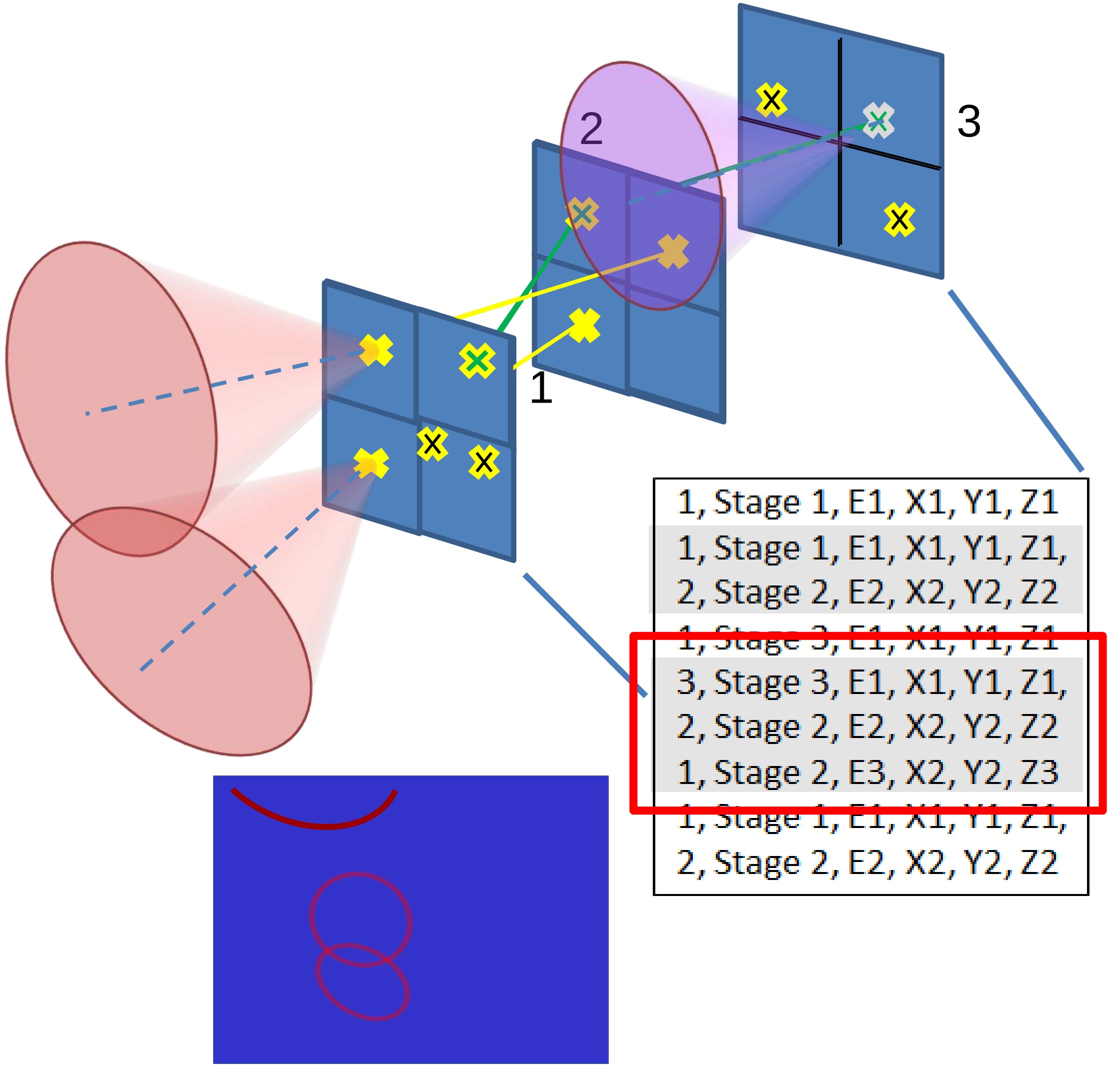
What went wrong

- How is the data recorded?

  - CC components have finite readout timing characteristics.

  - DS and TS events can be incorrectly recorded by the CC resulting in a “mis-ordered” (MO) event.

Chapter 3:3: Compton camera



What went wrong

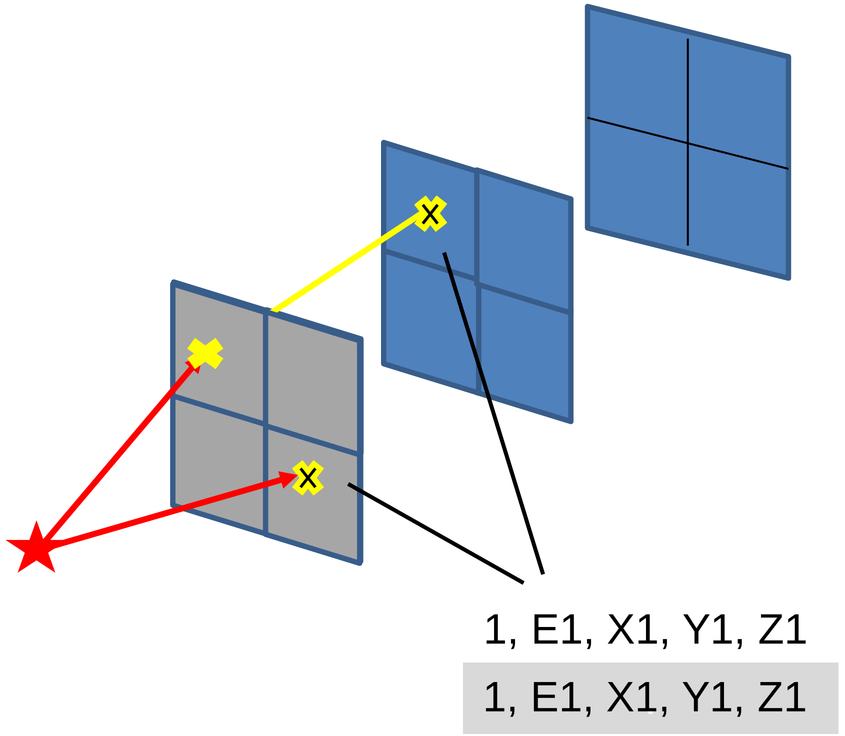
- How is the data recorded?

  - CC components have finite readout timing characteristics.

  - DS and TS events can be incorrectly recorded by the CC resulting in a “mis-ordered” (MO) event.

  - Back-projected cone no longer intersect with the source location.

Chapter 3:3: Compton camera



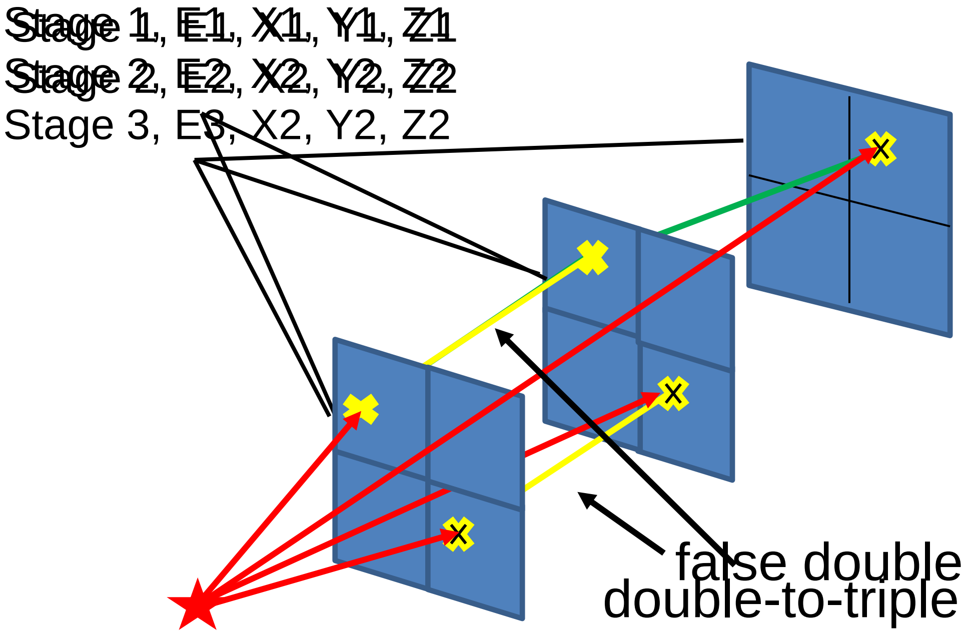
What went wrong

- How is the data recorded?

- The CCs are operating in *high count rate environments,* such as those encountered during proton radiotherapy:

- A detection stage may be in its “readout dead state” (“gray” 1st stage), meaning it is currently processing and recording the data from a previous gamma event. It is therefore unable to detect and readout the current gamma interaction. Thus the gamma DS or TS event would not be recorded.

Chapter 3:3: Compton camera



What went wrong

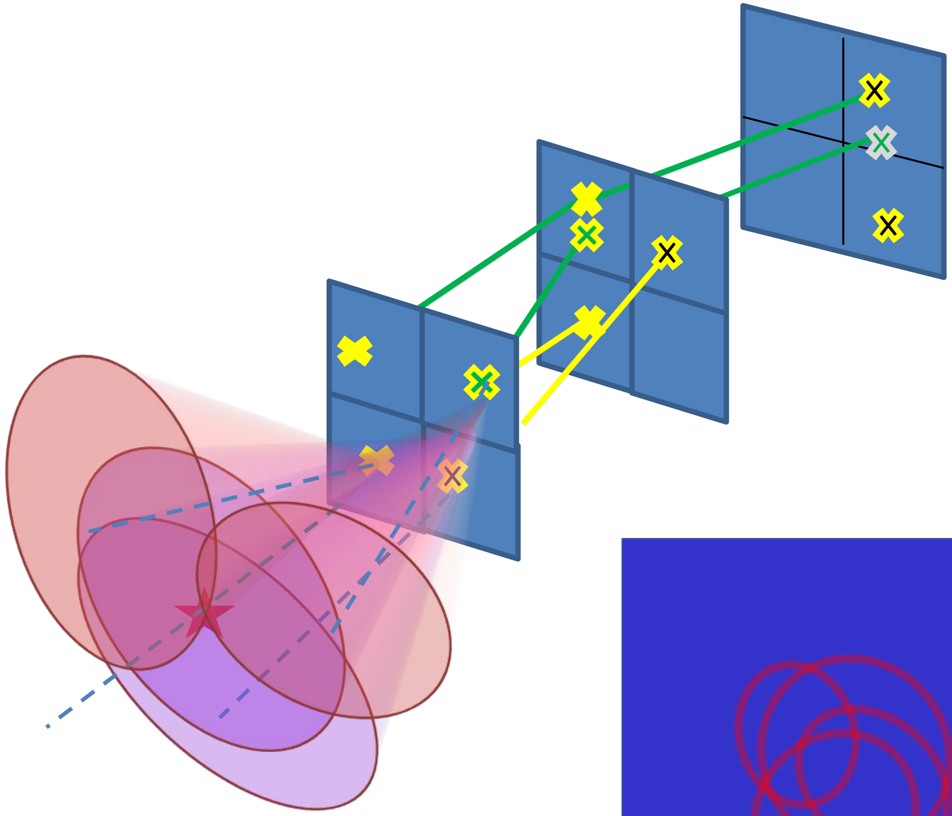
- How is the data recorded?

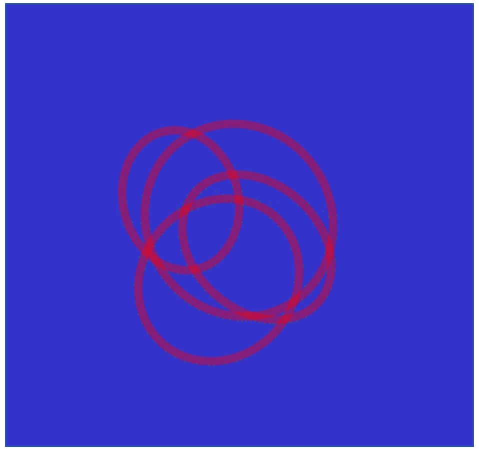
- The CCs are operating in *high count rate environments,* such as those encountered during proton radiotherapy:

  More than one gamma may interact within the active detection window, which can result in a “False” DS or TS event being readout

  - False DS and TS events, can arise from:
    - Two SS or three SS interactions from two or three separate gammas, or
    - A DS plus a SS from a separate gamma resulting in the DS being readout as a TS, creating a “double-to-triple” (D-to-T) event.

Chapter 3:3: Compton camera



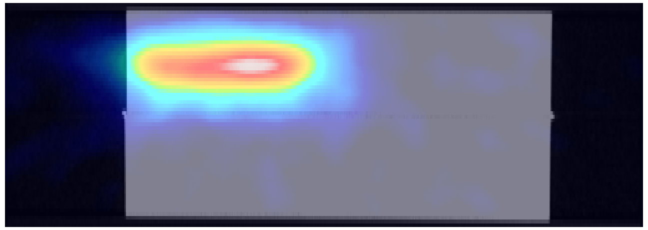


What went wrong

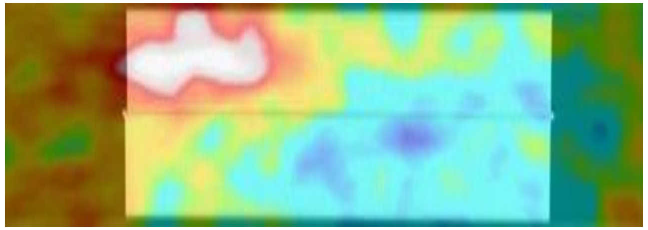
- How is the data recorded?

• These types of "false" events produce cone-of-origins that do not overlap with the source position, thus only contributing noise to the final image. This effectively reduces the number of cones-of-origin from "good" DS and TS events (i.e. that intersect the true source position) that will allow an image of the source to be reconstructed.

Chapter 3:3: Compton camera



Ideal image



High count rate image

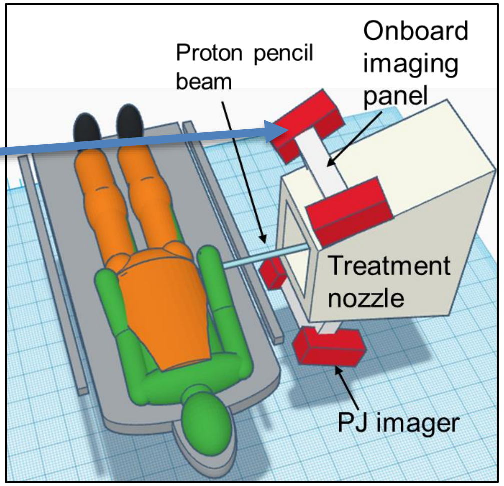
What went wrong

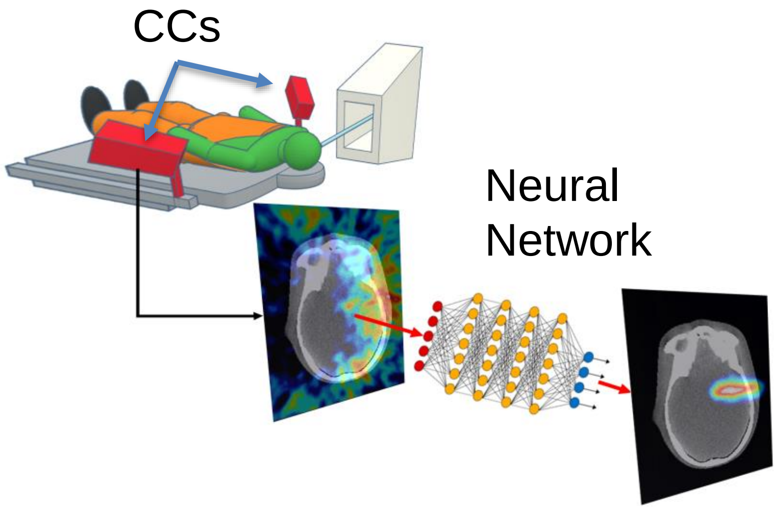
- What is the CC measuring?

For CC imaging in high count rate clinical proton therapy application the final PG image is greatly Degraded!

This issue, plus the large size and expensive components of many experimental CCs led many to conclude the CC imaging for PGI base proton range verification was not clinically viable.

Chapter 3:3: Compton camera





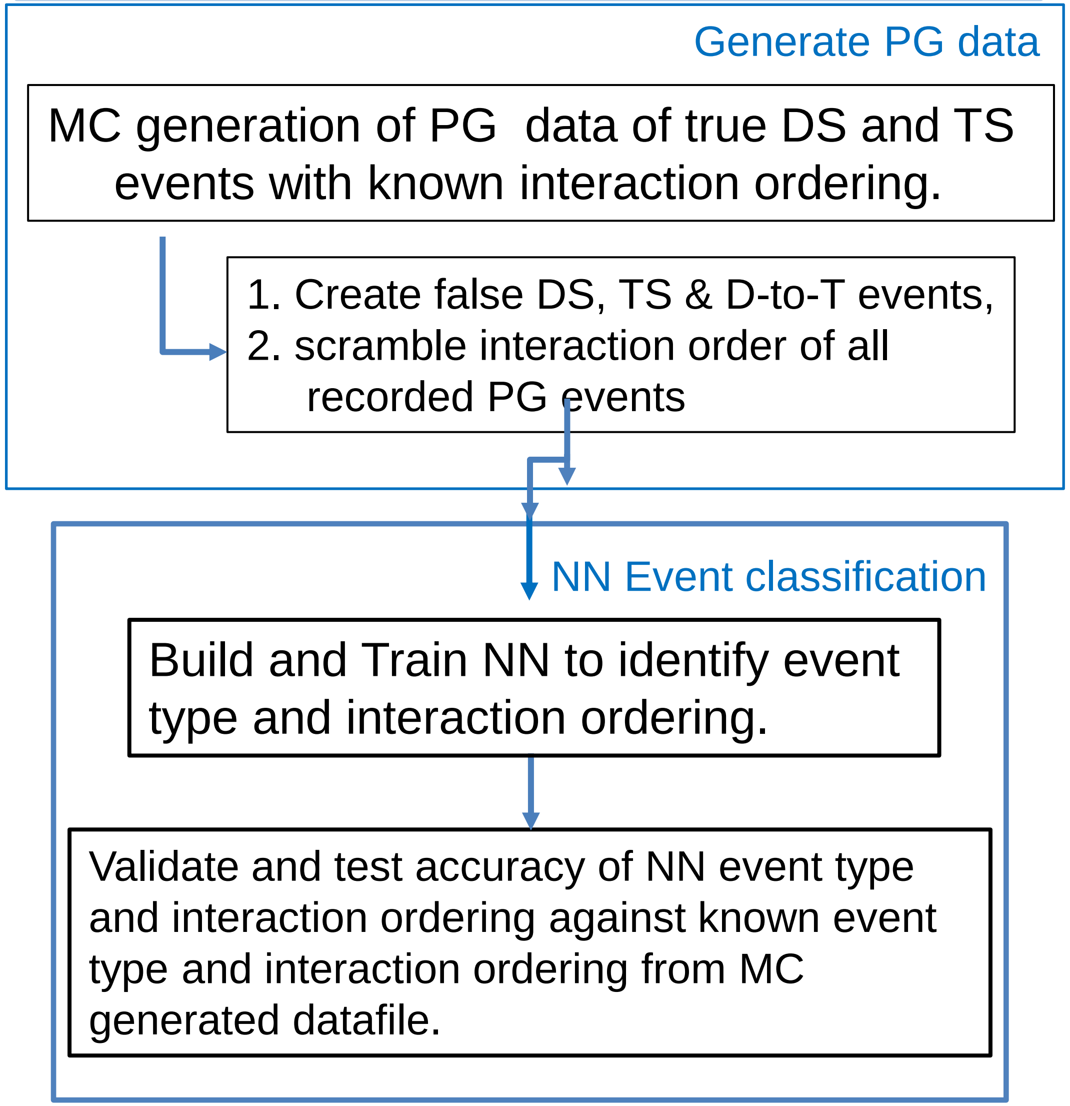
How it can still work

- Development of smaller, faster, cheaper CCs.
  - 5 cm x 5 cm x 12 cm
  - < 250 g
  - 0.1 – 9 MeV energy range
  - > 2 MHz count rate.
  - USB data streaming

- Mounting CC imagers to gantry
  - University of Maryland

- Machine learning.
  - Remove false events
  - Predict correct event ordering
  - Remove image artifacts
  - PG to dose transformation
  - Eliminate image reconstruction

Chapter 3:3: Compton camera

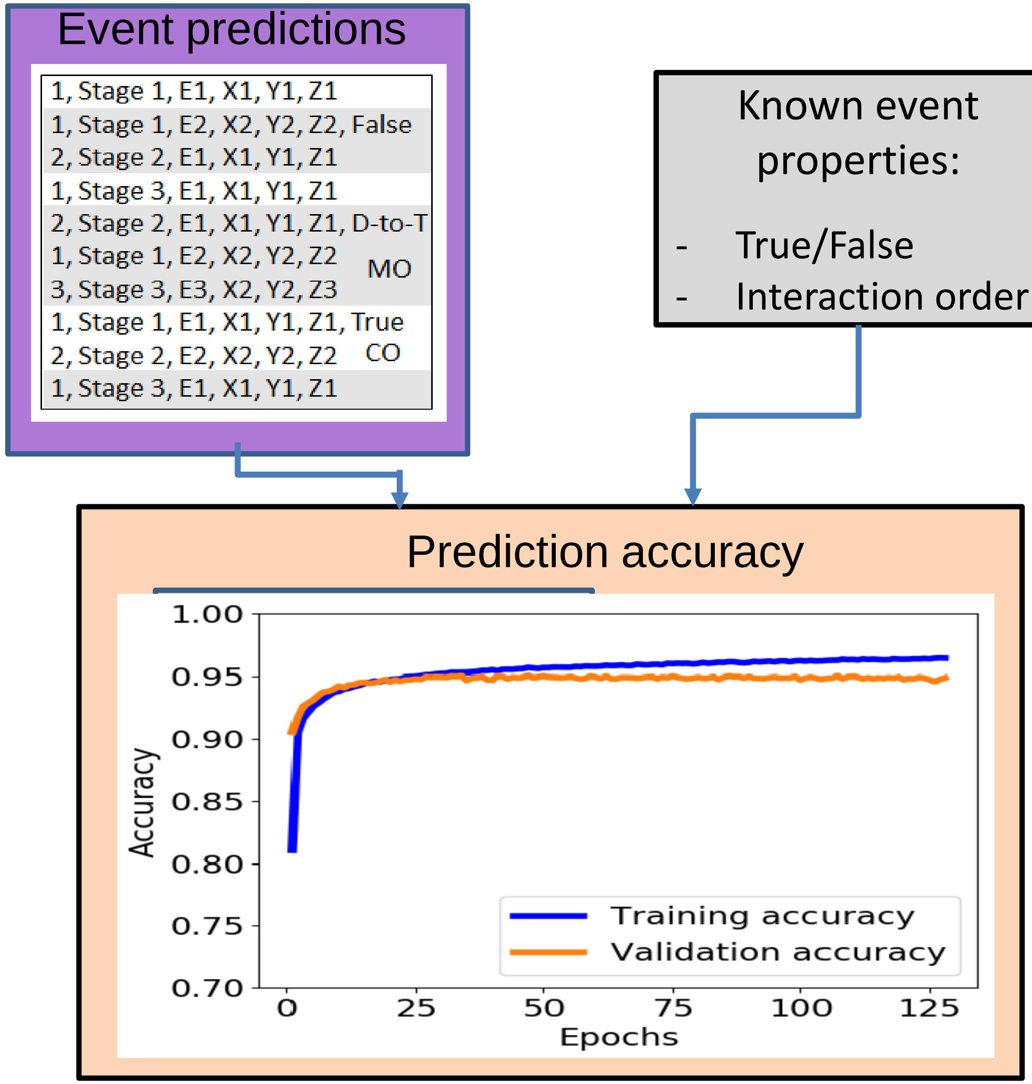


Courtesy of Dr. Carlos Barajas

How it can still work

- Machine learning.
  - Generate Monte Carlo “training” and “validation” data
  - Data must accurately reproduce measured data and contain:
    - Mis-ordered events
    - False events,
    - Etc.
  - Train Neural Network (NN) to accurately predict True/False events, and event order

Chapter 3:3: Compton camera



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- Machine learning.

  - Generate Monte Carlo “training” and “validation” data

  - Data must accurately reproduce measured data and contain:
    - Mis-ordered events
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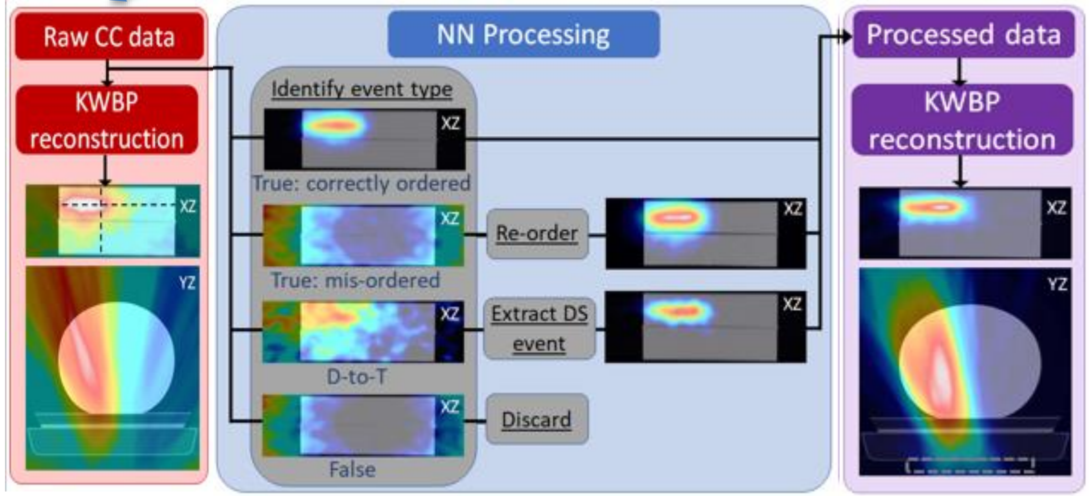
    - Etc.

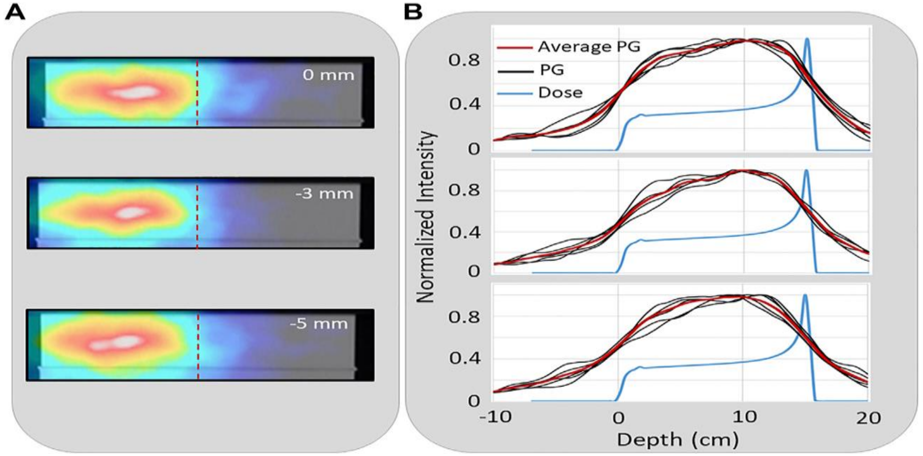
  - Train Neural Network (NN) to accurately predict True/False events, and event order

  - Validate on independent dataset

Chapter 3:3: Compton camera

Measured PG data





How it can still work

- Machine learning.

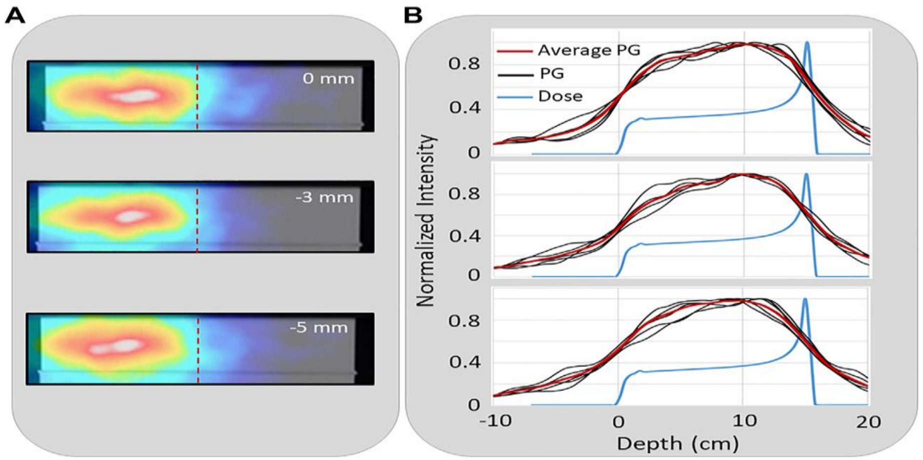
Measure PG emission with pre-clinical CCs
During clinical proton beam irradiation

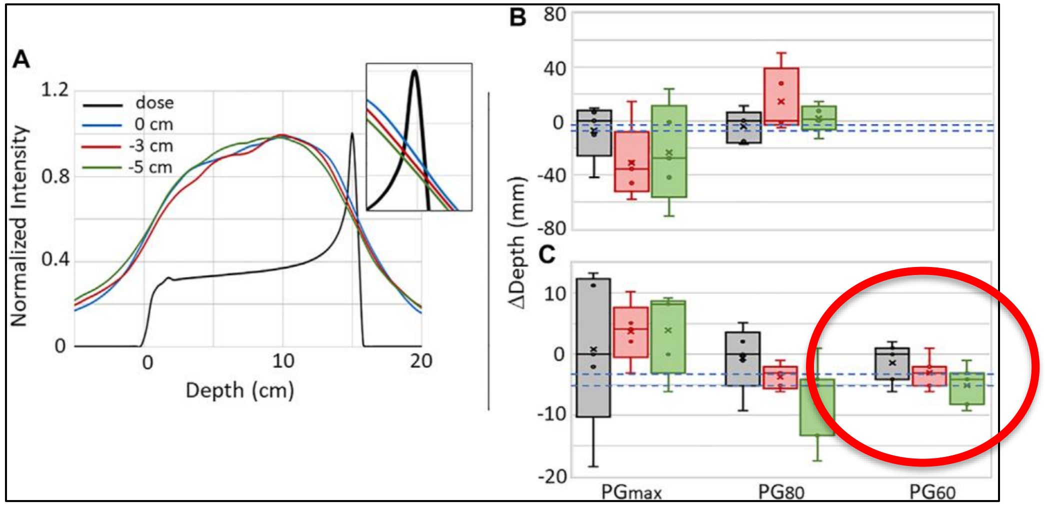
Process CC list-mode data with fully trained
Neural network (NN)

Reconstruct NN processed data.

Could see 3 mm and 5 mm shifts in delivered
Beam range.

Chapter 3:3: Compton camera





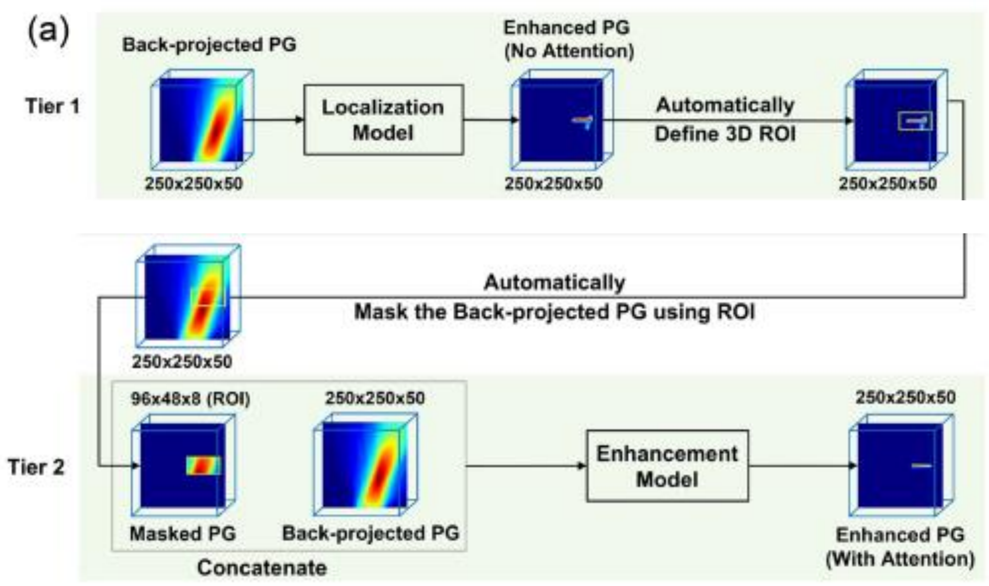
How it can still work

- Machine learning.

Could see 3 mm and 5 mm shifts in delivered Beam range.

PG 40% distal falloff as range metric.
- Minimum range shift was 3 mm.

Chapter 3:3: Compton camera



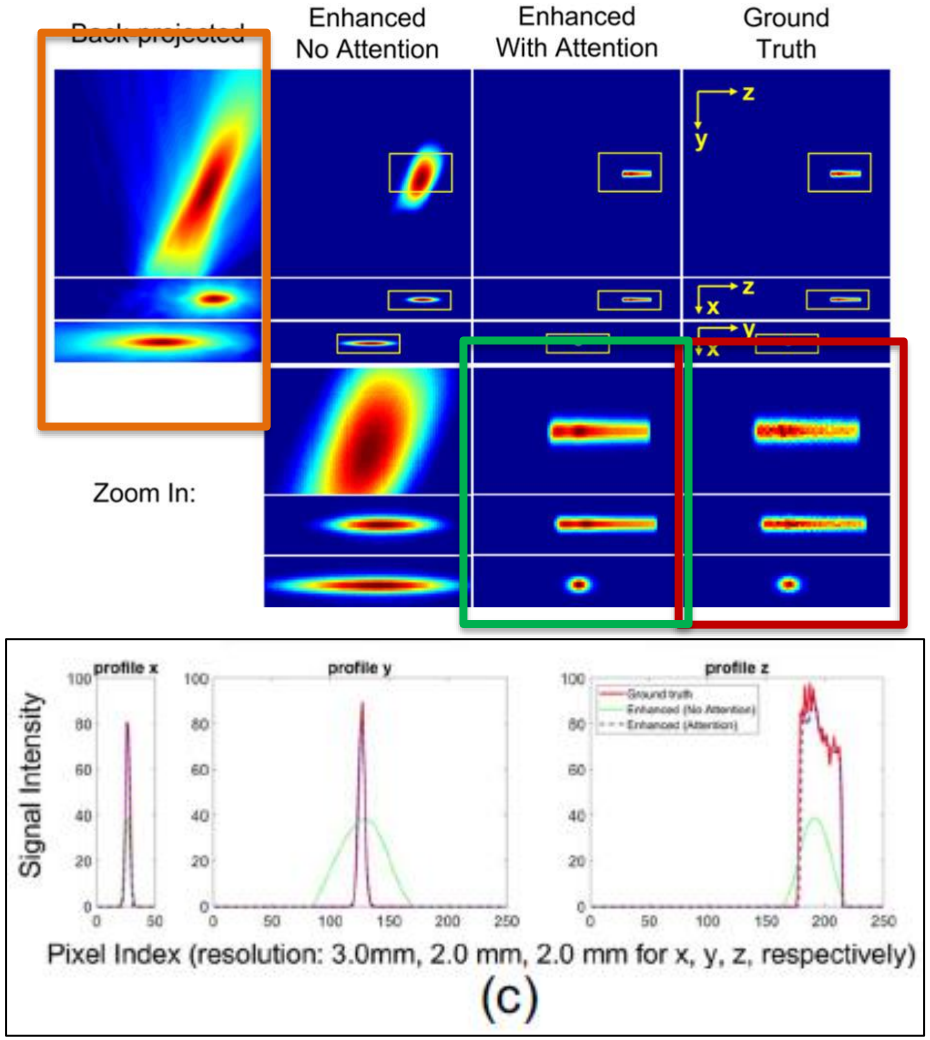
Jiang et al, (2023) Phys. Med. Biol. **68** 075001

How it can still work

- Machine learning.

Full 3D imaging of PG emission profile

Chapter 3:3: Compton camera



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How it can still work

- Machine learning.

Full 3D imaging of PG emission profile

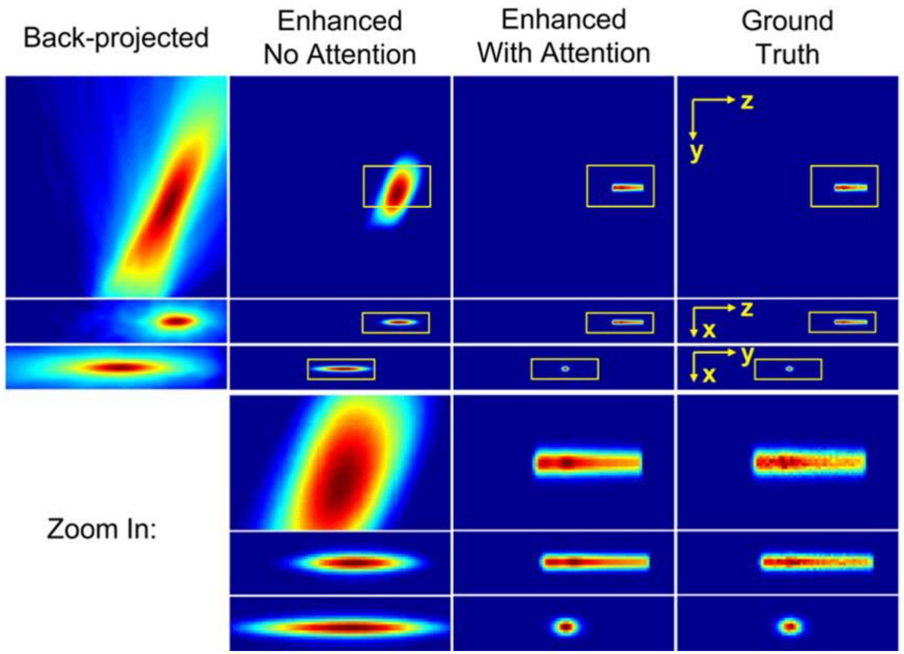
- Start with simple back-projected image

- Input back-projected image into trained NN

- Final 3D image of pencil beam

  - Good prediction of full pencil beam
  - No need for iterative reconstruction
  - 1st step to generating image *without* reconstruction algorithm

Chapter 3:3: Compton camera



Jiang et al, (2023) Phys. Med. Biol. **68** 075001

How it can still work

- Machine learning.

- Zoglauer A, Boggs SE. IEEE Nuclear Science Symposium Conference Record (2007). doi:10.1109/NSSMIC.2007.4437096

- Liu et al, Phys Med. 2020 69:110-119. doi: 10.1016/j.ejmp.2019.12.006.
- Kshirsagar, *et al. Sci Rep* **13**, 9948 (2023). https://doi.org/10.1038/s41598-023-36832-8
- Kozani et al, Phys Med Biol. 2022 67(15). doi: 10.1088/1361-6560/ac71f2.
- Lerendegui-Marco, J *et al. Sci Rep* **12**, 2735 (2022). https://doi.org/10.1038/s41598-022-06126-6
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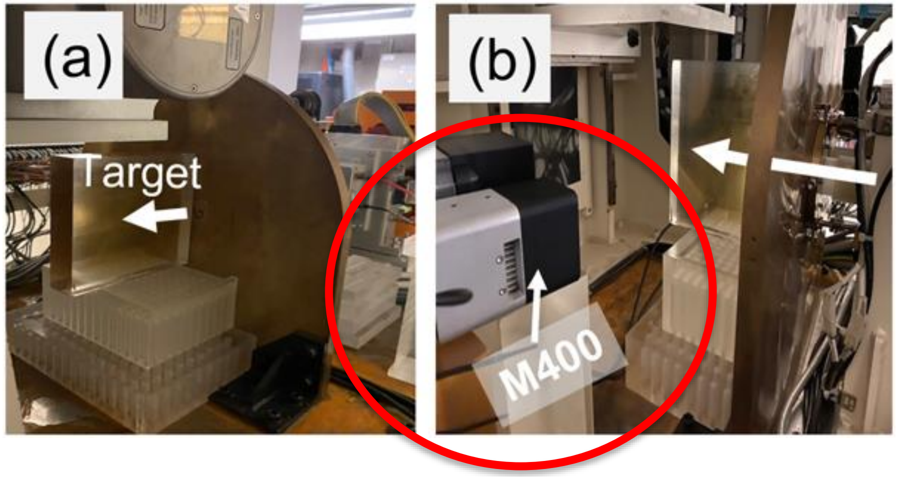
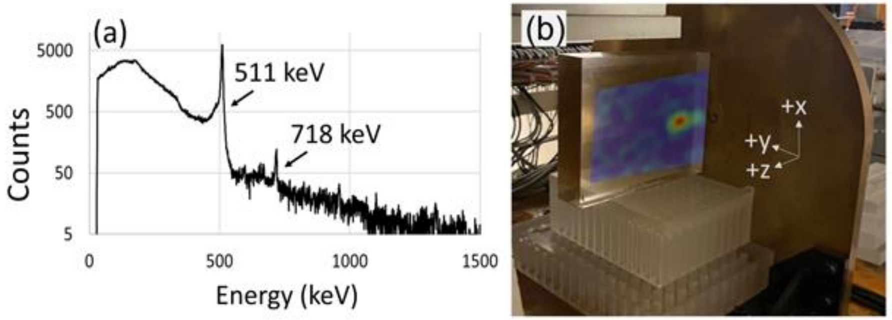
- Muñoz E et al. *Sci Rep* (2021) 11:9325. doi:10.1038/s41598-021-88812-5

Chapter 3:3: Compton camera





F Abouzahr *et al* 2023 *Phys. Med. Biol.* **68** 125001, DOI 10.1088/1361-6560/acd29e

How it can still work

- FLASH Radiotherapy

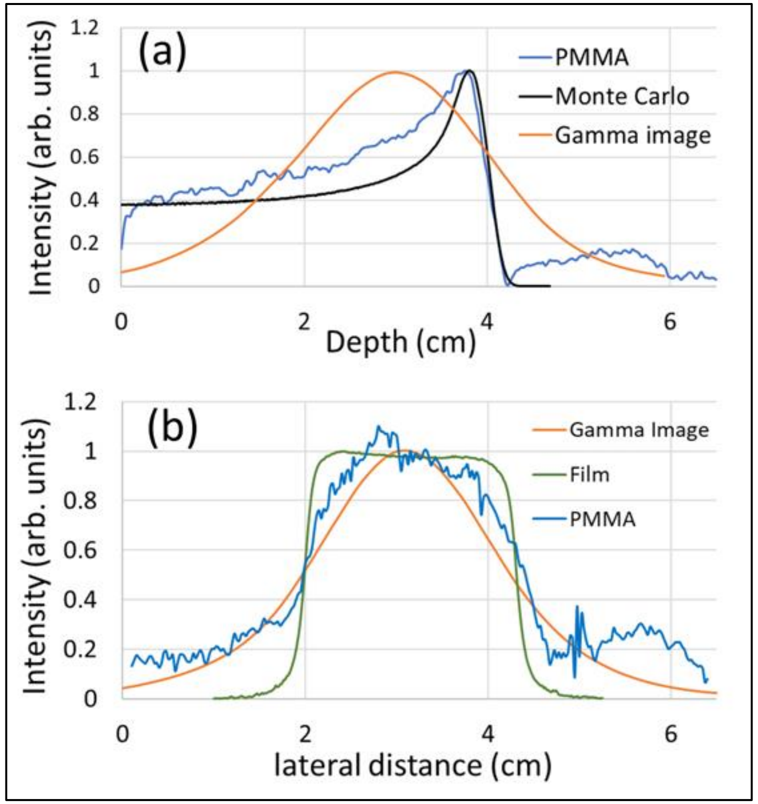
MD Anderson Proton Treatment Center

Dose delivered: 16.3 Gy
Dose rate: 161 Gy/sec

PG Imaging

- Online imaging (during beam delivery)
- 0.1 – 3 MeV gammas
- Simple back-projection imaging

Chapter 3:3: Compton camera



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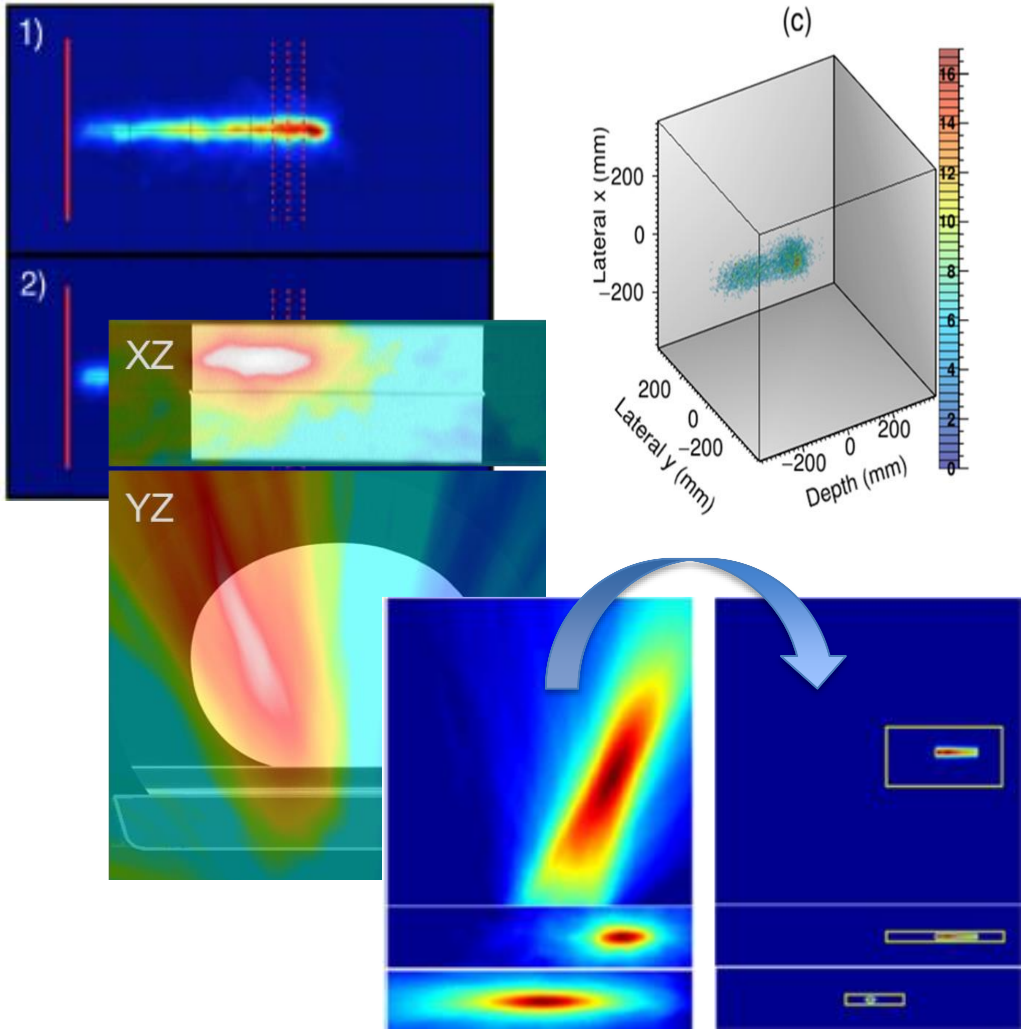
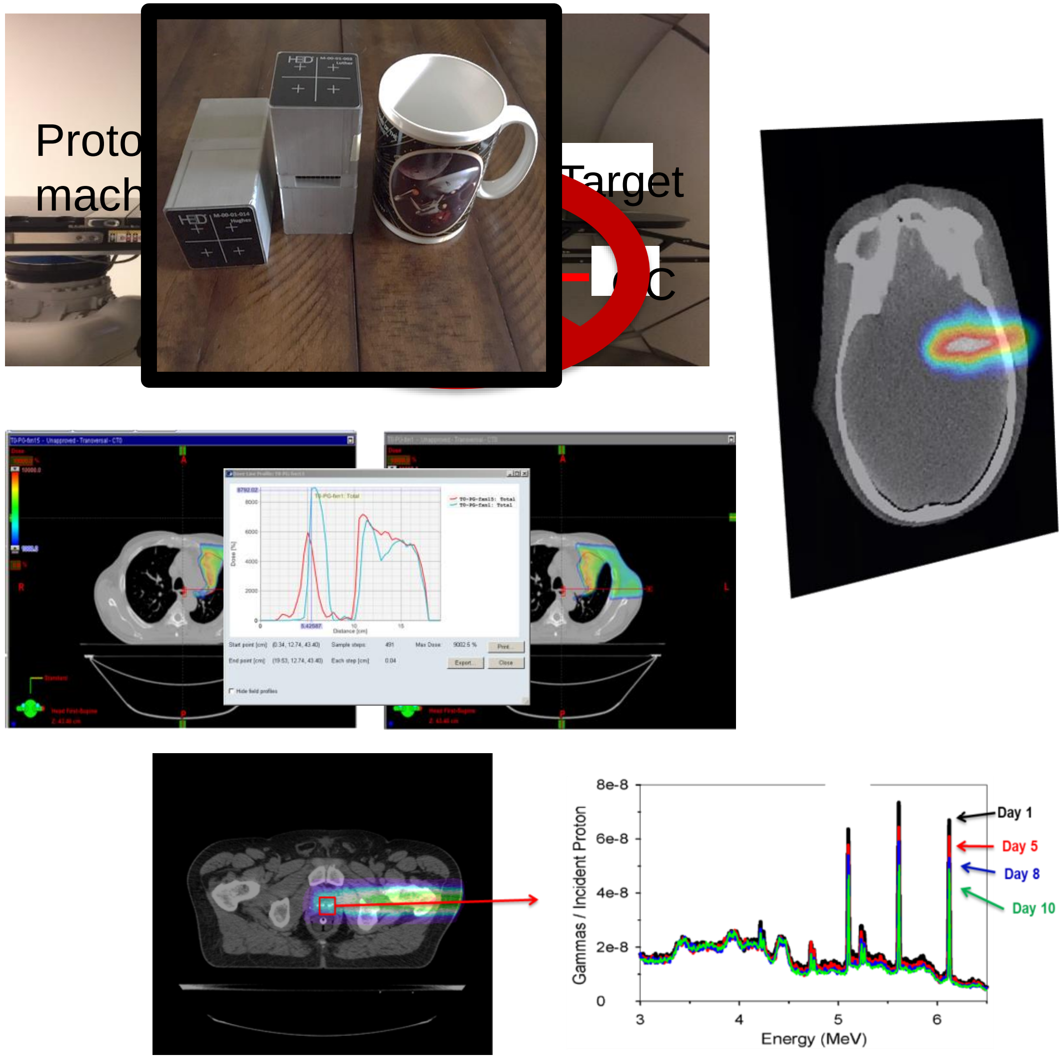


What we have learned

- Compton cameras can image PG emission during proton beam delivery.
- Can produce 3D images of PG emission
- PG imaging with clinical proton beams is (was) problematic
- Machine learning will make 3D (4D) PG imaging possible

Chapter 3:3: Compton camera



What is next

- New CCs:
  - Small, small, small
  - No impact to clinical treatment time
- 3D imaging:
  - Real-time overlay/display on daily CBCT
  - (4D imaging)
- Adaptive re-planning
  - Online
  - Post-daily fraction
- Functional imaging

Chapter 3:3: Compton camera

Please……

bring your brilliant new ideas

to Compton Camera research!!!!

Thank You!

Questions?