Medical radiography and tomography with proton beams

Pierluigi Piersimoni

Overview

- Introduction
- The *Range* problem
- Particle detection for proton imaging
- Proton radiography and CT systems
- Conclusions

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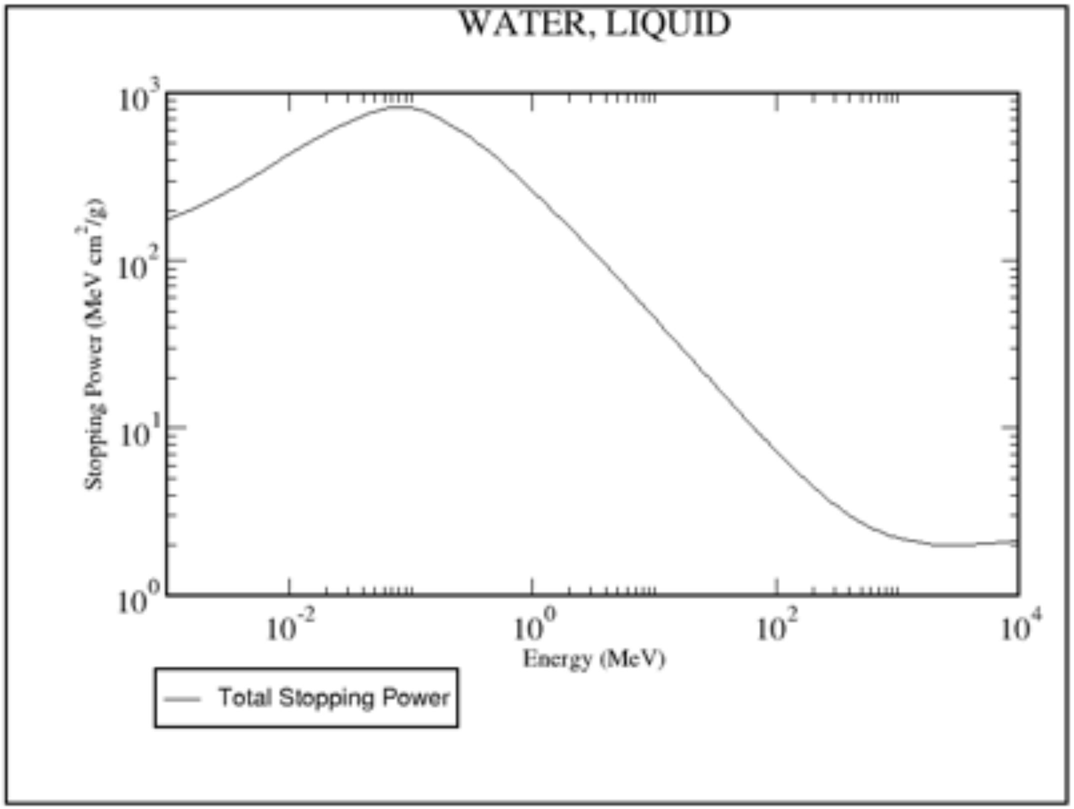
Introduction

Stopping power



$$\frac{dE}{dx} = \frac{4\pi e^2 Z_t Z_p^2}{m_e v^2}\left[ln\frac{2m_e v^2}{\langle I\rangle} - ln(1-\beta^2) - \beta^2 - \frac{C}{Z_t} - \frac{\delta}{2}\right]$$

$$\boldsymbol{S} = \frac{1}{\rho}\frac{dE}{dx}$$

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Range calculation

The **energy loss method** of charged particle radiography is based upon the effect on the **residual range** of the particles caused by the material being radiographed

$$E_i - E = -\int_0^L \frac{dE}{dx}(l')dl' = \int_0^L \rho(l')\boldsymbol{S}(l', E')dl' \qquad (1)$$

E_i: initial energy
E: final energy
L: length of the particle path
l': position along the path

K M Hanson et al 1981 Phys. Med. Biol. 26 965

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Range calculation

The range R_0 in a homogeneous medium for protons of energy E_i is defined as the distance the particles travel before losing all of their energy

$$E_i = \rho \int_0^{R_0} \boldsymbol{S}(E')dl' \qquad (2)$$

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Range

For a particle with E_i passing through a sample of possibly varying composition and density, the residual range ΔR is measured in some homogeneous reference material (water).

The residual range ΔR is:

$$\Delta R = R_0 - \int RSP(l', E')dl' \quad (3)$$

$$RSP(l', E') = \frac{\rho(l')\boldsymbol{S}(l', E')}{\rho_{ref}\boldsymbol{S}_{ref}(E')} \quad (4)$$

R_0: range in water corresponding to the incident E_i

RSP: relative stopping power

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Range and RSP

Particle mass stopping powers have the property that their ratios are approximately independent of the initial energy.

$$\Delta R = R_0 - \int RSP(l')dl' \quad (5)$$

The residual range, is simply related to the projection of *RSP(l')* along the particle path
The integral is equivalent to the water equivalent path length (**WEPL**) of the proton, which is used as input for CT reconstruction.
The reconstructed quantity for CT reconstruction is the ***RSP***

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The *Range* problem

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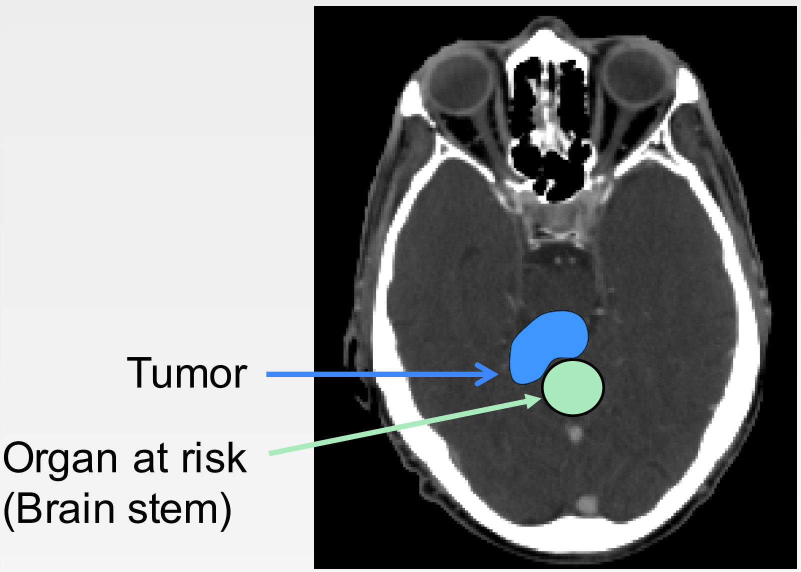
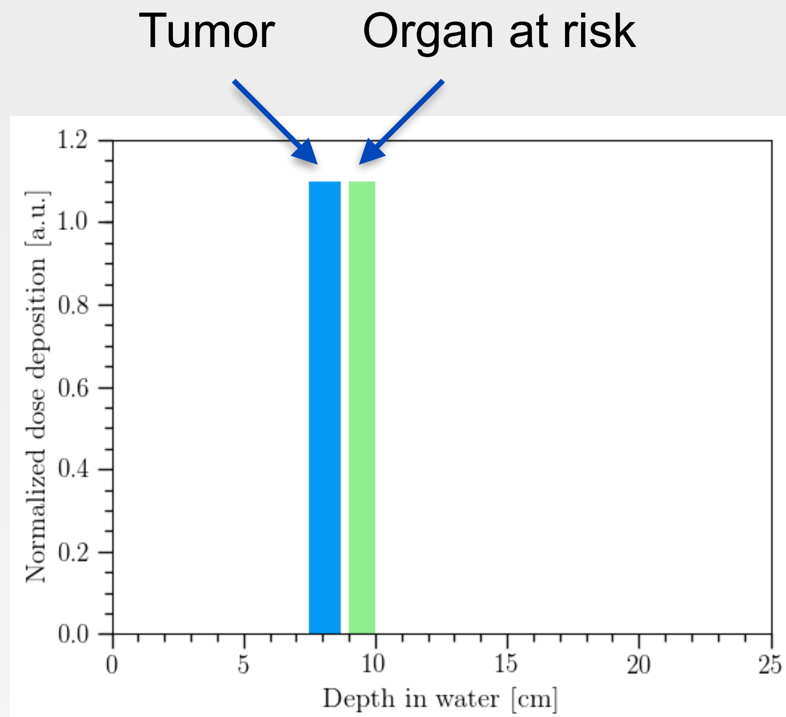
The Range problem





Ideal case: Prescribed dose to tumor volume, no dose to surrounding healthy tissue

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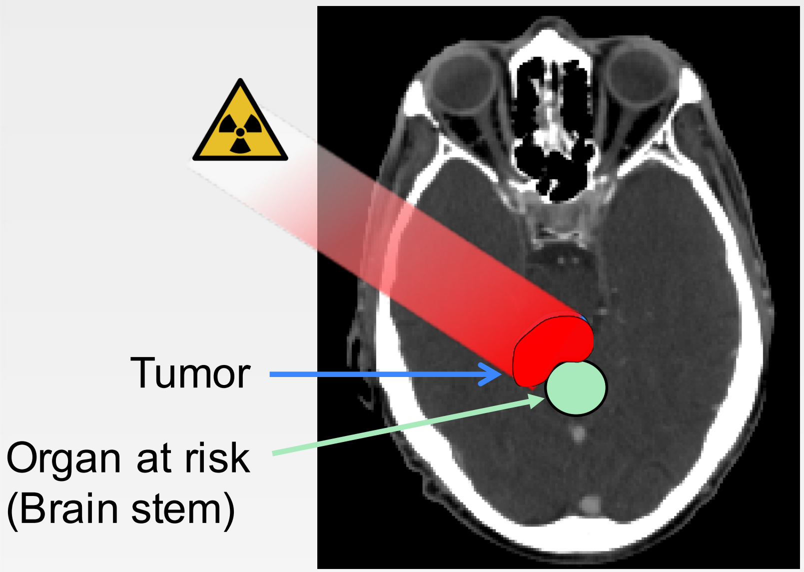
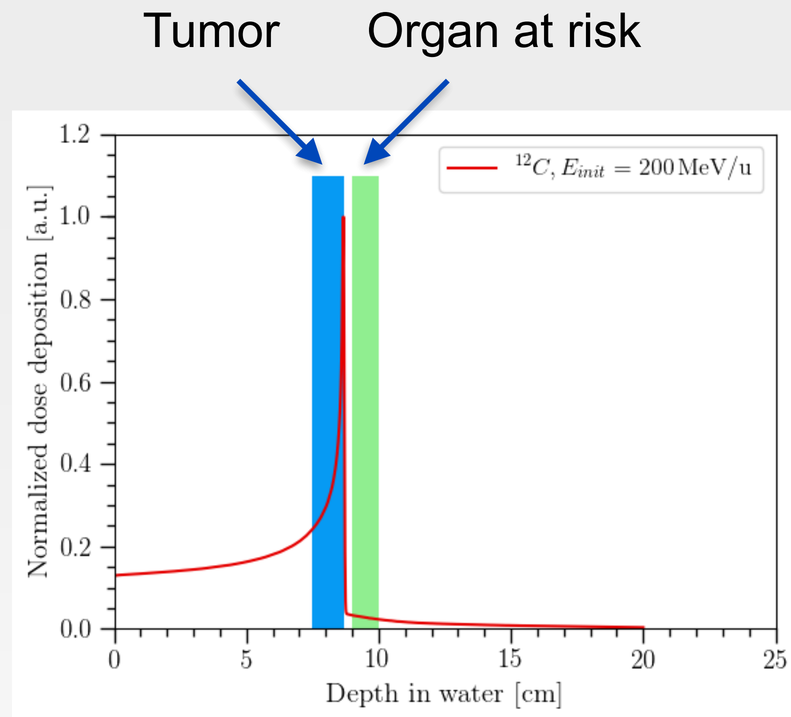
The Range problem





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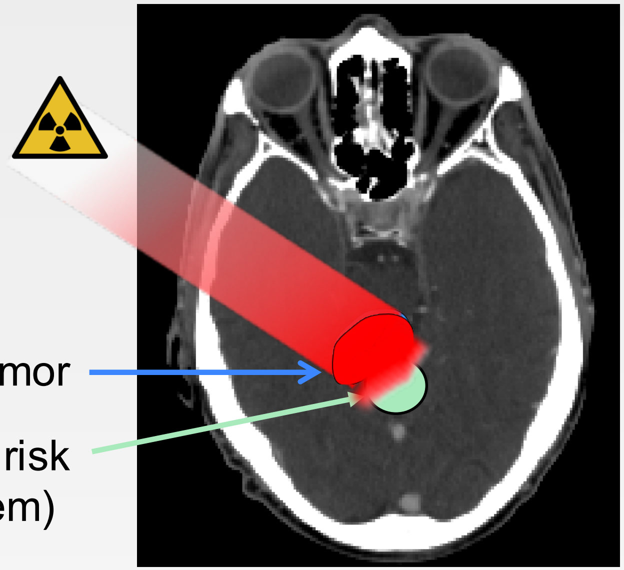

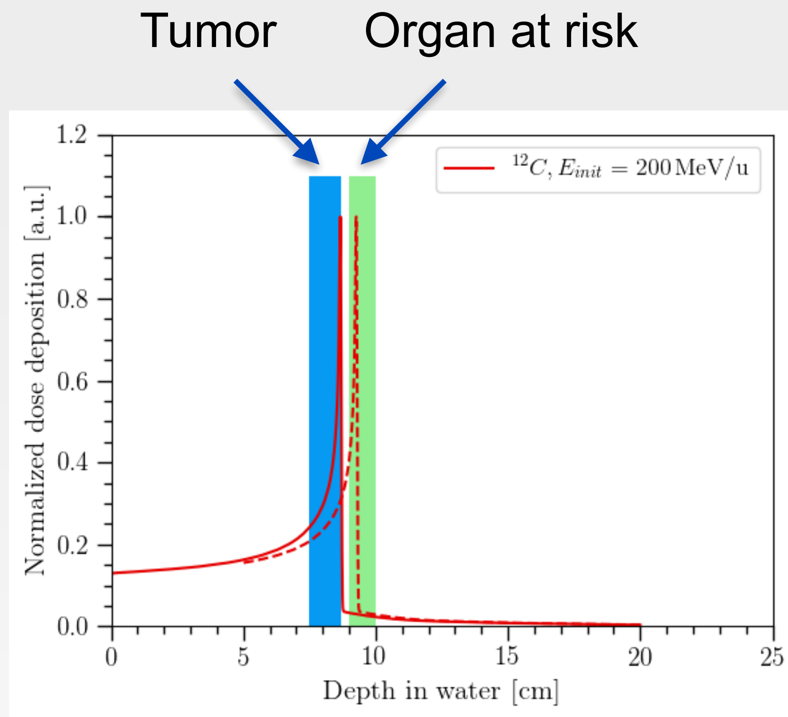

Ideal case: **Prescribed dose to tumor volume, no dose to surrounding healthy tissue**

Real Case: **Precise prediction of the Bragg-Peaks distal fall-off is critical due to *Range Uncertainties***

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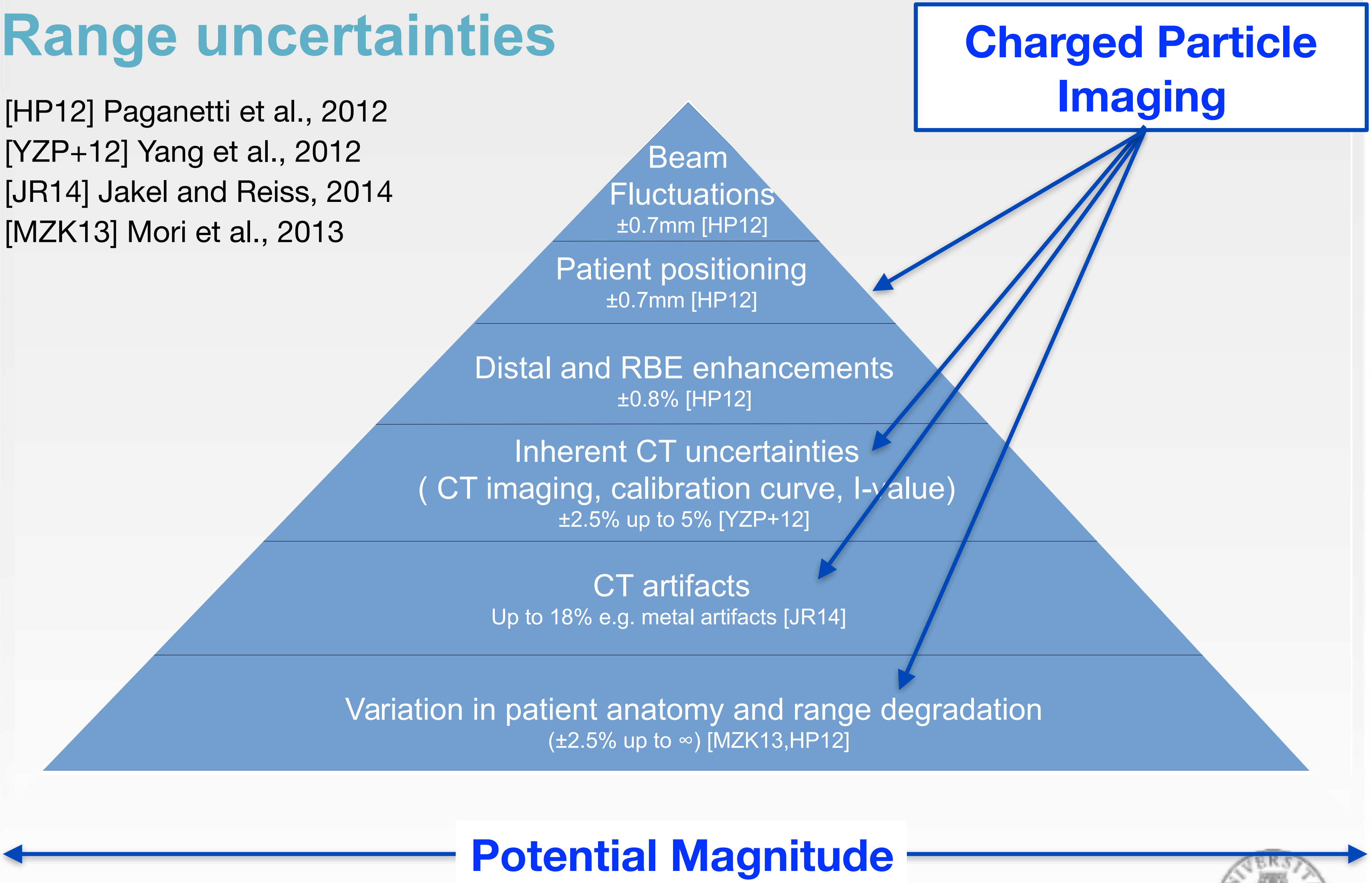
Range uncertainties

[HP12] Paganetti et al., 2012
[YZP+12] Yang et al., 2012
[JR14] Jakel and Reiss, 2014
[MZK13] Mori et al., 2013



Range uncertainties

Charged Particle Imaging

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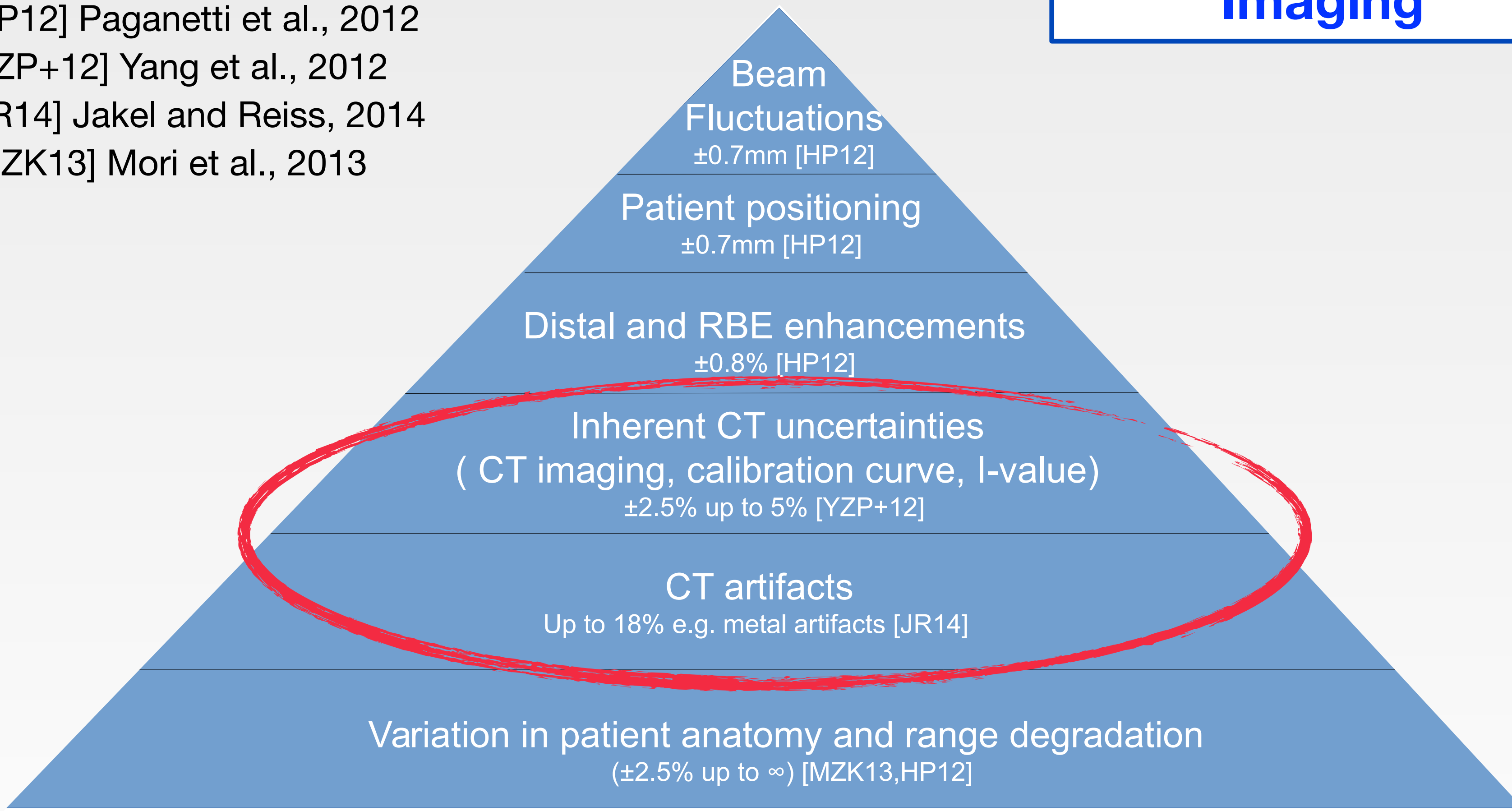

Potential Magnitude

Range prediction

Imaging

X-Ray CT

$\mu \propto \rho_e \, f(Z)$

→

Treatment planning

Photon therapy attenuation coefficient

$\Delta E \propto \mu e^{-\int \mu(x)dx}$

Range prediction

Imaging

Treatment planning

X-Ray CT

$\mu \propto \rho_e f(Z)$

Photon therapy
attenuation coefficient

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Charged particle therapy

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Range prediction

Imaging

X-Ray CT

$\mu \propto \rho_e f(Z)$

Treatment planning

Photon therapy attenuation coefficient

$\Delta E \propto \mu e^{-\int \mu(x) dx}$

Conversion uncertainties

Charged particle therapy

Range prediction

Imaging | **Treatment planning**

X-Ray CT

$\mu \propto \rho_e f(Z)$

Photon therapy
attenuation coefficient

$\Delta E \propto \mu e^{-\int \mu(x)dx}$

Conversion uncertainties

Particle CT

dE/dx

Charged particle therapy

$$\Delta E \propto \rho K \frac{Z}{A} \frac{z^2}{\beta^2} \cdot \left\{ \ln \frac{2 m_e c^2 \beta^2}{(1-\beta^2) I} - \beta^2 - \frac{\delta}{2} \right\}$$

Particle detection for proton imaging

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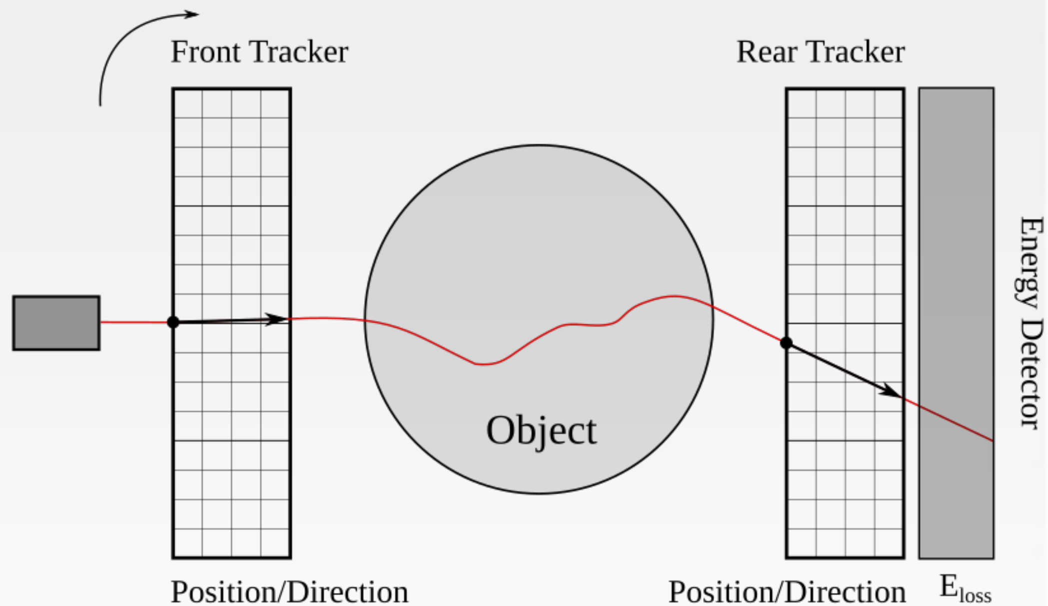
An ideal pCT

To achieve optimal spatial resolution and excellent energy-loss resolution, the trajectory and residual energy of each **single particle history** crossing an object from different directions must be measured



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- **Tracker system:**
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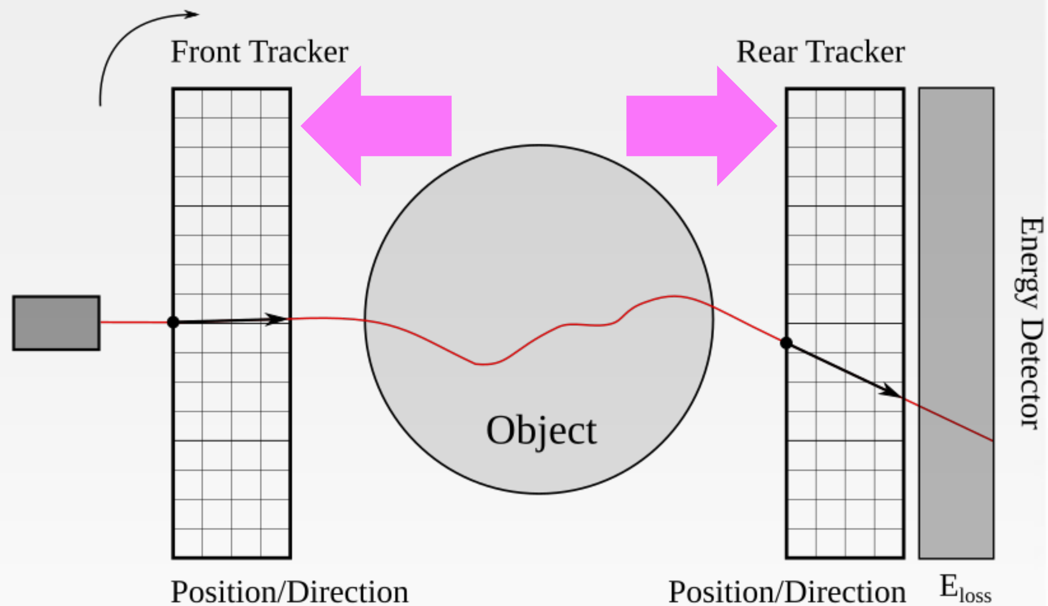

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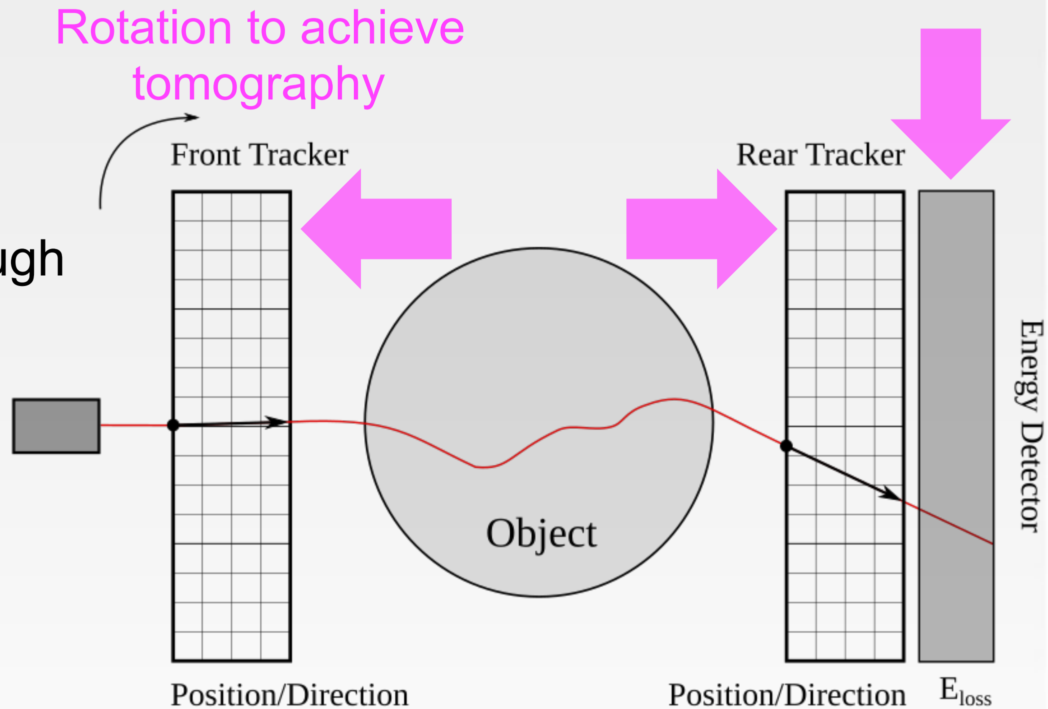
An ideal pCT

To achieve optimal spatial resolution and excellent energy-loss resolution, the trajectory and residual energy of each **single particle history** crossing an object from different directions must be measured

- **Tracker system:**
  entrance and exit points
- From tracker information,
  the 'most likely path' (**MLP**) through the phantom can be estimated
  The multiple Coulomb scattering (**MCS**) must be considered
- **Energy detector:**
  residual energy
- Residual Energy into **WEPL**



- **WEPL** and path information are used to reconstruct the **RSP** of each voxel in the target through iterative algorithms

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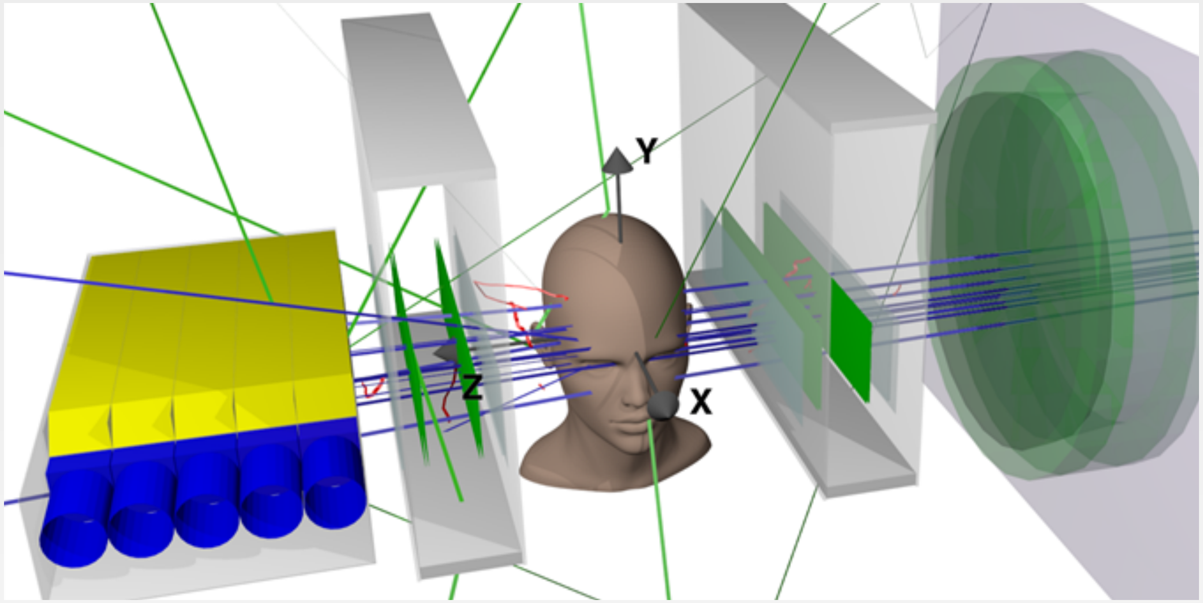
Choosing the optimal particle energy



- All of the incident protons must pass completely through the phantom, so that their energy loss may be measured
- The incident proton energy is generally at or near the maximum energy of the medical accelerator
  230-250 MeV
- This is not necessary to cross adult human body
- The aperture of most tracker detector is usually small
  ➡ some groups working on pCT concentrate on instruments that can image at least part of a human head

Choosing the optimal particle energy

Higher energies would produce reduced MCS ➡️ better spatial resolution

Rms width of the angular distribution for multiple Coulomb scattering projected onto a plane *(Beringer J. et al., 2012)*:

$$\theta_0 = \frac{13.6\,\mathrm{MeV}}{\beta c p}\sqrt{x/X_0}\,[1 + 0.038\,\ln(x/X_0)] \quad (6)$$

$\beta c, p$: proton's speed and momentum

$\frac{x}{X_0}$: number of radiation lengths of material traversed

Higher energies can result in more inelastic nuclear interactions and reduced WEPL resolution

The optimization depends on judgement of the relative importance of spatial versus WEPL resolution.

For treatment planning hen the objective is to map out the proton **RSP** on a useful spatial scale, not to make beautiful, high-resolution pictures.

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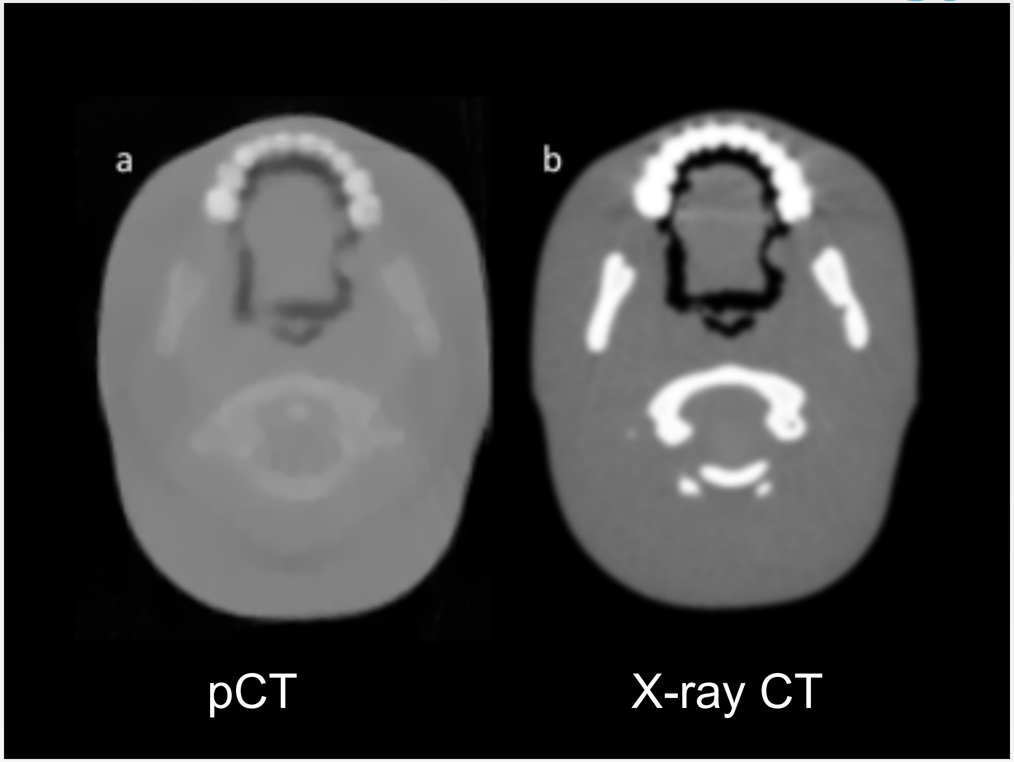
Choosing the optimal particle energy



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Spatial resolution

The spatial resolution for path reconstruction depends on:

- Traverse displacement error
- Angular error
- MCS in the detector material
- Systematic errors due to misalignment
- Proton passage through a typical phantom

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Spatial resolution

The spatial resolution for path reconstruction depends on:

The available detecting and read out electronics techniques can take care of these

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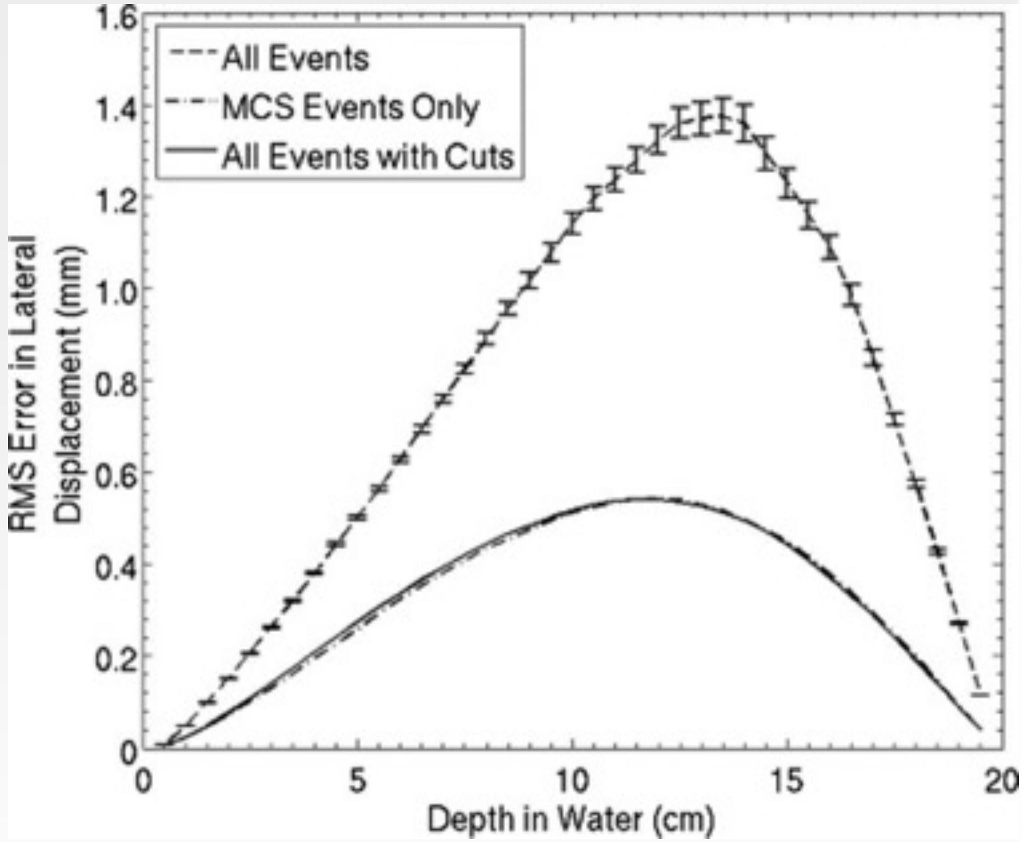
Spatial resolution

- Maximum error on the prediction of the path of a 200 MeV proton passing through 200 mm of water:
  0.5 mm - 0.6 mm
  ~115 mm from the phantom entrance
- The image spatial resolution near the phantom center will never be better than about 0.5 mm
- The ideal voxel size in the image reconstruction will be in the range of 0.5 mm to 1.0 mm

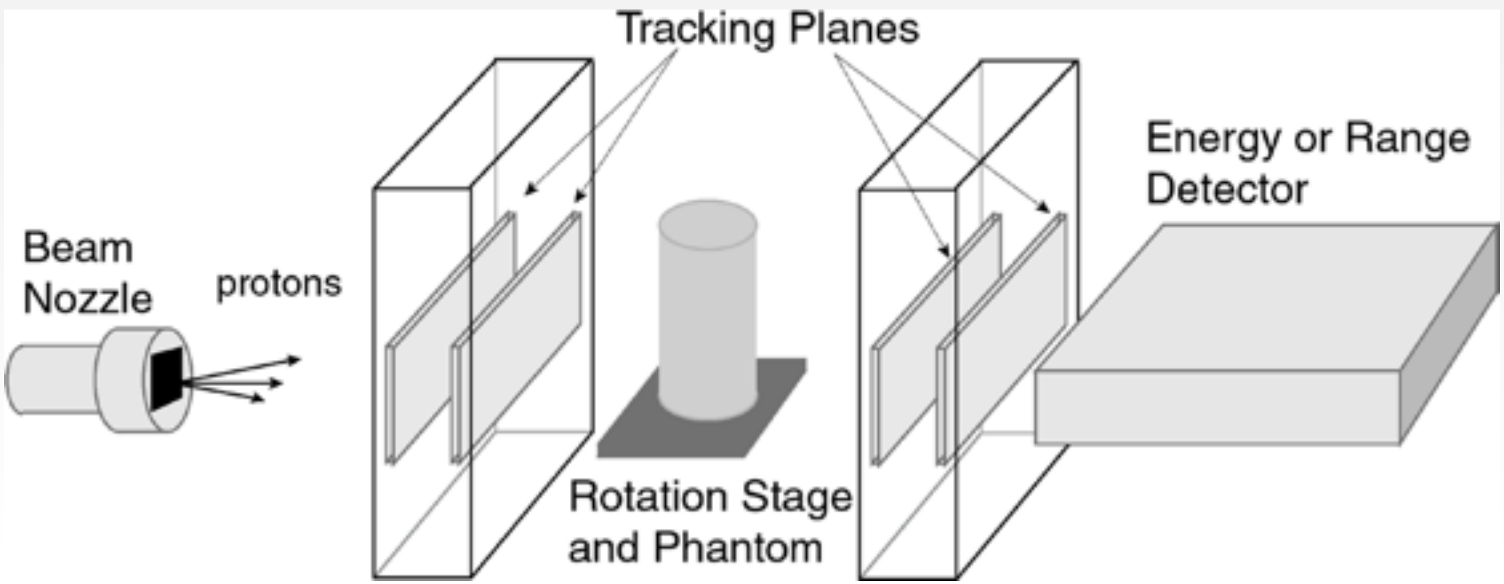


Schulte R et al. 2008 *Med. Phys.*

Efficiency

Detection efficiency must be as close as possible to100%

- Many of the available systems use technology coming from high energy physics: 200 MeV protons yield roughly double the ionization density of minimum ionizing particles typically of interest in particle physics
- a **95%** single-plane efficiency would results in a loss of **34%** of the events when 8 measurements are needed ➡️ increase of scan time and dose to the patient



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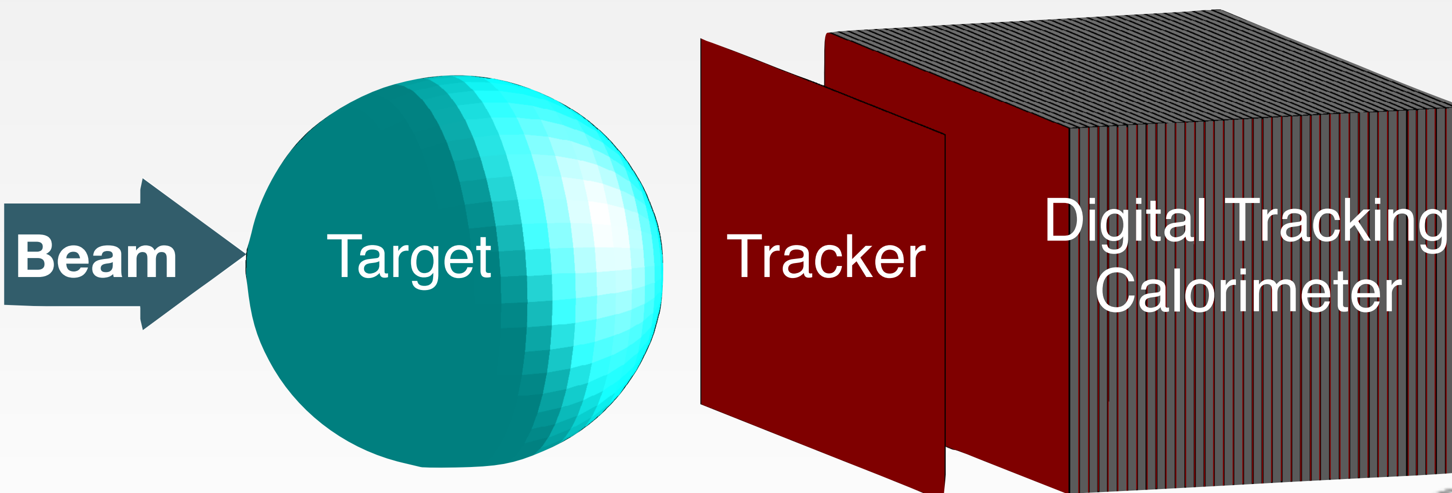
Efficiency

Detection efficiency must be as close as possible to100%

- If a range detector is used to measure the WEPL, then it is crucial for each of the *N* layers to be close to 100% efficient, in order to identify the proton's stopping point reliably
- achieving that result is aided by the increased ionization inherent in the Bragg peak



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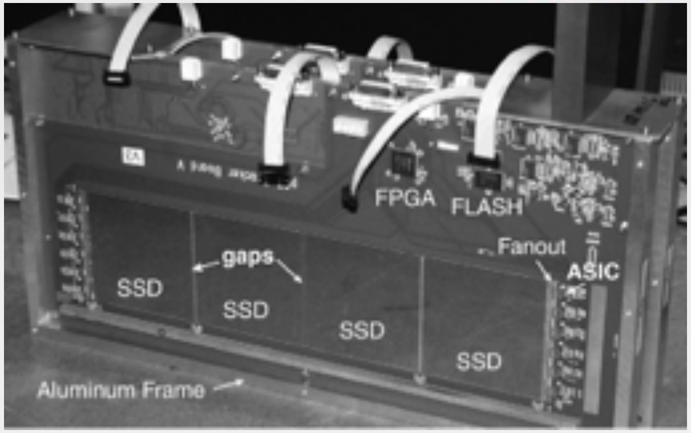
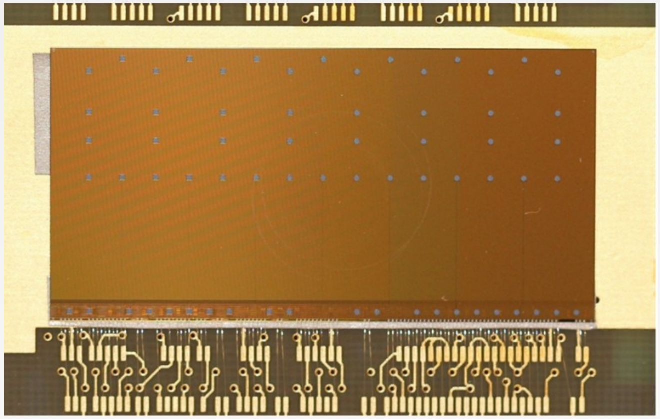
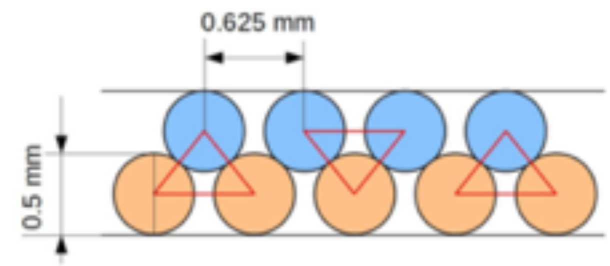
Efficiency

Most common detectors used for proton imaging

- **Silicon strip detectors:**
  efficiencies well above 99% with insignificant noise levels
- **Solid-state pixel detectors**
  efficiency close to 100%
- **Scintillating fibers:**
  comparatively marginal signal-to-noise performance, even when employing relatively large fibers (e.g. 1mm diameter) and some redundancy to cover gaps between fibers
  (mostly used for radiography)







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Efficiency

Event losses

- **Nuclear interactions:**
  occurring in 20% or more of proton events, depending on how much material is traversed
- **Hard Coulomb scattering:**
  events do not fit into the MLP framework used to analyze the data

➡ **Filters needed:**
binning proton events that follow similar trajectories to identify and cut out tails in the WEPL and angle distributions

~50% of the events from protons that pass through the regions of interest end up being useful for image reconstruction

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WEPL resolution

Resolution factors:

- design and performance of the detector system responsible for measuring residual energy or range
- natural fluctuations in energy loss (‘range straggling’) in any degrader placed upstream of the detector, in the tracking detector, in the phantom and, for the case of a range detector, in the WEPL detector itself

Quality assurance assessment of treatment delivery is expressed in terms of:
dose difference (Δ***D***) in %
distance to agreement (**DTA**) in mm

➡ **GOAL**: ΔD/DTA = 1%/1 mm *(Crowe S B et al. 2016)*

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RSP resolution and accuracy of 1%

⬇️

percent range prediction at a typical depth of 100 mm error < 1 mm *(Schulte R W et al 2005)*

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WEPL resolution

WEPL detectors

- **Calorimeter**:
  proton residual energy measured directly
  poor WEPL resolution at short depth (a large measured energy is subtracted from the known beam energy to yield a small result for the energy lost in the phantom)
- **Range telescope:**
  detects where the proton stops by means of many thin sensor layers interleaved with absorber material
  accuracy entirely determined by range straggling:
  ~3 mm for a 200 MeV proton in water is about
  1.1% of the range
- **Hybrid multi-stage scintillator:**
  N scintillation stages along the beam direction
  protons with small WEPL in the phantom pass through several stages before stopping

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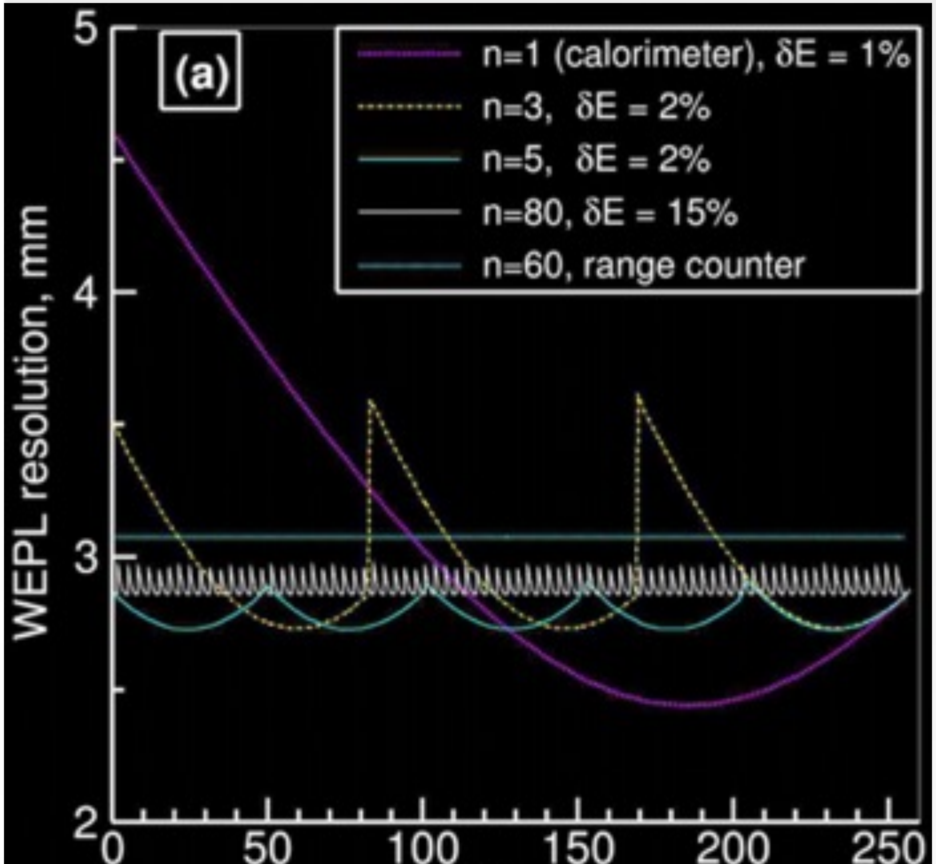
WEPL resolution



Bashkirov V A *et al* 2016

Advantages of a Hybrid N-stage

- far fewer channels than the range counter
- relatively cheap

Disadvantages:

- very complicated calibration in the conversion energy loss to WEPL, requiring correction for:

spatial variations in light collection

nonlinearity of electronics and of detectors (e.g. Birk's law)

time-varying gains and pedestals aging of components

variations from channel to channel

threshold and noise-dependent complexities for protons stopping near a boundary of two stages

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WEPL resolution

Not explored

- **magnetic spectrometers**

- **Time of flight detectors**

Avoid range fluctuations and nuclear interactions in the counters themselves

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WEPL resolution

Not explored

- **magnetic spectrometers**
  Too expensive
  Heavy and bulky
- **Time of flight detectors**

Avoid range fluctuations and nuclear interactions in the counters themselves

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WEPL resolution

Not explored

- **magnetic spectrometers**
  Too expensive
  Heavy and bulky
- **Time of flight detectors**
  timing resolution should be pushed to ~10 ps,
  nearly an order of magnitude beyond the capabilities of present technology

Avoid range fluctuations and nuclear interactions in the counters themselves

Detection rate

The scan time should be reasonably short

- Writing 100 MB/s it would take ~10 min to collect 300-400 M proton histories using a system which only keeps single events, due to the non lateral segmentation of the energy detector
- Simultaneous measurement of 2 or more proton tracks at the same time, the proton tracks have to be distinguishable
- Pixelated detectors can be the most suitable long as they are:
  fast
  cheap
  minimal need of read out electronics material to be added within the sensitive field
- Need of tracking algorithms

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Detection rate

- Efficiency from rate limitations of the tracking detectors can get severely aggravated when a narrow ‘pencil’ beam is used during imaging
- The beam scan rate is very slow compared with the particle rate, so the detector system responds as though a static narrow beam were impinging always on the same spot
- Silicon detectors with long strips have a distinct disadvantage in this regard, because of the relatively long signal-shaping time needed to achieve low noise

➡ low intensities required by proton CT and radiography in order to accommodate instrument rate limitations

➡ Intensities below what existing treatment facilities were designed to deliver.

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➡ low intensities required by proton CT and radiography in order to accommodate instrument rate limitations

➡ Intensities below what existing treatment facilities were designed to deliver.

➡ the accelerator operators typically have no instrumentation built into their system that can detect the presence or indicate the quality of the beam when operating at such low current

Summary of requirements

- Low beam intensity
- **200 MeV** energy for the head **250 MeV** or more for larger parts of the body
- The RSP resolution and accuracy of the image > 1%,
  spatial resolution **~0.5 mm** (limit allowed by multiple scattering in the phantom)
- Ideally a simple range counter
  WEPL measurements with **~3mm** accuracy, limited by range straggling,
  Can operate with stable calibration
- Optimal spatial resolution measuring each proton's trajectory before and after the phantom
  the spatial resolution is limited by scattering in the phantom
- High tracking efficiency to ensure good measurement of each proton tracks, lowering the scanning time and dose to the patient

Proton radiography and CT systems

Proton radiography or tomography?

Radiography is enough

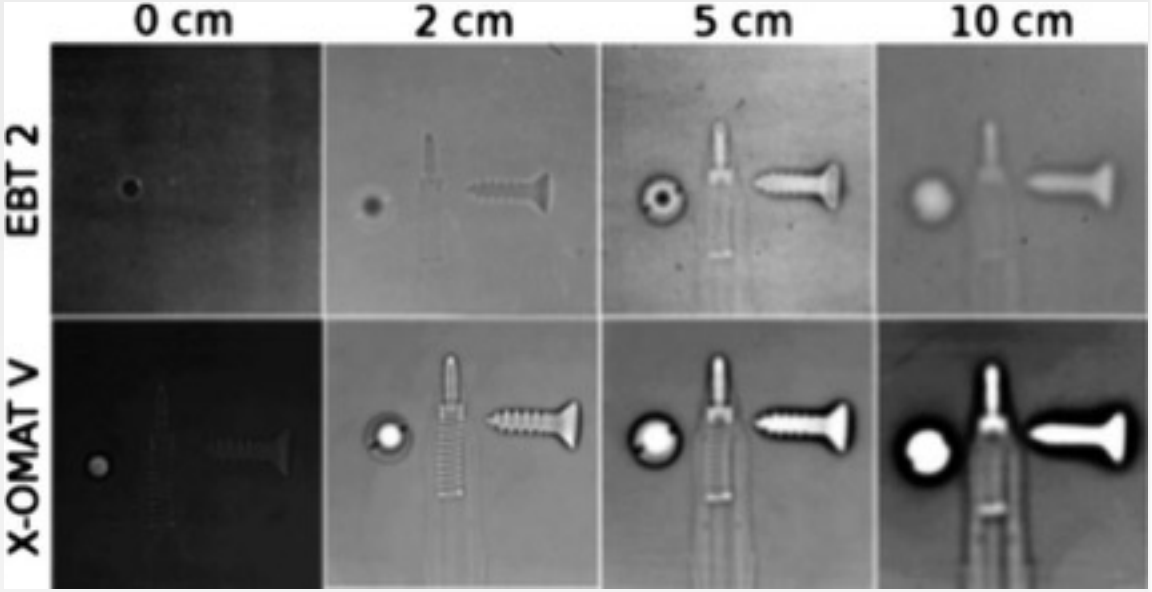
- proton radiography may be used more as a quality assurance: radiographs together with x-ray CT to solve the range problem.
- the WEPL map from a single proton radiograph may be compared with a corresponding x-ray image and the differences used to optimize the RSP map derived from x-ray CT *(Doolan P et al, 2015)*
- radiography doesn't require high data acquisition speed or computer power
- information on particle tracking before and after the phantom can be used to improve greatly the spatial resolution of a radiograph. Therefore, an optimal proton radiography detector system may closely resemble a system designed for pCT, but will have the advantage of producing an image in seconds

Tomography is needed

- Many groups are working with great effort to produce scanner able to be a complete substitute for X-ray CT in treatment planning, for which full pCT scans are needed

Integrating approaches

- The signal is due to the passage of an **undetermined number of incident protons**
- Dependence on both proton fluence and energy distribution
- Proton-integrating radiography assumes that the signal can be calibrated to average proton WEPL through the patient



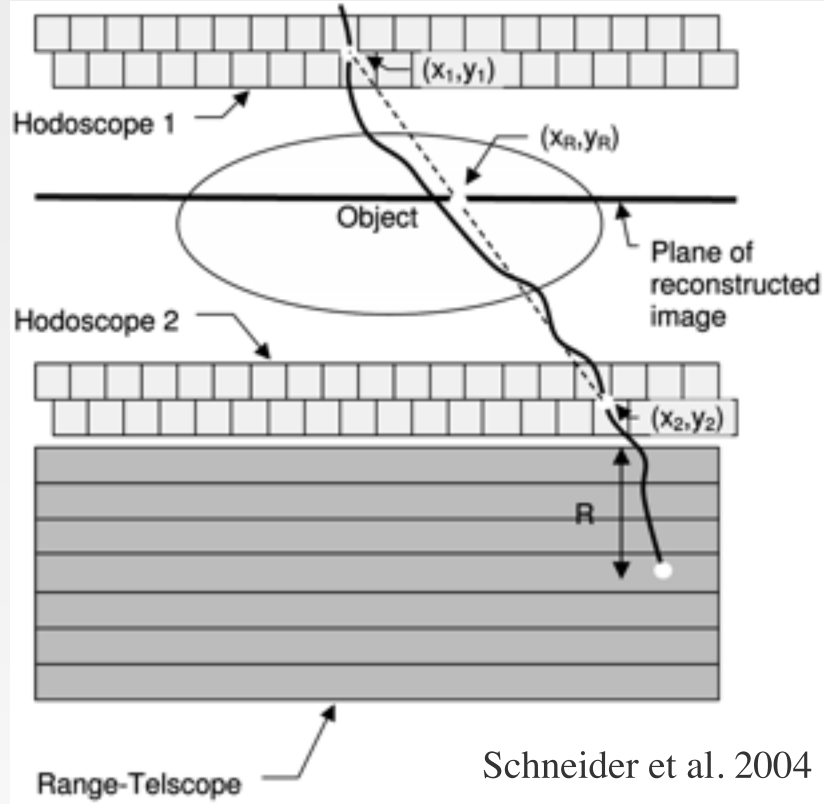
(Seco and Depauw, 2011)

"Halo" effect at material interfaces due to MCS and energy loss interplay, increasing with receptor offset.
The degradation in spatial resolution for integrating compared with tracking systems will depend on the patient anatomy and the detector–patient geometry.

Zygmanski P, et al., Phys Med Biol 2000 *Ryu H, et al., Phys Med Biol 2008*

PSI radiography system 1990

- **Tracking units:**
  scintillating fibre hodoscopes (Sci-Fis)
  2 orthogonal planes of 2x2 mm^2 plastic fibers
  Fibers made of plastic scintillator Bicron BCF 12 (decay time, 3.2 ns)
  each coupled to a channel of a photomultiplier tube
- **Energy detector:**
  range telescope consisting of 64 closely packed and optically isolated scintillator tiles 3 mm thick
  tiles material: Bicron BC404 (decay time, 1.8 ns)
- **Aperture:**
  22.0 x 3.2 cm^2
- **Event rates:**
  1 MHz



Schneider et al. 2004

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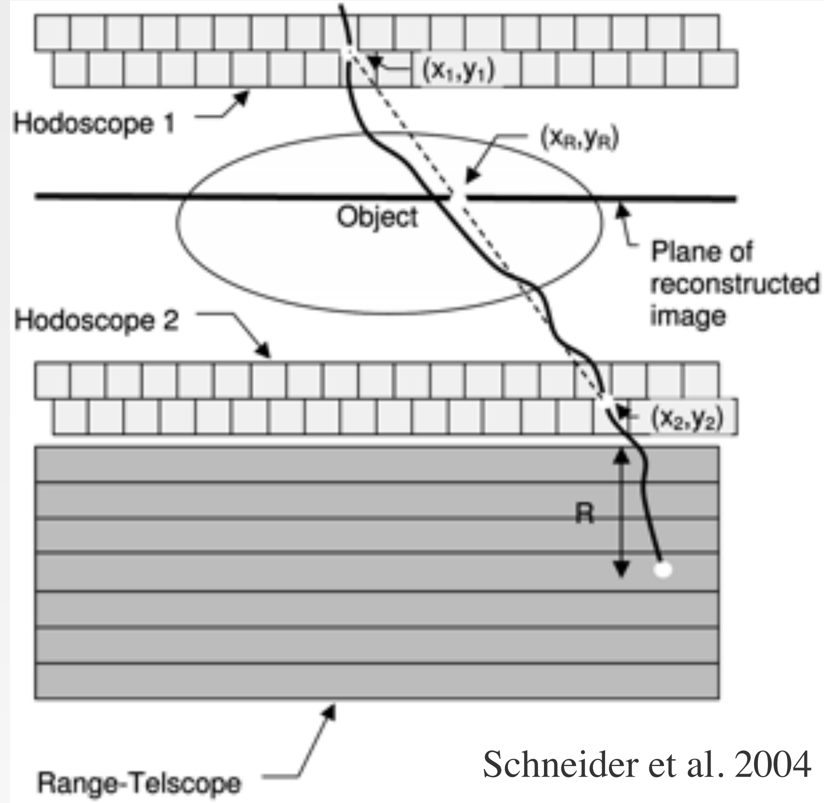

Schneider et al. 2004

The system would de suitable for pCT, but it was used only for radiography

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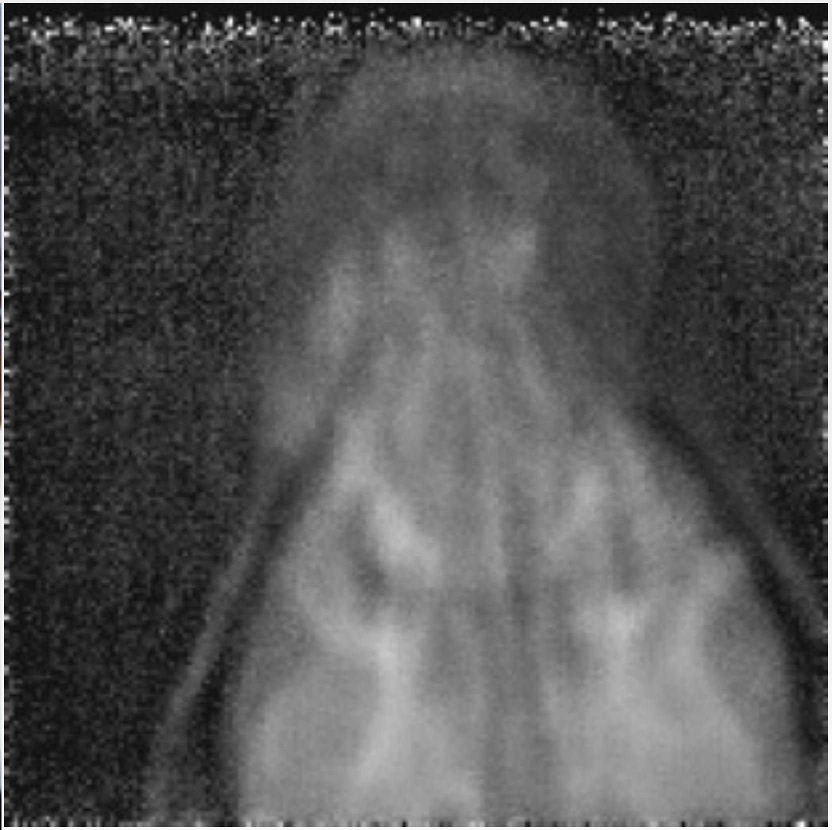
PSI radiography system 1990

Schneider et al. 2004



clinical conditions
clinical acceptable time
satisfying spatial resolution
good density resolution

Dose to the patient: ~50–100 times lower than for an x-ray image of the skull

Main limitation: each tracker is composed of only a single detector thus limiting the ability to define the MLP through the phantom

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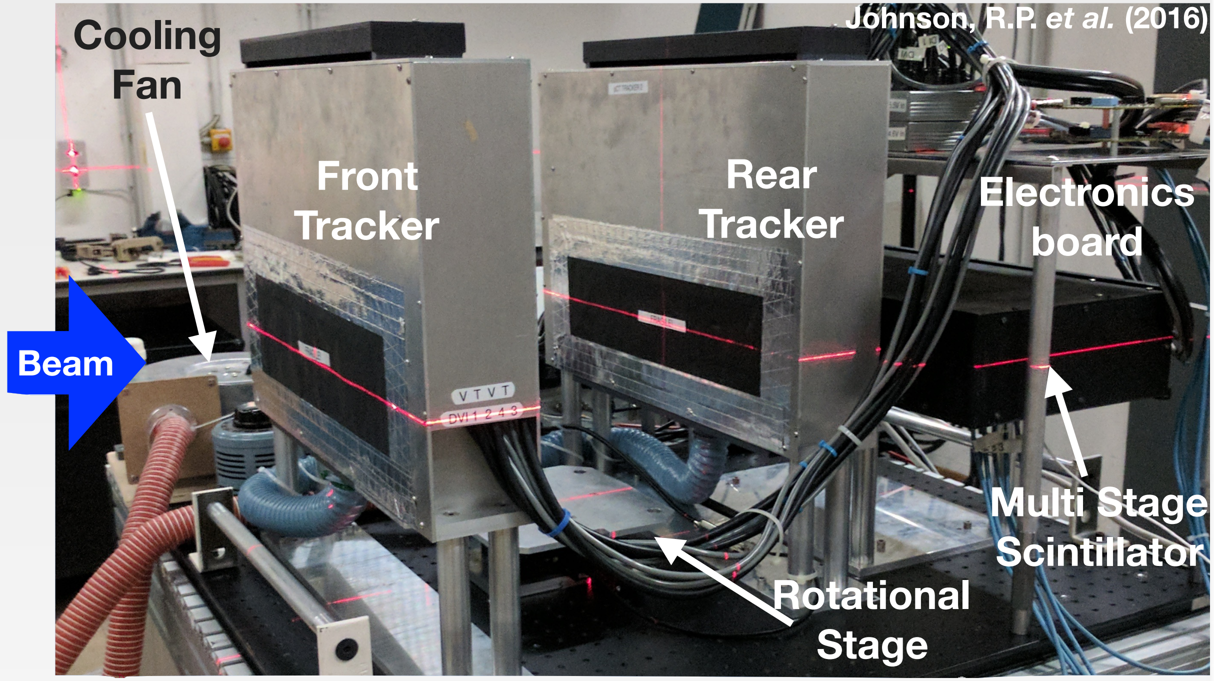
The U.S. pCT collaboration

- **Tracking units:**
  8 planes in total
  4 horizontal
  4 vertical
  4 silicon strip detectors (SSD) arranged per plane
  SSD sensitive area
  ~9x9 cm^2
  pitch 228mm
  thickness 400mm
- **Energy detector:**
  stack of 5 fast plastic scintillators read out by photomultiplier tubes
- **Aperture:**
  9 x 36 cm^2
- **Event rates:**
  1.2 MHz experimentally confirmed



Phase II pCT scanner

Loma Linda University
University of California Santa Cruz
Northern Illinois University
Baylor University

Good representation of the state of the art

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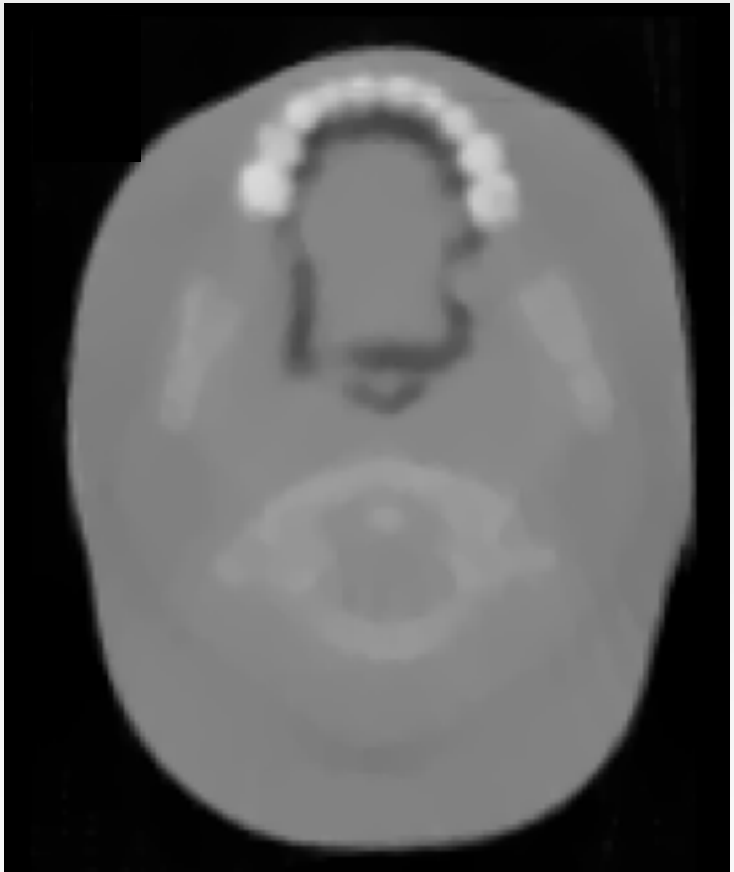
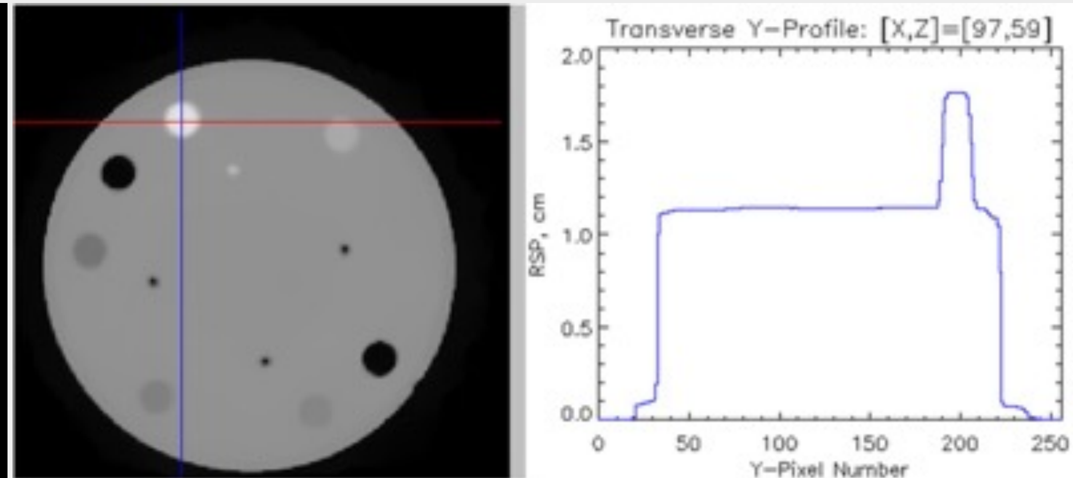
The U.S. pCT collaboration prototype



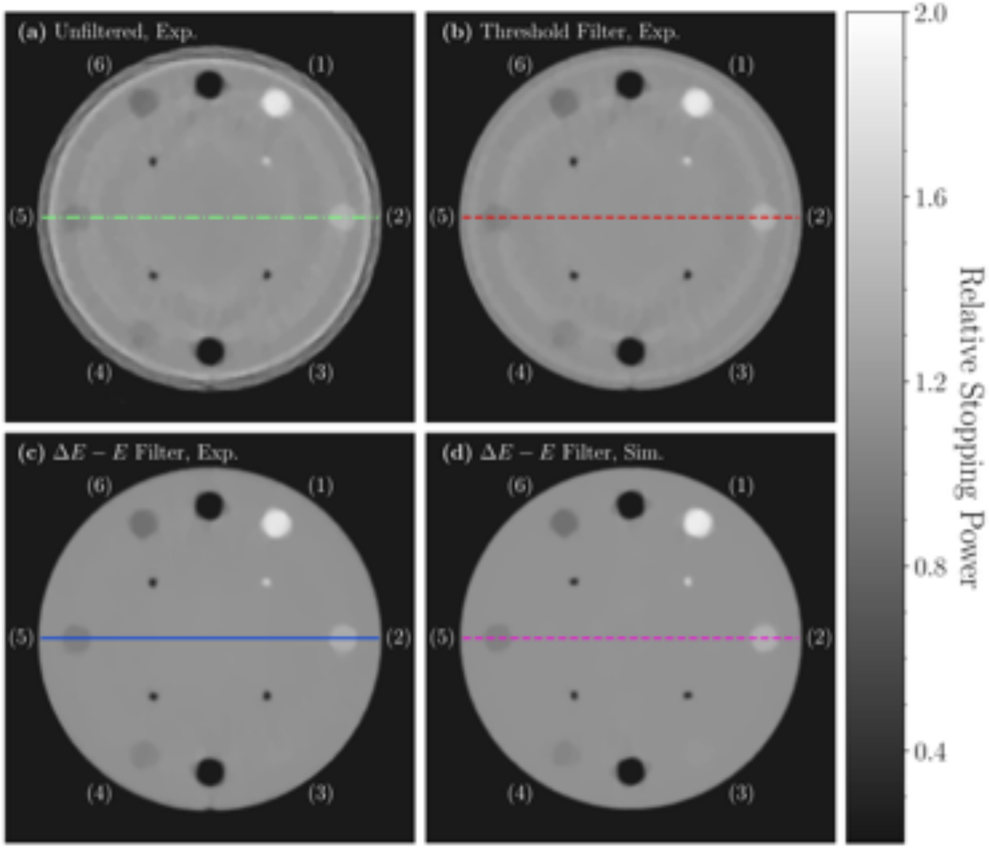
Johnson R P *et al* 2016

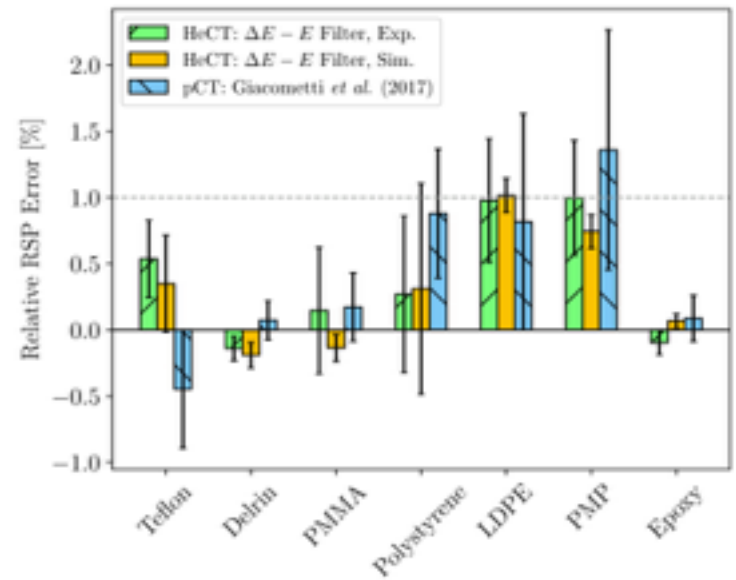


		DROP (10 blocks)		CARP	
Material	RSP	Mean ± std dev	Error	Mean ± std dev	Error
Teflon	1.790	1.774 ± 0.003	−0.89%	1.782 ± 0.019	−0.44%
PMP	0.883	0.897 ± 0.005	1.59%	0.882 ± 0.016	−0.11%
LDPE	0.979	0.986 ± 0.003	0.72%	0.971 ± 0.018	−0.82%
Polystyrene	1.024	1.031 ± 0.006	0.76%	1.017 ± 0.018	−0.68%
Delrin	1.359	1.349 ± 0.003	−0.74%	1.353 ± 0.015	−0.44%
Air	0.001 13	0.060 ± 0.003		0.029 ± 0.010	

Good RSP resolution close to 1%

The U.S. pCT collaboration prototype





Fragmentation is the main issue in HeCT: primaries are not distinguishable from secondary fragments, causing WEPL uncertainty and image artifacts

Volz, Piersimoni *et al* 2018

Catphan® CTP404

Applying a ΔE-E filter the RSP error was <1% for all the materials

Helium CT at HIT, Heidelberg

Robert P Johnson 2018 *Rep. Prog. Phys.* **81** 016701

Table 1. List of some contemporary efforts on prototype pCT systems and particle radiography (pRad) systems with particle tracking. For operational systems the rate is approximately what has been demonstrated to date. Earlier prototypes from the same collaborations are not listed.

Collaboration	Type	Aperture (cm^2)	Tracking technology	WEPL detector technology	Rate	Comment
AQUA [1]	pRad	10×10	GEM	Scint. range counter	10 kHz	1 MHz planned
LLU/UCSC phase-II [2]	pCT	36×9	Si strip	5 scint. stages	1.2 MHz	Operational
Niigata [3]	pCT	9×9	Si strip	NaI calorimeter	30 Hz	Larger, faster instr. planned
NIU, FNAL [4]	pCT	24×20	Sci Fi	Scint. range counter	2 MHz	Not operational
PRaVDA [5]	pCT	4.8×4.8	Si strip	CMOS APS telescope	2.5 MHz	Only tracker operating
PRIMA [6]	pCT	5.1×5.1	Si strip	YAG:Ce calorimeter	10 kHz	20×5 cm^2 1 MHz instr. planned
PSI [7]	pRad	22.0×3.2	Sci Fi	Scint. range counter	1 MHz	Program completed
QBeRT [8]	pRad	9×9	Sci Fi	Sci Fi range counter	1 MHz	Also a beam monitor

[1] Amaldi et al., 2011
[2] Johnson R P et al 2016
[3] Saraya Y et al. 2014
[4] Naimuddin M et al 2016
[5] Taylor J T et al 2015
[6] Scaringella M et al 2013
[7] Pemler P et al. 1999
[8] Lo Presti D et al 2016

Conclusions

Radiography

- Proton and ion radiography has seen very little use in the clinic, even for range verification and quality control
- Many efforts are underway this decade, interest appears to be growing along with the rapid worldwide growth in the number of proton and ion therapy centers
- Systems like the Phase-II scanner have demonstrated very high tracking reliability, and high data acquisition rate
- They can acquire a quality radiograph in a few seconds with a dose in the order of 0.01 mGy.
- Existing technology is thus ready for the task
- Further development will require industrial involvement to manufacture and market a standardized device ready for use

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Conclusions

Tomography

- Significant gains in treatment planning quality relative to, for example, dual-energy x-ray CT have to be proved
- Considerable added expense of bringing the patient into the proton beam line prior to treatment planning as well as for the treatment itself
- Limited beam energy (e.g. 230 MeV) available in most proton therapy centers, which would preclude doing pCT in some parts of the body, especially for larger patients.
- The best existing pCT system still requires ~10 minutes to complete a scan, and a similar time or longer, employing considerable computing resources, to generate an image
- An optimal system for radiography would look and perform very similarly to one of the existing tracking-based scanners designed for pCT

➡The device located in a treatment room could serve the needs of pCT in special cases for which the extra expense and time are warranted, while more frequently serving the needs of proton radiography for range verification and image guidance.

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