Dose Delivery Verification

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The role of dosimetry

1. Technical (beam-line) commissioning

- E.g. beam tuning

2. Clinical acceptance and commissioning

- Collection of data for the treatment planning system (TPS)
- Field characteristics
- Machine performance
- Absolute dosimetry

3. Quality checks, quality assurance (QA)

- Quality consistency checks:
- E.g. machine specific dosimetry
- E.g. patient specific dosimetry

Def. quality assurance (QA):
All planned and systematic actions necessary to provide confidence that a product will satisfy given requirements for quality

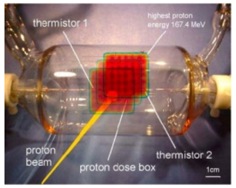
Def. clinical commissioning:
Characterization of the equipment's performance over the whole range of possible operation

The tasks of absolute dosimetry in particle therapy

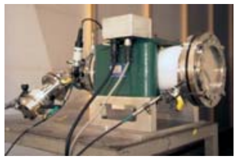
Absolute dosimetry

- Calibration of the primary monitor in the nozzle in terms of MU/p or MU/Gy

- Reference dosimetry with:
    - Calorimeters



    - Faraday cups



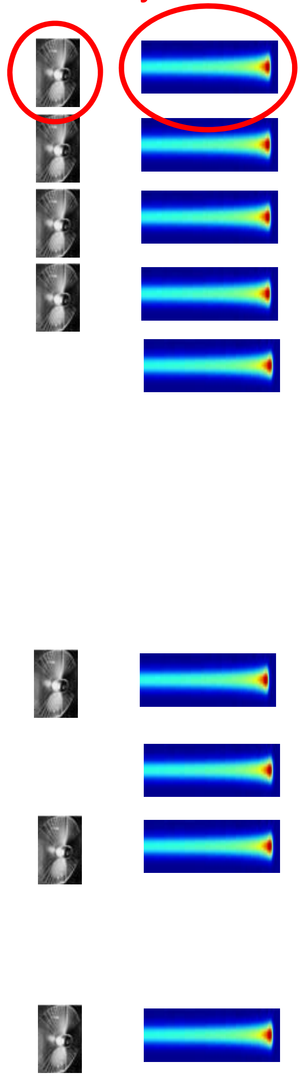
    - Ionisation chambers by following protocols (code of practice)

- Periodic Output measurements

The tasks of rel. dosimetry in particle therapy

SCANNING systems

SCATTERING systems



1. Rel. dosimetry orthogonal to the beam direction

- Lateral field geometries
- Position of field edges
- Lateral homogeneity
- Lateral penumbra
- Lateral beam width of individual pencil beams
  - Angular-spatial distribution
  - Spot position

2. Rel. dosimetry along the beam direction

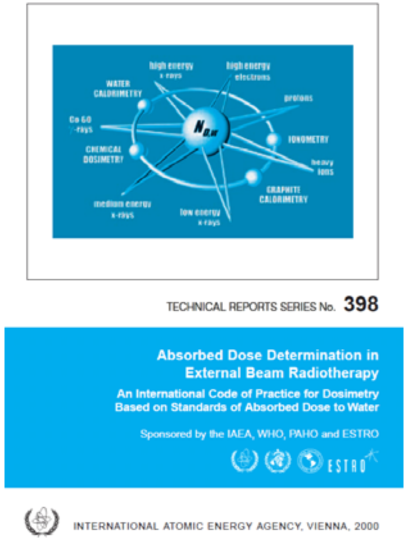
- Depth-dose profiles for homogenous SOBP (incl. distal fall-off)
- Depth-dose profiles for individual pencil beams (Bragg Peak curves)
- Range measurements

1+2 3D Dosimetry

- Dose distribution for small fields and by steep gradients

Absolute dosimetry

Absolute dosimetry: code of practice



IAEA TRS 398 (2000)

- Ionisation chamber dosimetry protocol
- Based on absorbed dose to water calibration coefficients
- Code of practice for photon, electron, protons, and heavy ions

ICRU 78 (2007) ('Prescribing, Recording, and Reporting Proton-Beam Therapy')

- Adoption of the IAEA TRS 398 code of practice
- Use of a generic relative biological effectiveness (RBE) value of 1.1

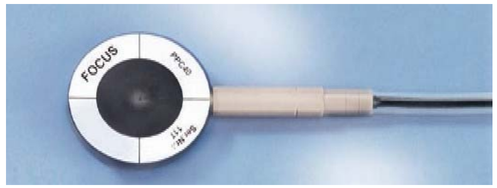
Absolute dosimetry: IC according to TRS 398

Ionisation chambers

- Both cylindrical and plane parallel chambers are recommended
- Plane-parallel chambers yield higher uncertainty in absolute Dw, although better suited for relative dosimetry
- Cylindrical ionisation chambers recommended for SOBP lengths $\geq$ 2cm
- Plane-parallel chambers must be used for SOBP lengths < 2 cm
- Many commercial systems available (usually not explicitly specified as proton chamber)

Cylindrical IC

Plane-parallel IC



Basic formalism according to TRS 398

Absorbed dose to water

The *absorbed dose to water* for a beam of quality *Q* is given by

$$D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0}$$

M_Q Instrument reading at users beam quality Q, corrected for all influence quantities other than beam quality, e.g.:

- k_{elec} calibration factor for electrometer
- k_{PT} temperature and air pressure
- k_s recombination losses

N_{D,w,Q_0} Absorbed dose to water calibration coefficient for calibration beam quality Q_0 (= ^{60}Co)

k_{Q,Q_0} Beam quality factor to correct for effects of differences between calibration beam quality Q_0 and user beam quality *Q*

This applies to any user beam quality (photons, electrons, protons, heavy ions)

Beam quality correction factor k_{Q,Q_0}

k_{Q,Q_0}

The *beam quality correction factor* is defined as the ratio, at the qualities Q and Q_0, of the calibration factors in terms of absorbed dose to water of the ionisation chamber

$$k_{Q,Q_0} \equiv \frac{N_{D,w,Q}}{N_{D,w,Q_0}} = \frac{D_{w,Q}/M_Q}{D_{w,Q_0}/M_{Q_0}}$$

General expression for k_{Q,Q_0}

As no primary standards for protons are available, all values of k_{Q,Q_0} are derived by calculation.

$$k_{Q,Q_0} \equiv \frac{(s_{w,air})_Q}{(s_{w,air})_{Q_0}} \frac{(W_{air}/e)_Q}{(W_{air}/e)_{Q_0}} \frac{p_Q}{p_{Q_0}}$$

$s_{w,air}$ water-to-air stopping-power ratio

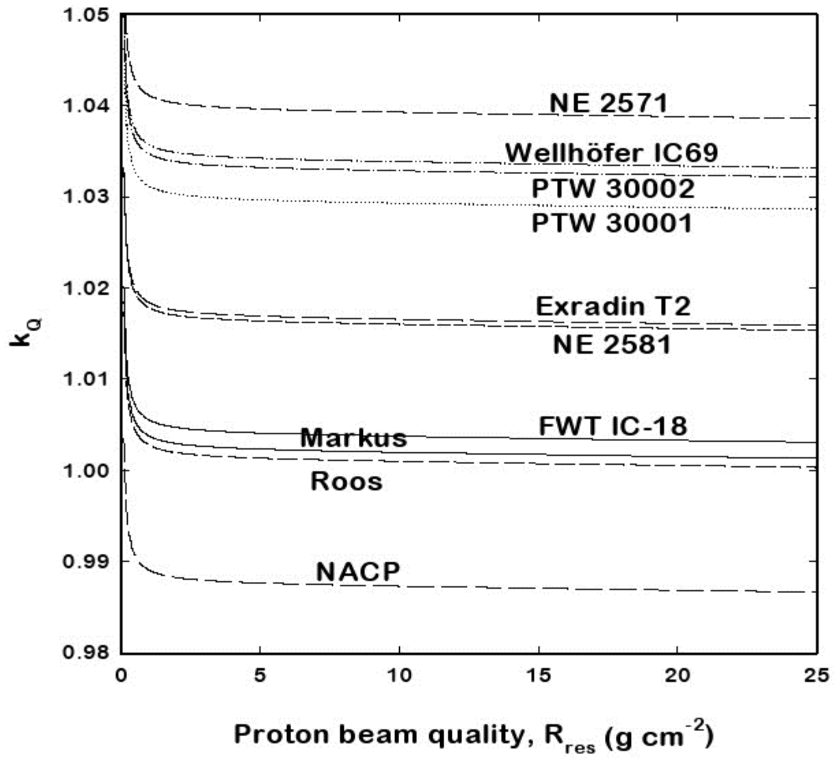
W_{air}/e mean energy expended in air per ion pair formed

$p_Q = p_{cav} p_{dis} p_{wall} p_{cel}$ perturbation factor

$p_Q \approx 1$ for protons

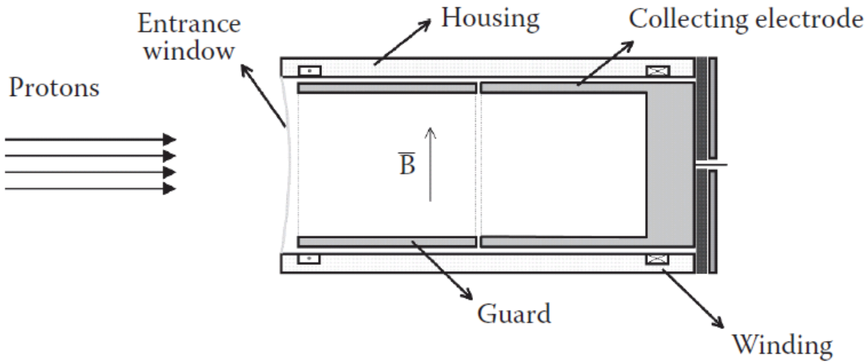
$p_{Q0} \neq 1$ for ^{60}Co

TRS 398

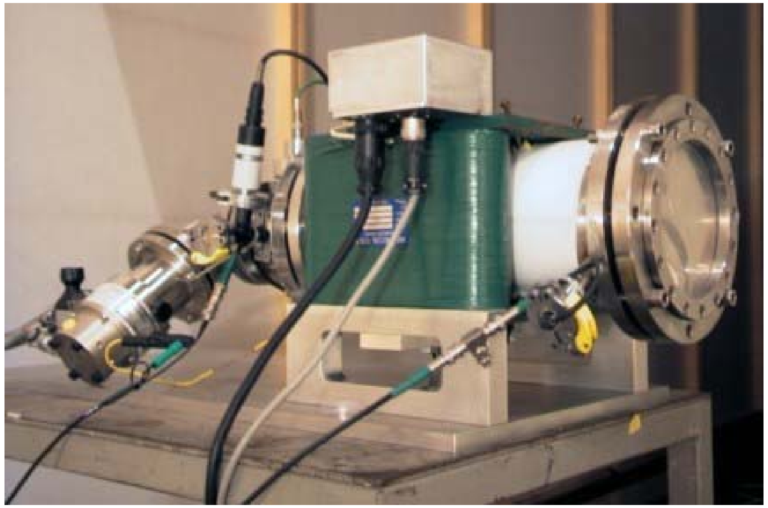


Gomà *at al*, PMB, **60** (2015) 3207-3216

Absolute dosimetry: monitor calibration with a FC



Schematic diagram of a reference dosimetry level Faraday cup with internal vacuum. Shown are the collecting electrode, the guard electrode (which is at negative potential with respect to the collecting electrode), the entrance window, and the windings creating a magnetic field, B, to suppress the loss of electrons generated in the collecting electrode.



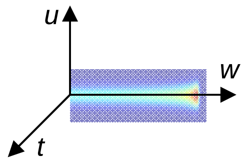
Faraday cup measurement

- Determines number of incident particles in a pencil beam
- Primary monitor calibration in terms of protons per MU

Example of PSI Gantry 1

Energy	Protons / MU
138 MeV	6555
160 MeV	7333
177 MeV	7921

Pencil beam dose model



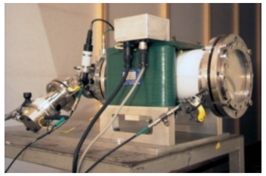
- Predicts absolute dose per incident proton
- $D_p(u,t,w) = T(w) \times G(t,\sigma_T(w)) \times G(u,\sigma_U(w))$
- Integral depth dose $T(w)$: based on first principles (Bethe-Bloch stopping power formula) including corrections for nuclear interactions
- Alternative: use Monte Carlo

$$D_P(u,t,w) = \frac{T(w)}{2\pi\sigma_T\sigma_U} e^{-\frac{t^2}{2\sigma_T^2(w)}} e^{-\frac{u^2}{2\sigma_U^2(w)}}$$

Absolute dosimetry at PSI

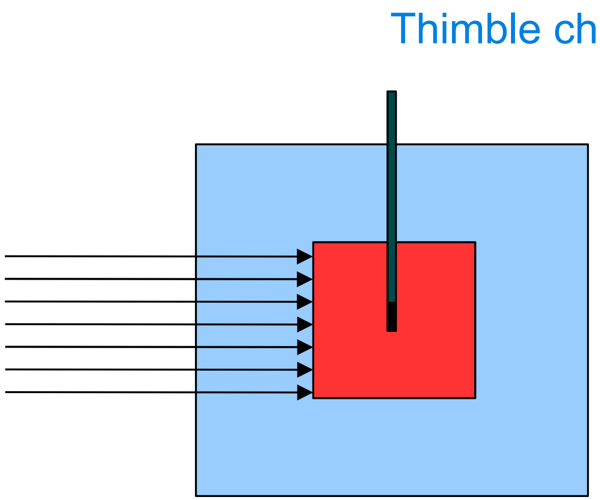
Faraday cup measurement

Number of protons/MU



Pencil beam dose model

Predicts number of protons (or MU) needed to fill a 10x10x10 cm^3 box with homogeneous dose of 1.0 Gy



Apply scan to phantom

Measure actual dose with certified thimble ionisation chamber following code of practice IAEA TRS 398

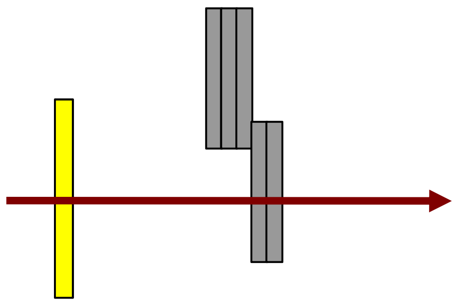
Compare predicted and measured dose

Correction factors for MU calculations

$\Delta = \pm 2\%$

Absolute dosimetry at PSI

Range Shifter
Gantry 1

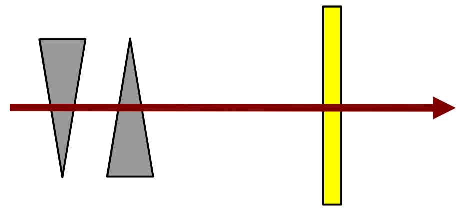


patient

MU chamber

- always "sees" constant proton energy during beam delivery
- MU calibration stays constant during beam delivery
- TRS 398 can apply

Fast Degrader
Gantry 2

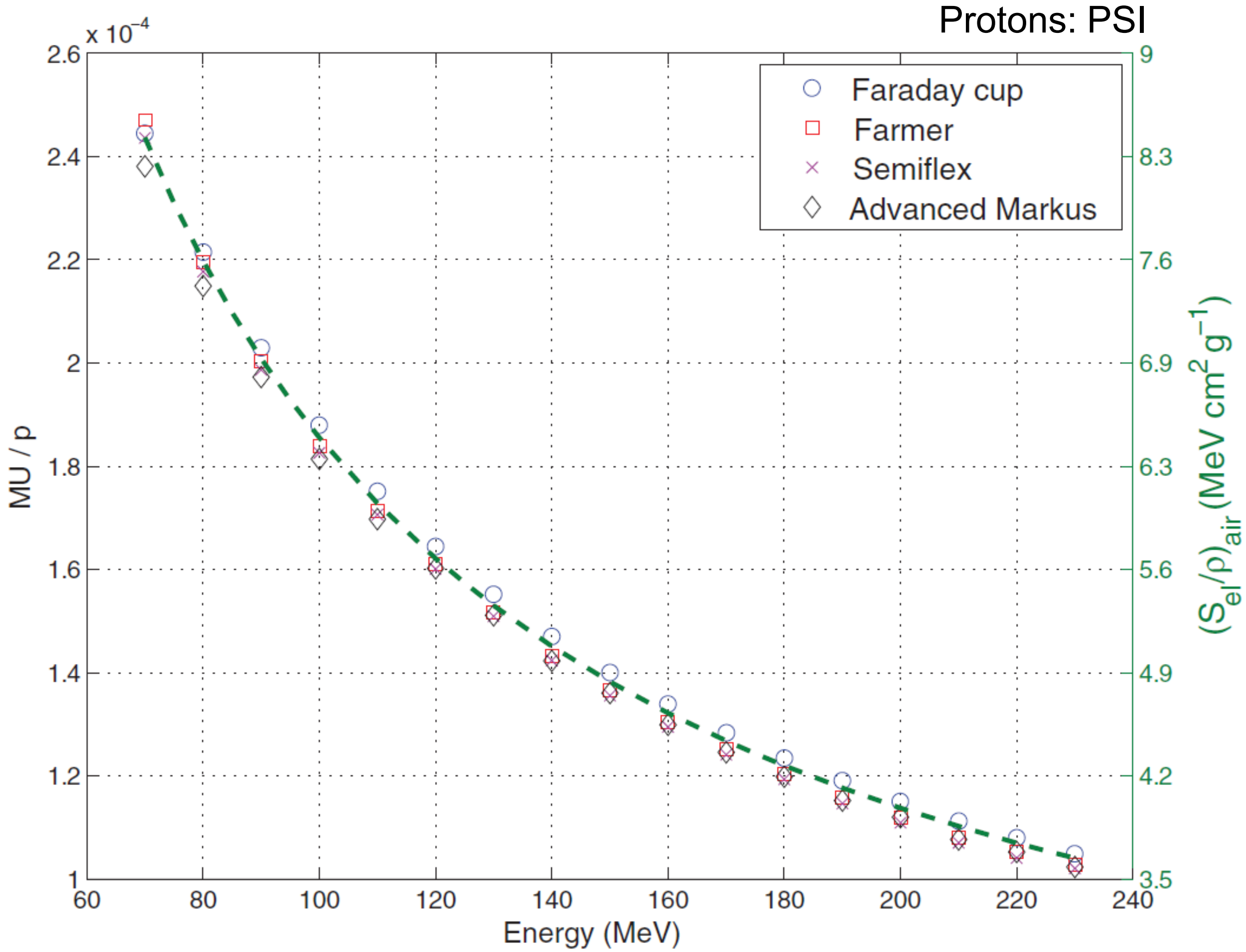


patient

MU chamber

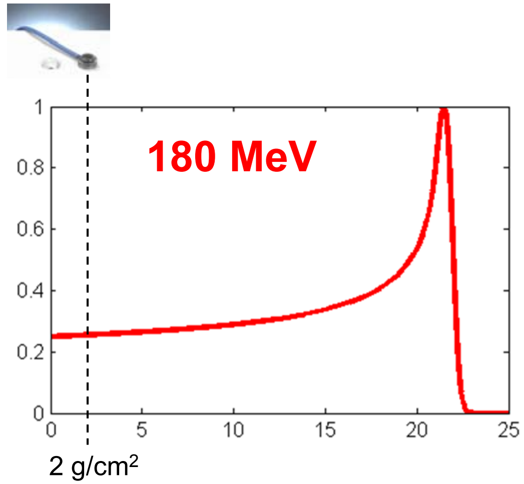
- "sees" varying proton energies during beam delivery
- MU calibration changes during beam delivery
- TRS 398 is inappropriate

Beam calibration: FC vs ICs



Gomà *at al*, PMB, **59** (2014) 4961-4971

Calibration with IC



- Deliver 10x10 cm^2 energy-layers
- Dose D_w at w_{ref} = 2 g/cm^2
  → calibration in MU/D_wA

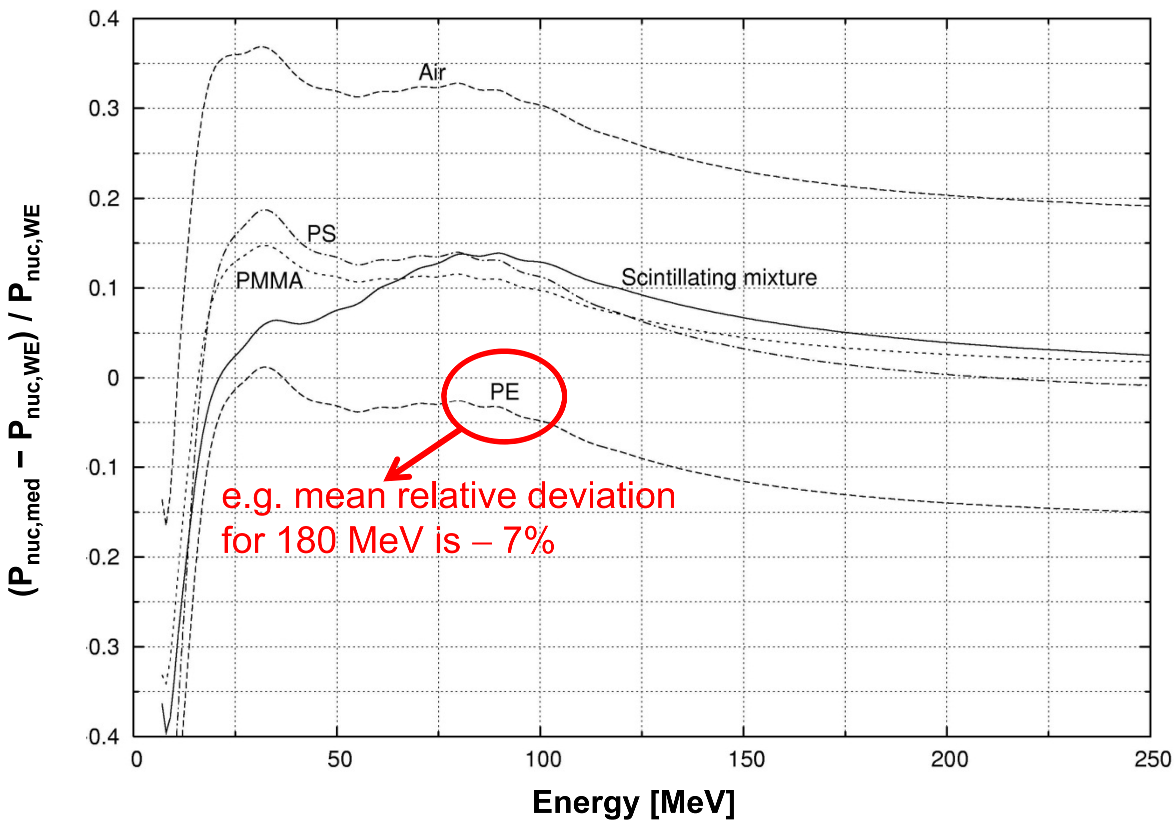
For comparison

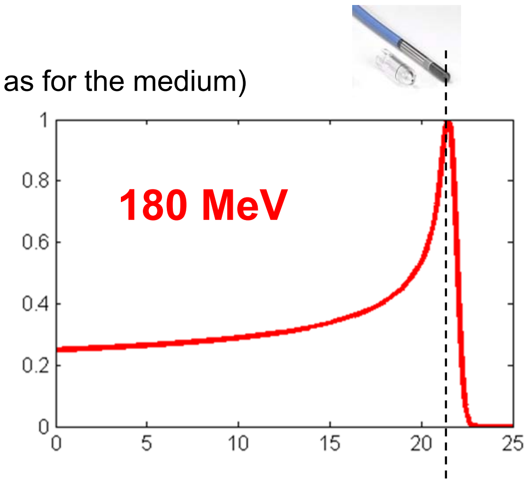
- Theoretical model: D_wA/p
  → calibration in MU/p

Jäkel *at al*, Med Phys, **31** (2004) 1009-13

Absolute dosimetry: in water only

$P_{nuc,med}$ = nuclear interaction probability in a given medium (thin layer)
$P_{nuc,WE}$ = nuclear interaction probability in an equivalent amount of water (same energy loss as for the medium)





P_{nuc} ?

Nuclear interaction probability

Water (W) Polyethylene (PE)

20.7% 19.2%

Δ = 1.5%

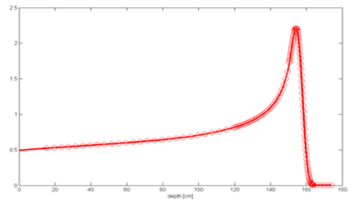
Dose ∝ fluence

$\Delta D/D$ = ~ 2%

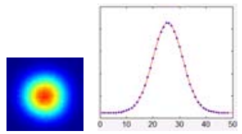
Dose in PE potentially ~ 2% higher than in water at Bragg peak but …
error reduced due to the propagation of secondary protons

Relative dosimetry: Pencil beam characteristic

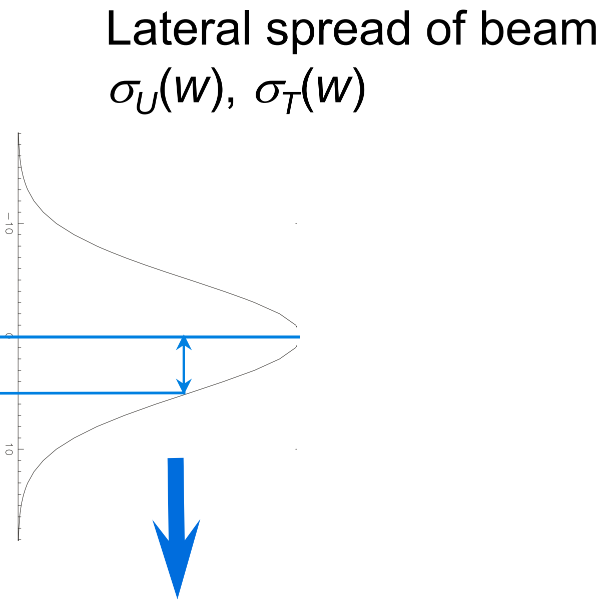
- Integral depth-dose curves

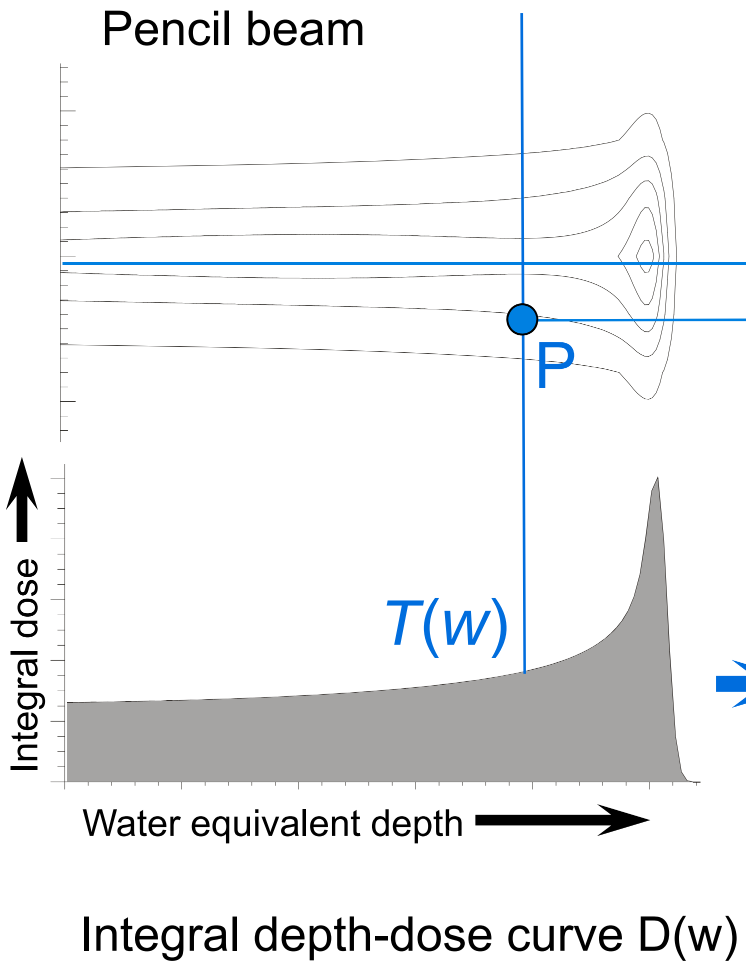


- Lateral beam width of individual pencil beams

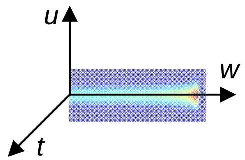


Pencil beam model

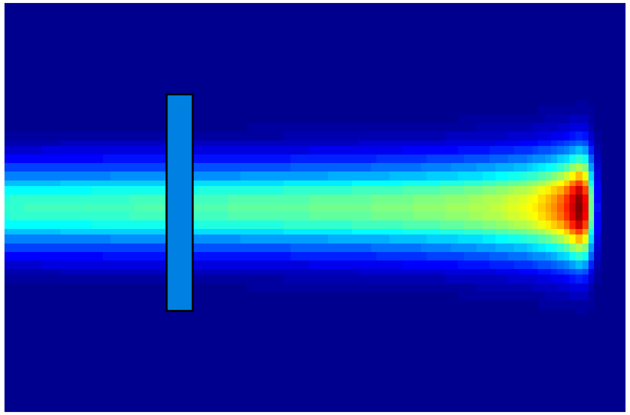


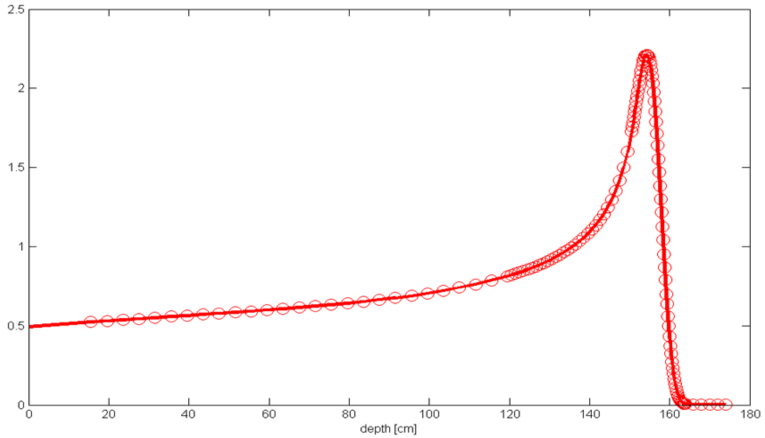


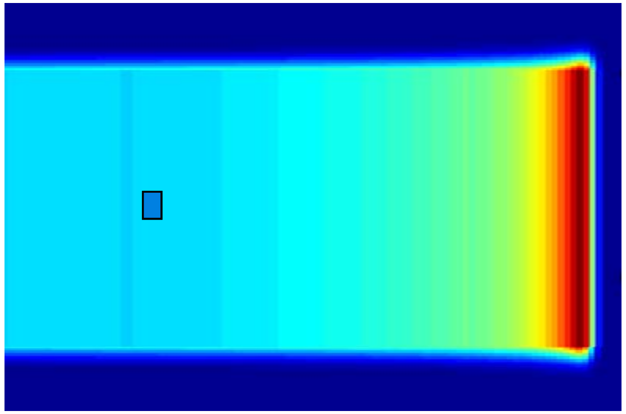
$$D_P(u,t,w) = \frac{T(w)}{2\pi\sigma_T\sigma_U} e^{-\frac{t^2}{2\sigma_T^2(w)}} e^{-\frac{u^2}{2\sigma_U^2(w)}}$$

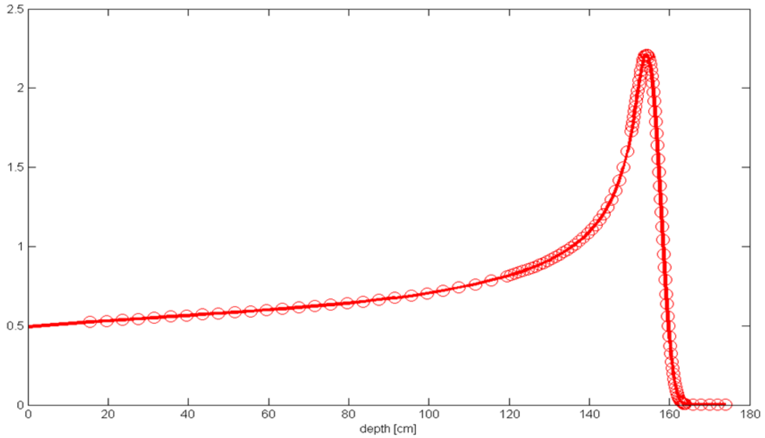


Small field big chamber vs small chamber big field

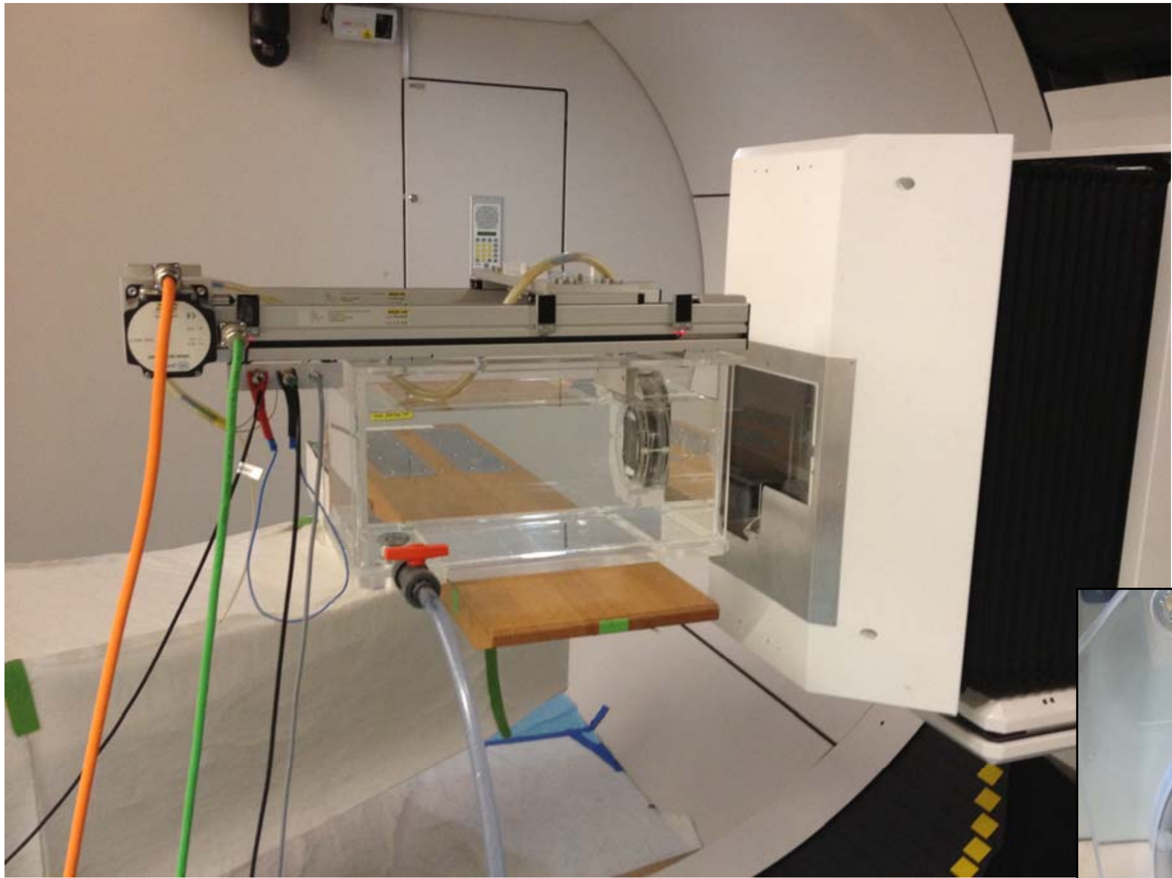






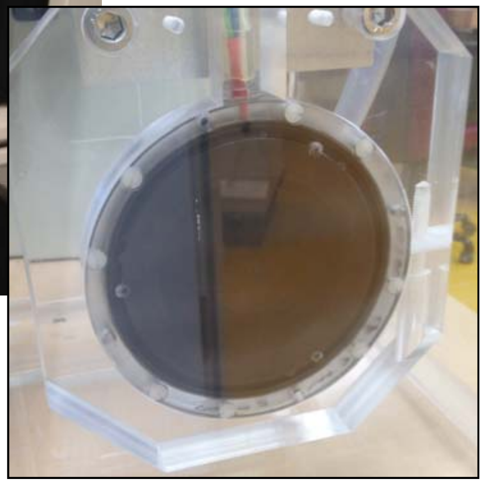


Integral depth dose curves at PSI



Range scanner

- water phantom
- 1D positioning system
- large diameter ionization chamber
- Using gantry MU as reference
- High resolution in one dimension
- High reproducibility



Large plane-parallel IC chamber (∅ 8cm)

Beam halo effect due to secondary protons

$$D(x,y,w) = T(w) \times \left((1 - f_{NI}(w)) \times G^{P}(\sigma^{p}(w)) + f_{NI} \times G^{NI}(\sigma^{NI}(w)) \right)$$

Models the lateral spread of long range secondary particles as a 2nd Gaussian in the dose calculation

T(w): Integral depth dose curve

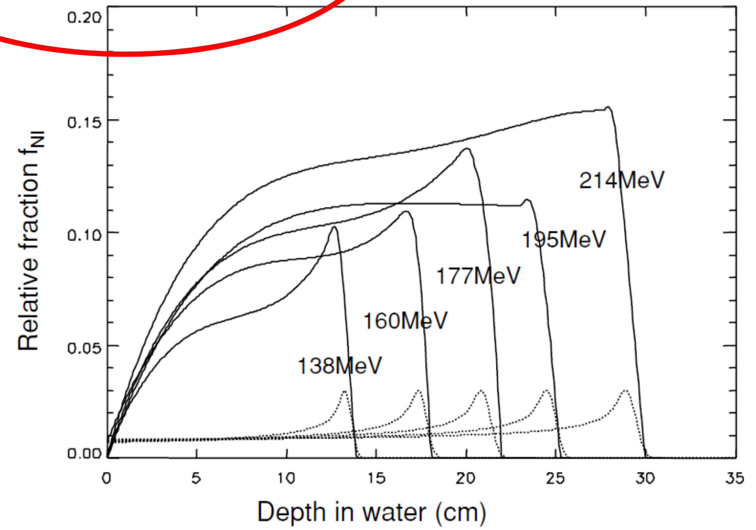
G^P: Gaussian distribution of primary beam

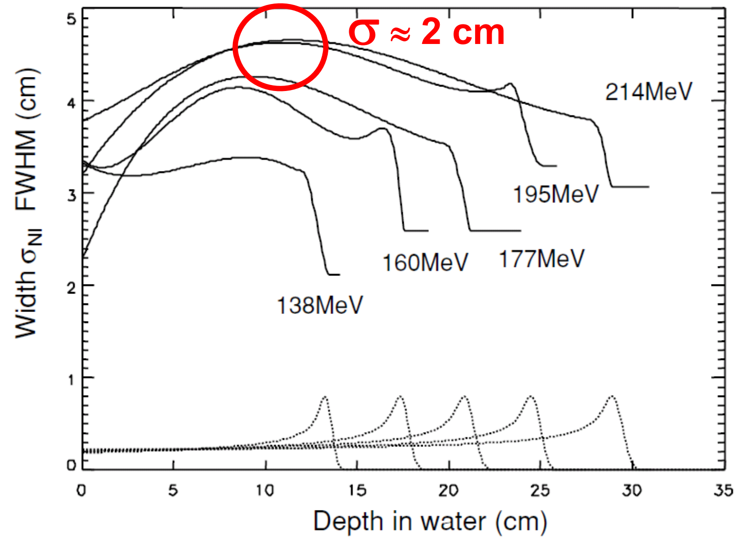
$\sigma^P(w)$: Beam width of primary beam at depth w

$f_{NI}(w)$: Fraction of total integral dose at depth w resulting from secondary particles

G^{NI}: Gaussian distribution of secondary particle distribution

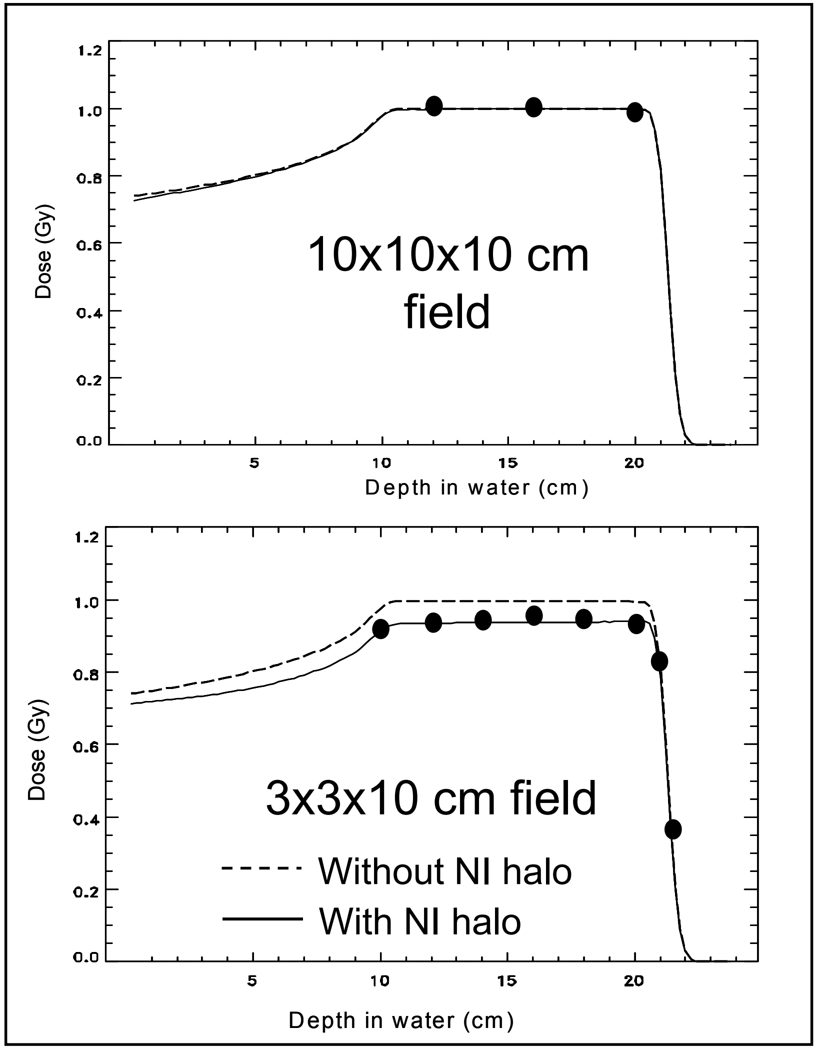
$\sigma^{NI}(w)$: Beam width of secondary particle distribution at depth w



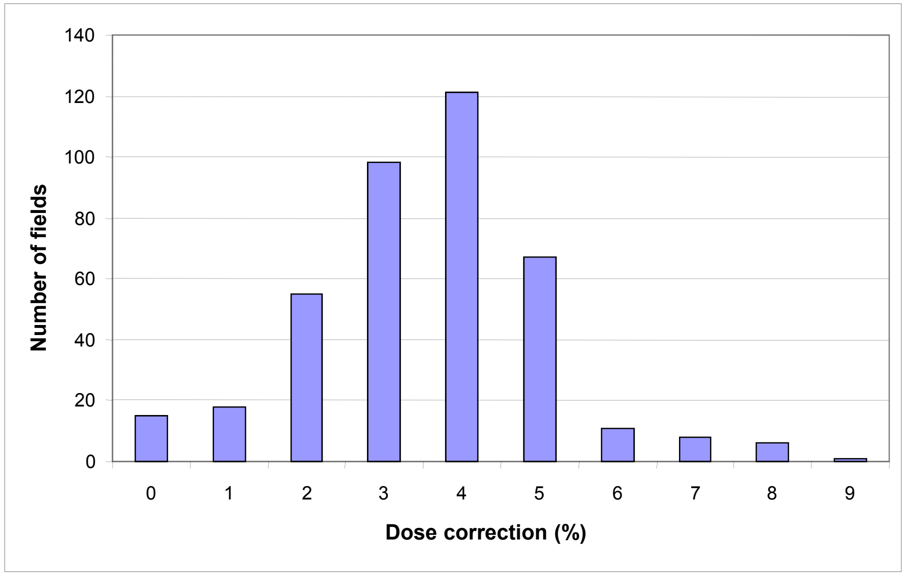


Pedroni et al, PMB, 50 (2005) 541-561

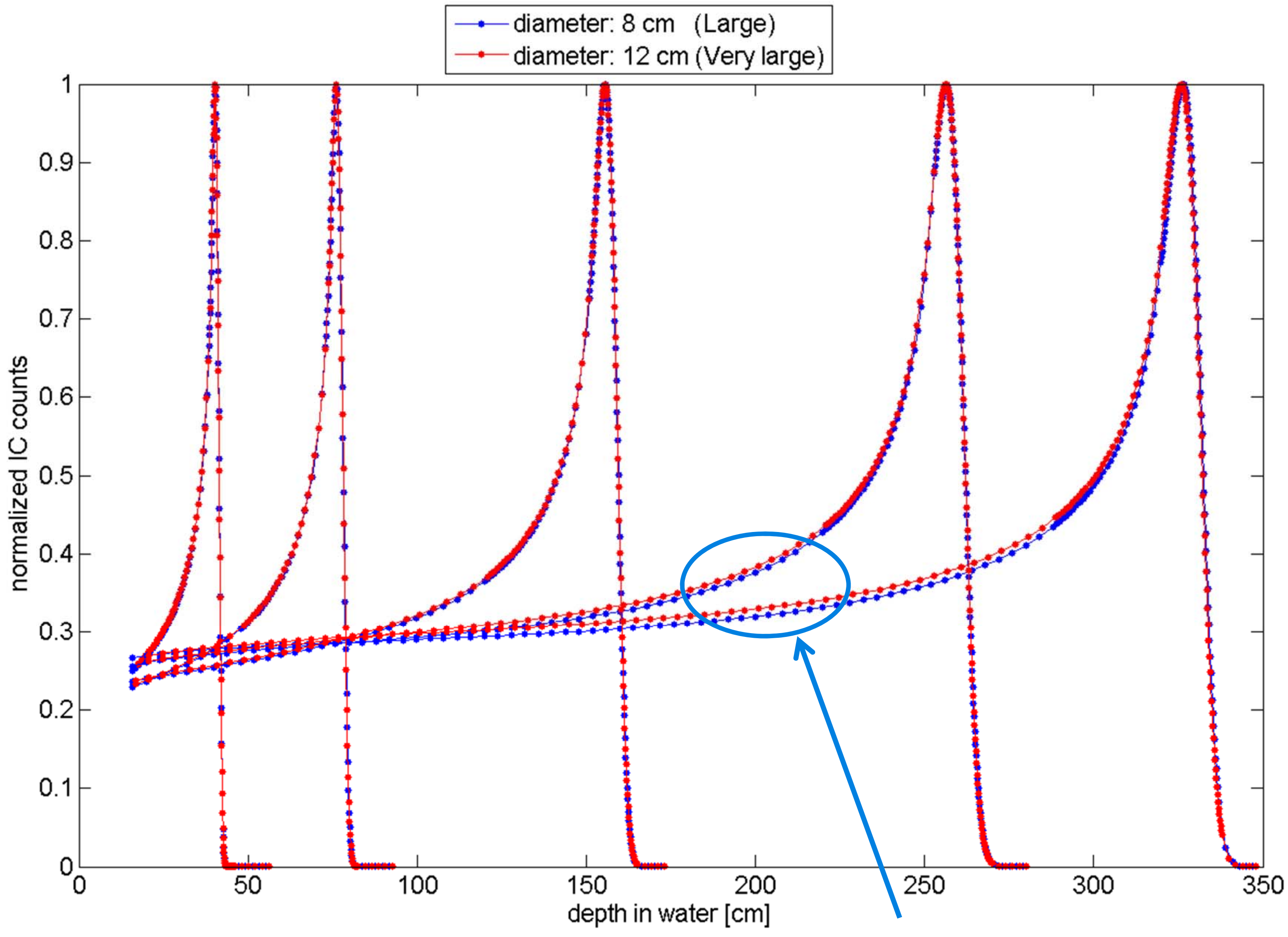
Experimental verification and clinical results



Global dose correction required due to NI effects over 390 measured fields measured at PSI

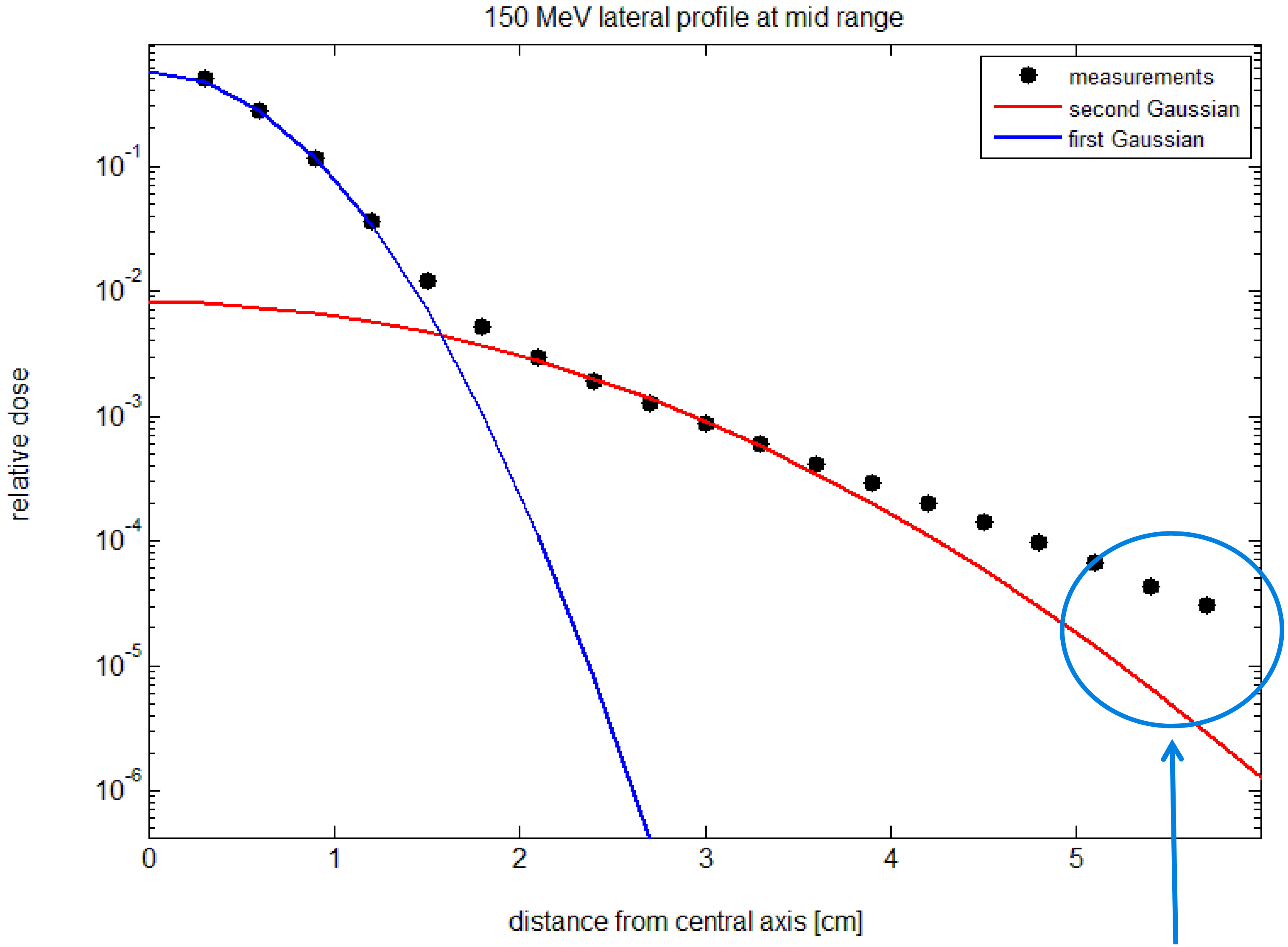


Large ICs: 8 cm vs 12 cm



Differences visible only for high energies

The two Gaussian model

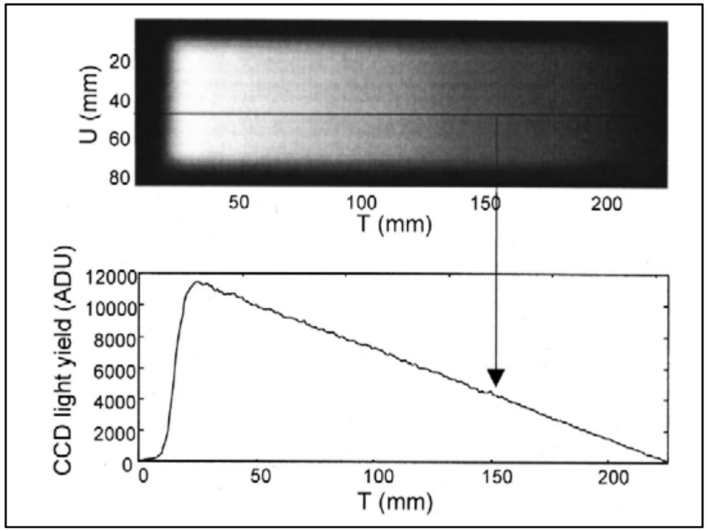


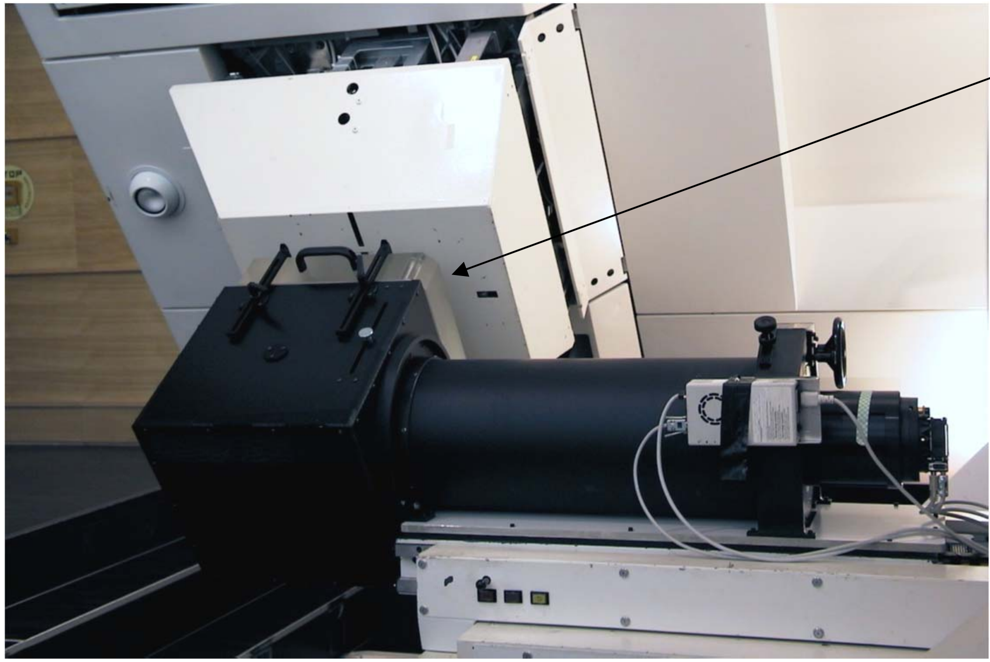
Residual dose outside the second Gaussian

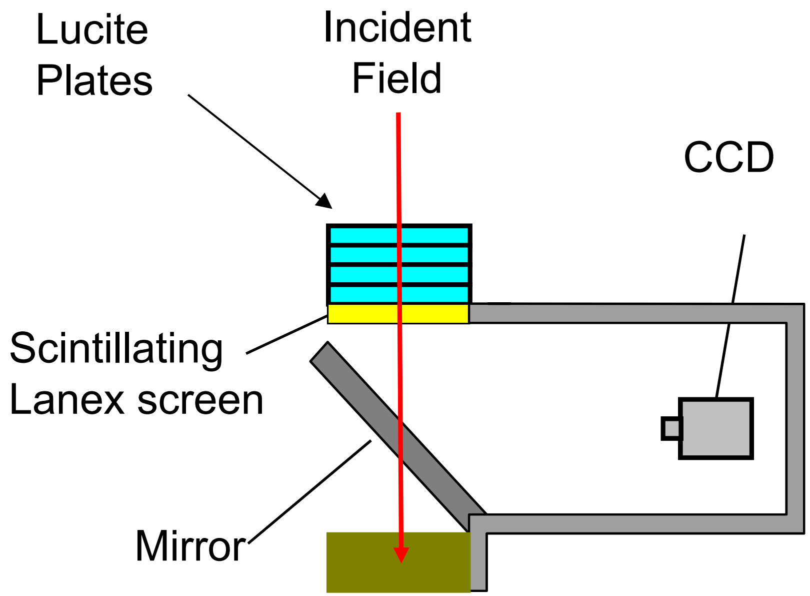
Lateral beam size measurement

CCD Camera with scintillating screen

- Lanex scintillating screen
- High spatial resolution: 0.5mm
- High reproducibility: 0.2%
- Fast data acquisition
- Linear response to dose
- Suitable tool for relative dosimetry
- Quenching effects (under-response to high LET)

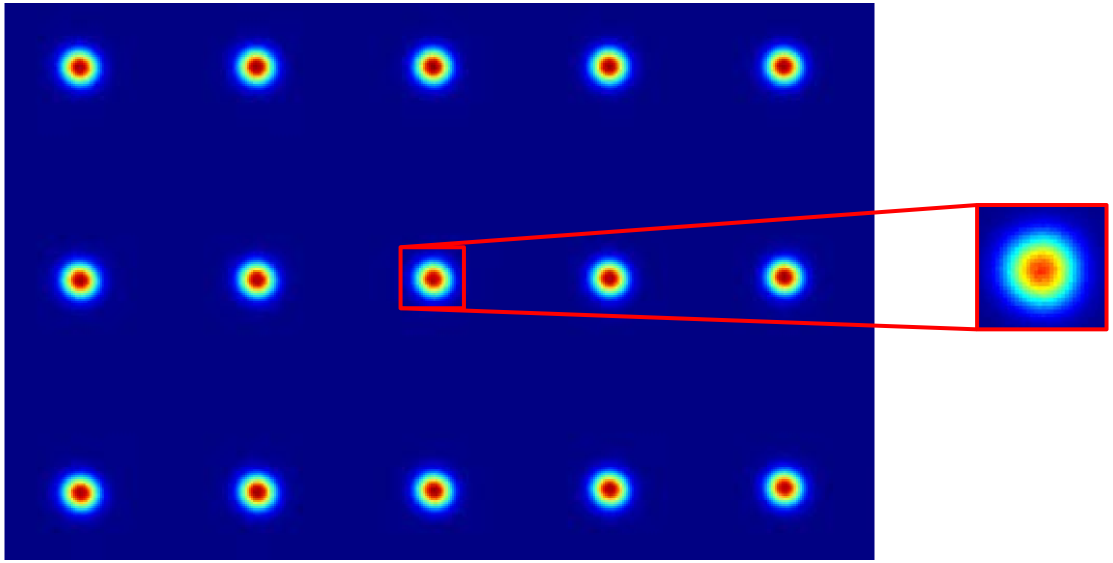


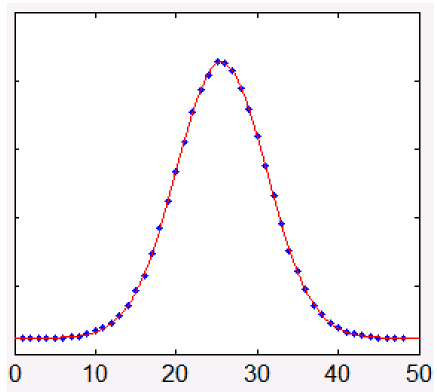




Lateral beam size measurement: example

150 MeV proton beam in air at different lateral positions





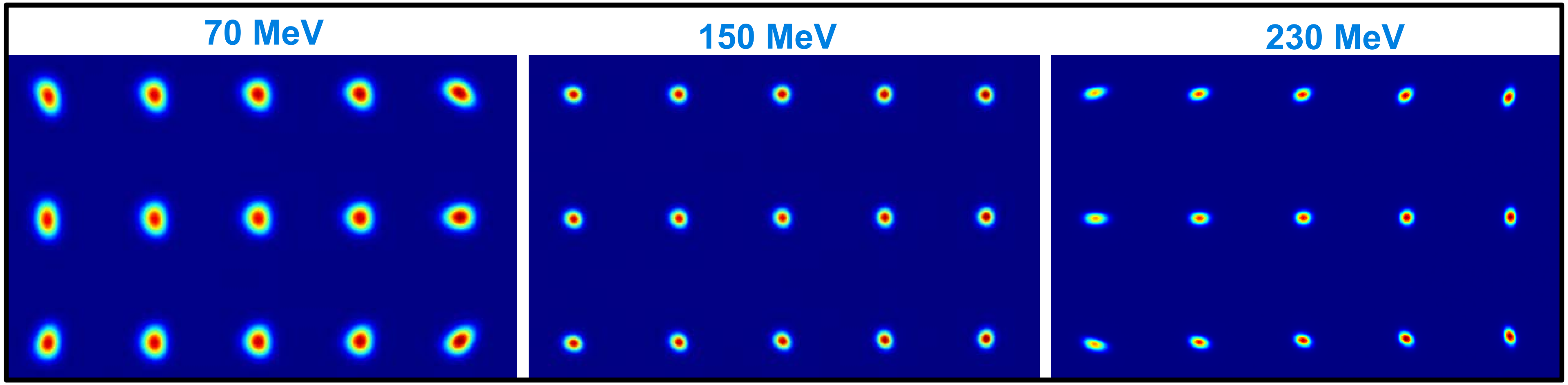
- 2D Gaussian fitting for each spot to determine σ_U and σ_T

Effective tool for commissioning when a large amount of data has to be collected

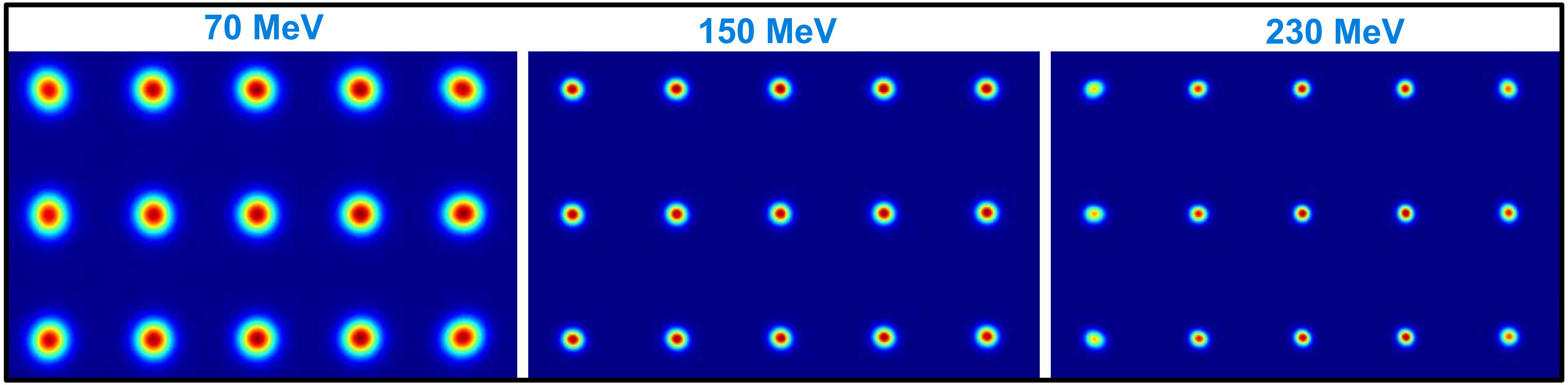
Delivered pencil beam in air at PSI Gantry 2

grid: U,T   20x12 cm   15 spots

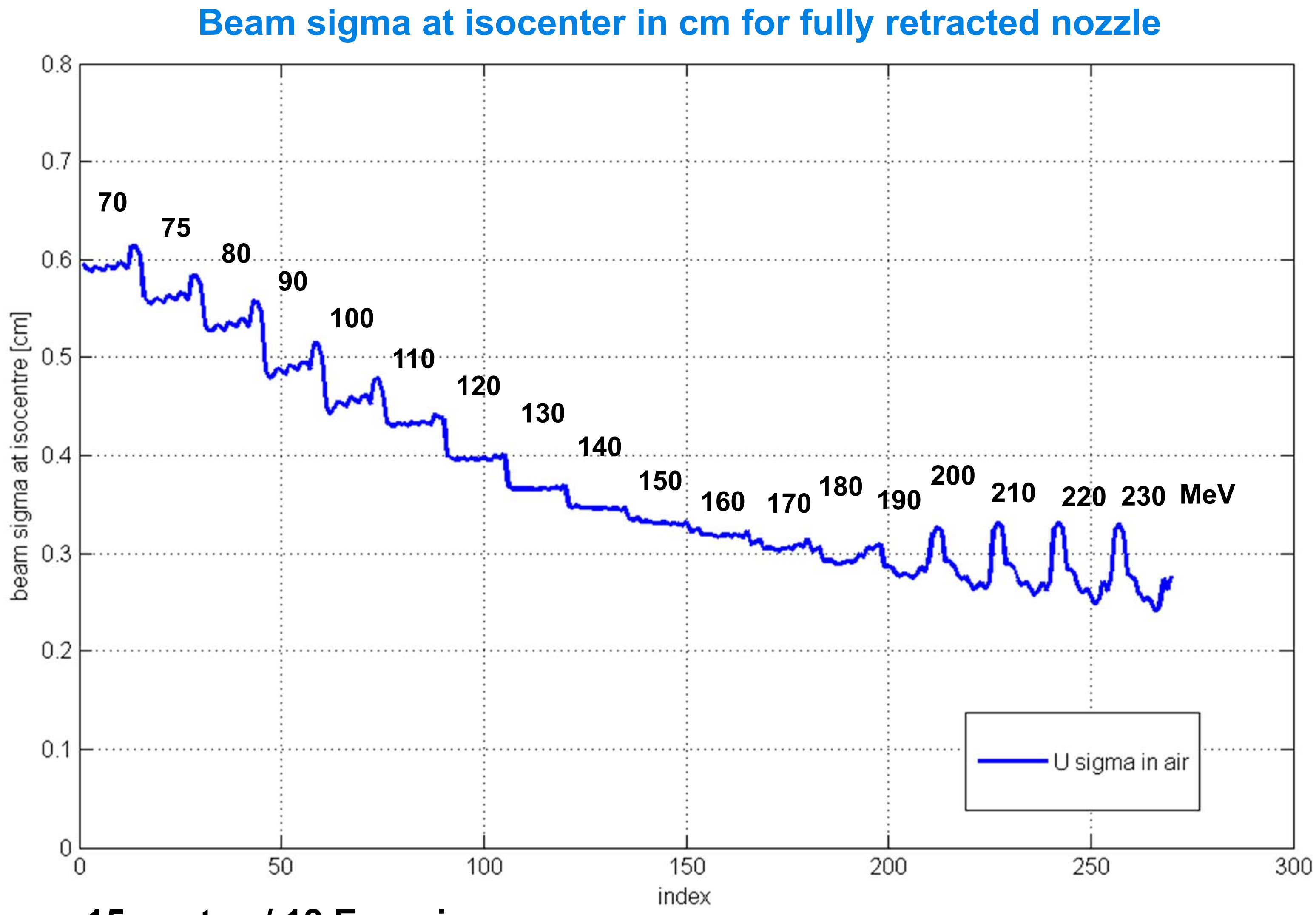
40cm above isocentre



At isocentre

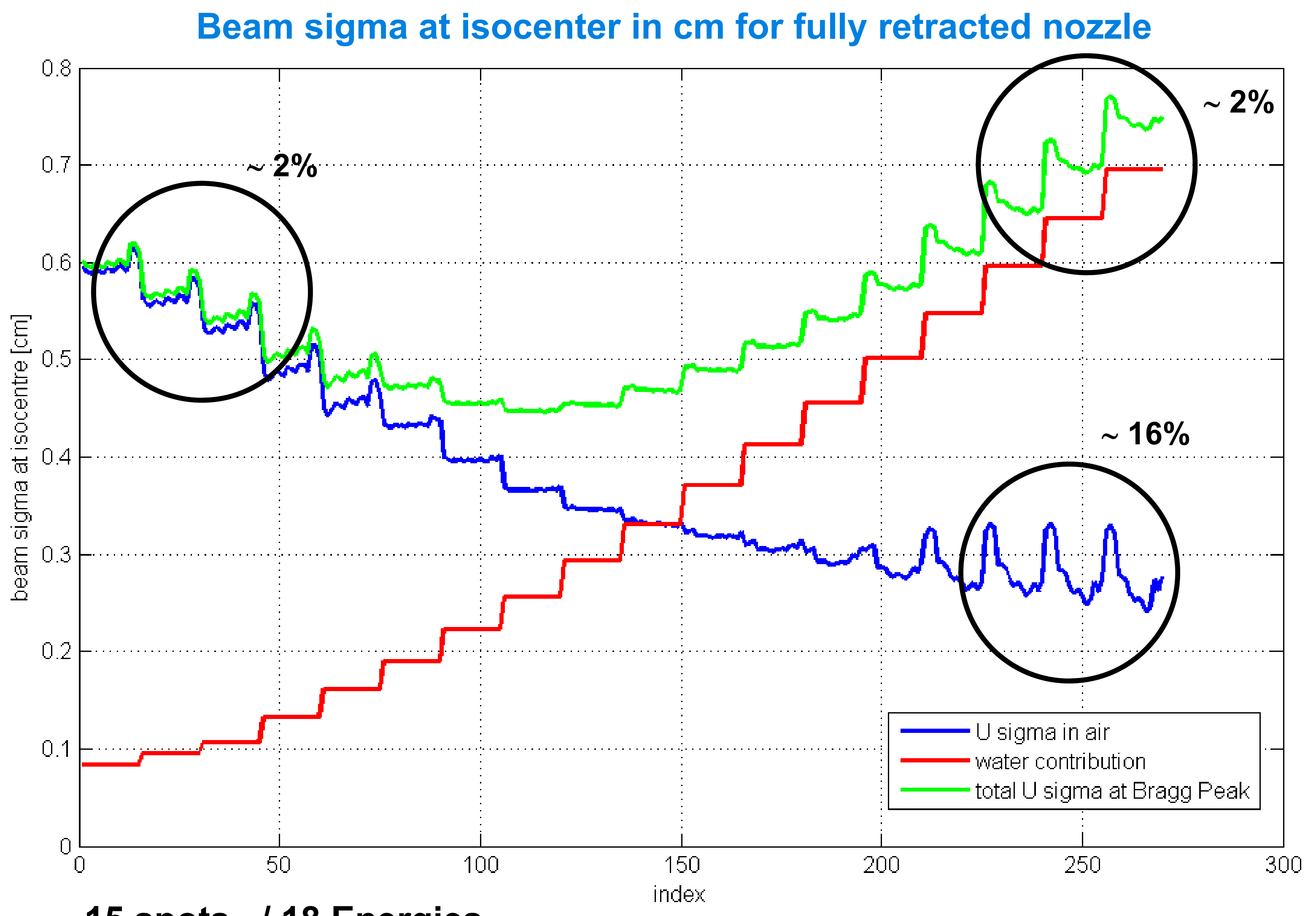


Delivered pencil beam in air at PSI Gantry 2



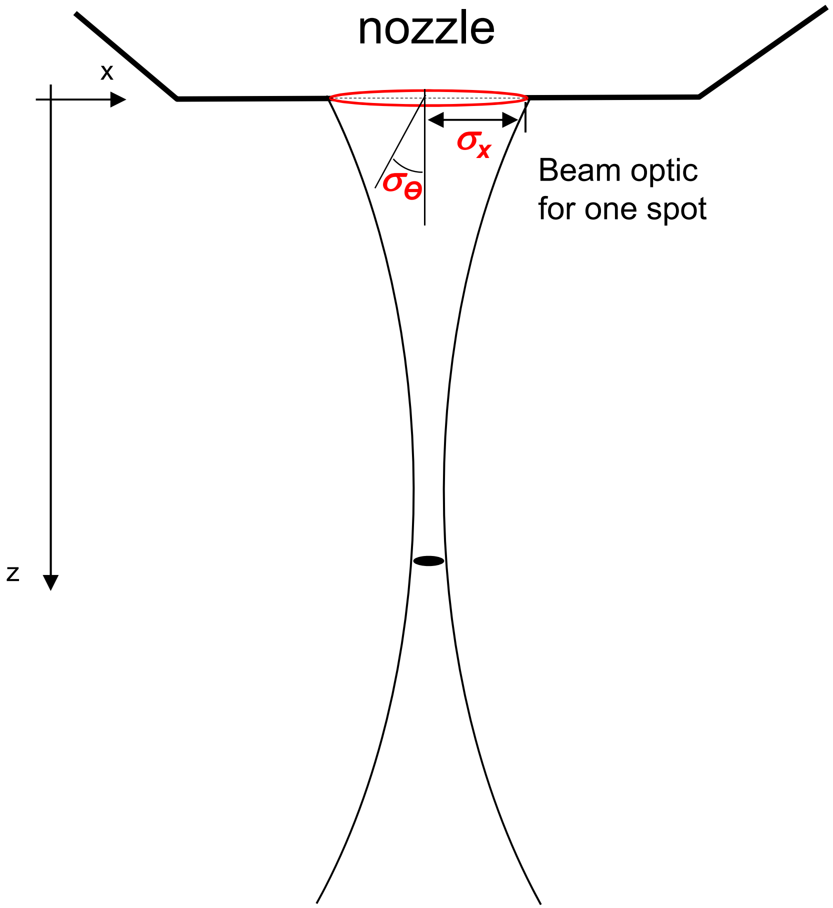
15 spots / 18 Energies

Delivered pencil beam in air at PSI Gantry 2



15 spots / 18 Energies

Beam propagation in air



The *moments* of the angular-spatial distribution of the pencil beam at z = 0

A_0, A_1, A_2

The angular-spatial distribution (Eyges solution to Fermi's diffusion equation):

$$P(x,\theta,z) = \frac{1}{\pi\sqrt{A_0 A_2 - A_1^2}} e^{-(A_0 x^2 - 2A_1 x\theta + A_2\theta^2)/(A_0 A_2 - A_1^2)}$$

$$A_2 = 2\sigma_x^2 \qquad A_0 = 2\sigma_\theta^2 \qquad A_1 = 2Cov(x,\theta)$$

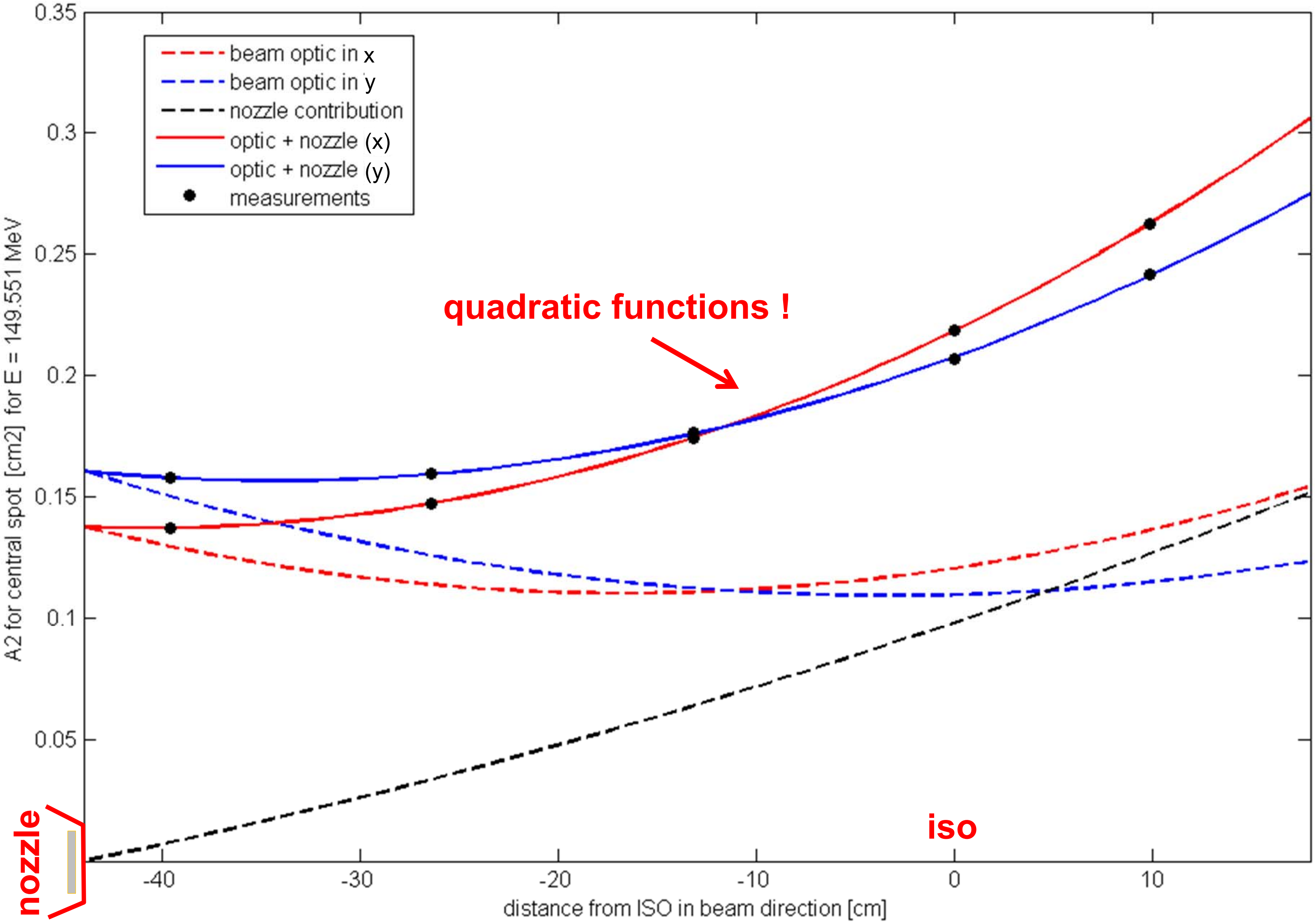
- $\sigma_x(z) \equiv$ spot size in air at z

From the generalized Fermi-Eyges theory:

$$A_2(z) = A_0 z^2 + 2A_1 z + A_2$$

Comparison with measurements at PSI

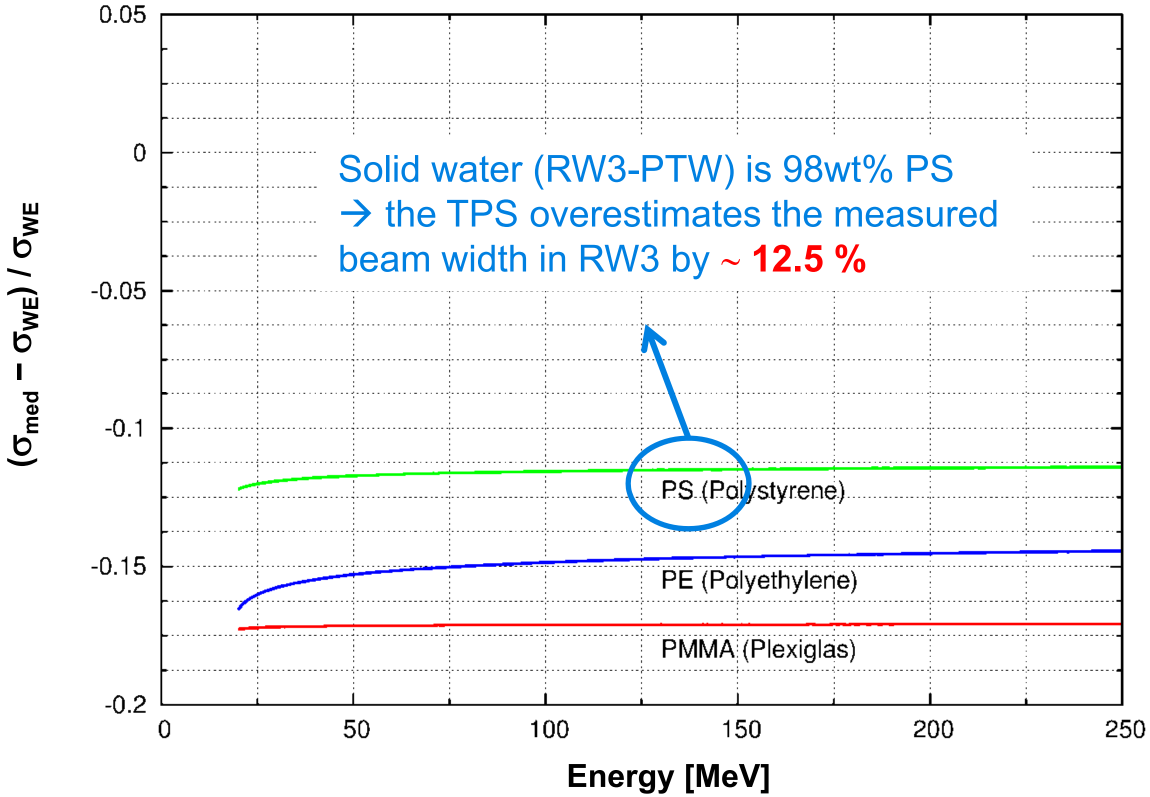
$A_2 = 2\sigma_x^2$ for the central spot for E = ~ 150 MeV (Gantry 2)

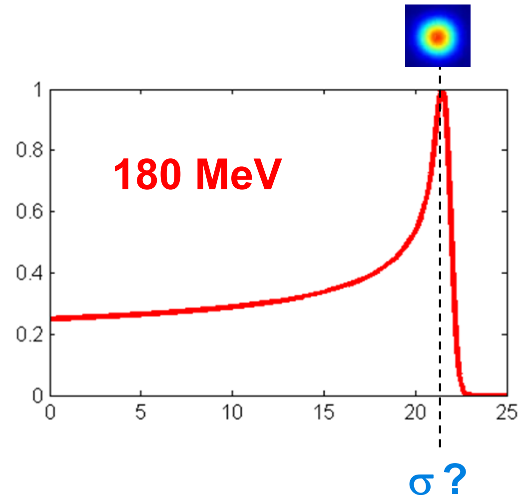


Beam propagation in a medium

σ_{med} = beam width due to scattering in a given medium

σ_{WE} = beam width due to scattering in an equivalent amount of water (same energy loss as for the medium)





Beam width (σ) at the Bragg peak

Water (W)	Polyethylene (PE)
0.46 cm	0.39 cm

Δ = 15 %

The beam width in PE is 15 % smaller than in water at the Bragg peak

Relative dosimetry: Field characteristics/Machine performance

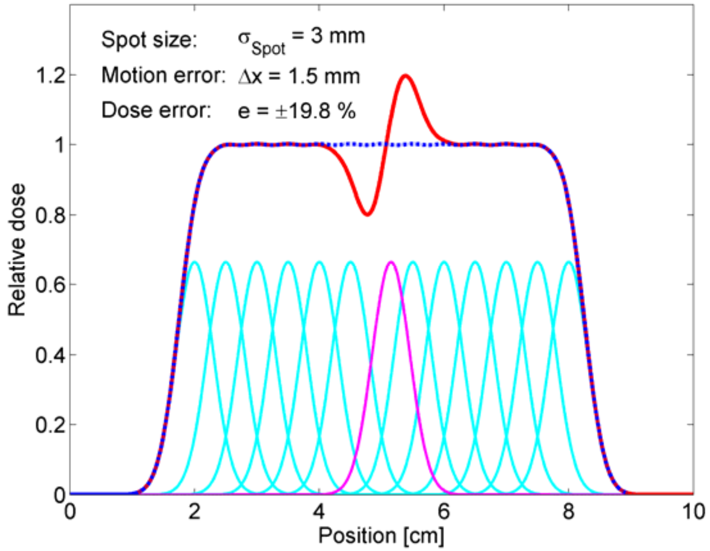
Geometrically well defined shapes

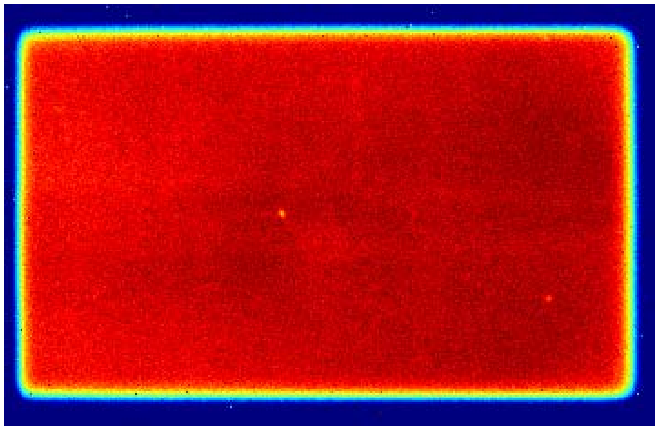
1. Monoenergetic homogeneous planes
2. Cubes, spheres

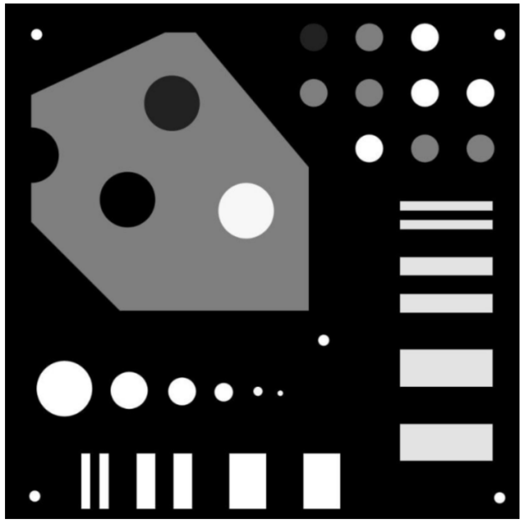
Checking of interplay of multiple factors

- Accurate spot spacing
- Accurate spot weighting
- Uniformity of monitor chamber

- Field uniformity (homogeneity)
- Distal and lateral fall-off
- Geometrical accuracy







Test pattern developed at MGH (J. Flanz)

Periodic checks: machine specific dosimetry

Machine specific dosimetry: daily QA

Dosimetry-specific checks

Check	Rational
1. Absolute dose (center of SOBP and opt. distal fall-off)	Problems with the monitor calibration and/or in general with the system
2. Pencil beam position and size (and parallelism)	Problems with the scanning system and/or beam line optic
3. Beam energy (range measurements)	Problems with the energy selection system and/or beam line

Machine specific dosimetry: daily QA

Dosimetry-specific checks

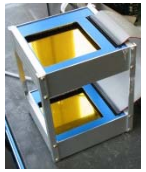
Device

1. Absolute dose
(center of SOBP and opt. distal fall-off)

Ionisation chambers (e.g., cylindrical Farmer FC65)

2. Pencil beam position and size
(and parallelism)

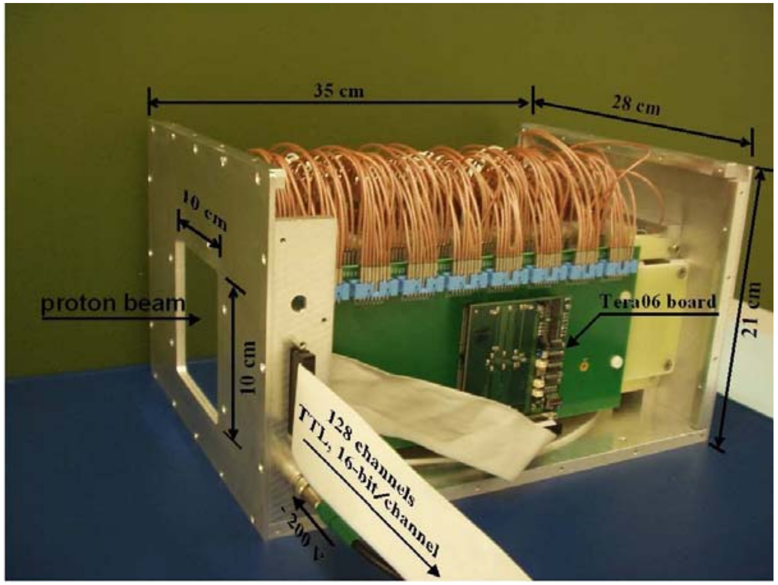
Strip chamber , amorphous-Si detectors



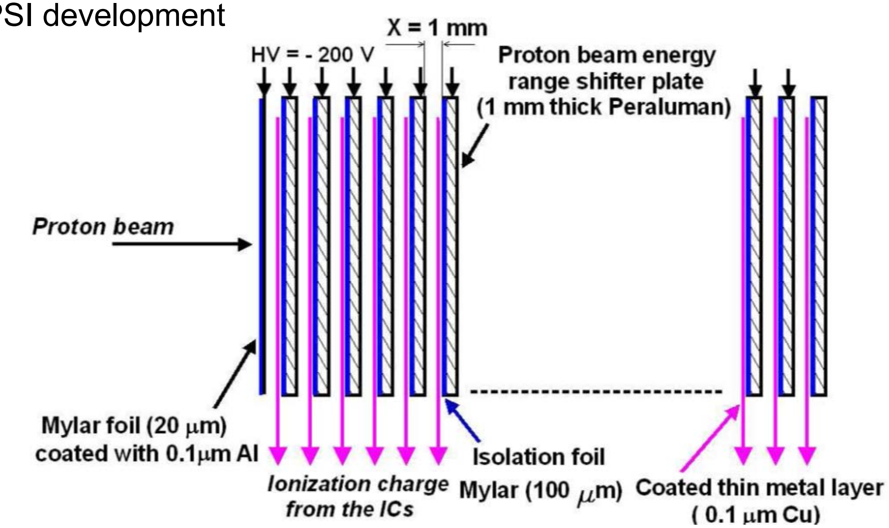
3. Beam energy
(range measurements)

Large Ionisation chamber or
Multi-Layer-IC (MLIC)

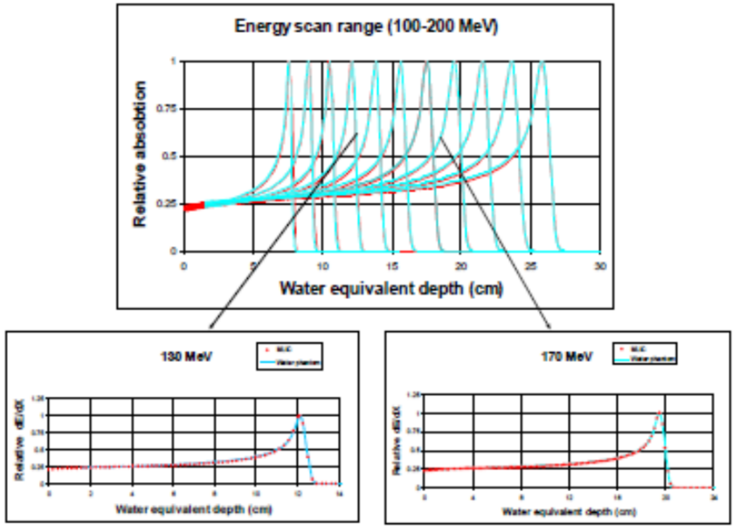
Multi Layer Ionization Chamber (MLIC)

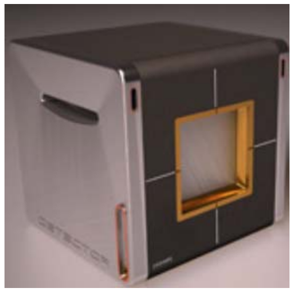


PSI development



- Stack of 128 IC's
- Interleaved with aluminium plates (1mm)
- Full Bragg curves recorded in a single measurement



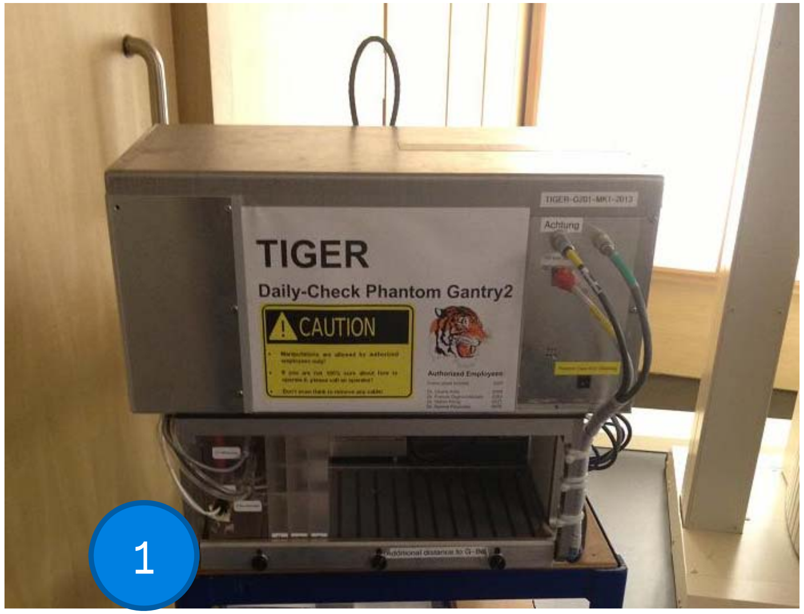


Commercial products

S Lin *et al.*, Med. Phys. **36** (2009), 5531-5540

Machine specific dosimetry: e.g., Gantry 2

Daily check phantom of Gantry 2

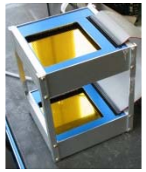


1. Absolute dosimetry

   ICs in PMMA phantom

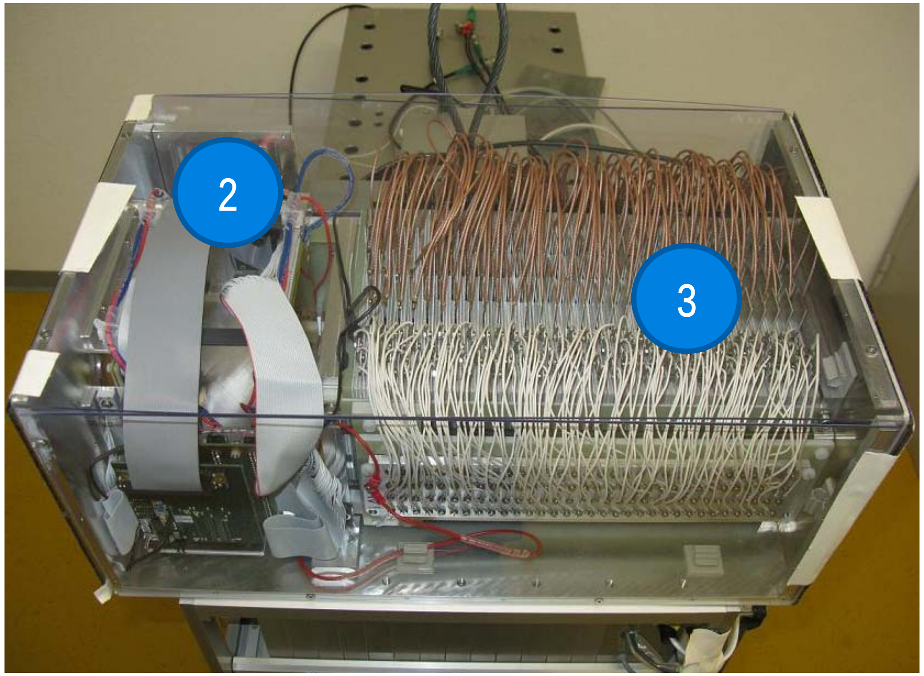
2. Beam position and size

   Strips chambers



3. Beam energy

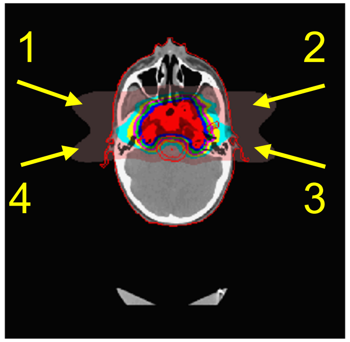
   Multi-layer-ICs



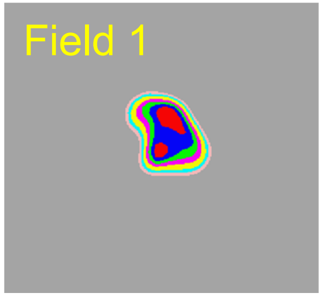
Periodic checks: patient specific QA

Patient specific dose verification

Patient

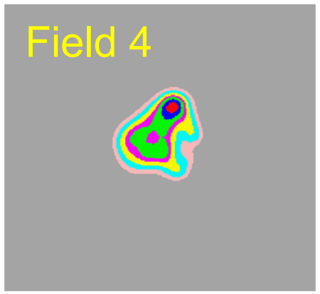


Treatment plan

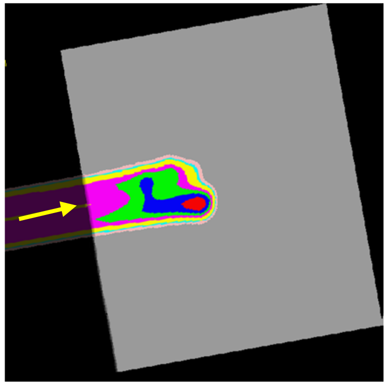


Fields

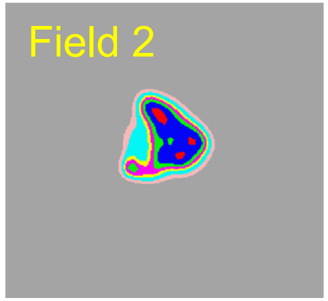
Spot weights



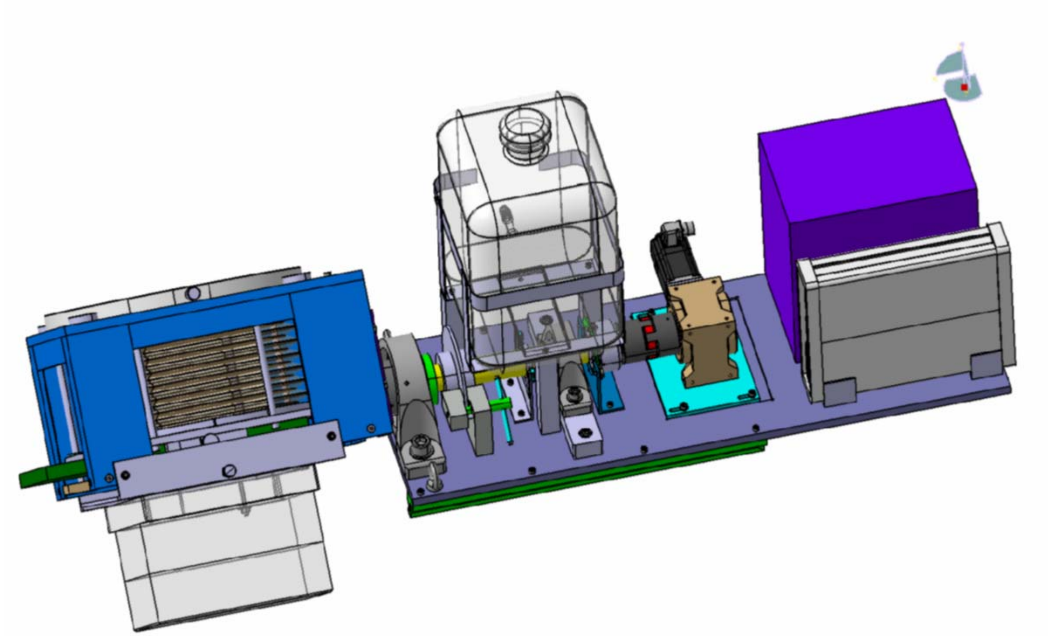
Phantom

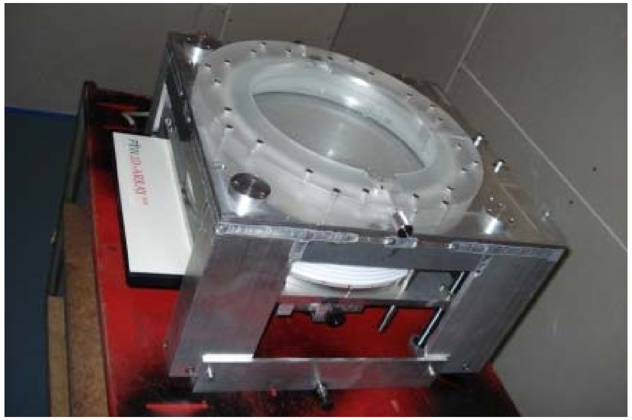


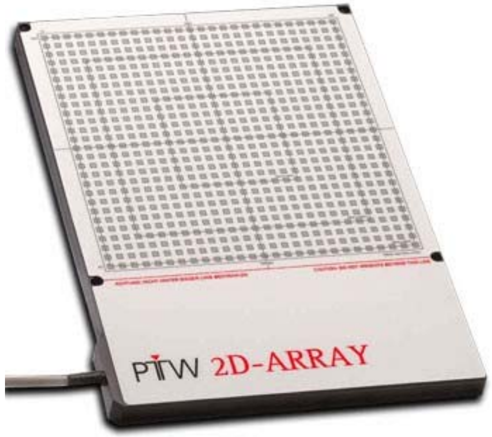
Recalculated 3D dose distribution



Patient specific dose verification







Equipment

- Dedicated rotatable water phantom
- Commercial available 2D-array
- Adjustable water column
- Readout interface to planning system

Reproducibility of the PTW 2D-array

Gamma analysis: the common definition

The gamma value

$$\gamma(\vec{r_m}) = min\{\Gamma(\vec{r_m},\vec{r_c})\}\forall\{\vec{r_c}\}$$

where

$$\Gamma(\vec{r_m},\vec{r_c}) = \sqrt{\frac{r^2(\vec{r_m},\vec{r_c})}{\Delta d_M^2} + \frac{\delta^2(\vec{r_m},\vec{r_c})}{\Delta D_M^2}}$$

and

$$r(\vec{r_m},\vec{r_c}) = |\vec{r_c} - \vec{r_m}|$$

$$\delta(\vec{r_m},\vec{r_c}) = D_c(\vec{r_c}) - D_m(\vec{r_m})$$

$\Delta d_M \equiv$ acceptance criteria for *DTA (C_{DTA})*

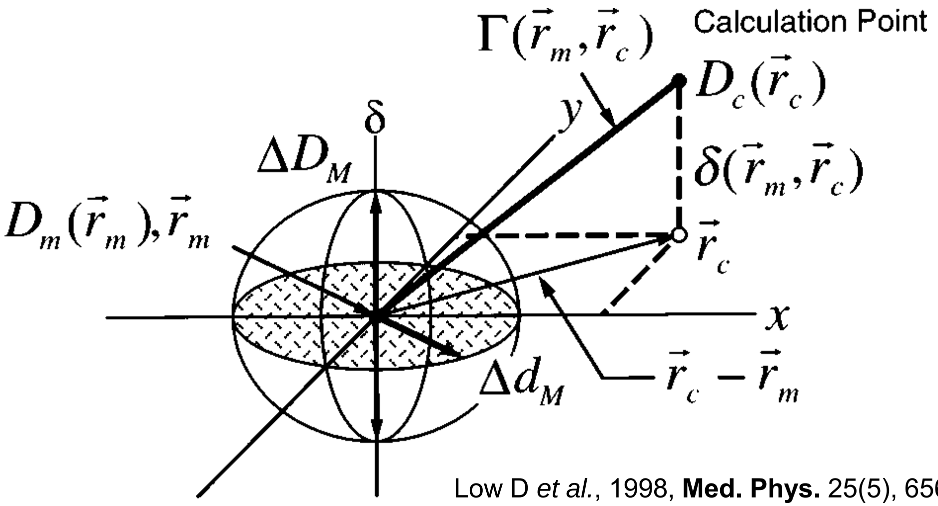
$\Delta D_M \equiv$ acceptance criteria for the dose-difference (C_{DD})

D_m and D_c are the measured and calculated dose, respectively (usually expressed as **relative dose**)

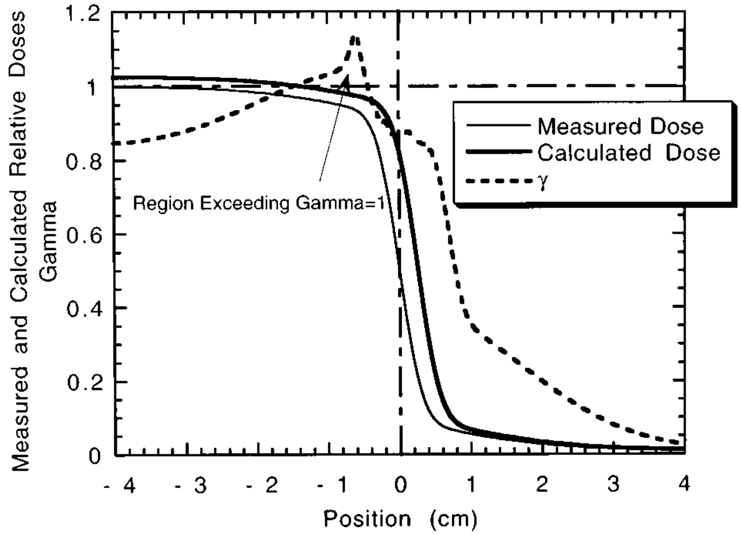
Typical passing criteria for Δd_M, ΔD_M : 3mm / 3%

Criteria for gamma: xx% of points have a gamma smaller than 1 (typical 95%)

It is at the user's discretion to assign clinically relevant values to Δd_M, ΔD_M and γ

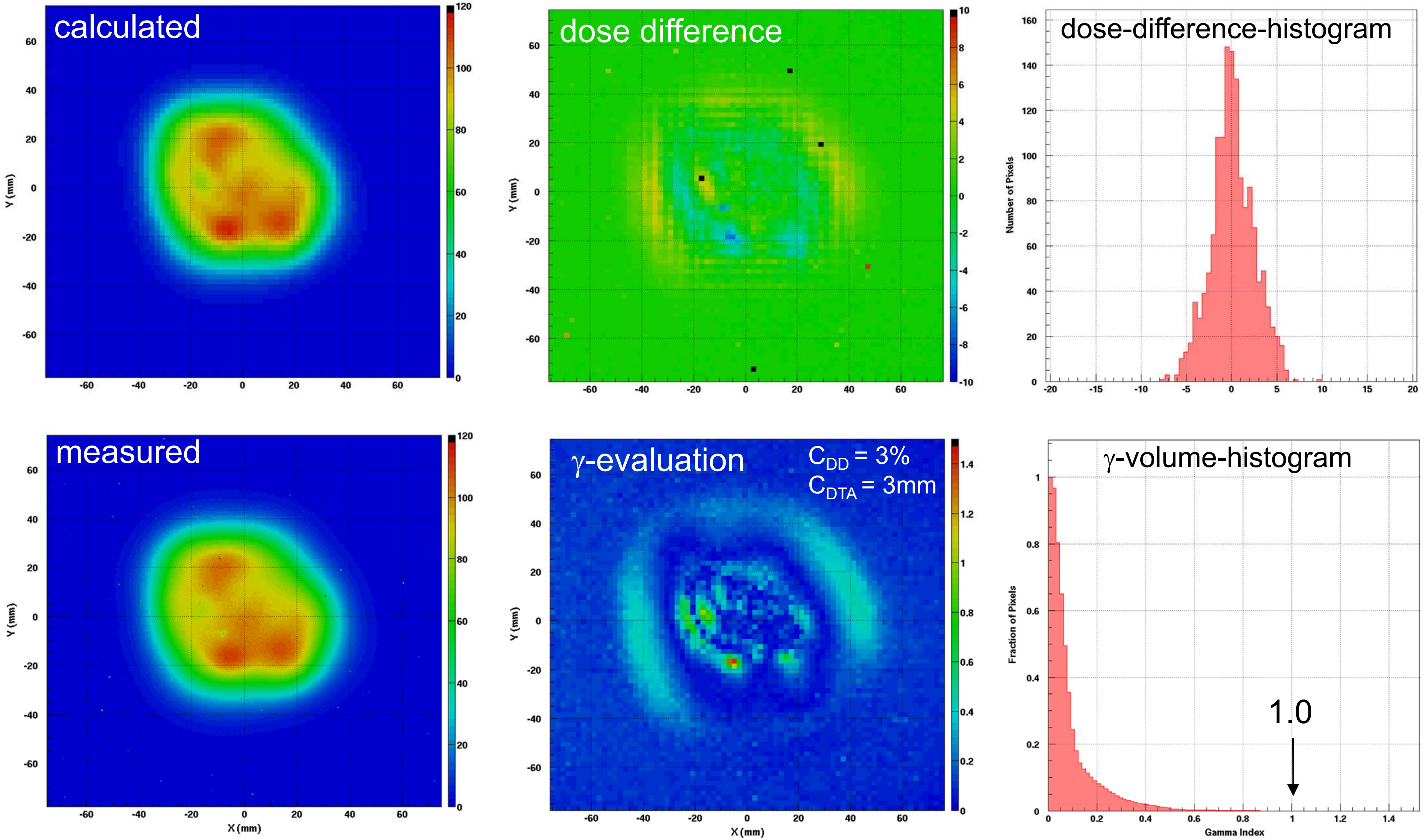


Low D *et al.*, 1998, **Med. Phys.** 25(5), 656-61



Scintillator-CCD dosimetry system

Field verification



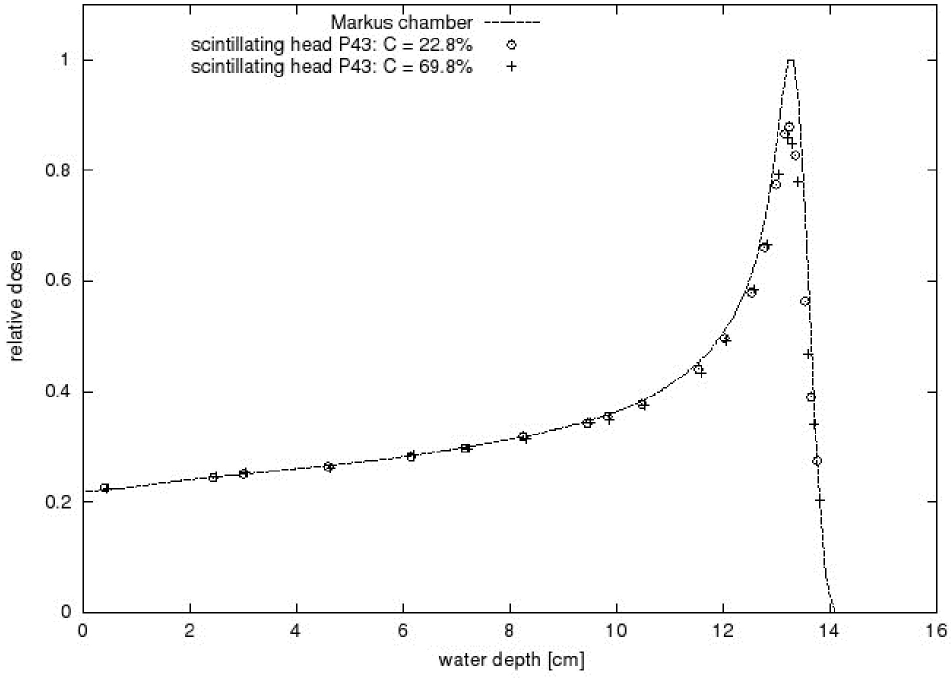
CCD Dosimetry System for field verification

Quenching Effects

- Under-response of scintillator in the Bragg peak region (high LET)

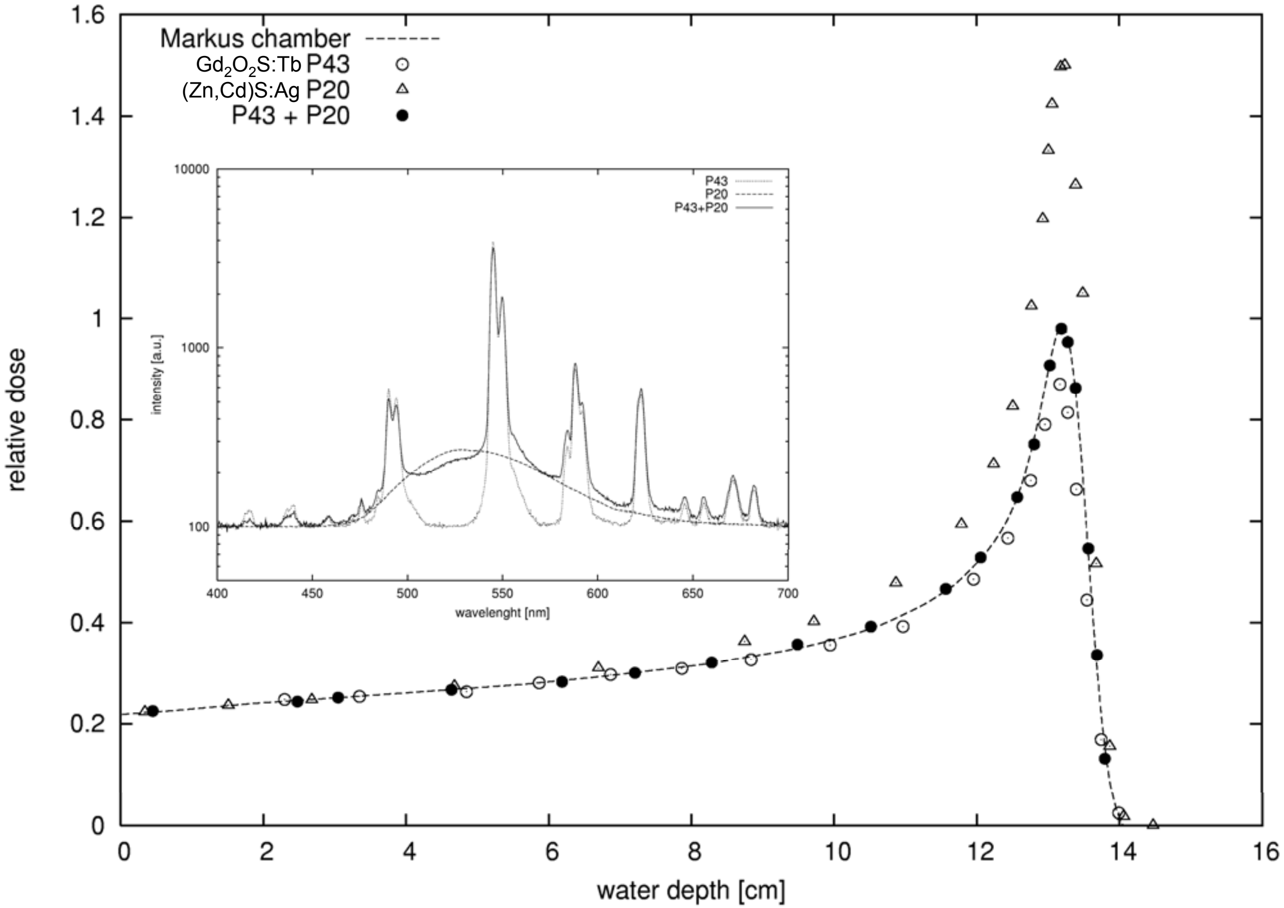
- Inclusion of quenching in dose calculation by (empirical) correction factor:

$$C = 1 / (1 + 0.008\ dE/dx)$$



CCD Dosimetry System for field verification

Mixture of two scintillating powders can minimize quenching effects at the Bragg peak

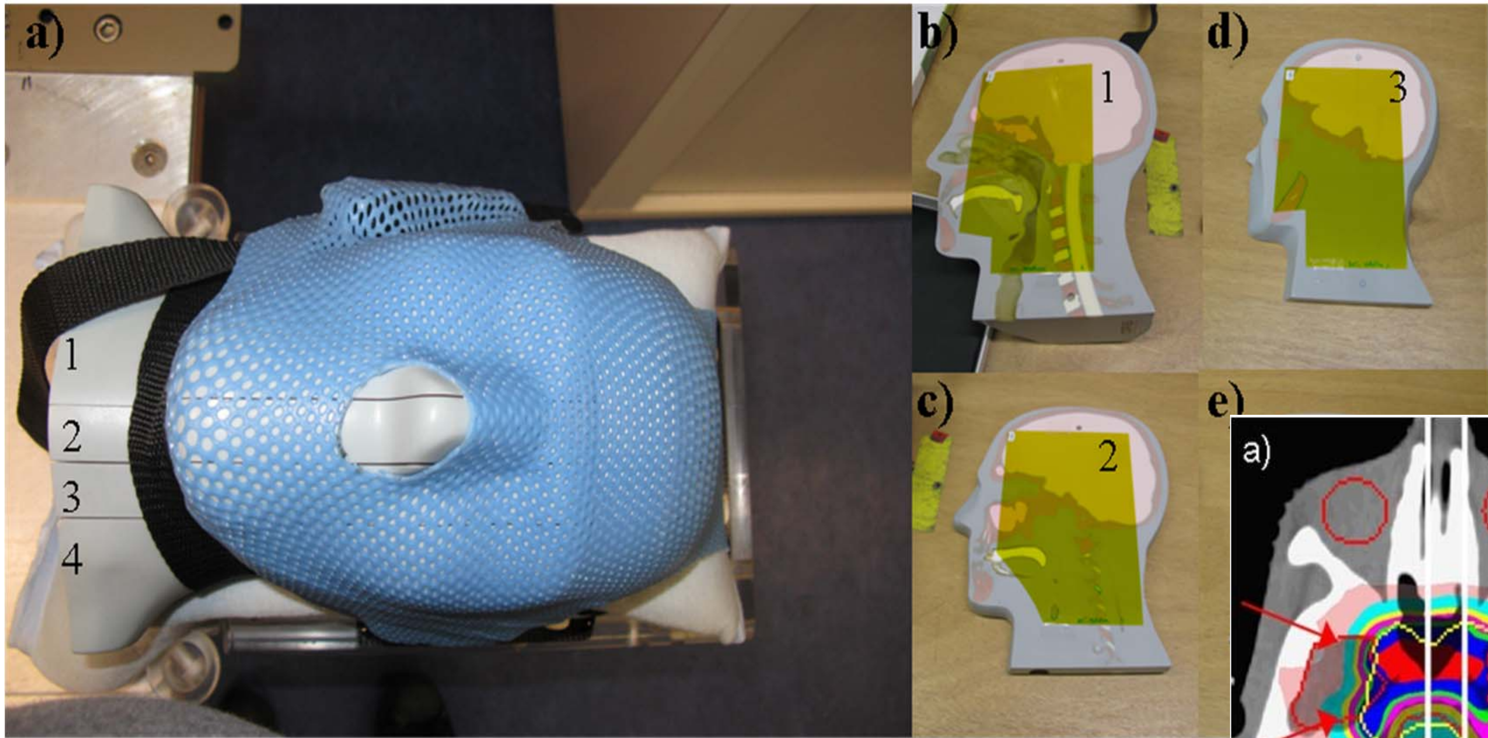


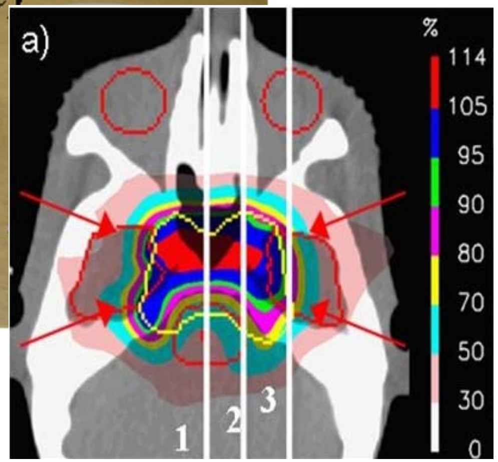
Safai *et al.*, PMB, **49** (2004) 4637-4655

Phantom measurements (Charly)

Antrophomorphic phantom
with sagital slicing

Gafchromic film



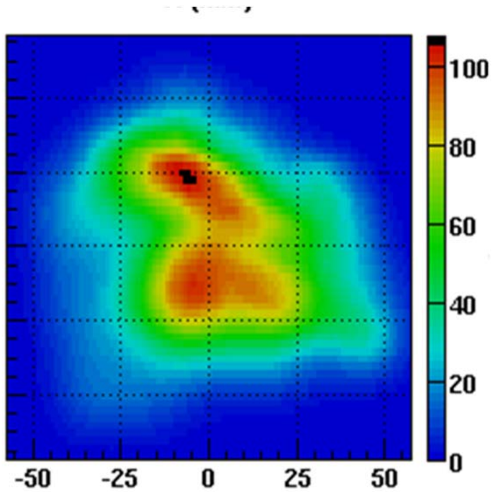


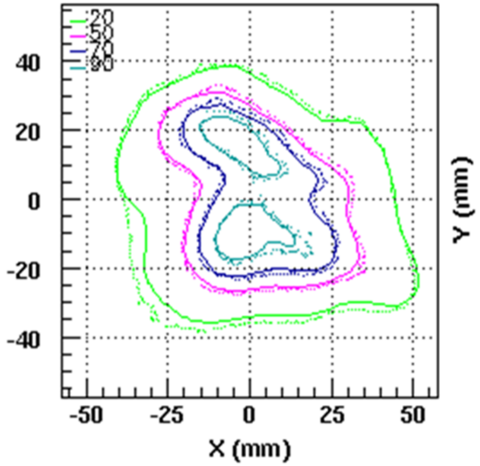
TPS dose distribution

Albertini *et al.*, PMB, **56** (2011) 4415-4431

Phantom measurements (Charly)

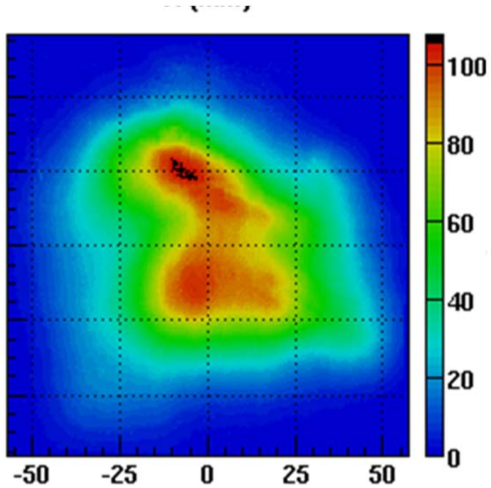
Dose
calculation

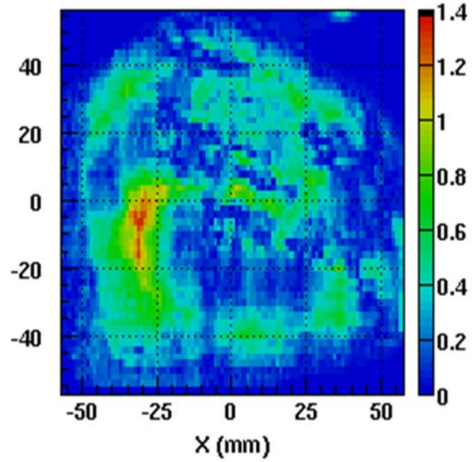




Isodose
overlay

Measurement





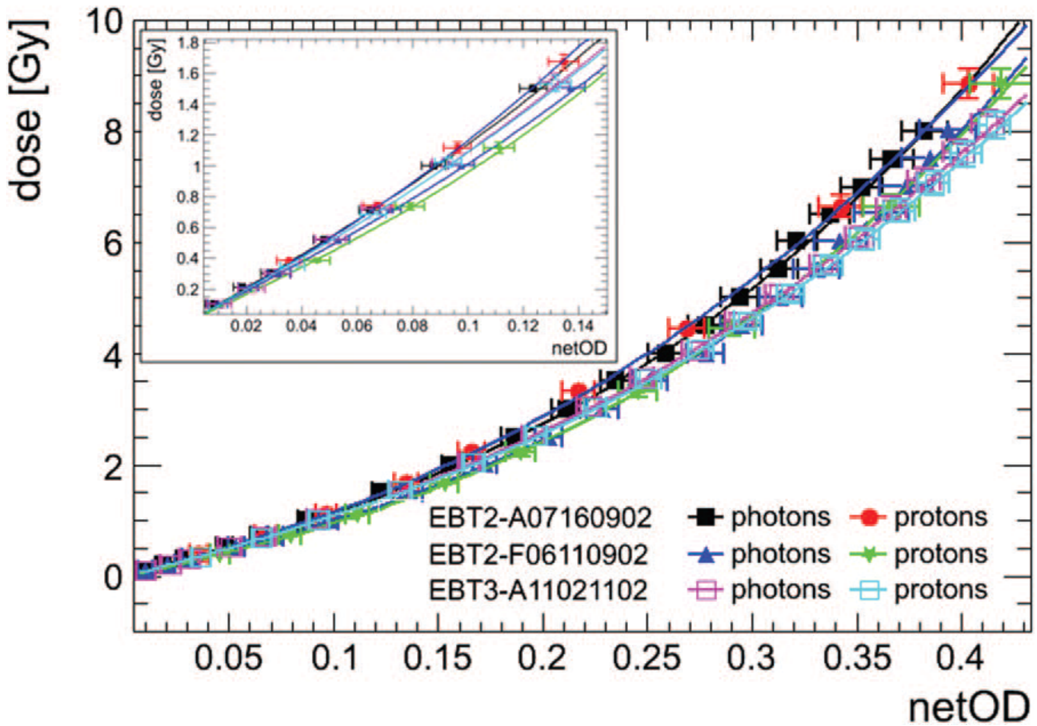
γ-analysis

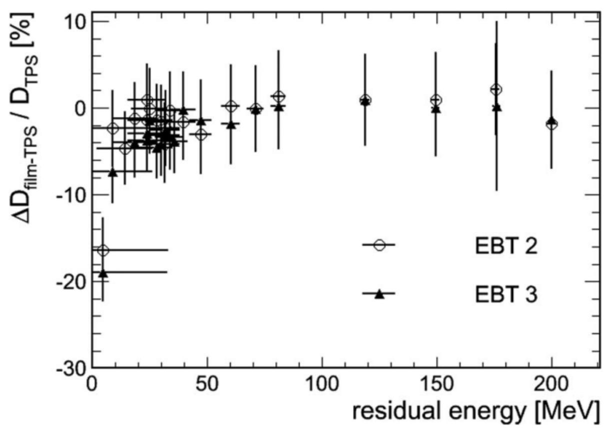
3 mm / 3%

>99%
agreement

Albertini *et al.*, PMB, **56** (2011) 4415-4431

Gafchromic EBT3





Reinhardt et al, Med. Phys., **39** (2012) 5257 - 61

EBT3 under the proton beam

- Almost linear response below 2 Gy
- Quenching in the Bragg peak:
  - underresponse up to 20% → LET dependence
- Film darkening: 7.6% within 24 h → increase in measured dose of over 10%
- Average batch-to-batch variation of up to 12 % (up to 4.6% for the same lot)
- Side orientation sensitivity eliminated compared to EBT2

LET dependence correction methods

Quenching factor QF: $\dfrac{1}{1 + k \cdot dE/dx}$

Two approaches to correct the LET dependence

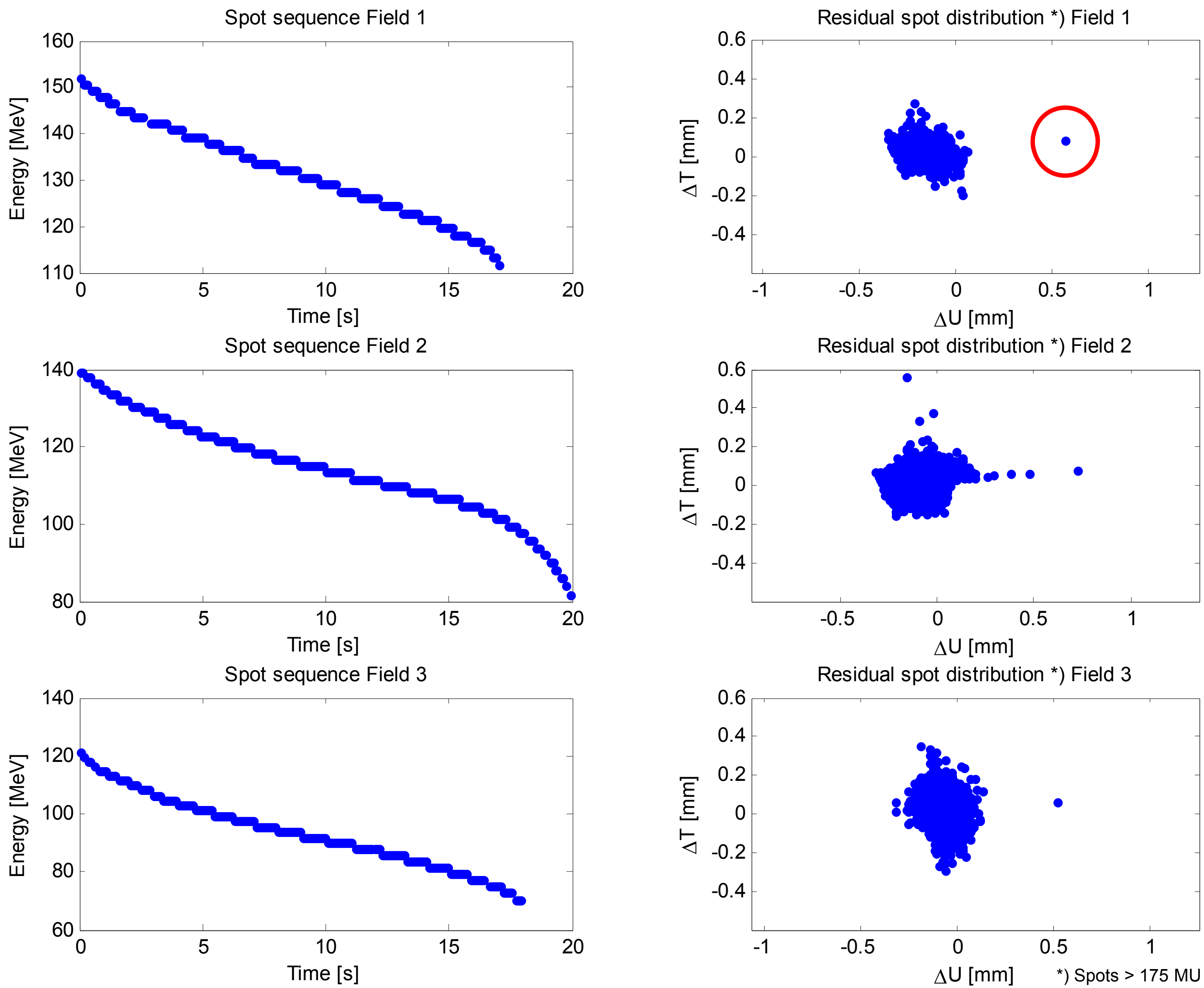
To reproduce the expected dose	To reproduce the measured dose
$D_{exp} = CF \cdot D_m$	$D_m = QF \cdot D_{exp}$
Use dose-weighted correction factors for mix fields	Recalculate dose distribution using beam data that matches the measured depth dose curves

Kohno et al., *J Appl Clin Med Phys*, **12** (2011), 326-37

Lu et al., *Med Phys*, **37** (2010), 5858-66

Log files analysis: example I

1st patient, 1st fraction in Gantry 2



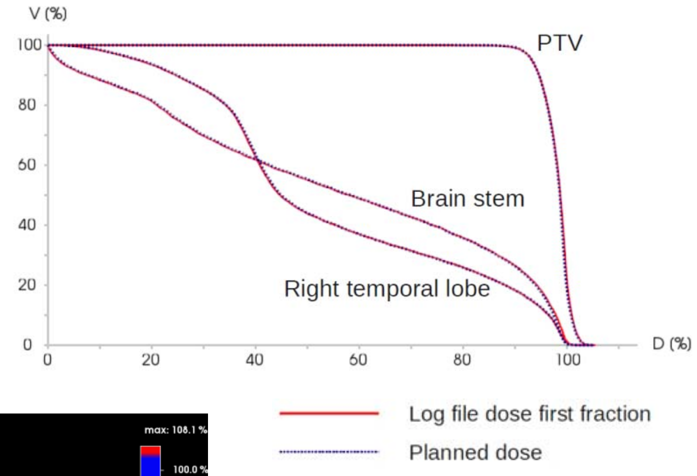
*) Spots > 175 MU

Log files contain important information such as the delivered beam positions that can be analyzed for retrospective QA purposes

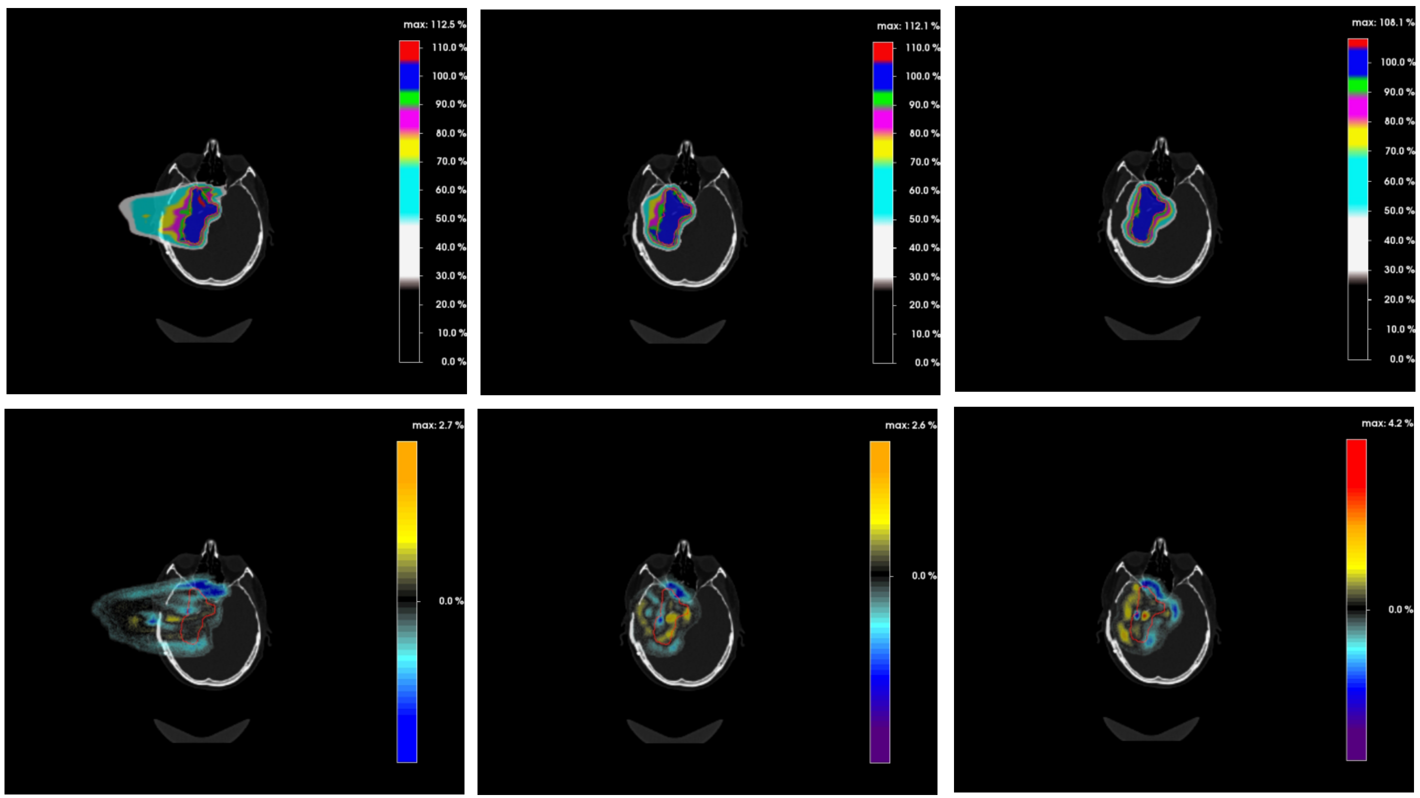
Log files analysis: example II

1st patient, 1st fraction in Gantry 2

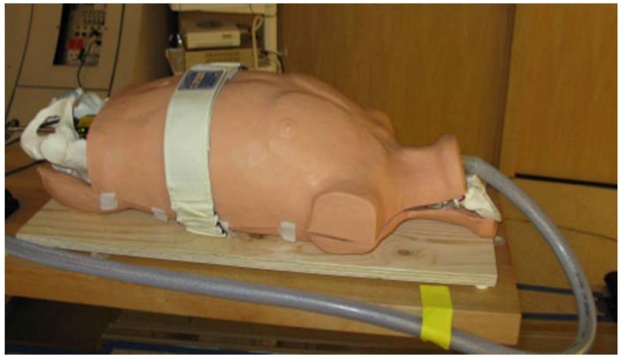
Log files can also be used to calculate the actual delivered dose on a particular day in the patient geometry → the clinical significance of possible delivery errors can then be better assessed



F0 **F1** **F2**

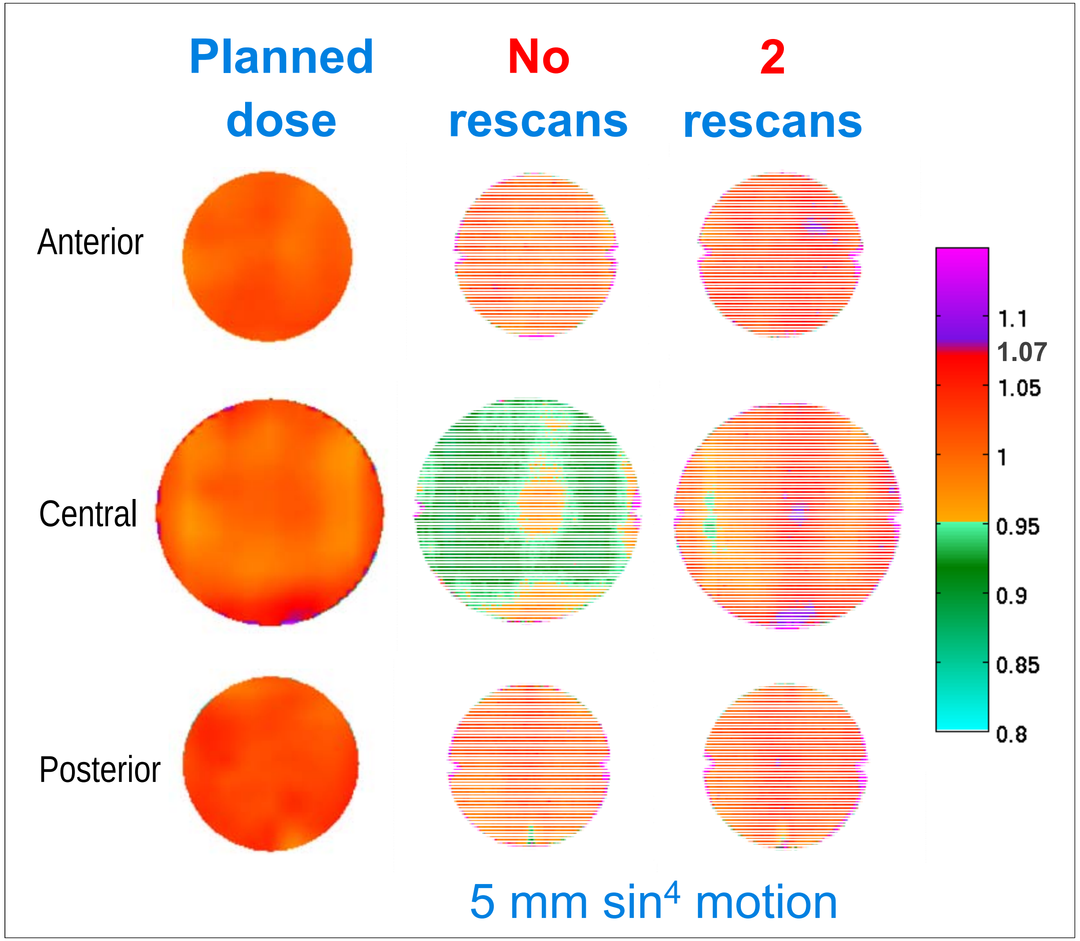


Dosimetric validation of 4D treatments



Phantom features

- Deforming lung with heart insert
- Deformable rib cage
- Skin covering
- “Tumour” target sliced for film insertions (X5)

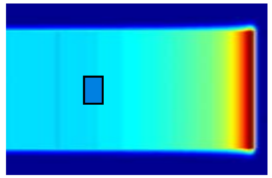
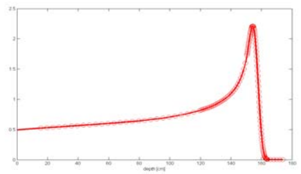
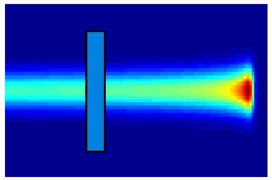
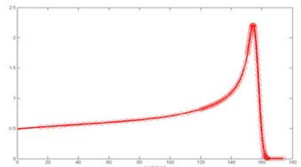


Additional information: dosimetry devices

- Ionisations chambers
- Radiochromics films and scintillating foils
- Semiconductors
- Gels
- Synthetic diamond detectors

Not presented here: TLDs, OSL, Alanine

Ionisation chambers

Device		Application	Note
Point-like chambers			
Cylindrical IC (typical ∅ 2 mm)		Lateral profiles, lateral penumbra	
Plane-parallel chambers			
Small plane-parallel (e.g Markus Chamber)		Bragg peak curves (incl. distal fall-off)	 
Large plane-parallel (∅ ≥ 8 cm)		Bragg peak curves	 

Collects the charge deposited by secondary protons due to nuclear interactions

Pro: - High accuracy and reproducibility
- Very small LET dependence

Con: Corrections for deviation from calibration conditions required

Film dosimetry incl. scintillating foils

Device	Application	Note
Radiochromic films (e.g. EBT3)	• Field geometry and homogeneity • Lateral profiles and penumbra • Beam width	**Pro:** - 2D measurements - High spatial resolution - self-developing - almost linear response below 2 Gy - stacking **Con:** - LET dependence - Complex evaluation - No electronic read-out - No linear response in the range 0 to 10 Gy
Scintillating foils (e.g. Lanex screens)	• Field geometry and homogeneity • Lateral profiles and penumbra • Beam width	**Pro:** - 2D measurements - High spatial resolution - linear response - Easy evaluation - Electronic readout **Con:** - LET dependence - large device

Semiconductors

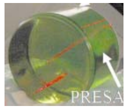
Device	Application	Note
Silicon diodes MOSFET	• Lateral profiles and penumbra • *In vivo* range verification	**Pro:** - High spatial resolution - High signal - Inexpensive - Electronic read-out - Small size **Con:** - LET, dose rate dependence (esp. MOSFET) - Decrease in sensitivity due to irradiation

There is still a lack of systematic studies on semiconductors and published results are to some extend contradictory

Grusell *and Medin*, PMB, **45** (2000) 2573-2582

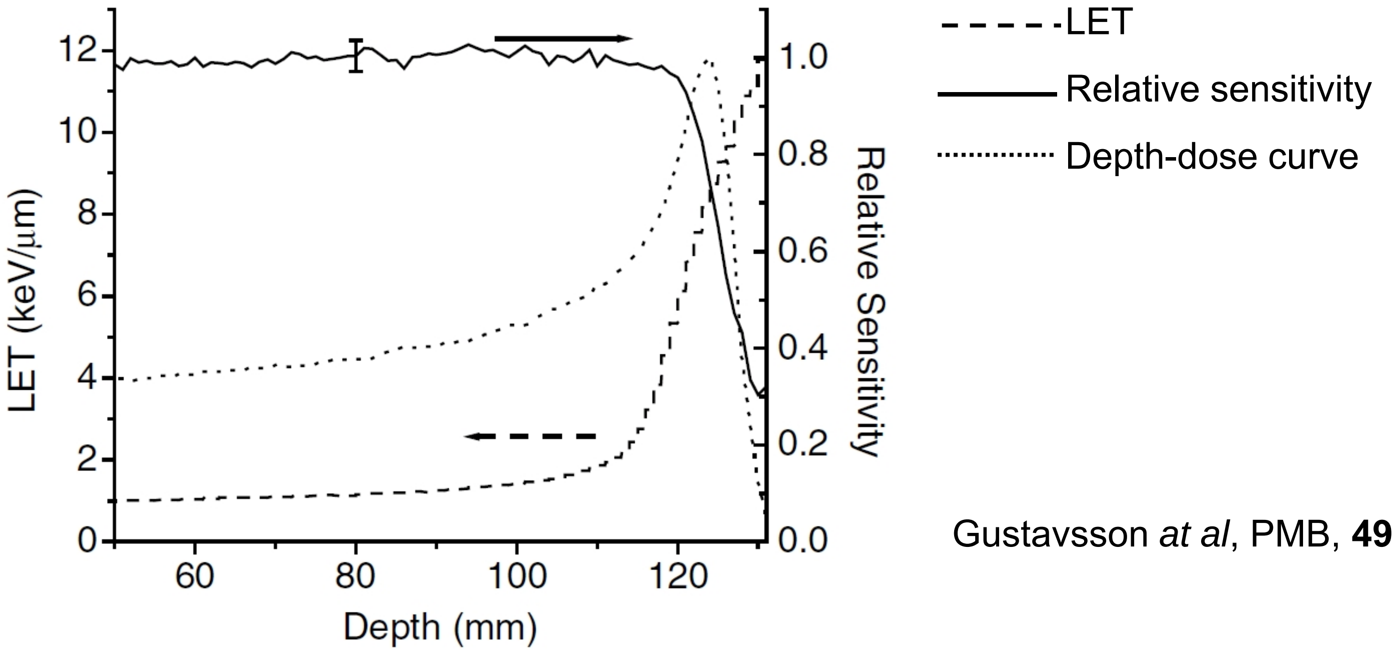
Kaiser *et al.*, Radiat Environ Biophys, **49** (2010) 365-371

3D dosimeters

Device	Application	Note
Polymer gels	3D dose distributions	**Pro:** - High resolution 3D dosimetry - Linear dose response **Con:** - LET dependence - Requires external containers - Difficult off-line evaluation
PRESAGE (solid dosimeter doped with radiochromic components) 	3D dose distributions	**Pro:** - High resolution 3D dosimetry - Linear dose response - Solid dosimeter **Con:** - LET dependence - Off-line evaluation (optical-CT) - Temperature dependence - Sensitive to UV and visible light

So far this kind of detectors are not yet employed routinely in the clinic

LET dependence for gels



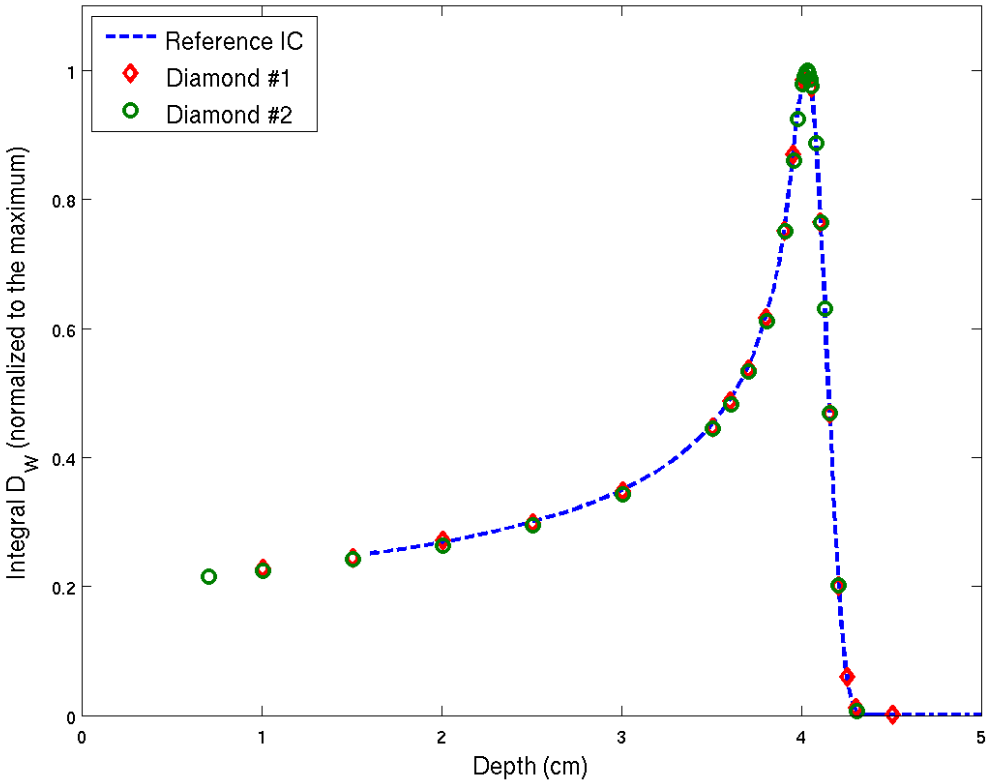
Gustavsson *at al*, PMB, **49** (2004) 3847-3855

Polymer gels under the proton beam

- Quenching in the Bragg peak:
  - underresponse of over 20% → strong LET dependence
- Similar effect with PRESAGE (Al-Nowais et al., *Appl. Rad. Isot.*, **67** (2009), 415-18)

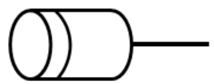
Synthetic single-crystal diamond detector

Integral depth-dose curve for a **70 MeV** beam



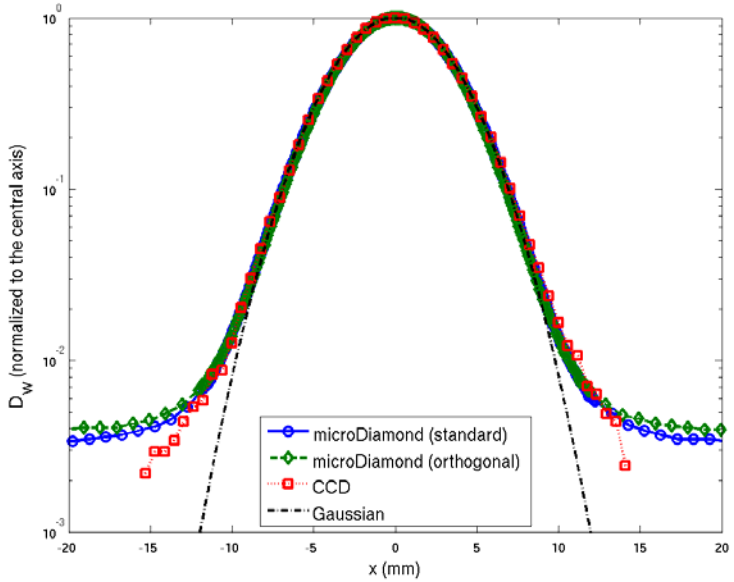
Characteristics

- No quenching (LET) dependence even at low energies
- Linear with dose
- Dose-rate independent



Disc

- 1.1 mm radius
- **1 μm** thickness



Conclusions

Commercial products designed for particle therapy dosimetry are slowly becoming available but more are needed. The integration of these devices with the delivery machine is still unsatisfactory (synchronization of data acquisition with beam delivery and table motion).