

Contrôle de l'hadronthérapie par détection de rayons γ prompts

É. Testa

pour les différentes collaborations " γ prompts"



Creatis

IPNL

LPC

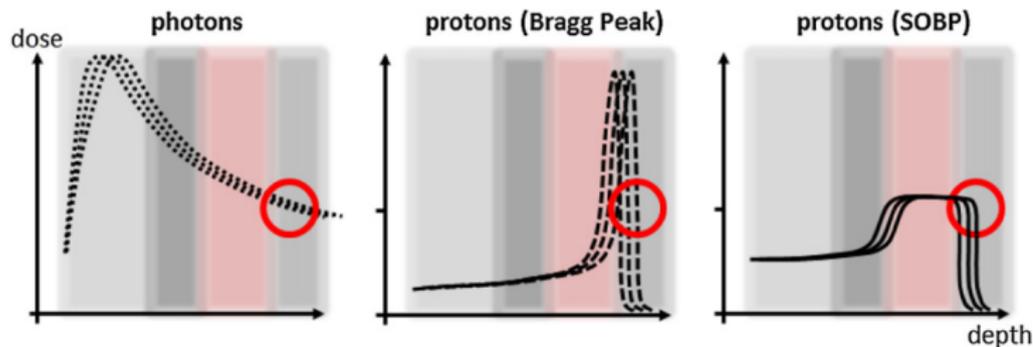
"Projet ProtoBeamLine au CAL"
3 décembre 2014

Outline

- 1 Rationale and principle
- 2 State of the art
- 3 Progress report
- 4 Projects

Ion ranges very sensitive to treatment uncertainties

Sensitivity



Depth-dose profiles with and w/o a density heterogeneity [Knopf PMB 2013]

Sources of uncertainties

Independent of dose calculation

- Organ motion
- Setup and patient variations

Dependent of dose calculation

- Dose calculation approximations
- Biological considerations

A critical issue

Examples of current margins in US

Centers	Margins*
MGH	3.5% + 1 mm
Houston, Loma Linda, Pennsylvania Florida	3.5% + 3 mm
Typical uncertainties w/o MC	2.5% + 1.5 mm
Typical uncertainties w MC	2.7% + 1.2 mm
Typical uncertainties w MC	2.4% + 1.2 mm

* Margins not fully generic. Adjustments are made for certain sites

⇒ Overshoot of 8 mm for a 20 cm range field in soft tissue at MGH!
[Paganetti, PMB 2012]

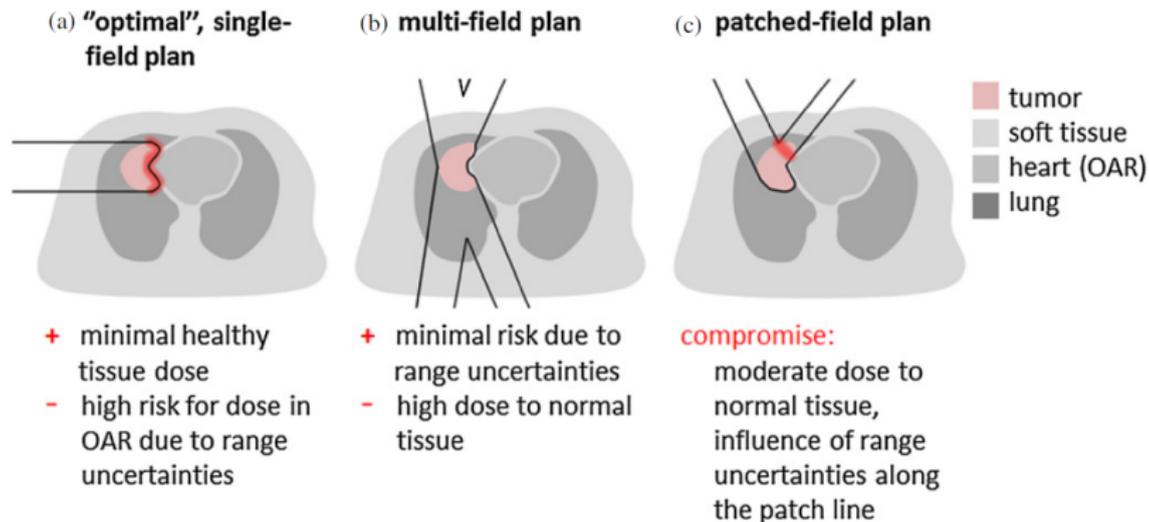
AAPM poll

30% of AAPM delegates considered that ion-range uncertainty is the main obstacle to proton therapy becoming mainstream (AAPM 2012)

Rationale for range verification

Safer treatment delivery

New irradiation fields



[Knopf, PMB 2014]

Prompt radiation monitoring

Emission yields of prompt γ radiation

- $\rightarrow \sim 10$ MeV
- \sim isotropic
- $\ll 10^{-9}$ s

Light charged particles

- \sim same velocity as “their” nucleus

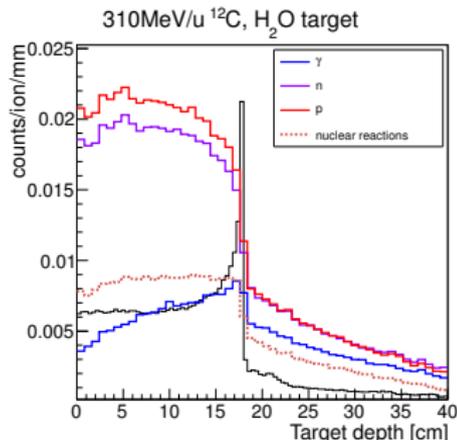
\Rightarrow Prob. to escape from patient:

- ▶ Proj. fragments: high
- ▶ Targ. fragments: very low

First “proof of principle”

- PG: measurements with proton beams [Min, APL 2006]
- Charged particles: simulations with C beams [Henriquet, PMB 2012]

Emission yields (Geant4 9.4)



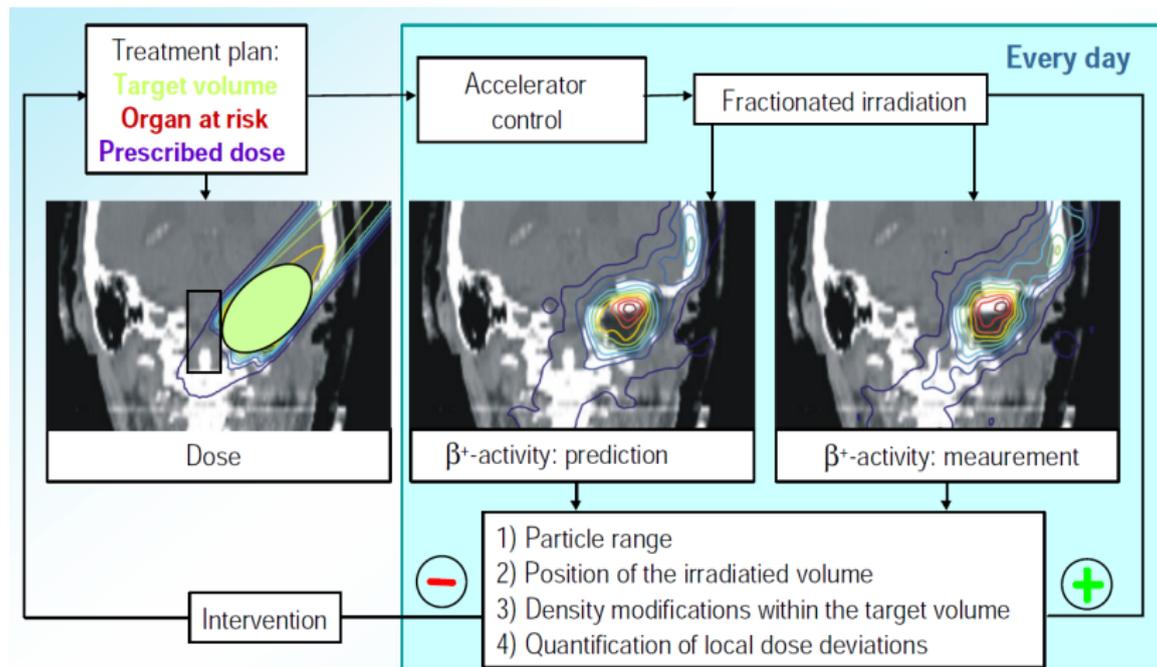
Concept of real time

Number of incident ions per pencil beam and energy slice

	Number of ions (Distal slice)	
	Proton	^{12}C
Beam		
Pencil beam (active delivery)	$\sim 10^8$	$\sim 10^6$
Energy slice (active or passive delivery)	$\sim 10^{10}$	$\sim 10^8$

[Grevillot PMB 2011, Smeets PMB 2012, Kraemer PMB 2000]

Clinical Implementation



Example of PET monitoring [Enghardt ENLIGHT meeting 2003]

- 1 Rationale and principle
- 2 State of the art
- 3 Progress report
- 4 Projects

Collimated cameras

2 kinds of collimated cameras

- **Multi-slit camera:** construction
- **Knife-edge camera:** prototype tested

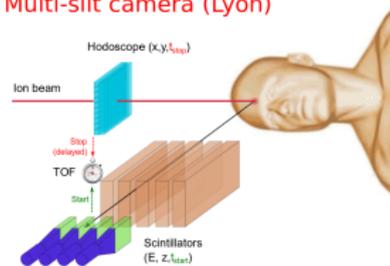
Advantages

- “Simplicity”
- Constant response of the camera along the ion range (multi-slit camera)

Drawback

- Mechanical collimation. . .

Multi-slit camera (Lyon)

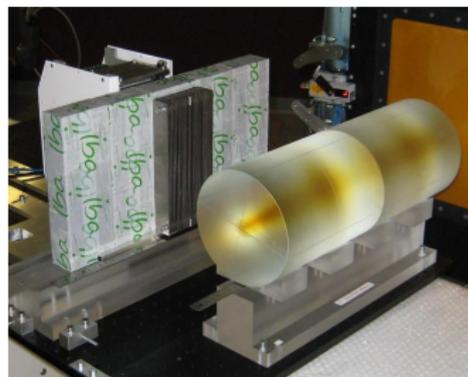


Knife-edge camera (IBA)



Multi-slit cameras without TOF

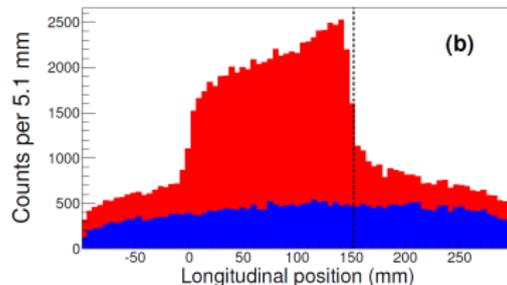
- Seoul
 - ▶ First optimization and measurements with single detector [Min, MP 2012]
 - ▶ Construction of a prototype [Dresden workshop 2014]
- IBA-Lyon [Roellinghoff, Patent 2014]
 - ▶ Collimator optimization on falloff retrieval precision (*FRP*)
 - ▶ LYSO detectors
 - ▶ Expected precision: $\sigma \sim 1$ mm
 - at a pencil beam scale (10^8 protons)
 - for a 20 cm height
 - ▶ **Spatial resolution**: Falloff Width (*FW*) ~ 15 mm



IBA test of a small size camera

Multi-slit cameras with TOF

- Delft (Project)
- Lyon [Pinto PMB 2014]
 - ▶ Collimator optimization on falloff retrieval precision (*FRP*)
 - ▶ BGO detectors
 - ▶ Expected precision: $\sigma \sim 1$ mm
 - at a pencil beam scale (10^8 protons)
 - for a 20 cm height
 - ▶ Spatial resolution: $FW \sim 8$ mm

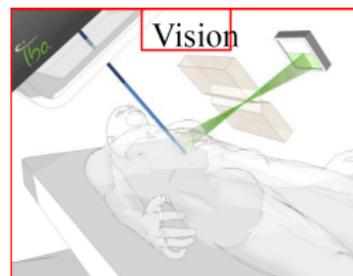


Profile obtained with an optimized TOF camera for 4×10^9 protons [Pinto, PMB 2014]



Knife-edge cameras

- Seoul [D. Kim, JKPS 2009]
 - ▶ First measurements and simulations
- Delft [Bom, PMB 2012]
 - ▶ Precision ~ 1 mm for single spot
- IBA
 - ▶ Prototype optimization [Smeets, PMB 2012]
 - $FRP \sim 1$ mm at a pencil-beam scale
 - ▶ Current status: Validated with IBA's C230 cyclotron [Perali, PMB 2014]
 - ▶ Studies with anthropomorphic phantoms in progress



Knife-edge camera (IBA)



IBA prototype

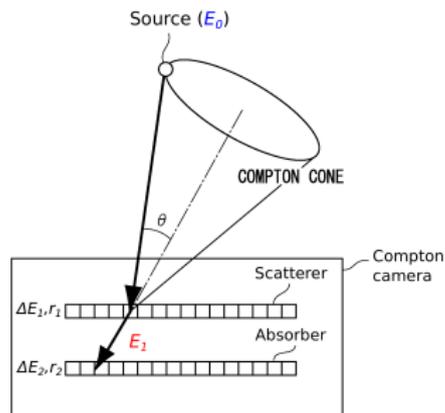
Compton camera: Basic principle

Physics

- Det.1: Compton scattering (scatterer)
- Det.2: 2nd interaction (absorber)

Compton scattering formula

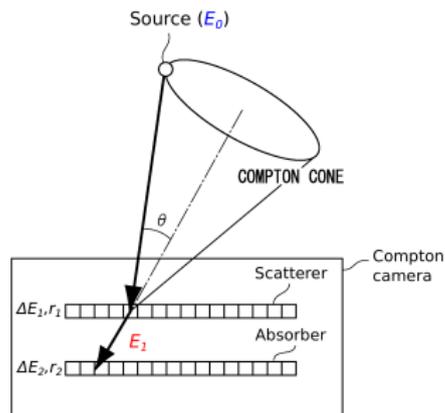
$$\cos \theta = 1 + m_e c^2 \left(\frac{1}{E_0} - \frac{1}{E_1} \right)$$



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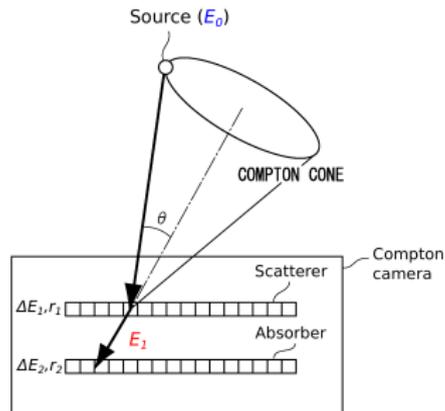
Absorption or not absorption?

Source	Known	Unknown
E_0	known	$E_0 = \Delta E_1 + \Delta E_2$
E_1	$E_0 - \Delta E_1$	$E_1 = \Delta E_1 + \Delta E_2$
Absorption	Not required	Required

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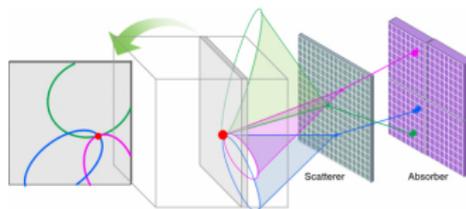
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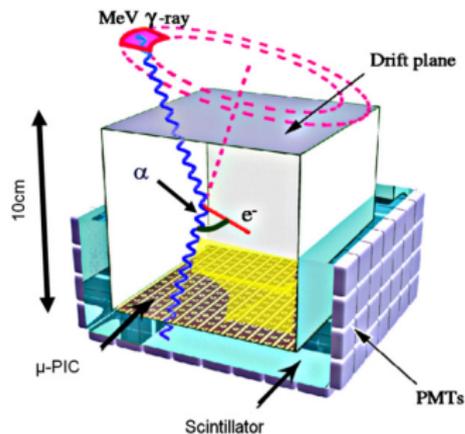
Source reconstruction



Some specific Compton cameras

Electron Tracking Compton Camera

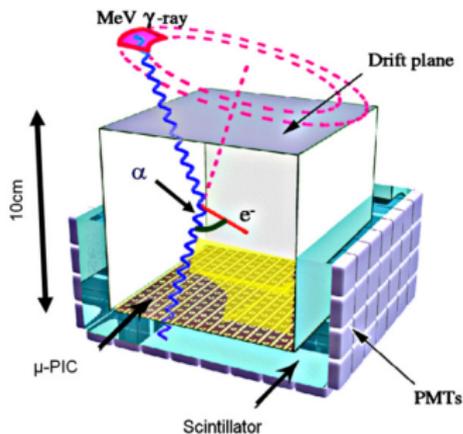
- Tracking of the Compton electron
- ⇒ Reconstruction of a line along the cone



Some specific Compton cameras

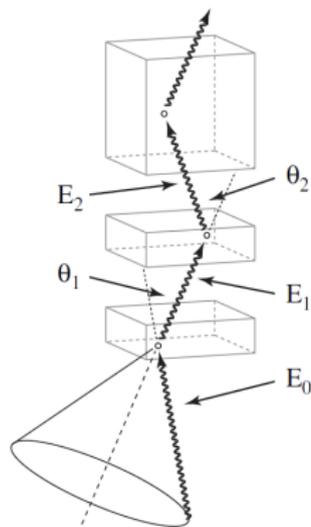
Electron Tracking Compton Camera

- Tracking of the Compton electron
- ⇒ Reconstruction of a line along the cone



3-stage camera

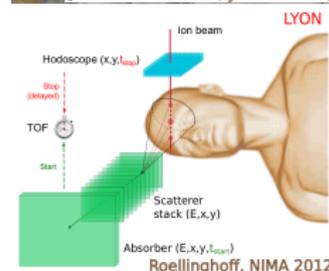
- **No need for a full absorption** in the absorber



Examples of Compton Cameras

Dedicated CC for hadrontherapy monitoring

Group	Scatterer	Absorber	Abs. size (mm)	Status
Valencia	LaBr ₃	LaBr ₃	~ 30	Components tested
Dresden	CdZnTe	LSO	~ 30	Components tested
Lyon	Si	BGO	~ 300	In development



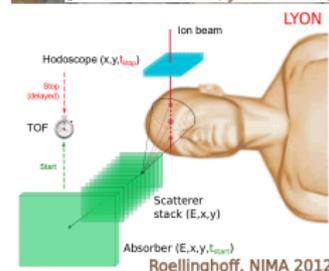
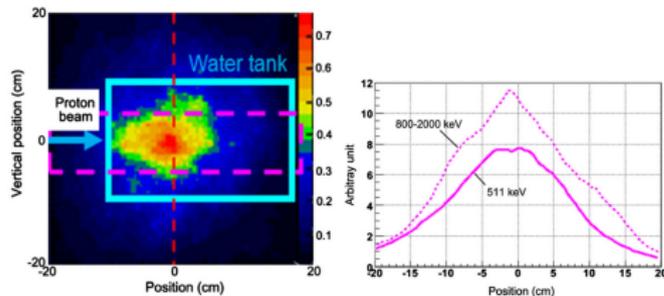
Examples of Compton Cameras

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Non-dedicated CC

- Electron Tracking Compton Camera
- First PG measurements with 2.5 pA p beam



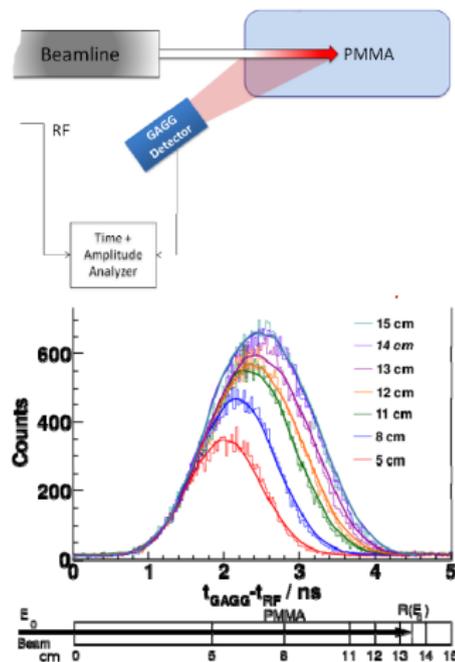
Prompt Gamma Timing

Principle

- PG TOF spectrum depends on ion range
 - ▶ Ion path in the target
 - ▶ PG travel from the emission to the detector

Experimental results

- KVI-CART Groningen
- Stacked PMMA target from 5 to 15 cm
- Measurement of **2 mm range deviation within few seconds**



[Golnik, PMB 2014]

Prompt Gamma Spectroscopy

Principe

- Unique correlation between proton energy and nuclear reactions

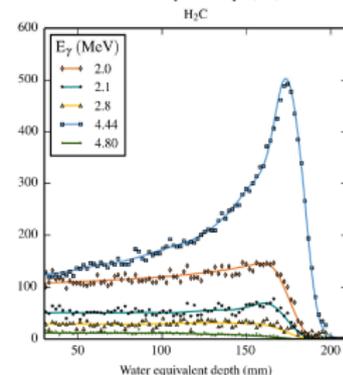
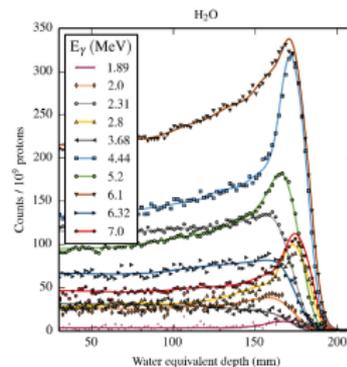
⇒ Determination of:

- ▶ Absolute water equivalent depth at detector position
- ▶ Elemental composition of irradiated tissue

Experimental results

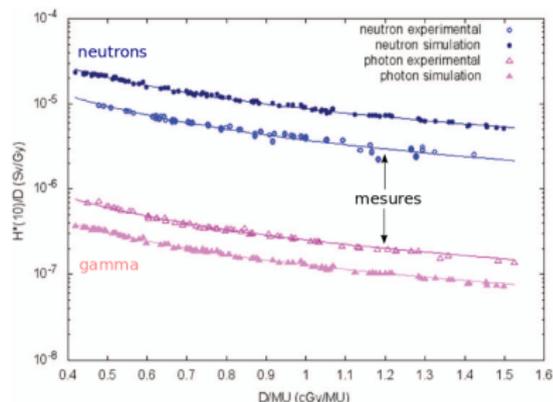
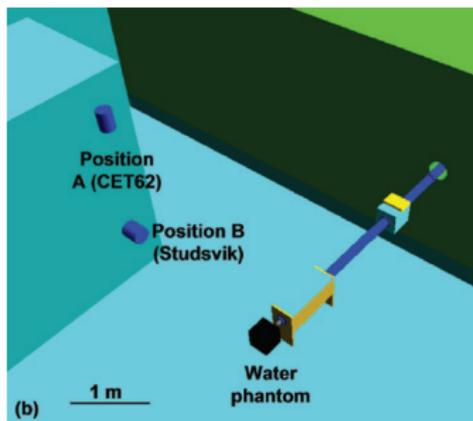
- Single collimated detector at the end of PG profiles
- Millimetric precision on proton range at \sim pencil beam scale

[Verburg PMB 2014]



Principe du contrôle de l'énergie déposée dans le patient

Première étude effectuée au CAL [Carnicer Med. Phys. 2012]



- Détecteur γ (A) : Grande chambre à ionisation
- Détecteur neutron (B) : BF_3

- $H^*(10)$: dose ambiante
- D : dose déposée dans le pic de Bragg
- MU : “unités moniteur”

Première étude effectuée au CAL : résultats

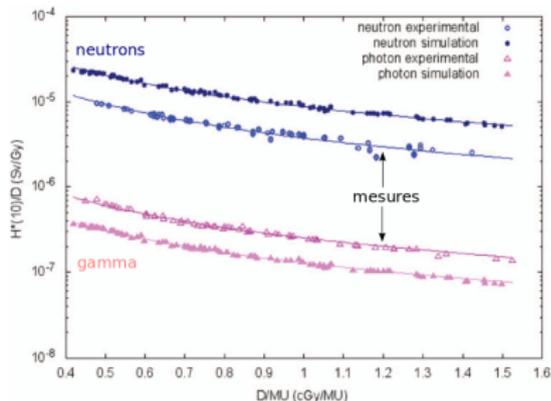
Résultats expérimentaux

- 66 mesures γ
- 177 mesures neutron
- Reproductib. de quelques %

⇒ Application clinique avec un seuil de détection de 5%

Résultats de simu (MCNPX)

- $H_{\gamma}^*(10)$ sous-estimée d'un facteur 2
- $H_n^*(10)$ sur-estimée d'un facteur 2
- Bonne description des variations de $H^*(10)$



- $H^*(10)$: dose ambiante
- D : dose déposée dans le pic de Bragg
- MU : “unités moniteur”

Conclusion (1/2)

Ion-range monitoring (collimated cameras)

- **Homogeneous** targets
 - ▶ p: pencil basis
 - ▶ C: energy-slice basis
- Heterogeneous targets
 - ▶ Studies under progress

Collimated cameras

- **First prototype tested in clinical conditions** (knife-edge IBA)
- Multi-collimated cameras: similar performances

Conclusion (2/2)

Compton cameras: Challenging but dynamic R&D

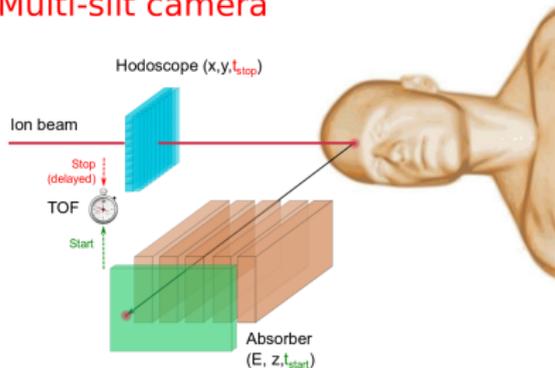
- High counting rates
- ++ Spatial resolution, 2D/3D imaging
 - Lower beam intensities may be required

Accelerator-dependent devices

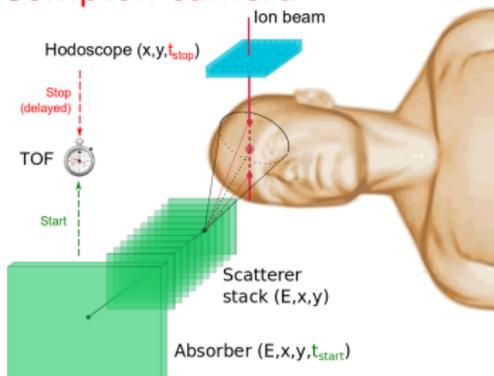
- Count rates
- TOF

Multi-slit and Compton cameras

Multi-slit camera



Compton camera



Common developments

- Absorber (Clermont)
- Hodoscope
- μ TCA acq. system (Marseille)
- Acq. software

Specific developments

- Scatterer
- Collimator

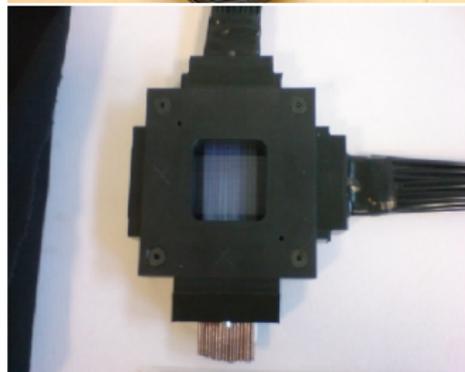
Hodoscope: 2 prototypes

Goals

- Position resolution: 1 mm
- Time resolution: 1 ns
- Count rate: 10^8 Hz

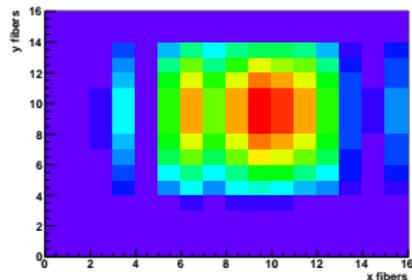
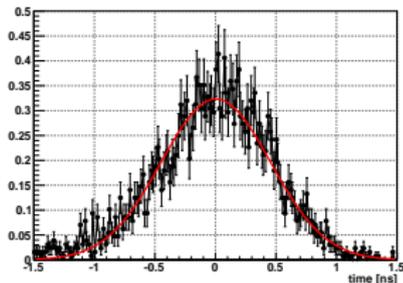
Prototypes

- array of scintillating fibers
(1×1 mm² BCF 10/12)
- prototypes: 2×32 and 2×128
fibers
- readout: optical fibers FORETEC
- coupling to multianode PM
H-8500



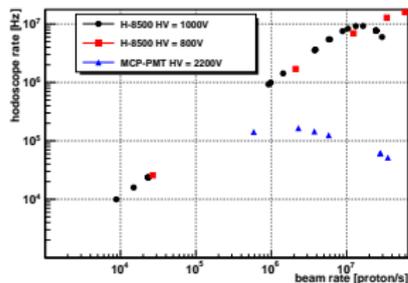
Performance tests

- GANIL: 75 MeV/u ^{13}C , IPN Orsay: 25 MeV protons
- time reference: cyclotron HF \Rightarrow time resolution 1 ns FWHM



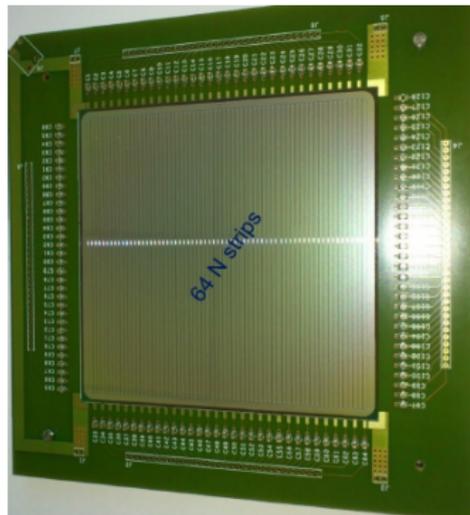
- Counting rate > 10 MHz at 800 V

[Krimmer et al. ICTR-PHE 2014]



Scatterer

- double sided **silicon strip** detectors
- size: $90 \times 90 \times 2 \text{ mm}^3$
- **7 planes** in total
- **2×64 strips**
(p- and n-side)
- bias voltage **-750 V**
(full depletion)
- **bonding** of detectors
at IPNL
- **PCB**: polarization resistors
decoupling capacitors
- **Front-end electronics**: dedicated
ASIC (under test)
[M. Dahoumane et al. IEEE NSS
MIC 2014]



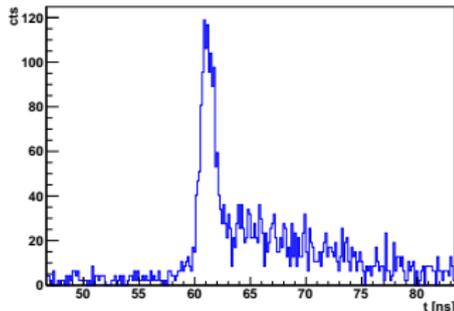
detector under characterization

Components: absorber

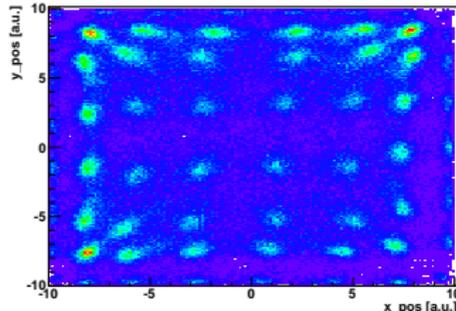


- streaked BGO crystals $35 \times 38 \times 30$ mm³ read by 4 PMs
- 8×8 (pseudo)-pixel, 96 crystals in total
- energy resolution 17% at 511 keV, time resolution 2 ns
- detector assembly and readout electronics (ASM boards): Clermont

BGO0 TDC 2d_cut_fore_perion 0



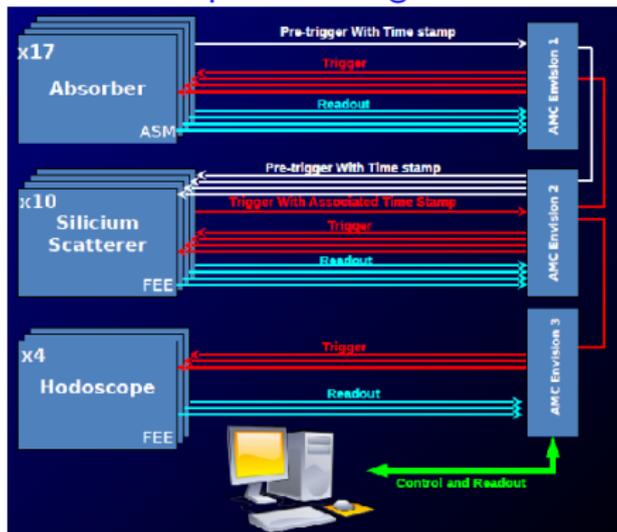
BGO2 2D cut perion



[J.K. et al. NDIP 2014, submitted to NIM A]

Fast DAQ system: μ -TCA

acquisition diagram



[C. Abellan ICTR-PHE 2014]

μ -TCA crate



AMC board (CPPM)



Le projet "GammaDosi"

But

- Amélioration de la technique développée par Carnicer et al. :
information **plus précise** et **en temps réel**
- Idée : Détection des **rayonnements** prompts provenant du patient grâce
à une sélection de TOF

⇒ Mesures, simulations et développement d'un prototype

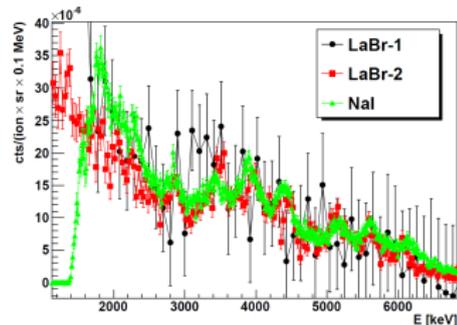
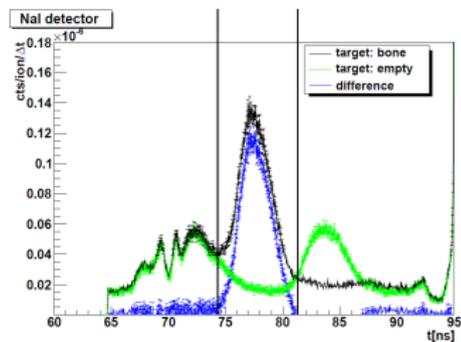
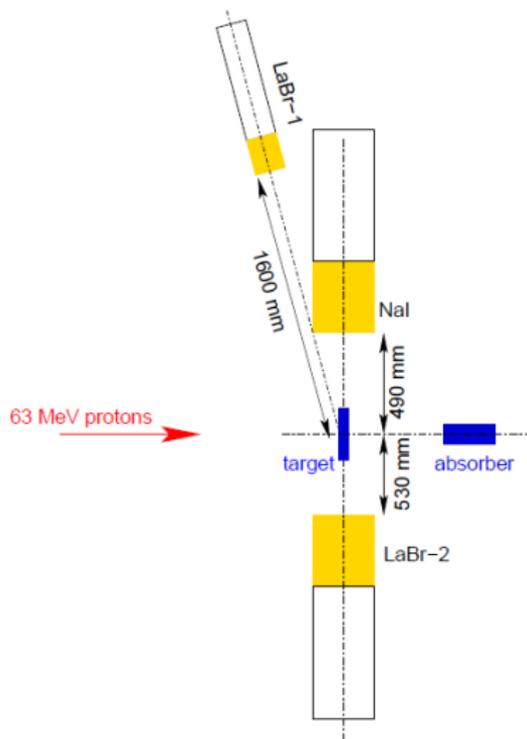
Projet Physique Cancer

- Partenaires: IPNL, CREATIS et CAL
- Période: 1/12/2013 - 30/11/2015

Mesures

- 4 expériences (WPE, HIT, GANIL, CAL)

p de 63 MeV (CAL) : spectres en énergie et TOF



Conclusion

Caméras γ prompts (+ hodoscope)

- Développement de 2 modalités avec des éléments en commun (absorbeur, hodoscope, acquisition)
- Première version de caméras:
 - ▶ Collimatée: fin 2015
 - ▶ Compton: mi-2016

Contrôle de l'énergie déposée dans le patient (GammaDosi)

- Prototype : mi-2015

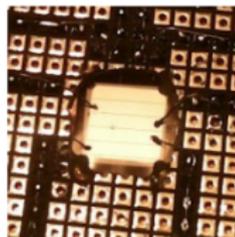
Projet MoniDiam: Contexte

- Hodoscope à fibres de 2 mm d'épaisseur : peut être limitant
 - Photomultiplicateurs: taux de comptage par voie limité ($< 10^7$ Hz)
 - Résistance aux radiations OK ($> 10^{12}$ carbone/cm²)
 - Résolution temporelle OK (< 1 ns)
- ⇒ Solution alternative: Diamant polycristallin

Performances actuelles

Travaux entrepris dans le cadre du projet Gamhadron

- Détecteurs de petites tailles fournis par le CEA LIST



Final configuration:

1x1 cm² EG pcCVD diamond (500 μm thick), Al 1.8 mm 4(X)x4(Y) strips with 100 μm pitch

Performances

- Résolution temporelle 100 ps
- Efficacité 100% avec protons 25 MeV
- Taux de comptage 100 MHz par strip

Cadre et objectifs du projet

Cadre

- Projet en cours (2015), collaboration IPNL, LPSC et CHU Grenoble
- Projet collaboratif : prises de contact avec d'autres laboratoires

Objectifs

- Test sur détecteurs commerciaux (Element 6)
- Cahier des charge pour la réalisation d'un moniteur de grande taille
 - ▶ Nécessité d'un trigger faisceau à chaque pulse, pour chaque énergie
 - ▶ A intensité réduite (1 proton/bunch): timing à 100 ps
 - ▶ Mode intégration (mesure du flux)
 - ▶ Electronique dédiée

Projet Physique Cancer "SPECTCO"

Soumission

Novembre 2014

Objectifs

- Développement d'un algorithme de reconstruction 4D (image spectrale) pour la caméra Compton
- ⇒ Prise en compte des absorptions partielles des photons dans la caméra
- Évaluation de l'apport de cette reconstruction sur la mesure du parcours des ions
- Prise de données en labo (sources radioactives) et sur faisceau (CAL) avec le prototype de caméra

Projet européen “Galn”

Soumission

- Appel à projet PHC-11 (H2020)
- Octobre 2014

Objectifs

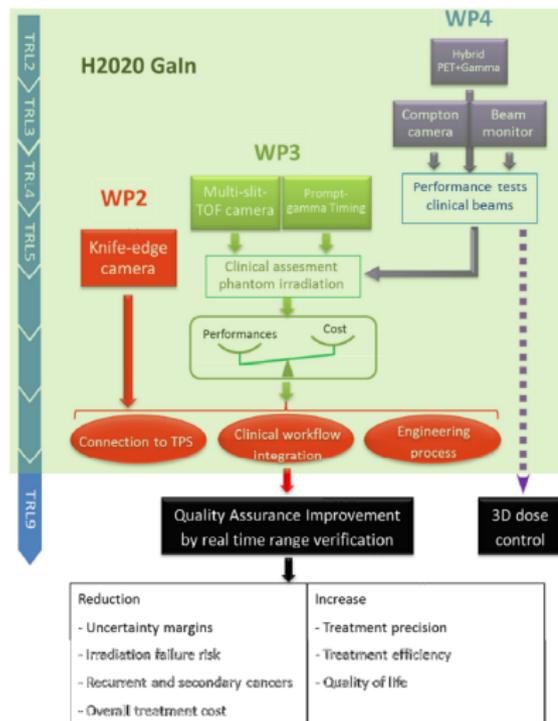
- Transfert vers le clinique des prototypes d’imageurs gamma prompts
- Évaluation sur faisceaux cliniques de détecteurs de “prochaines générations” (PGT, mutli-slit camera)
- Projet orienté vers le développement industriel

Consortium

Participant No.	Participant organisation name	Country
1 (coordinator)	University Hospital Dresden - UKD	Germany
2	Helmholtz-Centre Dresden-Rossendorf - HZDR	Germany
3	Centre national de la recherche scientifique - CNRS	France
4	Ion Beam Applications - IBA	Belgium
5	Institute of Corpuscular Physics - IFIC	Spain
6	Technical university of Munich - TUM	Germany
7	Université catholique de Louvain - UCL	Belgium
8	Politecnico Milano - POLIMI	Italy
9	Centro Nazionale do Adrotherapia Oncologica - CNAO	Italy
10	University hospital Heidelberg - HIT	Germany
11	Target Systemelektronik GmbH & Co. KG - TAR	Germany
12	Scionix Holland BV - SCI	The Netherlands
13	XGLab S.r.L. - XGL	Italy
14	AIMA S.A. - AIM	France
15	Centre Antoine-Lacassagne - CAL	France

CNRS : 3 post-doc de 12 mois (IPNL, CPPM, CREATIS)

Workpackages



Mesures à Nice

- Caractérisation des dispositifs sur faisceau
 - ▶ Caméras gamma et GammaDosi
 - ▶ Cibles homogènes et hétérogènes “simples”
- Performance des dispositifs sur le S2C2
 - ▶ $\sim 10^4$ protons par paquets de ~ 8 ns toutes les ~ 15 ns
 - ▶ Extraction de quelques dizaines de μ s toutes les 1 ms
- Mesures sur fantômes anthropomorphiques
 - ▶ Application d'une planification de traitement
- Mesures avec fantôme déformable
 - ▶ Collaboration avec le LIRIS sur la modélisation biomécanique du mouvement des organes

Thank you for your attention

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IPN Lyon

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 - ▶ M. Pinto (PhD)
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 - ▶ Y. Zoccarato
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Collaborators

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 - ▶ E. Hilaire (PhD)
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- LPC Clermont
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 - ▶ I. Rinaldi
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 - ▶ D. Prieels
 - ▶ J. Smeets

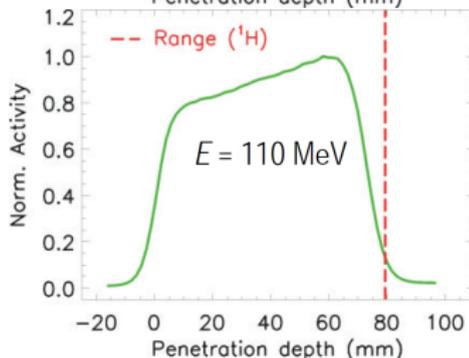
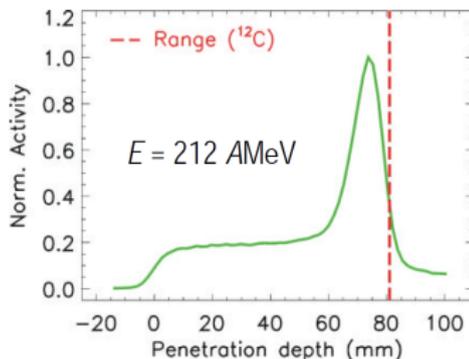
PET monitoring

Cross sections [Enghardt ENLIGHT meeting 2003]

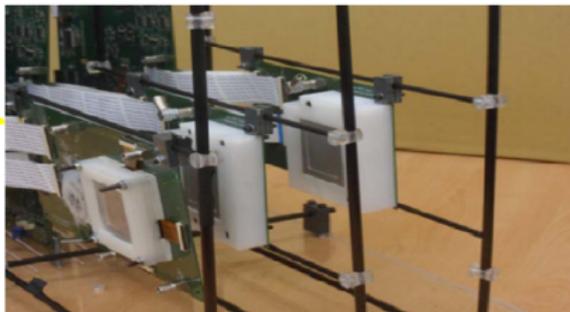
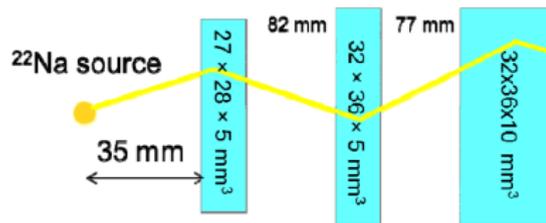
Beam	Reaction	σ (mb)	$T_{1/2}$
^{12}C	$(^{16}\text{O}, \text{X})^{15}\text{O}$	84	2 min
	$(^{12}\text{C}, \text{X})^{11}\text{C}$	56	20 min
	$(^{12}\text{C}, \text{X})^{10}\text{C}$	5	20 s
^1H	$(^{16}\text{O}, \text{pn})^{15}\text{O}$	50	2 min
	$(^{12}\text{C}, \text{pn})^{11}\text{C}$	40	20 min
	$(^{12}\text{C}, \text{p2n})^{10}\text{C}$	2	20 s

“Ion range – β^+ activity” correlation

- β^+ emitters have \sim same velocity as “their” nucleus
- \Rightarrow ^{12}C : peak with projectile-like emitters
- \Rightarrow p : no peak (target-like emitters)



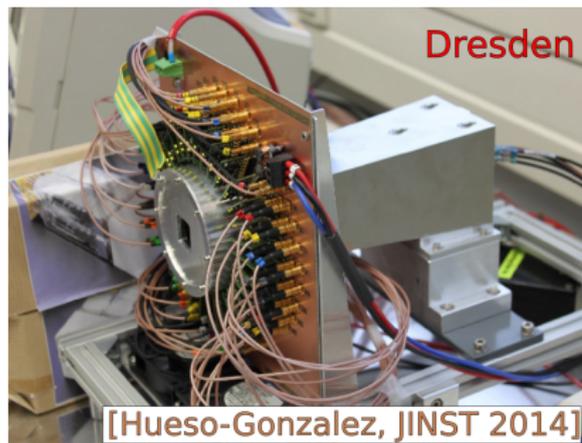
Compton camera: Valencia



[Llosa, NIMA 2012]

- 2 or 3 stages
- LaBr_3 crystals readout with SiPM ($\sim 30 \text{ mm} \times 30 \text{ mm} \times 5$ or 10 mm)
- Prototype components tested with sources

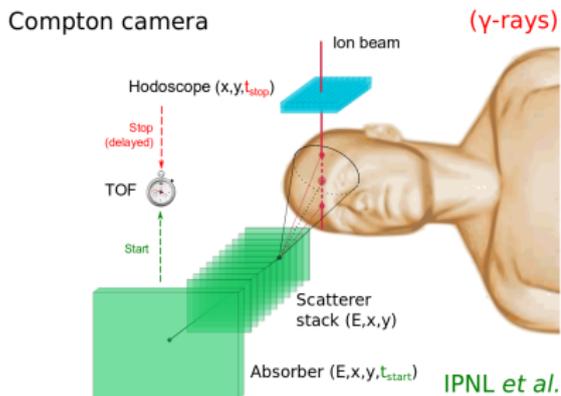
Compton camera: Dresden



[Hueso-Gonzalez, JINST 2014]

- 2 stages
- Scatterer: CdZnTe (20 mm×20 mm×5 mm)
- Absorber: LSO (52 mm×52 mm×20 mm) (PET block detector)
- Prototype components tested at 1-14 MeV Bremsstrahlung beam (ELBE)

Compton camera: Lyon

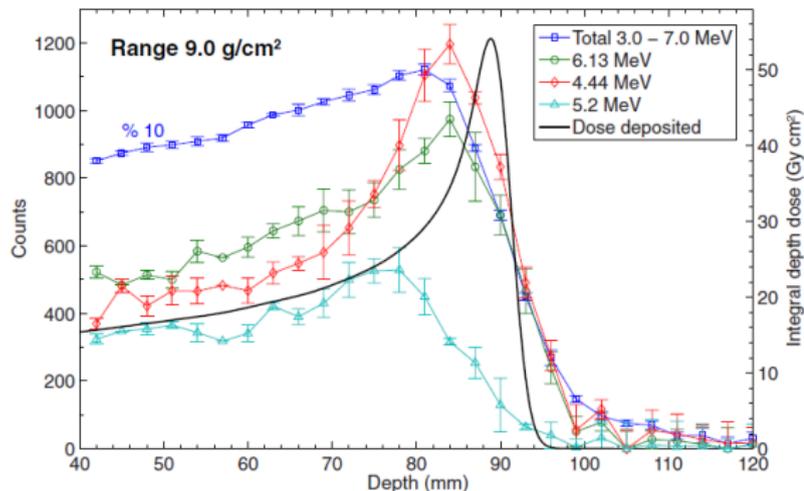


[Roellinoff NIMA 2011]

- 2 stages
- Scatterer: Double-Sided Silicon Detectors (90 mm \times 90 mm \times 2 mm)
- Absorber: BGO (380 mm \times 380 mm \times 30 mm)
- Large size camera in development

PG profiles vs γ -lines

110 MeV protons in H₂O [Verburg, PMB 2013]



⇒ Profiles strongly depend on γ -lines

PG profiles vs type of incident ions (p, C)

γ yields above 1 MeV in 4π

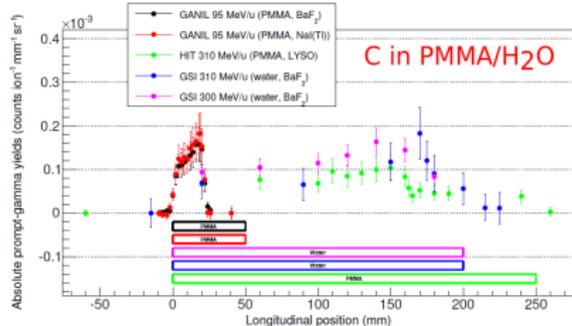
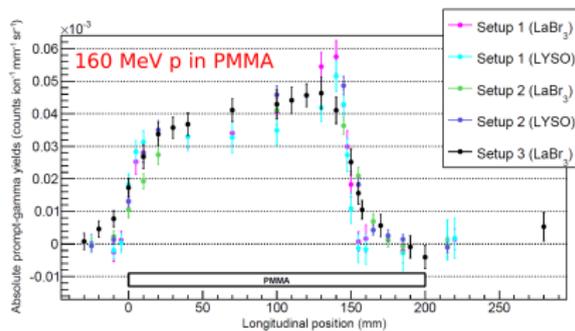
- p: 0.3%/cm per proton
- C: $\sim 2\%$ /cm per carbon

Material influence

$$T(\text{PMMA}) \sim \frac{3}{4} \times T(\text{H}_2\text{O})$$

Other measurements

- p: Seoul [Min, APL 2006], IBA [Smeets, PMB 2012], Texas Univ [Polf, PMB 2013]
- C: Lyon [M. Testa, REB 2010] INFN [Agodi, JINST 2011]



[Pinto, submitted to PMB]

PG modeling: code benchmarking

- General purpose codes vs dedicated nuclear reaction codes

[Verburg, PMB 2012]

- ▶ Variation up to factor 2

- Geant4/GATE vs FLUKA

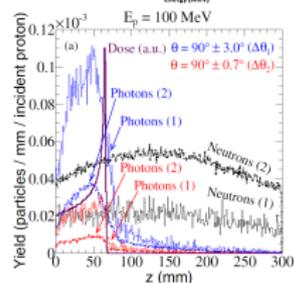
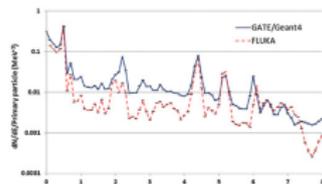
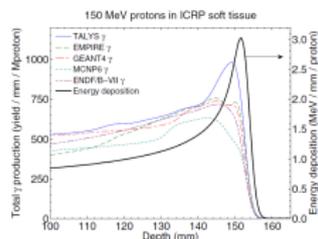
[Robert, PMB 2013]

- ▶ $T(\text{Geant4}) \sim 2 T(\text{FLUKA})$

- Geant4 vs MCNPX

[Biegun, PMB 2012]

- ▶ $T(\text{Geant4}) \sim 2 - 3 T(\text{MCNPX})$



Prostate treatment planning

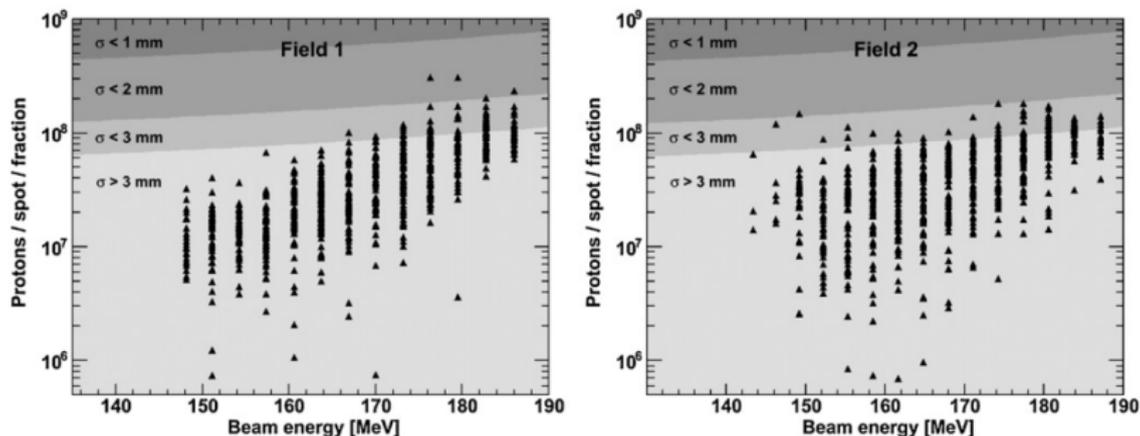


Figure 19. Beam energy and number of protons of every spot of a two-field prostate treatment plan delivered in pencil beam scanning mode in fractions of 2 Gy (Grevillot *et al* 2011). The grey-coloured regions indicate the standard deviation σ of range estimation by the current slit camera solution at 25 cm distance from the beam axis as a function of beam energy and number of protons.

[Smeets PMB 2012]