Prompt gamma imaging
for proton and carbon therapy

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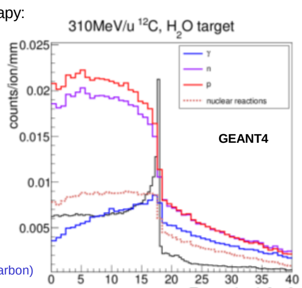
Outline

Basic features:
- prompt radiation production by nuclear reactions
- prompt gamma yields
  - Measurements
  - Simulations

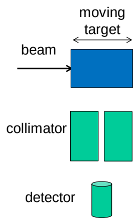
Online control with prompt gammas
- range verification
  - passive collimation systems
  - Time of Flight issue
  - active collimation: Compton cameras
  - no collimation: gamma-timing
- target composition: spectral information

Nuclear fragmentation

- Dose deposition during radiotherapy:
  - Ionization
- Hadrontherapy:
  - Nuclear fragmentation
    - High probability
    - Influence on dose deposition
    - Secondary particles
      - γ, *n*, *p*, fragments
      - Radioactive Isotopes (β^+)
  - Range control by means of nuclear reaction products:
    - β^+ annihilation (K. Parodi)
    - Secondary protons (only carbon)
    - **Prompt gamma**
      - ≤ 1 per nuclear reaction
      - ~ isotropic emission
      - Massive particles: background



Prompt gamma measurements
with collimated detectors



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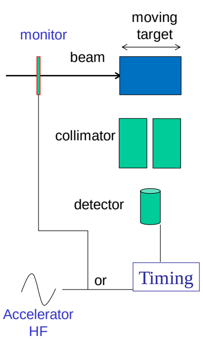

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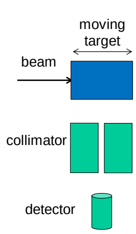
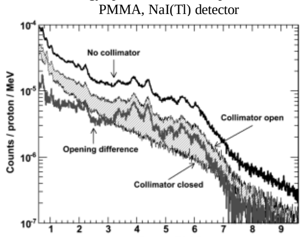


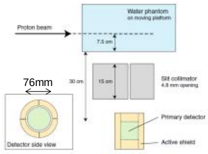
Energy spectrum 160 MeV protons in PMMA, NaI(Tl) detector



Smeets PMB 2012

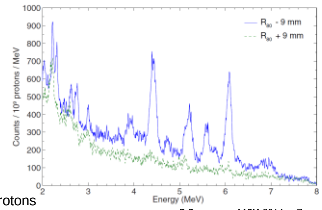
Energy: <1 MeV to 10 MeV
A small fraction is measured as discrete lines
Low energy gammas: larger scattered fraction
Synchronization with accelerator HF or monitor: Time of Flight

Fast timing and high energy resolution measurements



J. Verburg, PMB 2013
Talk WE-D-BRF-3

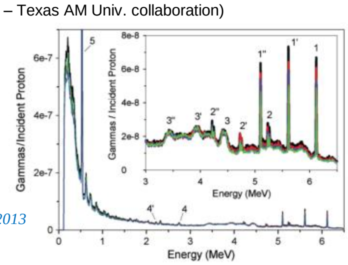
- Fast timing (2ns window)
- High spectral resolution
  (Large volume LaBr + Compton rejection BGO)
- Spatial resolution (~1cm FOV)



→ 10 – 100 counts/ peak for 10^9 protons

Monitoring the tissue composition
(Oklahoma – Texas AM Univ. collaboration)

- Experiment:
  - 48 MeV protons
  - Water target with various sucrose quantities
  - HP-Ge detector
    (ε ~10^{-5} – 10^{-6})

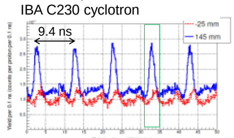


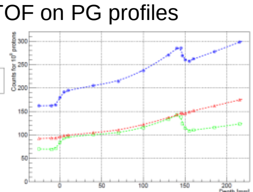
Polf, PMB 2013

- Result
  - 6.13 MeV oxygen gamma-lines proportional to oxygen concentration
  - Monitoring tissue oxygenation
- Comment
  - No spatial information (tumour vs healthy tissues)

Influence of TOF on PG profiles

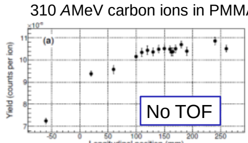
160 MeV protons in PMMA
IBA C230 cyclotron

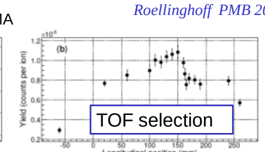




Roellinghoff PMB 2014

310 *A*MeV carbon ions in PMMA



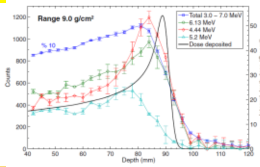


TOF : mandatory for carbon ions

M. Pinto, submitted New J Phys

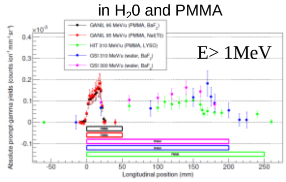
Prompt gamma measurements

110 MeV protons in water



J.Verburg, PMB 2013

95, 300, 310 MeV/u carbon in $H_2$0 and PMMA



M.Pinto, submitted New J Phys

PG yield above 1 MeV : ~ 0.3% /cm per proton ~ 2% /cm per carbon

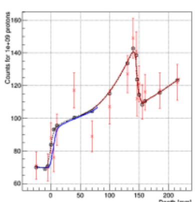
Other measurements (profiles and/or energy spectra):

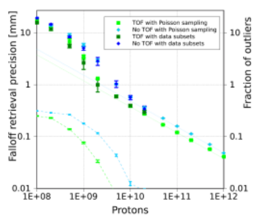
- **Protons:** Seoul (*Min, APL 2006*), IBA (*Smeets, PMB 2012*), Lyon (*Roellinghoff, PMB 2014, Pinto NJP (submitted)*), Texas Univ (*Polf, PMB 2009, PMB 2013*)
- **Carbon:** Lyon (*Testa REB 2010*), INFN (*Agodi, JINST 2011*)

+ astrophysics γ lines

Fall-off retrieval precision

160 MeV protons in PMMA
IBA C230 cyclotron

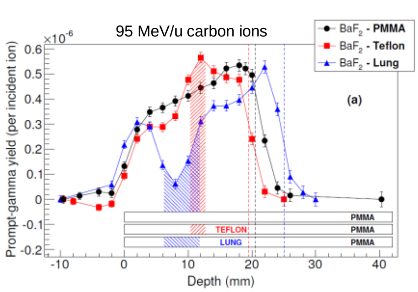




Measurement with single (small) detector
Real clinical detector 10 times more efficient → millimetric precision for a distal spot

Roellinghoff PMB 2014

Prompt gamma yields: heterogeneous targets



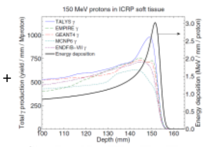
High resolution profiles: influence of heterogeneities close to the Bragg peak

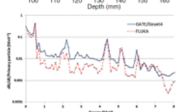
M. Pinto et al, submitted to Med Phys

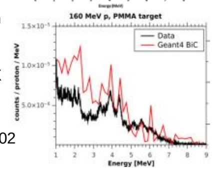
PG models benchmarking

Protons:

- *Verburg, PMB 2012*: comparison of simulation codes Geant4.9.5, MCNP6, TALYS, EMPIRE, + ENDF/B-VII library
  - Dedicated codes more precise
  - Variation up to factor 2
- *Robert, PMB 2013*: comparison Geant4/GATE and FLUKA
- *Dedes, PMB 2014*: Geant 4.9.4 – IBA data
  - Geant4-BIC overestimates by factor ~1.7 at 50 cm depth for 160 MeV protons in PMMA
- *Smeets, PMB 2012*: comparison data-MCNPX
  - Satisfactory agreement, except background
- *Biegun, PMB 2012*: Comparison Geant4.9.2p02 and MCNPX







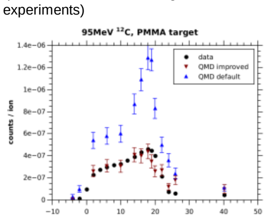
PG models benchmarking

Carbon ions:

Dedes, PMB 2014: comparison data with GEANT4.9.4, QMD model for nucleus-nucleus collisions

- Overestimation of PG yields by factor 2-3
- QMD tuning (free parameters : wave packet width and clustering size, adjusted according to fragmentation experiments)

Agreement at low energy (95 MeV/u)
High energy: overestimation by factor ~ 1.5 (proton, neutron contributions)



Online control with prompt gammas

What do we want ?

Online control with prompt gammas

What do we want ?

- Range verification with mm accuracy
  - For single pencil beam spot (distal)
    - Protons: 10^8 particles
    - Carbon ions: 10^6 particles

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  - For distal energy slide (statistics x10)
  - For whole fraction (Statistics x1000) or passive delivery

Online control with prompt gammas

What do we want ?

- Range verification with mm accuracy
  - For single pencil beam spot (distal)
    - Protons: 10^8 particles
    - Carbon ions: 10^6 particles
  - For distal energy slide (statistics x10)
  - For whole fraction (Statistics x1000) or passive delivery
- real time?
- 2D or 3D spatial information?
- target composition: spectral information

→ Compromise with statistics

Main features - Challenges

☺ Relatively large number of PG emitted ($>10^8$ per fraction)
☺ Correlated to ion range
☺ Real time information

☹ Poly-energetic
☹ E> 1MeV : minimum absorption
- Escape from patient
- Difficult to collimate and detect

→ Current SPECT devices not adapted:
New technologies/concepts needed

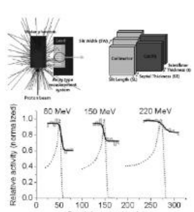
☹ Large background (neutrons…)

Collimated cameras

- Multi-slit cameras
  - **Seoul** *(Min, MP 2012)*

Independent optimization of 5 parameters:

Scint. thickness	3 mm
Slit width	2 mm
Slit length	150 mm
Septal thickness	2 mm
Energy window	4-10 MeV



Measurements with single detector:
~4 nA for 10s, 30mm height CsI
→ A few 10^2 counts

- **Lyon** : Multi-slit with TOF

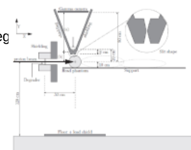
Collimator optimized on falloff retrieval precision *(Pinto, submitted PMB)*
BGO detector. Expected precision: ~1mm at pencil beam scale (10^8 protons)

- **Delft** : Multislit with TOF (project)

Collimated cameras

- **MGH**: TOPAS Simulation of collimated camera for passive delivery: Synchronization with range modulator wheel *(M. Testa, PMB 2014)*:

- Knife edge
  - **Seoul** *(D. Kim, JKPS 2009)*
    Measurements and simulations
    Single CsI détector (moving table)
    40 MeV protons (1nA, 30s) with Al plates deg



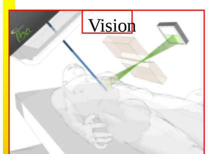
  - **Delft** : Simulation *(Bom, PMB 2012)*
    Efficiency: 2.6x10^{-4} for E > 1.5 MeV
    Precision 1σ = 1mm for single spot

  - **IBA** : Operational prototype

Knife-edge slit collimated γ–camera

Courtesy J. Smeets, IBA

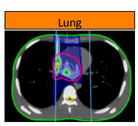
IBA

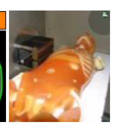


Design:
- Tungsten alloy collimator (53 kg)
- 2 rows of 20 LYSO crystal slabs (500 cm³)
- Lateral SiPM light readout (7 per slab)

Specifications:
- Up to 40 Mcps in fast counting mode (3-6 MeV)
- 10 cm FOV along beam axis

Status:
- Validated for tests with IBA's C230 cyclotron
- Beyond maximum clinical proton beam current
- 2nd unit ready in 2014



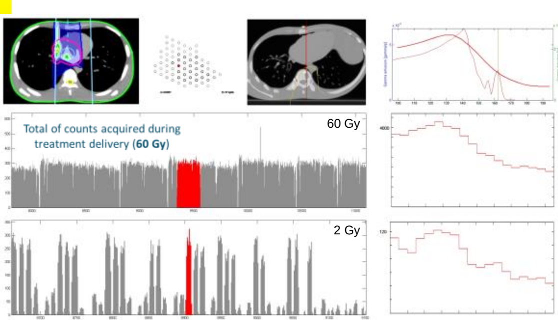


J. Smeets et al.: Phys. Med Biol. 57 (2012) 3371, Perali et al. (2012) IEEE NSS/MIC

Knife-edge slit collimated γ–camera: Test at the Praque PT

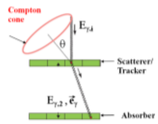
Courtesy J. Smeets, IBA

IBA



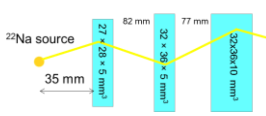
Compton cameras

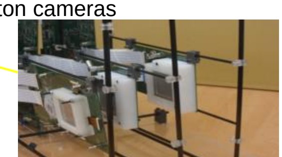
- No collimation: potentially higher efficiency
- Potentially better spatial resolution (< 1cm PSF)
- If beam position known → simplified reconstruction
- 3D-potential imaging (several cameras)



	Group	stages	scatterer	absorber	Efficiency (10^{-5})	Resolution (mm)	Proto/simu	ref
	Lyon	3	DSSD	LYSO	~1	6	simu	Richard 2010
	Baltimore - Texas		Ge CdZnTe	Ge/LaBr CdZnTe	~1 ?	?	Simu proto	Peterson 2010 **Polf Su-E-J-121**
	Seoul		DSSD	NaI	?	~12	Proto tested	Seo 2011
ENVISION	Valencia	2 -3	LaBr	LaBr	?	7.8	Proto tested	Llosa 2013
ENVISION	Lyon	2	DSSD	BGO	~25	~8	Simu/proto in prog	Roellinghoff 2011, Ley 2014
ENVISION	Dresden		CdZnTe	LSO/BGO	?		Proto tested	Hueso- Gonzalez 2014
	Munich		DSSD	LaBr	~1-100	~8	Proto in prog	**Thirolf Su-E-J-46**
ETCC	Kyoto	Gas: Ar+C_2H_6		GSO	0.3	?	Proto tested	Kurosawa 2012
ETCC	Seoul	γ conv.+hodo		CsI	0.6	100	Simus	Kim 2012

Compton cameras





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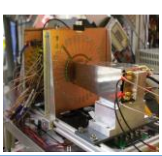
Compton cameras



Dresden small size prototype:
Tested at 1-14 MeV Bremsstrahlung beam (ELBE)

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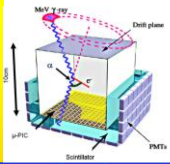
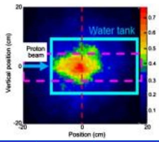
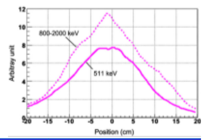
Compton cameras







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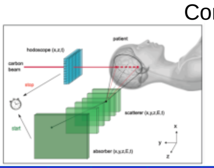
Compton cameras



Lyon project:
TOF and beam position with hodoscope
Large size camera

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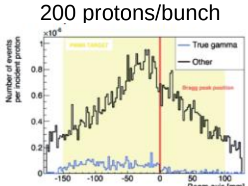
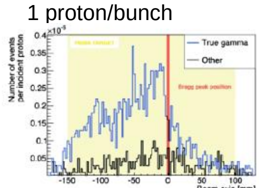
Compton-camera count rate issue

Simulation: line-cone reconstruction for Lyon prototype
1 distal spot (10^8 incident protons) incident on PMMA target, 160 MeV
Pulsed beam (IBA C230)

Clinical intensity:
200 protons/bunch



Reduced intensity:
1 proton/bunch



JL Ley, PTCOG 2014

Beam time-structure issue

- Counting rates
- TOF – precise timing measurements

		Synchrotron HIT		Synchrotron ProTom	Cyclotron C230 IBA	Cyclotron Varian	Synchro-cyclo S2C2 - IBA	Synchro-cyclo Mevion S250
		^{12}C	Protons					
Typical intensity (ions/s)		10^7	10^9		$\sim 10^{10}$	10^8 - 10^{10}	$\sim 10^{10}$	
Macro-structure	Period (s)	1 - 10		0.1 - 5	-	-	10^{-3}	0.005
Micro-structure	Bunch width (ns)	20		?	2	0.5	?	?
	Period (ns)	200		?	9.4	13.9	13	?
	Ions/bunch	2	200	?	200	2 - 200	4000	?

Steps toward clinical workflow integration

- IBA: analytical calculation of PG response (Talk E. Sterpin TH-C-BRD-1 Thursday), simulation for lung treatment (AAPM 2013)
- P. Gueth et al (PMB 2013): Machine learning-based algorithm for patient specific PG dose monitoring
- J. Polf et al (PMB2014) : position-dependent analytical estimate of PG

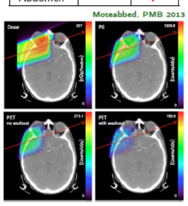
Moteabbed, PMB 2013

PG vs PET (MGH)

Simulations of treatments

	Passive	Active
Head-neck	✓	✓
Prostate	✓	
T-spine	✓	
Abdomen		✓

Moteabbed, PMB 2013



Profile features

- PG/PET production yields: 60-80
- PG/PET γ transmission: ~ 5
- PG falloff closer to the dose falloff by 5-10 mm
  - $\Rightarrow$ Advantage for pencil beams

Efficiency of CC/PET

- CC: $\sim 2 \times 10^{-4}$ (Roellinghoff 2011)
- in-room PET: $\sim 2 \times 10^{-2}$

Expected CC/PET statistics

- $\sim 3-4$
- CC: small Ω / PET: all the decays

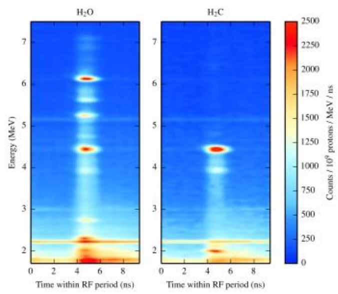
Energy- and time-resolved γ-ray detection

Courtesy J. Verburg, MGH

165 MeV proton beam stopped in water and polyethylene

Measurement 20 mm upstream of end-of-range with collimated detector

Prompt γ-rays resolved in energy and time within cyclotron RF period

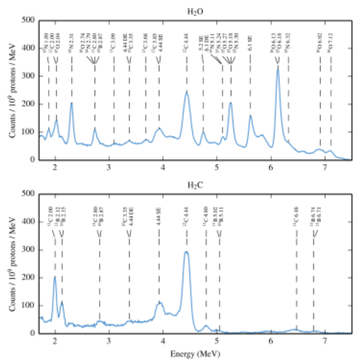


Joost Verburg, Thomas Bortfeld, Joao Seco
Department of Radiation Oncology
Massachusetts General Hospital and Harvard Medical School

Proton-induced prompt γ-ray spectrum

Courtesy J. Verburg, MGH

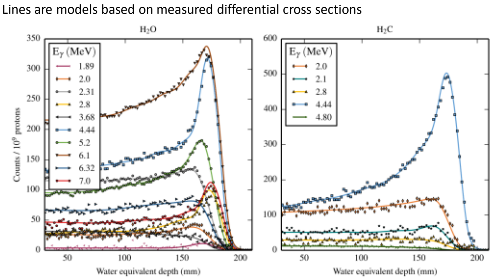
Averaged over last 30 mm of range of 165 MeV proton beam



Prompt γ-ray emissions along pencil-beam

Courtesy J. Verburg, MGH

Nuclear reactions have **unique correlations with proton energy**
Lines are models based on measured differential cross sections



165 MeV proton beam

Proton range verification

Courtesy J. Verburg, MGH

Simultaneous determination of **absolute water equivalent depth at detector position** and elemental composition of irradiated tissue, using small scale prototype detector:

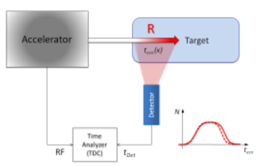
	Detected depth (mm)	Range error (mm)	Detected ^{16}O (g cm^{-3})	Detected ^{12}C (g cm^{-3})
Water Detector at 156.5 mm, 0.89 g cm^{-3} oxygen				
No range error	156.3 ± 1.3	0.1 ± 1.3	0.94 ± 0.07	0.05 ± 0.07
+ 2.3 mm shifter	158.6 ± 1.0	-2.2 ± 1.0	0.90 ± 0.07	0.02 ± 0.06
+ 5.2 mm shifter	161.6 ± 1.0	-5.2 ± 1.0	0.88 ± 0.07	0.04 ± 0.06
Plastic Detector at 157.1 mm, 0.21 g cm^{-3} oxygen, 0.70 g cm^{-3} carbon				
No range error	157.1 ± 1.4	0.0 ± 1.4	0.17 ± 0.04	0.70 ± 0.07
+ 2.3 mm shifter	159.3 ± 1.4	-2.3 ± 1.4	0.18 ± 0.03	0.70 ± 0.07
+ 5.2 mm shifter	162.4 ± 1.3	-5.4 ± 1.3	0.18 ± 0.04	0.69 ± 0.08

Based on five distal pencil-beams delivering 5 x 10^8 protons
Uncertainties ± 1σ, n = 90

Prompt gamma timing (PGT): Idea

Courtesy G. Pausch, Oncoray

- Physics of PGT
  1. Time-of-flight (TOF) effects
     - Range R
     - Flight path differences
     - TOF distribution width 33 ps/cm × cos(υ)
  2. Emission time effects
     - Range R
     - Stopping time
     - Emission time window
     - "TOF" distribution width > 67 ps/cm

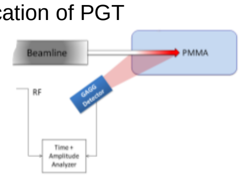


- Measure prompt gamma timing spectra with a "TOF" setup.
- "TOF" spectra broaden with R due to TOF and emission time effects.

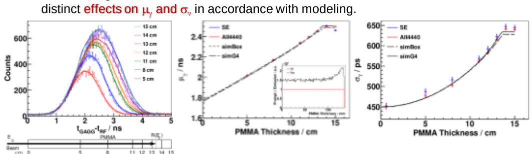
Experimental verification of PGT

Courtesy G. Pausch, Oncoray

Experiment at AGOR, KVI-CART Groningen
- 150 MeV proton beam on massive targets
- GAGG scintillation detector at 135^0
- Time and energy analysis



Stacked target 5 to 15 cm PMMA:
distinct effects on μ_γ and σ_γ in accordance with modeling.



Clinical applicability: 2mm range deviation measurable within few seconds

C. GOLNIK, PMB 2014 (accepted)

Concluding remarks

Prompt gamma = emerging technique **close to clinical translation**

- Physics models : still in progress
- Collimated systems
  - compatible size with patient treatment constraints
  - **Millimetric range-control at the pencil-beam scale for protons**
  - First prototype tested in clinical conditions (knife-edge IBA)
  - Multi-collimated cameras: similar performances
- Compton cameras: still under development
  (spatial resolution, 2-3D imaging).
- **New concepts** (with calibration issue)
  - PG timing
  - PG spectroscopy
- **Lower beam intensities** may be required for Compton cameras or precise timing: reduction of intensity for control of the distal spots (few seconds)?
- Use of **fast beam monitor for TOF** with long bunch time
- **Accelerator-dependent devices** (count rates, TOF)

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PRIMES UNIVERSITE DE LYON

ENVISION

Precise timing: fast monitor
Scintillating fibers hodoscope

Prototype

$1mm^2$ square fibers (128 +128 fibers)
Light transmission: optic fibers
Photomultiplier : Hamamatsu H8500
Home-made ASICs electronic readout : discriminator + TDC at 10^8 Hz rate capability (S. Deng 2011)
Tests:
- 0.5 ns resolution
- Admissible dose > 10^{12} carbon ions/cm^2
- Count rate < $4x10^6$ Hz per PMT: use of several PMTs