Feasibility of in-beam time-of-flight SPECT/PET gamma imaging based on Silicon Photomultipliers for high precision hadrontherapy

Sergey Vinogradov[1,2,3], Elena Popova[4], and Carsten Welsch[2,3]

[1] Lebedev Physical Institute of the Russian Academy of Sciences, Russia
[2] University of Liverpool, Department of Physics, UK
[3] Cockcroft Institute of Accelerator Science and Technology, UK
[4] National Research Nuclear University (MEPhI), Russia

Outline

- Motivation
  - In-beam gamma imaging modalities for hadrontherapy
  - Needs and challenges
- TOF SPECT/PET gamma imaging
  - New approach of prompt gamma timing (PGT) for dose range assessment
  - Feasibility of combined TOF SPECT/PET modality
  - Analysis of TOF SPECT signal detection
  - Algorithm of TOF SPECT image reconstruction
- Discussion
  - Harnessing SPECT and PET in one imager
  - Anticipating TOF SPECT/PET benefits and drawbacks
  - Moving forward: critical issues to be addressed (10 ps time resolution?!)

Gamma imaging modalities for hadron therapy verification

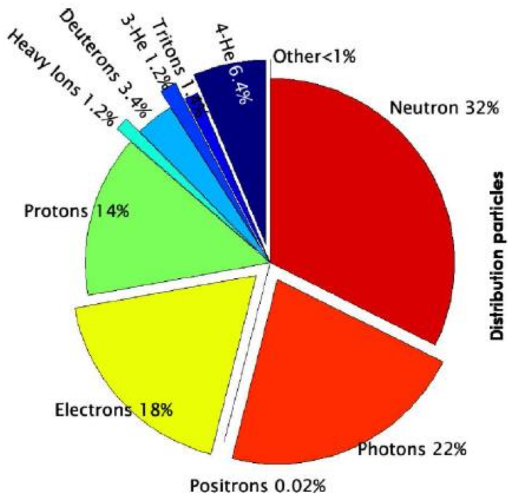
Imaging modalities	Pro	Contra
(TOF) PET	Clinically proven Good efficiency	Low statistics of events Large background Short decay time Metabolic washout Limited in-beam geometry
PGI	High yield of gammas	
Collimated cameras		Very low efficiency Scattering in collimator Complexity of collimation
Compton cameras		Low efficiency Overall complexity

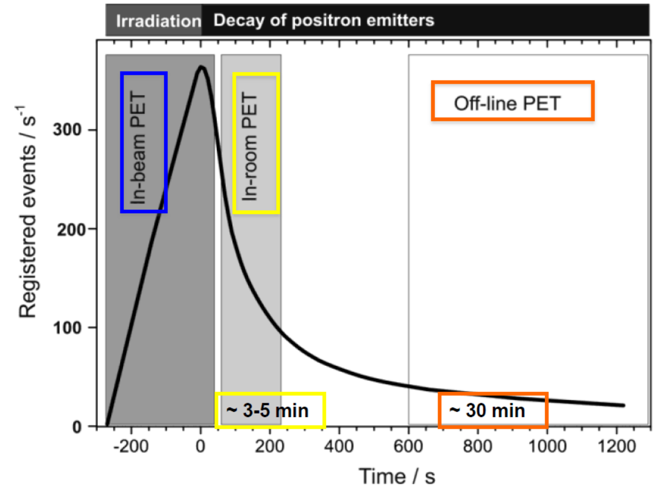
M. Dosanjh, ENLIGHT coordinator, in "ENLIGHT Highlights December 2015"

"…Alberto Del Guerra (Pisa, Italy), who reviewed the mechanisms of PET imaging in detail, ending with a firm conclusion that a combination of prompt gamma and PET imaging are required for the best estimations of dose placement."

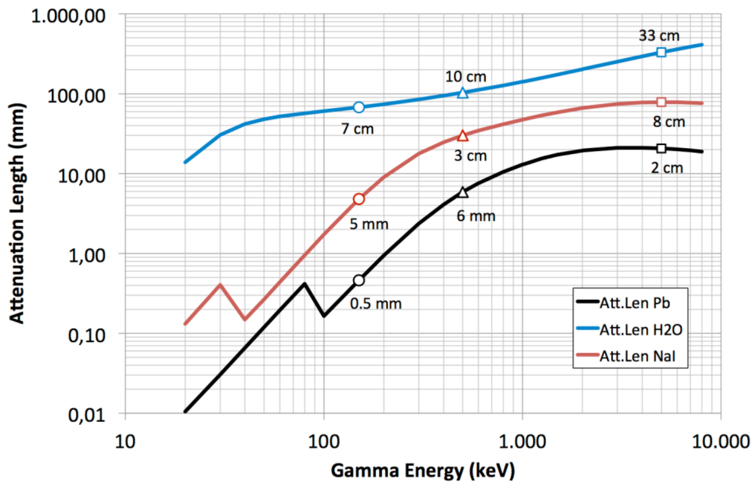
A. del Guerra, "The current status and challenges of detection and imaging in radiation therapy", *in ENLIGHT Meeting*, Kraków 18-20 September 2015.

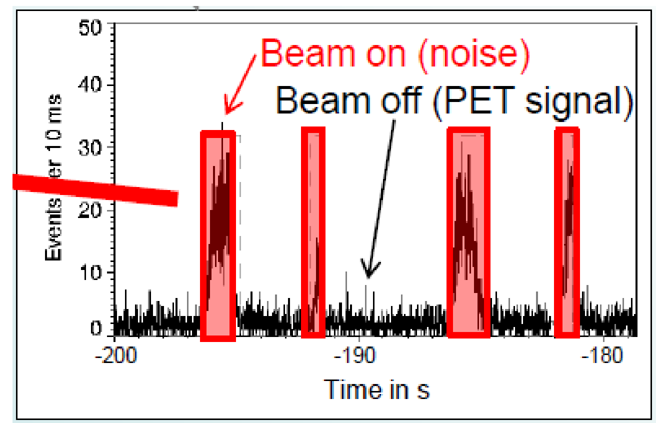
Prompt and annihilation gammas





F. Pennazio et al., "A Study of Monitoring Performances with the INSIDE System", 2015.

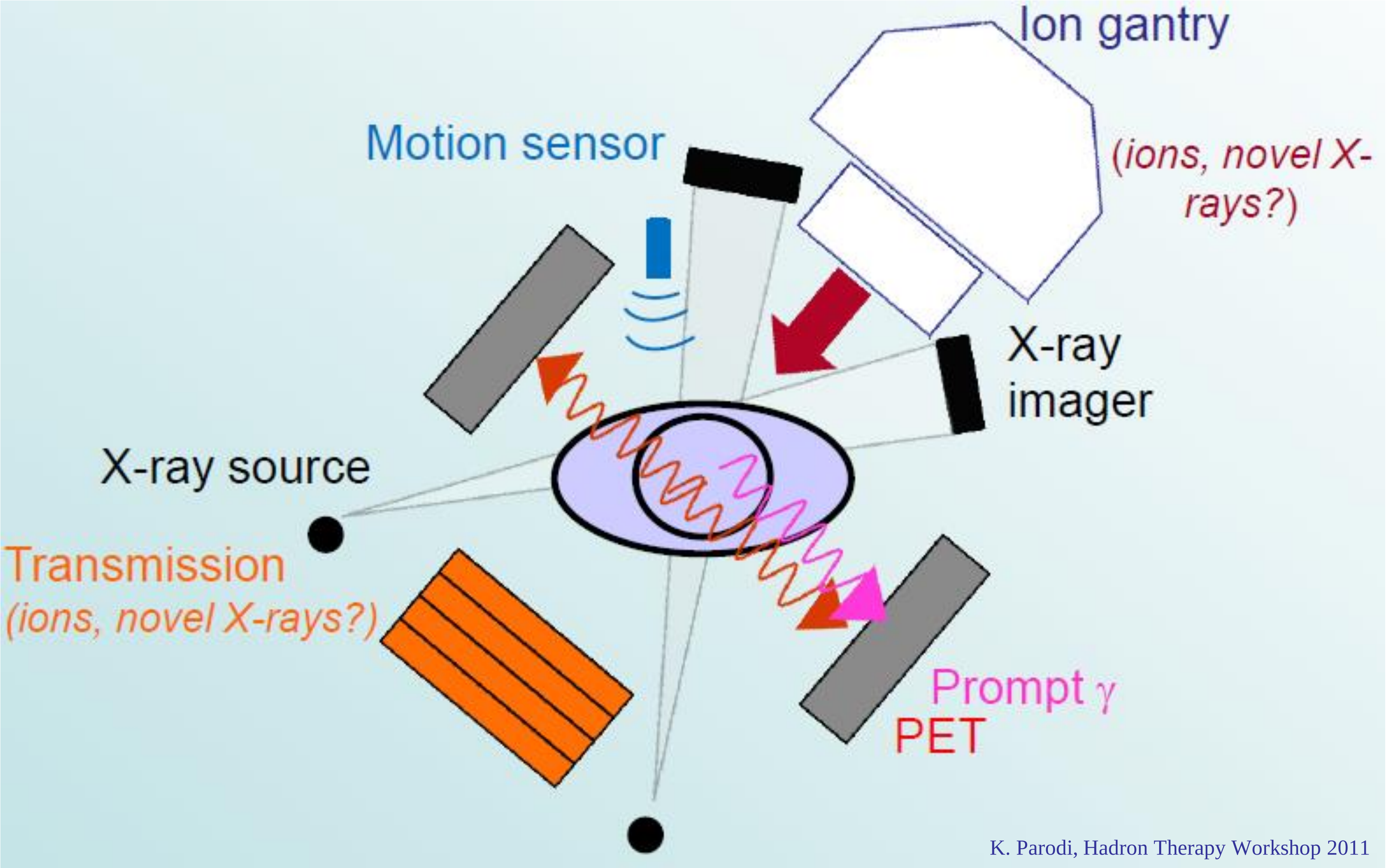




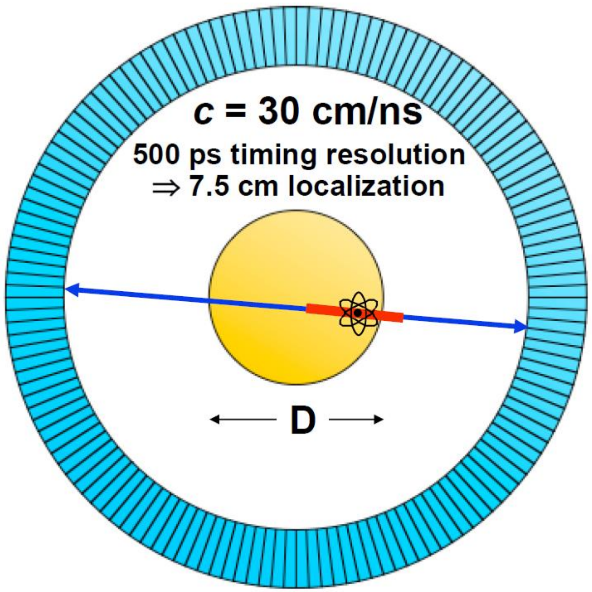
K. Parodi, Hadron Therapy Workshop 2011

Can we deploy common gamma cameras as used in nuclear medicine? No. – G. Pauch, 2015

Toward ideal imaging system

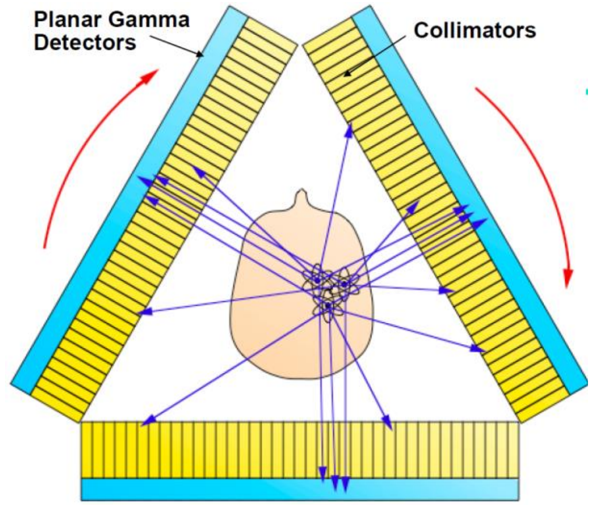


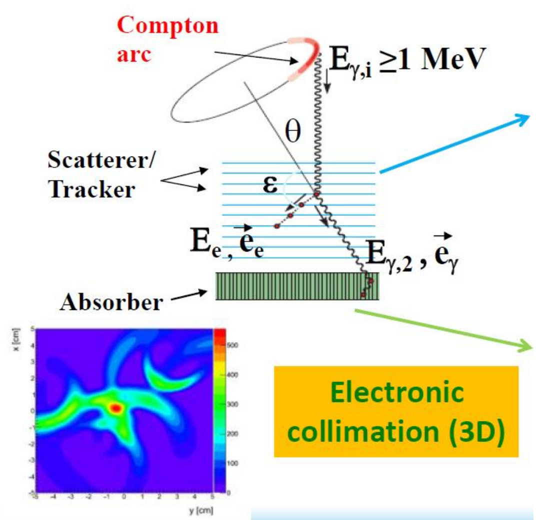
PET + PGI = ?



W. Moses, NDIP 2008

+





P. Thirolf, C. Lang, S. Aldawood, .., K. Parodi, LMU

= ?

Many approaches and projects in the area

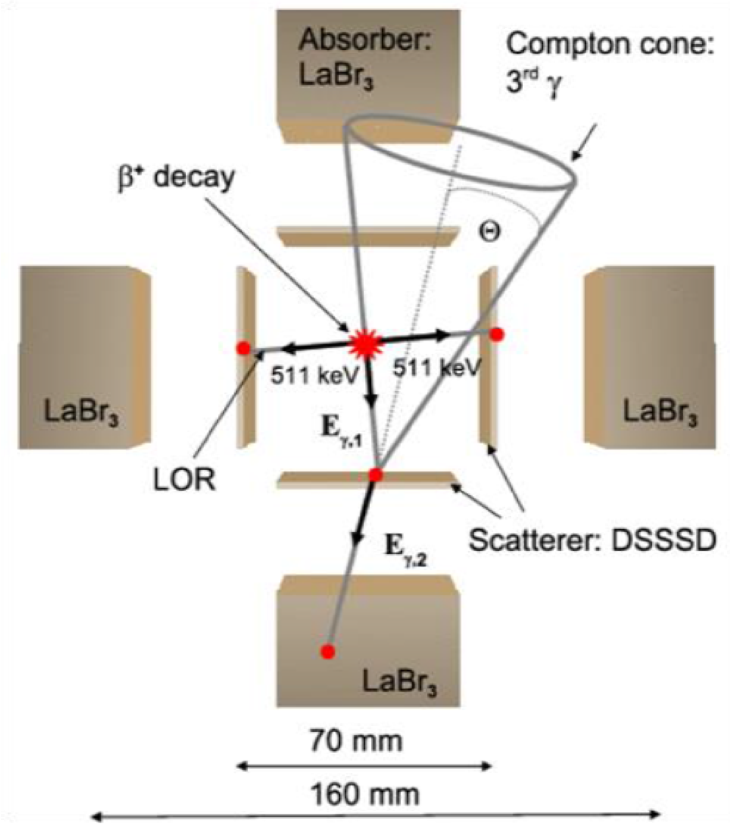
- In-beam TOF PET, SPECT, Compton @ENVISION project
- In-beam PET + Secondary charged particles profiler @INSIDE collaboration
- In beam TOF PET+dSiPM @TU Delft *"Turning the physical advantages of protons into true clinical benefits with in-beam TOF-PET"*
- TOF PGI (passive collimation) + dSiPM @TU Delft: *"A time-of-flight prompt-gamma camera for real-time, in-situ monitoring of particle radiotherapy"*
- J. Krimmer, et al., "*Collimated prompt gamma TOF measurements with multi-slit multi-detector configurations*", *JINST, 2015*

Compton camera concepts for prompt gamma imaging:
Various approaches differing in the detectors design

- Dresden: CZT + segmented LSO/BGO
- Munich: double-sided Si strip detectors + monolithic $LaBr_3$
- Lyon: double-sided Si strip detectors + segmented BGO
- Valencia: monolithic $LaBr_3$ + monolithic $LaBr_3$
- Baltimore: multistage CZT based on POLARIS

G. Pausch, Dresden, 2015

PET + Compton combination



P. Thirolf, C. Lang, S. Aldawood, .., K. Parodi, LMU

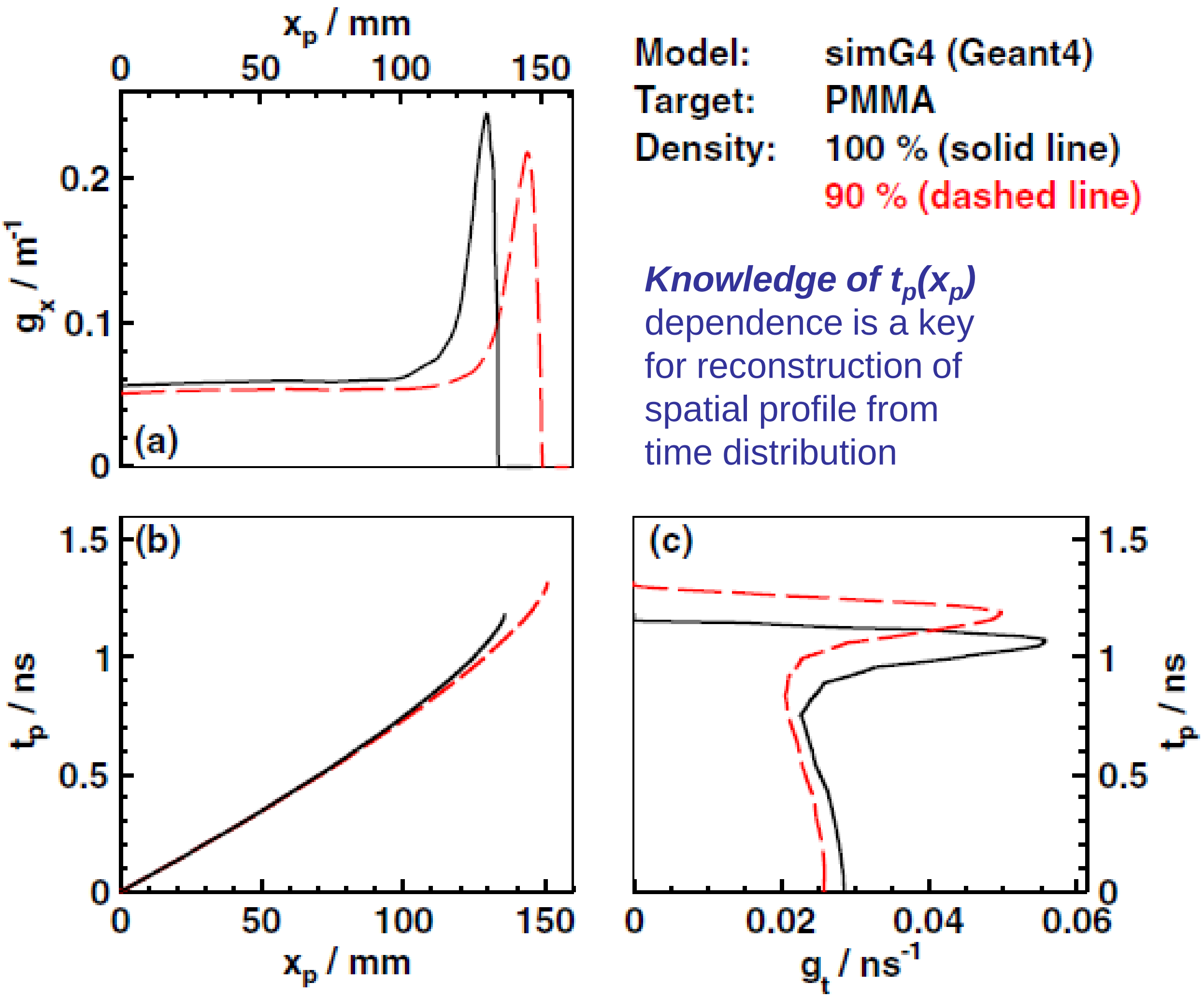
Hybrid detector concepts

Multi-purpose detectors could exploit complementary information on different time scales

E.g., we are considering imaging of prompt gamma during beam-on and (γ)-PET during beam interrupts *(depending on delivery time structure)*

Contra:
- Complexity
- Space consuming design
- Low efficiency in Compton mode
- ...Multiple trade-offs…

Prompt Gamma Timing (PGT) @OncoRay: emission TOF distribution ~ spatial profile



Model: simG4 (Geant4)
Target: PMMA
Density: 100 % (solid line)
90 % (dashed line)

Knowledge of $t_p(x_p)$ dependence is a key for reconstruction of spatial profile from time distribution

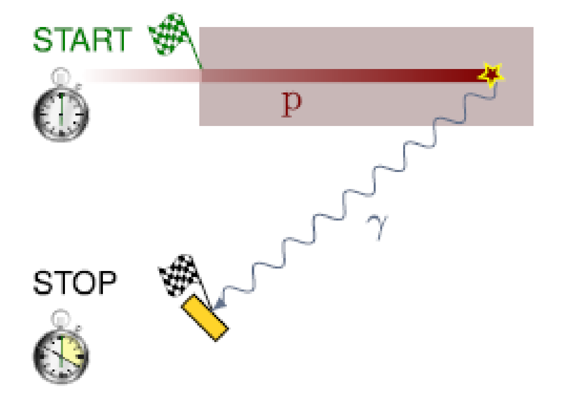
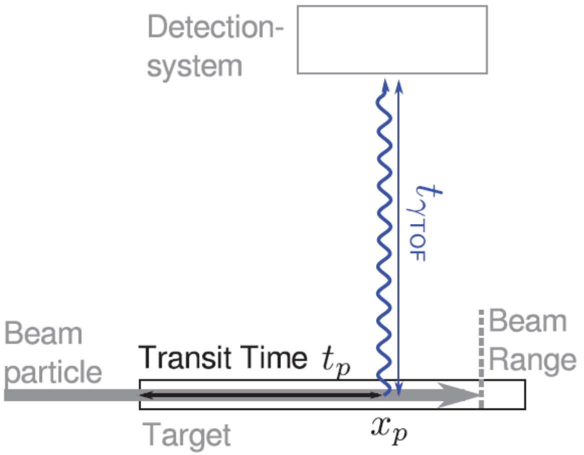
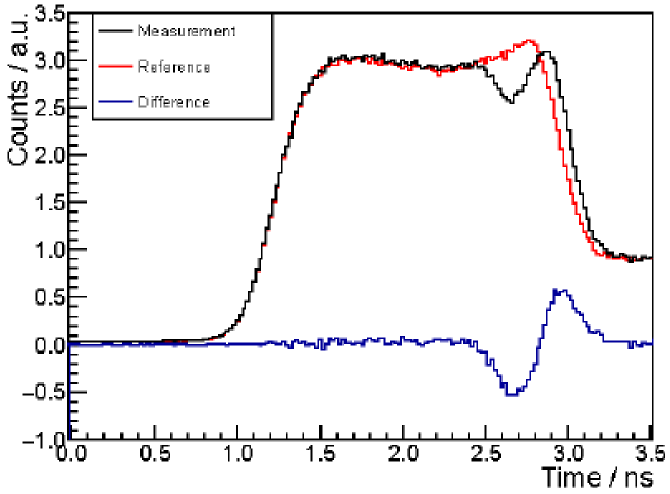


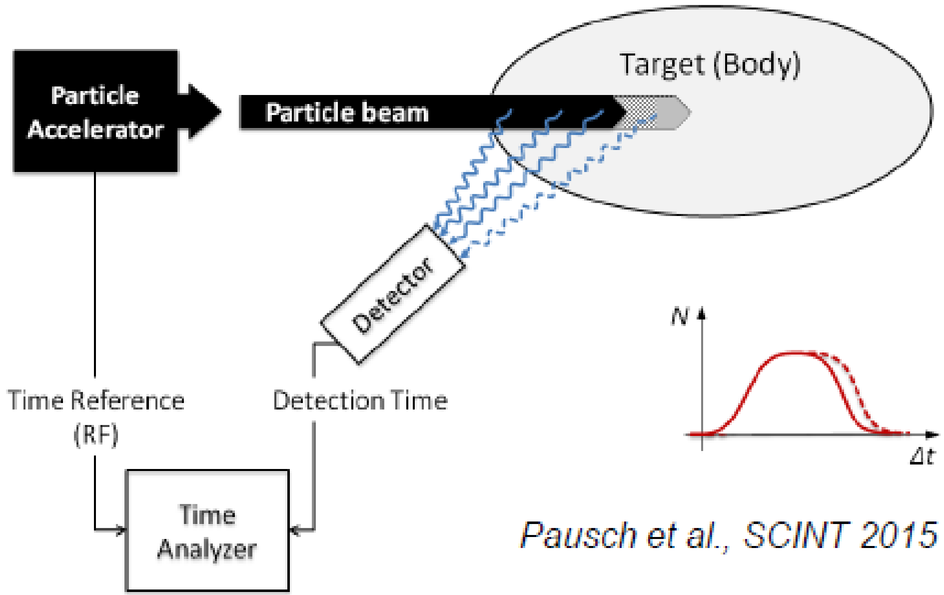
FIGURE 5 | Illustrative sketch of the PGT method. The therapeutic proton p (the projectile) slows down as it penetrates the target and interacts with a nucleus, which emits a prompt gamma ray. The time between the entrance of the proton to the target (the start flag) and the arrival of the gamma ray to the detector (the stop flag at the yellow rectangle) encodes the proton transit time and gamma time of flight, which can be correlated to the depth of interaction of the proton (gamma emission point).



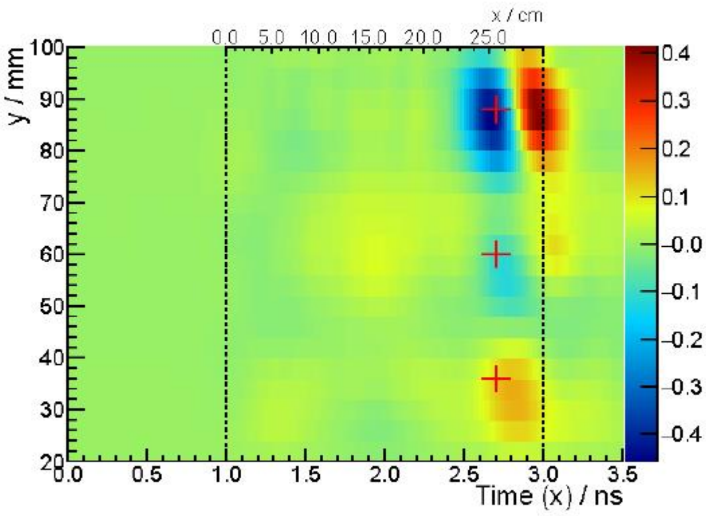
C. Golnik *et al,* Range assessment in particle therapy based on prompt γ-ray timing measurements, Phys. Med. Biol. **59** (2014) 5399

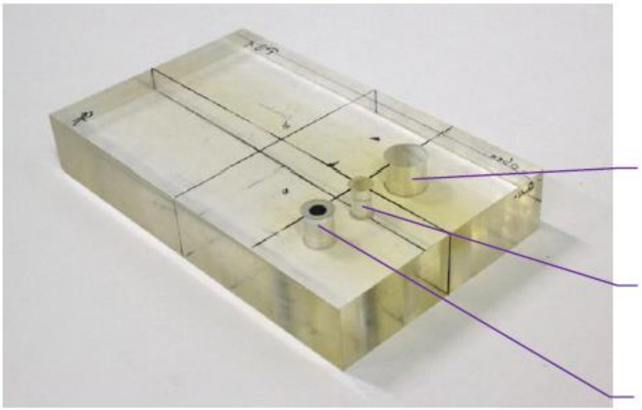
Latest results in PGT @OncoRay





Pausch et al., SCINT 2015



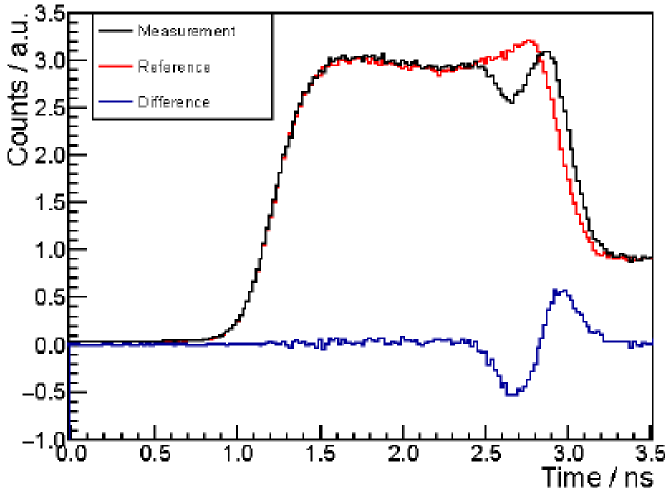


∅ 19mm (large) cavity

∅ 9mm (small) cavity

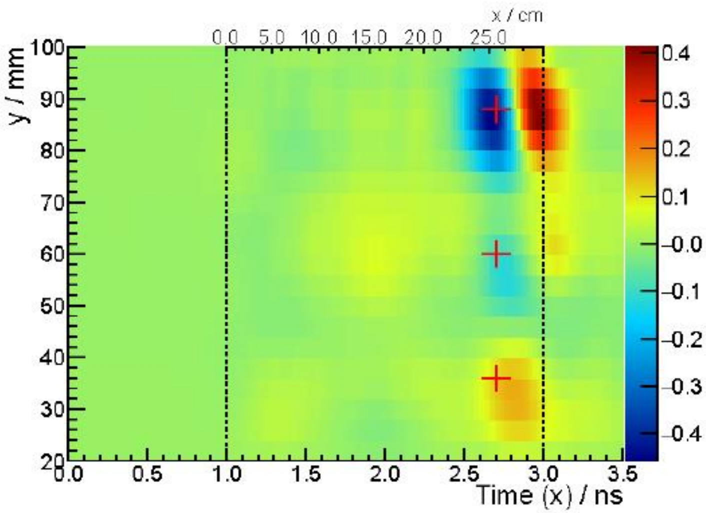
∅ 13mm filled cavity („marrowbone“)

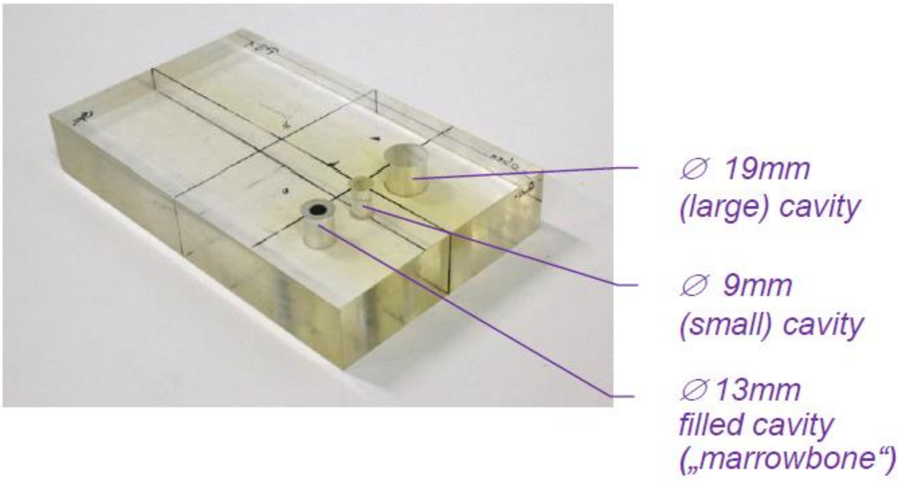
Latest results in PGT @OncoRay with proton pencil-beam



First prompt-gamma based image of target inhomogeneities and resulting proton beam overranges ever made!

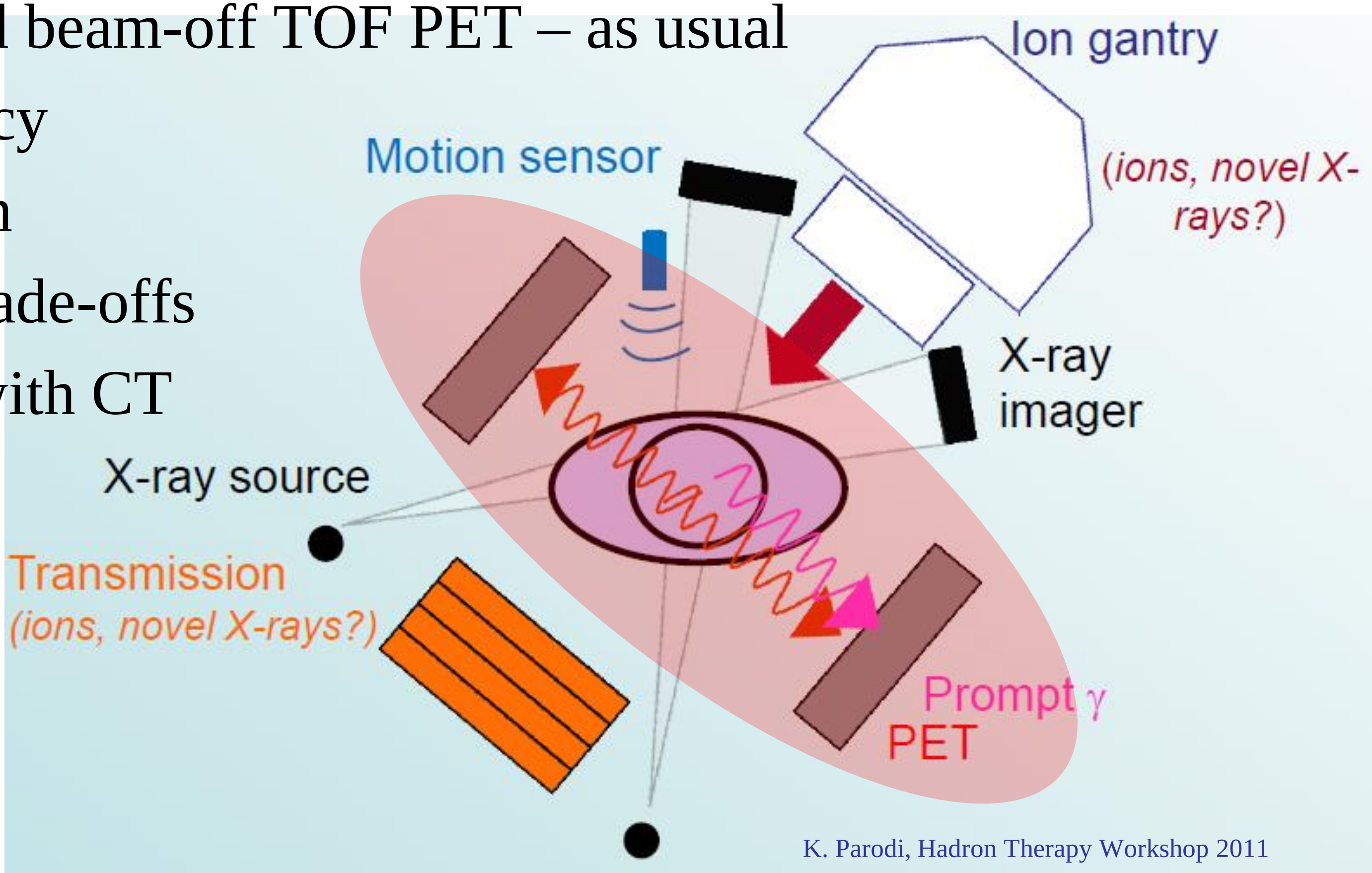
Not a clinical scenario:
High dose, maximum beam energy, long exposure (minutes per "spot")





TOF SPECT (PGT with detector array) + TOF PET

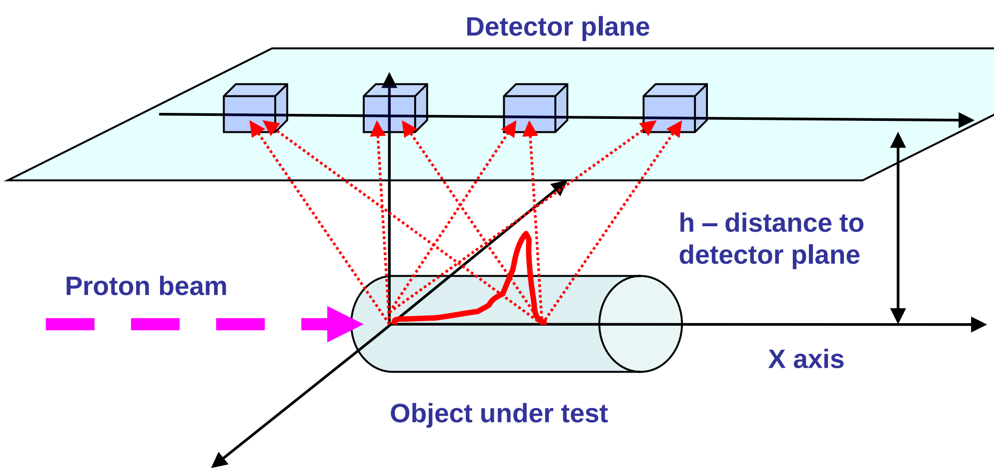
- Common scintillator–SiPM detector for prompt and annihilation γ
- In-spill TOF SPECT for prompt gammas
  - Analytical image reconstruction using known TOF & PSF for any points
- Inter-spill and beam-off TOF PET – as usual
- High efficiency
- Simple design
- Resolvable trade-offs
- Compatible with CT

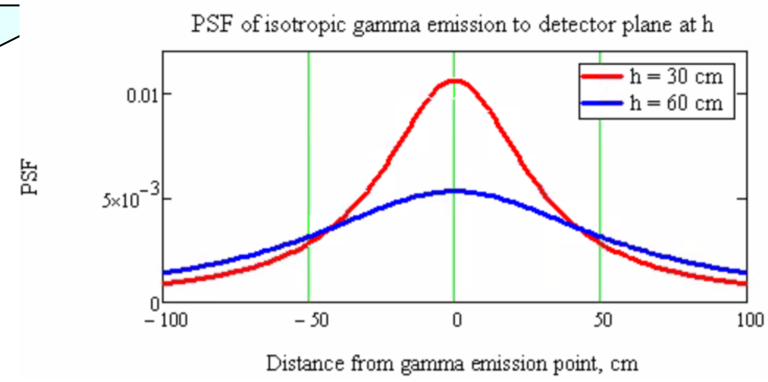


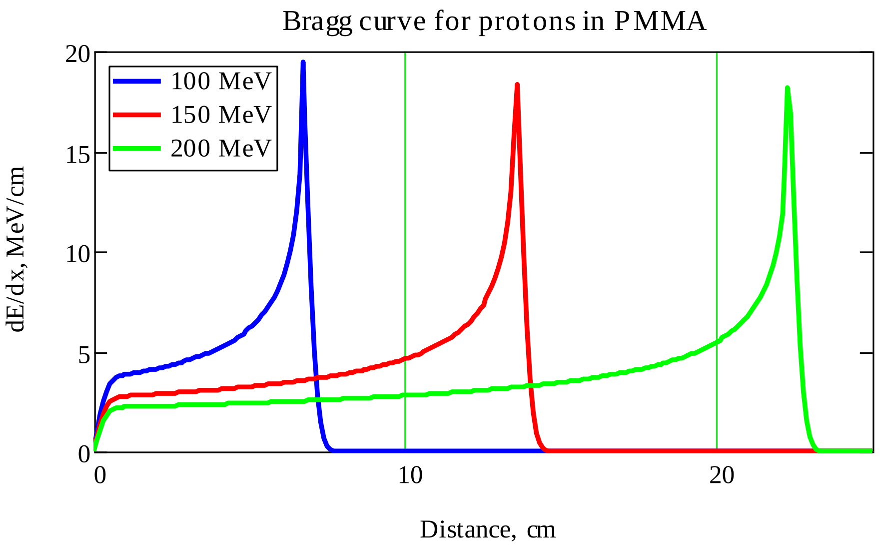
K. Parodi, Hadron Therapy Workshop 2011

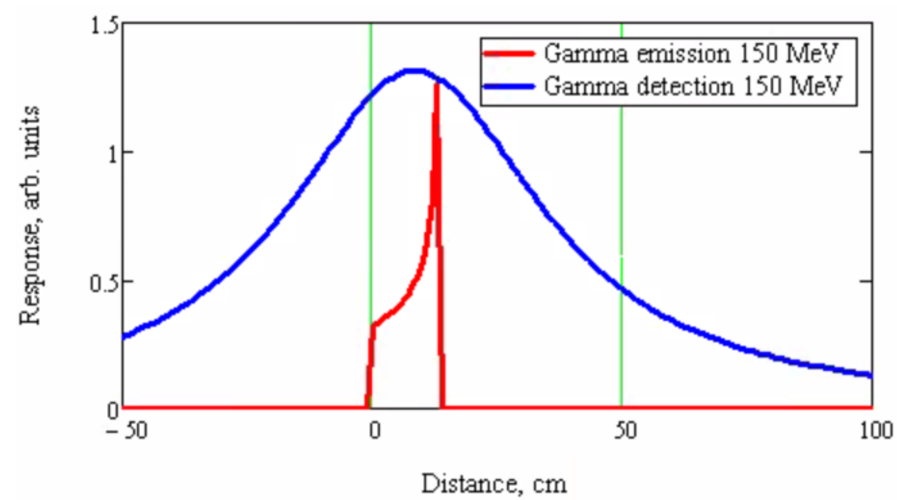
Gamma emission and detection spatial distributions of pencil-beam profile

SEVENTH FRAMEWORK PROGRAMME
UNIVERSITY OF LIVERPOOL
FAST Fast Advanced Scintillator Timing
The Cockcroft Institute of Accelerator Science and Technology
P.N.Lebedev Physical Institute of the Russian Academy of Science

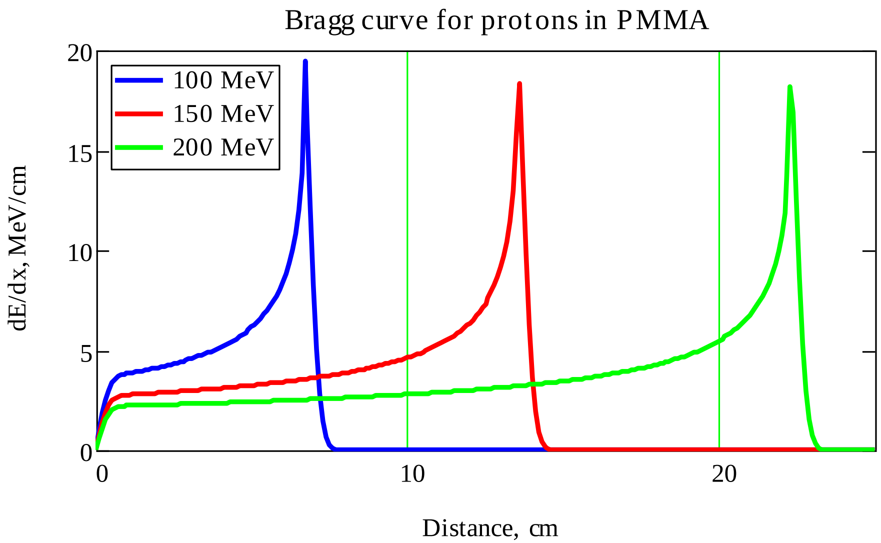






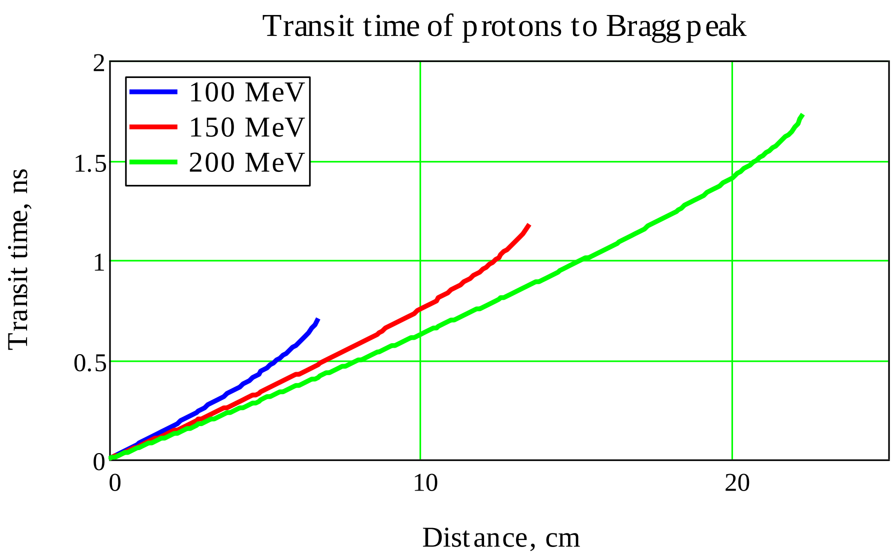


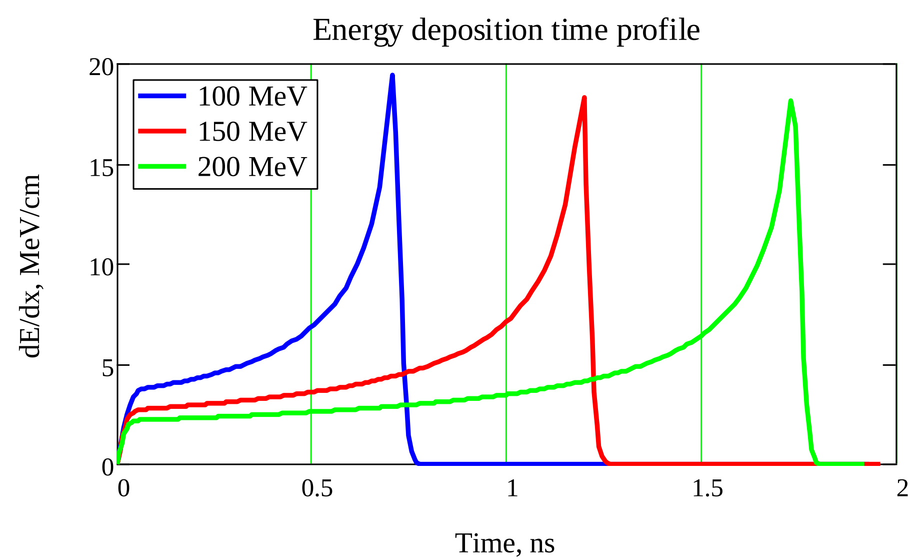
Analytical model: gamma emission time distribution with known *dE/dx*, *t(x)*



$$S(E) := \frac{dE}{dX} \qquad \frac{dX}{dt} = V(Ep) := c\cdot\sqrt{1 - \left[\frac{1}{\left(1 + \frac{Ep}{Em}\right)}\right]}$$

$$X(Ep, E0) := \int_{E}^{E0} \frac{1}{\rho \cdot S(E)}\, dE \qquad T(Ep, E0) := \int_{E}^{E0} \frac{1}{V(E)\cdot \rho \cdot S(E)}\, dE$$

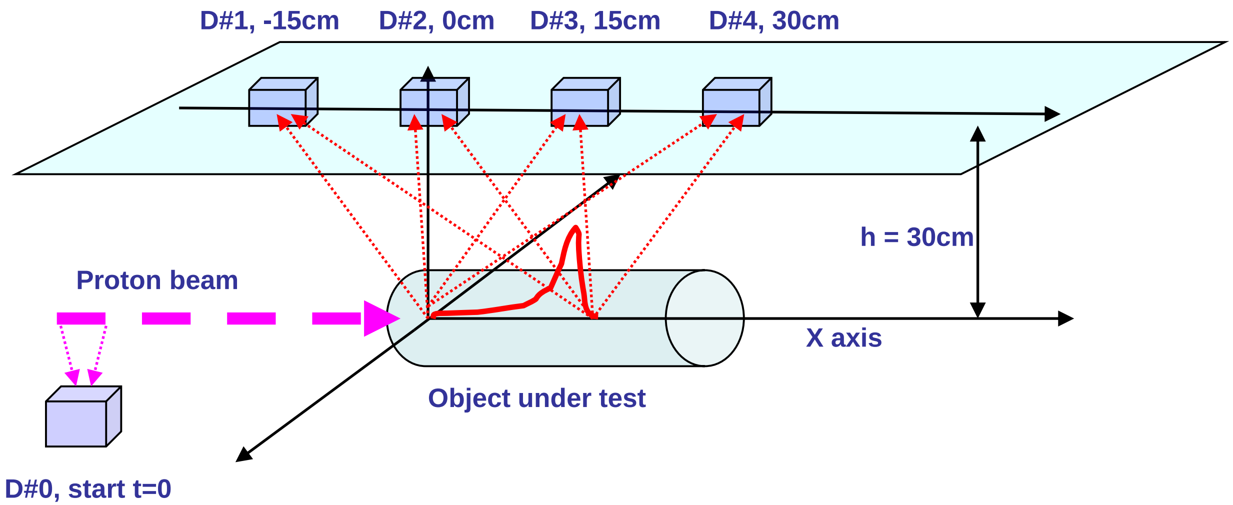




Analytical model: gamma detection time distribution

If energy deposition *S(x,E0)* and proton velocity *V(x,E0)* profiles are known,

the gamma signal *I(xd,t)* in a planar detector configuration can be calculated analytically



- Imaging optics formalism

Object: $O(x,t) = S(x,E0) * \delta(x - V(x,E0) \cdot t)$

Transfer function:

$$T(\Delta x,t) = PSF(\Delta x,h) * \delta(t - Td(\Delta x,h))$$

Image: $I(xd,t) = O(x,t) * T(\Delta x,t)$

Solution $I(xd,t)$ is implicit function of t:

$$I(xd,t) = S(x,E0) \cdot \frac{h}{\pi\left((xd-x)^2 + h^2\right)}$$

$$t = \int_0^x \frac{1}{V(x',E0)} dx' + \frac{h}{c}\sqrt{(xd-x)^2 + h^2}$$

- TOF probabilistic formalism

TOF is a sum of ind. random variables =

$= Tp\text{-}bunch + T\gamma\text{-}emission + T\gamma\text{-}detection$

$$\sigma^2(TOF) = \sigma^2(T_p) + \sigma^2(T_e) + \sigma^2(T_d)$$

$PDF(TOF) = PDF(T_p) * PDF(T_e) * PDF(T_d)$

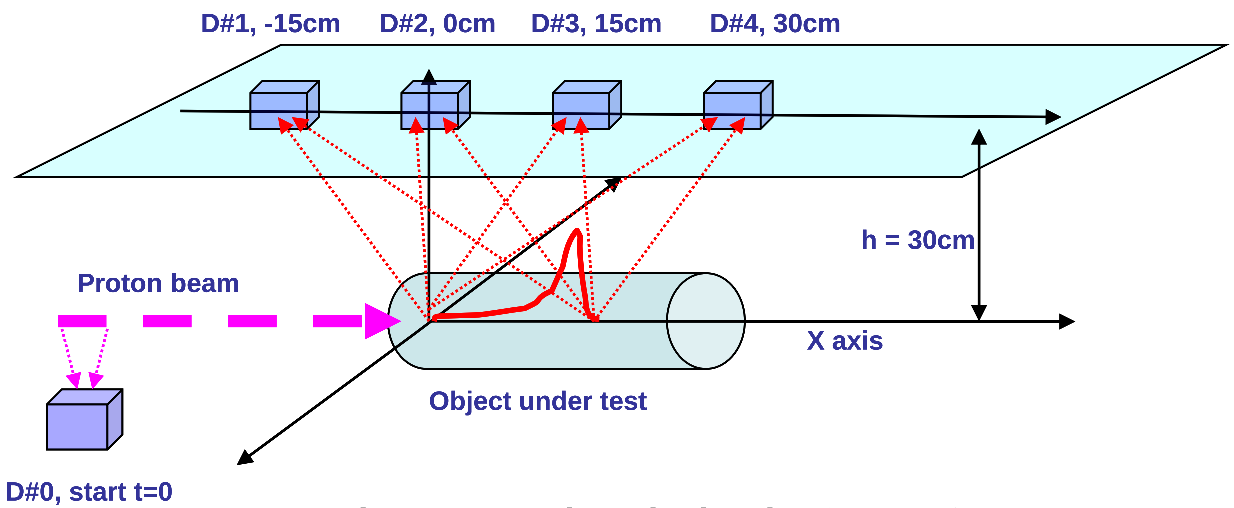
Where

$PDF(T_p) * PDF(T_e) = S(x,E0) * \delta(x - V(x,E0) \cdot t)$

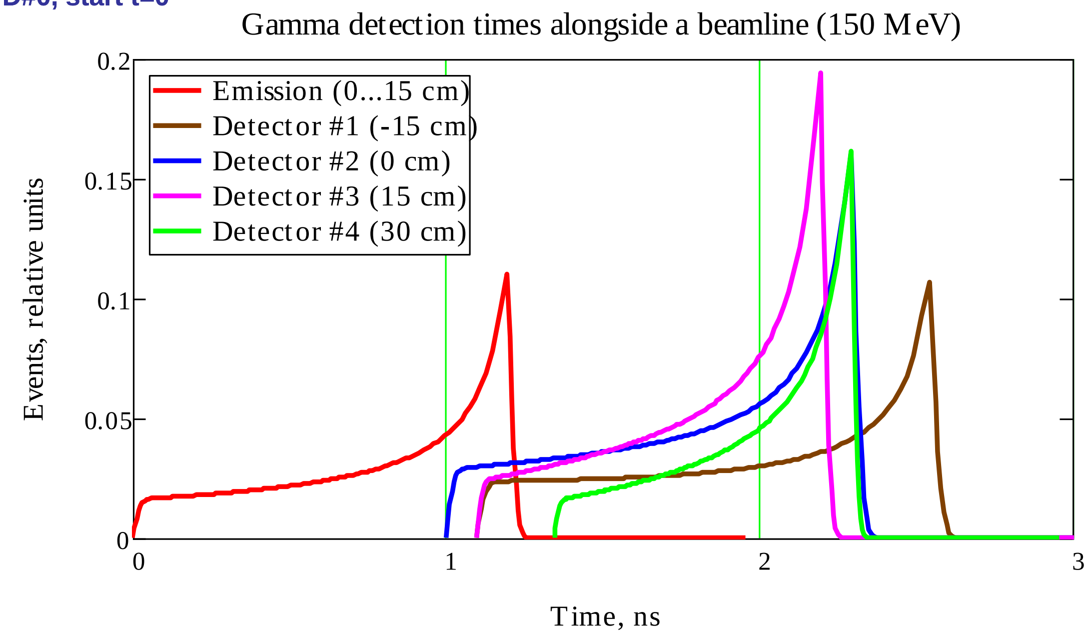
$PDF(T_d) = PSF(\Delta x,h) * \delta(t - TOF(\Delta x,h))$

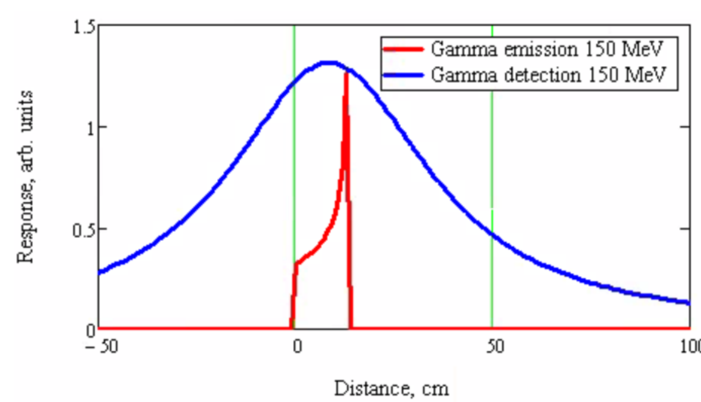
$PDF(TOF) = \langle N\gamma \rangle\, I(x,t)$

Analytical model: TOF detection distributions



1. How to reconstruct dose range without *apriori* known *t(x)?*
2. How to reconstruct dose profile without *apriori* known *S(x)?*



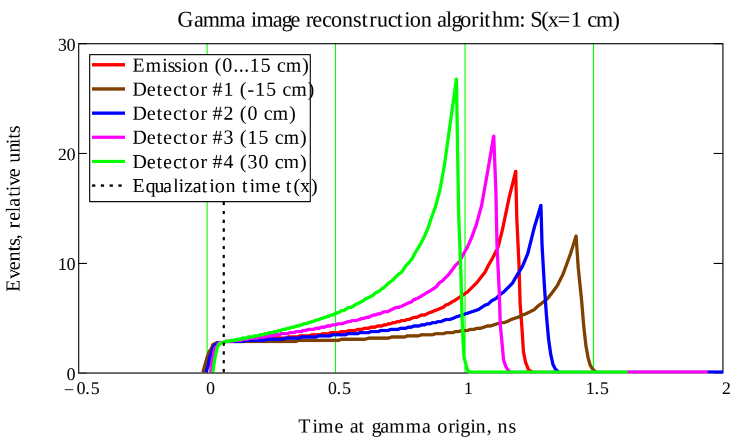


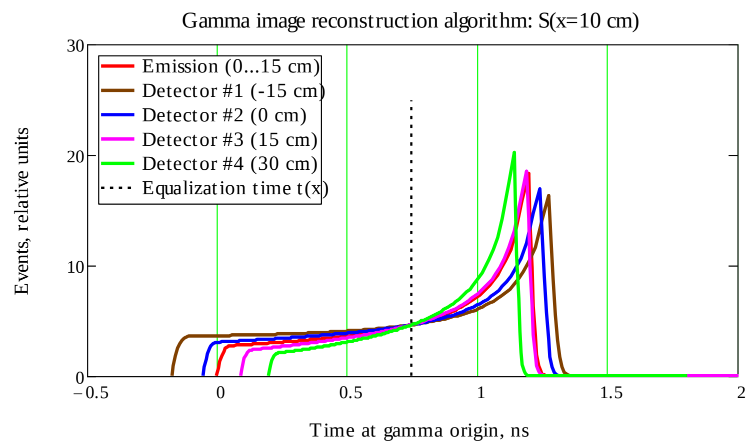
Analytical model: reconstruction algorithm with unknown S(x)=dE/dx and t(x)

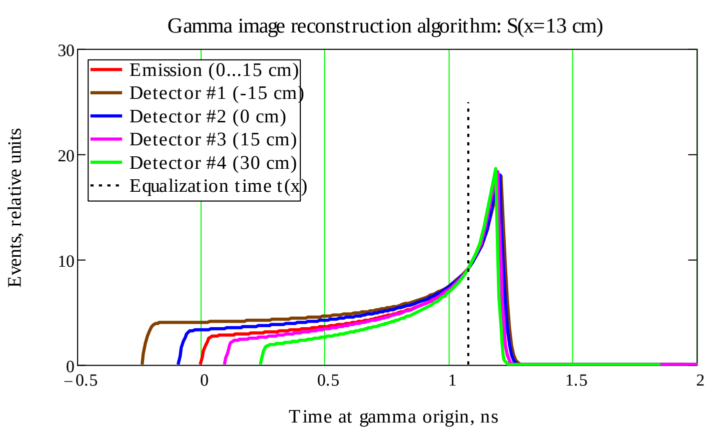
$$I(xd,t) = S(x,E0)\cdot\frac{h}{\pi\left((xd-x)^2+h^2\right)} \quad\Rightarrow\quad S(x) = I(xd,t(x))\cdot\frac{\pi\left((xd-x)^2+h^2\right)}{h}$$

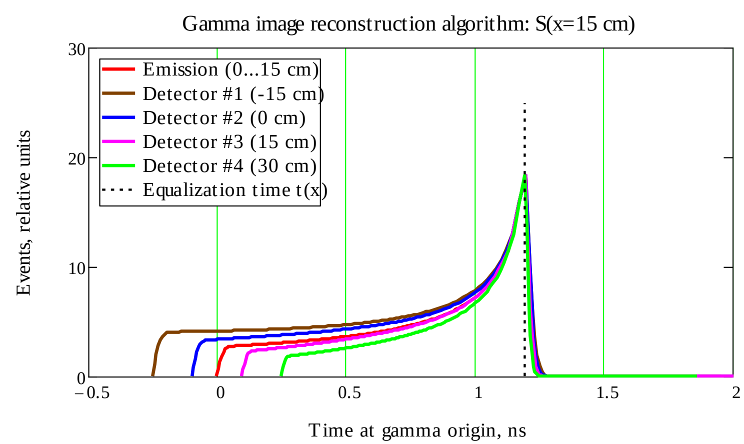
$$t = \int_0^x \frac{1}{V(x',E0)}dx' + \frac{h}{c}\sqrt{(xd-x)^2+h^2} \quad\Rightarrow\quad t(x) = t - \frac{h}{c}\sqrt{(xd-x)^2+h^2}$$

ALL detectors contribute to reconstruction at point x

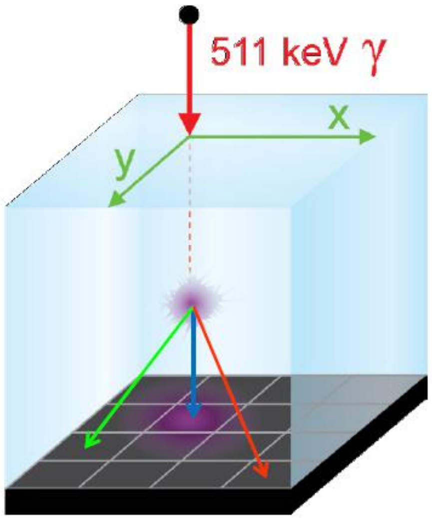


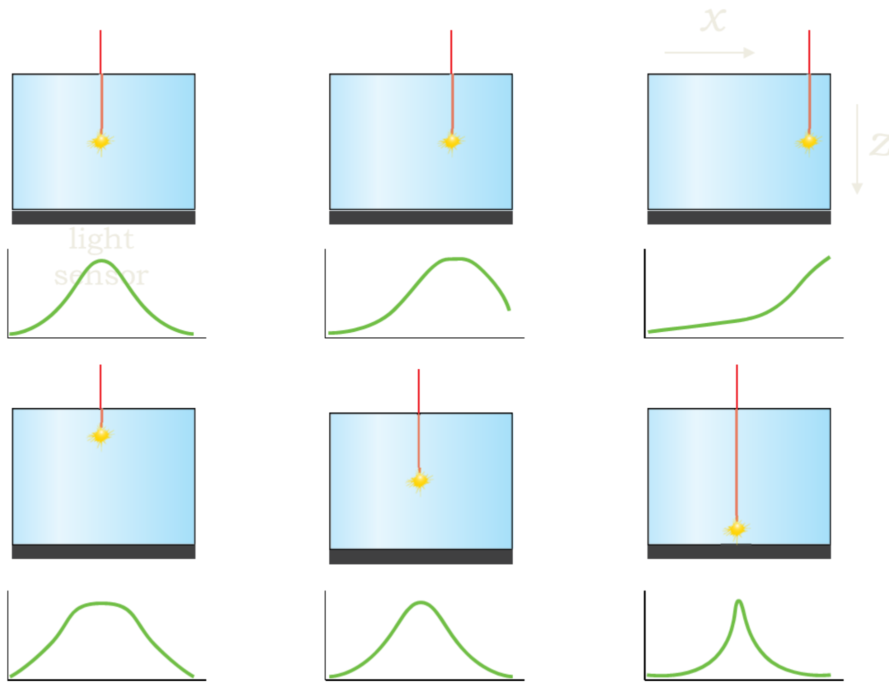






TOF DOI monolithic scintillator + SiPM for best estimation of interaction point (x,y,z, t)





Light distribution depends on the position of interaction …

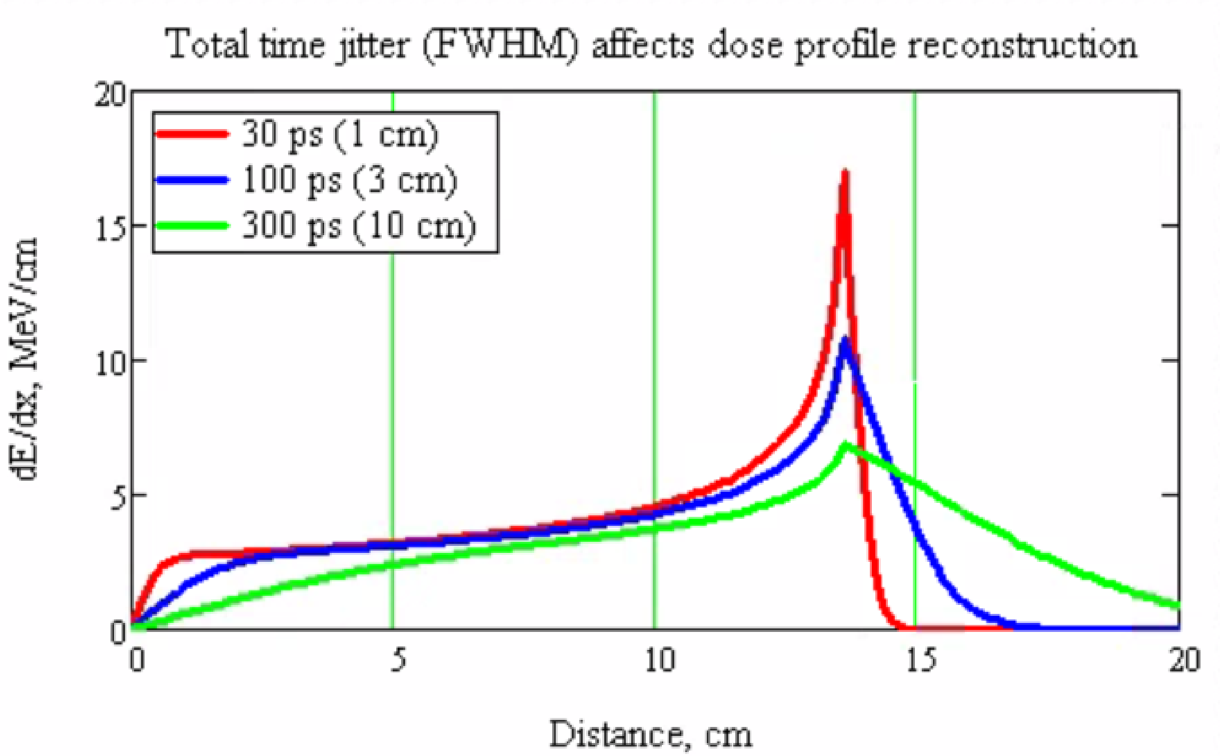
including the depth of interaction (DOI).

H.T. van Dam
S.Siefert
D. Schaart
…..
2013 -2014

Current results with LSO monolithic scintillators on dSiPM arrays:

Performance parameter		Monolithic	State of the art
Energy resolution	(% FWHM)	11 - 12	~12
Spatial resolution	(mm FWHM)	1.0 - 1.6	4 - 6
DOI resolution	(mm FWHM)	3 - 5 mm	None
CRT	(ps FWHM)	160 - 185	500 - 650

Main challenge: timing uncertainty due to bunch width + detector time resolution



"PGT method is not applicable at all clinical accelerators: only to those with a specific micro-time structure."
F. Hueso-González "Compton Camera and Prompt Gamma Ray Timing: Two Methods for In Vivo Range Assessment in Proton Therapy" Front. Oncol., 12 April 2016

Beam bunch time width: ~ 0.2 … 2 ns FWHM @ medical accelerators

SiPM time resolution ~ 50 ps FWHM @4…5 MeV (assuming ~100 ps @511KeV)

Gamma emission timing ~ 1 ps

Possible solutions from accelerator side?

New dedicated accelerators
with ps-short bunch time width?

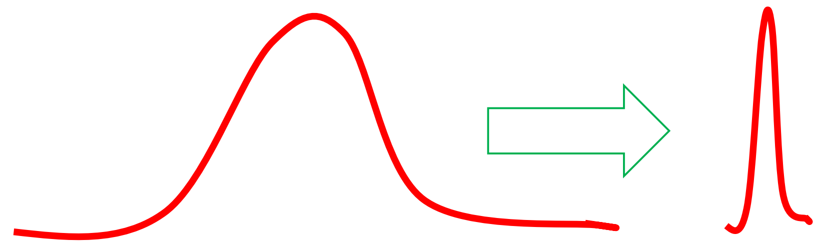
Laser-plasma wakefield accelerator?
MiniLinac?

CERN?
MIT?
Radiabeam?

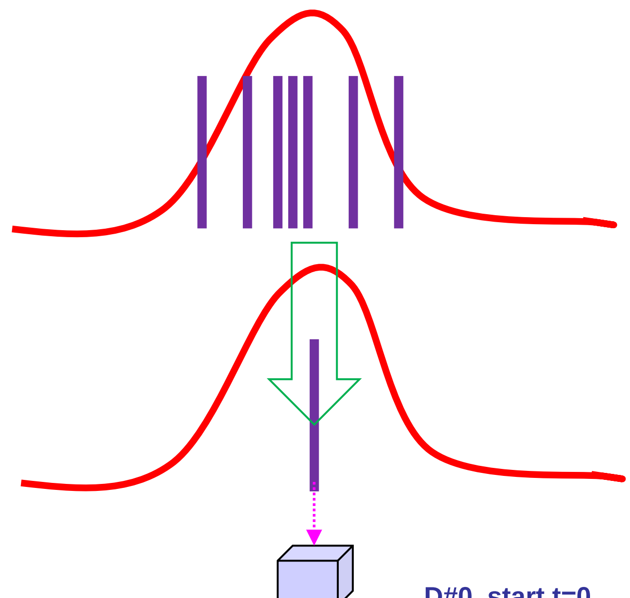
Serge Mathot with the first of the four modules that will make up the miniature accelerator (Image: Maximilien Brice/CERN)

Existing medical accelerators

A) Compressing bunch width from ns to ps scale ?

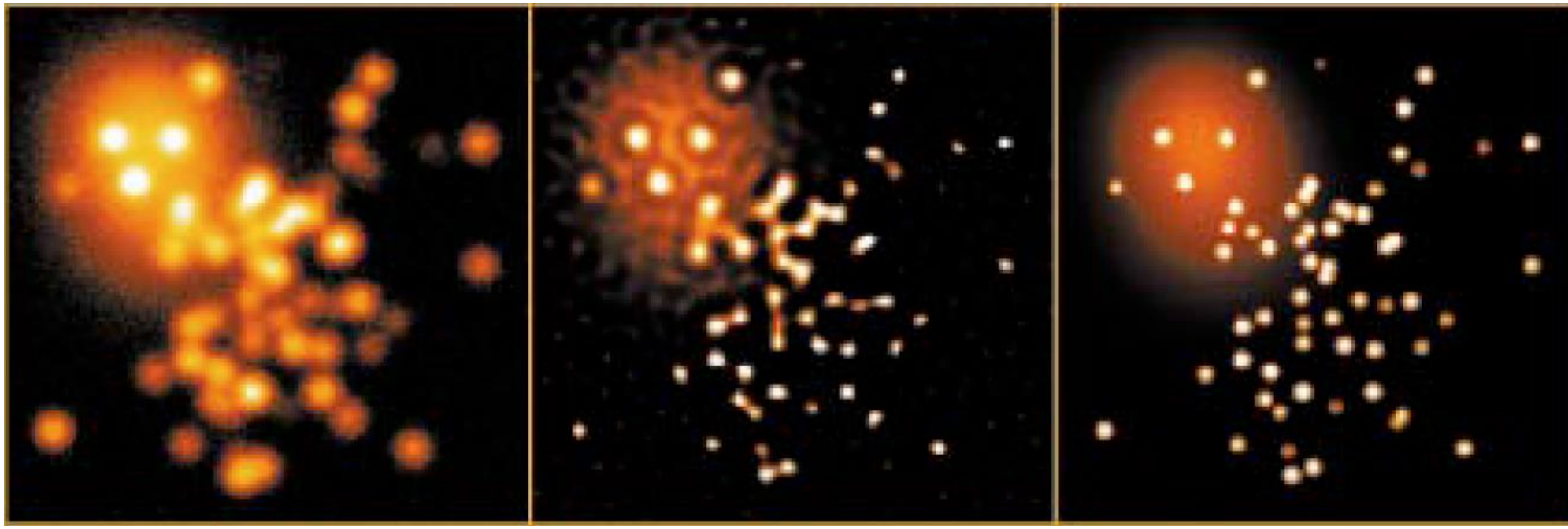


B) Reducing number of hadrons per bunch to a single one?



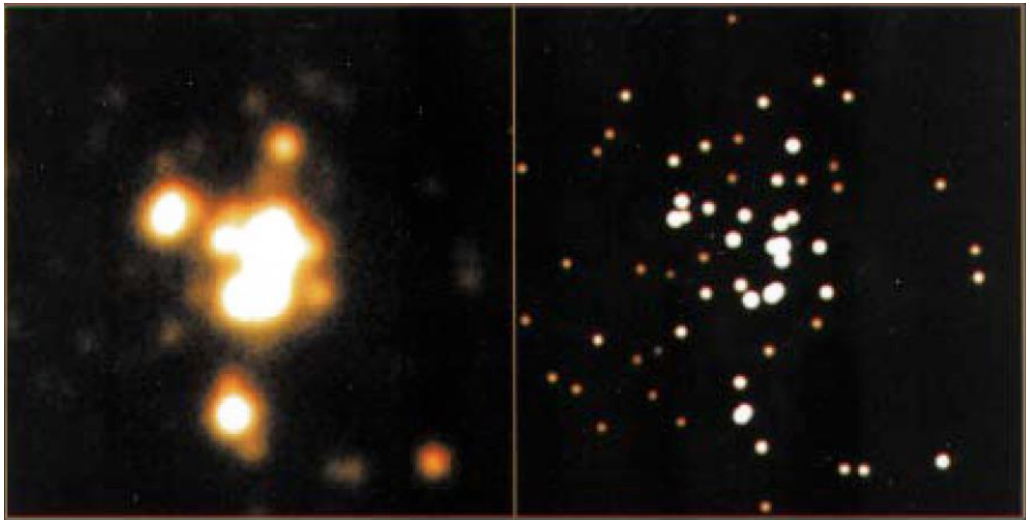
D#0, start t=0

Deconvolution as a possible solution?
high efficiency = high SNR



Original image | Standard deconvolution (50 iterat.) | Correct sampling deconvolution

(FWHM ~ 5 pixels)



P. Magain, F. Courbin, S. Sohy, Deconvolution with Correct Sampling, Astrophys. J., V. 494, 1, pp. 472-477 (1998)

Summary

- We propose TOF SPECT/PET imaging: very efficient and simple
- Information on a prompt gamma emission profile is collected “free of charge”, it complements TOF PET and improves imaging
- Trade-offs in the dedicated detector design are minimal (vs. e.g. PET/Compton) thus it could be easily developed and optimized
- TOF SPECT/PET is fully compatible with CT
- Perfect alignment with the FAST initiative toward 10 ps timing
- TOF SPECT/PET seems to be a good starting point for initiative on dedicated medical (mini-) accelerators to enable development of new generation of inexpensive reliable compact hadron treatment facilities of high precision
- We are looking for a broad collaboration on TOF SPECT/PET

Acknowledgements

- This work was supported in part by
  - EC under Grant Agreement 329100 “SiPM in-depth”
  - Megagrant program of Russia under Grant Agreement 14.A12.31.0006.

- This participation at MEDAMI was supported in part by
  - MEDAMI, Paul Lecoq
  - COST FAST, Etiennette Auffray

Thank you for your attention

Questions?

Objections?

Opinions?

…

Collaborations?

Vin@lebedev.ru