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Some applications of Nuclear Physics in Medicine

José A. Briz Monago

Thanks to E. Nácher, L.M. Fraile, O. Tengblad and A. Perea from whom I got a lot of slides and information

Applications in Medicine

- Nuclear Physics for radio-diagnostics:
  medical imaging (xCT, PET, NMR…)

- Nuclear Physics for radio-therapy: protontherapy

Radiodiagnostics: xCT & PET

- ***Computerized Tomography with X-rays* (xCT):**

Traditional diagnostics by X-rays transmission

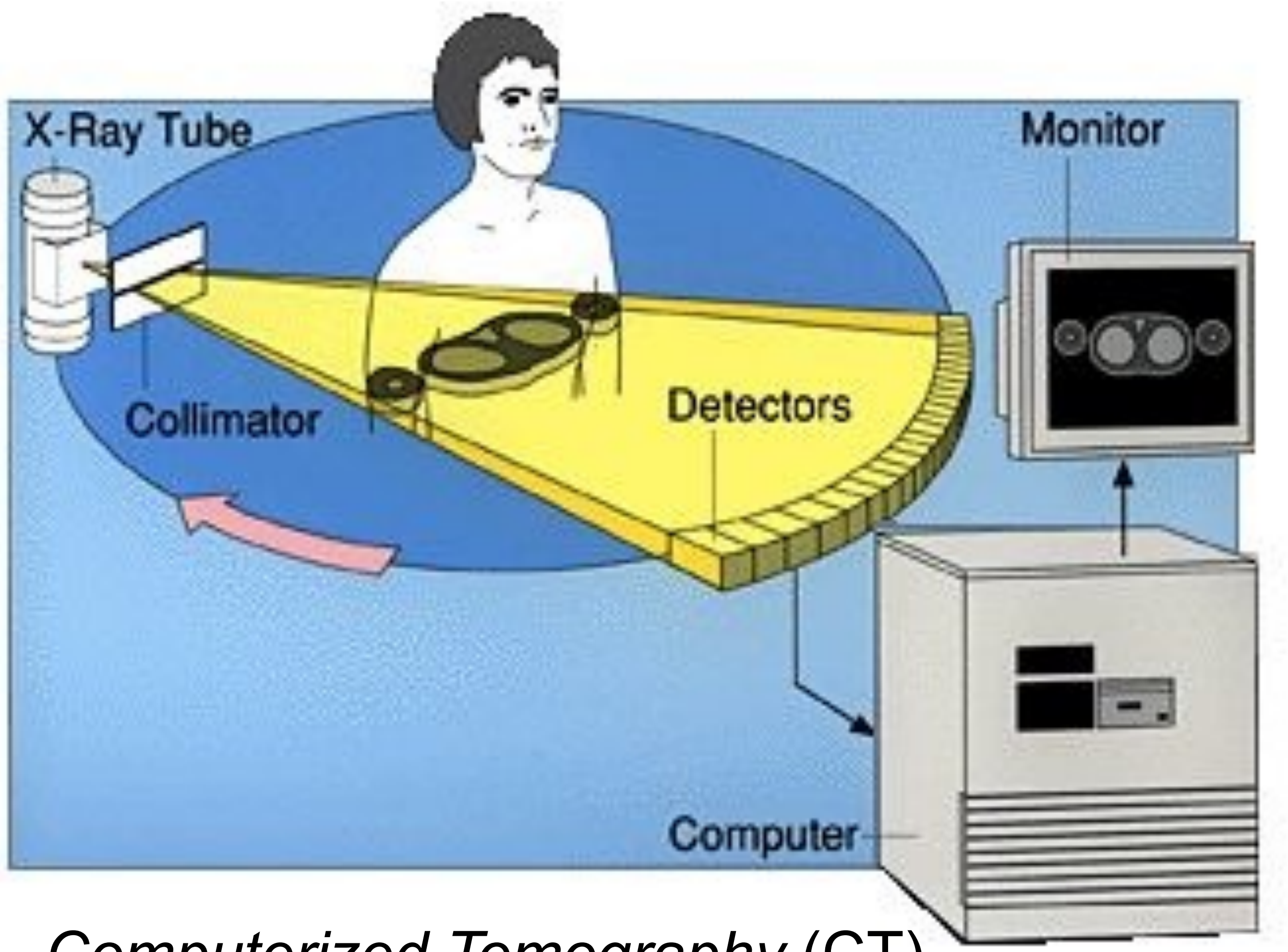
→ *Good morphological image*

- ***Positron Emission Tomography* (PET):**

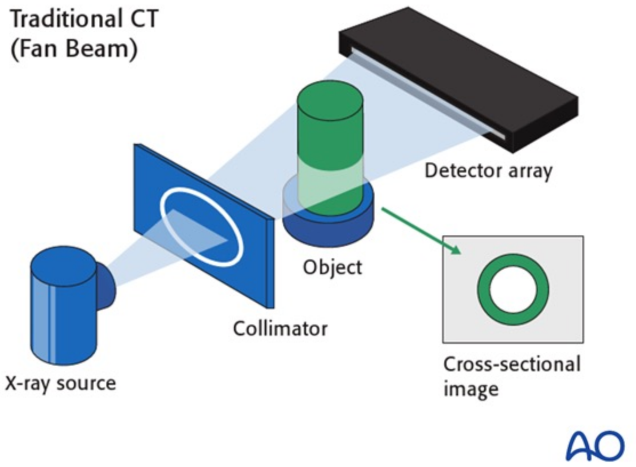
Use of radio-tracers and its accumulation in different organs in the body

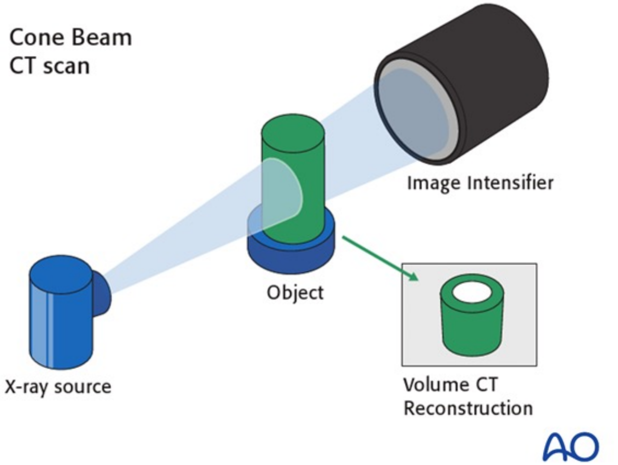
→ *Good functional image*

X-rays CT (xCT)



Computerized Tomography (CT)

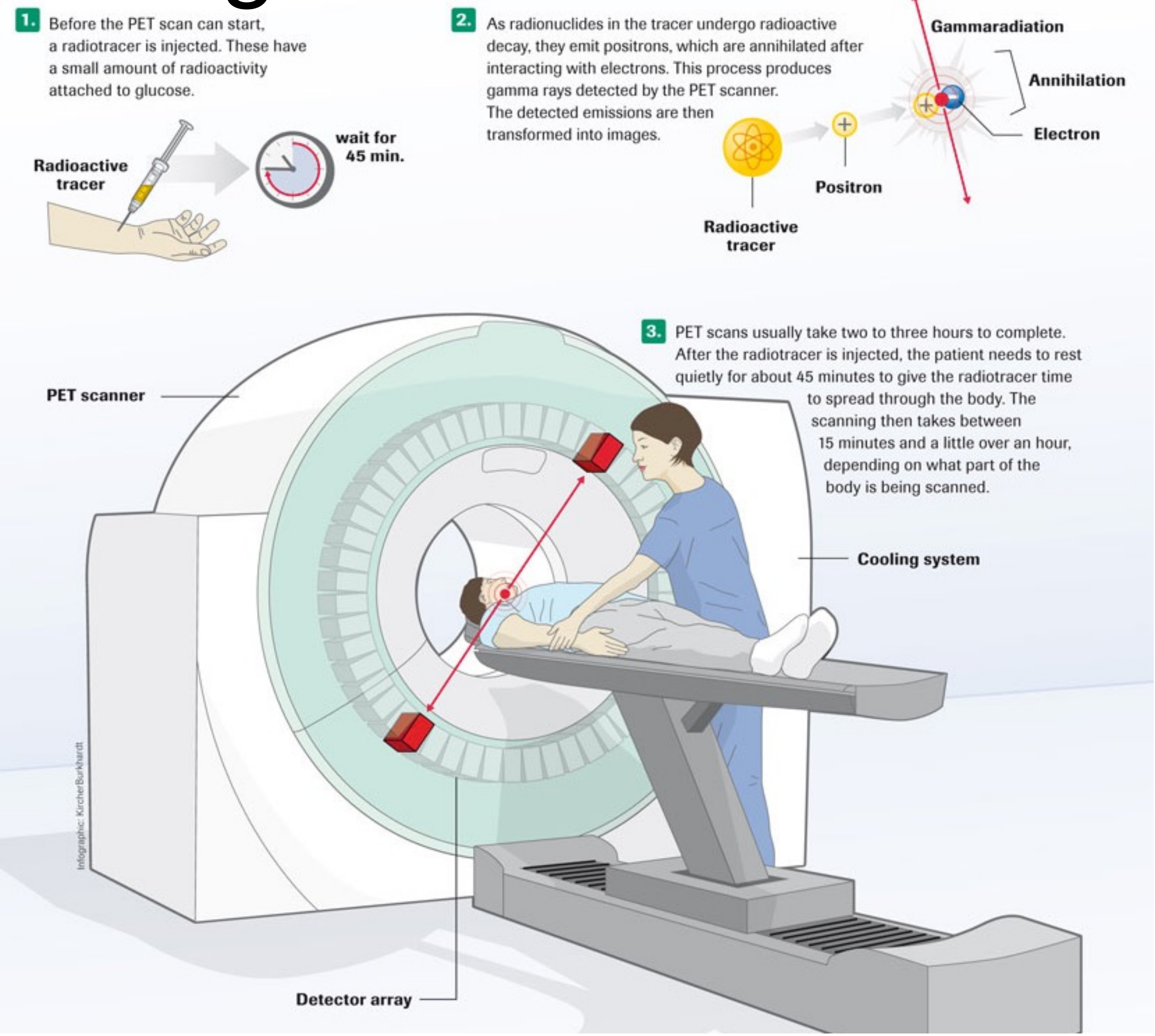




Source: Surgery reference web: https://surgeryreference.aofoundation.org/

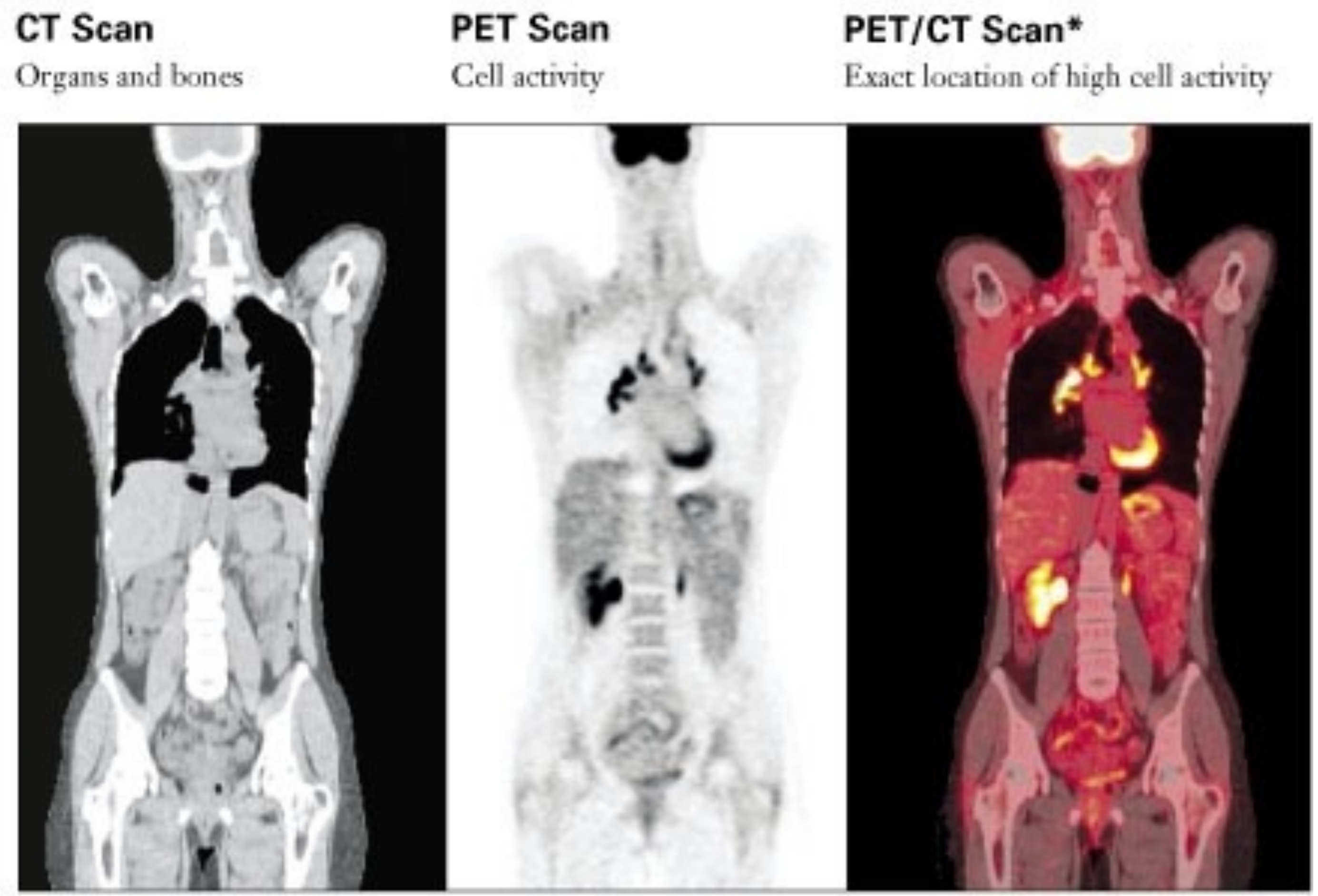
Radiodiagnostics: xCT & PET

Radiotracers:
FDG
(FluoroDeoxiGlucosa)
with ^{18}F for example



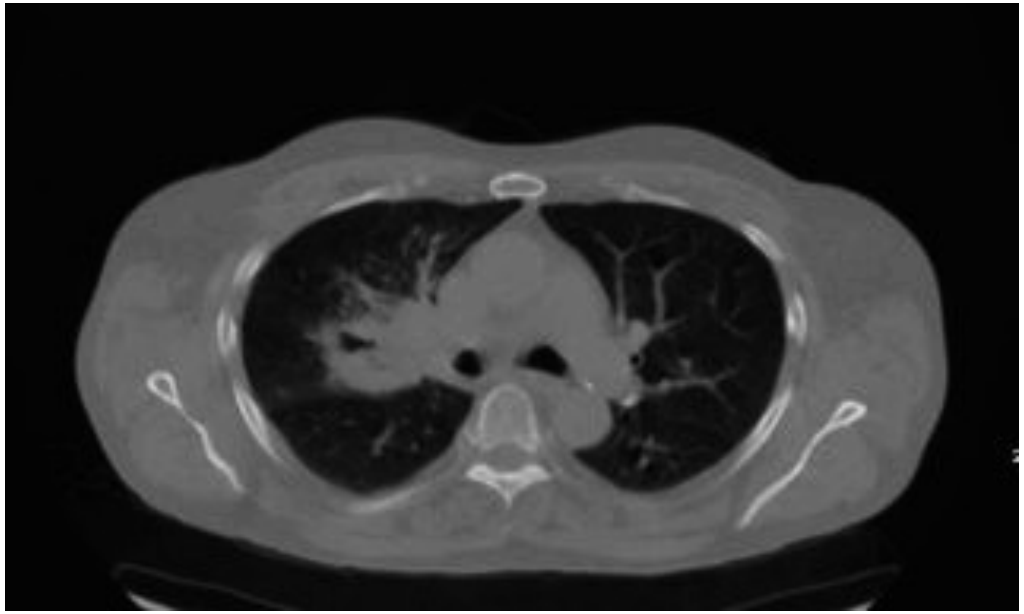
Positron Emission Tomography (PET)

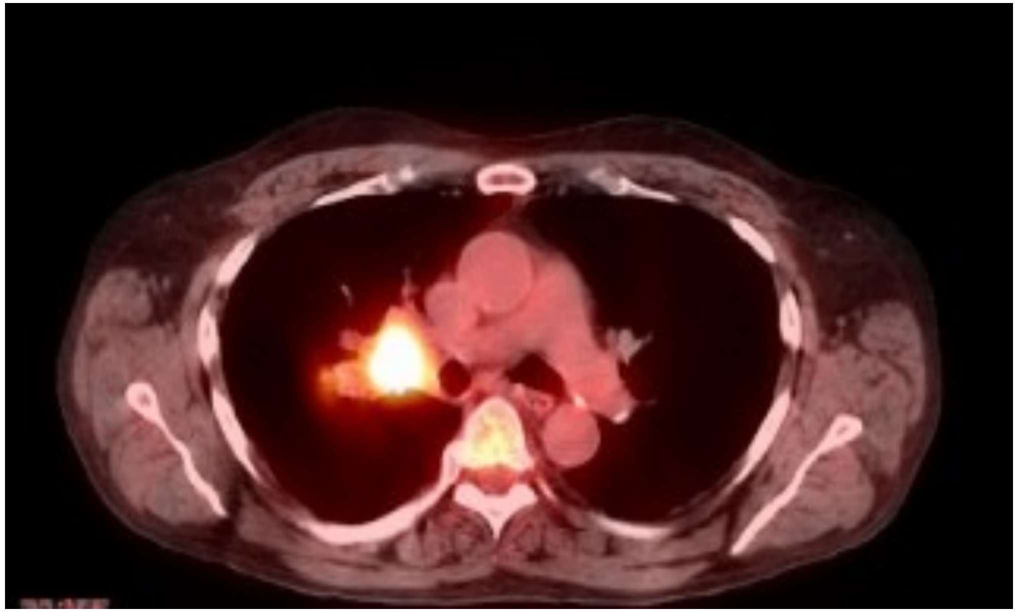
Radiodiagnostics: xCT & PET



PET/xCT combination: functional image with great definition and morphological quality

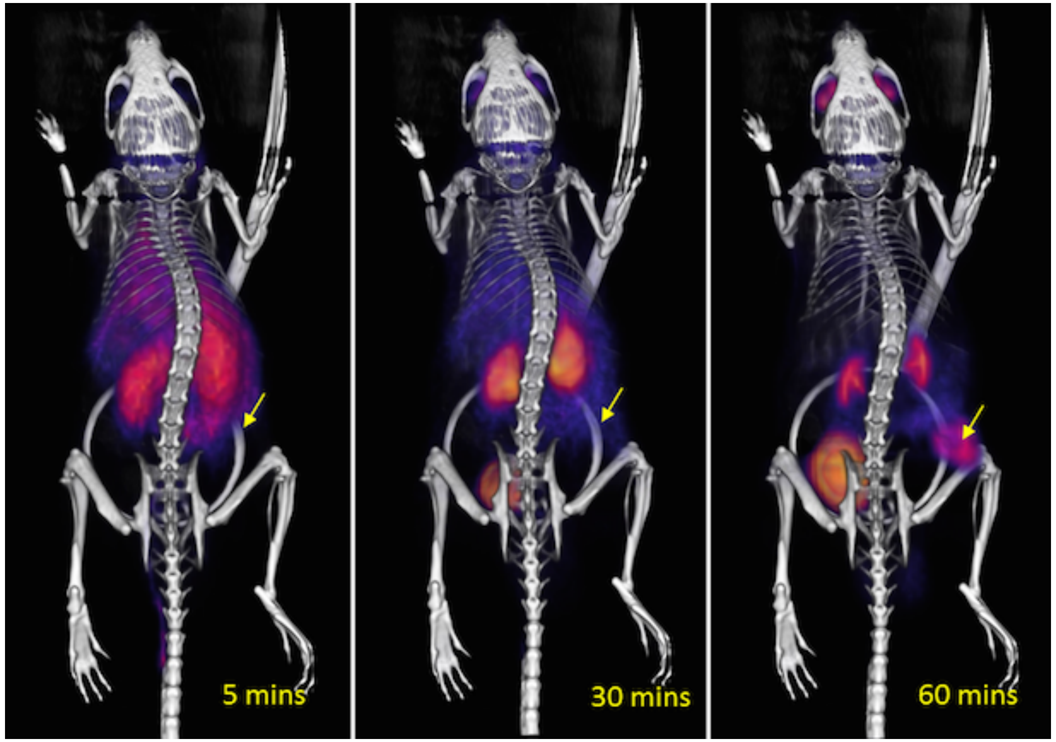
Radiodiagnostics: xCT & PET





PET/xCT combination:
functional image with great
definition and morphological quality

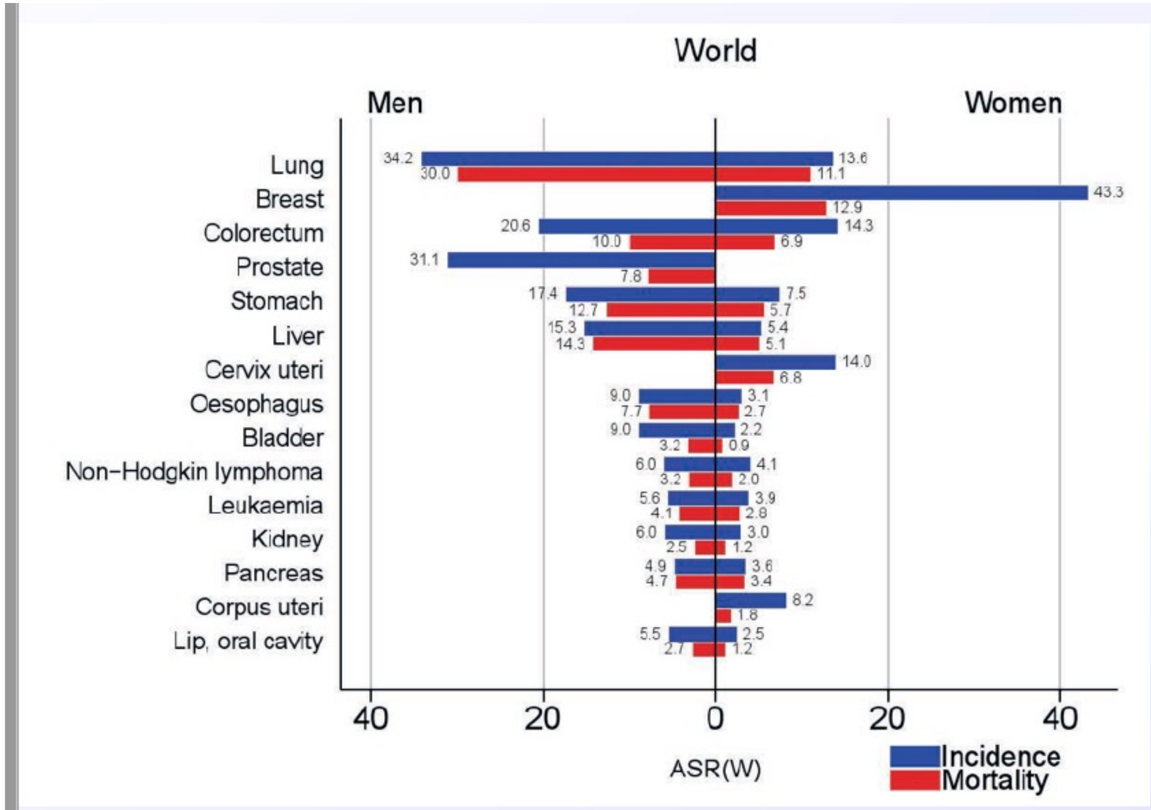
Radiodiagnostics: CT & PET

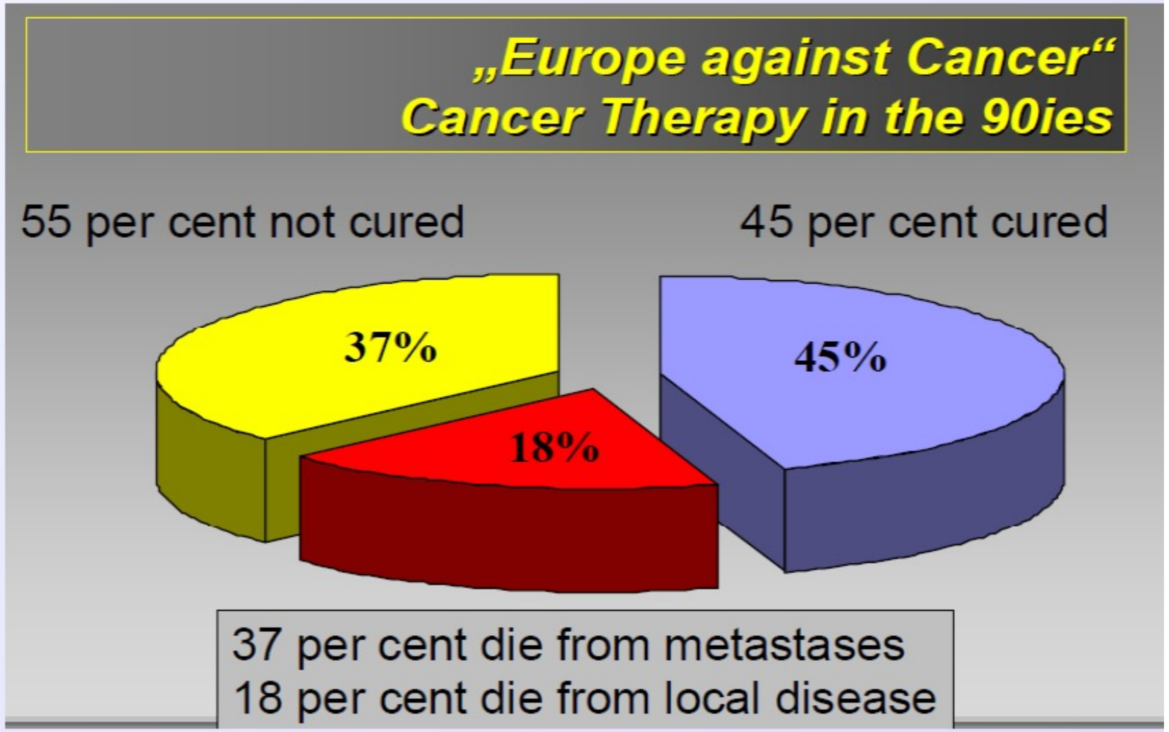


PET/xCT combination:
functional image with great
definition and morphological quality

PROTONTHERAPY

Cancer





[World Cancer Report 2014]

Taken from L.M. Fraile

Cancer is a leading cause of death worlwide, accounting for **nearly 10 million deaths in 2020**

(World Health Organization https://www.who.int/news-room/fact-sheets/detail/cáncer)

Radiotherapy

- ***Therapy with X- or γ–rays***

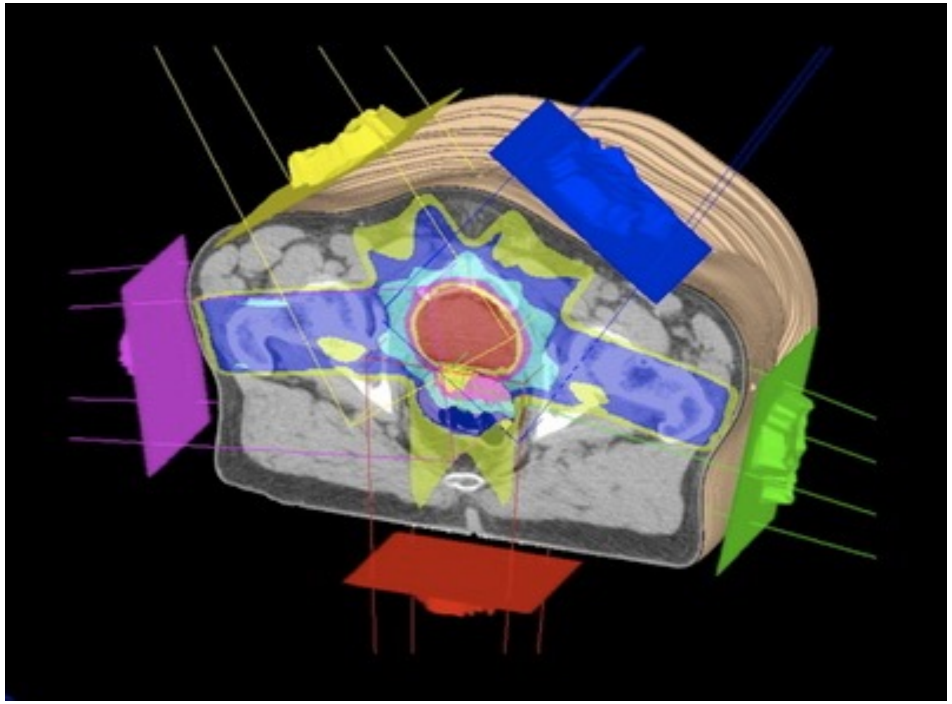
X-rays tubes, ^{60}Co source or electron linear accelerator (cheaper, less selective)

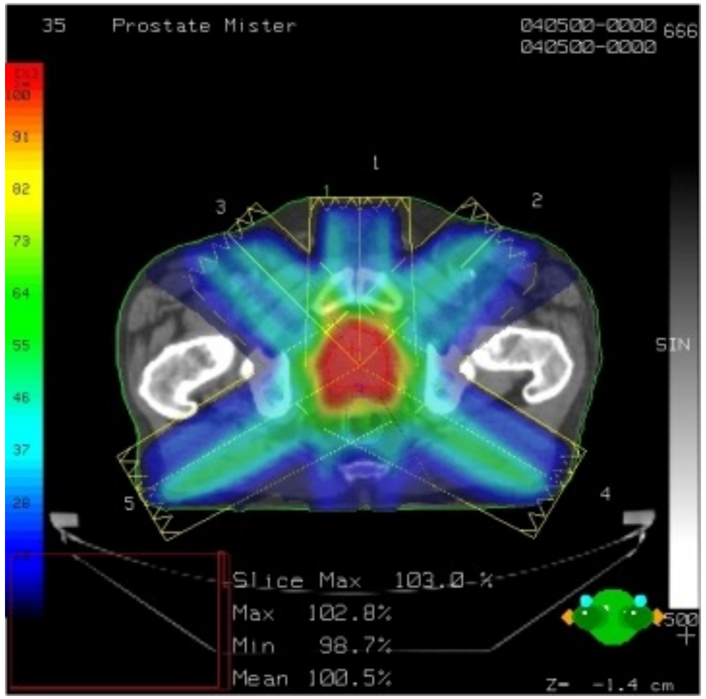
- ***Therapy with hadrons***

accelerators (ciclotrons or synchrotrons) of protons or ^{12}C (more expensive, very selective)

Radiotherapy:
X- or γ–rays *vs* hadrons (p,^{12}C)

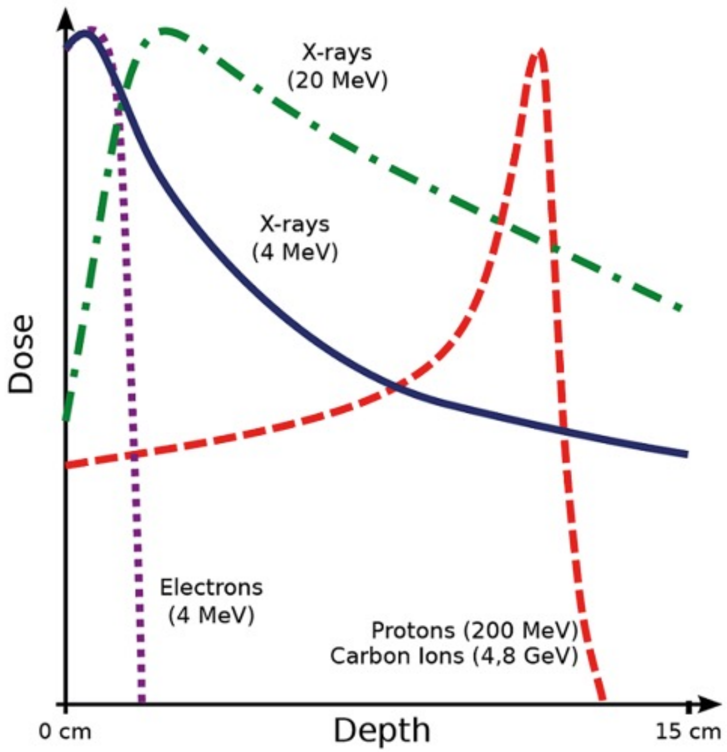
- Intensity Modulated Radiation Therapy (IMRT)
- 3D Conformal therapy

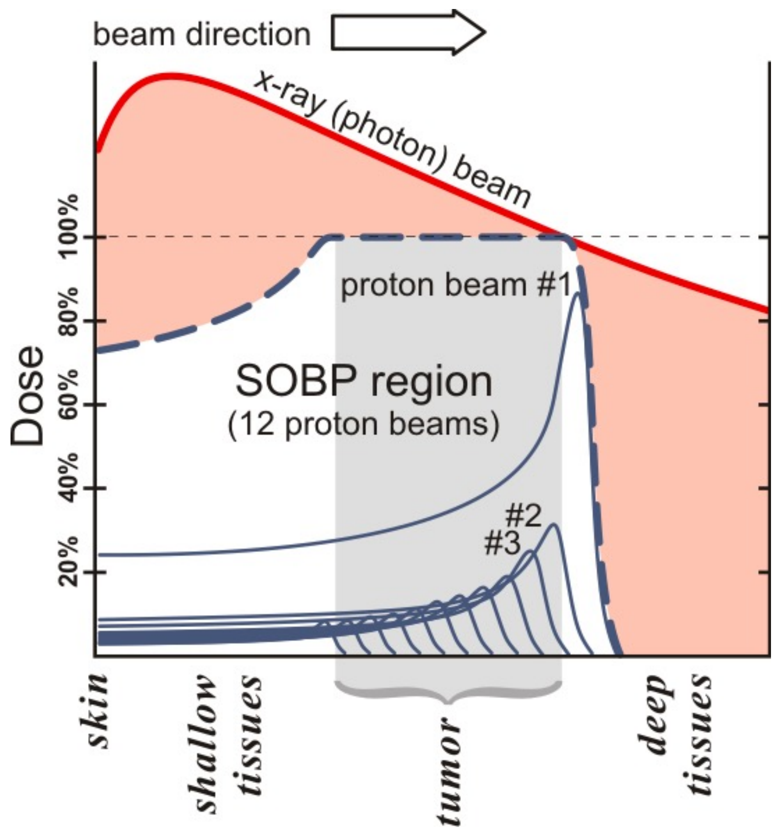




Radiotherapy: X- or γ–rays *vs* hadrons (p,^{12}C)

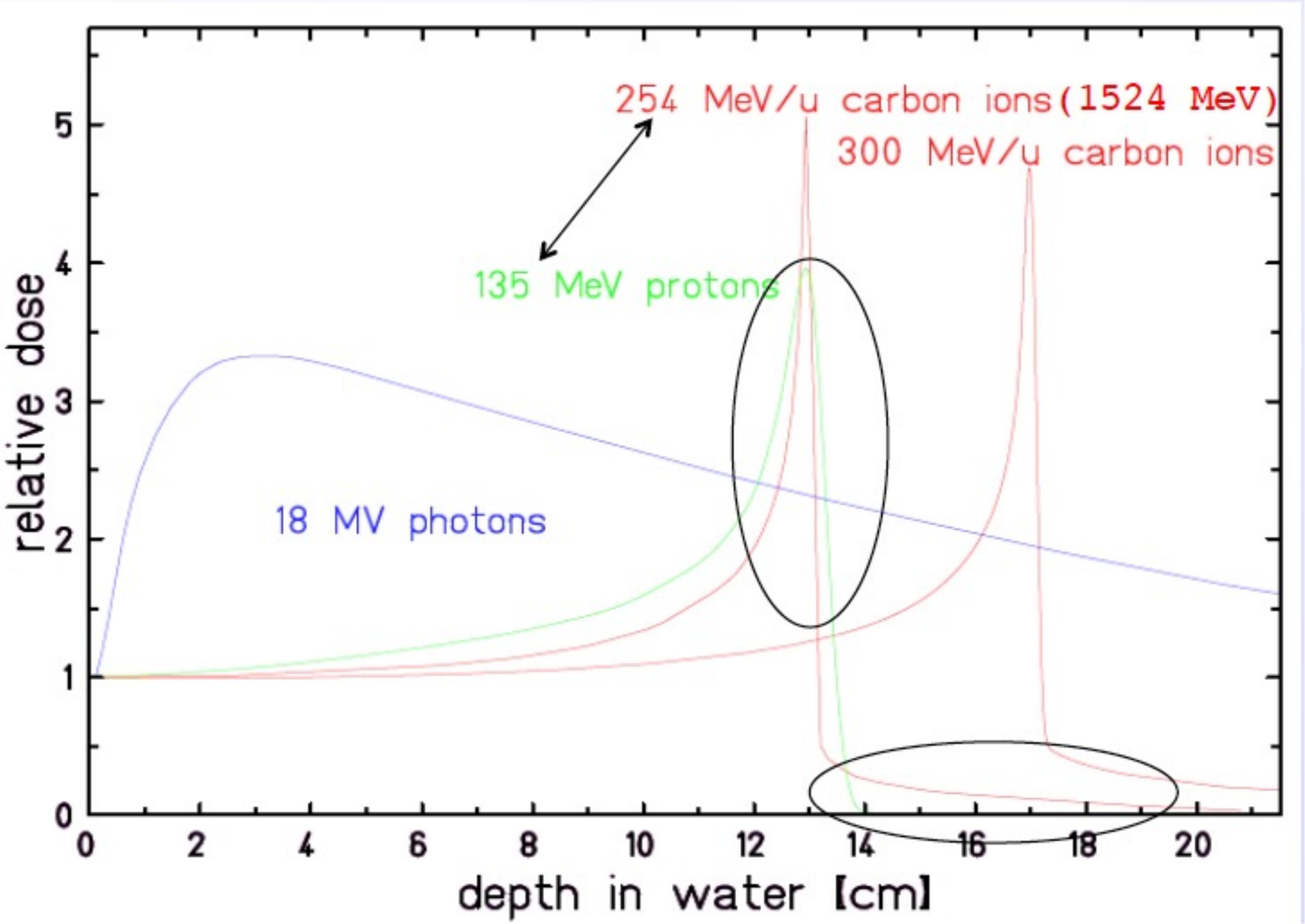
- *Hadrontherapy*: use of p or ^{12}C accelerated beams → very localized dose





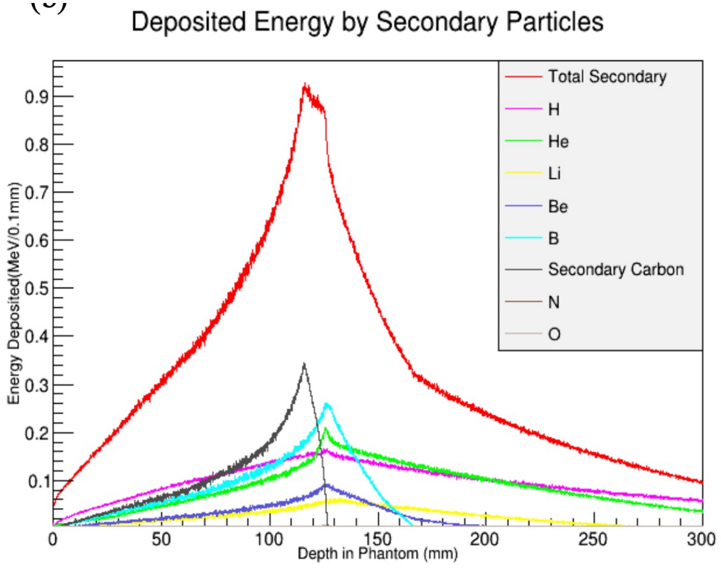
Red area:
Extra dosis
applied to
the patient

Radiation treatments



Proton vs Carbon ions:

- Bragg Peak (BP)
- Width of BP
- Tails beyond BP



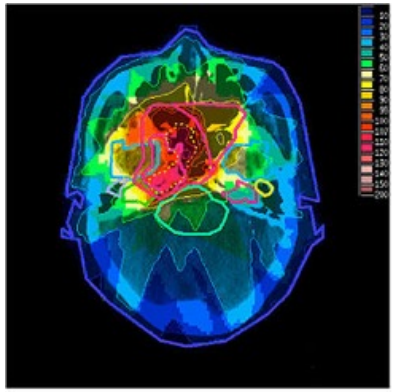
Source: C K Ying et al 2017 J. Phys.: Conf. Ser. 851 012033

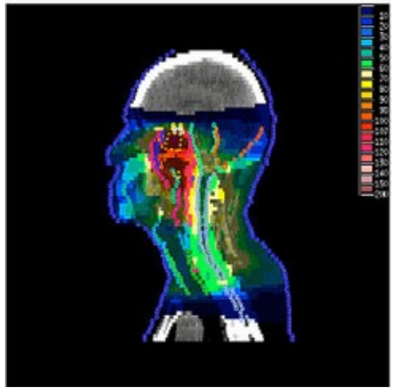
Radiotherapy:

X- or γ–rays *vs* hadrons (p,^{12}C)

nasopharyngeal carcinoma

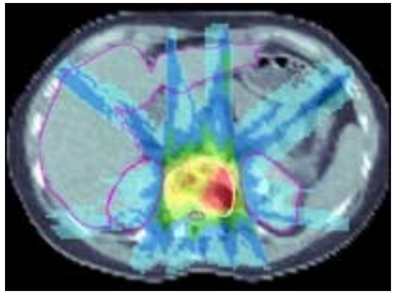
X-rays



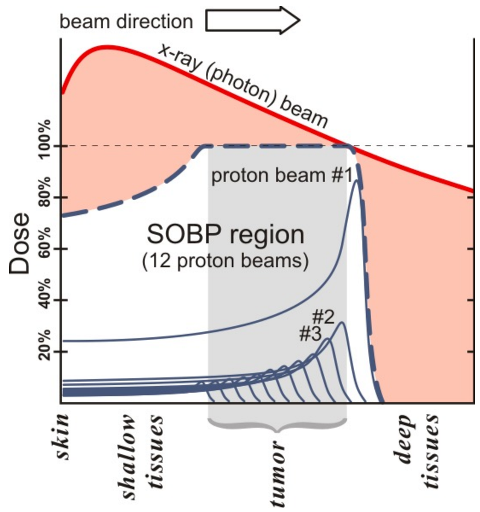


Medullary tumor

X-rays



Deposited energy with respect to depth:



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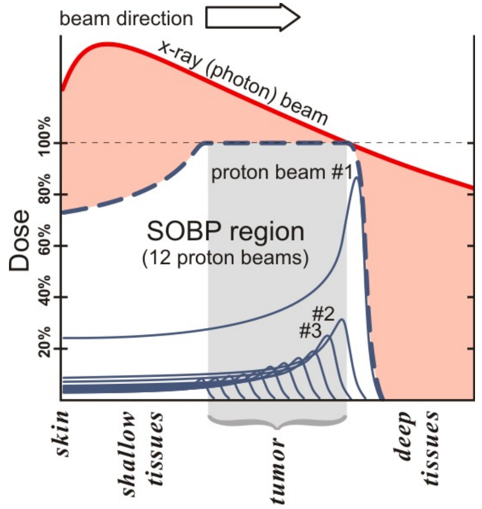
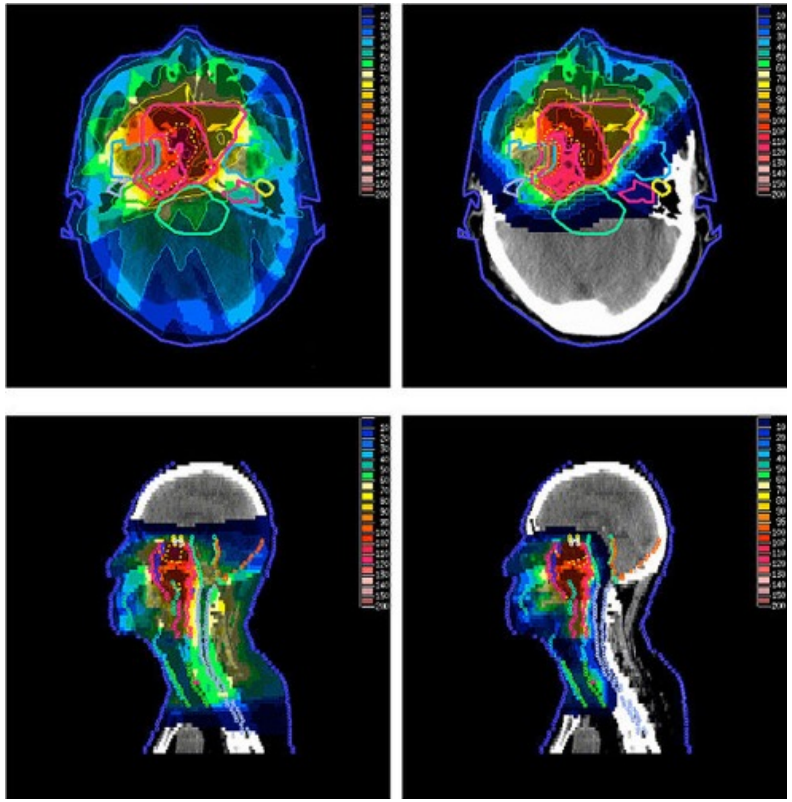
Radiotherapy:
X- or γ–rays *vs* hadrons (p,^{12}C)

Deposited energy with respect to depth:



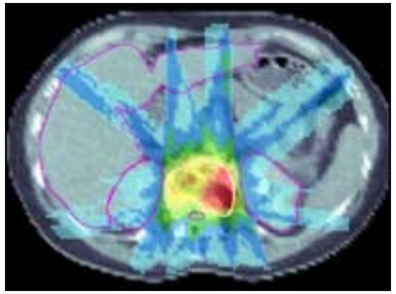
nasopharyngeal carcinoma

X-rays | protons

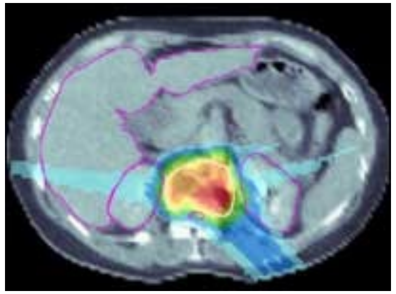


Medullary tumor

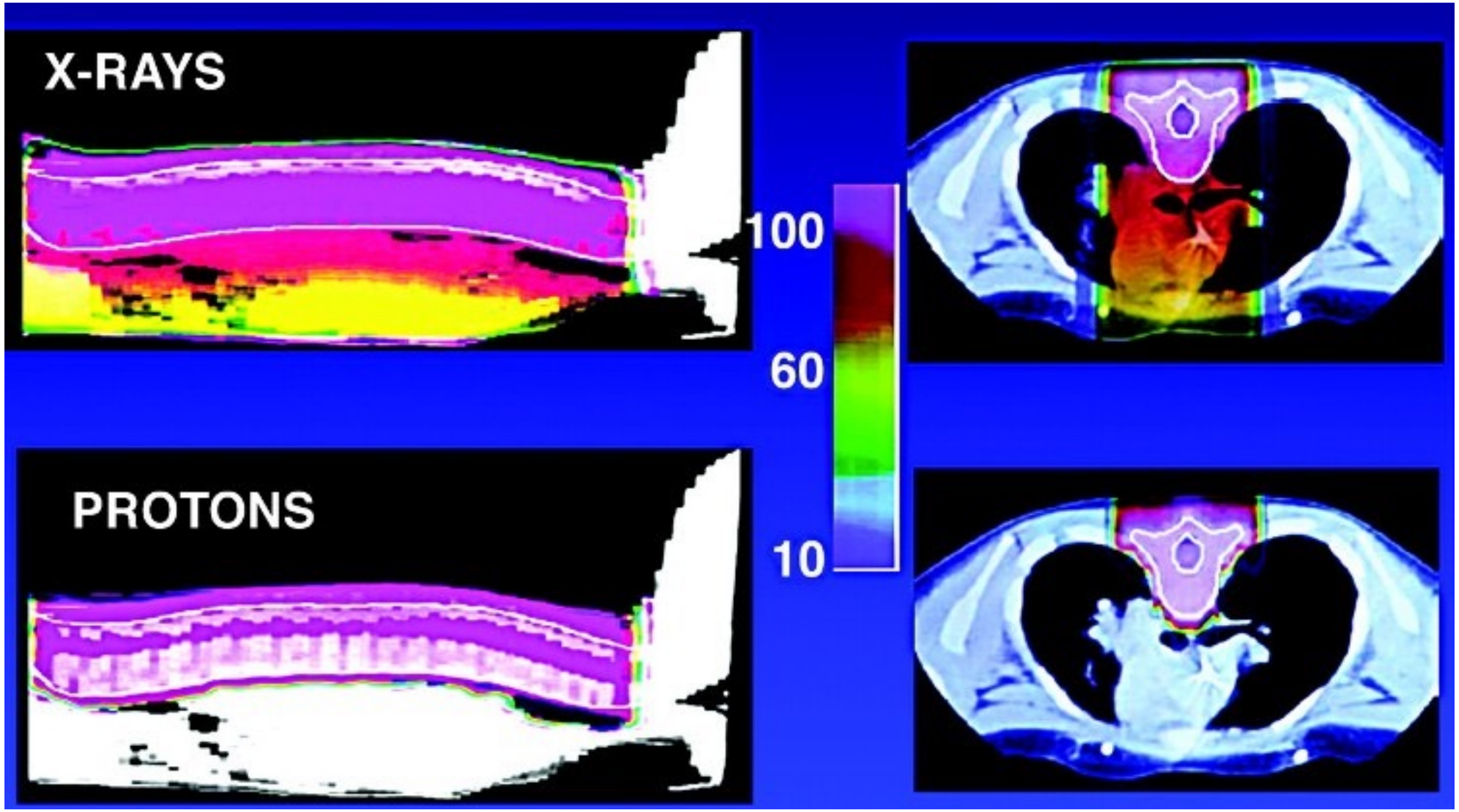
X-rays



protons



Radiotherapy:
X- or γ–rays *vs* hadrons (p,^{12}C)



Pediatric medulloblastoma

Protontherapy dose control

- Protons deposit dose in a very localised area
  - A **good control of dose deposition is required** since it makes the difference between applying high dose to tumor or healthy tissue
  - Treatment plans should be **very accurate and precise**
  - A system of dose verification is needed

Range Uncertainties

Reasons for range uncertainties:

- Organs motion
- Setup and anatomical variations
- Dose calculations
- Biological considerations

Source of range uncertainty in the patient	Range uncertainty without Monte Carlo	Range uncertainty with Monte Carlo
Independent of dose calculation		
Measurement uncertainty in water for commissioning	± 0.3 mm	± 0.3 mm
Compensator design	± 0.2 mm	± 0.2 mm
Beam reproducibility	± 0.2 mm	± 0.2 mm
Patient setup	± 0.7 mm	± 0.7 mm
Dose calculation		
Biology (always positive) ˆ	+∼0.8%	+∼0.8%
CT imaging and calibration	± 0.5%[a]	± 0.5%[a]
CT conversion to tissue (excluding I-values)	± 0.5%[b]	± 0.2%[g]
CT grid size	± 0.3%[c]	± 0.3%[c]
Mean excitation energy (I-values) in tissues	± 1.5%[d]	± 1.5%[d]
Range degradation; complex inhomogeneities	−0.7%[e]	± 0.1%
Range degradation; local lateral inhomogeneities *	± 2.5%[f]	± 0.1%
Total (excluding *, ˆ)	2.7% + 1.2 mm	2.4% + 1.2 mm
Total (excluding ˆ)	4.6% + 1.2 mm	2.4% + 1.2 mm

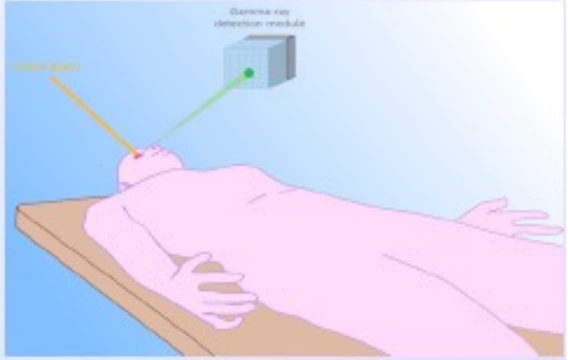
Source: H. Paganetti Phys. Med. Biol. 57 (2012) R99-R117

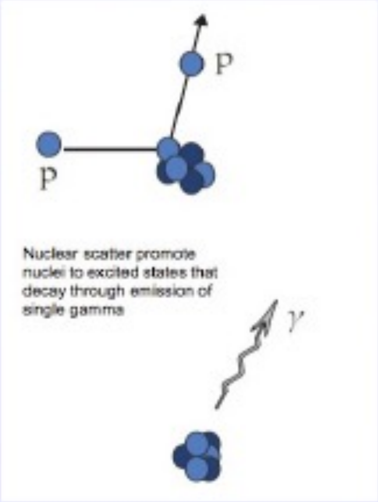
Treatment plans take into consideration an uncertainty of 3.5 % of the range plus 1-3 mm

For example, 3.5%+3 mm implies 1 extra cm for a tumor at 20 cm depth

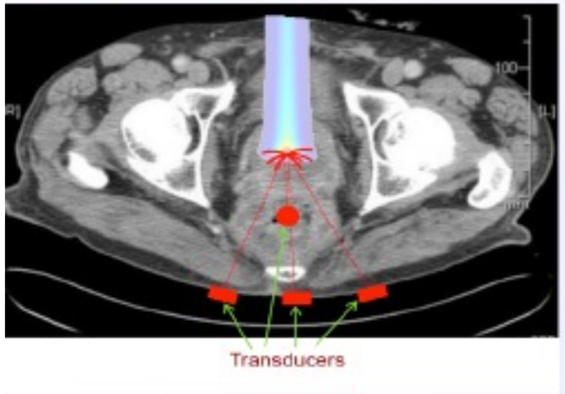
Dose verification

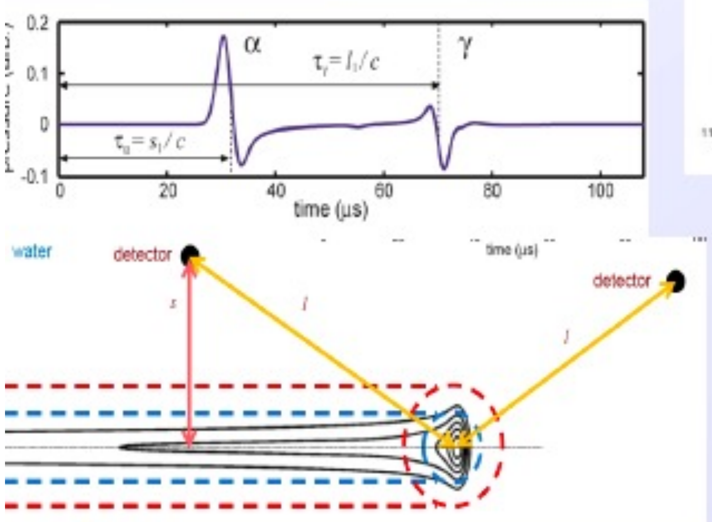
Prompt gamma-rays



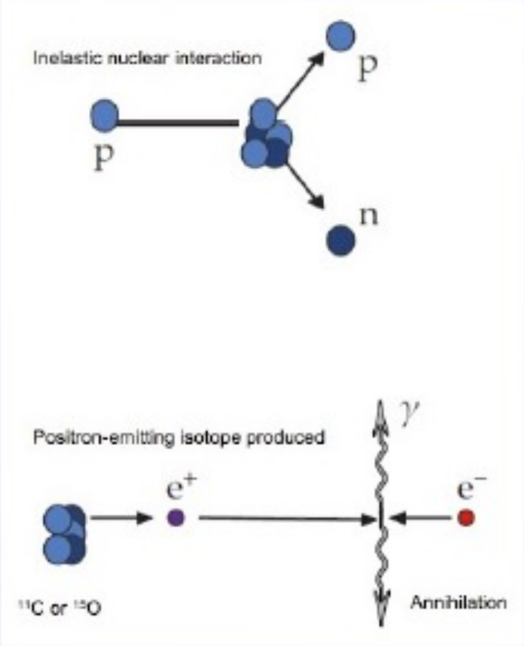


Protoacustics





PET, prompt PET



Taken from L.M. Fraile

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Hadrontherapy in Spain

- Currently, there are 98 protontherapy centers and, at least, 29 under construction and 12 of hadrontherapy with ^{12}C and 5 other under construction worlwide

- Protontherapy arrived recently to Spain with two centers (in Madrid):
  Quirónsalud y Clínica Universidad de Navarra.

EL MUNDO Cáncer

Llega a España el bombardeo de protones que cura los tumores más escondidos

LAURA TARDÓN Madrid 27 DIC. 2018 10:30

EFE: SALUD

Primer centro de protonterapia contra el cáncer en España empezará a funcionar en 2019

Javier Tovar | MADRID/EFE/REDACCIÓN SALUD Miércoles 06.06.2018

- 2 new centers in the Public Health System recently approved to be built in Cantabria and Cataluña (planned for 2025) : ElPais de 30 Abril 2021

CÁNCER >

La radioterapia más puntera aterriza en la sanidad pública para mil niños enfermos de cáncer al año

Cataluña y Cantabria construirán dos centros de protonterapia mientras Andalucía ignora un proyecto ultimado tras siete años de estudio

quirónsalud
La salud persona a persona

In operation since December 2019

https://www.quironsalud.es/es/centro-protonterapia

Clínica Universidad de Navarra

From March-April 2020

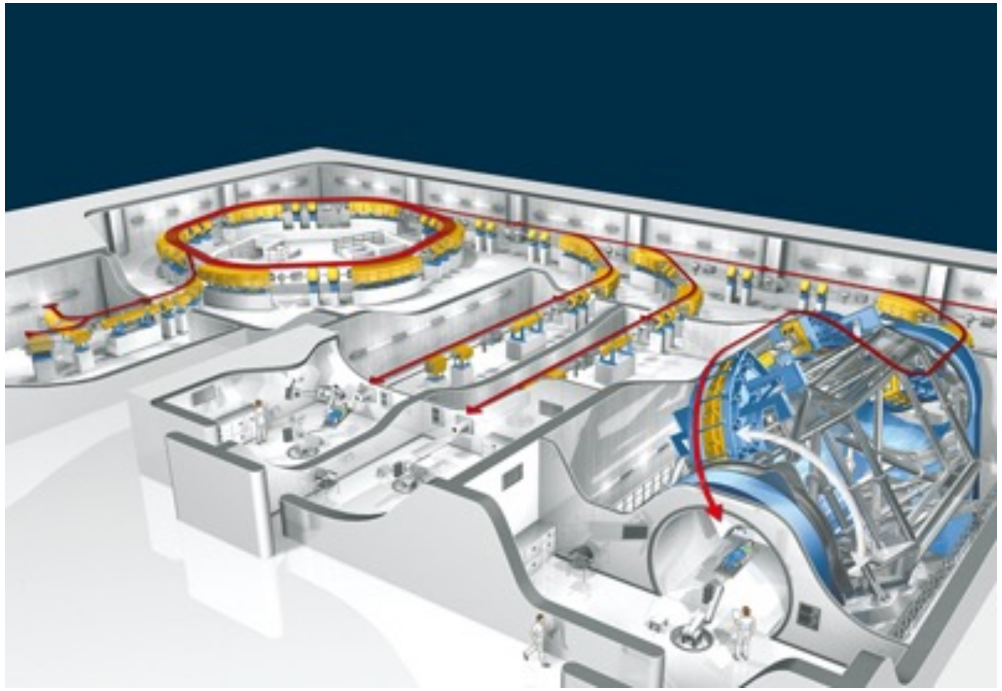
UNIDAD DE TERAPIA DE PROTONES

INICIO DE TRATAMIENTO A PACIENTES A PRINCIPIOS DE 2020

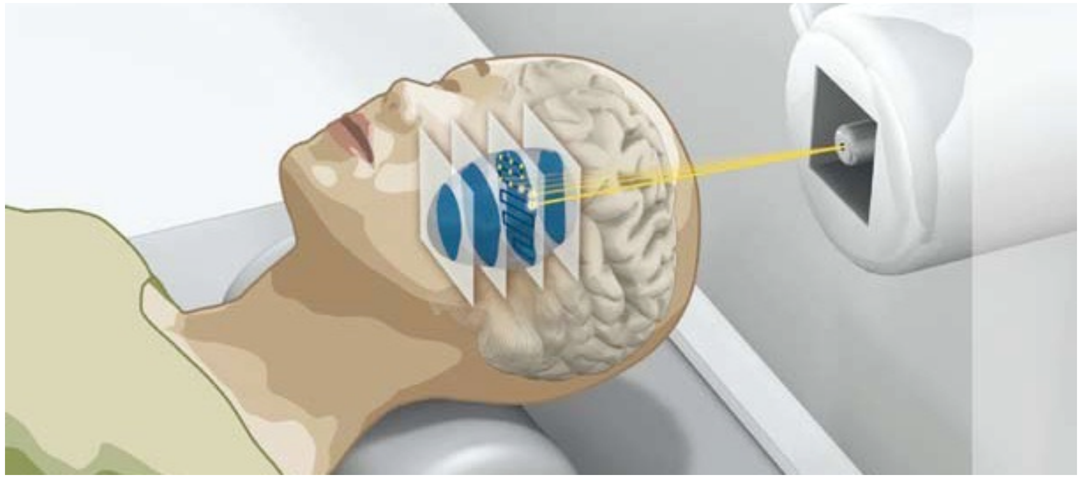
Con una superficie de 3.600m2 la nueva unidad cuenta con un acelerador de protones, dos salas de tratamiento para pacientes (gantrys), salas de trabajo y equipo e instalaciones de apoyo.

https://www.cun.es/protonterapia

HIT: Center of therapy with ion beams in Heidelberg (Germany)



- Therapy with both, protons and heavier ions
- Treating patients since November 2009
- Approx.: 750 patients per year
- Treatment of tumors with difficult chirurgical Access up to 30 cm deep



- CO_2 Ion beam, it produces ionized C_2
- Linear Accelerator with $\beta=v/c=0.1$
- Synchrotron accelerates C ions up to $\beta=0.73$

R&D IN PROTONTHERAPY

PRONTO-CM project

- Joint project: UCM-CSIC-Ciemat
- 4 years: 2018-2021
- R&D in protontherapy: proton range verification and proton imaging

B2017/BMD-3888
Programas de I+D en Biomedicina 2017
Comunidad de Madrid
UNION EUROPEA FONDO EUROPEO DE DESARROLLO REGIONAL

Pronto
Protontherapy and nuclear techniques for oncology

IEM-CSIC in PRONTO

- Design a proton-CT scanner

- Built using Nuclear Physics instrumentation

B2017/BMD-3888
Programas de I+D en Biomedicina 2017

Pronto
Protontherapy and nuclear techniques for oncology

The importance of proton-CT

Proton-therapy treatment plans are based on X-rays CT images (XCT)

Conversion

– Maps of Hounsfield Units (XCT) → RSP (Proton-therapy)

(relative stopping power)

$$HU = 1000 \times \frac{\mu - \mu_{\text{water}}}{\mu_{\text{water}} - \mu_{\text{air}}}$$

(μ → attenuation coefficients)

– **Conversion induces uncertainties in proton ranges of ~3%**

Using proton-CT (pCT) images: **uncertainties can be reduced to < 1%**

Challenge: design a pCT scanner providing high quality images

Dose applied to patient

Absorbed dose for a head

- radiograph: 0.01 mGy
- X-ray CT: 30-50 mGy
- proton CT: ~1.3-1.4 mGy

Source: Robert P. Johnson et al. Rep. Prog. Phys. 81 (2018) 016701

Advantages of proton-CT vs. xCT

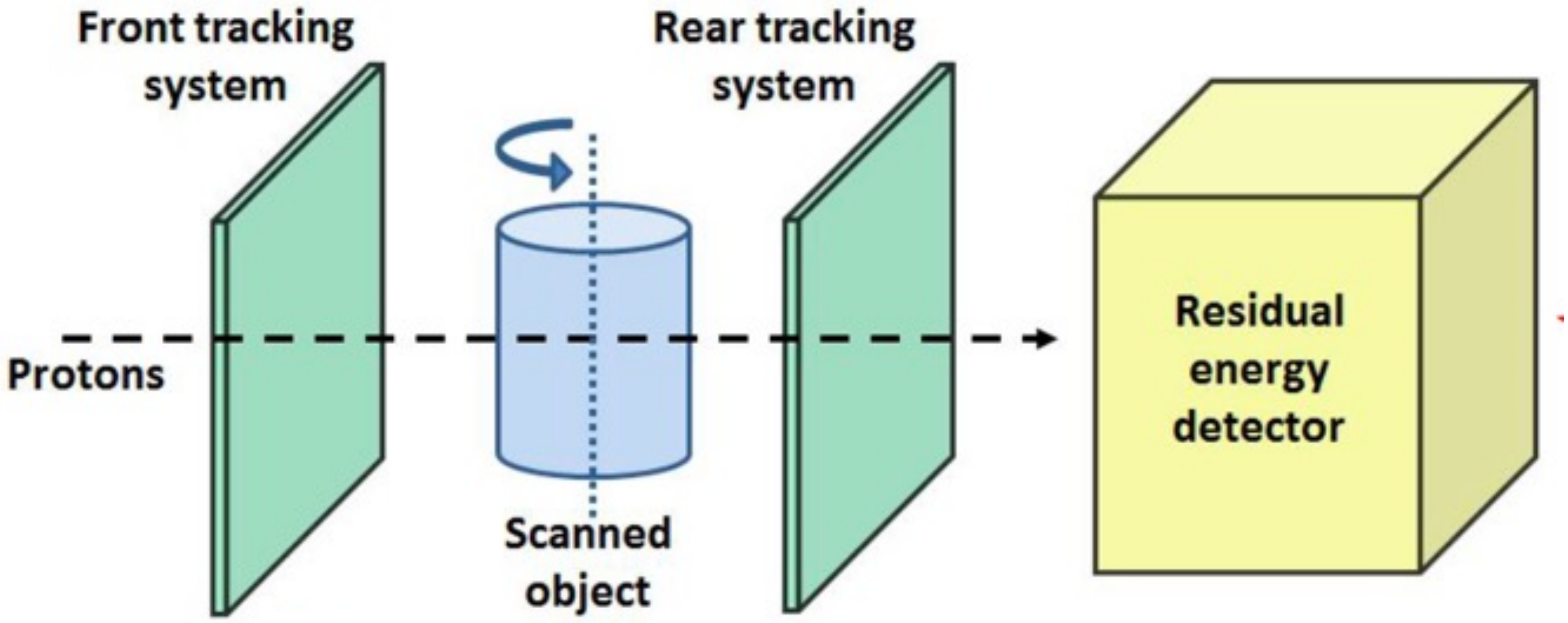
- Reduce uncertainties in proton ranges from 3% to <1%

- Avoid image artifacts originated by high-Z components
- Methalic elements such as dental implants, cardiac pacemaker, etc…

- More reduced dose to patient

- Generally speaking: lower spatial resolution but better density resolution

proton CT scanner



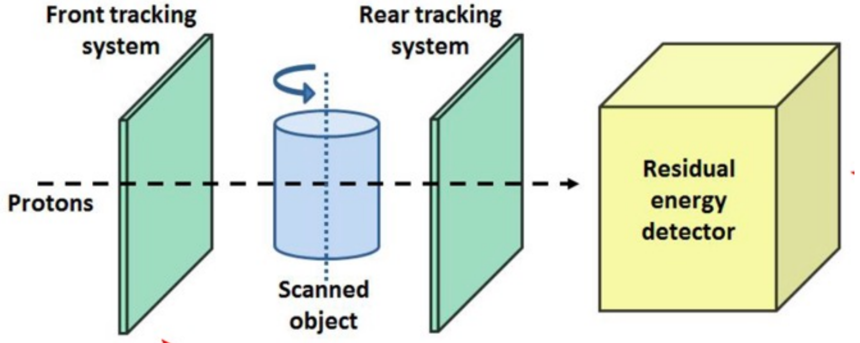
Prototypes of pCT scanners

Collaboration	Type	Aperture (cm^2)	Tracking technology	WEPL detector technology	Rate	Comment
AQUA [90] Italy	pRad	10×10	GEM	Scint. range counter	10 kHz	1 MHz planned
LLU/UCSC phase-II [51] USA	pCT	36×9	Si strip	5 scint. stages	1.2 MHz	Operational
Niigata [100] Japan	pCT	9×9	Si strip	NaI calorimeter	30 Hz	Larger, faster instr. planned
NIU, FNAL [93] USA	pCT	24×20	Sci Fi	Scint. range counter	2 MHz	Not operational
PRaVDA [102] UK	pCT	4.8×4.8	Si strip	CMOS APS telescope	2.5 MHz	Only tracker operating
PRIMA [95] Italy	pCT	5.1×5.1	Si strip	YAG:Ce calo-rimeter	10 kHz	20×5 cm^2 1 MHz instr. planned
PSI [84] Switzerland	pRad	22.0×3.2	Sci Fi	Scint. range counter	1 MHz	Program completed
QBeRT [88] Italy	pRad	9×9	Sci Fi	Sci Fi range counter	1 MHz	Also a beam monitor

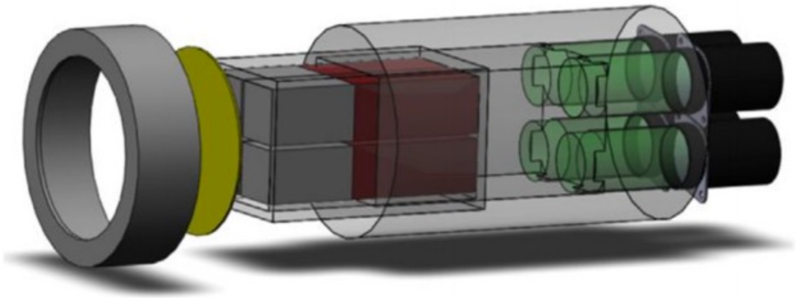
Source: Robert P. Johnson et al. Rep. Prog. Phys. 81 (2018) 016701

IEM-CSIC prototype of pCT scanner

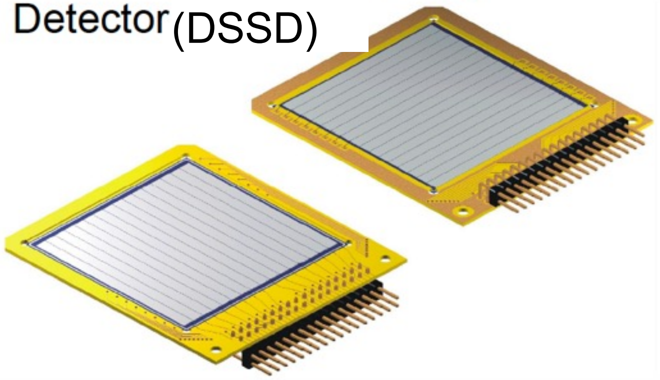
pCT scanner



CALIFA Endcap Phoswich Array (CEPA4)

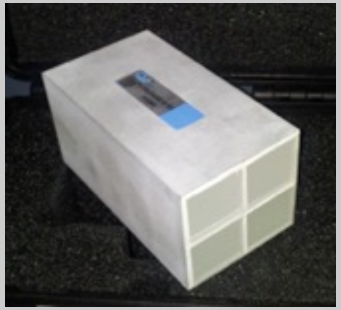


Double-sided Silicon Strip Detector (DSSD)



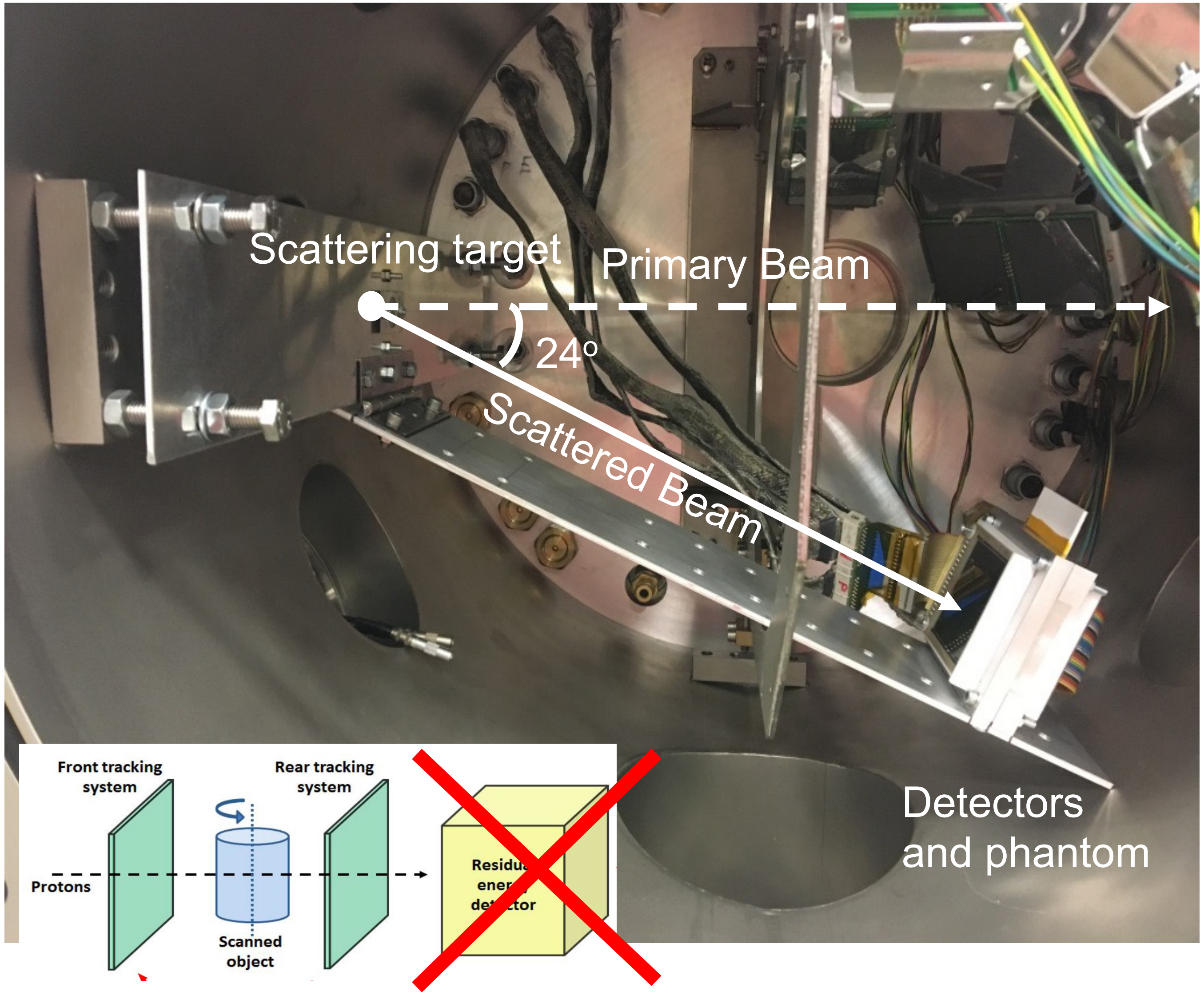
Area: 50 x 50 mm^2
Segmentation: 256 3x3 mm^2 pixels

- Phoswich: $LaBr_3$ (4 cm) + $LaCl_3$ (6 cm) in Array of four 27x 27mm^2
- Energy resolution:
  - 3 % for 1173 keV γ (^{60}Co)
  - 3-5 % for 60 – 130 MeV protons
- decay time 16 ns

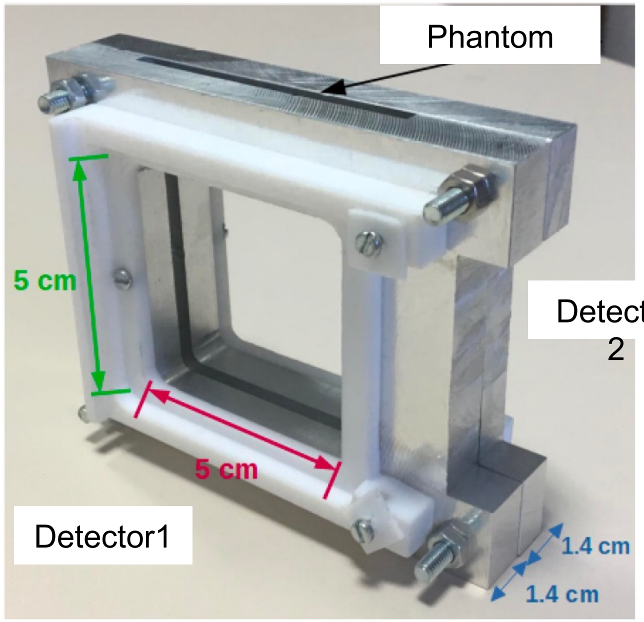


O. Tengblad et al. NIM A 704 (2013) 19-26

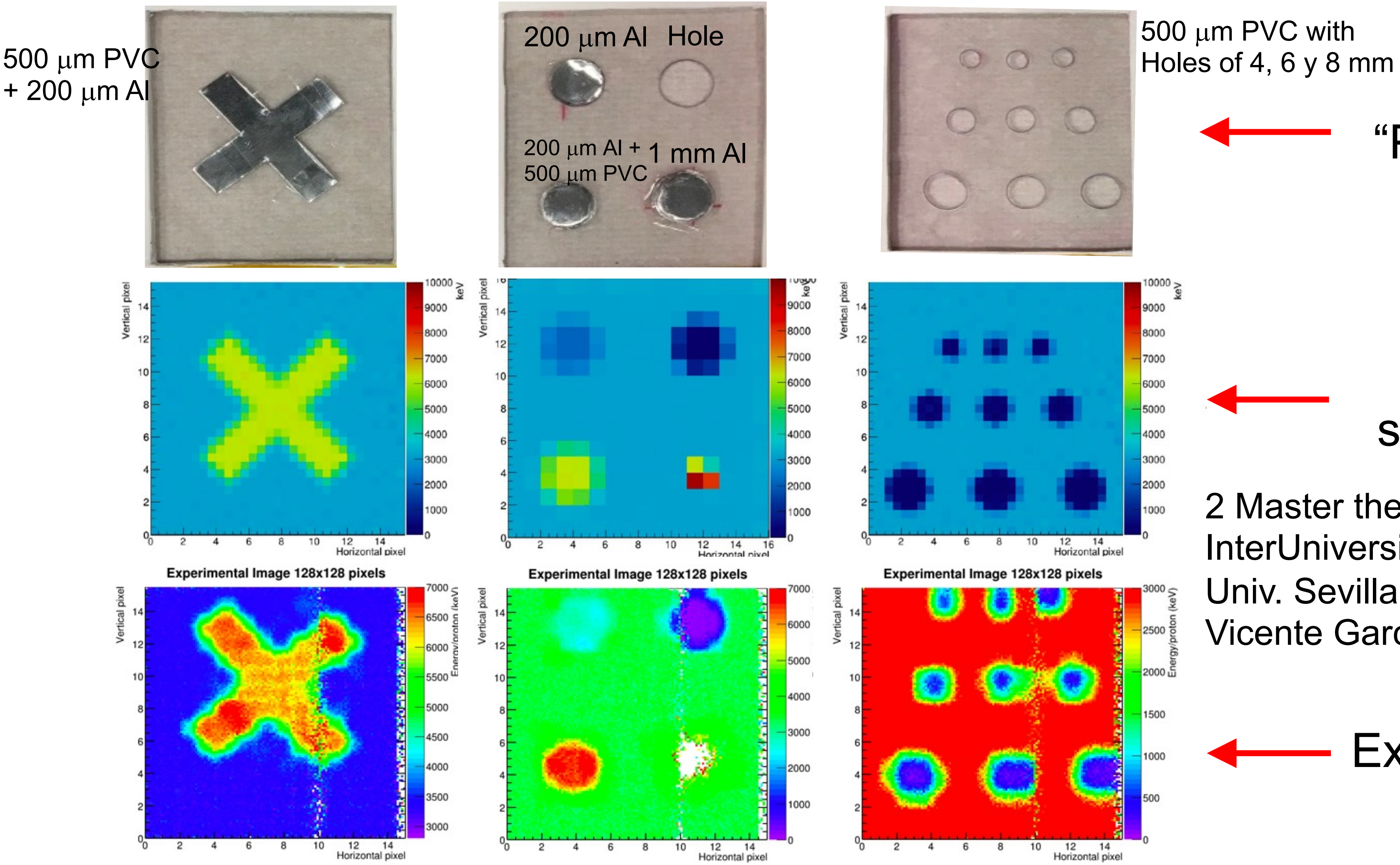
Proof-of-concept: CMAM Experiment



- Centro de MicroAnálisis de Materiales (UAM)
- 10 MeV protons → thin "phantoms" ~1 mm
- Beam intensity ~1 nA
- 2 DSSDs detectors:
  - 60 μm
  - 500 μm



Proof-of-concept: CMAM Experiment



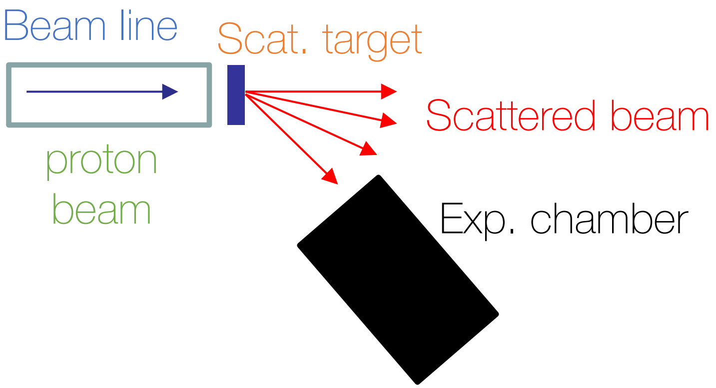
"Phantoms"

Geant4 simulations

2 Master theses from this Master InterUniversitario were defended in Univ. Sevilla in Sept 2019: Vicente García and Inma Posadillo

Experimental results

Future experiments



Cyclotron Centre Bronowice

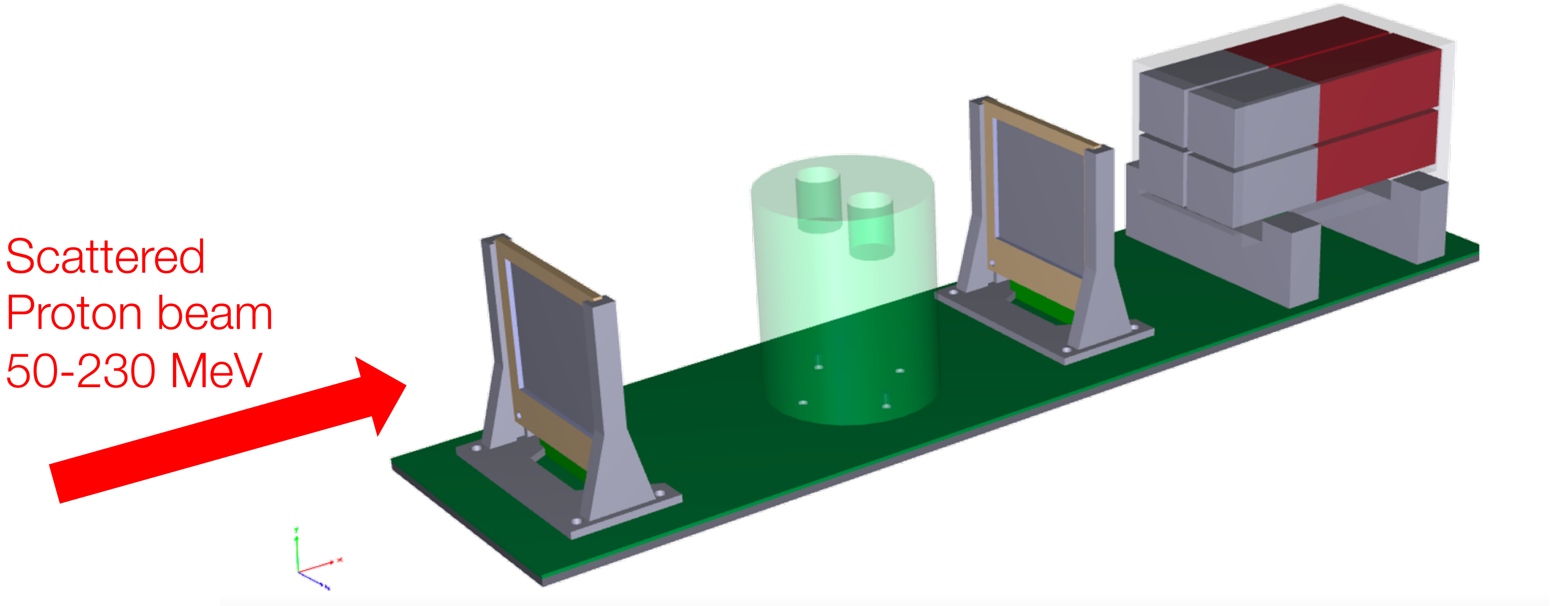
Experiments to be performed in 2021 at:

1º- KVI-CART (Groningen, Netherlands) → **28-30 Junio 2021**

2º- CCB (Krakow, Poland) → **4-6 Junio 2021**

Higher beam energies: 50-230 MeV

Larger phantoms: from 60 mm to 200 mm thickness



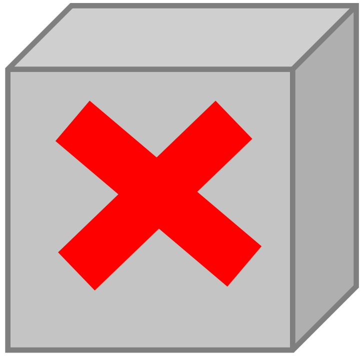
<u>Objectives</u>

- Properties of direct images (radiographs) (**Single projections)**
- Tomography of 3D objects (**Multiple projections**):
  - test of reconstruct. algorithms
  - evaluation of image properties

Phantoms

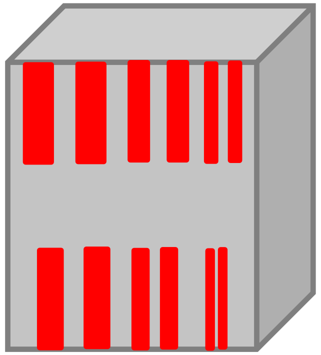
Single projection

Simple (Cross)



Aluminum inserts

Derenzo-type



- Sensitivity different materials
- Imaging spatial shapes

Spatial resolution

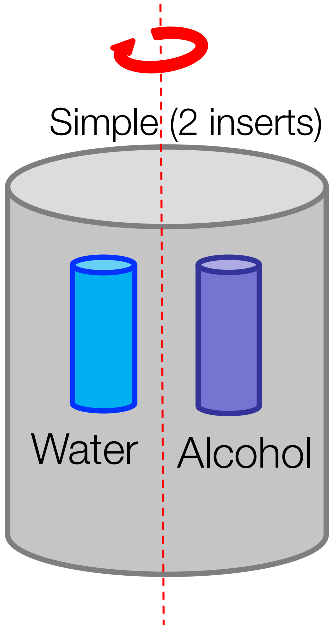
Radiograph mode

Materials

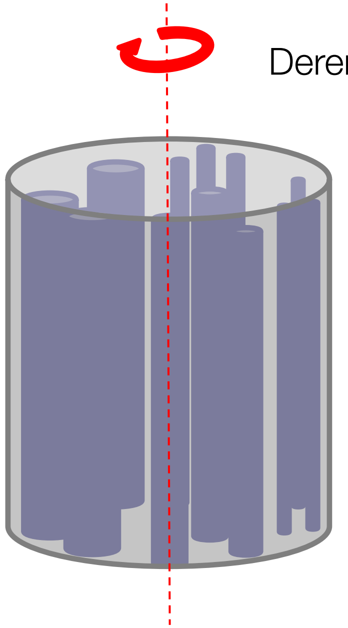
- PMMA
- Aluminum
- Air
- Water
- Alcohol

Multiple projections

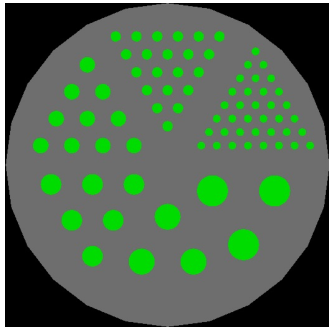
Simple (2 inserts)



Derenzo



Top view

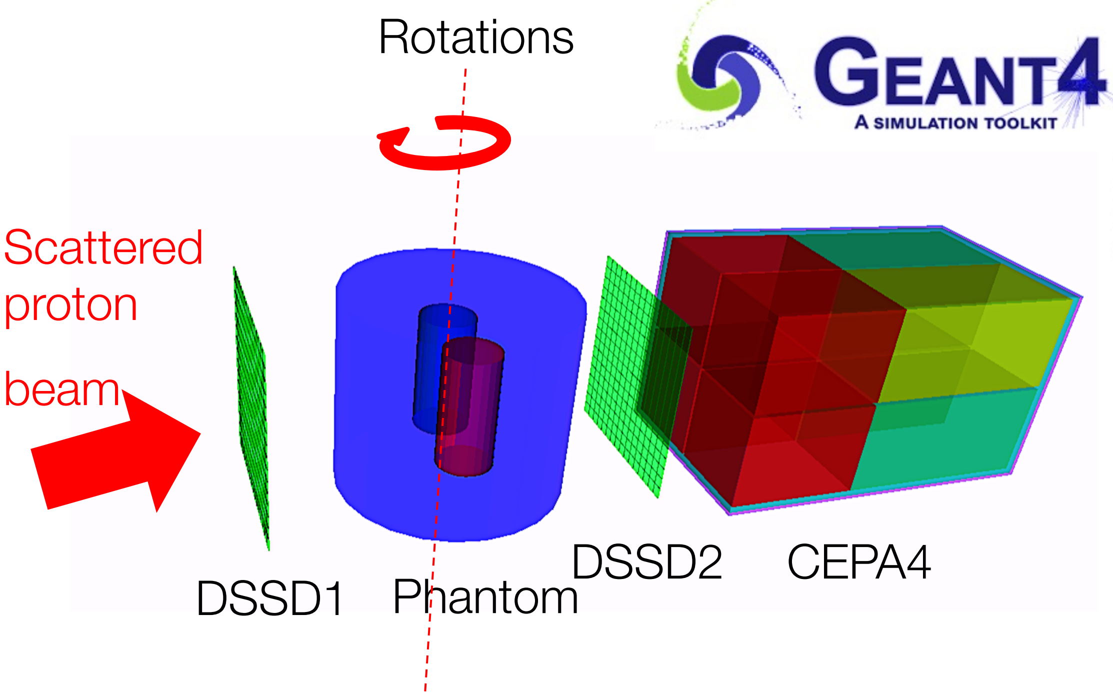


- Sensitivity different materials
- Imaging spatial shapes

Spatial resolution

Reconstructed CT images

pCT scans: Geant4 simulations



Geant4 geometry

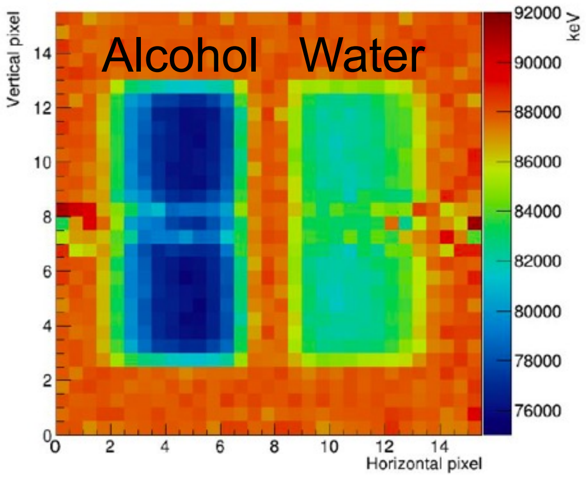
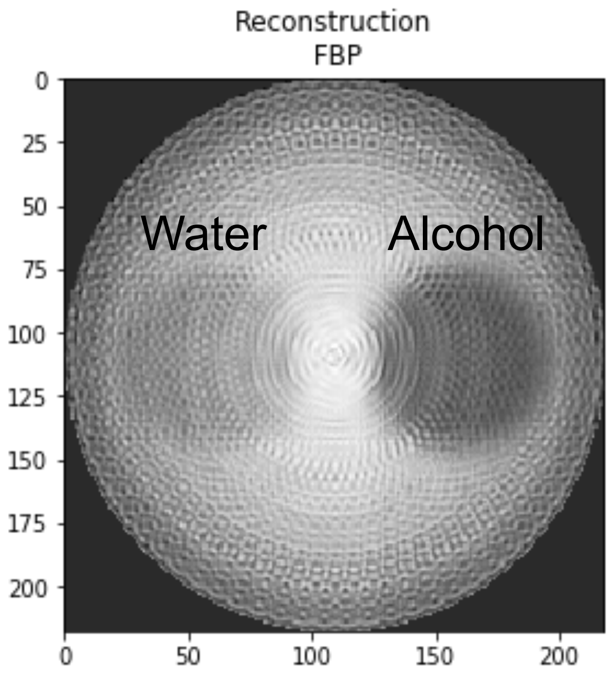


Image obtained at 0º

37 projections
in 5º steps from 0 to 180º

Reconstruction
algorithms



Reconstructed Image using Filtered-Back Projection algorithm (FBP)

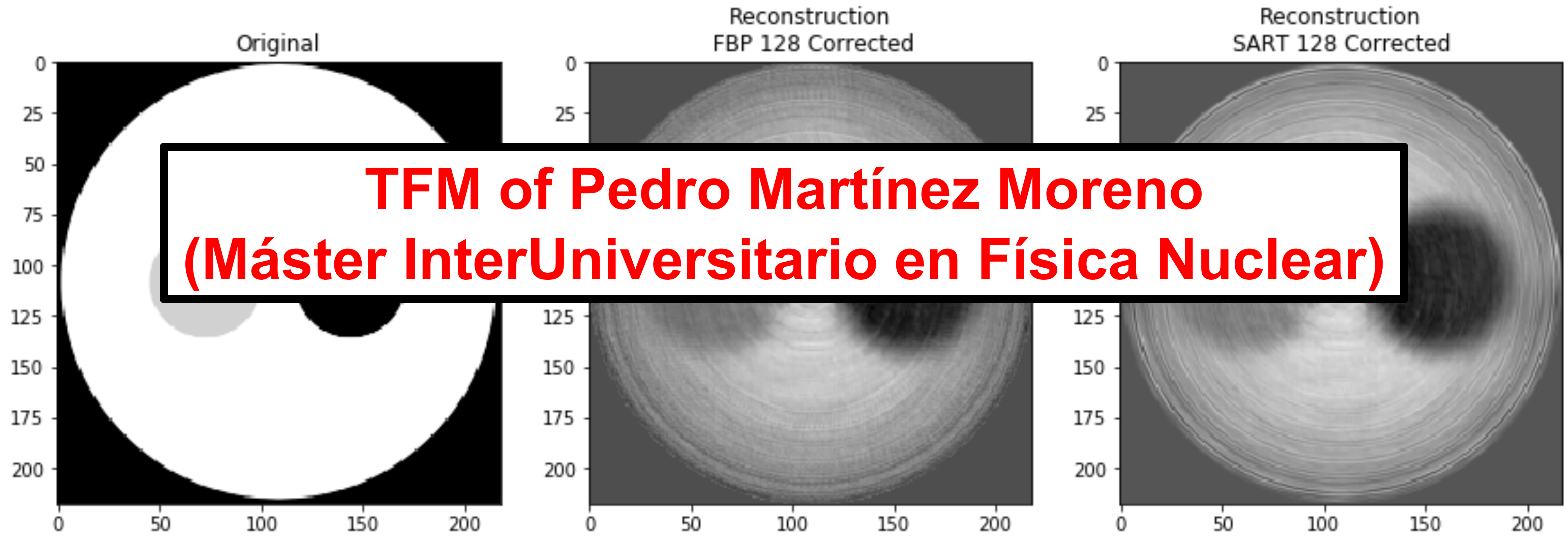
100 MeV proton beam

Extensive studies with simulations done and ongoing to optimize our setup

Reconstruction algorithms

FBP

SART (1 iter)



TFM of Pedro Martínez Moreno
(Máster InterUniversitario en Física Nuclear)

2º steps 0-180º

Images are corrected by Uniform

Preparation of Experimental setup

Experiments scheduled for June 2021:

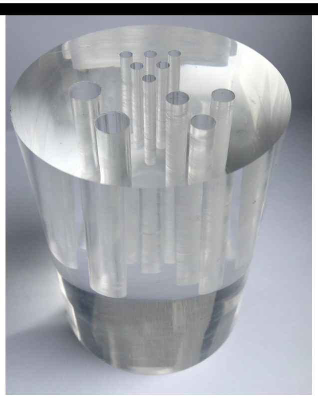
- -Krakow (Poland): 4-6 June
- -Groningen (Netherlands): 28-30 June

Cu

TFMs de

Carlos Ballesteros (Máster InterUniversitario en Física Nuclear)

Amanda Nerio (Máster Erasmus Mundus en Física Nuclear)



Experimental tests ongoing at IEM-CSIC Lab to use new digital electronics and test detectors.

Temática del TFM de Carlos Ballesteros (InterUniversitario) y Amanda Nerio (Erasmus Mundus en Física Nuclear)

Summary

- Imaging techniques: xCT and PET
- Treatment: radiotherapy with X-rays vs. protontherapy
  - Protontherapy is more selective, less harmful to surrounding tissue
  - Better control of dose applied
  - Range verification is required
  - Range uncertainties
  - pCT helps reducing uncertainties
  - IEM working in PRONTO project to build a pCT prototype

Thanks for your attention!

Questions?

If later a question disturbs you
contact me by email: jose.briz@csic.es