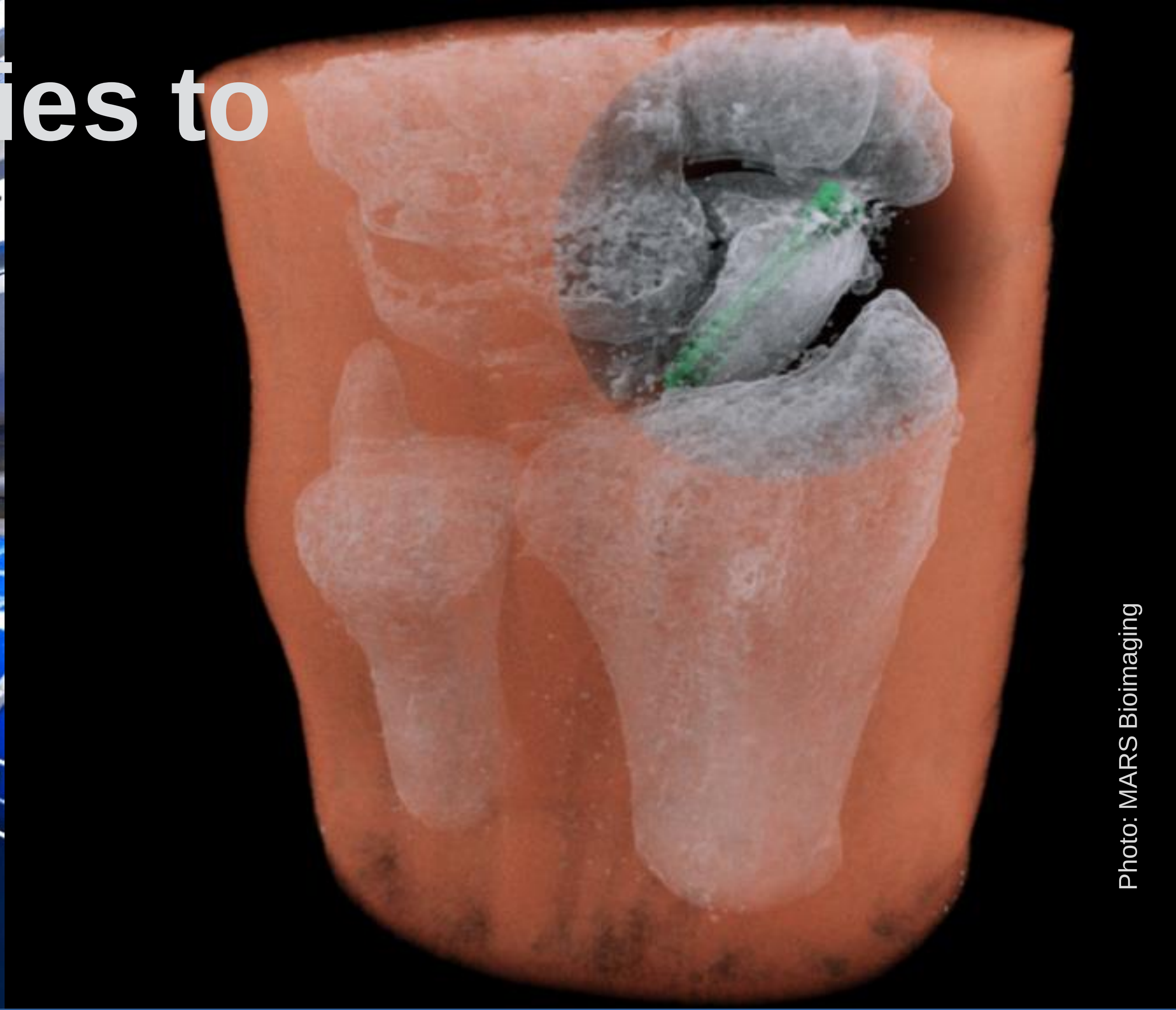
From CERN technologies to Medical Applications



Manuela Cirilli,
Medical Applications Advisor
CERN Knowledge Transfer group

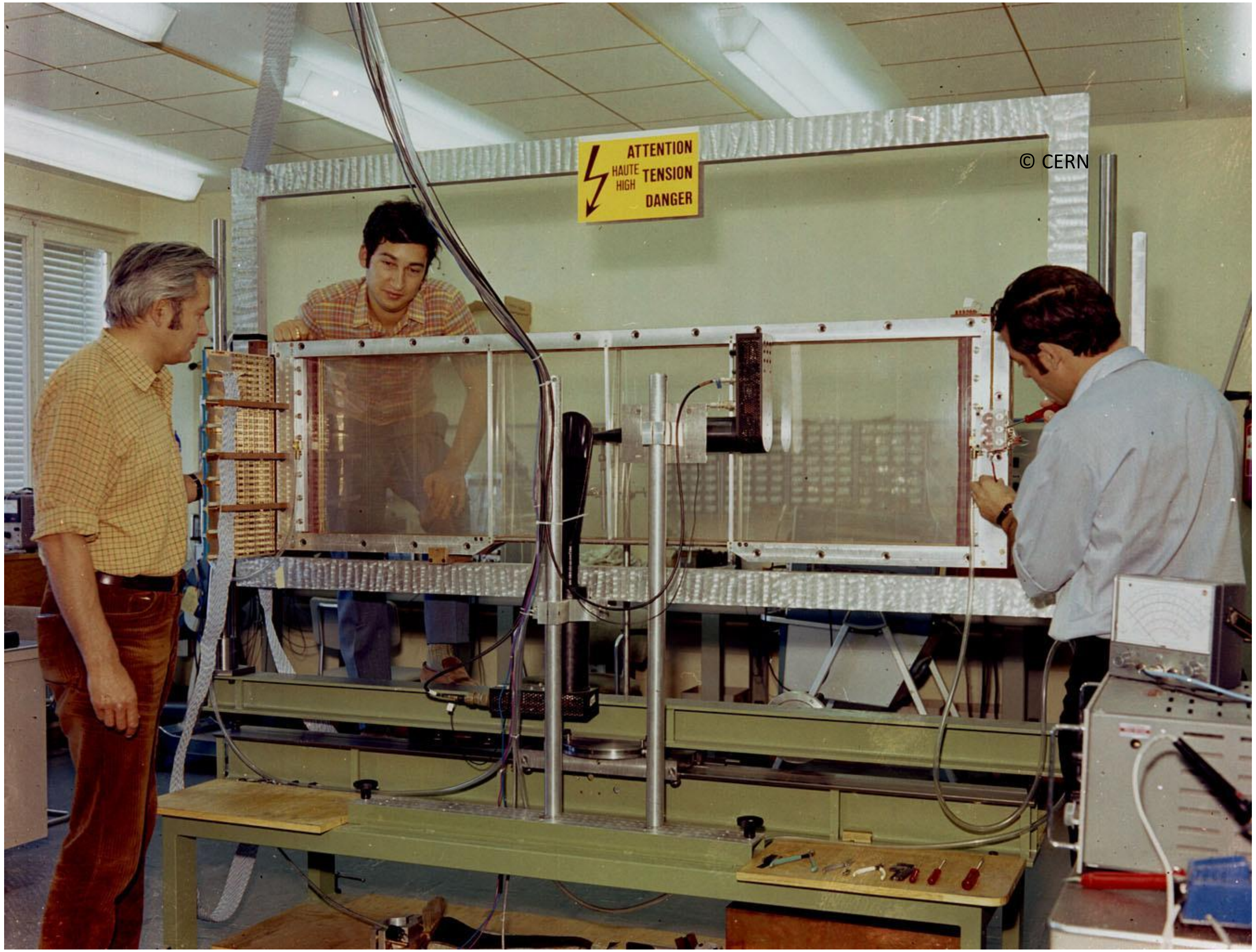
Knowledge Transfer
Accelerating Innovation

CERN's technological innovations have applications in many fields

CERN is the birthplace of the World Wide Web

And there are many more examples

Medical imaging, cancer therapy, material science, cultural heritage, aerospace, automotive, environment, health & safety, industrial processes.



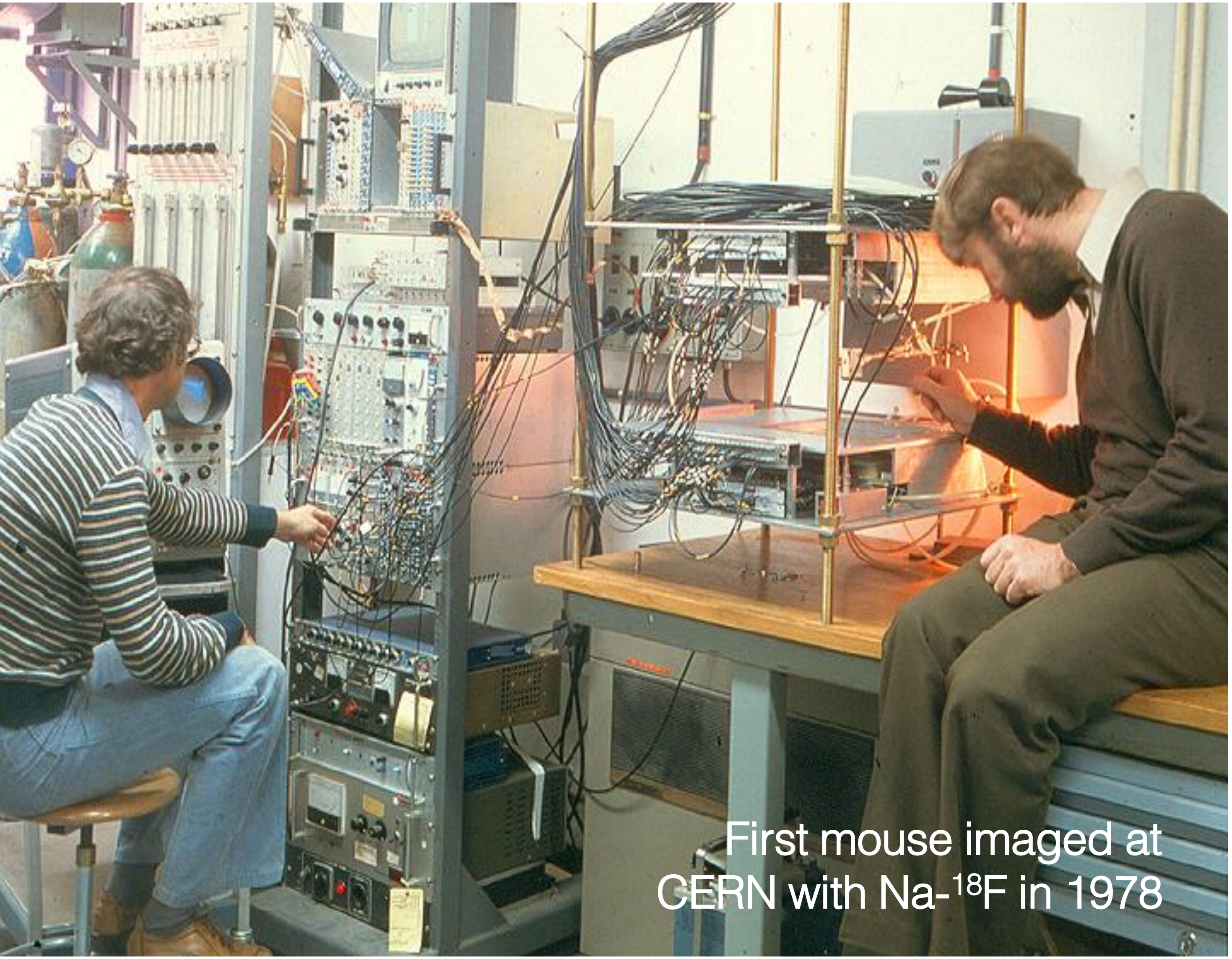
Radioprotection 2005 DOI: 10.1051/radiopro:2005010
Vol. 40, n° 2, pages 245 à 255

Produit nouveau

Une nouvelle imagerie ostéo-articulaire basse dose en position debout : le système EOS

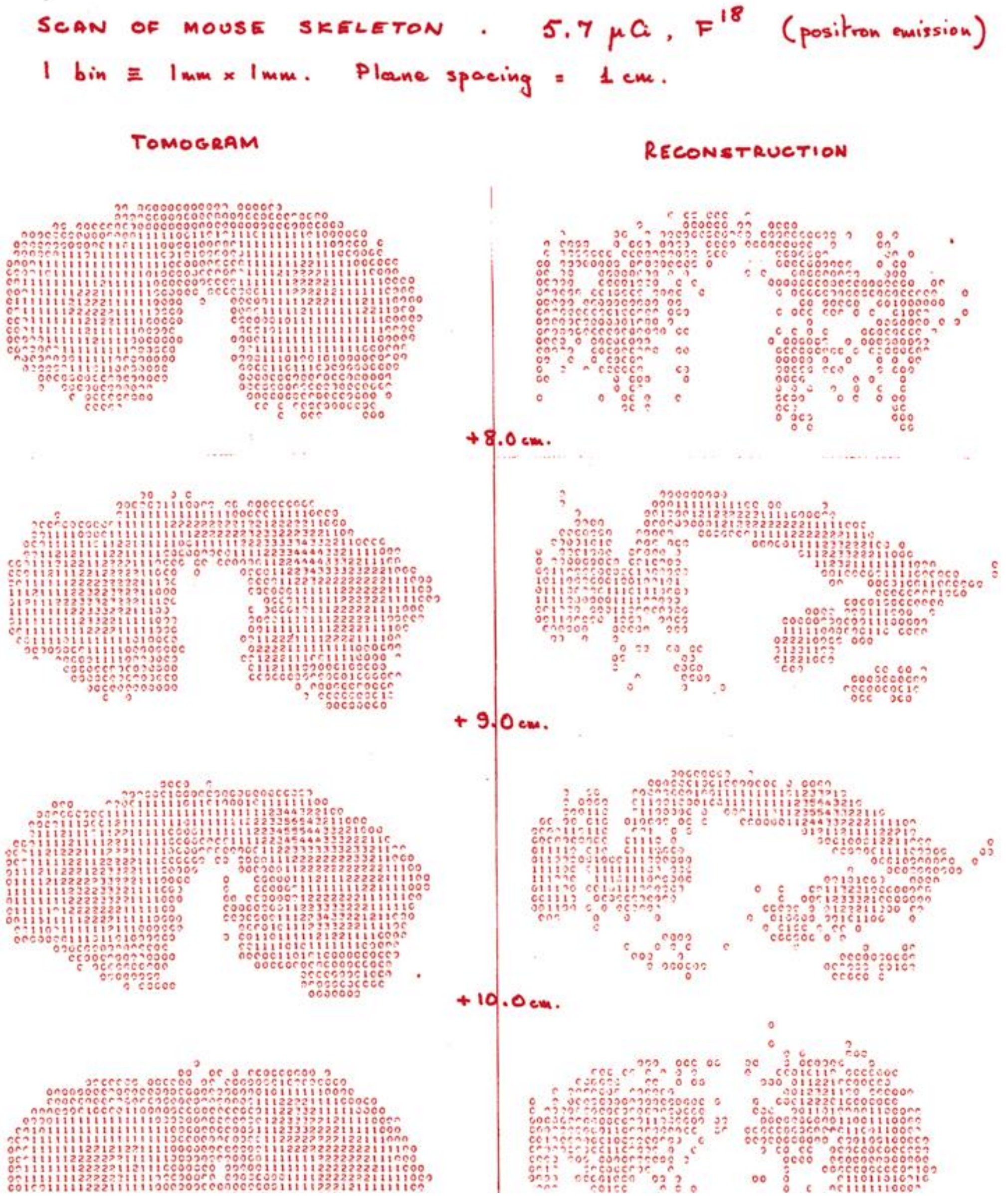
J. DUBOUSSET[1], G. CHARPAK[2], I. DORION[2], W. SKALLI[3], F. LAVASTE[3], J. DEGUISE[4], G. KALIFA[5], S. FEREY[5]

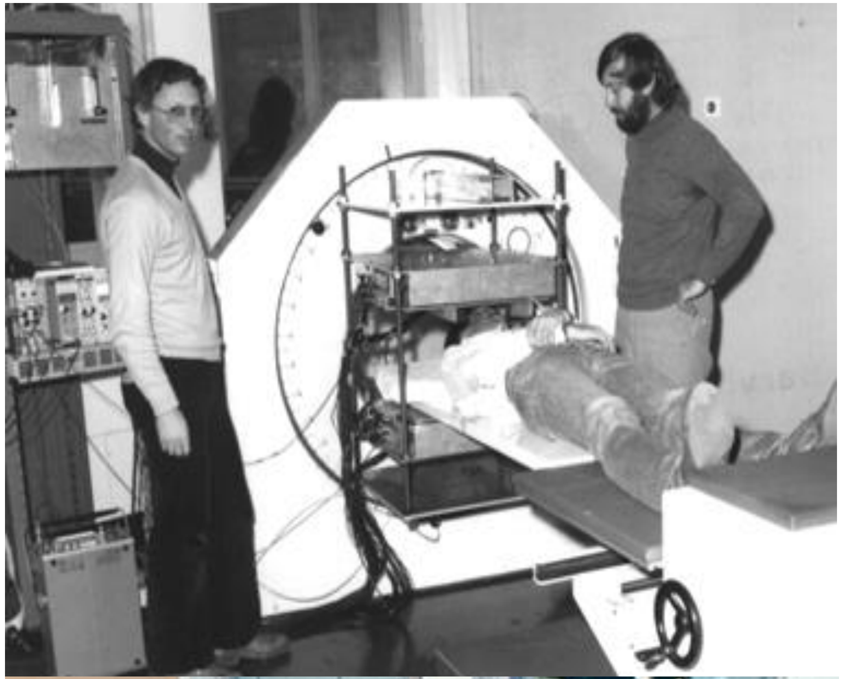
Georges Charpak, Fabio Sauli and Jean-Claude Santiard working on a multiwire chamber in 1970

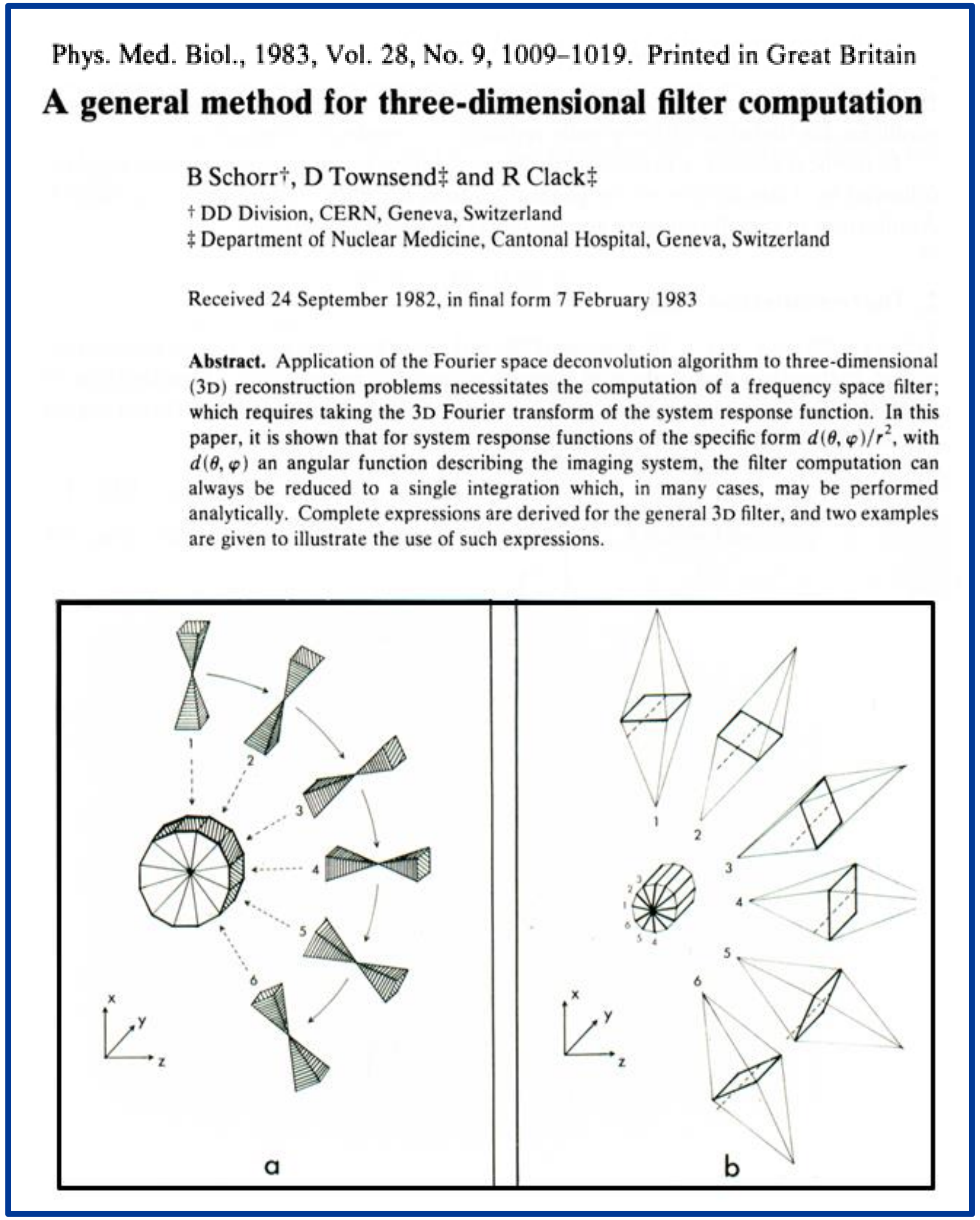


First mouse imaged at CERN with Na-^{18}F in 1978

David Townsend and Alan Jeavons







Phys. Med. Biol., 1983, Vol. 28, No. 9, 1009–1019. Printed in Great Britain

A general method for three-dimensional filter computation

B Schorr†, D Townsend‡ and R Clack‡

† DD Division, CERN, Geneva, Switzerland

‡ Department of Nuclear Medicine, Cantonal Hospital, Geneva, Switzerland

Received 24 September 1982, in final form 7 February 1983

Abstract. Application of the Fourier space deconvolution algorithm to three-dimensional (3D) reconstruction problems necessitates the computation of a frequency space filter; which requires taking the 3D Fourier transform of the system response function. In this paper, it is shown that for system response functions of the specific form $d(\theta, \varphi)/r^2$, with $d(\theta, \varphi)$ an angular function describing the imaging system, the filter computation can always be reduced to a single integration which, in many cases, may be performed analytically. Complete expressions are derived for the general 3D filter, and two examples are given to illustrate the use of such expressions.

bulletin

WEEK MONDAY 26 JANUARY N°5/81 SEMAINE DU LUNDI 26 JANVIER

Apparatus for growing broad beans which have been exposed to radiation. The roots are immersed in a tank of running water (CERN 439.10.80). Right: Chromosomal aberration (A) in a dividing cell (B) of Vicia Faba exposed to a 250 GeV hadron beam.

A gauche, dispositif de culture des fèves irradiées. Les racines plongent dans un bac d'eau courante (photo CERN 439.10.80). A droite, aberrations chromosomiques (A) parmi une cellule en division (B) de Vicia Faba exposée à un faisceau de hadrons de 250 GeV.

Beans in Beams

The CERN Radiobiology Group carries out experiments to study the effects of radiation on living cells. The purpose of the research is to compare the effects of different kinds of radiation, to ascertain how far these effects are modified by variations in dosage and application (i.e. one or several sessions) and to examine the repair mechanisms of cells following exposure to radiation. Tests were carried out on human blood, mice and broad beans. As the absorption of radiation causes the same types of damage for all cells, a relatively simple detector was chosen for a recent experiment — the broad bean, which is easy to handle. Its root-tip (or meristem) is composed of cells which are particularly sensitive to radiation, thus enabling rapid analysis of the damage to be made. Two kinds of investigation were carried out on the beans: physiological investigation to ascertain the reduction in the rate of growth of the roots after exposure to radiation, and microscopic investigation to ascertain the damage to the cells and chromosomes. In this way it has proved possible to study the effects of neutrons produced at the 600 MeV SC at doses as low as 200 millirads. The results obtained indicate that at the lower end of the range studied damage increases linearly with dose for both neutrons and gamma radiation. This is of considerable importance for our understanding of the effects of radiation. Studies of the effects of even lower energies of neutrons are in progress. Broad beans have also been used to study the biological effects of 250 GeV hadrons supplied by the SPS.

Des fèves dans le faisceau?

Le groupe de Radiobiologie du CERN se livre à une série d'expériences qui étudient les effets des radiations sur les cellules vivantes. Le but de ces recherches est de comparer les effets produits par divers types de rayonnements, d'étudier la variation des effets en fonction de la dose et de son mode d'administration (séance unique ou fractionnée) ainsi que les mécanismes de réparations cellulaires après irradiation. Plusieurs détecteurs biologiques sont employés : sang humain, souris, fèves. Etant donné que l'absorption des radiations cause le même type de dégâts dans toutes les cellules, on a choisi pour une expérience récente un détecteur relativement simple comme la fève qui est très facile à manipuler. L'extrémité de sa racine (ou méristème) est formée de cellules particulièrement sensibles aux radiations et permettant une analyse rapide des dégâts produits. Des recherches de deux types ont été effectuées avec les fèves : l'une (physiologique) est de déterminer la réduction de la croissance des racines après irradiation; l'autre (microscopique) consiste à évaluer les dégâts produits au niveau des cellules et des chromosomes. C'est ainsi qu'on a pu étudier les effets de neutrons produits par le synchro-cyclotron de 600 MeV à des doses aussi faibles que 200 millirads. Les résultats obtenus indiquent que les dégâts augmentent de façon linéaire avec la dose, à la limite inférieure de la gamme étudiée, aussi bien pour les neutrons que pour les rayons gamma. Cela est d'un grand intérêt et permet de mieux comprendre les effets des radiations. L'étude des effets de neutrons à des énergies plus faibles est en cours. Les fèves ont aussi permis d'étudier les effets biologiques produits par des hadrons de 250 GeV fournis par le SPS.

1980s: Marilena Streit-Bianchi and the CERN Radiobiology group

Strategy and framework approved by CERN Council in 2017

CERN/SPC/1091/RA
CERN/FC/6125/RA
CERN/3311/RA
Original: English
23 May 2017

ORGANISATION EUROPEENNE POUR LA RECHERCHE NUCLEAIRE
CERN EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

Action to be taken		*Voting Procedure*
For information	SCIENTIFIC POLICY COMMITTEE 304th Meeting 12 & 13 June 2017	-
For information	FINANCE COMMITTEE 360th Meeting 13 & 14 June 2017	-
For approval	RESTRICTED COUNCIL 185th Session 16 March 2017	Simple majority of Member States represented and voting

Strategy and framework applicable to knowledge transfer by CERN for the benefit of medical applications

The Council is invited to approve the strategy and framework set out in this document for medical applications-related activities, and to take note of the information contained in Annexes I and II.

Updated strategy paper

Approved by CERN Council in June

https://cds.cern.ch/record/2864317?ln=en

CERN/SPC/1091/Rev.
CERN/FC/6125/Rev.
CERN/3311/Rev.
Original: English
6 June 2023

ORGANISATION EUROPEENNE POUR LA RECHERCHE NUCLEAIRE
CERN EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

Action to be taken		*Voting Procedure*
For information	**SCIENTIFIC POLICY COMMITTEE** 334th Meeting **19-20 June 2023**	-
For information	**FINANCE COMMITTEE** 386th Meeting **20-21 June 2023**	-
For decision	**RESTRICTED COUNCIL** 212th Session **22-23 June 2023**	Simple majority of Member States represented and voting

Updated strategy and framework applicable to knowledge transfer by CERN for the benefit of medical applications

The Council is invited to take note of the information set out in this document and to approve the updated strategy and framework for medical-applications-related projects set out therein.

ICT for medical applications

Nuclear Medicine

Medical Imaging

Radiotherapy

Radiation Monitoring and Dosimetry

Robotics

Medical devices

Over **70 companies and institutes produce accelerators for industrial applications**; these organizations sell more than **1,100 industrial systems per year** — almost twice the number produced for research or medical therapy — at a **market value of $2.2B**.

Over **$1B** of this amount is generated by the sales of accelerators for **ion implantation** into materials — primarily semiconductor devices — whose worldwide value of production is about $300B.

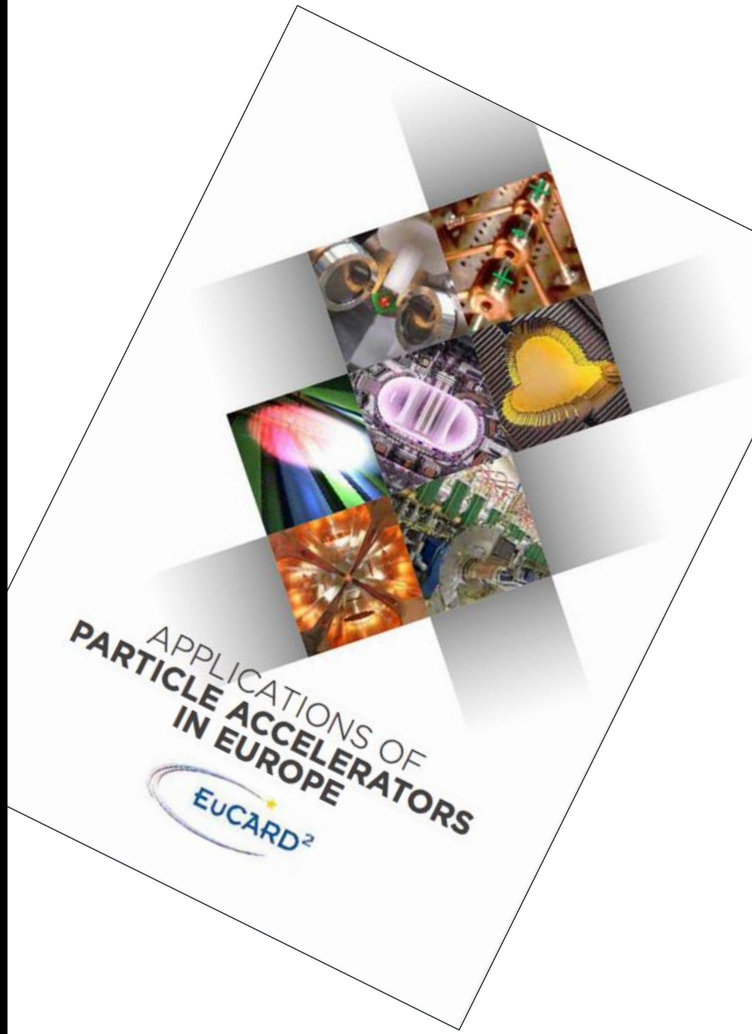
Hamm,R.andHamm,M.(2012).Industrial accelerators and their applications. World Scientific Publishing Co.

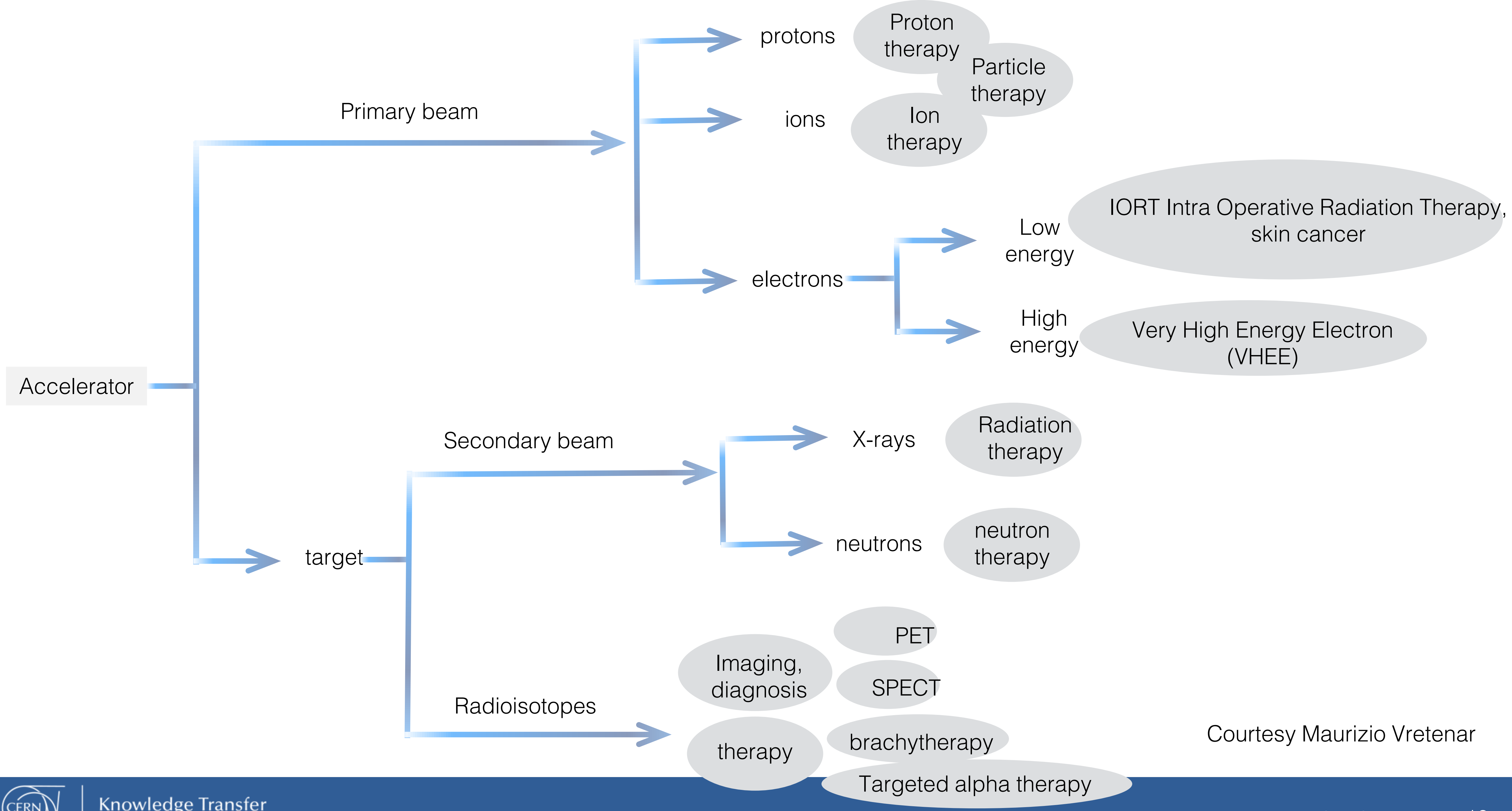
As of 2014 there were **42,200** accelerators worldwide:
27,000 (64%) in industry,
14,000 (33%) for medical purposes
1,200 (3%) for basic research.

These figures exclude electron microscopes and x–ray tubes, and the security and defense industries.

Chernyaev, A. P. and Varzar, S. M. (2014). Particle accelerators in modern world. Physics of Atomic Nuclei, 77(10):1203–1215.

Area	Application	Beam	Accelerator	Beam energy/MeV	Beam current/mA	Number
Medical	Cancer therapy	e	linac	4-20	10^{-2}	>14000
		p	cyclotron, synchrotron	250	10^{-6}	60
		C	synchrotron	4800	10^{-7}	10
	Radioisotope production	p	cyclotron	8-100	1	1600
Industrial	Ion implantation	B, As, P	electrostatic	< 1	2	>11000
	Ion beam analysis	p, He	electrostatic	<5	10^{-4}	300
	Material processing	e	electrostatic, linac, Rhodatron	≤10	150	7500
	Sterilisation	e	electrostatic, linac, Rhodatron	≤10	10	3000
Security	X-ray screening of cargo	e	linac	4-10	?	100?
	Hydrodynamic testing	e	linear induction	10-20	1000	5
Synchrotron light sources	Biology, medicine, materials science	e	synchrotron, linac	500-10000		70
Neutron scattering	Materials science	p	cyclotron, synchrotron, linac	600-1000	2	4
Energy – fusion	Neutral ion beam heating	d	electrostatic	1	50	10
	Heavy ion inertial fusion	Pb, Cs	Induction linac	8	1000	Under development
	Materials studies	d	linac	40	125	Under development
Energy – fission	Waste burner	p	linac	600-1000	10	Under development
	Thorium fuel amplifier	p	linac	600-1000	10	Under development
Energy – bio-fuel	Bio-fuel production	e	electrostatic	5	10	Under development
Environmental	Water treatment	e	electrostatic	5	10	5
	Flue gas treatment	e	electrostatic	0.7	50	Under development





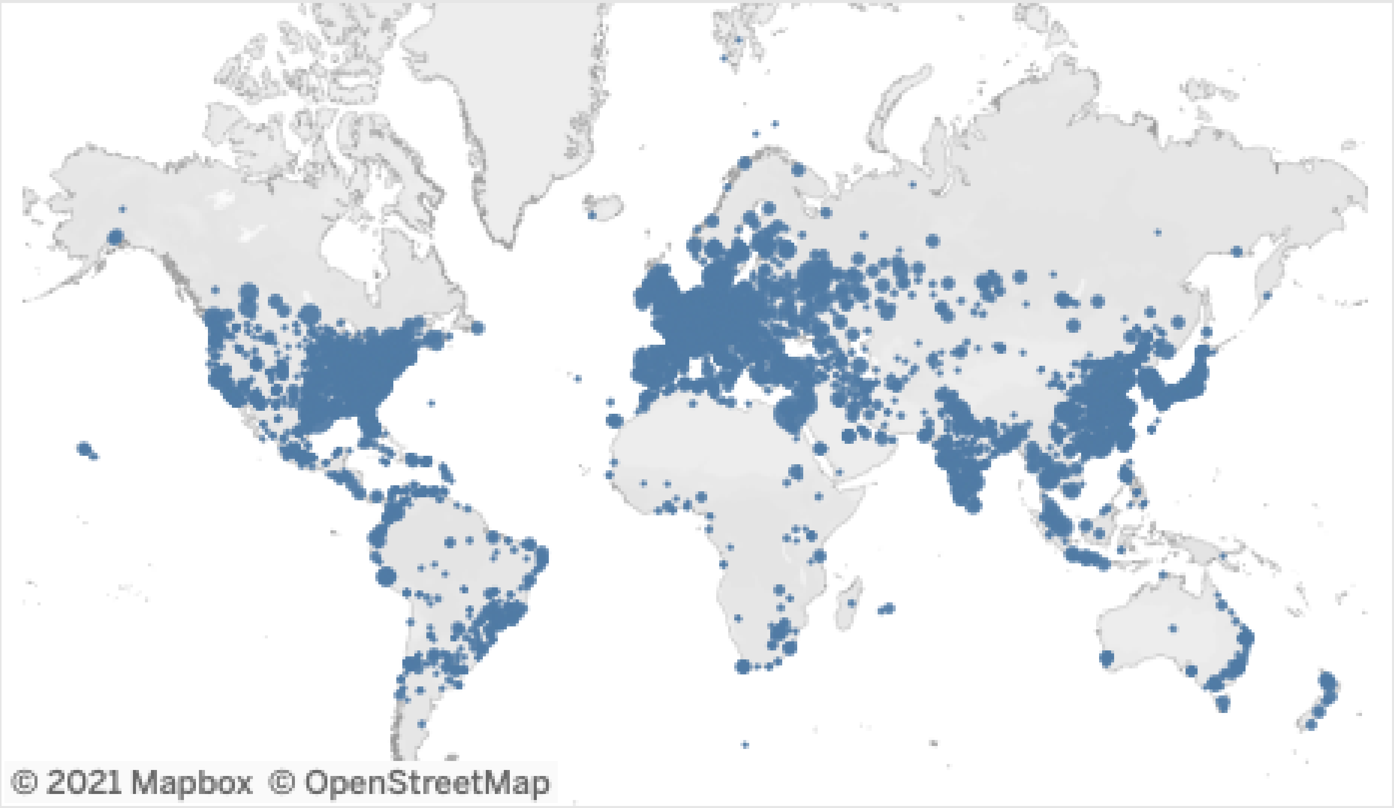
Courtesy Maurizio Vretenar

Status of Radiation Therapy Equipment

155 Countries

7602 RT Centres

14875 MV Therapy



Equipment type

(Updated on : 23/06/2021 09:19:53)

Equipment type	Number
MV Therapy	14,875
Brachytherapy	3,318
Light Ion Therapy	110

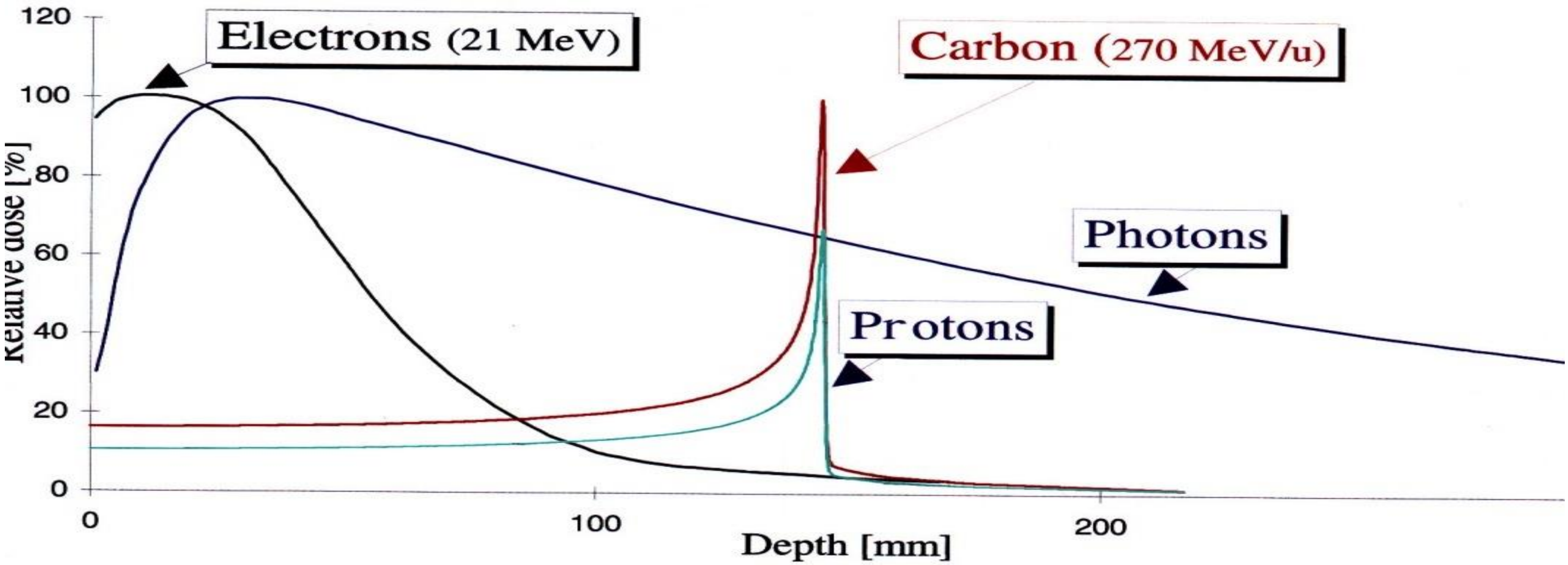
Equipment per income groups

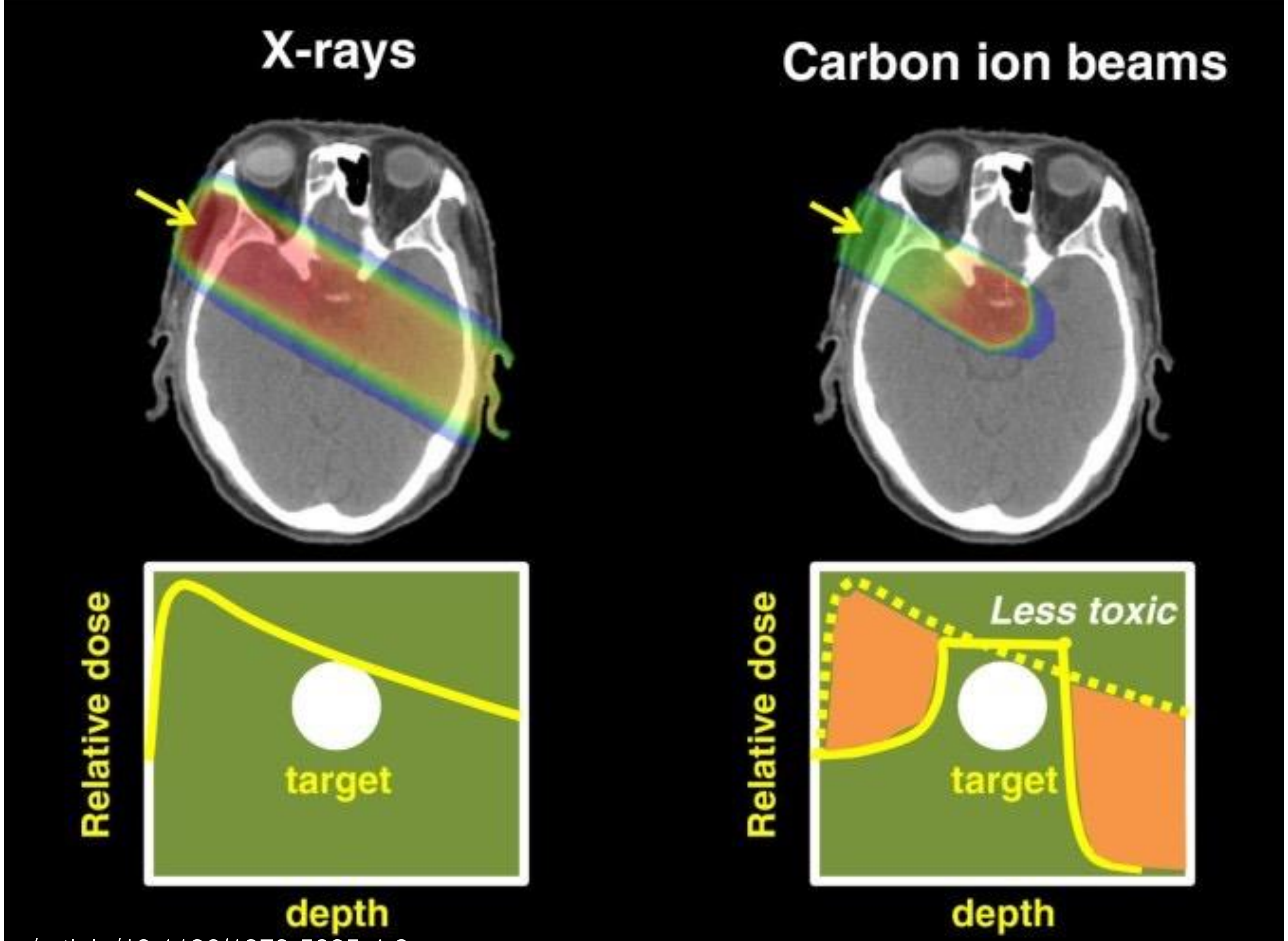
(Updated on : 23/06/2021 09:19:53)

Income group	Number
High income (H)	9,365
Upper middle income (UM)	4,165
Lower middle income (LM)	1,303
Low income (L)	39
Temporarily unclassified (NC)	3

IAEA DIRAC Directory of Radiotherapy Centres

Protons, ions: hadron therapy, particle therapy, (light, heavy) ion therapy





m/article/10.1186/1878-5085-4-9

Status of Radiation Therapy Equipment

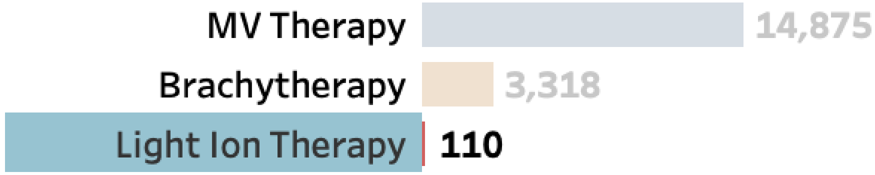
20 Countries

106 RT Centres

110 Light Ion Therapy

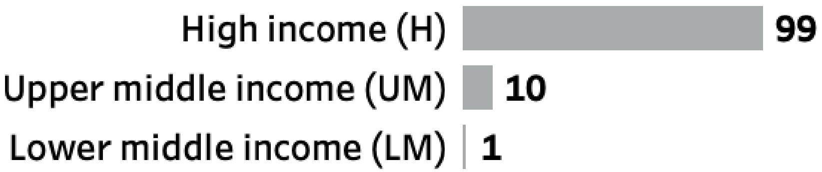
Equipment type

(Updated on : 23/06/2021 09:19:53)



Equipment per income groups

(Updated on : 23/06/2021 09:19:53)



From the PIMMS Study @ CERN → TERA

EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH
CERN - PS DIVISION

CERN/PS 2000-007 (DR)

PROTON-ION MEDICAL MACHINE STUDY (PIMMS) PART II

Accelerator Complex Study Group*
supported by the Med-AUSTRON, Onkologie-2000 and the TERA Foundation
and hosted by CERN

ABSTRACT

The Proton-Ion Medical Machine Study (PIMMS) group was formed following an agreement between the Med-AUSTRON (Austria) and the TERA Foundation (Italy) to combine their efforts in the design of a cancer therapy synchrotron capable of accelerating either light ions or protons. CERN agreed to support and host this study in its PS Division. A close collaboration was also set up with GSI (Germany). The study group was later joined by Onkologie-2000 (Czech Republic). Effort was first focused on the theoretical understanding of slow extraction and the techniques required to produce a smooth beam spill for the conformal treatment of complex-shaped tumours with a sub-millimetre accuracy by active scanning with proton and carbon ion beams. Considerations for passive beam spreading were also included for protons. The study has been written in two parts. The more general and theoretical aspects are recorded in Part I and the specific technical design considerations are presented in the present volume, Part II. An accompanying CD-ROM contains supporting publications made by the team and data files for calculations. The PIMMS team started its work in January 1996 in the PS Division and continued for a period of four years.

*Full-time members: L. Badano[1)], M. Benedikt[2)], P.J. Bryant[2)] (Study Leader), M. Crescenti[1)], P. Holy[3)], A. Maier[2)+4)], M. Pullia[1)], S. Reimoser[2)+4)], S. Rossi[1)],
Part-time members: G. Borri[1)], P. Knaus[1)+2)]
Contributors: F. Gramatica[1)], M. Pavlovic[4)], L. Weisser[5)]
1) TERA Foundation, via Puccini. 11, I-28100 Novara.
2) CERN, CH 1211 Geneva-23.
3) Oncology-2000 Foundation, Na Morani 4, CZ-12808 Prague 2.
4) Med-AUSTRON, c/o RIZ, Prof. Dr. Stephan Korenstr.10, A-2700 Wr. Neustadt.
5) Sommer & Partner Architects Berlin (SPB), Hardenbergplatz 2, D-10623 Berlin.

Geneva, Switzerland
May 2000

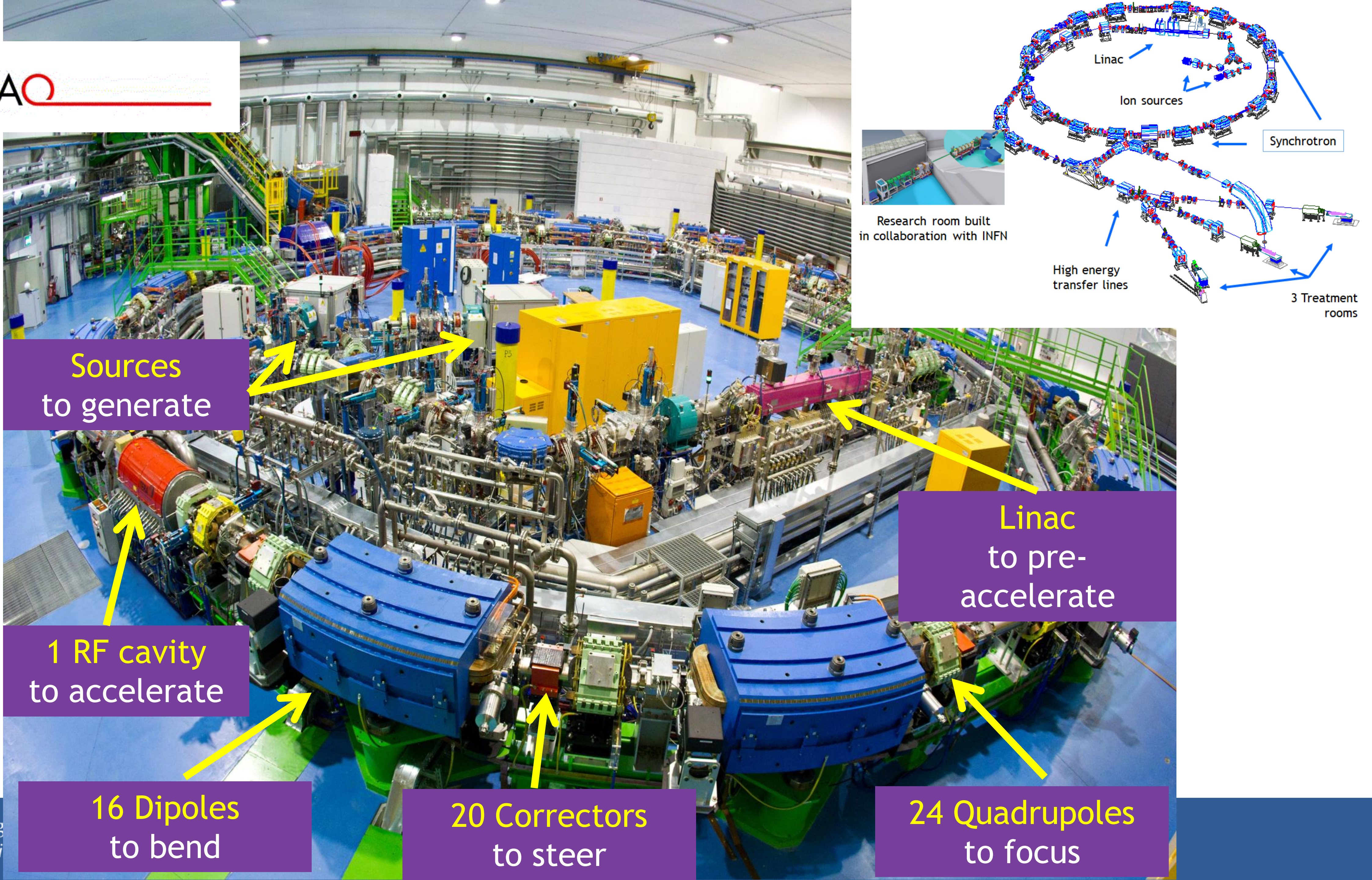
PIMMS August 2000

INFN

fondazione CNAO

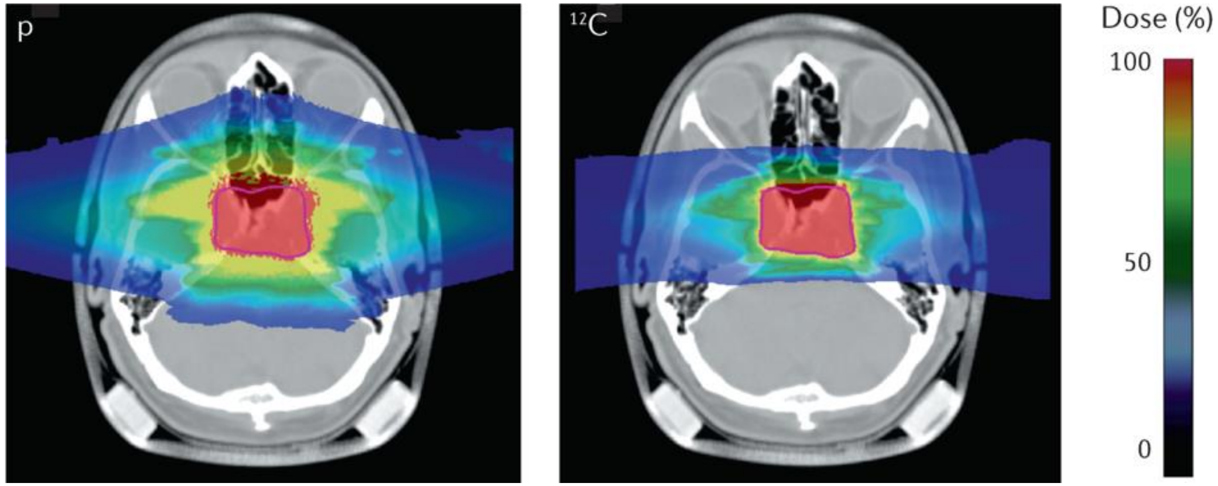
MedAustron

fondazione CNAO



From pioneering rasterscanning & carbon ion pilot project @ GSI

440 patiens
1998-2008



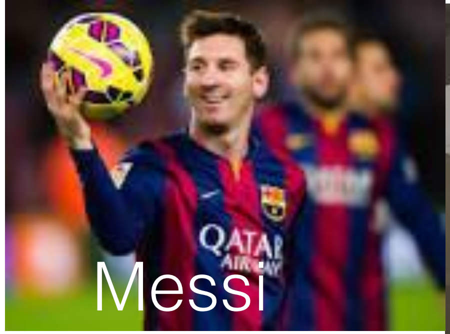
The image shows an optimized plan with two opposite fields for a chordoma patient using protons (left) or 12C ions (right).

HIT Heidelberger Ionenstrahl-Therapiezentrum

Since 2009*:
2841 patients with p
3793 patients with C-ion

* Until Dec 2020, source ptcog.ch

200



Multi heavy ions
(protons +
carbon ions)

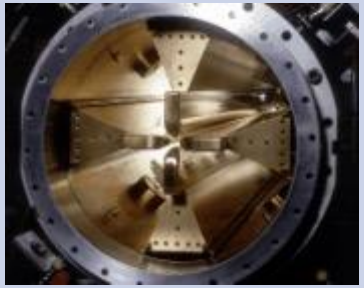
oton multi-room

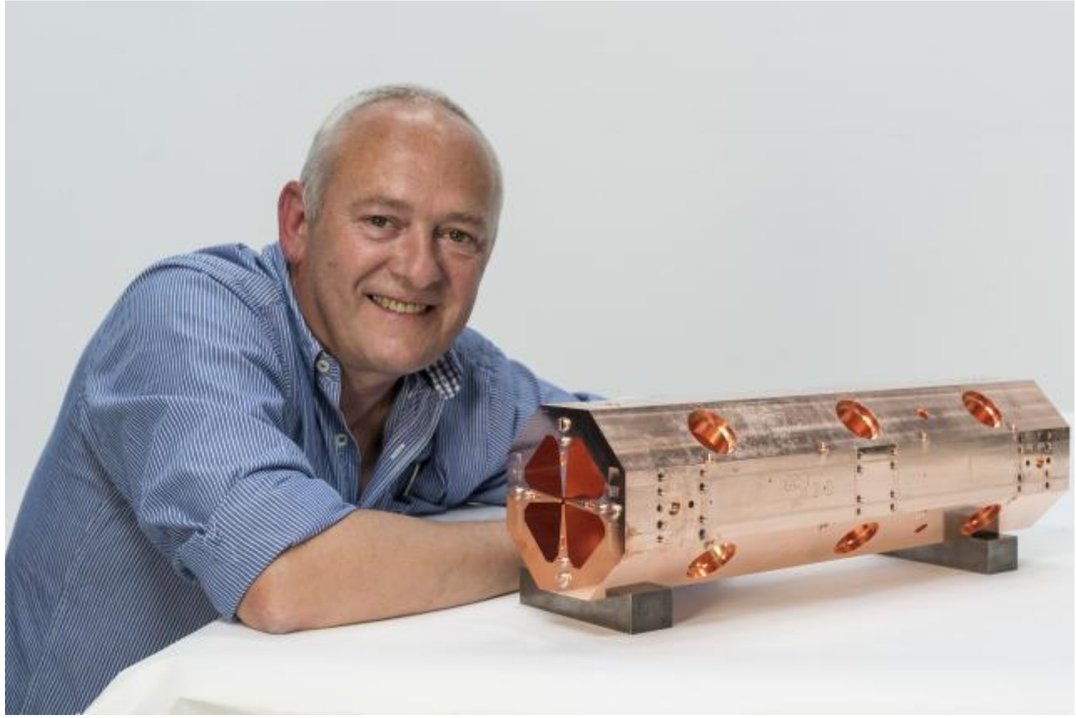
2

on single-
room

Courtesy
(I'll never thank him enough!)
Marco Durante (GSI)
JENAS 2019
https://indico.ijclab.in2p3.fr/event/5418/timetable/#20191016.detailed

Protons: the LINAC way

1990 RFQ2 200 MHz 0.5 MeV /m Weight :1200kg/m Ext. diametre : ~45 cm	2007 LINAC4 RFQ 352 MHz 1MeV/m Weight : 400kg/m Ext. diametre : 29 cm	2014 HF RFQ 750MHz 2.5MeV/m Weight : 100 kg/m Ext. diametre : 13 cm
		



Compact High-Frequency Radio Frequency Quadrupole (RFQ)

M. Vretenar, A. Dallocchio, V. A. Dimov, M. Garlasché, A. Grudiev, A. M. Lombardi, S. Mathot, E. Montesinos, M. Timmins, “A Compact High-Frequency RFQ for Medical Applications”, in Proc. LINAC2014, Geneva, Switzerland, September 2014

Licensed to AVO-ADAM

Next Ion Medical Machine Study (NIMMS)

Why ions?
Proton therapy is now commercially available.
Ion therapy (mainly carbon) still bespoke facilities.

An R&D programme based at CERN for critical technologies related to ion therapy

Focus on the development of key technologies (a toolbox) corresponding to CERN core competences.

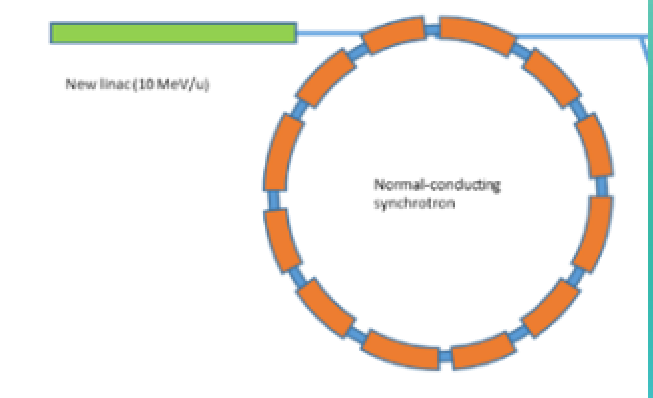
Manuela.Cirilli@cern.ch

Three alternative accelerator designs

Improved synchrotron (warm)

Equipped with several innovative features: multi-turn injection for higher beam intensity, new injector at higher gradient and energy, multiple extraction schemes, multi-ion.

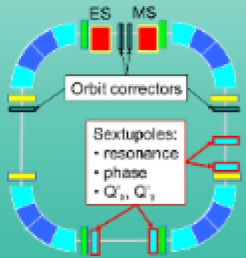
Circumference ~ 75 m



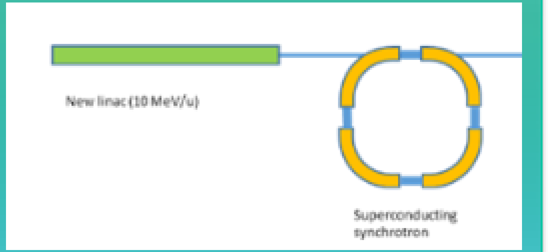
Improved synchrotron (superconducting)

Equipped with the same innovative features as warm, but additionally 90^0 superconducting magnets.

Circumference ~ 27 m



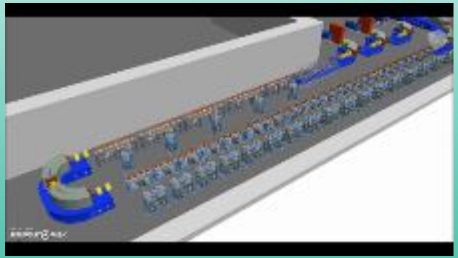
Courtesy: TERA

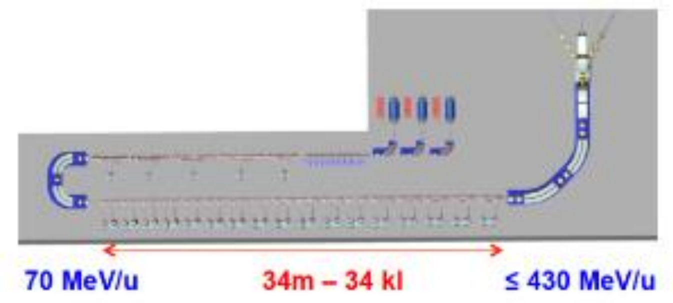


Linear accelerator

Linear sequence of accelerating cells, high pulse frequency.

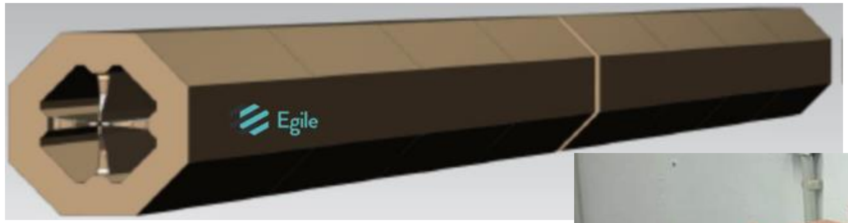
Length ~ 53 m

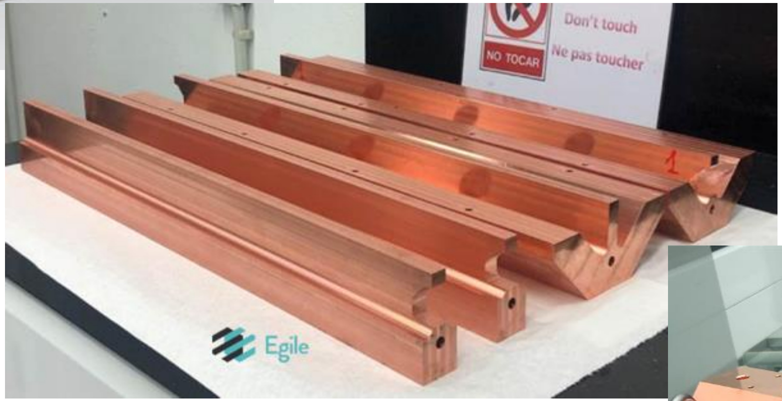


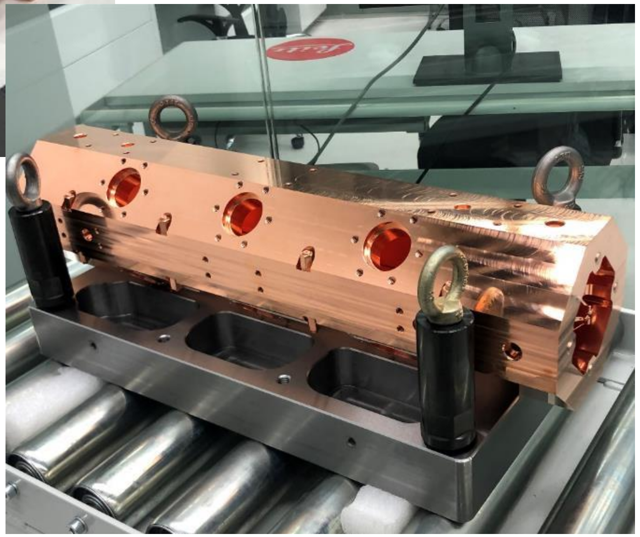


Other options considered as less interesting because of cost and/or required R&D: RC synchrotron, FFAG, SC cyclotron, PWFA

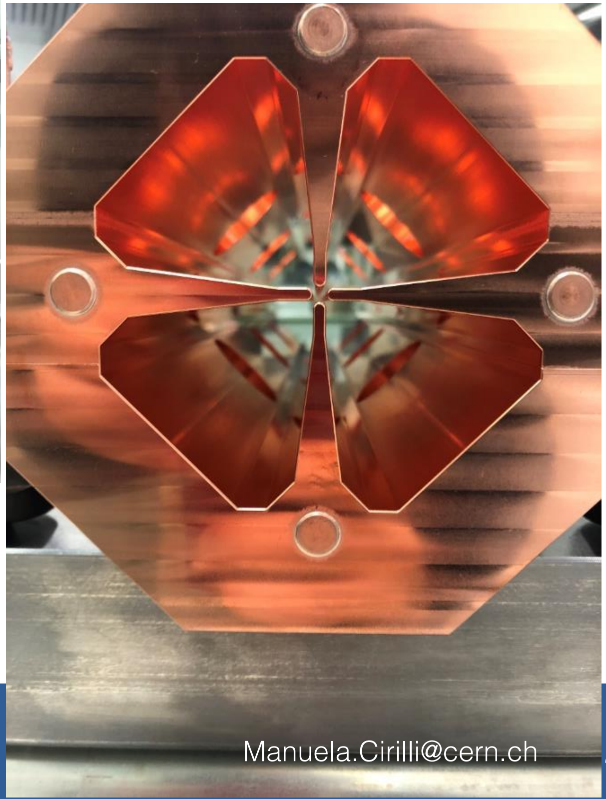
The RFQ for C^{6+} LINAC option







First (of 4 sections) completed



Collaboration CERN-CIEMAT-CDTI-Spanish industry

2.0 m long

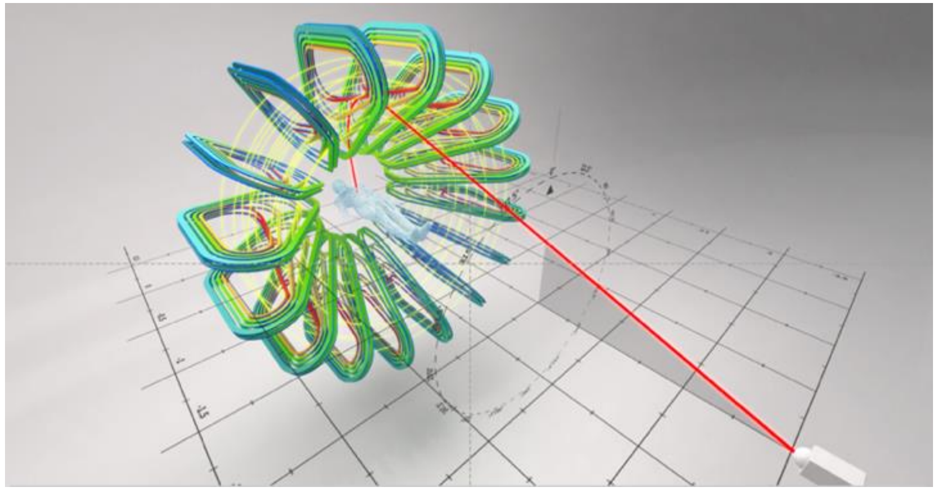
750 MHz

Will deliver Carbon (or Helium) at 5 MeV (total energy)

Designed at CERN built in Spanish Industry

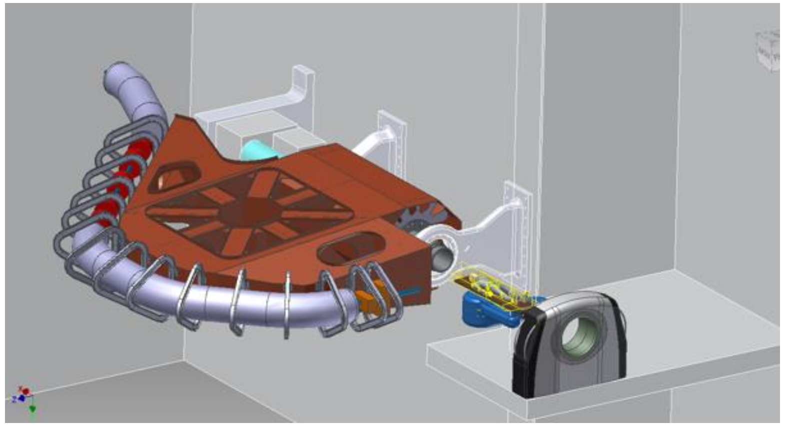
R&D on gantries

GaToroid: A Novel Concept for a Superconducting Compact and Lightweight Gantry for Hadron Therapy



CERN

Collaboration CNAO-INFN-CERN-MedAustron start 2022



EuroSIG

INFN

70 ANNI DI RICERCA DISEGNANDO IL FUTURO
1951 2021 infn

Superconducting Ion Gantry

CSN5 – Call 2021

SIG

Superconducting Ion Gantry

Lucio Rossi

Università di Milano e sezione INFN di Milano – LASA

R. Musenich INFN-GE, L. Sabbatini LNF, S. Giordanengo e E. Fiorina INFN-TO

FLASH therapy – a growing clinical interest

NATURE May 23, 1959 VOL. 183

Modification of the Oxygen Effect when Bacteria are given Large Pulses of Radiation

D. L. DEWEY
J. W. BOAG

Research Unit in Radiobiology,
British Empire Cancer Campaign,
Mount Vernon Hospital,
Northwood.

> Sci Transl Med. 2014 Jul 16;6(245):245ra93. doi: 10.1126/scitranslmed.3008973.

Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

Vincent Favaudon [1], Laura Caplier [2], Virginie Monceau [3], Frédéric Pouzoulet [4], Mano Sayarath [4], Charles Fouillade [4], Marie-France Poupon [4], Isabel Brito [5], Philippe Hupé [6], Jean Bourhis [7], Janet Hall [4], Jean-Jacques Fontaine [2], Marie-Catherine Vozenin [8]

Affiliations + expand

PMID: 25031268 DOI: 10.1126/scitranslmed.3008973

In vitro studies suggested that sub-millisecond pulses of radiation elicit less genomic instability than continuous, protracted irradiation at the same total dose. To determine the potential of ultrahigh dose-rate irradiation in radiotherapy, we investigated lung fibrogenesis in C57BL/6J mice exposed either to short pulses (≤ 500 ms) of radiation delivered at ultrahigh dose rate (≥ 40 Gy/s, FLASH) or to conventional dose-rate irradiation (≤ 0.03 Gy/s, CONV) in single doses. The growth of human HBCx-12A and HEp-2 tumor xenografts in nude mice and syngeneic TC-1 Luc(+) orthotopic lung tumors in C57BL/6J mice was monitored under similar radiation conditions. CONV (15 Gy) triggered lung fibrosis associated with activation of the TGF-β (transforming growth factor-β) cascade, whereas no complications developed after doses of FLASH below 20 Gy for more than 36 weeks after irradiation. FLASH irradiation also spared normal smooth muscle and epithelial cells from acute radiation-induced apoptosis, which could be reinduced by administration of systemic TNF-α (tumor necrosis factor-α) before irradiation. In contrast, FLASH was as efficient as CONV in the repression of tumor growth. Together, these results suggest that FLASH radiotherapy might allow complete eradication of lung tumors and reduce the occurrence and severity of early and late complications affecting normal tissue.

FLASH therapy – a growing clinical interest

Vozenin et al
Clin Cancer Res
2018

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis[a,b,*], Wendy Jeanneret Sozzi[a], Patrik Gonçalves Jorge[a,b,c], Olivier Gaide[d], Claude Bailat[c], Fréderic Duclos[a], David Patin[a], Mahmut Ozsahin[a], François Bochud[c], Jean-François Germond[c], Raphaël Moeckli[c,1], Marie-Catherine Vozenin[a,b,1]

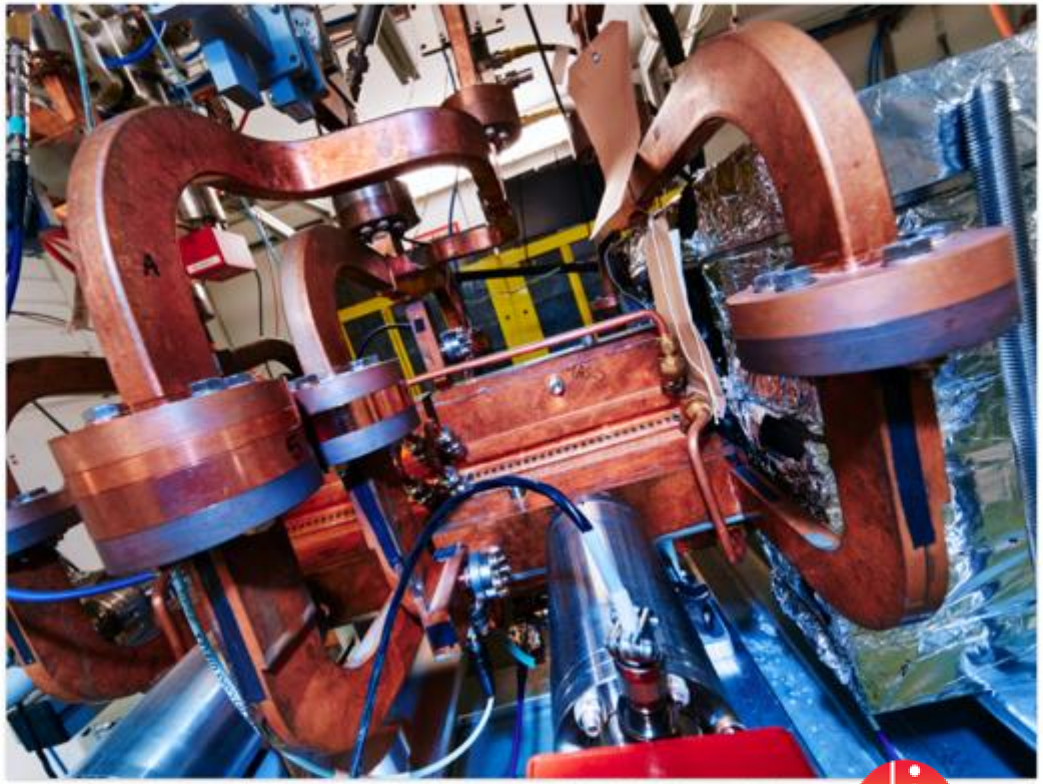
[a] *Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne;* [b] *Radiation Oncology Laboratory, Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne;* [c] *Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne; and* [d] *Department of Dermatology, Lausanne University Hospital and University of Lausanne, Switzerland*

Fig. 1. Temporal evolution of the treated lesion: (a) before treatment; the limits of th PTV are delineated in black; (b) at 3 weeks, at the peak of skin reactions (grade 1 epithelitis NCI-CTCAE v 5.0); (c) at 5 months.

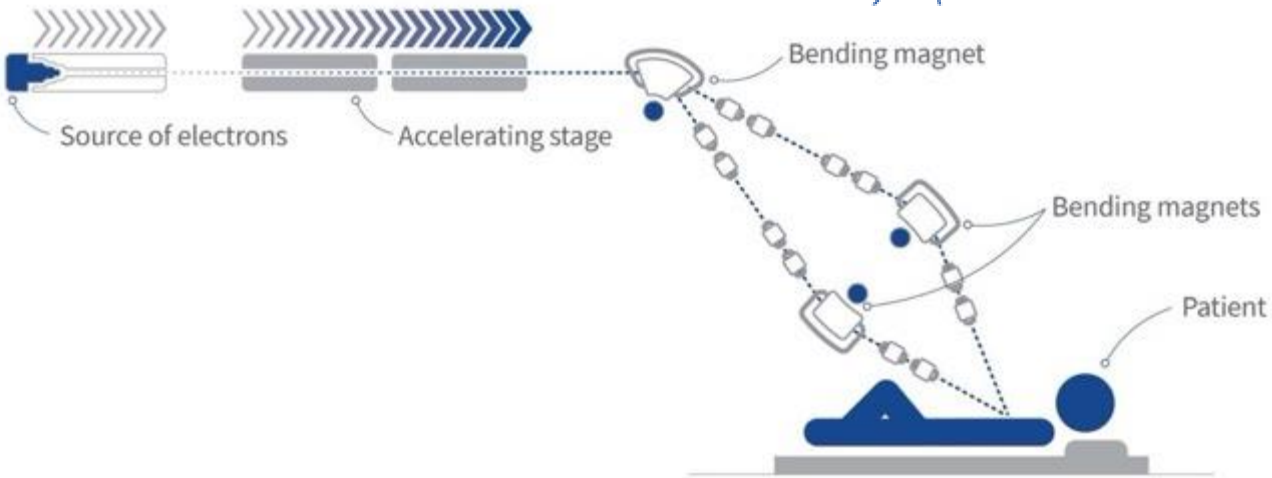
First human patient – skin cancer treated with 10 MeV-range electrons

FLASH VHEE therapy

CLIC technology for a FLASH VHEE facility being developed in collaboration with CHUV (Lausanne University Hospital) and THERYQ (ALCEN Group)



Close-up of the Compact Linear Collider prototype, on which the electron FLASH design is based (Image: CERN)



An intense beam of electrons is produced in a photoinjector, accelerated to around 100 MeV and then is expanded, shaped and guided to the patient.

The design of this facility is the result of an intense dialogue between groups at CHUV and CERN.

Jean Bourhis from CHUV:
"The clinical need that we have really converges with the technological answer that CERN has."

The remarkable connection between CLIC technology and FLASH electron therapy

Very intense electron beams

CLIC – to provide brightness needed for delicate physics experiments
FLASH – to provide dose fast for biological FLASH effect

Very precisely controlled electron beams

CLIC – to reduce the power consumption of the facility
FLASH – to provide reliable treatment in a clinical setting

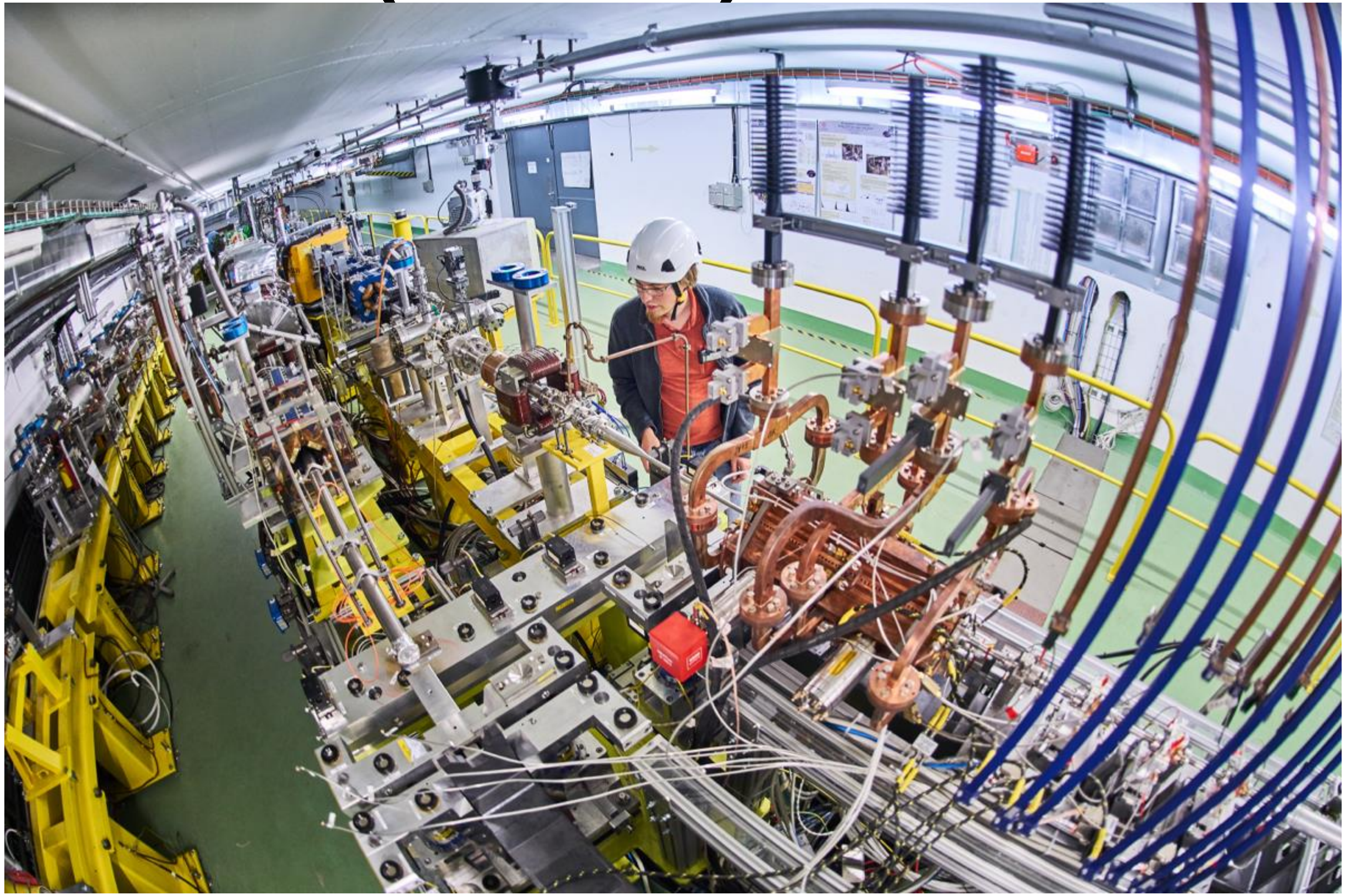
High accelerating gradient (that is high beam energy gain per length)

CLIC – fit facility in Lac Leman region and limit cost
FLASH – fit facility on typical hospital campuses and limit cost of treatment

CERN KT Seminar on April 26th, 2021
https://indico.cern.ch/event/975980/

The CERN Linear Electron Accelerator for Research (CLEAR)

CLEAR is a versatile 200 MeV electron linac + a 20m experimental beamline, operated at CERN as a multi-purpose user facility.



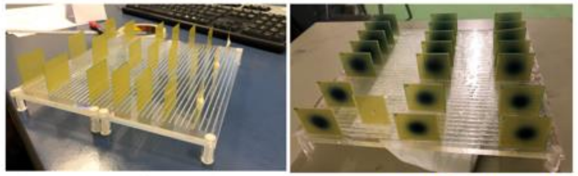
VHEE activities in CLEAR

Calibration of operational medical dosimeters – nonlinear effects with high-dose short pulses

Verification of FLASH effect using biological dosimeters

Experimental verification of dose deposition profiles in water phantoms

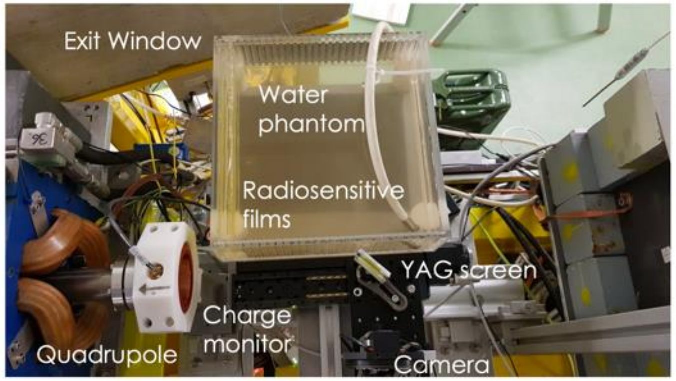
Demonstration of “Bragg-like peak” deposition with focused beams



Films set-up for profile depth dose, CHUV Lausanne (M.C. Vozenin, C. Bailat, R. Moeckli et al.)

Calorimeter and ROOS chamber, Nat. Phys. Lab. UK (A. Subiel et al.)

Advance Markus chambers and SRS Array, Oldenburg University and PTW (B. Poppe, D. Poppinga et al.)



Strathclyde and Manchester

A. Lagdza, R. Jones et al., Influence of heterogeneous media on Very High Energy Electron (VHEE) dose penetration and a Monte Carlo-based comparison with existing radiotherapy modalities, Nuclear Inst. and Meth. in Physics Research, B, 482 (2020) 70-81.

M. McManus, A. Subiel et al., The challenge of ionisation chamber dosimetry in ultra-short pulsed high dose-rate Very High Energy Electron beams, Nature Scientific Reports (2020) 10-9089.

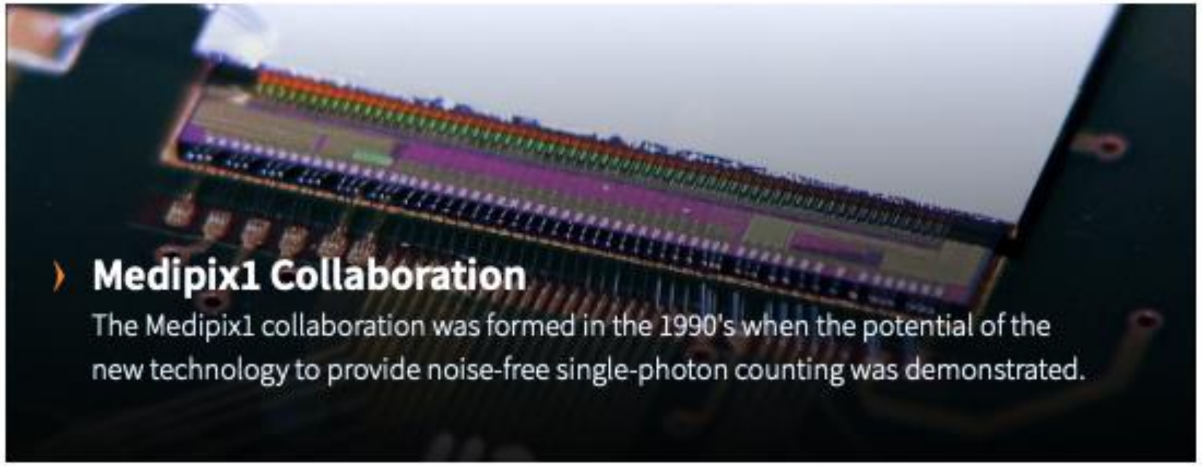
Small, K.L., Henthorn, et al., Evaluating very high energy electron RBE from nanodosimetric pBR322 plasmid DNA damage, Nature Sci. Rep. 11, 3341 (2021).

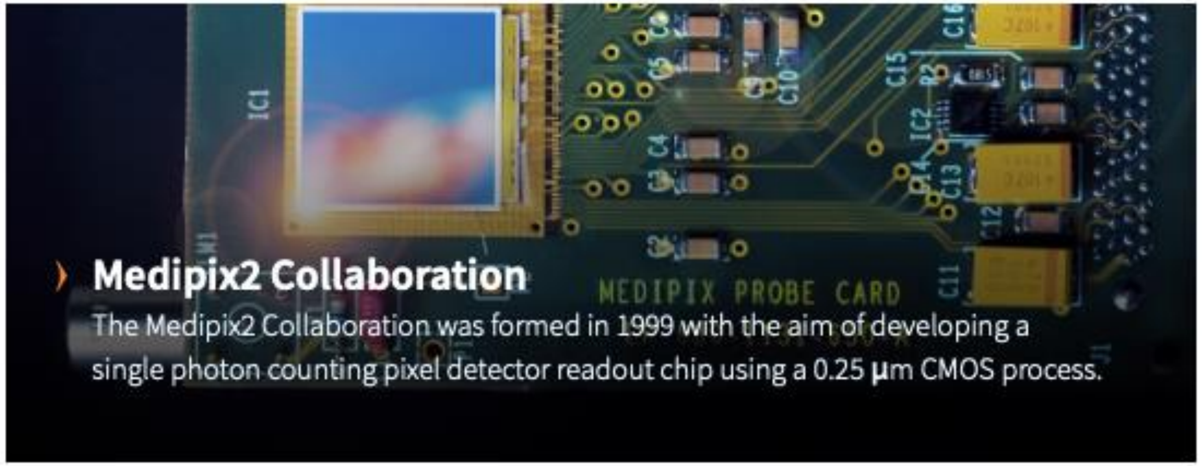
D. Poppinga et al., VHEE beam dosimetry at CERN Linear Electron Accelerator for Research under ultra-high dose rate conditions, 2021 Biomed. Phys. Eng. Express 7 015012.

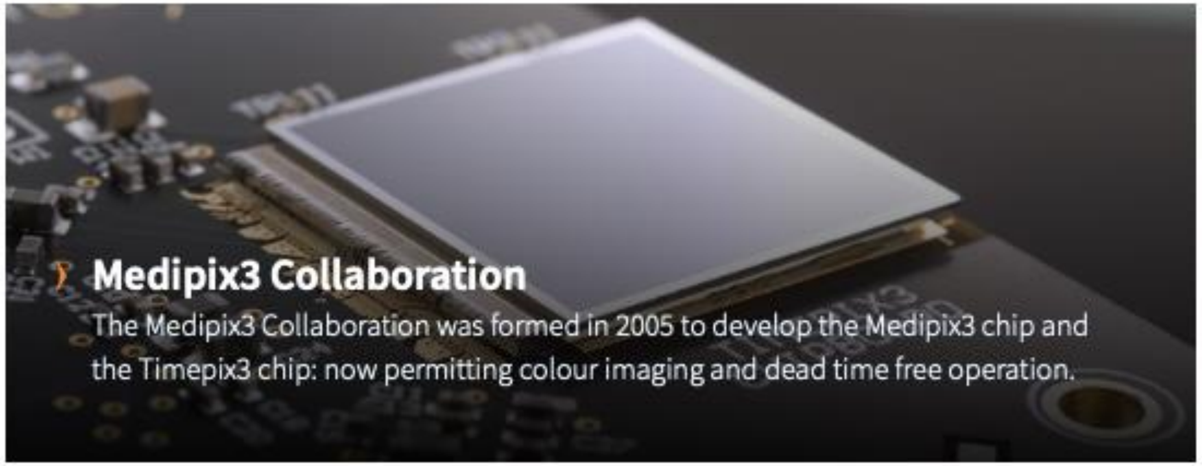
Kokurewicz, K., Brunetti, E., Curcio, A. et al. An experimental study of focused very high energy electron beams for radiotherapy, Nature Commun. Phys. 4, 33 (2021).

Medipix

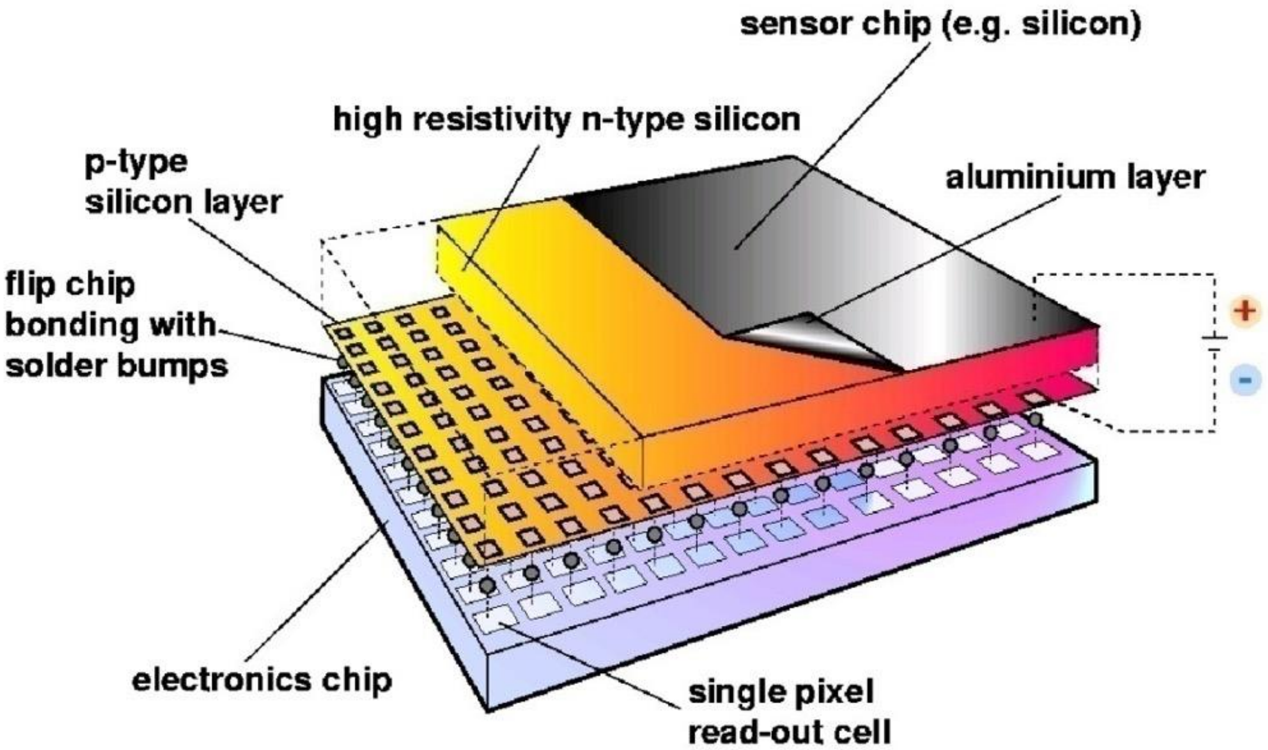
A family of pixel detector read-out chips for particle imaging and detection developed by the Medipix Collaborations

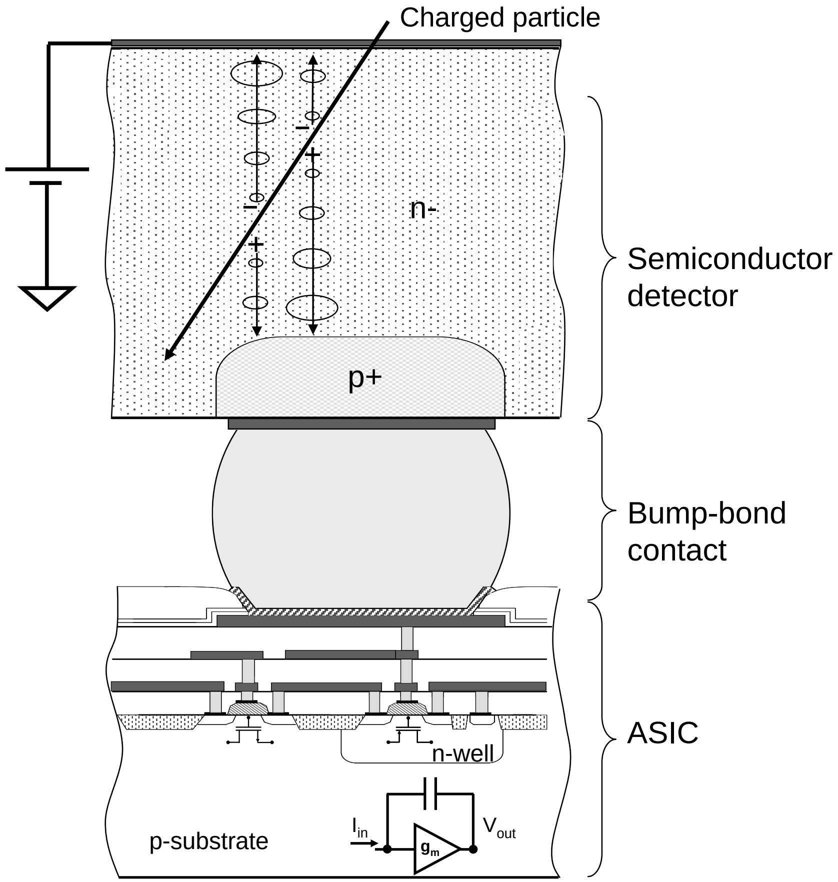




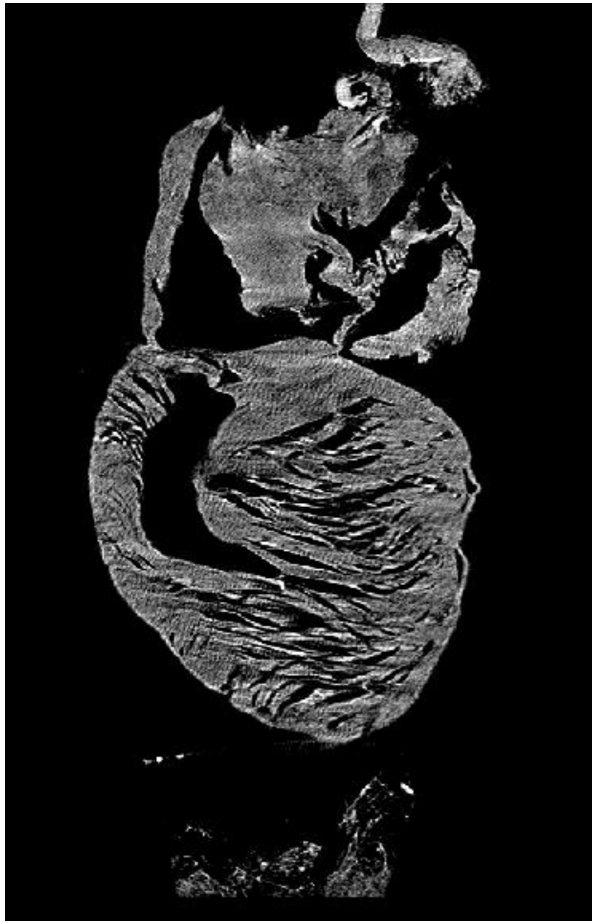


Hybrid Silicon Pixel Detectors



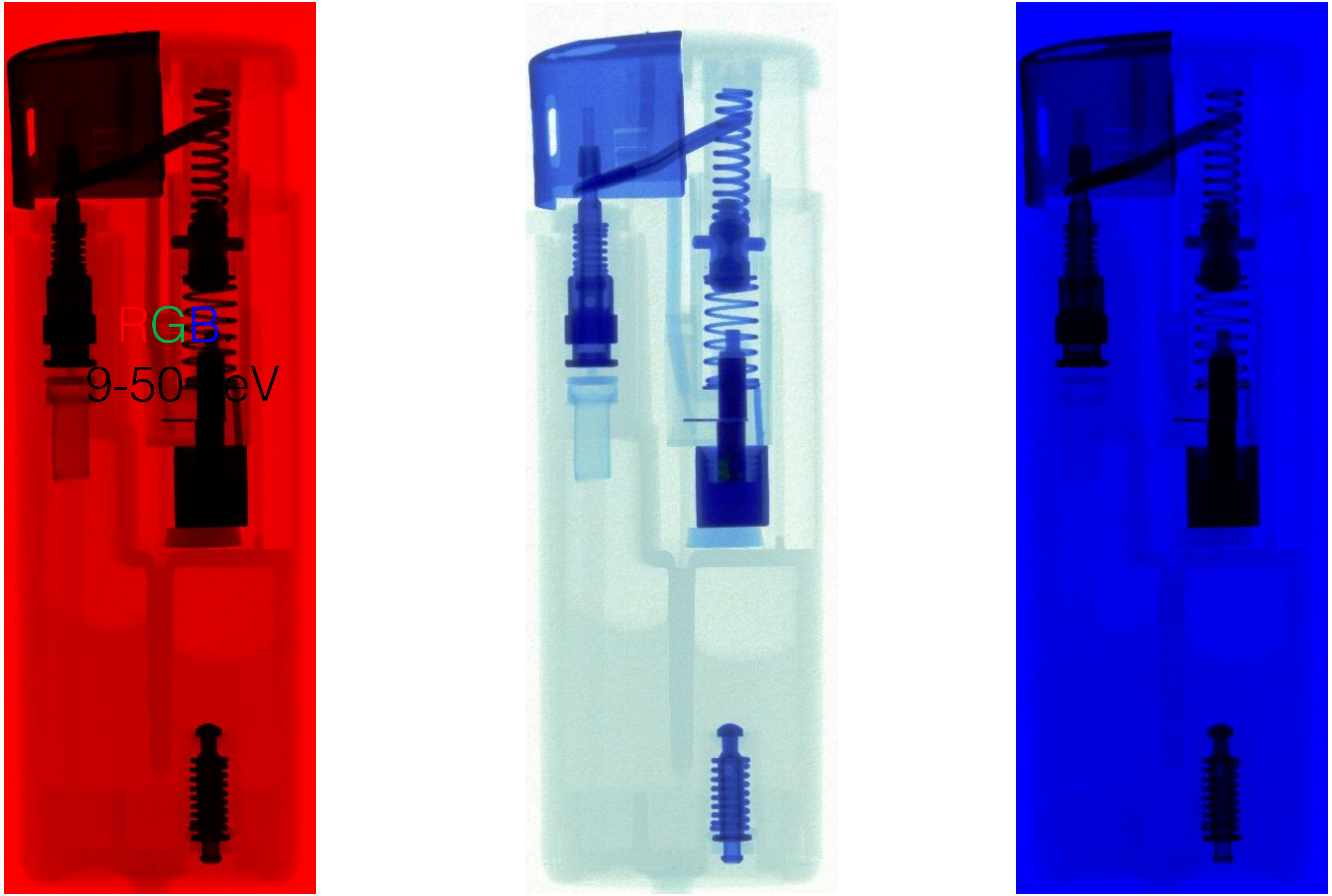


Noise-hit free particle detection
Standard CMOS can be used allowing on-pixel signal processing
Sensor material can be changed (Si, GaAs, CdTe..)



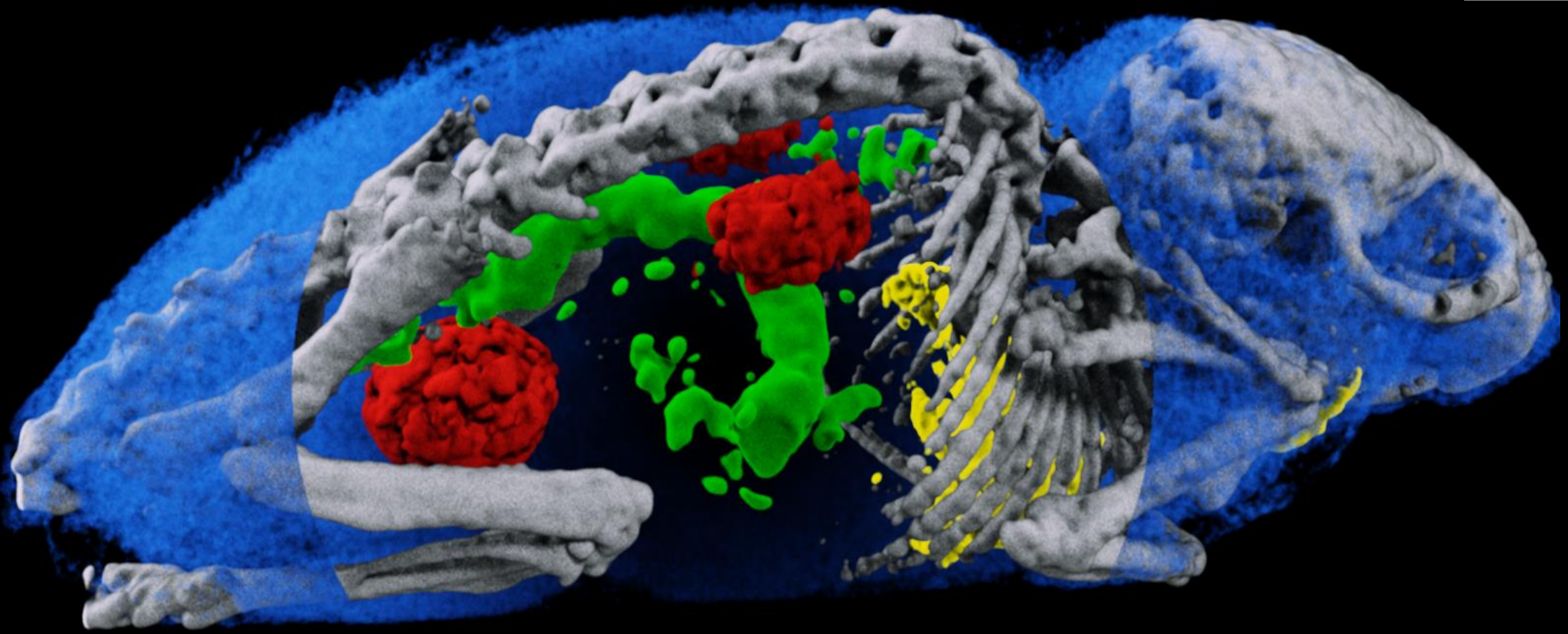
Ethanol-preserved mouse heart scanned using the WidePIX$_{10x5}$ detector
60 kVp tungsten spectrum
720 projections, 5 seconds per projection (one hours total)
Spatial resolution ca. 7 μm
Reconstructed using Volex, visualized using CTVox and Amide software

Colour x-ray of a lighter



S. Procz et al.

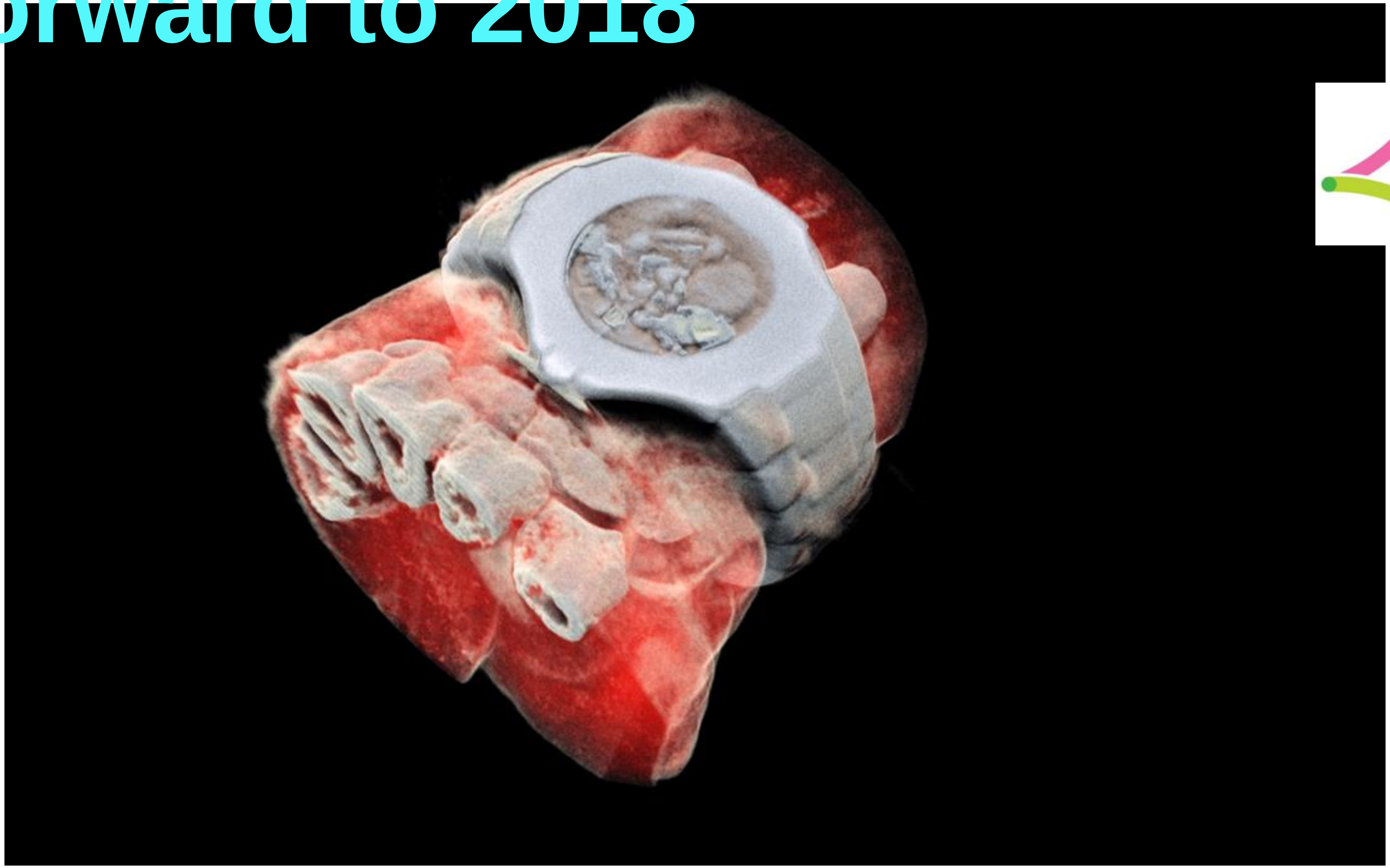
Spectroscopic information permits material separation



The water has been partly cut away to reveal the bone, gold, gadolinium and iodine

Images presented and the European Congress of Radiology, Vienna, March 2017.

Fast forward to 2018



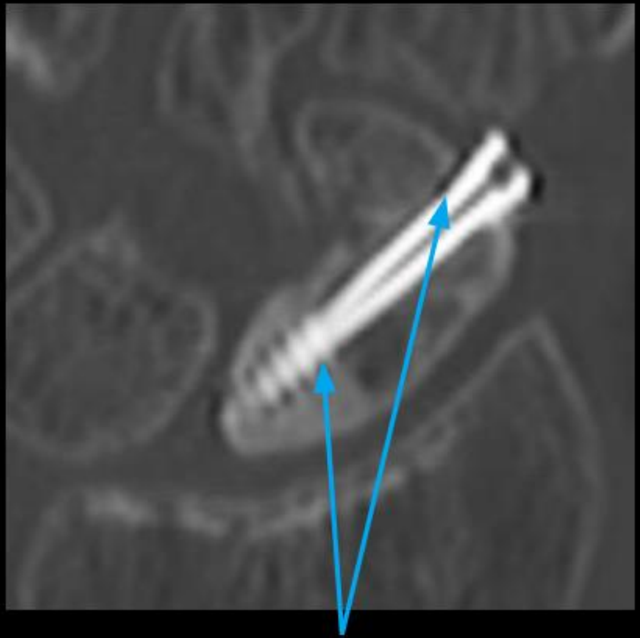
mars

CT versus MARS

Standard CT

Metal artefact

MARS



Scaphoid screw

Metal artifact hides the bone-metal interface

The bone-metal interface is visualised enabling assessment of peri-implant infection and osteolysis

MARS SPCCT Imaging technology is in concept development for human use. It is not a product and is not cleared or approved by the US FDA or any other regulator for commercial availability outside of New Zealand

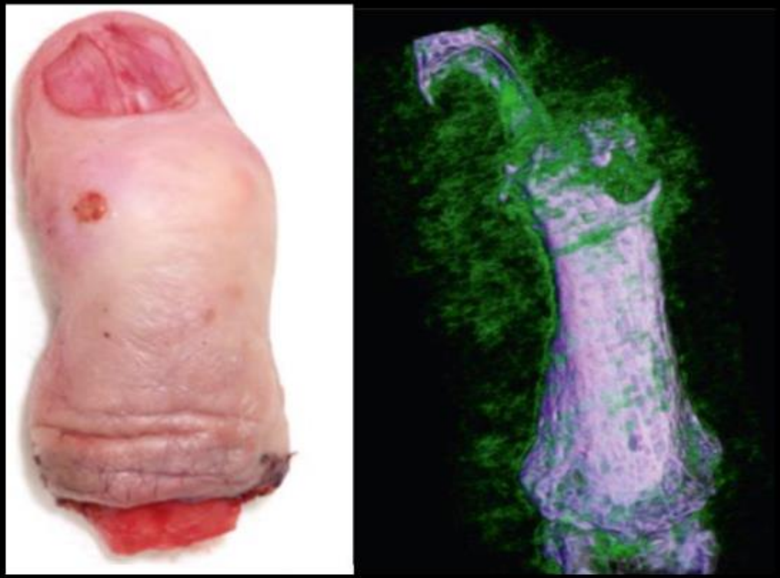
mars

Slide courtesy of Anthony Butler, University of Canterbury

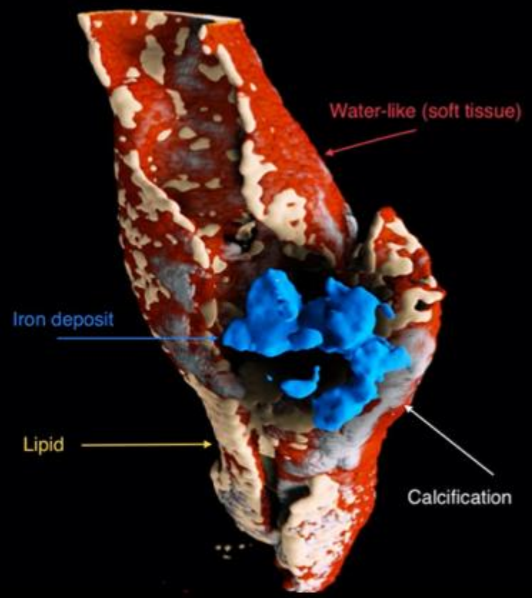
Presented at 6th Workshop on Medical Applications of Spectroscopic X-ray Detectors, 29 Aug 2022, CERN

Molecular versus MARS

MARS - intrinsic information



Gout crystal characterisation
(Collab with CHUV)



Carotid plaque with quantitative measurements of fat, water, calcium, and iron

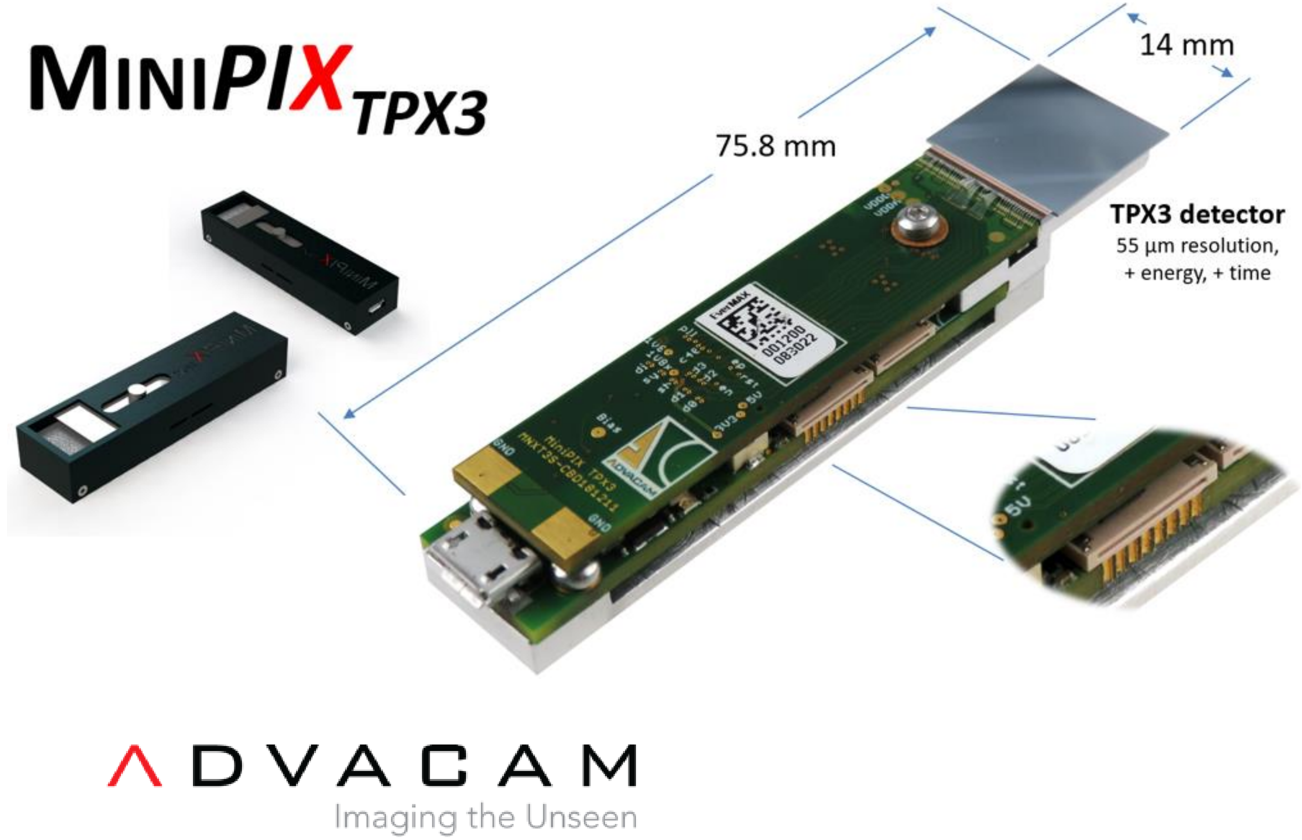
MARS SPCCT Imaging technology is in concept development for human use. It is not a product and is not cleared or approved by the US FDA or any other regulator for commercial availability outside of New Zealand

mars

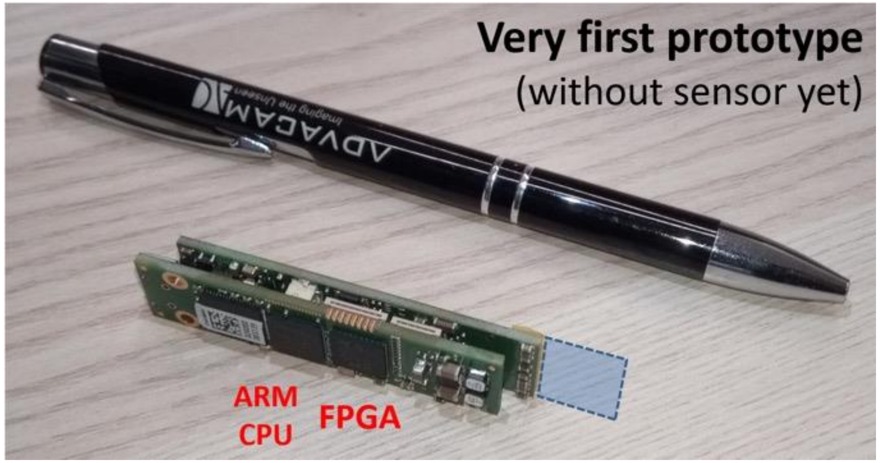
Slide courtesy of Anthony Butler, University of Canterbury

MiniPIX TPX3

Miniaturized spectral camera supporting Si and CdTe sensors

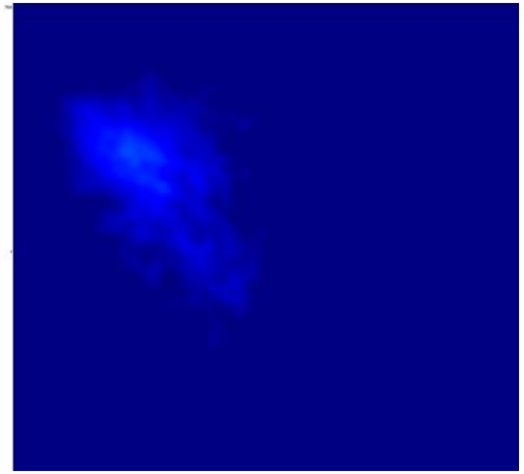


It's really small...



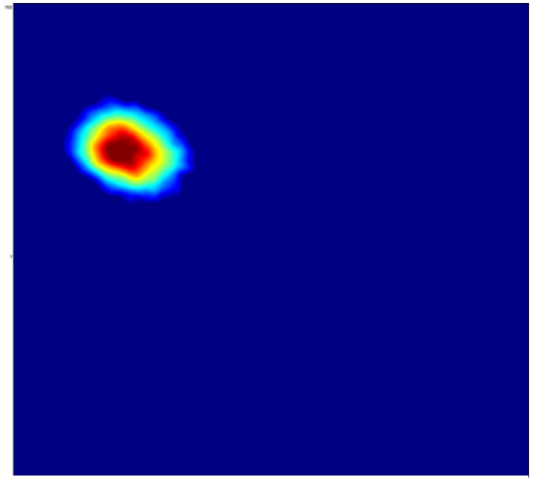
Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

250 – 300 keV



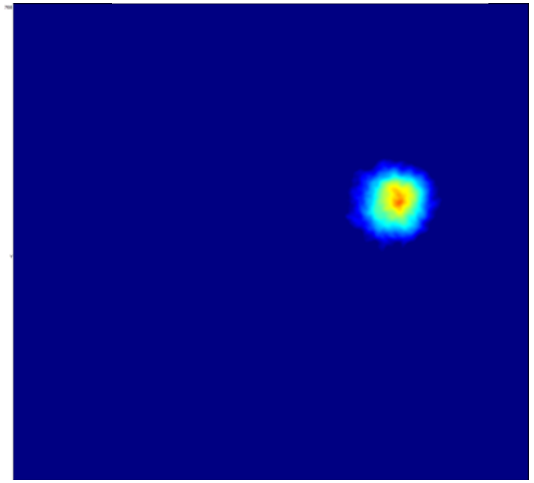
^{131}I 284 keV (7%)

350 – 400 keV



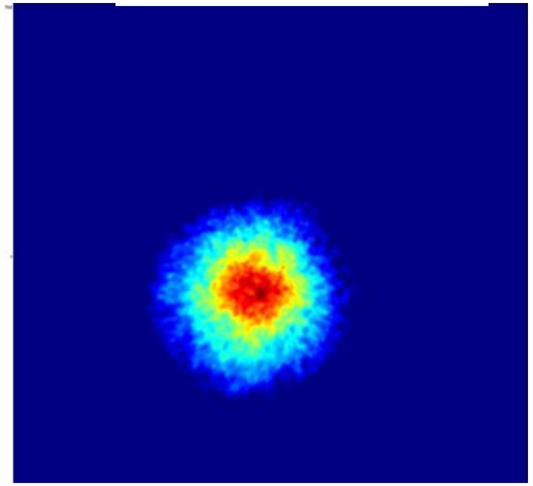
^{131}I 364 keV

500 – 550 keV

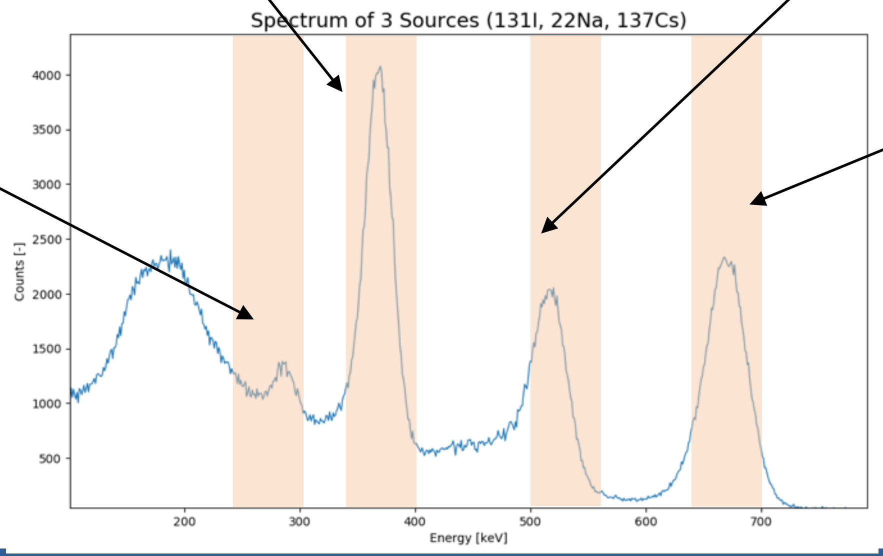


^{22}Na 511 keV

650 – 700 keV



^{137}Cs 662 keV



Gamma camera applications: Thyroid diagnostic

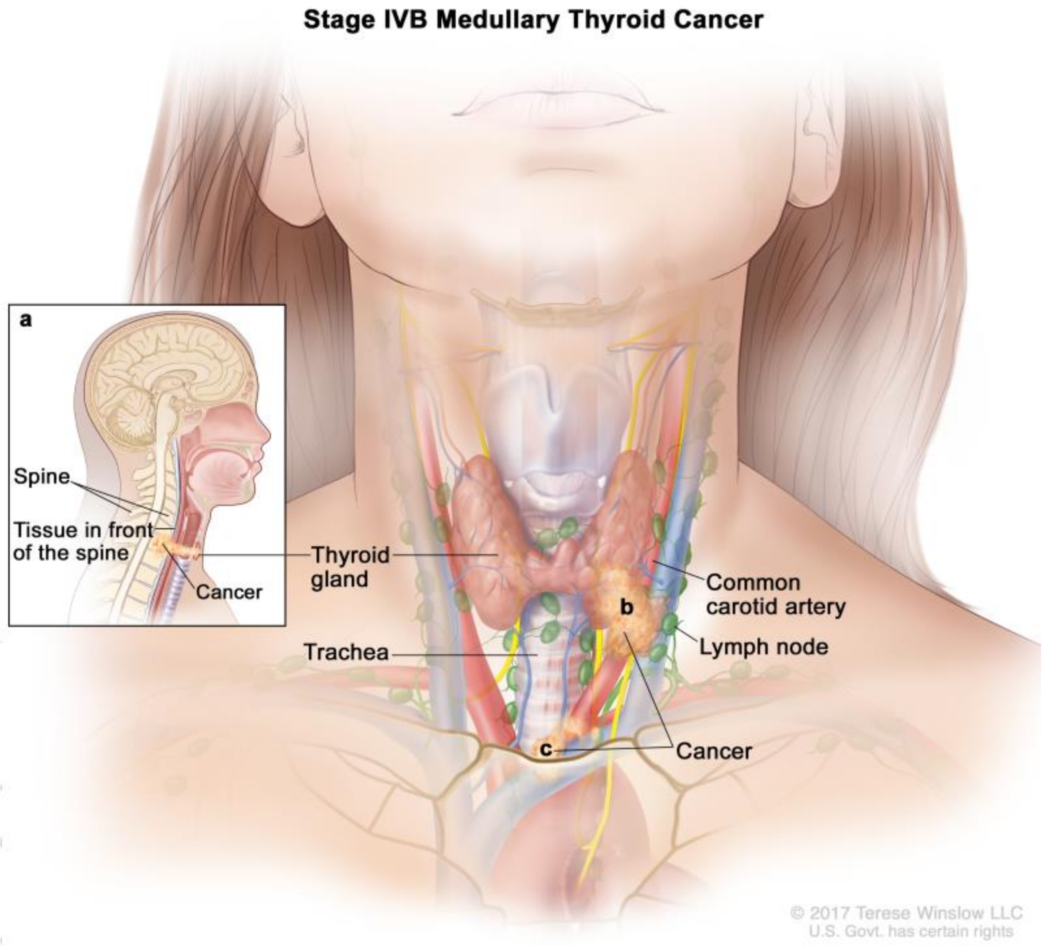
Thyroid cancer diagnostics and treatment monitoring:

The second most frequent cancer for women (after breast cancer)

Current imaging methods offer resolution of about 12 mm in 2D

Our technology allows

- 5 times better resolution and 3D (2.5 mm)
- 4 times lower dose



TimePIX 3 photon fluence measurement in hospital theatres

Reference person: 1.76 m

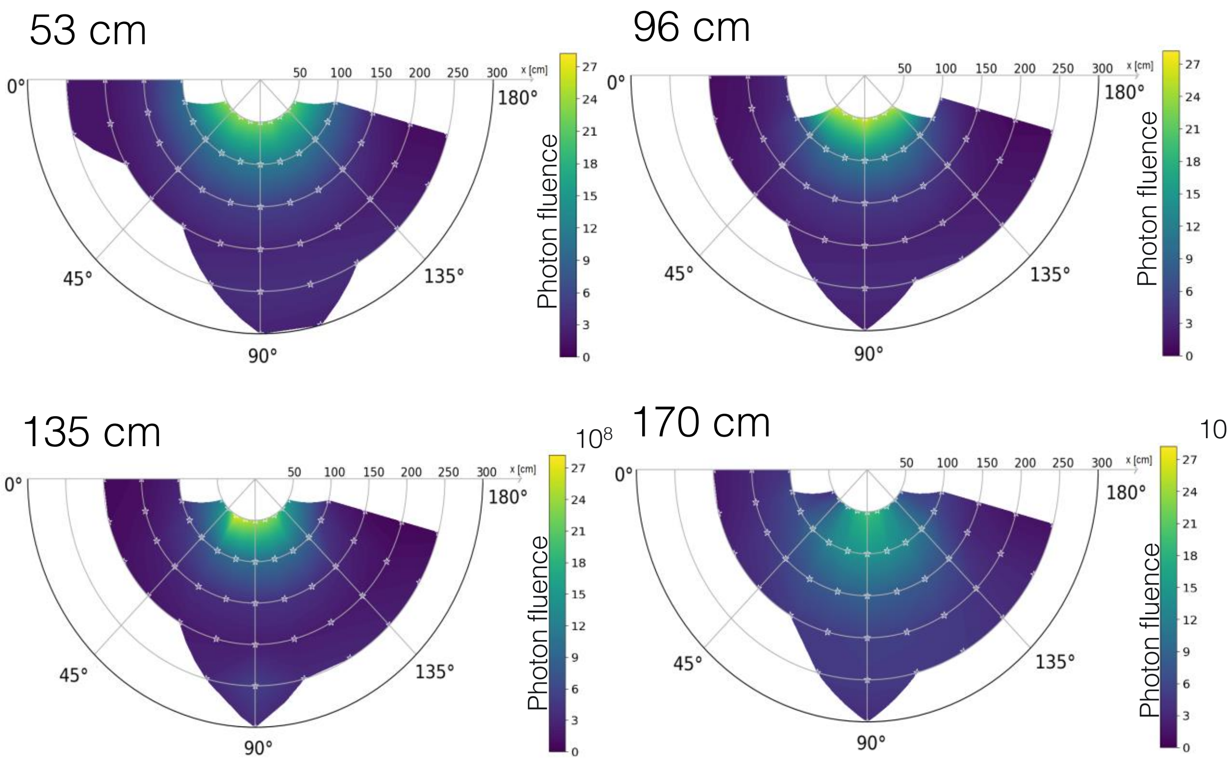
Eye lens - 170 cm

Chest - 135 cm

Belt - 96 cm

Knee - 53 cm

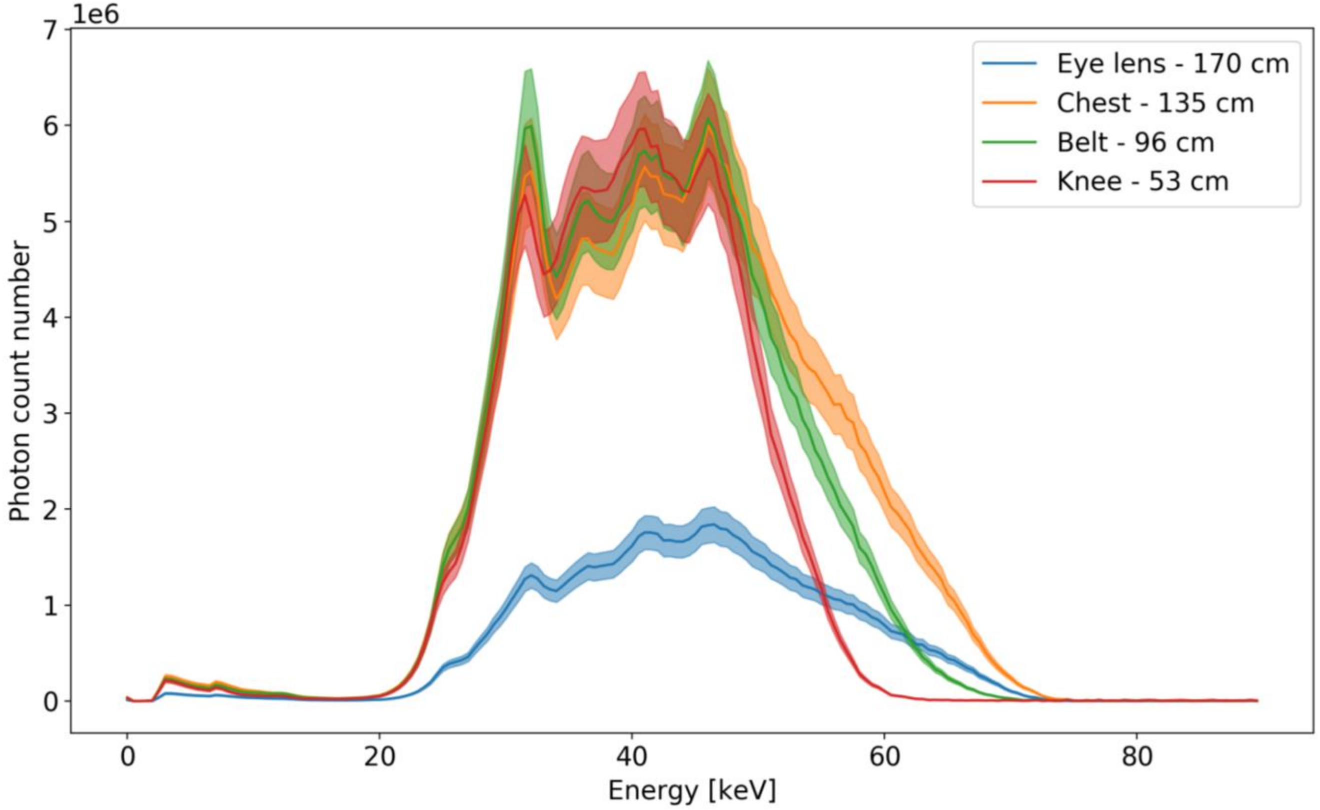
Courtesy of M. Nowak

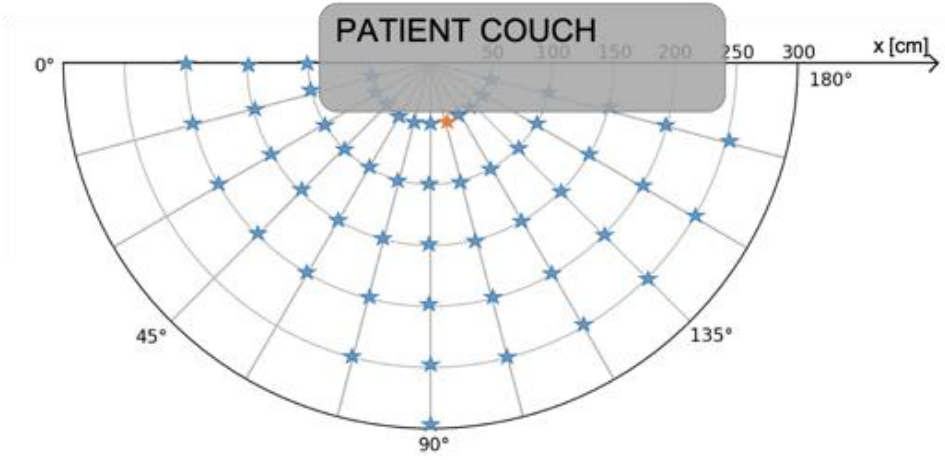


Colour maps of the photon fluence measured with a Timepix III in an hospital theatre at four horizontal eights.

TimePIX 3 photon fluence measurement in hospital theatres

Energy spectra for each height for a given person

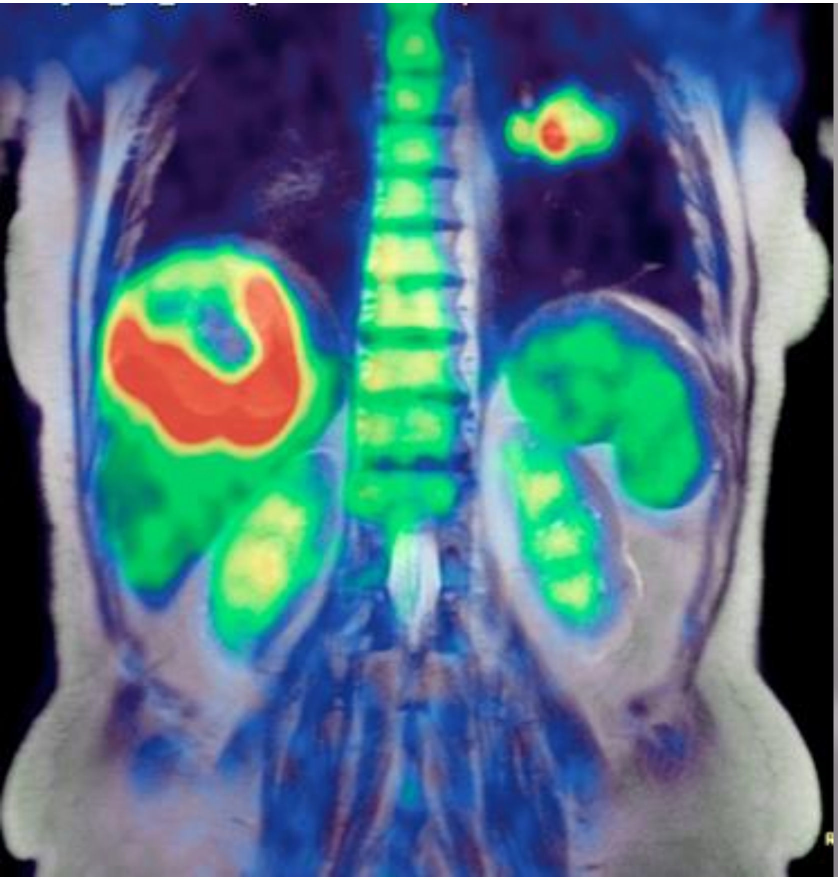


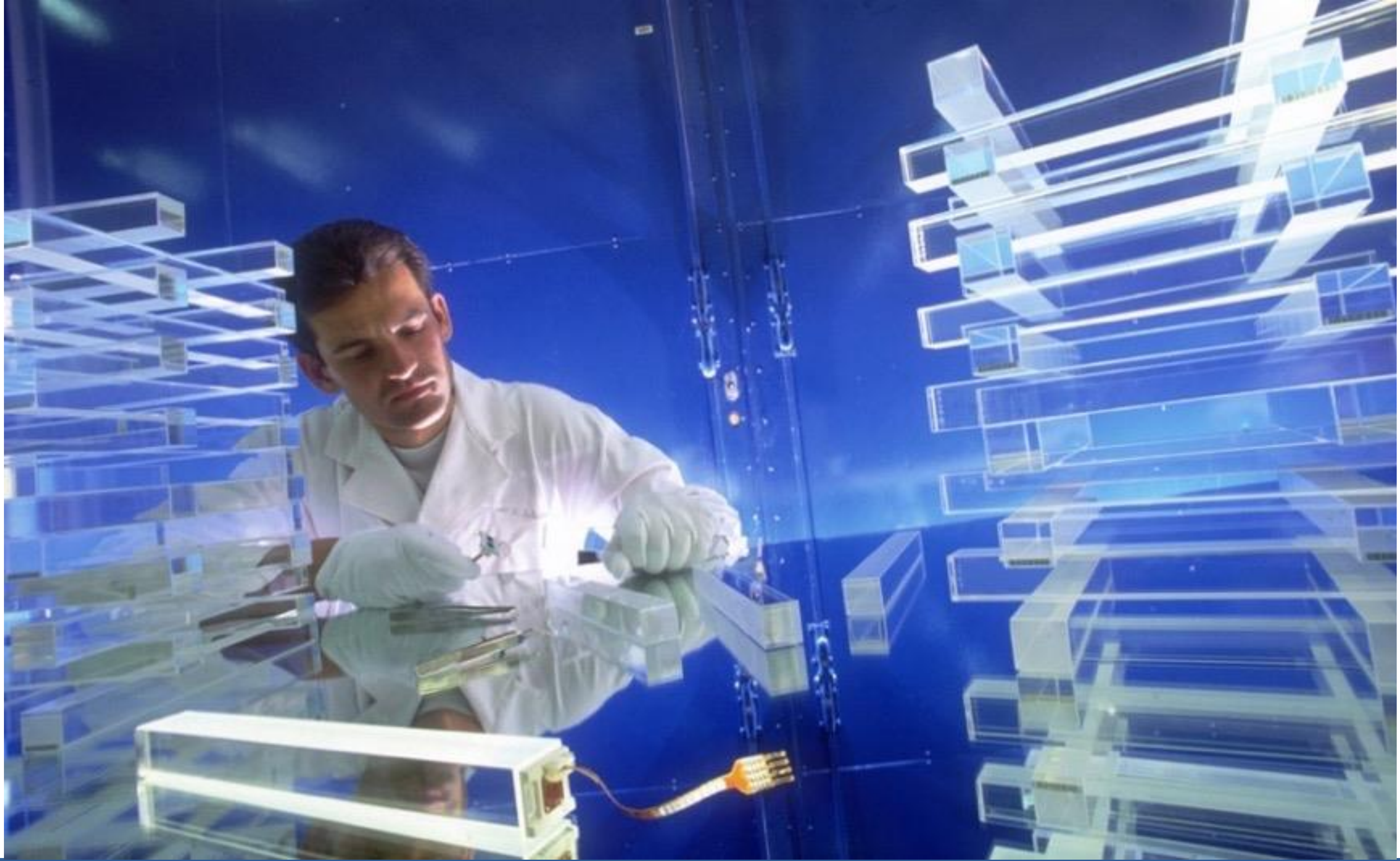


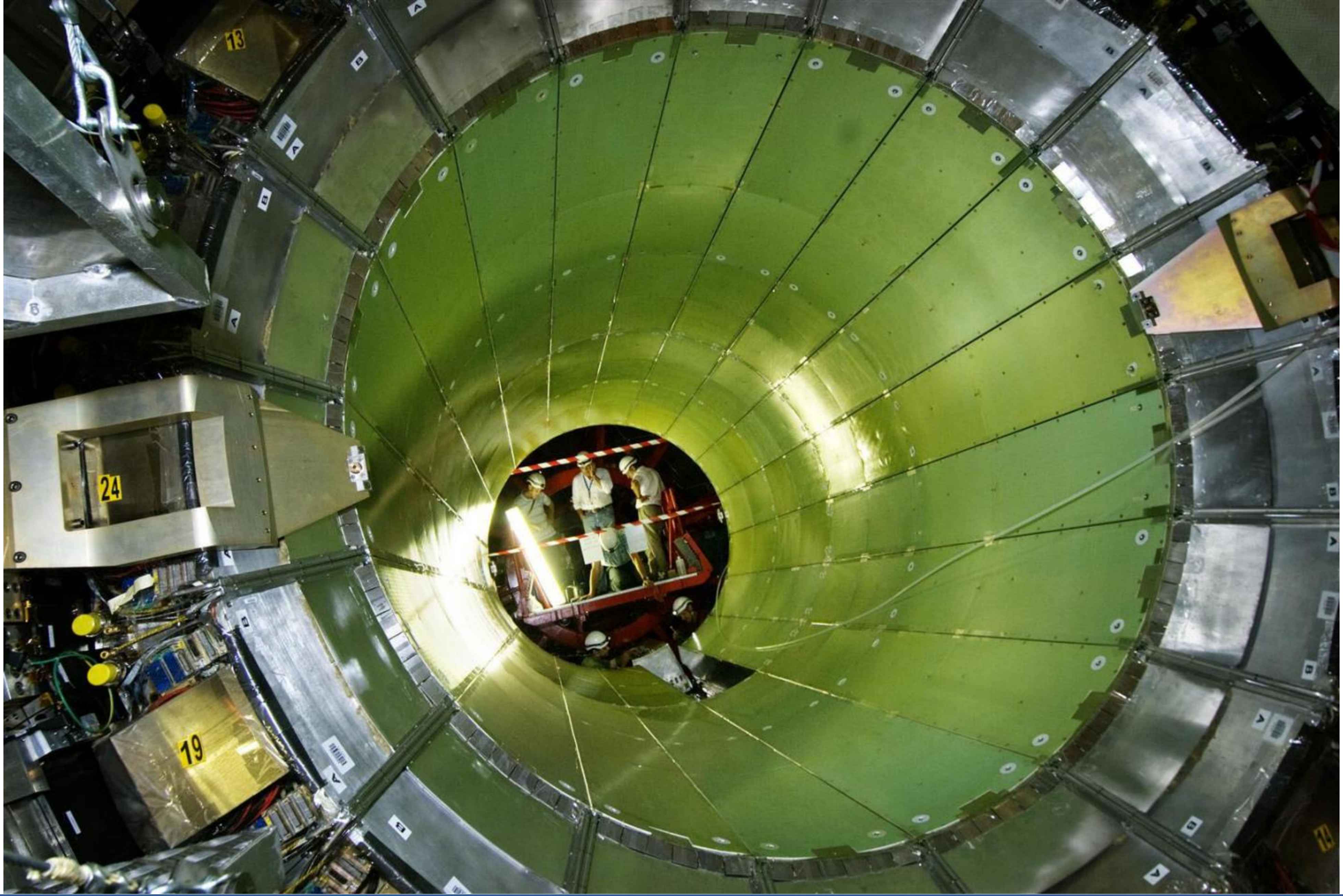
Courtesy of M. Nowak

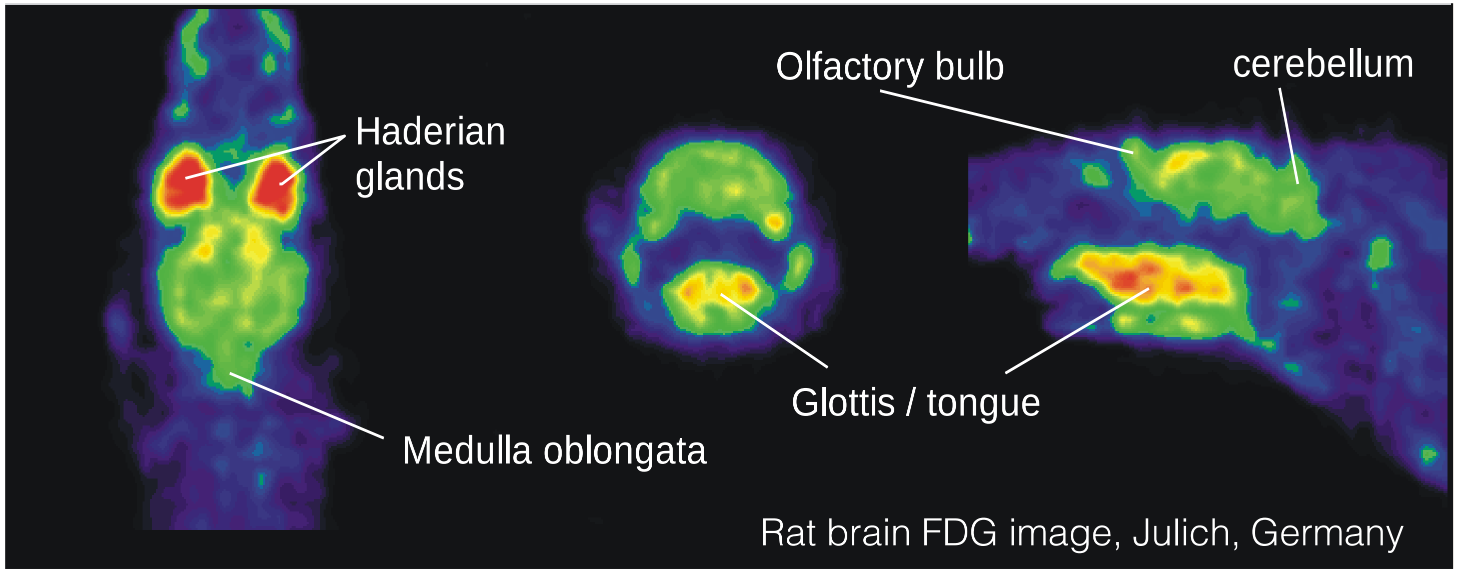
➡ Shift in energy from head to toes = non homogenous exposure

PET

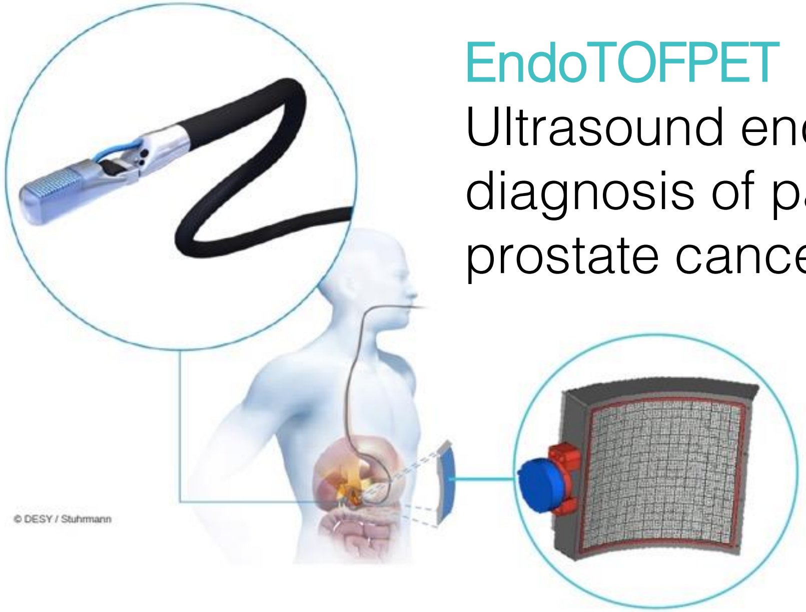




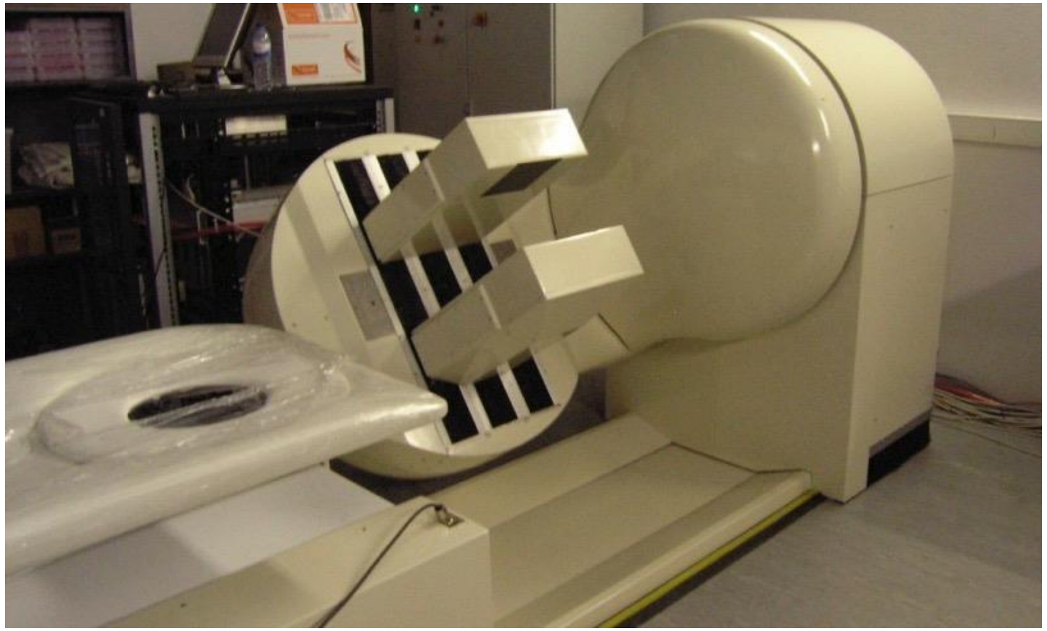

13
24
19



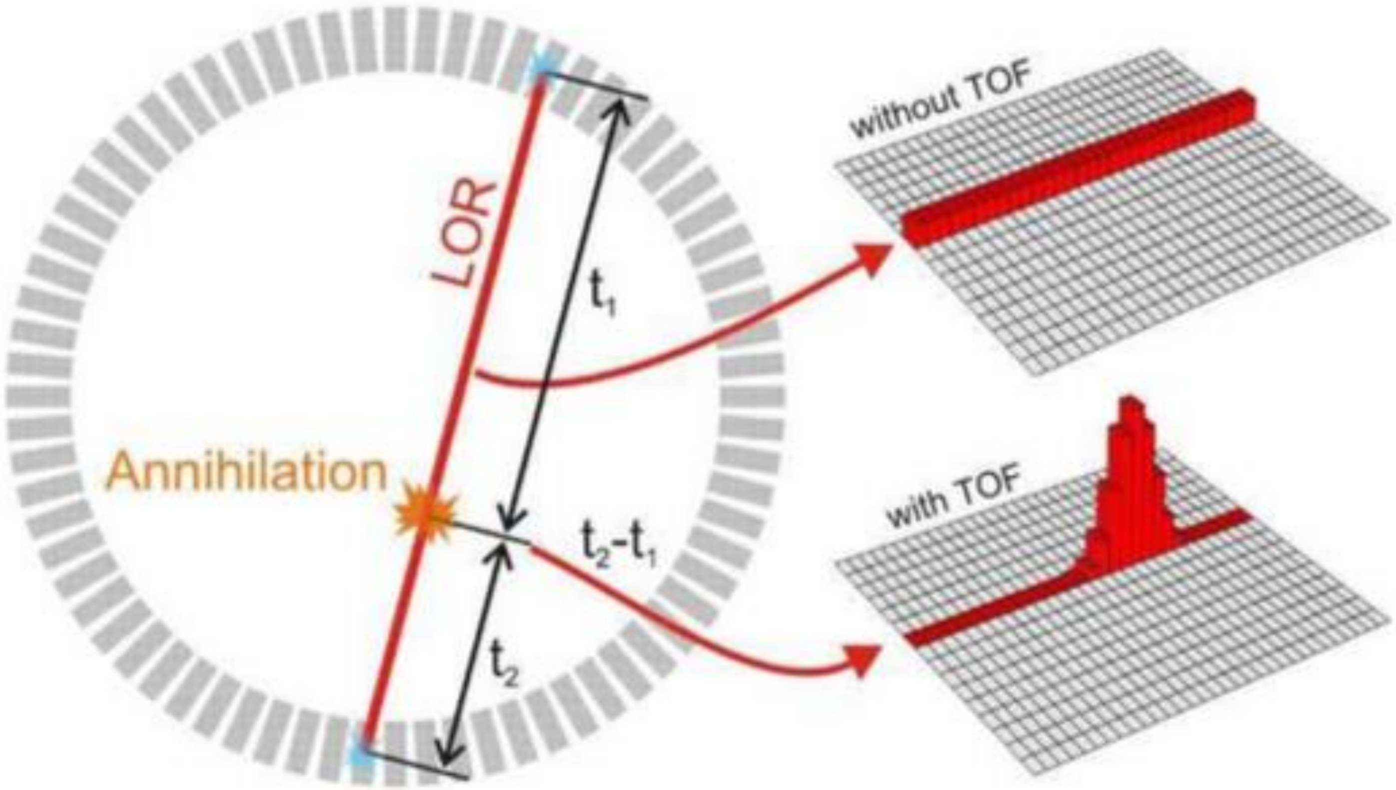
ClearPET
PET for small anymals



EndoTOFPET
Ultrasound endoscopic PET for diagnosis of pancreas & prostate cancer



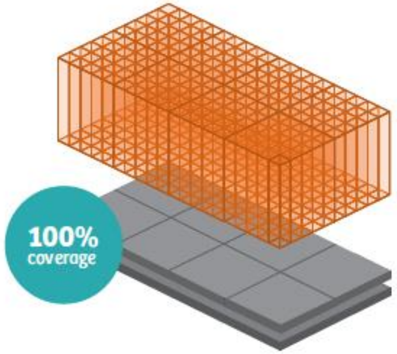
ClearPEM
Dedicated scanner for breast imaging


LOR
Annihilation
t_1
t_2
t_2-t_1
without TOF
with TOF

Current status commercial TOF-PET

TOF PET SIEMENS: BIOGRAPH VISION

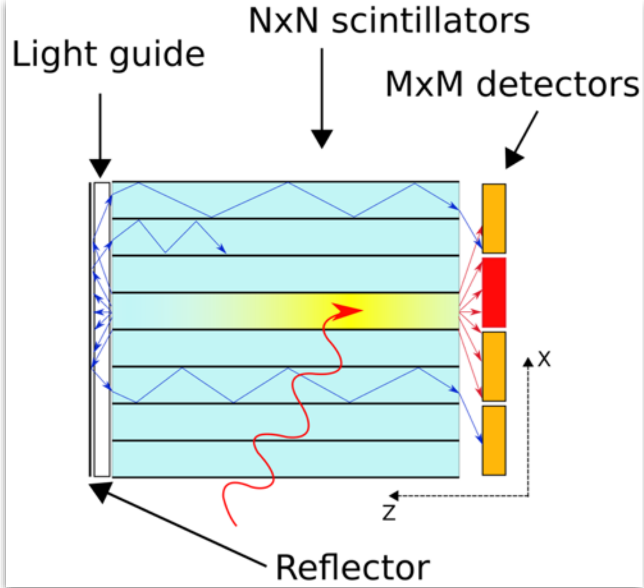
3.2mm section crystals
CTR 215ps

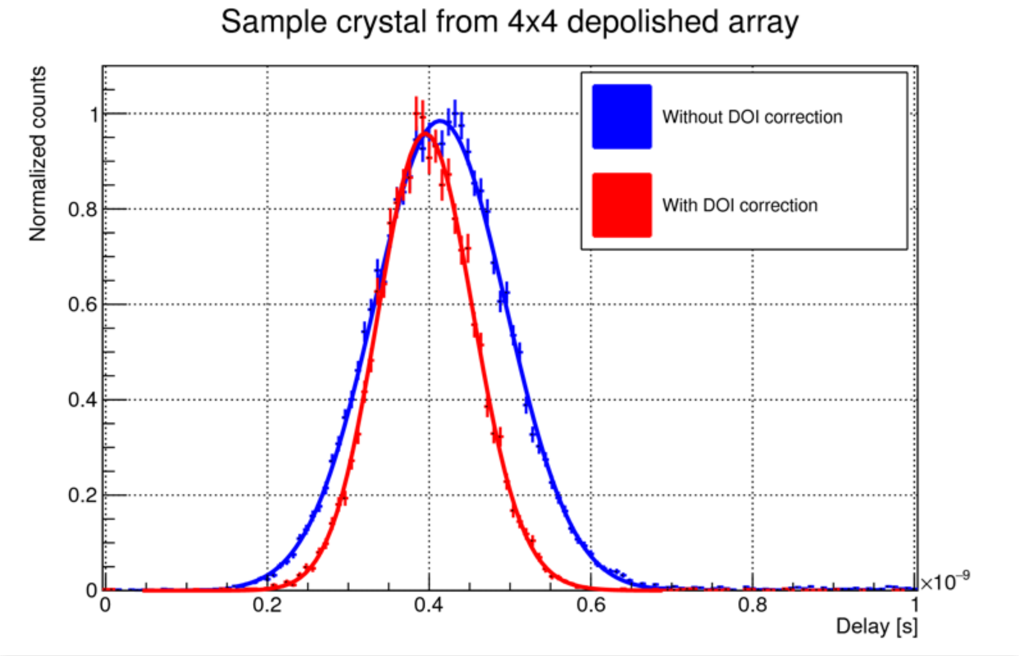


Webpage SIEMENS:
https://static.healthcare.siemens.com/siemens_hwem-hwem_ssxa_websites-context-root/wcm/idc/groups/public/@global/@imaging/@molecular/documents/download/mda4/mzmy/~edisp/biograph_vision_technical_flyer-05440720.pdf

See presentation KT/EP seminar 6 September 2021 from Maurizio Conti

In the CERN Crystal Clear group: <160 ps with DOI





Type of array	Crystals dim. [mm³]	DOI resolution FWHM [mm]	En. Res. FWHM @ 511 keV [%]	CTR FWHM [ps], central pixels	
				No correction	*With DOI correction*
DOI	3.1 x 3.1 x 15	3.0 ± 0.1	8.9 ± 0.2	234 ± 2	157 ± 2

DOI information extracted without degradation of timing properties

M. Pizzichemi et al, Phys. Med. Biol. 61 (2016) 4679

nature International weekly journal of science

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Archive > Volume 504 > Issue 7479 > News Feature > Article

NATURE | NEWS FEATURE

Radioisotopes: The medical testing crisis

With a serious shortage of medical isotopes looming, innovative companies are exploring ways to make them without nuclear reactors.

Richard Van Noorden

11 December 2013

PDF | Rights & Permissions

Radioisotopes & Nuclear Medicine

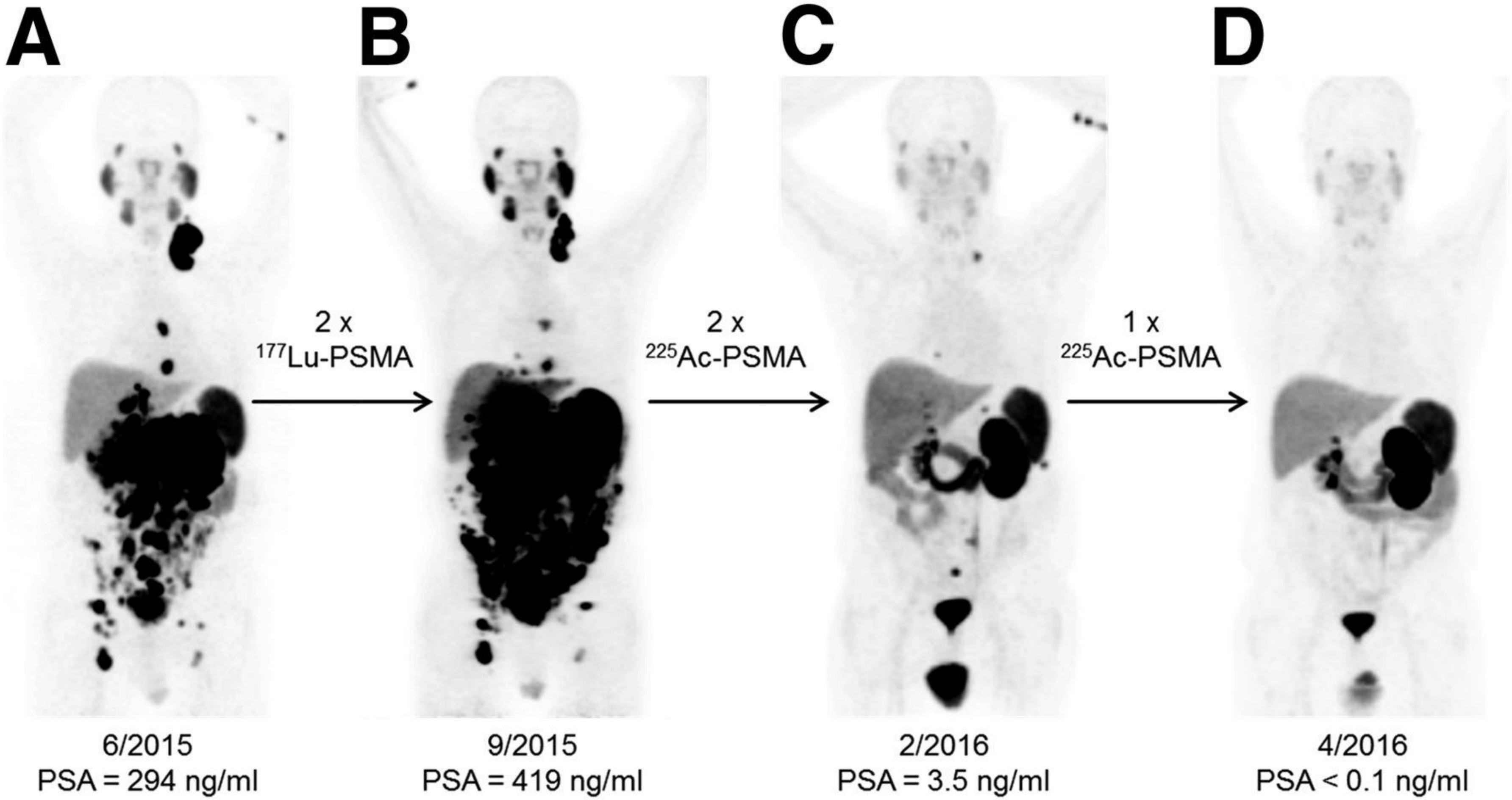
Classification of isotopes for Medicine:

1. Established isotopes → Industrial suppliers
^{99m}Tc, ^{18}F, ^{123,125,131}I, ^{111}In, ^{90}Y

2. Emerging isotopes → Small innovative suppliers
^{68}Ga, ^{82}Rb, ^{89}Zr, ^{177}Lu, ^{188}Re

3. R&D isotopes → Research labs
^{44,47}Sc, ^{64,67}Cu, ^{134}Ce, ^{140}Nd, ^{149,152,155,161}Tb, ^{166}Ho, ^{195m}Pt, ^{211}At, ^{212,213}Bi, ^{223}Ra, ^{225}Ac,…

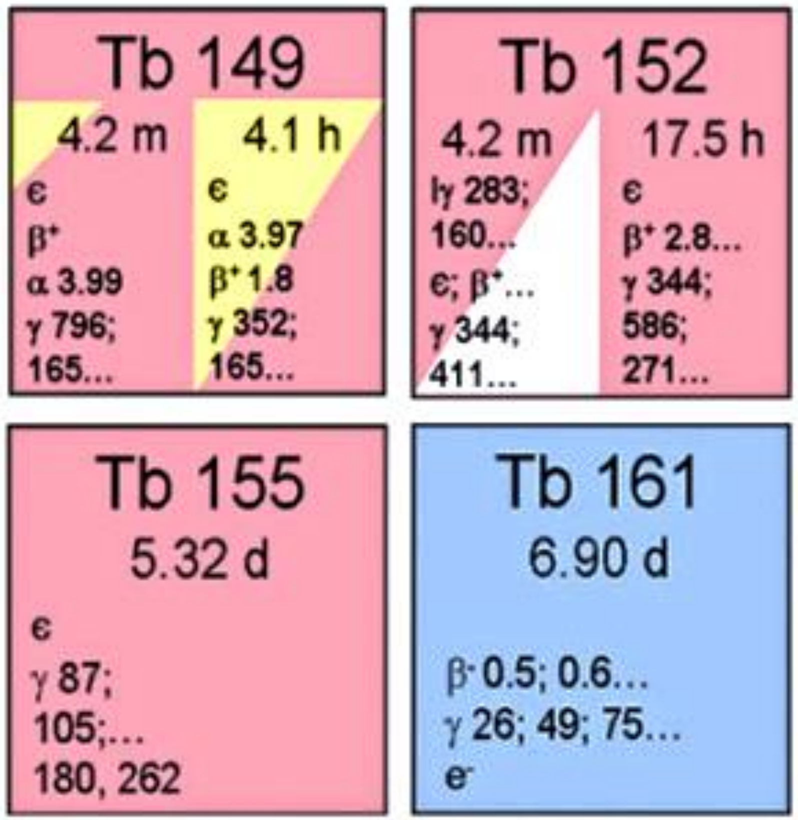
Courtesy U. Koester



68Ga-PSMA-11 PET/CT scans of patient B. In comparison to initial tumor spread (A), restaging after 2 cycles of β-emitting 177Lu-PSMA-617 presented progression (B).
Clemens Kratochwil et al. J Nucl Med 2016;57:1941-1944

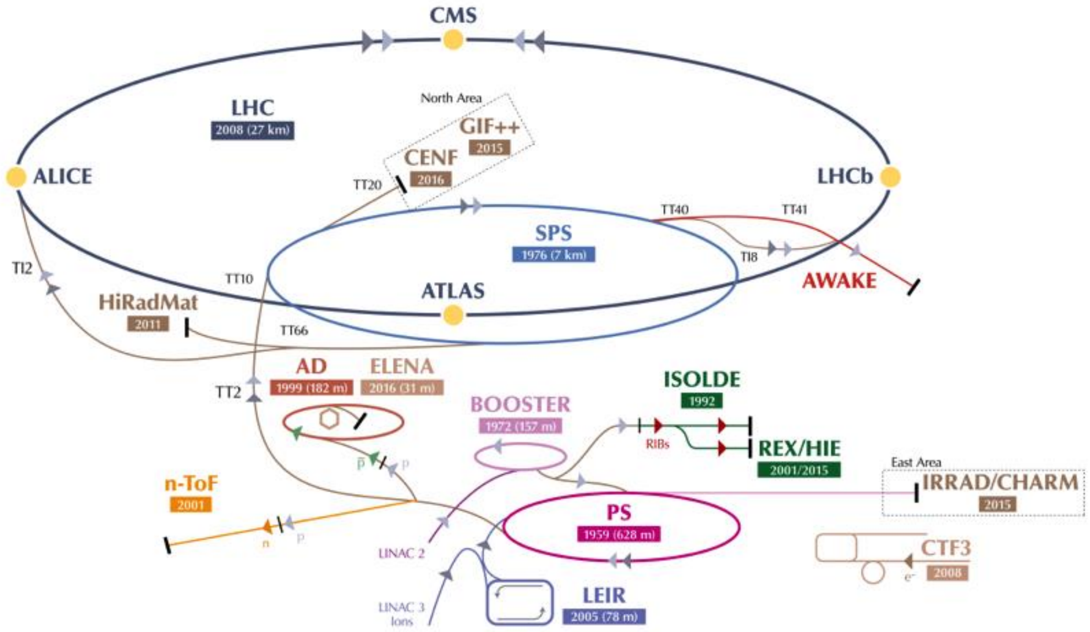
The Journal of NUCLEAR MEDICINE

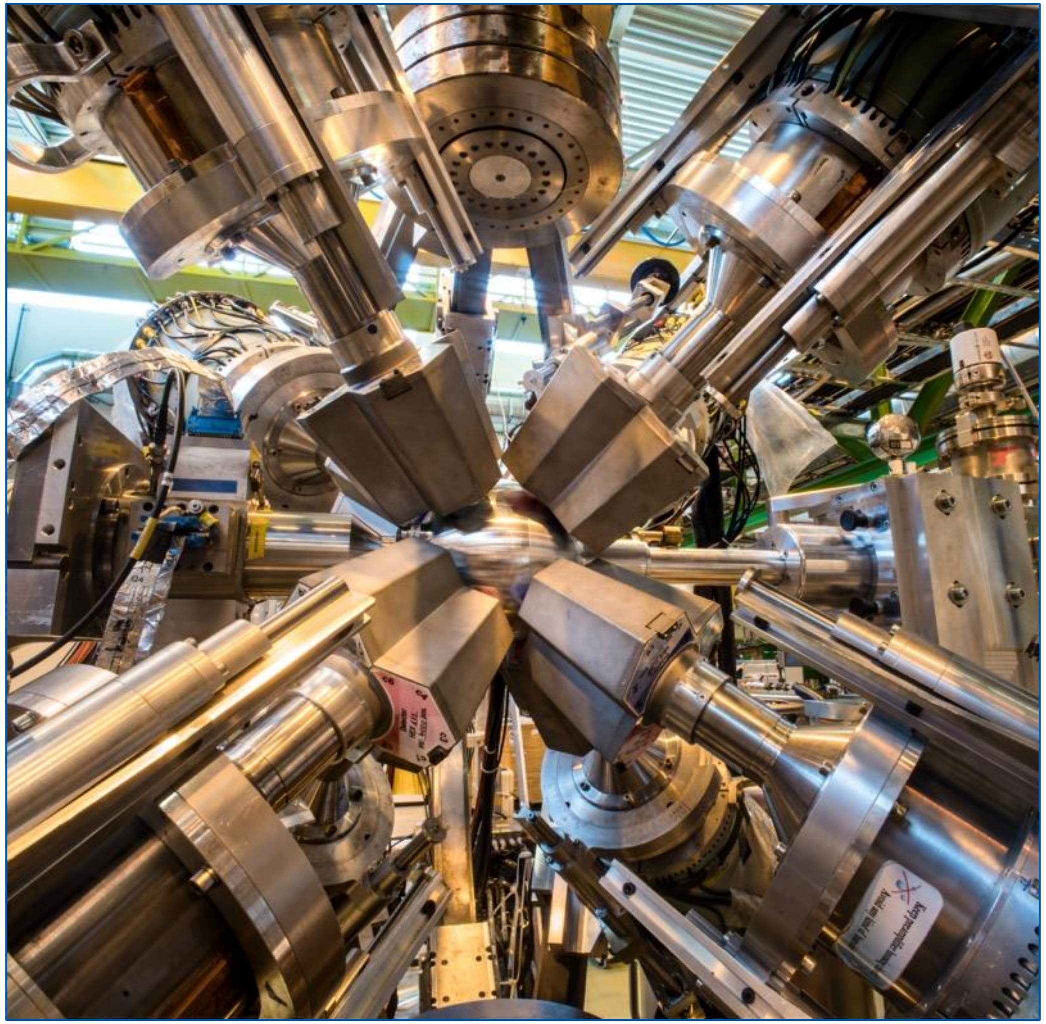
Theranostics



A Unique Matched Quadruplet of Terbium Radioisotopes for PET and SPECT and for α- and β⁻-Radionuclide Therapy: An In Vivo Proof-of-Concept Study with a New Receptor-Targeted Folate Derivative
Cristina Müller, Konstantin Zhernosekov, Ulli Köster, Karl Johnston, Holger Dorrer, Alexander Hohn, Nico T. van der Walt, Andreas Türler and Roger Schibli
Journal of Nuclear Medicine December 2012, 53 (12) 1951-1959; DOI: https://doi.org/10.2967/jnumed.112.107540

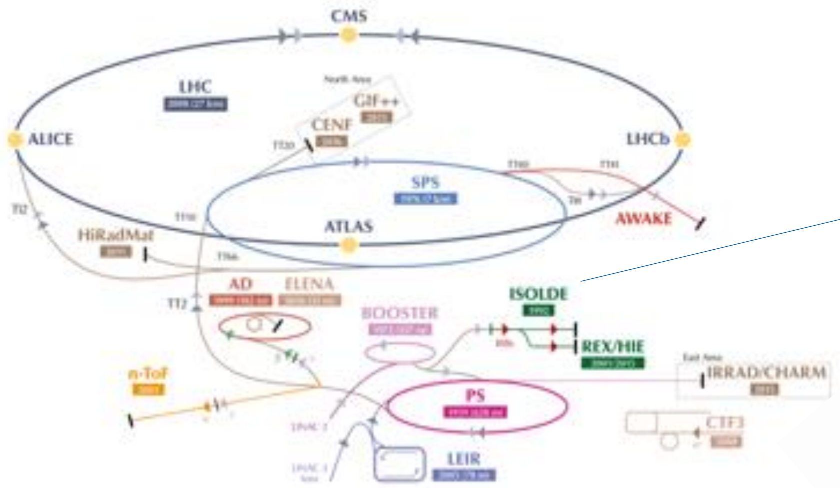
ISOLDE has been running @CERN for > 50 years

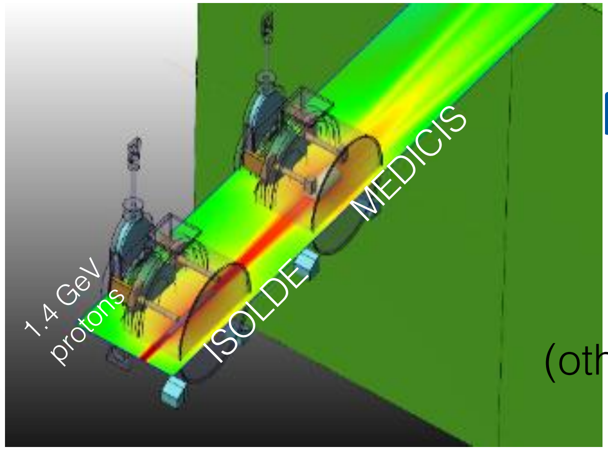




CERN-MEDICIS

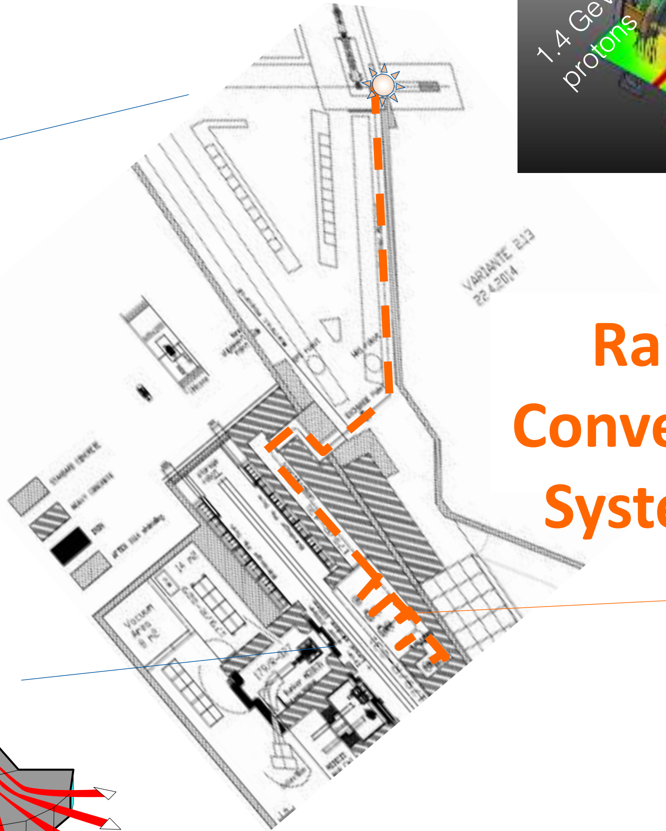
Non-conventional isotopes collected by mass separation for new medical applications



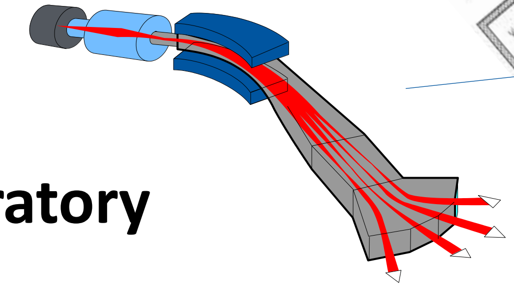


MEDICIS Target Irradiation

"Free" proton beam
(otherwise lost in the dump)

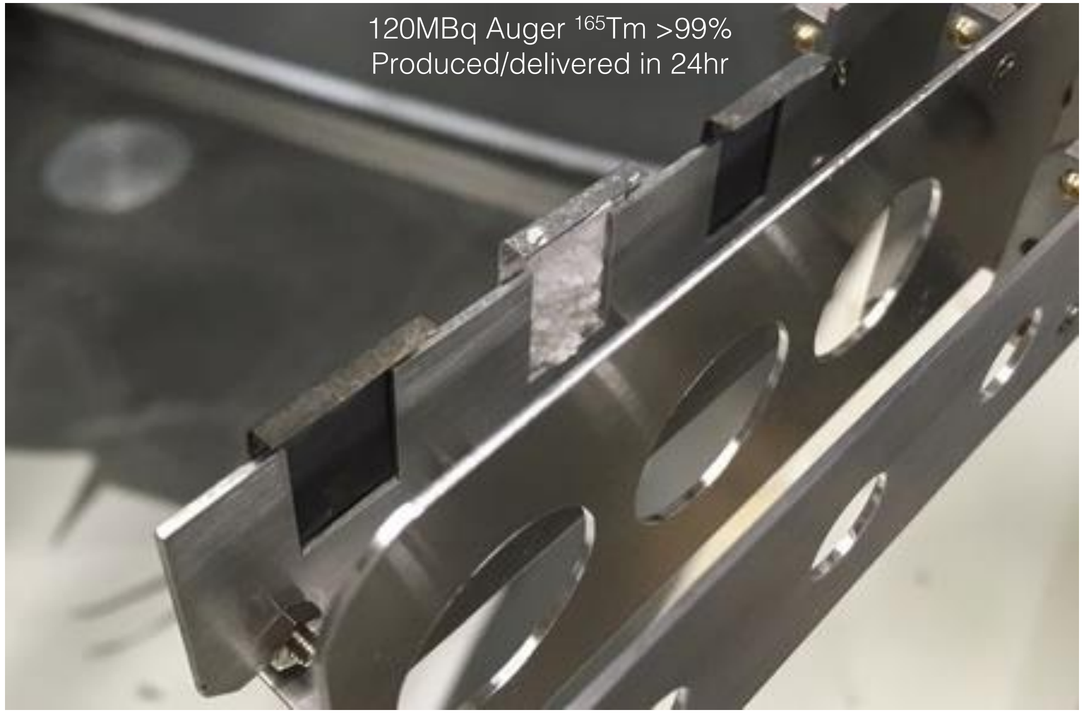


Rail Conveyor System



MEDICIS Laboratory

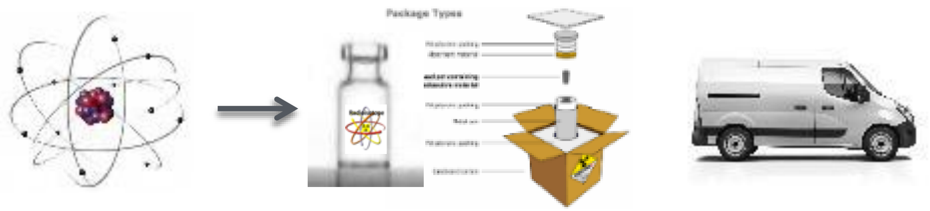
CERN-MEDICIS



Some **MEDICIS isotopes** :

High activity Sm-153, Ba/Cs-128, Tm/Er-165

Defined by the MEDICIS CB board,
1st-proof-of-concepts type of studies



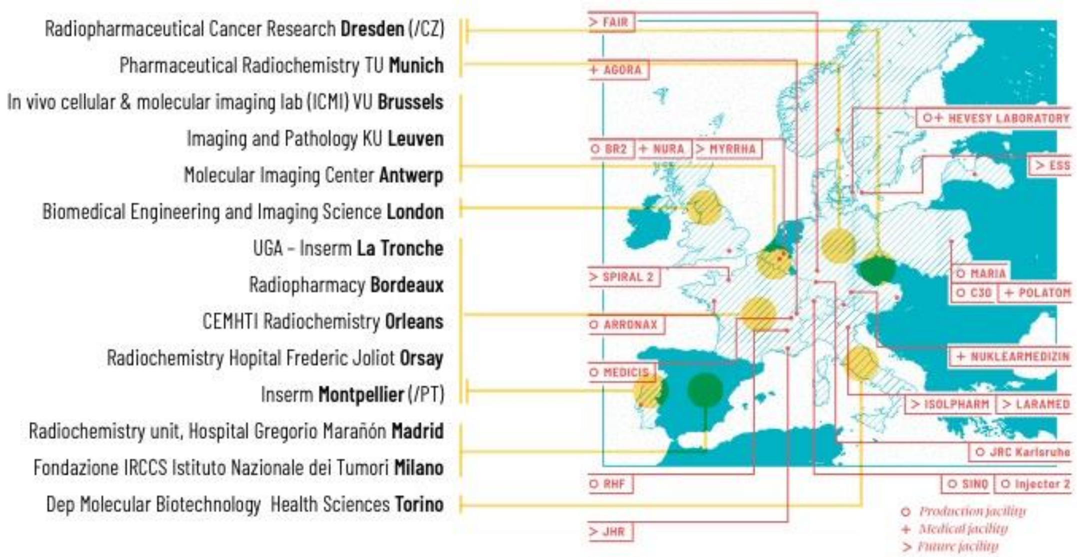
From CERN-MEDICIS to the lab/Hospital
(Countries: BE, CH, FR, PK, PT, LV, UK)

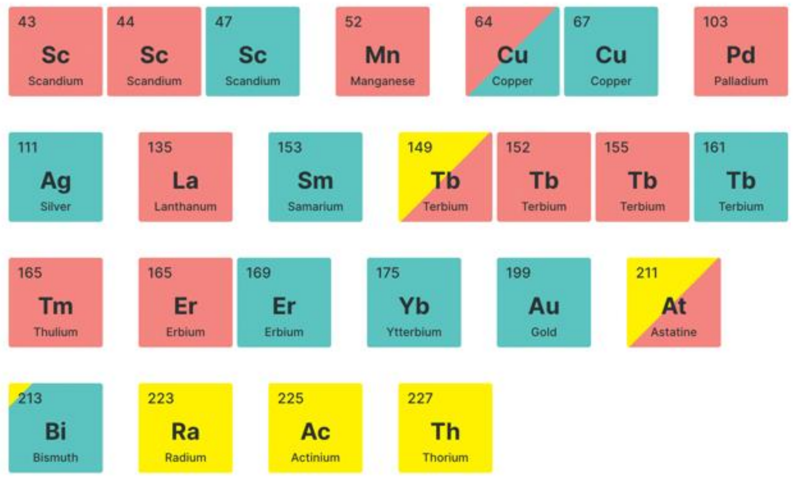
PRISMAP – The European medical radionuclides programme

Achievements in 2022:

15 projects for biomedical research with novel radionuclides selected across Europe

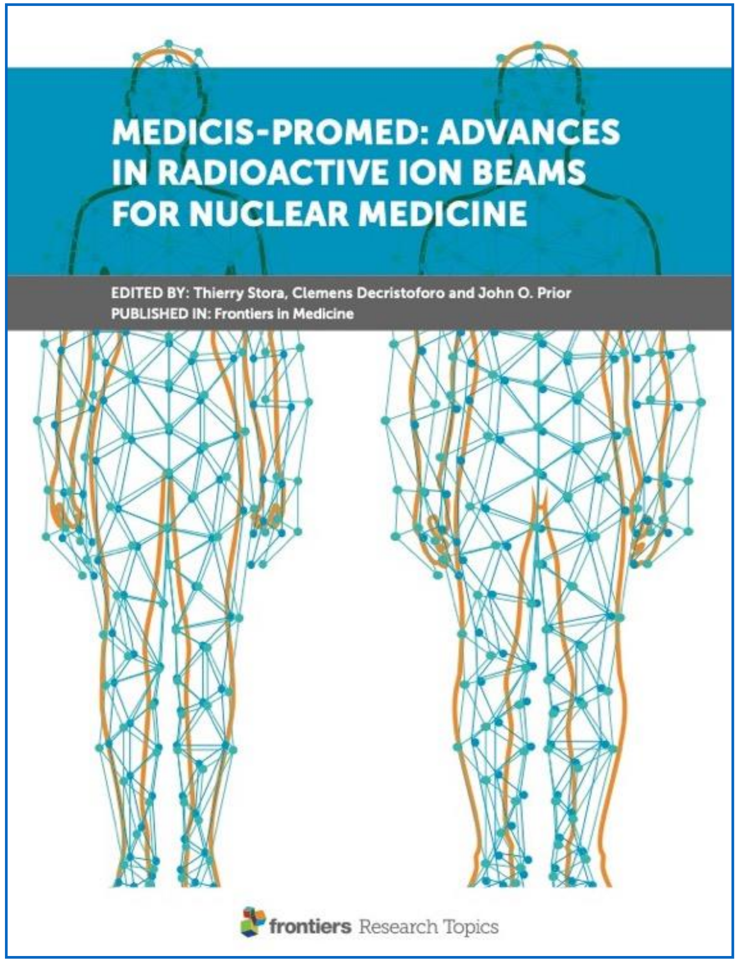
www.prismap.eu/access/user-projects (BE, CZ, DE, ES, FR, IT, PT, UK)





PRISMAP invited to present research needs in the field of novel biomedical radionuclides to the EU Commissioner for research and education Mariya Gabriel

New “theranostics” (therapy+diagnostics) radionuclides



Research Topical issue in Frontiers in Medicine

Cicone F et al: Internal radiation dosimetry of a (152)Tb-labeled antibody in tumor-bearing mice. EJNMMI Res. 2019 Jun 11;9(1):53. doi:10.1186/s13550-019-0524-7

Talip Z., et al;; Production of mass separated erbium-169 towards the first preclinical in vitro investigations. Frontiers in Medicine (2021), doi: 10.3389/fmed.2021.643175

Project 12 entitled “*Added Value using Terbium-161 over Lutetium-177 in Combination with the metabolically more stable GRPR Ligand AMTG for Targeted Radiotherapy of GRPR-expressing Malignancies? – A Preclinical Evaluation*” started on 15 November 2022 with the first delivery of Tb-161 by PSI, followed by two additional deliveries in December 2022 by PSI and SCK CEN (https://www.prismap.eu/news/newsletter-feed/)

https://medicis.cern/approved-projects (32 projects), 23 scientific articles published

Gamma-MRI project

Development of a new medical diagnostic modality

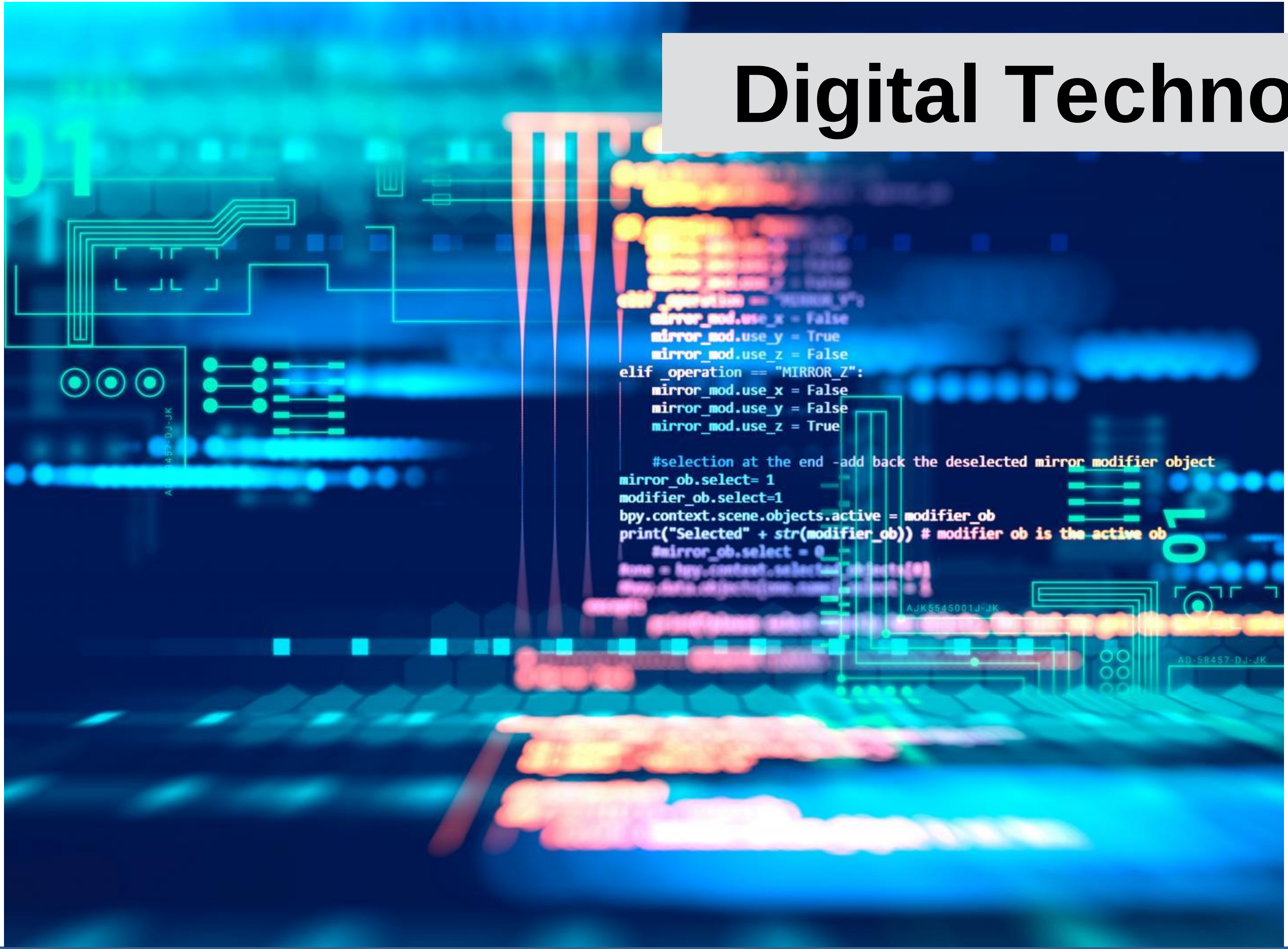
Combine high spatial resolution (MRI) and high sensitivity (radiotracer)

Proof-of-principle by U Virginia: Y. Zheng, et al., Nature 537, 652 (2016)

- Polarised gamma-emitting tracer => anisotropic decay

	Detection efficiency	Spatial resolution
PET and SPECT	high	Low (e.g. >5mm for 82Rb)
MRI	low	High

Digital Technologies



Geant4 – a simulation toolkit

Open source

CERN strongly contributes to its core development

Other Geant4 collaboration members developed specific capabilities and applied them in G4 medical applications

Medical Applications

G4DNA
    Geant4-DNA project

G4MED (in Japanese)
    Geant4 Medical Physics in Japan

G4NAMU
    Geant4 North American Medical User Organization

GAMOS
    Geant4-based Architecture for Medicine-Oriented Simulations

GATE
    Geant4 Application for Tomographic Emission

GHOST
    Geant4 Human Oncology Simulation Tool

TOPAS
    Geant4 Monte Carlo Platform for Medical Applications

Human phantoms

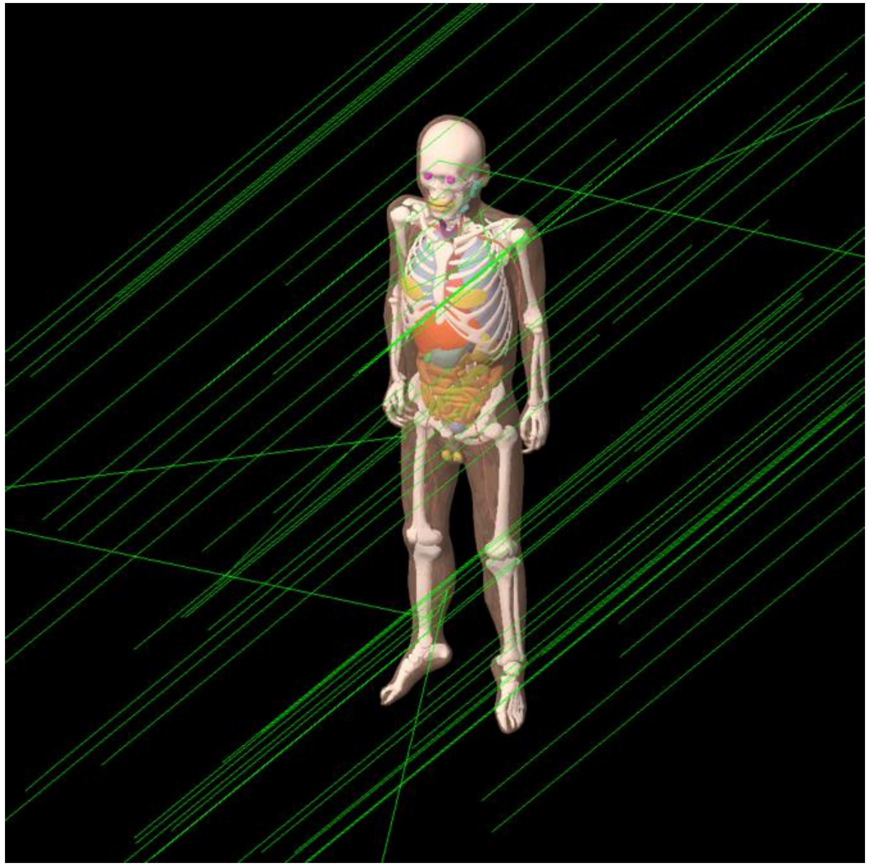
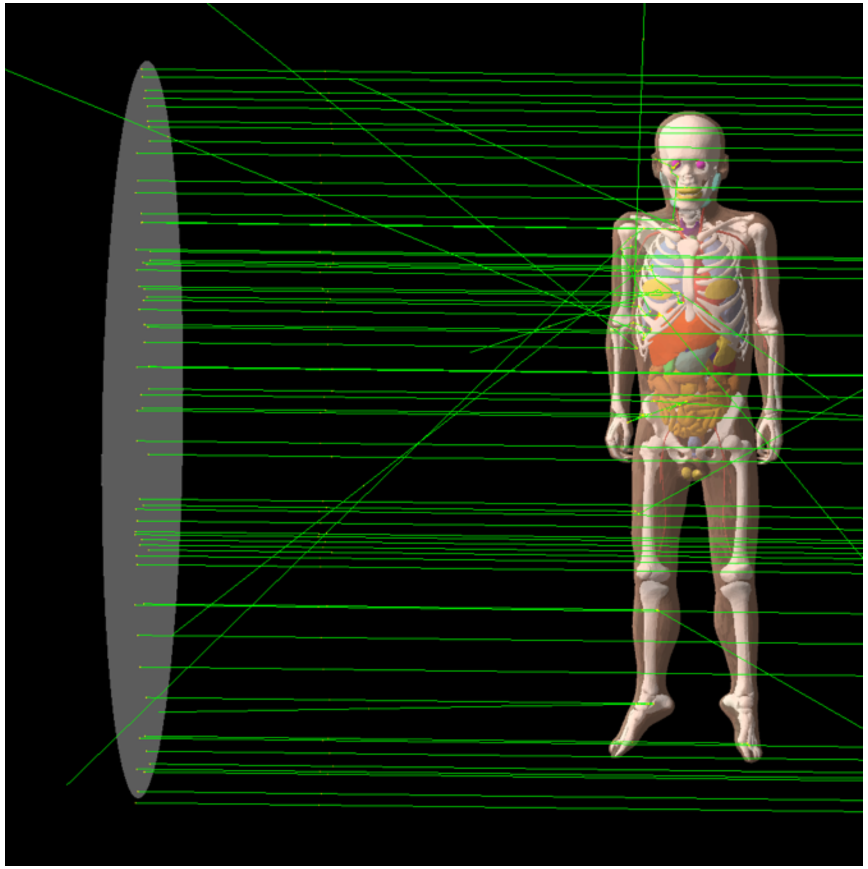
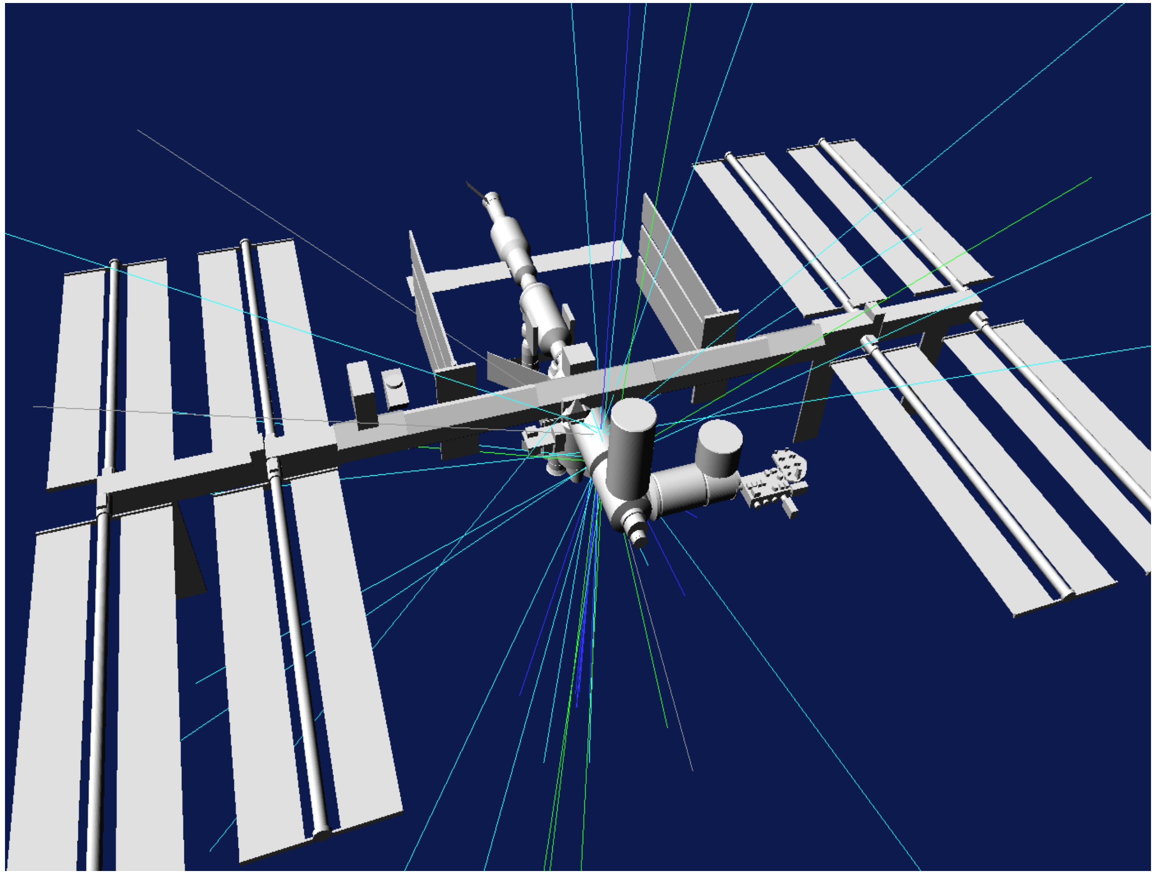



Image of Polygon-Surface Reference Korean Male Phantom (PSRK-Man), implemented in Geant4. Courtesy of C.-H. Kim & C. Choi, Hanyang Univ.

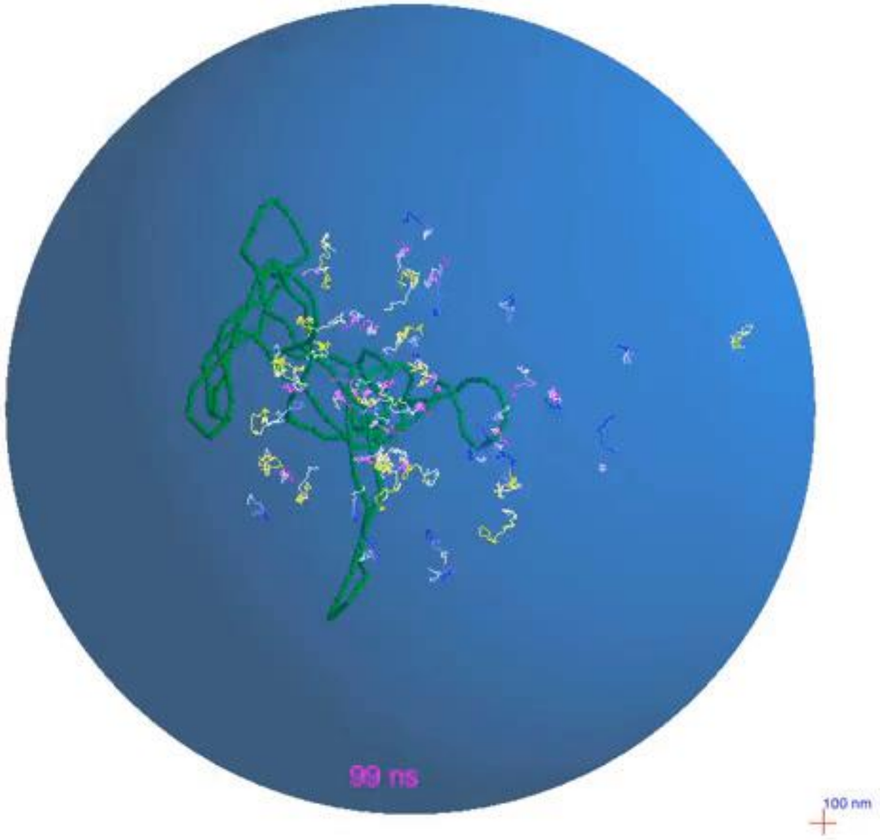
Radiation Environment – model of space station



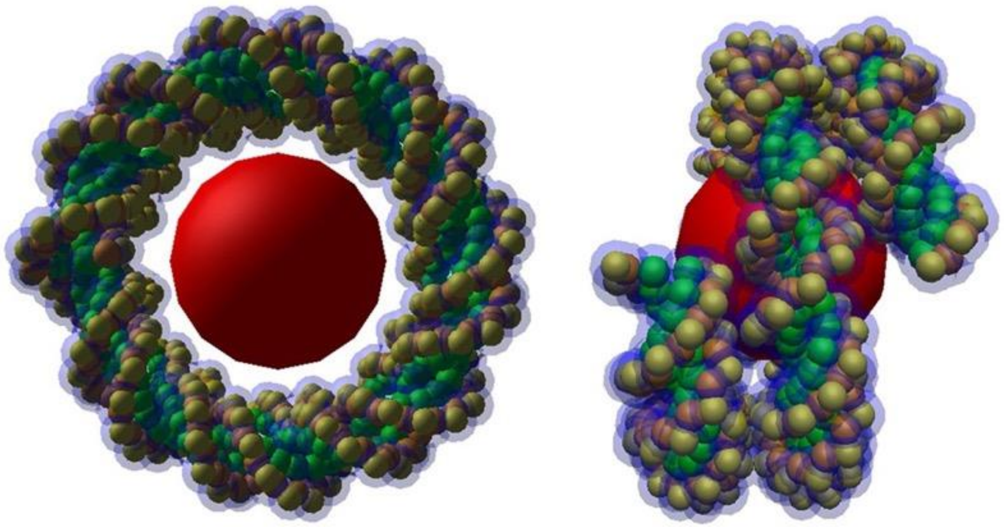
Courtesy T. Ersmark, KTH Stockholm

Geant4-DNA applications

Simulation using Geant4-DNA of irradiation of a pBR322 plasmid, including radiolysis



- movie courtesy of V. Stepan (NPI-ASCR/CENBG/CNRS/IN2P3/ESA



Model of nucleosome created using DnaFabric*, imported into Geant4 to model irradiation, repair mechanisms.

* S. Meylan et al, Comp. Phys. Comm. 204 (2016) p159

Tools for specific applications

based on Geant4

Tools provide specific capabilities for creating setups, measuring

create setup, steer simulation via ‘text commands’

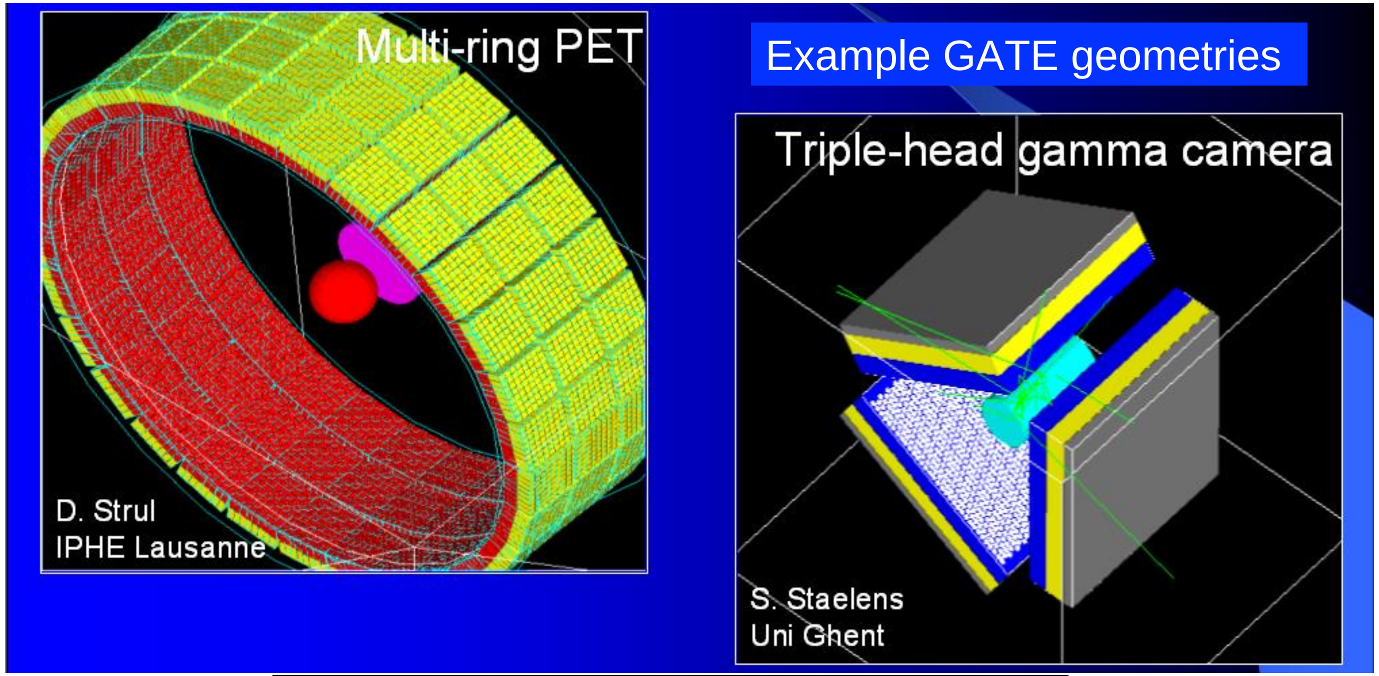
output adapted for application-area

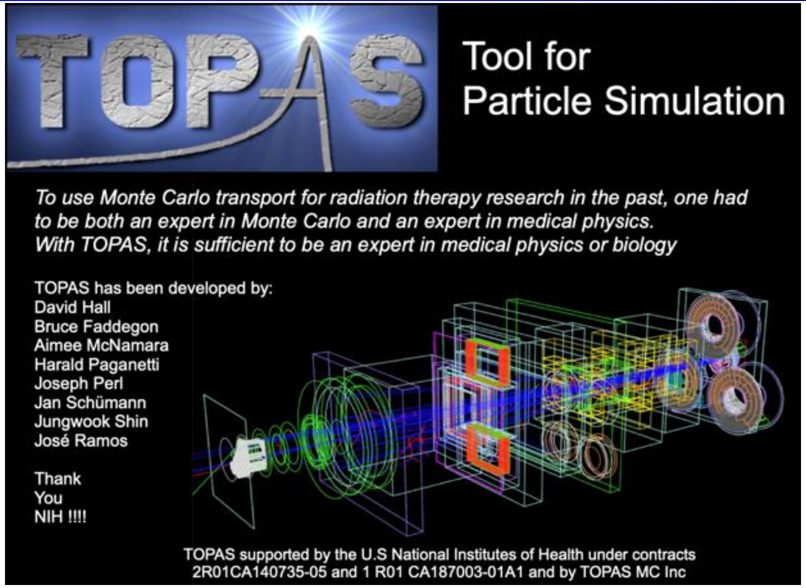
GATE (FR, DE, GR, PL, AT) - PET/SPECT,

TOPAS (US) - protontherapy

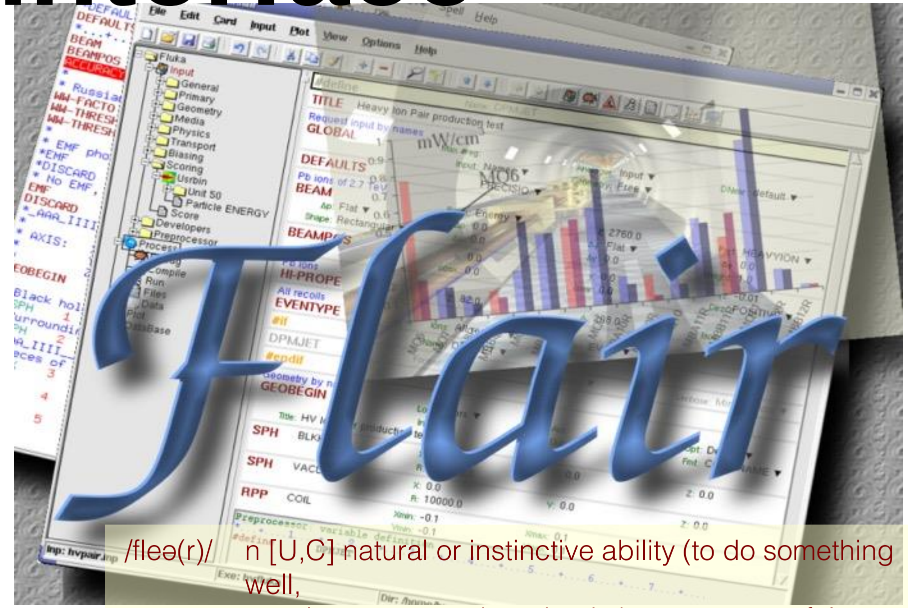
GAMOS (ES) - for nuclear medicine applications

Developed by external parties - using capabilities of G4 toolkit





Flair – fluka advanced interface



/fleə(r)/ n [U,C] natural or instinctive ability (to do something well,
to select or recognize what is best, more useful, etc.
[*Oxford Advanced Dictionary of Current English*]

is more than a graphical Interface

→ is a complete integrated working environment for FLUKA

Greatly enhanced productivity
→ users focus on their problem rather than on technicalities

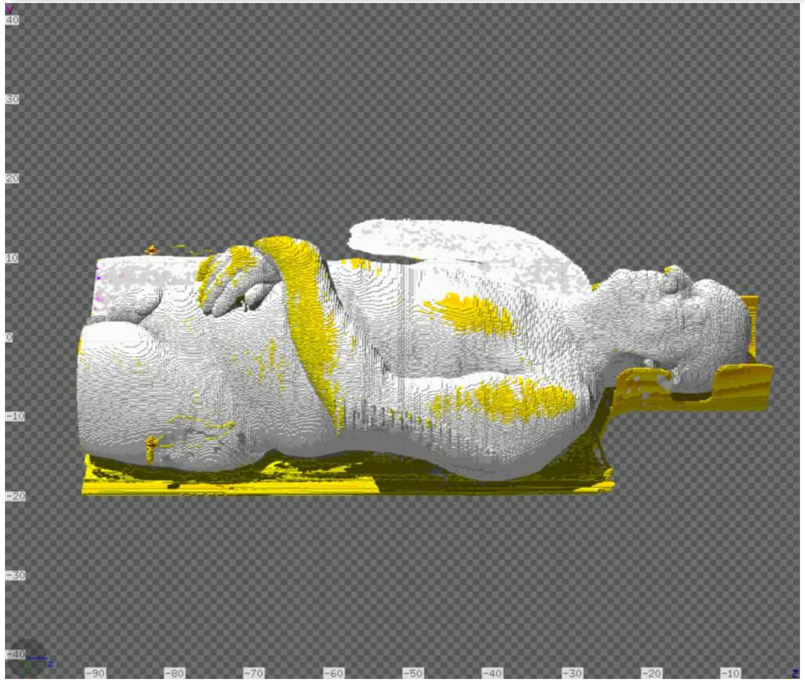
Improvements for medical simulations

Process **DICOM standard files** for radiotherapy purposes

Provides easy-to use tool for **treatment plan re-simulation** and quantitative comparison

- Enables precise description of patient model and beam delivery system

In this presentation: a selection of results obtained by the CERN group



3D spatial dose distribution simulated with FLUKA

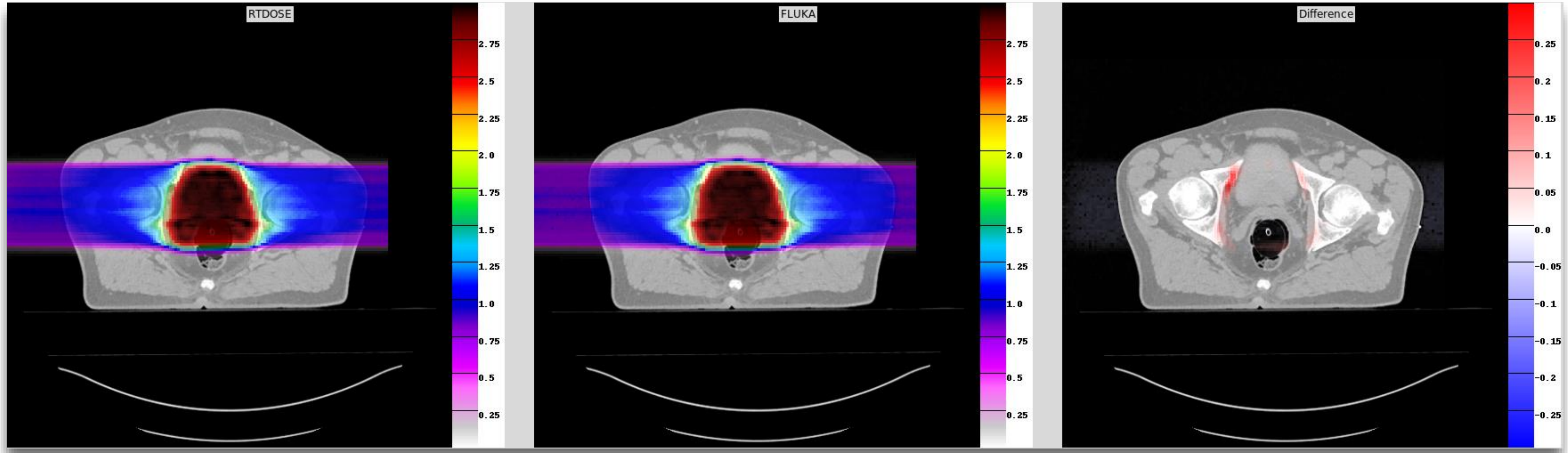
Importing the RT DOSE with the activity mapping of ^{68}Ga

Simulation of the ^{68}Ga decays

Very fast setup time
less than a few minutes with a few clicks from the user

Run FLUKA simulations with no programming skills or file editing requirements!

Sensitivity studies of Monte Carlo TP recalculations

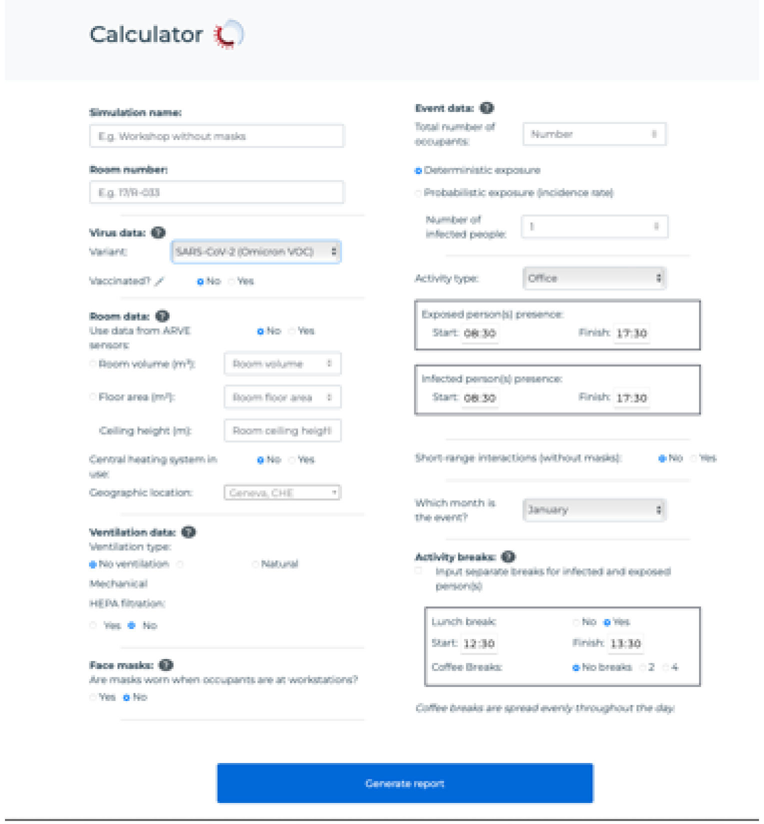


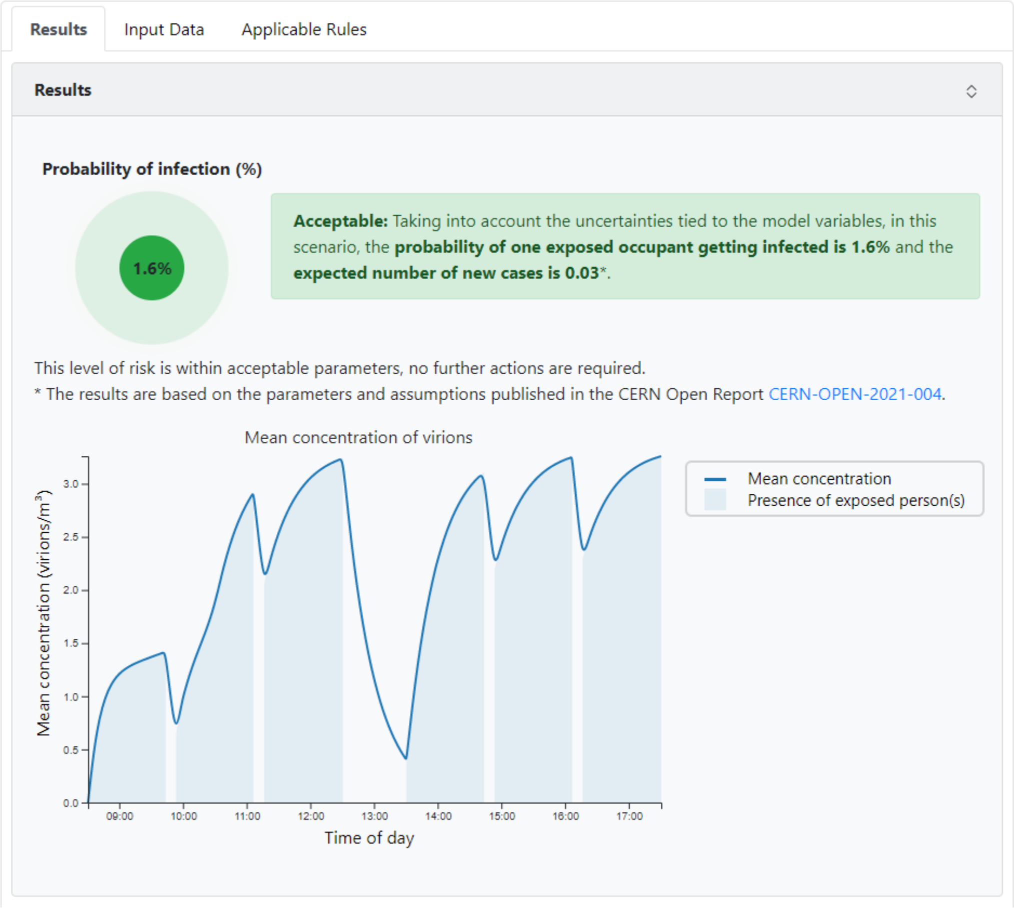
Proton prostate patient case
(MedAustron)
W.Kozlowska PhD

CAiMIRA

CERN Airborne Model for Indoor Risk Assessment

Developed by CERN personnel to assess the COVID airborne risk in indoor spaces with a risk-based approach.





Extension to the medical field of AI tools for

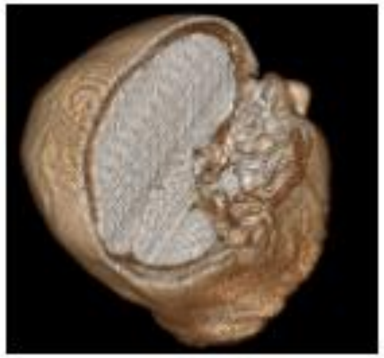
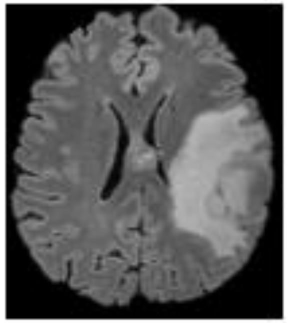
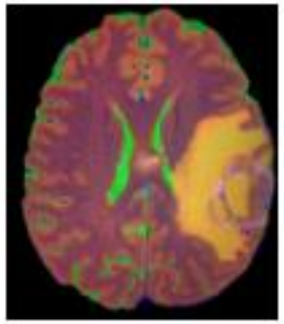
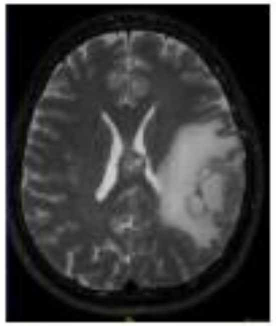
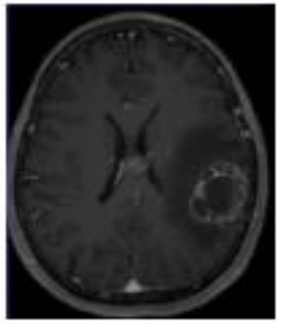
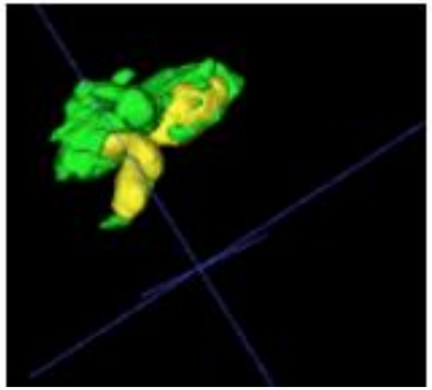
- functional and dependency analysis of complex critical infrastructure
- digital imaging for radiography autonomous defects detection

Background work:

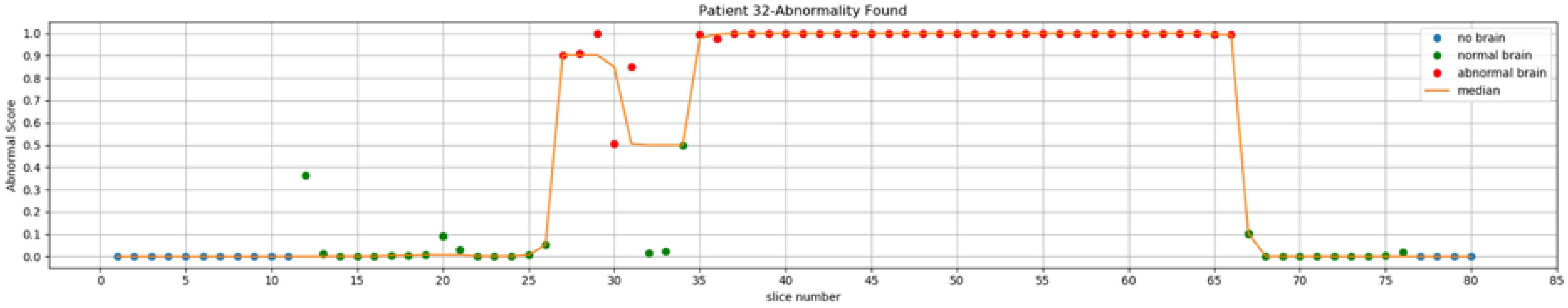
- the CASO platform: AI-assisted diagnosis and predictive maintenance for critical infrastructures operation
- the CAFEIN platform: AI-assisted X-ray image analysis for quality control of LHC welds

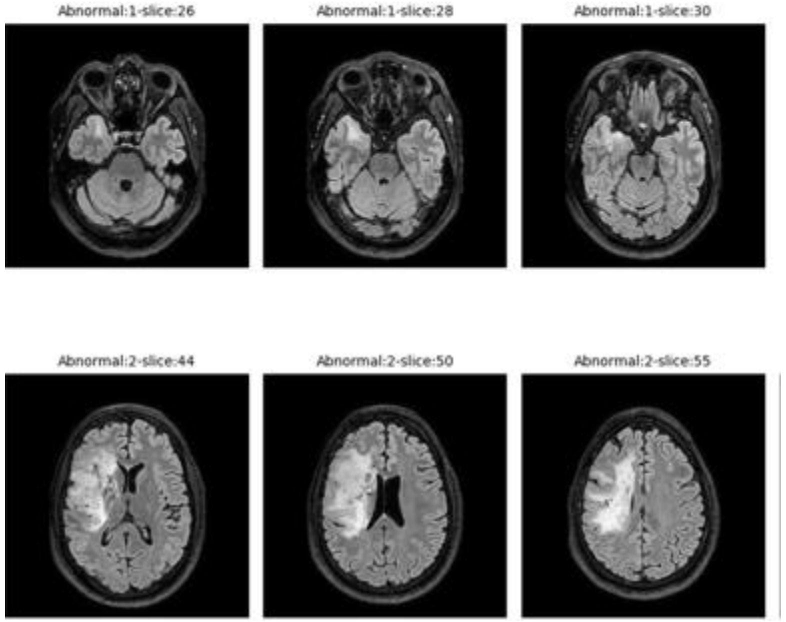
- **Field of application:**
  - Semi-automated analysis and modelling of medical data and images
  - Diagnosis and treatments based on multiple features and data beyond human perception
  - Federated learning and distributed computing to ensure privacy for a wide and safe international collaboration as well as access to diagnostic models in remote areas

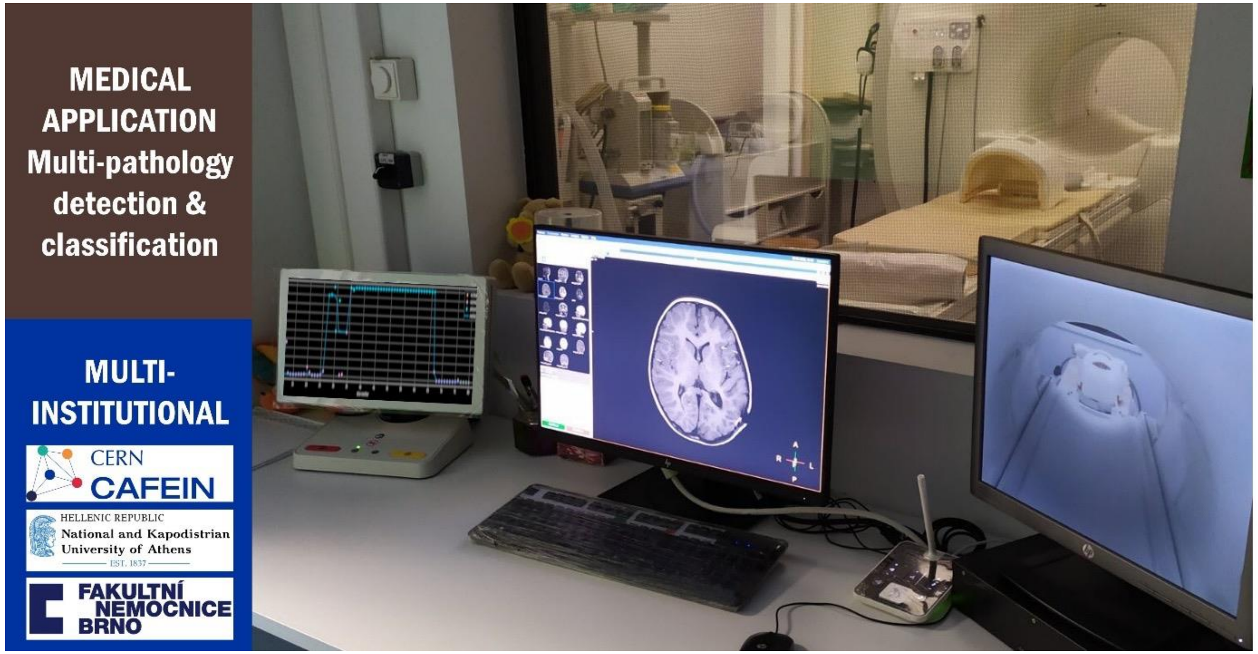
- **Medical application:**
  - Brain pathologies detection, analysis and segmentation based on CNN applied to MRI images

Final Output- Screening Tool







MARCHESE: Remote Monitoring of Health Parameters

Background: response time of a rescue team of CERN Fire Brigade could take up to 22 minutes in the LHC tunnel.

The research is oriented towards the development of robotic solutions: workers' detection and health contactless monitoring during emergencies situations is important to support in search and rescue scenarios.

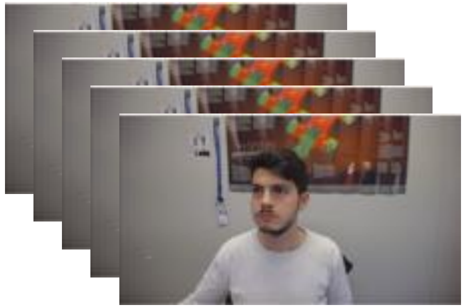
PHOTOPLETHYSMOGRAPHY

- Optical technique used to detect volumetric changes in the blood in the peripheral circulation.
- Blood volume changes in microvascular tissue (i.e. at cheeks and forehead level)

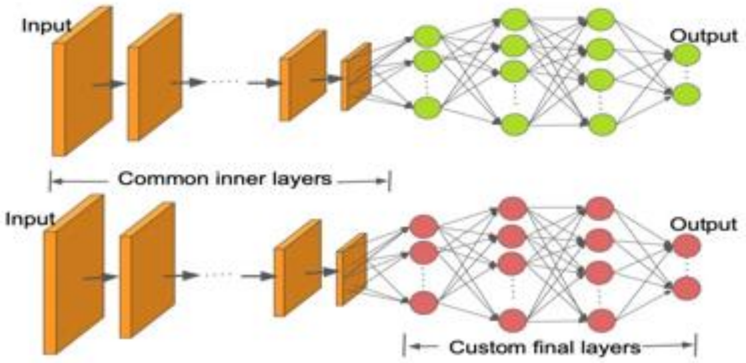
Remote PPG: Video pre-processing

30 FPS

30 images/second
Logitech 1080p FULL HD
GPU NVIDIA GTX 1080p

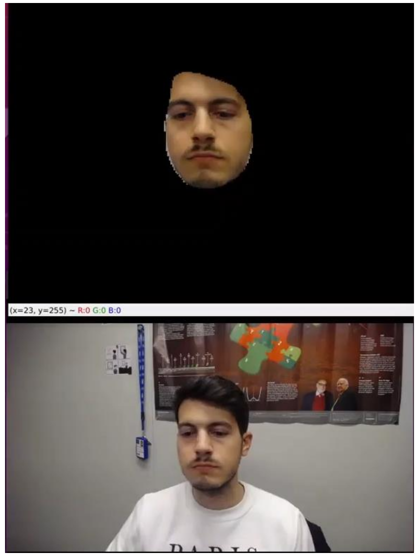


NEURAL NETWORK



SEPARATION of SKIN PIXELS from NO-SKIN PIXELS

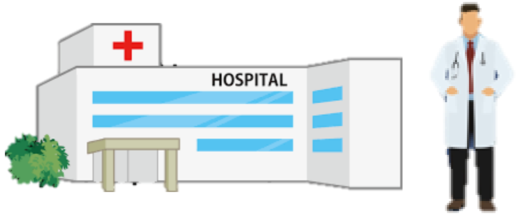
REAL TIME



Medical Applications

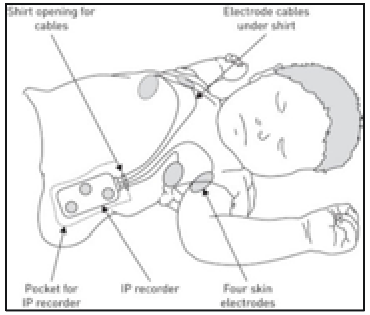
In contact with Medical Staff in the Hospital

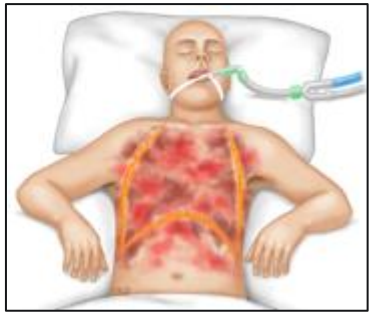
➡ **Understand which are the needs of the real scenario**



NEWBORN and PATIENTS WITH BURNS

- Fragile skin
- No abrasions and damage of epidermis
- Continuous and constant monitoring





ASSISTIVE ROBOTIC REHABILITATION

- adjust the exercise level (increase or decrease) according to the patient's physiological response
- Exploit residual patient capabilities (assistance-as-needed)

SMART HOSPITAL ROOM

- Hospital room for remote monitoring
  - Avoid medical staff infections
- Hospitalization more comfortable for patients
- Group or single patient monitoring

Photo: CERN

Photo: CNAO treatment room

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