From (Particle) Physics to Healthcare

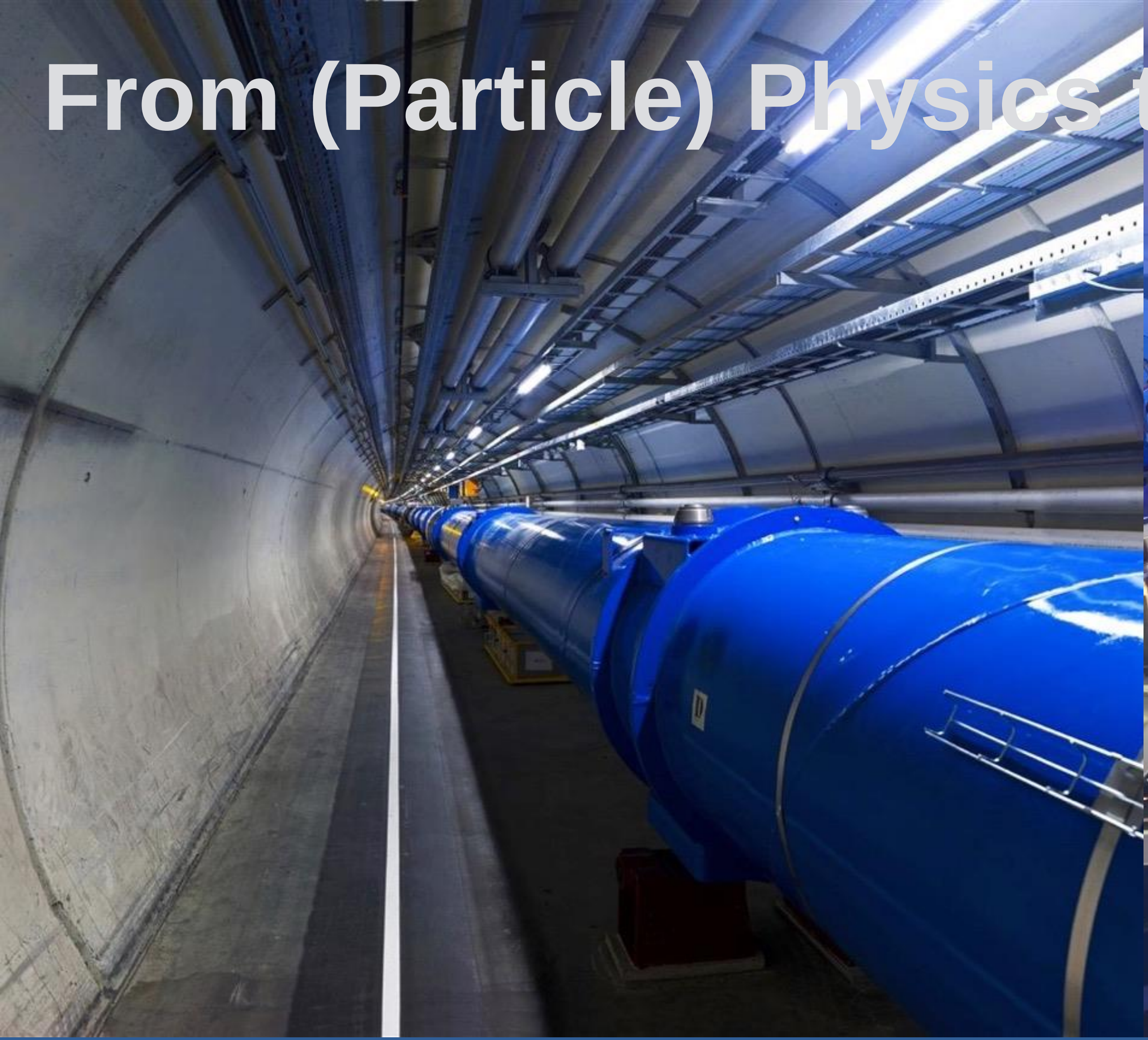


Photo: CNAO treatment room

Manuela Cirilli
Medical Applications Adviser
CERN Knowledge Transfer group

CERN Knowledge Transfer
Accelerating Innovation

Disclaimer(s) & Acknowledgments

Of course, I had to select the material to be included.
And of course, Physics ≠ HEP and HEP is not just CERN
(but a lot of HEP in this talk, and many CERN examples).

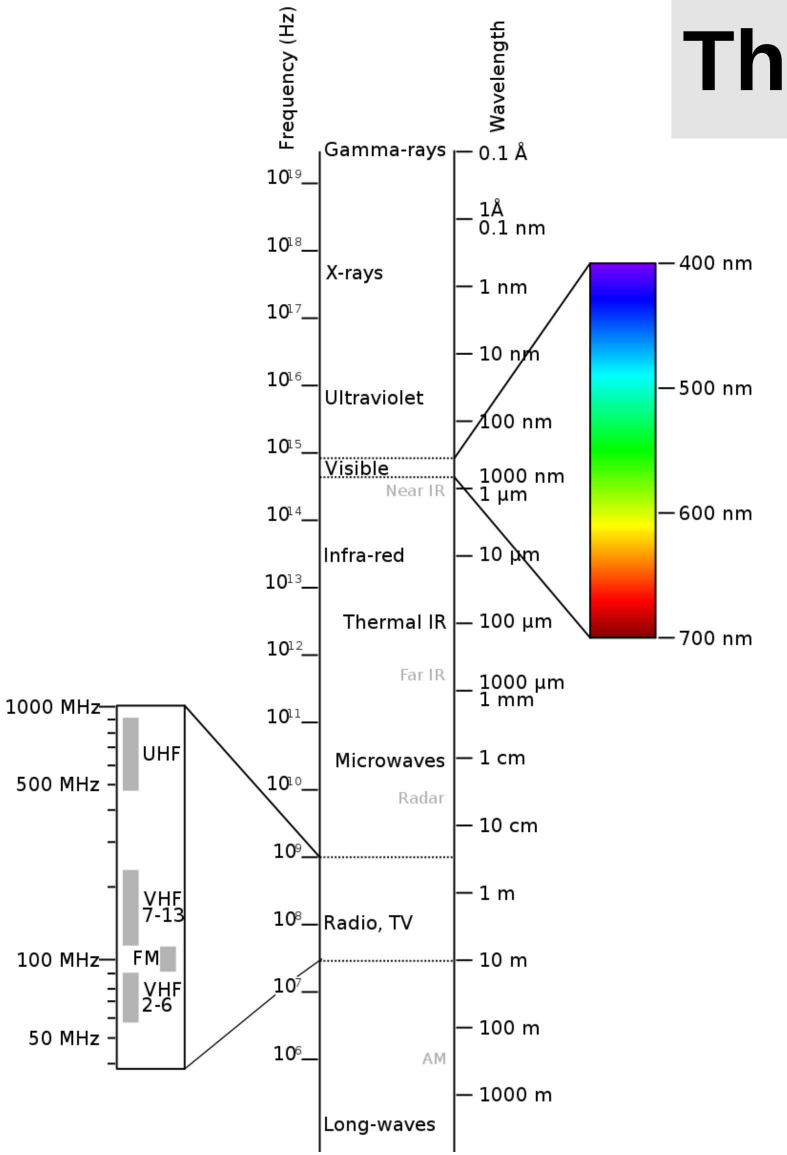
The CERN medical applications-related projects presented in this talk are realized by the CERN scientists and engineers: most names are acknowledged on the respective slides, but there are many more.

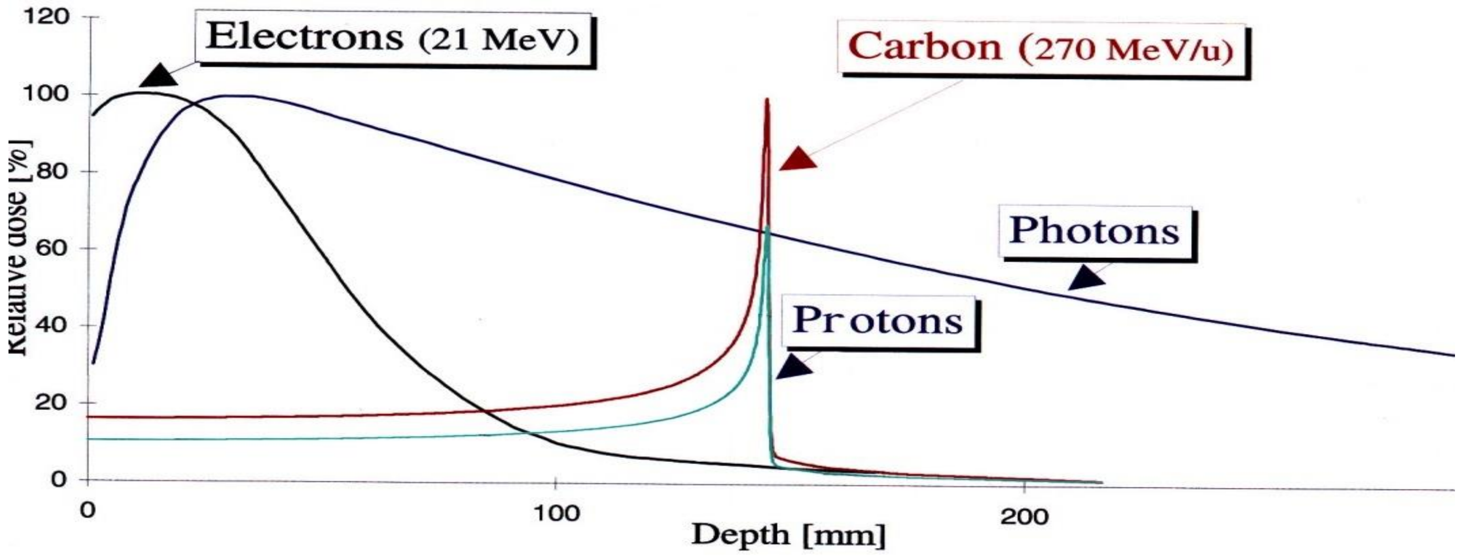
The KT group and myself are privileged to have the opportunity to support these projects in a tailored way, and to help bridge the gap between CERN technologies and society.

Many thanks to all the colleagues from CERN, CNAO, CHUV, GSI, MedAustron, INFN, TERA who have shared their material and wisdom with me; special thanks to Ugo Amaldi and Manjit Dosanjh.

I am neither a doctor, nor a medical physicist, nor a technical expert in most of the technologies I present, so let's see how many of your questions I'm able to answer! ☺

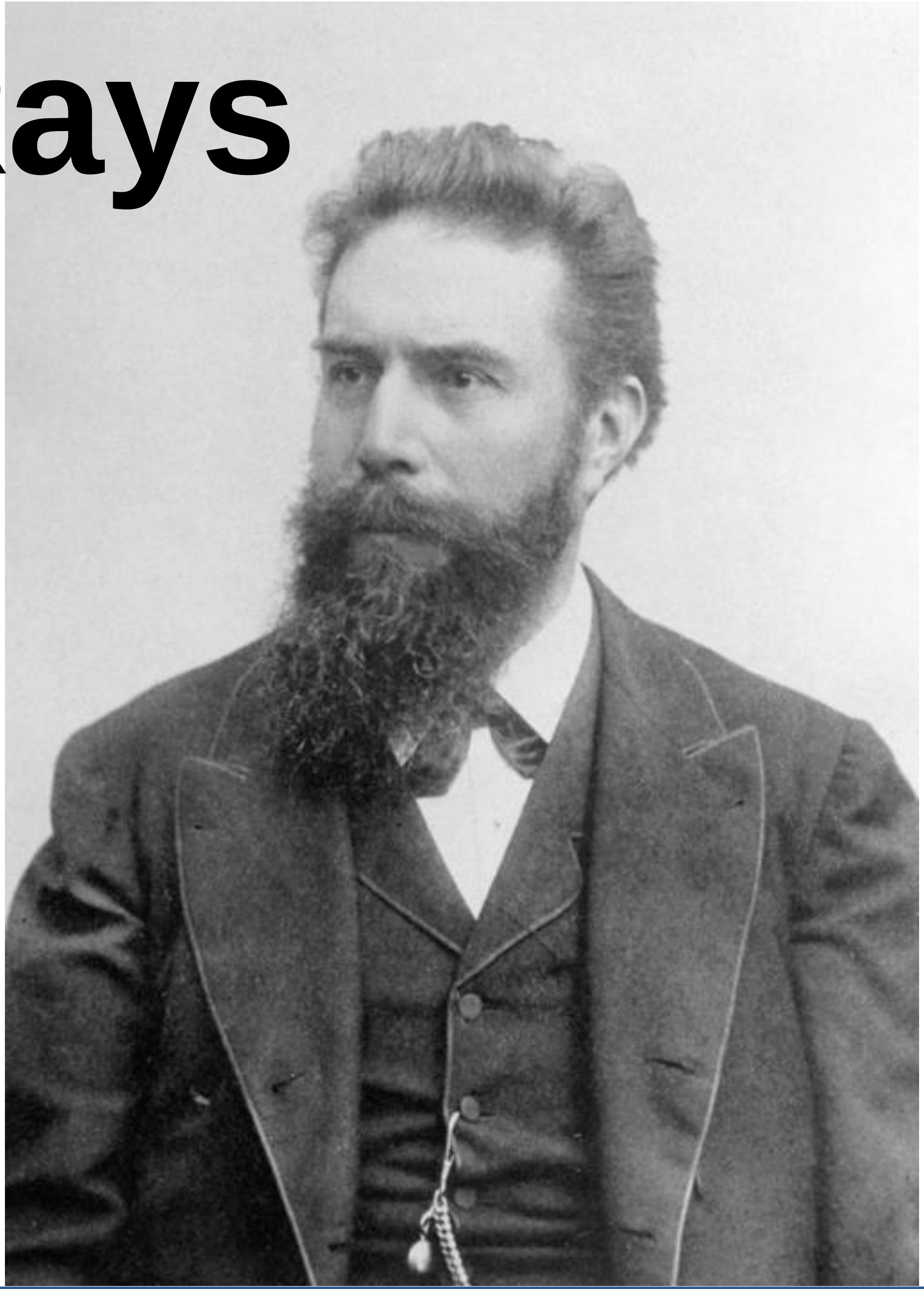
The physics itself

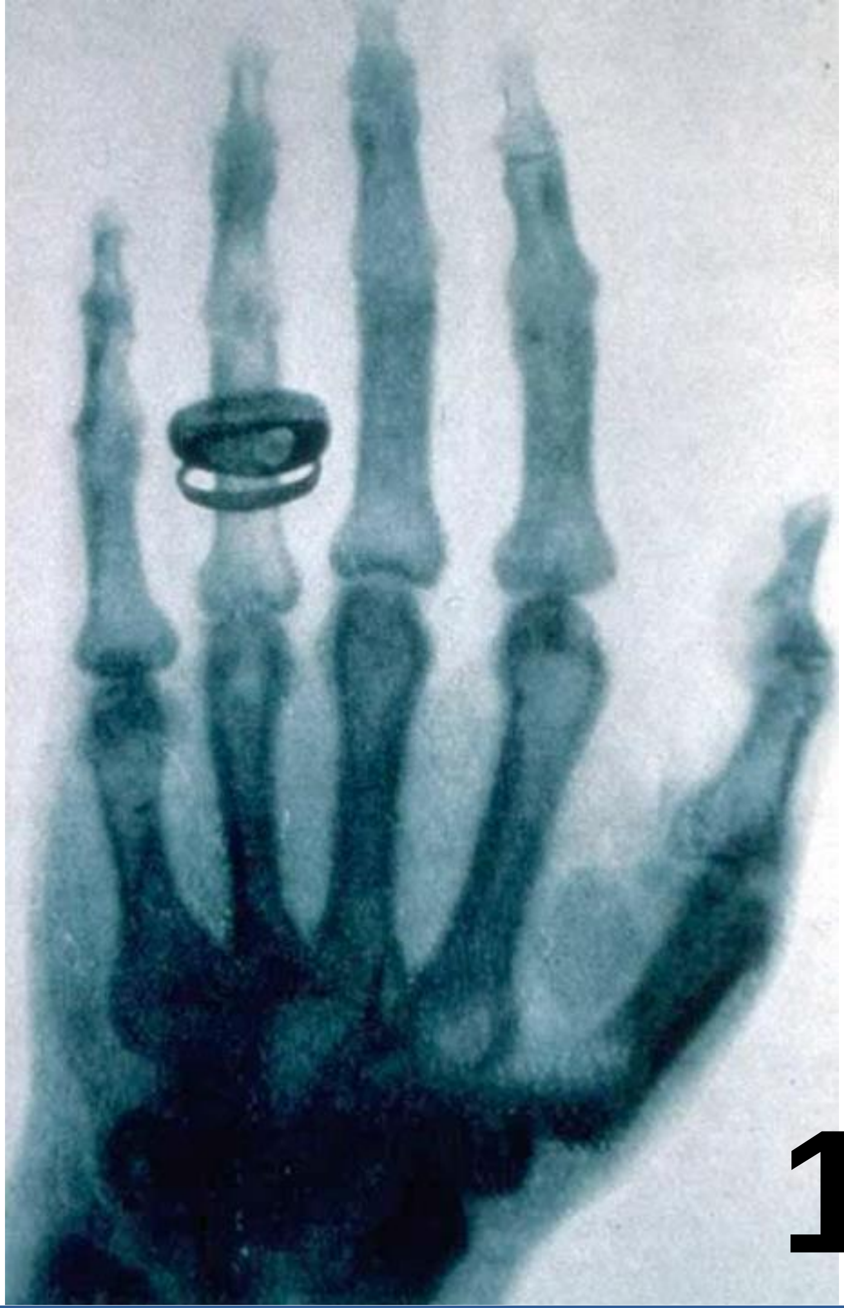




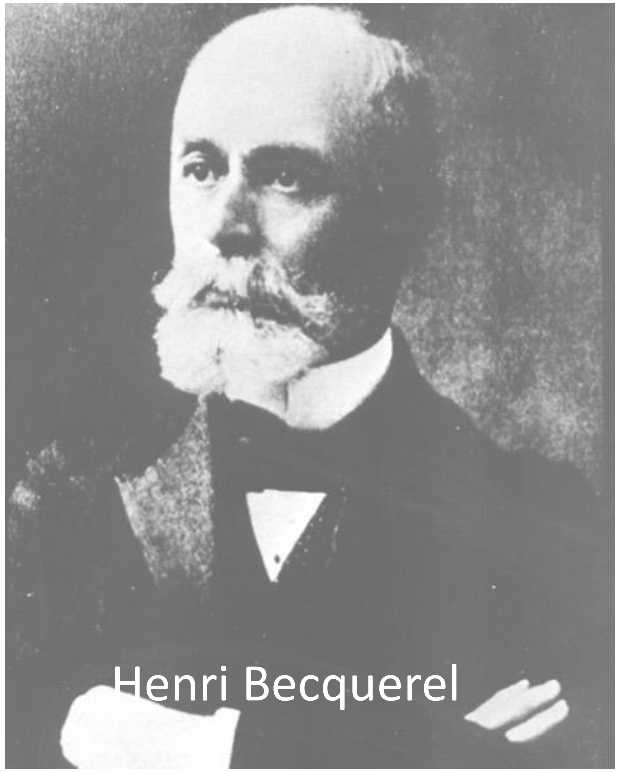
By Original: Penubag Vector: Victor Blacus - Own work based on: Electromagnetic-Spectrum.png, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=22428451

X-Rays





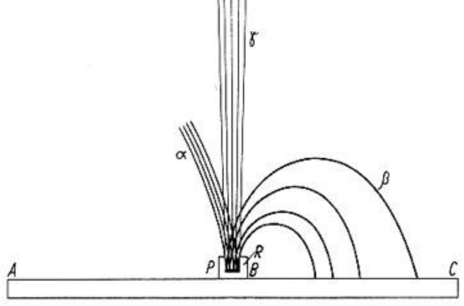
1895



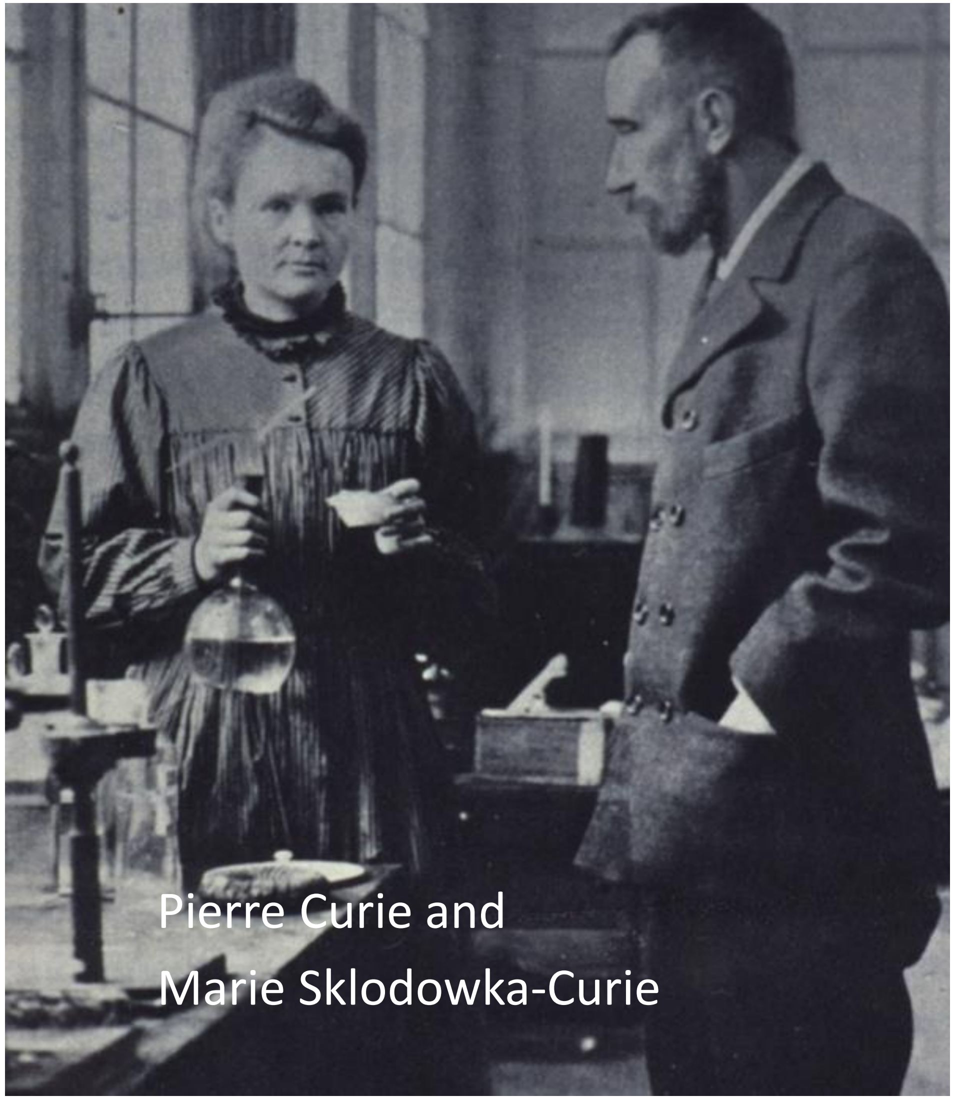
Henri Becquerel

1896: accidental discovery of natural radioactivity

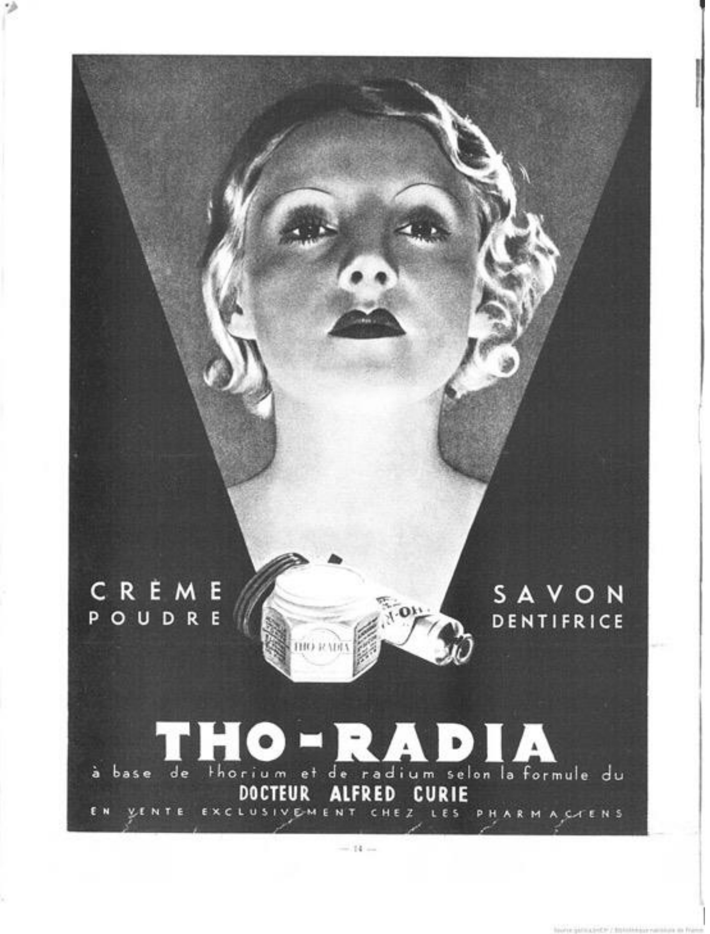
Mme. Curie thesis – 1904
α, β, γ in magnetic field



1898: by studying the strange uranium rays, they soon discovered polonium, thorium, radium



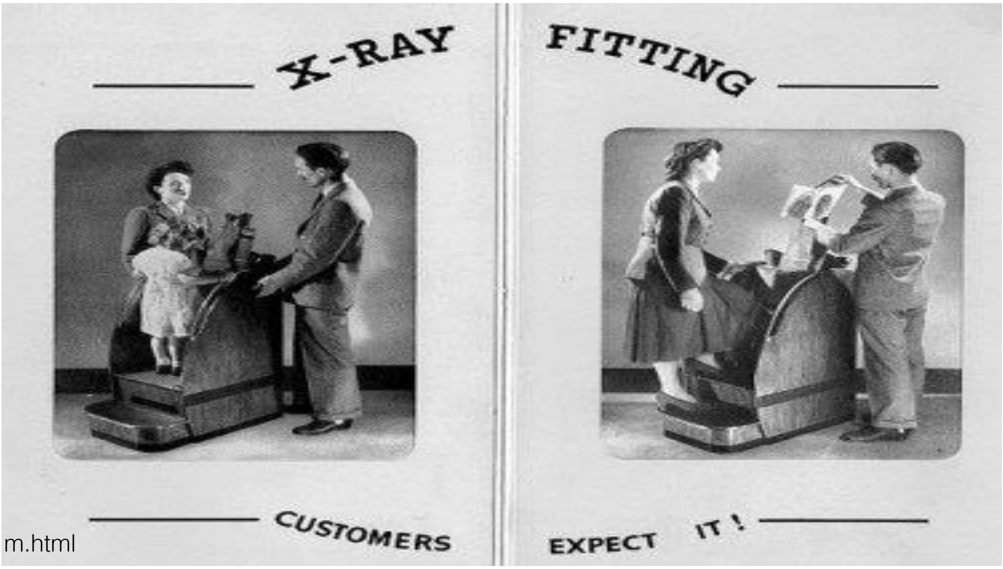
Pierre Curie and
Marie Sklodowka-Curie



Par Cinémagazine, 14 février 1935 — https://gallica.bnf.fr/ark:/12148/bpt6k2000628h, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=97956453

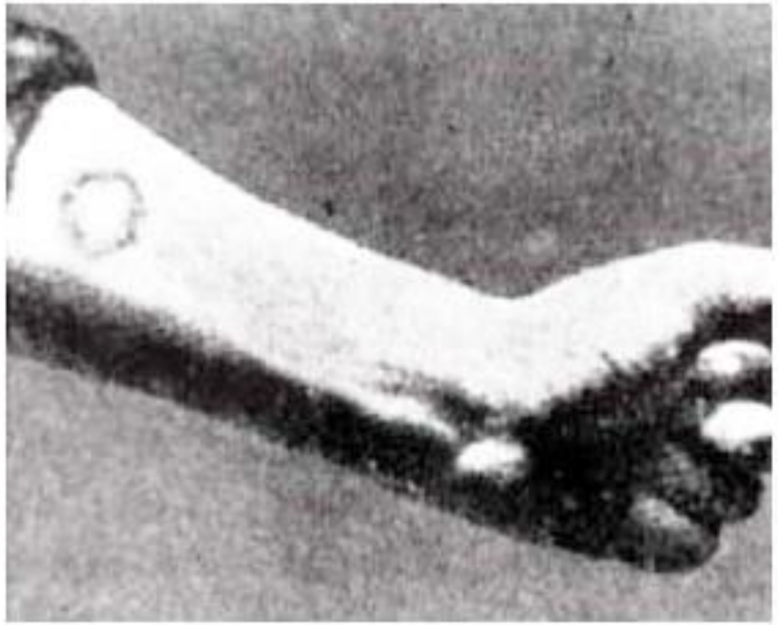
Par Radior cosmetics — sitead New York Tribune Magazine, page 12, Domaine public, https://commons.wikimedia.org/w/index.php?curid=35047170

Par Sam LaRussa from United States of America — Radithor, CC BY-SA 2.0, https://commons.wikimedia.org/w/index.php?curid=57841049



https://www.smh.com.au/national/nsw/from-the-archives-1956-ban-urged-of-x-ray-machines-at-shoe-shops-20210318-p57c1m.html

Friedrich Giesel
1852-1927



Burning of Pierre Curie's arm

Pierre Curie
1859-1906

Photo of Pierre Curie's arm, burned by radium salt applied for 10 hours. In 1900, the German dentist Walkhoff noted that radium rays act energetically on the skin in a manner analogous to that of X-rays. This observation was confirmed a few weeks later by the German chemist F. Giesel, with whom Pierre and Marie maintained regular correspondence.

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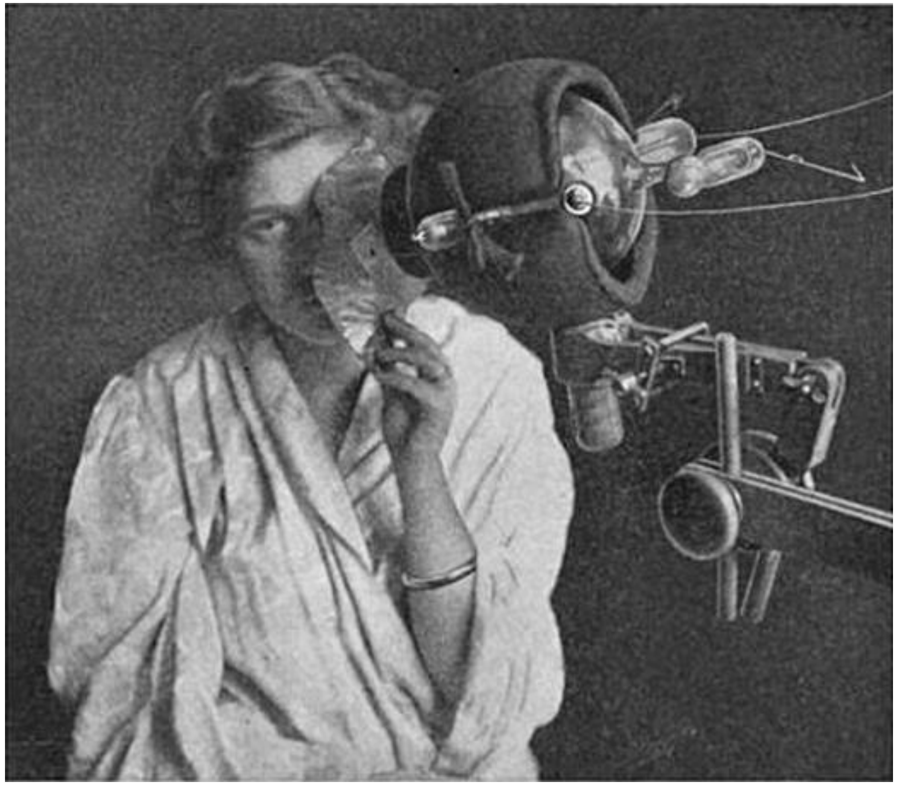


X-ray apparatus used for treatment of epithelioma of the face, 1915.

Small tubes containing radium salts are strapped to a woman's face to treat what was either lupus or rodent ulcer, 1905.

The Nobel Prize in Physics 1944

Photo from the Nobel Foundation archive.

Isidor Isaac Rabi

Prize share: 1/1

The Nobel Prize in Physics 1944 was awarded to Isidor Isaac Rabi "for his resonance method for recording the magnetic properties of atomic nuclei."

The Nobel Prize in Physics 1952

Photo from the Nobel Foundation archive.

Felix Bloch

Prize share: 1/2

Photo from the Nobel Foundation archive.

Edward Mills Purcell

Prize share: 1/2

The Nobel Prize in Physics 1952 was awarded jointly to Felix Bloch and Edward Mills Purcell "for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith."

The Nobel Prize in Physiology or Medicine 2003

Photo from the Nobel Foundation archive.

Paul C. Lauterbur

Prize share: 1/2

Photo from the Nobel Foundation archive.

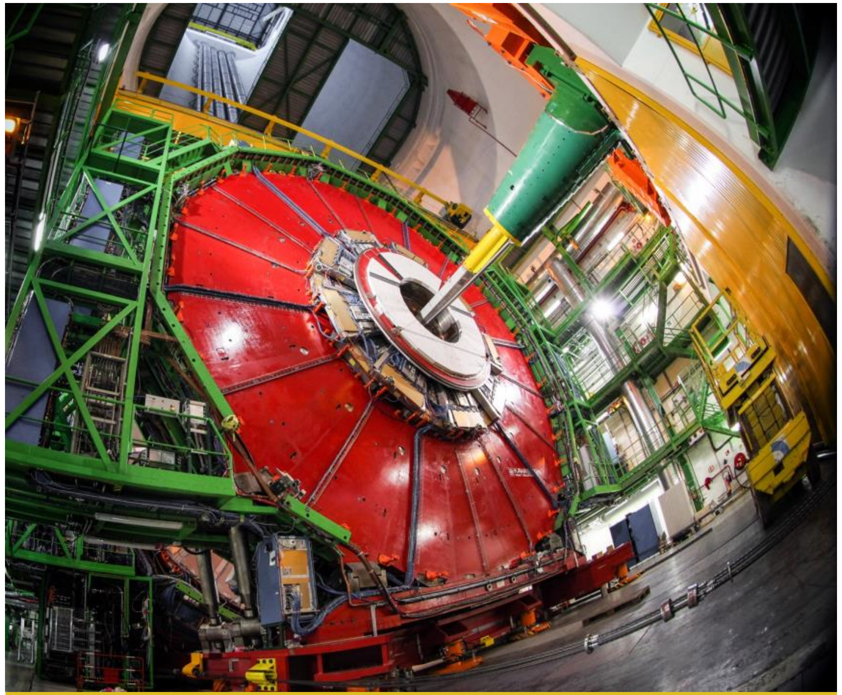
Sir Peter Mansfield

Prize share: 1/2

The Nobel Prize in Physiology or Medicine 2003 was awarded jointly to Paul C. Lauterbur and Sir Peter Mansfield "for their discoveries concerning magnetic resonance imaging."

The technologies

ACCELERATORS



DETECTORS

COMPUTING


sound reproduction
data management
testing satellite components
astronauts' radiation exposure
understanding turbulence
food sterilization
medical implants
homeland security
finding oil, gas, water
geological dating
scientific linux
curing of epoxies and plastics
medical imaging
x-ray diffractometry
spacecraft shielding
radiology
medical equipment sterilization
medical radioisotopes
non-destructive testing
nuclear waste transmutation
ion implantation
rad-hard electronics
shrink wrap
radiotherapy
PET
terrestrial reproduction of space radiation
simulations
industry 4.0
digital data preservation
optimised irrigation systems
drug development
safety
www
open hardware
powering complex biological simulations
industrial control systems
power transmission
analysis of satellite data
treatment planning systems
volcano tomography
space applications
sealing food packages
autonomous vehicles
isotope production
smoke detectors
hadron therapy
cultural heritage
MRI
cleaner air and water
ink curing
cargo screening
computer chips manufacturing
studying the retina
medical dosimetry
material science


Accelerators for America's Future
U.S. DEPARTMENT OF ENERGY
Particle physics – it matters
A forward look at UK research into the building blocks of the Universe and its impact on society
In partnership with
Science & Technology Facilities Council
Accelerating science and innovation
Societal benefits of European research in particle physics
Tools, Techniques, and Technology Connections of Particle Physics
Task force chairs:
Marcel Demarteau
Argonne National Laboratory
Katie Yurkewicz
Fermi National Accelerator Laboratory
U.S. DEPARTMENT OF ENERGY
Office of Science
Accelerators and Beams
TOOLS OF DISCOVERY AND INNOVATION
4th Edition
Published by the Division of Physics of Beams of the American Physical Society
APPLICATIONS OF PARTICLE ACCELERATORS IN EUROPE
EuCARD²
Accelerators for Society
Particle accelerators are being applied throughout society. Originally developed for fundamental research, today they are used for a range of applications, from healthcare to manufacturing silicon chips to reducing pollution.
TIARA
From Physics to Daily Life
Applications in Informatics, Energy, and Environment
Edited by Beatrice Bressan
WILEY Blackwell

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.

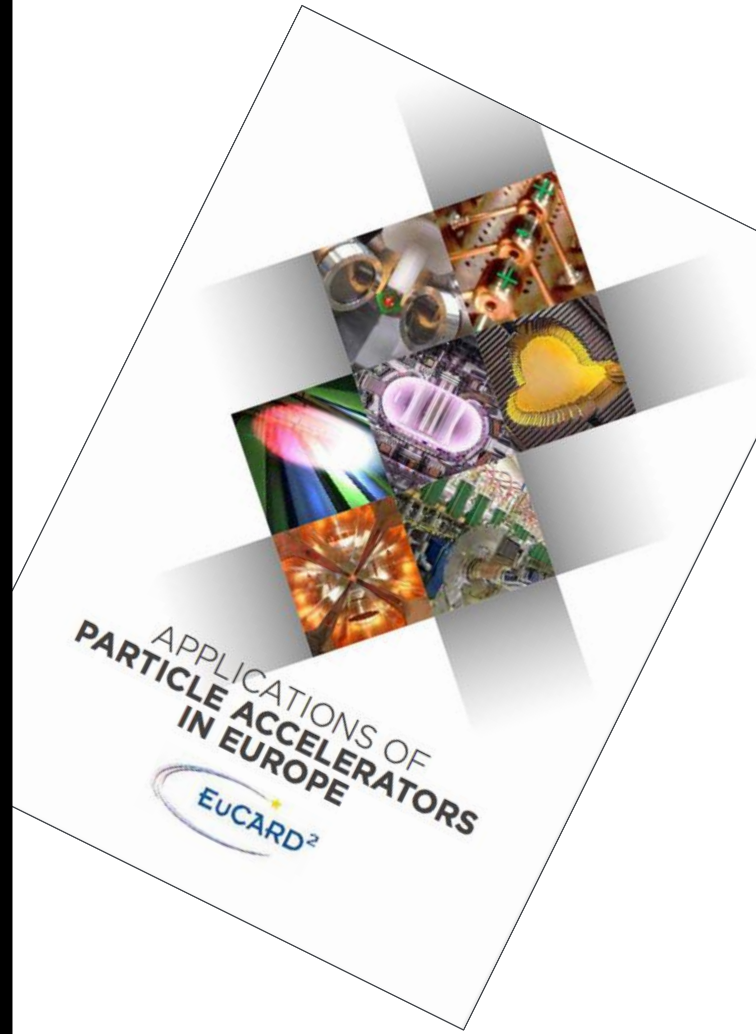
As of 2014 there were **42,200** accelerators worldwide:
27,000 (64%) in industry,
14,000 (33%) for medical purposes
1,200 (3%) for basic research.

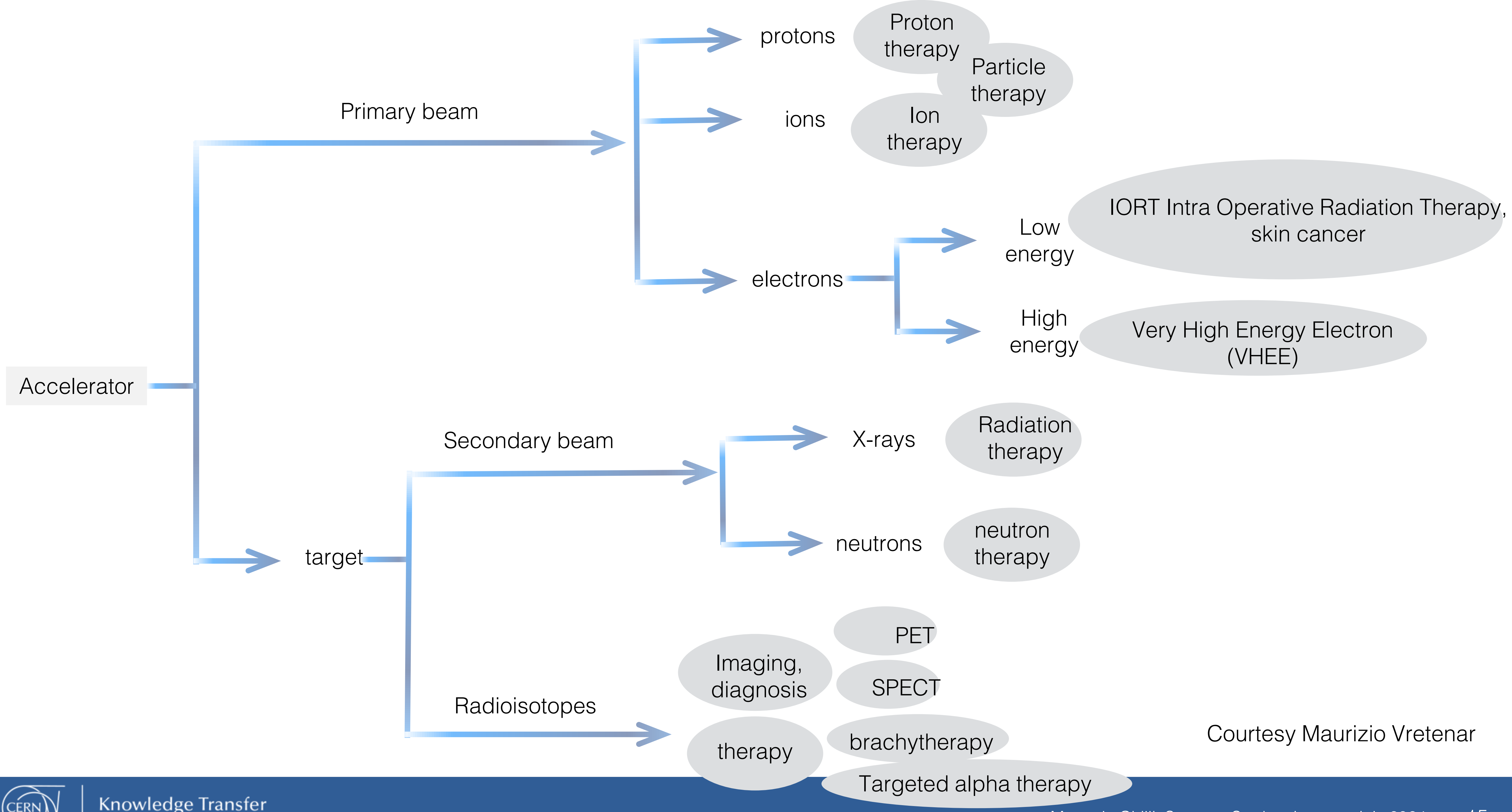
These figures exclude electron microscopes and x–ray tubes, and the security and defense industries.

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

Los Alamos National Laboratory/Flickr, CC BY-NC-ND

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

Radiotherapy

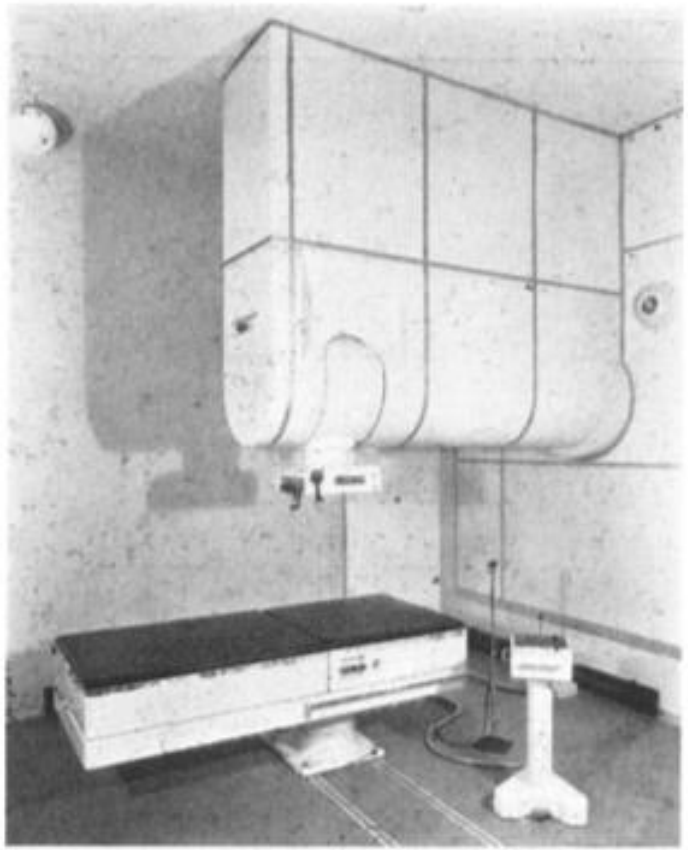
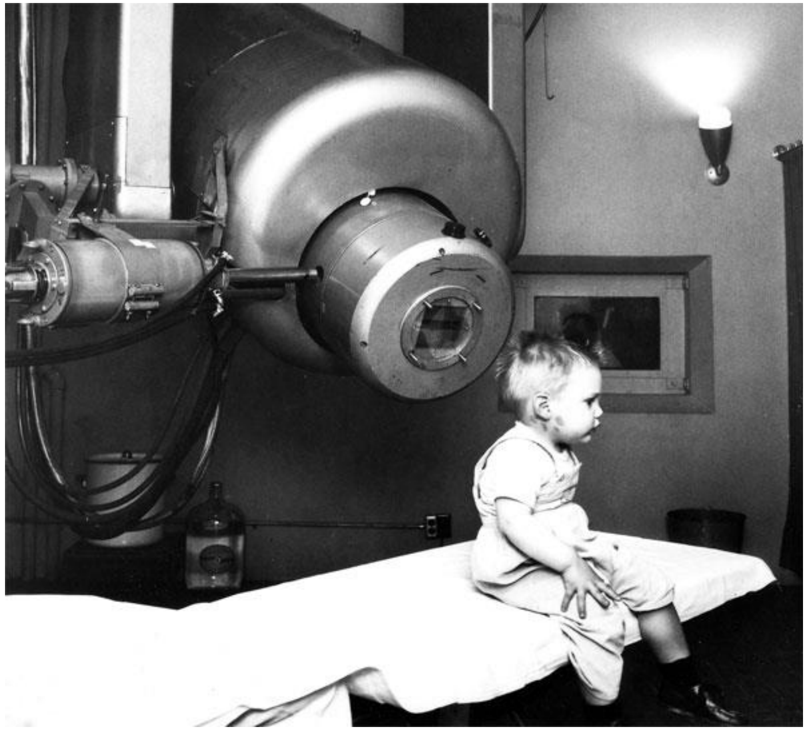


Fig. 1. The 8 MeV linear accelerator (Metropolitan-Vickers) at Hammersmith Hospital with the angle of the roentgen head adjusted to give a beam directed vertically downwards.

1953



1956: The first patient to receive radiation therapy from the medical linear accelerator at Stanford was a 2-year-old boy.

Approx. date of introduction	Model and location	Manufacturer	Beam energy and modality
1953	Hammersmith Hospital, London	Metropolitan-Vickers	8 MV X-rays
1954	St. Bartholomew's Hospital, London	Mullard	15 MeV X-rays and electrons
1954	Christie Hospital, Manchester	Metropolitan-Vickers AEI	4 MV X-ray
1954	Newcastle	Mullard	4 MV X-ray
1955	Stanford	Stanford	5 MV X-ray
1955	Argonne Cancer Hospital, Chicago	Stanford, HVE and Argonne	5–50 M electr
1955	Michael Reese Hospital, Chicago	Stanford. M. Reese and Helene Curtis	45 Me electr
1962	Newcastle	Vickers Research	4 MV X-ray
1962	Clinac 6	Varian	6 MV X-ray
1965	Mevatron 8	Applied Radiation	6–8 MV X-rays 3–10 MeV electrons
1965	SL-75	Mullard	6–8 MV X-rays 8–10 MeV electrons

Table 1 (*cont.*)

Approx. date of introduction	Model and location	Manufacturer	Beam energy and modality
1967	Sagittaire, Paris	CSF	16 MV X-rays 12–32 MeV electrons
1968	Clinac 4	Varian	4 MV X-rays
1969	Mevatron VI & XII	Applied Radiation	6 or 8 MV X-rays 3–11 MeV electrons
1969	LMR-13	Toshiba	8 and 10 MV X-rays 8–13 MeV electrons
1970	Therapi 4	SHM	4 MV X-rays
1970	Clinac 35 Hiroshima	Varian	8 and 25 MV X-rays 7–28 MeV

P. Howard-Flanders (1954) The Development of the Linear Accelerator as a Clinical Instrument, Acta Radiologica, 41:sup116, 649-655, DOI: 10.3109/00016925409177244

C J Karzmark and N C Pering 1973 Phys. Med. Biol. **18** 321

Status of Radiation Therapy Equipment

156 Countries

7687 RT Centres

15130 MV Therapy

Equipment type

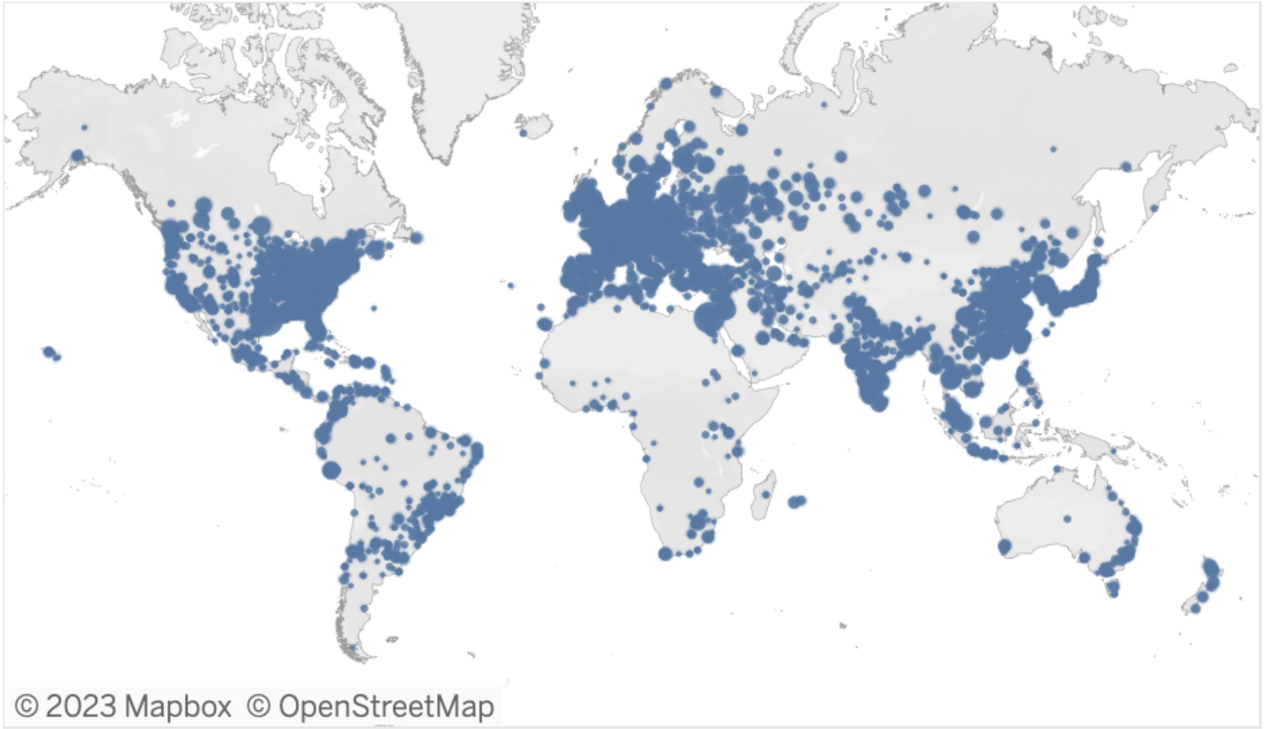
(Updated on : 09/03/2023 13:55:27)

MV Therapy	15,130
Brachytherapy	3,336
Light Ion Therapy	107

Equipment per income groups

(Updated on : 09/03/2023 13:55:27)

High income (H)	9,449
Upper middle income (UM)	4,023
Lower middle income (LM)	1,615
Low income (L)	40



IAEA DIRAC Directory of RAdiotherapy Centres

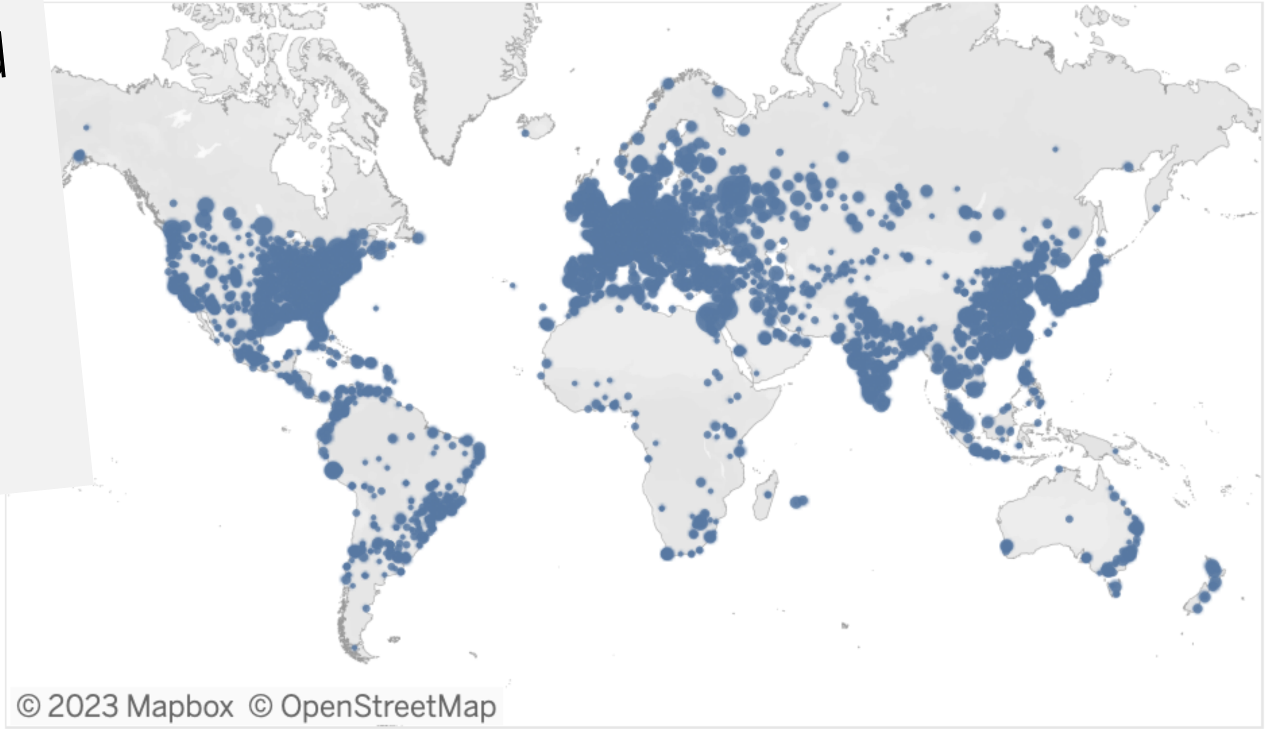
Status of Radiation Therapy Equipment

156 Countries

7687 RT Centres

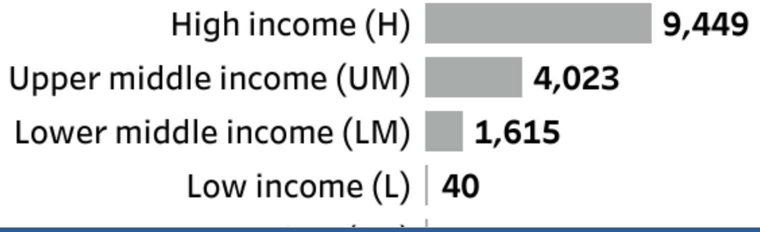
15130 MV Therapy

STELLA (Smart Technologies to Extend Lives with a Linear Accelerator) formed to address the lack of radiotherapy in challenging environments. Supported by ICEC, UK STFC, Lancaster, Oxford, Daresbury lab, CERN, users in LMICs



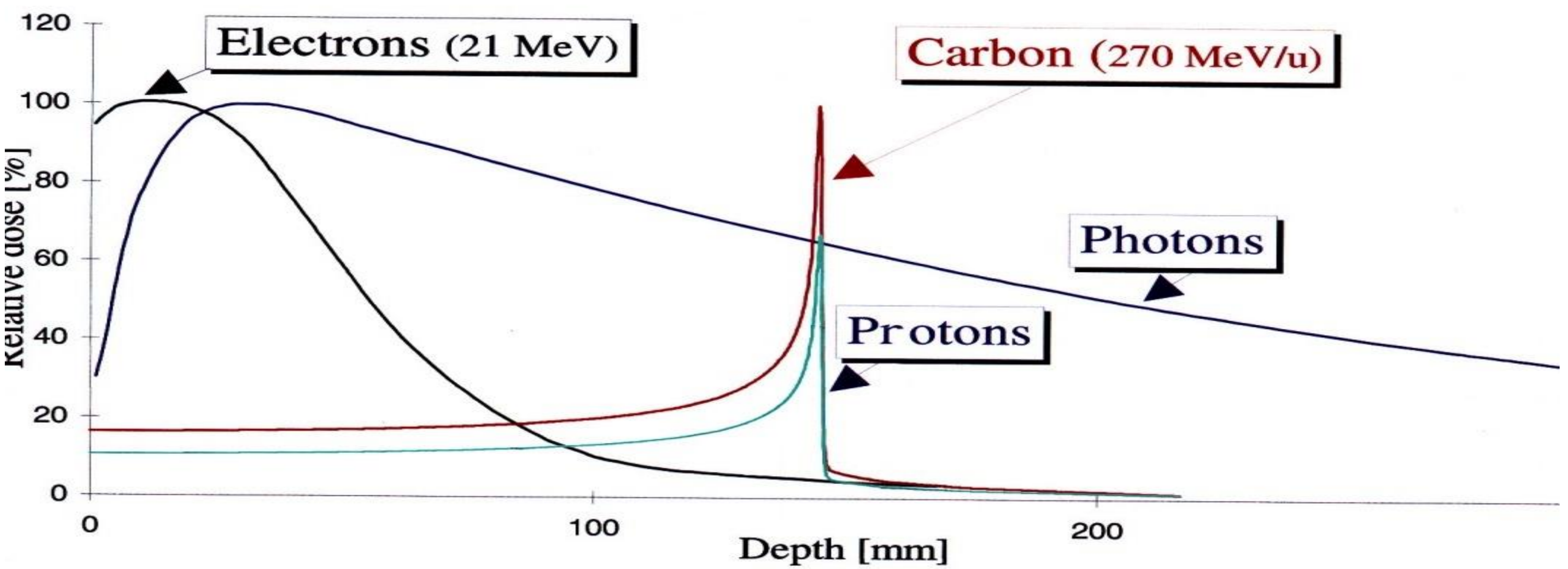
Equipment per income groups

(Updated on : 09/03/2023 13:55:27)

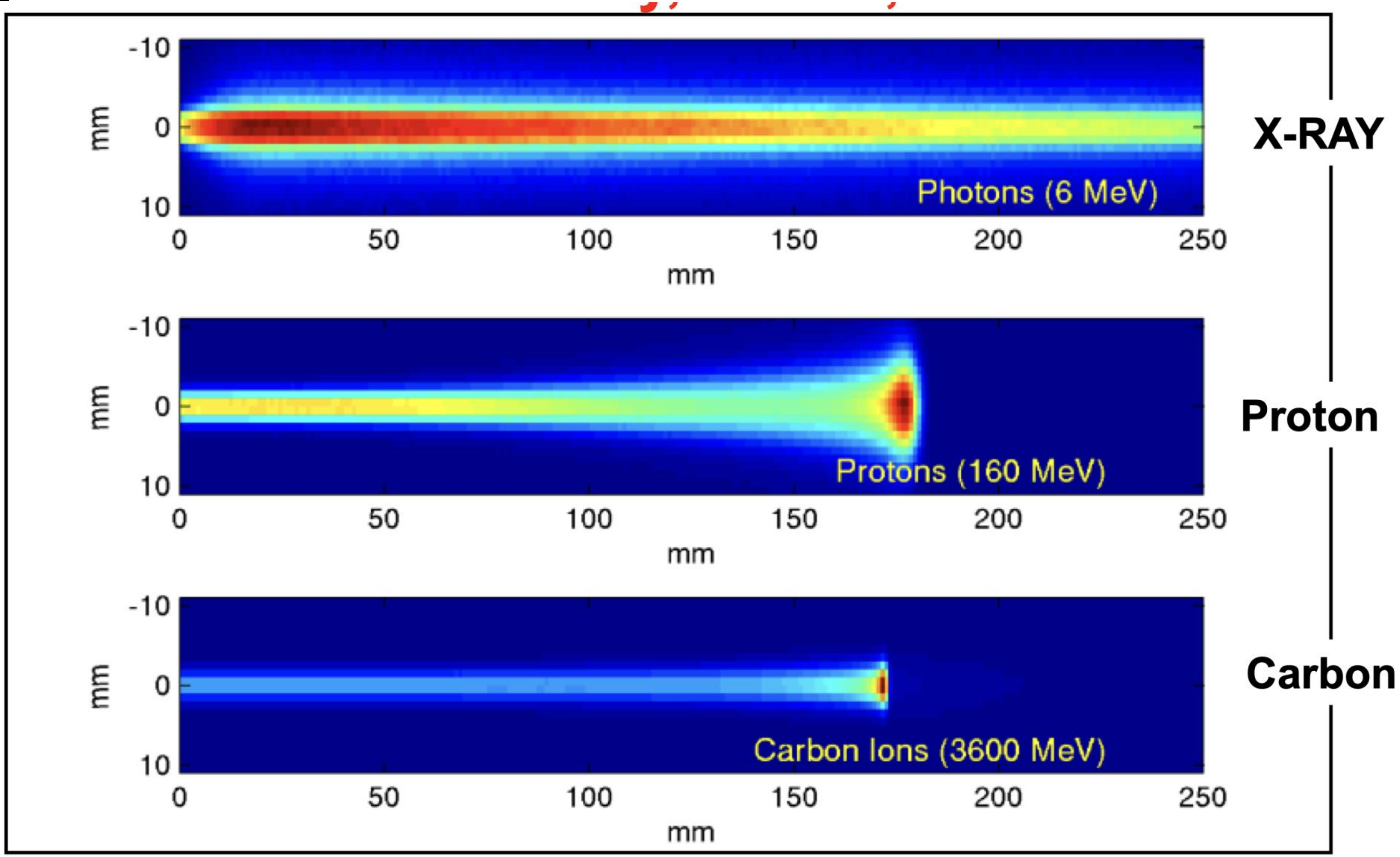


IAEA | DIRAC Directory of RAdiotherapy Centres

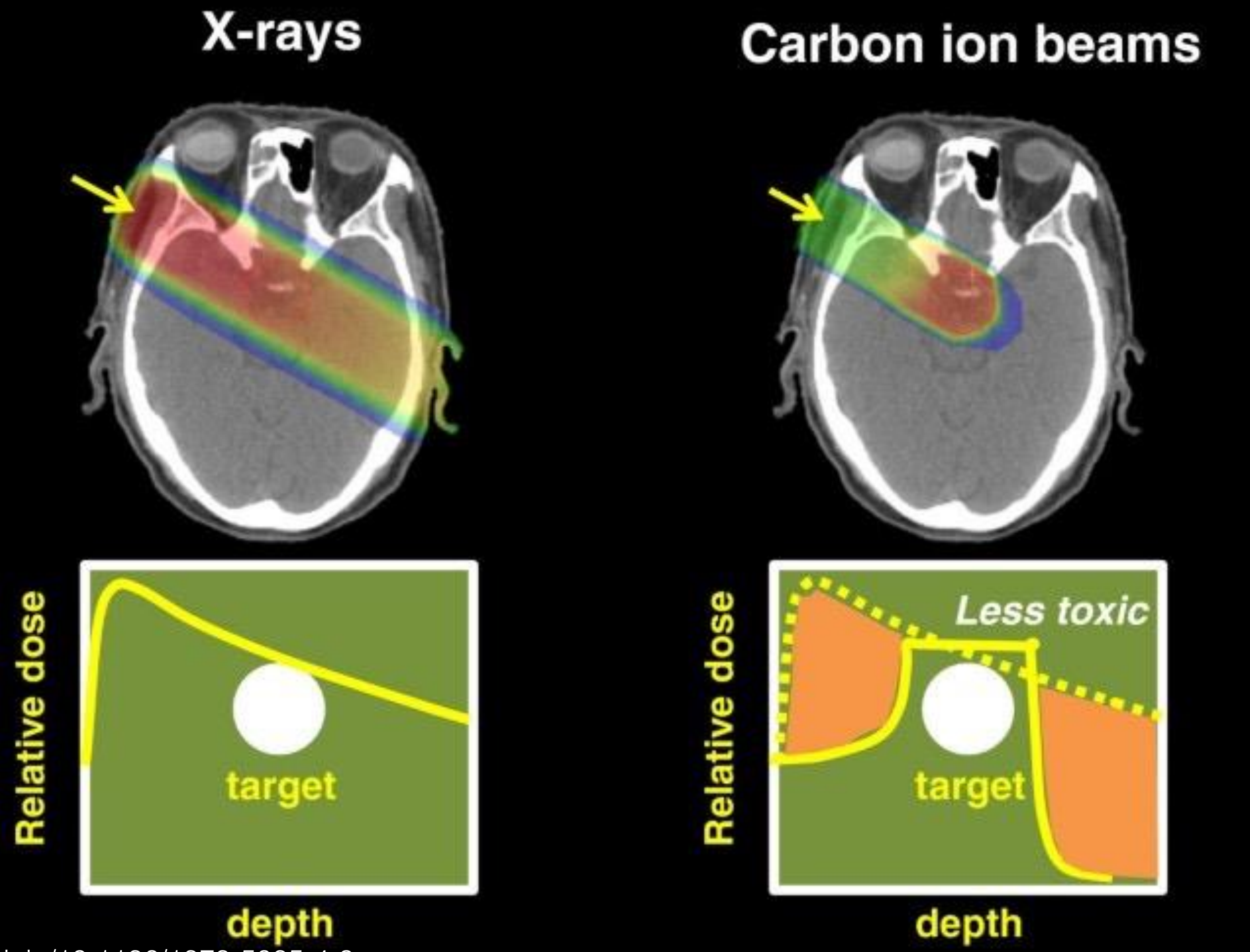
Protons, ions: hadron therapy, particle therapy, (light, heavy) ion therapy



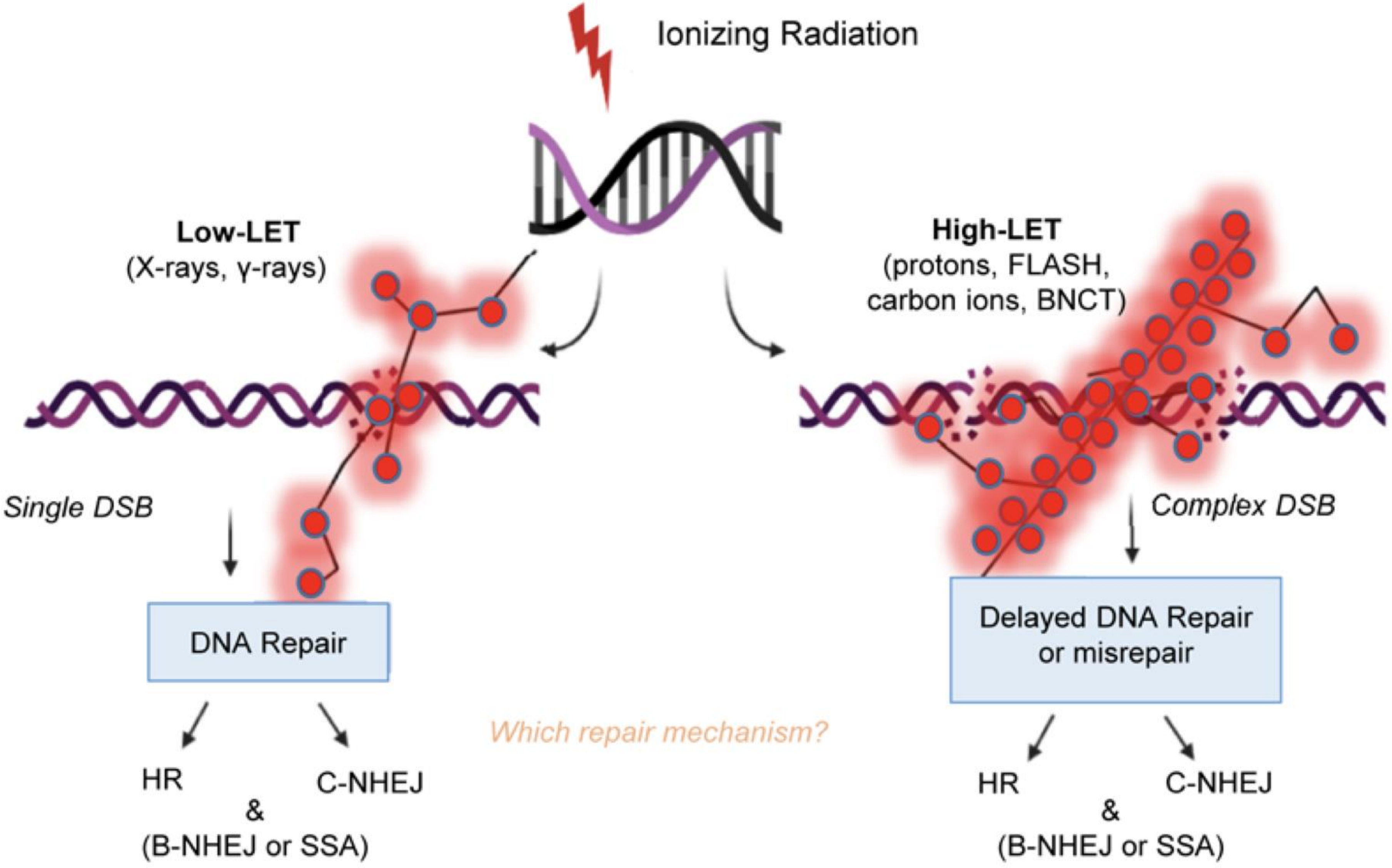
Beam profiles



Kraft, G. History of heavy-ion therapy at GSI



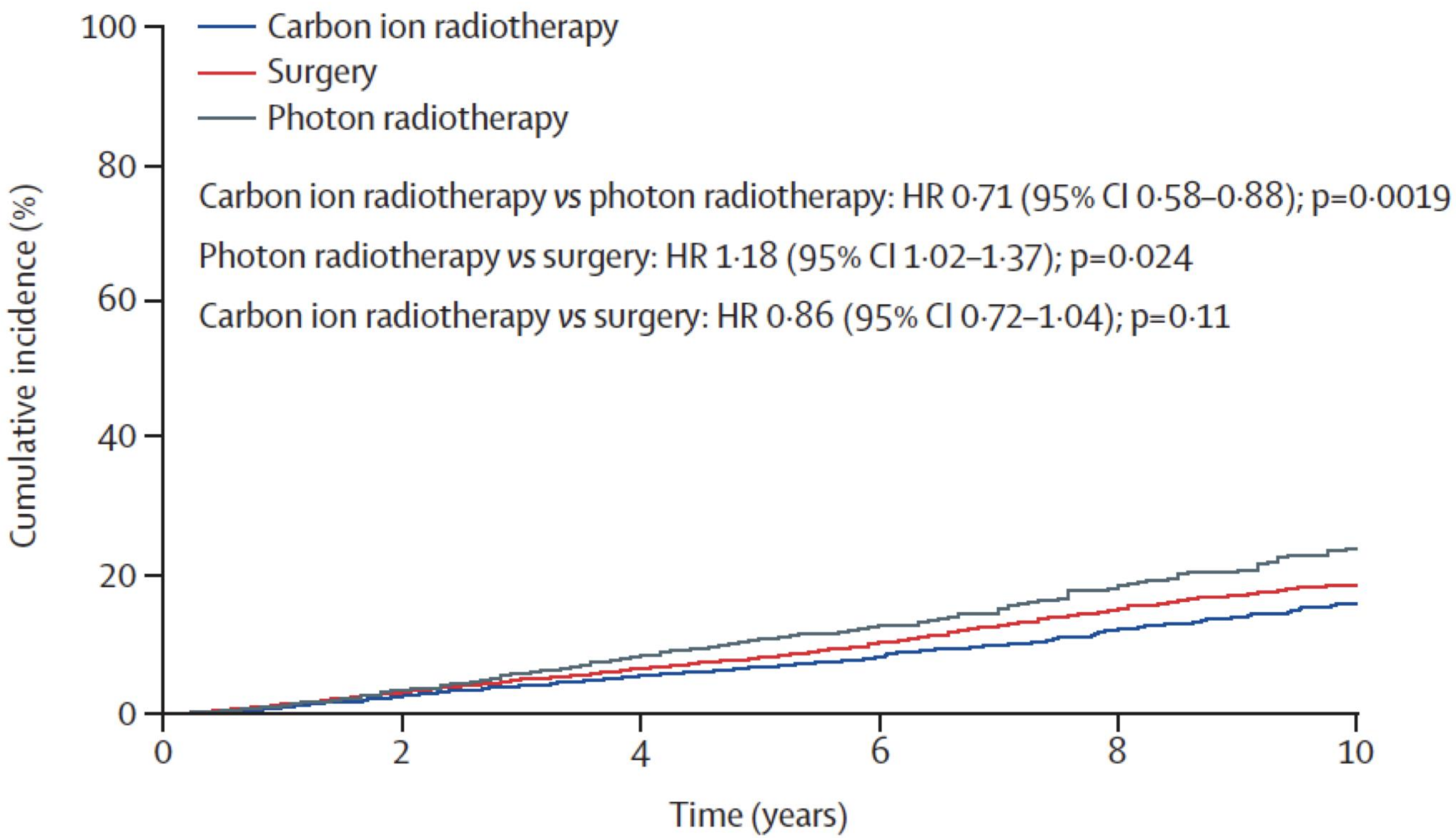
https://link.springer.com/article/10.1186/1878-5085-4-9



Nikitaki Z, Velalopoulou A, Zanni V, Tremi I, Havaki S, Kokkoris M, Gorgoulis VG, Koumenis C, Georgakilas AG (2022).
Key biological mechanisms involved in high-LET radiation therapies with a focus on DNA damage and repair.
Expert Reviews in Molecular Medicine 24, e15, 1–15. https:// doi.org/10.1017/erm.2022.6

Risk of subsequent primary cancers after carbon ion radiotherapy, photon radiotherapy, or surgery for localised prostate cancer: a propensity score-weighted, retrospective, cohort study

Osama Mohamad, MD; Takahiro Tabuchi, MD; Yuki Nitta, MD; Akihiro Nomoto, MD; Akira Sato, MD; Goro Kasuya, MD et al. The Lancet Oncology, VOLUME 20, ISSUE 5, P674-685, MAY 2019



Status of Radiation Therapy Equipment

20 Countries

104 RT Centres

107 Light Ion Therapy

Equipment type
(Updated on : 09/03/2023 13:55:27)

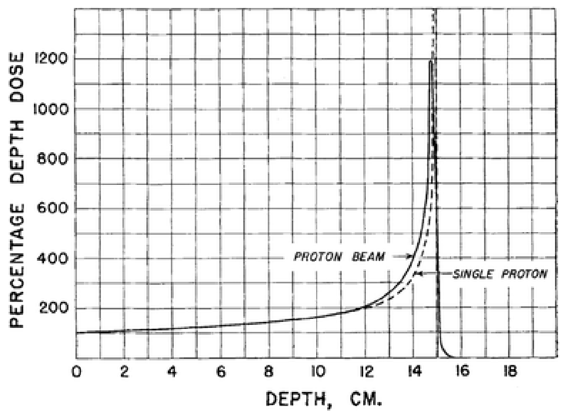
Equipment type	Count
MV Therapy	15,130
Brachytherapy	3,336
Light Ion Therapy	107

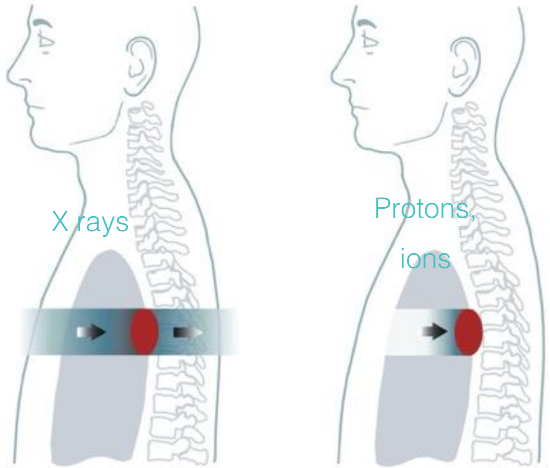
Equipment per income groups
(Updated on : 09/03/2023 13:55:27)

Income group	Count
High income (H)	96
Upper middle income (UM)	10
Lower middle income (LM)	1

IAEA DIRAC Directory of RAdiotherapy Centres

Berkeley
1931 Invention of cyclotron (Ernest Lawrence)
1946 RR Wilson published his seminal paper on particle therapy
1952 First biological investigation with accelerated nuclei (C Tobias and JH Lawrence)
1954 First therapeutic exposure of humans to protons and alphas (Tobias and JH Lawrence)
1975 Clinical trials with accelerated light ions at LBL (Castro)





Gustav Werner Institute and Theodor Svedberg Laboratory
1949 Synchrocyclotron at the Gustav Werner Institute (Uppsala)
1950s Pre-therapeutic physical experiments with high energy protons (B. Larsson)
1957 First patient treated with proton beam

π^- beam therapy

1935 Yukawa theory on pi meson

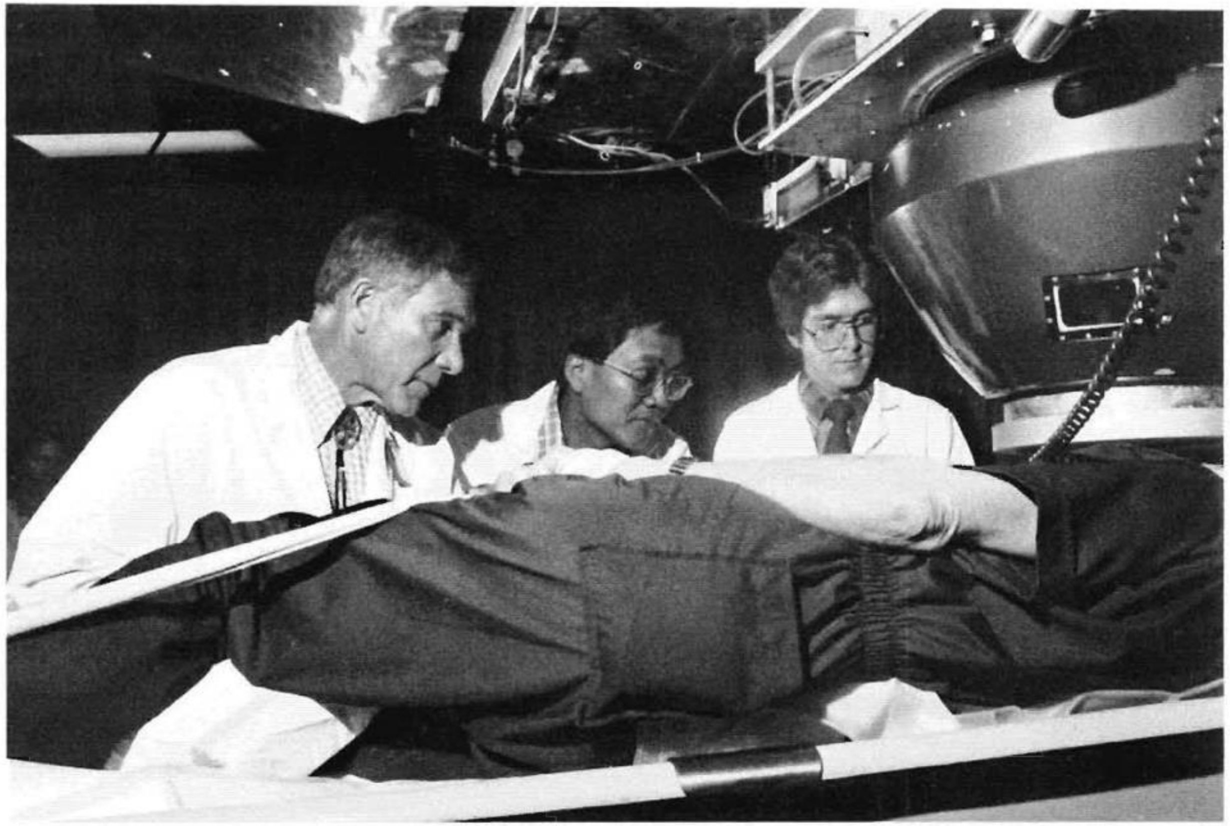
1947 Discovery of pions

1951 Possibility of using negative pions for cancer therapy (Tobias and Richman)

1961 Clinical use of π^- advocated (Fowler and Perkins, Nature 1961)

'70-'80s Clinical trials of negative pions at LAMPF, TRIUMF, PSI and Stanford

William T. Chu
EO Lawrence Berkeley National Laboratory
PTCOG From 1985 to Present and Future

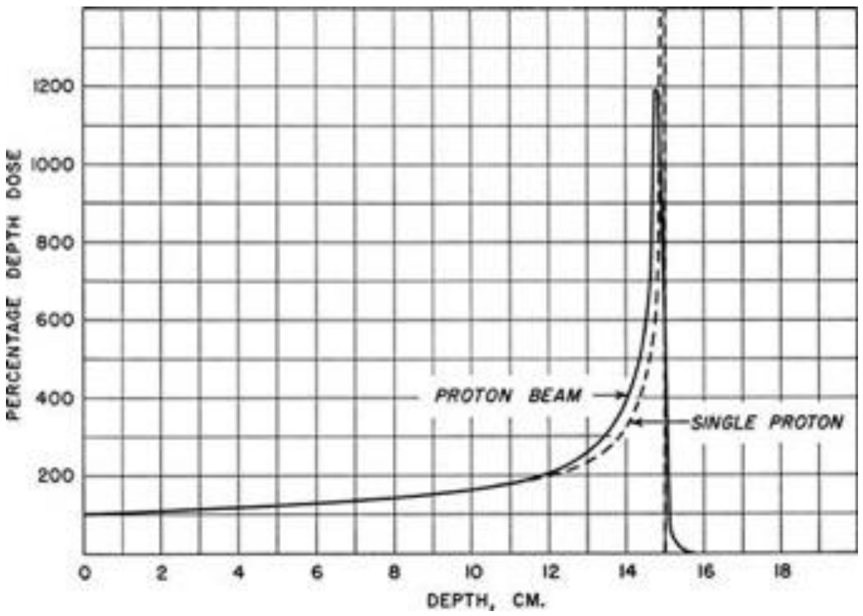


In a pilot experimental program at LAMPF's Biomedical Facility, about 250 patients were treated with negative pions for a variety of advanced deep-seated tumors. Compared to conventional x-ray therapy, pion therapy is expected to provide improved dose localization and biological effectiveness. Shown positioning a patient under the pion radiotherapy beam are (left to right) Dr. Morton Kligerman, former Director of the University of New Mexico's Cancer Research and Treatment Center, a visiting radiotherapist from Japan, and Dr. Steven Bush, formerly of the University of New Mexico. The hardware at the upper right includes a beam collimator, a dose monitor, and a device for changing the penetration depth of the pions.

LAMPF: a dream and a gamble

From physics labs…

1932 - E. Lawrence
First cyclotron

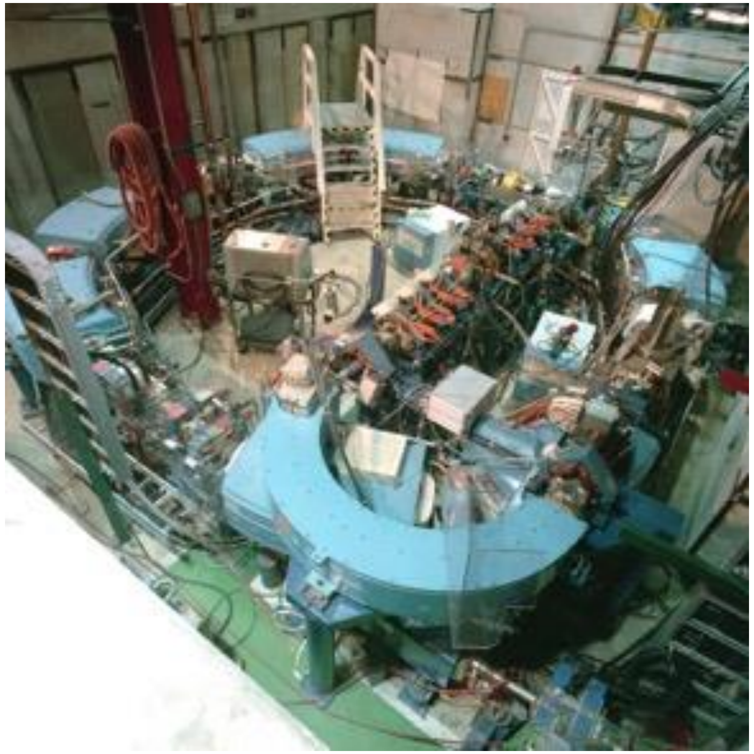


1946 – proton therapy
proposed by R. Wilson

1954 – Berkeley treats
the first patient

...to clinics

1989
Clatterbridge UK



1990
Loma Linda USA

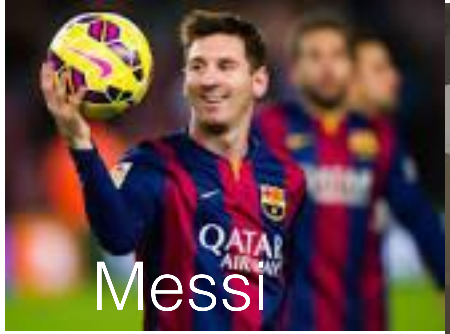
1994
HIMAC Japan

Pioneers in scanned beam delivery

Building Gantry 1 back in the 1990s
(Photo: Paul Scherrer Institute)

1998
Pilot project at GSI
Germany and proposal for HIT facility

200



Multi heavy ions (protons + carbon ions)

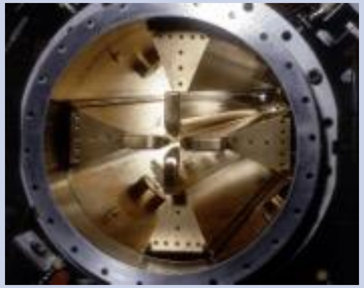
oton multi-room

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

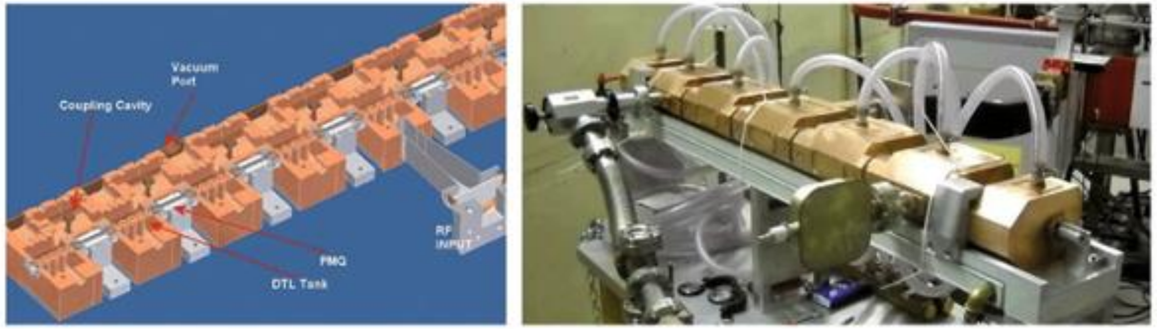
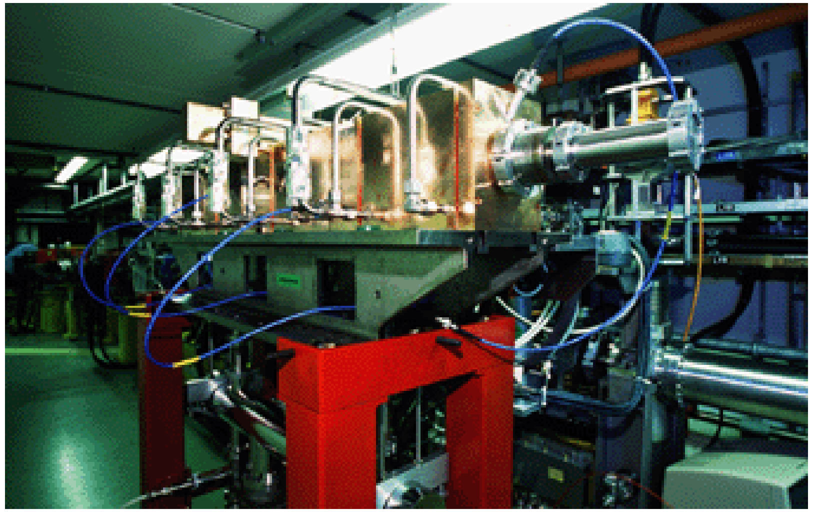


Fig. 4. TOP-IMPLART SCDTL structure: (left) schematic (right) 18–24 MeV booster built for the SPARKLE Company.

TOP IMPLART

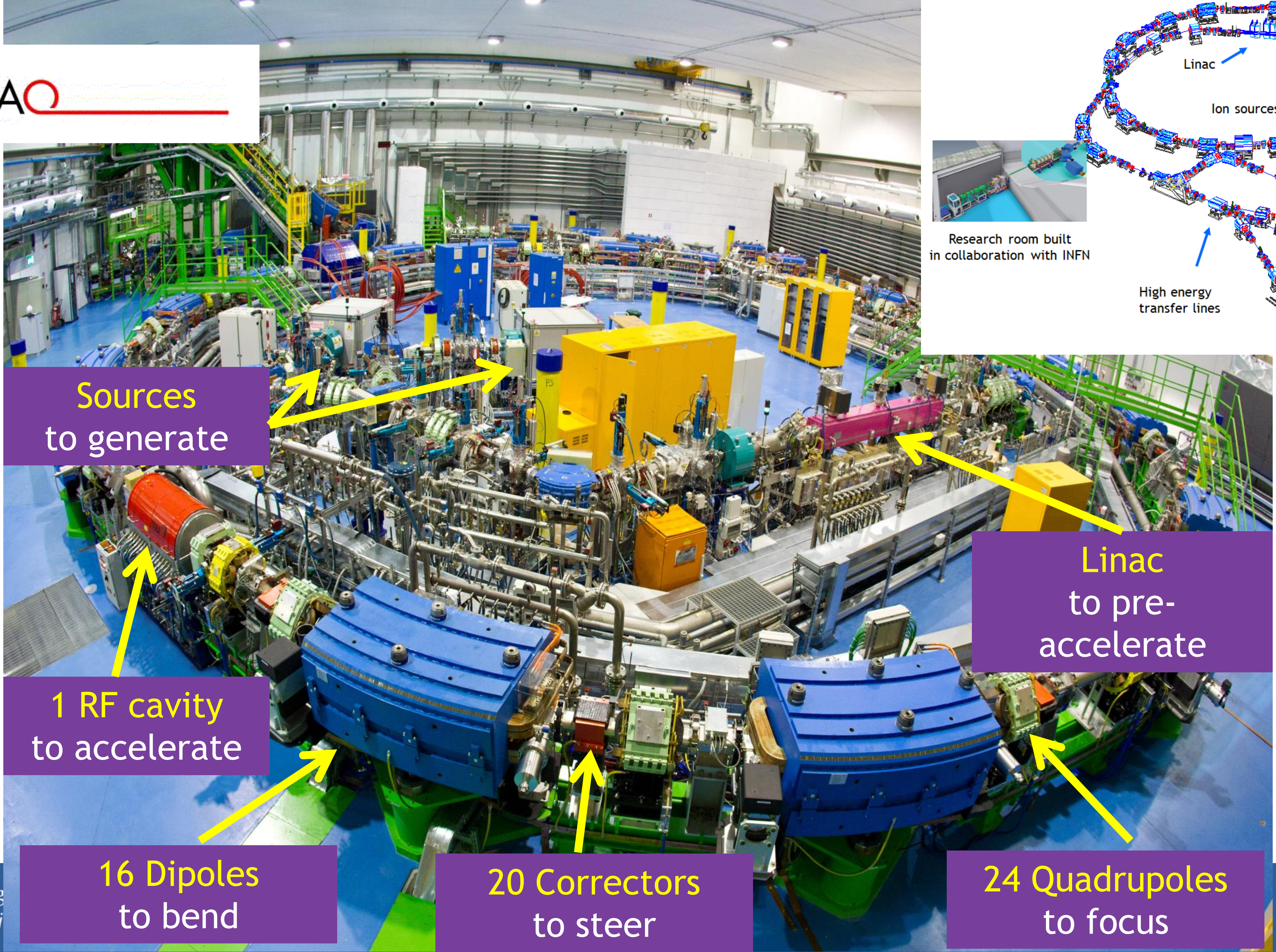
C. Ronsivalle, M. Carpanese, C. Marino, G. Messina, L. Picardi, S. Sandri, E. Basile, B. Caccia, D.M. Castelluccio, E. Cisbani, S. Frullani, F. Ghio, V. Macellari, M. Benassi, M. D’Andrea, L. Strigari, The TOP-IMPLART project, Eur. Phys. J. Plus 126: 68 (2011) 1–15, http://dx.doi.org/10.1140/epjp/i2011-11068-x.

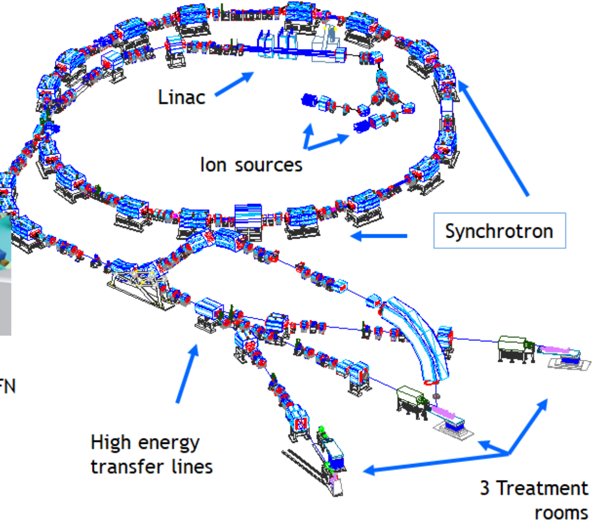


LInac BOoster (LIBO)

U. Amaldi et al., “LIBO-a linac booster for protontherapy: construction and test of a prototype,” Nucl. Instrum. Meth- ods Phys. Res. A, vol. 521, pp. 512-529, 2004.

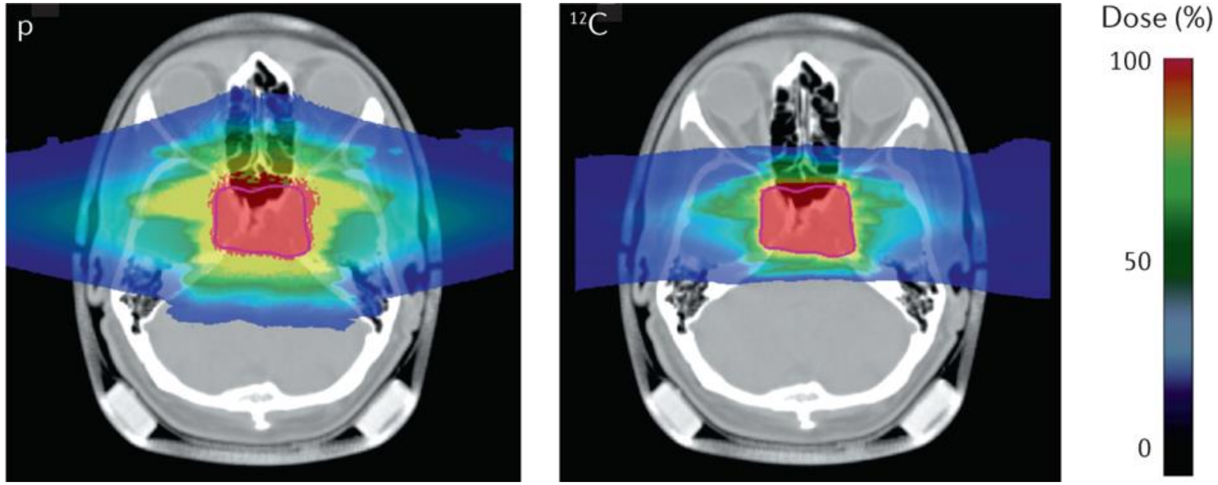
fondazione CNAO





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).

Image from the GSI patient project archive,
distributed under Creative Commons CC BY 4.0.

HIT Heidelberger Ionenstrahl-Therapiezentrum

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

* Until Dec 2020, source ptcog.ch

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

From PIMMS @ CERN

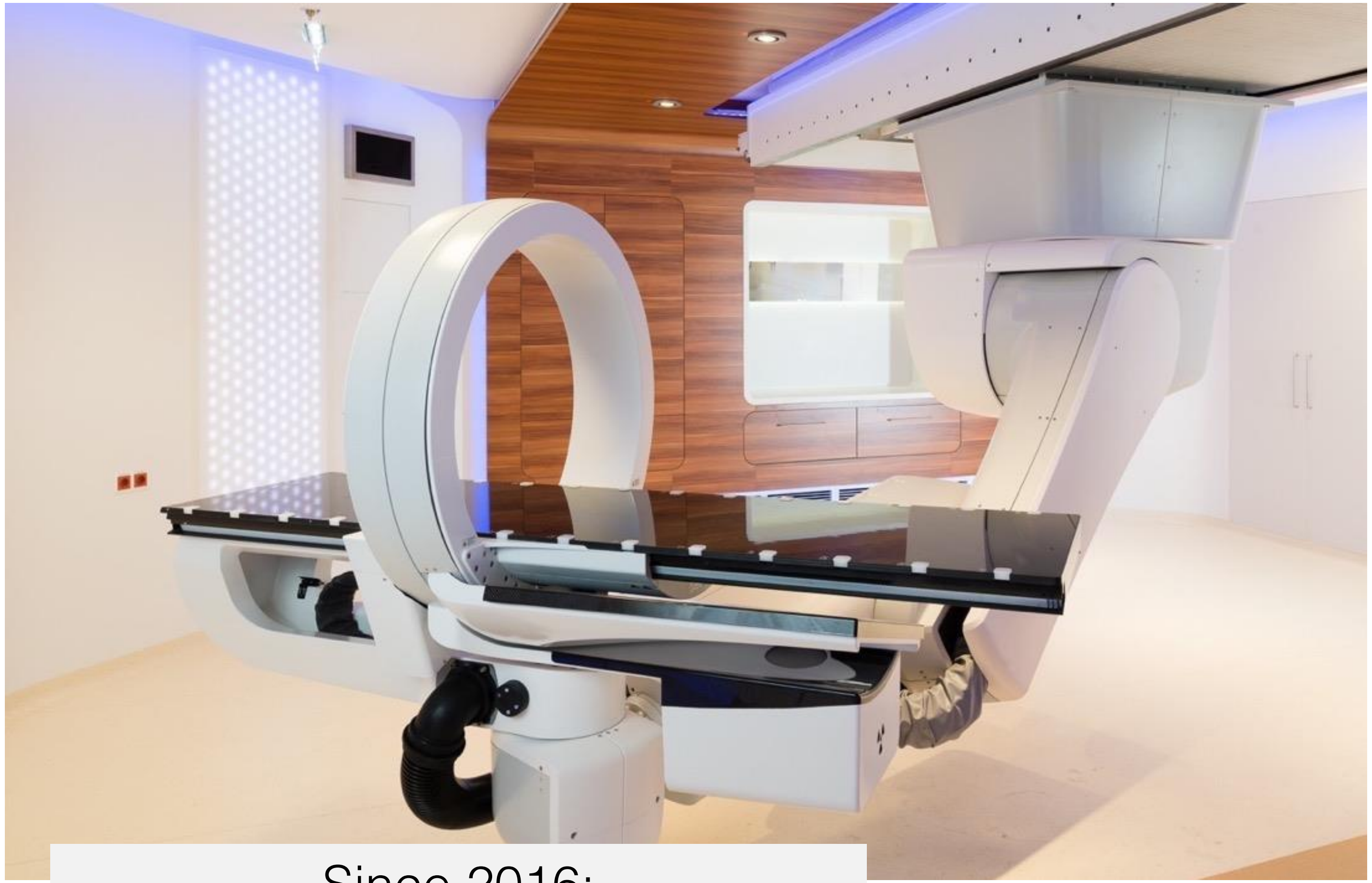
TERA

INFN

fondazione CNAO

MedAustron

Patient treatment at MedAustron



Since 2016:
1174 Patients
30600 Single Fractions

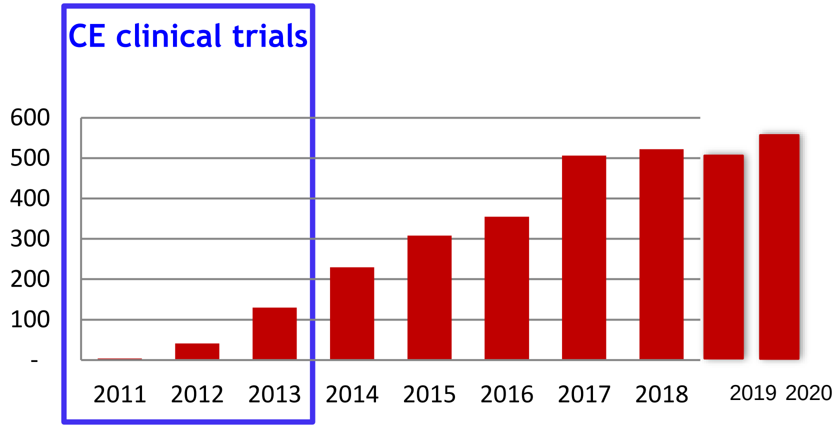
MedAustron

CNS	28%
Head & Neck	20%
Pediatrics	15%
Re-Irradiation	15%
Sarcoma	9%
Skull Base	7%
Prostate	3%
Gastrointestinal (upper)	2%
Gastrointestinal (lower)	<1%
Gynecological Tumors	<1%
Urogenital Tumors	<1%
Breast/Mamma-Ca	<1%

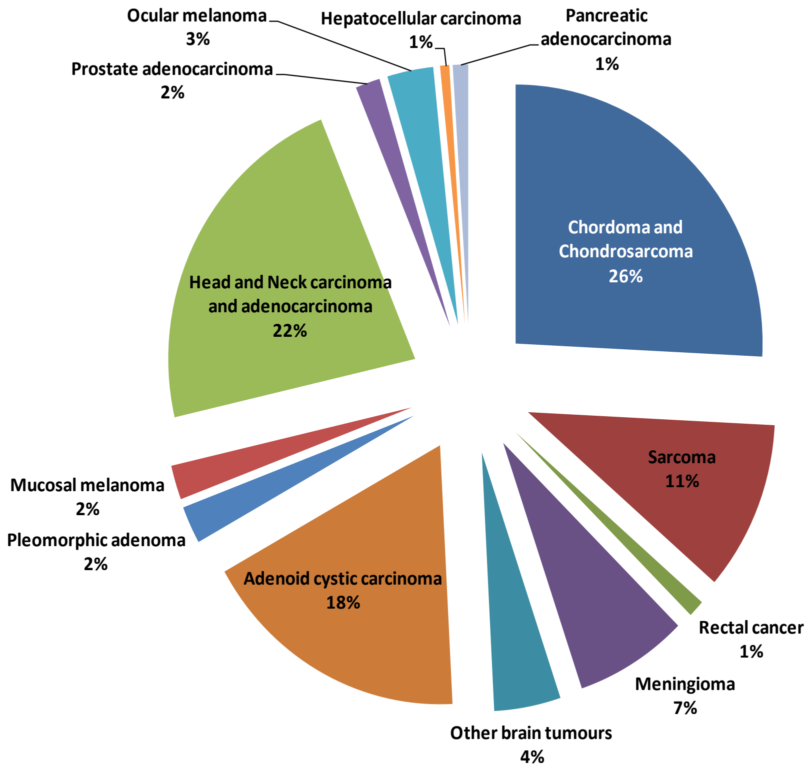
Values October 2021 • values rounded

Patient treatment at CNAO

Since 2011:
3700 Patients
55% C-ions
45% Protons



Patients per year



fondazione CNAO

Non oncological application: ventricular arrhythmia (Collaboration with San Matteo Hospital, Pavia) Published: European Journal of Heart Failure

SCIENTIFIC REPORTS

OPEN

Feasibility Study on Cardiac Arrhythmia Ablation Using High-Energy Heavy Ion Beams

Received: 08 August 2016
Accepted: 09 November 2016
Published: 20 December 2016

H. Immo Lehmann[1,*], Christian Graeff[2,*], Palma Simoniello[2], Anna Constantinescu[2], Mitsuru Takami[1], Patrick Lugenbiel[3], Daniel Richter[2,4], Anna Eichhorn[2], Matthias Prall[2], Robert Kaderka[2], Fine Fiedler[5], Stephan Helmbrecht[5], Claudia Fournier[2], Nadine Erbeldinger[2], Ann-Kathrin Rahm[3], Rasmus Rivinius[3], Dierk Thomas[3], Hugo A. Katus[3], Susan B. Johnson[2], Kay D. Parker[2], Jürgen Debus[6], Samuel J. Asirvatham[1], Christoph Bert[2,4], Marco Durante[2,7] & Douglas L. Packer[1]

> Eur J Heart Fail. 2020 Nov 12. doi: 10.1002/ejhf.2056. Online ahead of print.

The First-in-Man Case of Non-invasive Proton Radiotherapy to Treat Refractory Ventricular Tachycardia in Advanced Heart Failure

Veronica Dusi [1 2], Viviana Vitolo [3], Laura Frigerio [1 4], Rossana Totaro [1 4], Adele Valentini [5], Amelia Barcellini [3], Alfredo Mirandola [3], Giovanni Battista Perego [6], Michela Coccia [2], Alessandra Greco [4], Stefano Ghio [4], Francesca Valvo [3], Gaetano Maria De Ferrari [7], Massimiliano Gnecchi [1 2], Luigi Oltrona Visconti [4], Roberto Rordorf [1 4]

Affiliations + expand

PMID: 33179329 DOI: 10.1002/ejhf.2056

Challenges for next-generation particle-therapy machines

Cost-effective technologies

Reduced footprint

New treatment regimes (e.g. FLASH, microbeams) and fractionation schedules

Multi-ions

Radiobiology research integrated in the facility

Many challenges in common with those for future particle physics facilities. Various initiatives starting/on-going.

KT Seminars

The CERN Next Ion Medical Machine Study: towards a new generation of accelerators for cancer therapy

by Maurizio Vretenar (CERN)

Monday 19 Oct 2020, 14:00 → 16:30 Europe/Z

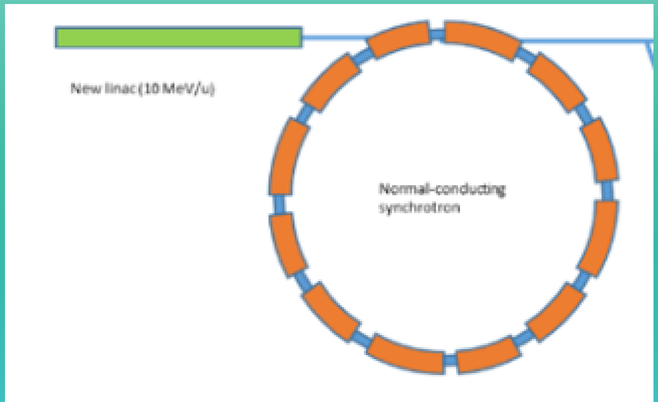
https://indico.cern.ch/event/956260/

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.

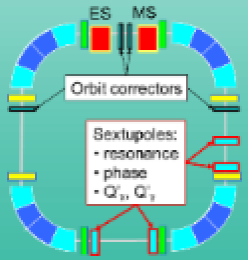
Circumference ~ 75 m



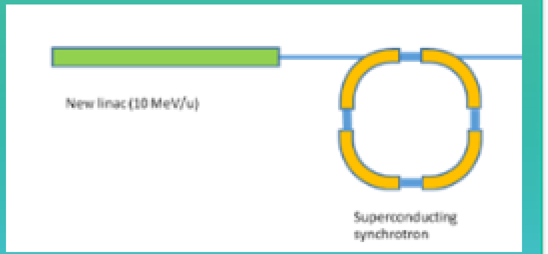
Improved synchrotron (superconducting)

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

Circumference ~ 27 m



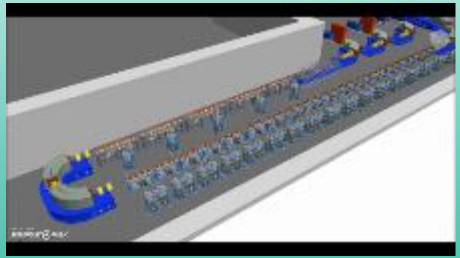
Courtesy: TERA

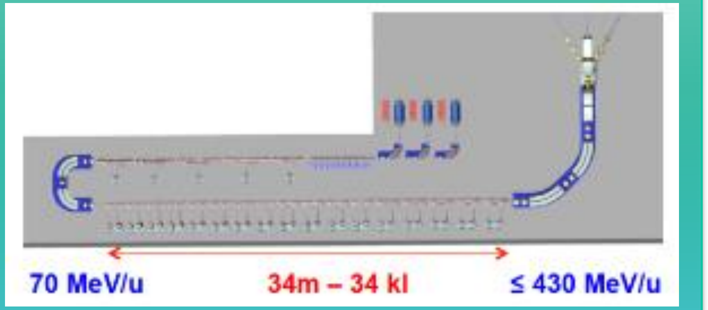


Linear accelerator

Linear sequence of accelerating cells, high pulse frequency.

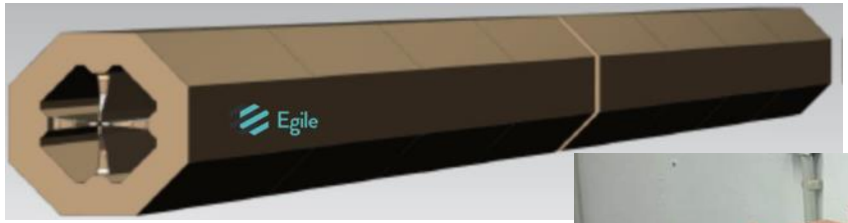
Length ~ 53 m

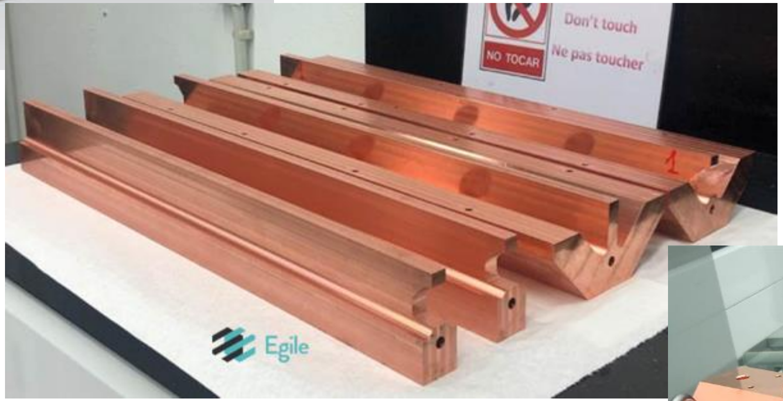


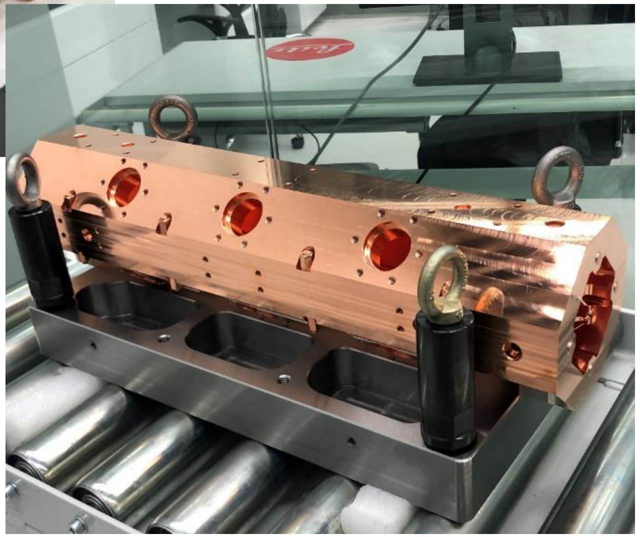


Other options considered as less interesting because of cost and/or required R&D: RC synchrotron, FFAG, SC cyclotron, PWFA

The RFQ for C^{6+} LINAC option







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

Collaboration CNAO-INFN-CERN-MedAustron

Developing enabling technologies for a next-generation compact and lightweight rotating gantry

Protons stop…but where?

(Range uncertainty)

Courtesy Marco Durante

Range monitoring

Dosimetry

Moving organs

Clinical Trials

Combining Heavy-Ion Therapy with Immunotherapy: An Update on Recent Developments

Alexander Helm; Daniel K. Ebner; Walter Tinganelli; Palma Simoniello; Alessandra Bisio; Valentina Marchesano; Marco Durante; Shigeru Yamada; Takashi Shimokawa

Int J Part Ther (2018) 5 (1): 84–93.

https://doi.org/10.14338/IJPT-18-00024.1

Impact of proton therapy on antitumor immune response

Céline Mirjolet, Anaïs Nicol, Emeric Limagne, Carole Mura, Corentin Richard, Véronique Morgand, Marc Rousseau, Romain Boidot, François Ghiringhelli, Georges Noel & Hélène Burckel

Scientific Reports **11**, Article number: 13444 (2021) | Cite this article

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

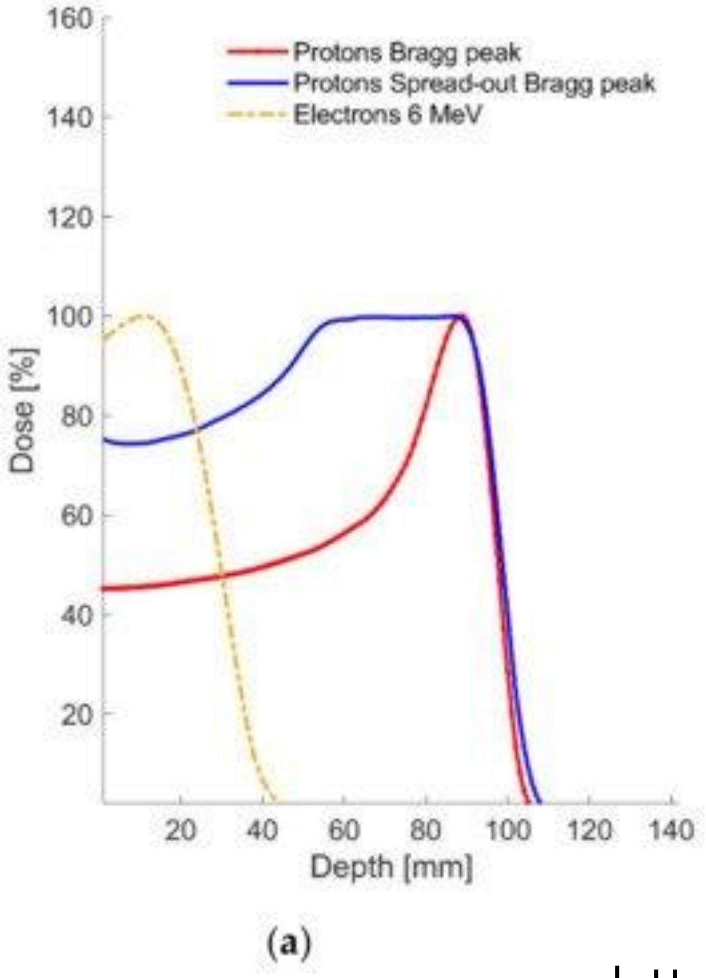
Treatment of a first patient with FLASH-radiotherapy

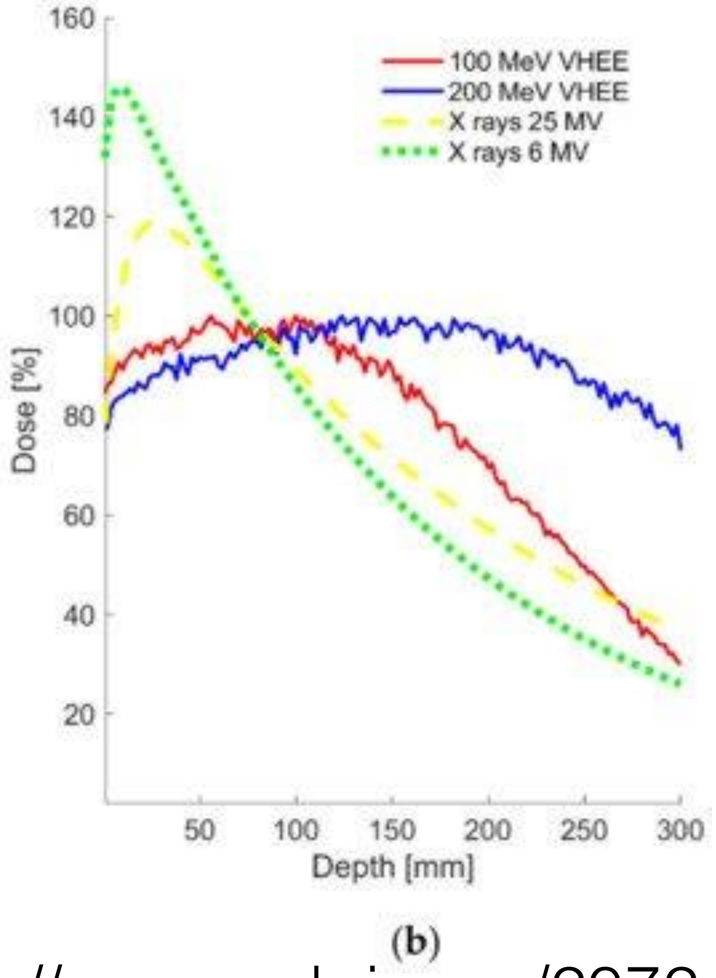
Jean Bourhis [a,b,*], Wendy Jeanneret Sozzi [a], Patrik Gonçalves Jorge [a,b,c], Olivier Gaide [d], Claude Bailat [c], Fréderic Duclos [a], David Patin [a], Mahmut Ozsahin [a], François Bochud [c], Jean-François Germond [c], Raphaël Moeckli [c,1], Marie-Catherine Vozenin [a,b,1]

[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

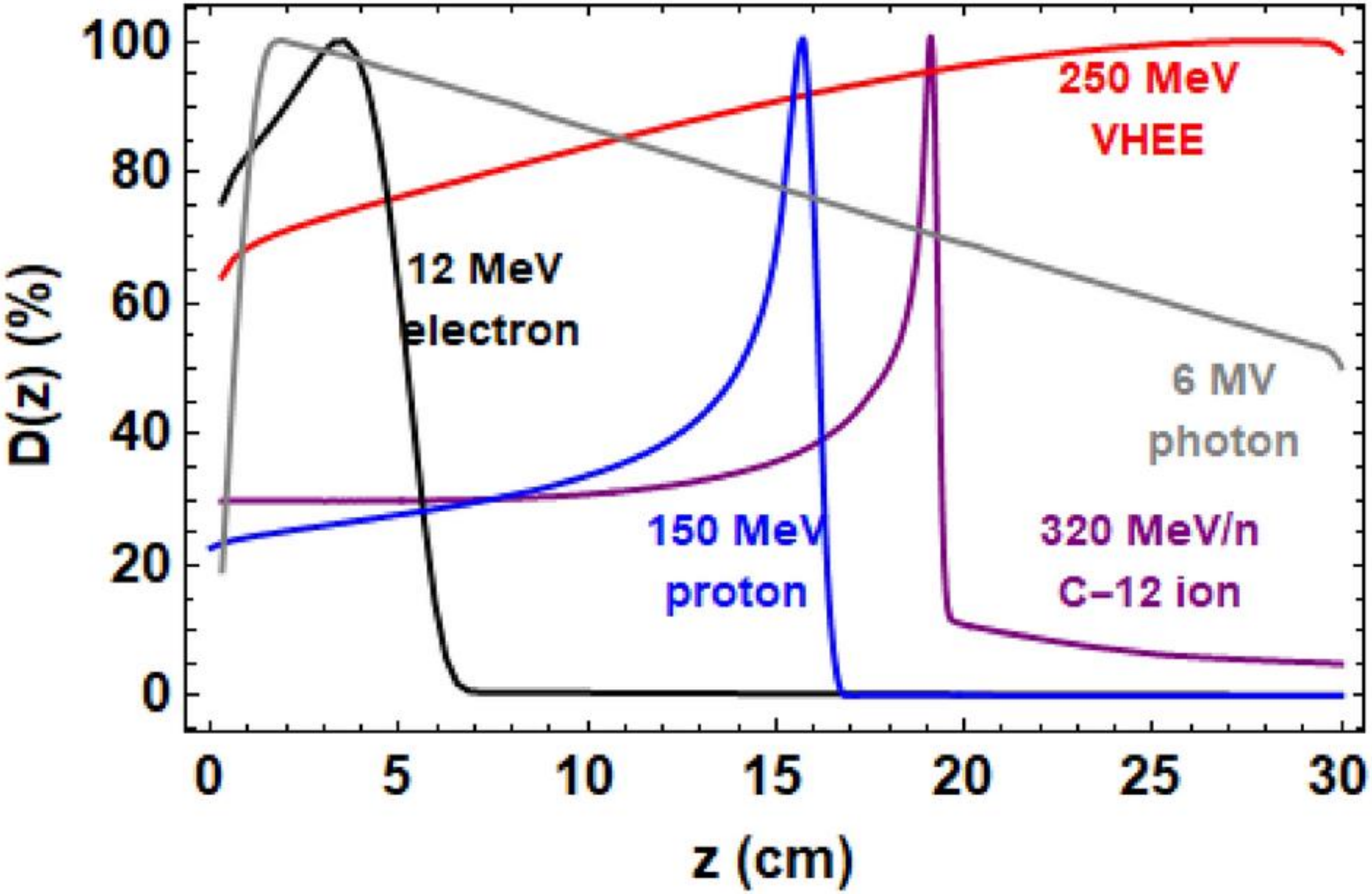
Fig. 1. Temporal evolution of the treated lesion: (a) before treatment; the limits of th PTV are delineated in black; (b) at 3 weeks, at the peak of skin reactions (grade 1 epithelitis NCI-CTCAE v 5.0); (c) at 5 months.

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





https://www.mdpi.com/2072-6694/13/19/4942/htm



TOPAS-based Monte Carlo simulations of the integrated normalised dose deposited in the plane parallel to the direction of an incident Gaussian beam (σ=4mm). All beams are in the absence of focusing

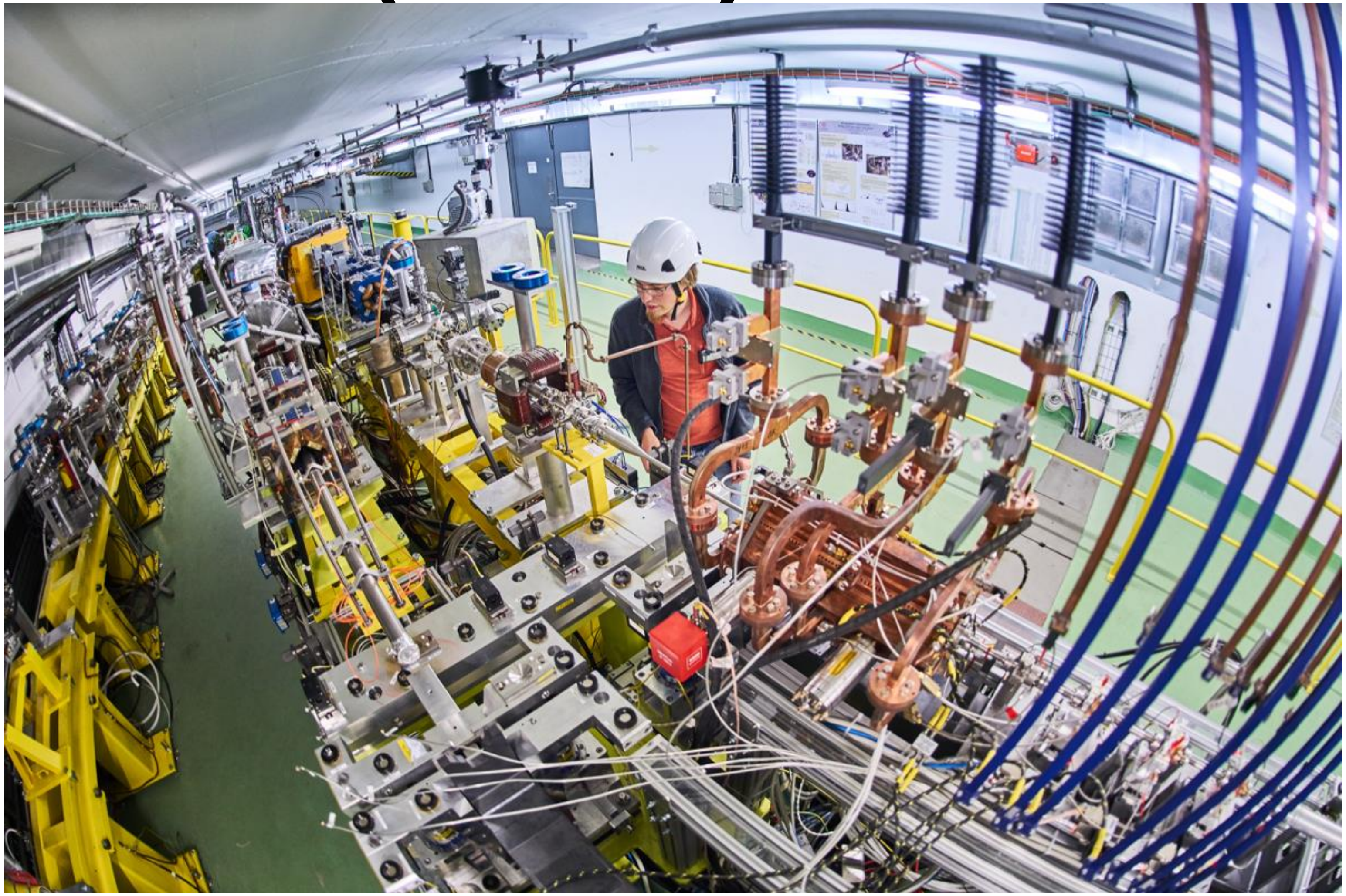
https://www.nature.com/articles/s41598-021-93276-8#Fig1


VHEE2020
5-7 October 2020
Cherenkov in water
Exit Window
Water phantom
Radiosensitive films
YAG screen
Charge monitor
Camera
Quadrupole


VHEE'17
Very High Energy Electron
Radiotherapy: Medical & Accelerator Physics Aspects Towards Machine Realisation
JULY 24 – 26, 2017
COCKCROFT INSTITUTE
Scientific Programme Committee:
Roger M. Jones — University of Manchester/Cockcroft Institute, UK– Chair
Colleen DesRosiers — Indiana University, USA
Angeles Faus-Golfe — IFIC, Spain, and CNRS/LAL, France
Dino Jaroszynski — University of Strathclyde, UK
Karen Kirkby — University of Manchester, UK
Ranald Mackay — The Christie, UK
Peter McIntosh — STFC Daresbury Laboratory, UK
Hywel Owen — University of Manchester/Cockcroft Institute, UK
Jiaru Shi — Tsinghua University, China
Sami Tantawi — SLAC National Accelerator Lab, USA
Marcel Van Herk — The Christie/Manchester University, UK
Alan Wheelhouse — STFC Daresbury Laboratory, UK
Local Organizing Committee:
Deepa Angal-Kalinin — STFC Daresbury Laboratory – Chair
Roger M. Jones — University of Manchester/ Cockcroft Institute
Nirav Joshi — University of Manchester/ Cockcroft Institute
Peter McIntosh — STFC Daresbury Laboratory
Hywel Owen — University of Manchester/ Cockcroft Institute
Sue Waller — STFC Daresbury Laboratory
This workshop will explore fundamental issues associated with the development of a radiotherapy machine capable of delivering 250 MeV electrons at a high dose. We will explore both the dose delivery aspects, and the potential to realise a radiotherapy machine suitable for patient treatment.
www.cockcroft.ac.uk/events/VHEE17
The Cockcroft Institute
Science & Technology Facilities Council
IOP Institute of Physics
EuCARD²

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.



Roberto Corsini (CERN)

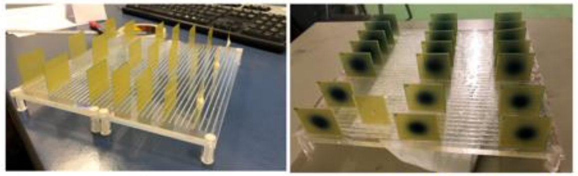
VHEE activities in CLEAR

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

Verification of FLASH effect using biological dosimeters

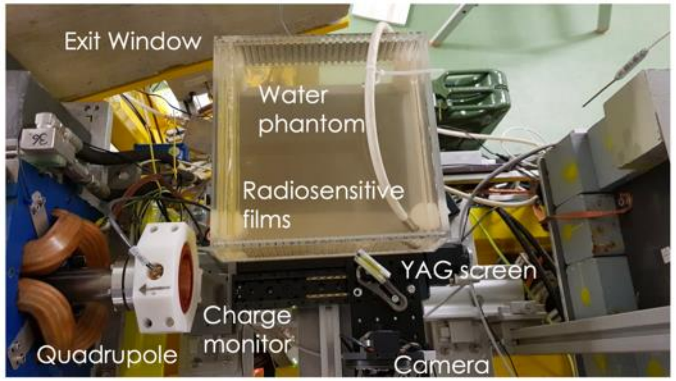
Experimental verification of dose deposition profiles in water phantoms

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).

Table 1. Main parameters for the VHEE sources cited in this document.

Beam Parameters	CLEAR	SPARC	NLCTA
Energy (MeV)	50–220	170	50–120
Bunch charge (pC/shot)	150	60	30
Bunch length rms (ps)	0.1–10	0.87	1
Repetition rate (Hz)	0.8–10	0.1–10	0.1–10
Beam size at water phantom surface (σ mm)	1.2	3.4	2

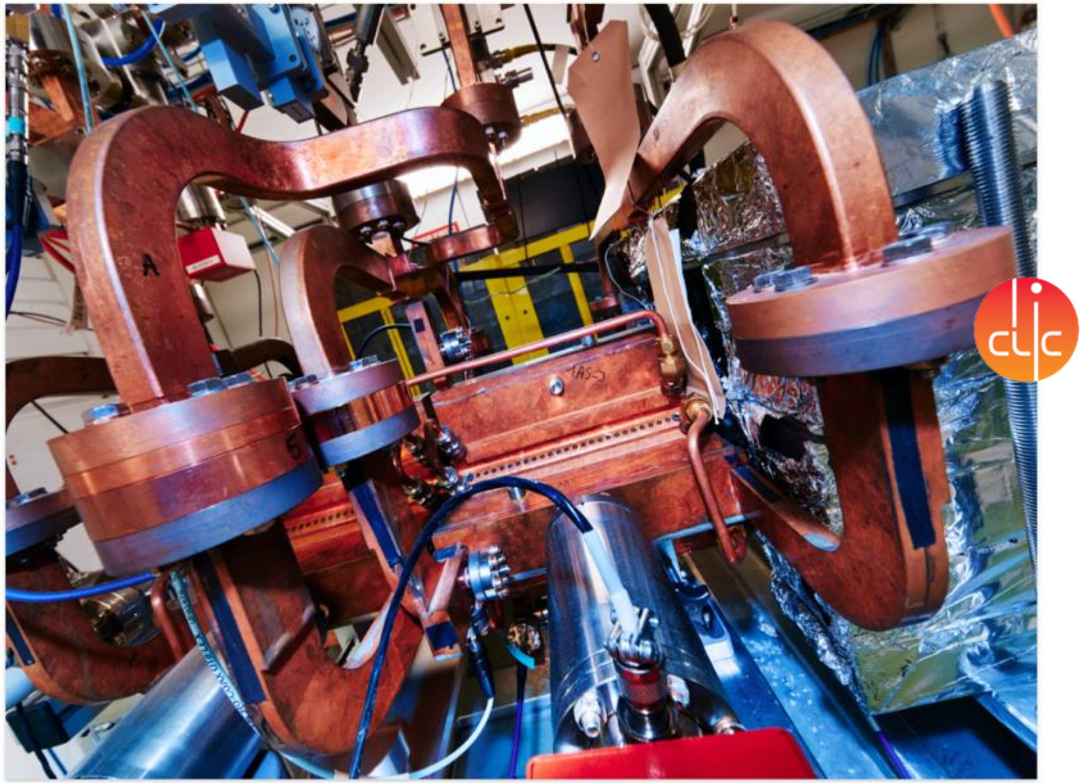
Table 2. List of facilities or accelerators under development for VHEE production.

Beam Parameters	PHASER	CLARA	PITZ	Argonne	Tsinghua University
Energy (MeV)	100–200	50 (−250)	20 (−250)	6–63	45 (−350)
Bunch charge (pC/shot)	-	20–100	0.1–5000	$100–10^5$	200
Bunch length rms (ps)	3.10^5	0.3–5	30	0.3	<2
Repetition rate (Hz)	10	10 (−100)	10	0.5–10	5–50

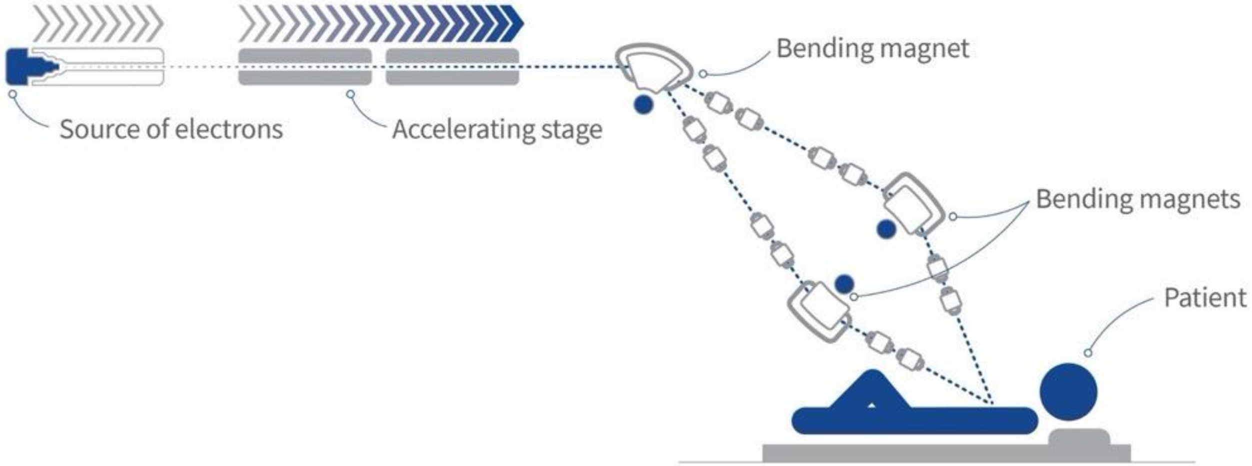
https://www.mdpi.com/2072-6694/13/19/4942/htm

FLASH VHEE therapy

CLIC technology for a FLASH VHEE facility designed by CERN in collaboration with CHUV that will be realized by THERYQ



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)

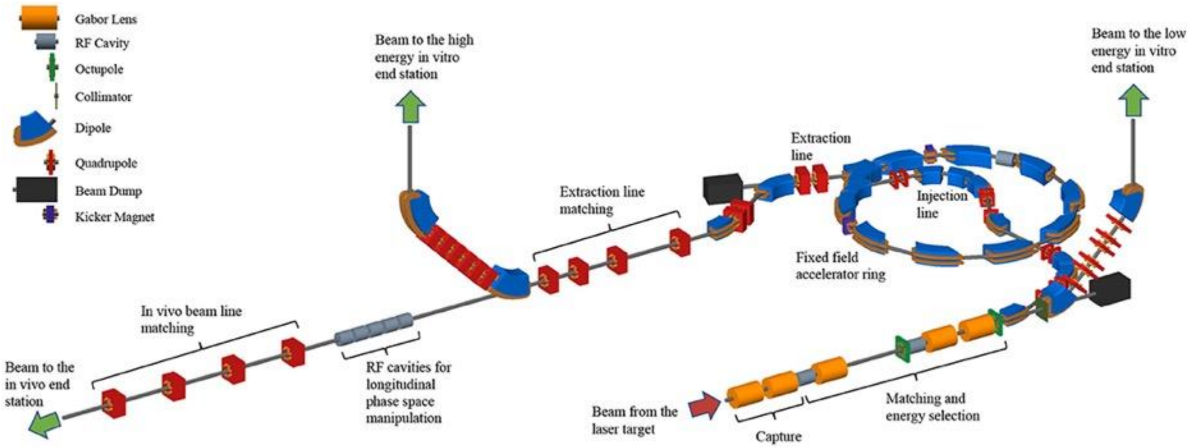
CLIC – fit facility in Lac Leman region and limit cost

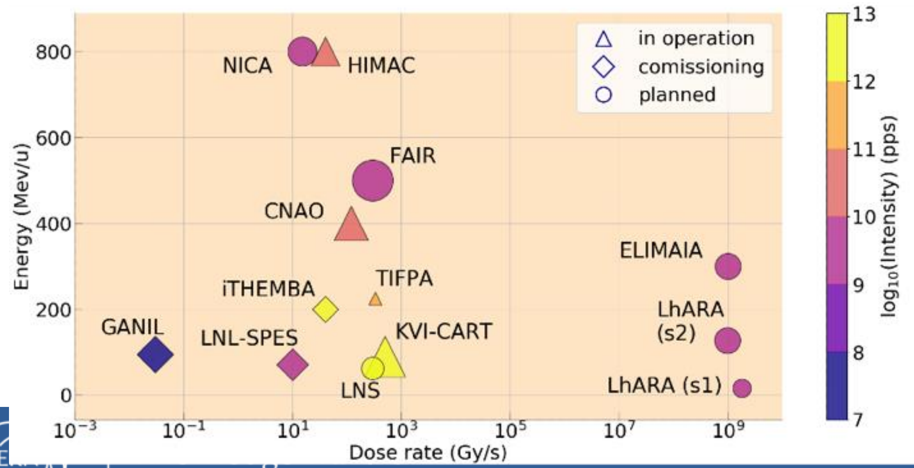
FLASH – fit facility on typical hospital campuses and limit cost of treatment

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

Look even further

Laser-hybrid Accelerator for Radiobiological Applications

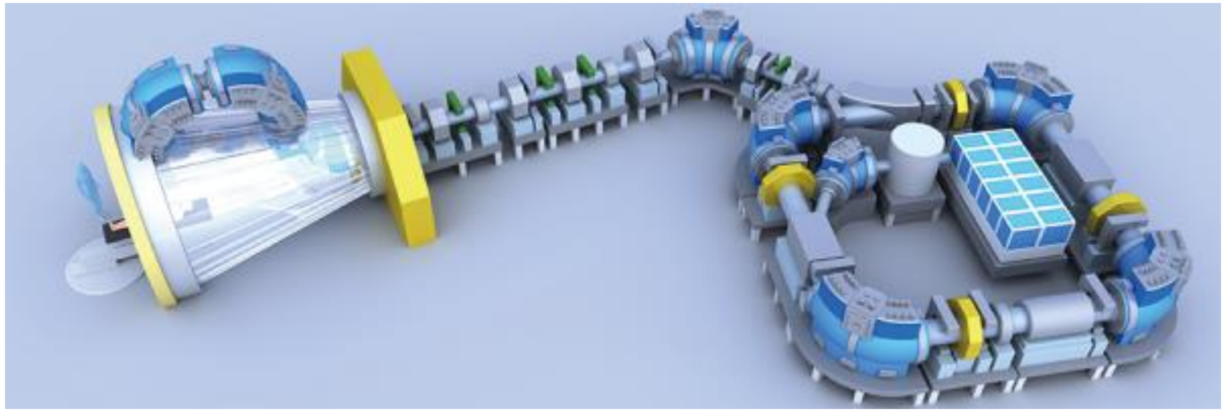




Credit: LhARA Consortium

Quantum Scalpel

National Institutes for Quantum Science and Technology



5th generation facility:

Superconducting synchrotron

Multi-ion irradiation system

Injector with laser acceleration technology

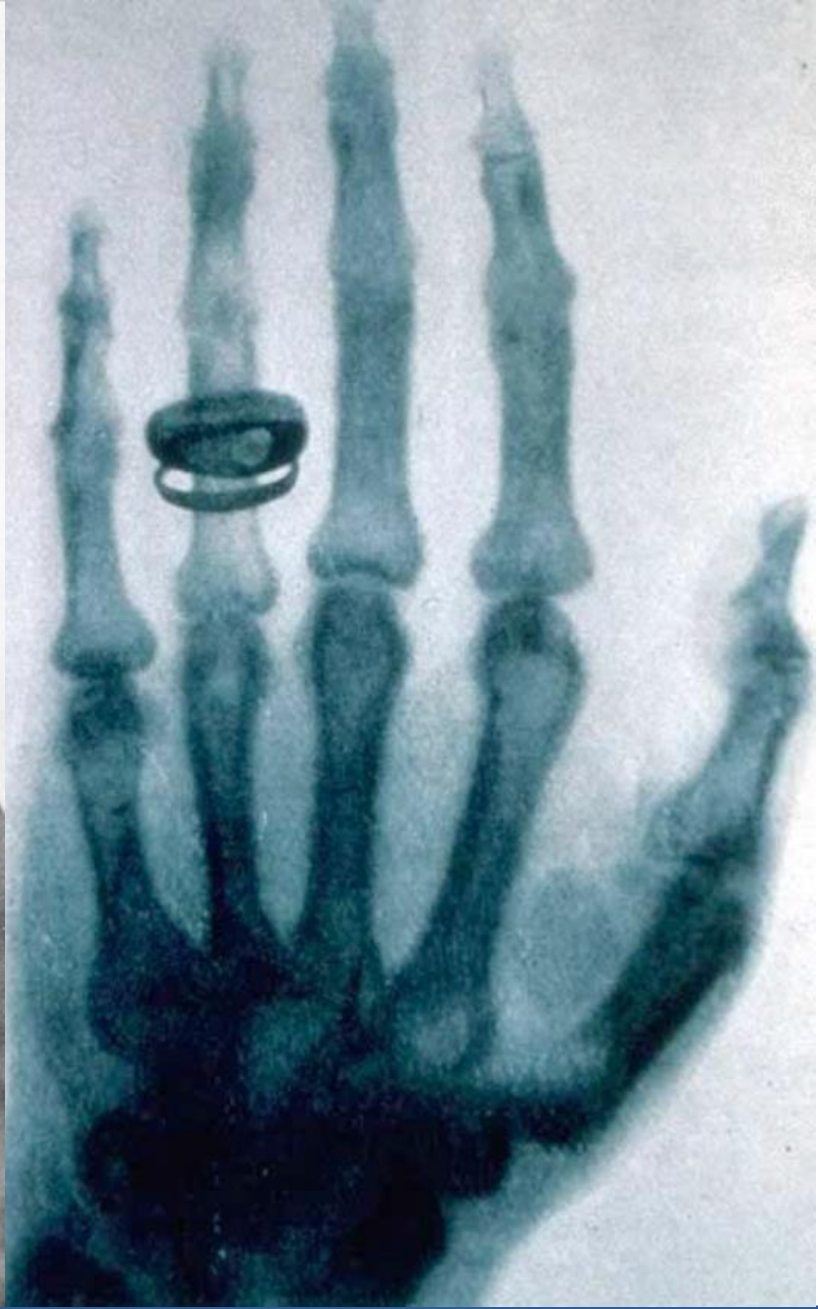
Rotating gantry with HTS magnets

Microsurgery system

End part I

Photo: CNAO treatment room

X RAYS



Georges Charpak’s MWPC

EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

File: Charpak chambers

EF-1

THE USE OF MULTIWIRE PROPORTIONAL COUNTERS
TO SELECT AND LOCALIZE CHARGED PARTICLES

G. Charpak, R. Bouclier, T. Bressani, J. Favier
and Č. Zupančič

CERN, Geneva, Switzerland.

ABSTRACT

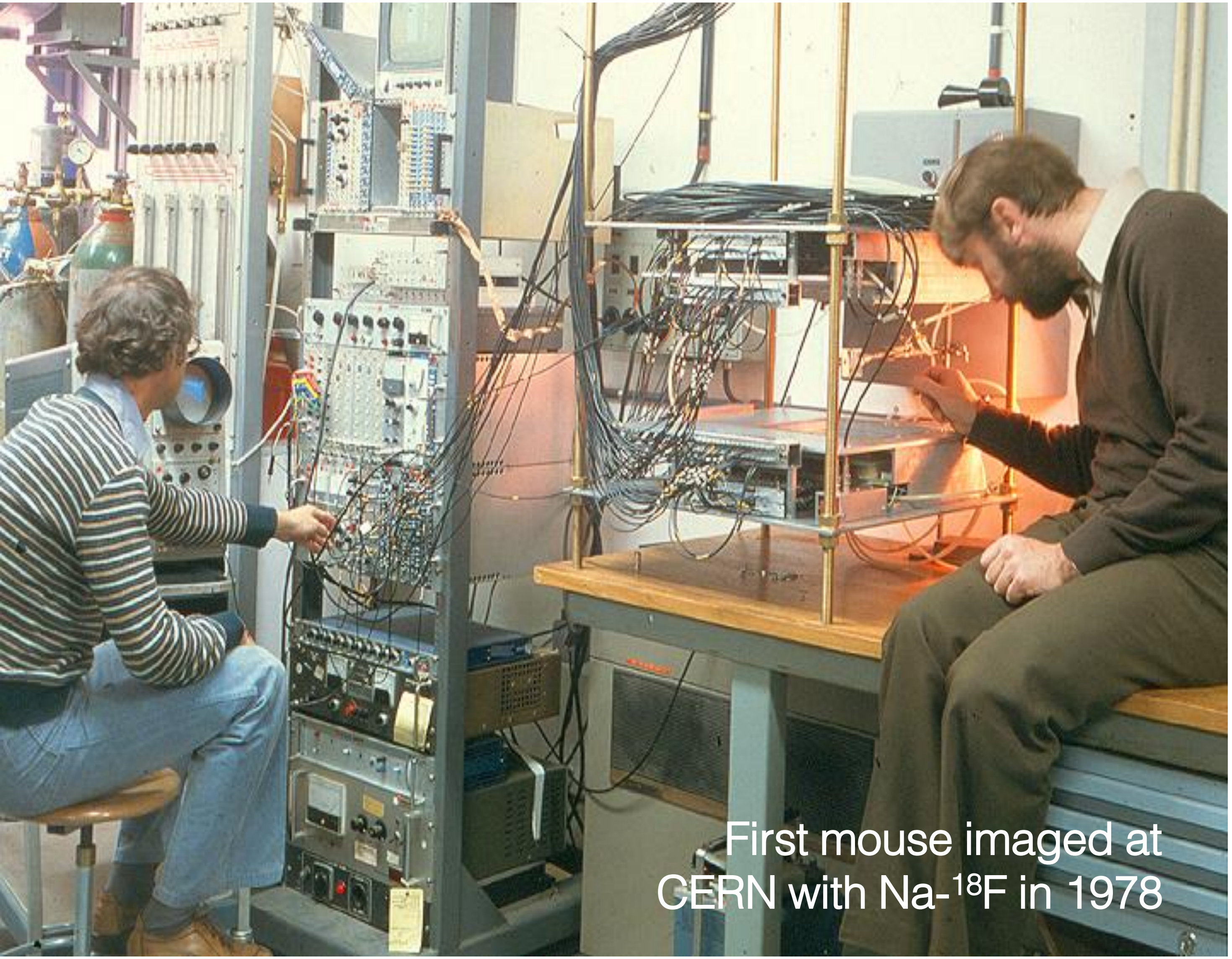
Properties of chambers made of planes of independent wires placed between two plane electrodes have been investigated. A direct voltage is applied to the wires. It has been checked that each wire works as an independent proportional counter down to separation of 0.1 cm between wires.

- Counting rates of 10^5/wire are easily reached.
- Time resolutions of the order of 100 nsec have been obtained in some gases.
- It is possible to measure the position of the tracks between the wires using the time delay of the pulses.
- Energy resolution comparable to the one obtained with the best cylindrical chambers is observed.
- The chambers can be operated in strong magnetic fields.

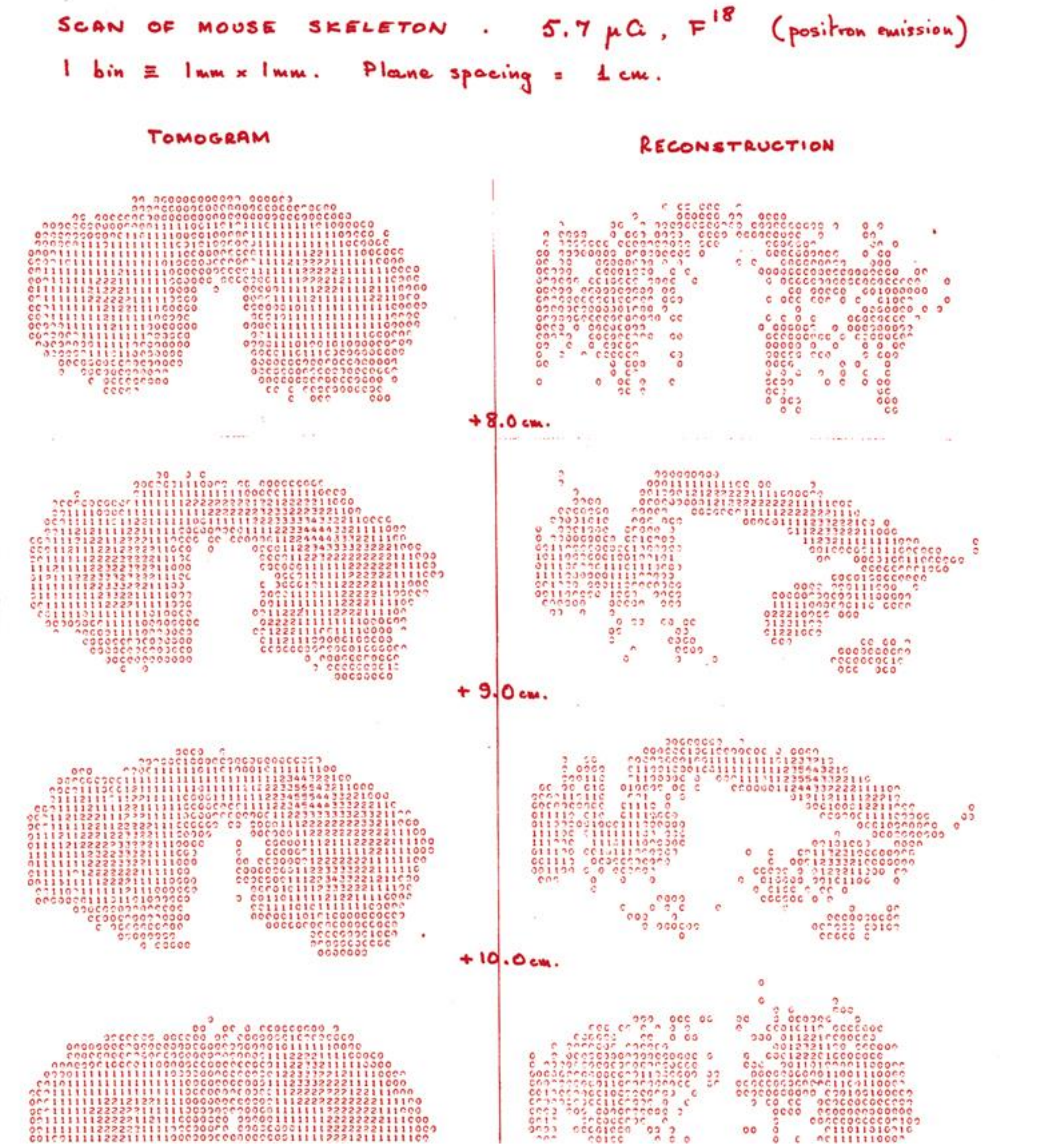
Geneva - 23 February, 1968
(Submitted to Nucl. Instrum. and Methods)

SIS/kw/sb

David Townsend, Alan Jeavons



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



David Townsend, Alan Jeavons

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

A general method for three-dimensional filter computation

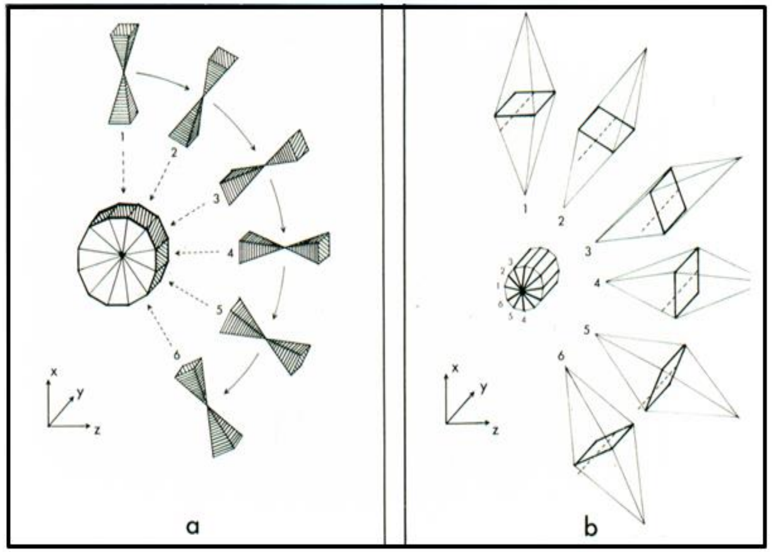
B Schorr†, D Townsend‡ and R Clack‡

† DD Division, CERN, Geneva, Switzerland

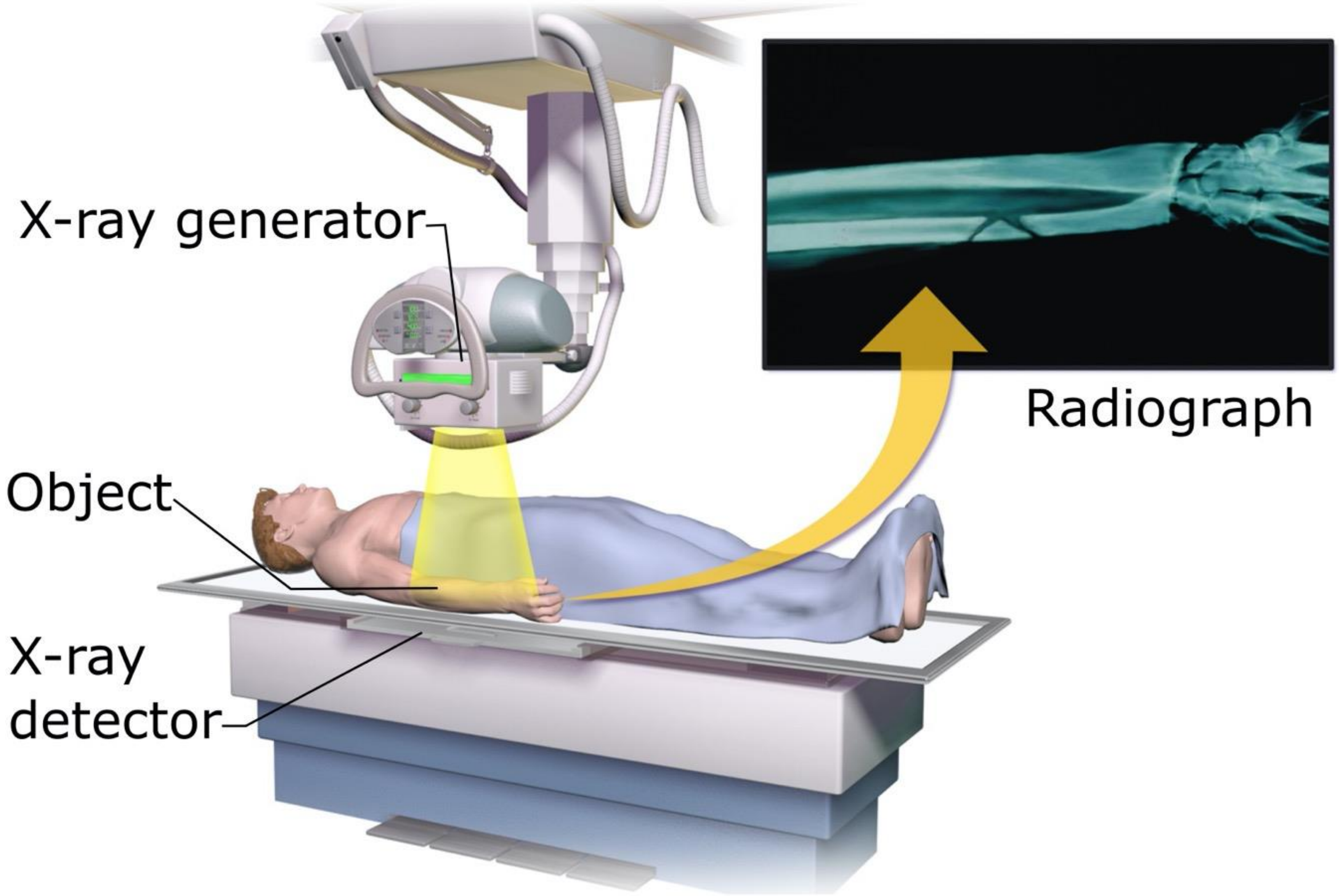
‡ Department of Nuclear Medicine, Cantonal Hospital, Geneva, Switzerland

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.

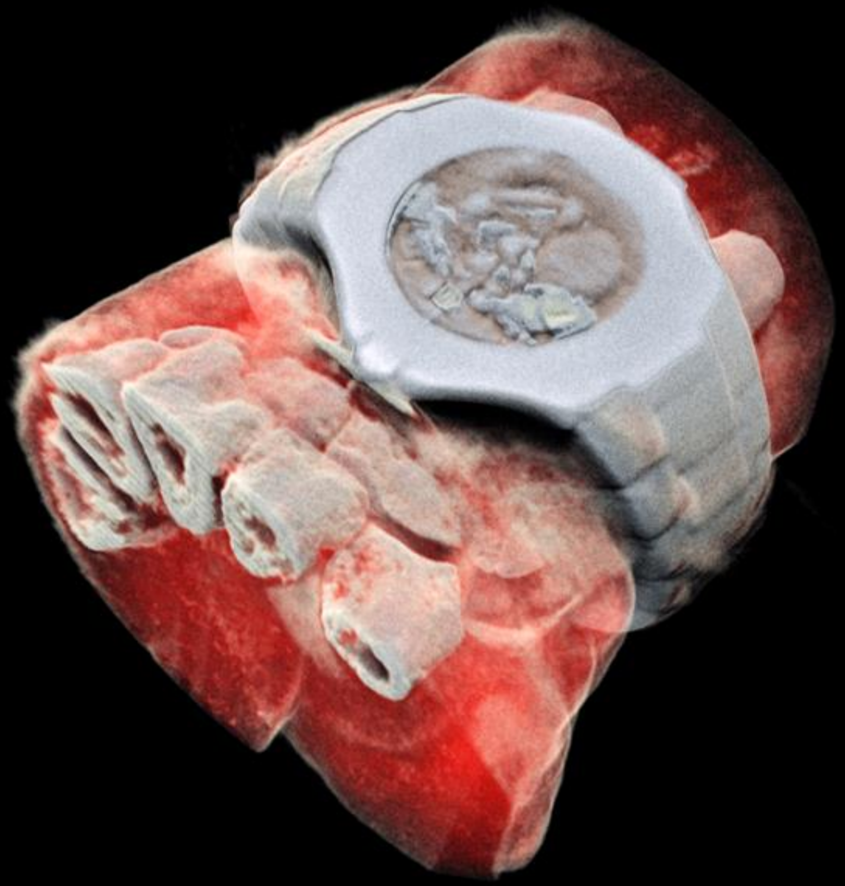


Projectional radiography



https://en.wikipedia.org/wiki/X-ray_detector#/media/File:Projectional_radiography_components.jpg
Blausen Medical Annotations by Mikael Häggström - By Blausen Medical.
https://creativecommons.org/licenses/by-sa/4.0/

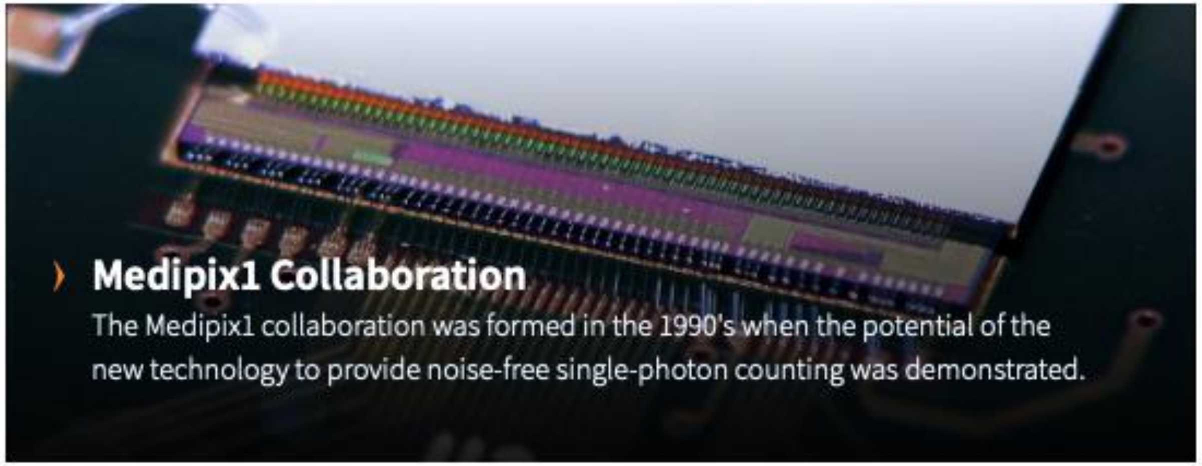
Fast forward to 2018

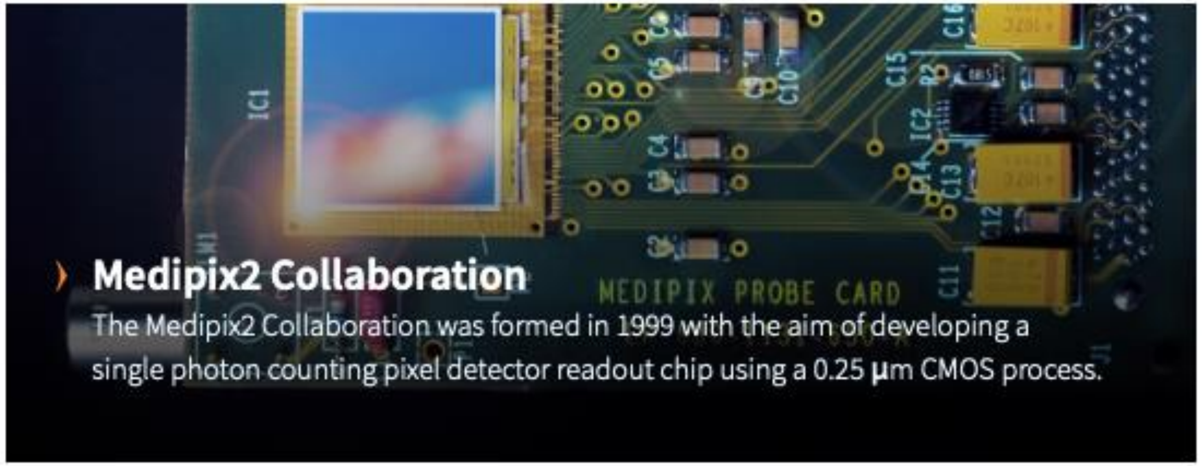


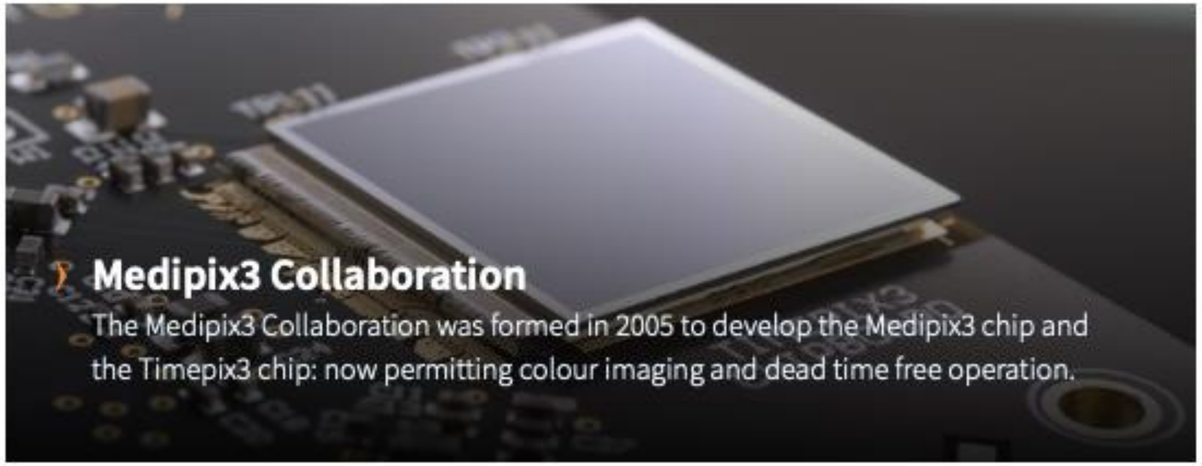
First 3D colour X-ray of human extremities using the Medipix3 technology developed at CERN

Medipix

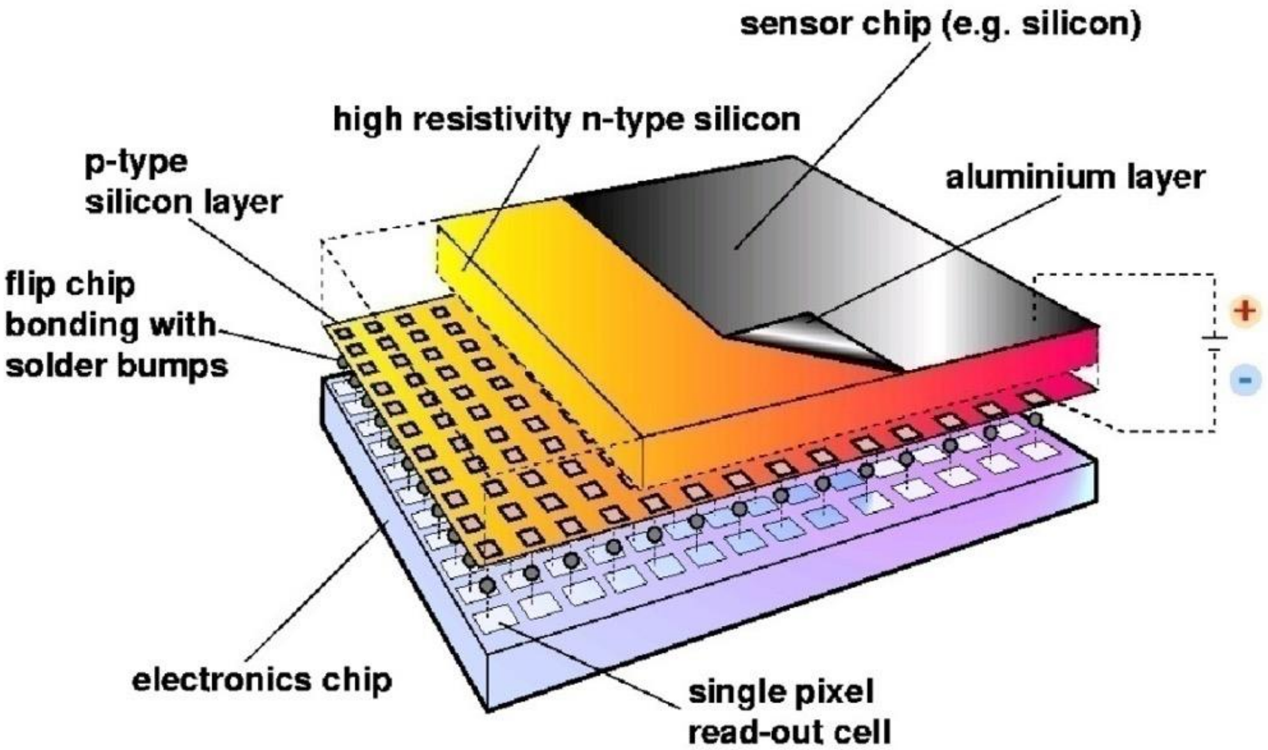
A family of pixel detector read-out chips for particle imaging and detection developed by the Medipix Collaborations

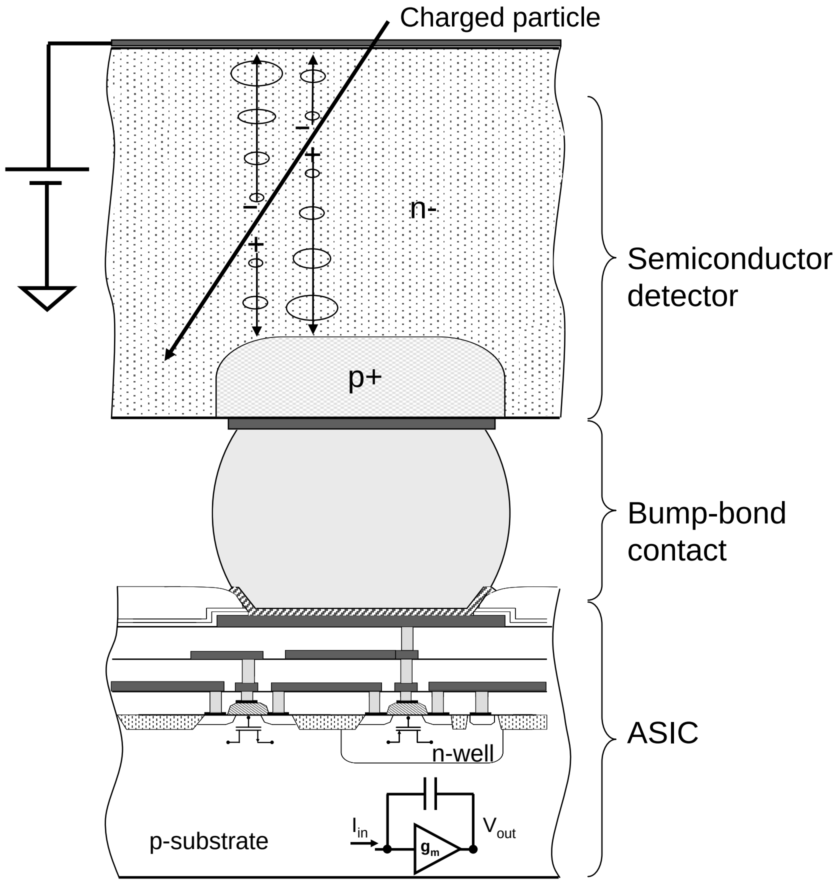






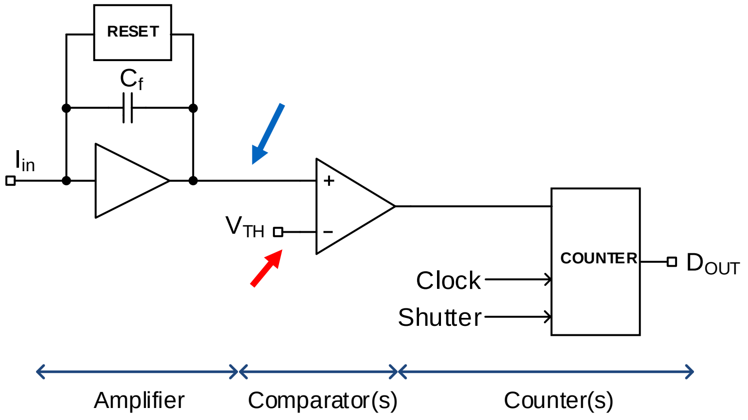
Hybrid Silicon Pixel Detectors

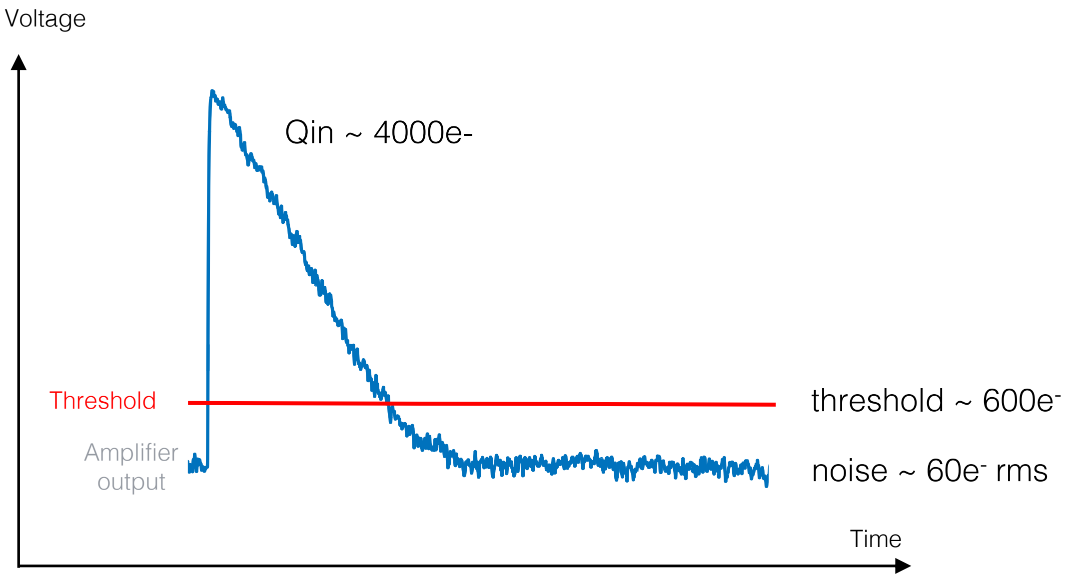


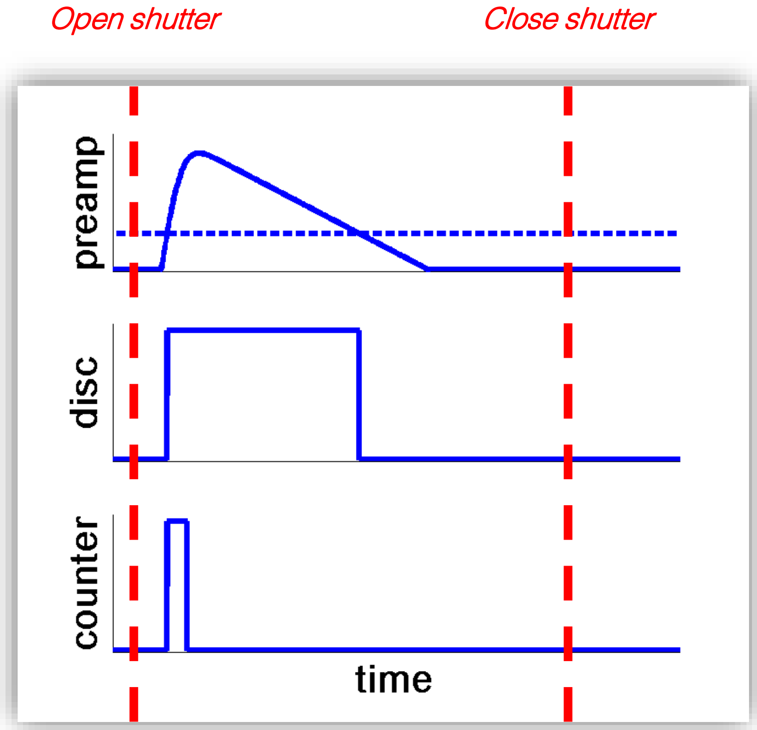


Noise-hit free particle detection
Standard CMOS can be used allowing on-pixel signal processing
Sensor material can be changed (Si, GaAs, CdTe..)

Hybrid Silicon Pixel Detectors: counting electronics

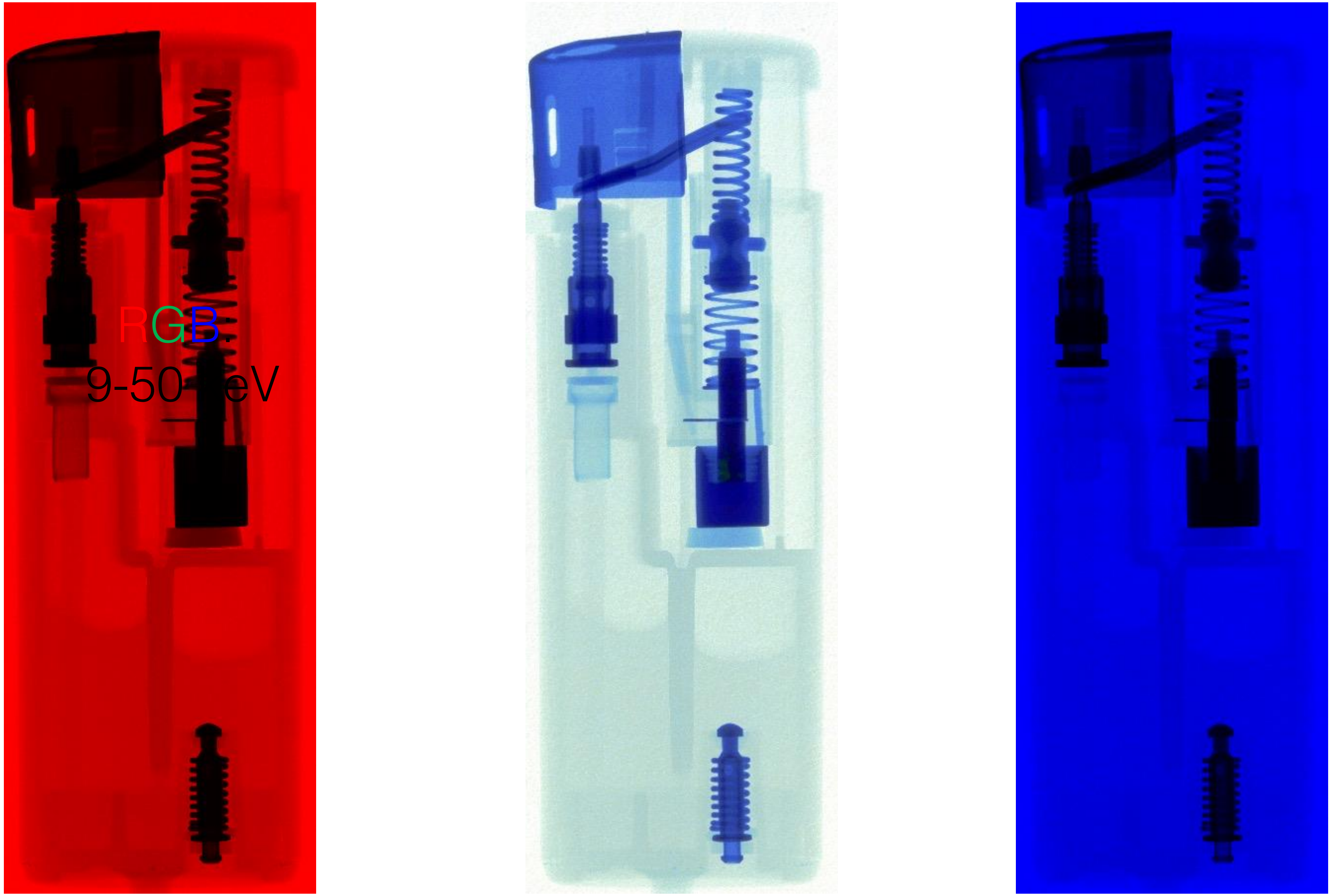






→ Noise hit free imaging

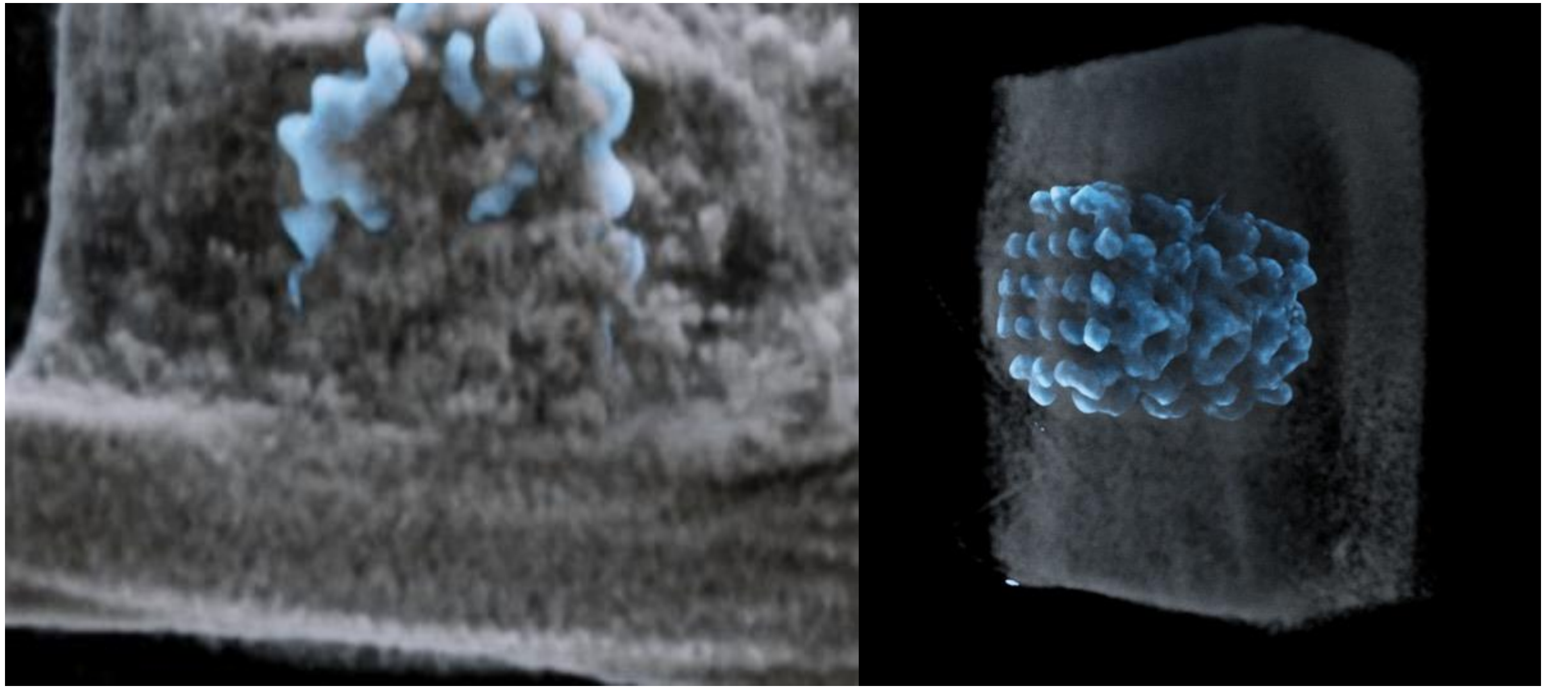
Colour x-ray of a lighter



S. Procz et al.

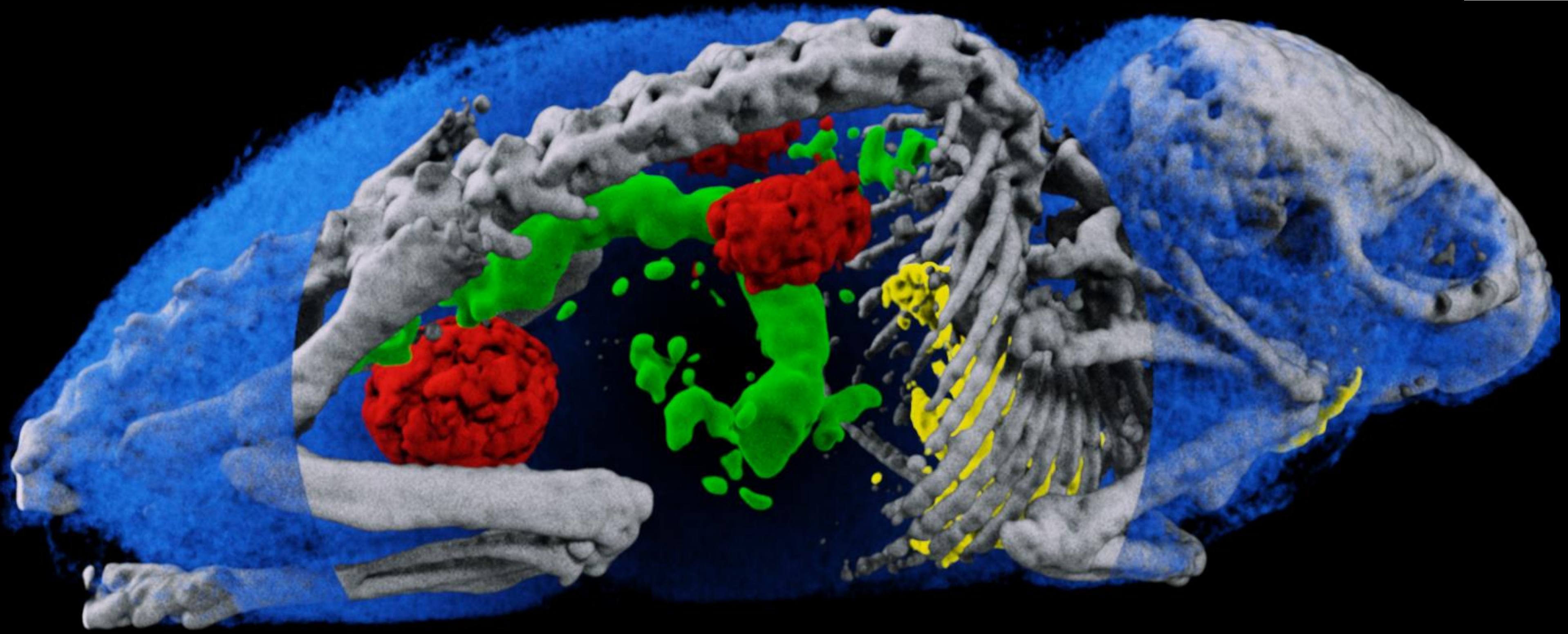
Spectral imaging of Joints

Titanium implant in sheep bone



Enables better understanding of
- process of bone ingrowth
- bone / implant interface

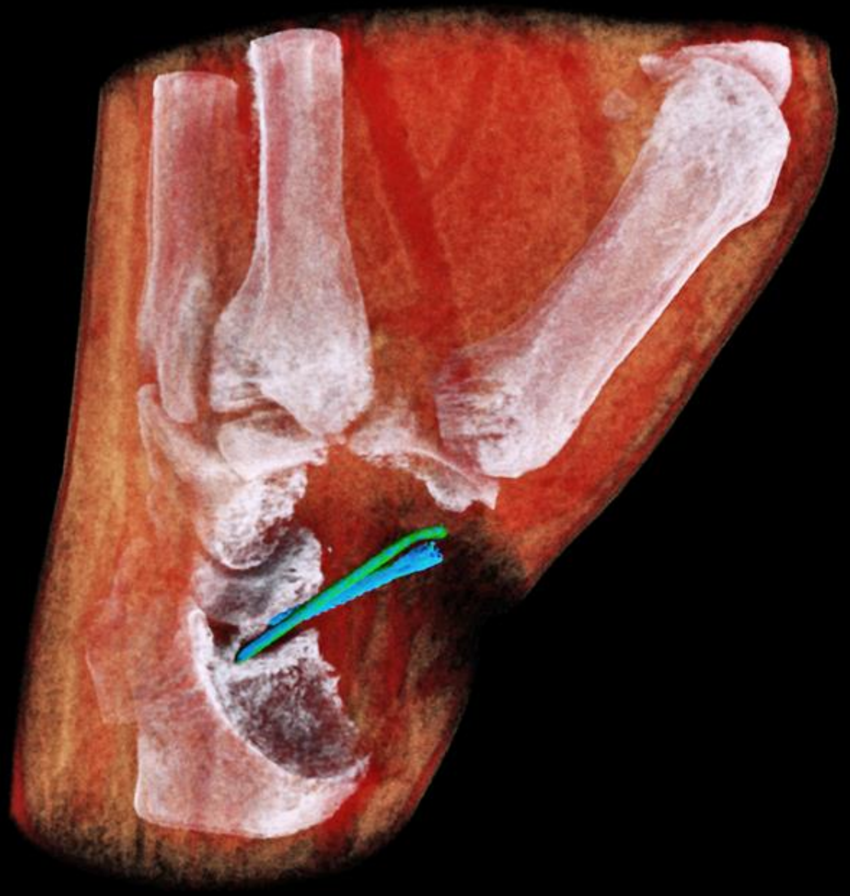
Spectroscopic information permits material separation



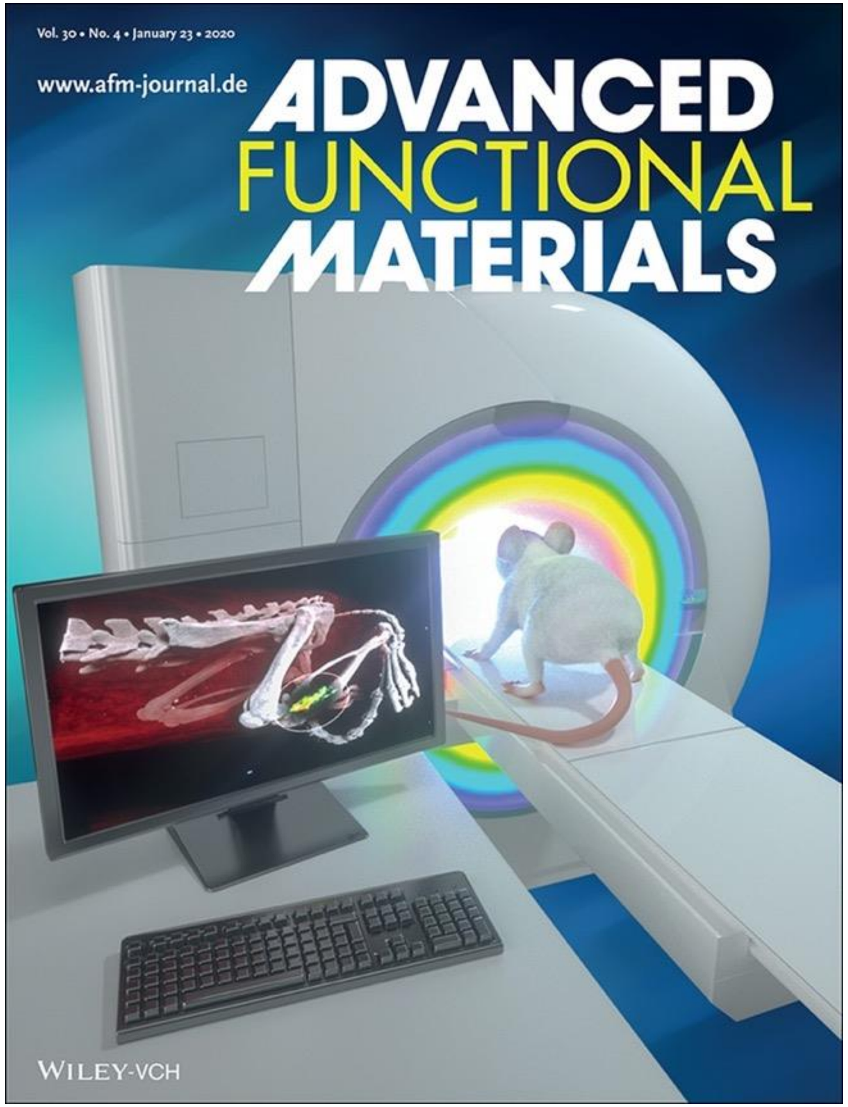
The water has been partly cut away to reveal the bone, gold, gadolinium and iodine

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

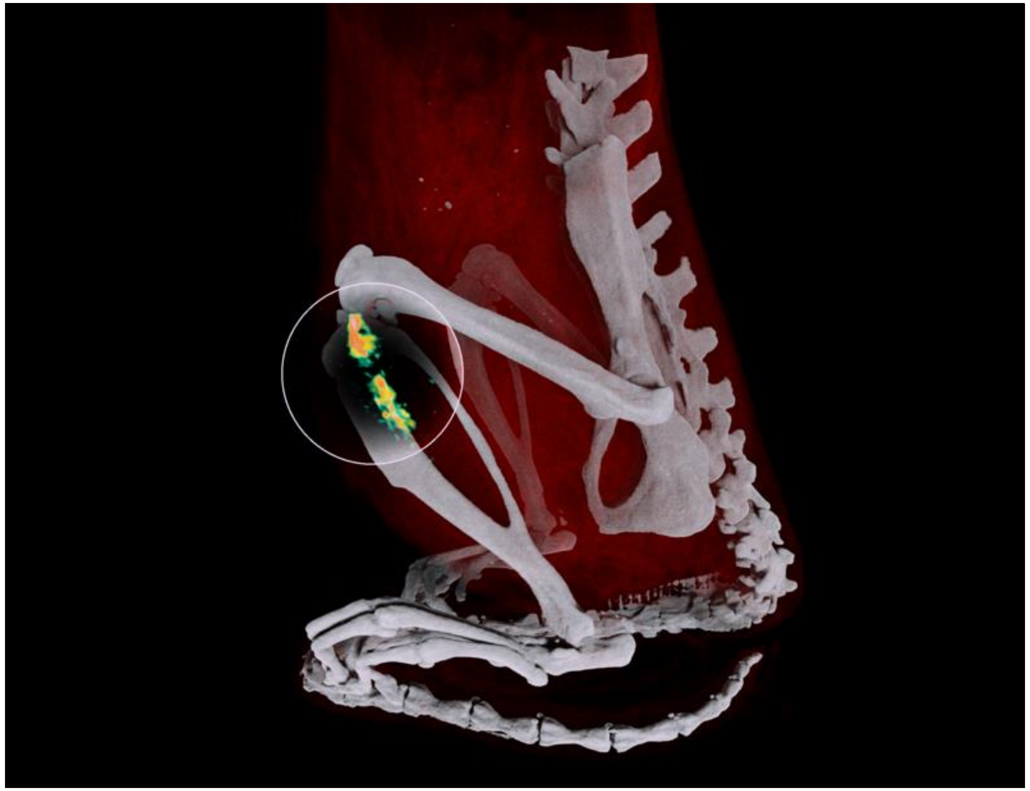
Spectral CT image showing wrist implant



Hafnia accumulation at bone microcracks



mars

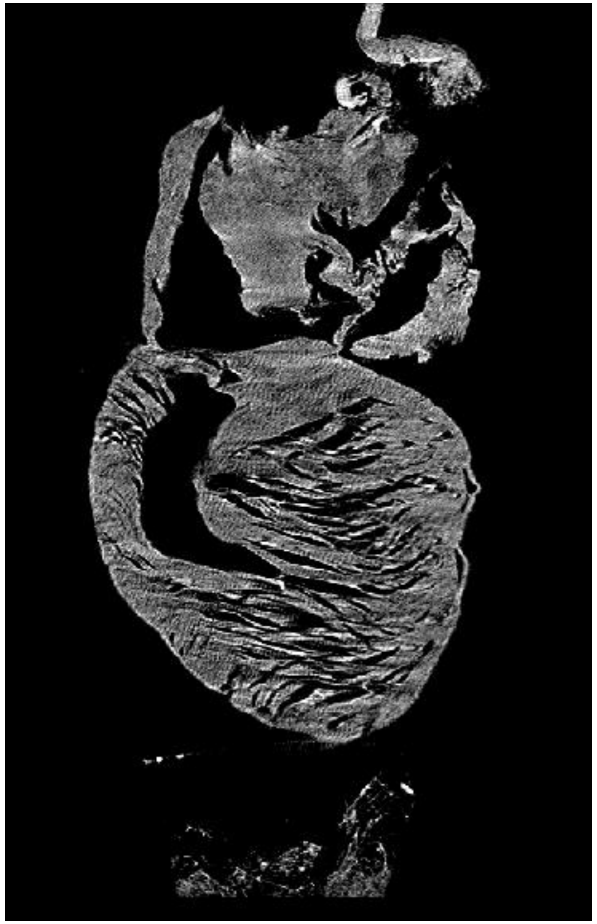


Molecular imaging using metal nanoparticles - spectral CT

Colour 3D X-ray image of a fatty deposit on an artery (carotid plaque) taken using a Medipix3 detector

Image by Mars Bio-Imaging
Feature article link:
https://rdcu.be/bOFuR

mars

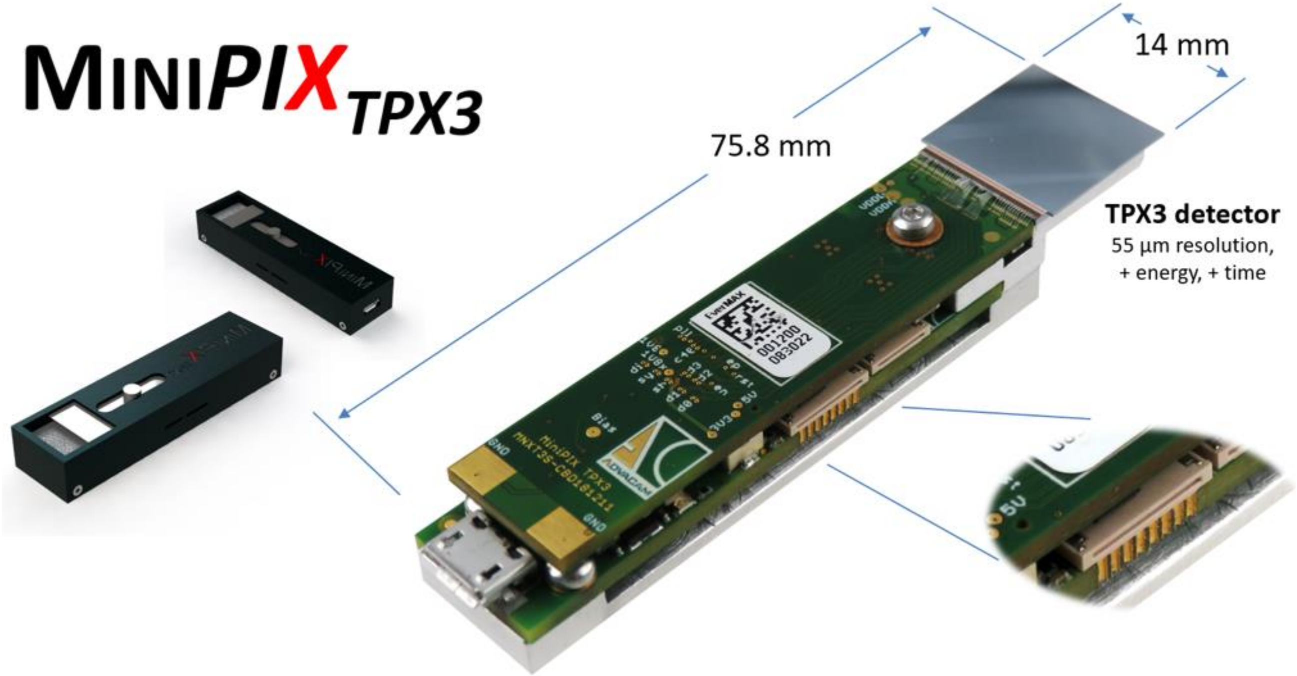


Ethanol-preserved mouse heart scanned using the WidePIX$_{10x5}$ detector
60 kVp tungsten spectrum
720 projections, 5 seconds per projection (one hours total)
Spatial resolution ca. 7 μm
Reconstructed using Volex, visualized using CTVox and Amide software

MiniPIX TPX3

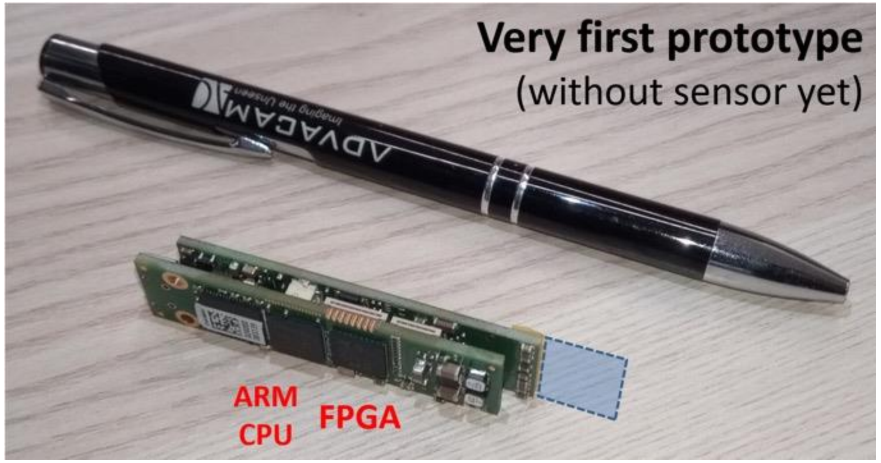
Miniaturized spectral camera supporting Si and CdTe sensors

MiniPIX TPX3

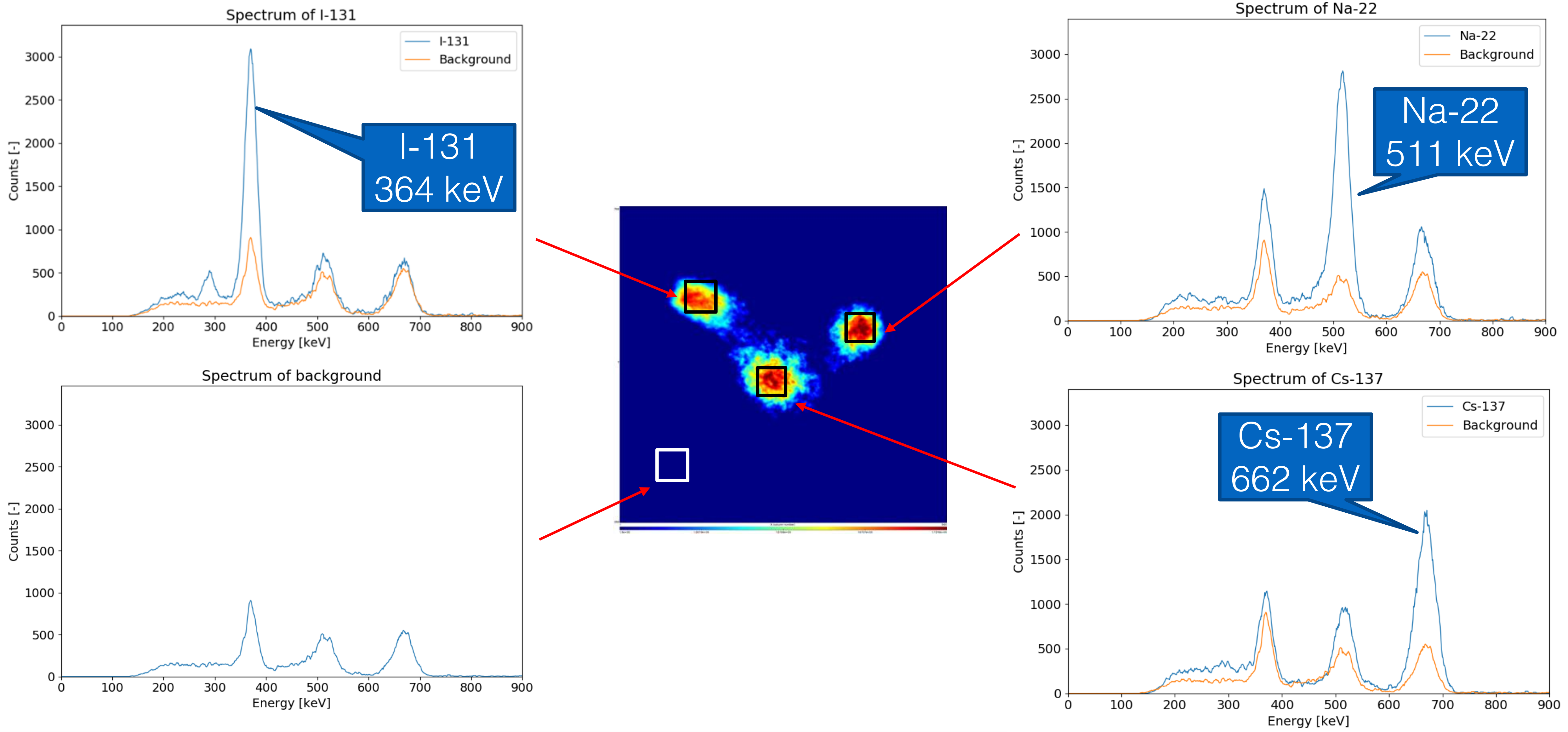


ADVACAM
Imaging the Unseen

It's really small...



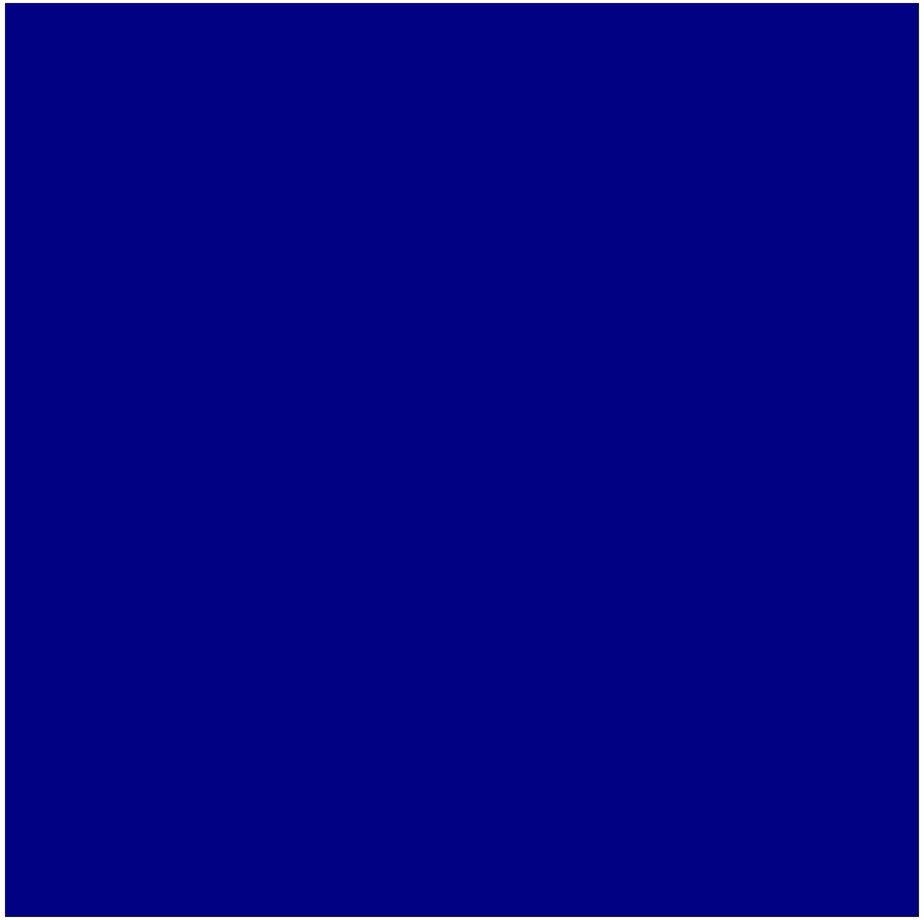
Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

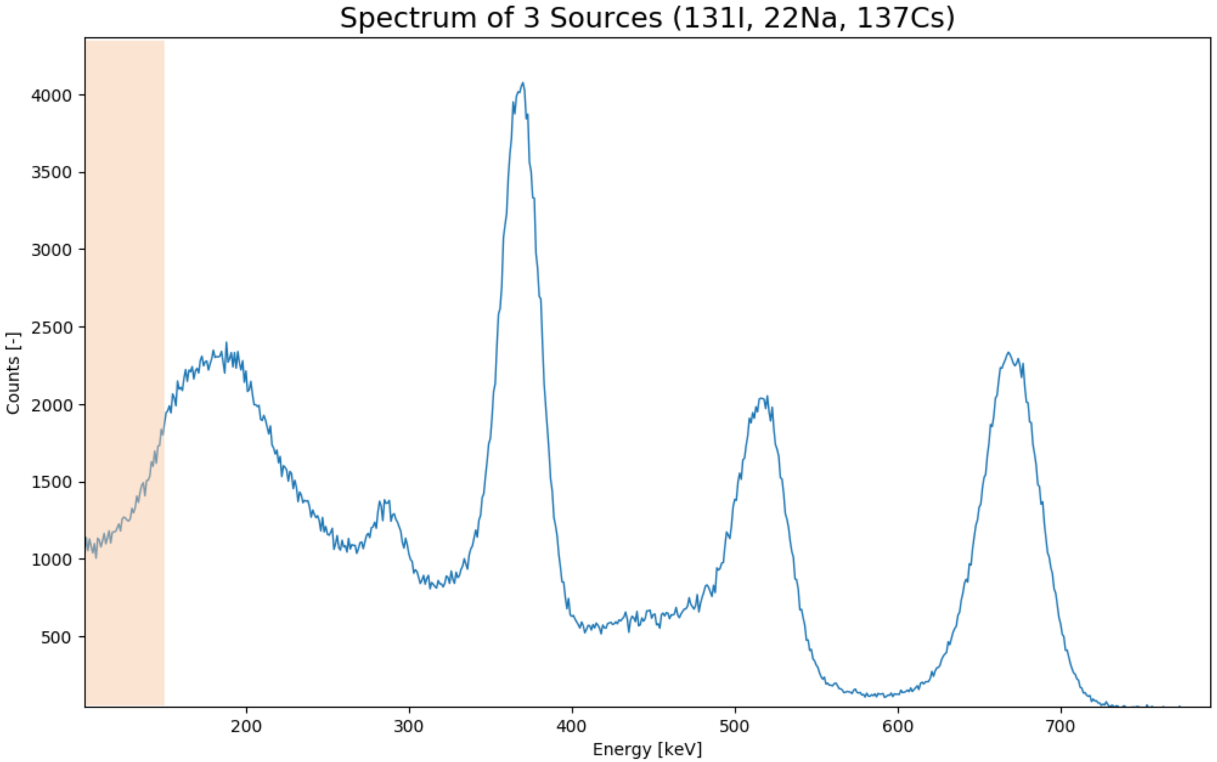


Slide courtesy of D. Turecek, ADVACAM s.r.o.

Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

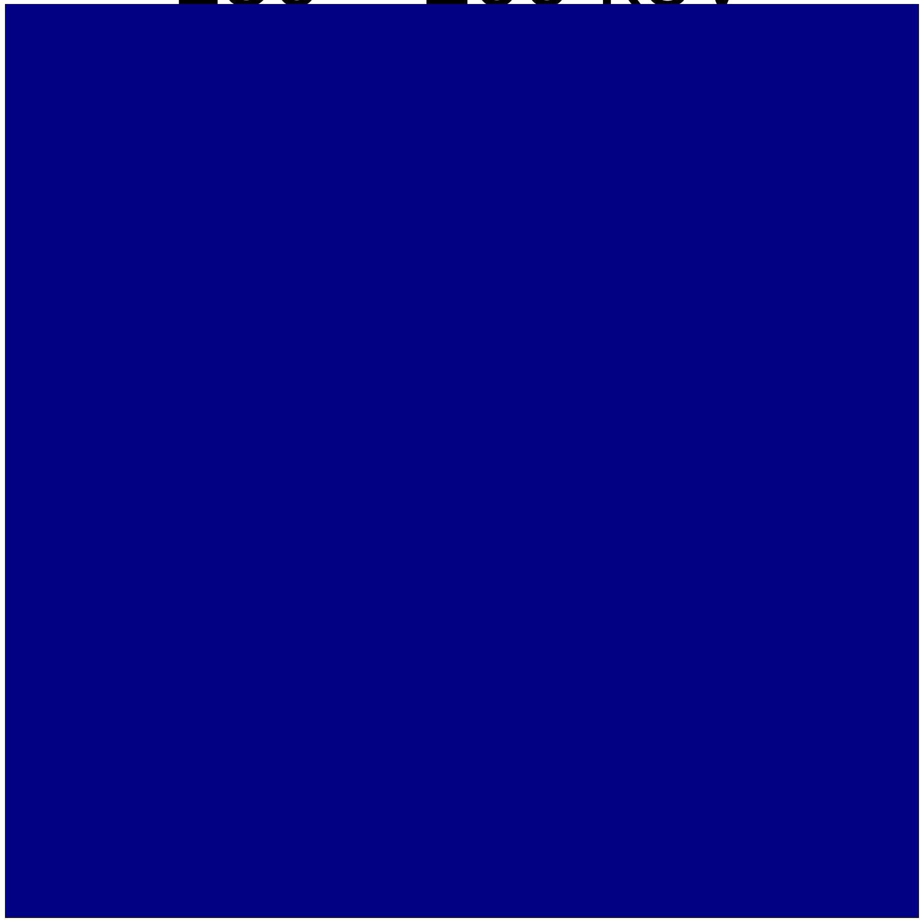
100 – 150 keV

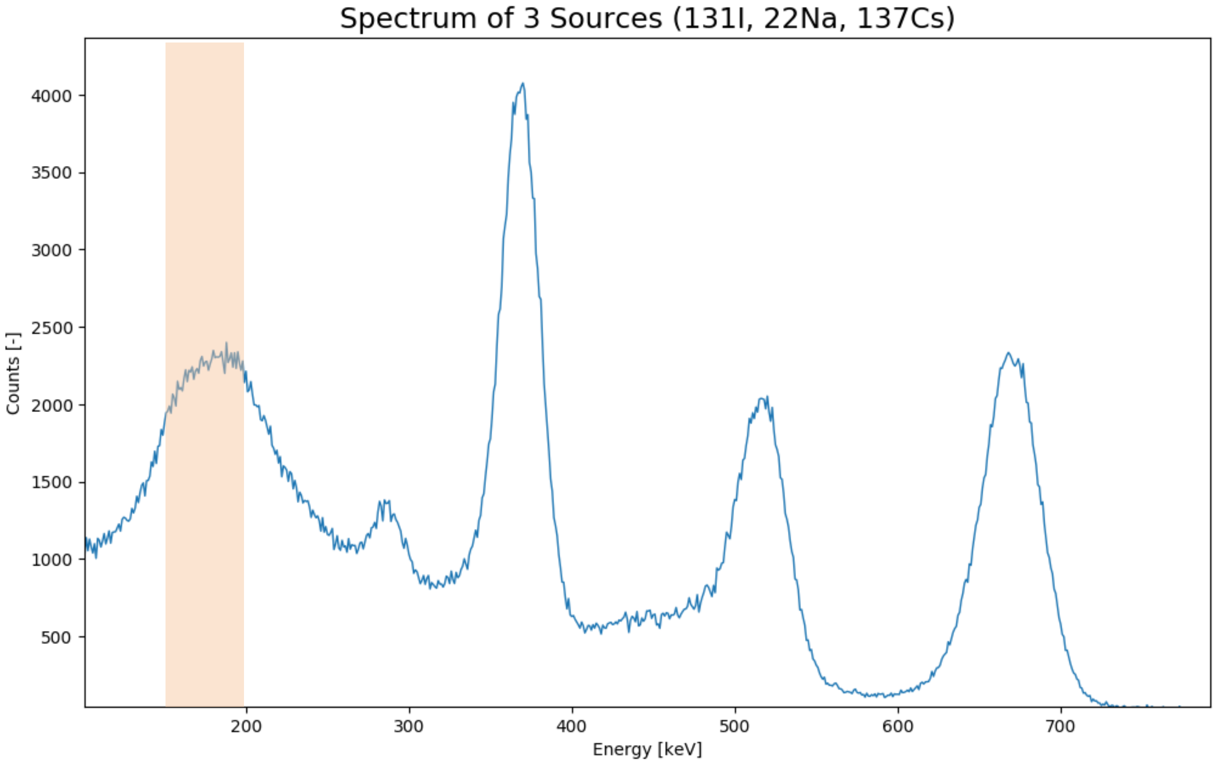




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

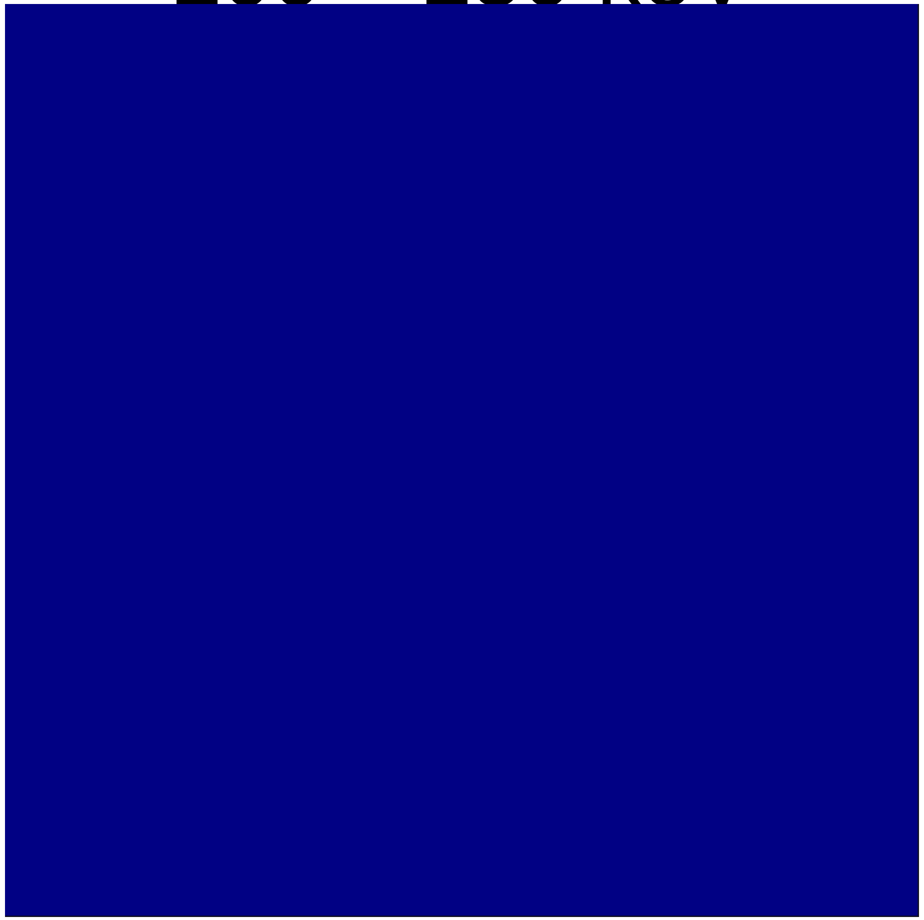
150 – 200 keV

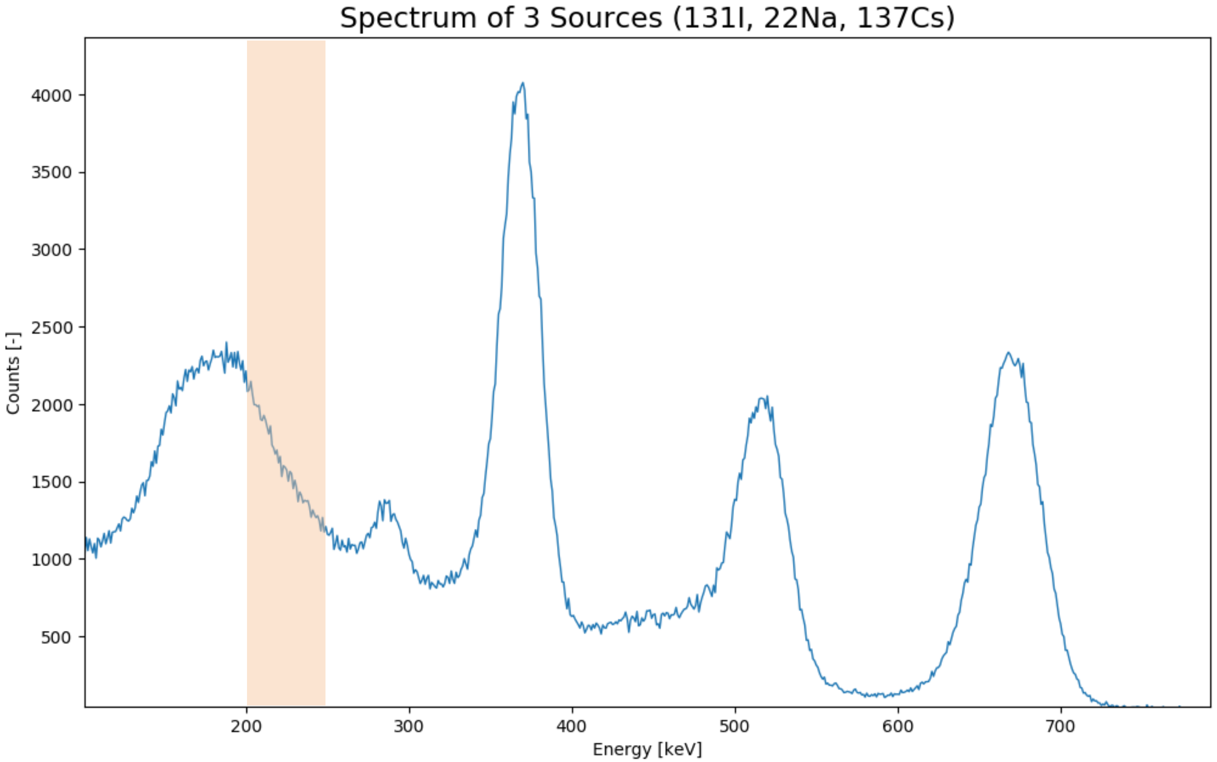




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

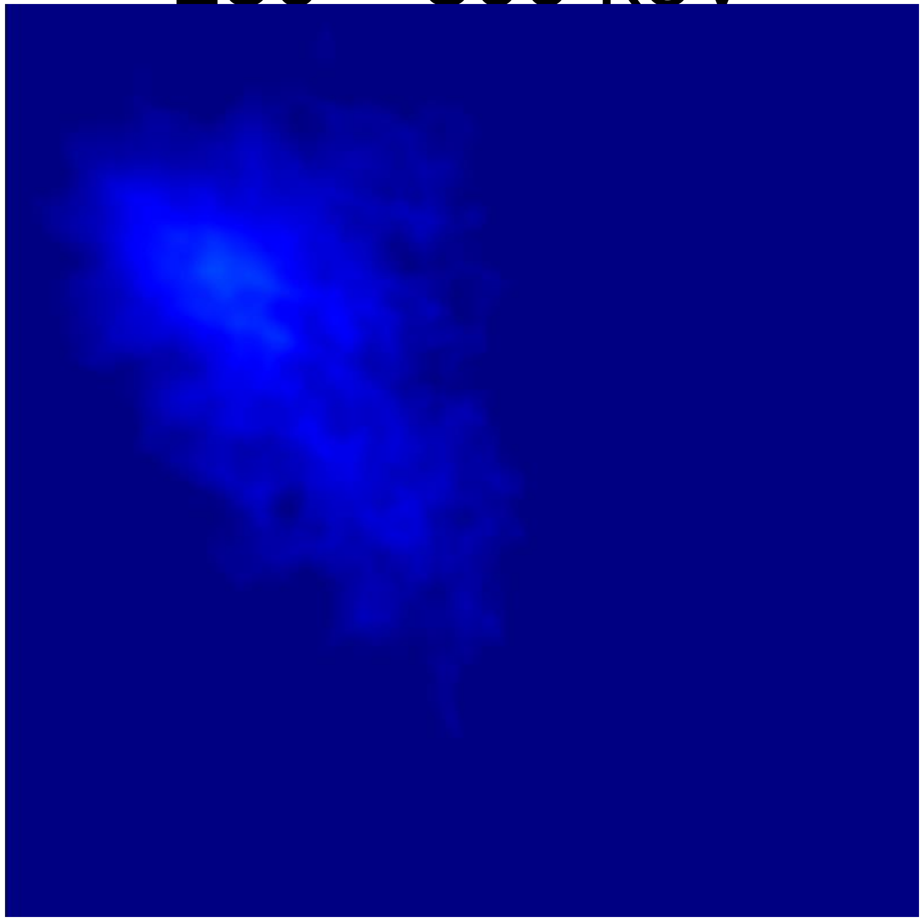
200 – 250 keV

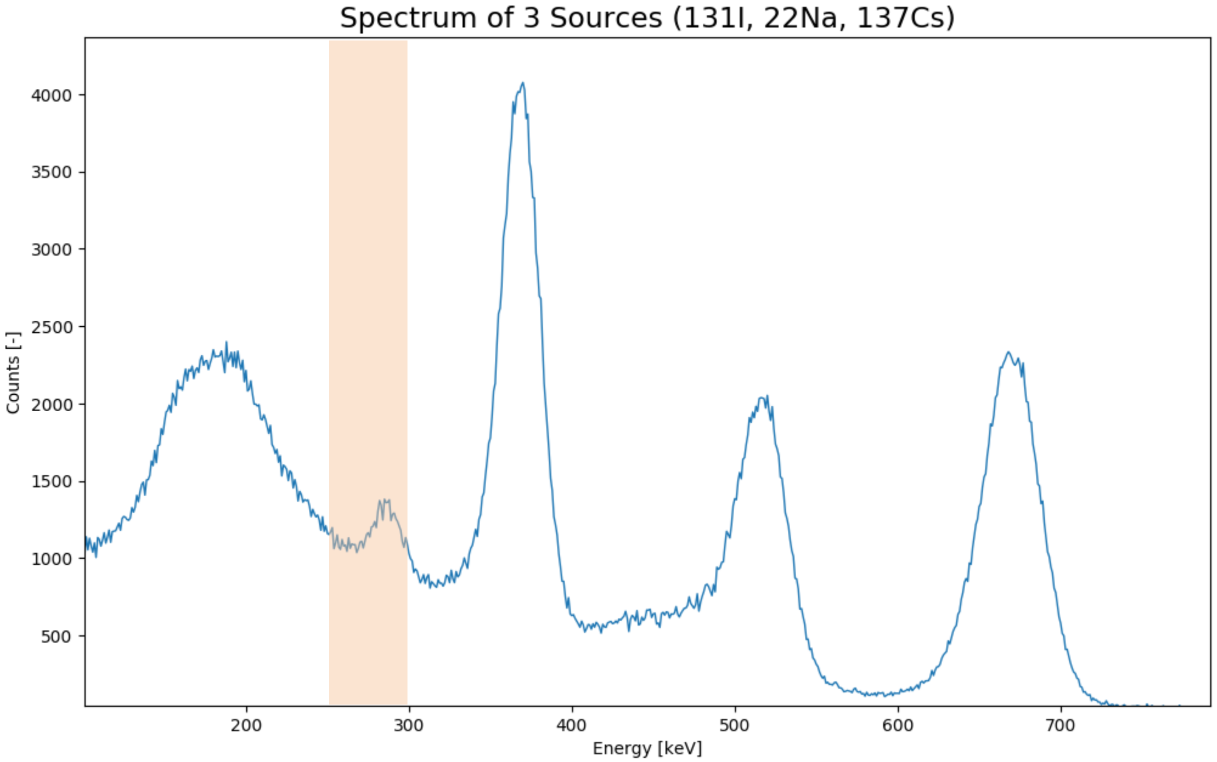




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

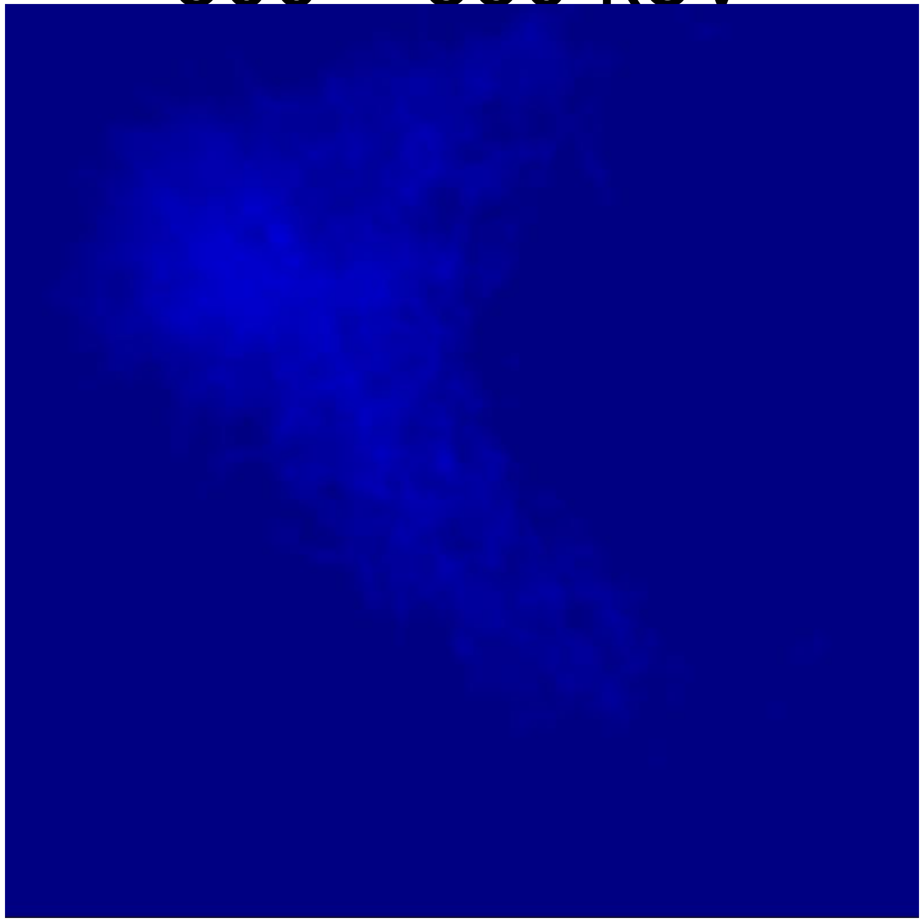
250 – 300 keV

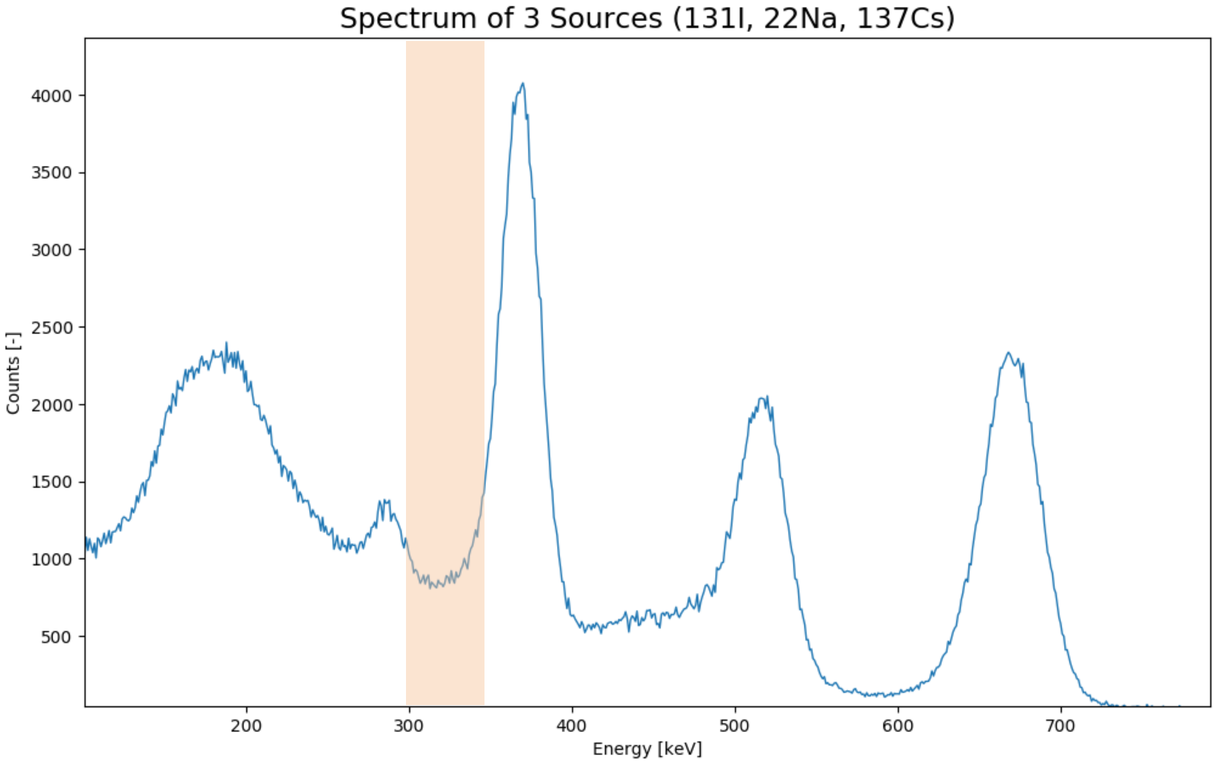




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

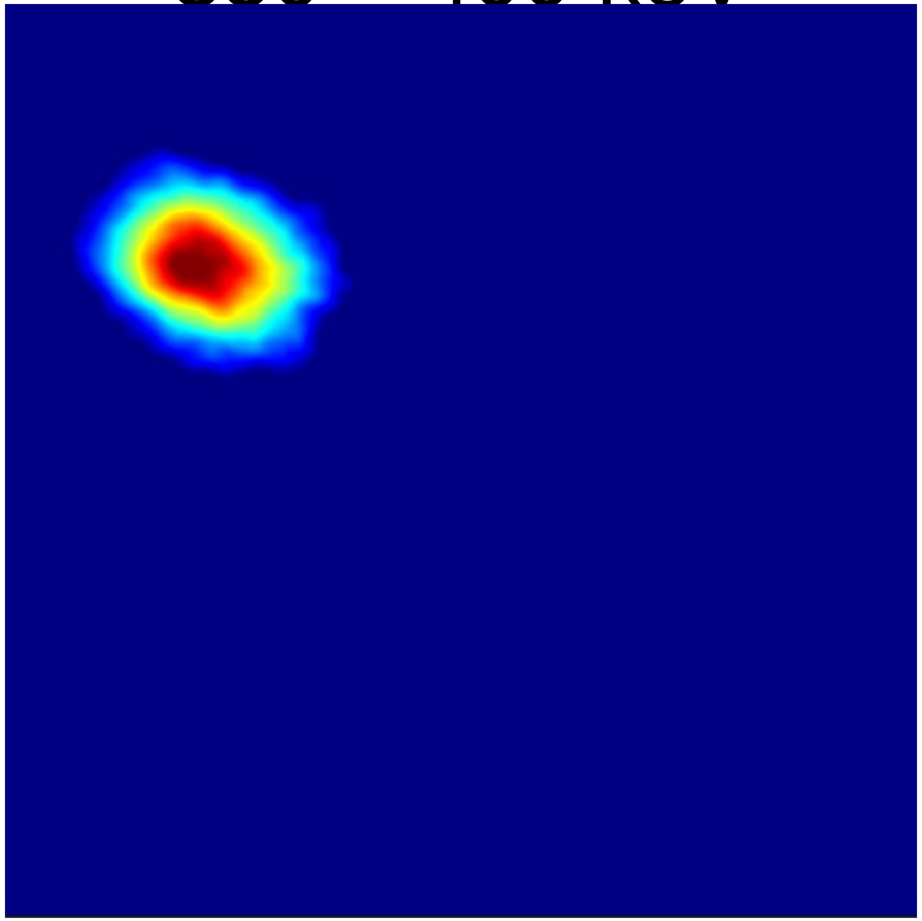
300 – 350 keV

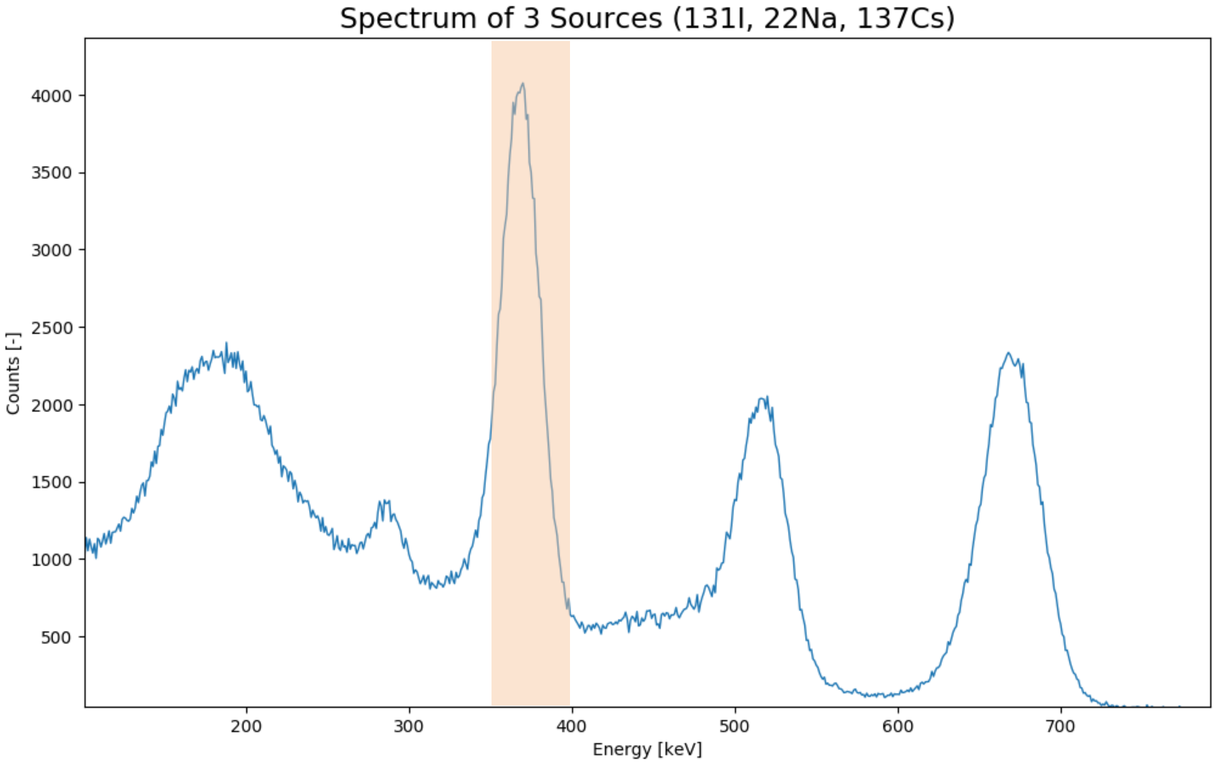




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

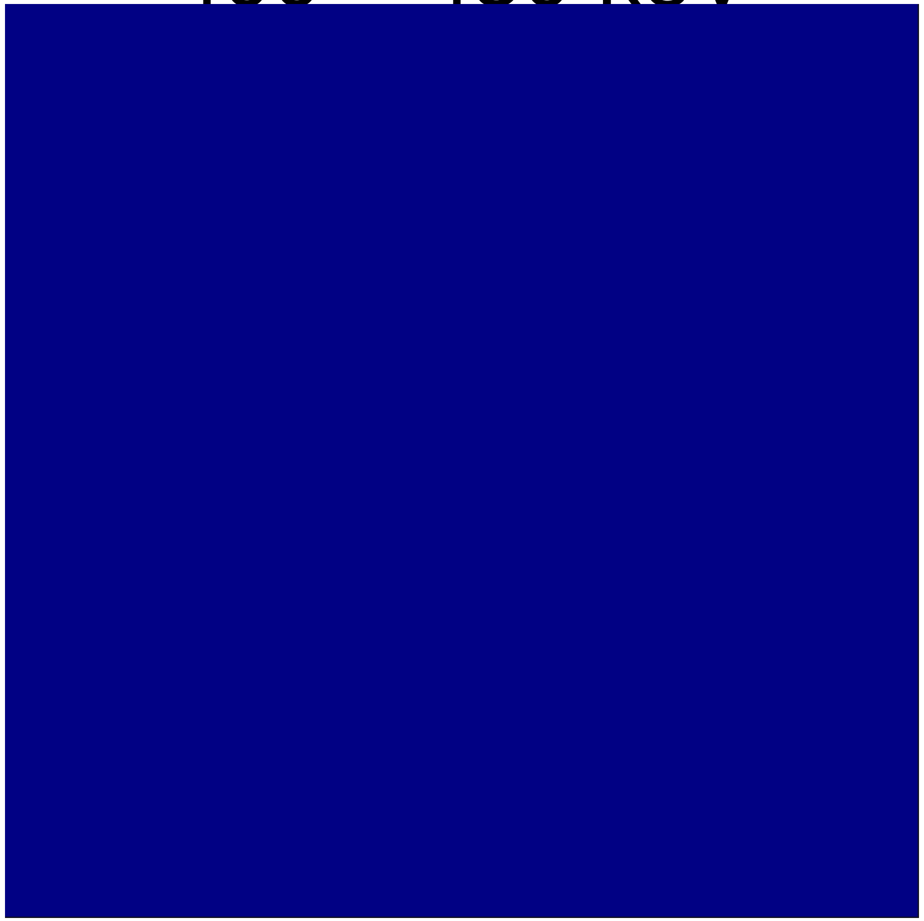
350 – 400 keV

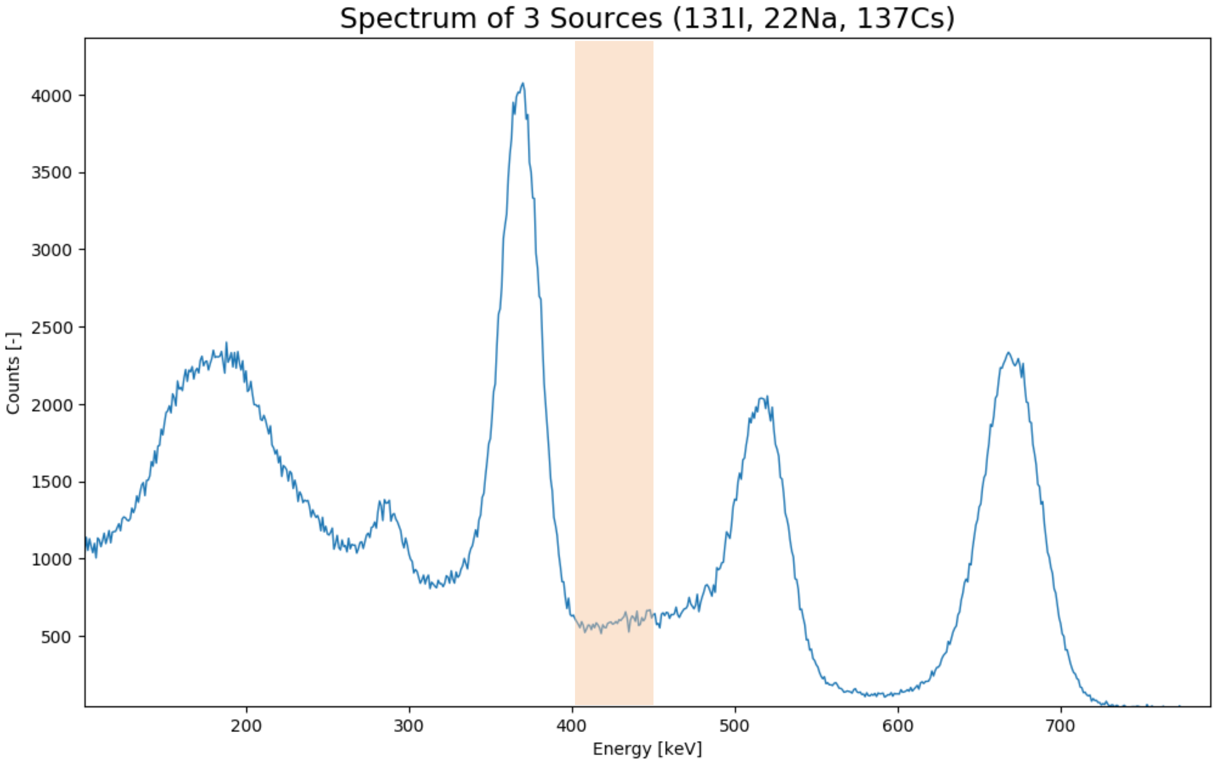




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

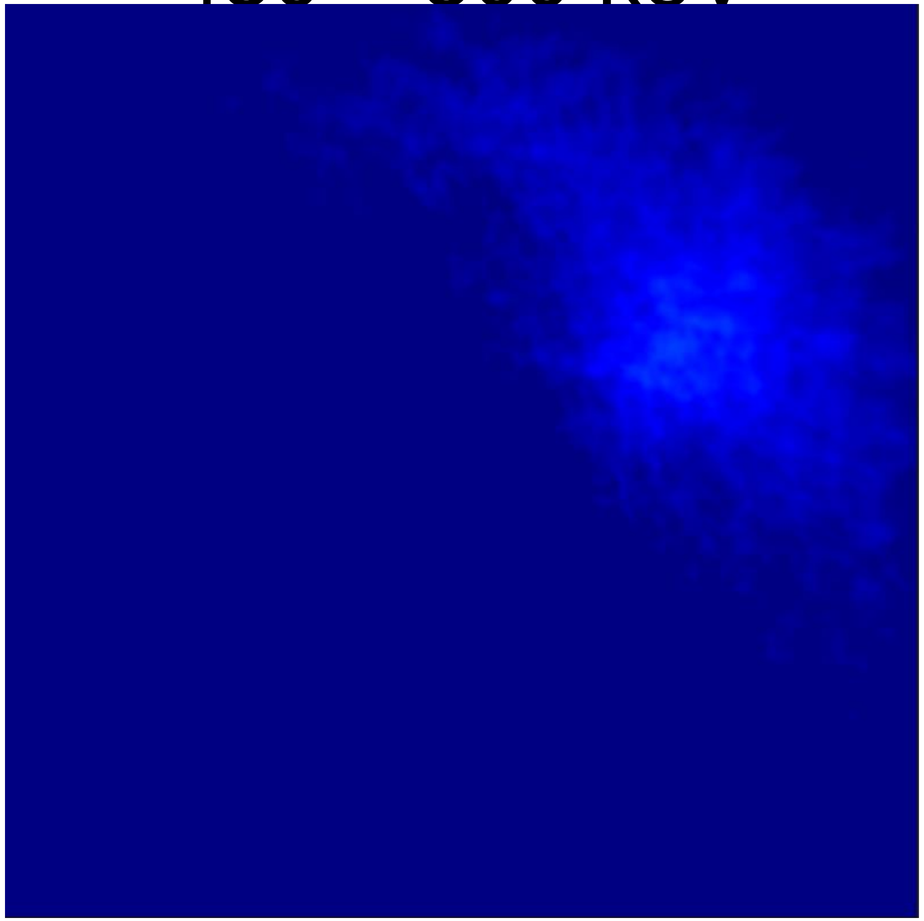
400 – 450 keV

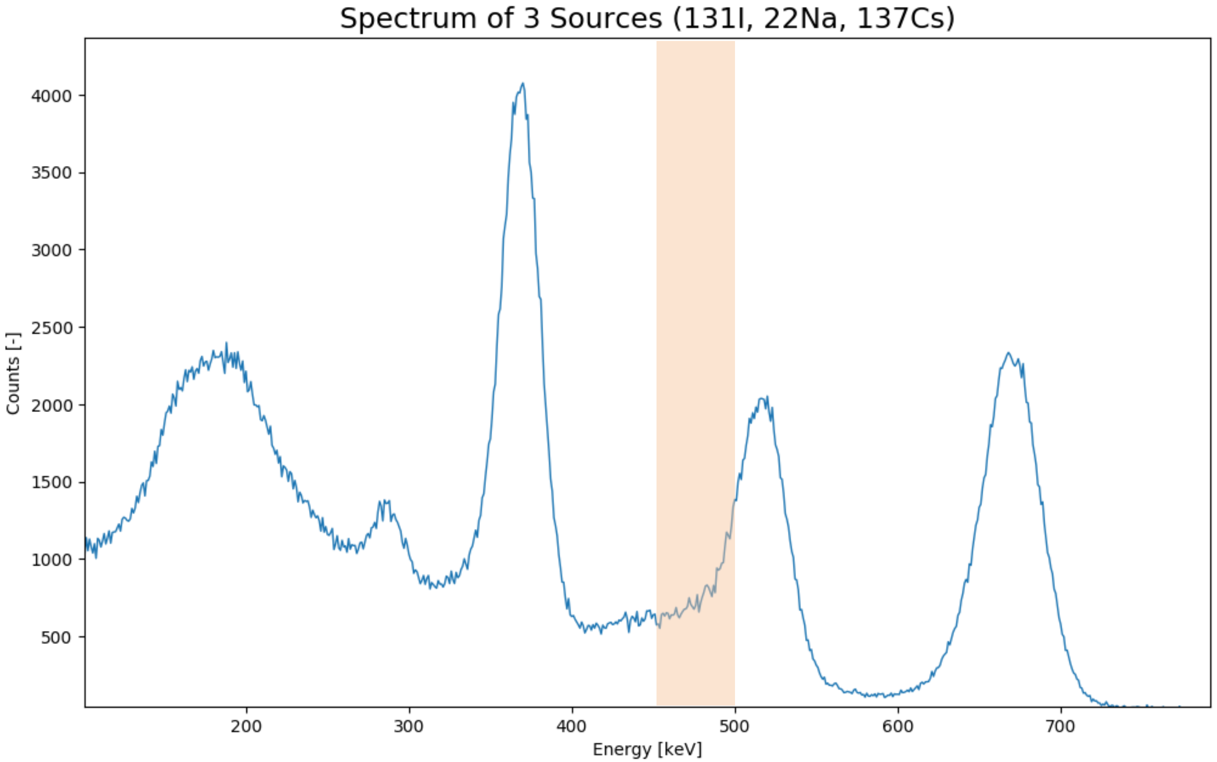




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

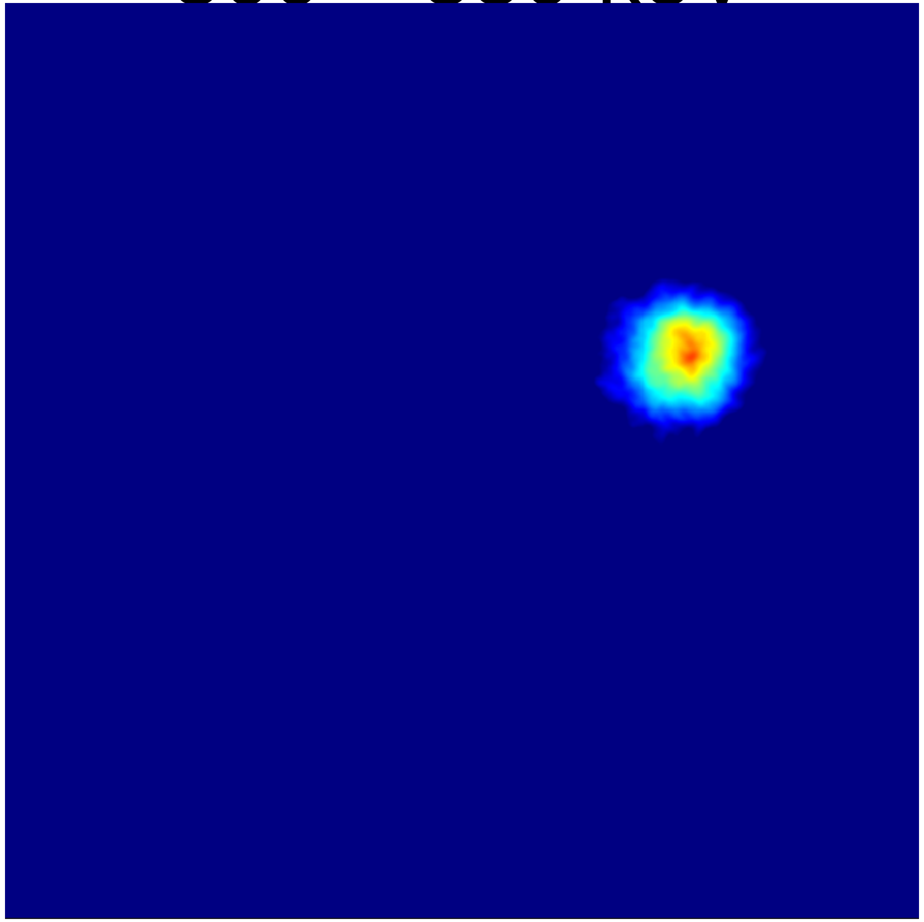
450 – 500 keV

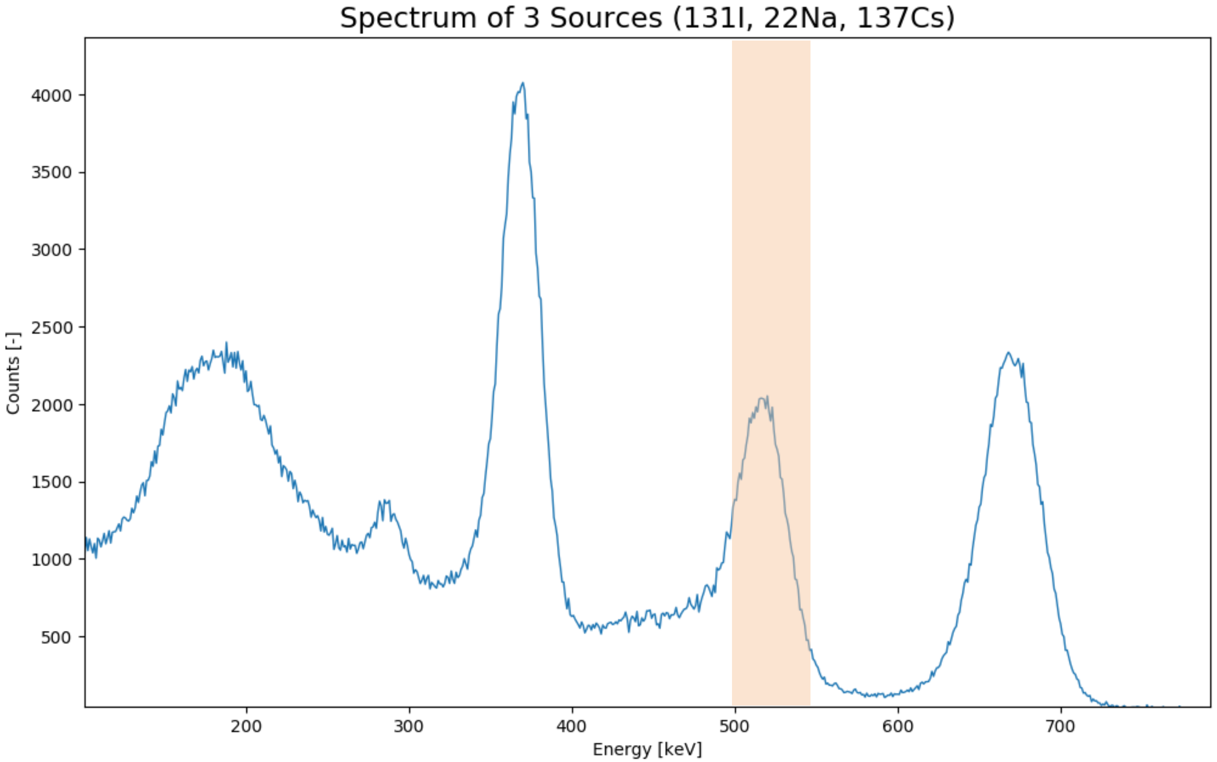




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

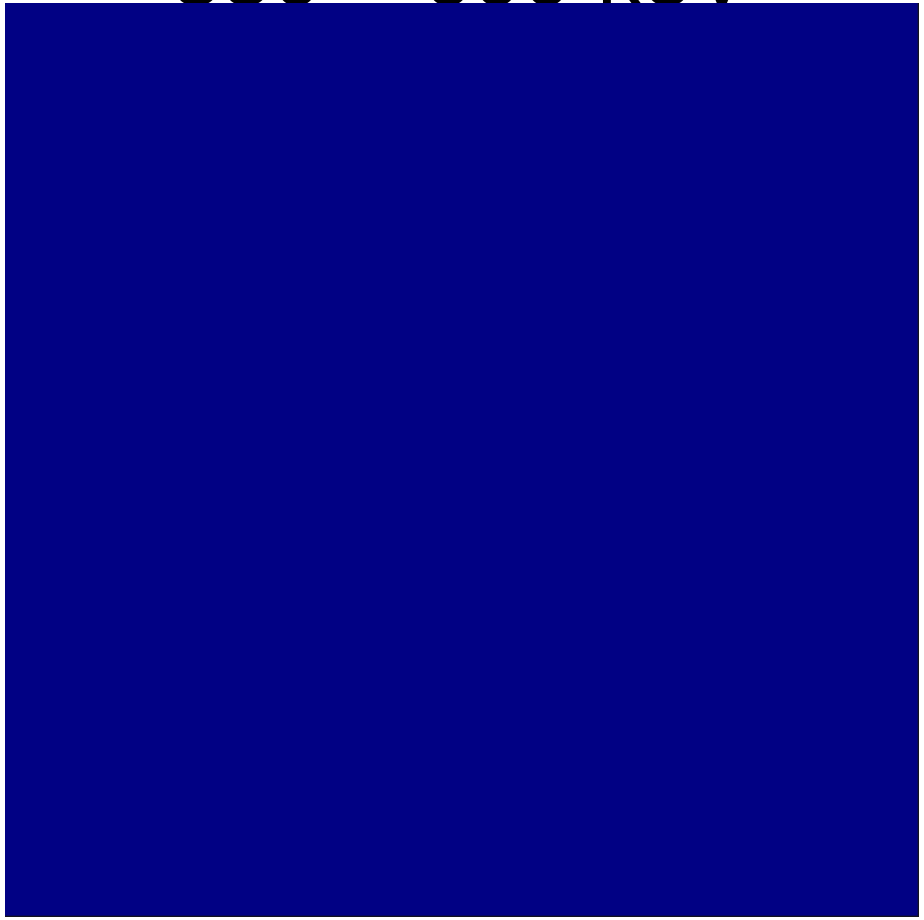
500 – 550 keV

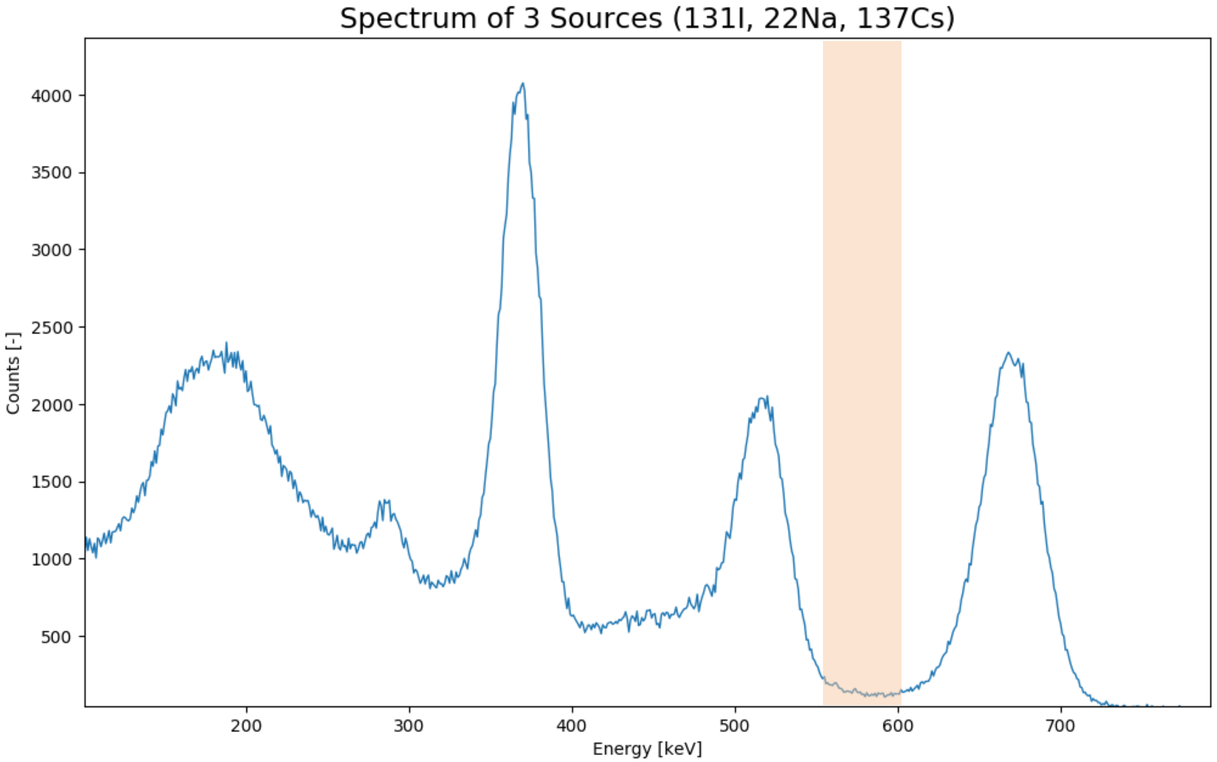




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

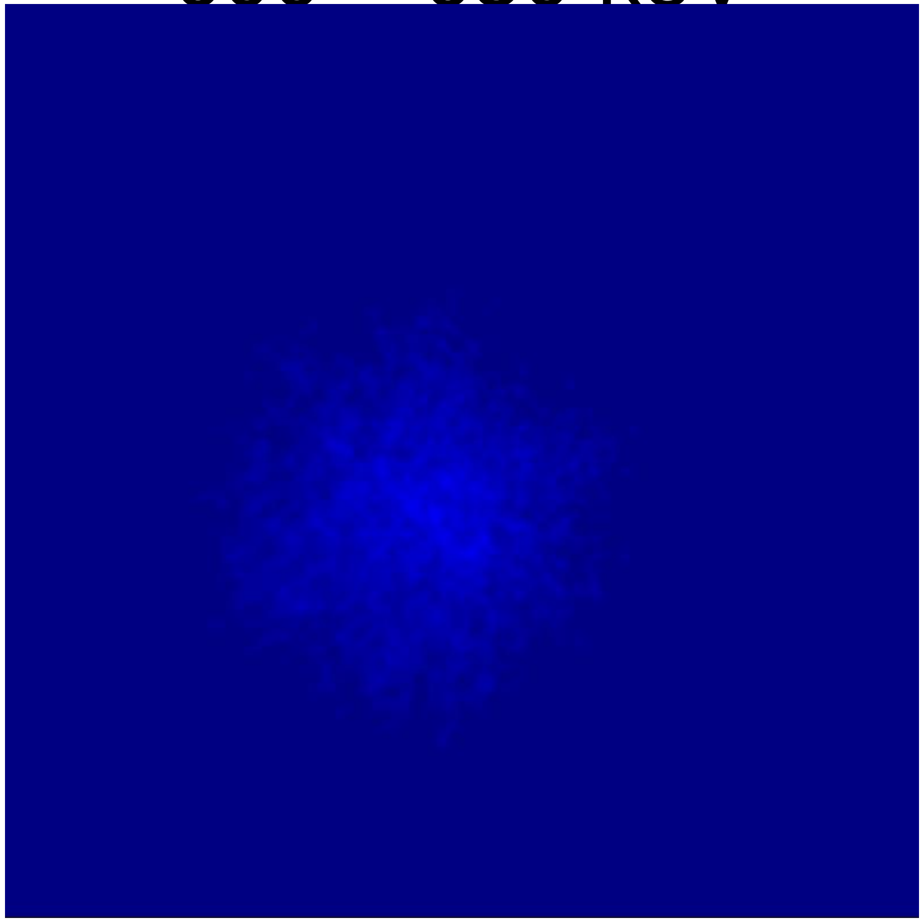
550 – 600 keV

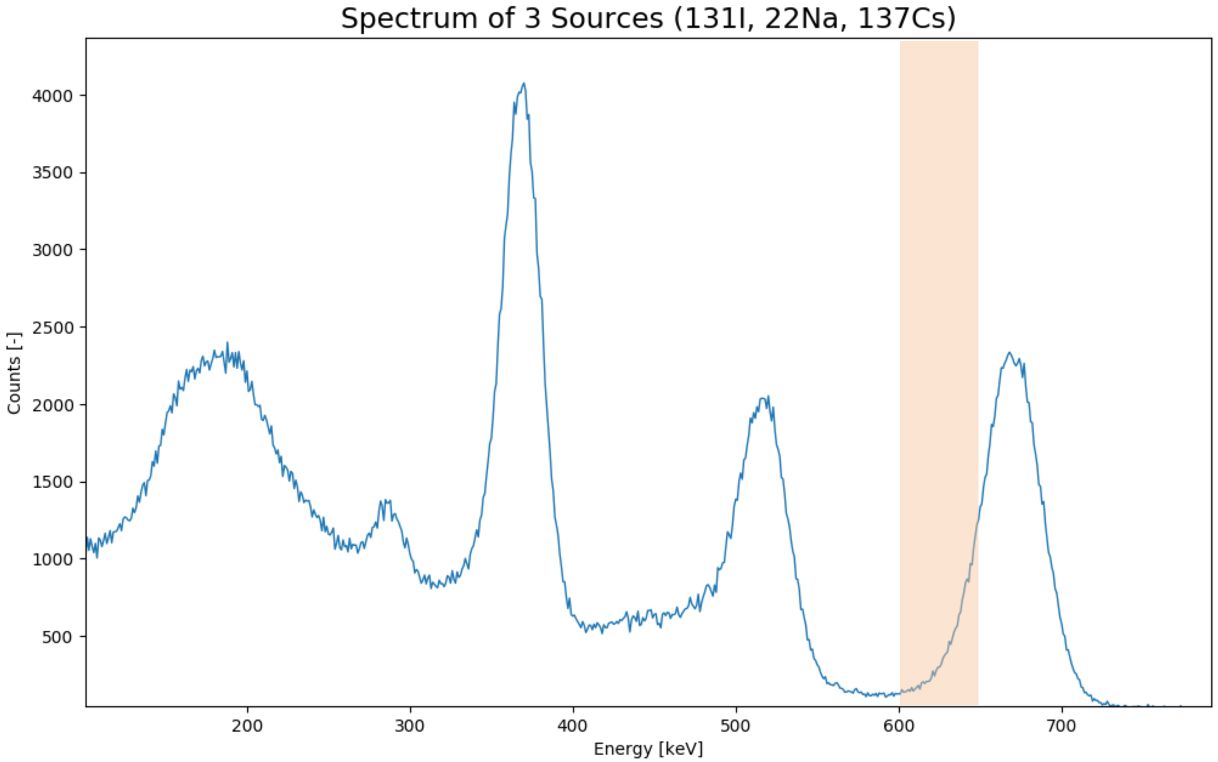




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

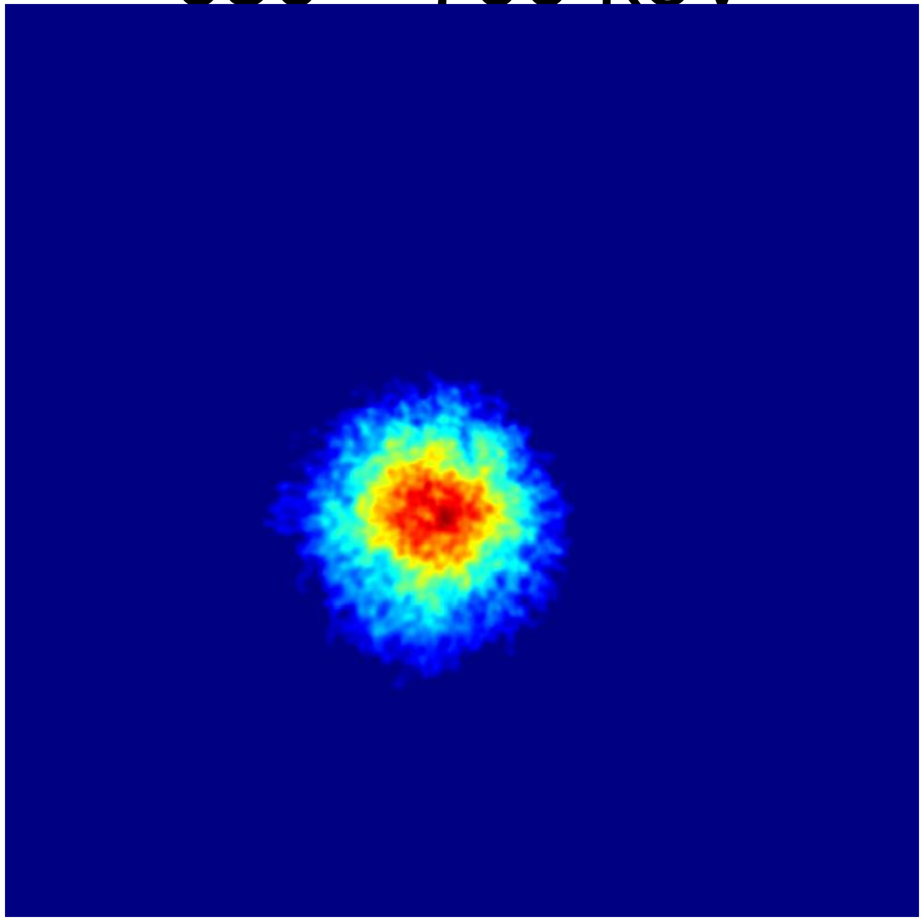
600 – 650 keV

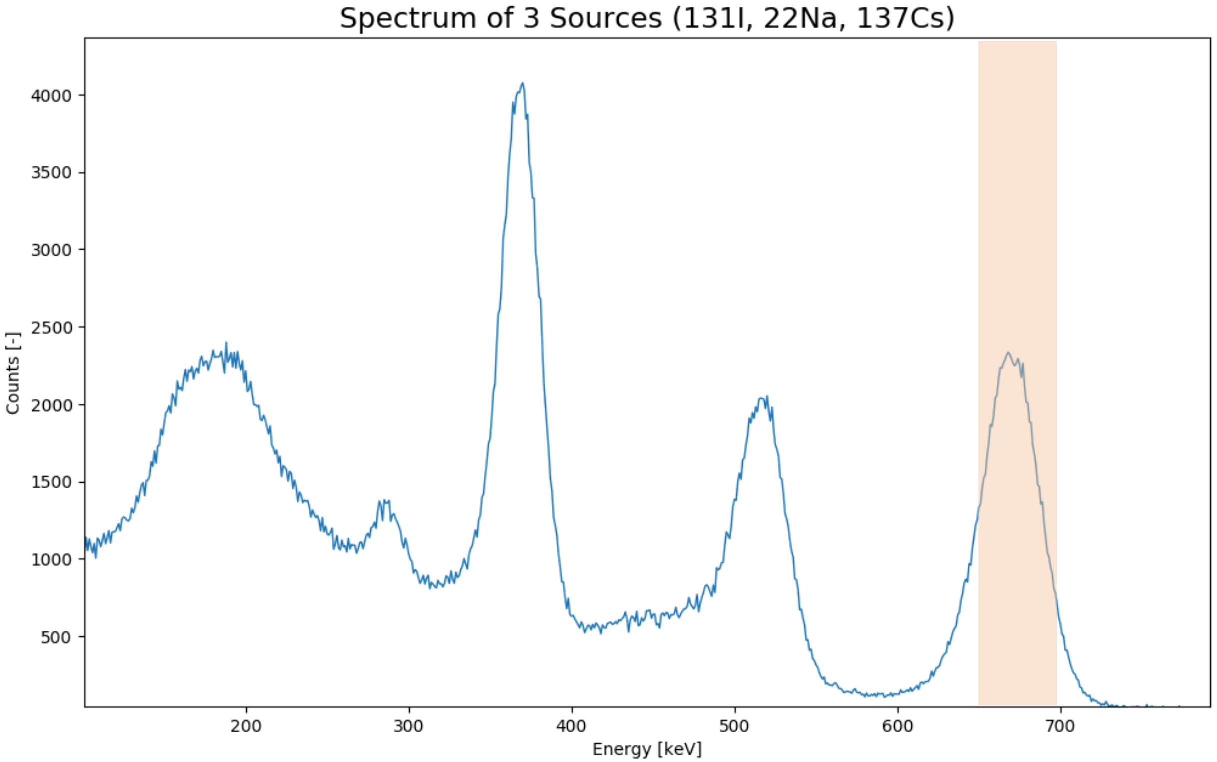




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

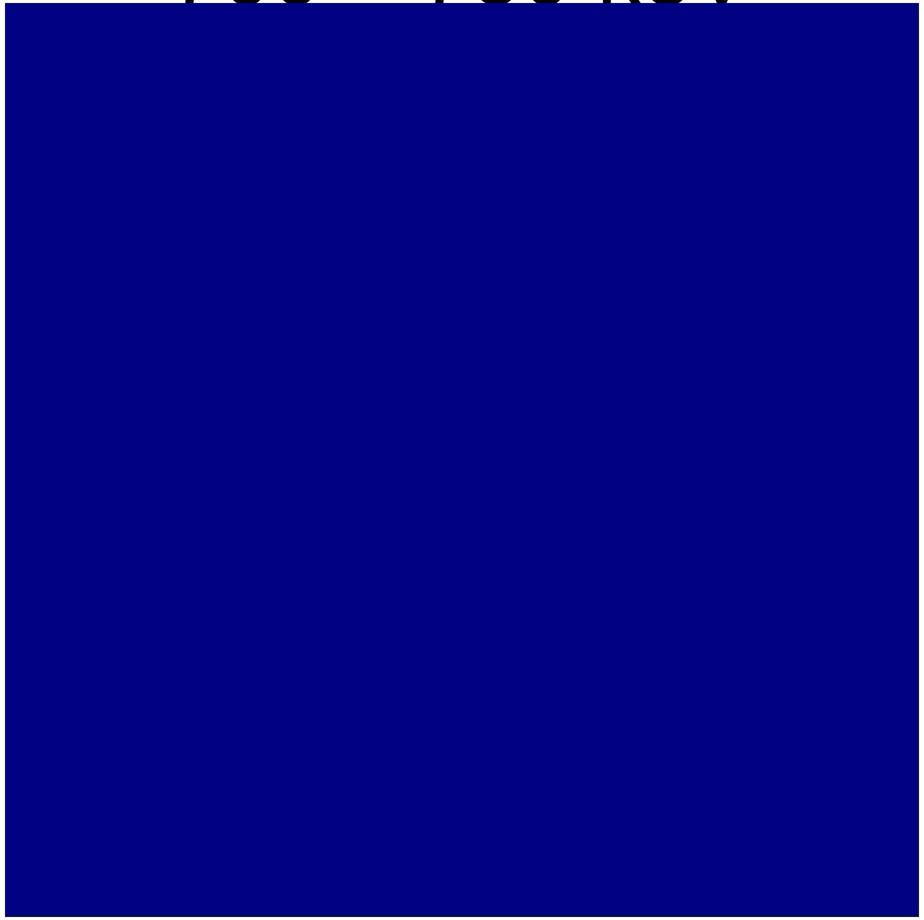
650 – 700 keV

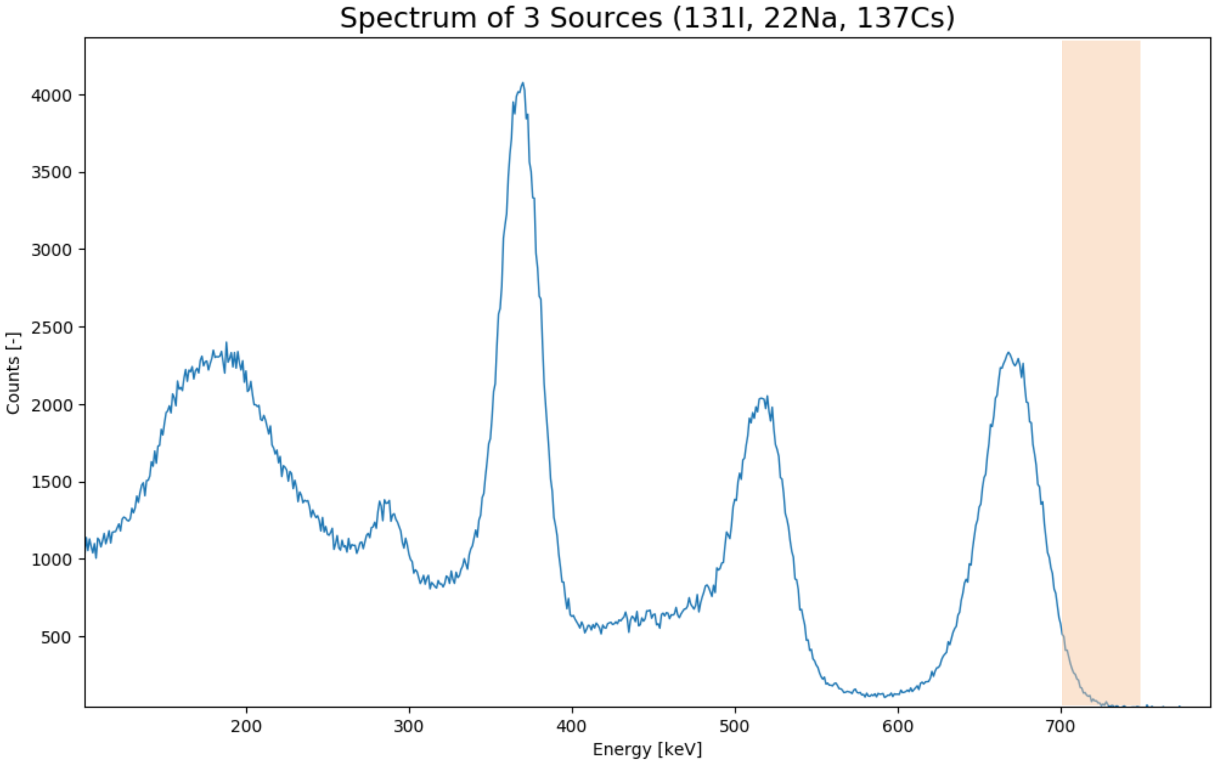




Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

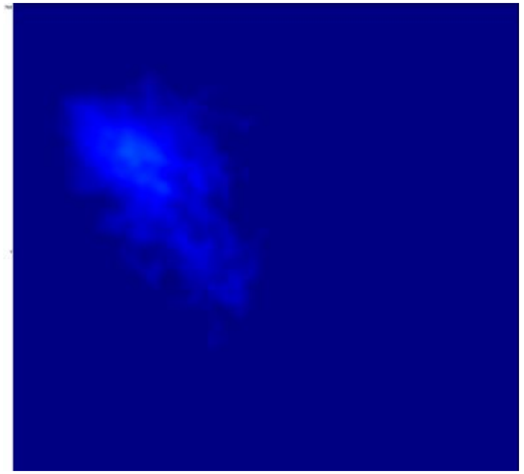
700 – 750 keV





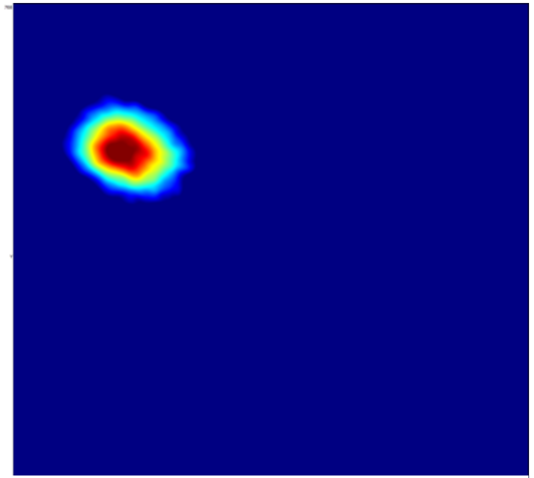
Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

250 – 300 keV



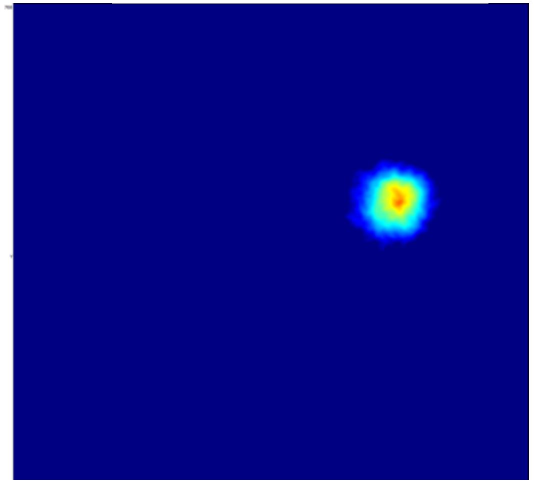
^{131}I 284 keV (7%)

350 – 400 keV



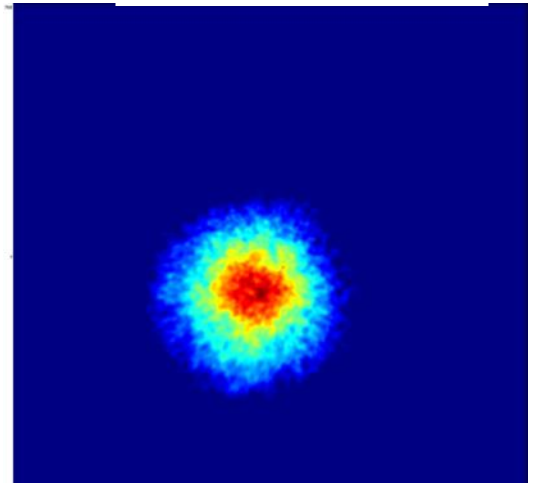
^{131}I 364 keV

500 – 550 keV

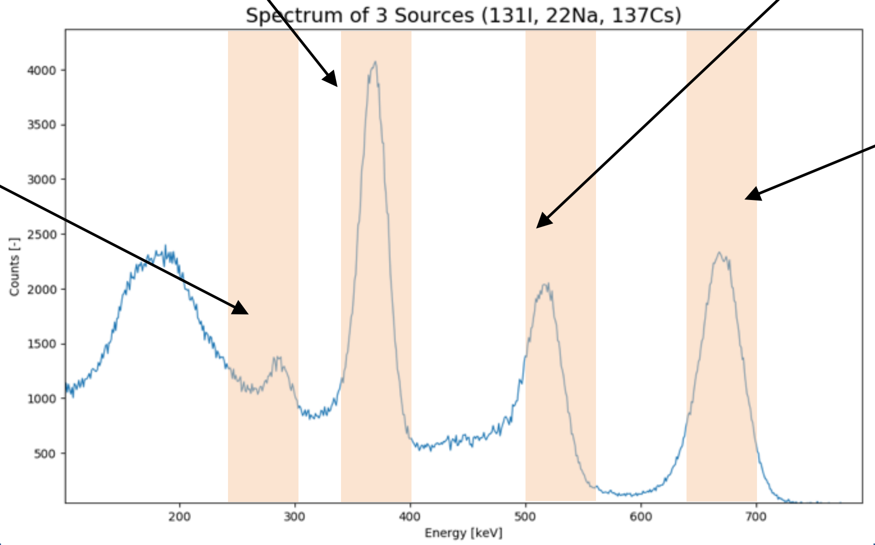


^{22}Na 511 keV

650 – 700 keV



^{137}Cs 662 keV



Gamma camera applications: Thyroid diagnostic

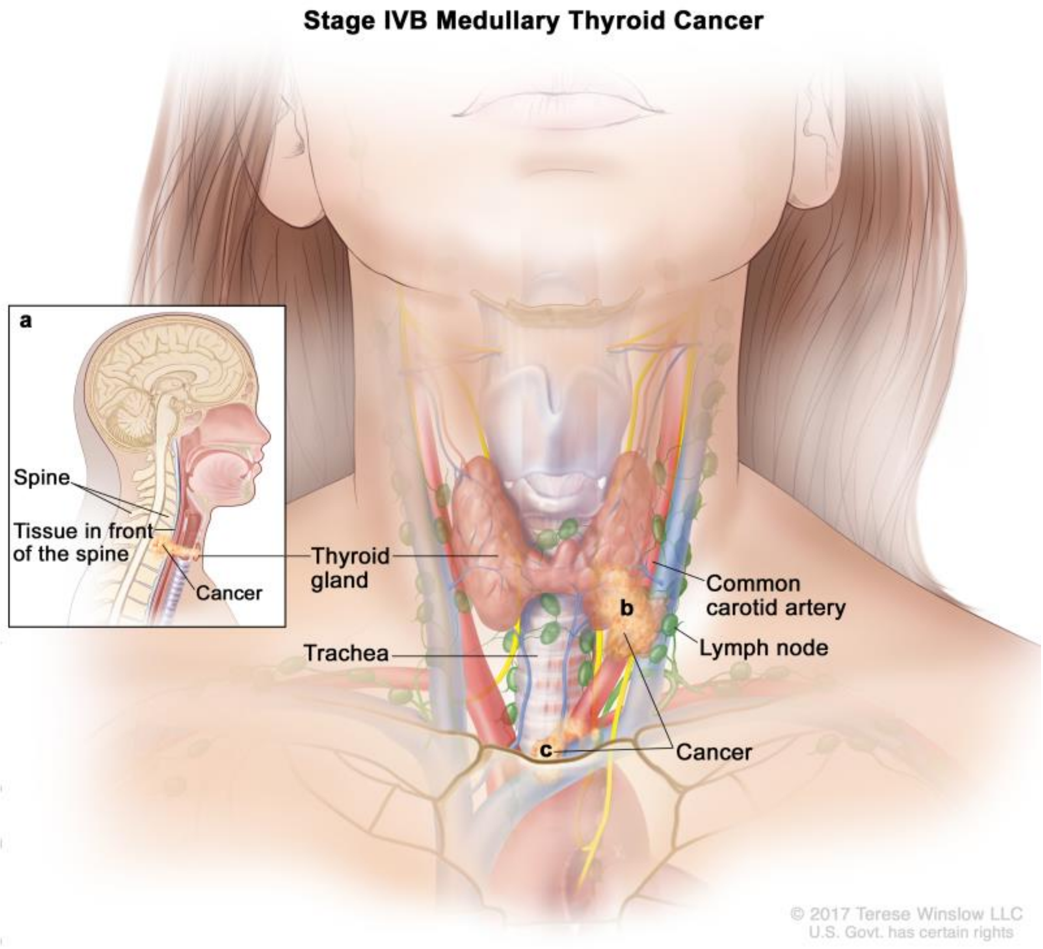
Thyroid cancer diagnostics and treatment monitoring:

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

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

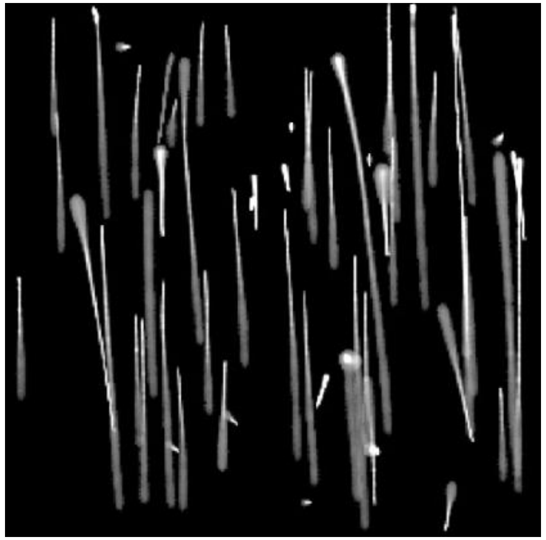
This technology allows

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



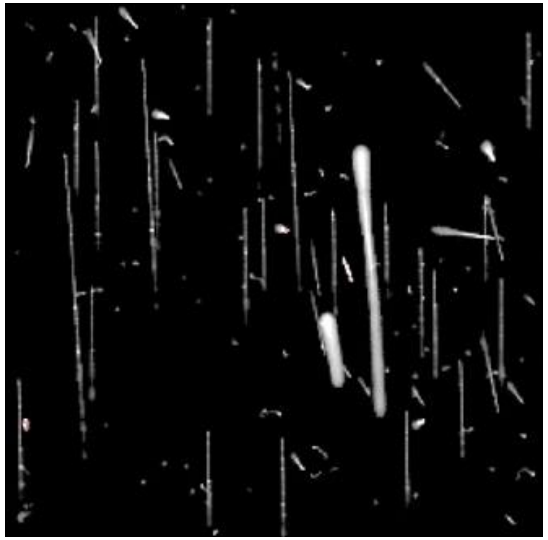
In-line images of a hadron therapy beam

Protons 48 MeV



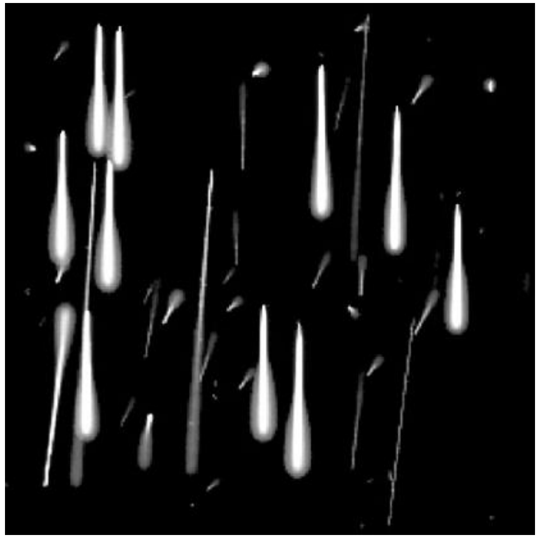
Only protons and their scattering, no secondaries.

Protons 221 MeV



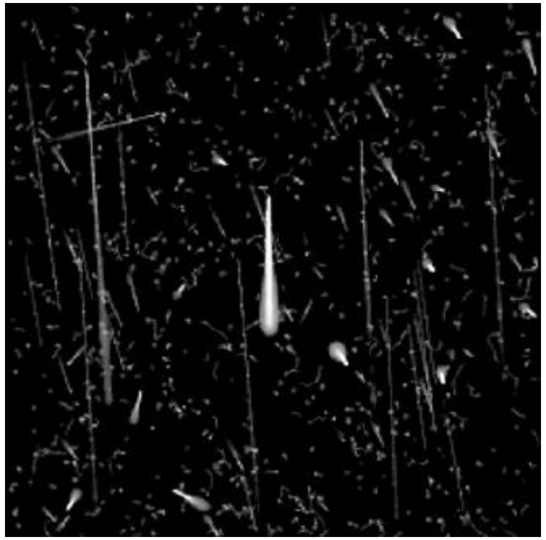
Many secondaries, (delta electrons fragments).

Carbons 89 MeV/u



Carbons and protons and their scattering, no secondaries.

Carbons 430 MeV/u

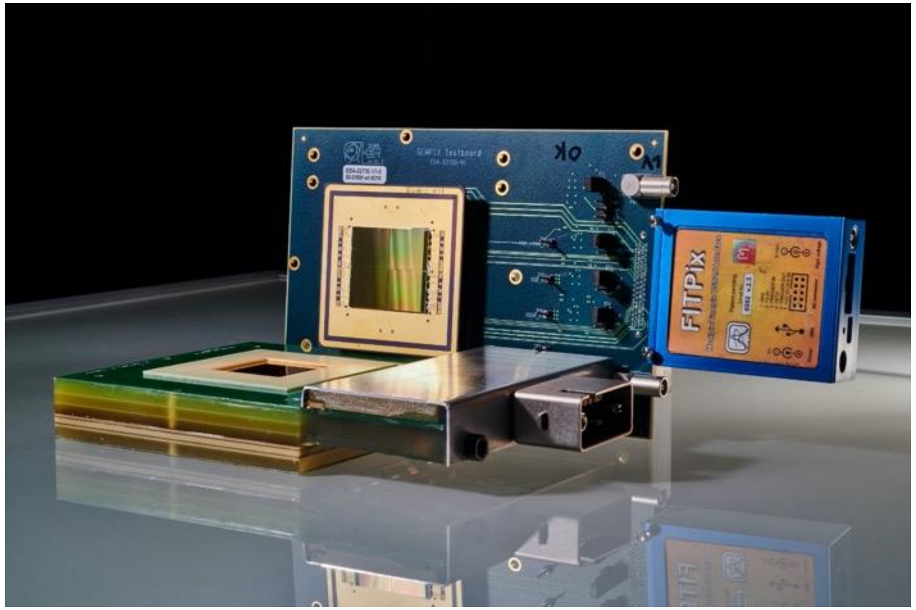


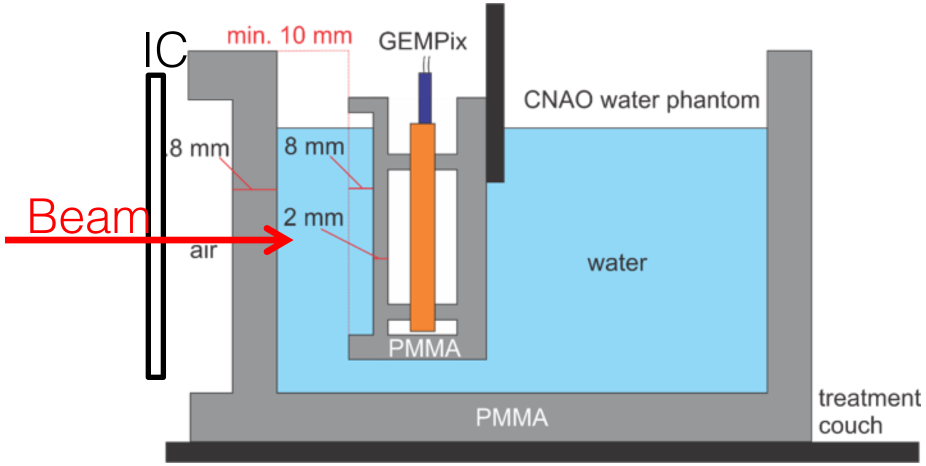
Carbons and many secondaries.

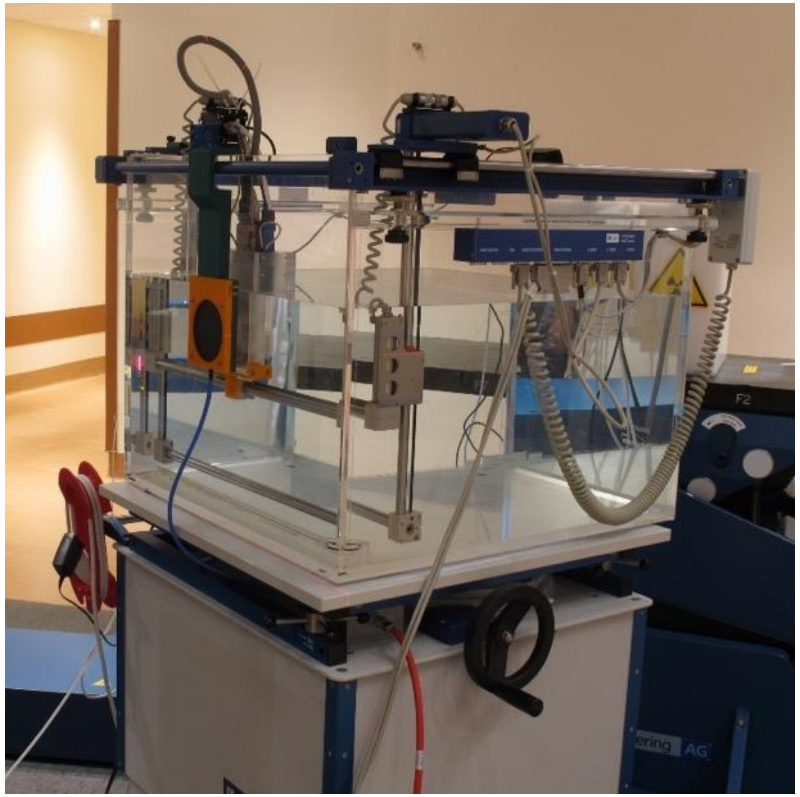
Timepix chip combined with Si detector

Timepix on the ISS

GEMPix for QA in Hadron Therapy







Water phantom donated from Luzern hospital equipped with GEMPIx, reference PTW ion chamber + readout

Ion chamber, GEMPix and movement in water phantom integrated in one system (HW/SW)

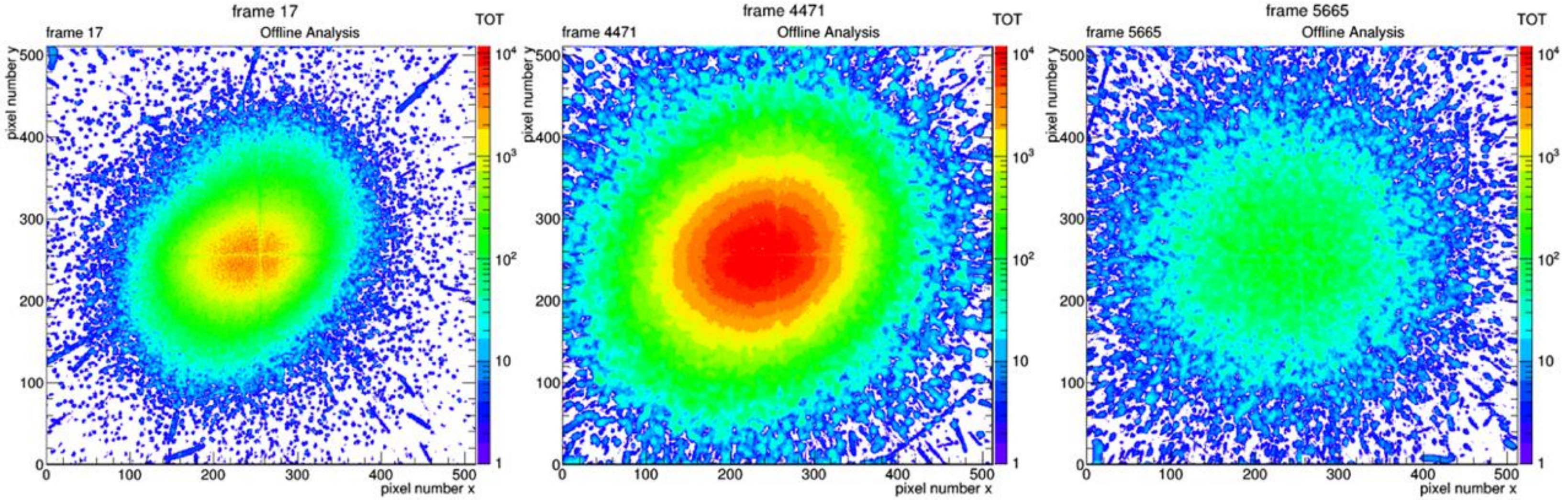
Measurements at CNAO – Italian National Centre for Oncological Hadron therapy

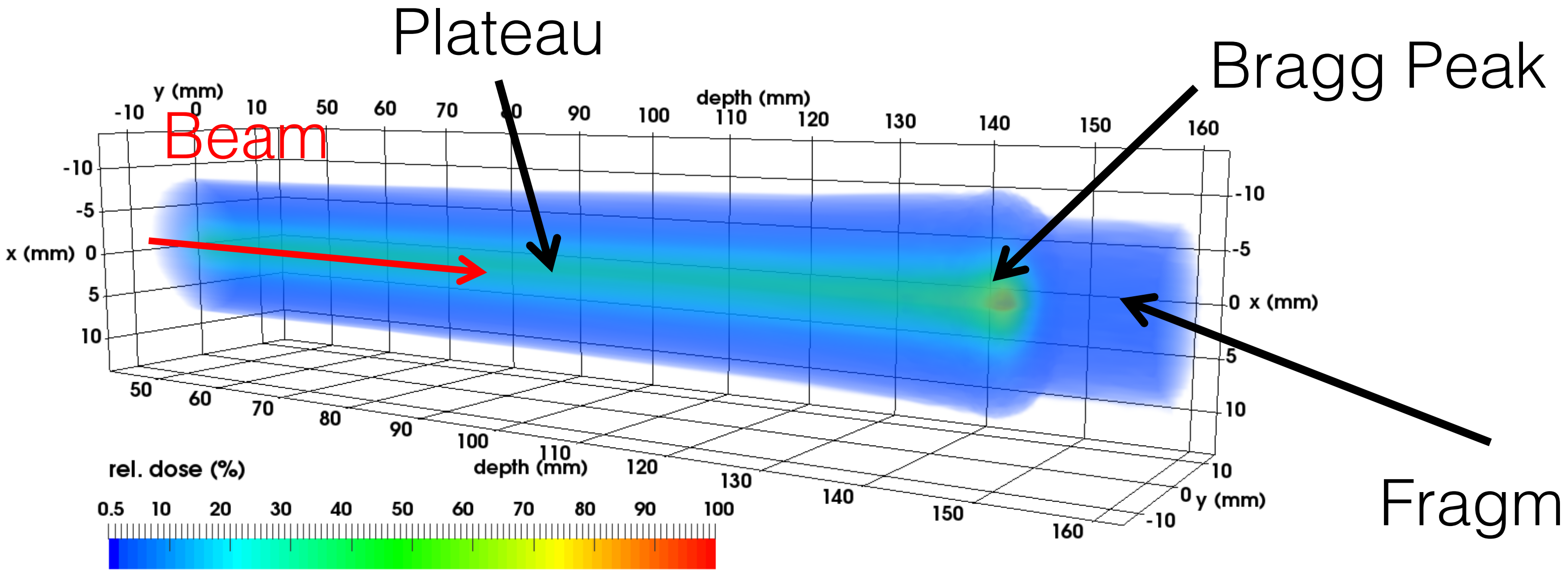
J. Leidner, M. Ciocca, S. P. George, A. Mirandola, F. Murtas, A. Rimoldi, M. Silari and A. Tamborini. 3D Energy deposition measurements with the GEMPix detector in a water phantom for hadron therapy. Journal of Instrumentation 13, P08009 (2018)

J. Leidner, M. Ciocca, A. Mairani, F. Murtas and M. Silari. A GEMPix-based integrated system for measurements of 3D dose distributions in water for carbon ion scanning beam radiotherapy. Medical Physics 47, 2516-2525 (2020)

GEMPix: measurements with a ^{12}C beam at CNAO

2D images with much better spatial resolution than with an ion chamber





TimePIX 3 photon fluence measurement in hospital theatres

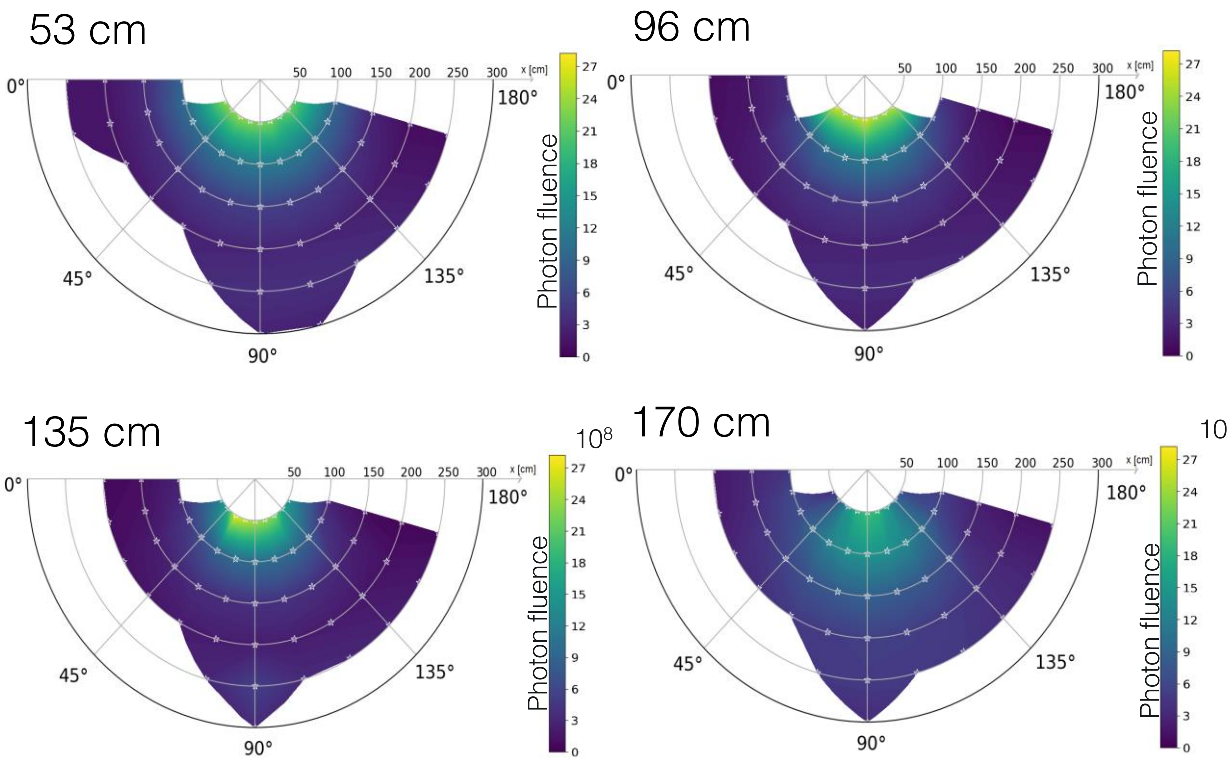
Reference person: 1.76 m

Eye lens - 170 cm

Chest - 135 cm

Belt - 96 cm

Knee - 53 cm

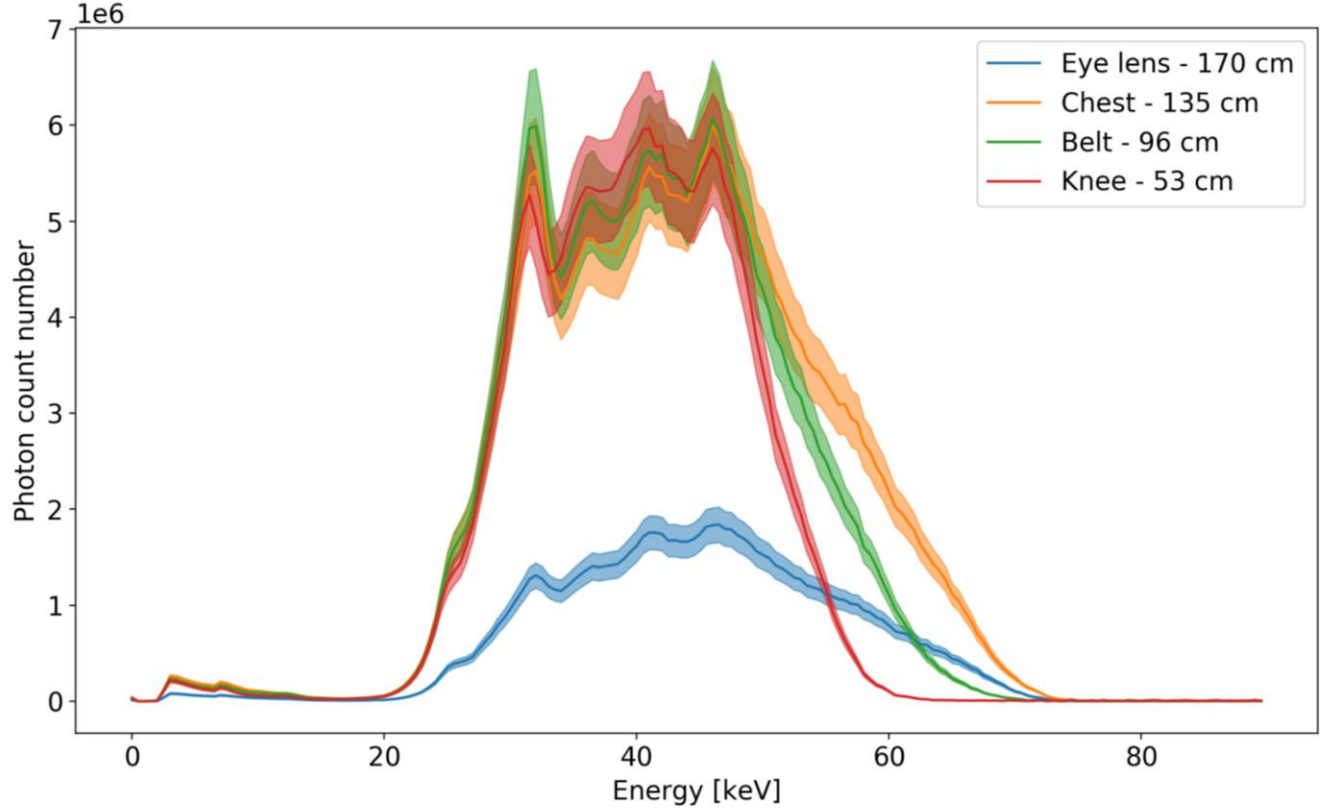


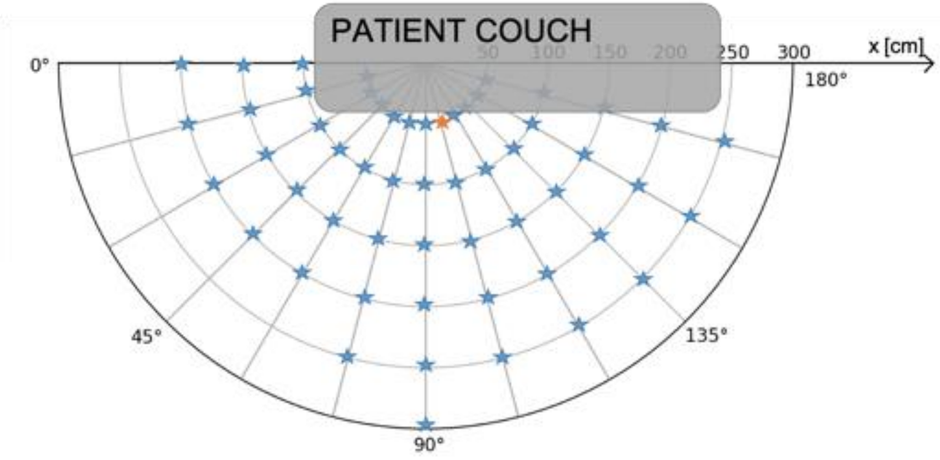
Colour maps of the photon fluence measured with a Timepix III in an hospital theatre at four horizontal eights.

Courtesy of M. Nowak

TimePIX 3 photon fluence measurement in hospital theatres

Energy spectra for each height for a given person

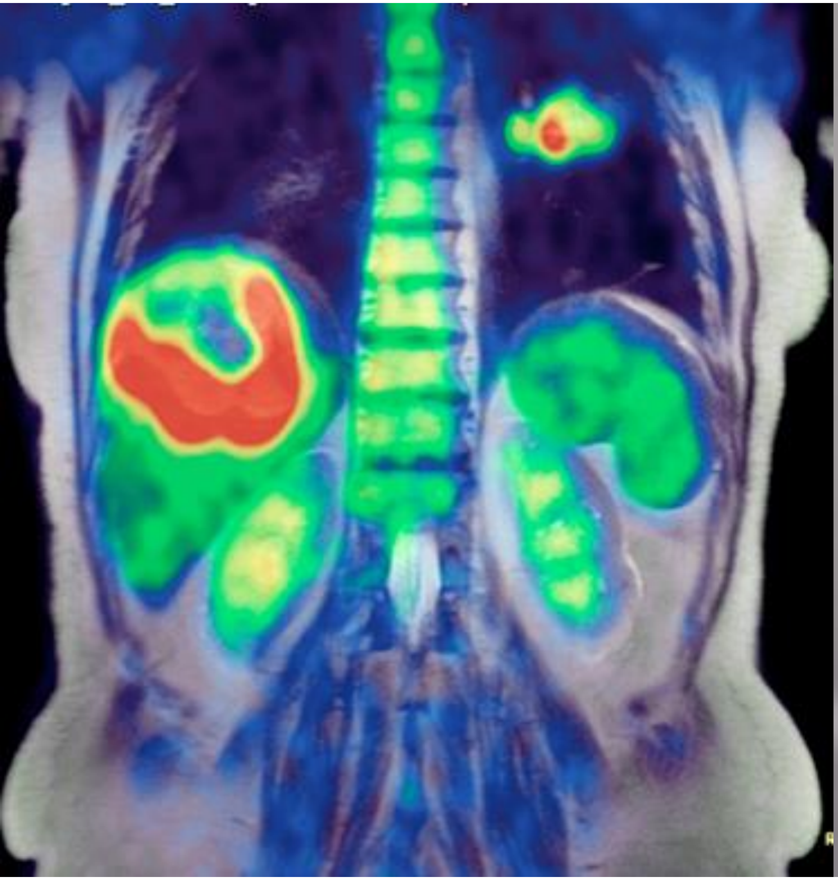




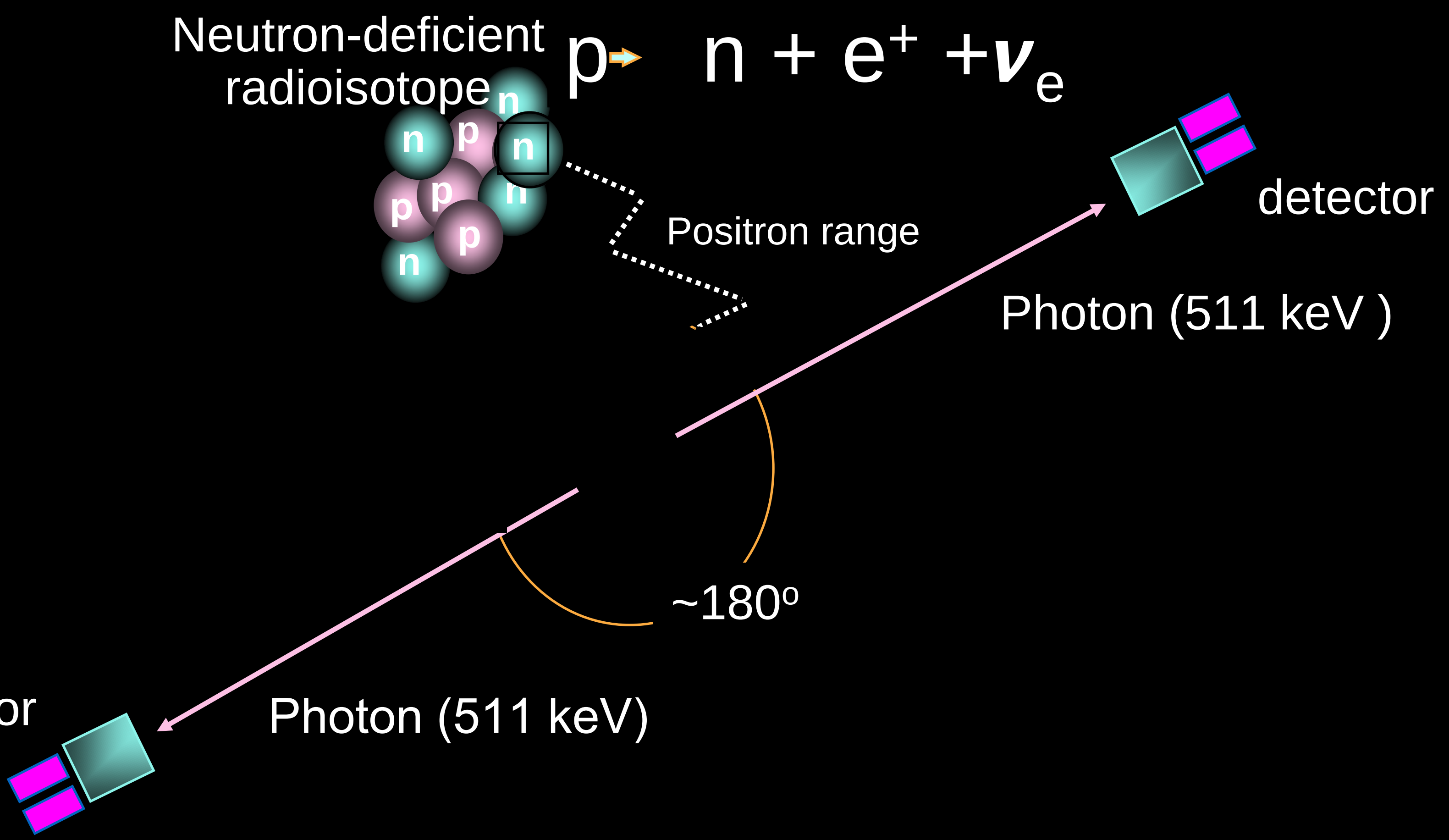
Courtesy of M. Nowak

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

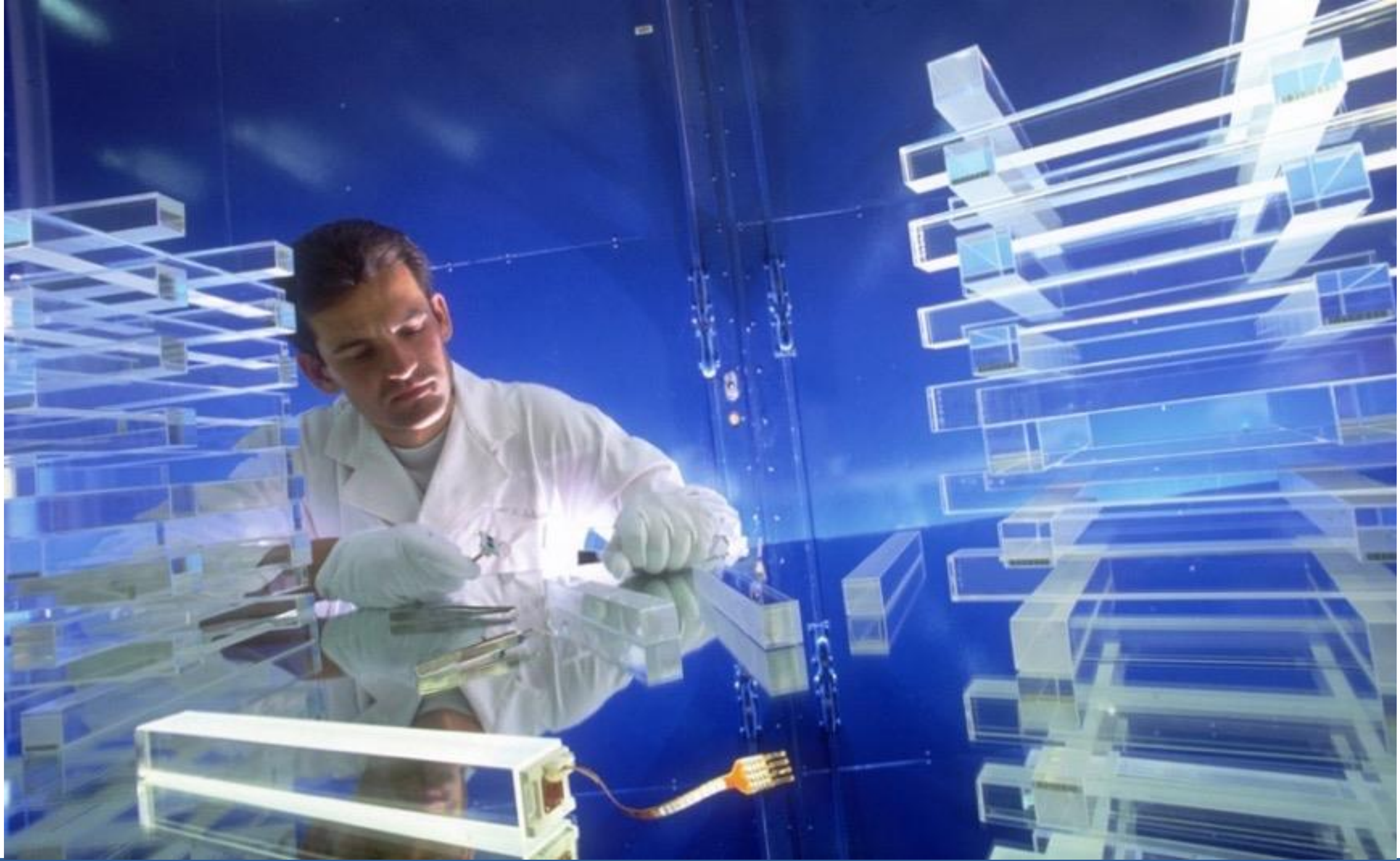
PET

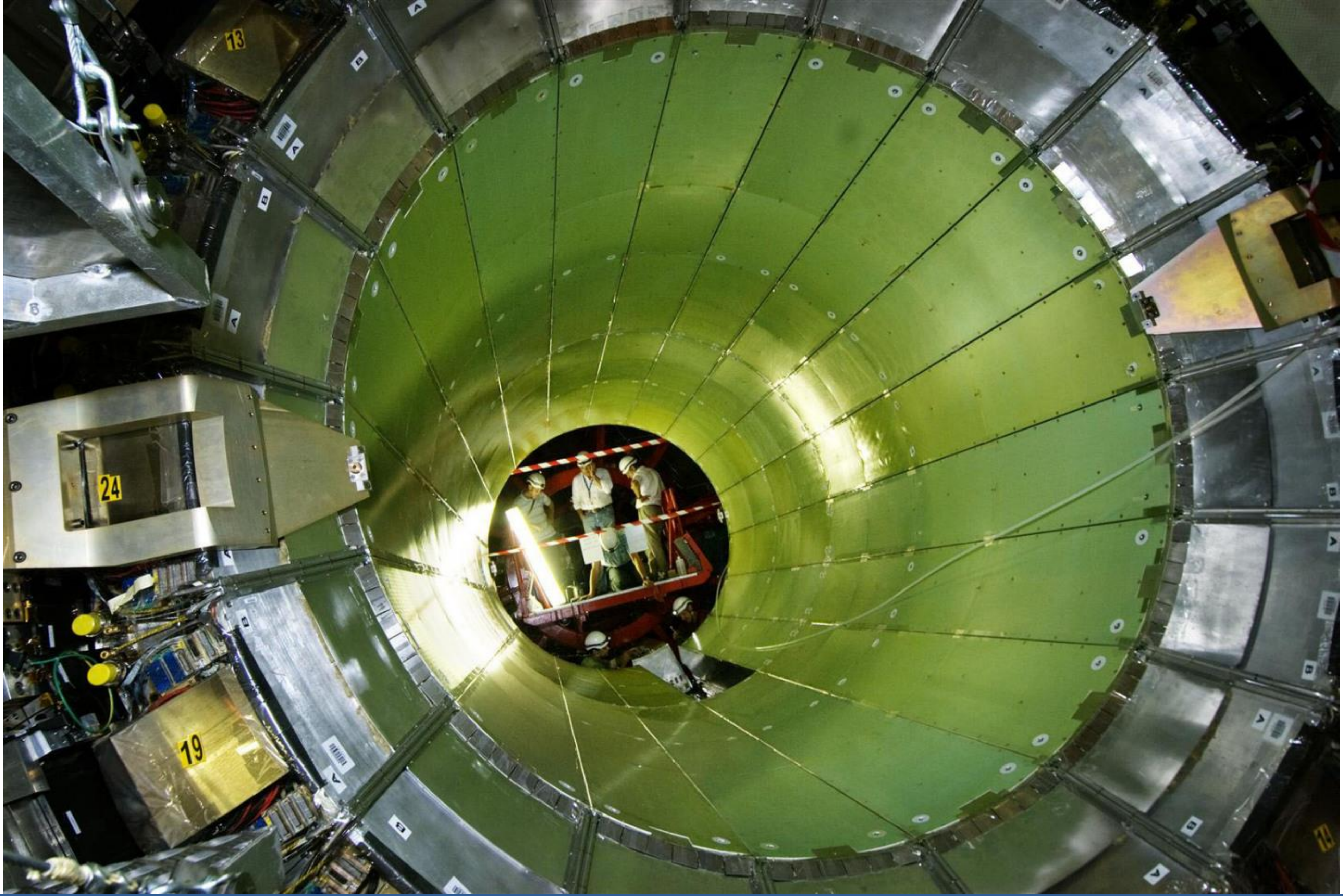


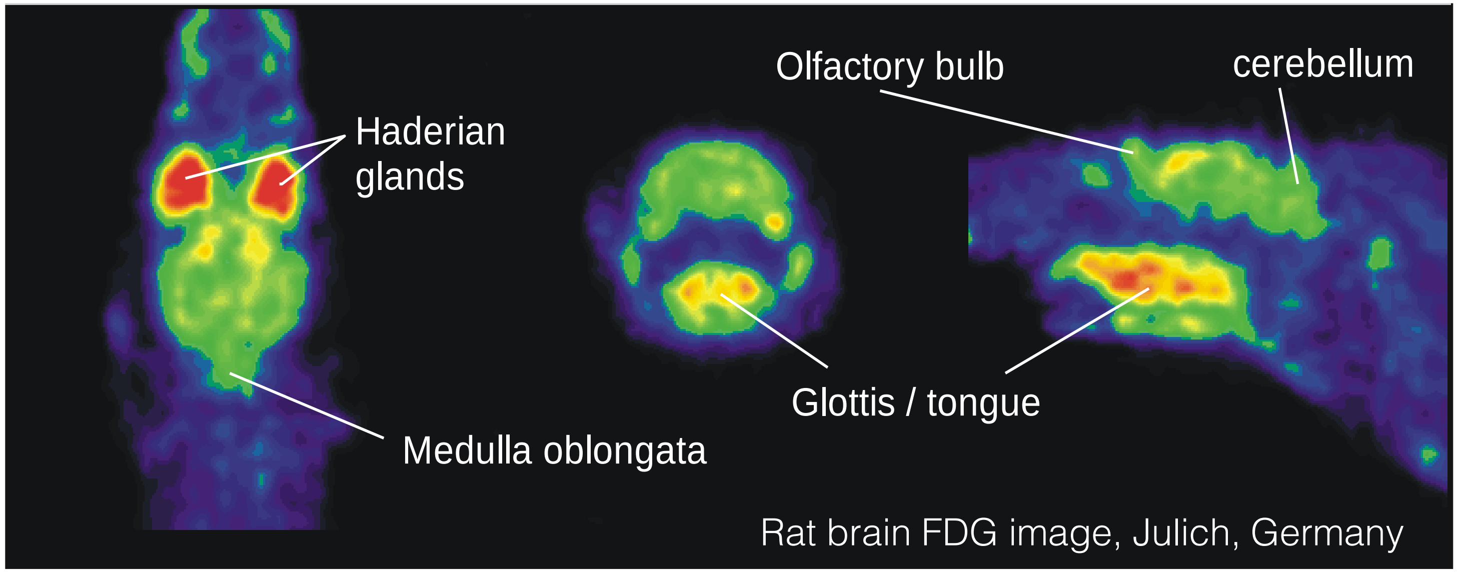
Positron Emission Tomography



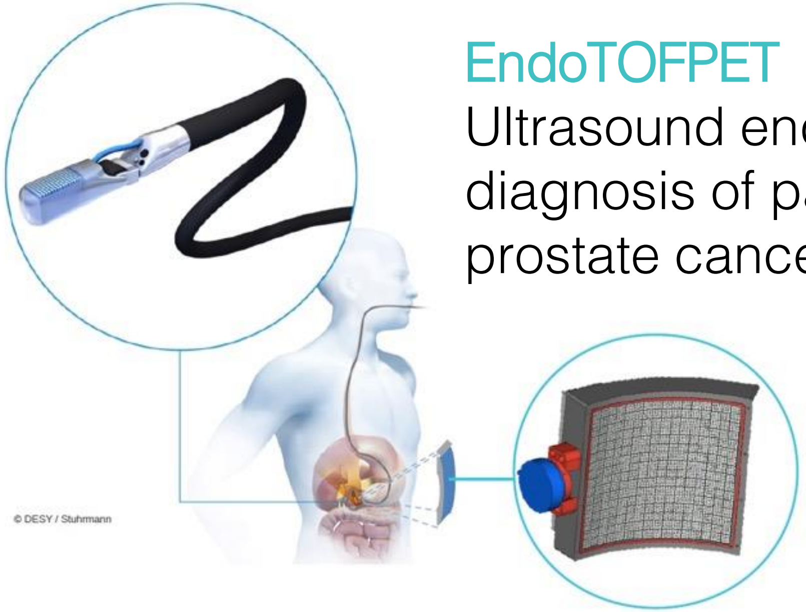
https://www.facebook.com/watch/?v=18454476357039



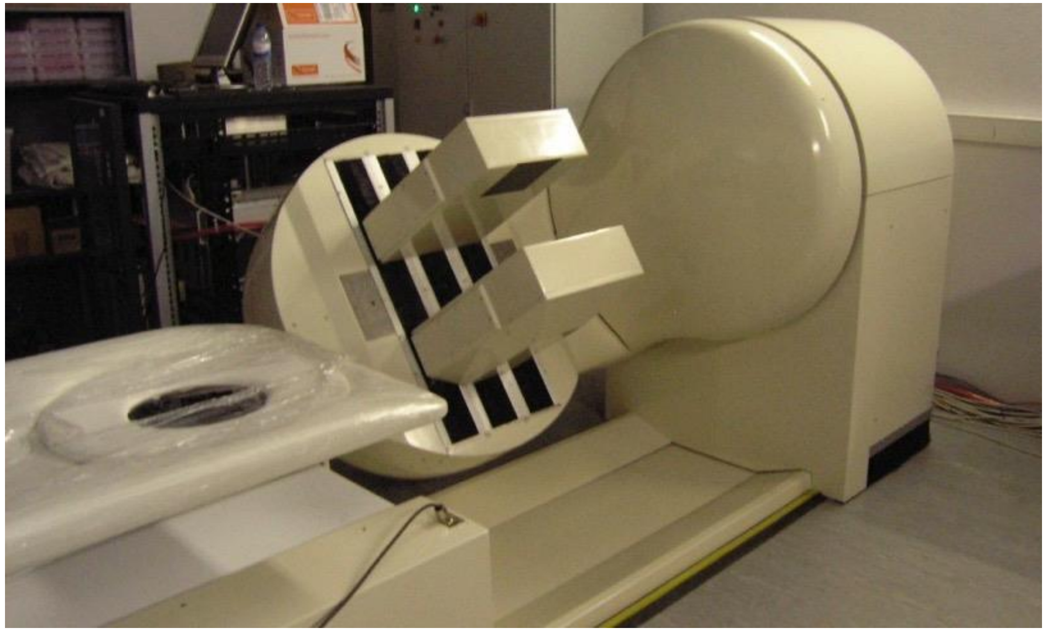

13
24
19



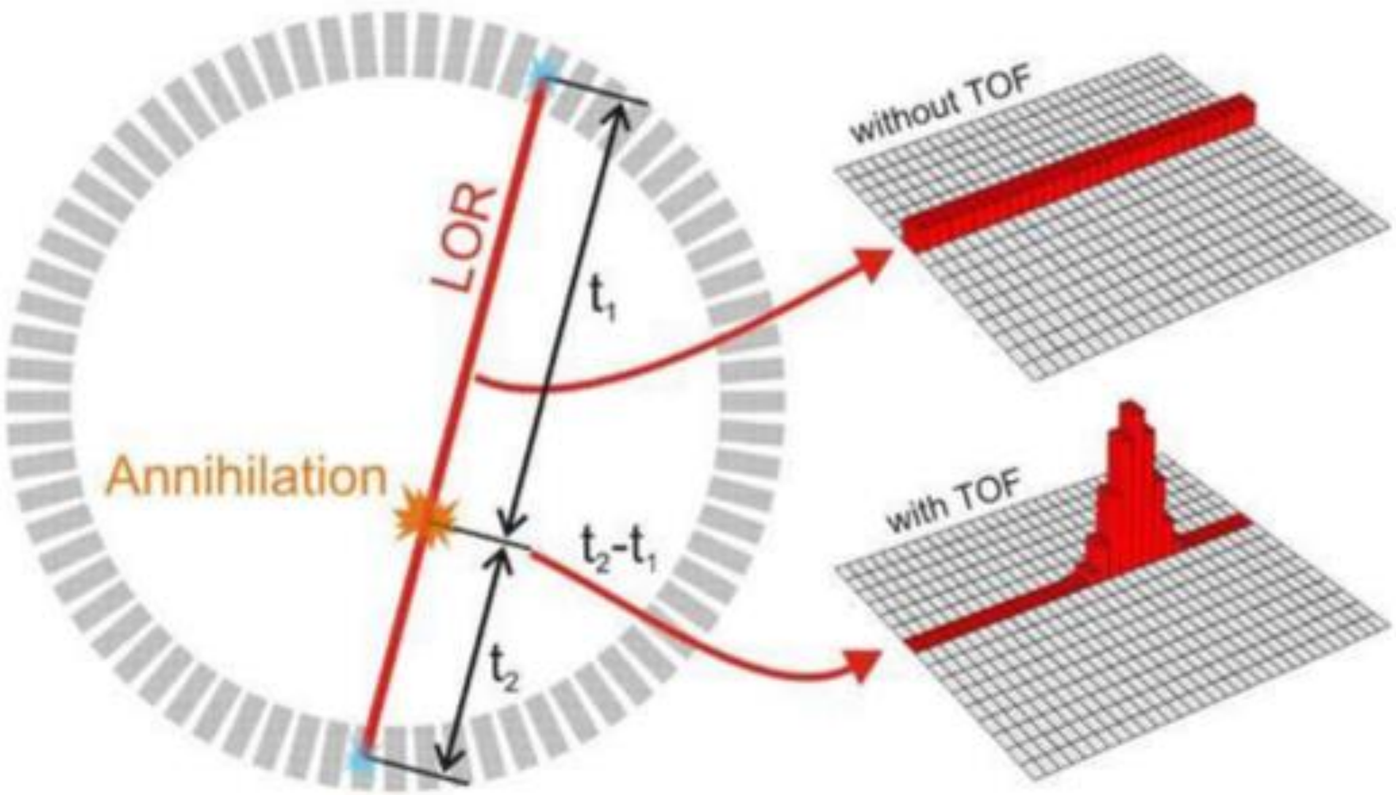
ClearPET
PET for small anymals



EndoTOFPET
Ultrasound endoscopic PET for diagnosis of pancreas & prostate cancer



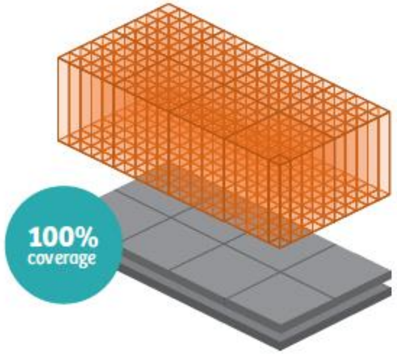
ClearPEM
Dedicated scanner for breast imaging


without TOF
LOR
t_1
Annihilation
t_2-t_1
with TOF
t_2

Current status commercial TOF-PET

TOF PET SIEMENS: BIOGRAPH VISION

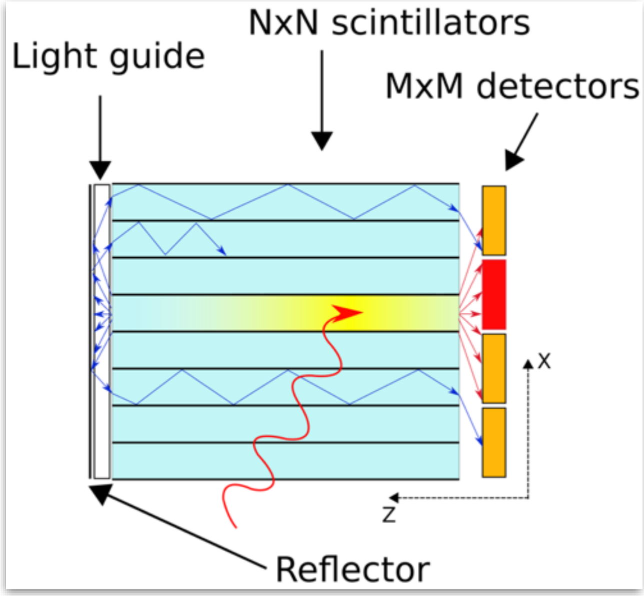
3.2mm section crystals
CTR 215ps

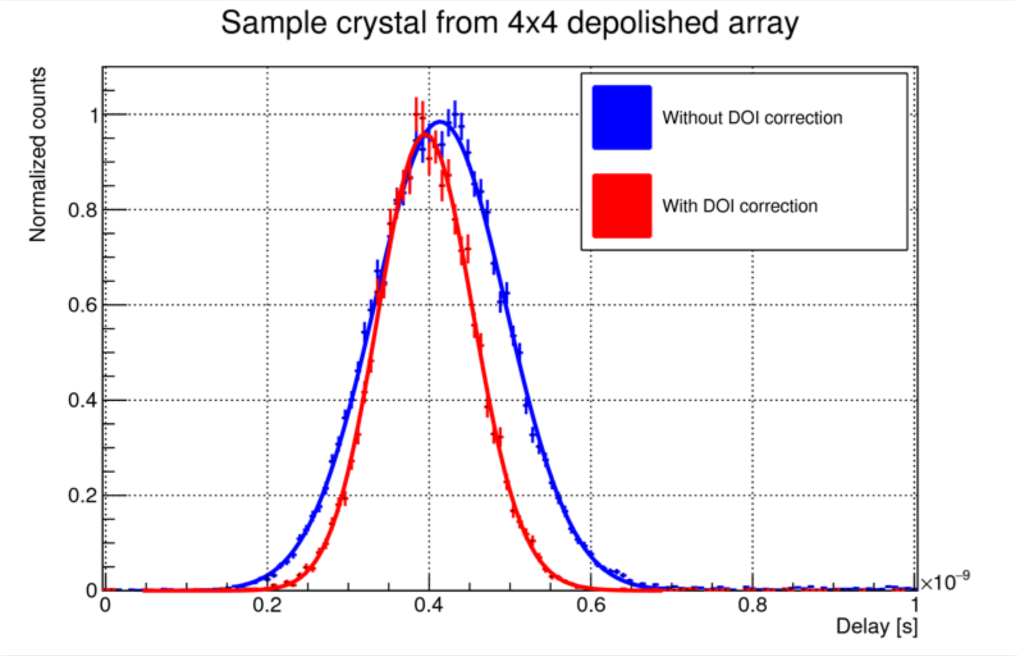


Webpage SIEMENS:
https://static.healthcare.siemens.com/siemens_hwem-hwem_ssxa_websites-context-root/wcm/idc/groups/public/@global/@imaging/@molecular/documents/download/mda4/mzmy/~edisp/biograph_vision_technical_flyer-05440720.pdf

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

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



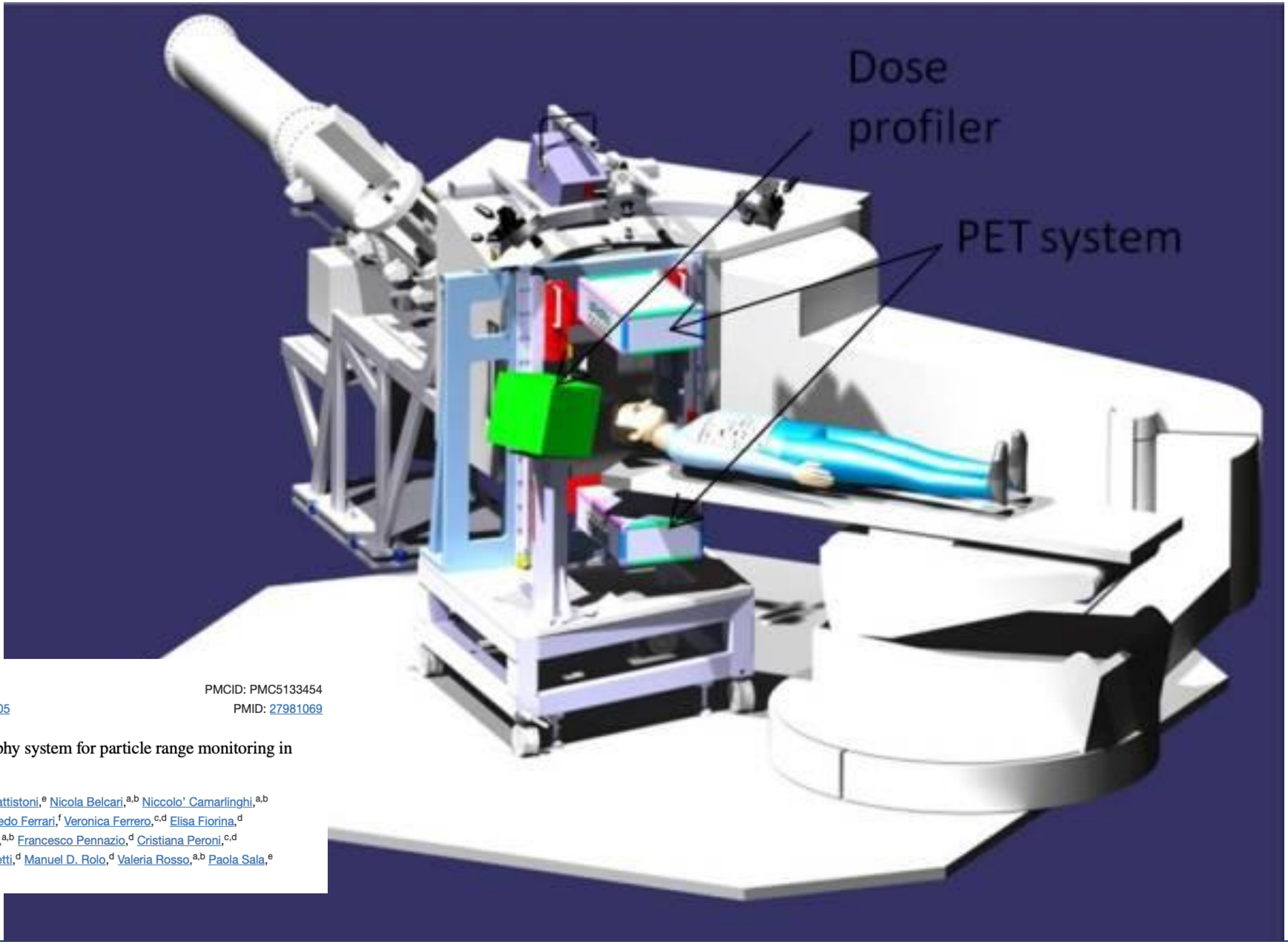


Type of array	Crystals dim. [mm^3]	DOI resolution FWHM [mm]	En. Res. FWHM @ 511 keV [%]	CTR FWHM [ps], central pixels	
				No correction	*With DOI correction*
DOI	3.1 x 3.1 x 15	3.0 ± 0.1	8.9 ± 0.2	234 ± 2	157 ± 2

DOI information extracted without degradation of timing properties

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


PET DETECTOR
ENVISION

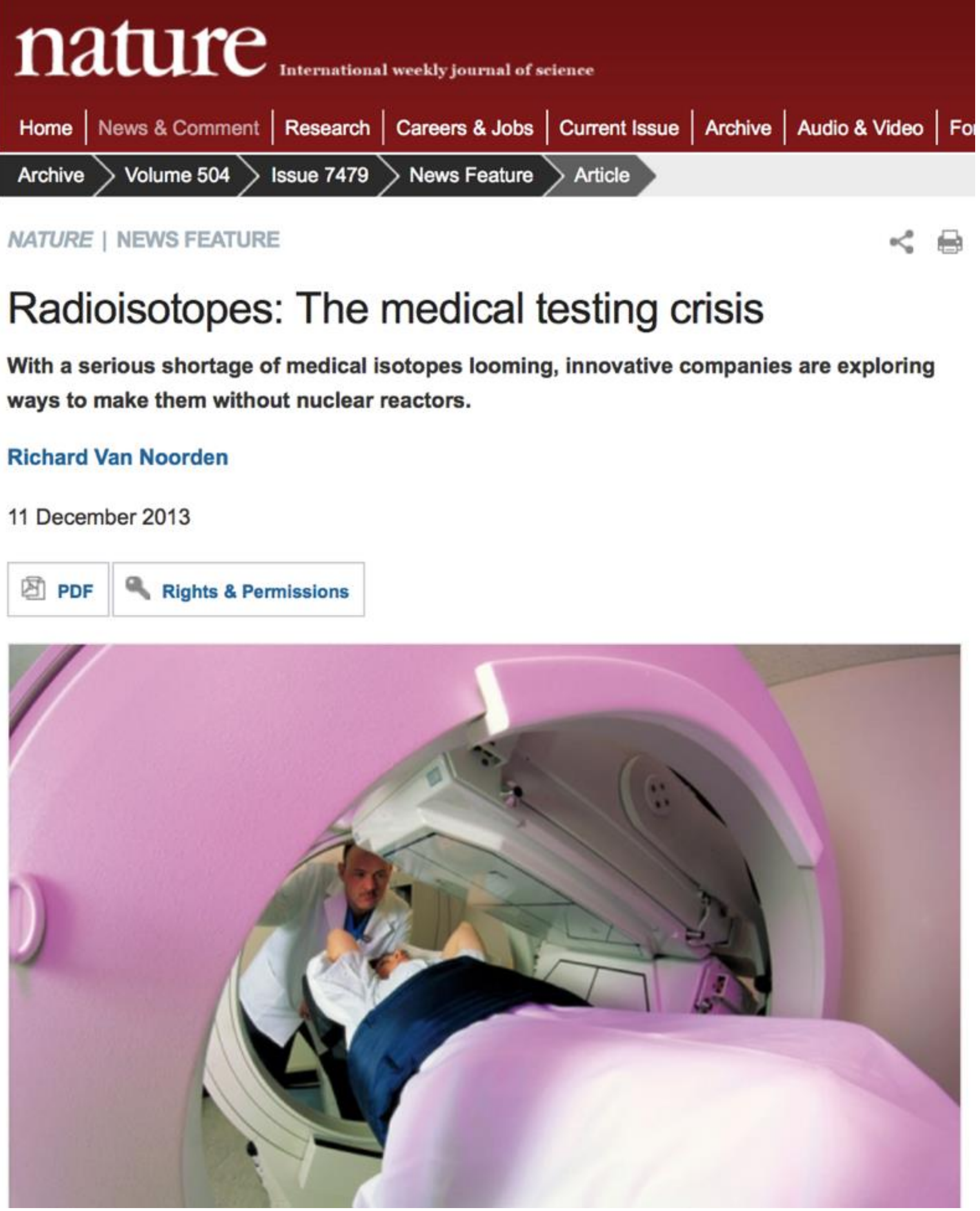


J Med Imaging (Bellingham). 2017 Jan; 4(1): 011005.
Published online 2016 Dec 2. doi: 10.1117/1.JMI.4.1.011005
PMCID: PMC5133454
PMID: 27981069

INSIDE in-beam positron emission tomography system for particle range monitoring in hadrontherapy

Maria Giuseppina Bisogni,[a,b,*] Andrea Attili,[c,d] Giuseppe Battistoni,[e] Nicola Belcari,[a,b] Niccolo' Camarlinghi,[a,b] Piergiorgio Cerello,[d] Silvia Coli,[d] Alberto Del Guerra,[a,b] Alfredo Ferrari,[f] Veronica Ferrero,[c,d] Elisa Fiorina,[d] Giuseppe Giraudo,[d] Eleftheria Kostara,[b] Matteo Morrocchi,[a,b] Francesco Pennazio,[d] Cristiana Peroni,[c,d] Maria Antonietta Piliero,[a,b] Giovanni Pirrone,[a,b] Angelo Rivetti,[d] Manuel D. Rolo,[d] Valeria Rosso,[a,b] Paola Sala,[e] Giancarlo Sportelli,[a,b] and Richard Wheadon[d]

Radioisotopes


nature International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audio & Video | Fo

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

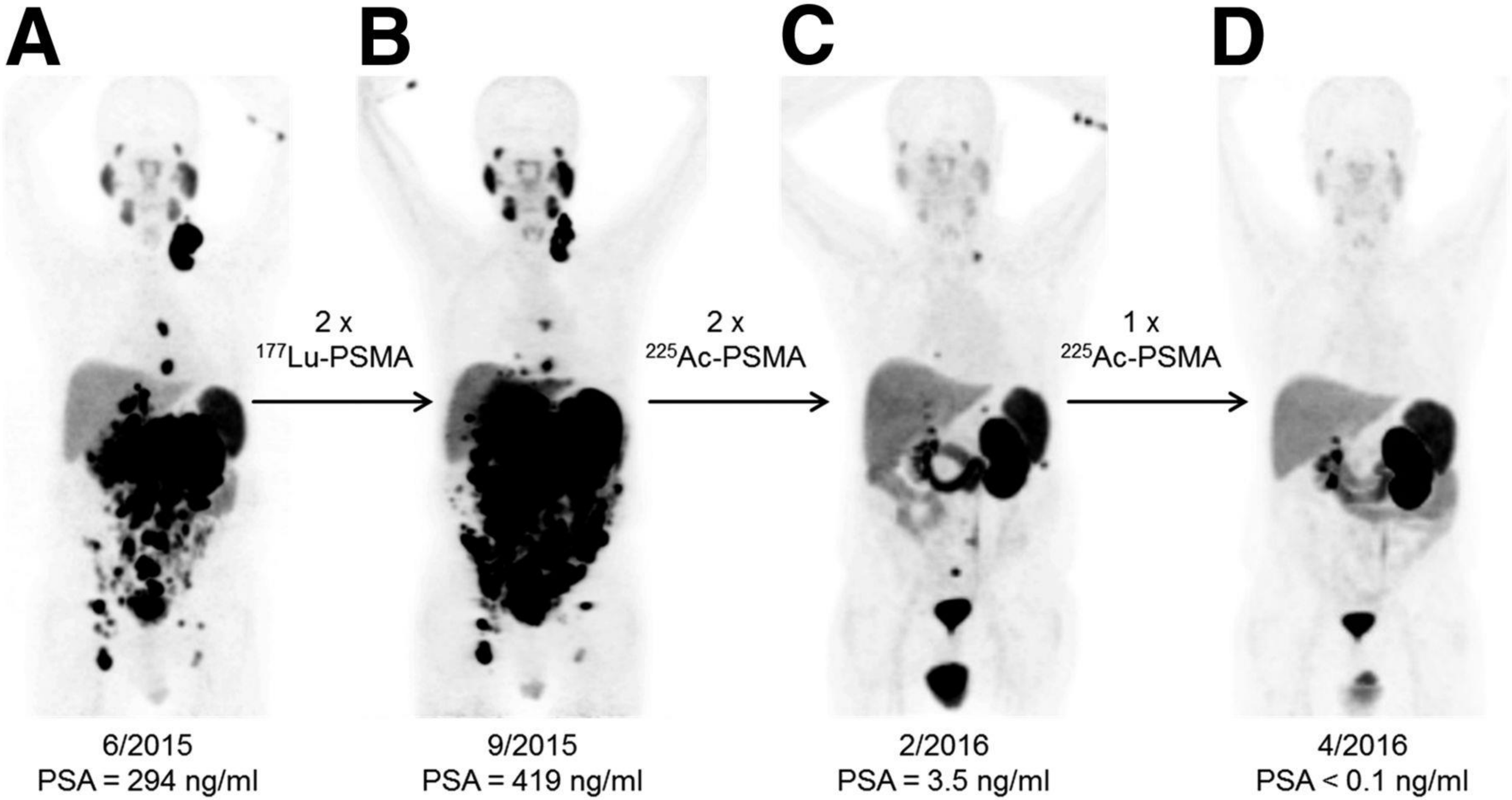
Classification of isotopes for Medicine:

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,…

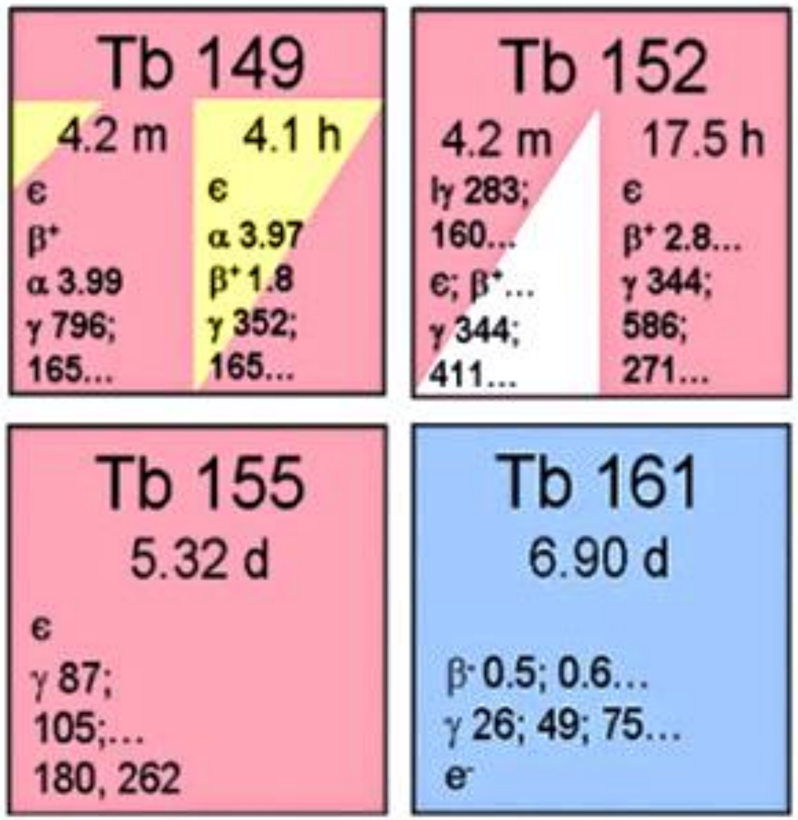
Courtesy U. Koester



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

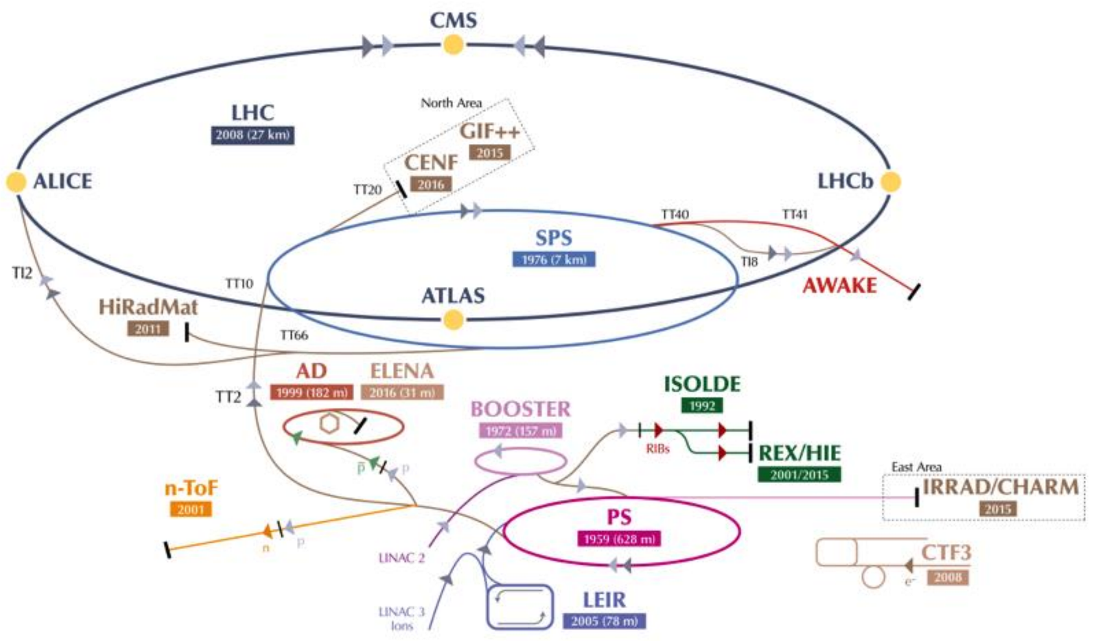
JNM The Journal of NUCLEAR MEDICINE

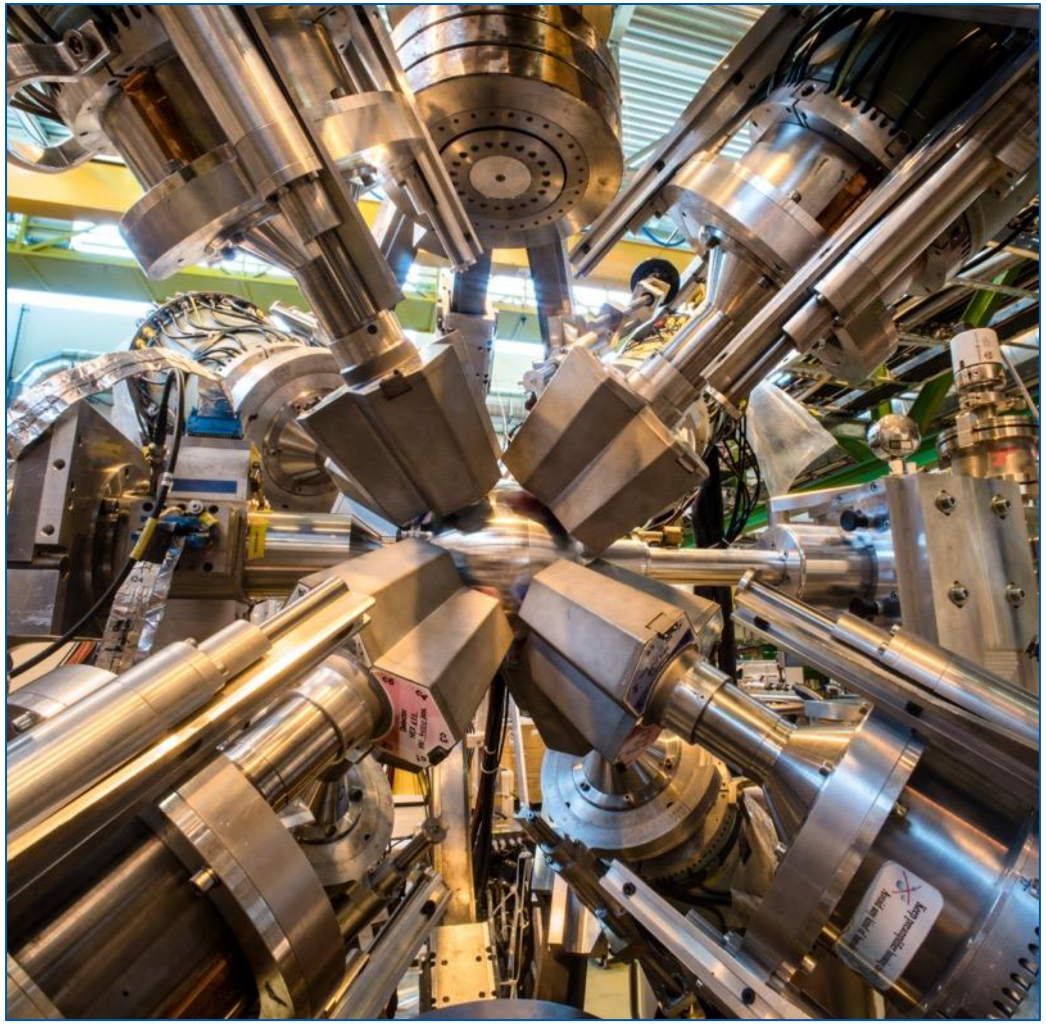
Theranostics



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



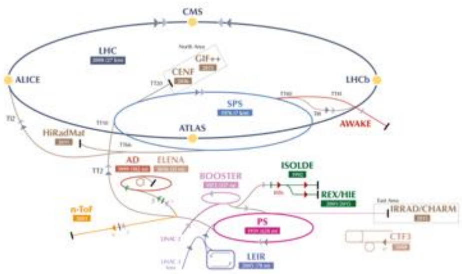


CERN-MEDICIS

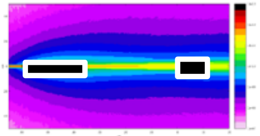
Non-conventional isotopes collected by mass separation for new medical applications

Principle of isotope production

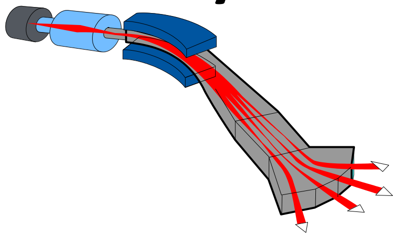
CERN protons

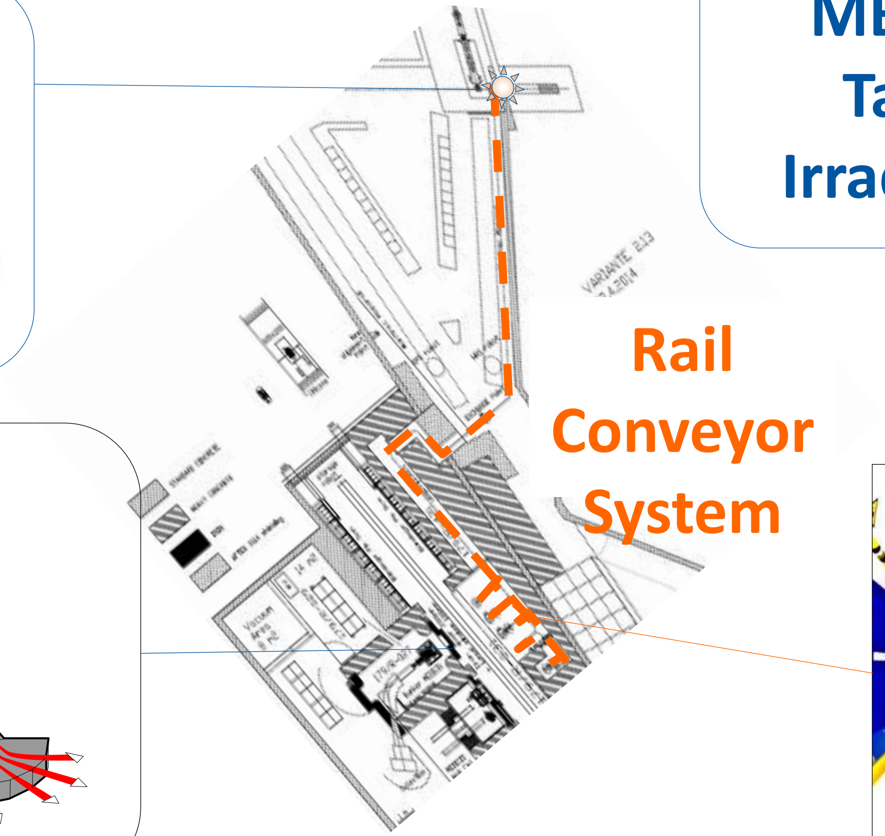


MEDICIS Target Irradiation



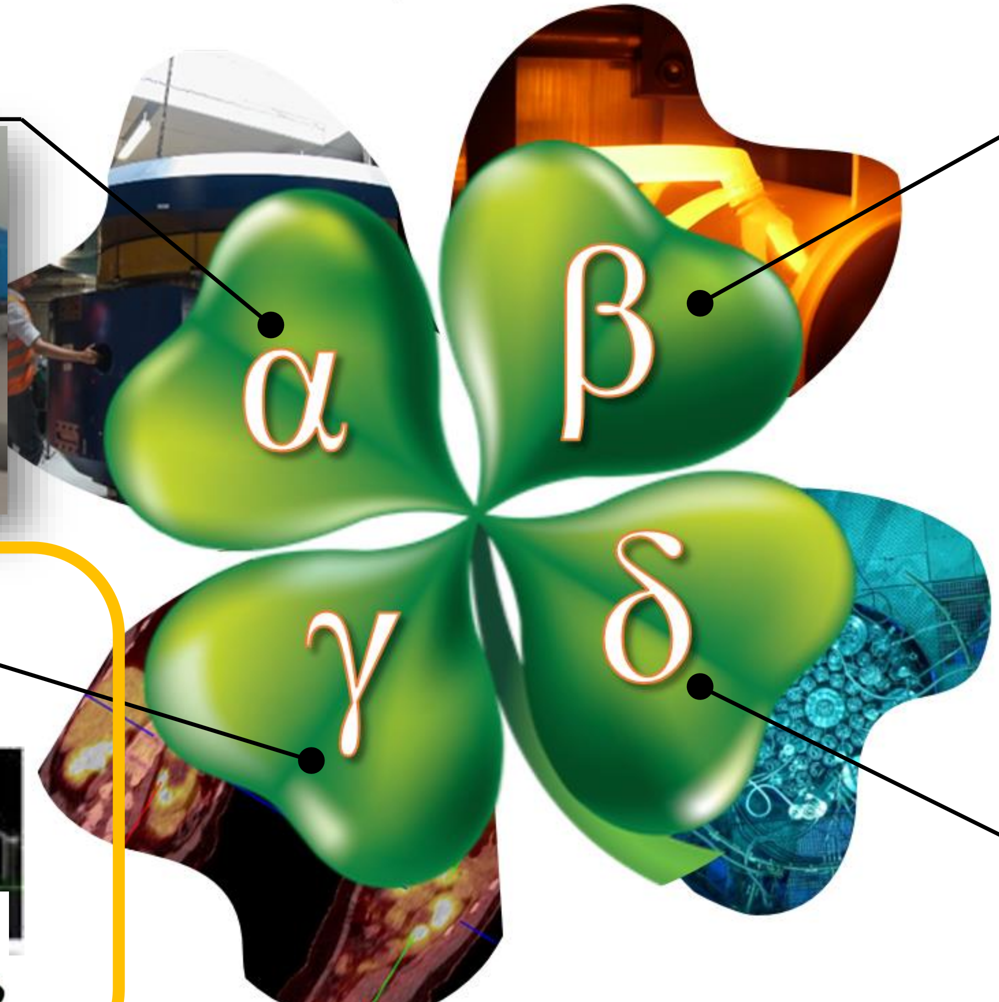
MEDICIS Laboratory



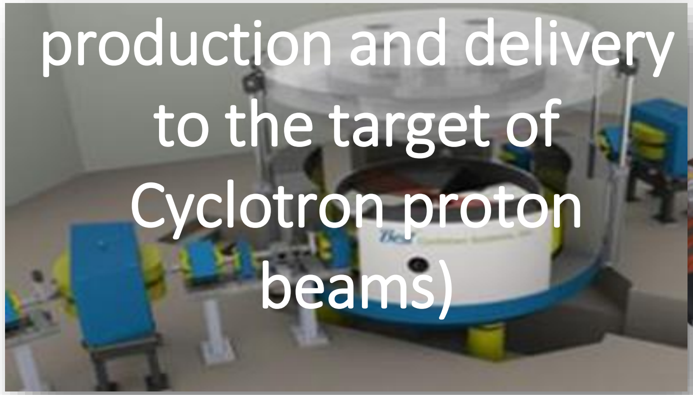


Rail Conveyor System

SPES -Selective Production of Exotic (nuclear) Species @ LNL

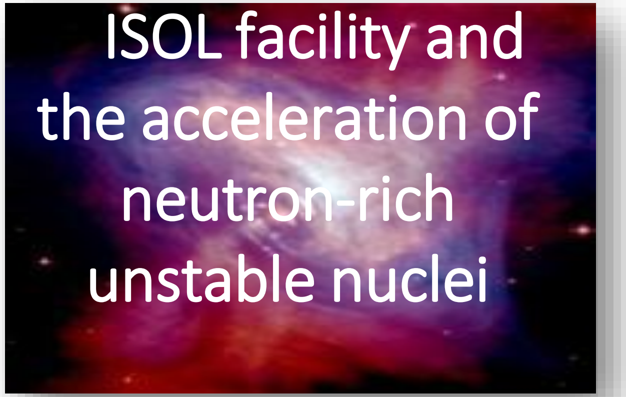


SPES-α



production and delivery to the target of Cyclotron proton beams)

SPES-β



ISOL facility and the acceleration of neutron-rich unstable nuclei

SPES-γ

Radioisotopes for medical applications

ISOLDE PHARM Knowledge Transfer Accelerating Innovation & LARAMED

SPES-δ

Neutron source for applied physics and industry

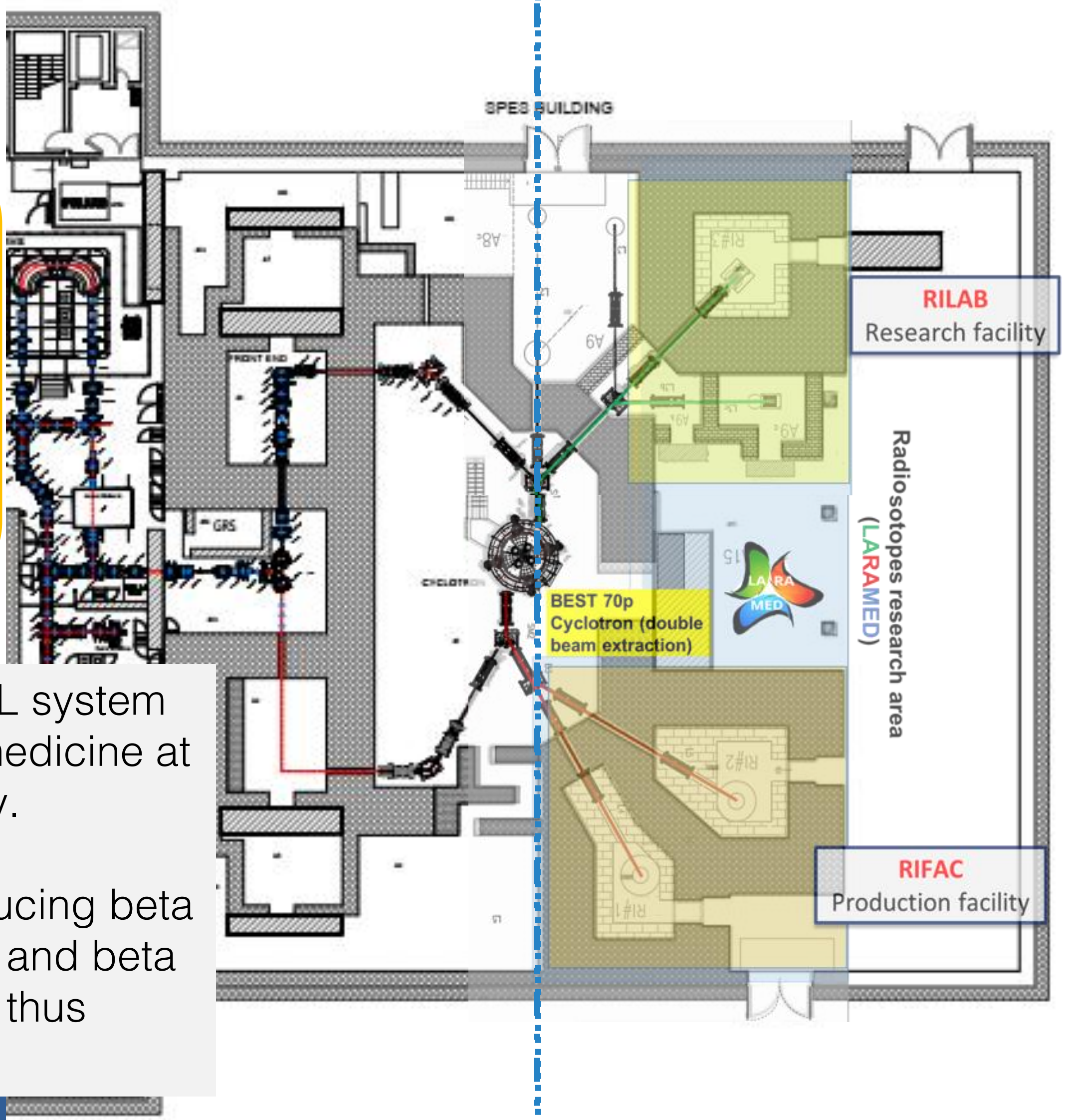
SPES-γ: innovative radioisotopes for medical applications

Production of radiosiotopes for medical applications via **ISOL technique**

ISOLPHARM
SPES exotic beams for medicine

Focused on the use of the ISOL system to produce radioisotopes for medicine at high specific activity and purity.

INFN patent «Method for producing beta emitting radiopharmaceuticals and beta emitting radiopharmaceuticals thus obtained»



Production of radiosiotopes for medical applications via **dire n**

LAboratory of Radionuclides for MEDicine

molecules MDPI

Letter

LARAMED: A Laboratory for Radioisotopes of Medical Interest

Juan Esposito [1], Diego Bettoni [1,2], Alessandra Boschi [3], Michele Calderolla [1], Sara Cisternino [1], Giovanni Fiorentini [2], Giorgio Keppel [1], Petra Martini [1,3,*], Mario Maggiore [1], Liliana Mou [1], Micòl Pasquali [1], Lorenzo Pranovi [1], Gaia Pupillo [1], Carlos Rossi Alvarez [1], Lucia Sarchiapone [1], Gabriele Sciacca [1], Hanna Skliarova [1], Paolo Favaron [1], Augusto Lombardi [1], Piergiorgio Antonini [1] and Adriano Duatti [1,4]

[*] Esposito J et al., Molecules **2019**, 24, 20; doi:10.3390/molecules24010020

Gamma-MRI project

Development of a new medical diagnostic modality

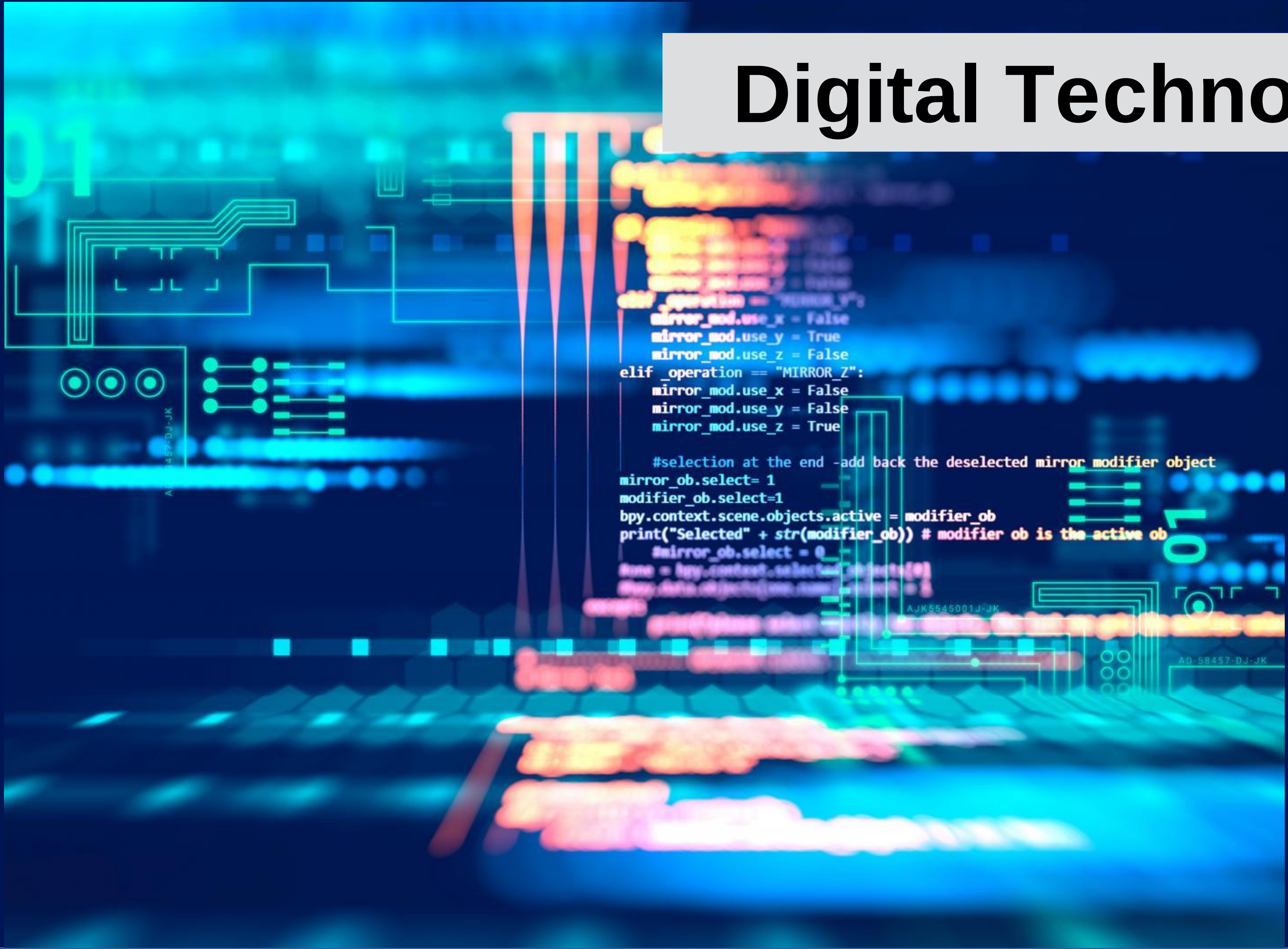
Combine high spatial resolution (MRI) and high sensitivity (radiotracer)

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

GEANT4 collaboration
A SIMULATION TOOLKIT

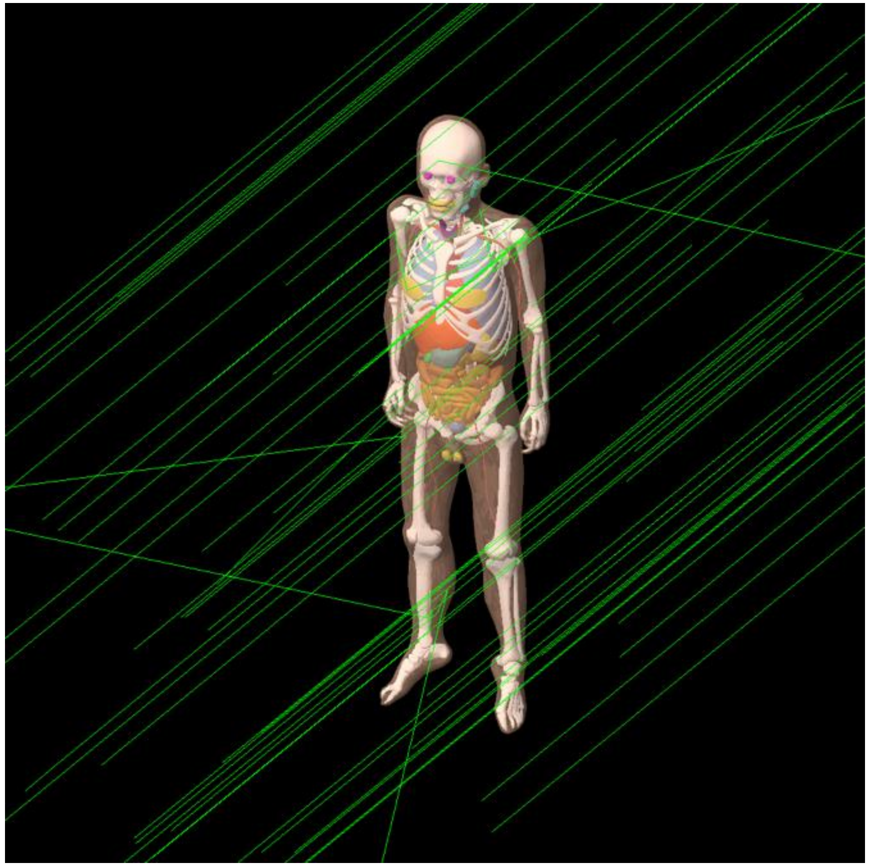
http://geant4.cern.ch/

Geant4: a simulation toolkit
S. Agostinelli *et al.*
NIM A, vol. 506, no. 3, pp. 250-303, 2003

Geant4 Developments and Applications
J. Allison *et al.*
IEEE Trans. Nucl. Sci., vol. 53, no. 1, pp. 270-278, 2006

Recent Developments in Geant4
J. Allison *et al.*
NIM A, vol. 835, pp. 186-225, 2016

Human phantoms



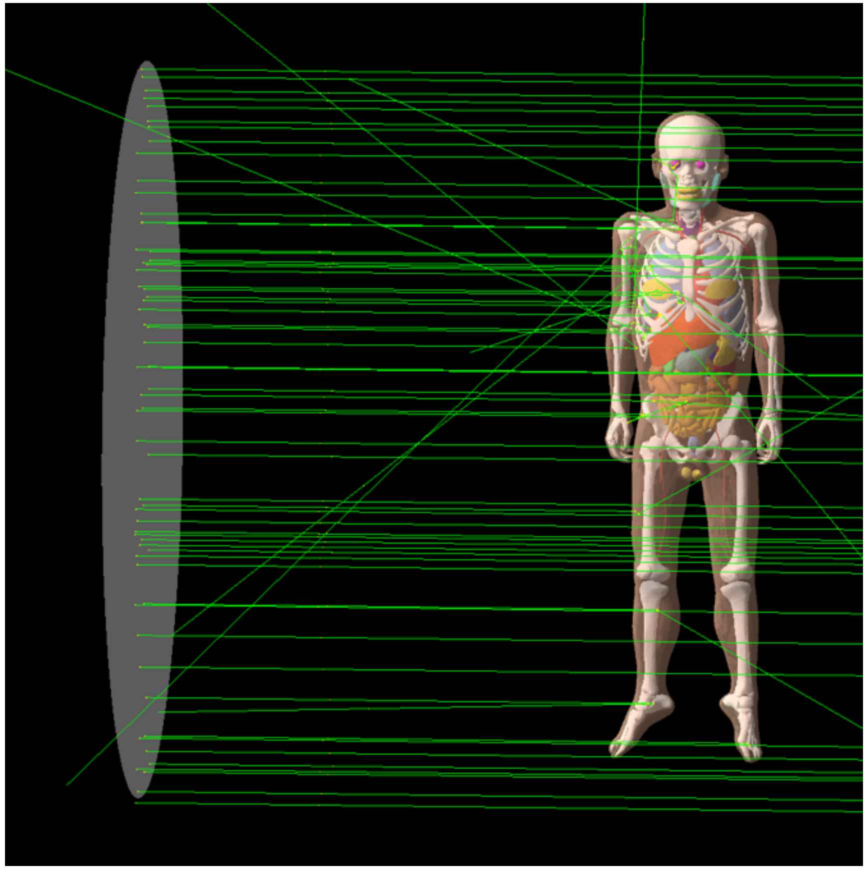
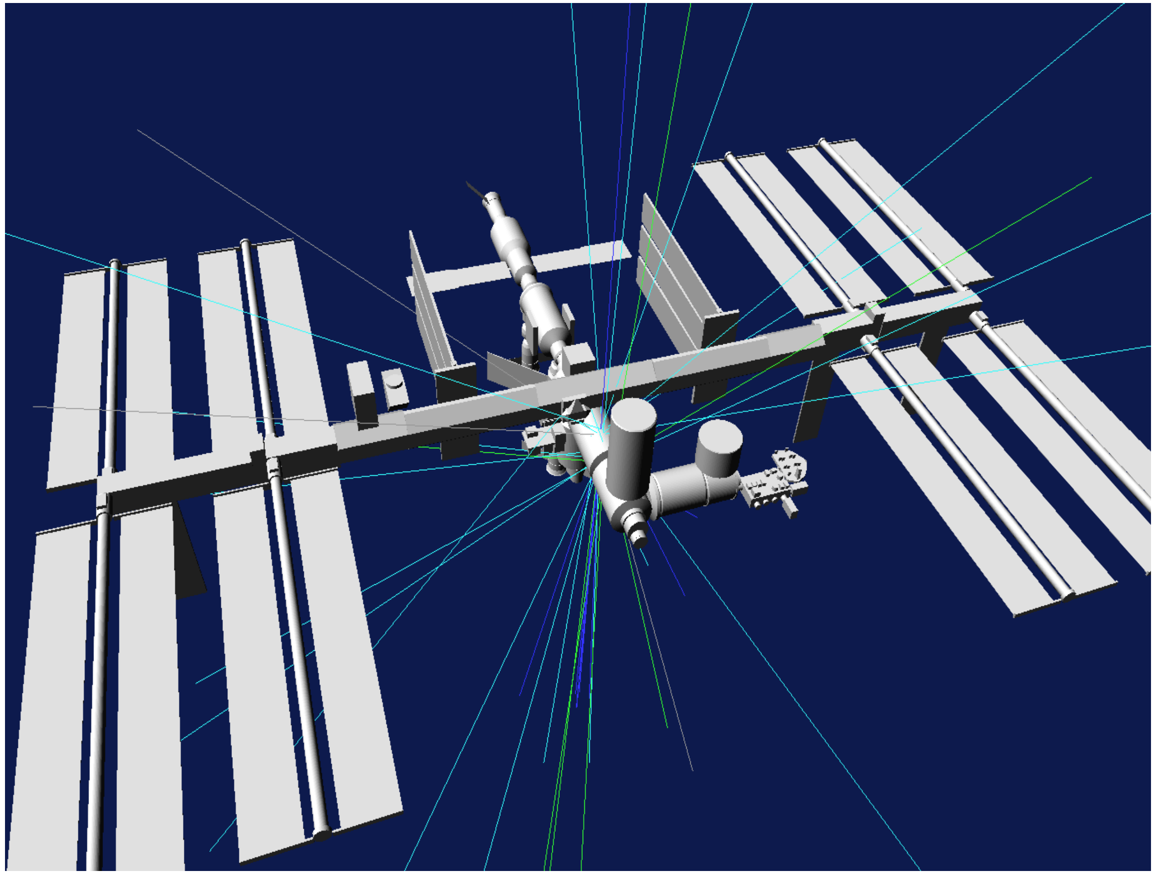


Image of Polygon-Surface Reference Korean Male Phantom (PSRK-Man), implemented in Geant4. Courtesy of C.-H. Kim & C. Choi, Hanyang Univ.

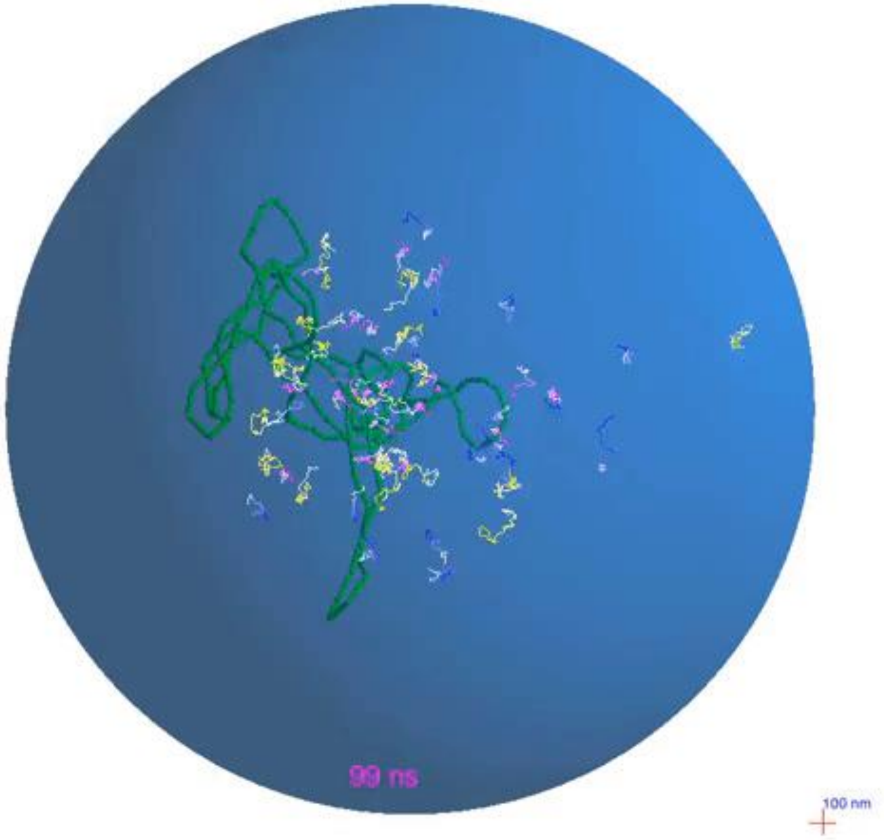
Radiation Environment – model of space station



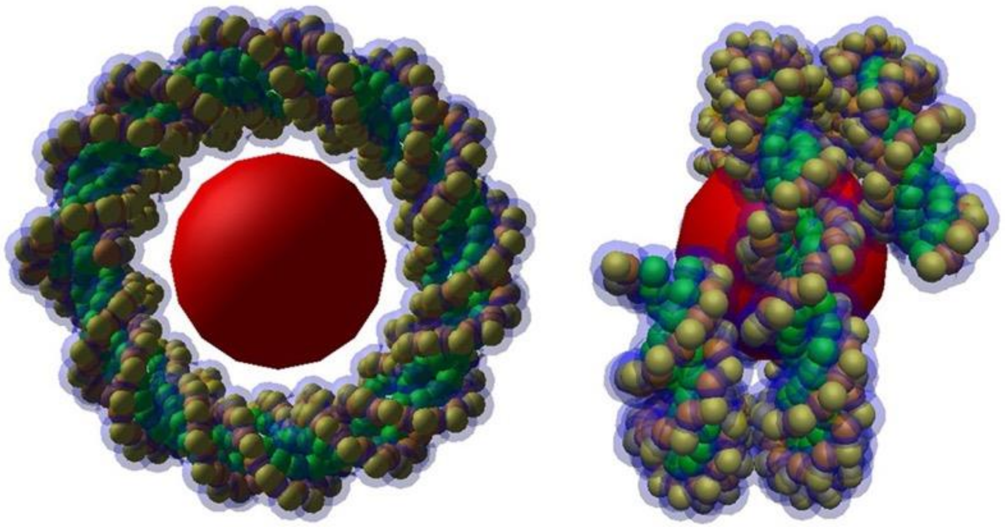
Courtesy T. Ersmark, KTH Stockholm

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’

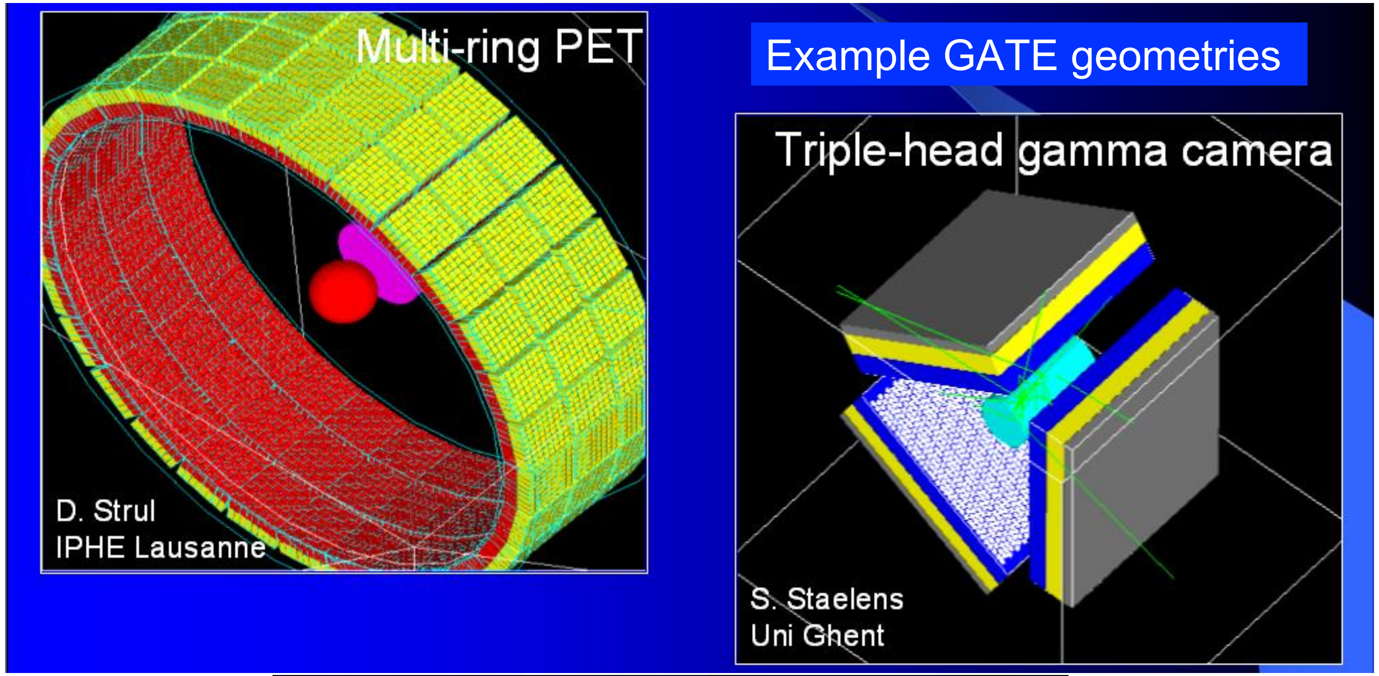
output adapted for application-area

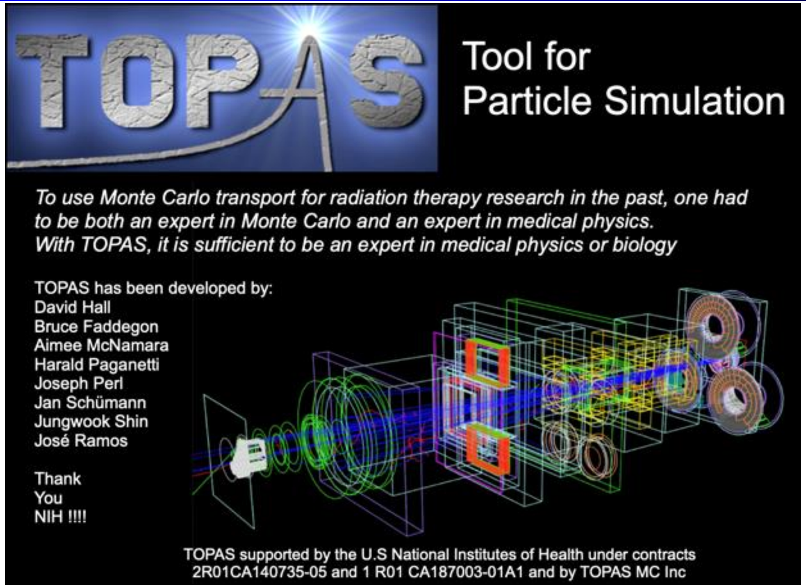
GATE (FR, DE, GR, PL, AT) - PET/SPECT,

TOPAS (US) - protontherapy

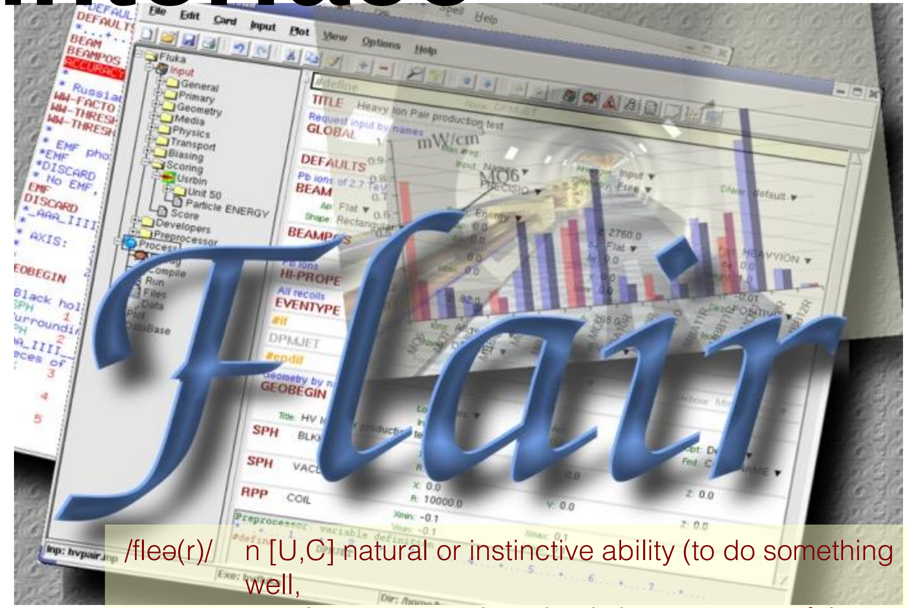
GAMOS (ES) - for nuclear medicine applications

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

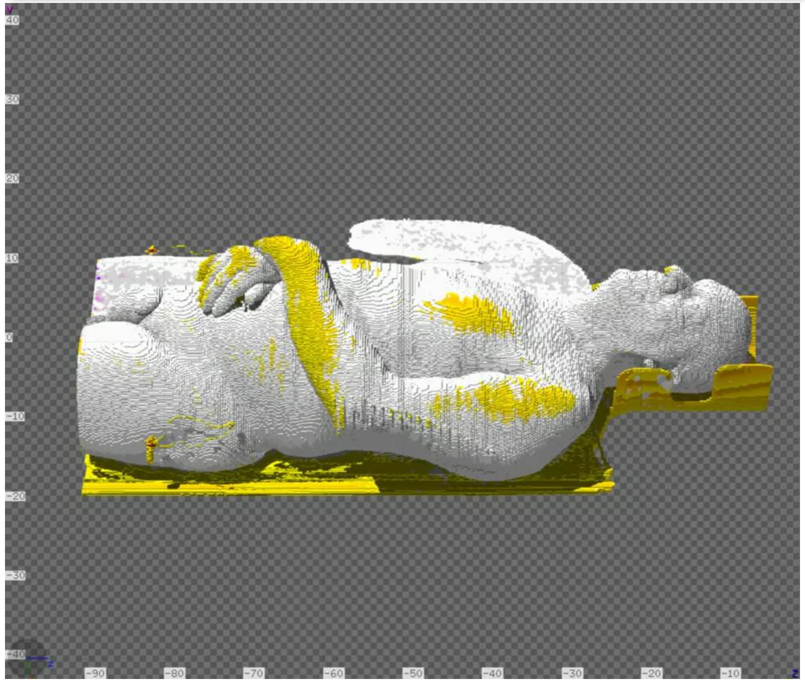
Improvements for medical simulations

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

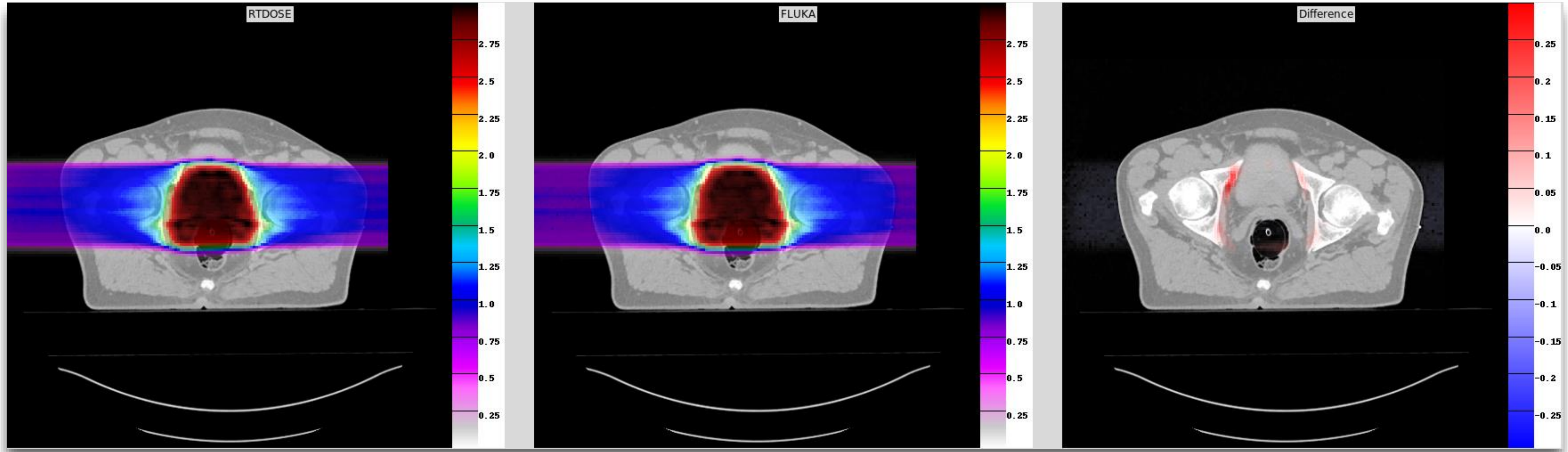
Importing the RT DOSE with the activity mapping of ^{68}Ga

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!

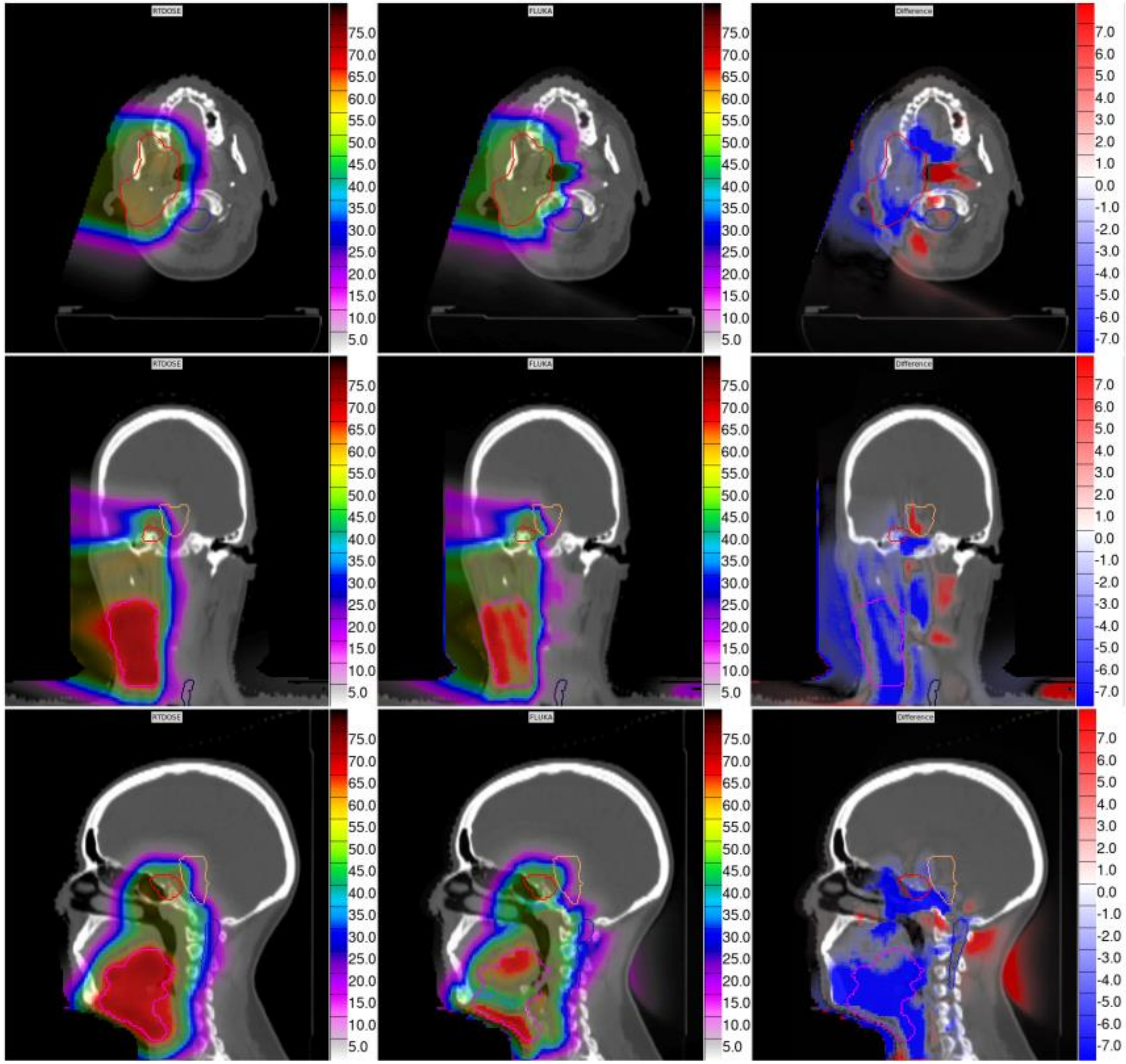
Sensitivity studies of Monte Carlo TP recalculations



Proton prostate patient case (MedAustron) W.Kozlowska PhD

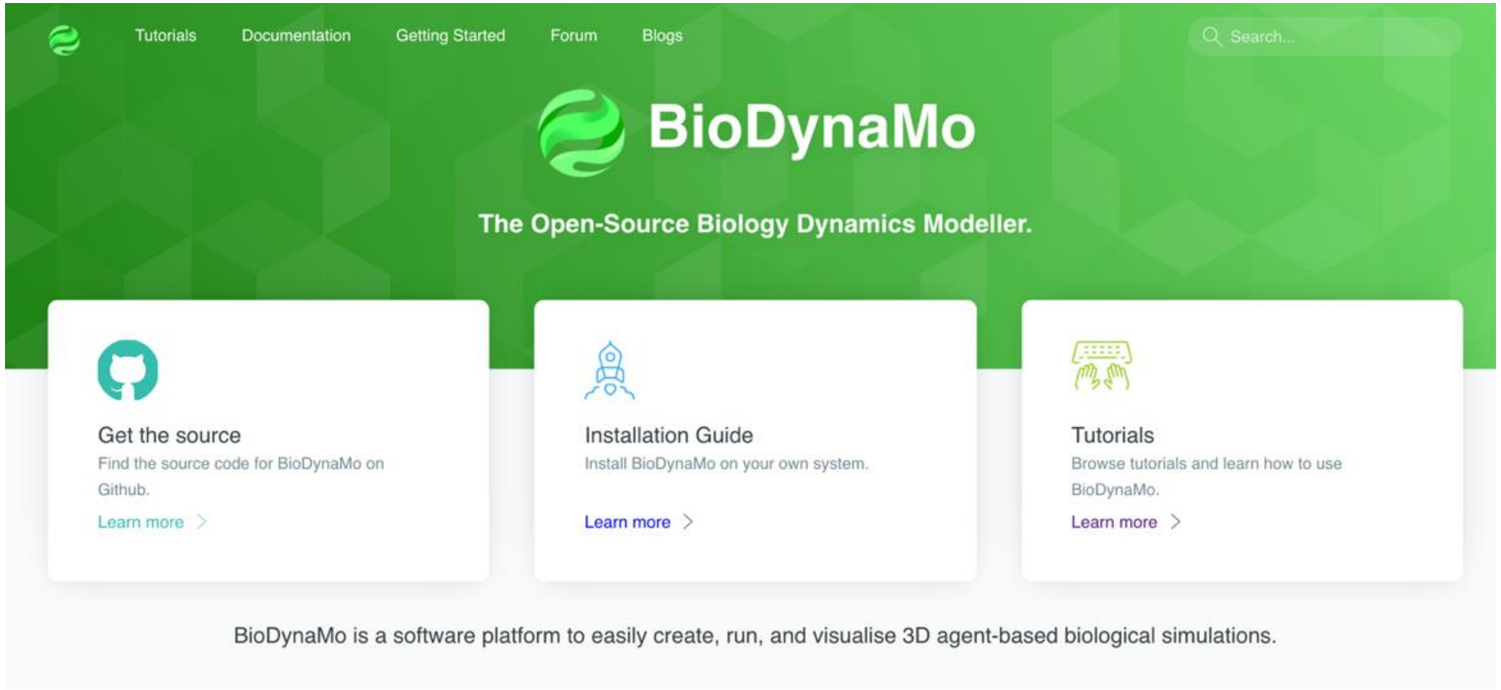
FLUKA

Head and Neck case



Head and Neck case (CNAO)
W.Kozlowska PhD

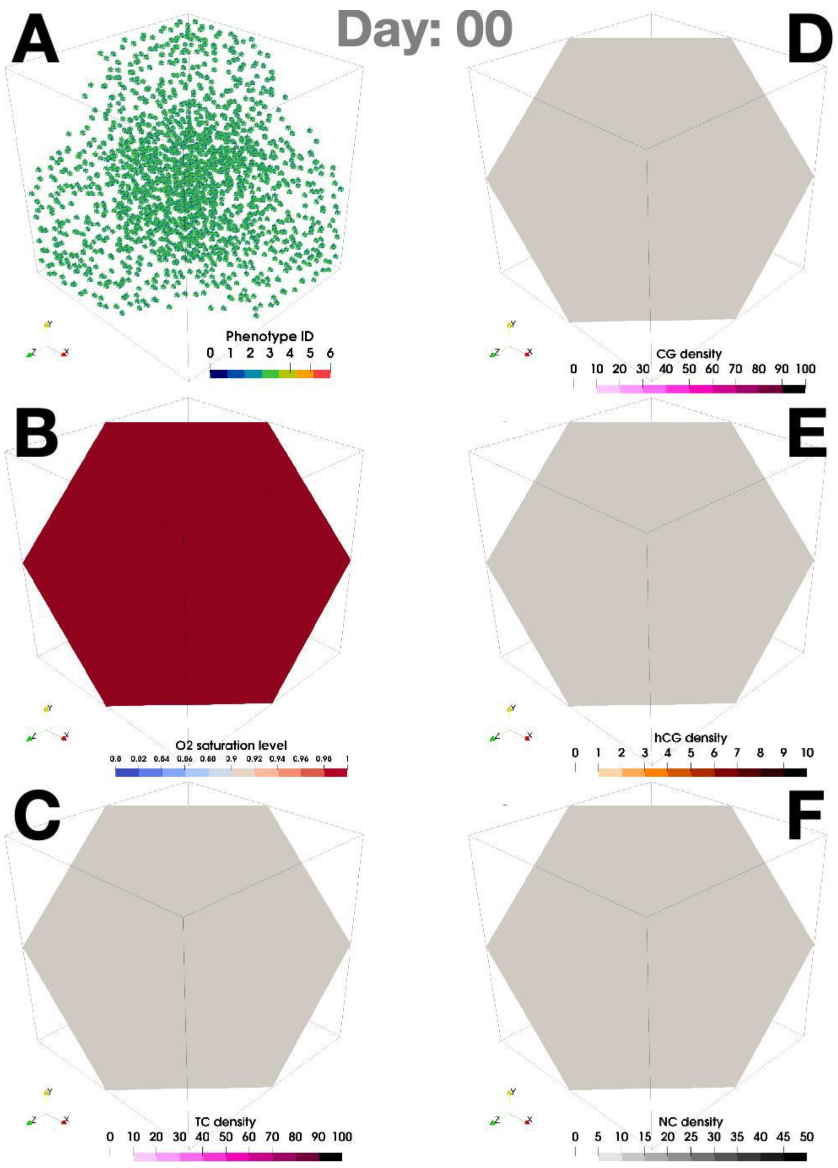
BioDynaMo: An open-source software framework



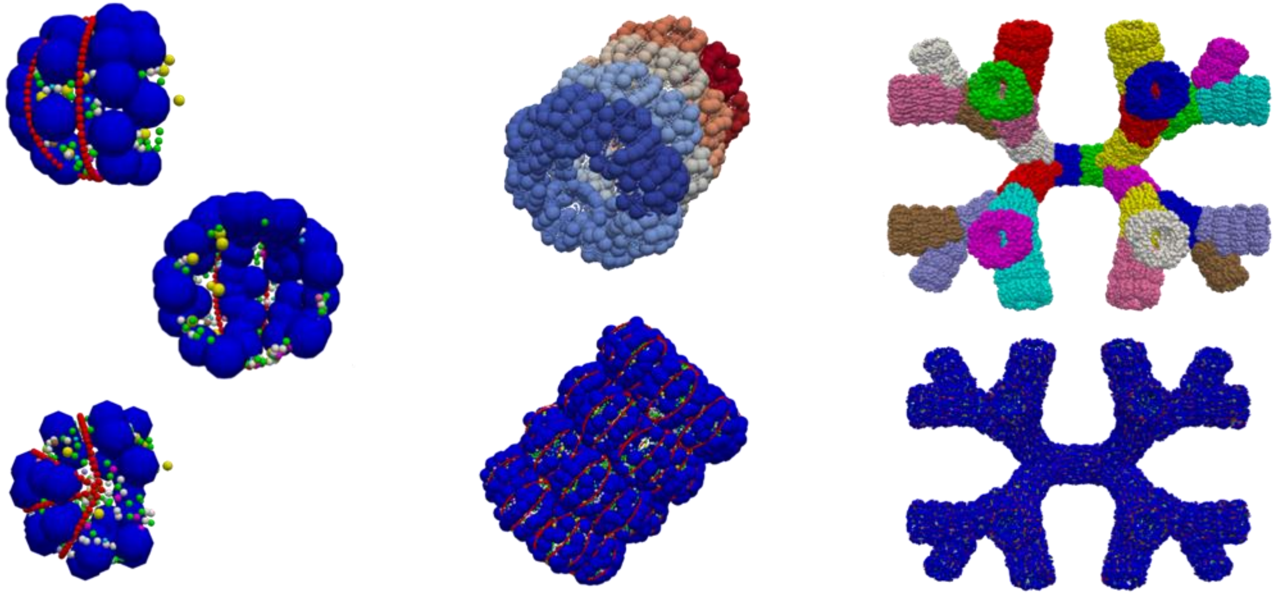
An open-source software platform to easily create, run, and visualise 3D agent-based simulations, built up around CERN-developed technologies

www.biodynamo.org

Newcastle University
CERN
University of Cyprus
GSI
Scimpulse foundation
UNIVERSITÉ DE GENÈVE
UNIVERSITY OF SURREY
Statistics Netherlands
ImmunoBrain Checkpoint



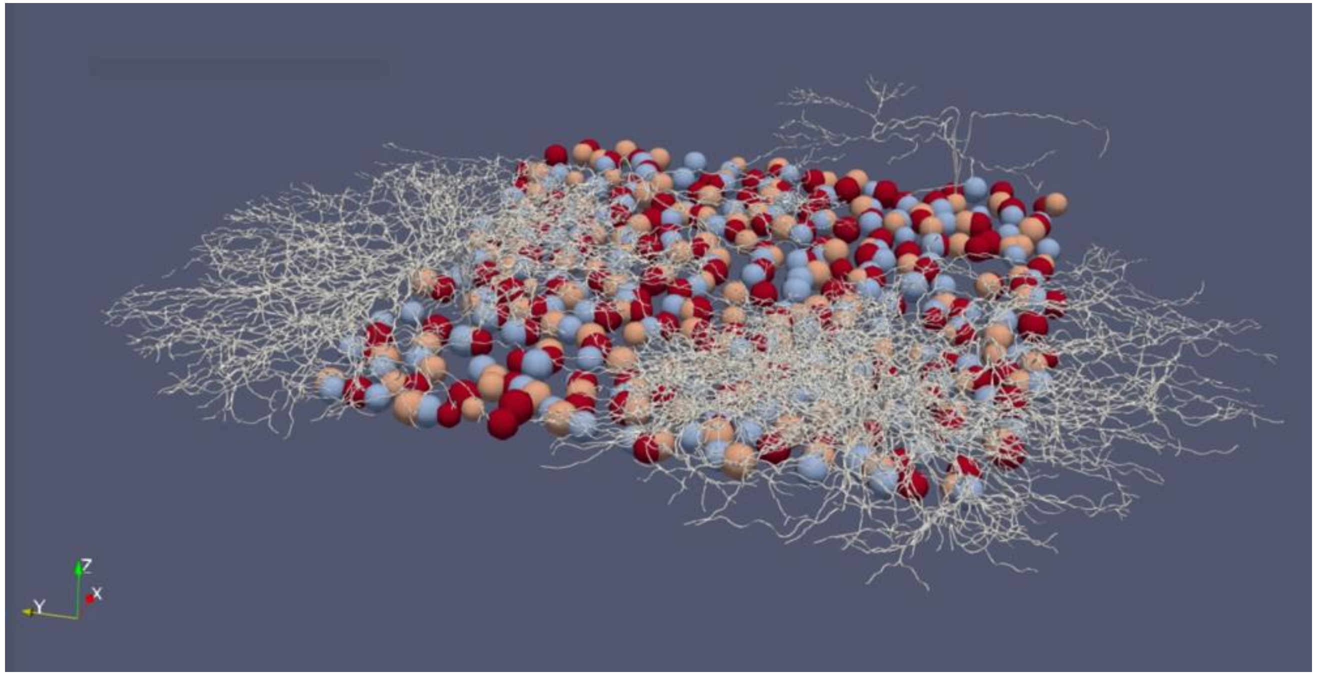
BioDynaMo
Biology Dynamics Modeller

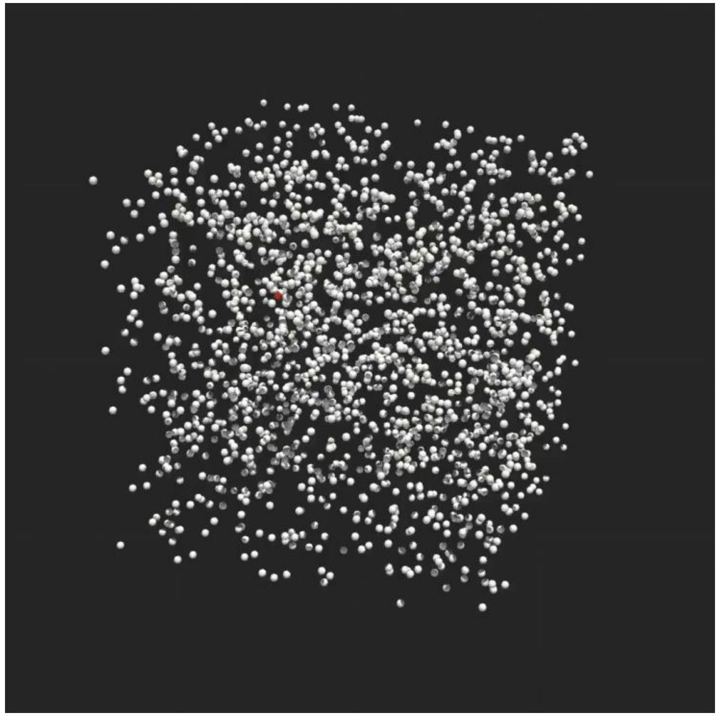


Courtesy Nicolo Cogno, TU Darmstadt (Germany)

From De Montigny et al., Methods, 2020

BioDynaMo
Biology Dynamics Modeller





Courtesy Jean de Montigny and Roman Bauer

CERN openlab
UNIVERSITÉ DE GENÈVE

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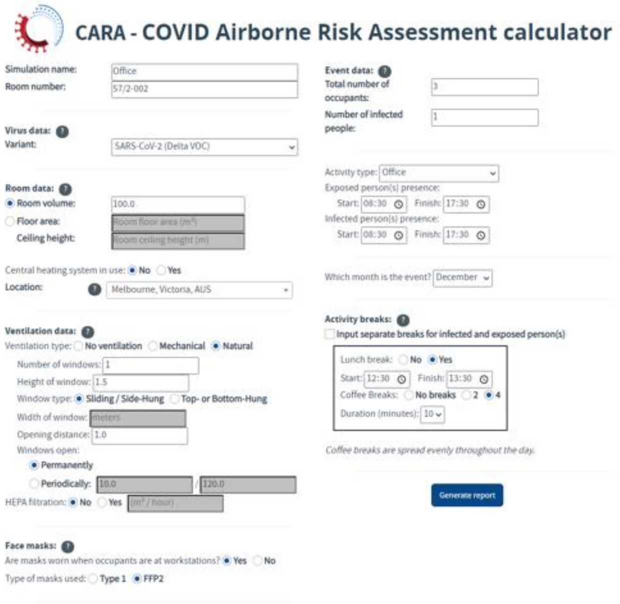
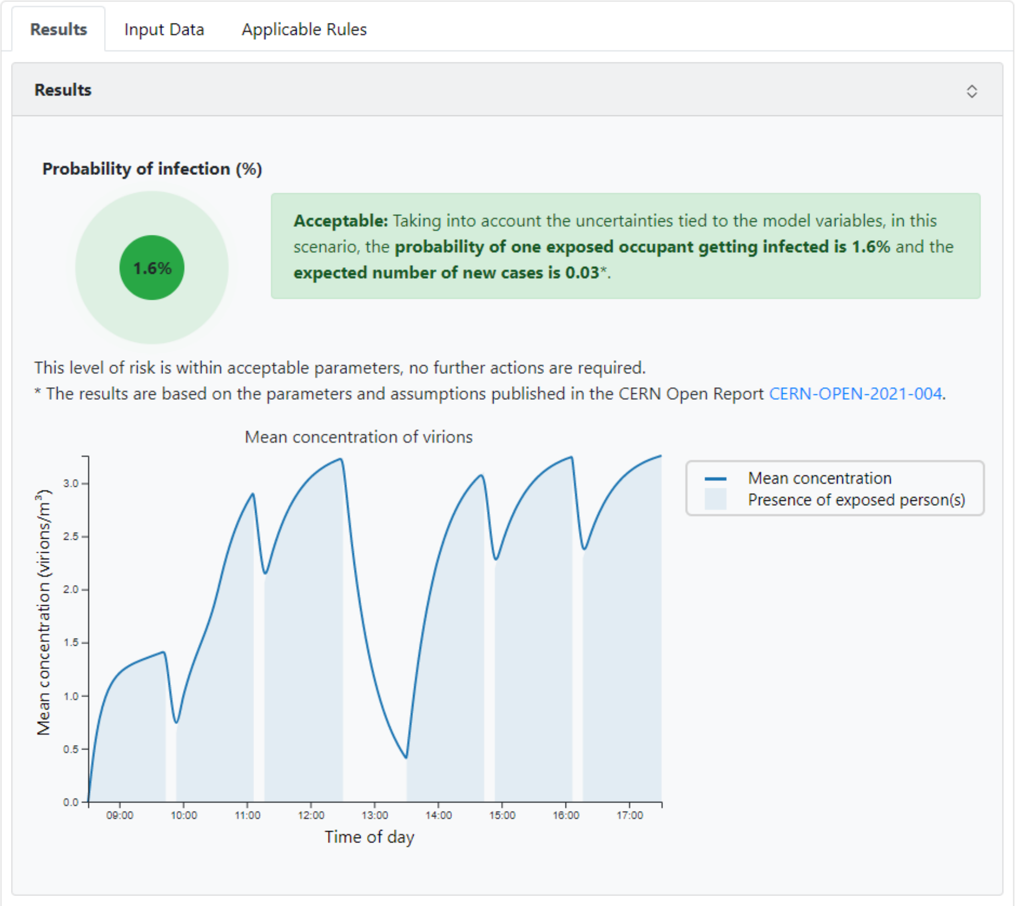
COVID Airborne
Risk Assessment





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

Includes hourly fluctuations in outdoor temp (GVA data) and detail window modelling for natural ventilation, complex occupancy and ventilation profiles.

Andre Henriquez (CERN)

CS4OD
CERN Science for Open Data

Data size

overcome barriers related to data governance and storage defining **common principles**

Data heterogeneity

overcome barriers of data access defining a **global coordination** of **open data from multi-domain fields**

Data analysis

overcome barriers of analysis diversity defining **common pipelines and approaches**

Data overload

overcome barriers of excess of information by complying with **results reproducibility and multi-disciplinary expertise's exchange**

SWAN EOS CERNBox reana zenodo

SCIENCE AND TECHNOLOGY BRIEFINGS

PARLIAMENTARY OFFICE FOR SCIENTIFIC AND TECHNOLOGICAL ASSESSMENT

ASSEMBLÉE NATIONALE — SÉNAT

Briefing n° 12 — **Large particle accelerators** — February 2019

Ring segment of a particle accelerator
© fotonat67 / Adobe Stock

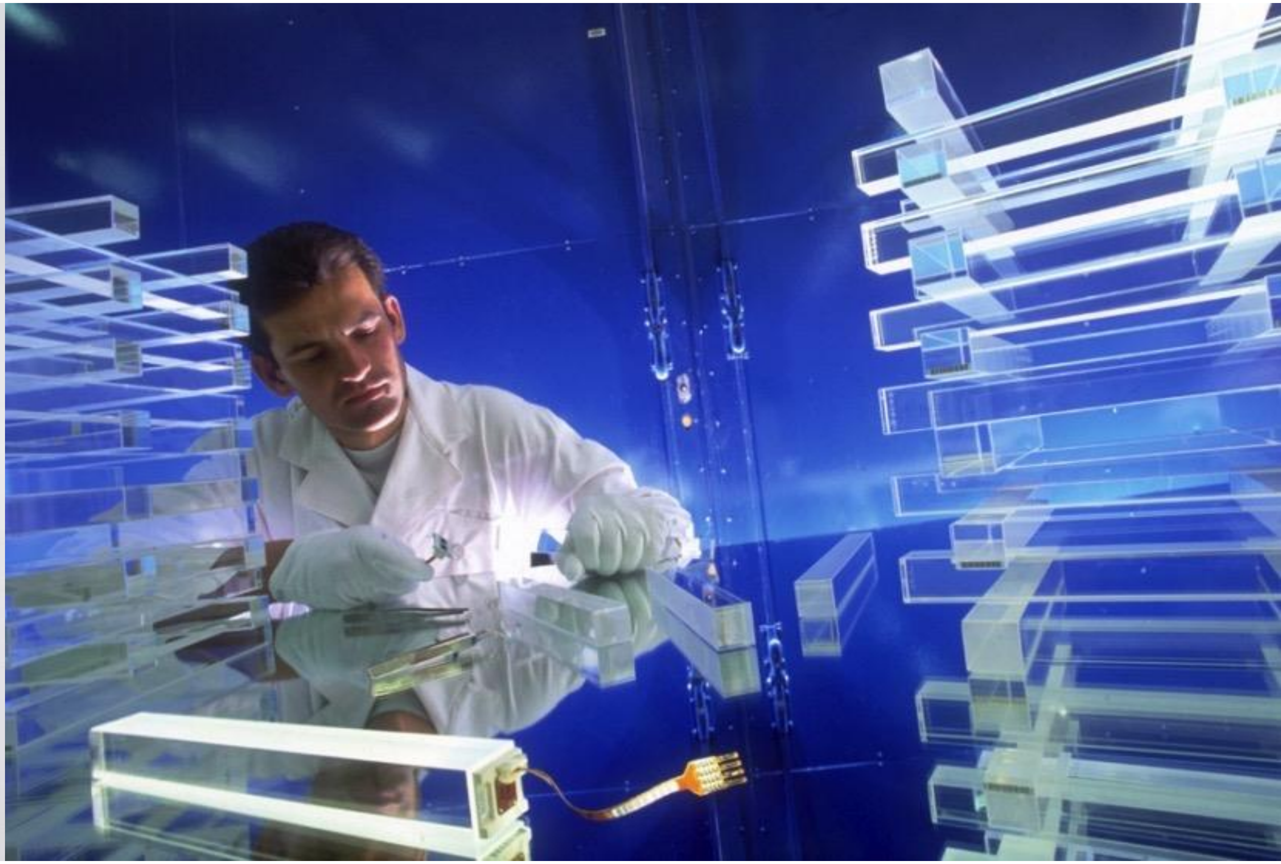
Summary

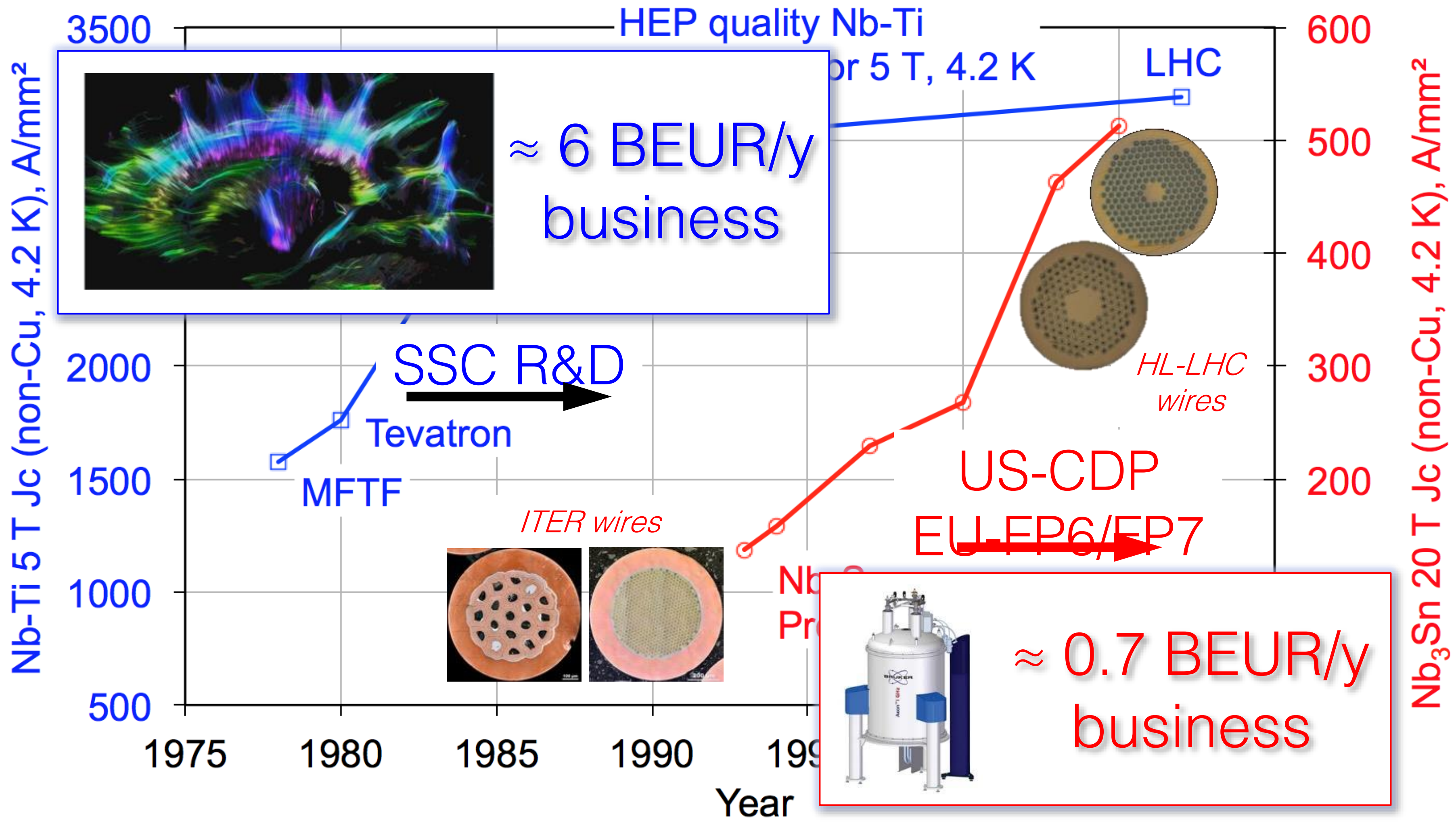
- *Particle accelerators, like other kinds of "very large research infrastructure" (VLRI), make it possible to manage cutting-edge projects and respond to strategic issues: acquiring knowledge, enhancing scientific attractiveness, preparing for technological breakthroughs, scientific diplomacy, etc.*
- *CERN, the European particle physics laboratory, currently operates the biggest circular particle accelerator in the world, the LHC, which achieves the highest energies produced to date.*
- *A decision by the Japanese government is exp… accelerator project, the ILC, proposed sinc… scientific community.*
- *Thinking on the future European strategy for… 2018 and should be presented in spring 2020. I… confirms its interest in ILC, this European stra… this fact: a possible contribution from Europe… must be assessed in terms of scientific return, c…*

Mr. Cédric Villani, MP (National Assembly), First Vice-Chairman

CERN has also had a very strong societal impact via **the creation of the *World Wide Web* (WWW)** in 1989[21] under the leadership of Tim Berners-Lee and his collaborator Roger Cailliau. It was originally a response to researchers' need to exchange a high volume of data simply and instantaneously for international collaborations. CERN published software

From HEP to society:
a long and winding road…



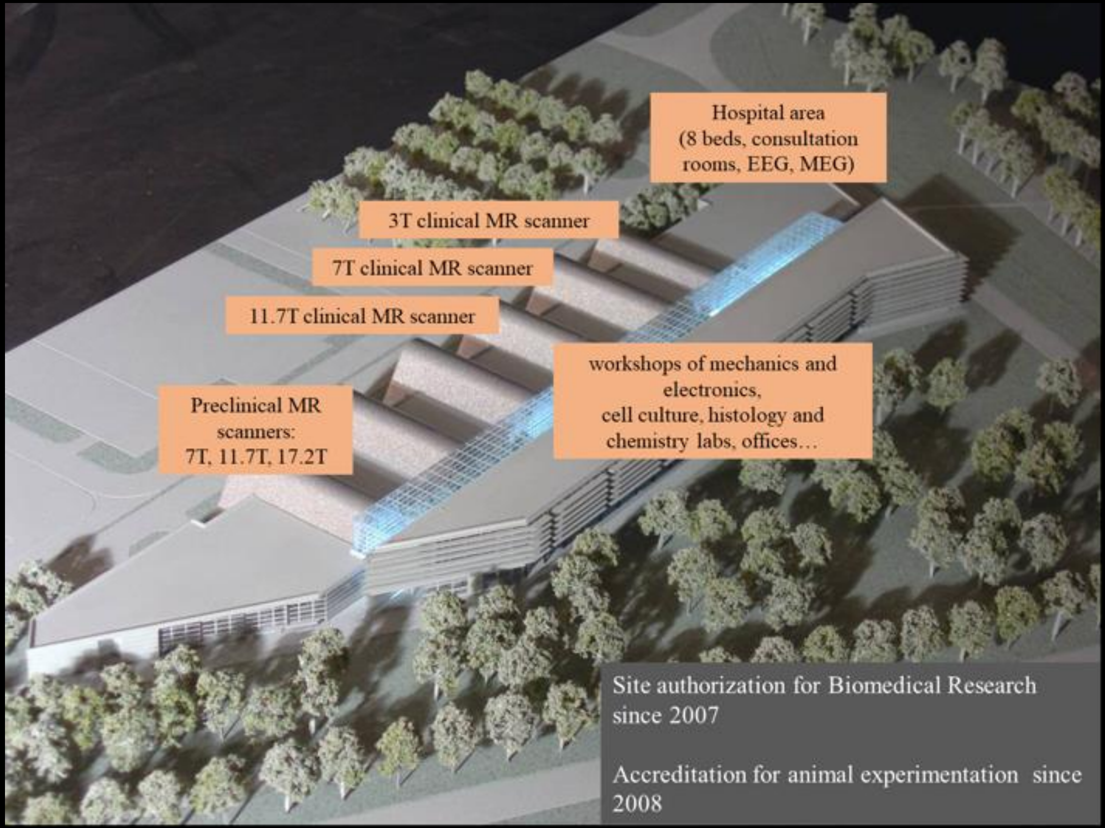


Courtesy Luca Bottura (CERN)

On the unreasonable request of high J_C

The ISEULT whole body 11.7 T MRI magnet

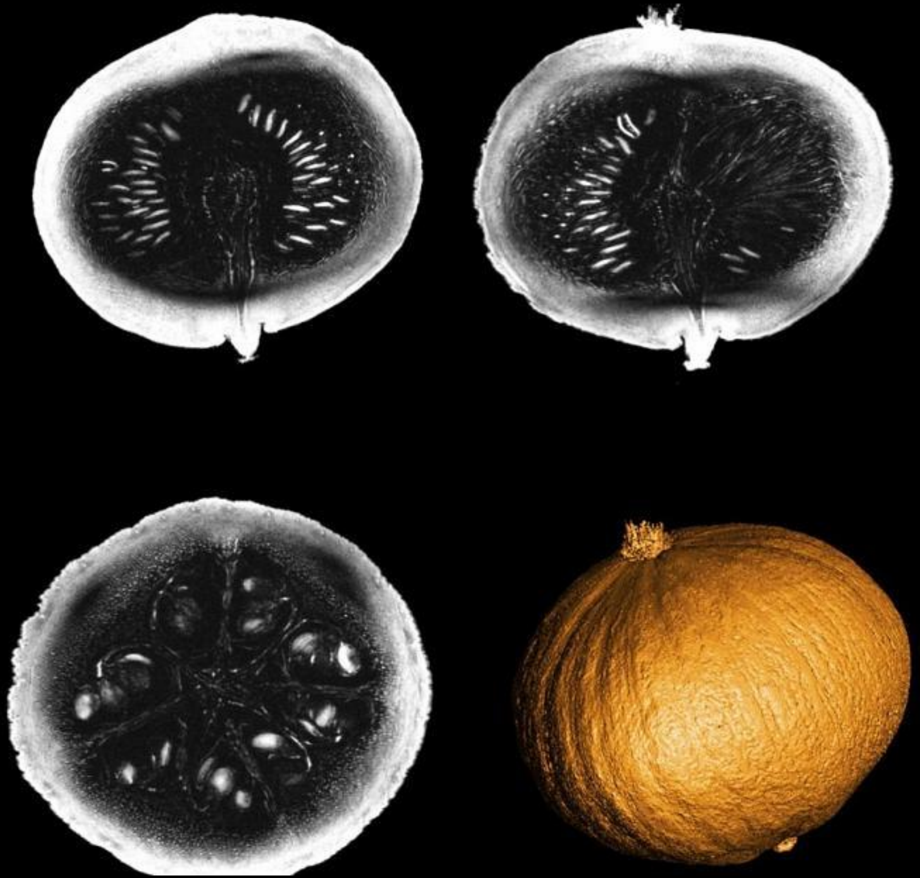
NEUROSPIN: a unique concept in neuroscience research



The ISEULT whole body 11.7 T MRI magnet

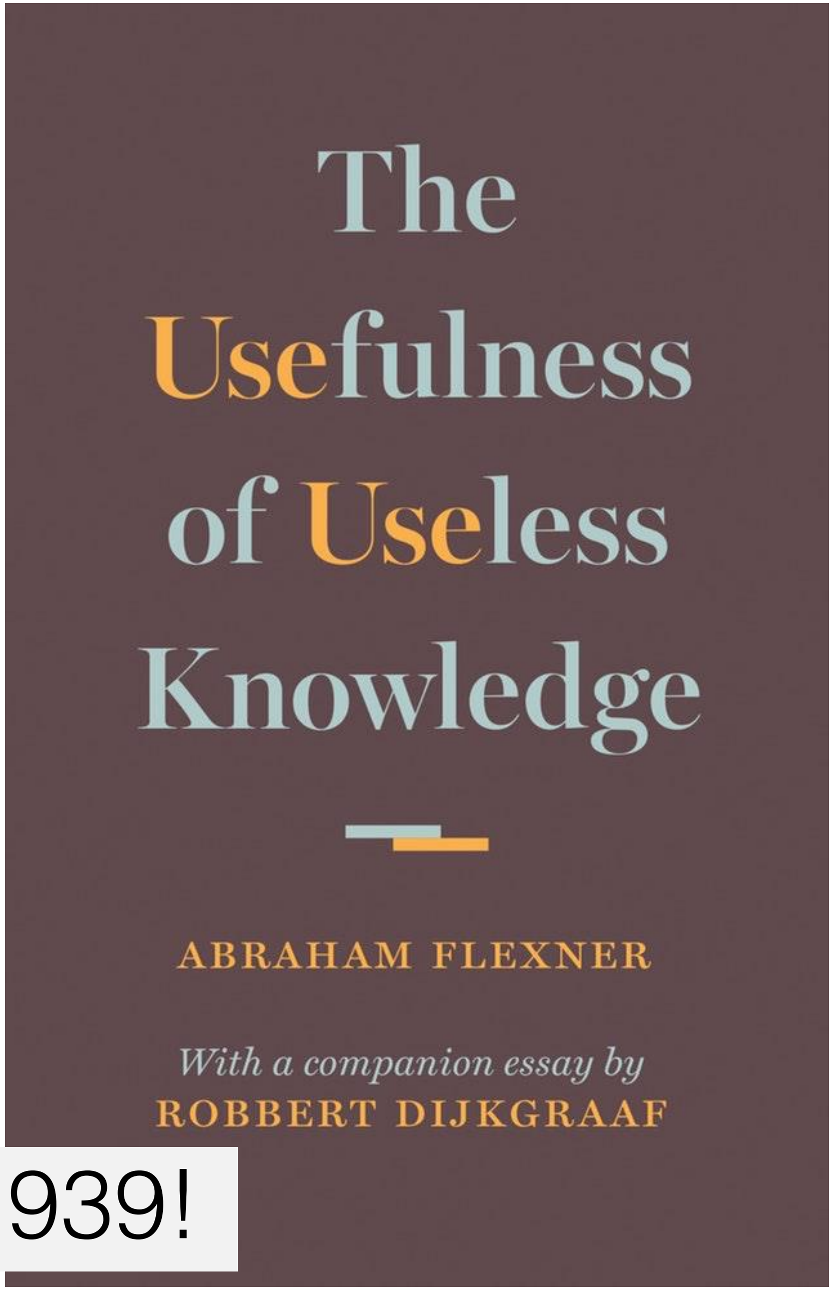
The ISEULT magnet -
a French-German initiative

Full field of 11.72 teslas achieved on July 18, 2019



First images released Oct. 7, 2021

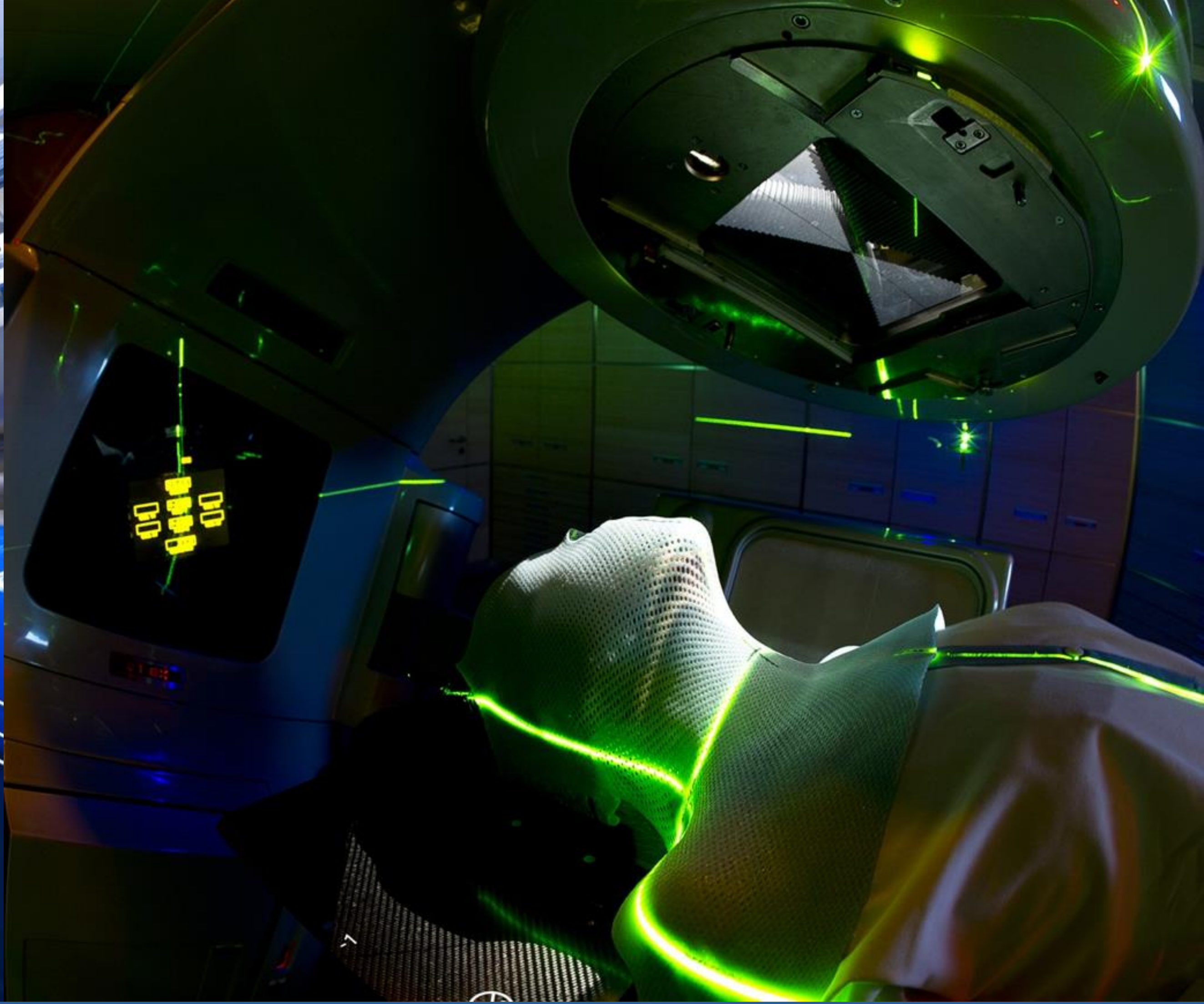
https://www.cea.fr/presse/Pages/actualites-communiques/sante-sciences-du-vivant/premieres-images-irm-iseult-2021.aspx



1939!

In the end, utility resulted, but it was never a criterion to which his (*Faraday's, ndr*) ceaseless experimentation could be subjected.

I am not for a moment suggesting that everything that goes on in laboratories will ultimately turn to some unexpected practical use or that an ultimate practical use is its actual justification.



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