From CERN technologies to Medical Applications


Photo: CERN


Photo: CNAO treatment room

Manuela Cirilli,
Medical Applications Advisor
CERN Knowledge Transfer group

CERN | Knowledge Transfer
Accelerating Innovation

SYMPOSIUM
30TH ANNIVERSARY OF THE TERA FOUNDATION
15 SEPTEMBER 1992 - 15 SEPTEMBER 2022

TERA

How I met TERA

Acknowledgements

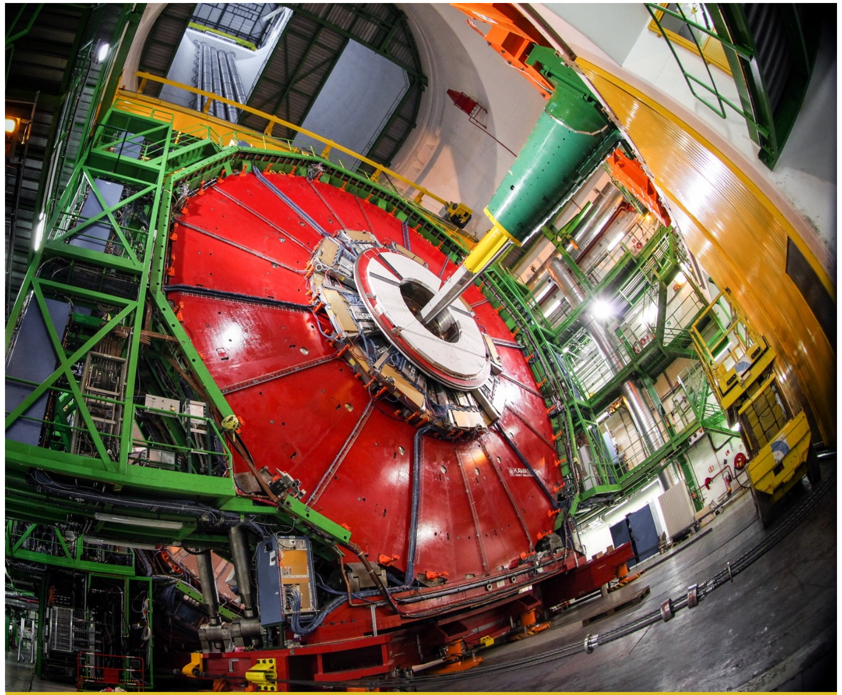
The medical applications-related projects presented in this talk are carried out by the CERN scientists and engineers: without their skills, ingenuity, and dedication, there would be no knowledge to transfer!

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.

Warm thanks (in no particular order) to all those who shared with me material, insights, stories, throughout the years, and apologies to those I unintentionally forgot.
Ugo Amaldi, Manjit Dosanjh, Sandro Rossi, Enrico Felcini, Silvia Meneghello, Christoph Kurfürst, Etiennette Auffray, Luca Bottura, Michael Campbell, Roberto Corsini, Alberto Di Meglio, Ariel Haziot, Mikko Karppinen, Alessandra Lombardi, Diego Perini, Marco Silari, Thierry Stora, Davide Tommasini, Maurizio Vretenar, Walter Wuensch, Giovanni Anelli, Benjamin Frisch, Alessandro Raimondo

We develop technologies in three key areas

ACCELERATORS



DETECTORS

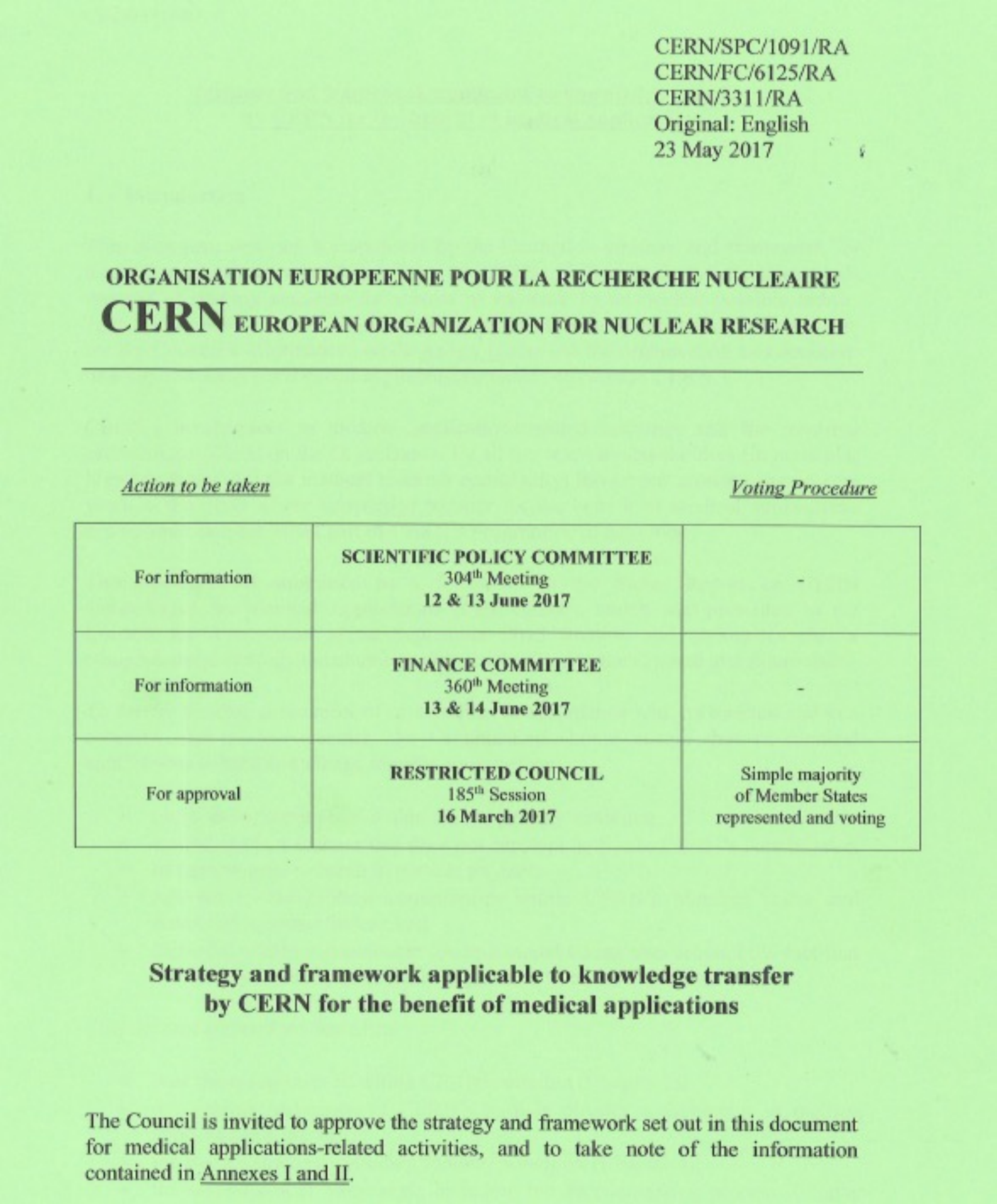
COMPUTING

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.

Strategy and framework approved by CERN Council in 2017



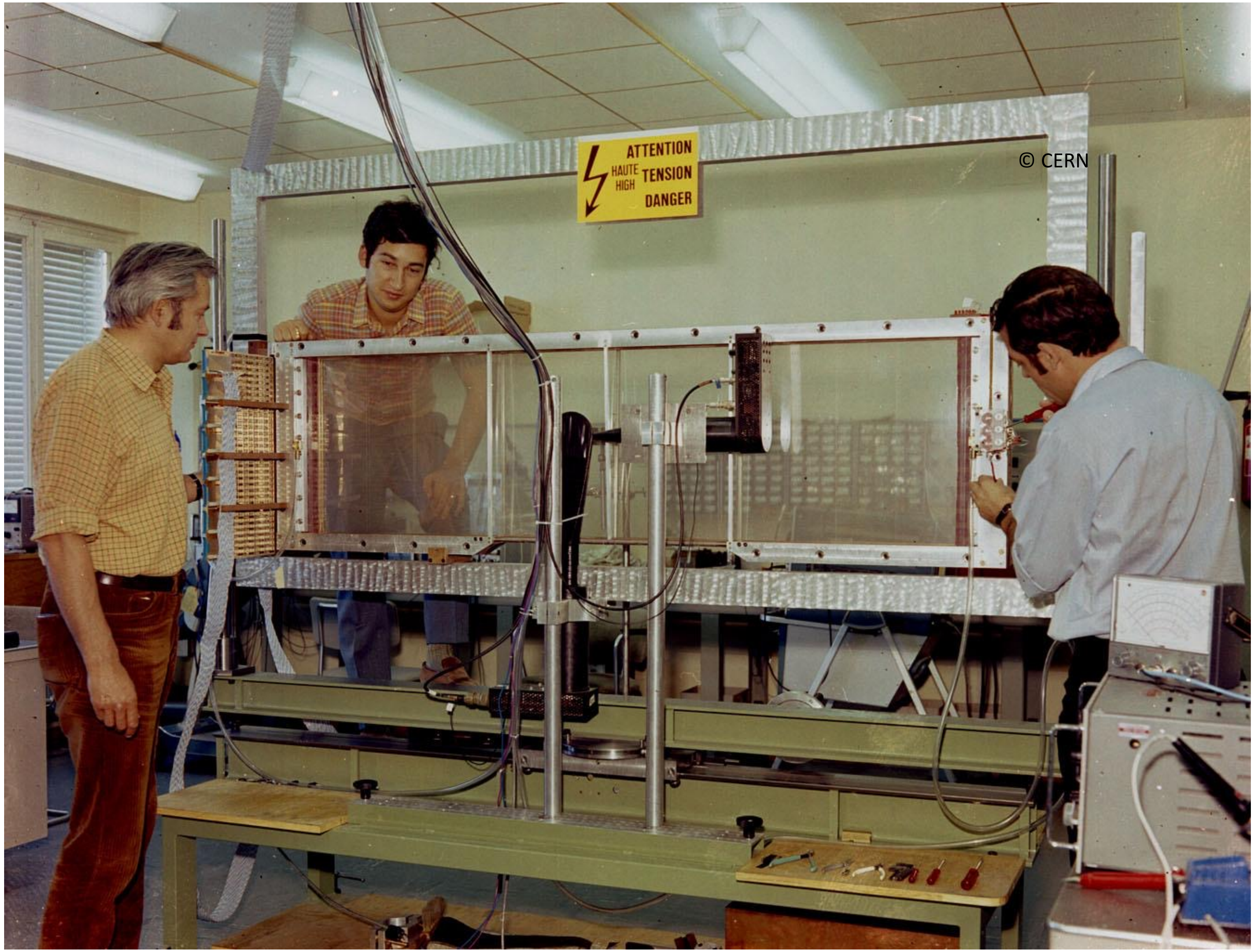
CERN/SPC/1091/RA
CERN/FC/6125/RA
CERN/3311/RA
Original: English
23 May 2017

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.



© CERN

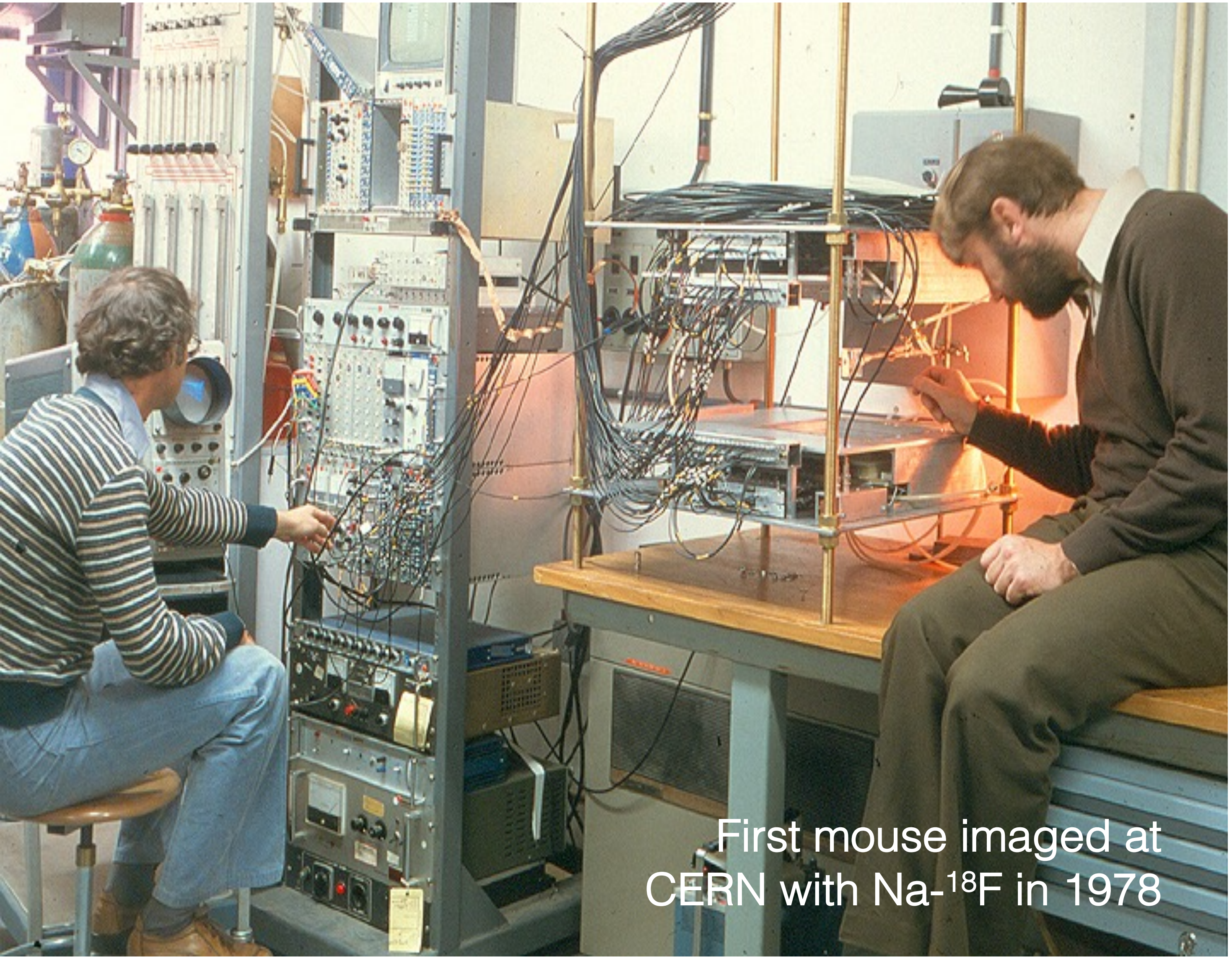

Radioprotection 2005 DOI: 10.1051/radiopro:2005010
Vol. 40, n° 2, pages 245 à 255

Produit nouveau

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

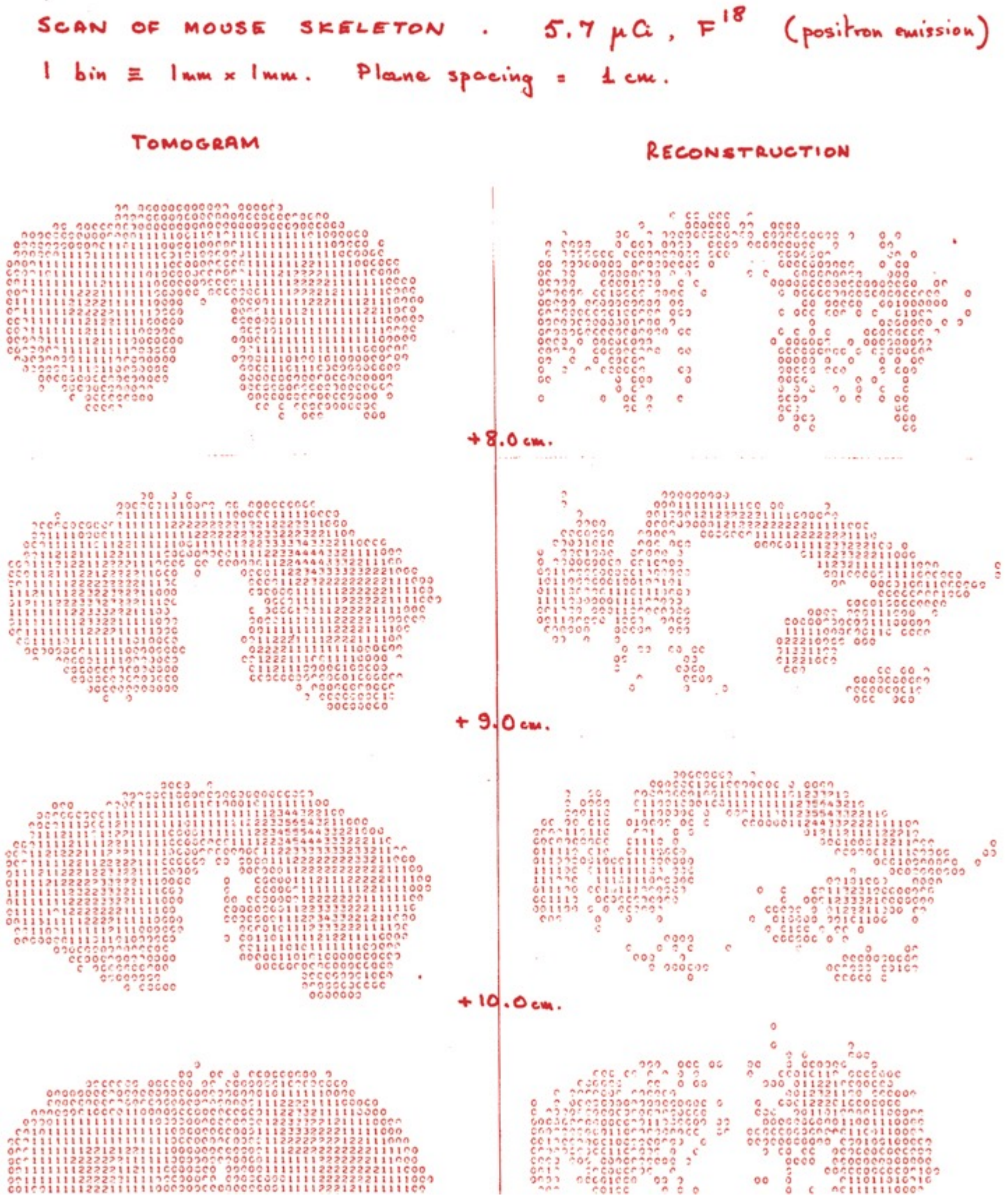
J. DUBOUSSET[1], G. CHARPAK[2], I. DORION[2], W. SKALLI[3], F. LAVASTE[3],
J. DEGUISE[4], G. KALIFA[5], S. FEREY[5]

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



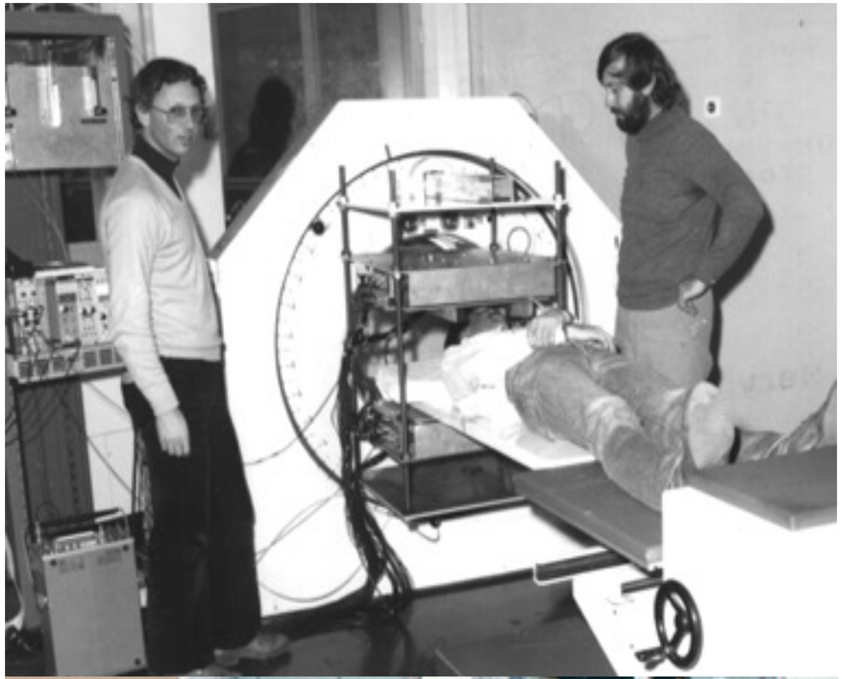
First mouse imaged at CERN with Na-^{18}F in 1978

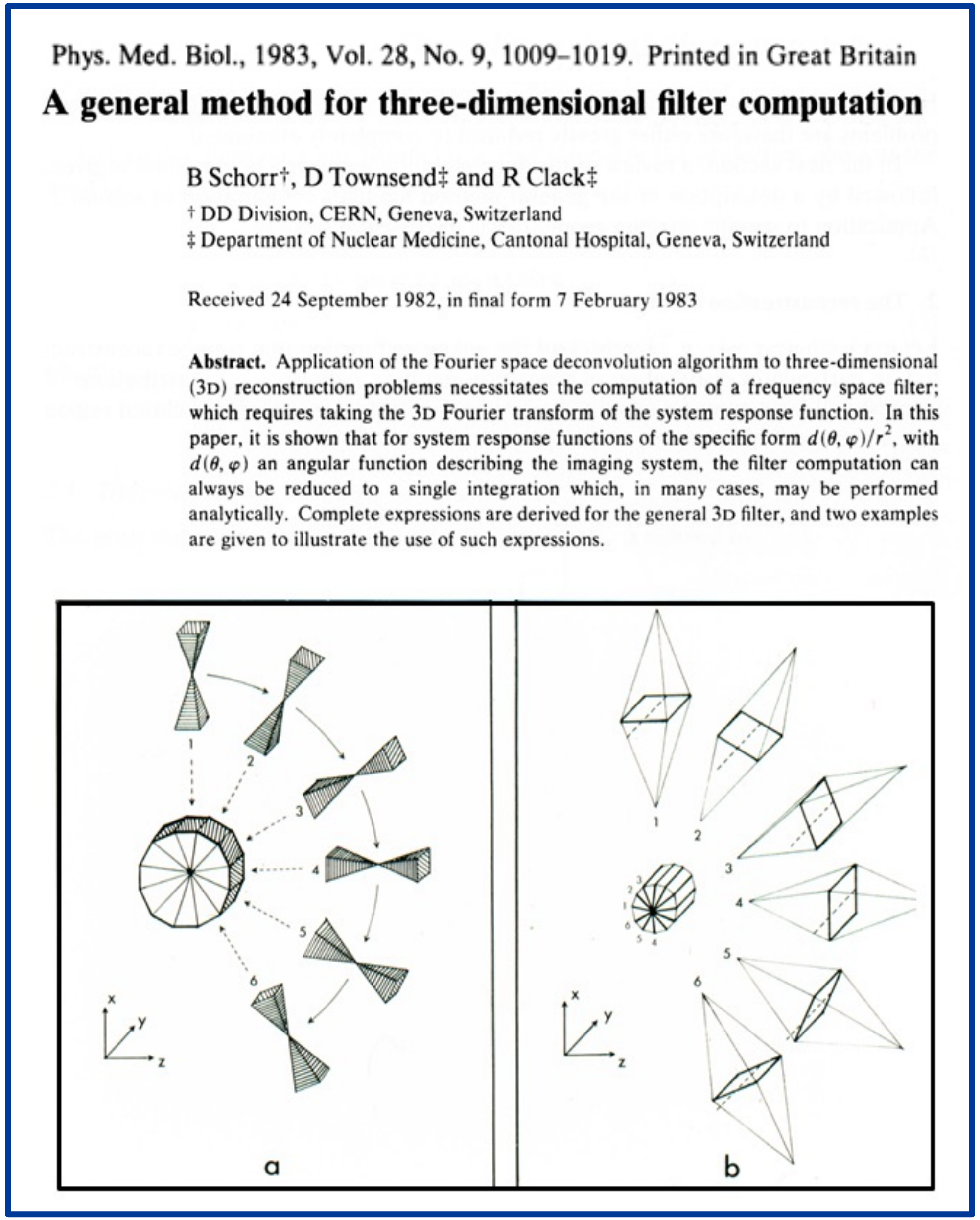
David Townsend and Alan Jeavons



SCAN OF MOUSE SKELETON . 5.7 μCi , F^{18} (positron emission)

1 bin ≡ 1mm x 1mm. Plane spacing = 1 cm.





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.

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

bulletin

WEEK MONDAY 26 JANUARY

Nº5/81

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.

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. Badano1), M. Benedikt2), P.J. Bryant2) (Study Leader), M. Crescenti1), P. Holy3), A. Maier2)+4), M. Pullia1), S. Reimoser2)+4), S. Rossi1),
Part-time members: G. Borri1), P. Knaus1)+2)
Contributors: F. Gramatica1), M. Pavlovic4), L. Weisser5)
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

Radiotherapy and Oncology 128 (2018) 76–82

ELSEVIER

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

ENLIGHT

ENLIGHT: European network for Light ion hadron therapy

Check for updates

Manjit Dosanjh [a,*], Ugo Amaldi [b], Ramona Mayer [c], Richard Poetter [d], on behalf of the ENLIGHT Network

[a] CERN, Geneva, Switzerland; [b] TERA Foundation, Novara, Italy; [c] Former Medical Director of MedAustron, Wiener Neustadt; and [d] Department of Radiotherapy, Medical University of Vienna, Austria

ENLIGHT was established to co-ordinate European efforts in using ion beams for radiation therapy and to catalyse collaboration and co-operation among the different disciplines involved. ENLIGHT had its inaugural meeting in February 2002 at CERN and was funded by the European Commission for its first 3 years.

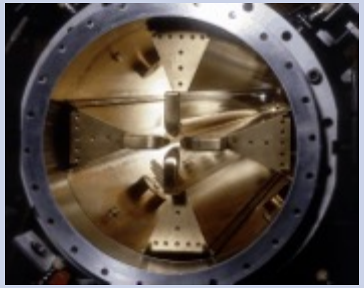
While the ENLIGHT network itself flourishes without direct dedicated funding since 2006, the R&D and training activities under the umbrella of ENLIGHT have been funded primarily through European Commission (EC) projects.

http://cern.ch/enlight

ENLIGHT

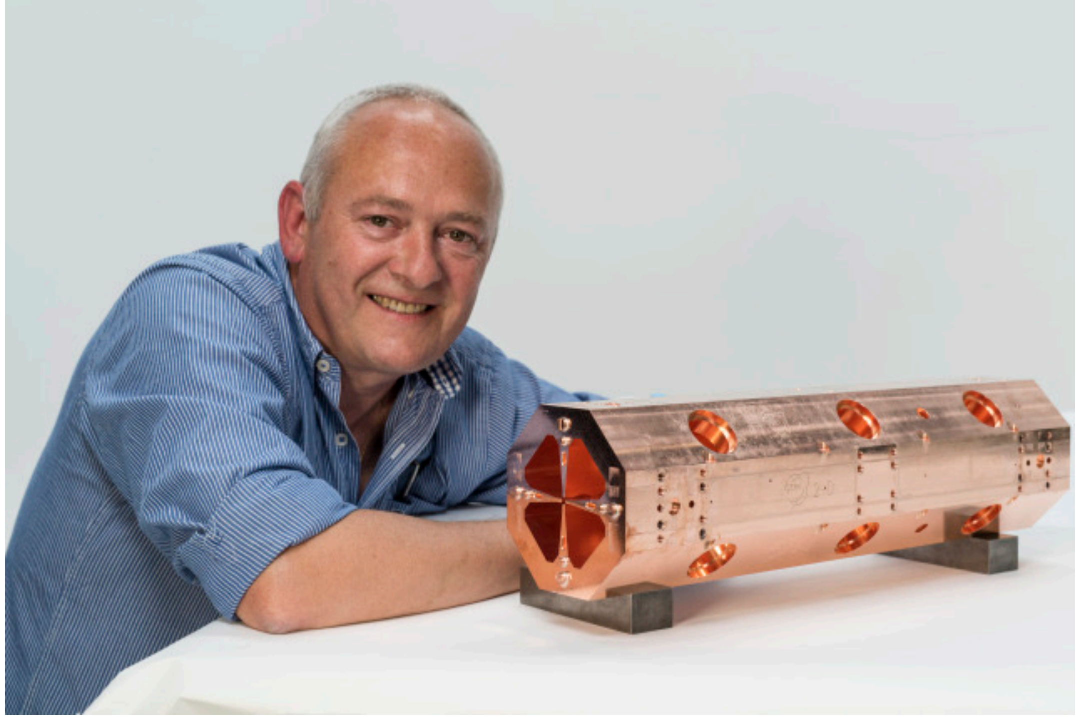
2012: Manjit Dosanjh, ENLIGHT co-ordinator, and members of the ENLIGHT network at the ENLIGHT 10th anniversary meeting

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.

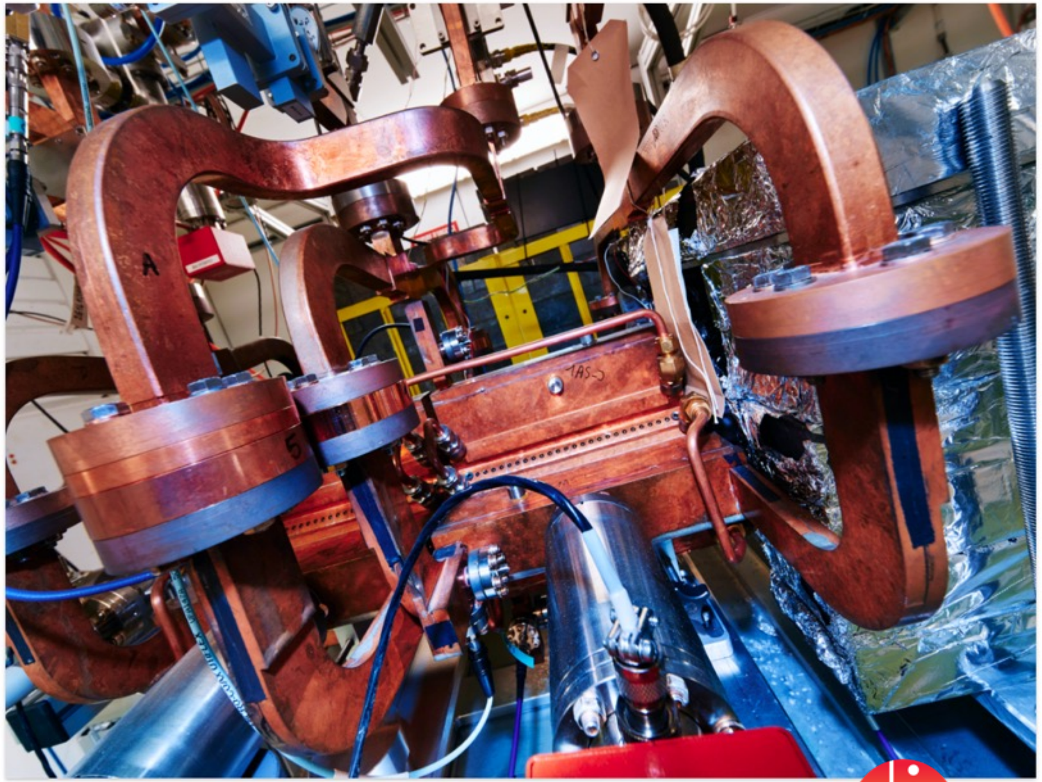
An R&D programme based at CERN for critical technologies related to ion therapy

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

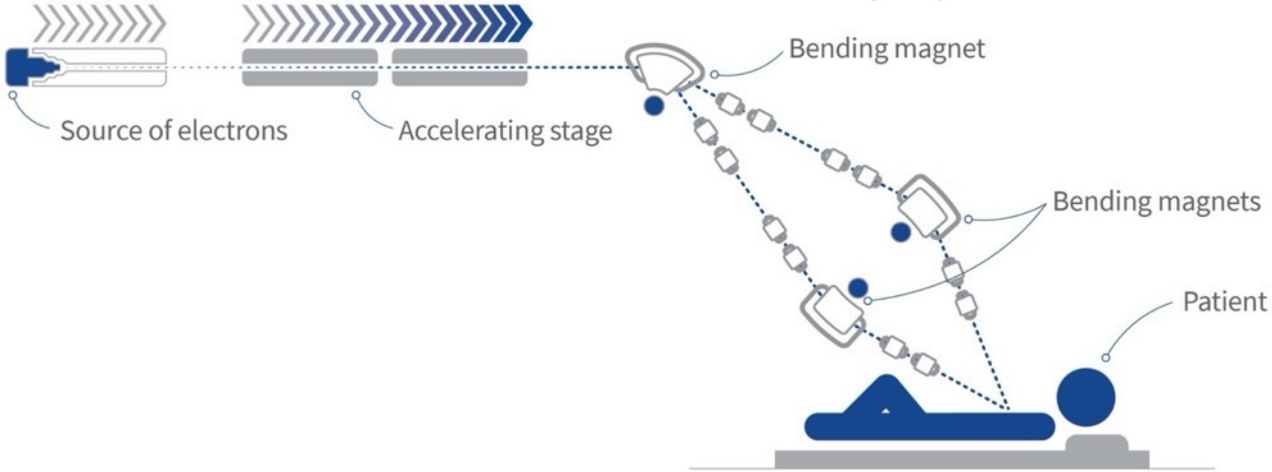
See the talk from Maurizio Vretenar, NIMMS Coordinator

CERN – CHUV collaboration on FLASH VHEE therapy

CLIC technology for a FLASH VHEE facility being designed in collaboration with Lausanne University Hospital CHUV



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.

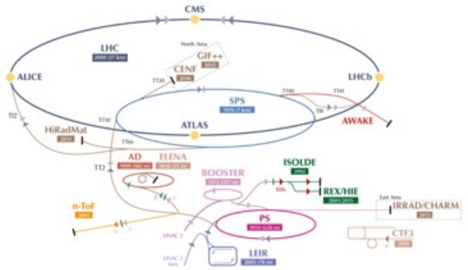
The design of this facility is the result of an intense dialogue between groups at CHUV and CERN.

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

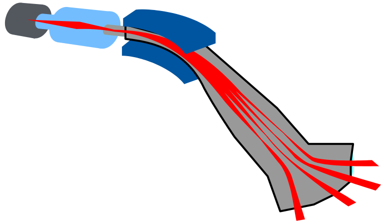
CERN-MEDICIS

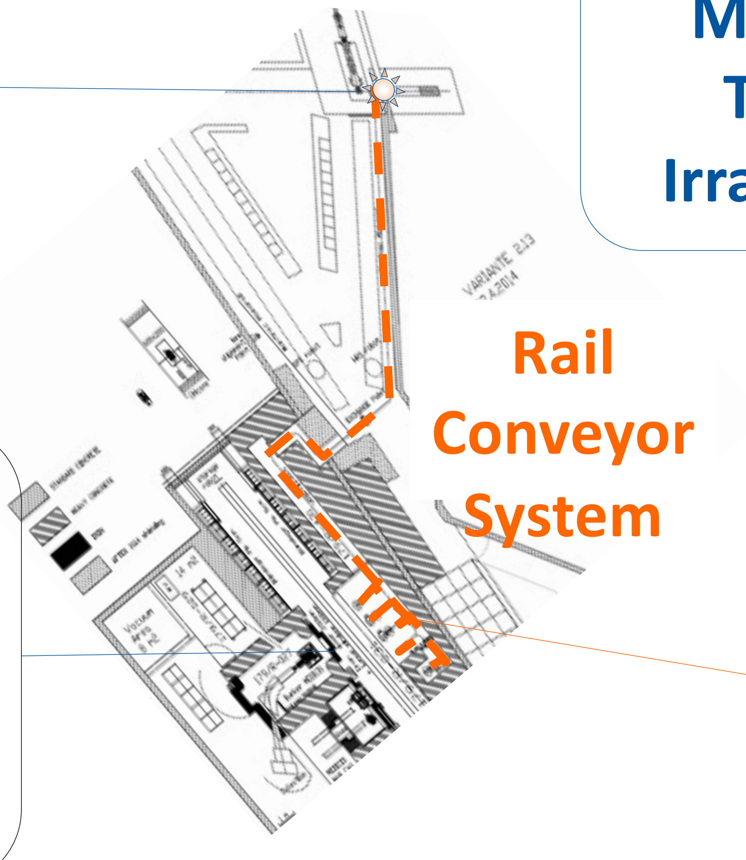
Non-conventional isotopes collected by mass separation for new medical applications

CERN protons



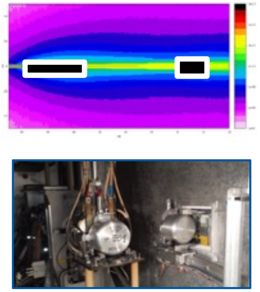
MEDICIS Laboratory





Rail Conveyor System

MEDICIS Target Irradiation



Thierry Stora (CERN)

Crystal Clear Collaboration – CERN RD18 Experiment

Initiated in 1990 by P. Lecoq, approved in 1991 by CERN for R&D for future LHC detectors

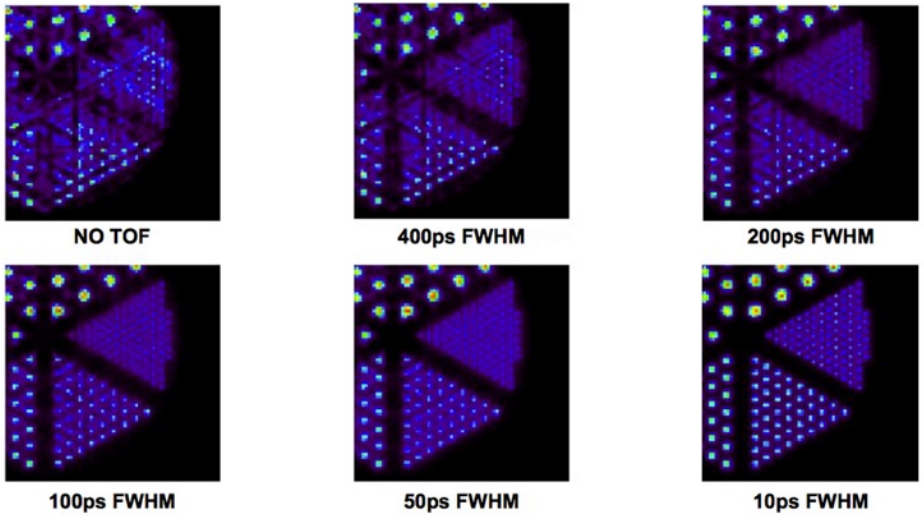
R&D on inorganic scintillators for HEP, medical imaging, industry

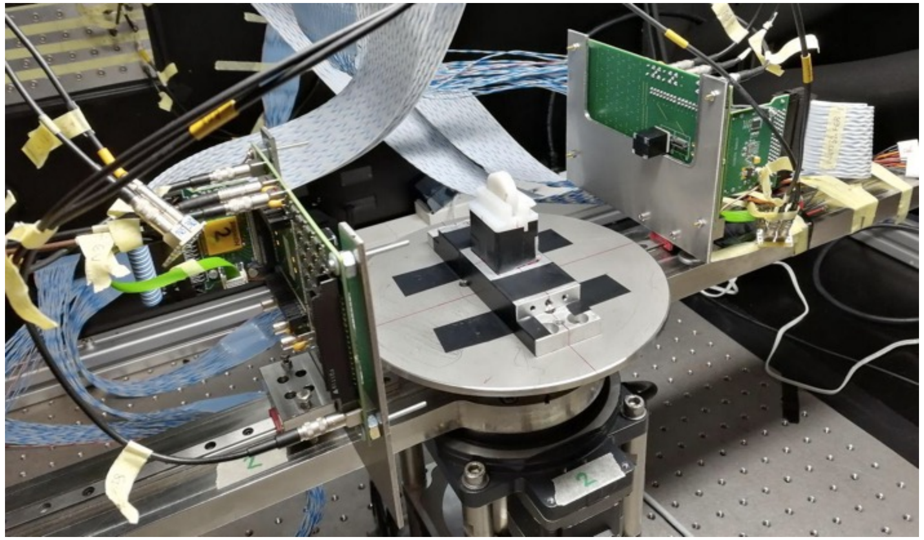
A CERN group very active in Positron Emission Tomography (PET), now focusing on:

Flexible testing facility to test “any” PET detector configuration

Scintillating heterostructures

pushing the limit of TOF-PET resolution



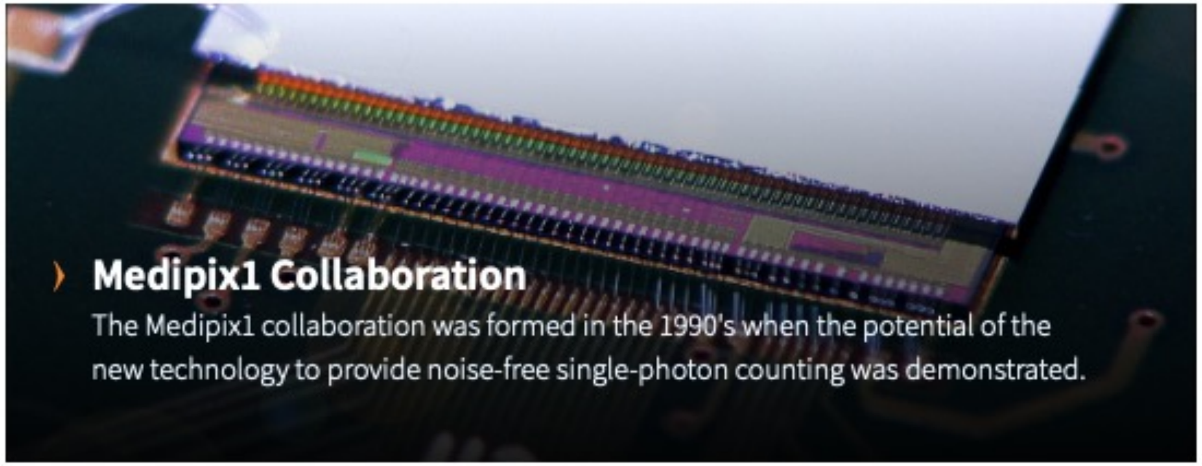


Development of a versatile PET scanner prototype, Polesel et al, IEEE MIC 2019 (Manchester), poster M-13-168

Etiennette Auffray (CERN)

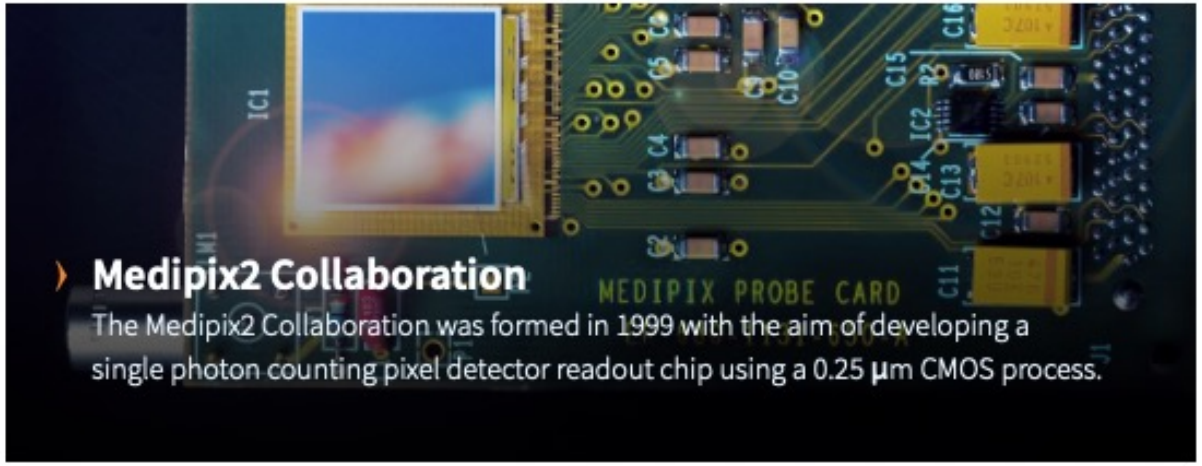
Medipix

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



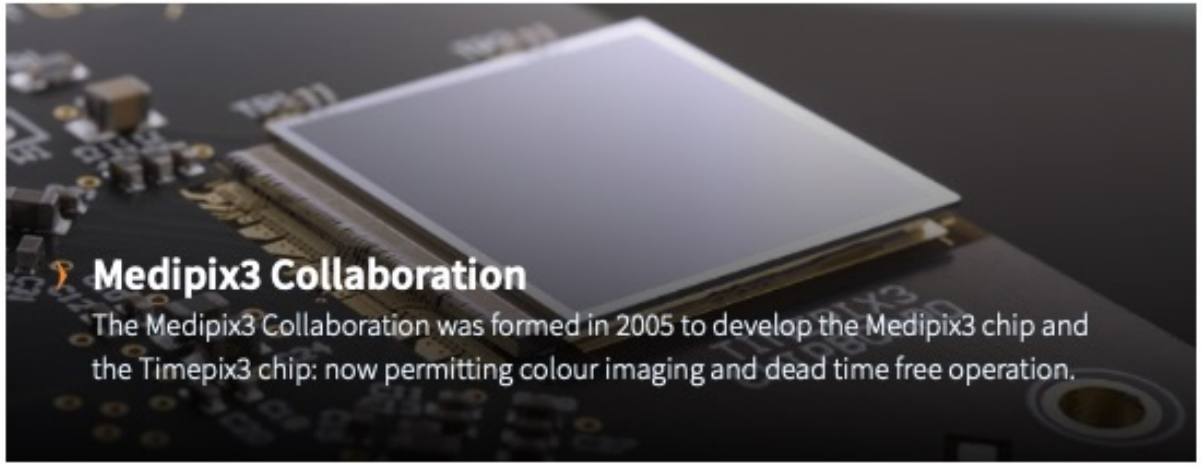
Medipix1 Collaboration

The Medipix1 collaboration was formed in the 1990's when the potential of the new technology to provide noise-free single-photon counting was demonstrated.



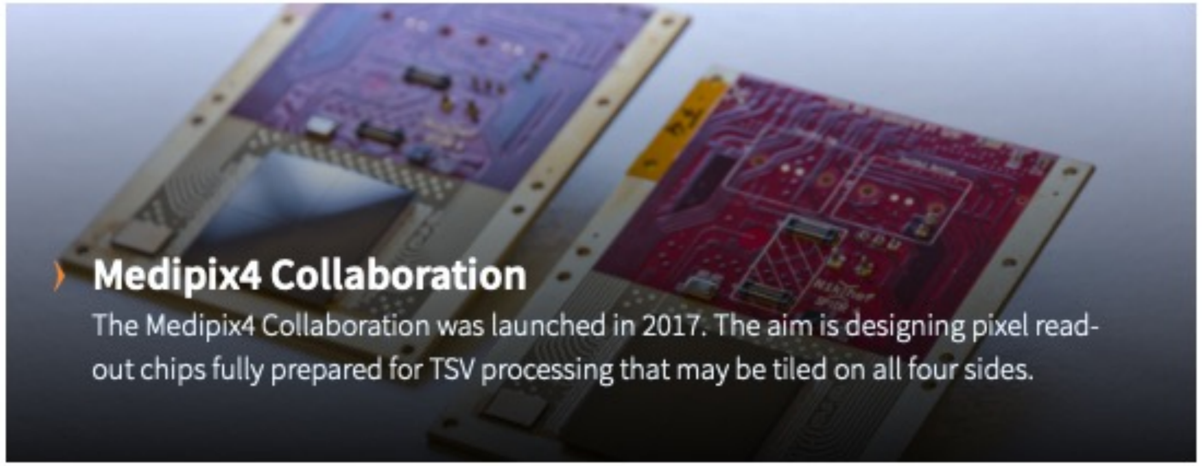
Medipix2 Collaboration

The Medipix2 Collaboration was formed in 1999 with the aim of developing a single photon counting pixel detector readout chip using a 0.25 µm CMOS process.



Medipix3 Collaboration

The Medipix3 Collaboration was formed in 2005 to develop the Medipix3 chip and the Timepix3 chip: now permitting colour imaging and dead time free operation.

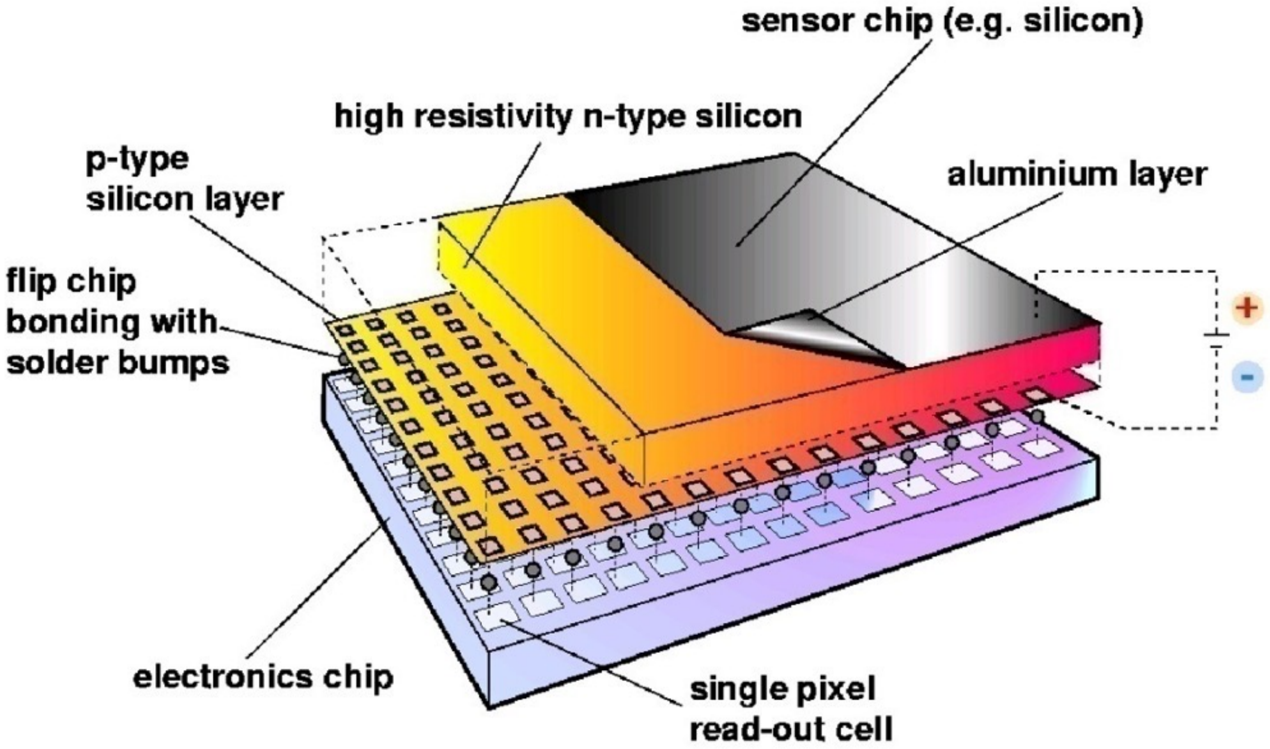


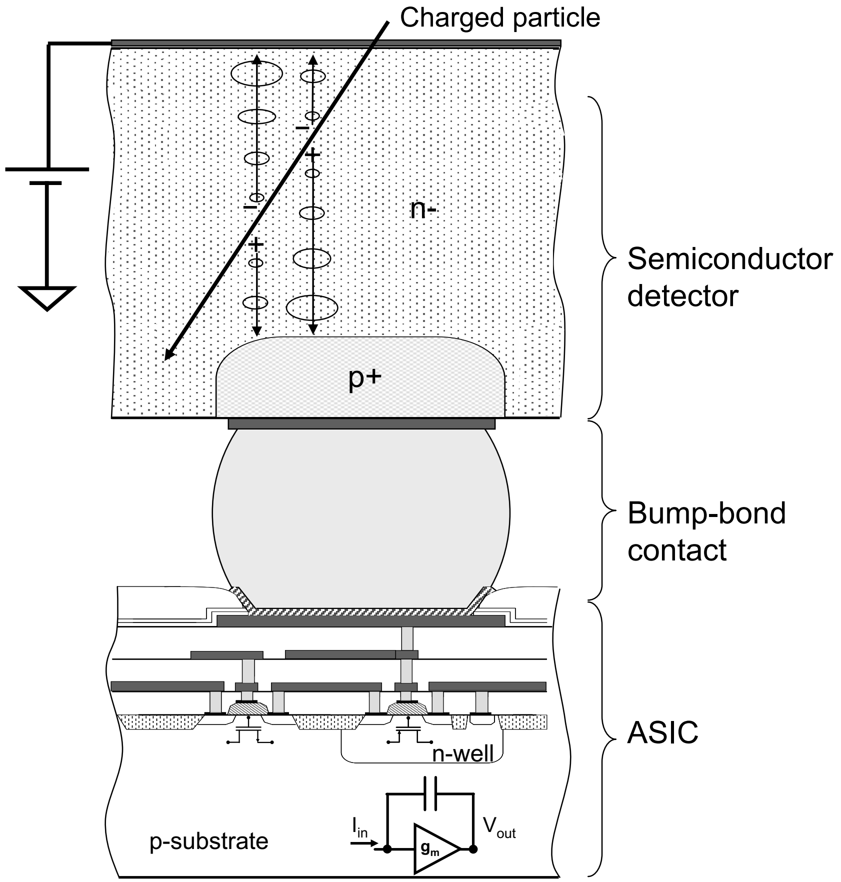
Medipix4 Collaboration

The Medipix4 Collaboration was launched in 2017. The aim is designing pixel read-out chips fully prepared for TSV processing that may be tiled on all four sides.

Michael Campbell (CERN)

Hybrid Silicon Pixel Detectors

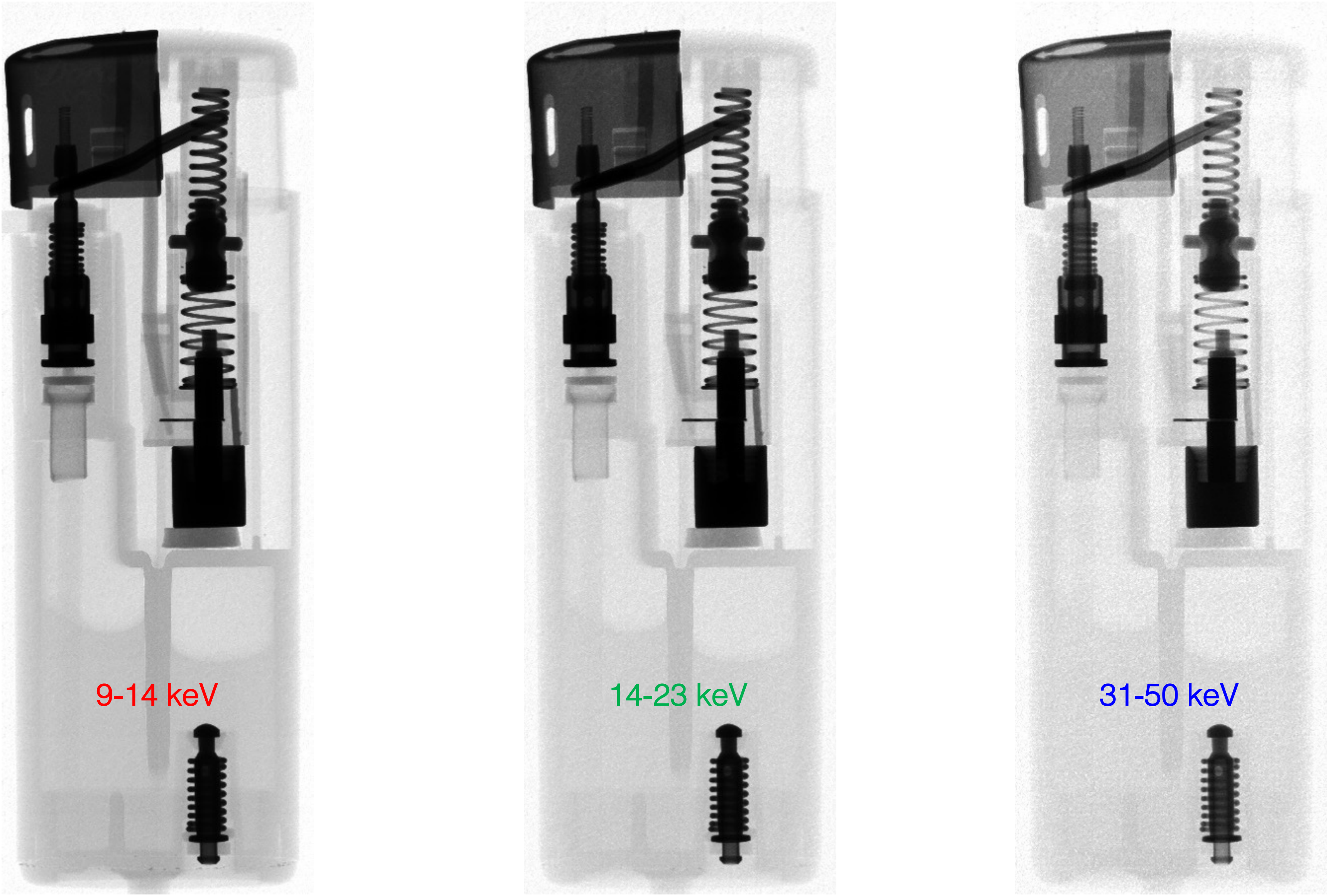




Noise-hit free particle detection
Standard CMOS can be used allowing on-pixel signal processing
Sensor material can be changed (Si, GaAs, CdTe..)

Michael Campbell (CERN)

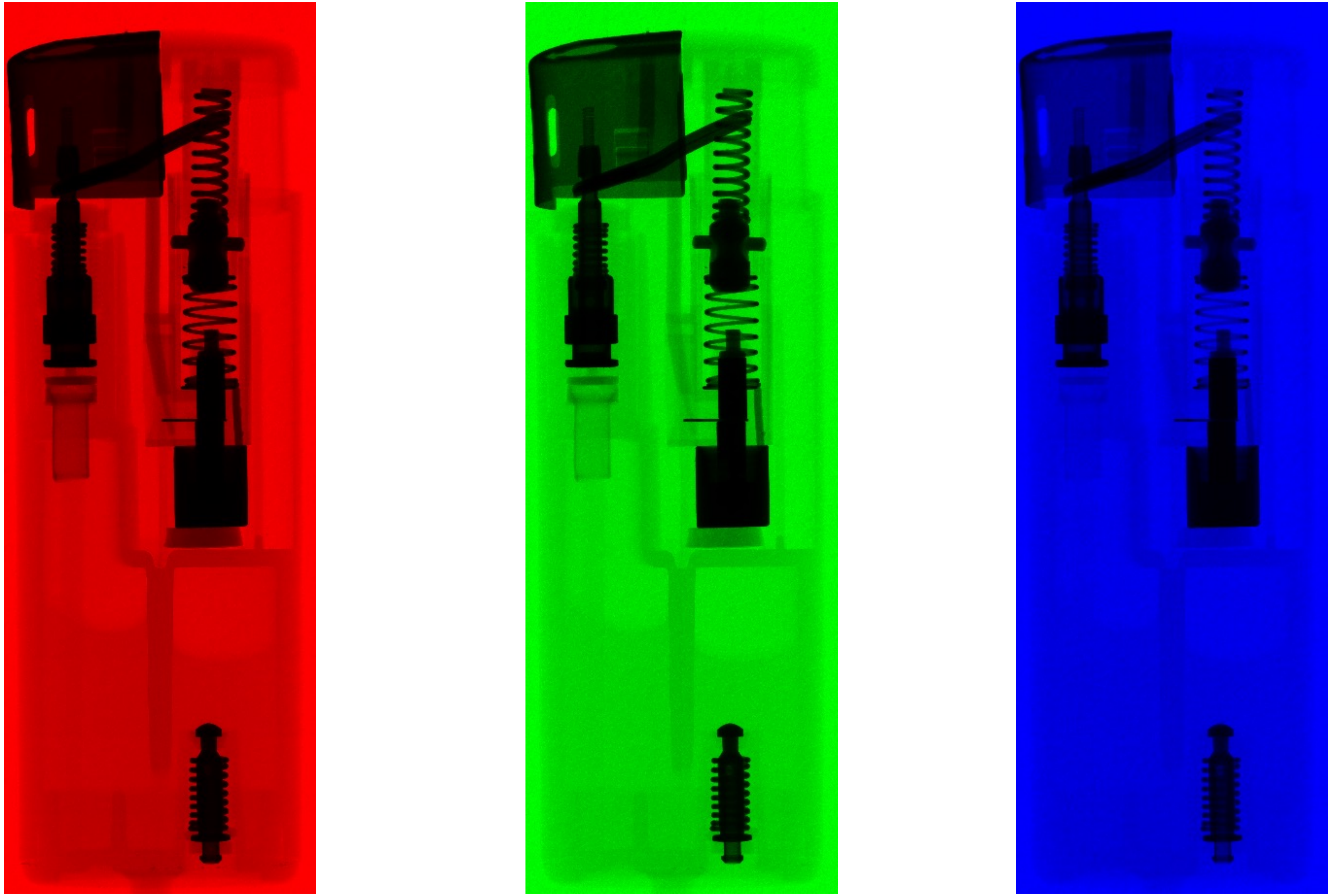
Colour x-ray of a lighter



S. Procz et al.

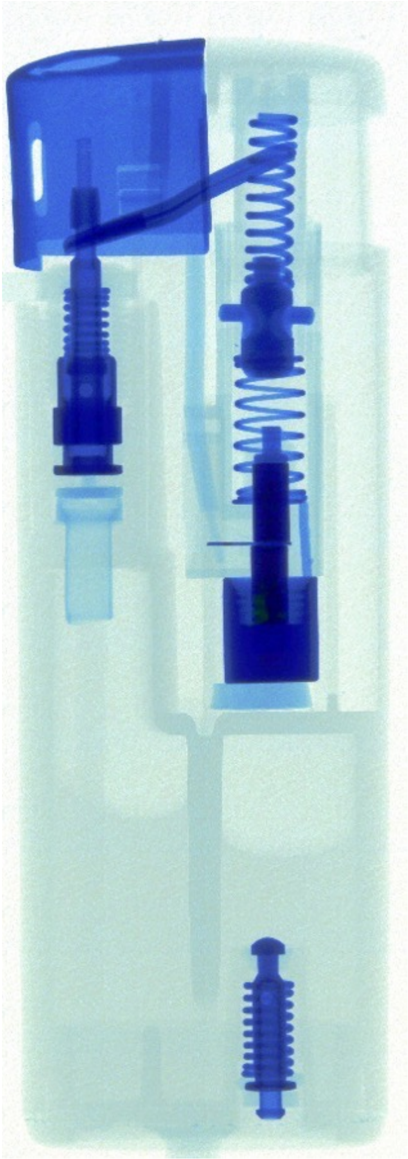
Colour x-ray of a lighter

RGB:
9-50 keV



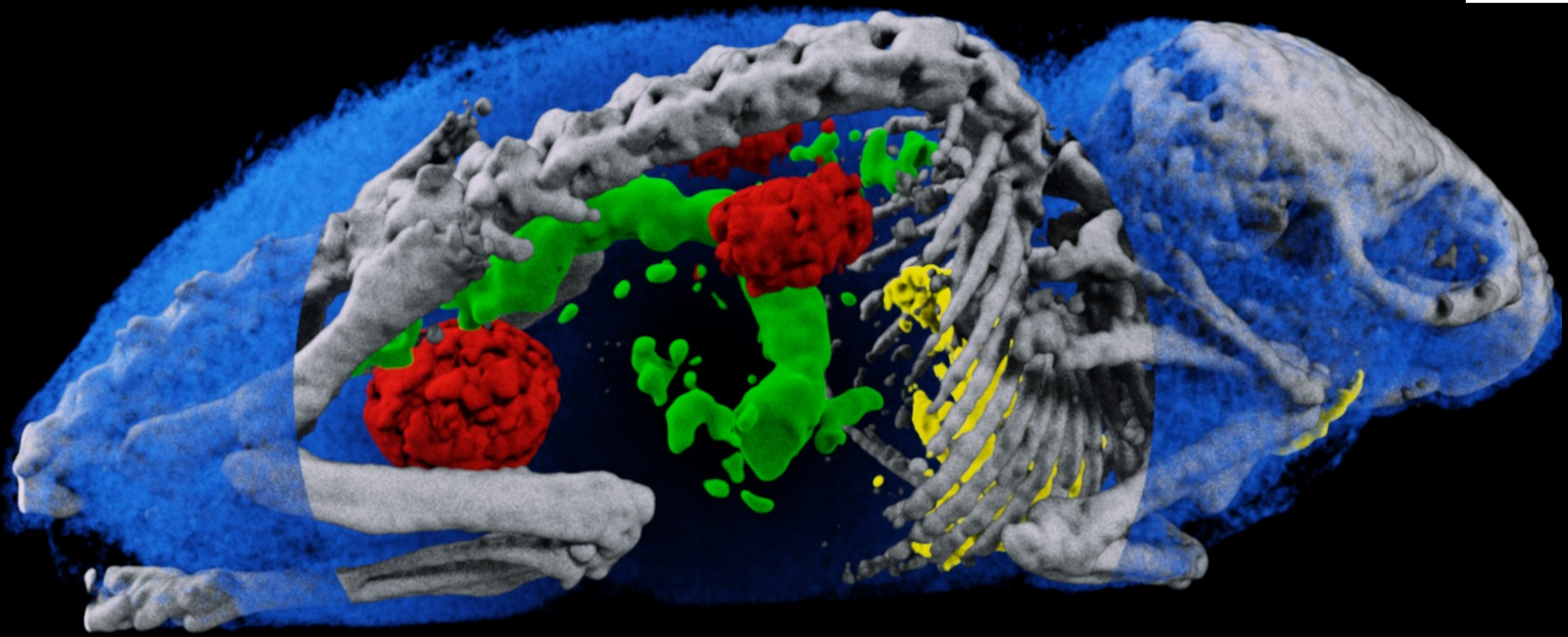
S. Procz et al.

Colour x-ray of a lighter



S. Procz et al.

Spectroscopic information permits material separation

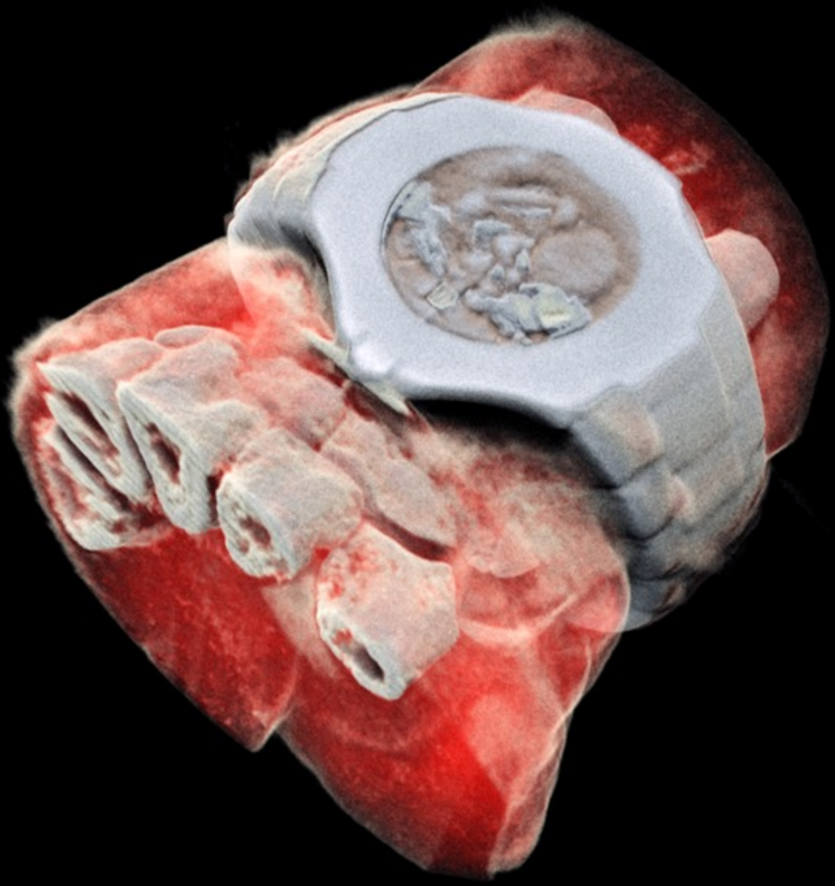


The water has been partly cut away to reveal the bone, gold, gadolinium and iodine

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

A. Butler, University of Canterbury

Fast forward to 2018

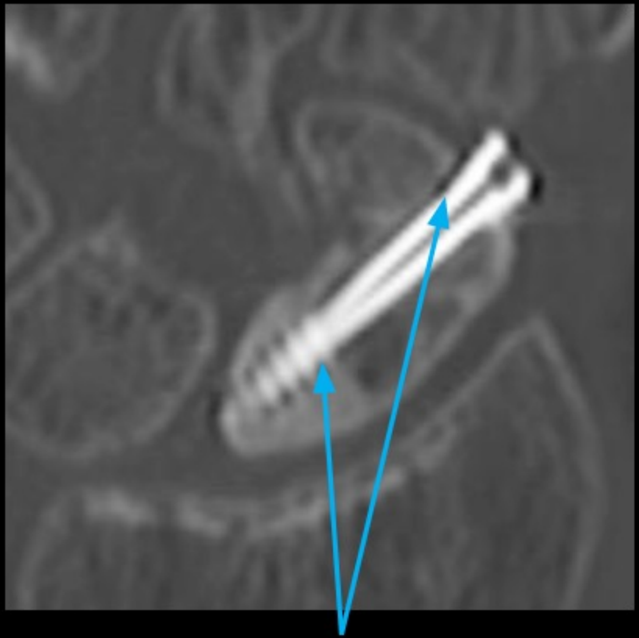


First 3D colour X-ray of a human using the Medipix3 technology developed at CERN

CT versus MARS

Metal artefact

Standard CT



Metal artifact hides the bone-metal interface

Scaphoid screw

MARS

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

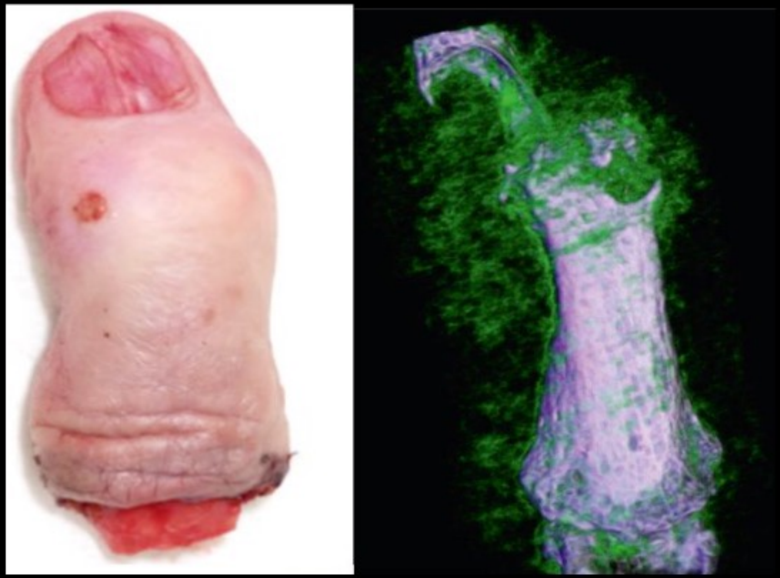
MARS SPCCT Imaging technology is in concept development for human use. It is not a product and is not cleared or approved by the US FDA or any other regulator for commercial availability outside of New Zealand

Slide courtesy of Anthony Butler, University of Canterbury

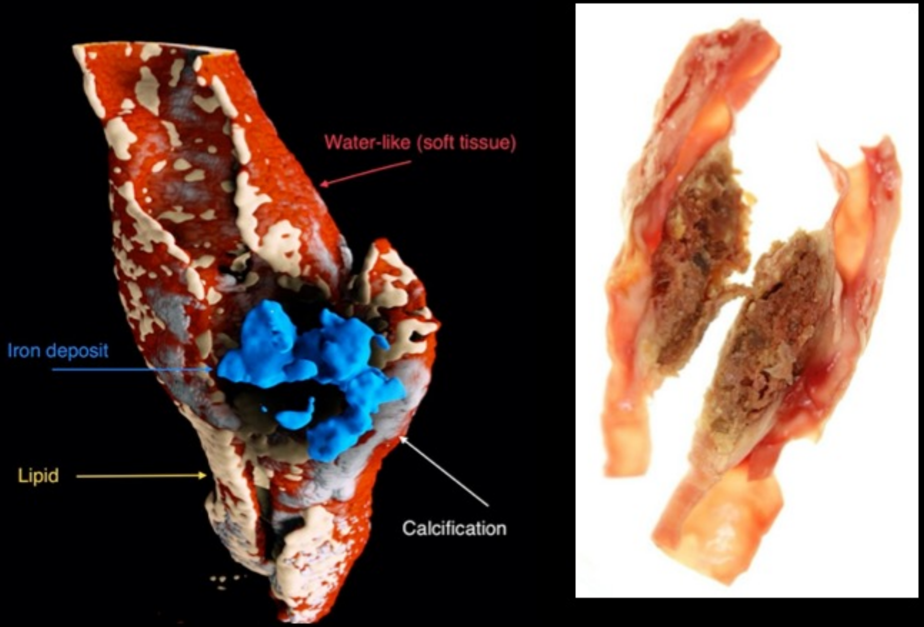
Presented at 6th Workshop on Medical Applications of Spectroscopic X-ray Detectors, 29 Aug 2022, CERN

Molecular versus MARS

MARS - intrinsic information



Gout crystal characterisation
(Collab with CHUV)

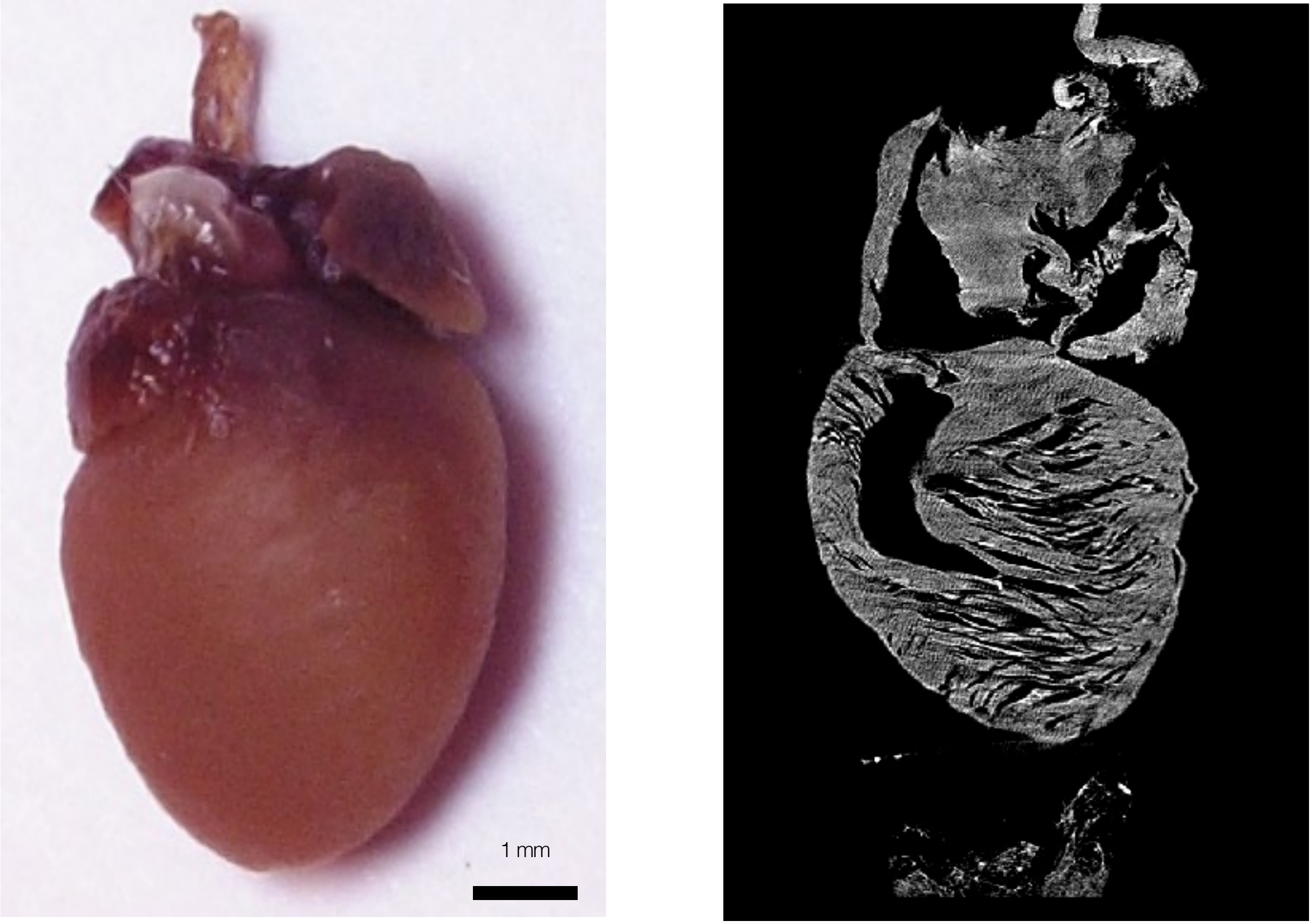


Carotid plaque with quantitative measurements of fat, water, calcium, and iron

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

Slide courtesy of Anthony Butler, University of Canterbury

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



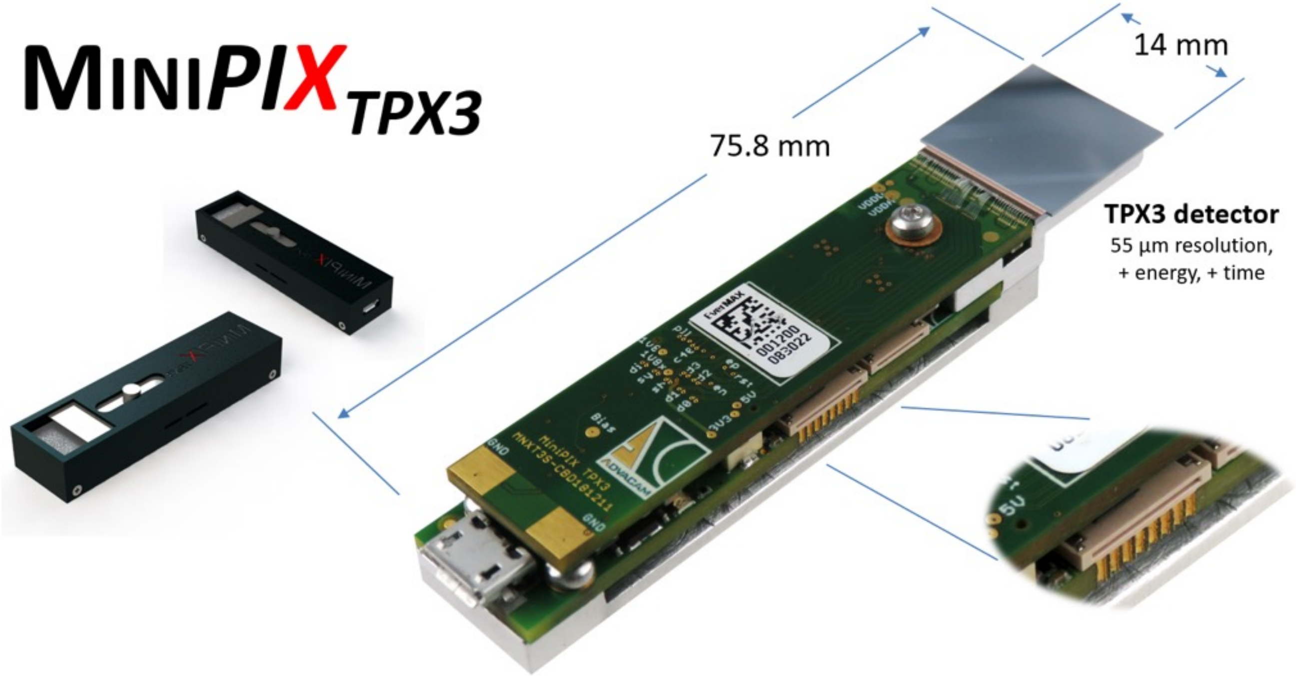
Ethanol-preserved mouse heart scanned using the WidePIX$_{10x5}$ detector
60 kVp tungsten spectrum
720 projections, 5 seconds per projection (one hours total)
Spatial resolution ca. 7 μm
Reconstructed using Volex, visualized using CTVox and Amide software

Slide courtesy of J. Dudak, IEAP, Czech Technical University

MiniPIX TPX3

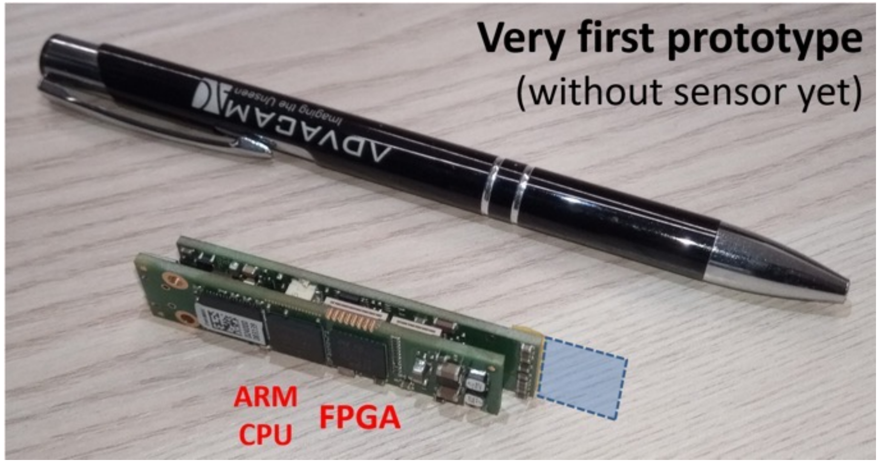
Miniaturized spectral camera supporting Si and CdTe sensors

MiniPIX TPX3



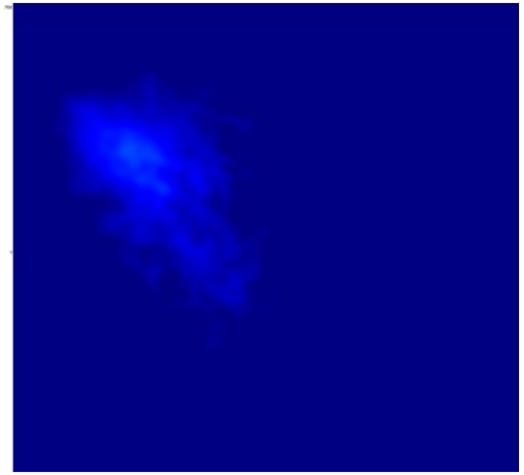
ADVACAM
Imaging the Unseen

It’s really small...



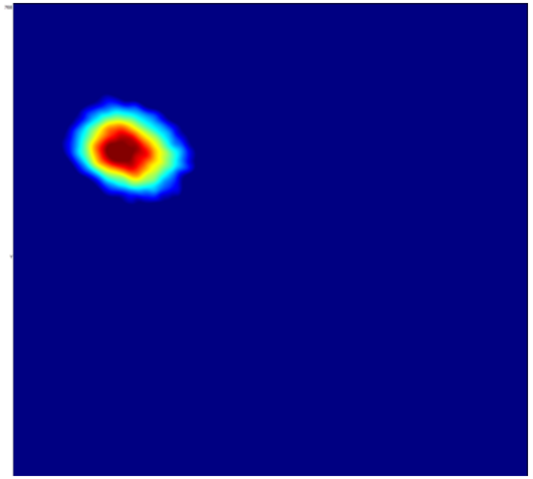
Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

250 – 300 keV



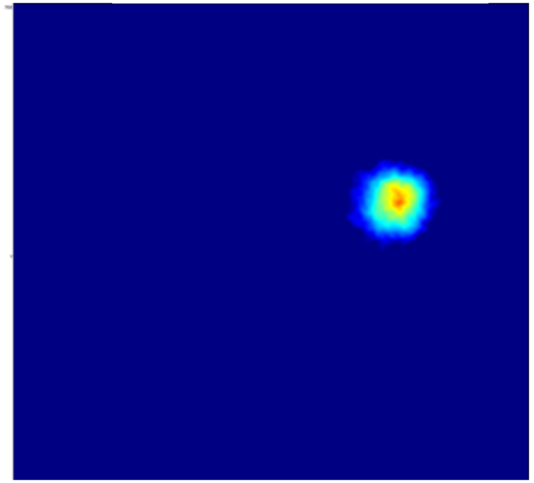
^{131}I 284 keV (7%)

350 – 400 keV



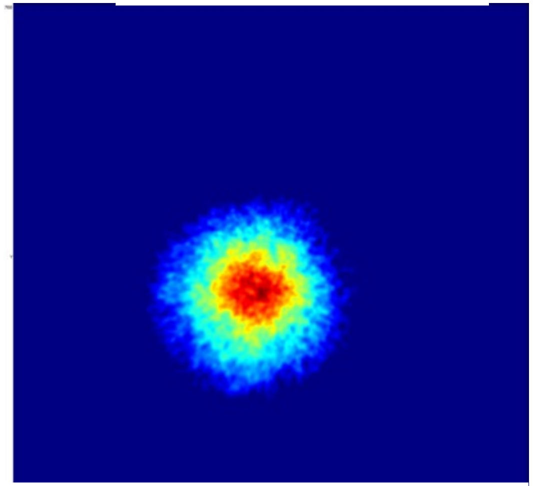
^{131}I 364 keV

500 – 550 keV

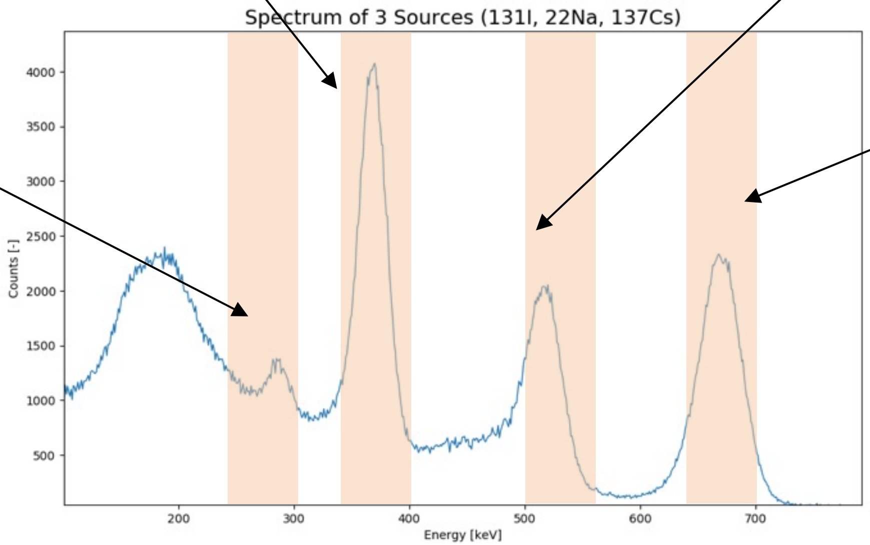


^{22}Na 511 keV

650 – 700 keV



^{137}Cs 662 keV



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

Gamma camera applications: Thyroid diagnostic

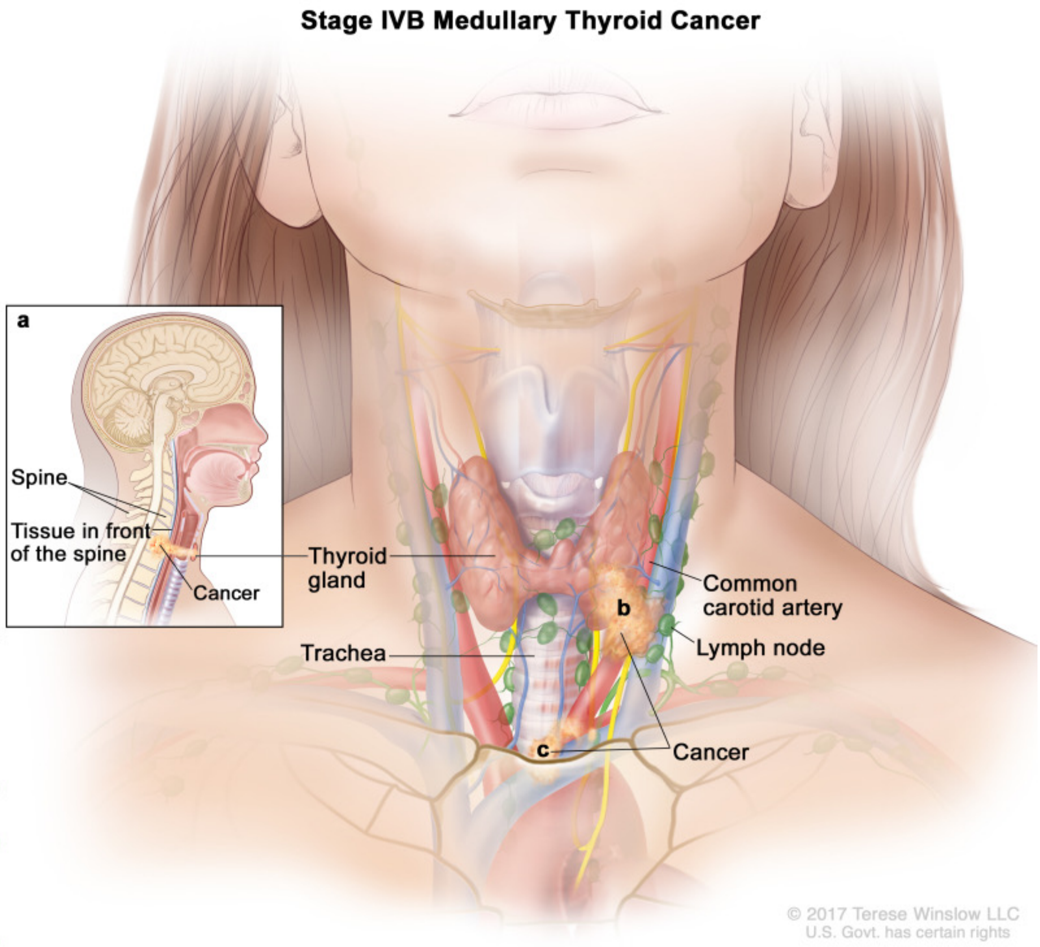
Thyroid cancer diagnostics and treatment monitoring:

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

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

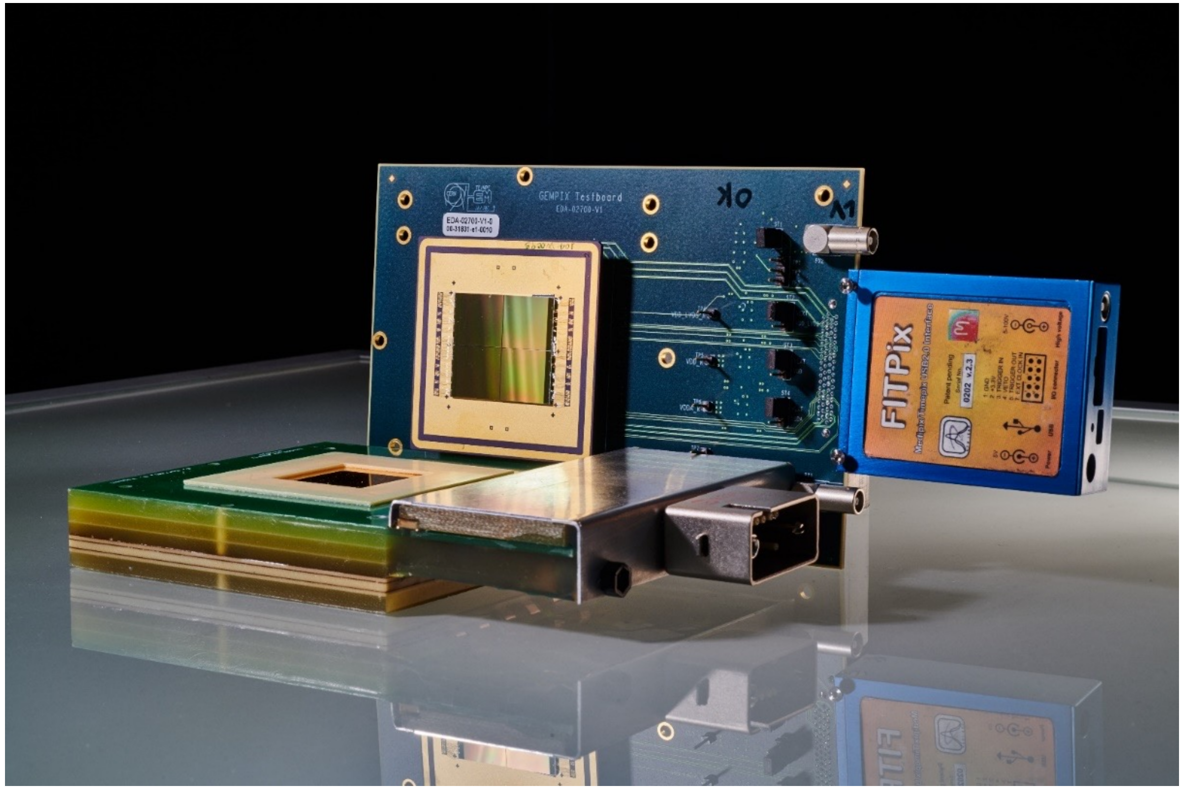
Our technology allows

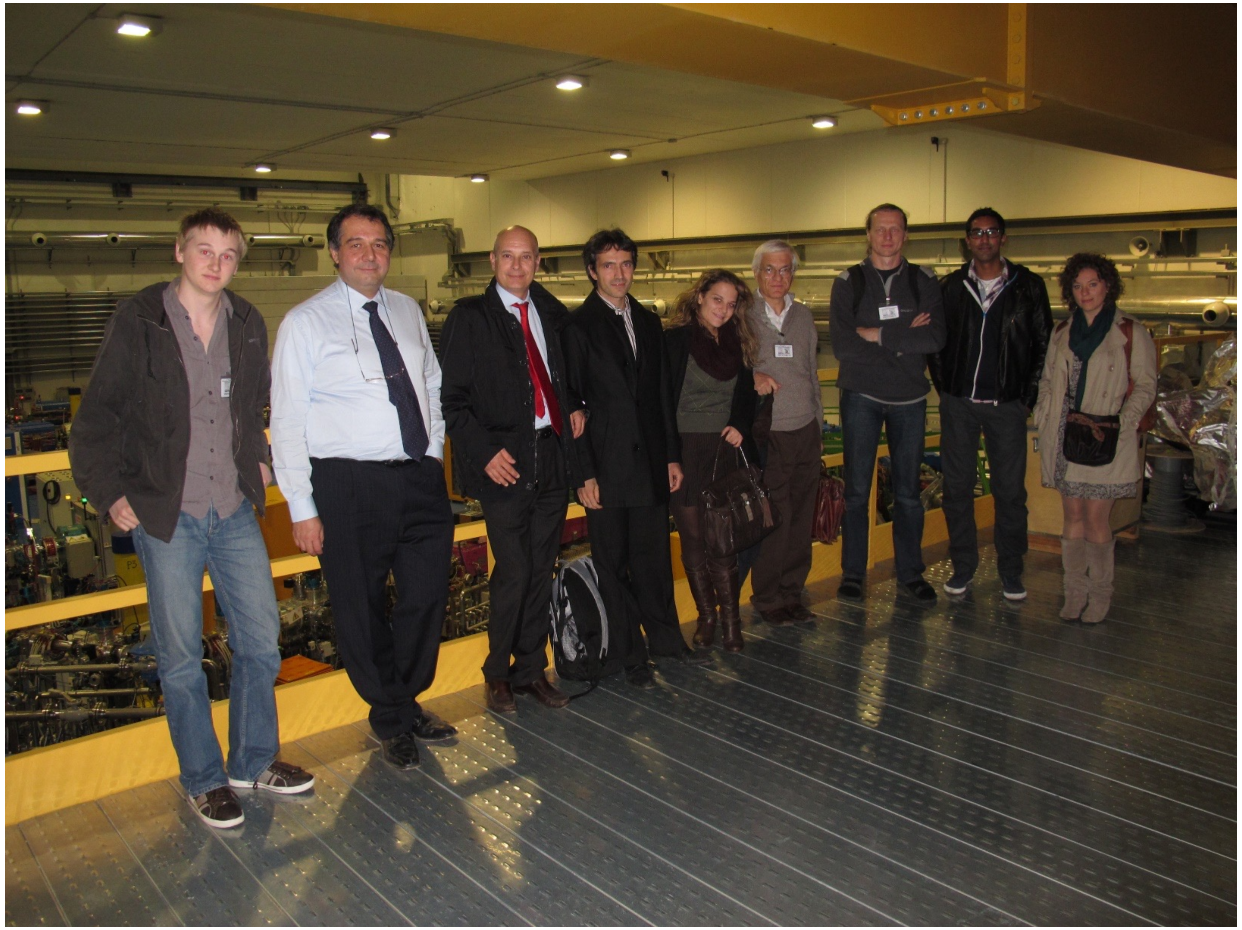
- 5 times better resolution and 3D (2.5 mm)
- 4 times lower dose



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

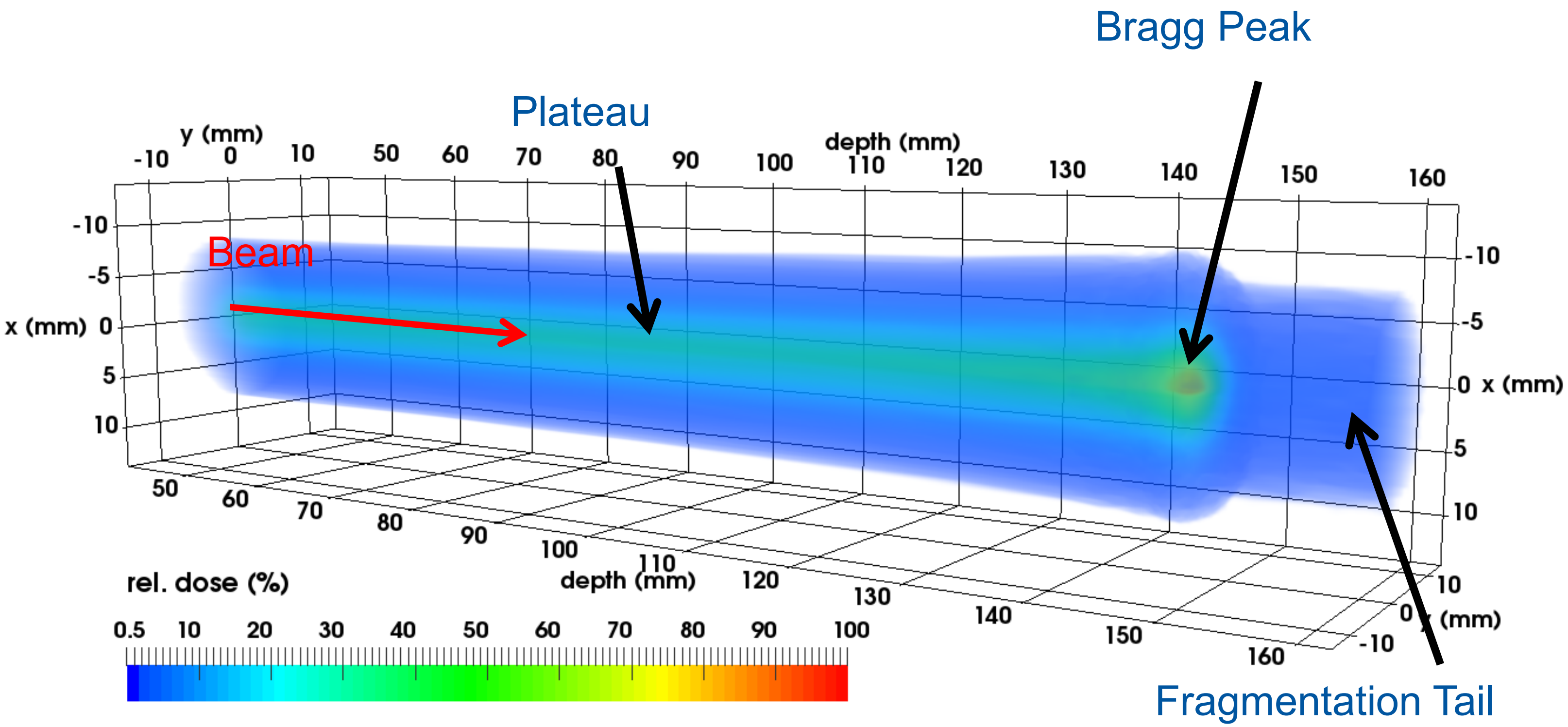
ARDENT at CNAO on 19 October 2012 – The birth of the GEMPix





Marco Silari (CERN)

GEMPix for hadron therapy



3D dose reconstruction after depth scan at CNAO

Marco Silari (CERN)

TimePIX 3 photon fluence measurement in hospital theatres

Reference person: 1.76 m

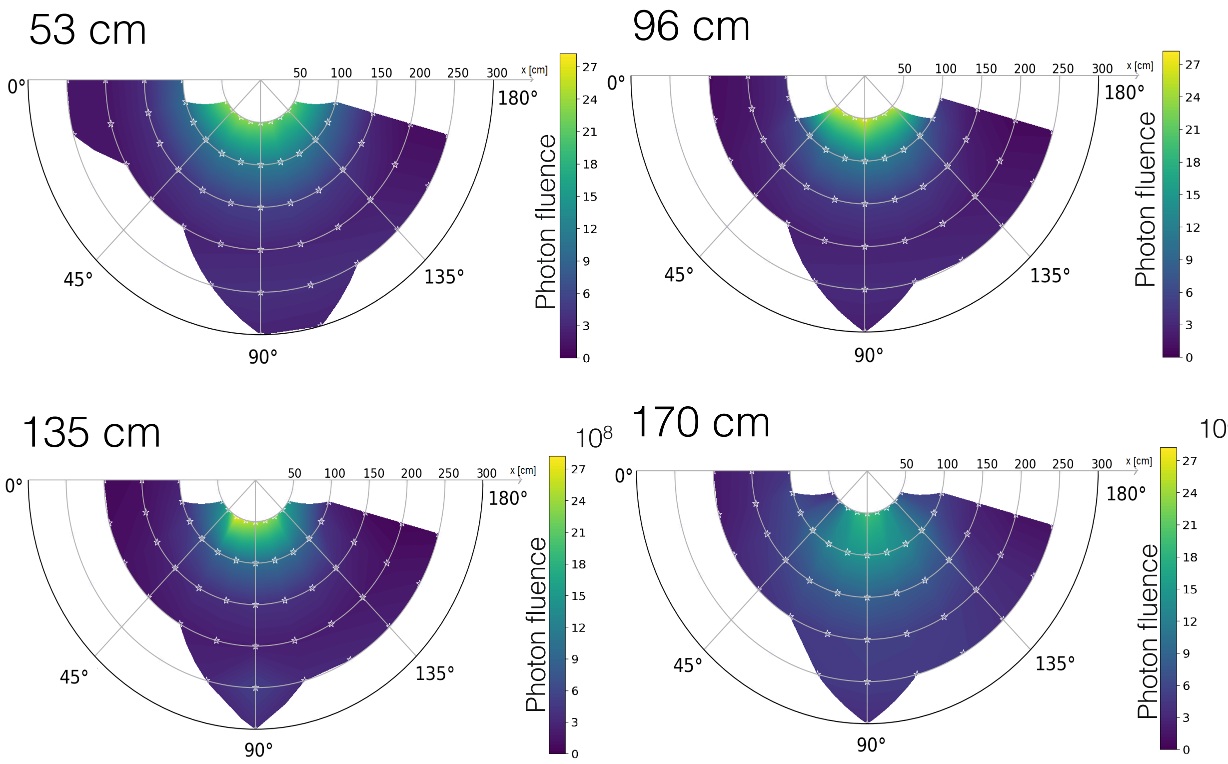
Eye lens - 170 cm

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.

Pierre Carbonez (CERN)
Marie Nowak CERN PhD. Student 2017-2020

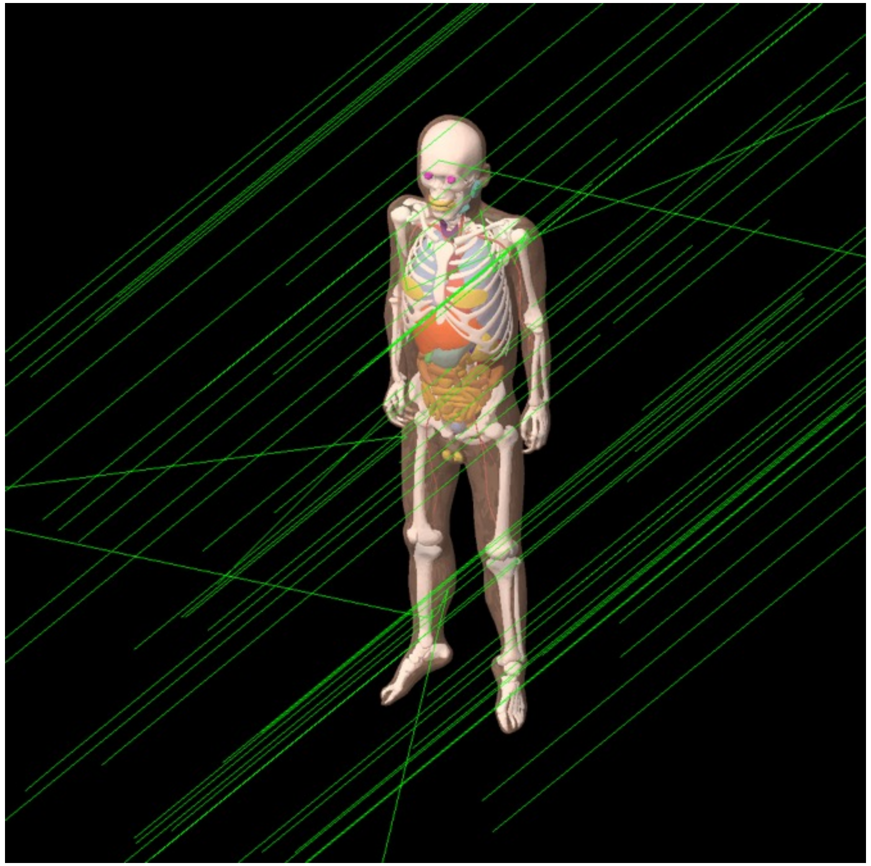
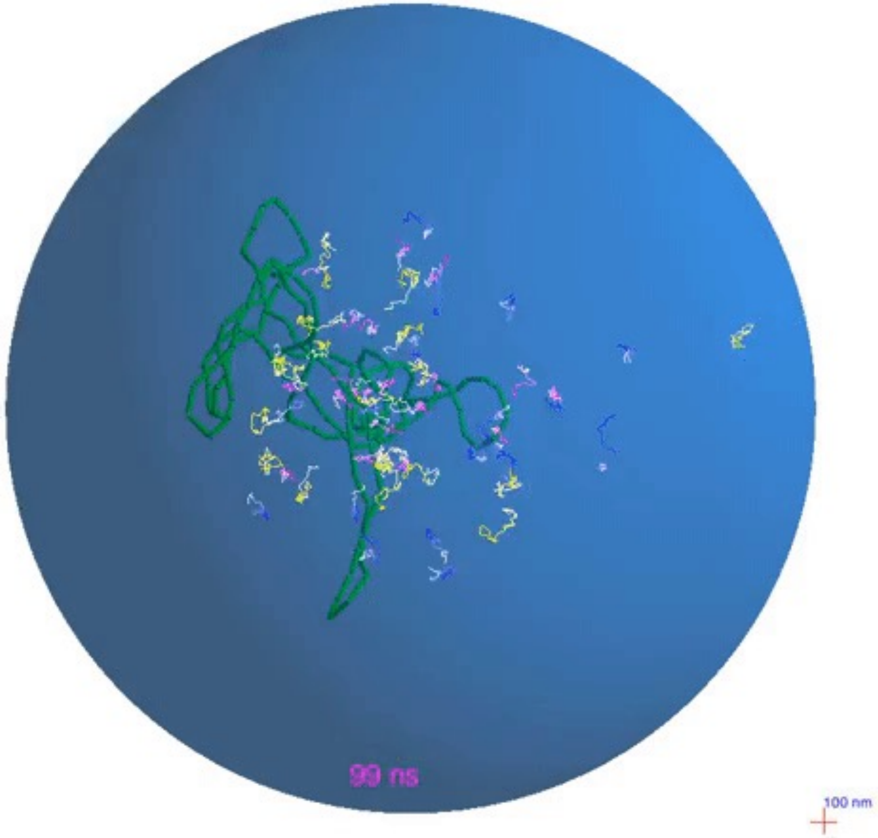


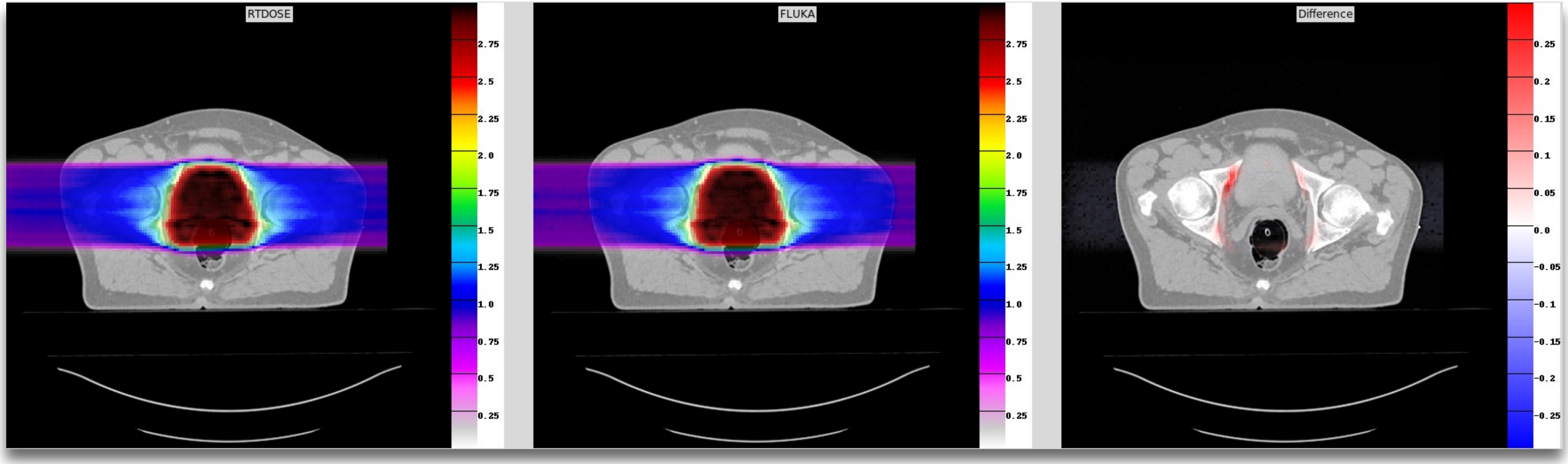
Image of Polygon-Surface Reference Korean Male Phantom (PSRK-Man), implemented in Geant4. Courtesy of C.-H. Kim & C. Choi, Hanyang Univ.

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



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

Sensitivity studies of Monte Carlo TP recalculations

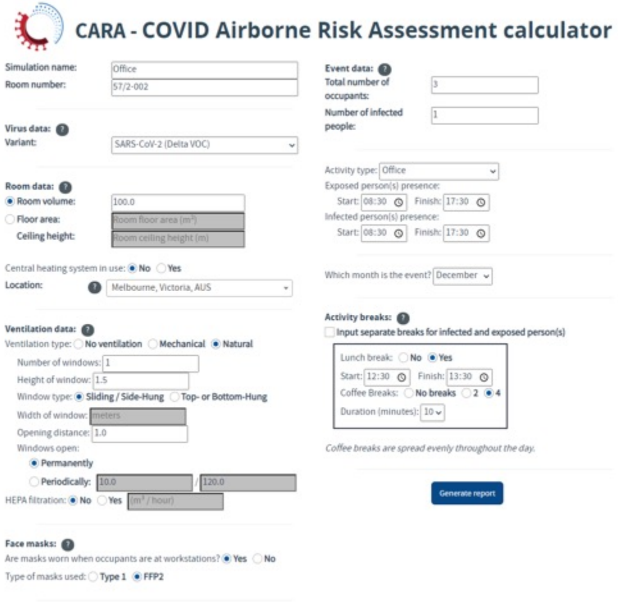


Proton prostate patient case
(MedAustron)
W.Kozlowska PhD

Calibration of HU to density
HU to tissue conversion methods
Size of the scoring grid
Ionization potentials of tissue materials
Accuracy of primary beam description

Vasilis Vlachoudis (CERN)
Wioleta Kozlowska, CERN PhD student

COVID Airborne
Risk Assessment



CARA - COVID Airborne Risk Assessment calculator

Simulation name: Office
Room number: 57/2-002

Virus data: ?
Variant: SARS-CoV-2 (Delta VOC)

Room data: ?
● Room volume: 100.0
○ Floor area: Room floor area (m²)
Ceiling height: Room ceiling height (m)

Central heating system in use: ● No ○ Yes
Location: ? Melbourne, Victoria, AUS

Ventilation data: ?
Ventilation type: ○ No ventilation ○ Mechanical ● Natural
Number of windows: 1
Height of window: 1.5
Window type: ● Sliding / Side-Hung ○ Top- or Bottom-Hung
Width of window: meters
Opening distance: 1.0
Windows open:
● Permanently
○ Periodically: 10.0 / 120.0
HEPA filtration: ● No ○ Yes (m³ / hour)

Face masks: ?
Are masks worn when occupants are at workstations? ● Yes ○ No
Type of masks used: ○ Type 1 ● FFP2

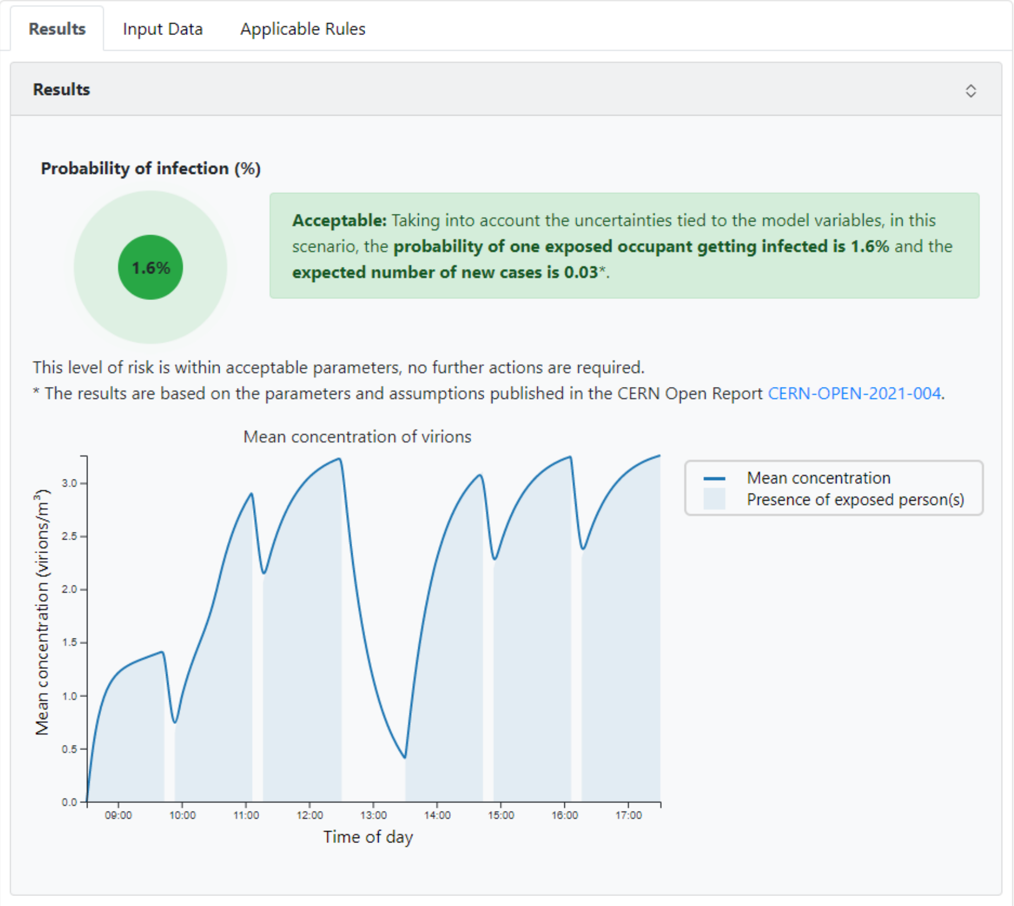
Event data: ?
Total number of occupants: 3
Number of infected people: 1

Activity type: Office
Exposed person(s) presence:
Start: 08:30 Finish: 17:30
Infected person(s) presence:
Start: 08:30 Finish: 17:30

Which month is the event? December

Activity breaks: ?
☐ Input separate breaks for infected and exposed person(s)
Lunch break: ○ No ● Yes
Start: 12:30 Finish: 13:30
Coffee Breaks: ○ No breaks ○ 2 ● 4
Duration (minutes): 10

Coffee breaks are spread evenly throughout the day.



Results

Probability of infection (%)

1.6%

Acceptable: Taking into account the uncertainties tied to the model variables, in this scenario, the **probability of one exposed occupant getting infected is 1.6%** and the **expected number of new cases is 0.03***.

This level of risk is within acceptable parameters, no further actions are required.
* The results are based on the parameters and assumptions published in the CERN Open Report CERN-OPEN-2021-004.

Mean concentration of virions

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)

CAFEIN

A modular platform to support medical analysis, diagnosis and forecast

Luigi Serio (CERN)

Living lab

a big-data analytics platform for large-scale studies of data under special constraints, such as information that is privacy-sensitive, or that has a varying level of quality, associated provenance information, or signal-to-noise ratio.

Alberto Di Meglio (CERN)

MARCHESE

Machine learning based human recognition and health monitoring system

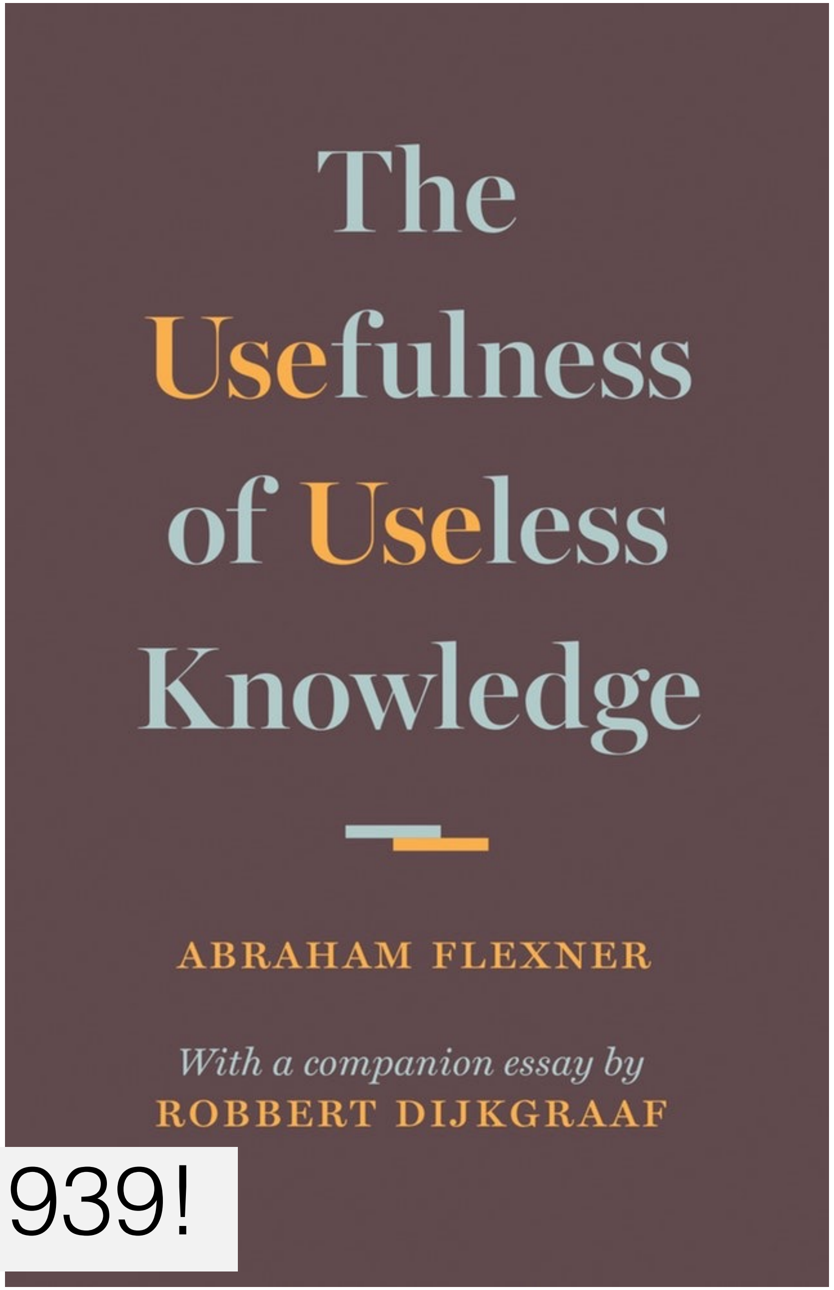
Mario Di Castro (CERN)

MediBox

ScienceBox for medical data analysis

Pere Mato(CERN)

CS4OD
CERN Science for Open Data



The
Usefulness
of Useless
Knowledge

ABRAHAM FLEXNER

With a companion essay by
ROBBERT DIJKGRAAF

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.

From HEP to society: a long and winding road…

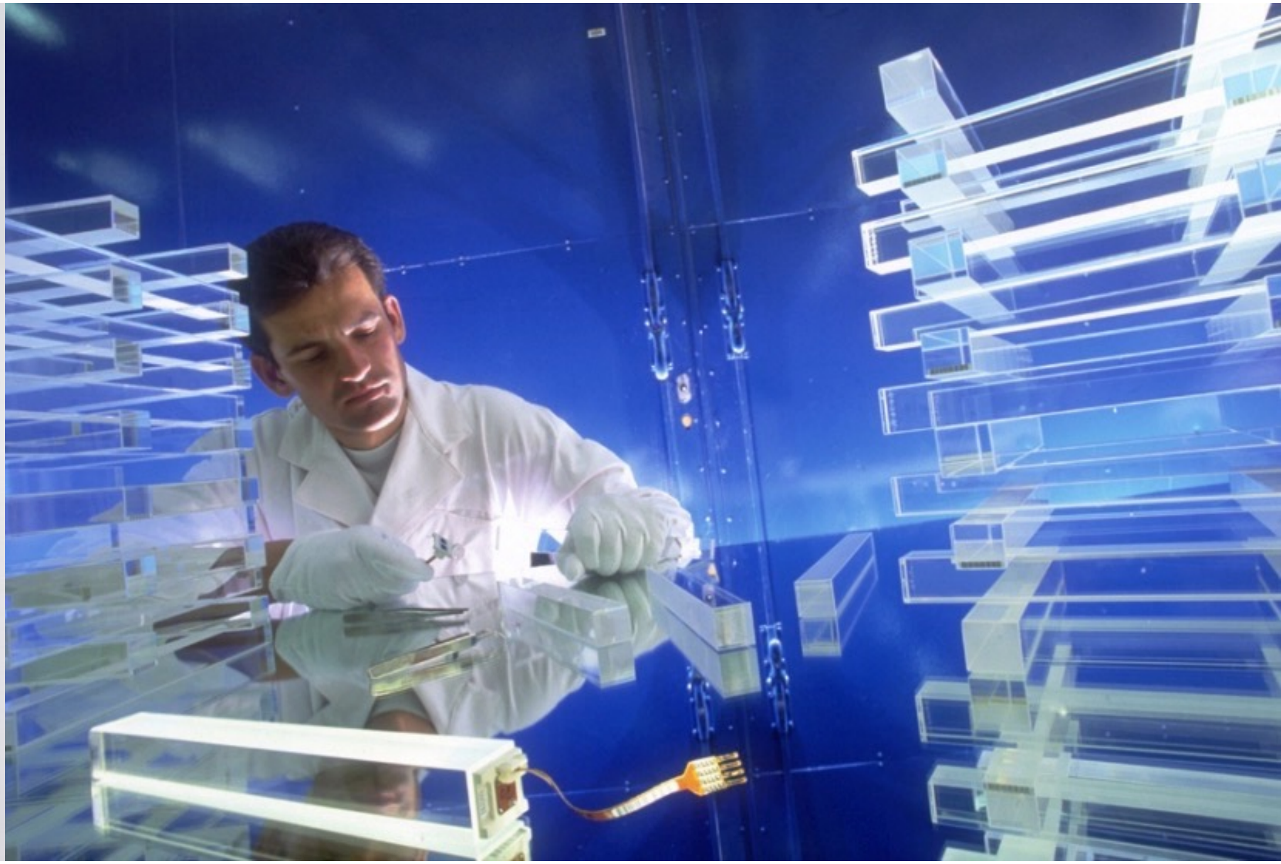


Photo: CERN

Photo: CNAO treatment room

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