From CERN technologies to Medical Applications

Manuela Cirilli,
Medical Applications Advisor
CERN Knowledge Transfer group
How I met TERA

Manuela Cirilli - TERA 30th anniversary
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
Une nouvelle imagerie ostéo-articulaire basse dose en position debout :
le système EOS

J. Dubouset¹, G. Charpak², I. Dorion², W. Skalli³, F. Lavaste³,
J. Dequise⁴, G. Kalifa³, S. Ferey³

Georges Charpak, Fabio Sauli and Jean-Claude Santiard working on a
multiwire chamber in 1970
First mouse imaged at CERN with Na-\textsuperscript{18}F in 1978

David Townsend and Alan Jeavons

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 $d(\theta, \phi)/r^2$, with $d(\theta, \phi)$ 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
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, Oncologie-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 Oncologie-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.

*Part-time members: L. Badawia, M. Bonadelli, P.J. Bryant (Study Leader), M. Courrent, P. Holy, A. Macek, M. Pelle, E. Reitberger, S. Rusi

Part-time members: O. Boer, F. Kraus

Contributors: P. Granata, M. Pacheco, L. Weisner

1) TERA Foundation, via Parini 11, 28100 Novara.
2) CERN, CH-1211 Geneva 23.
4) Med-AUSTRON, c/o BZ, Prof. Dr. Stephan Karwatzki II, A-2700 Wv, Neumarkt.
5) Sonnen & Partner Architektur Berlin (SPB), Hohenschönhausen 2, D-10623 Berlin.

Geneva, Switzerland
May 2000

PIMMS August 2000
ENLIGHT was established to co-ordinate European efforts in using ion beams for radiation therapy and to catalyse collaboration and cooperation 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

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

<table>
<thead>
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<th>Year</th>
<th>Model</th>
<th>Frequency (MHz)</th>
<th>Energy (MeV/m)</th>
<th>Weight (kg/m)</th>
<th>Ext. Diameter (cm)</th>
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<td>RFQ2</td>
<td>200</td>
<td>0.5</td>
<td>1200</td>
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<tr>
<td>2007</td>
<td>LINAC4 RFQ</td>
<td>352</td>
<td>1</td>
<td>400</td>
<td>29</td>
</tr>
<tr>
<td>2014</td>
<td>HF RFQ</td>
<td>750</td>
<td>2.5</td>
<td>100</td>
<td>13</td>
</tr>
</tbody>
</table>

Compact High-Frequency Radio Frequency Quadrupole (RFQ)


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
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 Target Irradiation

Rail Conveyor System

MEDICIS Laboratory

Manuela Cirilli - TERA 30th anniversary
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
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 readout chips fully prepared for TSV processing that may be tiled on all four sides.
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..)

Manuela Cirilli - TERA 30th anniversary
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


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

Standard CT

Metal artefact

MARS

Scaphoid screw

Metal artifact hides the bone-metal interface

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

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

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\textsubscript{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

It’s really small...

Very first prototype
(without sensor yet)

ARM CPU FPGA
Single Layer Compton Camera with MiniPIX TPX3 – Multiple Gamma Sources

- $^{131}I$ 284 keV (7%)
- $^{131}I$ 364 keV
- $^{22}Na$ 511 keV
- $^{137}Cs$ 662 keV

Spectrum of 3 Sources ($^{131}I$, $^{22}Na$, $^{137}Cs$)
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
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

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

- 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

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
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.
Cafein
A modular platform to support medical analysis, diagnosis and forecast
Luigi Serio (CERN)

Marchese
Machine learning based human recognition and health monitoring system
Mario Di Castro (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)

MediBox
ScienceBox for medical data analysis
Pere Mato (CERN)
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…