Medical Applications at CERN

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The CERN Accelerator School and MedAustron are organizing a course on

**Accelerators for Medical Applications**

26 May - 5 June, 2015

Eventhotel Pyramide, Vösendorf, Austria

This course will mainly be of interest to staff in accelerator laboratories, university departments, particle therapy centres and companies manufacturing therapy systems and associated accelerator equipment.

Following introductory lectures on radiobiological and oncological issues, the basic requirements on accelerators and beam delivery will be reviewed. The medical applications of linear accelerators, cyclotrons and synchrotrons will then be treated in some detail, followed by lectures on the production and use of radioisotopes and a look at some of the acceleration techniques for the future.

A full day visit to the MedAustron centre in Wiener Neustadt will provide a practical insight into the field. Participants will also have the opportunity to work on realistic case studies as an integral part of the program.
ICERN: Particle Physics and Innovation

- **Interfacing** between fundamental science and key technological developments

- **CERN Technologies and Innovation**
  - Accelerating particle beams
  - Detecting particles
  - Large-scale computing (Grid)
What Everyone Knows

Hadrontherapy vs. radiotherapy

The BRAGG Peak

- Tumours close to critical organs
- Tumours in children
- Radio-resistant tumours

The physics properties of light ions (Bragg) may make them much more efficient in treating some kinds of tumours

Energy deposition
Comparison of Collateral Damage
History and Reminders
Initiative: Accelerator reminder PIMMS

“In 1996, CERN initiated the Proton Ion Medical Machine Study (PIMMS), which aimed at designing a synchrotron optimized for the treatment of moving organs with carbon ions (and protons). Together with CERN part-time staff, the study participants were the TERA Foundation (Italy), the MedAustron project (Austria) and Oncology 2000 (Czech Republic). The design was summarized in two reports issued in 2000. The project was adapted by TERA and used as a basis for the CNAO centre, which has just been completed in Pavia by the CNAO Foundation and INFN. The MedAustron facility utilises the same synchrotron design, and is currently being built in Wiener Neustadt (Austria).”
CNAO (Pavia) is treating patients
CNAO in Pavia
MedAustron is building a centre in Wiener Neustadt
PIMMS1 design has been a big service to the community

- 2 source branches installed
- Beam commissioning
- Synchrotron hall installation
What has happened since 2000 on the technology side?

- **LHC accelerator technology development**
  - Operation of 8T magnets
  - Testing of 11T magnets for Luminosity upgrade
  - Development of 18-20T magnets for energy upgrade

- **LHC Detectors developments**
  - Crystal scintillators improvements
  - Medipix proliferation and enhancements
  - Developments of new vertex detectors for LHC luminosity upgrade
  - Development of TOF resolution for Luminosity Upgrade

- **CLIC**
  - Accelerating structure frequency reduced from 30GHz to 12GHz
  - Development of room temperature structures for 100MV/m gradient
  - Proposals for structures of 3 and 5.7 GHz with 30 and 50 MV/m for medical applications

- **LHC Grid**
  - Demonstration of the efficiency and reliability
  - Rapid adoption to new domains; Medicine

- **Developments of medical simulations with FLUKA/GEANT**
  - Treatment planning, medical research
Animation of Hadron Cancer Therapy

European NoVel Imaging Systems for ION therapy
What should an **ideal** facility do?

- Treat the tumour and only the tumour
  - monitor and control, the *ideal* dose to the tumour
  - Minimal collateral radiation “outside” the tumour
  - Minimal radiation to nearby critical organs

  - Even if the tumour is moving

- Be affordable
  - Capital cost ?
  - Operating costs ?
  - Increased number of treated patients per year ?

- **Compact**: Fit into a Teaching Hospital ?
Dimensional comparison for carbon ion accelerators

[Diagram showing dimensional comparison for different carbon ion accelerators including TERA cyclinac CABOTO, IBA / ARCHADE SC cyclotron, HIT synchrotron Heidelberg, iRCMS (BNL) synchrotron, and CNAO synchrotron Pavia.]
Cost Questions (user Specs)

• **Compactness**
  
  • Specification of “maximum” dimensions...MA
  
  • Balance of importance of compactness vs cost..MA

• **Cost Effectiveness .. The Over-riding Parameter**
  
  • What is a reasonable cost parameter (e.g. relative cost per patient compared with conventional therapy? Survival parameter?)..MA
  
  • Reduction of capital cost... Acc + MA
    
    • Number of treatment rooms + number and specs of gantries
  
  • Reduction of running and operational costs (experts...)..Acc + MA
    
    • Number of treatment rooms + gantries
  
  • number of patients treated per year...MA +Acc
Technical/Medical Questions (user Specs)

- **Beam Specs (needs R&D)**
  - Type of Light Ion (protons to Carbon or multiple ion capability)...
  - Central beam energy and energy range (?multiple energies for different functions)....M
  - Beam size (h+v) (emittance).....M
  - Energy spread of beam....M

- **Beam Distribution (gantry)**
  - Required angular coverage.....M
  - Allowed rate of change of beam energy...Acc + M
  - Degree of allowed movement of patient.....M

- **Diagnostics and Imaging (needs Test bed and simulations)**
  - Dose: requirements and precision deposition....M
  - Beam control devices.....Acc
  - Requirements for imaging (update rate, precision, resolution)... M
Technical/Medical Questions (user Specs)

- **Spot Scanning (Needs R&D)**
  - Comparison of specs for spot scanning (fast with low dose per shot or large dose per shot)...
  - Optimum spot scanning parameters, rate, dose, etc...
  - Control of dose per deposition...

- **Type of Accelerator ...Acc**
  - Synchrotron (normal or rapid cycling)
  - Linac
  - Cyclotron
  - Or a combination of the above (SC, Cyclo-Linac, etc)

The agreed specs will influence decision on type of accelerators and design of gantries.
Dealing with Organ Movement

• Time gating: apply dose when the organ is in the correct position. E.g. respiration cycle
• Fast rescanning: very rapid multiple painting. Statistically distribute the dose
• Tumour tracking: diagnostics and imaging

All methods need high scanning speeds
The New CERN Initiatives

1. Medical Accelerator Design
   - coordinate an international collaboration to design a new compact, cost-effective accelerator facility, using the most advanced technologies

2. Biomedical Facility
   - creation of a facility at CERN to provide particle beams of different types and energies to external users for radiobiology and detector development
   - Iterative experimental verification of simulation results

3. Detectors for beam control and medical imaging

4. Diagnostics and Dosimetry (pot) for control of radiation

5. Radio-Isotopes (imaging and possibly treatment)

6. Large Scale Computing and data (simulations, treatment planning, telemedicine etc)

Each Initiative is part of a package but also important as a stand-alone project.
User Specifications

1. Beam parameters:
   - Particle type(s),
   - Measured position,
   - Energy range
   - Required dose,
   - Real time feedback from detectors

2. Distributing the beam
   - Rep rate,
   - Spot scanning,
   - Gantry

3. Accelerator type,

4. Cost-effectiveness and compactness parameters

Radio-Oncologists, Radio-Biologists

Medical Physicists,

Accelerator Physicists

Detectors and imaging
• Many of these questions can only be answered with
  – experimental verifications
  – significant simulations
  – Development of diagnostics (imaging, dosimetry)

• ⇒ We need a dedicated test facility
We have many accelerators at CERN

But, one is a perfect test-bed, LEIR

**LEIR** (Low Energy Ion Ring)
- part of LHC injection chain
- accumulator for LHC ion programme (lead ions)
  - only used for several weeks / year
- Plan to *establish facility* for
  - Test-bed for medical instrumentation
  - Diagnostics and dosimetry
  - *radiobiology*
  - basic physics studies such as fragmentation of ion beams
Biomedical Research Facility at LEIR
Two experimental beamlines are foreseen

- **Horizontal** beamline up to maximum energy
- **Vertical** beamline up to 2.6 Tm (75 MeV/u C)
- **Pencil beam** 5-10 mm FWHM and broad beam 5x5 cm$^2$ considered
- 4 bending magnets (max 1.6 T, ± 40 mm gap) and 12 quadrupoles (max 23 T/m, max 40 mm radius) in total
Radiobiological Facility @ CERN

## Collection of requirements for Radiobiology Facility

### What radiobiological experiments are of interest?

**What are the desired beam properties?**
- ion species & energies
- beam intensities & duration
- beam size
  - (micro vs. broad beam)
- beam homogeneity

**How could an end-station for radiobiological experiments be designed?**
- Precision of beam-cell positioning
- Setup and Tooling

### Also a test bed for diagnostics

<table>
<thead>
<tr>
<th>Ions</th>
<th>Priority Rating</th>
<th>Why</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protons</td>
<td>5</td>
<td>Clinical</td>
</tr>
<tr>
<td>(molecular ion) H₂</td>
<td>2</td>
<td>Correlated particle experiments</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Experiments - Spatial distribution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Variation in response</td>
</tr>
<tr>
<td>Helium³</td>
<td>5</td>
<td>Possibly clinical</td>
</tr>
<tr>
<td>Helium⁴</td>
<td>4</td>
<td>Stable and possibly clinically relevant</td>
</tr>
<tr>
<td>Li⁶</td>
<td>4</td>
<td>Radiobiologically interesting, not clinically useful</td>
</tr>
<tr>
<td>⁴D</td>
<td>4 (if clean), 0 (if not)</td>
<td>RBE greater than P</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fragmentation tail shorter, less dose deposited past the distal edge</td>
</tr>
<tr>
<td>B₅¹⁰</td>
<td>2</td>
<td>Potentially clinical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fragmentations more than Li, better than C</td>
</tr>
<tr>
<td>C₆¹²</td>
<td>5</td>
<td>Clinical</td>
</tr>
<tr>
<td>N₇¹⁴</td>
<td>3</td>
<td>Radiobiological Studies</td>
</tr>
<tr>
<td>O₈¹⁶</td>
<td>4</td>
<td>Possibly clinically relevant</td>
</tr>
<tr>
<td>Ne₂₀¹⁰</td>
<td>3-4</td>
<td>Radiobiological Studies</td>
</tr>
<tr>
<td>Ne-Fe</td>
<td>1</td>
<td>To analyse radiobiological trends across the ions</td>
</tr>
<tr>
<td>Ca₂₀⁴⁰</td>
<td>1</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biologically important trace element</td>
</tr>
<tr>
<td>Fe₂⁵⁶</td>
<td>3</td>
<td>Radiobiological interpolation</td>
</tr>
</tbody>
</table>

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OPENMED Facility Summary

• With a new Front End (Source)
  – LEIR can provide ions of interest for biomedical studies up to <430 MeV for fully stripped $^{12}\text{C}$ or $^{16}\text{O}$ ions
  – Facility can also be used to test detectors and diagnostics as well as test the results of medical simulations
  – Study well under way:
    • (Re-)implementation of slow ejection with longitudinal and/or transverse excitation
    • New extraction channel (septa) and transfer line to experiment

• Need the Funding for Implementation
Detectors

• Continuous development on particle physics detectors at CERN
• Scintillating crystals
• Medipix
• Diamond detectors
Radio-Isotopes (1)

- Radioisotopes are used in medicine for applications ranging from imaging to treatment.
- The most used tracers are 99mTechnecium, often locally made available in hospitals from so-called generators created at nuclear reactors, for SPECT imaging.
- The most popular PET tracer 18F, is produced either in hospitals or in distributed cyclotron centres.
- Novel isotopes are emerging, either as imaging or treatment isotopes, exhibiting a range of chemical and decay properties.
- CERN has been hosting the Isolde facility for about 50 years.
- Over 1000 radioisotopes of more than 70 chemical elements have become available for fundamental and applied research.
- The technique of isotope mass-separation for medical isotope production will now be taken one step further with the construction of the CERN-MEDICIS facility.
Key Points: Radio-Isotopes

• Securing an adequate supply of radioisotopes is a big challenge, (not only for $^{99}$Mo/$^{99m}$Tc) but even more for promising "new" radioisotopes such as alpha emitters for radio-immunotherapy.

• A European user facility to be created to supply innovative radioisotopes (produced at ISOLDE-CERN, ILL, PSI, Arronax,...) for R&D in life sciences (preclinical and clinical studies).

• Medicis on ISOLDE
Isotope production in the dump and mass separation in the lab

1.4 GeV protons

- Spallation
- Fragmentation
- Fission

1000+ isotopes of 70+ chemical elements
**The scope**

- **Scope**: Life sciences, Medicine
- Innovative protocols (Surgery/brachytherapy/combination)
- Innovative isotopes

<table>
<thead>
<tr>
<th>Field of Application</th>
<th>Radiation</th>
<th>Chemical elements</th>
<th>Half lives</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET</td>
<td>$\beta^+$</td>
<td>Alkaline earth, Halogen, Lanthanide, Transition metals</td>
<td>10’s min. Hours</td>
</tr>
<tr>
<td>SPECT</td>
<td>$\gamma$</td>
<td></td>
<td>Days Months</td>
</tr>
<tr>
<td>TAT</td>
<td>$\alpha$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta therapy</td>
<td>$\beta^-$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auger therapy</td>
<td>$e^-$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Studies on cells, animals (« preclinical »)
  
  *possibly extended to clinical phases*

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The scope

\[ ^{161} \text{Tb-DOTA-RM6} \] in PC3 tumor bearing mice for SPECT-CT and treatment

At 3 hours
Civil Engineering is on track

September 4th 2013
Planning ...

<table>
<thead>
<tr>
<th>Phase</th>
<th>Construction</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE I</td>
<td>Commissioning: No beam</td>
<td>end 2015</td>
</tr>
<tr>
<td>PHASE II</td>
<td>Commissioning with beam and light targets to gain operational experience</td>
<td>2016</td>
</tr>
<tr>
<td>PHASE II B</td>
<td>Isotope production with light targets</td>
<td>mid 2016</td>
</tr>
<tr>
<td>PHASE III</td>
<td>Extending to heavy targets up to Tantalum</td>
<td>end 2016</td>
</tr>
<tr>
<td>PHASE IV</td>
<td>Collection of short lived alpha emitters (e.g. 149Tb)</td>
<td>2017</td>
</tr>
<tr>
<td>PHASE IVB</td>
<td>Operation with Lasers</td>
<td></td>
</tr>
<tr>
<td>PHASE V</td>
<td>Operation with Uranium targets/possible proton beam upgrade</td>
<td>2018</td>
</tr>
</tbody>
</table>
The CERN HF-RFQ for Medical Applications
First prototype under construction @ CERN

Injector for Protontherapy Linac:

→ Compact: 5 MeV in only 2 meters
→ High Frequency: 750 MHz
→ For injection into 3 GHz structures
RFQ Main Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Input/Output Energy</td>
<td>40 keV / 5 MeV</td>
</tr>
<tr>
<td>Length</td>
<td>1.964 m</td>
</tr>
<tr>
<td>Vane voltage</td>
<td>67.6 KV</td>
</tr>
<tr>
<td>Min aperture radius</td>
<td>1 mm</td>
</tr>
<tr>
<td>Maximum modulation</td>
<td>3</td>
</tr>
<tr>
<td>Final synchronous phase</td>
<td>-15 deg</td>
</tr>
<tr>
<td>Output current (max.)</td>
<td>300 µA</td>
</tr>
<tr>
<td>Beam transmission</td>
<td>30 %</td>
</tr>
<tr>
<td>Output transv. rms emit.</td>
<td>0.027 p.mm.mrad</td>
</tr>
<tr>
<td>Output phase spread</td>
<td>± 2 deg</td>
</tr>
<tr>
<td>Output energy spread</td>
<td>± 20 KeV</td>
</tr>
<tr>
<td>RF Frequency</td>
<td>750 MHz</td>
</tr>
</tbody>
</table>

(M. Vretenar et al, Linac14, Geneva, 2014)

Highest lost particle energy = 500 KeV.
99.5% of the lost particles @ E < 100 KeV → No activation of the structure.

Overall peak RF power = 399 KW.
4 IOT-based amplifiers, one per module.

Cooling for max. 5% duty cycle.
HF-RFQ Advantages

- Compactness and shielding limited to the target
- Reduced weight
- Highly reduced activation of the accelerating structure
- Highly reliable and very simple to use with limited maintenance
- Modular: addition of modules to change the energy
- Compatible with proton, deuteron and alpha particles
- Safe: Immediate cut-off in case of beam loss
- No power consumption in beam off mode
- No conditioning time
HF-RFQ Medical Applications

→ Protontherapy Injector: 1 RFQ
  ~2 meters – 5 MeV p⁺ – low current – low duty cycle

→ PET Isotope Production: 2 RFQ
  ~4 meters – 10 MeV p⁺ - 20 µA average current – 4% duty cycle
  ==> Production of \(^{18}\text{F}\) AND short lived isotopes (\(^{15}\text{O},^{11}\text{C},^{13}\text{N},\ldots\))

→ High energy proton source for \(^{99m}\text{Tc}\) Production: 2 RFQ + 1 DTL
  ~10 meters – 18 MeV p⁺ - 2 mA average current – 10% duty cycle
  Low cost – Direct production by \(^{100}\text{Mo}(p,2n)^{99m}\text{Tc}\)
  Reduce Nuclear Wastes - No need of \(^{235}\text{U}\)
CMA Initiatives: Where are we?

- Obtained some “seed” funding from CERN, as well as donations from outside
- “CERN Medical Applications Workshop” followed the ICTR-PHE (15-16 February)
- Attracted ~80 top experts from all over the globe
- Funding, governance,... “institute or..”
- International Strategy Committee (Nov 2014)
- CERN as a medical data repository (HUG, EPFL, CHUV, NCI)
- Radio-isotopes project well under way
- White paper well under way
- RFQ development
DRAFT Structure (to be decided)
Large Scale Computing and Data
• Clinical data
• Simulations
• Medical data storage, transfer and analysis
Hadron Therapy

• Bioinformatics has become an increasingly important domain of life and health sciences, as technological progress and data handling go hand-in-hand.

• The requirements are well beyond the current state-of-the-art and the applicability of developments from basic research, including solutions implemented for CERN’s Large Hadron Collider, is being explored.

• Standard information-processing tools need to be adapted to the complexity of medical data, which are more heterogeneous than physics data, and hence present new challenges for data mining. The confidentiality of patient information is also a major issue in medical data sharing.
Hadron Therapy

• We are investigating the application of grid computing and analytical software tools in data storage, handling, sharing and analysis, as well as the use of modern Monte Carlo (MC) calculation techniques.

• The high-level software systems will be effectively complemented by a user-friendly MC-based TPS capable of handling photon and ion therapy in various configurations, and by the MC modelling of the physical and biological behaviours of alternative ion species as well as of protons and carbon ions (followed by experimental verification).
Towards full picture of individual’s health status

- Biosensors
- Biochips
- Environmental Data
- Genomic data

Phenomic data

ICT Systems

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Courtesy Marco Manca
Thank you for your attention
SPOT SCANNING

ENERGY

POSITION

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PET Principle

A positron emitting radiopharmaceutical is injected into the patient: the distribution.

The emitted positrons annihilate with electrons in the tissue producing back-to-back photons detected by scintillating crystals.

After some time the patient is placed in the imaging scanner.

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Auffray
PET (Positron Emission Tomography) Imaging

[Diagram showing positron emission tomography process]

Brain Metabolism in Alzheimer’s Disease: PET Scan

(normal subject vs. cocaine addict)
Superconducting magnet technology developments at CERN can be applied to improve MRI scanners.
Scintillators are used in High Energy Physics to detect electromagnetic particles and measure their energy.

Scintillators convert incident energy to light, which is then detected by photo detectors, e.g. photomultiplier tubes (PMTs)

The intensity of the measured light is proportional to the energy of the incident particle

The detectors are called Electromagnetic calorimeters
In the CERN Large Hadron Collider (LHC) 2 experiments use scintillating crystals: Lead tungstate crystals: PbWO$_4$

Alice: 18,000 crystals

CMS

75,000 crystals = 100 tons
Higgs Bosons in 2 gamma

Particle Physics

Medical Physics

Slightly lower energy photons!!
Similar Challenges in HEP and medical imaging

CMS Electromagnetic calorimeter

Positron Emission Tomograph (PET)

Scale is the difference