ICTR-PHE 2016

OPENMED
Conceptual Design Report

Ghislain Roy – CERN

Uniting physics, biology and medicine for better healthcare

Background and context

- 2012 brainstorming meeting:
  "A community call for a *dedicated radiobiological research facility […]*"
- Concepts presented and discussed, e.g. in [Brainstorming Meeting on LEIR in 2012]
- Proof of principle also presented, e.g. in global feasibility study ([Abler et al.]) and study of transfer line ([Abler et al.])
- Need to go beyond this initial work and establish a coherent proposal based on solid requirements and assumptions
- Should reflect the views of a "community" and not of a single institute
- CDR is basis for initial approval of a project
- Then a Technical Design Report, following R&D and detailed technical studies, is basis for construction.
- A CDR is also the fruit of a Collaboration, whereby several institutes elaborate the concept together.


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Editorial

A community call for a dedicated radiobiological research facility to support particle beam cancer therapy

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Recently more than one hundred researchers followed an invitation to a brainstorming meeting at CERN on the topic of a future dedicated radio-biological and radio-physical research center. Many more joined the meeting via webcast. After a day of presentations and discussions it was clear, that an urgent need for such a development exists, resulting in a community call for the construction of a dedicated laboratory. Below we comment on the essential points.

Why is it needed?

Over the last decade particle beam cancer therapy has developed into a major treatment option. Many new centers have been built, and more are under construction. Currently 35 proton therapy centers and six carbon ion centers are in operation and 24 and 4, respectively are in construction or in the planning stage [1]. Many of these centers are driven by financial considerations and are heavily concentrating on treating large patient numbers. It was actually financial considerations, and not technical or medical ones, which led to the premature closure of two new carbon ion facilities in Germany. This situation encourages neither large-scale fundamental research nor clinical use for complicated and high-risk cases. Following the positive experiences of the initial research at GSI, Darmstadt [2] and the recent start-up of the Heidelberg Ion Therapy Centre (HIT) [3–5] this situation is expected to change.

Particle therapy is believed to have a physical advantage over even the most modern X-ray delivery methods (IMRT) based on the physical properties of particles depositing the main portion of the dose to tissue in the Bragg peak, minimizing the dose to the entrance channel, and delivering virtually no dose beyond the distal edge of the Bragg peak. Heavier ions (i.e. carbon), in addition, due to the higher density of ionization events along the particle track, exhibit a higher relative biological effectiveness than X-rays or protons, especially in the Bragg peak region, making them prime candidates for the treatment of radio-resistant tumors [6,7].

Still, all these advantages are mere speculations based on a scatter of physical and biological studies, spread over many years, and performed in multiple centers under different conditions, resulting in significant uncertainties [8]. The criticism that no large-scale clinical or pre-clinical studies are available to support these perceptions seems justified. Consequently, to fully utilize the benefits of particle therapy, a concerted research effort is called for to provide the biological and physical data set to help clinicians in their decision on which the most appropriate cancer incidences for this advanced therapy are, and to give guidance to the biologists and physicists on how to improve the potential capabilities of particle therapy.

This need is widely recognized in the community [9] but existing centers do not have the beam time available for the basic research efforts needed. Their focus is on clinical use, and research time is often limited to a few hours at a time, not adequate for well-organized data campaigns. Obviously a dedicated center for physics and radiobiology research, offering extended blocks of beam time, with a variety of ions and energies provided, is desperately needed.

What is it needed for?

Particle irradiation and the impact in vitro have been reported in a number of publications, resulting in a large range of RBE data from a number of different cell lines and endpoints [8]. These studies have been very useful in confirming to a large extent the hypotheses of the effect of particle irradiation. Nonetheless, the heterogeneity between the different studies makes it hard to combine the obtained data and to draw any definite final conclusions.

At this point, for further use in clinical research, there is a need for a large range of systematically obtained in vitro data, using identical cell lines in the same setup and under identical conditions, enlightening the effects and side effects of different particle irradiation. This will require a broad panel of different cell lines, representing cancer cells from a range of different tissues, cancer stem cells, and virus infected cells (e.g. Human Papillomavirus, which has been demonstrated in head and neck cancer to have an effect on outcome of radiotherapy [10]), irradiated with different particle types and LET-values.

A similar systematic approach must be used to test the effect of cytostatica or radiosensitizers, as for example Nimorazole, in context with particle irradiation [11–14].

Ultimately, to be able to study the impact on both tumor and normal tissue in the more complex situations presented in a living

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- CERN colleagues and management

- ISC led by M. Baumann, S. Myers and M. Dosanjh
  - Michal Waligorski, Philippe Lambin

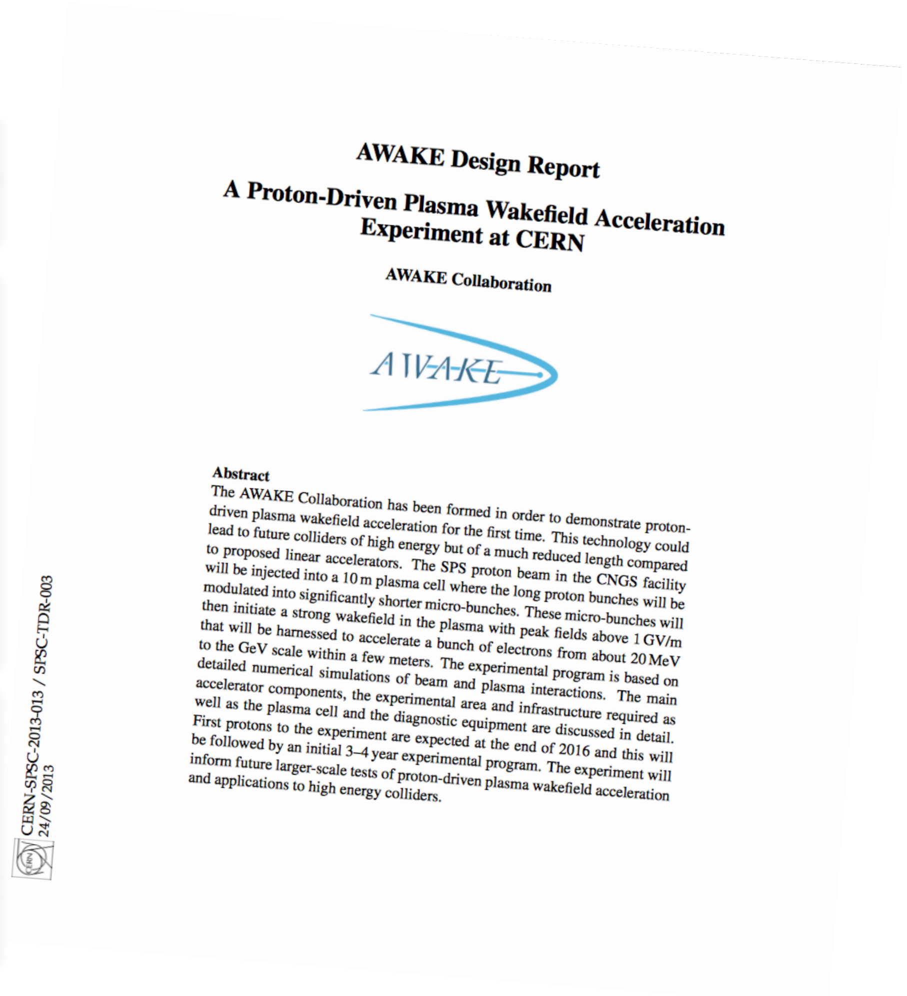
CDR Layout

- Collaboration and Organization
- Requirements and Parameters

- Ion Source
- Frontend & LINAC
- Injection Transfer Line
- LEIR Beam Dynamics
- Beam Extraction
- Transfer Lines to Experimental Area
- Biomedical Experimental Area

- Radiation Protection
- Integration and General Services
- Controls
- Operation
- Safety

- Project Planning



AWAKE Design Report

A Proton-Driven Plasma Wakefield Acceleration Experiment at CERN

AWAKE Collaboration

Abstract

The AWAKE Collaboration has been formed in order to demonstrate proton-driven plasma wakefield acceleration for the first time. This technology could lead to future colliders of high energy but of a much reduced length compared to proposed linear accelerators. The SPS proton beam in the CNGS facility will be injected into a 10 m plasma cell where the long proton bunches will be modulated into significantly shorter micro-bunches. These micro-bunches will then initiate a strong wakefield in the plasma with peak fields above 1 GV/m that will be harnessed to accelerate a bunch of electrons from about 20 MeV to the GeV scale within a few meters. The experimental program is based on detailed numerical simulations of beam and plasma interactions. The main accelerator components, the experimental area and infrastructure required as well as the plasma cell and the diagnostic equipment are discussed in detail. First protons to the experiment are expected at the end of 2016 and this will be followed by an initial 3–4 year experimental program. The experiment will inform future larger-scale tests of proton-driven plasma wakefield acceleration and applications to high energy colliders.

CERN-SPSC-2013-013 / SPSC-TDR-003
24/09/2013

3: Ion source

- Define source characteristics (intensity, charge state) from irradiation requirements

- Identify range of light ions that can be produced with intensity & charge states

- Sources under consideration:
  - Pantechnik Supernanogan
  - **AISHA (LNS Catania)**

- Install & characterize a test source
  - Intensity and charge states
  - Fast switching of ion species
  - Operability

Collaboration opportunity with INFN LNS
Interest at CNAO

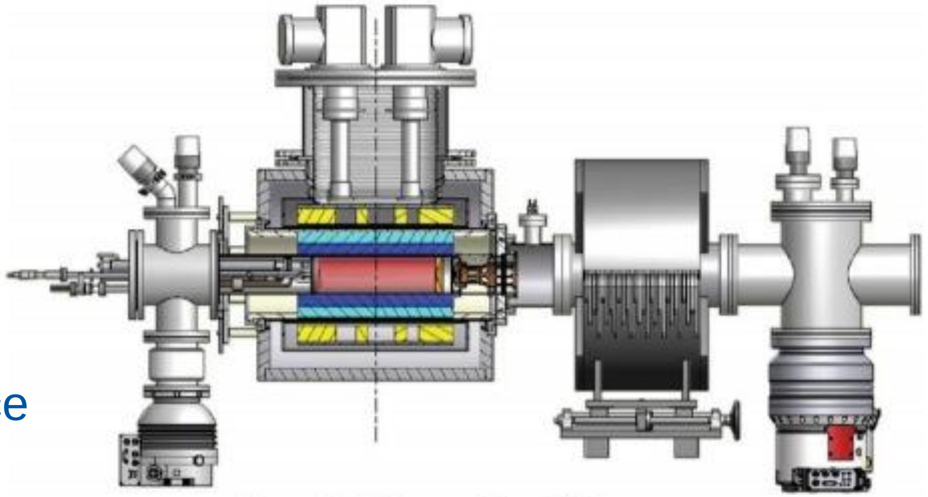


Figure 1: The layout of the AISHa source.

D. Kuchler, V. Toivanen

4: Frontend and LINAC

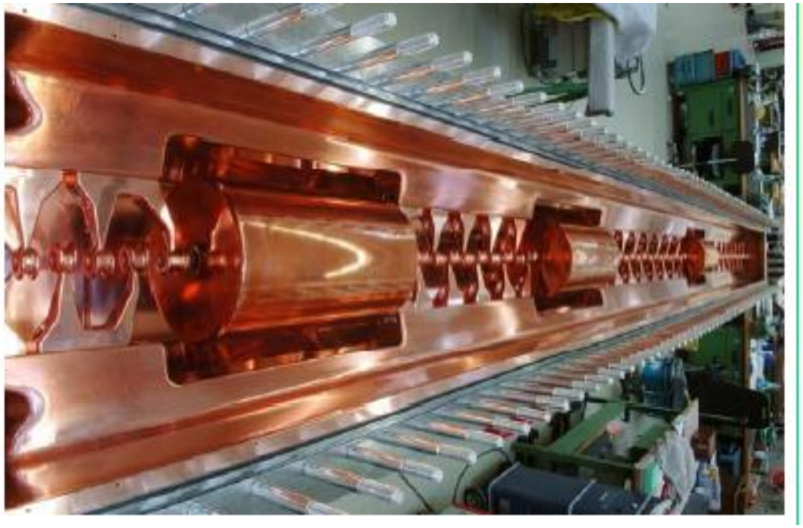
Design the frontend for optimal matching between source and LINAC

- Design of source output shaping
- Design of new beamline elements (RFQ)

Design of a new light ion LINAC5

- q/m ratio ?
- final design with source characterization input

Opportunity to reuse LINAC2 area

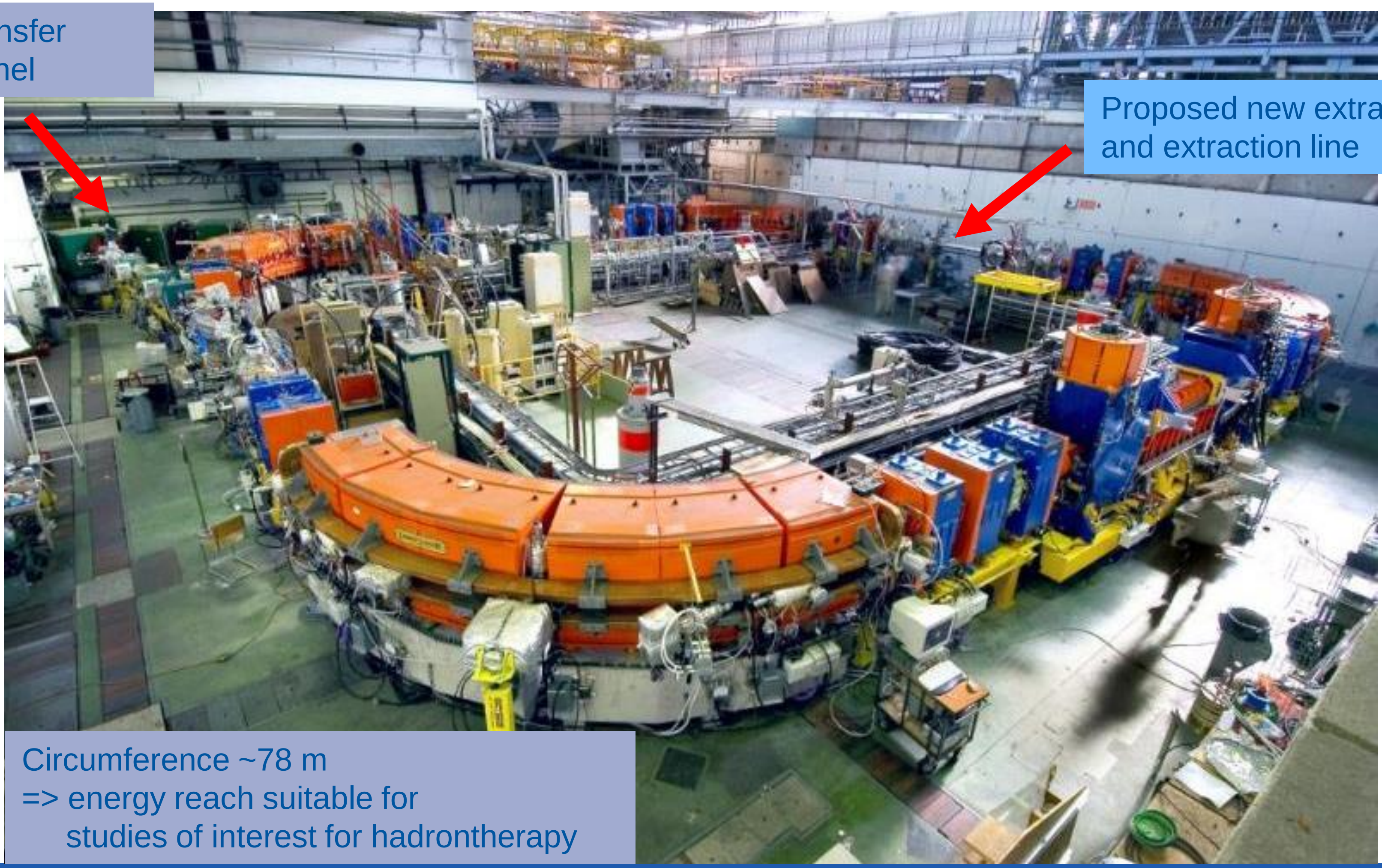


Interest from CNAO

A. Lombardi, J-B. Lallement

OPENMED facility outline

OPENMED facility outline II

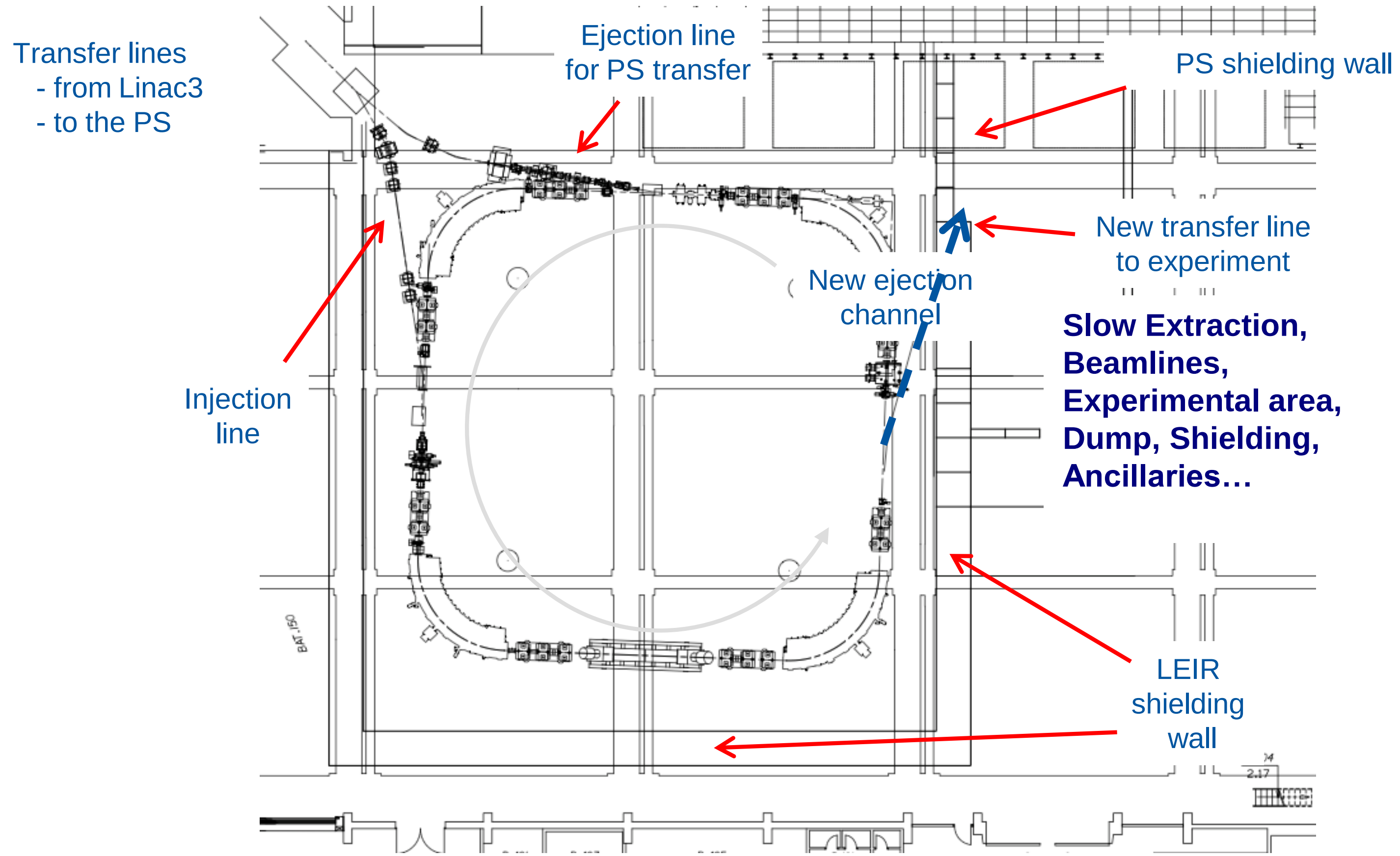


Transfer tunnel

Proposed new extraction and extraction line

Circumference ~78 m
=> energy reach suitable for
studies of interest for hadrontherapy

OPENMED facility outline III



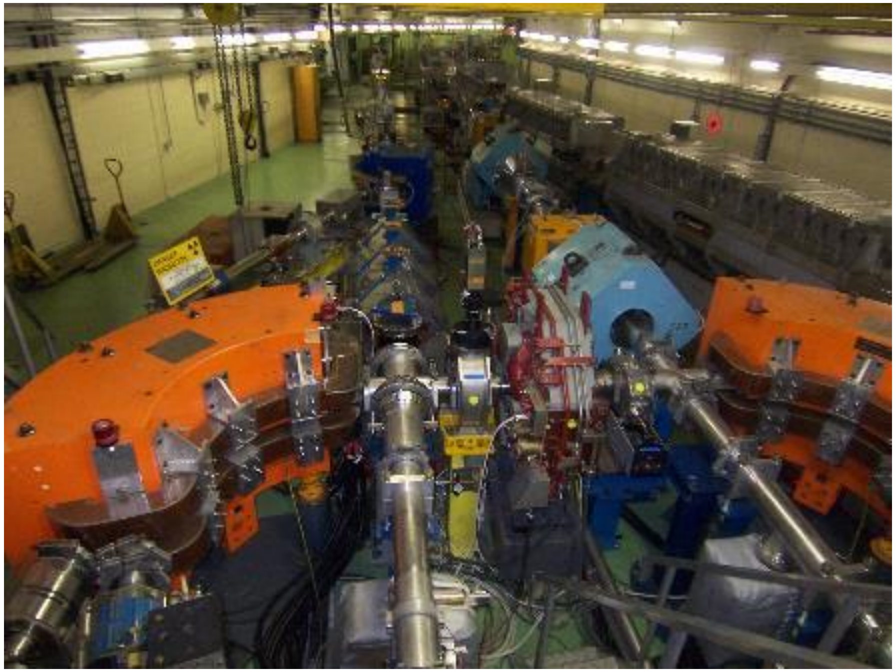
Slow Extraction,
Beamlines,
Experimental area,
Dump, Shielding,
Ancillaries…

5: Injection Transfer Line

Design of the transfer line between LINAC5 and LEIR

- Preserve existing lines
  LINAC3 to LEIR (heavy ions)
  LINAC4 to PSB (protons)
- Minimum of new elements

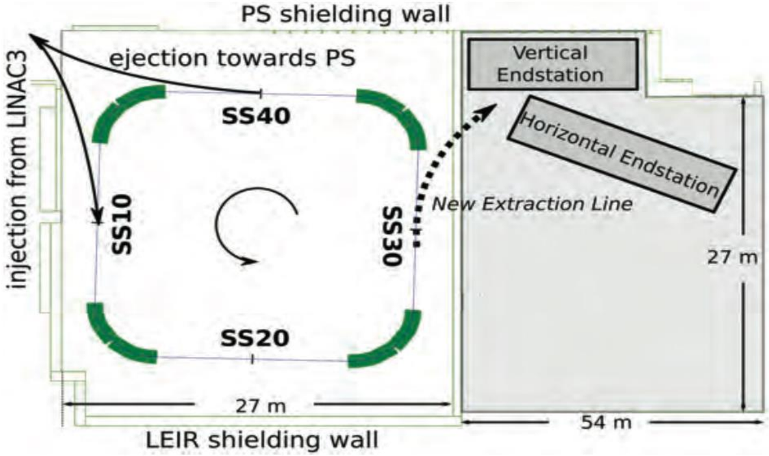
Issues for integration and planning



6: LEIR Beam Dynamics

Beam dynamics studies to verify LEIR for use with full range of light ions at energies up to 440 MeV and as low as 20 MeV

- Study of LEIR beam optics
  - Impact of magnet saturation after magnet power supply upgrade
  - Study effect of electron cooling and/or solenoid on light ions operation
- Fast ion switching in LEIR from operational point of view
- Beam dump
- etc.



7: Beam Extraction

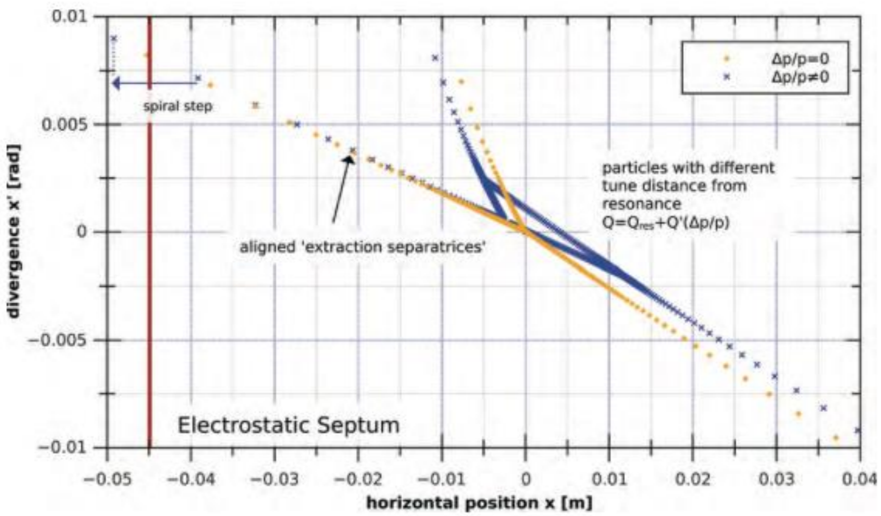
Collaboration opportunity with HIT, positive experience

Study and design beam extraction mechanism and specification of required equipment

Review applicability of extraction via RF knock-out (better beam quality) & required hardware

Review quad. driven slow extraction preliminary design and parameters (intensity fluctuations)

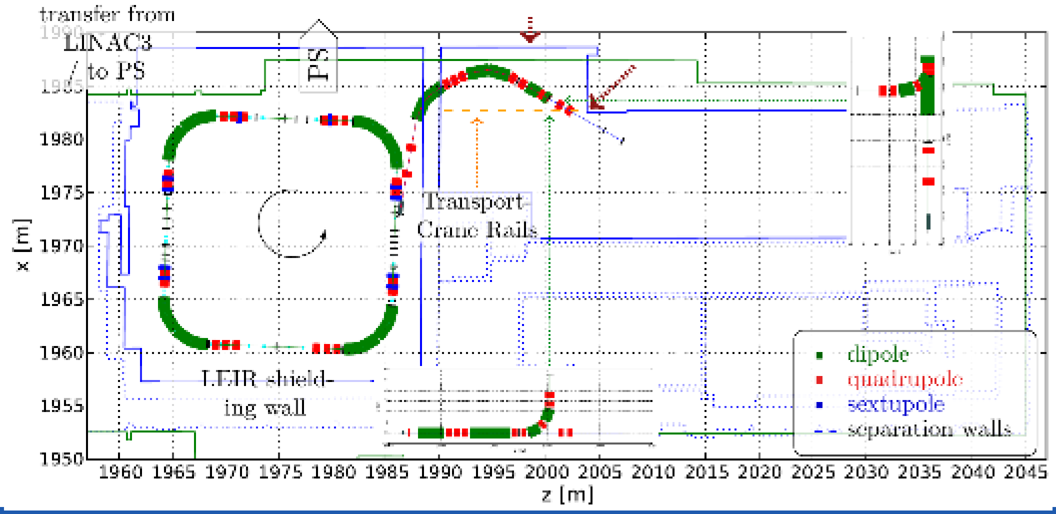
Impact of electron cooler on slow extraction



8: Transfer Lines to Experimental Area

Design of beam transfer lines to the biomedical experimental area

- common extraction transfer line
- 2 or 3 final beam lines
  - vertical beam line (going upwards, 70 MeV/u)
  - horizontal beam line (440 MeV/u for clean cell work)
  - horizontal beam line (440 MeV/u for more technical work)



Collaboration with
University of Huddersfield, UK

D. Abler,
T. Amin, R. Barlow,
S. Ghithan

9: Biomedical Experimental Area

Design of the biomedical experimental area providing common instrumentation & sample/detector mounts, access & area control.

- Biomedical laboratory for experimental preparation (fridges, incubators)
- Provision for cell imaging
- Design of user access to the irradiation areas and integration of the area
- Beam delivery design to experiments
- Beam Instrumentation
- Provision for an X-ray irradiation control
- Provision of generic sample mount – possible robotic placement system
- Provision of local experimental control

Collaboration with University of Oxford, UK

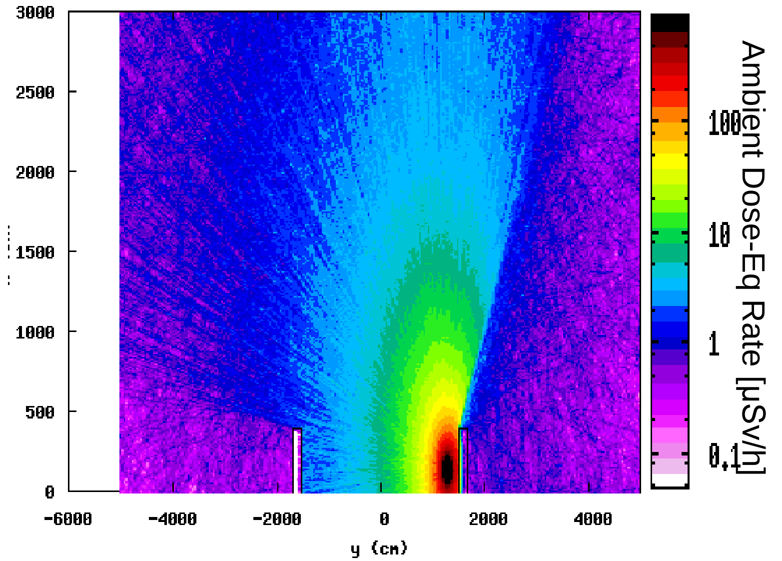
B. Jones, B. Vojnovic

10: Radiation Protection

Study all aspects of radioprotection for the OPENMED facility and necessary shielding implementation

- necessity of a shielding roof over LEIR for light ion operation ?
- Shielding requirements for the transfer lines
- Beam dump in end user station
- Impact of stray radiation from PS on OPENMED
- Neutron and gamma at the end user station

- Provide FLUKA simulations for nuclear safety & beam characteristics
- Study dosimetry requirements in the enduser station
- Access control requirements for the enduser station



Collaboration with University of Huddersfield , UK

S. Damjanovic,
R. Rata, R. Barlow

12, 13: Controls & Operation

Full integration of OPENMED controls into CERN accelerator controls

Local control for the enduser stations (beam on/off…)

Manpower requirements

Infrastructure requirements (local or remote)

Integration in CERN beam planning

- Independence of LINAC3 and LINAC5
- Requirements from HEP community for Heavy Ions from LEIR

2. **Requirements** / Parameters

Information collected

- ISC working groups (see next talks)
- in discussions with CNAO, MedAustron, PSI, HIT, …

Thanks!

Draft document listing all collected requirements, which still need clarifications and setting priorities.

Document available to those who can and want to contribute.

2. Requirements / **Parameters**

- **H, He, Li, Be, B, C, N, O** with Linac 5
- Heavier ions from Linac 3 (to be studied)
- Single source if rapid ion change
- Two sources would allow mixed irradiation

- Energies down to 50 MeV/u
- Energies up to 440 MeV/u (after PC upgrade)
- Higher energies in other CERN facilities

- Cycle time of 2.4s minimum (2 basic periods)
- Slow extraction
- Energy change at synchrotron, and/or range shifter

2. Requirements / **Parameters**

- Intensities to be refined with source and linac design

First estimate by C. Carli

Species	C	N	O	Ne
Intensity	$1.4\ 10^9$	$0.4\ 10^9$	$1.1\ 10^9$	$0.25\ 10^9$

- Can we increase for high dose ?
  - Stacking in LEIR ?

2. Requirements / **Parameters**

- Vertical (upwards) beam line < 70 MeV/u
- Horizontal beam line at full energy
- Second horizontal beam line ?

- Wide beam 50x50 mm2
- 1-2% homogeneity (w/o collimation ?)
- Beam interception as upstream as possible

- Pencil beam with multispot (both lines ?)

2. Requirements / **Parameters**

- Dosimetry and fluence monitoring
- Reference irradiator (X-ray or Co-60 ?)

- Target area with translators and basic equipment

- Laboratory space – clean room

2. Requirements / **Parameters**

Simple to operate and maintain

- Operating costs
- Operation for heavy ions for LHC…

High availability to serve the users

- Accelerator development come second
- Facility is first the experimental area

Disclaimer

- Following slides represent my own views.
- These views have been discussed and are shared by some colleagues.
- But they do not represent the official position of CERN.

CERN Environment

- International environment
  - Outside of jurisdiction of States
  - Council of 21 Member States

- Large lab with many specialists
  - cross-fertilization, translational research
  - expertise onsite, e.g. detectors, instrumentation and controls
  - but lacks biomedical expertise

Experiments at CERN

- Large experiments driven by Collaborations.
- Small experiments selected on basis of open call, and merit evaluation by a board.
- Beam-time is not charged to experiments.
- Results must be made available and published.

Roadmap

We have gauged a lot of interest in the community, officially and from personal contacts, both in the research and in contributing directly to the facility.

We have also received a number of statements of support from Europe and worldwide.

University of Huddersfield	MedAustron
University of Oxford	CNAO
INFN-LNS	PSI
IN2P3-CNRS	HIT

Roadmap

Still diverse requirements, interests

Research program at OPENMED ?

- Topics list, with priorities.
- Ideally, research hard to do at other facilities.
- Complement to the CDR

Collaboration ?

Can we find a number of institutes with similar interests, to get together in order to refine the proposal, assess the resources, formalize the request for OPENMED around LEIR at CERN, and bring the project to reality ?

And CERN must be a partner, of course.

CERN