

# Feasibility study for a biomedical experimental facility based on LEIR at CERN

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In light of the recent European developments in ion beam therapy, there is a strong interest from the biomedical research community to have more access to clinically relevant beams. Beamtime for pre-clinical studies is currently very limited and a new dedicated facility would allow extensive research into the radiobiological mechanisms of ion beam radiation and the development of more refined techniques of dosimetry and imaging. This basic research would support the current clinical efforts of the new treatment centres in Europe (for example HIT, CNAO and MedAustron). This paper presents first investigations on the feasibility of an experimental biomedical facility based on the CERN Low Energy Ion Ring LEIR accelerator. Such a new facility could provide beams of light ions (from protons to neon ions) in a collaborative and cost-effective way, since it would rely partly on CERN's competences and infrastructure. The main technical challenges linked to the implementation of a slow extraction scheme for LEIR and to the design of the experimental beamlines are described and first solutions presented. These include introducing new extraction septa into one of the straight sections of the synchrotron, changing the power supply configuration of the magnets, and designing a new horizontal beamline suitable for clinical beam energies, and a low-energy vertical beamline for particular radiobiological experiments.

**Keywords:** ion beam therapy; hadrontherapy; radiobiology; dosimetry; imaging

## INTRODUCTION

The use of charged particles for external beam radiotherapy (ion beam therapy) aims at reducing collateral dose to important healthy tissues and organs, thus allowing in principle a safer dose escalation to the tumour. Nearly 100 000 patients have been treated with charged particles around the world [1] over the past 60 years, and the number of new centres is doubling approximately every 8 years. The vast majority (80%) of these treatments used proton beams. Following the positive pioneering work in treatments with carbon ion beams in Japan, two 'multiparticle' centres have recently come into operation in Germany (HIT) and Italy (CNAO), and a third is under construction in Austria (MedAustron). Indeed, 'heavy' ion therapy (carbon, helium, boron, lithium) is expected to be superior to proton therapy for some tumour types, due to its enhanced radiobiological effectiveness and smaller lateral penumbra. More basic research in this field is needed to help clinicians make full use

of the benefits of ion beam therapy and to improve treatment outcomes for the patients. In this perspective, the creation of a dedicated biomedical research experimental facility is proposed at CERN, based on the existing Low Energy Ion Ring (LEIR). The reasons supporting this project are presented here, along with the technical challenges that it entails.

## MOTIVATION

### Research challenges and beamtime demand

Despite the increased availability of clinical ion beams in Europe, beamtime for pre-clinical radiation biology, chemistry and physics studies is insufficient, considering how crucial they are for the future development of ion beam therapy [2]. Operational clinical facilities work with beams of protons and carbon ions (as well as helium and oxygen in the near future at HIT), concentrating on clinical use and related quality assurance.

However, the development of accurate detector response models needed for dosimetry of scanned and passive beams require availability of ion species beyond those available at clinical ion beam facilities [3]. These beams could be provided by nuclear physics research centres, which offer a variety of beams in terms of ion species and characteristics, tailored to the experiments' needs. Their beamtime availability for biomedical applications, however, is often very limited, as physics experiments have the priority. Clinical practice could also greatly benefit from a coherent, uniform and systematic set of radiobiological experimental data comparing different beam characteristics, ion species, irradiated cell lines and tissues under the same protocol [4]. Studies on the interactions of ion beam therapy with drugs (sensitivity modifiers, chemotherapy, among others) should also be carried out more extensively. In parallel, the development of more precise imaging techniques and their respective detector systems would allow improved monitoring of the dose conformality during treatment, which is critical in particular for the treatment of moving targets and hypoxic tumour regions [5]. Finally, detailed information on particle fragmentation and nuclear cross-sections is important for simulations of advanced clinical treatment planning.

This report describes a proposal to upgrade the LEIR synchrotron to host a dedicated biomedical research facility. LEIR has similar characteristics to the accelerators used in ion beam therapy and has actually been proposed to act as a medical accelerator in the past [6–7]. CERN would be well-placed to host this facility, considering the existing competences in accelerators and detectors, experience in handling large collaborative projects and the opportunity to make use of the existing infrastructure. This proposed facility is strongly supported by the relevant research community [4, 8–9].

### The low-energy ion ring at CERN

LEIR is a low-energy accumulator of heavy ions, used to achieve the required luminosity for lead ion collisions in the Large Hadron Collider (LHC) [10] and, more recently, to provide beams for fixed target experiments at the Super Proton Synchrotron (SPS). Several long, low-intensity pulses of  $\text{Pb}^{54+}$  at 4.2 MeV per nucleon from the linear accelerator LINAC3 are accumulated in LEIR, by alternating a special stacking mechanism in transverse and longitudinal phase space and electron cooling. High-intensity, small emittance bunches of 72.2 MeV per nucleon are then extracted to the Proton Synchrotron (PS) for further acceleration. As most LHC runs use protons, LEIR is presently only used for about two months per year for LHC and SPS fixed-target experiments. A schematic of LEIR and the new experimental area is shown in Fig. 1. The synchrotron structure consists of four  $90^\circ$  bending magnets and four straight sections for a total length of 79 m. One of the straight sections (SS10) is used for injection, a second (SS20) houses the electron cooler, a third (SS30) kicker magnets for fast extraction and the fourth

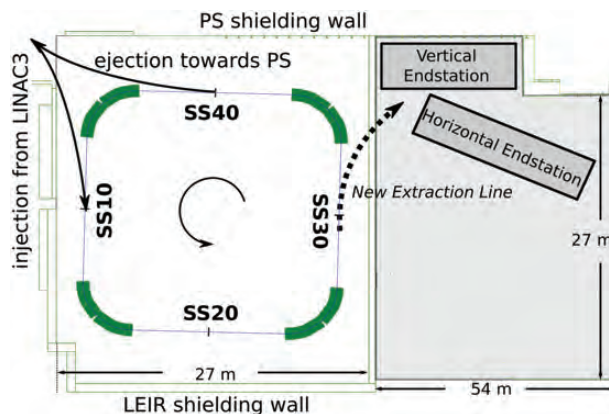


Fig. 1. LEIR facility layout.

(SS40) the extraction septum towards the PS and the radio-frequency cavities. LEIR has five families of quadrupoles (two triplets in SS20/40 and two doublets in SS10/30), along with two families of sextupoles in SS10 and SS30 used for chromaticity correction. In addition, two weaker sextupoles are present in SS40 and the bending magnets are equipped with entrance and exit pole face windings producing dipolar and sextupolar magnetic fields.

### Objectives for feasibility study

Research is ongoing at CERN, with the objective of assessing the feasibility of using LEIR to provide beams required for a dedicated facility for biomedical research. The study comprises two main topics of investigation. First, a dedicated ejection scheme must be implemented. This scheme will have to satisfy the requirements imposed by the experiments and will require slight modification of the current LEIR layout to introduce new elements. These modifications must not affect the performance of the accelerator for LHC operation, and in particular must not reduce its large acceptance. Second, short beamlines from the ejection point to the experiments will be designed. Both horizontal and vertical beamlines are under consideration to be able to perform a wide variety of radiobiological investigations.

In parallel to the studies on LEIR upgrades presented in this report, various options for upgrades of the LEIR injector are presently being investigated (personal communication from D Kuchler, A Lombardi, JT Stafford-Haworth *et al.*, CERN). One of them foresees the use of a commercial Electron Cyclotron Resonance (ECR) ion source, acceleration in a new Radio Frequency Quadrupole (RFQ) and injection in the present LINAC3 line with a switchyard.

## TECHNICAL CHALLENGES

### General considerations on slow extraction

The current power supply of the bending magnets limits the maximum magnetic rigidity of the circulating beam to

4.8 Tm, corresponding to a beam energy of 250 MeV/u (for fully stripped carbon ions), which is sufficient for most studies. However, with a new power supply, carbon ion beams could be accelerated up to 430 MeV/u (6.7 Tm), allowing investigations with all clinically relevant energies. The available machine aperture and tune stability determine the minimum extraction energy, whereas the limited strength of the magnets (for all but the main dipoles) makes it more difficult to find a solution for slow extraction at high energy and this may restrict the maximum beam energies for the experiments. Two main methods of extraction are used in synchrotrons: fast extraction, based on fast kickers deflecting the beam, and slow extraction, based on resonant amplitude growth. In order to send the beam towards the new experimental area for biomedical studies, extraction needs to be performed in SS30. The proposal foresees the implementation of a slow extraction from SS30 since this is better suited for experiments (control over the ion flux that can be provided to the experiments), and since the implementation of another fast extraction is not easily feasible due to layout constraints (lack of space for kicker magnets, and usage of existing kickers would require delicate closed-orbit manipulations). A slow extraction based on the third order integer resonance is therefore being studied. Such an extraction has already been used for antiprotons in the Low Energy Antiproton Ring (LEAR), the ancestor of LEIR, and is currently employed by all ion beam therapy centres based on synchrotrons [11]. The basic principle is to excite a third order resonance by powering appropriately located sextupoles [12]. The horizontal phase space is thus distorted to a characteristic triangular shape, as shown in Fig. 2. Particle trajectories inside the triangular shape, delimited by three separatrices, are stable and these particles can circulate for many turns. Particles outside this triangular region are

unstable and feature fast increase of the transverse oscillation amplitude with particles returning to the same separatrix every three turns. This quadratic increase in transverse amplitude allows some particles to jump over a thin septum, where they are kicked away from the circulating beam and towards the extraction line (Fig. 2).

The flux of extracted particles is linked to the rate at which particles become unstable. This process is carefully adjusted so that only a small fraction of the beam is extracted at each turn. The simplest method to bring the beam gradually to resonance is to modify the tune by varying the strength of one or more quadrupoles in the lattice. This method has been effectively used at GSI to provide beams for patient treatment. It suffers, however, from the sensitivity to tune ripples, and from a variation of the characteristics of the extracted beam over the duration of the spill. More sophisticated alternatives, requiring additional hardware, are the RF-Knock-Out (RF-KO), as used in HIT, or stochastic extraction for low extracted particle fluxes, as previously implemented in LEAR [13]. RF-KO would probably be the most versatile method, as stochastic extraction is more suitable for very long spill lengths. However, compared to the simpler tune variation method, RF-KO results in different transverse characteristics in the extracted beam. Band-limited noise signals (up to 100 kHz width) are used to excite the beam in horizontal phase space. The kicks needed for 1–10 s spill lengths are moderate (5  $\mu$ rad maximum) and—in combination with appropriate noise signal generators—existing machine elements could be used for this purpose.

### New lattice elements for extraction

The septa introduced in the previous section separate the circulating and extracted beams. They have to be very thin in order to limit the loss of particles. The first and thinnest

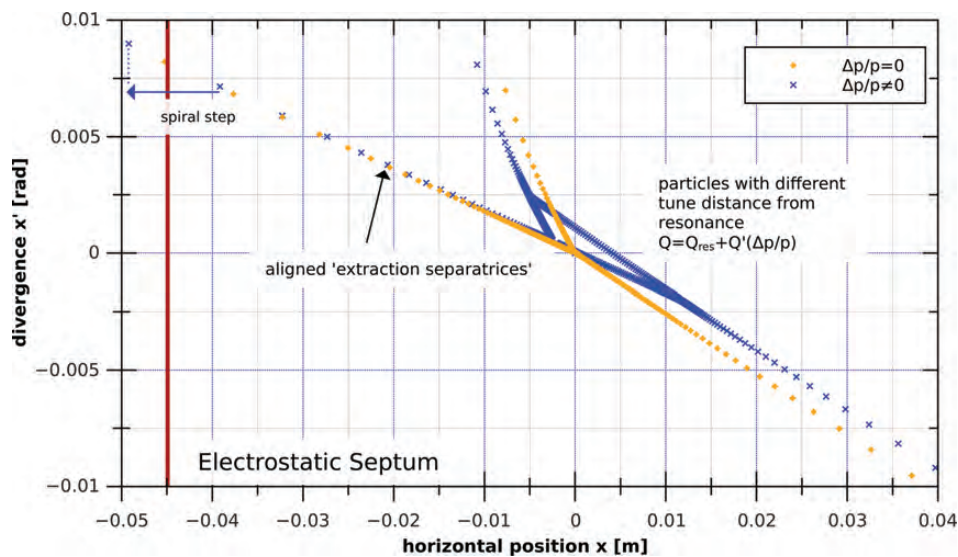


Fig. 2. Extraction of unstable particles with the third integer resonance.



septum is typically an electrostatic septum. Once sufficient separation has been achieved between the circulating and the extracted beam, a (thicker) septum magnet is added. It provides a stronger kick to the extracted beam, resulting in the beam finally exiting the accelerator through an extraction line. Considering the free space available in SS30 (see Fig. 3), the first septum has to be placed between the end of the bending magnet connected to SS20 and the first quadrupole doublet. Other septa can be placed in the 5 m-long drift space between the two kickers used for extraction of the lead ion beam. This only requires the adjustment of the position of some elements of minor importance. Since these new septa should not restrict the available aperture for normal LHC operation, their minimal transverse distance from the centre of the beampipe has to be 45 mm for the first septum and 50 mm for the others. Realistic parameters for the septa are summarized in Table 1.

It should be noted that the maximum kick achievable by the electrostatic septum is limited by the available longitudinal space and by the conducting material in order not to deteriorate the high vacuum needed for lead ion operation (personal communication from J Borburgh, CERN). Achieving a beam separation of at least 23 cm between extracted and circulating beam at the second kicker, is essential in order not to lose particles at the kicker magnet and to free sufficient transverse space to place the first quadrupole as soon as possible in the extraction line.

**Table 1.** Realistic parameters for the septa needed for slow extraction (personal communication from J Borburgh, CERN)

Septa	Electrostatic	Magnetic
Physical length	86 cm	120 cm
Effective length	66 cm	100 cm
Septum thickness	0.1 mm	10 mm
Maximum field strength	7 MV/m	0.5 T
Maximum kick (400 MeV/u $C^{6+}$ )	3.4 mrad	80 mrad

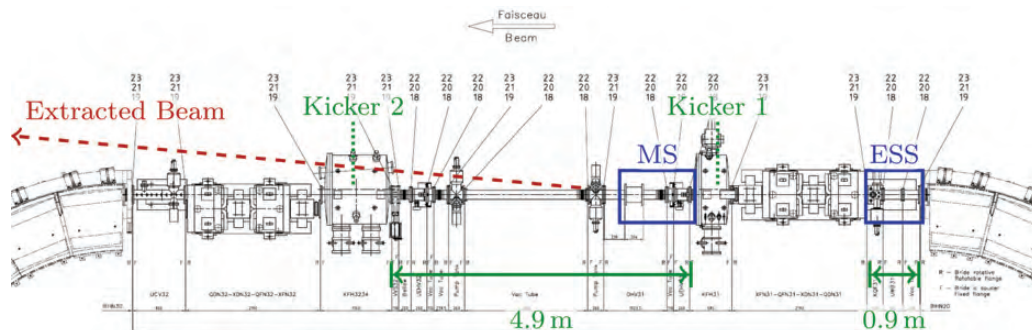
### Optical settings for slow extraction

Two optical configurations are under investigation: one where the optical functions are very similar to those used for LHC operation (in this case, the  $5/3$  horizontal resonance is excited), the other where the optical functions are very similar to those previously used in LEAR (in this case, the  $7/3$  horizontal resonance is excited). This is shown in Fig. 4.

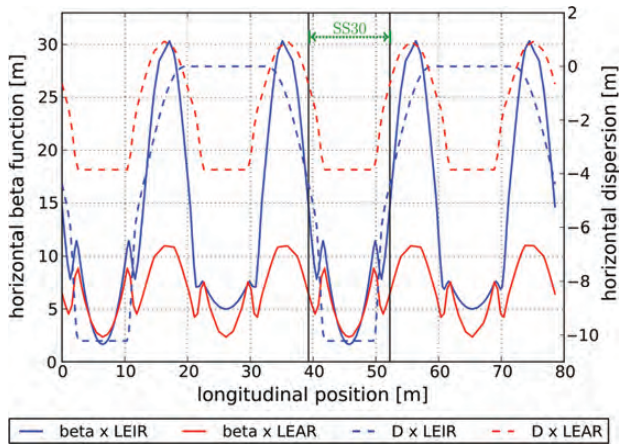
The difference in optical functions (beta and dispersion) results in different powering configurations for the sextupoles, which provide the correct resonance excitation and chromaticities. This relation derives from the Hardt condition, which ensures the alignment of the separatrices for particles with slightly different momenta from the design momentum, and thus limits losses at the electrostatic septum [12]. Considering the non-zero dispersion at the septum and assuming reasonable virtual normalized sextupole strength of  $30 \text{ m}^{-1/2}$ , the required horizontal chromaticity is 9 for the ‘LEIR-like’ lattice and 3 for the ‘LEAR-like’ lattice. Both conditions can be achieved even for the highest possible energies by using the normal sextupoles in SS10/30 and two of the pole face windings in the bends. Finally, an appropriate orbit bump in SS30 has to be foreseen, to ensure that particles are not lost at an aperture restriction somewhere else in the ring before reaching the electrostatic extraction septum. This central orbit distortion will be produced by the four orbit bumpers placed at the entrance and exit of the two bending magnets delimiting SS30. A first study, not taking into account the current strength limits of LEIR sextupoles, indicates that the maximum bump needed to extract a beam with horizontal (geometric) emittance of  $20 \pi\text{-mm}\cdot\text{mrad}$  would be 40 mm. Assuming that a ‘Supernogan’ (Pantechnik SA) source is used to produce the ions, and considering the emittances of CNAO and LEIR, an injected (normalized, RMS) emittance of  $0.9 \pi\text{-mm}\cdot\text{mrad}$  is estimated. The previous configuration would then correspond (assuming a  $2.5\text{-}\sigma$  beam envelope) to extracting a beam of 35 MeV/u [10, 14].

### Beamlines

Two beamlines are being studied: a horizontal beamline for energies up to the maximum extraction energy and a lower-



**Fig. 3.** Extraction process in SS30, involving an Electrostatic Septum (ES) and a Magnetic Septum (MS).



**Fig. 4.** Optical functions for the two envisaged slow extraction settings ('LEIR-like' and 'LEAR-like').

energy vertical beamline, allowing measurements of the biological effect on the plateau region of the stopping power curve for most relevant ions. The vertical beamline would also facilitate *in vitro* experiments, particularly those involving drugs such as radio-sensitizers or protectors (personal communication from K Peach, B Jones, B Vojnovic, M Hill, C Timlin *et al.*, PTCRi, University of Oxford).

The 1000 m<sup>2</sup> storage area adjacent to LEIR provides ample space for the installation of beam transport lines, connected experimental endstations and laboratories (Fig. 1). The initial location of the vertical beamline next to the PS radioprotection wall has been chosen in order to maximize vertical space availability, which is limited due to the presence of transport cranes: ~7.5 m from ground level at the position indicated in Fig. 1 compared with only ~5.5 m in any other location. The final positions of horizontal and vertical beamlines are subject to the outcome of the ongoing beamline design.

After extraction from LEIR, the beam properties in vertical phase space are similar to those of the circulating beam, whereas in horizontal phase space, the beam is characterized by a very small divergence and a large transverse size, resulting in very small emittances and forming the so-called 'bar of charge'. The use of the extracted beam for biomedical experiments demands variable beam sizes from a few millimetres, for clinical pencil beams, to broad beams with at least 5 × 5 cm<sup>2</sup> and dose uniformity > 95%.

The simplest method of producing a broad beam is by adjusting focusing elements in the beamlines. This approach would be the easiest to implement in a first stage and be capable of delivering beams of different sizes, while preserving the purity of the beam. Pencil beam scanning in a vertical beamline could be achieved by means of a translatable setup table that allows the positioning of samples relative to the beam. In the long term, a beam scanning system, as in modern ion beam treatment centres, would provide

maximum flexibility, allowing the simulation of complex beam deliveries for medical physics experiments while at the same time providing the possibility of delivering homogeneous dose distribution across a large target area [15–16]. Good field homogeneity can also be achieved by other active (using higher order optical elements, or beam 'wobbling') or passive methods (using scatterers) [17–19].

## CONCLUSION

This paper presents first investigations on the feasibility of using the CERN LEIR synchrotron as an accelerator for a new biomedical research facility. The scope of this facility would be to provide relevant beams for research in support of the recent clinical efforts of the new ion beam therapy centres in Europe. The main technical challenges introduced in this report are linked to the implementation of a new slow extraction scheme. This requires introducing new extraction septa in one of the straight sections of the lattice, as well as allowing different powering levels and configurations for most of the active elements of LEIR. Finally, a new extraction line and two experimental lines (a horizontal beamline suitable for all clinically relevant beam energies, and a low-energy vertical beamline for special radiobiological manipulations) need to be designed.

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