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DEVELOPMENTS TOWARDS A COMPACT CARBON ION LINAC FOR CANCER THERAPY*

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Abstract

Hadron therapy offers improved localization of the dose to the tumor and much improved sparing of healthy tissues, compared to traditional X-ray therapy. Combined proton/carbon therapy can achieve the most precise dose confinement to the tumor. Moreover, recent studies indicated that adding FLASH capability to such system may provide significant breakthrough in cancer treatment. The Advanced Compact Carbon Ion Linac (ACCIL) is a conceptual design for a compact ion linac based on high-gradient accelerating structures operating in the S-band frequency range. Thanks to this innovation, the footprint of this accelerator is only 45 m, while its capabilities are well beyond the current state of the art for hadron therapy machines and include: operation up to 1000 pulses per second, pulse to pulse energy variation to treat moving tumors in layer-by-layer regime. ACCIL is capable of accelerating all ions with mass-to-charge ratio A/q ~2 to a full energy of 450 MeV/u, and that includes protons, helium, carbon, oxygen and neon. With very short beam pulses of ~1 μs and high instantaneous dose delivery, ACCIL is capable of delivering FLASH-like doses (>100 Gy/sec) for most ion species. In close collaboration between Argonne and Radiabeam, we have developed different design options and prototypes of the high-gradient structures needed for ACCIL. Following an overview of the ACCIL design and its capabilities, the most recent results from the high-gradient structure R&D and future plans will be presented and discussed.

ACCELERATORS IN HADRON BEAM THERAPY – WHY NOT A LINAC?

Cyclotrons are currently dominating the field of proton therapy while synchrotrons are being used for ion beam therapy, especially carbon ions. A cyclotron is a continuous-wave (cw) fixed-energy machine; it does not offer the flexibility of adjusting the time structure or the energy of the beam by simple tuning. Energy degraders are used to adjust the beam energy, these are material blocks that also degrade the primary beam quality and generate secondary radiation requiring significant shielding.

Synchrotrons are pulsed accelerators which offer more flexibility in pulse structure and pulse-to-pulse change in energy without significant radiation or deterioration in beam quality. However, due to the multi-turn acceleration in a synchrotron and typical beam extraction, these changes could take a few seconds.

Being a single-pass machine, a pulsed linear accelerator (linac) is in principle capable of adjusting the pulse repetition rate and the beam energy hundreds of times per second (~200 Hz). So, why ion linacs are not deployed in cancer therapy? Linacs have already been proposed for protons [1], but using the same technology used for high-intensity research machines [2], such a linac would be hundreds of meters long. This have limited their deployment in a hospital or university setting, and it is the main reason why synchrotrons are currently dominating the field of ion beam therapy.

However, the intensity requirements for ion beam therapy are rather modest, 10^{10} p/s for proton and 10^{9} p/s for carbon, which could in principle be delivered in very short pulses (~μs) at a relatively low duty cycle (~10^{-4}). Combined with the possibility of using small-aperture accelerating sections, these features enable the use of high-frequency high-voltage copper cavities. Due the wide-spread use and commercial availability of S-band RF sources, the frequency range of ~3 GHz was a natural choice. And, taking advantage of high-gradient accelerating structure developments for CLIC [3], an accelerating gradient of 50 MV/m seems quite achievable in this frequency range, and was taken as a goal for current and future therapy linac proposals [4].

Finally, a fast-pulsed linac will enable the much-desired flexibility in beam tuning and the fast and efficient beam scanning to allow 3D dose painting, as well as real-time image-guided therapy and targeting of moving targets. By changing the pulse repetition rate, the beam intensity could be adjusted up to 10^{9} ions per second (10^{10} for protons), typically needed for therapy. The carbon beam energy could be changed continuously up to the full energy of 430 MeV/u required to penetrate the depth of a human body, which is equivalent to a 30 cm of water. The beam delivery from a linac will be similar to synchrotron beam delivery through fixed beam lines or gantry systems. However, the beam quality of the linac could enable much smaller magnets and therefore more compact gantries.

ACCIL – THE ADVANCED COMPACT CARBON ION LINAC

The Advanced Compact Carbon Ion Linac (ACCIL) is the most compact full-energy carbon ion linac proposed for therapy [5]. In Europe, there are proposals for a combined cyclotron and linac (cyclinac) and an all-linac for carbon beams [6], in addition to the ongoing LIGHT project for a

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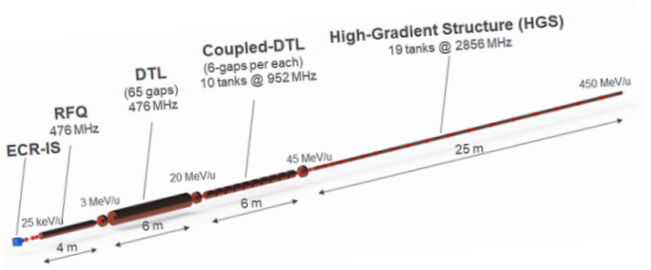

Figure 1: A schematic layout of the ACCIL linac design.A schematic layout of the ACCIL linac design.

proton therapy linac [7]. ACCIL is designed to deliver a full energy of 450 MeV/u which exceeds the energy required for carbon ion therapy. It is also capable of accelerating protons and many other ion beams to the same energy per nucleon. Figure 1 presents a schematic layout of the ACCIL design. The system is about 45 m long, but could, in principle, be folded into two 25 m long sections.

The linac is comprised of an electron cyclotron resonance ion source, followed by a radio-frequency quadrupole accelerating the carbon beam to 3 MeV/u, which is further accelerated in a drift tube linac (DTL), then in a coupled DTL linac up to 45 MeV/u. The most essential features to achieve compactness in the ACCIL design are high-gradient structures, each capable of delivering 50 MV/m, that accelerate the beam to the full energy of 450 MeV/u in ~25 m.

Main Design Features

In order to satisfy the ion beam requirements, the following design choices were made, which reflect the main design features of the ACCIL linac:

- The required carbon beam intensities can be provided by a commercial ECR ion source. A 5^+ charge state is selected for carbon ions to avoid contaminants.
- The acceleration starts with a 476 MHz RFQ designed for $^{12}C^{5+}$, followed by stripping to a 6^+ charge state.
- Further acceleration is provided by a DTL with permanent-magnet quadrupoles (PMQs) designed to focus both proton and carbon beams without tuning.
- A frequency transition to 972 MHz and further acceleration is provided by a CCDTL with compact electromagnetic quadrupoles for alternating focusing.
- The transition to an S-band frequency of 2856 MHz happens at 45 MeV/u, where a CCL using high-gradient structures is designed taking advantage of commercially available klystrons as RF sources and recent developments in high-gradient acceleration.
- High accelerating gradients up to 50 MV/m in S-band structure are possible due to very short RF pulse, less than 1 µs, and manageable voltage breakdown rates. Such short pulses are acceptable because of the low average beam current requirement.
- A relatively high repetition rate of beam pulses, ~100 Hz or higher, is required for fast tumor scanning. This is manageable by adjusting the pulse length while keeping the same overall duty cycle.

Design Parameters of the Different Linac Sections

Table 1 summarizes the most important design parameters for the different sections of the ACCIL linac:

Table 1: Main Design Parameters of ACCIL Sections

Parameter	RFQ	DTL	CCDTL	CCL
Design beam	C^{5+}	C^{6+}	C^{6+}	C^{6+}
Frequency (MHz)	476	476	972	2856
Input energy (MeV/u)	0.025	3	20	45
Output energy (MeV/u)	3	20	45	450
Section length (m)	4	6	10	25
Aperture radius (mm)	2	5	5	3
Kilpatrick factor	2.6	2	2	2.2
Accel. Gradient (MV/m)	1	3.5	12	50
Focusing lattice	–	FODO	FD	doublets
Focus. strength (T/m)	–	140	90	200
Focusing period	–	4 βλ	15 βλ	8 βλ

Being a pulsed machine with a low duty cycle (~10^{-4}), the accelerating structures could be operated at relatively high peak surface fields (Kilpatrick factor). The RFQ can be a brazed four-vane structure similar to the linac-4 RFQ operating at 352 MHz [8]. In the DTL, the focusing strength of the non-tunable PMQs is selected to satisfy the carbon beam dynamics while still providing a stable motion for the proton beam. Since the accelerating rate is the same for both beams, the transverse phase advance for protons is significantly larger, 97 deg vs. 23 deg for carbon.

Proton and Carbon Beam Dynamics Simulations

Figure 2 shows results of proton beam simulations from the ion source to the end of the linac while Fig. 3 shows the same results for carbon. The input and output beam parameters are summarized in Table 2.

Table 2: Input and Output Parameters for Proton and Carbon Beams for the ACCIL Linac

Parameter	Proton	Carbon
Input 4*$\epsilon_{t,rms,n}$ ($\pi \cdot$ mm $\cdot$ mr)	0.33	0.33
Input energy spread (%)	0.1	0.1
Output 4*$\epsilon_{t,rms,n}$ ($\pi \cdot$ mm $\cdot$ mr)	0.35	0.36
Output 4*$\epsilon_{l,rms,n}$ ($\pi \cdot$ ns $\cdot$ keV/u)	0.93	0.89
Beam transmission (%)	92	92

It is important to note that the 92% transmission corresponds to the RFQ acceleration efficiency and that no beam loss was observed through the rest of the linac. These results assume 99% stripping efficiency of C^{5+} to C^{6+} at 3 MeV/u following the RFQ.

DEVELOPMENT OF HIGH-GRADIENT STRUCTURES FOR ION BEAMS

As mentioned earlier, the essential part of the ACCIL linac are the S-band high-gradient accelerating structures

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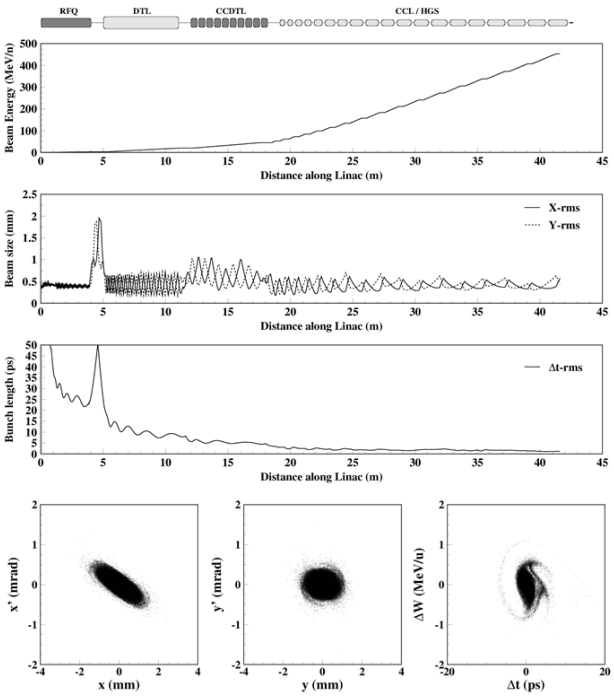

Figure 2: Simulation results for a proton beam in the ACCIL linac up to 450 MeV.

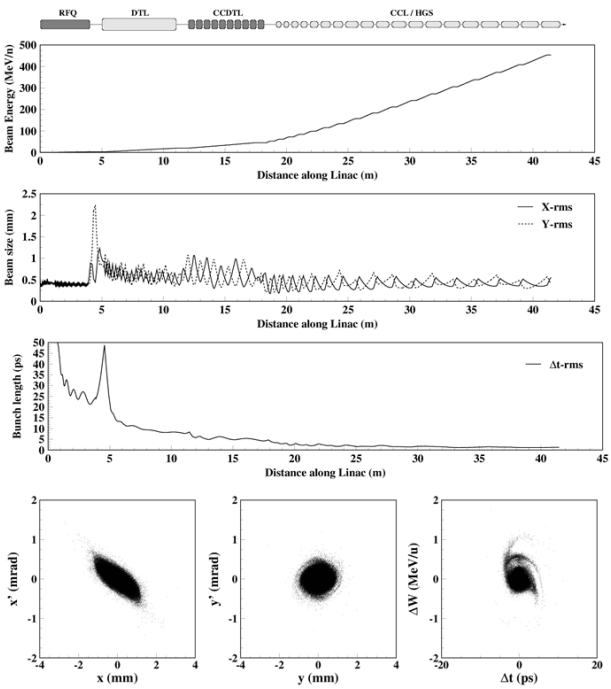

Figure 3: Simulation results for a carbon beam in the ACCIL linac up to 450 MeV/u.

used in the high-energy section of the linac and making it possible to be compact with a footprint under 50 meters.

Such a technology is well developed for electron beams, which become relativistic at an early stage of acceleration and benefit from speed of light accelerating cells, $\beta \sim 1$. In fact, a voltage gradient as high as 52 MV/m has been demonstrated at Argonne for a five-cell electron beam structure operating at the same frequency (2856 MHz) and pulse structure required for ACCIL [5]. However, ACCIL requires these structures for ion acceleration with a relative velocity β in the 0.3–0.8 range. This makes the accelerating cells more compact compared to $\beta \sim 1$ electron cavity cells, especially at the lowest β. A shorter and more compact cell increases the rate of electric breakdowns and makes dissipating the power required for operation at such high gradients very challenging.

Research and development (R&D) in this field is being pursued at CERN [9], other European institutions and recently in the US by Radiabeam and Argonne [10]. In collaboration with Radiabeam, we have developed a novel design for a $\beta \sim 0.3$ negative harmonic traveling-wave structure capable of delivering such accelerating gradients, ~50 MV/m [11]. Designing the cavity to operate in the negative space harmonic leads to a longer cell where reentrant noses can be added for more efficient acceleration while easing power dissipation due to the larger cell volume. This special cavity design for the lowest velocity ions is what distinguishes ACCIL and makes it more compact than other linacs. It allows the transition to high-gradient acceleration to take place at 45 MeV/u, which is much lower than the 70 MeV/u proposed for other linacs.

Standing wave $\pi/2$-mode options such as side-coupled (SCS) and annular-coupled structures (ACS) are promising designs capable of similar performance. These structures are made of alternating accelerating and coupling cells. The coupling is off axis on one side in the case of SCS, while it's annular surrounding the accelerating cells in the ACS design. Development and prototyping is required for low and medium velocity high-gradient structures to populate the high-energy section of the ACCIL linac.

In collaboration with Radiabeam, we have built and tested at high-power a full prototype NHS cavity for $\beta \sim 0.3$. Figure 4 shows the design, construction and test results for the NHS cavity. A power corresponding to a 50 MV/m accelerating gradient was attained, more details can be found in [12]. We have also designed and built a cold model for an ACS cavity for an ion beam velocity of $\beta \sim 0.4$ as the next accelerating cavity for ACCIL, following the NHS cavity [13]. Figure 5 shows the RF design, fabrication and testing of the cold model for the ACS cavity.

More recently, and due to the need for fast beam scanning for 3D tumor painting, an advanced model of the NHS has been designed to operate at a repetition rate as high as 1 kHz [14]. Figure 6 shows the cell geometry, rf design and engineering model of the latest NHS design. It will be built and tested in the near future.

ACCIL CAPABILITIES AND POTENTIAL APPLICATIONS

The main advantages of ACCIL are fast pulse-to-pulse beam energy change and ion beam switching capabilities. Different ion sources could be used in the front-end to allow

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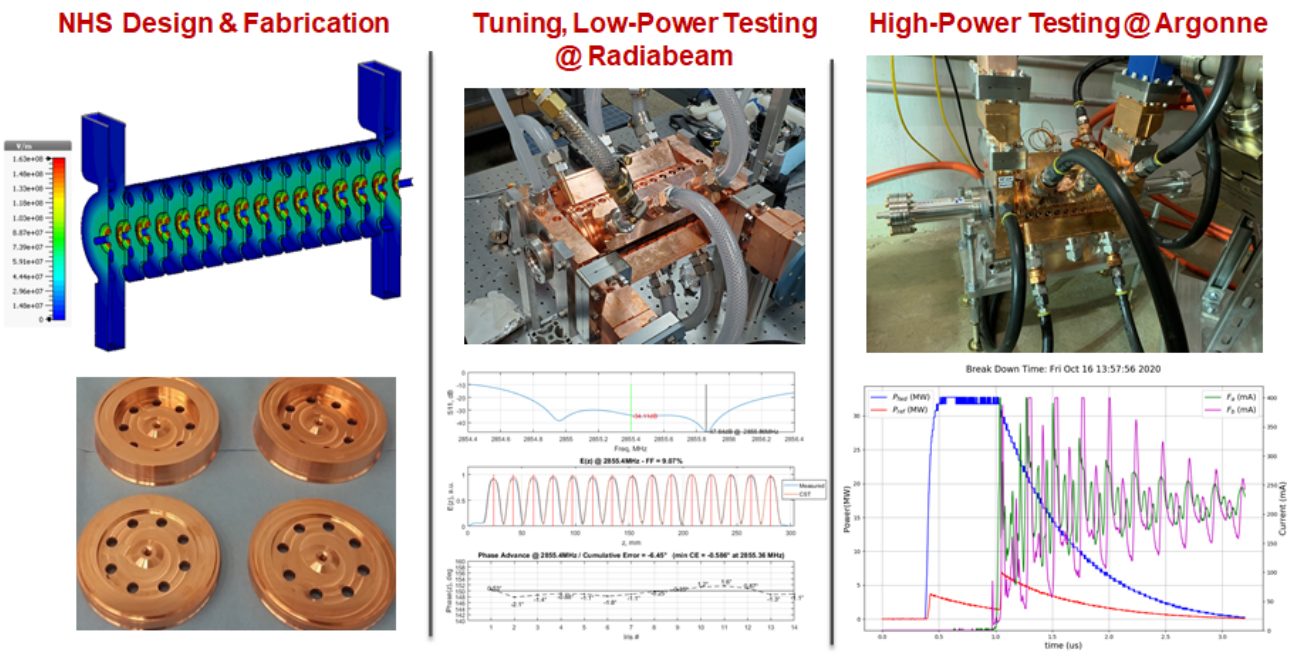

Figure 4: Design, fabrication and high-power testing of the β ~0.3 negative-harmonic traveling-wave structure (NHS) developed by Radiabeam in collaboration with Argonne.

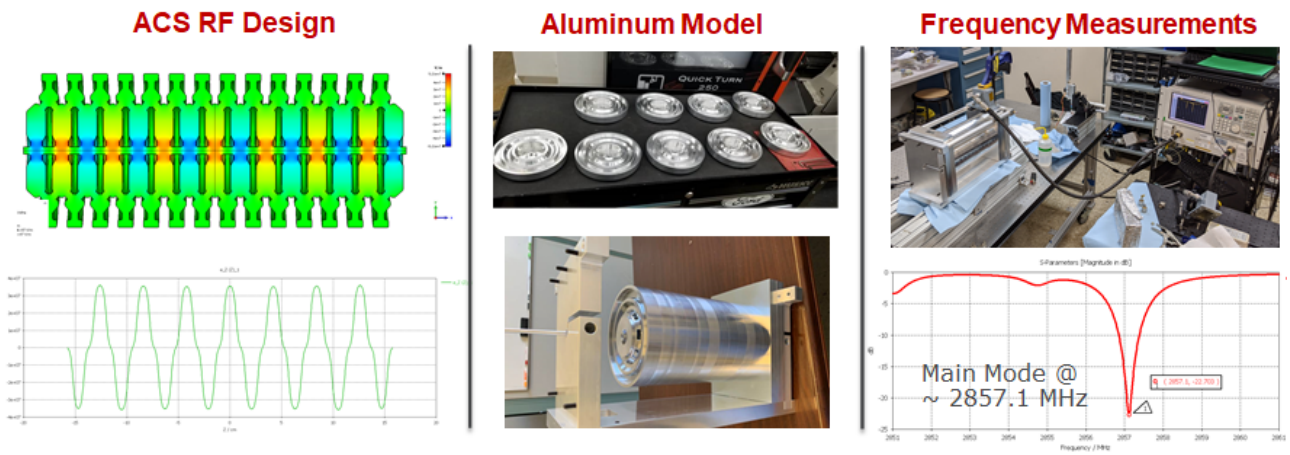

Figure 5: Design, cold model and measurements of the β ~0.3 annular-coupled structure (ACS) developed by Argonne in collaboration with Radiabeam.

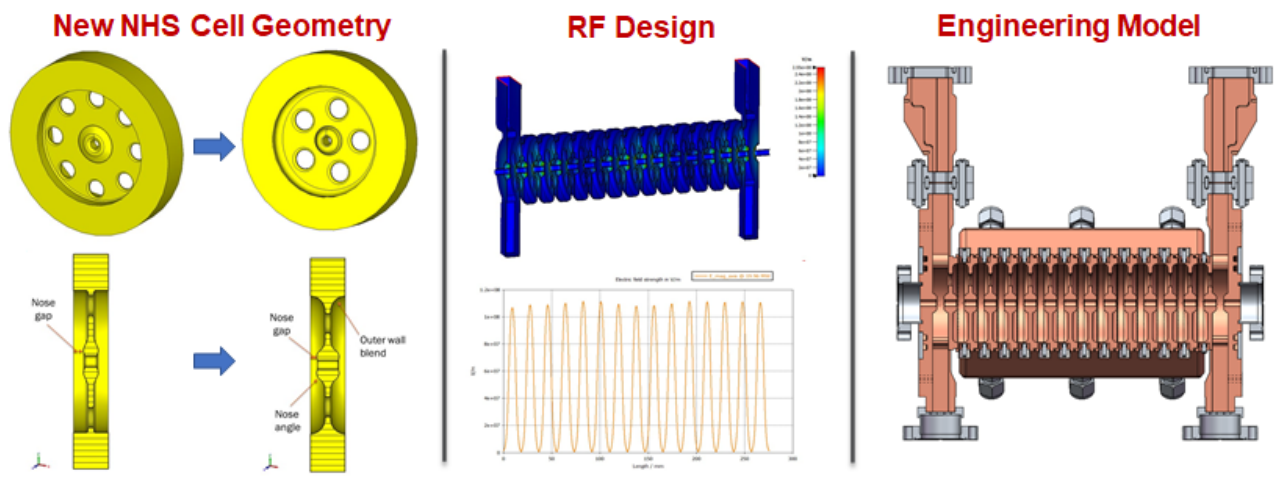

Figure 6: New cell geometry, rf design and engineering model for the latest NHS design developed by Radiabeam.

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fast beam switching between different ion species. The delivered beam intensity could also be controlled by adjusting the pulse length at the source or changing the pulse repetition rate, typically from 100 to 400 pulses per second (pps) are possible, and R&D for accelerating structures capable of operating at 1000 pps is ongoing. Ultimately, the tuning flexibility of the ACCIL design will allow fast and effective variable-energy and intensity-modulated multi-ion beam therapy.

ACCIL is capable of accelerating a variety of ion beams from proton to neon, up to a maximum energy of 450 MeV/u. At this energy, ions lighter than carbon, including protons and helium ions, have ranges exceeding the depth of the human body and could therefore be used for imaging purposes, as in proton tomography. It is also possible to deliver these beams with lower energies for treatment. Despite having ranges shorter than the human body, ions heavier than carbon, like oxygen and neon, could still be used for treatment at adjustable energies up to the full linac energy.

As for FLASH therapy, ACCIL's capability is comparable to other existing proton and ion machines [15]. For example, for a proton beam of 230 MeV, losing about half of its energy in the last 10 cm, the energy deposited at 10^{10} p/s in a spot size of ~5x5 mm^2 corresponds to a delivered dose rate of ~60 Gy/s, which is well within the FLASH dose requirement of 40 Gy/s to 100 Gy/s. For a carbon ion beam of 430 MeV/u, losing about half of its energy in the last 10 cm, the energy deposited at 10^9 p/s in the same stopping volume corresponds to a dose rate of ~150 Gy/s, which exceeds the FLASH dose requirement and calls for a larger beam spot size. However, in order to satisfy all cases, for all tumor sizes and beam energies, we would need at least 10 times more particles per second (10^{11} protons/s and 10^{10} carbon/s), which is feasible within the current ACCIL design. In addition, the higher rep. rate of ~1 kHz, being developed, will allow faster beam scanning and more flexibility in beam delivery.

FUTURE DEVELOPMENTS AND PLANS

In addition to the general development of high-gradient accelerator structures for low-velocity ions, we identify few areas of R&D of special importance for compact ion linacs and their applications in the medical and industrial sectors, namely:

- Investigating and pushing the beam current limit of compact ion linacs.
- Increasing the repetition rate of high-gradient structures.
- Developing RF sources capable of delivering the required high pulsed power.

In particular, to enable this technology for ion beam therapy, establishing a linac-based advanced ion therapy research center in one of the US National Labs would be a significant step forward and would allow the following applications and further developments:

- Cancer therapy and radiobiology research with all ion species up to neon.
- Imaging and Tomography with ions lighter than carbon: proton, helium, …
- Combined real-time MRI imaging with beam delivery, significantly enhancing the outcome of ion beam therapy.
- PET imaging using positron emitters (C-11, N-13, O-15, …) produced in the tumor for dose verification.
- FLASH ion therapy and other applications .

We mention, in particular, an ACCIL-type linac could be installed at the former IPNS site at Argonne National Lab. with the existing required infrastructure [16], which represents a significant cost saving compared to a green field installation. Following the development and commissioning phases, an initial research program including cellular radiobiology and animal therapy could be conducted prior to human therapy and clinical trials for FDA approval.

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