Review of pre-CDR of the project "Laser-hybrid Accelerator for Radiobiological Applications (Lhara)"

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This review evaluates the content of the document 2020-03-24_Lhara-pre-CDR-d1.0.pdf and the presentations given by K. Long, J. Parson, and A. Kurup, during the meeting held on the 25th of March of 2020.

LhARA, Laser-hybrid Accelerator for Radiobiological Applications, is conceived as a novel and very versatile facility devoted to charged particle radiobiology research. LhARA uses a hybrid approach in which laser-driven beams are post-accelerated by a fixed-field accelerator (FFA). This approach enables radiobiological investigations in completely new regimes as it allows the unique properties of the laser-driven source—extremely high instantaneous flux in an extremely sort pulse over a tiny area, flexibility in the time and spatial structure of the beam —to be preserved and exploited.

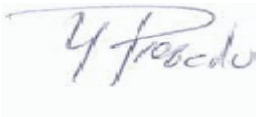
This is a very promising project, offering unique beam features and much-needed research infrastructure for radiobiology research. The main characteristics to be highlighted are:

- Flexibility
  The flexible temporal and spatial beam structure would enable exhaustive investigations of the impact of the beam parameters (i.e. pulse length, repetition rate, average dose rate) on the biological response. These comprehensive evaluations are not possible at clinical centres, where the clinical beams cannot be tuned. Among others, this flexibility would allow assessing the precise beam characteristics required and the thresholds in Flash therapy. Along this line, LhARA may also contribute to unravel the underlying mechanisms in Flash therapy.
- Different beam species
  The availability of several ion beams (from protons to heavier ions) at the same facility will aid the inter-comparisons among different charged articles for therapy.
- Accessibility
  The greater accessibility of LhARA in comparison to clinical centres would allow: -The assessment of different temporal fractionation schemes. Linked to that, evaluations of different combinations with immunotherapy or chemotherapy could be performed with fewer constraints that at clinical centres.

-performing exhaustive evaluations of RBE using more complex endpoints (ie. angiogenesis, inflammation, etc). The possibility of performing in vivo experiments is very valuable as there is an important lack of in vivo data in charged particle therapy.

- The negligible divergence of the beam to be provided by LhARA is an important advantage for the investigations in spatially fractionated radiotherapy.
- The potentially more stable beams to be delivered by LhARA in comparison with other laser-based systems is a very relevant characteristic to obtain reliable and reproducible results in biology experiments.

In conclusion, LhARA has the potential to drive a change in current clinical practice by increasing the wealth of radiobiological knowledge. This in turn may be used to devise new approaches decreasing the radiotoxicity on normal tissue, while maintaining or even enhancing, the tumour-kill probability.



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