

**REVIEW FORUM** Corresponding Author

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- ✓ 1. Initial Validation
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- 6. Final Validation
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**LhARA: The Laser-hybrid Accelerator for Radiobiological Applications**

Galen Aymar, Tobias Becker, [Stewart Boogert](#), Marco Borghesi, Robert Bingham, Ceri Brenner, Philip N Burrows, Oliver C Ettlinger, [Titus-Stefan Dascalu](#), Stephen Gibson, Timothy Greenshaw, Sylvia Gruber, Dorothy Gujral, Claire Hardiman, Jonathan Hughes, W Gareth Jones, Karen Kirkby, Ajit Kurup\* , Jean-Baptiste Lagrange, [Kenneth Richard Long\\*](#) , Wayne Luk, John Matheson, Paul McKenna, [Ruth Mclauchlan](#), Zulfikar Najmudin, Hin Tung Lau, [Jason Luke Parsons](#), Jaroslaw Pasternak, Juergen Pozimski, [Kevin Prise](#), [Monika Puchalska](#), Peter Ratoff, [Giuseppe Schettino](#), William Shields, Susan Smith, John Thomason, Stephen Towe, Peter Weightman, Colin Whyte and Rachel Xiao

**Original Research, Front. Phys. – Medical Physics and Imaging**

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History

Editor  
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Reviewer 2  
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**Reviewer 1**

Independent review report submitted: 09 Jul 2020

Interactive review activated: 09 Jul 2020

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**Submit all comments** AND **Re-submit manuscript**

**EVALUATION**

**Q 1** Please summarize the main findings of the study.

Reviewer 1 | 09 Jul 2020 | 11:44 #1

Since the paper is a design study on a novel facility based on an innovative particle acceleration system, there are no specific finding. See a more detailed discussion in the detailed report attached.

Add comment

**Q 2** Please highlight the limitations and strengths.

Reviewer 1 | 09 Jul 2020 | 11:44 #1

The main strength is that, if implemented, the facility envisioned in this study will potentially allow to gain insights on the radiobiological mechanisms at play in phenomena such as the reduced radiation-induced toxicity in normal tissue warranted by the FLASH effect as well as the use of proton mini/micro beams. The clinical relevance of the study in the outlined facility is also a major point. The major limitation is a dichotomy between excessive simplicity and verbosity in describing well-known concept (e.g. RBE) on one side and an excessive detail on technicalities regarding the design of the beam line. In addition, there appears to be a vagueness about the actual implementation of such an ambitious and clearly extremely well-thought out programme: no time frame, no cost-effectiveness evaluation, no mention on the actual overall cost. This may be important in light of the argued need to abate costs for hadrontherapy. See a more detailed discussion in the detailed report attached.

Add comment

KL; 10Jul20: No action.

KL; 10Jul20: responses:  
 \* Will fix text to reduce dichotomy <sup>1</sup>  
 \* Vagueness about implementation unavoidable at this stage. Deal with this in cover letter. <sup>2</sup>

**Q 3** Please comment on the methods, results and data interpretation. If there are any objective errors, or if the conclusions are not supported, you should detail your concerns.

Reviewer 1 | 09 Jul 2020 | 11:44 #1

I don't think this is rigorously applicable for this paper. The rationale, simulation-based approach and consequent results are sound.

Add comment

KL; 10Jul20: No action.

**Q 4** Check List

Reviewer 1 | 09 Jul 2020 | 11:44 #1

Is the English language of sufficient quality?  
- Yes

Is the quality of the figures and tables satisfactory?  
- Yes

Does the reference list cover the relevant literature adequately and in an unbiased manner?  
- Yes

Are the statistical methods valid and correctly applied? (e.g. sample size, choice of test)  
- Not Applicable

Are the methods sufficiently documented to allow replication studies?  
- Yes

Are the data underlying the study available in either the article, supplement, or deposited in a repository? (Sequence/expression data, protein/molecule characterizations, annotations, and taxonomy data are required to be deposited in public repositories prior to publication)  
- Not Applicable

Does the study adhere to ethical standards including ethics committee approval and consent procedure?  
- Not Applicable

Have standard biosecurity and institutional safety procedures been adhered to?  
- Not Applicable

Add comment

KL; 10Jul20: No action.

**Q 5** Please provide your detailed review report to the editor and authors (including any comments on the Q4 Check List):

Reviewer 1 | 09 Jul 2020 | 11:44 #1

Although I checked that the reference list is adequate, there is a disagreement on two of those, which I strongly believe must be replaced as illustrated in the attached detailed report.

[Review supporting file - 48618](#)

Add comment

KL; 10Jul20: Fix in paper, comment in letter.

3

QUALITY ASSESSMENT

<b>Q 6</b> Originality	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Q 7</b> Rigor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Q 8</b> Significance to the field	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Q 9</b> Interest to a general audience	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Q 10</b> Quality of the writing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Q 11</b> Overall quality of the study	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

REVISION LEVEL

**Q 12** What is the level of revision required based on your comments:

Reviewer 1 | 09 Jul 2020 | 11:44 #1

Minor revisions

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KL; 10Jul20: No action.

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