DOTTORATO DI RICERCA IN
BIOINGEGNERIA E BIOINFORMATICA

UNIVERSITA' DI PAVIA IL

COORDINATORE

PhD THESIS EVALUATION FORM
Confidential to the PhD Final Evaluation Committee

Year**	**2024**
PhD Student	**Giada Loi**
Reviewer	**Carmelo De Maria**
Reviewer Affiliation	**carmelo.demaria@unipi.it**
Date of the review	**28/11/2024**

Title of the PhD thesis*	**Frontespizio non presente**

Overall Assessment. Please suggest a possible outcome of the evaluation among the choices:

☐ PhD thesis not ready to be defended;
X PhD awardable;
☐ PhD awardable *cum laude* (top 10%)

Evaluation Table 1 of 2 (Please tick as appropriate: 4 – Excellent, 3 – Very Good, 2 – Good, 1 – Fair, 0 – Poor,Not App: Not Applicable). Please add a short comment if the evaluation is Fair or Poor

Scientific soundness and significance	4	3	2	2	0	Not App	Comment
Wide relevance/interest of the research theme	X						
Objectives well defined and scientifically supported		X					
Adequacy of the methodological approach		X					
Quality of the experimental setup		X					
Novelty of the approach		X					
Contribution to knowledge in the field		X					
Quality of the results		X					
Discussion and conclusions valid and properly supported		X					

Evaluation Table 2 of 2 (Please tick as appropriate: 4 – Excellent, 3 – Very Good, 2 – Good, 1 – Fair, 0 – Poor, Not App: Not Applicable). Please add a short comment if the evaluation is Fair or Poor

Written Document	4	3	2	1	0	Not App	Comment
Quality of the Abstract (is it exhaustive?)		X					
Document organization. Suitable balance of he component parts of the thesis		X					

c/o Dipartimento di Ingegneria Industriale e dell'Informazione - via Ferrata 5 - 27100 Pavia - Italy tel.: +39 0382 985350 – fax: +39 0382 985373 - e-mail: silvana.quaglini@unipv.it

Adequacy of the references		**X**					
Clarity		**X**					
Communication effectiveness		**X**					
Properly supported discussion and conclusions		**X**					

Comments/Notes

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Please add here any further comments/notes that might be useful to the PhD Candidate for improving the final version of the thesis.

PLEASE NOTE THAT THE FOLLOWING SECTION WILL BE FORWARDED TO THE PhD CANDIDATE

Use additional pages if needed

RELEVANCE OF THE TOPIC

The PhD research is focused on the optimization of the Bioprinting process for tissue engineering application, which is relevant and timely topic. Indeed, despite several recent advances the growing number of research papers, the Bioprinting field has not yet had a significant impact on patient management due to theoretical, experimental, and technological gaps.

MAIN OBJECTIVES and NOVELTY

The main objective of the PhD research is the integration of the extrusion-based bioprinting process with the mechanical stimulation of the bioprinted construct, by developing a custom platform, ie. a bioreactor, able to provide tensile or compression stresses.
This combination is underexplored in the field, which is more focused of combining fluid dynamic-based stimulation and extrusion-based bioprinting.
Nevertheless this novelty should be better framed and valorized by integrating/discussing/comparing with current research trends (see comments on discussion).

STATE OF THE ART

The state of the art is mainly described in chapter 1 and it is very concise (about 10 pages). It is suggested to includes (at least) analysis of other bioprinting technologies (e.g. inkjet or light based) and approaches (e.g. in situ bioprinting, non-planar extrusion bioprinting).
Furthermore, it is suggested to better organize the information regarding the combination of bioprinting and bioreactors, using tables to better visualize the comparison.

METHODS AND EXPERIMENTAL SETUP

Being an intrinsic multidisciplinary topic, the methods span from fabrication processes, to mathematical (mainly Finite Elements Model) and biological tests. An entire chapter is devoted to the design and development of the mechanical platform.

Specific comments:

- The stretchable support is at the core of the thesis and are introduced at the beginning of chapter 2. However, their rationale/shape/dimensions much better explained in chapter 3, and finally in chapter 4 (see figure 4.1). Please consider to introduce a more clear figure in chapter 2 for illustrating the rationale since the beginning.
- Are there any specific issues related to the different temperatures in the co-printing

process of PCL and the hydrogel?

- Was the mechanical characterization of PCL performed?
- The geometric symmetry along the z direction was not exploited. Please explain why.
- It is not clear how the interaction between the stretchable support and the hydrogel was modelled.
- It is not clear which materials were used to create the prototype of the platform (cfr page 39 and pages 45-46)
- The thesis claim that PA12 can be autoclaved, but please consider the effects of multiple wet thermal treatment on mechanical properties.
- Please try to use always mks unit of measurements.
- The experimental setup regarding the bioprinting process in the bioreactor is provided in chapter 4, but with limited details. E.g. how the zeroing process was managed?

RESULTS and DISCUSSION

Overall, the results are very good, but should be more in depth and clearly discussed.

- Are the results of the mechanical characterization of PDMS in line with literatures (see e.g. https://doi.org/10.1016/j.msea.2010.11.025)?
- the accuracy of the printing/coprinting/"in platform" printing should be presented and discussed.
- Please consider to compare the approach proposed in this thesis with the challenges/opportunities of robotic and in situ bioprinting.
- Please compare the results of biological experiments with similar studies
- The sentence "The in-silico study confirmed the experimental trend." should be better explained.

The above-mentioned comments should help to improve not only chapter 4 but also chapter 5

MANUSCRIPT

The structure of the thesis is good and the language is overall globally correct, but please consider revise the style with more short concise sentences.

References are adequate, but more should be added for improving the discussion.

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