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	**Diana Massai**
Reviewer Affiliation	**Politecnico di Torino**
Date of the review	**09.12.2024**

Title of the PhD thesis*	**Missing first page and title in the pdf**

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%)

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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**					

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

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Comments/Notes

General comment

The PhD thesis describes an original work regarding the design, manufacturing, and benchmarking of a bioprinted-integrated mechanical platform for tissue engineering applications in the field of skeletal muscle regenerative medicine. In particular, the platform was designed for mechanically stimulating elastic supports that contained cell-loaded hydrogels directly bioprinted inside the bioreactor.

After a brief introduction to the bioprinting technique and an overview of the phases for bioreactor development, with a state of the art of bioreactors for providing native-like mechanical stimulations aimed at promoting tissue maturation, the candidate highlights the gaps to be filled in terms of mechanical stimulation applied to bioprinted constructs and, even more challenging, about the integration of bioprinting and mechanical stimulation.

The first phase of the study was dedicated to the design, manufacturing, and preliminary biological testing of stretchable supports for housing bioprinted constructs, produced by adopting two different techniques (3D co-printing and molding). The second phase of the study was dedicated to design and prototype the platform, with the support of computational tools. Finally, the third phase involved the performance assessment in terms of mechanical stimulation and bioprinting feasibility and, lastly, biological validation culturing C2C12 murine cells.

Overall, the work is of high level and the amount of work done by the candidate is significant. Moreover, it is clear that the candidate dealt with several engineering methods in the bioprinting field and for the development of biomimetic culture conditions, also adopting computational tools for supporting the design and validation phases. The adopted methodology is appropriate and correct. The work is well organized and the text is well written, providing clearly described methods and good results.

Chapter 2

The preliminary tests for assessing the biocompatibility of the co-printed supports were performed checking the cell differentiation. The term “biocompatibility” should refer to the ability of the material to avoid any toxic effect on the cells, which is normally assessed by performing viability tests. Thus, the candidate should refer to these tests using different words, or providing also data on cell viability tests.

Moreover, the number of replicates for each conditions and for the different time-points should be provided in the text and in the figure captions for all the biological tests performed. Without this information, the results for day 14 are questionable. Indeed, it is particularly “impressive” the difference among bioprinted and co-printed supports at day 14, especially considering that a different trend is observed at day 21. The reviewer suggests verifying the results for day 14 and performing the tests in parallel, rather than comparing them with previous data.

Chapter 4/Conclusions

The authors refer contamination issues related to the porosity of the material adopted for manufacturing the SPD and propose a solution based on coating with PDMS the internal surfaces of the culture chamber. Although the proposed solution could temporarily work for few and preliminary experiments, it is not suitable for an intensive use of the bioreactor and does not guarantee process reliability over time. Indeed, the PDMS degrades with time and autoclave cycles, thus this procedure should be reiterated over time. In Chapter 4 and in the Conclusions chapter the candidate should recall this aspect, referring to a more reliable and effective solution, e.g., proposing a different selection of the manufacturing technique and material for the SPD.

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Minor comments

Figure 1.2. – The pictures from different studies can be used if the studies are cited in the caption, in this case the work from Gabetti et al. [78] should be cited.

Figure 2.2. – In the caption, the showed genes should be cited.

Chapter 4, pag. 51 and 60 - The following sentence is unclear and could be improved: “Furthermore, from a biological point of view, the mechanical platform should impact the in-vitro proliferation and differentiation of cells encapsulated within the hydrogel. Therefore, to meet these requirements, the platform must ensure sterility and be biocompatible”. The reviewer suggests to modify it, clarifying that a fundamental requirement for the platform is to allow sterilizability and biocompatibility of its materials, in order to be useful for influencing cell proliferation and differentiation.

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