INSTITUTE OF MACHINE AND INDUSTRIAL DESIGN

FME

Faculty of Mechanical Engineering
Brno University of Technology

Review of Doctoral Thesis

1. PhD candidate
Ing. Alexandra Streďanská/ Alexandra.Stredanska@vut.cz
2. Name of PhD programme
Design and Process Engineering
3. Title of PhD thesis
The influence of hyaluronic acid on friction and lubrication of fascia

4. Principal supervisor
prof. Ing. Martin Vrbka, Ph.D./ Martin.Vrbka@vut.cz
5. Co-supervisor
doc. Ing. David Nečas, Ph.D./ David.Necas@vut.cz

6. Reviewer
Professor Michael Bryant / m.g.bryant@bham.ac.uk
University of Birmingham

7. Overview of the scope of PhD thesis[1]
Evaluate:
Justification for evaluation: 100 – 200 words.

8. Significance of the topic and clarity of problem statement
Very good
The motivation for the project is clearly articulated, with strong reference to quantitative clinical drivers such as burden and current intervention limitations. The industry need is well framed, particularly in relation to the increasing demand for reliable and durable interventions in an ageing population. However, the justification would have been strengthened by an explicit discussion of the limitations of current methods / ISO standards for preclinical testing. Highlighting these gaps would reinforce the rationale for focusing on tribology as a key enabling technology. For instance, current standards may inadequately represent real-world tissue interfaces. Further elaboration on the clinical indications for intervention, and their downstream consequences (e.g. pain, reduced mobility, need for surgery) would enhance the translational impact. Including this detail would clarify how the proposed work directly addresses clinical and regulatory unmet needs.

[1] Overview of the scope of PhD thesis is a short description of objectives of PhD thesis's research and summary of main findings and scientific achievements.

9. Knowledge of existing literature
Very good
The proposal would benefit from a more comprehensive articulation of fasia mechanics and their contribution to disease progression, particularly with reference to quantitative data. Key pathophysiological factors such as inflammation and hyaluronic acid (HA) depletion are only briefly mentioned; their mechanistic links to altered lubrication, tissue damage, and pain could be more clearly established. While HA is discussed primarily in terms of viscosity, a broader review incorporating its structural properties, hydration shell, and interactions within the extracellular matrix (ECM) would strengthen the case. The hypothesised lubrication mechanisms of HA, including its role as a boundary lubricant, are underexplored. Additionally, the discussion of friction mechanisms is narrow, with an emphasis on viscoelastic lubrication and rubber/elastomer analogies. The rationale for this focus is unclear, and key concepts such as hydration lubrication, relaxation theory, and interfacial energy dissipation, well established in cartilage and mucosal tribology bit relevant, are notably absent. A more inclusive literature review would improve scientific rigour.

10. Choice of methods and technical soundness
Good
The methods employed in the study are broadly appropriate and align with standard approaches in the field. However, the rationale for material selection and their relevance to the intended application could have been more thoroughly justified, particularly in terms of mechanical properties, surface characteristics, and biocompatibility. Similarly, the chosen tribological parameters, such as load, speed, contact geometry, and lubrication regime, would benefit from clearer alignment with physiological or clinically relevant conditions. In this field, testing is typically comparative or benchmarking in nature, and it is unclear whether such a framework was adopted. Figure 17 refers to in vivo degradation of hyaluronic acid (HA), but the methodology and analytical techniques used to assess this are insufficiently described in the thesis (but detailed in the papers). Details are also lacking regarding how contact conditions (e.g. migratory vs occluded contact) were defined, and why specific lubricants (e.g. low-viscosity oils vs PBS) were selected. These decisions require further explanation to support reproducibility and relevance.

11. Quality, originality and significance of the results
Very good
The application of tribology to this specific context is novel and largely unexplored, making this thesis a valuable step toward addressing a clear knowledge gap. The work presents a thoughtful integration of tribological principles into a field where such analysis has been limited, and as such, has the potential to significantly advance understanding. The impact is multifaceted, with promising implications for the development of new preclinical test standards, improved product performance, and more predictive in vitro models. However, a clearer articulation of how the experimental outcomes map onto clinical indications or thresholds required for regulatory approval and product development would strengthen the translational relevance. Greater clarity on these links would help situate the findings within a clinical or industrial context, highlighting their applicability and informing future design criteria.

12. Quality of attached papers
Very good

Justification for evaluation: Papers are of excellent with a good use of figures and schematics throughout. All are in top tier journals for the field. It is great to see the engineering work been supplemented with biology/animal studies. It would have been nice to see some analysis of tissues so as to directly link tribological observations with biological outcomes. This would also help to serve as a validation measure for the surrogate materials.

13. Overall assessment, strengths and weaknesses (based upon the above evaluation categories 8–12)

Very good

Justification for evaluation: The thesis addresses a novel application of tribology, contributing to an underexplored area with potential impact on test standards and product development. Strengths include a clear motivation, relevant clinical drivers, and alignment with industrial needs. However, weaknesses lie in limited detail on clinical indications, unclear mapping of outcomes to product thresholds, and insufficient justification for material and test parameter choices. The discussion of HA is overly focused on viscosity, lacking depth in structural and mechanistic insights. Broader tribological literature could be better integrated, and methodological aspects such as lubricant choice and contact condition definitions require clearer rationale.

14. Questions and comments

How did you determine the relevance and clinical applicability of your tribological test parameters, and how do they compare to physiological or regulatory benchmarks?

Can you elaborate on the role of hyaluronic acid beyond viscosity, specifically in terms of structure, hydration, and boundary lubrication, and how your findings relate to its degradation in vivo?

Your work highlights gaps in current tribological standardshow might your findings inform the development of new or modified testing protocols for medical devices?

15. Conclusion

PhD thesis is an independent scientific work that presents a novel solution to a significant problem in the research area and demonstrates the candidate's ability to conduct independent research.

YES

16. Date and signature

01/06/2025

Please note

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doc. Ing. David Nečas, Ph.D./ **David.Necas@vut.cz**

6. Reviewer
Associated Professor Ana Paula Serro / **anapaula.serro@tecnico.ulisboa.pt**
Instituto Superior Técnico

7. Overview of the scope of PhD thesis[1]
Excellent
Justification for evaluation: This thesis addresses a complex biomedical challenge: developing an innovative hyaluronic acid (HA)-based viscosupplement to treat non-specific low back pain (NSLBP). Recognizing that pathological changes in the thoracolumbar fascia are among the primary causes of NSLBP, the initial objective was to identify a tribological model that simulates the frictional behaviour of fascia tissues under in vivo-like conditions. Subsequently, the study aimed to determine the key factors influencing HA lubrication and assess their impact on fascia lubrication mechanisms using predefined models. Additionally, a pharmacokinetic study was conducted to predict the in vivo stability of HA formulations and select the most suitable for minimizing friction between fascia layers. The findings indicate that HA molecular weight and concentration are critical in optimizing lubrication, and that HA derivation can slow the compound degradation in the organism. The research is well-structured, progressing logically with increasing complexity. It is pioneering and ambitious, integrating knowledge from biomechanics, materials science, pharmacokinetics, and clinical practice. More, it successfully bridges fundamental and applied research, providing a foundation for future translational work.

[1] Overview of the scope of PhD thesis is a short description of objectives of PhD thesis's research and summary of main findings and scientific achievements.

8. Significance of the topic and clarity of problem statement
Very good
Justification for evaluation: The topic is timely and has significant socioeconomic implications. Data indicate that non-specific low back pain (NSLBP) is a leading cause of disability worldwide, often resulting in patient absenteeism from work and reduced participation in social activities. Its increasing prevalence has raised concerns and highlighted the need for more effective solutions. The proposed tribological interpretation offers a novel and underexplored avenue for treatment. The candidate clearly articulates the clinical gap, identifying the limitations of current therapies and the absence of tribological models for fascial tissues. While the problem statement is generally clear, it could have been more concisely framed in the introductory section. Nonetheless, the justification for developing new HA-based solutions, particularly those targeting fascial adhesion and stiffness, is robust and well-substantiated by epidemiological and anatomical data.

9. Knowledge of existing literature
Excellent
Justification for evaluation: The literature review is comprehensive and well-organized, covering not only the histology and biomechanics of fascia but also the physicochemical and rheological properties of hyaluronic acid (HA). Relevant research in biotribology, compliant contact mechanics, and viscosupplementation is thoroughly cited, with key findings clearly presented. Importantly, the review identifies a significant knowledge gap: the absence of validated tribological models for fascia and a lack of studies focused on developing injectable HA-based products to treat NSLBP. This positions the thesis within a critical context, highlighting the need for innovative approaches in this area. Additionally, the review provides an adequate discussion of previous work on HA modifications and tissue-specific degradation profiles, reflecting a solid command and critical engagement with both biomedical and engineering domains.

10. Choice of methods and technical soundness
Very good
Justification for evaluation: The methods employed are technically sound and well-suited to the research objectives. The use of the Bruker UMT TriboLab, alongside rheological and electron microscopy analyses, ensured the acquisition of essential data for optimizing the HA solutions. The development of multiple model systems (ranging from PDMS and PU gels to real rabbit fascia) demonstrates a thoughtful attempt to create accessible yet representative platforms for addressing the problem in laboratory studies. A comprehensive evaluation of various parameters that may influence the lubricating performance of HA solutions (e.g., sliding velocity, material stiffness, pin radius, test duration, material preload, HA molecular weight, and concentration) was conducted, enabling a detailed understanding of frictional responses under different movement conditions. The inclusion of multiple HA formulations, including chemically modified derivatives, adds scientific depth to the study. The discussion makes appropriate references to boundary and mixed lubrication regimes. However, the statistical analysis lacks clarity regarding whether data normality and variance homogeneity were assessed, and if so, how. Another area for improvement would be a more explicit justification for the selected HA concentrations and normal preload values.

11. Quality, originality and significance of the results
Excellent

Justification for evaluation: The research presents original and significant findings in the development of hyaluronic acid (HA)-based viscosupplements for treating NSLBP. Through the creation of innovative tribological models, extensive testing, and comprehensive analysis, the study identifies optimal combinations of HA molecular weight and concentration that effectively reduce fascial friction. Notably, it challenges traditional assumptions from joint viscosupplementation by demonstrating that lower viscosity HA solutions can yield superior tribological performance in fascia. The tribological models developed are novel and have potential applications beyond fascia tribomechanical studies, advancing the field of biomedical engineering. Additionally, the integration of pharmacokinetic data enhances the clinical relevance of the findings, providing a foundation for selecting the most suitable HA formulations for therapeutic applications. Overall, these contributions not only deepen our understanding of HA's role in tissue lubrication but also pave the way for the development of more effective and personalized treatments for NSLBP.

12. Quality of attached papers

Very good

Justification for evaluation: The four publications stemming from this research work are of high quality, appearing in renowned scientific journals (three from Elsevier, one from MDPI) with significant impact factors. Specifically, the International Journal of Biological Macromolecules boasts an impact factor of 7.7 and is in the Q1 quartile for Biochemistry & Molecular Biology, Applied Chemistry and Polymer Science. The Journal of the Mechanical Behavior of Biomedical Materials has an impact factor of 3.3, ranking in the Q2 quartile for Biomedical Engineering and Q3 for Materials Science and Biomaterials. Lubricants holds an impact factor of 3.1 and is in the Q2 quartile for Mechanical Engineering. The journal Biotribology, while directly relevant to the research topic, is not indexed in major databases. The candidate is the first author on three of these publications, reflecting her significant contribution to the research. The sequence of papers demonstrates a logical progression from model development to applied testing and pharmacological considerations, effectively addressing the scientific questions posed in the thesis. The figures and tables are clear, and the arguments are well-supported, enhancing the overall quality and impact of the research.

13. Overall assessment, strengths and weaknesses (based upon the above evaluation categories 8–12)

Excellent

Justification for evaluation: This is an excellent PhD thesis that addresses an unmet clinical need: the development of an effective new alternative to treat NSLBP. The thesis combines a solid theoretical foundation with a robust experimental design and strong translational relevance. Key strengths include: (1) the development of novel tribological models specifically designed to simulate the mechanical behaviour of fascial tissues; (2) a multidisciplinary approach that integrates biomechanics, materials science, and pharmacology; and (3) the validation of HA derivatives as potential therapeutic agents for NSLBP. Importantly, the work was conducted in collaboration with Contipro a.s., an industrial leader in HA production, facilitating technology transfer and ensuring that the research is grounded in real-world applicability. This partnership enhances the potential for future clinical translation and commercial development. The work is coherent, well-documented, and original, offering a new therapeutic strategy that could improve health outcomes for a large patient population and have a significant socioeconomic impact. Minor weaknesses include some redundancy in the text and a few instances where parameter choices could have been more clearly justified. Nonetheless, these do not detract from the overall scientific merit or innovation of the thesis.

14. Questions and comments
What modifications could be incorporated into the tribological model to better represent the characteristics of pathological fascia? Given the short in vivo half-life of some HA solutions, do you envision combining HA with delivery matrices for sustained release? Could the models developed be adapted for use in other soft tissues where HA plays a role, such as tendons or pleura?

15. Conclusion
PhD thesis is an independent scientific work that presents a novel solution to a significant problem in the research area and demonstrates the candidate's ability to conduct independent research.
YES

16. Date and signature	
06/06/2025	

Please note

A. *Evaluate categories 7 to 13 using the following scale: unacceptable, acceptable, satisfactory, good, very good, excellent. The qualification of 'excellent' should only be given for a PhD Thesis in the top 3% of the research in your field of expertise.*
B. *E-mail the completed form to:* Klara.Javorcekova@vut.cz

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Principal supervisor's final report on the PhD study

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2. Name of PhD programme
Design and Process Engineering
3. Title of PhD thesis
The Influence of Hyaluronic Acid on Friction and Lubrication of Fascia

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Prof. Ing. Martin Vrbka, Ph.D. / martin.vrbka@vut.cz
5. Co-supervisor
Doc. Ing. David Nečas, Ph.D. / david.necas@vut.cz

6. Stays at other institutions (min. 7 days)
09/2021 Contipro a.s., Dolní Dobrouč, Czech Republic (Dr. Jarmila Husby). 05/2023 University of Groningen, Biomedical Engineering Dept. of University Medical Center Groningen, Groningen, Netherlands (Assoc. Prof. Prashant K. Sharma). 05-09/2024 Kyushu University, Faculty of Engineering Department of Mechanical Engineering, Fukuoka, Japan (Prof. Yoshinori Sawae, Assoc. Prof. Seido Yarimitsu).

7. Teaching activities
Machine Design – Machine Elements (5KS, winter semester). Machine Design – Mechanical Drives (6KT, summer semester). Machine Design and Machine Elements (CKP, winter semester).

8. List of main publications
Paper in SCOPUS indexed journal: **STREĎANSKÁ, A.**, D. NEČAS, M. VRBKA, I. KŘUPKA, M. HARTL, E. TOROPITSYN, J. HUSBY. Development of Tribological Model of Human Fascia: The Influence of Material Hardness and Motion Speed. *Biotribology*, 2022, vol. 30. ISSN 2352-5738. Doi: 10.1016/j.biotri.2022.100209. **Papers in journals with IF:** NEŠPOROVÁ, K., J. MATONOHOVÁ, J. HUSBY, E. TOROPITSYN, L. DIVOKÁ STUPECKÁ, A. HUSBY, T. SUCHÁNKOVÁ KLEPLOVÁ, **A. STREĎANSKÁ**, M. ŠIMEK, D. NEČAS, M. VRBKA, R. SCHLEIP, V. VELEBNÝ. Injecting hyaluronan in the thoracolumbar fascia: A model study. *International Journal of Biological Macromolecules*, Vol. 253, Part 3, 2023. ISSN 0141-8130. Doi: 10.1016/j.ijbiomac.2023.126879.

STREĎANSKÁ, A., D. NEČAS, M. VRBKA, J. SUCHÁNEK, J. MATONOHOVÁ, E. TOROPITSYN, M. HARTL, I. KŘUPKA, K. NEŠPOROVÁ. Understanding frictional behavior in fascia tissues through tribological modeling and material substitution, *Journal of the Mechanical Behavior of Biomedical Materials*, Volume 155, 2024, 106566, ISSN 1751-6161. Doi: 10.1016/j.jmbbm.2024.106566.

STREĎANSKÁ, A., M. ŠIMEK, J. MATONOHOVÁ, D. NEČAS, M. VRBKA, J. SUCHÁNEK, V. PAVLIŇÁKOVÁ, L. VOJTOVÁ, M. HARTL, I. KŘUPKA, K. NEŠPOROVÁ. Optimizing Hyaluronan-Based Lubricants for Treating Thoracolumbar Fascia Pathologies: Insights from Tribological and Pharmacokinetic Studies, *Lubricants*, 2025, 13, 184. Doi: 10.3390/lubricants13040184.

9. Assessment of the supervision process

Very good

The supervision process followed the pre-set rules for PhD study. The process was based on one-month main meetings and on-demand discussions with the supervisor, co-supervisor and colleagues from the Biotribology Research Group (BioTribo lab). Cooperation was also carried out with the scientific team of the application partner (Contipro company), as the dissertation was solved within the joint project of the Technology Agency of the Czech Republic (TACR). The candidate was always well prepared to discuss the issues of the dissertation including a reflection of critical comments. The final PhD thesis was prepared in time and very good quality. The PhD thesis resulted from four research papers, of which the candidate is the main author of three. The dissertation defence is slightly delayed due to the acceptance of the last publication. The teaching activities of the candidate were focused especially on tutorials of courses of Machine Design – Machine Elements, Machine Design – Mechanical Drives and Machine Design and Machine Elements. The candidate attended three international conferences where she presented partial results of her research: 5th International Conference on BioTribology 2021 (online - live and on-demand, 1st prize in Best poster Award), Nordic Tribology Symposium 2022 (Ålesund, Norway) and 9th International Tribology Conference 2023 (Fukuoka, Japan). The candidate has completed three internships as part of her PhD studies (see next paragraph).

10. Assessment of the candidate's ability to work independently

Good

The candidate worked independently, based on the discussion with me, co-supervisor and my colleagues from the BioTribo lab and other experts from the field of tribology, chemistry and biochemistry. Sometimes, the PhD candidate lacked self-motivation and independent initiative. I would like to highlight the cooperation with the Contipro company, where the candidate completed a month-long internship and carried out rheological measurements of individual HA solutions and measurements of mechanical properties of rabbit fascia. The second one-month internship of the candidate (Groningen) was focused on the preparation of fascia samples and their tribological tests with different HA solutions. The third and longest (five-month) internship (Kyushu) continued to develop the PhD candidate's knowledge and understanding of compliant contacts. The internship involved a range of experiments ranging from rheological tests of synovial fluid through tribological measurements of unique pHEMA and PVA hydrogels to permeability tests of the previously mentioned materials. In her dissertation, the candidate independently designed a methodology of experiments based on the state of the art, performed the individual experiments, and, according to the results analyses, she formulated conclusions. All publications, where she is listed as the main author, she prepared herself. The candidate also supervised one bachelor thesis in the field of biotribology.

11. Assessment of the contribution that the research makes to knowledge in the field
Very good
The PhD thesis is composed of four papers. One paper was published in the journal in Scopus database ("Biotribology") and the other three were published in the journals with impact factor ("International Journal of Biological Macromolecules", "Journal of the Mechanical Behavior of Biomedical Materials" and "Lubricants"). The main scientific output of this thesis is to understand the tribological behaviour of the human thoracolumbar fascia and to select an optimized HA-based viscosupplement injected into the fascia layers for the treatment of lower back pain. For this purpose, six unique tribological models of the thoracolumbar fascia were developed to simulate the frictional behaviour of fascial tissues under in vivo-like conditions. The main findings demonstrated that sliding velocity, material stiffness, pin radius, preload, and HA molecular weight and concentration are the critical factors influencing the frictional behaviour of the thoracolumbar fascia. Lower molecular weight HA solutions, particularly those with reduced viscosity, were found to significantly reduce friction by facilitating smoother movement between tissue surfaces. The type of HA derivation had no effect on fascia lubrication, i.e. molecular weight and HA concentration remain the dominant factors. Based on extensive tribological analyses, clear recommendations were established for the Contipro manufacturer. A product called Fascigel was developed and is currently in clinical trials. Thus, Fascigel is now on a promising path to regulatory approval and has the potential to relieve pain and improve the quality of life for people affected by lower back pain. The results of the PhD thesis have a very strong socio-economic impact. Certain weaknesses of the PhD thesis are the lack of a deeper analysis of the results and what it means for up-to-date fascia lubrication (what lubrication regimes are present) and what it means for fascia wear (only friction was analysed). In the thesis, I also miss the better variability of experiments with real rabbit fascia.

12. Other comments
The candidate has been involved in various activities of the institute during her PhD studies. Especially in PR activities, where she presented study programs (e.g. open days, Gaudeamus) or maintained social networks (Facebook and Instagram).

13. Conclusion
PhD thesis is an independent scientific work that presents a novel solution to a significant problem in the research area and demonstrates the candidate's ability to conduct independent research.
YES

16. Date and signature	
22/05/2025	

Please note

A. *Evaluate categories 9 to 11 using the following scale: unacceptable, acceptable, satisfactory, good, very good, excellent.*
B. *In each category 9 to 11 explain reasons for evaluation using between 100–200 words.*
C. *E-mail the completed form to:* Klara.Javorcekova@vut.cz