

## Review of Doctoral Thesis

<b>1. PhD candidate</b>
Ing. David Rebenda / david.rebenda@vut.cz
<b>2. Name of PhD programme</b>
Design and Process Engineering (Mechanical Engineering Design)
<b>3. Title of PhD thesis</b>
Effect of Viscosupplementation on Friction of Articular Cartilage

  

<b>4. Principal supervisor</b>
doc. Ing. Martin Vrbka, Ph.D. / martin.vrbka@vut.cz
<b>5. Co-supervisor</b>
Ing. David Nečas, Ph.D. / david.necas@vut.cz

  

<b>6. Reviewer</b>
Prof. Yoshinori Sawae / sawa@mech.kyushu-u.ac.jp
Department of Mechanical Engineering, Faculty of Engineering, Kyushu University

  

<b>7. Overview of the scope of PhD thesis<sup>1</sup></b>
<b>Very good</b>
Justification for evaluation: 100 – 200 words. Motivation and purpose of the dissertation thesis are clearly defined based on practical needs in the orthopedic field and research hypotheses are established based on the intensive review of relevant literatures. Experimental plans are carefully organized to verify research hypotheses by referring several previous studies. They are mostly reasonable to obtain necessary experimental data about rheological characteristics of HA solutions and viscosupplements in addition to their impacts on the frictional behavior of articular cartilage. Significant amounts of experimental results have been accumulated to deliver some valuable insights related to the research target of this thesis. The above-mentioned information is well summarized in Abstract and Conclusions.

  

<b>8. Significance of the topic and clarity of problem statement</b>
<b>Excellent</b>
Justification for evaluation: 100 – 200 words. This study aims to characterize rheological properties of HA solutions and commercial viscosupplements (VSs) and to evaluate their effects on frictional behavior of articular cartilage. It is perfectly matched with a strong

<sup>1</sup> 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.

demand for scientific researches in the aged modern society. HA-based VSs have been used preferably in a palliative treatment for the early stage of osteoarthritis and their demand is now continuously increasing worldwide with a progress of aging in the society. However, many uncertainties are still remained in the background mechanisms of physiological effects caused by VSs. Research outcomes from this study are expected to contribute to better understanding of therapeutic effects of viscosupplementation and improvement of its effectiveness. In addition, research hypotheses are appropriately formulated based on careful analyses of previous studies. They are mostly reasonable and consistent with the research motivation.

#### 9. Knowledge of existing literature

Very good

Justification for evaluation: 100 – 200 words. A wide range of literatures related to the synovial joint lubrication has been reviewed and certain amount of relevant knowledge has been accumulated. Especially, an extensive correction of rheological data of healthy and pathological synovial fluids is impressive. However, some important references for the boundary lubrication mechanism by synovial fluid constituents are missing from the literature review in Chapter 2 and the literature list in Pages 114 to 118, for example Hills and Buttler 1984, Higaki et al. 1998 (even though they appeared in reference list of attached manuscripts). Research on the boundary lubrication effect of HA and lubricin has a long history and following classic literatures are worth including in the literature review to deepen the knowledge about them. 1) A.G. Ogston, J.E. Stanier, J Physiol, 119, 244-252 (1953). 2) E.L. Radin, D.A. Swann, Nature, 228, 377-378 (1970). 3) D.A. Swann, et al., J Biol Chem, 256, 5921-5925 (1981). 4) D.A. Swann, et al., Arthritis Rheum, 24, 22-30 (1981). 5) B.L. Schumacher, et al., Arch Biochem Biophys, 311, 144-152 (1994). 6) S.G. Rees, et al., Matrix boil, 21, 593-602 (2002). In addition, certain literatures about hydrated hydrogel friction would be useful to understand the frictional behavior of PVA hydrogel.

#### 10. Choice of methods and technical soundness

Good

Justification for evaluation: 100 – 200 words. In this study, rheological properties of HA solutions, VSs and model synovial fluid supplemented with VS were explored by using two types of rotational rheometer. The most suitable combination of rheometer and measurement set up was carefully selected for each measurement; HR-3 with cone-plate set up was used for the steady shear test to measure shear rate-dependent viscosity and AR-G2 with parallel plates was chosen for the oscillatory test to obtain viscoelastic properties. The appropriate selection of experimental set up contributed the successful high-accuracy measurements of rheological properties. Friction of cartilage specimens were measured by utilizing a commercially available friction tester. The specimen setting and experimental conditions were decided by referring successful previous studies. However, more discussions about the relevance of whole experimental procedure and test conditions of friction measurement would be necessary, since repeatability of friction measurements in this study was certainly insufficient. Especially, some questions are remained about preparation and storage method of cartilage specimens.

<b>11. Quality, originality and significance of the results</b>
<b>Good</b>
Justification for evaluation: 100 – 200 words. Rheological data of VSs and model synovial fluids supplemented with VS obtained in this study have enough novelty and certain scientific values. They filled a remained vacancy in the knowledge about rheological characteristics of VSs and physical influences of viscosupplementation as the medical treatment. Also, prospective friction reduction effects of VSs in synovial joints could be estimated by using PVA hydrogel as a model of hydrated articular cartilage tissue. In addition, certain difference in the friction reduction effect could be confirmed among 5 VSs. It is also a valuable achievement of this study. Experimental results obtained in this study might provide some logical background for the selection of VSs to orthopedic surgeons.
<b>12. Quality of attached papers</b>
<b>Good</b>
Justification for evaluation: 100 – 200 words. The first paper contains results of comprehensive friction measurements for fresh cartilage specimens with 13 different lubricants and effects of synovial fluid compositions have been discussed. Overall structure of the manuscript is well organized. A large number of experimental results were systematically summarized and subsequently the importance of interaction of globulin, HA and PHs was emerged. The second paper intended to clarify the relationship between rheological properties and lubrication effects of HA solutions. However, sufficient repeatability of friction measurements could not be obtained and it made conclusions of this study relatively weak. In the third paper, rheological properties of 5 VSs were intensively studied and clearly demonstrated their differences in shear rate-dependent viscosity and viscoelastic properties. It also contains clear friction test results which contributed to elicit firm conclusions.
<b>13. Overall assessment, strengths and weaknesses (based upon the above evaluation categories 8–12)</b>
<b>Very good</b>
Justification for evaluation: 100 – 200 words. Overall, the manuscript has enough novelty and scientific impacts as a dissertation thesis of PhD study. The major strength of this thesis is a significant accumulation of experimental data. Especially, experimental data of the shear rate-dependent viscosity and viscoelastic properties of HA solutions and VSs obtained in this study can be utilized in future studies about the synovial joint lubrication and medical treatments for osteoarthritis. The manuscript still has a clear weakness in the methodology of the friction measurement for natural articular cartilage. It results in relatively large scatter of COF and subsequently makes conclusions about the influence of VSs on cartilage friction relatively weak.
<b>14. Questions and comments</b>
1. Do you think the specimen configuration with a stable cartilage pin on a moving glass plate is best for evaluating the frictional behavior of articular cartilage? Have you tried to use another specimen configuration or much wider range of test condition in sliding tests to

improve the repeatability of friction measurement? 2. Have you examined effects of the preparation procedure and the storage method of cartilage specimens on results of the friction test? 3. More detailed discussion is necessary to justify the relevance of PVA hydrogen as a cartilage tissue model based on comparison of physical properties between PVA hydrogel and articular cartilage tissue, since results obtained with PVA hydrogel were completely different from frictional behavior of actual cartilage tissue in the second attached paper.

#### 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

30/07/2021



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.Javorcekkova@vut.cz](mailto:Klara.Javorcekkova@vut.cz)