The Biochemical Process of Lubricant Film Formation inside Hip Joint Replacement

Risha Rufaqua

Supervisor: Doc. Ing. Martin Vrbka, Ph.D.

Brno University of Technology
Faculty of Mechanical Engineering
Institute of Machine and Industrial Design

Defense of the PhD thesis

Brno 29th June 2021

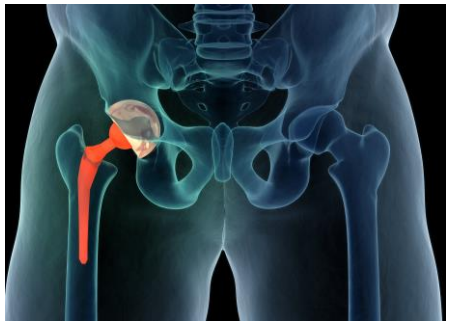
INSTITUTE OF **MACHINE**
AND **INDUSTRIAL DESIGN**

Content

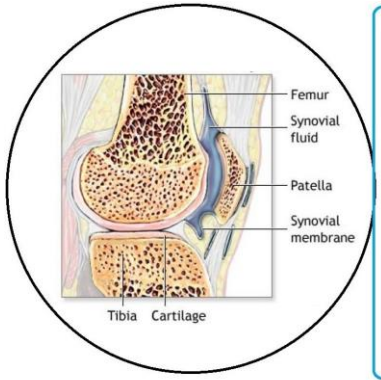
- Motivation
- Introduction
- Lubrication mechanism of joint replacement
- Analysis of literature review
- Aim of the thesis
- Scientific questions and hypothesis
- Materials and Methods
- Results
- Discussion
- Conclusions

Motivation

Synovial fluid film formation is a complex procedure



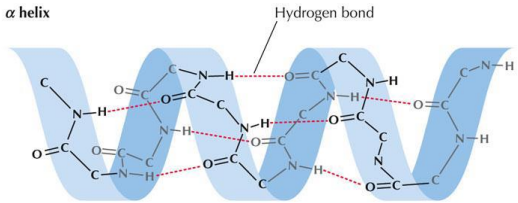
Chemical adsorption of the lubricant film on implant material



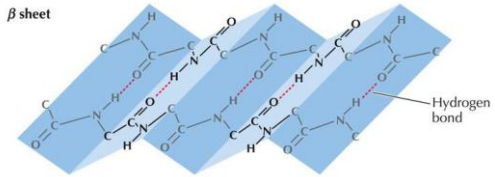
The chemical composition of synovial fluid film

Individual fluid components reacting with implant materials

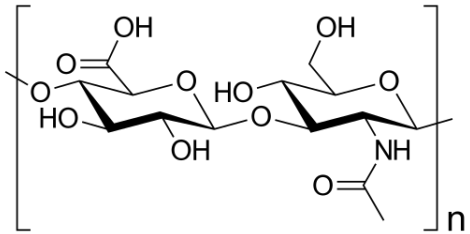
Albumin



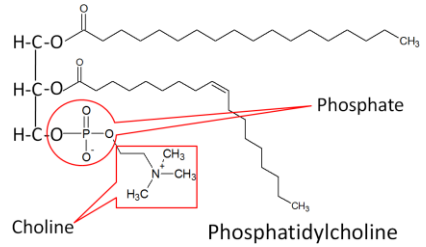
γ-Globulin



Hyaluronic Acid



Phospholipid



Introduction

50 years

CoCrMo Alloy Hip Implant

CoCrMo Chemical Composition

- Chromium, Cr 27–30%
- Molybdenum, Mo 5–7%
- Iron, Fe <0.75%
- Nickel, Ni <1%
- Carbon, C <0.35%
- Silicone, Si <1%
- Manganese, Mn <1%
- Tungsten, W <0.2%
- Sulfur, S <0.02%
- Nitrogen, N <0.25%
- Aluminium, Al <0.3%
- Titanium, Ti <0.1%
- Boron, B <0.01 %
- Phosphorus, P <0.02%
- Cobalt, Co *Balanced Amount*

(ISO 5832-4)

30 years

BIOLOX®forte Hip Implant

BIOLOX®forte Chemical Composition

- Alumina, Al_2O_3 **Ultra pure**
- Magnesium oxide, MgO *(Trace amount)*

(ISO 6474)

20 years

BIOLOX®delta Hip Implant

BIOLOX®delta Chemical Composition

- Alumina, Al_2O_3 75%
- Zirconia, ZrO_2 24%
- Strontium oxide, SrO
- Yttrium oxide, Y_2O_3
- Chromium oxide, Cr_2O_3

→ *(Trace amount)*

(ISO 6474-2)

Introduction

50 years

30 years

20 years

CoCrMo Alloy Hip Implant

BIOLOX®forte Hip Implant

BIOLOX®delta Hip Implant

Lubrication mechanisms

Tribological performance

Service-life of the implant

- Ion release
- Corrosion & Wear debris
- Micro-cracking
- Phase transformation

Lubrication mechanism of joint replacement - State of the Art

Film formation and thickness analysis → Coefficient of friction concerning joint implants → Spectroscopic analysis of synovial joint → Material analysis of joint implants

2014

Vrbka et al. In situ measurements of thin films in bovine serum lubricated contacts using optical interferometry

- Film thickness measurement as a function of time
- Optical interferometry method usage based on phase shifting interferometry

2015

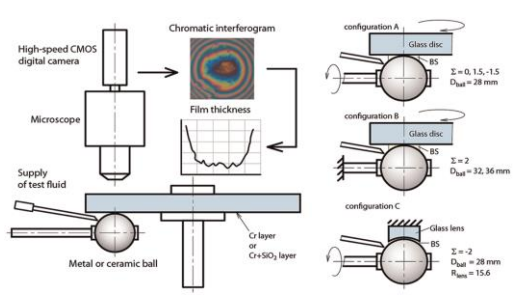
Parkes et al. Synovial fluid lubrication: the effect of protein interactions on adsorbed and lubricating films

- Film formation impact with different pH
- Film thickness with different compositions of synovial fluids

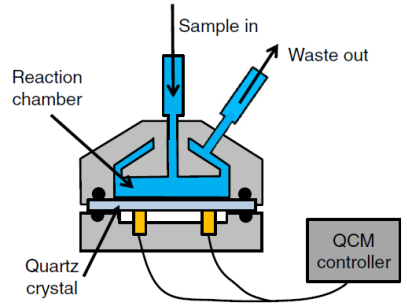
2018

Nečas et al. In situ observation of lubricant film formation in THR considering real conformity

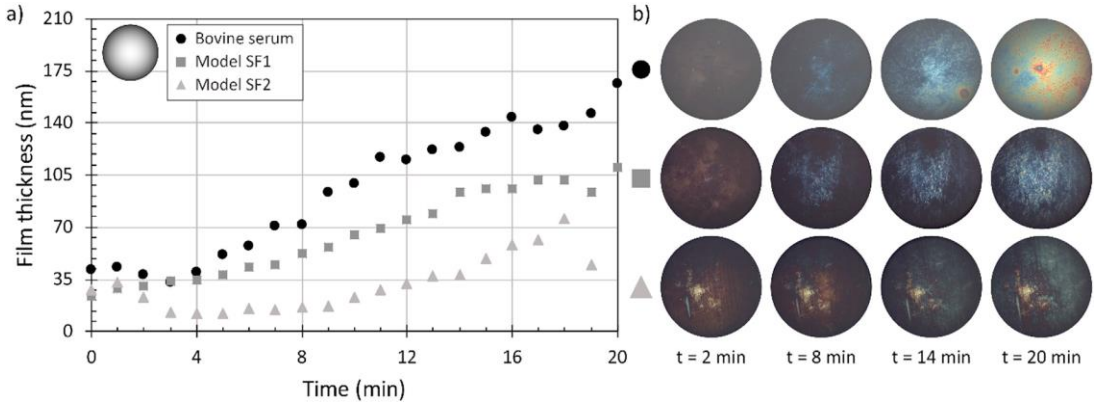
- In situ measurements with pendulum hip joint simulator
- Effects of material, load and compositions of synovial fluids



Optical test rig experimental approach



Quartz Crystal Microbalance with flow cell



Lubrication mechanism of joint replacement - State of the Art

Film formation and thickness analysis → **Coefficient of friction concerning joint implants** → Spectroscopic analysis of synovial joint → Material analysis of joint implants

2012

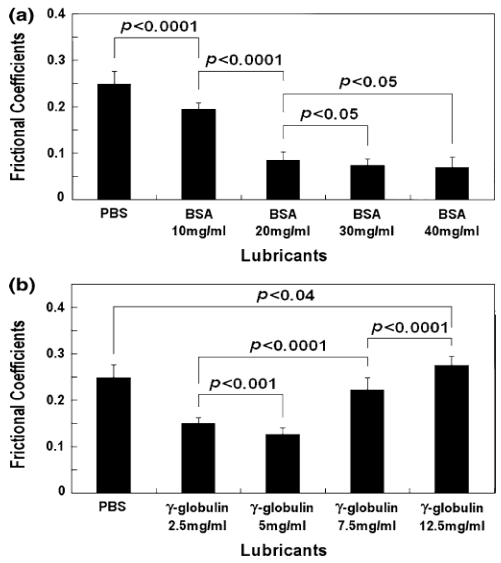
Duong et al. Effect of protein concentrations of bovine serum albumin and γ-globulin on the frictional response of a cobalt-chromium femoral head

- Concentration levels dependency of BSA and γ-globulin on the lubricating ability
- Friction coefficients with boundary lubricants calculation for CoCr femoral head .

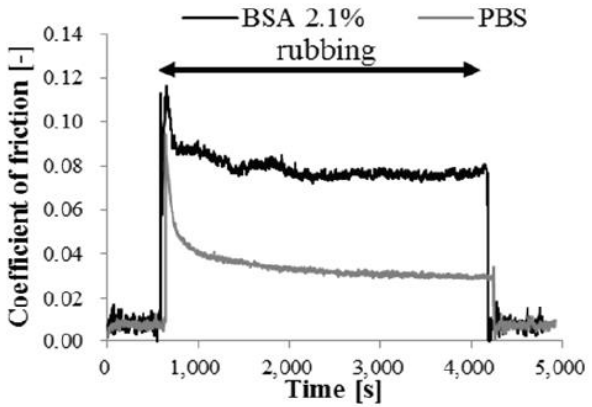
2015

Kazuhiro et al. Behavior of adsorbed albumin film on CoCrMo alloy under in-situ observation

- Adsorption and frictional property in rubbing condition.
- Reciprocating pin-on-disk tribo-meter with electrochemical method



AFM frictional coefficients of the CoCr femoral head measured



The effect of friction transition under OCP condition

Lubrication mechanism of joint replacement - State of the Art

Film formation and thickness analysis → Coefficient of friction concerning joint implants → **Spectroscopic analysis of synovial joint** → Material analysis of joint implants

2014

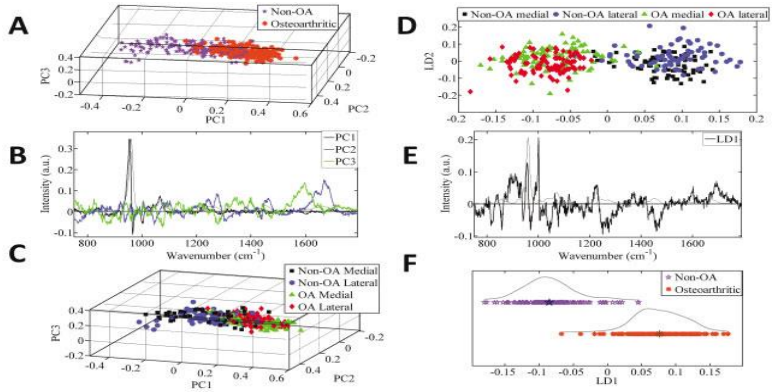
Kerns et al. Evidence from Raman spectroscopy of a putative link between inherent bone matrix chemistry and degenerative joint disease

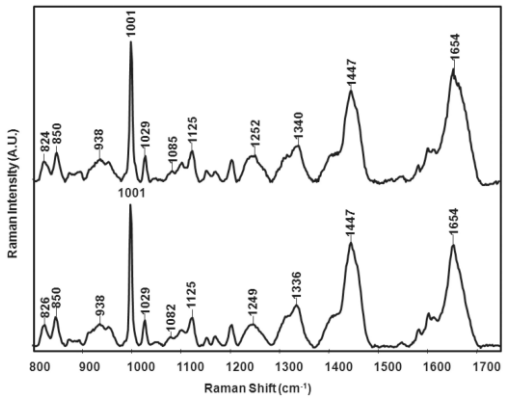
- Molecular structures of tibial plateaus of healthy joints and joints with total replacements due to osteoarthritis
- Comparison of medial and adjacent compartments of subchondral bones with different load baring sites

2009

Esmonde-White et al. Raman spectroscopy of synovial fluid as a tool for diagnosing osteoarthritis

- Biochemical compositions difference of healthy joint synovial fluids and synovial fluids of OA patients
- Drop deposition/Raman Spectroscopy protocol utilization





Raman Spectra of human SF dried drops

Lubrication mechanism of joint replacement - State of the Art

Film formation and thickness analysis → Coefficient of friction concerning joint implants → Spectroscopic analysis of synovial joint → **Material analysis of joint implants**

2012

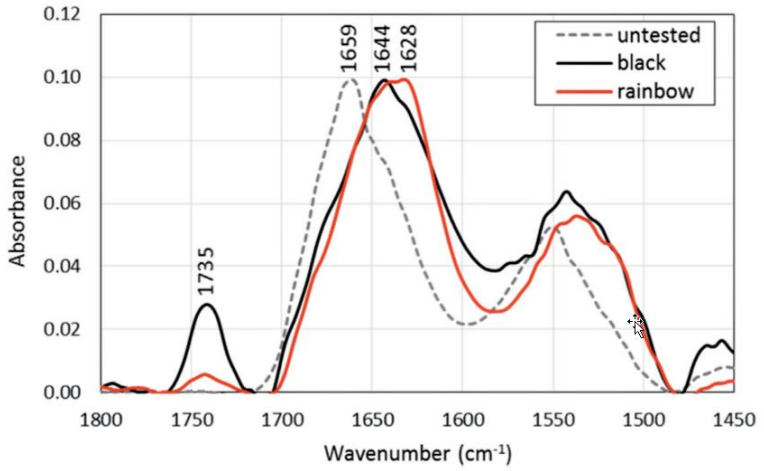
Taddei et al. Raman and fluorescence investigations on retrieved Biolox®delta femoral heads

- The molecular level characterization of BIOLOX®delta retrievals
- Material properties alteration of BIOLOX®delta femoral heads observation.

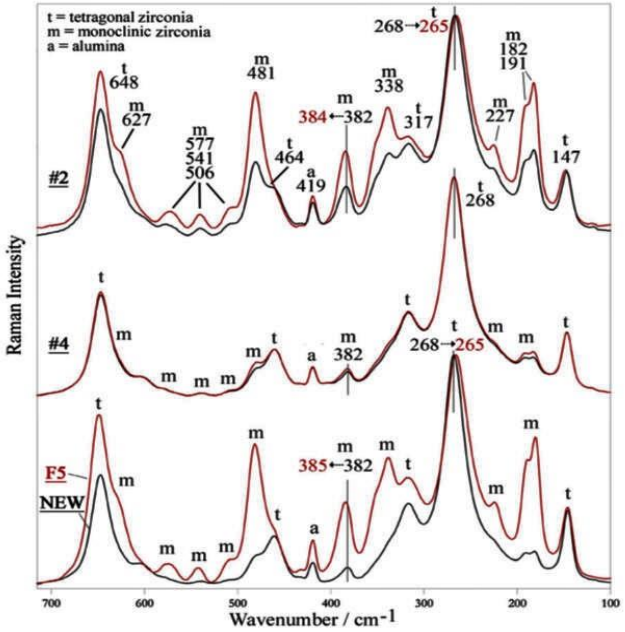
2019

Stevenson et al. The role of denatured synovial fluid proteins in the lubrication of artificial joints

- 25 wt% bovine calf serum and human synovial fluid
- Micro InfraRed Reflection Absorption Spectroscopy



Micro-IRRAS analysis of surface films of human SF

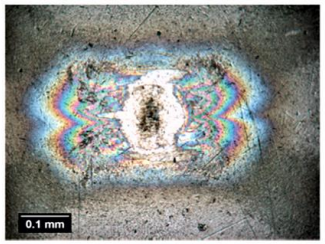


Average micro-Raman spectra of BIOLOX®delta femoral heads

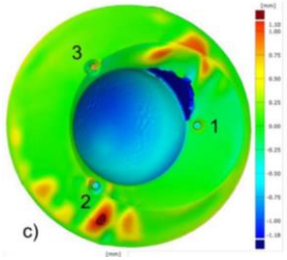
Analysis of Literature Review

Film formation on implant material:

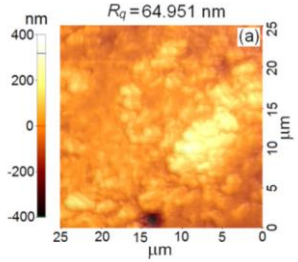
- ✓ Adsorption and desorption of protein
- ✓ Film thickness in different pH and concentration
- ✓ Friction, wear and shear force
- ✓ Boundary lubrication and rheology
- Frictional coefficient and chemical change
- Combination of bio-tribology and tribo-chemistry



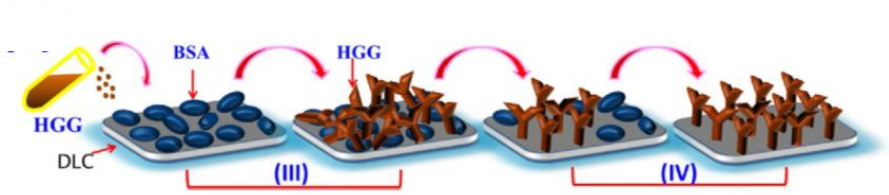
Wear scar deposits
(Stevenson et al.)



Mapped Surface deviation
(Choudhury et al.)



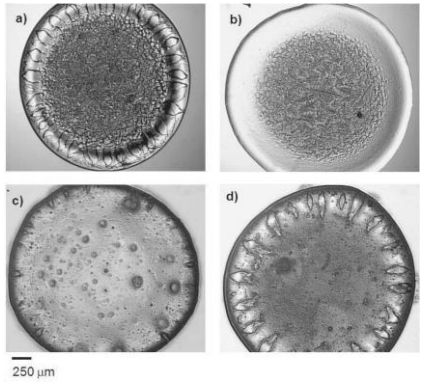
AFM image of CoCr head
(Park et al.)



Sequential adsorption of BSA and HGG
(Wu et al.)

Biochemical analysis of synovial fluid:

- ✓ Composition and concentration of synovial fluid components of osteoarthritis patients
- ✓ Spectroscopic analysis of the healthy and osteoarthritis specimens of synovial fluids
- ✓ Molecular structures healthy joints and joints with total replacements with osteoarthritis



Microscope images of human SF dried drops
(Esmonde-White et al.)

- Biochemical composition of film formation on implant materials
- Chemical structural change of synovial fluid components after joint replacements

Aims of the Thesis

Main Aim:

The research aims to clarify the chemistry of film formation on hip implant material surfaces with synovial fluids components.

Partial Aims:

- Design of the methodology of Raman spectroscopic technique for the analysis of lubricant film formation inside hip joint replacement.
- Observation of the chemical structural changes of synovial fluid components in interaction with implant materials.
- Measurement of the friction coefficient for different hip implant materials lubricated by synovial fluid.

Scientific questions and hypothesis

Scientific questions:

From chemical perspective:

- Which components of synovial fluids are adsorbing chemically on hip implant material surfaces while lubricant film formation within artificial joint replacement?

- How is synovial fluid changing the chemical structure of its constituents due to artificial hip implant?

From tribological perspective:

- How frictional coefficients are differing with this chemical change in the hip joint replacement?

Hypothesis:

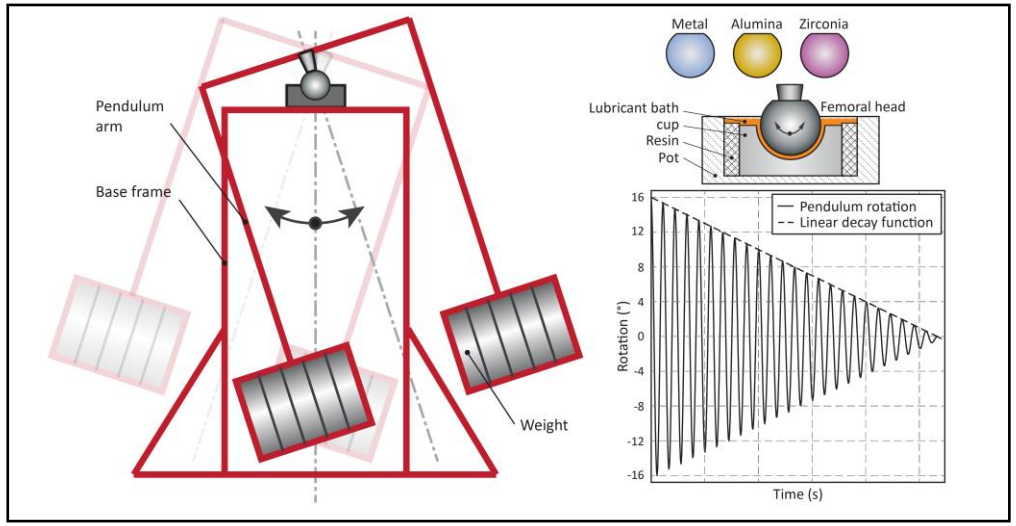
- On the surface of implant material, protein content is a significant factor for chemical interaction and involving chemisorbed film formation rather than HA and phospholipids.

- Metal hip implant materials are more chemically reactive with synovial fluid components to form tribo-film on the surface and could act as heterogeneous catalyst to form lubricant film within replaced joint. While ceramic implant materials are less chemically reactive to sustain chemisorption process with synovial fluid contents.

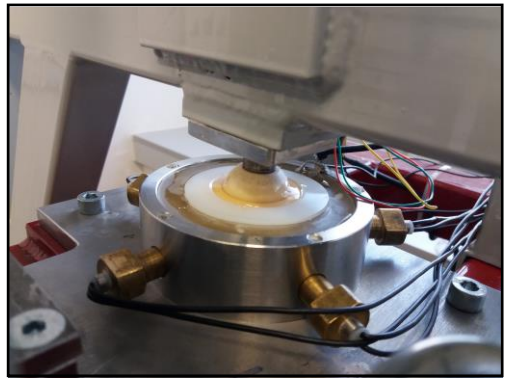
- With the elevation of chemical reaction occurring within a certain arrangement of implant materials and the lubricants, the coefficient of friction of the contact pairs is probably increased.

Materials and Methods

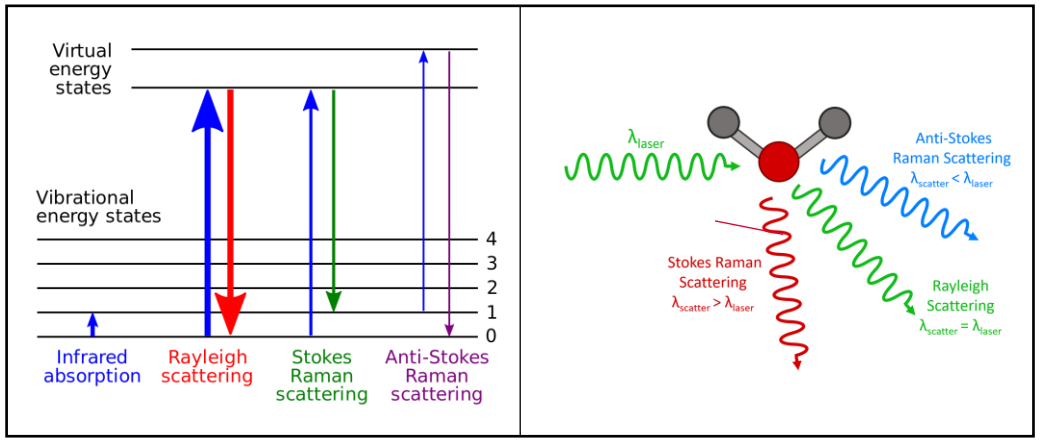
Tribological test condition:
- Time 5 minutes
- Load 532 N
- Temperature 37 ºC



Schematic diagram of Pendulum hip simulator



Raman analysis condition:
- Laser 532 nm Green
- Laser power 1 mW
- Exposure time 100 s



Raman Spectroscopic technique

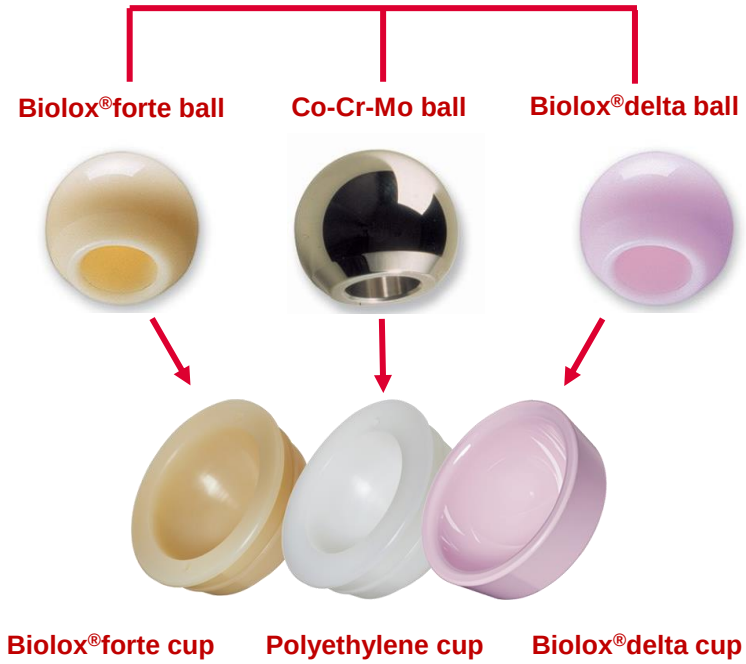
Materials and Methods

Materials for the experiment:

- **Lubricants:** 25% *BSA, Albumin, γ –globulin, hyaluronic acid and three types of Model Synovial fluids*
- **Ball on cup configuration**

Test Fluid	Albumin (mg/ml)	γ-globulin (mg/ml)	Hyaluronic Acid (mg/ml)	Phospholipid (mg/ml)
Bovine Serum Albumin	25%			
Albumin	28			
γ-globulin		11		
Hyaluronic Acid			2	
Healthy Joint (SF1)	20	3.6	2.5	0.15
After Total Joint Replacement (SF2)	26.3	8.2	0.87	0.35
Joint with Osteoarthritis (SF3)	24.9	6.1	1.49	0.34

Synovial fluid lubricants



Different types of hip implant balls and cups

Materials and Methods

Experimental Process:

Tribological test

The analysis of developing method of lubricant film formation in hip replacement, by using Pendulum hip simulator

Friction coefficient measurement

Measurement of coefficient of friction for three different contact pairs within all the synovial fluid lubricants

*Preserved for 24 hours in **4 °C***

Raman spectroscopic analysis

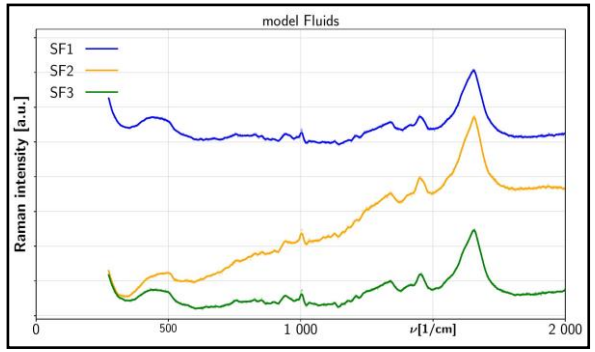
Raman spectroscopic measurement for the lubricants and the implant surface (After and Before the experiment process of The tribological performance of contact pair)

Data analysis

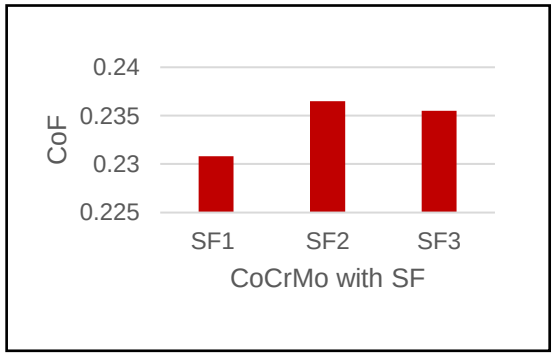
Analysis of Raman spectra to obtain chemical structure of film and chemical change in lubricants

+

Observation of correlation within Raman data and coefficient of friction data obtained



+



→ ?

Results – Raman spectroscopic data for CoCrMo ball

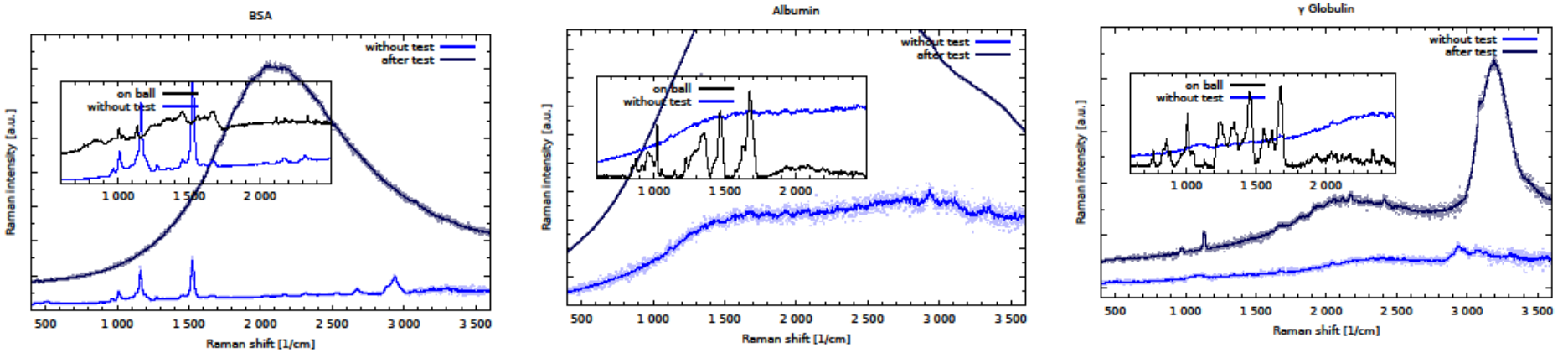
Coefficient of friction

Raman Analysis

CoCrMo

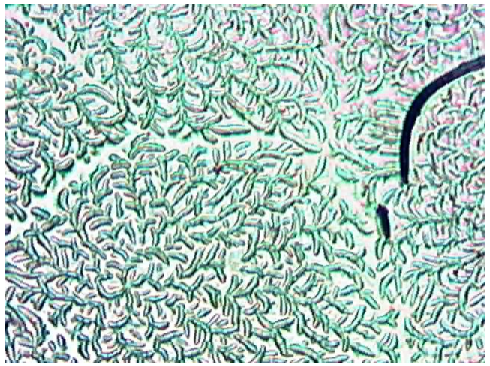
Biolox®forte

Biolox®delta

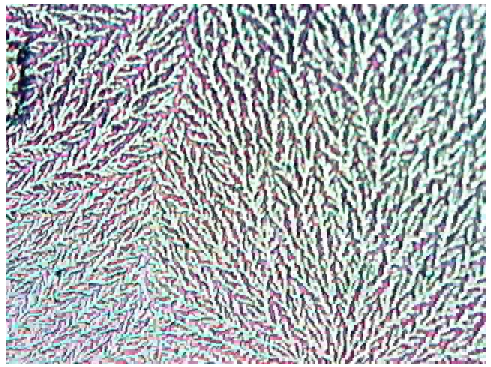


Raman Spectroscopic Data of film of Bovine serum, Albumin and γ –Globulin respectively on CoCrMo

Film formed by Bovine serum



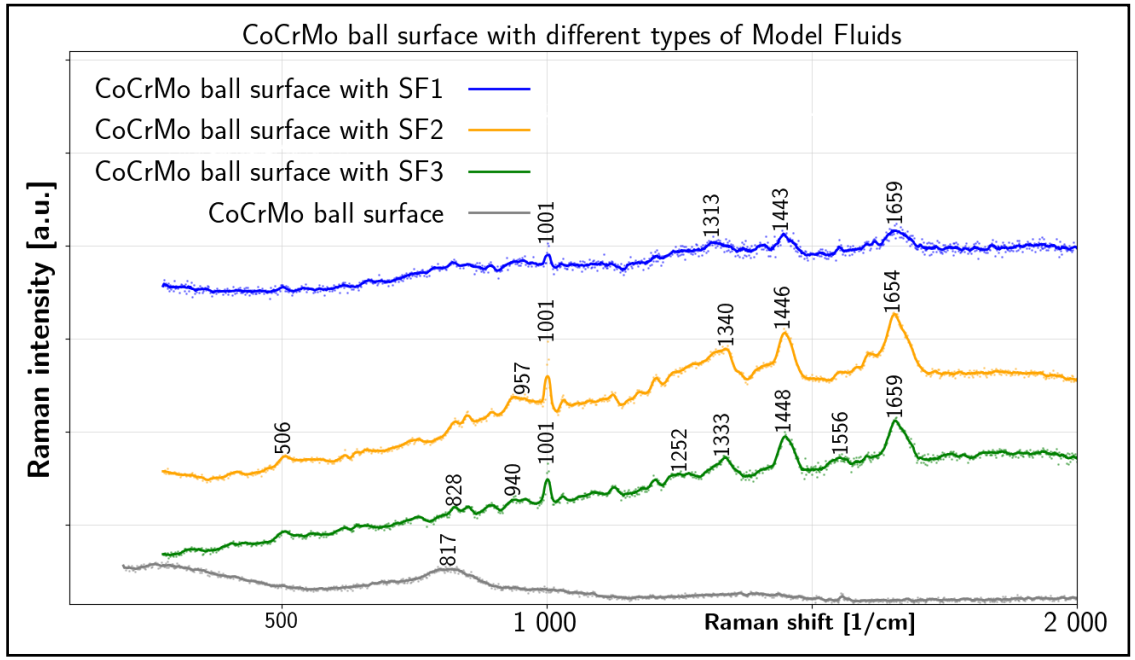
Film formed by Albumin



Film formed by γ –Globulin

Microscopic Images of Protein films on CoCrMo Ball

Results – Raman spectroscopic data for CoCrMo ball



Types of Model Synovial Fluids	
SF1	Healthy Joint
SF2	After Total Joint Replacement
SF3	Joint with Osteoarthritis

Raman Range (cm^{-1})	Chemical Structure	
1660-1645	C=O stretch (C-N, C-N-H)	α- helix Amide I
1473-1443	CH_3, CH_2 deformations	n-Alkanes
1300-1265	C-H, N-H deformation	α- helix Amide III
1411-1174	CH_2-CH_3 wagging	
1150-1010	C-C, C-OH, C-N stretch, C-O-C glycosidic linkage	Protein backbone.
1001	C-C in-phase symmetric motion	Ring breathing
900-800	C-C Skeletal Stretch	n-Alkanes
500-460	C-C Skeletal Stretch -$CH(CH_3)_2$,	Branched alkanes
817	CoCrMo Surface without lubricants	

Coefficient of friction

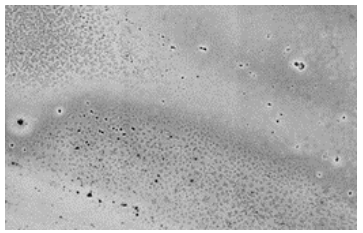
Raman Analysis

CoCrMo

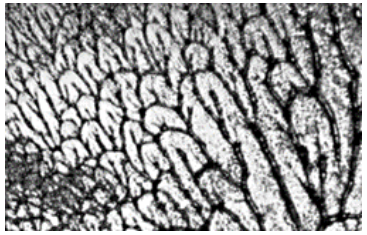
Biolox®forte

Biolox®delta

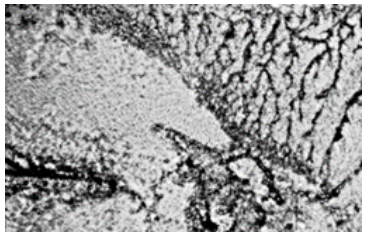
Raman data of model Synovial Fluid Films on CoCrMo Ball Surface



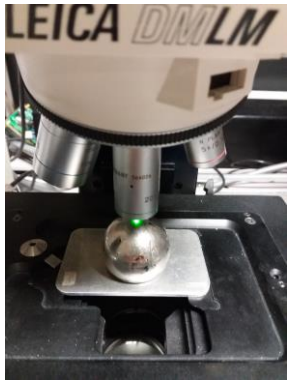
CoCrMo Ball SF1 on surface



CoCrMo Ball SF2 on surface

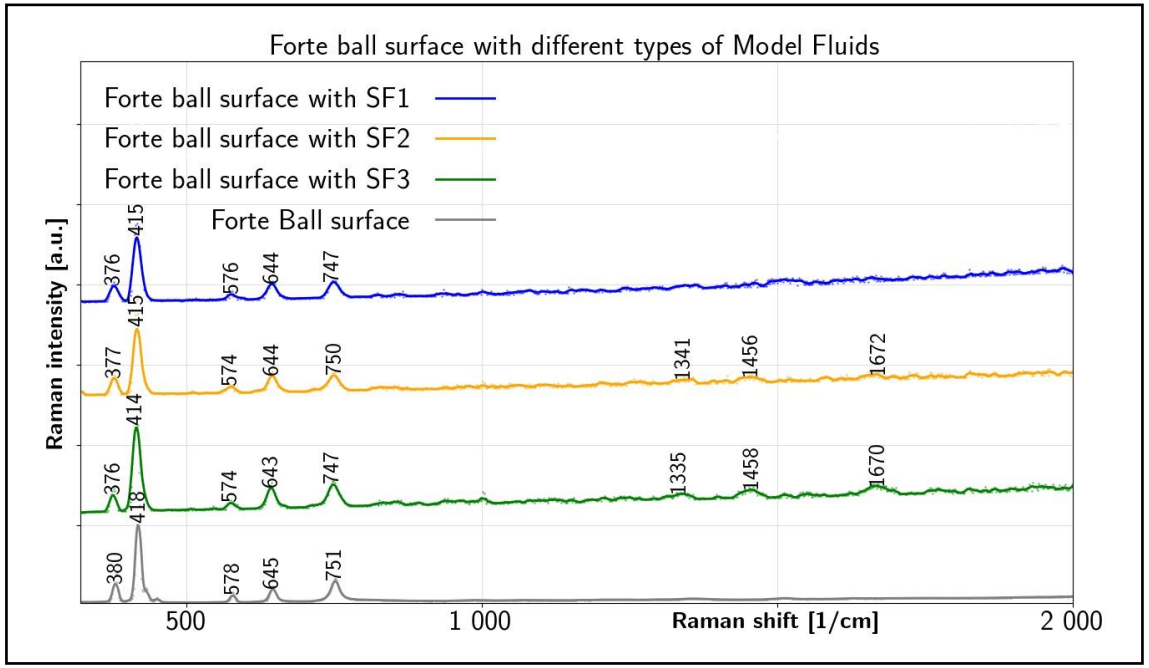


CoCrMo Ball SF3 on surface



Raman Spectroscopic measurements for CoCrMo implant surfaces with SF Lubricant

Results – Raman spectroscopic data for Biolox®forte ball



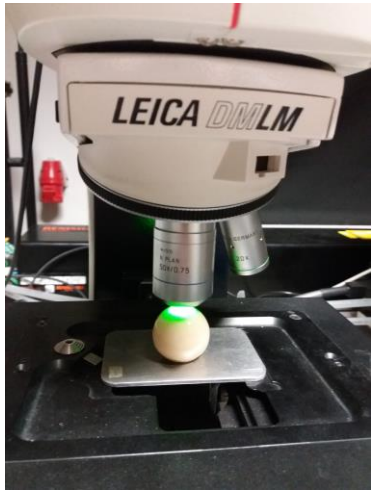
Raman data of model synovial fluid films on BIOLOX®forte ball surface

Types of Model Synovial Fluids	
SF1	Healthy Joint
SF2	After Total Joint Replacement
SF3	Joint with Osteoarthritis

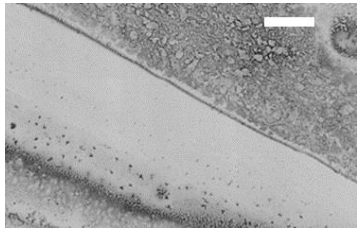
Raman Range (cm^{-1})	Chemical Structure	
1680-1665	C=O stretch (C-N, C-N-H)	β sheet Amide I
1473-1446	CH_3, CH_2 deformations	n-Alkanes
1411-1174	CH_2-CH_3 wagging	
414-421	Alumina	
Rest	Marker bands of implant material	

Coefficient of friction

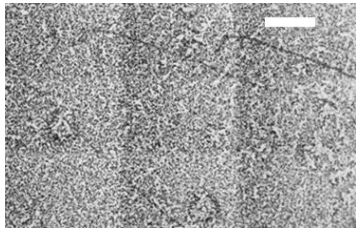
- Raman Analysis
- CoCrMo
- Biolox®forte
- Biolox®delta



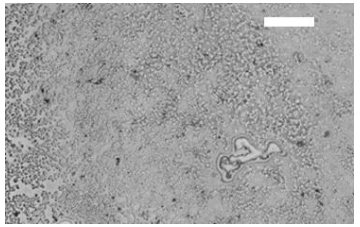
Raman Spectroscopic measurements for* BIOLOX®forte *implant surfaces with SF Lubricant



BIOLOX®forte Ball SF1 on surface



BIOLOX®forte Ball SF2 on surface



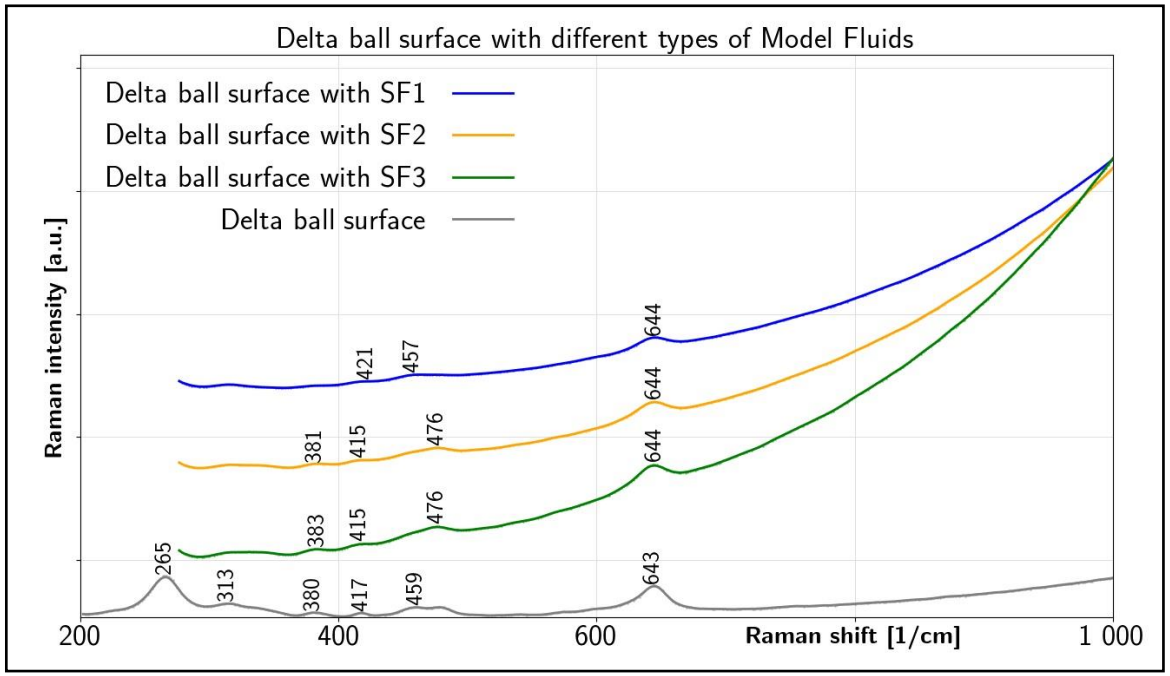
BIOLOX®forte Ball SF3 on surface

Results – Raman spectroscopic data for Biolox®delta ball

Coefficient of friction

Raman Analysis

- CoCrMo
- Biolox®forte
- Biolox®delta

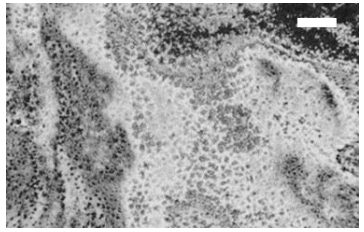


Raman data of model synovial fluid films on BIOLOX®delta ball surface

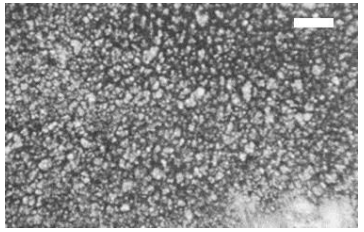
Types of Model Synovial Fluids	
SF1	Healthy Joint
SF2	After Total Joint Replacement
SF3	Joint with Osteoarthritis

Raman Range (cm^{-1})	Chemical Structure
414-421	Alumina
Rest	Marker bands of implant material

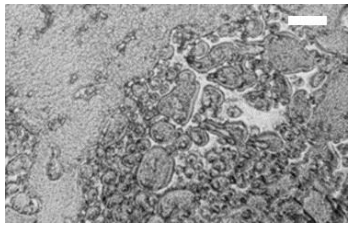
Raman Spectroscopic measurements for SF Lubricant



BIOLOX®delta Ball SF1 on surface

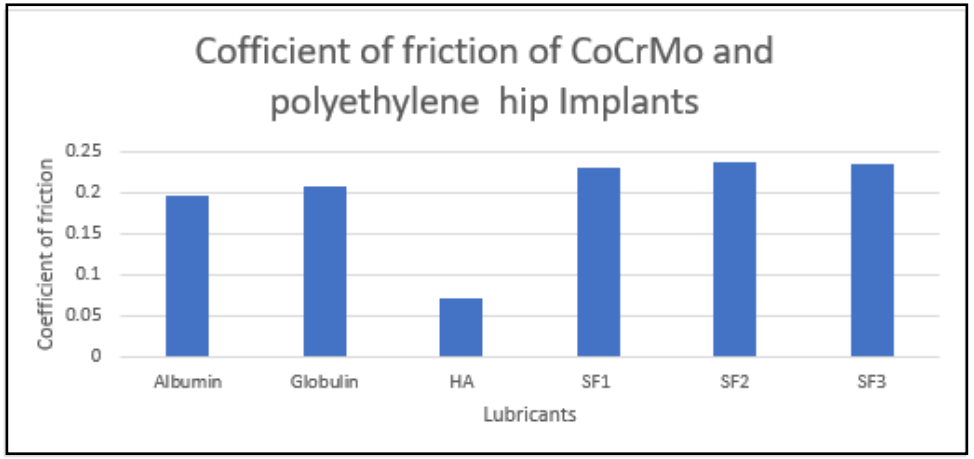


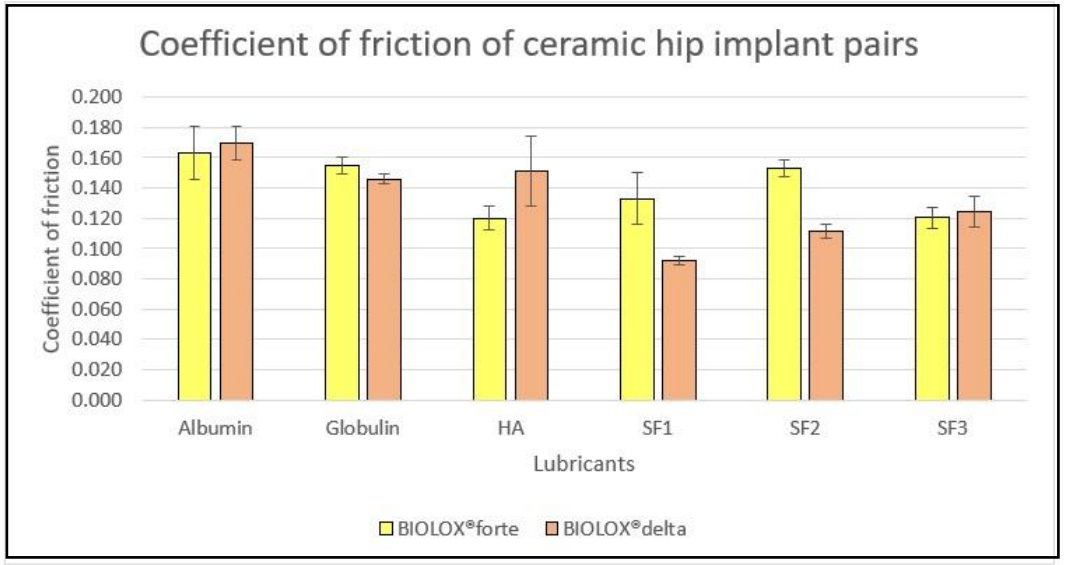
BIOLOX®delta Ball SF2 on surface



BIOLOX®delta Ball SF3 on surface

Results – Coefficient of friction of different hip implant pairs





Raman Analysis

Coefficient of friction

CoCrMo

Biolox®forte

Biolox®delta

CoCrMo and polyethylene pairs

- Lowest friction with HA **0.072**
- Higher for Model SF **0.2365-0.2308**

Types of Model Synovial Fluids	
SF1	Healthy Joint
SF2	After Total Joint Replacement
SF3	Joint with Osteoarthritis

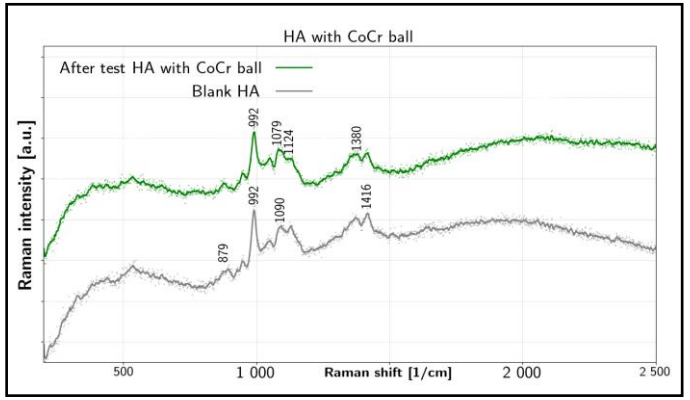
Ceramic contact pairs

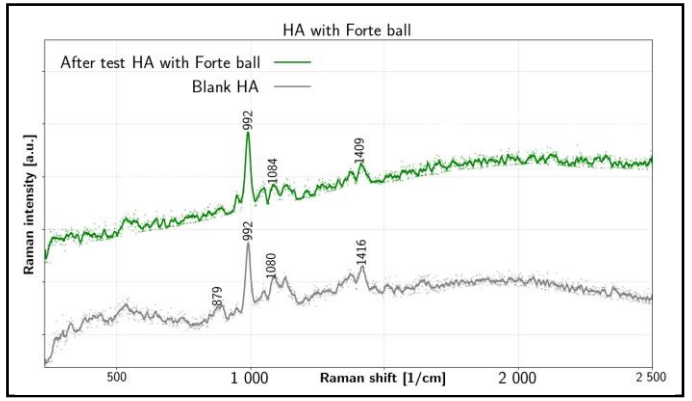
- Both proteins and SF3 show smaller differences for both ceramics
- BIOLOX®delta shows higher mean value for HA **0.151** than BIOLOX®forte **0.12**
- BIOLOX®forte provide higher mean values for SF1 **0.133** and SF2 **0.153** than BIOLOX®delta
- BIOLOX®delta shows mean value for SF1 **0.092** and SF2 **0.111**

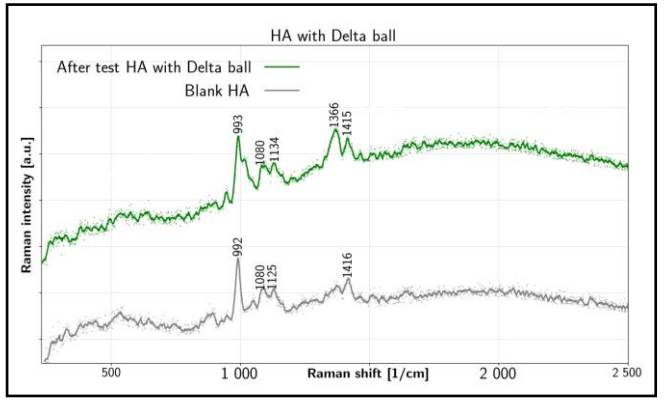
Discussion

- Pendulum hip simulator used to visualize the lubricating films between artificial head and cup in real geometry and in situ observation of lubricant film formation. (Vrbka et al. 2015)
- Raman spectoscopy provides information on the chemical structure of compounds through identification and analysis of functional groups. (Depciuch et al. 2016)
- The authors observed the Raman spectra of lubricant film formed on the ball, to address the chemical structural changes within the synovial fluid.
- The main Raman markers of HA at 1047 cm^{-1}, 1372 cm^{-1} and 1406 cm^{-1} are connected with C-C and C-O stretching, C-H bending and combination of C-N stretching and C-H deformation, respectively (Essendoubi et al. 2016)

Ball-on-cup Configuration within hip joint simulator

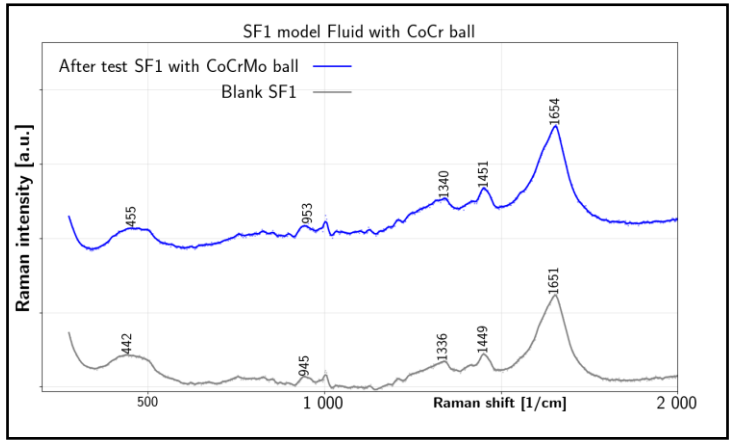


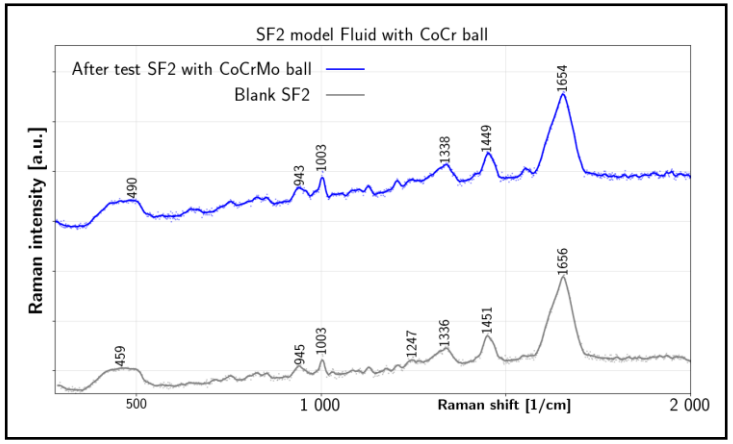


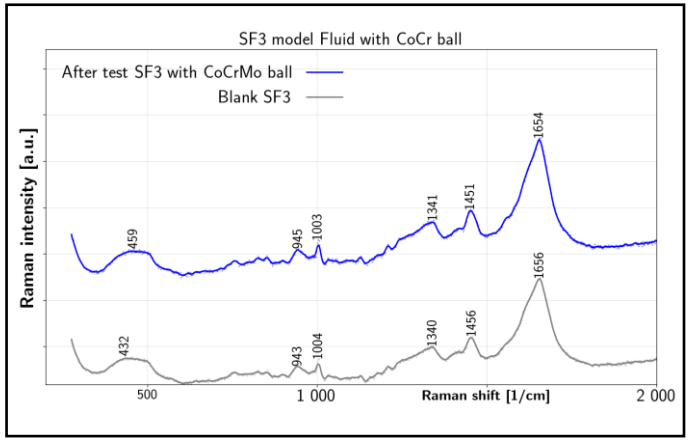


Discussion

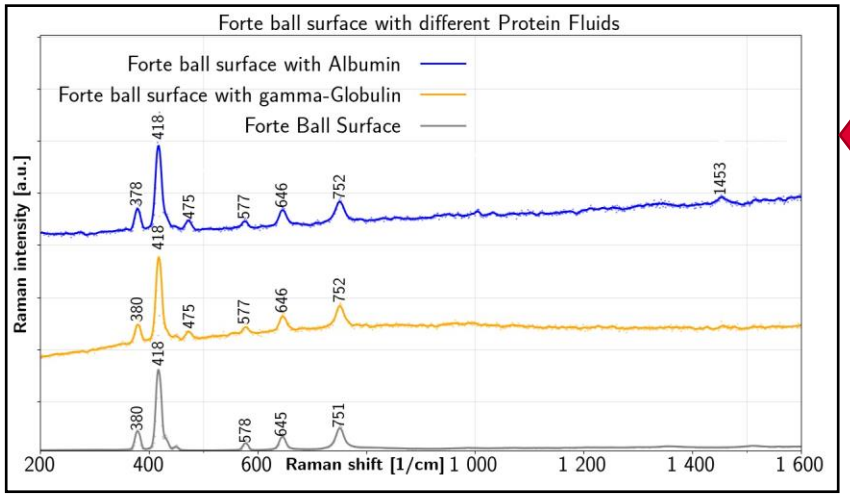
- Inside the contact of hip replacements, lubrication mechanisms and film formation depend on the composition of synovial fluid (Nečas et al. 2018)
- The formation of insoluble, denatured protein films is thought to be the primary lubrication mechanism contributing to surface protection during rubbing. (Stevenson et al. 2019)
- Concerning specifically albumin, its Amide I and III bands are located near 1656 cm^{-1} and 1250 cm^{-1}, respectively. In addition, intense bands near 1340 cm^{-1} due to side-chain stretching are observed (Rygula et al. 2013)
- Albumin marker band near 940 cm^{-1} is also reported (Parachalil et al. 2019)





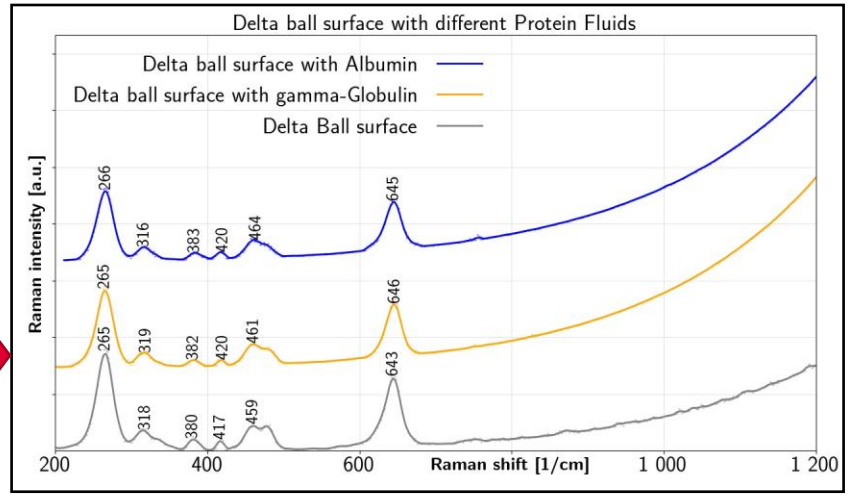


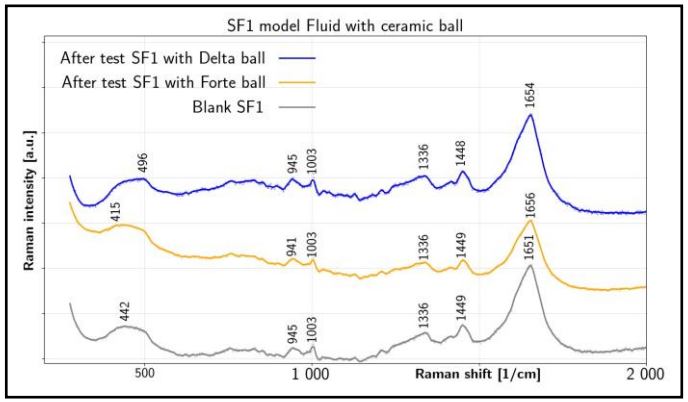
Discussion

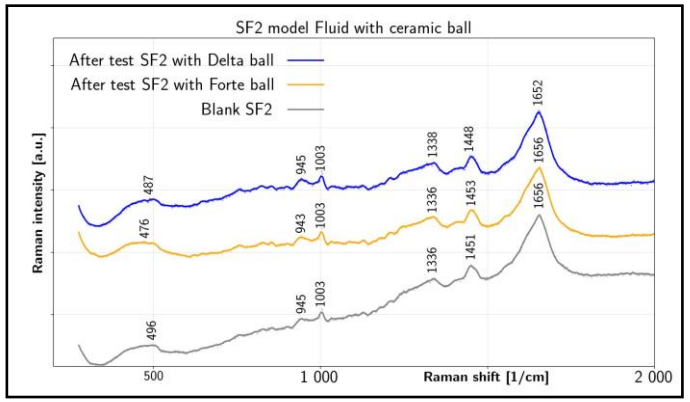


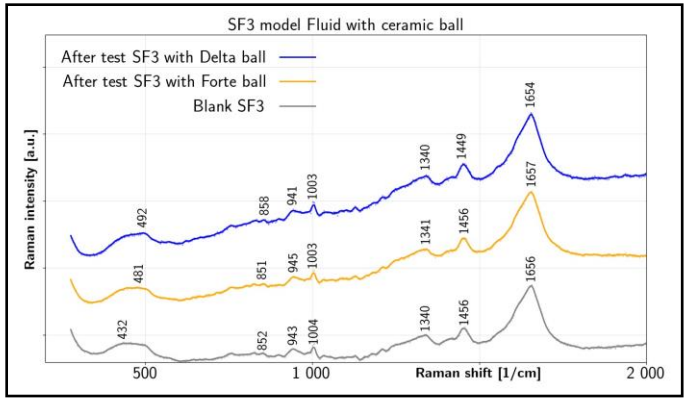
On the BIOLOX®forte ball surface, albumin and γ-globulin individual chemisorption is demonstrated by Raman spectroscopy

There was no significant reaction between BIOLOX®delta material and albumin or γ-globulin



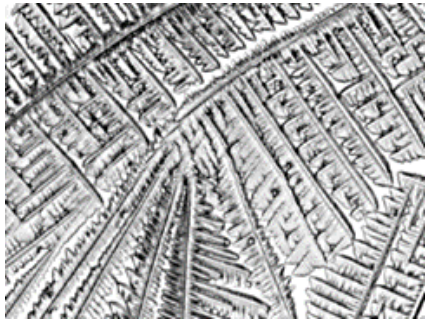


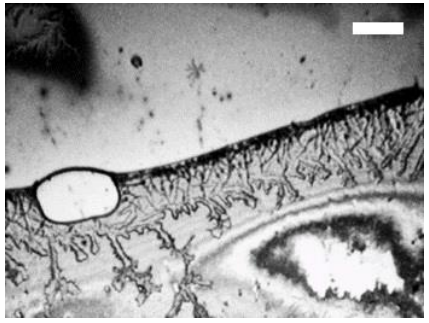




Discussion

- Frictional behaviour of the hip replacements is essential for overall implant lifespan specially during running-in phase (Nečas et al. 2020)
- Limited effect on friction was found when protein-based lubricants were applied with variation of fluid constituents' concentration in the range corresponding to physiologic and osteoarthritic SF (Furmann 2020)
- No consistency is revealed for frictional coefficients of different contact pairs with each individual component of the synovial fluid
- The Coefficient of friction is not an influencing factor of the chemisorption process of SF on the metal and ceramic surface.





Conclusions

Scientific questions

From chemical perspective:

Q1 Which components of synovial fluids are adsorbing chemically on hip implant material surfaces while lubricant film formation within artificial joint replacement?

Co-Cr-Mo Surface
- Evidence of Chemisorption **albumin**, **γ-globulin**, **HA** and all **three model fluids**
- Traces of albumin (**α-helix structure**) from the combination of synovial fluid components
- Diseased and operated joint fluids are more chemically reactive in film formation
- Possibility of heterogeneous catalysis process in case of albumin, γ-globulin.

BIOLOX®forte Surface
- Chemical adsorption of **albumin**, **γ-globulin**, HA and **model SF of the diseased and operated joint**
- Presumably, γ-globulin and/or HA are adsorbed chemically from OA joint fluid and total joint replacement fluid.

BIOLOX®delta Surface
- No significant chemical reactivity observed Albumin, γ-globulin and all three model fluids
- **HA** adsorbed chemically while used individually

Conclusions

Scientific questions

From chemical perspective:

Q2 How is synovial fluid changing the chemical structure of its constituents due to artificial hip implant?

Proteins: Albumin and γ-globulin
- **Tribological effect changes** the chemical structure with **Co-Cr-Mo** with UHMWPE and **BIOLOX®forte** contact pairs
- Proteins remain unchanged after tribological test with **BIOLOX®delta** contact pairs

Hyaluronic Acid
- Alters chemical structure with both **ceramic** contact pairs
- Exhibits similar characteristics without and with **Co-Cr-Mo** and UHMWPE contact pairs

Model Synovial Fluids
- No significant chemical structural modifications observed with any of the contact pairs after tribological activity

From tribological perspective:

Q3 How frictional coefficients are differing with this chemical change in the hip joint replacement?

Coefficient of Friction
- Consistencies not maintained for the CoF values and chemisorption occurrence
- Not indicating the chemisorption process of SF lubricant on the implant materials.

Conclusions

Hypothesis:

1. On the surface of implant material, protein content is a significant factor for chemical interaction and involving chemisorbed film formation rather than HA and phospholipids.

- **SF model imitating OA joint fluid and total joint replacement fluid are more intended to be chemically adsorbed**
- **Elevated concentrations of proteins could be the prime reason of chemisorption**

(Hypothesis H1 confirmed)

2. Metal hip implant materials are more chemically reactive with synovial fluid components to form tribo-film on the surface and could act as heterogeneous catalyst to form lubricant film within joint replace. While ceramic implant materials are less chemically reactive to sustain chemisorption process with synovial fluid contents.

- **BIOLOX®delta implant material found mostly chemically inert and Co–Cr–Mo head shows maximum reactivity for chemisorption**

(Hypothesis H2 partially confirmed)

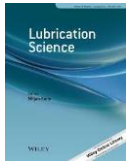
3. With the elevation of chemical reaction occurring within a certain arrangement of implant materials and the lubricants, the friction coefficient of friction of the contact pairs is probably increased.

- **No linear relationship was observed for the coefficient of friction values and chemisorption**

(Hypothesis H3 falsified)

List of Publications

Articles in peer-reviewed journals



- Rufaqua Risha, Martin Vrbka, Dipankar Choudhury, Dušan Hemzal, Ivan Křupka, and Martin Hartl. "A systematic review on correlation between biochemical and mechanical processes of lubricant film formation in joint replacement of the last 10 years." *Lubrication Science* 31, no. 3 (2019): 85-101.

(J_{imp} – *IF 1.812*)

- Rufaqua Risha, Martin Vrbka, Dušan Hemzal, Dipankar Choudhury, David Rebenda, Ivan Křupka, and Martin Hartl. "Raman analysis of chemisorbed tribo-film for metal-on-polyethylene hip joint prostheses.“ *Biosurface and Biotribology,* (2021): 1-11.

(J_{scopus} – *CiteScore 0.2*)

- Rufaqua Risha, Martin Vrbka, Dušan Hemzal, Dipankar Choudhury, David Rebenda, Ivan Křupka, and Martin Hartl. "Analysis of Chemisorbed Tribo-Film for Ceramic-on-Ceramic Hip Joint Prostheses by Raman Spectroscopy." *Journal of Functional Biomaterials* 12, no. 2 (2021): 29.

(J_{scopus} – *CiteScore 4.1*)

Conference paper

- Rufaqua, Risha, Martin Vrbka, Dipankar Choudhury, Dušan Hemzal, Ivan Křupka, and Martin Hartl."The biochemical process of lubricant film formation in joint replacement." (2018). 24th International Conference, Engineering Mechanics, Svratka, Czech Republic.

List of Publications

Conference abstracts

- Rufaqua, R., Vrbka, M., Choudhury, D., Hemzal, D., Křupka, I., and Hartl, M. The biochemical process of lubricant film formation in joint replacement. 24th International Conference, Engineering Mechanics 2018, Svratka, Czech Republic.

- Rufaqua, R., Vrbka, M., Choudhury, D., Hemzal, D., Rebenda, D., Křupka, I., and Hartl, M. Raman spectroscopic analysis of the biochemical reaction of hyaluronic acid in joint replacement. 74th STLE meeting and exhibition 2019, Nashville, Tennessee USA.

Thank you for your attention

Risha Rufaqua

Risha.Rufaqua@vut.cz

INSTITUTE OF **MACHINE**
AND **INDUSTRIAL DESIGN**

www.**ustavkonstruovani**.cz