PhD course in Health & Technologies

Yearly PhD student report – 2018/2019

34th cycle

Percutaneous Cement Discoplasty: biomechanical and clinical assessment of an innovative treatment of intervertebral disc disease

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Year 1 – In-vitro *evaluation of degenerated intervertebral disc stability following treatment with Percutaneous Cement Discoplasty*

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Funding:
European Union's Horizon 2020 Marie Skłodowska- Curie ITN grant SPINNER No. 766012.

1. Introduction

Intervertebral Disc (IVD) Degeneration is one of the main causes of low back pain, a large socio-economic burden for society which affects 80% of the over 80 y.o. [1]. The most common surgical treatment requires an open surgery which last hours and is often associated with important blood loss, long recovery, and general anaesthesia which are not suitable for oldest patients or the ones with comorbidities. Because this disease appears with age, finding minimally invasive treatments is crucial to treat the most complex cases. Percutaneous Cement Discoplasty (PCD) is a surgical technique minimizing the surgical morbidity and complications risks, applied when a vacuum phenomenon is observed inside the InterVertebral Disc (IVD) resulting in the collapse of the adjacent vertebra and in nerve compression. In order to recover the disc height and free the nerve, an injected acrylate cement is injected to fill the empty disc [2] [3] (Fig. 1). Discoplasty was shown to positively affect spine stability by recovering the lumbar alignment in 27 patients [4].

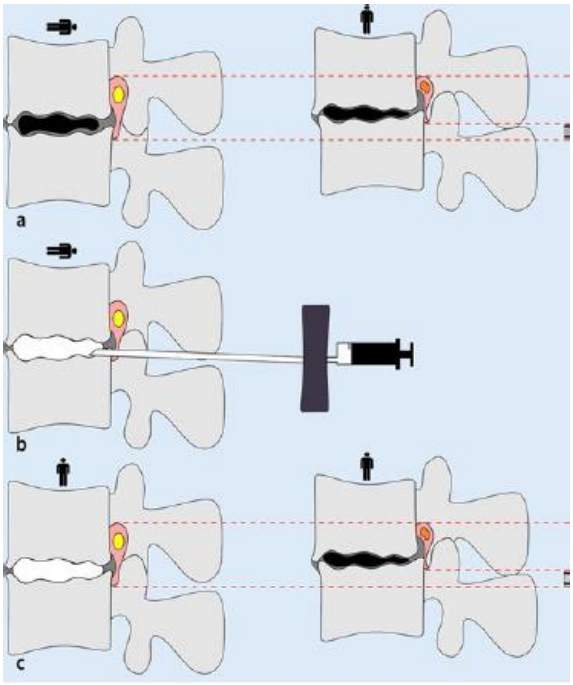

Figure 1: Percutaneous Cement Discoplasty, a recovery of the neuroforamen space by cement injection to treat degeneration [1]

The project aims at understanding mechanical competence of vertebrae and spine segments after being treated by PCD. In particular, the first year was dedicated to the development of a proper biomechanical testing to investigate this technique. An *in vitro* mechanical set up testing spinal repair has been performed to quantify the mechanical stability of the spine after treatment. The mechanical modeling is performed comparatively on animal and cadaver spines in order to fully understand the spine failure mechanisms.

2. Activities of the first year

As preliminary research, I investigated first the stability of animal spines (porcine in this case) in order to optimize the *in vitro* testing before applying the protocol to human specimens for more accurate study of the *in vivo* biomechanics.

2.1. Modeling of degenerative discs

One of the first steps of the *in vitro* testing was to define a biomechanical protocol modelling disc condition and discoplasty treatment. Since porcine specimens were young and healthy, their discs did not present the degenerative criterion for discoplasty. I had to artificially model the degenerated disc state: an empty disc. Several approaches were considered such as a chemical degeneration of the Nucleus Pulposus (NP), or its removal by the mean of a syringe. Discussing with the surgeons Peter Eltes and Aron Lazary, and after some trials, we concluded that the best mean to clear the disc inside was by opening the Annulus Fibrosus, and scratching out the NP and the endplate cartilages in order to reproduce the void observed in patient degenerated discs.

2.2. Overview of the animal study

2.2.1. Experimental protocol

Preliminary study aimed at developing a testing protocol and running an animal study as first insight of the spine stability after PCD. For that, ten spinal segments were transected from young and healthy

porcine specimens grown for alimentary purpose. The segments were cleaned from soft tissue, keeping intact the load transmission actors: some ligaments and the facet joints. Each segment was aligned based on a horizontal disc orientation and its extremities were potted with acrylic cement.

The specimens were tested in 3 conditions (Fig. 2):

- With intact discs
- With manually degenerated discs (as explained above). This step was called nucleotomy.
- After discoplasty. In this case, PMMA cement was injected by the tear to fill the disc.

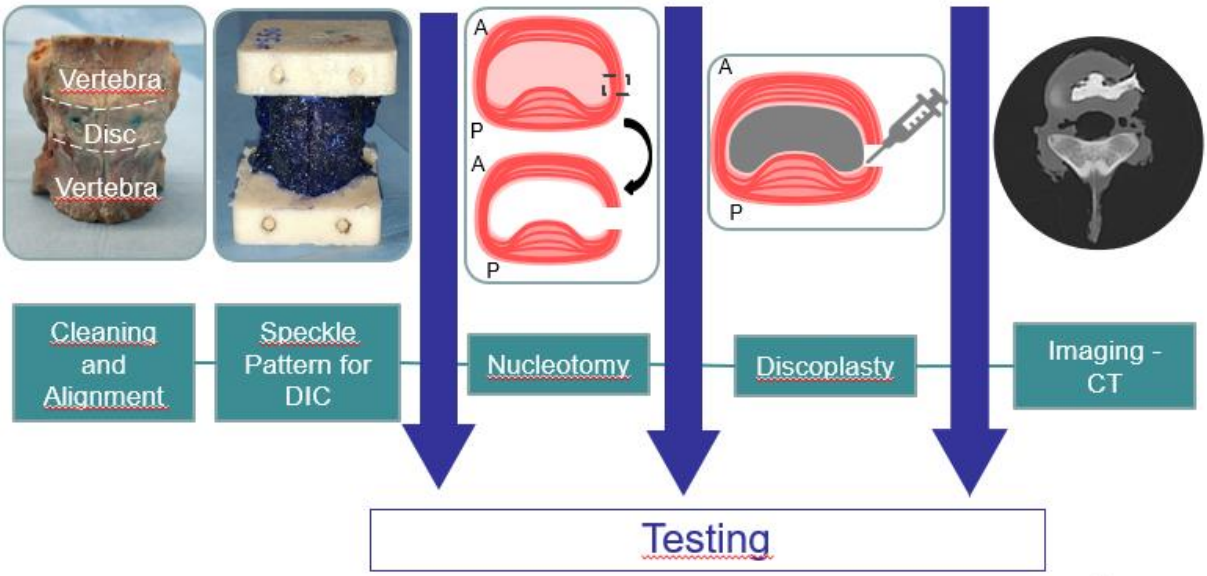

Figure 2: Experimental workflow. A: anterior, P: posterior

For each condition, the specimens were tested in flexion, extension and lateral bending (the bending side was selected as the undamaged side) applying a moment was in the physiological range (Fig. 3). Cycles were performed after a high frequency preconditioning. The last cycle was used for data extraction.

During testing, pictures of the specimen were recorded by an optical 3D-DIC system tracking the displacements of dots of a speckle pattern previously painted on the specimens. Images were acquired by two cameras converging to the same Region Of Interest (ROI). The parameters for the images acquisition and the correlation analysis have been previously optimized to minimize the error. In order to investigate the biomechanical behaviour of the spine, two different acquisitions are performed:

- lateral view in flexion and extension with the cameras pointing to the neuroforamen
- frontal view in lateral bending with the cameras pointing to the selected bending side of the specimen

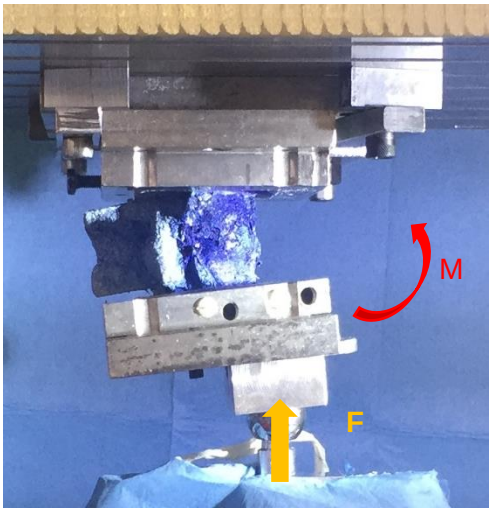

Figure 3: Experimental set-up in flexion loading, lateral view of the specimen

From the testing, load-displacement curves were extracted and stiffness was computed. In addition, the Range of Motion (ROM) of the segment was derived by tracking the vertebra position during the test. Specimen disc height in the back of the specimen, close to the neuroforamen, was measured at load peak in each condition. Finally, principal strains were measured over the specimen surface at peak load in order to prevent disc large deformations.

2.2.2. Results and Discussion

The study showed a decrease of the disc height after nucleotomy and significant (Wilcoxon's test) recovery of the height after discoplasty attesting that PCD acted as a spacer to maintain a normal gap between the vertebra and therefore open the nerve space (Fig. 4). This supported the clinical observations and confirmed that PCD recovered the disc height and neuroforamen space, the first goal of the surgery. The ROM and the stiffness did not show any significant difference between the degenerated and treated cases. Thus, discoplasty did not seem to impact spine flexibility.

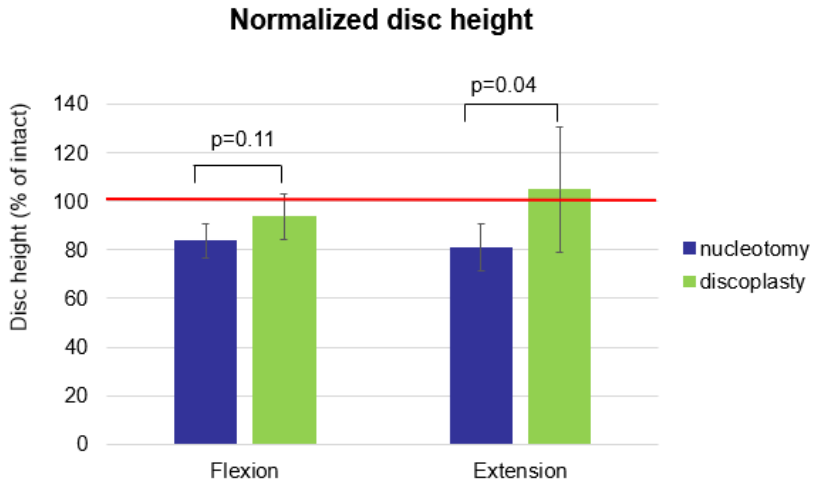

Figure 2: Normalized disc height after nucleotomy and discoplasty, in flexion and extension

Principal strains showed more intense values on the disc after nucleotomy whereas strain distribution after discoplasty looked closer to the intact condition (Fig. 5). The stomatic analysis of the strain values over the disc showed that the average strain recorded on its surface was not impacted by the disc condition. However, the extreme strain values (maximum and minimum) appeared higher after discoplasty, sign that discoplasty enhanced local strain concentrations, leading to large deformations. Moreover, such abnormal strain values could lead to damage initiation in the annulus.

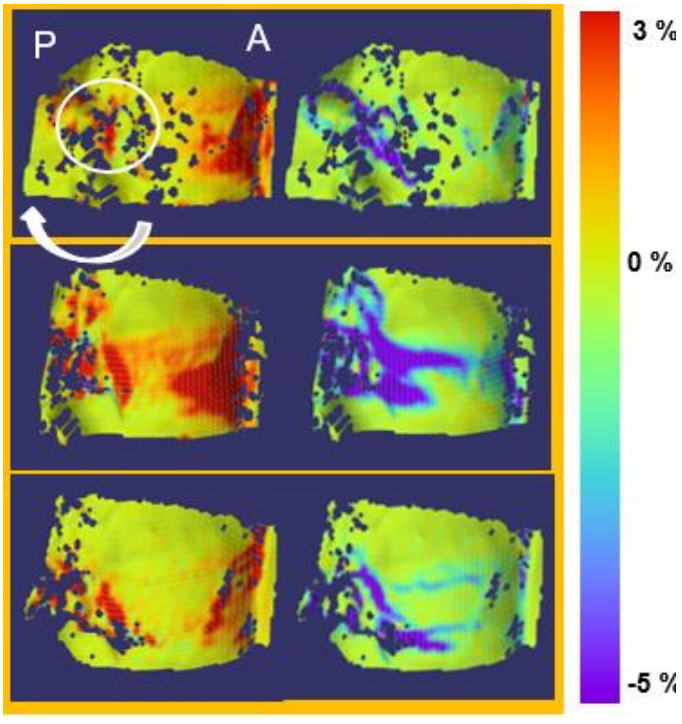

Figure 3: First (left) and second (right) true principal strain mapping of the specimen surface. A: anterior, P: posterior. The arrow shows the bending direction, here in extension. Circled area: neuroforamen

Some limitations however could be raised. Among them, the small number of specimens (10) led to wide variability of results. This prevented statistical significance between the cases although I tried to limit the geometrical factor by normalizing the results after nucleotomy and discoplasty to the intact case. Nucleotomy also presented two main differences with the natural degenerated disc: the disc was empty but no negative pressure was applied on the annulus fibrosus, and the annulus had sectioned fibers. However, it has been acknowledged albeit the tear neglection, that the ROM values corresponded to literature. To quantify the disturbance implied by the degenerated disc modelling, a study will be conducted on human spines comparing the tear shapes and sizes.

2.3. Overview of the human study

After the preliminary work on animal specimens, the central study will focus on human surrogates. Since the PhD project is a MSCA project in partnership with the National Centre for Spine Disorders in Budapest, a first selection of donors was performed by their surgeons among the body bank available at the hospital. In accordance to ethical agreements, 10 spines were received in Bologna from them. In addition, six spines obtained from the US in compliance with ethical regulations were added. CT scans have been performed by clinicians in order to select the levels for the study. Discs with a total fusion were disqualified by surgeons, as well as in case of endplate or vertebrae fracture. In total, 27 segments were segmented, cleaned and potted following the same protocol as for the porcine study. P. Eltes, surgeon in Budapest, proceeded at the nucleotomy of the dedicated levels according the previous protocol. In case of patient surgery, clinicians treat an already void disc, consequently, they are not interested in comparing discoplasty with healthy discs but with degenerated discs.

2.4. Other projects

On the side of my PhD project, I was also involved in a study led by the clinicians in Budapest about discoplasty. My task was to segment the injected cement on post-surgery CT scans. The data were anonymized.

3. Activities planned for the second and third years

I will complete the works in progress:

- **the animal study**. After the first conclusions drawn from the study, I want to investigate more deeply the mechanics of the segment and the impact of the cement on the strain by analysing its distribution within the disc. For that, CT have been performed and I will derive the cement volume in each specimen as well as the volume ratio cement to disc. The shape of the cement will be compared with local high strain values. Then a paper will be published and the study conclusions will serve to improve the testing protocol of the human study
- **the human study**. As stated previously, the human study has started. The testing plan will have to be defined according to the full conclusions of the animal study and the literature, and then the testing will start. Then, data analysis and the publication of my results will be the main activities.
- During spring, and according to the MSCA grant agreement, I will have to move to Budapest, at the NCSD for the second half of the PhD. There, I will apply a clinical approach to PCD, analysing patient images and being part of their follow-up. The activities being supervised by Budapest, it is still too early to have a precise plan.

4. Education

I followed two courses: i) 88003 *Image processing*, Pr. Nico Lanconelli and ii) *An Overview of Design of Experiments*, Prof. M. Scagliarini.

As part of MSCA PhD, students are entitled to train in all fields relevant to their interests and research. Thus, I attended:

- training sessions given in Tuttlingen (Germany) in December 2018, and in Bologna in February 2019 about surgical cases/treatments, spinal implants and surgical tools, publications and the process of article reviews, how to make a presentation.
- I attended as well 1-hour seminars given by academics about their research in Medical Engineering.
- I attended the 3rd International Workshop Spine Loading and Deformation in July 2019 in Berlin (Germany).
- Also, I attended two congresses: European Society of Biomechanics Vienna and ESB-ITA Bologna congresses, with sessions focused on spine and *in silico* modelling.

5. Dissemination

One requirement of a MSCA PhD is to disseminate my results, and to promote to various audiences the project. For that, I attended 2 conferences: ESB 2019 in Wien (Austria) and ESB Italy 2019 in Bologna (Italy) to present the developments of my research through two oral presentations of 10-15 min.
The papers presented in conferences are cited below:

C.Techens, M.Palanca, M.L.Ruspi, L.Cristofolini, "*IN VITRO EVALUATION OF DEGENERATED INTERVERTEBRAL DISC STABILITY FOLLOWING TREATMENT WITH DISCOPLASTY"*, oral presentation at ESB-ITA, Bologna 30 Sept-1Oct 2019

C.Techens, M.Palanca, M.L.Ruspi, L.Cristofolini, "*EVALUATION OF STABILIZATION FOLLOWING DISCOPLASTY OF DEGENERATED DISCS*", oral presentation at ESB, Wien 7 Jul-10 Jul 2019

A paper summarizing the porcine study is currently under preparation.

6. Teaching

- A seminar to Master students, where I presented the spine surgery types, the diseases treated by them, and I detailed the problem of disc degeneration and presented my research with discoplasty – "Clinical approach of spinal diseases" (1 hour)
- I supervised students during lab course on Mechanical Properties of Living Tissues
- I also supervised undergrad students:
    - Guillermo Collado, "Analysis of the biomechanical behaviour of healthy, degenerated and PMMA cemented pig lumbar intervertebral discs", Mar-Jul 2019
    - Sara Montanari, "Effect of intervertebral disc incision on the human spine biomechanics", Sept 2019

References

[1] « Low Back Pain Fact Sheet | National Institute of Neurological Disorders and Stroke ». [En ligne]. Available on: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Low-Back-Pain-Fact-Sheet. [Consulté le: 20-oct-2019].

[2] P. P. Varga, G. Jakab, I. B. Bors, A. Lazary, et Z. Szövérfi, « Experiences with PMMA cement as a stand-alone intervertebral spacer », *Orthop.*, vol. 44, n° 1, p. 1-8, nov. 2015.

[3] C. Sola *et al.*, « Percutaneous cement discoplasty for the treatment of advanced degenerative disk disease in elderly patients », *Eur. Spine J.*, mars 2018.

[4] L. Kiss, P. P. Varga, Z. Szoverfi, G. Jakab, P. E. Eltes, et A. Lazary, « Indirect foraminal decompression and improvement in the lumbar alignment after percutaneous cement discoplasty », *Eur. Spine J.*, avr. 2019.