

## Reproducible Disc Degeneration Scale in a Large Animal Model

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### Introduction

To study the efficacy of novel regenerative strategies is necessary to develop new models that do not implement annulus fibrosus (AF) damage. We hypothesize an ideal preclinical model to study novel biological therapies for nucleus pulpous (NP) regeneration can be achieved by approaching the NP via the endplate (EP) route through a minimal invasive transpedicular approach.<sup>1</sup> The aim of the study is to characterize a preclinical ovine model triggering EP damage and repair with or without mechanical nucleotomy, while keeping the AF intact.

### Material and Methods

Sheep ( $n = 12$ , 3 years old), were used. Throughout the transpedicular approach, a 2mm tunnel was drilled to the NP. Nucleotomy was performed using a shaver resector. The tunnel was sealed using a press-fit porous polyurethane (PU) cylinder. Five lumbar discs were assigned to different groups: EP tunnel (A); EP tunnel + nucleotomy (B); EP tunnel + repair with PU scaffold (C); EP tunnel + nucleotomy + repair (D); no treatment (E). X-ray and MRI was performed at 0, 1, 3 and 6 mths after. Disc height and MRI indexes were calculated and disc macro- and micro-morphology were analyzed. MRI images and gross anatomy photographs were graded using both Pfirrmann<sup>2</sup> and Thompson<sup>3</sup> grading systems.

### Results

MRI analysis showed a progressive decrease of NP signal intensity with different degrees of degeneration. According to Pfirrmann degenerative grade, the C group showed a grade II, group A appeared as grade III, group D looked as grade IV and group B appeared as grade V. Morphologically, all stages of the degenerative process from Thompson grade I to grade V were also observed with the same association. Histological analysis revealed progressive disc narrowing, fragmentation of the NP matrix in D and B group. The scaffold in the tunnel of C and D groups appeared colonized by cells without sign of bone formation at all time point. NP tissue was in the tunnel with infiltration of inflammatory cells in A and B groups.

### Conclusion

A new preclinical model to study tissue-engineering strategies for NP regeneration has been developed and characterized by approaching the NP via the EP route through a minimal invasive transpedicular approach [1]. Keeping the AF intact, the different degrees of IDD have been observed according to Pfirrmann and Thompson grading system. The sealing of the tunnel prevents the NP to leak out of the disc space.

This represents a significant contribution toward the translation of new regenerative strategies for biological restoration of early and mild IVD degenerative.

### Acknowledgment

The support of the Italian Ministry of Instruction, University and Research Grant (PRIN-200938NT8Z), the Young Investigator Research Grant of the Italian Ministry of Health (GR-2010-2318448) and the BIOSPINA Award of the Italian Society of Spine Surgery (SICV&GIS) are gratefully acknowledged.

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