# HISTOLOGICAL STUDY OF THE CHONDROGENIC REGENERATION CAPACITY OF A GELATIN-HYALURONIC ACID MICROGEL IN A PORCINE MODEL OF ARTICULAR CARTILAGE INJURY

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## Introduction/aim

The histological characteristics of hyaline cartilage, mainly its avascular nature, dictate its poor regenerative capacity. High-grade local cartilage injuries induce unbalanced mechanical stresses within the joint which exacerbate the damage and often progress to osteoarthritis. The regeneration of articular cartilage requires of three key elements: (i) the recruitment of chondrogenic cells to the defect site; (ii) the use of a biomaterial able of generating a three-dimensional environment capable of providing the necessary biomechanical cues; and finally, (iii) provide the essential biochemical factors to induce cells towards the adoption of the hyaline cartilage chondrocyte phenotype.

In this work we combined subchondral bone damage by microdrilling to produce bleeding at the defect site and create a pathway for migration of mesenchymal stem cells from the subchondral bone, with the use of a mixture of gelatin and hyaluronic acid microspheres containing platelet-rich plasma to provide a chondrogenic friendly environment with the idea to improved cartilage regeneration.

## **Methods**

We use a model of joint damage developed in pigs. We included 2 experimental groups, one treated with microdrilling and the other with microdrilling in combination with the microgel containing platelet-rich plasma (PRP). We used 8 animals for each experimental group. The animals were sacrificed after nine months, and the histological characteristics of the regenerated cartilage as well as the biomechanical properties were evaluated. Neocartilage morphology was characterized by thickness, cell density, and interdigitation of the cartilage and subchondral bone. Microscopic features of the cartilage were also evaluated using the ICRS grading scaling as previously described [1], using hematoxylineosin and toluidine blue histological stains.

### Results

The results show a great variability between the different animals of the two experimental series, since we observed cases in which the regenerated tissue has all the characteristics of hyaline cartilage, while in other animals, although the regenerated tissue filled the defect, its structure was more like fibrous tissue or fibrocartilage.

Although the series in which only the subchondral bone was damaged seems to present poorer results, we only found significant differences in terms of cartilage thickness (in the group with microdrilling and microgel it was greater than in the group with only microdrilling). Other quantitative variables analyzed did not show significant differences. We also did not find variations in relation to the biomechanical characteristics of the groups analyzed, being similar in terms of hardness and recovery.

## Conclussion

It seems that the use of the microgel loaded with PRP represents an improvement over the use of microdrilling alone because, on the one hand, the thickness of the cartilage of the animals included in this experimental group is greater, while, on the other hand, the area of the matrix with high glycosaminoglycan content is thicker. It would be necessary to increase the "n" to demonstrate if there are significant differences between groups.

## References

1. Zurriaga Carda J et al. J Biomed Mater Res B Appl Biomater, 108(4):1428-1438, 2020.

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