

# Novel Chitosan Hydrogels for the treatment of osteoarthritis: Mechanical support, Lubrication and Prevention of Cartilage degradation in a rabbit Model of osteoarthritis

Y Henrotin<sup>1,2</sup>, F Oprenyeszki<sup>1</sup>, F Comblain<sup>1</sup>, J-E Dubuc<sup>3</sup>, C Boileau<sup>4</sup>, M Chausson<sup>5</sup>,  
R Lecler<sup>5</sup>, G Rocasalbas<sup>5</sup>, P Douette<sup>5</sup>, S Gautier<sup>5</sup>

<sup>1</sup>B.C.R.U., Arthropôle Liège, University of Liège, Belgium

<sup>2</sup>Physical Therapy and Rehabilitation Department, Princess Paola Hospital, Marche-en-Famenne, Belgium

<sup>3</sup>Orthopaedic Department, Cliniques Universitaires St Luc, Brussels, Belgium

<sup>4</sup>Artialis S.A., Liège, Belgium

<sup>5</sup>Synolyne Pharma S.A., Herstal, Belgium



## BACKGROUND

Chitosan, a glucosamine polysaccharide, is a good candidate for viscosupplementation in OA joints. Herein, we report the physico-chemical properties and the effects of an innovative chitosan hydrogels in the rabbit anterior cruciate ligament model ACLT model of OA.

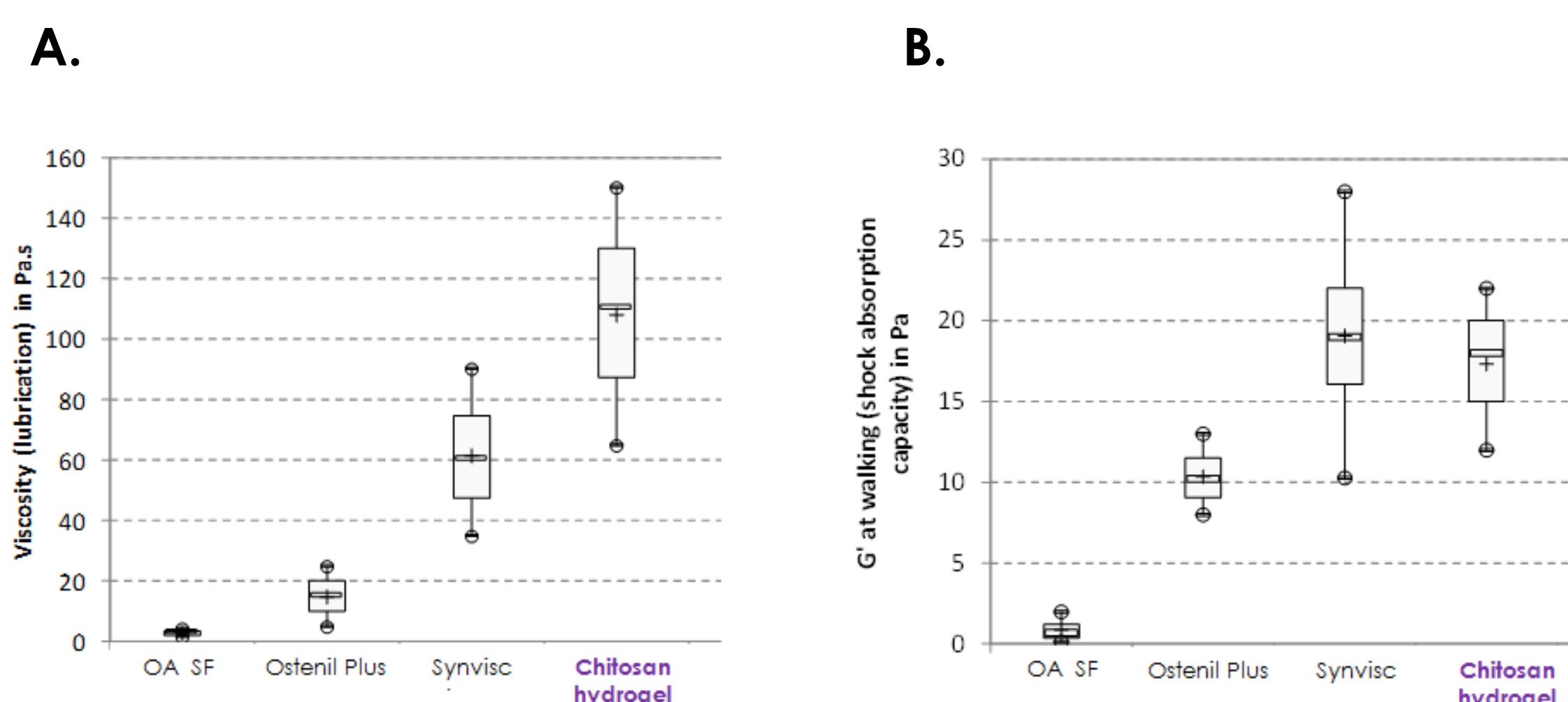
## METHODS

The ability to absorb shocks at walk frequency, the lubrication (viscosity at rest), and the biodegradation kinetics of animal-free ultrapure chitosan hydrogels - Vegetech inside™ - (Synolyne Pharma, Belgium) were evaluated using a mechanical compression equipment (Instron, US) and the Discovery Hybrid DHR-2 rheometer (TA Instruments, US). The properties were compared with those measured in synovial fluids and in hyaluronan viscosupplements. In addition, the chitosan hydrogels were mixed with patient synovial fluid (in a 1:1 ratio, v/v), and the ex vivo rheological properties of the mix were characterized.

OA was surgically induced by the transection of the anterior cruciate ligament (ACLT) in female Hyla albino rabbits. One week after surgery, animals were randomly divided into 2 groups. One group (n=9) was injected intra-articularly (right knee) with saline solution (control) and the other group (n=10) with a chitosan hydrogel (Synolyne Pharma, Belgium). X-rays from the right knee were performed at the time of sacrifice and scored with the Kellgren and Lawrence (K&L) scale. Animals were euthanized 9 weeks after surgery and a macroscopic evaluation of cartilage was done. Histological sections of cartilage areas and of synovial membrane were evaluated according to the OARSI histopathology initiative.

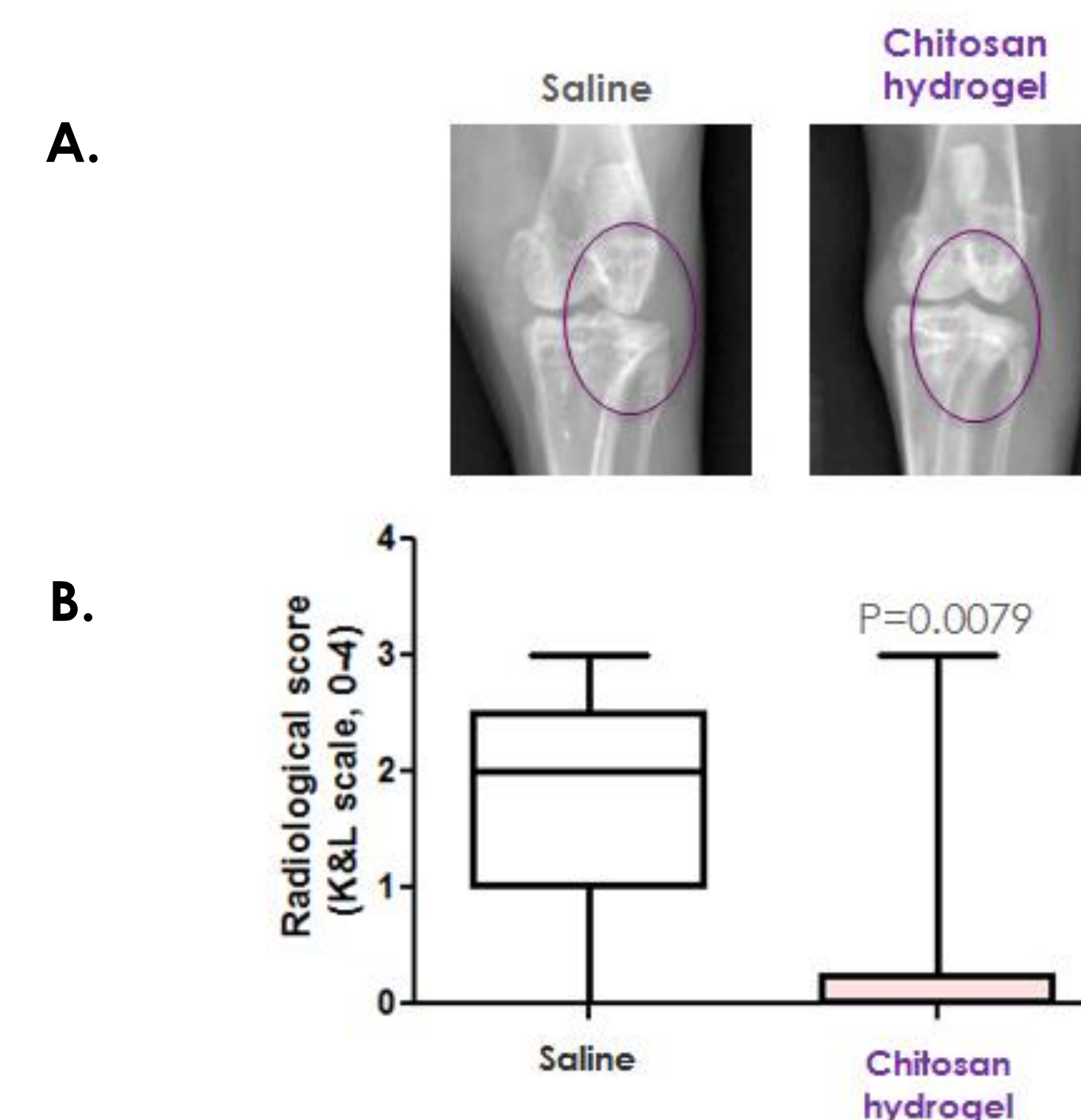
## RESULTS

**Chitosan hydrogel improves the lubrication and shock absorption capacity of OA SF.**



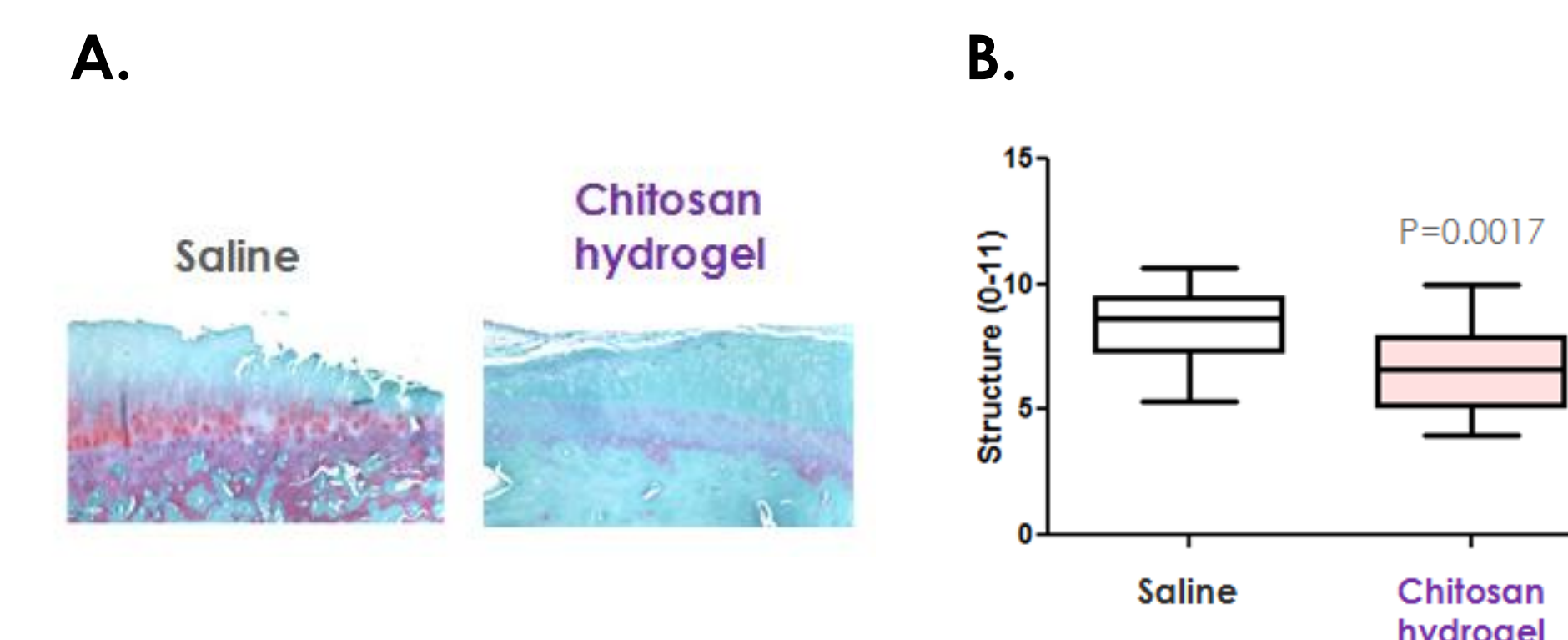
**Figure 1:** A. Lubrication capacity evaluated by the viscosity at rest and expressed in Pa. s. B. Shock absorption capacity evaluated by the viscoelasticity at walk frequency and expressed in Pa. Rheology of OA SF / gel (1:1) after 1 hour at 37°C.

**Based on the reduction of Kellgren & Lawrence scale, chitosan hydrogel prevents significantly the development of OA.**



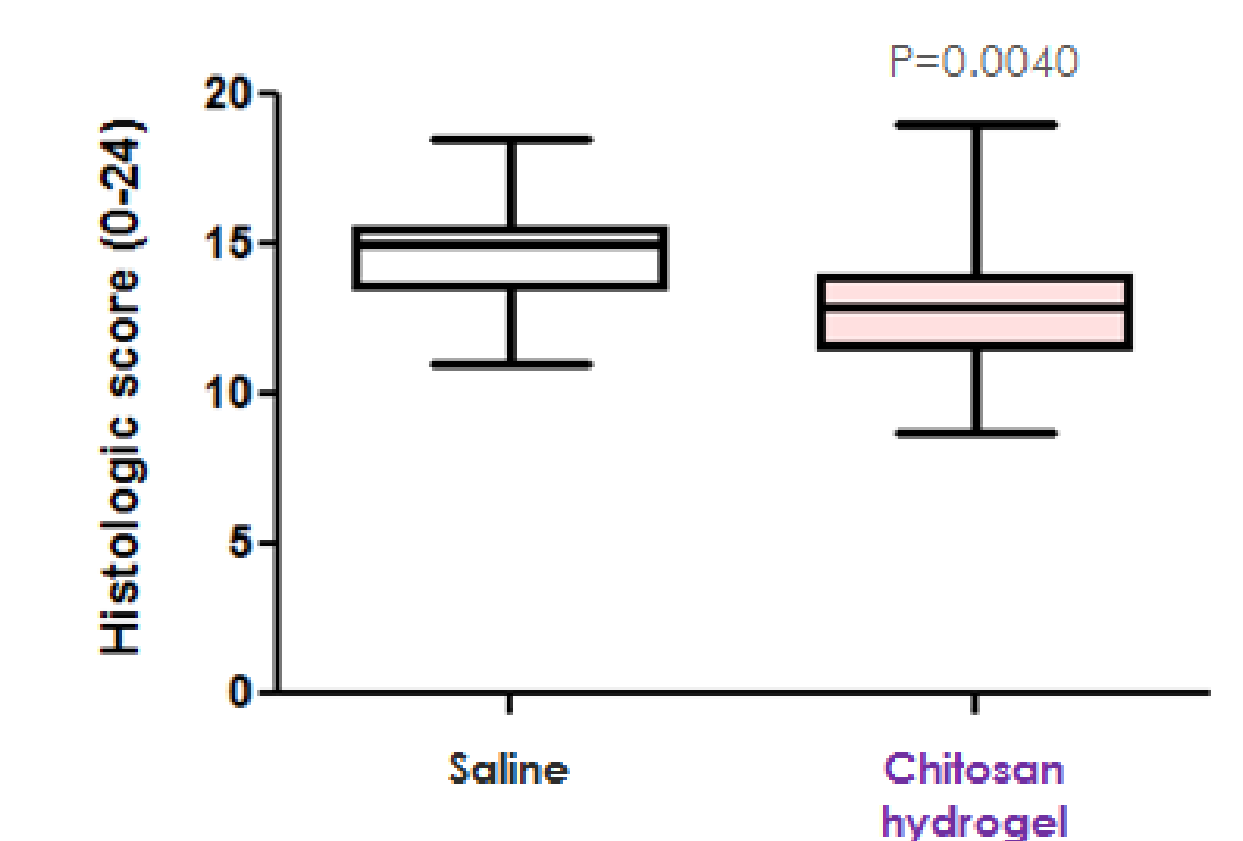
**Figure 2:** A. Representative X-rays from each group before sacrifice (9 weeks after surgery) B. X-ray grading according to the K&L scale. Data were analyzed with Mann and Whitney U test.

**The injection of chitosan hydrogel improves significantly the structure of cartilage.**



**Figure 3:** A. Histologic sections showing the full thickness of cartilage and subchondral bone in the weight bearing zone stained with Safranin-O/ Fast green in each group. B. Cartilage structure score. Data were analyzed with Mann and Whitney U test.

**Chitosan hydrogel reduces also significantly the synovial membrane inflammation.**



**Figure 4:** Synovial membrane histological global score. Data were analyzed with Mann and Whitney U test.

## CONCLUSIONS

These results are confirming the high potential of the mono-dose viscosupplementation with non crosslinked chitosan hydrogels specifically designed to protect cartilage and decrease the symptoms associated with OA.