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Chitosan hydrogel

- Thermo-sensitive
- Easily injectable
- Extended residency time
 (> 4 weeks in the rabbit)
Rheological properties

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

Rheology of OA SF / gel (1:1) after 1 hour @ 37°C
Material & Methods

- 20 HYLAL albino adult rabbits
- ACLT induced OA
- A single intra-articular injection of:
  - Chitosan hydrogel gel
  - Saline solution

The study endpoints were:
- Radiological Kelgren and Lawrence score
- Macroscopic evaluation of cartilage
- Histological evaluation of synovial membrane and cartilage (OARSI)
**Study design**

**Day 0**
- anterior cruciate ligament transection

- **HYLA albinos**

**Day 7**
- Single injection:
  - Chitosan hydrogel (n=10)
  - Saline solution (n=10)

**Induction of OA**
- one week

**X-rays**
- 600 µl

**Histological Macroscopic evaluation**

**Sacrifice**

**8 weeks**
X-ray – K&L score

<table>
<thead>
<tr>
<th>Saline solution</th>
<th>Chitosan hydrogel</th>
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<tbody>
<tr>
<td><img src="image1.png" alt="Saline solution X-ray" /></td>
<td><img src="image2.png" alt="Chitosan hydrogel X-ray" /></td>
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<tr>
<td><img src="image3.png" alt="Saline solution X-ray" /></td>
<td><img src="image4.png" alt="Chitosan hydrogel X-ray" /></td>
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**Mann and Whitney U test**

*P* < 0.05 is considered significant

*P* = 0.0079
Macroscopy

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<tr>
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<tr>
<td>Femoral condyles</td>
<td>![Image]</td>
<td>![Image]</td>
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<tr>
<td>Tibial plateaus</td>
<td>![Image]</td>
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OARSI Global score
Size x Severity

Mann and Whitney U test
P<0.05 is considered significant

P=0.0041

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Histology - cartilage

Saline solution

- Dedradated matrix
- Clusters
- Important loss of matrix staining
  => loss of proteoglycans
- Focal hypocellularity
- Confluent hypocellularity
- Severe fibrillations
- Deep erosion through calcified cartilage
- Toward total cartilage loss

Chitosan hydrogel

Structural changes

Mann and Whitney U test
P<0.05 is considered significant

P=0.0017

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Histology – Synovial membrane

**Control**
- Villous hyperplasia
- Bone/cartilage debris
- Synoviocyte proliferation and hypertrophy
- Blood vessels
- Proliferation of fibrocytes
- Inflammatory infiltrate

**Chitosan hydrogel**

Global score

![Histological changes](image)

Mann and Whitney U test

*P*<0.05 is considered significant
Conclusions

- A single injection of a thermo-sensitive chitosan gel prevents cartilage degradation and synovial membrane inflammation in ACTL-induced OA in rabbit.

→ **A good candidate for viscosupplementation**
  - Ultrapure, animal-free & well tolerated
  - Easy to inject (thermo-sensitive)
  - High lubrication & viscoelasticity
  - Extended intra-articular residency
  - Resistant to oxidative stress
  - Bioadhesive (cartilage filling)

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Thank you for your attention!

International collaborations:
F Blanco (La coruna, Spain)
T Conrozier (CHU Lyon, France)
V Kraus (Duke University, USA)
L Punzi (University of Padova, Italy)
A Mobasher (University of Nottingham, UK)
J Monfort (Hospital del mare (Spain)
P Richette (Lariboisiere, France)
J Runhaar (Erasmus MC, Rotterdam)
Histology- Synovial membrane

**Synoviocytes proliferation/hypertrophy**
- Control: [Graph showing data]
- Vi002: [Graph showing data]

**P = 0.0289**

**Inflammatory infiltrate**
- Control: [Graph showing data]
- Vi002: [Graph showing data]

**P = 0.0011**

**Synovial stroma**
- Villous hyperplasia, blood vessels, cartilage/bone detritus

- Control: [Graph showing data]
- Vi002: [Graph showing data]

Mann and Whitney U test

P<0.05 is considered significant
Histology - cartilage

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<tr>
<th>Matrix staining</th>
<th>Structure</th>
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<tr>
<td><img src="image" alt="Box plot" /></td>
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Matrix staining and structure comparisons with Mann-Whitney U test. P=0.0017 is considered significant.

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<th>Cluster formation</th>
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Cellularity and cluster formation comparisons with U test.