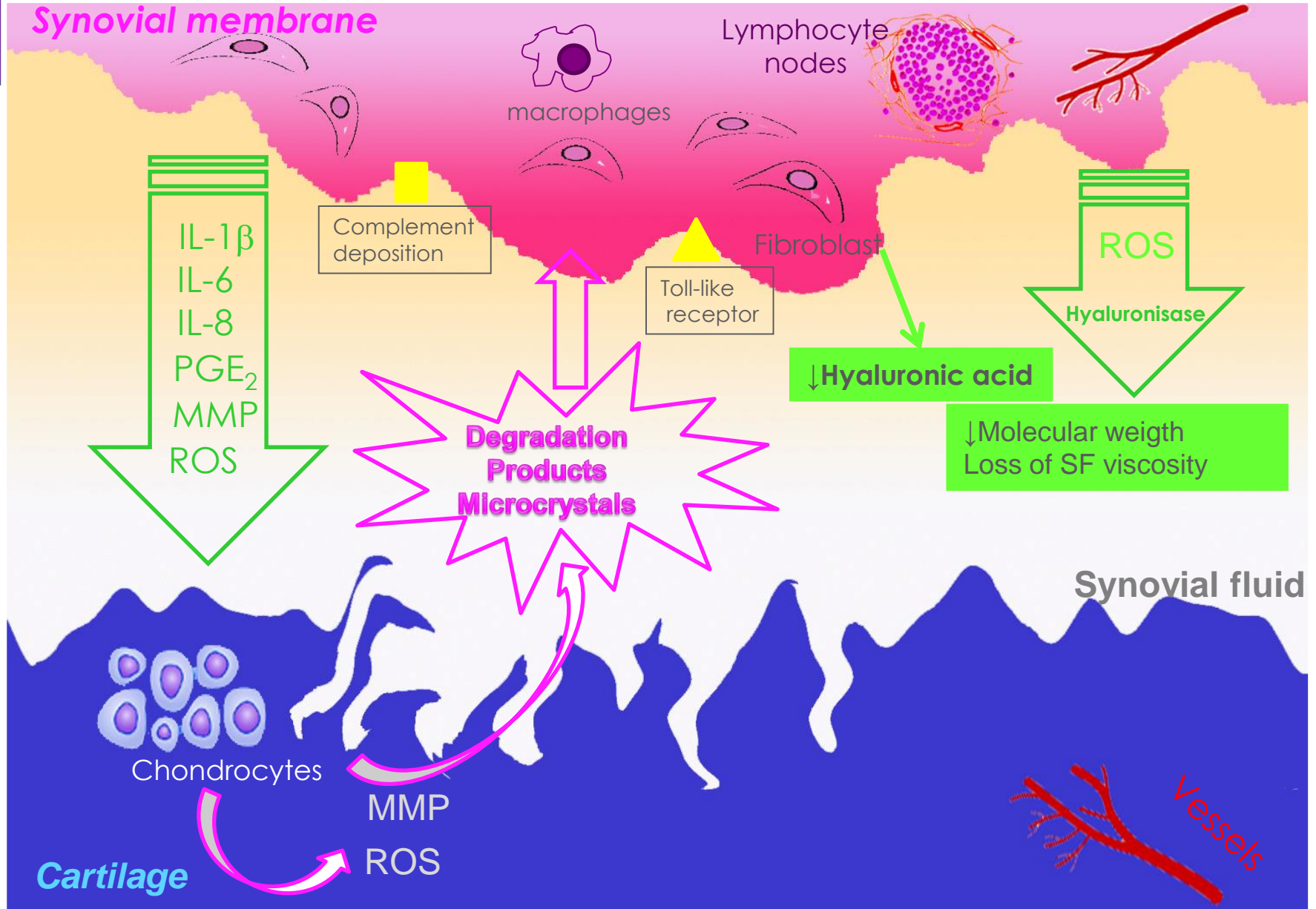


# Recent advances and innovation in viscosupplementation

Pr Yves Henrotin  
University of Liège



# Synovial membrane



# Viscosupplementation

“Viscosupplementation is the process that restores the normal rheological environment in the synovial fluid, synovial tissue...and reestablishes the protection, lubrication, shock absorption and barrier effects.”

## 4 KEYS PROPERTIES

- Visco-elasticity
- Shock absorbing
- Lubrication
- Barrier effect

## Hyaluronic acid





# Hyaluronic acid: limitations and needs

- Low residency time
- Low to moderate clinical efficacy
- Not recommended in recent guidelines



**Need of new  
products**

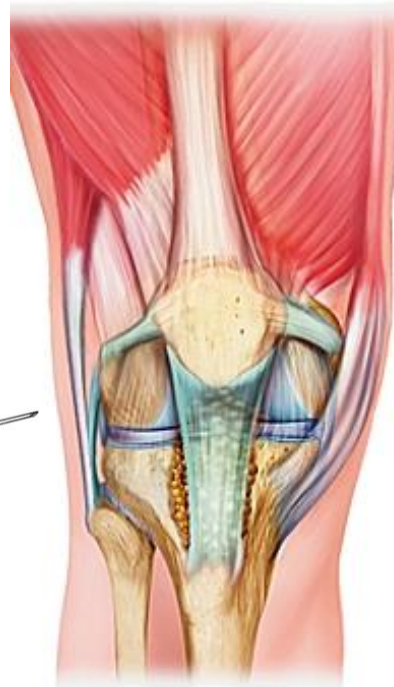
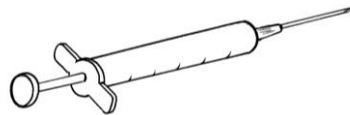
- **with a longer residency time**
- **a better clinical efficacy**
- **a disease modifying effect**

# Viscosupplementation: new directions

Present

## HYALURONIC ACID

Animal origin  
Bacterial fermentation  
Chemically Cross-linked



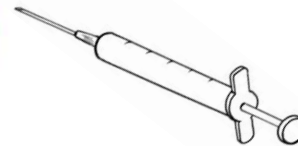
Future

## HA PROTECTION

Manitol  
Sorbitol  
Tocopherol

## DRUGS/ANTIBODY DELIVERY

NSAIDS/Coxibs  
Chlondine  
Triamcinolone  
Doxycycline  
☀️ **Chondroitin sulfate**  
ADAMTS inhibitors

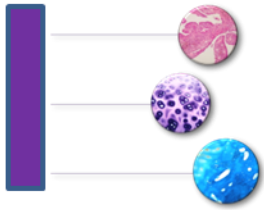


## NEW MOLECULES

☀️ **Chitosan (Arthrovisc)**

Lubricine

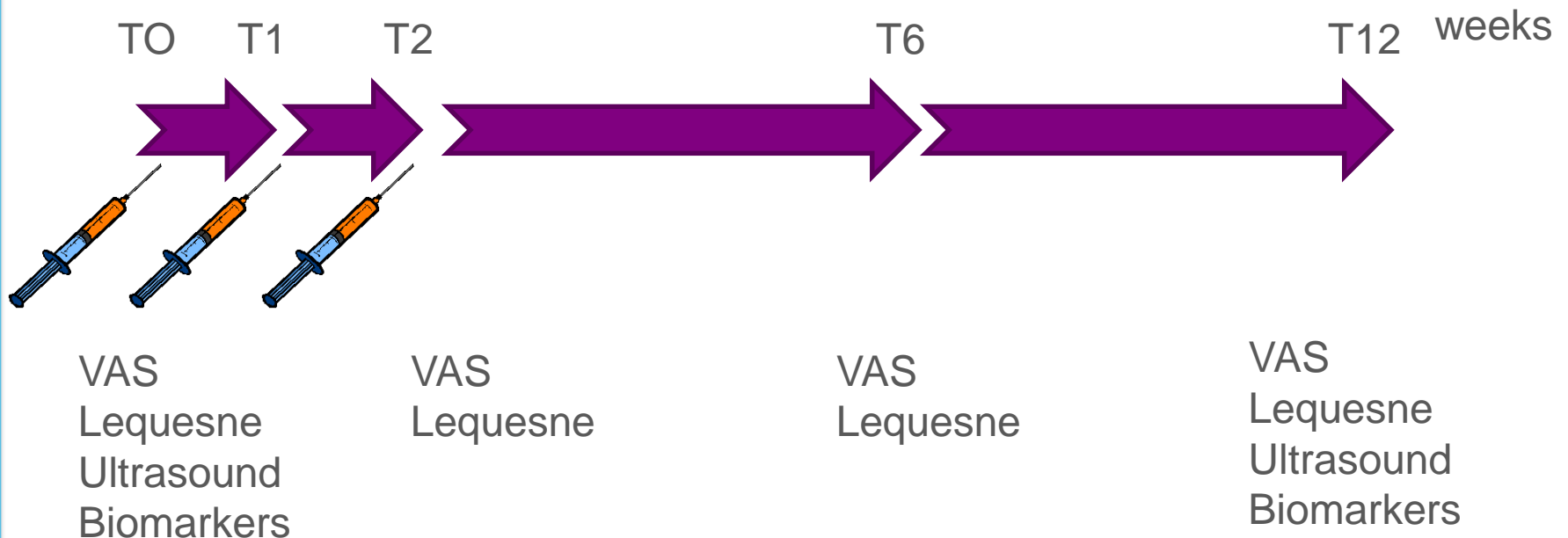
Polynucleotides (Chondrotide)

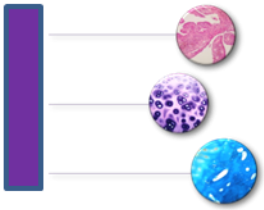


# HA+CS (Structovial CS)

## A pilot open uncontrolled study

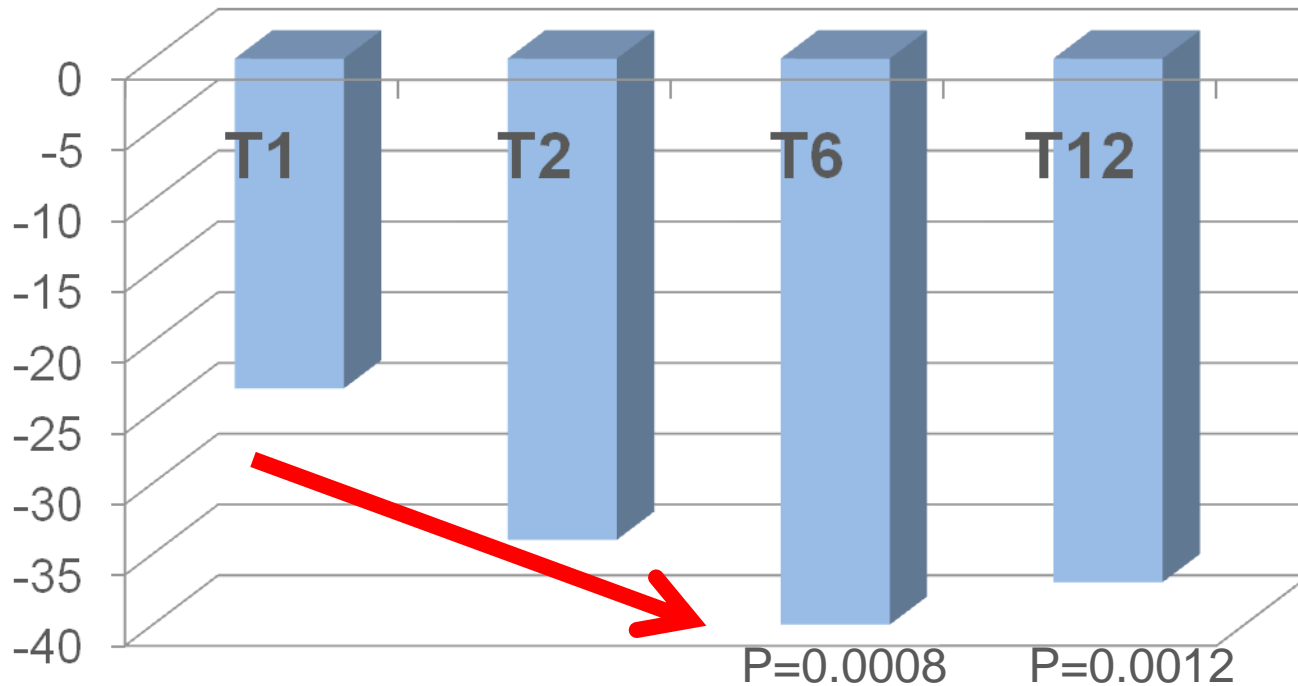
- 30 patients with femoro-tibial OA
- 2 ml containing 24 mg HA and 60 mg CS
- 3 injections on a weekly basis





# HA+CS

## Pain intensity



80 % reach a clinical reponse according OARSI/OMERACT criteria

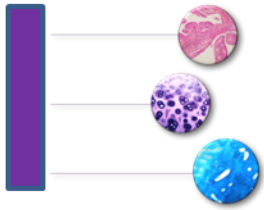


# HA + CS Biomarkers

	$\Delta T0 - T12$	Trends	
Coll2-1 (nM)	$-11 \pm 78$	↓	<b>Degradation</b>
Coll2-1NO2 (nM)	$-0.06 \pm 0.41$	↓	<b>Oxidative stress</b>
CS-846 (ng/ml)	$+1 \pm 17$	↑	<b>Synthesis</b>
CPII ng/ml)	$-41 \pm 867$	↓	<b>Synthesis</b>
IL-6 (pg/ml)	$-5667 \pm 21769$	↓↓↓	<b>Inflammation</b>

Biomarkers changes suggest that HA/CS tends to promote return to cartilage homeostasis





# Chitosan smartbeads®+ chitosan hydrogel = Arthrovisc®

- Diameter: 600-900 μm
- Mushroom Chitosan :  
0.5% - 42Kda
- Alginate (Pronova UP) :  
1.4%



chitosan (C) smartbeads

+

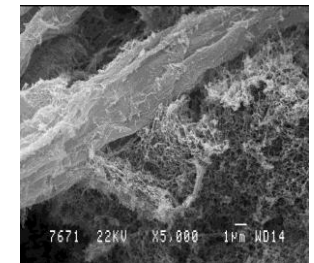
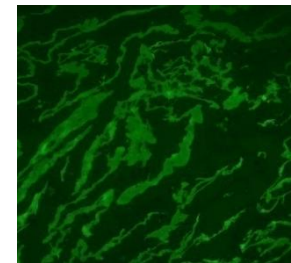
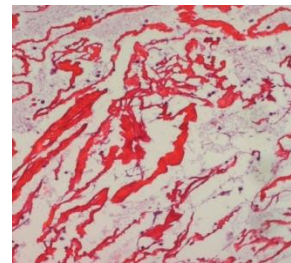
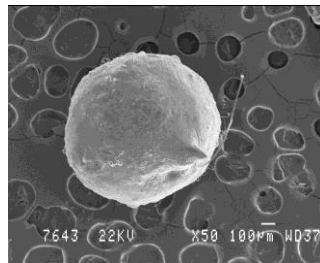
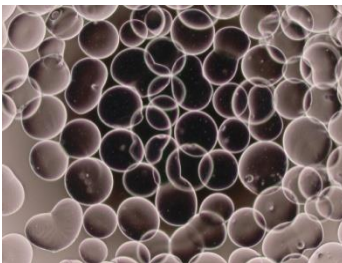


Chitosan-derived hydrogel

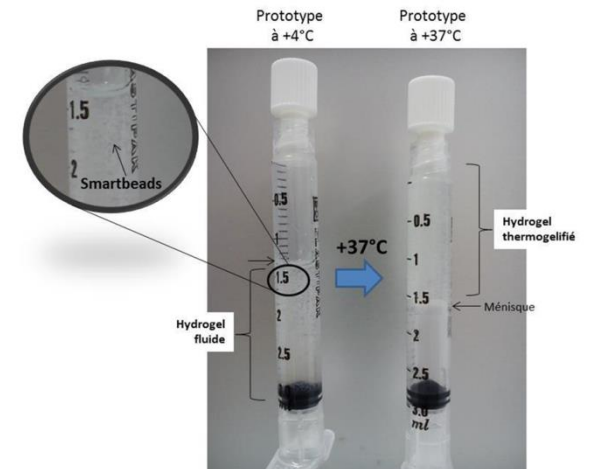
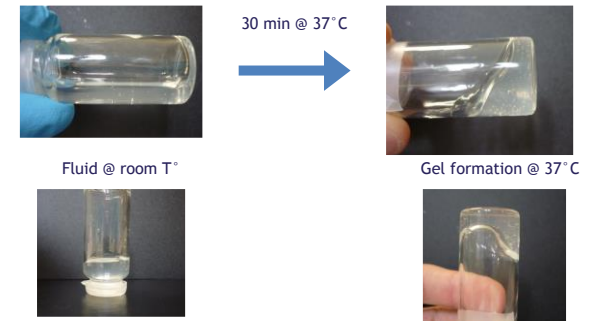
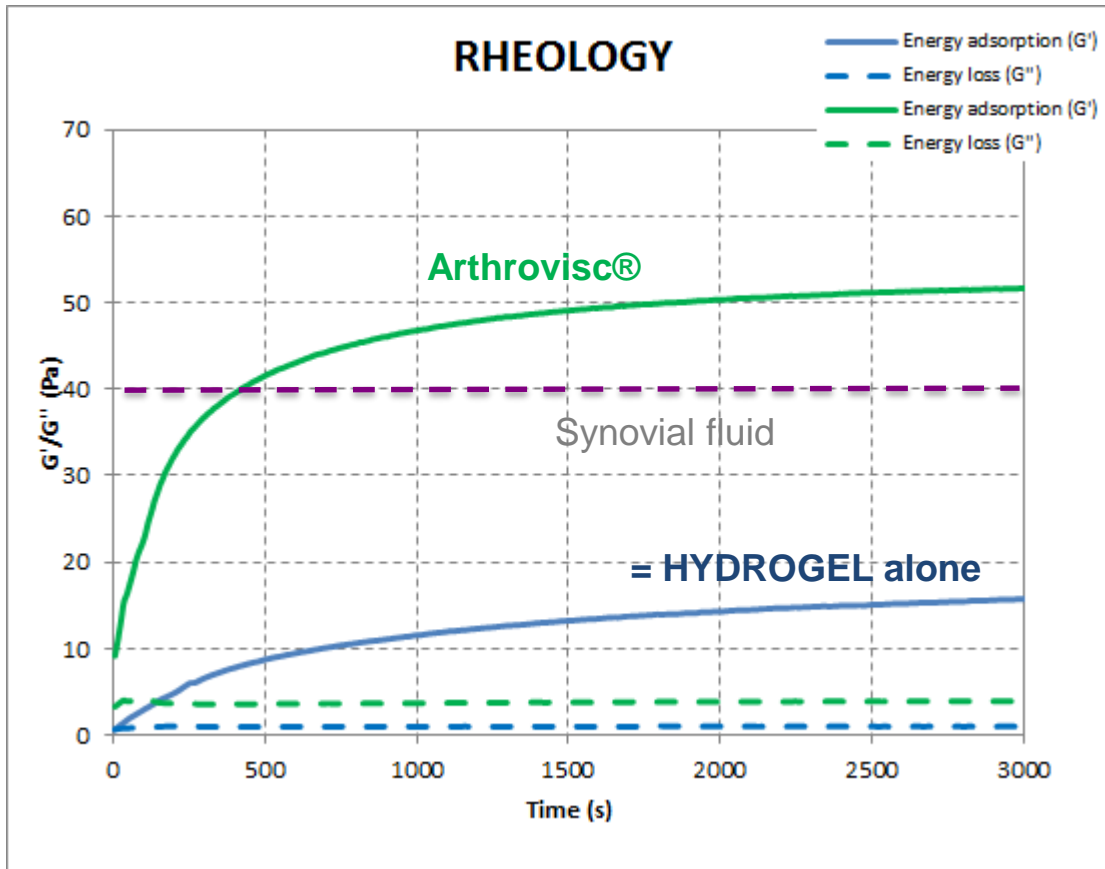
- Thermogelling
- 1% trimethylchitosan
- 132 Kda

**Biphasic biomaterial**

**Ratio 1/1 w/w**



# A thermogelling hydrogel mimicking synovial fluid



# Study design

Day 7  
Single injection :

- 900 µl Arthrovisc® (n=7)
- 900 µl Hydrogel alone (n=7)
- 900 µl saline (n=7)

Histological evaluation  
of cartilage  
and  
synovial membrane  
OARSI score

Day 0  
anterior cruciate  
ligament  
transection



Hyla albinos

Induction of OA  
one week

6 weeks

Sacrifice

Analysis

X-rays



X-rays

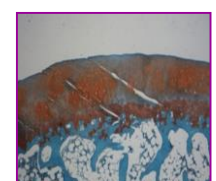
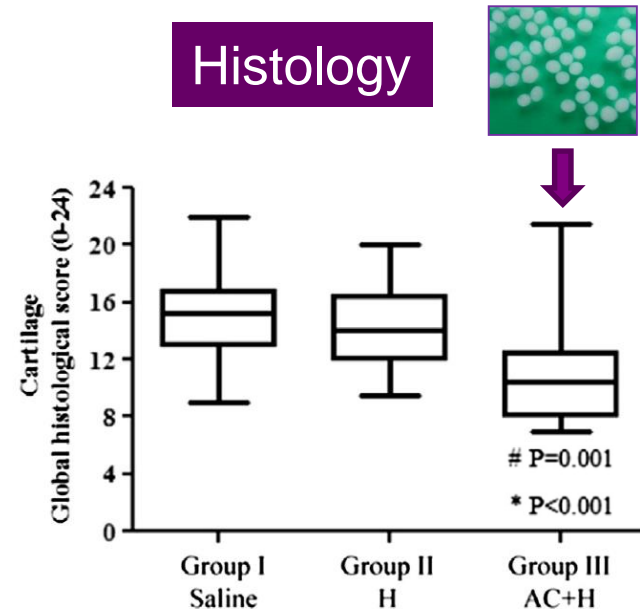
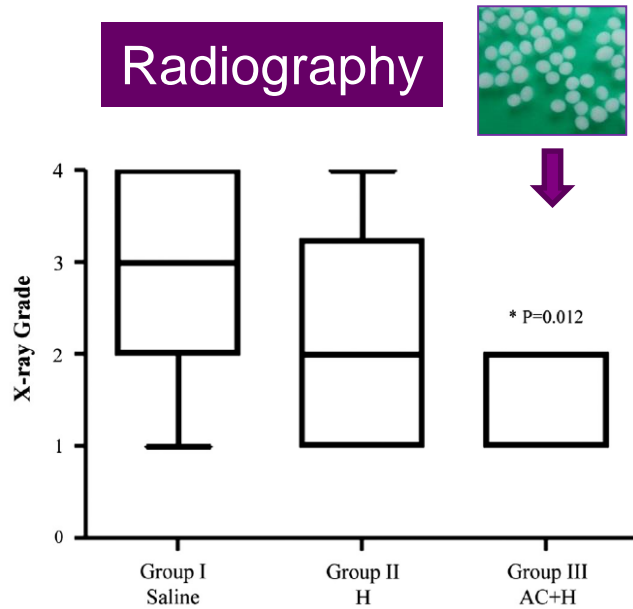


X-rays

K&L  
score

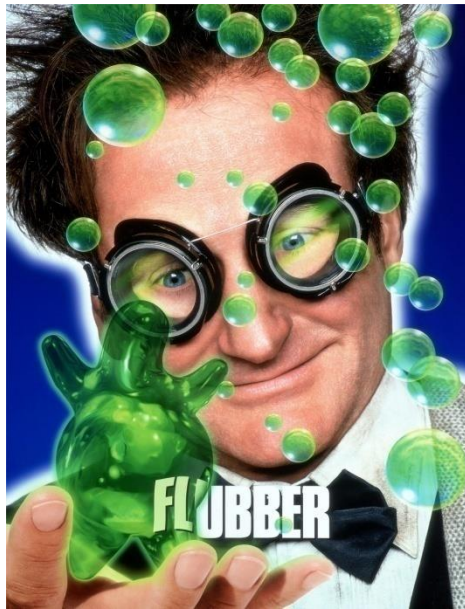


# Arthrovisc® decreases OA progression



# Conclusions

So...What's about the future?



Perhaps not only a dream!





# Thank you for your attention !

## International collaborations:

- F Blanco (La corona, 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)

