DOES INJECTABLE 2.5% POLYACRYLAMIDE HYDROGEL RESTORE SYNOVIAL HOMEOSTASIS IN THE OSTEOARTHRITIC JOINT?

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Background & Purpose

Osteoarthritis & Synovial Changes

- OA causes synovial changes leading to pain, stiffness, and reduced function
  - Mechanical stress activates pro-inflammatory and nociceptive pathways
- Synovial fibrosis is associated with increased pain and limited joint function

2.5% iPAAG (2.5% Injectable Polyacrylamide Hydrogel)

- 2.5% iPAAG is a soft synovial implant shown to reduce pain and improve function in humans and animals with OA
- 2.5% iPAAG integrates into the synovial membrane
  - Its exact mechanism of action is still not fully understood

Purpose

- **Mathematical simulations** were performed to assess how an iPAAG implant within the synovial membrane affects tissue stress distribution
- An **ex vivo study** was conducted to measure synovial membrane stiffness from horses, allowing evaluation of iPAAG effects using the equine osteochondral fragment model of osteoarthritis (OA)

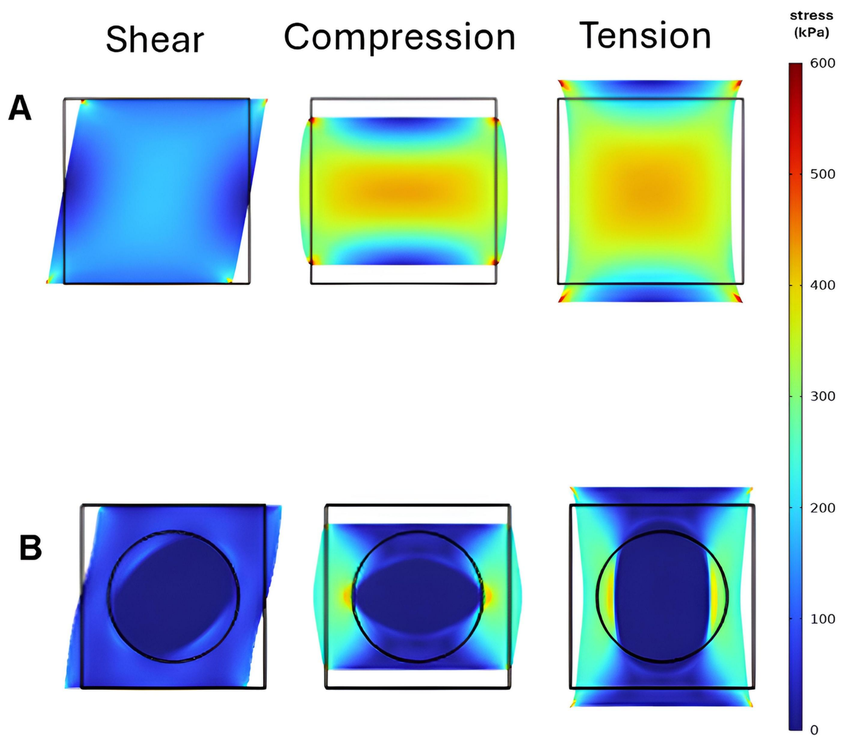


Figure 1.
Cross-sectional midplane stress distribution in synovial tissue with no hydrogel filling (**A**) or with a single spherical hydrogel filling of 15% v/v (**B**) under 10% shear, compression and tension.

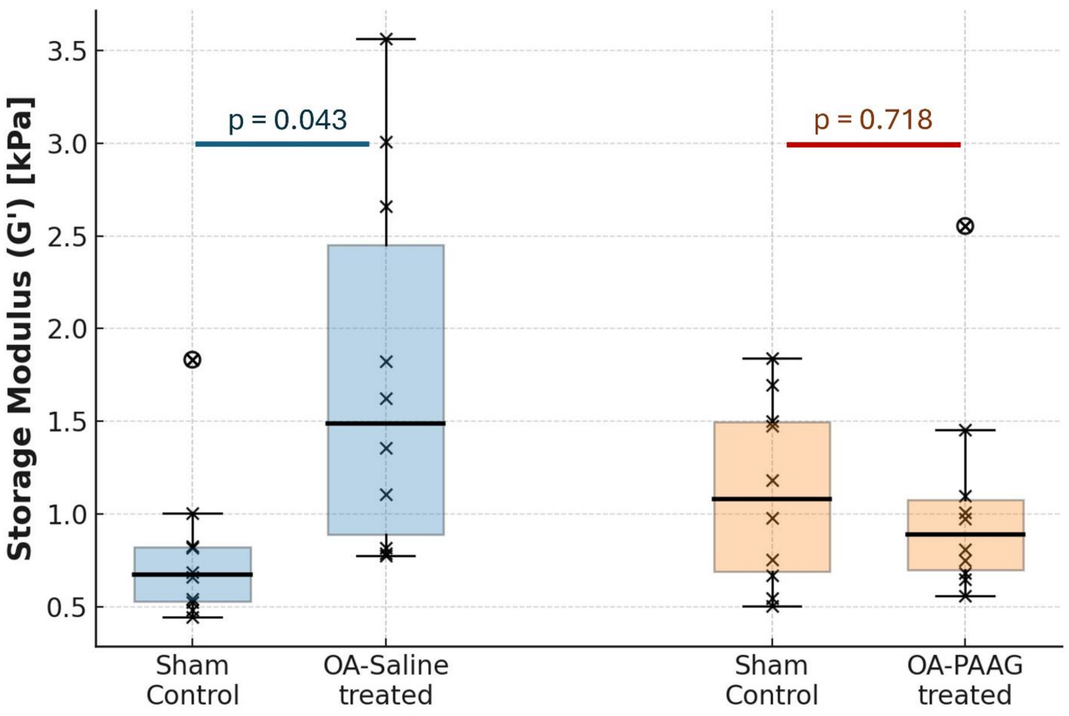


Figure 2.
Storage moduli of OA treated vs. contralateral sham-operated samples. Encircled data points are recognized as outliers but included in the overall dataset because the reason cannot be determined.

Methods

Mathematical Simulations

- Used stationary modeling to evaluate each deformation mode until equilibrium
- Applied boundary conditions to isolate:
  - Pure shear | Pure compression | Pure tension
- Only one deformation mode was applied at a time
- Conducted parametric analysis to assess the stress–strain response of hydrogel embedded in surrounding tissue

Ex Vivo Study

- Included 32 synovial membrane samples from 16 horses
- Each horse provided an OA-induced joint and contralateral sham control
  - OA-induced joints received either: iPAAG treatment (n=8) or saline (n=8)
- 2 circular plugs (8 mm Ø) excised from each membrane using an OATS-punch
- Experimental and control samples were tested concurrently
- Shear stiffness measured using a commercial rheometer
- Tissue stiffness quantified as storage modulus (G′)
- OA vs. contralateral sham joints compared using paired t-tests ($\alpha = 0.05$)

Results

Mathematical Simulation (Figure 1)

- Hydrogel reduces stress distribution within the synovial membrane
  - Primary reasons for stress reduction:
    - Hydrogel volume carries negligible stress, lowering overall tissue stress when embedded.
    - iPAAG's softness limits tissue deformation, making the membrane effectively softer and improving stress distribution

Ex Vivo Study (Figure 2)

- OA joints injected with saline showed:
  - Increased stiffness vs. contralateral controls
    - Storage modulus: 1824 ± 1105 Pa vs. 1002 ± 495 Pa
      - Significant difference: p = 0.043
- OA joints injected with 2.5% iPAAG showed:
  - Storage modulus similar to contralateral controls
    - 2.5% iPAAG: 1099 ± 647 Pa vs. Control: 1184 ± 504 Pa
      No significant difference: p = 0.718

Conclusion

Mathematical simulations and ex-vivo study suggest that 2.5% iPAAG restores synovial elasticity in OA joints.

Future work involves further investigation of the biological mechanisms underpinning these observed responses.

Disclosure

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