Team #33: Biological Joint Resurfacing

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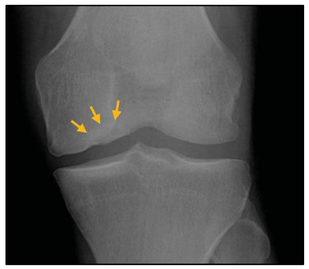
Background

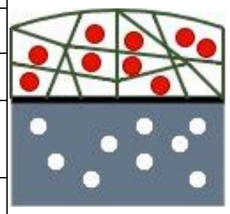
- Cartilage damage occurs commonly on medial/lateral femoral condyles, trochlear groove
- Cartilage cushions load and distribute stress across the joint
- Microfracture, autograft/allograft, autologous chondrocyte implantation



[1] Medial femoral condyle defect (Peterson L. 2009)

Design Overview and Objectives

Double-diffusion bioreactor
Provides platform to generate osteochondral grafts
Live Chondrocytes
Provides graft biocompatibility, secretes ECM materials
Type II Collagen
Provides *tensile* load resistance to cartilage
Proteoglycan
Provides *compressive* load resistance in cartilage
Trabecular Bone Scaffold
Provides Base layer for graft

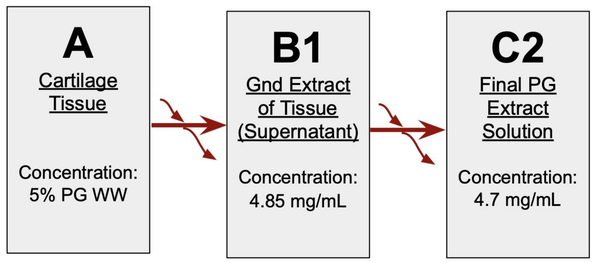


1. Proteoglycan Extraction

Aim: Extract >90% of proteoglycan from 2 grams of cartilage (~70 mg)
A. *Use Proteinase K proteoglycan extraction as a control of amount of sGAGs*
B. *Verify extraction efficiency with DMMB assay*

Results:

- Guanidine HCL Extraction with 15% efficiency
- Proteinase K Digestion completed
- DMMB assay analysis

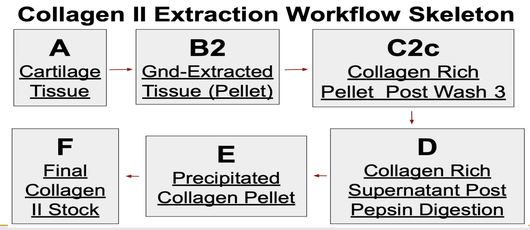


2. Type II Collagen Extraction

Aim: Develop simple, repeatable extraction protocol compatible with the proteoglycan removal workflow

Design Changes:

- Reduced treatment conditions
- Clarified procedure
- Creation of flow chart

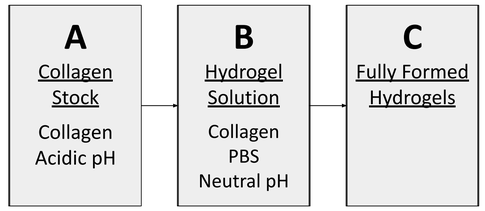


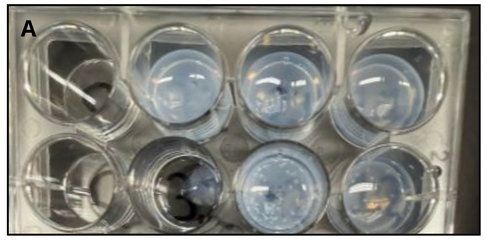
3. Hydrogel Formation

Aim: Create type I telocollagen hydrogels that can withstand cell culture conditions for 7 days

Results

1. Hydrogels successfully fabricated
2. Hydrogels withstood cell culture conditions for 7 days





Gels post 7 day trial

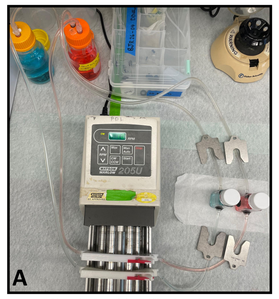
4. Double Diffusion Mineralization

Aim: Use a simplified double diffusion system to diffuse calcium and phosphate from opposite sides of a hydrogel and react to form hydroxyapatite (HAp) at the midpoint

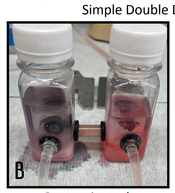
Design Improvements: Flow rate of 0.0052 cm^3/s, gravimetric pump calibration, simplified system with epoxy-sealed reservoirs

Results: 24 hr run with 2% agarose gel

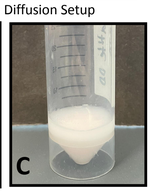
- Solution bypassed along chamber walls
- Excess hydroxyapatite formed in reservoirs
- Collected hydroxyapatite for future analysis



Simple Double Diffusion Setup



Reservoirs and Gel Chamber



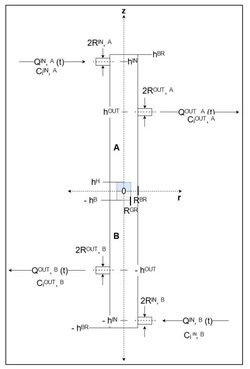
Collected Hydroxyapatite

5. Bioreactor Study

Aim: Validate bioreactor dimensions & define the key geometric/transport variables controlling HAp formation.

Results:

- MicroCT dimensional analysis (32um) confirmed the bioreactor components met design requirements.
- Key variables: flow, concentration, pressure, axial heights, radial lengths, dynamic/kinematic viscosity, & fluid velocity.
- This analysis creates a platform to quantify inputs for a trial run.



Conclusions & Future Directions

Proteoglycan Extraction

- Remove other contaminants
- High throughput validation of proteoglycan yield across multiple bovine tissue sources

Type II Collagen Extraction

- Experimental validation of extraction protocol
- Characterization of extracted collagen
- Integration into hydrogel

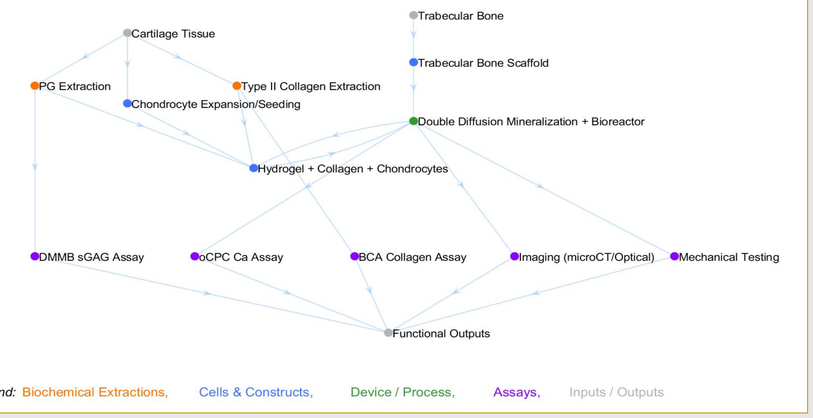
Hydrogel Formation

- Incorporate cells into hydrogel formulation
- Switch to type II telocollagen
- Include aggrecan and ideally hyaluronan in formulation

Double Diffusion & Bioreactor

- Improve gel sealing
- oCPC to quantify hydroxyapatite
- MicroCT to measure localization

Flowchart



Acknowledgements

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References

[1]Journal of Orthopaedic & Sports Physical Therapy. "Reliability and Validity of Observational Risk Screening in Evaluating Dynamic Knee Valgus." Journal of Orthopaedic & Sports Physical Therapy, vol. 39, 2009, pp. 665–674, doi:10.2519/jospt.2009.3004.