Osteoinductive Hydrogels for Treatment of Vertebral Compression Fractures: an Osteopenic Rabbit Model

Veterinary Research Scholars Program
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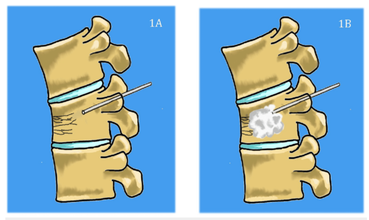
Introduction

- 1.5 Million Vertebral Compression Fractures (VCFs) occur each year in the United States.
- Osteoporosis is the major risk factor for VCFs, which have up to 25% lifetime incidence in post-menopausal women.
- Standard Treatment: Vertebroplasty using polymethylmethacrylate (PMMA) bone cement.



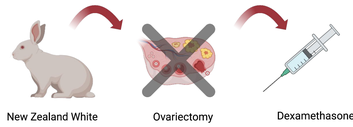
- Problem: PMMA is much stiffer than bone, with compressive strength being one to two orders of magnitude greater than surrounding bone. This results in breakdown of bone adjacent to the vertebroplasty site and the need for future vertebroplasties.
- Calcium phosphate-loaded, chitosan-based osteoinductive hydrogels have been shown to be effective in a rabbit model vertebral fusion procedure[1]. This efficacy may translate to vertebroplasty as well.

Objective

- Determine the feasibility of chitosan-based hydrogels to treat VCFs based on biocompatibility, compressive strength, and *in vivo* testing using an osteopenic rabbit model

Methods

- Induce osteopenia in 24 rabbits through ovariectomy followed by 8 weeks of steroid treatment (dexamethasone at a dose of 0.6 mg/kg/day).



- Transcutaneous vertebroplasty of the L5 vertebra will be performed on all 24 rabbits. Half (12) will receive PMMA and 12 will receive the osteoinductive hydrogel formulated in our previous rabbit vertebral fusion study.
- CT scans will be taken at 0, 6, and 12 weeks following vertebroplasty.
- Rabbits will be euthanized at 12 weeks post-vertebroplasty. All L5 vertebrae will be removed, with 12 samples being analyzed by histological assessment, and 12 being evaluated mechanically by compression testing.
- Results will be analyzed for evidence of fracture stabilization and osteoinduction.

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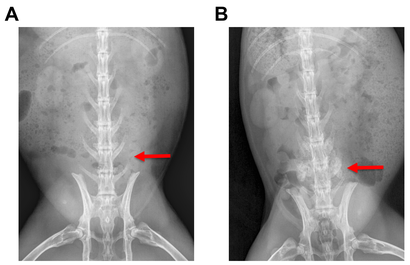
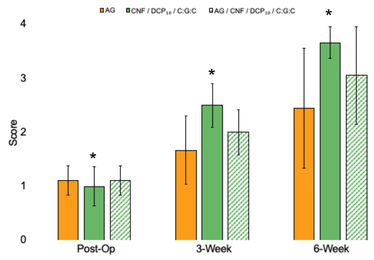
In Vivo Ossification

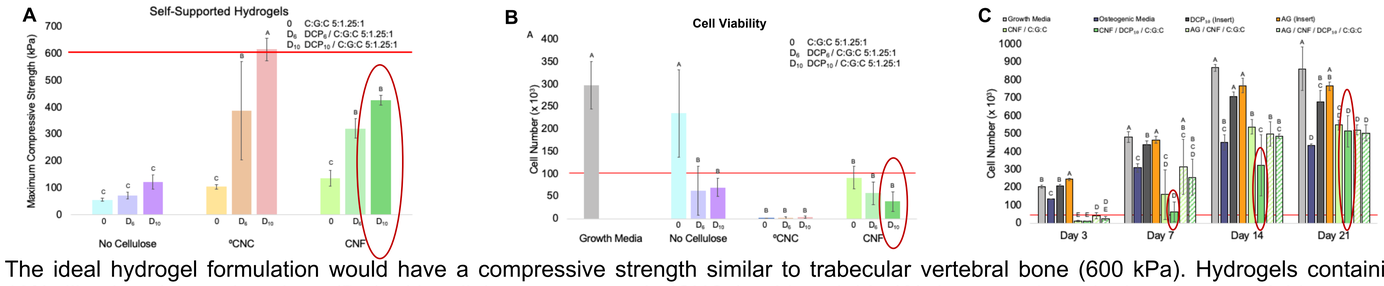


Radiographs from the previous spinal fusion rabbit study taken 6 weeks following spinal fusion of L5-L6 utilizing Allograft only (**A**) and cellulose nanofiber (CNF) / dibasic calcium phosphate (DCP) loaded hydrogel (**B**).



Manual palpation scoring demonstrating degree of vertebral immobilization in allograft, CNF/DCP hydrogel, and allograft/CNF/DCP hydrogel. The hydrogel without added allograft (*) achieved the most immobility following the spinal fusion procedure[1].

Hydrogel Formulation and Bioreactivity

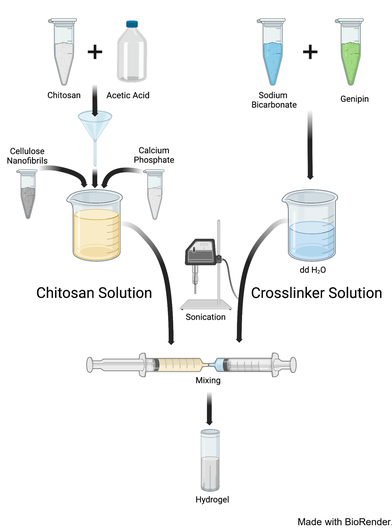


The ideal hydrogel formulation would have a compressive strength similar to trabecular vertebral bone (600 kPa). Hydrogels containing 10% dibasic calcium phosphate (D_{10}) with cellulose nanocrystals (CNCs) achieved this (**A**), however these hydrogels were highly cytotoxic when cultured with cells (**B**). A cell proliferation assay demonstrated that cellulose nanofiber (CNF) loaded hydrogel was less toxic (**C**). Hydrogels containing cellulose nanofibrils (CNFs) produced an acceptable compromise between compressive strength (~ 400 kPa) and cell viability[1].

Additional cell culture tests demonstrated cell viability with alamarBlue assay, osteoinductivity by ALP assay, and calcium deposition by alizarin red staining.

Histology following implantation of the D_{10}/CNF hydrogel into the quadriceps muscle of mice produced minimal cellular evidence of rejection[1].

Hydrogel Preparation



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Conclusions & Future Work

- Our osteoinductive hydrogel demonstrates superior osteomodulatory effects to allograft, the current gold standard for vertebral fusion procedures. We expect these osteoinductive effects to translate to our ongoing VCF rabbit study. CT scans, histological analysis, and mechanical testing will be conducted to determine the osteoinductive effects of our hydrogel.
- Further work is needed to optimize the hydrogel formulation to increase compressive strength while maintaining biocompatibility and feasibility for vertebral body injection.
- Osteoinductive hydrogels may have a future clinical utility in the repair of other types of fractures.

Acknowledgements & References

1. Darkow, Blake; Herbert, Joseph; Messler, Mark; Grisolano, Abigail; Hemmerla, August; Kimes, Austin; Lanza, Julien; Sun, Yisheng; Crim, Julia; Stensby, Derek; Wan, Caixia; Moore, Don; Ulery, Bret. Spinal Fusion Properties of Mechanically-Reinforced, Osteomodulatory Chitosan Hydrogels. BioRxiv [Preprint]. May 28, 2022 [Accessed June 27, 2022]. Available from https://doi.org/10.1101/2022.05.26.493540

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