

Acrylated Hyaluronic-Acid Based Hydrogel for the Treatment of Craniofacial Volumetric Muscle Loss

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Introduction/Objectives

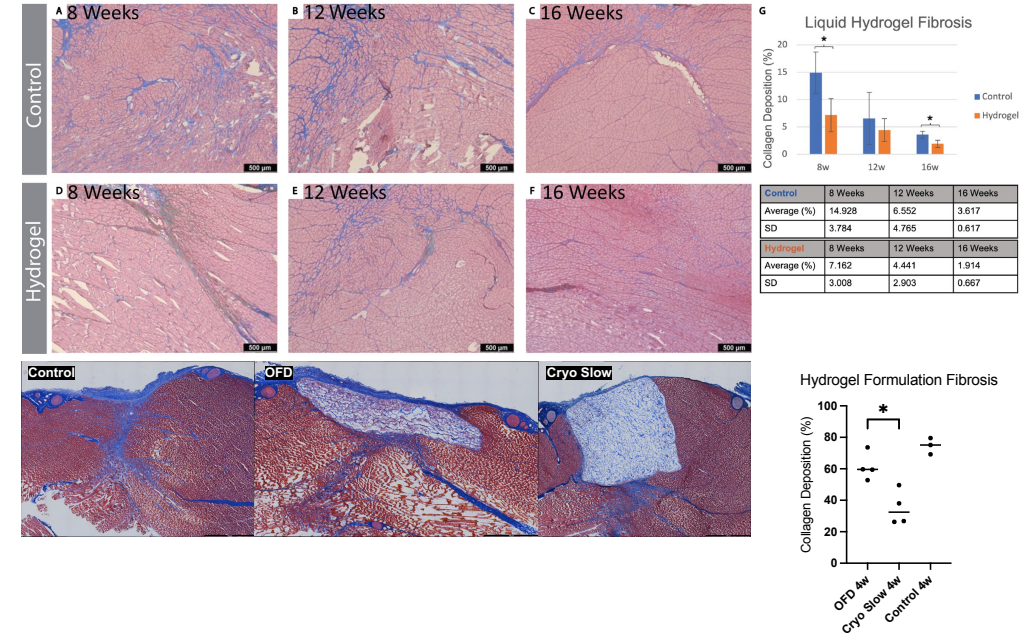
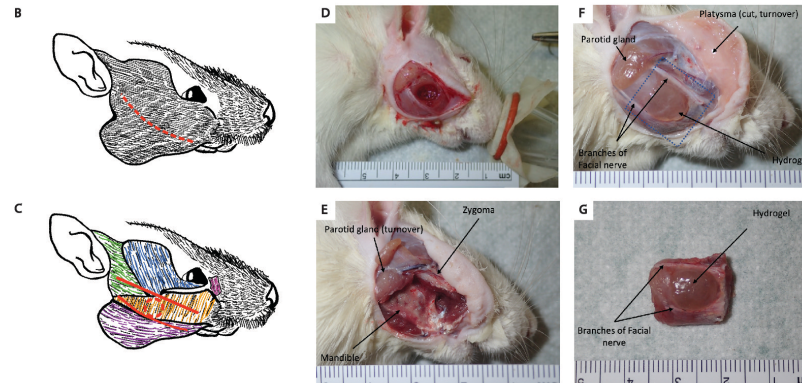
- Current treatment options for craniofacial volumetric muscle loss (VML) have disadvantages and are unable to fully restore normal function.
- In vivo* studies of tissue engineering strategies in animal models of extremity VML have shown promise, however very little research in craniofacial VML has been conducted.
- Hydrogels, such as semi-synthetic hyaluronic acid (HyA) hydrogels, can fill irregularly shaped defects, resemble natural extracellular matrix, and induce a minimal inflammatory response.
- We aimed to compare different formulations of an AcHyA hydrogel to optimize retention and evaluate histological outcomes of administration of an AcHyA hydrogel in a novel rodent model of VML.

Methods

- All animals underwent a surgically created VML injury that consisted of removal of approximately 10% of the right superficial masseter using a 5mm biopsy punch.
- The acrylated HyA (AcHyA) hydrogel contains bsp-RGD(15) adhesion peptide, MMP-sensitive crosslinker (MMP-13), and thiolated heparin macromers.
- Three different types of hydrogel were tested: liquid, OFD, and cryogel. Formulations of these 3 types included 3 different volumes of liquid (42 vs. 60 vs. 80 μ L) and 2 different heights and 3 different MMP-sensitive crosslinkers in the cryogel scaffolds.
- Masseter muscles were explanted at sacrifice and stained with Hematoxylin and Eosin (H&E) to assess defect size and with Masson's trichrome to compare collagen deposition between hydrogel-treated and nonrepaired control masseters.

Results

- A reduction in collagen deposition was observed among slow-breakdown cryogel-treated tissue compared to nonrepaired controls at 4 weeks (cryogel 35.20 ± 11.0 vs. control 74.64 ± 5.13 ; $p=0.002$), and among slow-breakdown cryogels compared to OFD hydrogels at 4 weeks (cryogel 35.20 ± 11.0 vs. OFD 61.40 ± 8.74 ; $p=0.01$).
- A reduction in collagen deposition was observed among liquid hydrogel-treated tissue compared to nonrepaired controls at 8 weeks (control 14.93 ± 3.78 vs. hydrogel 7.16 ± 3.01 ; $p=0.03$) and 16 weeks (control 3.62 ± 0.62 vs. hydrogel 1.91 ± 0.67 ; $p=0.02$).
- A lesser decrease in defect size among masseters treated with liquid hydrogel was observed compared to unrepaired controls at 2 and 4 weeks.
- The hydrogel was well-tolerated by the recipient animals, with no signs of infection, seroma, or rejection.



Conclusion

- AcHyA hydrogel is well tolerated and results in a decreased degree of fibrosis relative to an untreated control following masseter VML.
- These findings suggest the potential for use of hydrogel-based treatments for craniofacial VML and demonstrate a system for evaluating subsequent iterations of materials in VML injuries.

Ongoing Experiments

- The cryogel formulation had the greatest retention in the wound and the least degree of fibrosis and will be the formulation of choice in future studies.
- Continue analyzing masseters & comparing degradation of hydrogel *in vivo* between slow, medium, and fast cryogels at 8 and 12 weeks.
- Analyze the following parameters of muscle regeneration between cryogel formulations: Fiber cross-sectional area, muscle fibers with centrally located nuclei, eMHC expression, satellite cell activity, neovascularization, reinnervation.