



Collagen Type 0 as a non-mammalian bulk filler alternative for *in vivo* applications

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WHAT ARE BULK FILLERS?

Injectable bulking agents are space filling substances used to increase tissue bulk. Bulk fillers can be comprised of body fat, collagen, or another approved filler substance.

Bulk fillers are commonly used in the following applications:

- Dental bone void filler
- Incontinence injections
- Bone void fillers
- Dermal fillers
- Other injectable matrices

COLLAGEN AS BULK FILLERS

Collagen is an ideal choice for injectable bulk fillers, the resorbable nature of collagen reduces the long-term risk of a granuloma compared to permanent filler options. Collagen also benefits from being formulated into flowable suspensions allowing for a smaller injection site at the target tissue than more viscous solutions.

Mammalian sourced collagen can transfer multiple diseases to humans that non-mammalian sources cannot e.g., transmissible spongiform encephalopathies (TSEs) and foot and mouth disease (FMD). This risk of disease transmission has sparked regulatory concerns. In addition to regulatory concerns there are many religious and ethical issues that plague the use of mammalian collagen for medical applications.

Collagen is the most abundant protein in the extracellular matrix of connective tissue and has roles in signalling new tissue formation. Jellagen collagen is extracted from *Rhizostoma Pulmo* (the 'barrel jellyfish') and processed for medical applications, has been defined as Collagen Type 0 due to its ancient origin. Collagen Type 0 has proven biocompatibility, biodegradability, low immunogenicity, and cell-adhesive properties. Therefore, Collagen Type 0 is an ideal biomaterial for the reconstruction of tissue *in vivo*, without the drawbacks of mammalian-sourced collagens.



Study 1. A comparative MRI study of Jellyfish collagen, Hyaluronic acid and Acellular cadaver dermis in an in vivo model of injection medialisation laryngoplasty.

In this in vivo model the left recurrent laryngeal nerve was sectioned to create vocal cord paralysis. Two weeks later injection laryngoplasty was performed with Jellagen's Collagen Type 0, Hyaluronic acid and Collagen Type I (Human). MRI and histology were used to compared the injected materials.

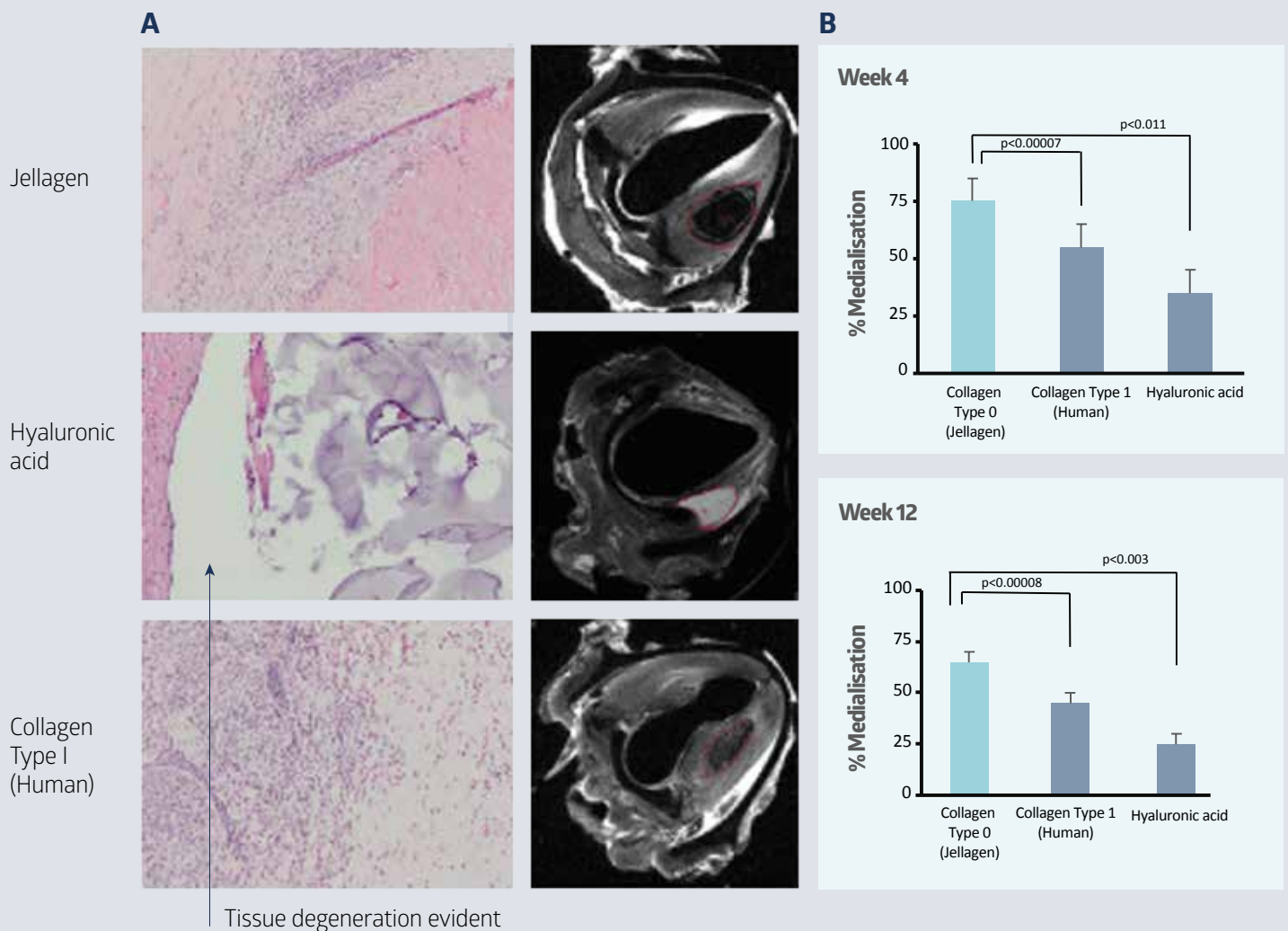


Fig. 1
 Superior cell and tissue structure shows Collagen Type 0 outperforms standard of care hyaluronic acid and human collagen type I (Fig.1A).
 MRI data demonstrates that Collagen Type 0 outperforms standard of care hyaluronic acid and human collagen type I and provides improved medialisation as well as increased glottal benefit with minimal tissue pathology (Fig.1B).



Study 2. Larynx proteomics after jellyfish collagen IL : Increased ECM /collagen and suppressed inflammation

Proteomic profile analysis was performed on paraffin embedded laryngeal tissues sections using nanoflow liquid chromatography electrospray ionisation tandem mass spectrometry followed by reactome gene ontology pathway analysis.

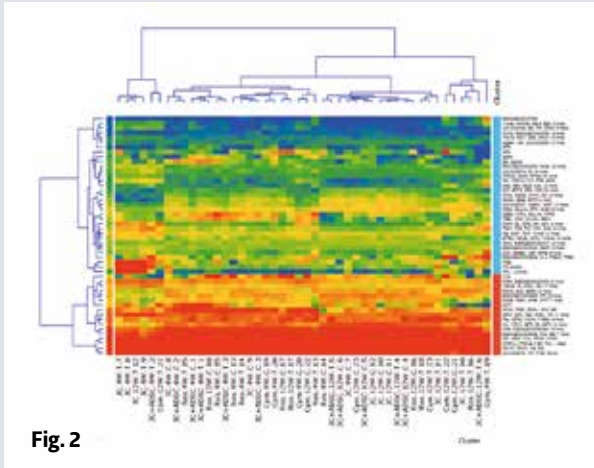


Fig. 2

Proteomic pathway data confirms Collagen Type 0 uniquely suppresses T1 specific inflammation. Collagen Type 0 was shown to enable angiogenesis which is vital for effective tissue repair. Additionally Collagen Type 0 upregulated Beta-oxidation pathways known to promote formation of new muscle fibres and the larger context of pre-regenerative signals. An important potential clinical benefit is the upregulation of fatty acid oxidation which may decrease scar formation (Fig.2)

CONCLUSIONS

Collagen Type 0- demonstrated superior cell & tissue structure and outperforms widely used hyaluronic acid and human cadaver collagen type 1.

Using MRI it was discovered that Collagen Type 0 medialisation volumes were 40% and 100% greater compared to Collagen type I (human) and hyaluronic acid respectively. No overt adverse reactions were noted with Collagen Type 0, whereas hyaluronic acid injections were associated with higher frequency of myocytic loss.

Unlike mammalian collagens and hyaluronic acid, Collagen Type 0 increased ECM formation, promoted collagen biosynthesis, elastic fibre formation and de novo protein translation and cellular metabolism. This is all indicative of a positive effect on cell metabolism and tissue regeneration.

Leading bulk filler products have short lived benefits. Collagen Type 0 has controlled batch reproducibility and optimal type B collagen fibres that support tissue regeneration. Injected Collagen Type 0 has shown no overall cytotoxicity which aids in the decreased resorption time. The increased retention of Collagen Type 0 in the tissue allows for prolonged benefits compared to predicate biomaterials.

FUTURE OPPORTUNITIES

Due to the unique properties of Collagen Type 0 described, we are investigating its potential in several clinical areas. Firstly, and as described in this case study, as a bulk filler in medical applications. Secondly, we are looking at how the unique biocompatible and regenerative properties of Collagen Type 0 can be utilised for other medical treatments. These include in the treatment chronic wounds and treatment of osteoarthritis with cartilage repair strategies.

Please see our case study on Collagen Type 0 in the treatment of chronic wounds.

References:

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