Biomaterial delivery vehicles improve acute retention of cells in the infarcted heart

Ellen T. Roche^{1,2*}, Conn L. Hastings^{3*}, Sarah A, Lewin², Dmitry E. Shvartsman², Yevgeny Brudno², Nikolay V. Vasilyev⁴, Fergal J. O'Brien³, Conor J. Walsh^{1,2}, Garry P. Duffy³, David J. Mooney^{1,2}

- 1. School of Engineering and Applied Sciences, Harvard University
- 2. Wyss Institute of Biologically Inspired Engineering
- 3. Royal College of Surgeons in Ireland
- 4. Boston Children's Hospital

* Authors contributed equally

<u>Introduction and Hypothesis:</u> Cell delivery to the infarcted heart has emerged as a promising therapy, but is limited by very low acute retention and engraftment of cells. The hypothesis was that acute retention can be improved with a biomaterial carrier, and the study compared several.

<u>Methods</u>: Cells were quantified 24 hours post-implantation in a rat myocardial infarct model Fig. 1a) in five groups (n=8per group); saline injection (current clinical standard), two injectable gels (alginate, chitosan) and two epicardial patches (alginate, collagen). For injectable groups 60ul of saline or gel containing 400,000 human mesenchymal stem cells was injected intramyocardially in the infarct border zone. 400,000 cells were seeded on alginate or collagen patches, and implanted on the epicardial surface at infarct border zone. At 24 hours, retained cells were quantified with an *in vivo* imaging system. Hearts were perfused and sectioned to stain for retained cells.

<u>Results:</u> All biomaterials significantly improved retention compared to a saline control, with 8 and 14-fold increases for alginate and chitosan injectables, and 47 and 59-fold increases achieved with collagen and alginate patches, respectively (Fig. 1b-c). Immunohistochemical analysis qualitatively confirmed these findings (Fig. 1d). Encapsulated/seeded cell survival was assessed in hypoxia/ischemia to further compare biomaterials.

<u>Conclusion</u>: Injectable gels and epicardial patches were demonstrated to improve acute retention of cells when compared to a saline control. Injectable gels enable immediate myocardial delivery while epicardial patches facilitate superior retention and could potentially sustain cell delivery over extended periods. These biomaterial approaches should be considered for future cell therapy applications.

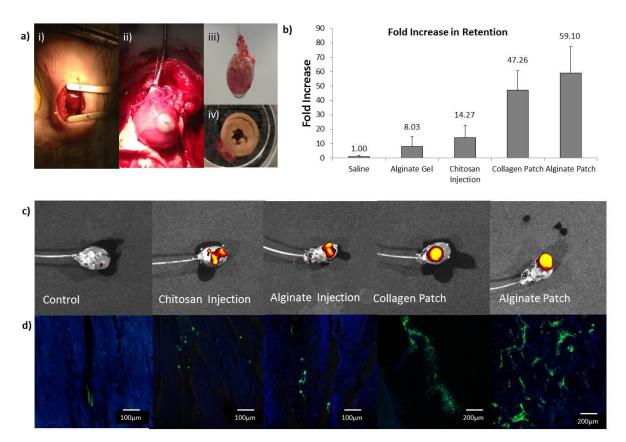


Figure 1: a) Procedural snapshots b-c) Cell retention after 24 hours d) Ventricle wall showing DAPI and implanted cells with GFP antibody (green) for each group