Appendix A. Supplementary Material

Appendix A.1. Histological sectioning

After diffusion tensor imaging, the injected specimens underwent serial histological sectioning. The tissue samples were fixed in 10% neutral buffered formalin, immersed in 70% ethanol, and embedded in paraffin. 20 5-µm sections were obtained with a step size of 300 µm, spanning across the thickness of each specimen, and Masson's trichrome staining was used to identify the myofibers, collagen fibers, and hydrogel. Sections were photographed with a Nikon SMZ 800 microscope. Histology was performed at Histoserv, Inc. (Germantown, MD).

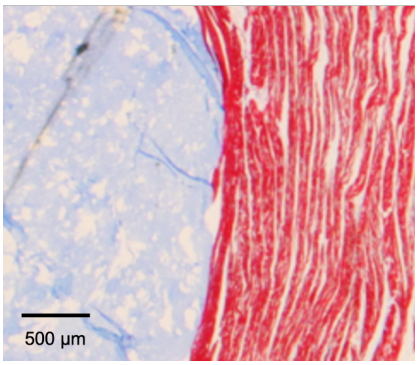

Fig. A.1: Histology. Masson trichrome stain of injected myocardium showing interface of tissue (red) and hydrogel (blue).

Appendix A.2. Maximum tangent modulus vs. injection volume

Maximum tangent modulus m was determined using the reaction forces computed on the mesh boundaries in all deformation modes for each of the parametric simulations. Simulations varied by injection placement in the transmural direction, injection volume, hydrogel stiffness, and post-MI myocardium material parameters. We simulated the myocardium without hydrogel inclusion to emulate the control response, using n = 3 meshes with identical fiber orientation mappings and material properties. To assess maximum tangent modulus m as a function of injection volume, group averages of all transmural placements (endo, mid, epi) were computed at each volume (0%, 1.5%, 5%, and 17%), n = 3 for each group. These computations were done separately for both post-MI time points (0 WK and 4 WK).

Group-averaged m was displayed as mean ± standard error of the mean (SEM). We used a two sample t-test to compare group averages, and p-values ≤ 0.05 were considered statistically significant. All statistical analysis was performed using MATLAB.

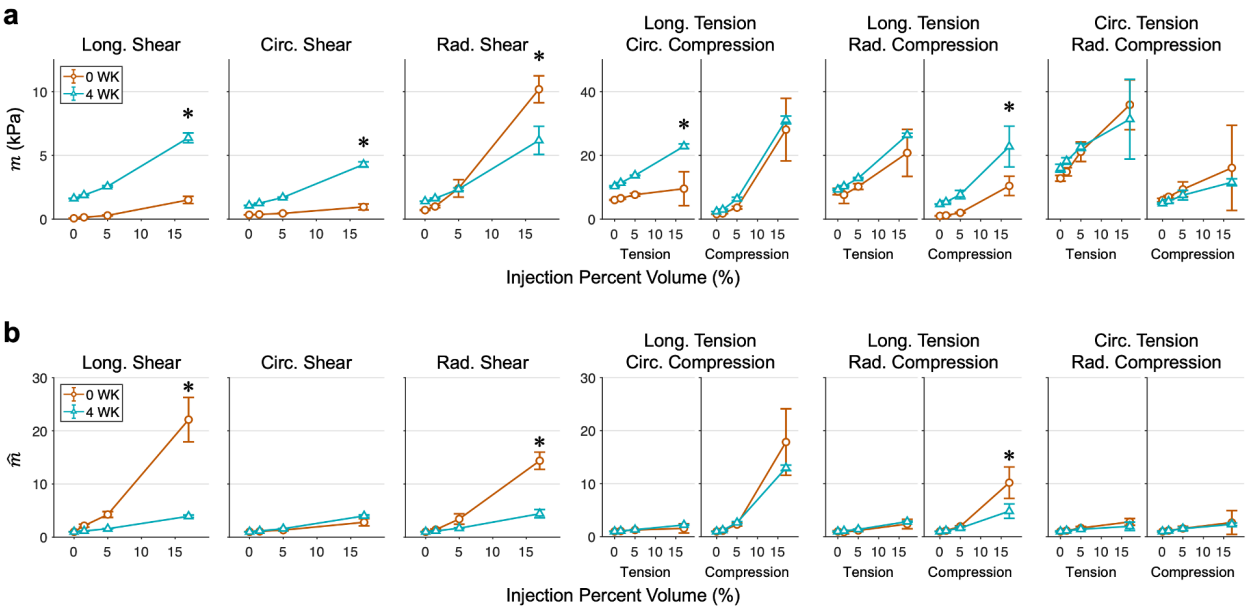

Fig. A.2: Maximum tangent modulus as a function of injection volume. (a) Absolute m and (b) normalized $\hat{m}$ derived from finite element simulations of injected myocardium with hydrogels of increasing volume for the 0 WK (orange) and 4 WK (blue) post-MI time points. Quantities displayed as Mean ± SEM. Significant differences between the 17% injection of the 0 WK and 4 WK time points indicated with $^*p \leq 0.05$.

Appendix A.3. Maximum principal strain vs. injection volume

At maximum deformation, the Green-Lagrange strain tensor $\mathbf{E}$ was calculated for all myocardium elements within a spherical region of interest centered in the cube domain, excluding both distal myocardium elements and hydrogel elements. A volume-averaged strain tensor $\bar{\mathbf{E}}$ was obtained by averaging each corresponding component of $\mathbf{E}$ across all elements in the region of interest and used to determine the maximum principal strain for the myocardium in each deformation mode. The maximum principal strain in each deformation mode E_1 was evaluated for all placement-volume combinations at both post-MI time points.

To assess maximum principal strain E_1 as a function of injection volume, group averages of all transmural placements (endo, mid, epi) were computed at each volume (0%, 1.5%, 5%, and 17%), n = 3 for each group. These computations were done separately for both post-MI time points (0 WK and 4 WK). Group-averaged E_1 was displayed as mean ± standard error of the mean (SEM).

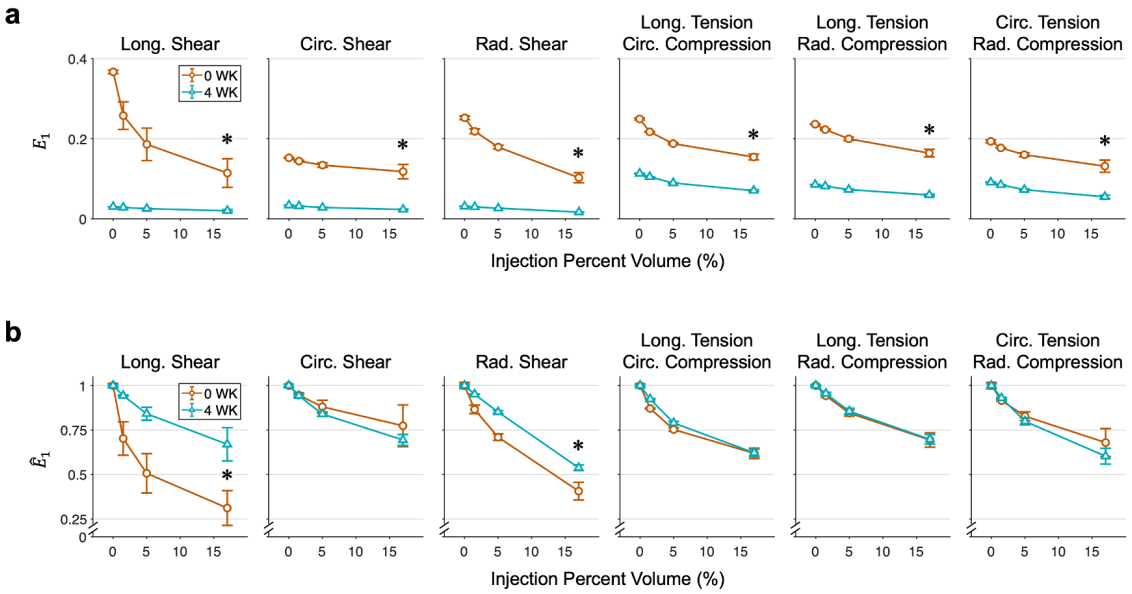

Fig. A.3: Maximum principal strain as a function of injection volume. (a) Absolute E_1 and (b) normalized $\hat{E}_1$ derived from finite element simulations of injected myocardium with hydrogels of varying placement and volume for the 0 WK (orange) and 4 WK (blue) post-MI time points. Quantities displayed as Mean ± SEM. Significant differences between the 17% injection of the 0 WK and 4 WK time points indicated with *p $\leq$ 0.05.

Appendix A.4. Maximum principal strain vs. injection stiffness

The maximum principal strain in each deformation mode E_1 was evaluated as a function of hydrogel modulus for the mid-placed inclusion of 17% cuboid volume. Evaluating changes in maximum principal strain as a function of hydrogel stiffness was performed using only the 17% injection volume with a mid placement.

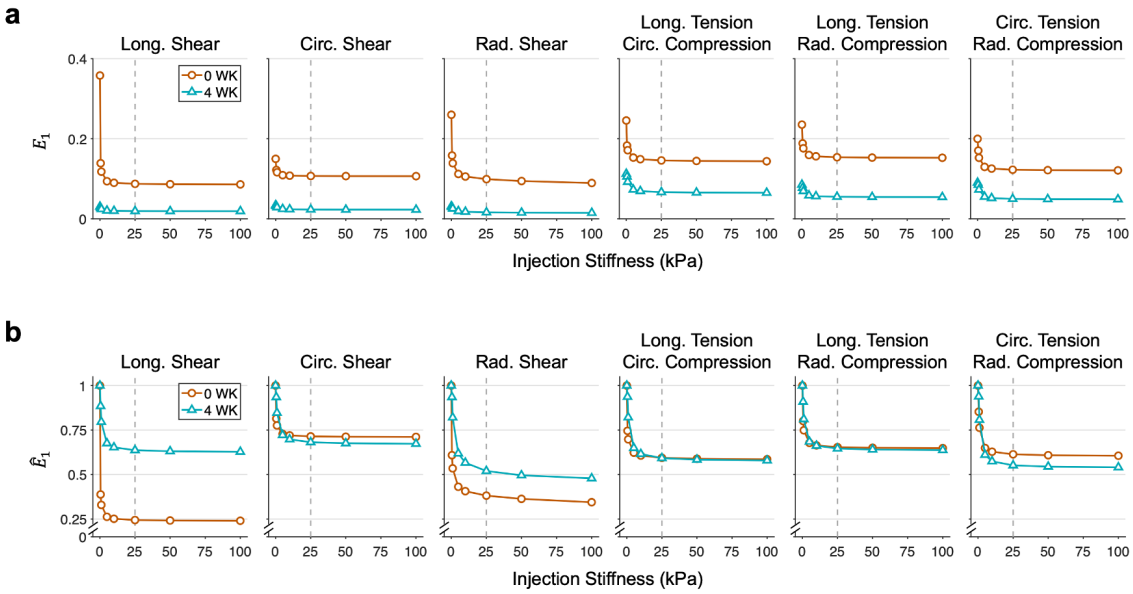

Fig. A.4: Maximum principal strain as a function of injection stiffness. (a) Absolute E_1 and (b) normalized $\hat{E}_1$ derived from finite element simulations of the 0 WK and 4 WK post-MI time points undergoing optimal deformations modes with increasing hydrogel modulus. The largest injection volume (17%) at mid placement is evaluated. Further increases in modulus have a minimal effect beyond stiffness values indicated by the dotted gray lines.