

# Injectable Hydrogel Scaffold Incorporating Microspheres Containing Cobalt-Doped Bioactive Glass for Bone Healing

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Table S1. Nominal and measured compositions of bioactive glasses.

| Bioactive<br>glass code | Nominal Composition (% mol) |       |                   |                               |      | Measured Composition (% mol)* |       |                   |                               |      |
|-------------------------|-----------------------------|-------|-------------------|-------------------------------|------|-------------------------------|-------|-------------------|-------------------------------|------|
|                         | SiO <sub>2</sub>            | CaO   | Na <sub>2</sub> O | P <sub>2</sub> O <sub>5</sub> | CoO  | SiO <sub>2</sub>              | CaO   | Na <sub>2</sub> O | P <sub>2</sub> O <sub>5</sub> | CoO  |
| G                       | 46.25                       | 26.87 | 24.37             | 2.50                          | -    | 46.41                         | 27.46 | 24.20             | 1.93                          | -    |
| G3Co                    | 45.56                       | 25.97 | 23.49             | 2.47                          | 2.47 | 46.12                         | 26.02 | 23.56             | 1.80                          | 2.50 |
| G5Co                    | 44.30                       | 25.82 | 23.33             | 2.42                          | 4.10 | 44.26                         | 27.08 | 22.81             | 1.82                          | 4.03 |
| G7Co                    | 43.14                       | 25.56 | 23.12             | 2.36                          | 5.79 | 43.21                         | 26.24 | 22.91             | 1.79                          | 5.85 |

\* Measured by X-ray fluorescence spectroscopy. G: cobalt-free bioactive glass; GxCo: 3%, 5% and 7% w/w cobalt-doped bioactive glass.

Table S2. Release of cobalt ions from the bioactive glasses and MHSs.\*

| Cobalt Concentration (ppm) (mean $\pm$ SD) |                   |                  |                  |                 |                 |                  |
|--------------------------------------------|-------------------|------------------|------------------|-----------------|-----------------|------------------|
| Time                                       | Bioactive glasses |                  |                  | MHSs            |                 |                  |
|                                            | G3Co              | G5Co             | G7Co             | A-S-G3Co        | A-S-G5Co        | A-S-G7Co         |
| Day 3                                      | 4.70 $\pm$ 0.27   | 7.20 $\pm$ 0.36  | 11.00 $\pm$ 0.10 | 2.73 $\pm$ 0.12 | 6.76 $\pm$ 0.12 | 9.20 $\pm$ 0.10  |
| Day 7                                      | 5.50 $\pm$ 0.61   | 14.09 $\pm$ 0.08 | 18.20 $\pm$ 0.70 | 3.26 $\pm$ 0.06 | 9.36 $\pm$ 0.11 | 13.70 $\pm$ 0.17 |
| Day 14                                     | 4.20 $\pm$ 0.30   | 12.76 $\pm$ 0.06 | 7.03 $\pm$ 0.05  | 1.70 $\pm$ 0.10 | 7.5 $\pm$ 0.20  | 8.60 $\pm$ 0.10  |

\* Microsphere-containing hydrogel scaffolds. GxCo: 3%, 5% and 7%w/w cobalt-doped bioactive glass; A-S-GxCo: alginate hydrogel containing microspheres made from silk fibroin/gelatin loaded with bioactive glass doped with 3%, 5% and 7% w/w cobalt.

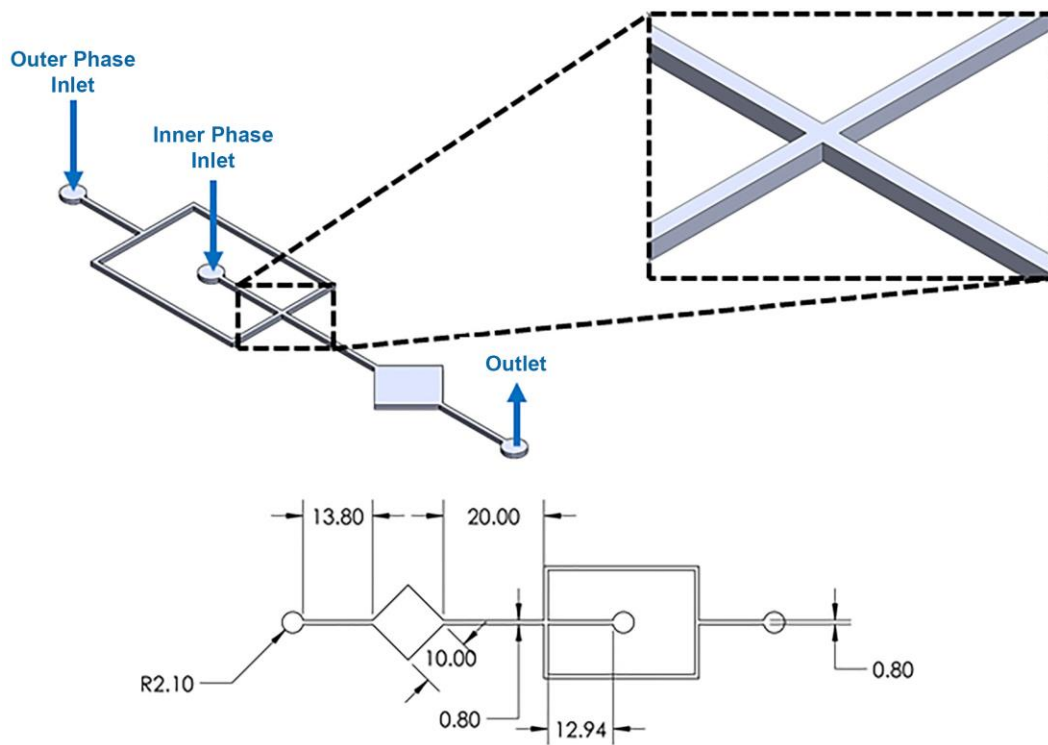


Figure S1. Microfluidic device design. (a) Schematic view of the microfluidic device used to generate silk fibroin/gelatin microspheres loaded /not loaded with bioactive glass, (b) a view of the main dimensions (all dimensions are in mm).

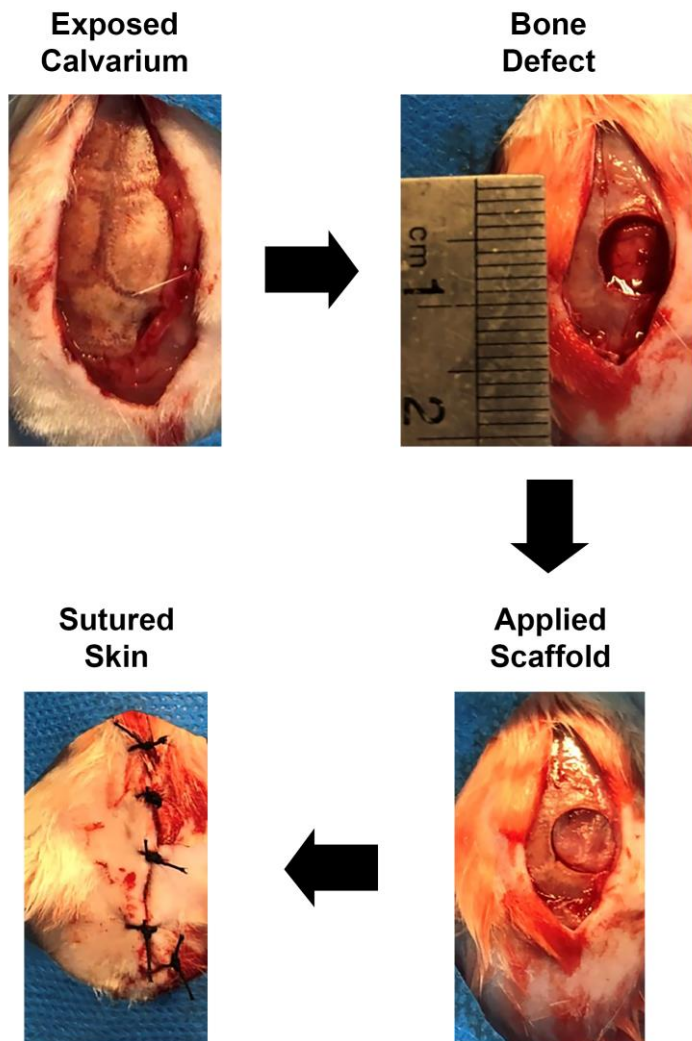


Figure S2. Surgical procedure involving surgical interventions to create calvarial defect in rats and application of the scaffold at the defect site.