

## Bioactive Glass Scaffolds for Bone Tissue Engineering

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### Introduction

In materials science, the ability to develop porous constructs with high mechanical strength is important for a broad range of emerging applications, including filters, catalyst support, and tissue engineering scaffolds. Particularly for orthopedic surgery, the regeneration of large bone defects in load-bearing limbs remains a challenging problem that require scaffolds that combine the strength required for a load bearing application with the large porosities needed to ensure cell survival and tissue regeneration.

Direct ink write as a layer-by-layer assembly technique has been used to fabricate constructs with materials including polymeric, sol-gel, and ceramic inks. The technique can be used to build scaffolds whose structure follows a computer design. In that way, the scaffold architecture can be controlled and optimized to achieve the desired mechanical response, accelerate the bone-regeneration process, and guide the formation of bone with the anatomic cortical-trabecular structure. The aim of this work was to fabricate bioactive 6P53B glass scaffold by direct-ink-write assembly of a hydrogel-based ink, and to evaluate their in vitro degradation and mechanical response.

### Experimental

Bioactive 6P53B glass with the composition (wt%): 52.7 SiO<sub>2</sub>, 10.3 Na<sub>2</sub>O, 2.8 K<sub>2</sub>O, 10.2 MgO, 18.0 CaO, and 6 P<sub>2</sub>O<sub>5</sub> was used in the present study. Glass inks were created by mixing 30 vol% glass particles in 20 wt% Pluronic® F-127 solution. Glass scaffolds were fabricated by printing the inks through a 100 μm nozzle (EFD precision tips, EFD, East Providence, RI) using a robotic deposition device (RoboCAD 3.0, 3-D Inks, Stillwater, OK). After printing, the scaffolds were air-dried and sintered at 700°C for 1 hr.

The porosity of the sintered glass scaffolds was measured using the Archimedes method. Scanning electron microscopy, SEM, (Hitachi S-4300, Tokyo, Japan) was used to observe the microstructure of the scaffolds. Synchrotron X-ray micro computed tomography (SR microCT) was used to obtain a three-dimensional perspective of the scaffold. Scanning was conducted at the Advanced Light Source (ALS-LBNL, Berkeley, CA) with 22 keV monochromatic X-rays and a 4.4 μm voxel size (resolution). The degradation of the scaffolds and their conversion to HA were evaluated as a function of immersion time of the scaffolds in an SBF with a starting pH = 7.2 at 37°C, as described in detail elsewhere [1]. The degradation and conversion process is accompanied by a weight loss, and this weight loss versus time was used to monitor the conversion kinetics. The compressive

strength of the glass scaffolds was measured by performing uniaxial tests on cubic blocks (3 × 3 × 3 mm) cut from the sintered specimens. Surface grinding was conducted on the blocks to ensure that the two tested ends were flat and parallel. The samples were compressed in the direction parallel to the pore orientation on a servo-hydraulic testing machine (MTS810, MTS Systems, Eden Prairie, MN) at a cross-head speed of 0.5 mm/min. At least eight samples were tested to get statistically reliable values.

### Results

Three-dimensional glass scaffolds with precisely defined rod diameter, spacing, and number of layers were patterned by extruding the glass ink through the 100 μm tip (**Figure 1**). **Figure 1a** shows the sintered scaffold consisting of square pores with the size of 250 μm. The printed rods had a smooth surface and bonded well to the previous layer (**Figure 1b**).

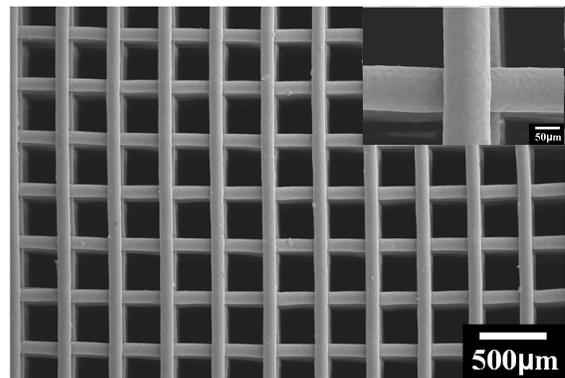


Fig. 1 SEM image of sintered scaffold and detailed adhesion of the rods (inset)

The porous glass scaffold had a compressive strength of 136 MPa representing specific properties comparable to that of cortical bone but with porosity comparable to trabecular bone (60%). The strength of this porous glass scaffold is ~ 100 times that of polymer scaffolds and 4 - 5 times that of ceramic and glass scaffolds with similar porosity reported elsewhere (**Figure 2**). The elastic modulus, determined from the approximately linear region in the stress-strain curve, was 2.0 GPa, within the range of the value for trabecular bone (0.1 - 5 GPa). The high mechanical strength of the freeze-cast scaffold is attributed to its anisotropic structure consisting of parallel ceramic lamellae. Anisotropic structure has been commonly observed in biological systems like wood, bone, cork, and glass sponge, and has been reported to be responsible for the ability to efficiently optimize the

strength-to-density and stiffness-to-density ratio. The work in this study might provide a new avenue for the fabrication of light yet strong materials.

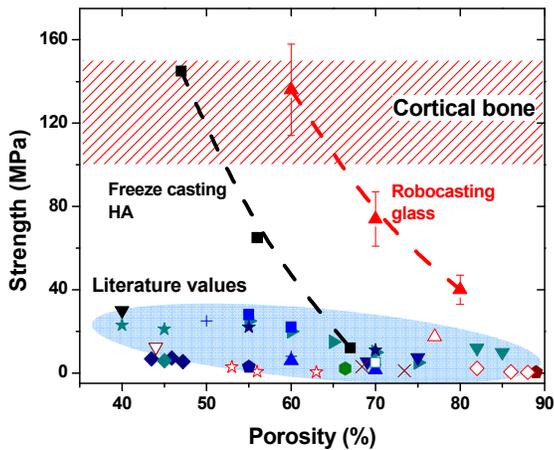


Fig. 2 Compressive strength vs. porosity of glass scaffolds compared with literature values. As a reference, the compressive strength of cortical bone has been reported to be in the range of 100-150 MPa in the direction parallel to the axis of orientation (long axis) [2,3]

The scaffolds showed a gradual degradation when immersed in SBF, and the pH of the solution increased with the immersion time (Figure 3). The weight loss of the scaffold increased rapidly during the first 100 h of immersion, slowed between 100–400 h, and reached a nearly constant, limiting value above ~400 h. The limiting weight loss was 4.5 %. The change in pH of the SBF, resulting from the reactions accompanying the conversion of the glasses to HA, followed the same trend as the weight loss data.

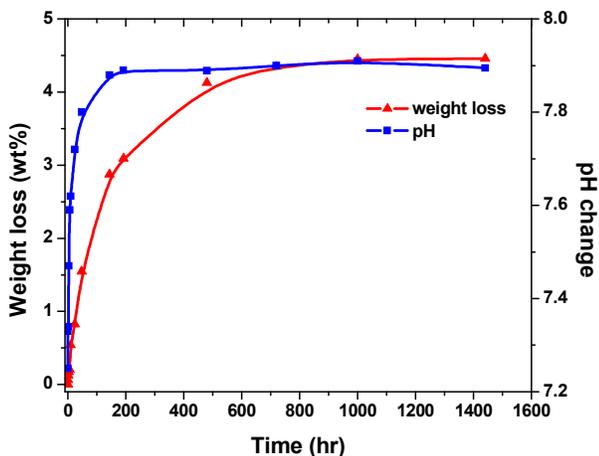


Fig. 3 Weight loss of glass scaffolds and pH change of the solution upon immersion in SBF.

After two weeks, the scaffold surface was covered with a layer of nanosized crystals (Figure 4), which was confirmed to be HA by X-ray diffraction. The thickness of the layer was determined to be ~5  $\mu\text{m}$  by observing the

cross sections using SEM. The formation of the HA on the glass surface has been reported to be responsible for the strong bonding between the scaffold and hard tissues. The fast formation of the nanosized HA layer is usually considered an indication of good in vitro bioactivity. Our processing approach does not crystallize or degrade the bioactive behavior of the 6P53B glass.

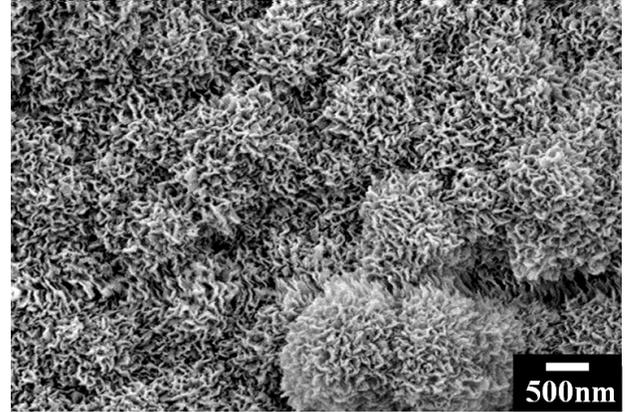


Fig. 4 Microstructure of the rod surface after immersion in SBF for 14 days.

## Conclusions

We have developed highly porous and strong glass scaffolds by direct-ink-write assembly of a hydrogel-based glass ink. The sintered glass scaffolds show a compressive strength comparable to human cortical bone, an indication of their excellent potential for the repair and regeneration of load-bearing bone defects. The use of glasses also opens new possibilities, as their composition can be easily tailored to manipulate bioactivity and biodegradation rates as well as the release kinetics of different ions.

## References

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