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Modelling of the strength–porosity relationship in glass-ceramic foam scaffolds for bone repair

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Abstract

Foam-like glass-ceramic scaffolds based on three different glass compositions (45S5 Bioglass and two other experimental formulations, CEL2 and SCNA) were produced by sponge replication and characterized from morphological, architectural and mechanical viewpoints. The relationships between porosity and compressive or tensile strength were systematically investigated and modelled, respectively, by using the theory of cellular solids mechanics or quantized fracture mechanics. Models results are in good agreement with experimental findings, which highlights the satisfactory predictive capabilities of the presented approach. The developed models could contribute to improve the rational design of porous bioceramics with custom-made properties. Knowing the scaffold recommended strength for a specific surgical need, the application of the models allows to predict the corresponding porosity, which can be tailored by varying the fabrication parameters in a controlled way so that the device fulfils the desired mechanical requirements.

Keywords: Scaffold; Glass-ceramic; Strength; Cellular solids mechanics; Quantized fracture mechanics

1. Introduction

Bioceramics constitute a subset of ceramic materials that are specially designed for the repair and reconstruction of diseased or damaged parts of the body. As reported by Dorozhkin in a valuable historical review,[1] plaster of Paris (calcium sulphate) was the first experimented artificial bioceramic: ancient literature dating back to 975 AD notes that calcium sulphate was useful for setting broken bones in *ex vivo* applications and, by the end of the 19th century, orthopaedic surgeons began to use plaster of Paris as a bone-filling substitute *in vivo*. Over the years, tens of bioceramic compositions have been tested, ranging from inert ceramics (*e.g.* alumina, zirconia and composites thereof) and calcium orthophosphates (due to the chemical similarity to mammalian bones and teeth) to bioactive glasses (amorphous ceramics).[2]

To date, bioceramics have been preferentially proposed for hard tissue repair covering all areas of the skeleton (*e.g.* healing of bone defects, fracture treatment, total joint replacement, bone augmentation, cranio-maxillofacial and orbital reconstruction, spinal surgery, dental field),[3–7] but in the last two decades their suitability for soft tissue engineering (*e.g.* glass fibres for muscle and nerve regeneration) has been also suggested.[8,9]

Since the invention of 45S5 Bioglass® by Hench and associates in the early 1970s,[10] silicate bioactive glasses have been the subject of great interest in the field of bioceramics due to their unique property to form both *in vitro* and *in vivo*, when exposed to physiological fluids, a surface apatite layer having the ability to tightly bond to the surrounding bone tissue. This is a key feature, as the clinical success of an implantable biomaterial primarily requires the achievement of a stable interface with host tissue, as well as an adequate matching of the mechanical behaviour of the implant with the tissue to be replaced.[11] In order to fulfil

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the latter requirement, bioactive glasses are often designed into the form of three-dimensional (3-D) porous scaffolds, which act as templates supporting and directing tissue in-growth and regeneration.[12,13] In this regard, different methods have been proposed to produce glass or glass-ceramic (depending on the sintering conditions) scaffolds, including starch consolidation,[14] H_2O_2 foaming,[15] gel-casting,[16] sponge replication,[17–21] polyethylene (PE) particles burning-out,[22–24] directional freeze drying[25,26] and software-guided manufacturing methods.[27–29]

One of the key challenges in scaffold design is the achievement of a satisfactory balance between adequate porosity, that should allow biological fluid flow and cells migration, and mechanical strength, that should be comparable to that of cancellous bone; hence, under this perspective, the development of porosity–strength relationships are of utmost importance in the attempt at optimizing the architectural properties of scaffolds, ideally at a pre-processing stage. Looking at the broad field of ceramic science, many mechanical property–porosity relationships for porous ceramics have been proposed over the years, as critically discussed by Pabst et al. in a valuable review[30]; as to porous bioactive glasses and bioceramics in general, however, the relevant literature is relatively scarce.

Reviewing the data from the literature, Gerhardt and Boccaccini[12] applied linear fitting and, in most cases, found an acceptable negative linear relationship between glass scaffold porosity and compressive strength (Fig. 1); however, the linear interpolation fails to hold for ultra-porous 45S5 Bioglass® scaffolds (porosity above 90 vol.%)[17] due to the onset of instability phenomena promoting the collapse of the scaffold micro-architecture. Baino et al.[23] proposed quadratic and cubic models correlating the theoretical porosity, established at the design stage, with the final pore content and compressive strength of glass-ceramic scaffolds fabricated by PE burning-out method; second-order polynomial fitting was also proposed to obtain compressive strength–porosity relationships for bioactive glass foams.[21]

A linear correlation was also established between porosity and elastic modulus of glass-ceramic scaffolds using ultrasonic wave propagation;[31] a second-order polynomial Young's modulus–porosity relationship was assessed in the modelling of the mechanical properties of a face-cubic-centred scaffold microstructure.[32] Hellmich and associates modelled the non-linear relationship between porosity and elastic modulus of different porous bioceramics by applying homogenization of heterogeneous materials and micromechanical theory of porous solids.[33]

Following the hierarchical structure of natural bone, Chen et al.[34,35] recently used a bottom-up approach and proposed a geometrical, general model for porous scaffolds with a structural hierarchy to optimize tissue regeneration; they studied its basic mechanical constants and elastic-plastic stress–strain behaviour, showing that the mechanical properties are comparable to those of natural bone. Tancret et al.[36] considered the porosities at both the micro- and macro-scale and presented a hierarchical model to predict the mechanical behaviour of biphasic calcium phosphate scaffolds.

It is worth mentioning that finite element methods (FEMs) have been gradually employed to study the mechanical behaviour of bone tissue engineering scaffolds,[37] often in combination with advanced imaging techniques (*e.g.* X-ray micro-computed tomography[38,39]), by which the precise geometric model of the scaffold can be reconstructed. The method can thoroughly examine the stress–strain responses of scaffolds and the FEM-based quantitative analysis is helpful in understanding the mechanical stimuli on cells and local stress distribution in the scaffolds.

In this work, foam-like scaffolds based on three different bioactive glass formulations were produced by the sponge replication method and characterized from morphological, architectural and mechanical viewpoints. The relationships between porosity and compressive or tensile strength were modelled following two different approaches, involving the application of cellular solids or quantized fracture mechanics(QFM) theories, respectively.

2. Experimental

2.1. Synthesis of the starting glasses

Three melt-derived glass formulations were used as starting materials for producing 3-D scaffolds by the sponge replication method. The molar compositions of the glasses are reported in Table 1 and correspond to Hench's 45S5 Bioglass, well known in the biomedical field since the early 1970s and commercialized worldwide since 1985,[10] and CEL2 and SCNA, two experimental SiO_2-based glasses that have been originally developed and studied by Vitale-Brovarone and associates at Politecnico di Torino.[18,40–43] All glasses were prepared by melting the required quantities of high-purity reagents (purchased from Sigma–Aldrich) in a platinum crucible in air (raw products and melting conditions are reported in Table 1). The melt was then quenched into cold water to obtain a "frit" that was later ground by using a six-ball zirconia mill, and the glass powders were eventually sieved through stainless steel sieves (Giuliani Technologies, Italy) to obtain particles with size below 32 μm to be used for scaffolds fabrication.

For comparative purposes, a commercial 45S5 Bioglass® powder (NovaBone, USA), with a particle size below 5 μm, was used as received for making a reference batch of scaffolds.

From here on, the two types of 45S5 Bioglass powders will be distinguished as follows: the melt-derived 45S5 Bioglass sieved below 32 μm will be referred to as BG32, whereas the commercial one will be denoted as BG5.

2.2. Scaffolds fabrication

Sponge replication was chosen for making scaffolds due to its excellent suitability to obtain porous bioceramics with trabecular architecture closely mimicking that of cancellous bone.[13,17] The processing schedule adopted in this work has been extensively described elsewhere.[19] Briefly, small cubic blocks of a commercial open-cells polyurethane (PU) sponge (density of the porous polymer about 20 kg m^{-3}) were coated with glass powder by being impregnated in a water-based