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Short communication

A numerical model of heterogeneous surface strains in polymer scaffolds

Elbert Baas*, Jan Herman Kuiper

Institute of Science & Technology in Medicine, Keele University, Thornburrow Drive, Hartshill, Stoke-on-Trent, Staffordshire ST4 7QB, UK

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Abstract

In vitro bone tissue growth inside porous scaffolds can be enhanced by macroscopic cyclic compression of the construct, but the heterogeneous strain generated inside the construct must be investigated to determine appropriate levels of compression. For this purpose a linear micro-finite element (μFE) technique based on micro-computed tomography (μCT) was verified for the calculation of local displacements inside polymer scaffolds, from which local strains may be estimated. Local displacements in the axial direction at the surface of microstructures inside the scaffold in 60 locations were calculated with the μFE model, based on compression simulation of a μCT reconstruction of the scaffold. These displacements were compared with accurately measured displacements in the axial direction in the same polymer scaffold at the same 60 locations, using a micro-compression chamber and μCT reconstructions of the scaffold under two fixed levels of compression (5% and 0%). The correlation between the calculated and the measured displacements, after correction for the dependence of the axial displacement on the axial position, was $r = 0.786$ ($r^2 = 0.617$). From this we conclude that the linear μFE model is suitable to estimate local surface strains inside polymer scaffolds for tissue engineering applications. This technique can not only be used to determine appropriate parameters such as the level of macroscopic compression in experimental design, but also to investigate the cellular response to local surface strains generated inside three-dimensional scaffolds.

Keywords: In vitro skeletal tissue engineering; Polymer scaffolds; Micro-computed tomography; Local surface strain; Micro-compression

1. Introduction

Applying cyclic mechanical strains to bone cells seeded in scaffolds can increase the production of markers for bone tissue formation (El Haj et al., 1990; Walker et al., 2000; Mullender et al., 2004). Typically, the applied strain is determined from the macroscopic deformation of the scaffold in which the tissue is growing (Yang et al., 2004; Wood et al., 2006). However, uniform macroscopic compression of a porous material can generate a very inhomogeneous distribution of local strains inside the sample, as shown by micro-finite element (μFE) modelling of trabecular bone (Van Rietbergen et al., 1999). The same is likely to hold for porous three-dimensional (3D) scaffolds as used for skeletal tissue engineering. If true, then determining the range of local strains inside these scaffolds will be important to determine the appropriate external deformation regimes for these scaffolds. Determining local strains will also be important to link between local bone formation and local strains.

Mechanical analyses of various types of scaffolds are regularly conducted using micro-computed tomography (μCT) reconstructions and numerical μFE modelling, to determine the apparent macroscopic properties of scaffolds (Jacques et al., 2004). The feasibility of this technique to estimate local strain inside these scaffolds has only been published for hydroxyapatite and bioglass-composite scaffolds (Lacroix et al., 2006). These scaffold materials with high stiffness form a fraction of the materials commonly used in bone tissue engineering applications. Biodegradable polymers, e.g. poly(L-lactic acid) (PLA, PLLA), chitosan and PLGA, form a wide range of alternative scaffold materials. Their linear elastic range can be as small as 1% (Rezgui et al., 2005), which may pose problems when using voxel-based linear μFE methods. The aim of this study was to experimentally verify the suitability of these methods for local surface displacement estimation inside 3D polymer

*Corresponding author. Tel.: +44 1782 554 253; fax: +44 1782 717 079.
E-mail address: e.baas@med.keele.ac.uk (E. Baas).

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scaffolds and to determine the distribution of surface strain inside 3D polymer scaffolds.

2. Materials and methods

2.1. Scaffold preparation

A scaffold (diameter = 9 mm, height = 4 mm, porosity = 90% ± 2 SD) was made from medical grade poly(L-lactic acid) (PLLA) (Plurasorb™, Gorinchem, The Netherlands) (Yang et al., 2002). Briefly, the polymer was dissolved in chloroform, mixed with 250–355-μm-diameter sodium chloride crystals (Sigma, UK) of irregular shape, and placed into a cylindrical mould (diameter = 9 mm). Following chloroform evaporation, salt was leached out in gently stirred and regularly refreshed double-distilled water over a period of 3 days. The resulting porous PLLA cylinder was cut to a height of 4 mm with a single-edged blade in a guiding cutting tool, to obtain plane–parallel surfaces for compression.

2.2. Micro-compression

An experiment was designed in which the scaffold, while under compression, was scanned with a μCT scanner. For this purpose a micro-compression chamber was built (Fig. 1) with a radio-translucent window, in which a scaffold could be held and imaged under fixed compression. The chamber was similar in concept to a device for μCT imaging of trabecular bone samples under microscopic levels of compression (Müller et al., 1998), but specifically designed for the lower load levels associated with micro-compression of polymer scaffolds. Micro-compression was applied with a purpose-made PC-controlled loading rig with 1.25 μm step resolution.

2.3. μCT imaging and post-processing

For the verification measurement, the scaffold was scanned under macroscopic uniaxial compression of 5% (200 μm) and rescanned after relaxation with a μCT scanner (μCT40, Scanco Medical AG, Zürich, CH, Table 1). An integrated scanner software was used to generate image reconstructions using a filtered back projection algorithm. A Gauss-filter was applied (sigma = 1.2, support = 2) to reduce the noise in the reconstructed 3D images. The resultant voxel dimensions were 15 μm in *X*-, *Y*- and *Z*-direction (15^3 μm^3).

To generate a μFE model, another μCT scan of the relaxed scaffold was made in a smaller sample holder using the same scan parameters to obtain a reconstruction at a resolution of 6^3 μm^3. This reconstruction was then downscaled to 15^3-μm^3-voxel resolution, giving a reconstruction with improved structural quality compared with that of the relaxed scaffold inside the micro-compression chamber. The downscaled reconstruction was aligned with the reconstructions of the micro-compression experiment.

The scaffold-phase in each reconstruction was segmented using a threshold of 20. Values below 20 were labelled as void, values of 20 or above as scaffold. The images of the compressed and relaxed scaffold from the micro-compression chamber and from the sample holder were stored as matrices μCT-$R_{5\%}$, μCT-$R_{0\%}$ and μCT-R_{fe}, respectively.

2.4. μFE model

The linear μFE model was based on μCT-R_{fe}. Loosely connected microstructures were removed from the reconstruction. The FE mesh was generated with FE-software v1.04 (Scanco Medical AG, Zürich, Switzerland), by converting each scaffold-voxel of μCT-R_{fe} to 8-node isotropic elastic brick elements (Van Rietbergen et al., 1996; Young's

Table 1
Parameters used for μCT acquisition of polymer scaffolds

Beam-type	Cone-beam
Intensity	145 μA
Energy	55 kV
No. of projections	2000
Integration time	200 ms
Frame averaging	5 ×
Acquisition time	±4.5 h

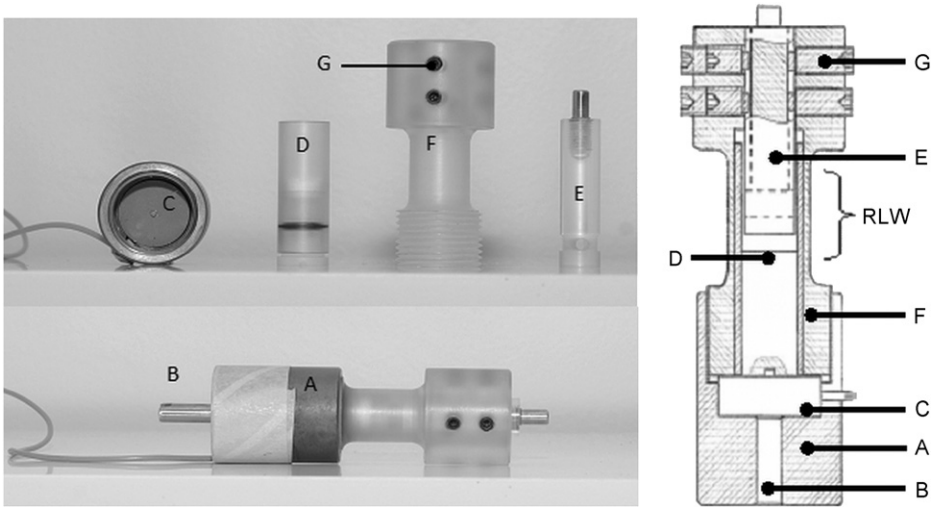

Fig. 1. An image and complementary schematic drawing of the micro-compression chamber. The micro-compression device is made up of a brass base (A) that can be mounted in the micro-CT scanner with a stainless-steel pin (B). A 30 N load cell (DS-Europe, BC302) is embedded in the base (C). On top of the load cell rests a free-moving polycarbonate watertight cup in which the scaffold is placed (D). A polycarbonate piston (E) comes down into this cup to compress the scaffold. The piston contains a hole near its end to take care of the rising liquid level due to compression of a wet sample and to prevent hydrostatic pressure. An outer polycarbonate cylinder is screwed tight into the base to guide the cup and piston (F). Four grub screws are inserted at the top of the outer cylinder to fix the piston at the desired level for compression of the piston (G). The grub screws have a brass pad that fits into a slot in the piston to prevent friction and/or rotation during compression and damage to the piston during fixation. The thin polycarbonate walls of the cup and the outer cylinder around the sample space create a radiolucent window (RLW) for μCT imaging.