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Research Paper

Novel methodology for assessing biomaterial–biofluid interaction in cancellous bone

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ABSTRACT

Understanding the cement flow behaviour and accurately predicting the cement placement within the vertebral body is extremely challenging. Vertebral cancellous bone displays highly complex geometrical structures and architectural inhomogeneities over a range of length scales, thus making the scientific understanding of the cement injection behaviour difficult in clinical or cadaveric studies. Previous experimental studies on cement flow have used open-porous aluminum foam to represent osteoporotic bone. Although the porosity was well controlled, the geometrical structure of each of the foams was inherently unique. This paper presents novel methodology using customized, reproducible and pathologically representative three-dimensional bone surrogates to help study biomaterial—biofluid interaction. The aim was to provide a robust tool for comprehensive assessment of biomaterial injection behaviour through controlling the bone surrogate morphology and the injection parameters (i.e. needle gauge, needle placement, flow rate and injected volume), measuring the injection pressure, and allowing the visualization and quantitative analysis of the spreading distribution. This methodology provides a clinically relevant representation of cement flow patterns and a tool for validating computational simulations.

1. Introduction

Osteoporosis and other skeletal pathologies such as spinal metastasis and multiple myeloma, compromise the structural integrity of the vertebra, thus increasing its fragility and susceptibility to fracture (Bouxsein, 2003; Currey, 2001; Myers and Wilson, 1997). During vertebral augmentation procedures, bone cement is injected through a cannula into the cancellous bone of a fractured vertebra with the goal of relieving pain and restoring mechanical stability. Further, prophylactic surgical stabilization is often performed to reinforce a structurally compromised vertebra adjacent to the index level and decrease its susceptibility to

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fracture (Ortiz and Mathis, 2010; Mathis and Wong, 2003). The bone cements used are chemically complex, multi-component and non-Newtonian with their viscosity having differing degrees of time and shear rate dependency. These cements interact with the porous structures though which they flow and with other fluids present within the porous media. The most widely used cement, poly(methyl methacrylate) (PMMA), is generally assumed insoluble in any biofluid (bone marrow) it comes into contact with, thus the cement-marrow displacement is characterized as a two-phase immiscible flow in porous media (Pinder and Gray, 2008; Widmer and Ferguson, 2011). As vertebral cancellous bone displays highly complex geometrical structures and architectural inhomogeneities over a range of length scales, the pore-scale cement viscosity varies due to its non-linear dependency on shear rates, which are affected by variations in the local tissue morphology. Furthermore, the vertebral cancellous bone microarchitecture varies among the patients being treated, thus making the scientific understanding of the cement flow behaviour difficult in clinical or, indeed, cadaveric studies (Bohner et al., 2003; Widmer Soyka et al., 2013a,b). Previous experimental studies on cement flow (Bohner et al., 2003; Baroud et al., 2006; Habib et al., 2010; Loeffel et al., 2008; Mohamed et al., 2010) have used open-porous aluminum foam to represent osteoporotic bone. Although the porosity was well controlled, the geometrical structure of each of the foams was inherently unique. This paper presents novel methodology using customized, reproducible and pathologically representative three-dimensional bone surrogates to help study biomaterial–biofluid interaction. The aim is to provide a clinical representation of cement flow distribution and a tool for validating computational simulations.

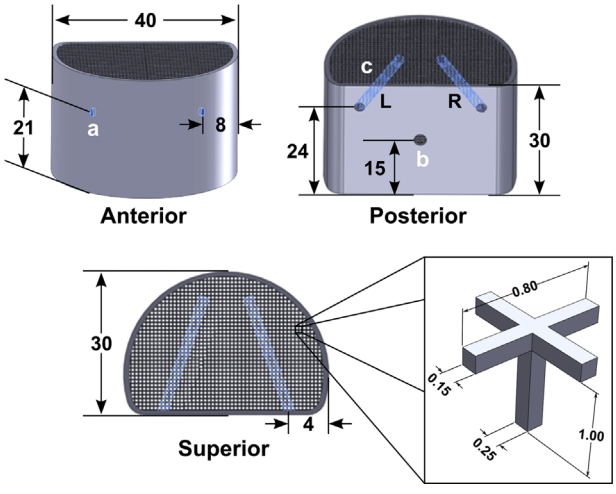

Fig. 1 – The boundary of the 3D bone surrogates showing: (a) two identical and symmetrical elliptical openings 2 mm in height and 1 mm in width applied to mimic breaches due to anterior blood vessels, (b) one circular opening 3 mm in diameter applied to mimic posterior breaches due to the basivertebral veins, and (c) the insertion channels that were incorporated to allow consistent needle placement during injection. The superior and inferior surfaces of the surrogates were kept open due to manufacturing restrictions. All dimensions are in millimetres.

2. Materials and methods

2.1. *Bone surrogate development*

Three-dimensional bone surrogates were developed to mimic the human vertebral body (Fig. 1). The surrogates were designed in SolidWorks (Dassault Systèmes, Vélizy, France) then manufactured using a rapid prototyping technique (Projet HD 3000, 3D Systems, Rock Hill, South Carolina, USA). The structure of the surrogates was tailored to mimic three skeletal pathologies: osteoporosis (Osteo), spinal metastasis (Lesion) and multiple myeloma (MM). Fig. 2 illustrates the developed bone surrogates and Table 1 describes the elements incorporated into each surrogate. Once the surrogates were manufactured, microCT (μCT 100, Scanco Medical, Switzerland) was used to assess the variability in their morphology. Eight of the Osteo surrogates were scanned at a spatial resolution of 24.6 μm (isotropic voxel size). Then, a cylindrical volume of interest 15 mm in diameter and 15 mm in length was consistently defined at the centre of each specimen. Within this volume of interest, a threshold of −120 HA mg/ccm (based on Ridler's method (Ridler and Calvard, 1978)) was applied and the three-dimensional morphometric indices were determined using proprietary software (Scanco Medical, Switzerland). Only the bone volume fraction, BV/TV (%), trabecular thickness, Tb.Th (mm), and trabecular separation, Tb.Sp (mm) were compared. The porosity of the specimens was obtained from the micro-CT data and validated using Archimedes' suspension method of measuring volume (Hughes, 2005) which was performed using six cubes ($2 \times 2 \times 2\ cm^3$) with the same structure as the Osteo surrogates. One of the six cubes was also used to measure the permeability of the Osteo structure using Darcy's law (Baroud et al., 2004; Widmer and Ferguson, 2012). Furthermore, static contact angle analysis (FTA 4000, First Ten Angstroms, Virginia, USA) was performed on the material to compare the surface wettability to that of cortical bone from a dry human femur and a fresh ovine vertebra.

2.2. *Experimental protocol*

The surrogates were filled with bone marrow substitute prepared using an aqueous solution of 2.5% w/w carboxymethyl cellulose ($M_w \sim 250{,}000$—sodium carboxymethyl cellulose, Sigma-Aldrich, Missouri, USA) with a nominal viscosity of 0.4 Pa s which has been reported as the approximate value for red bovine marrow (Bryant et al., 1989). Superior and inferior plates were used to create a tight seal and confine the marrow within the surrogates. Following this, the surrogates were placed into the experimental set-up (Fig. 3) and Simplex P bone cement (Stryker Corporation, Michigan, USA) was injected into each bone surrogate under a constant flow rate of 3 mL/min. A modified formulation for Simplex P was prepared using 10 mL liquid monomer, 9 g PMMA powder and 1 g $BaSO_4$. The cement was mixed (Bou-Francis et al., 2014) then transferred into a 10 mL syringe and injected at 4 and 8 min from mixing (SP4 and SP8, respectively) to assess the effect on the flow behaviour. The same syringe, needle and cement were used to perform the two injection time points into separate surrogates. The flow behaviour was tested in each structure, and all injections were repeated three times.