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Research paper

Biomechanical analysis of a salt-modified polyvinyl alcohol hydrogel for knee meniscus applications, including comparison with human donor samples

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ABSTRACT

The primary objective of this research was the biomechanical analysis of a salt-modified polyvinyl alcohol hydrogel, in order to assess its potential for use as an artificial meniscal implant. Aqueous polyvinyl alcohol (PVA) was treated with a sodium sulphate (Na_2SO_4) solution to precipitate out the polyvinyl alcohol resulting in a pliable hydrogel. The freeze–thaw process, a strictly physical method of crosslinking, was employed to crosslink the hydrogel. Development of a meniscal shaped mould and sample housing unit allowed the production of meniscal shaped hydrogels for direct comparison to human meniscal tissue. Results obtained show that compressive responses were slightly higher in PVA/Na_2SO_4 menisci, displaying maximum compressive loads of 2472 N, 2482 N and 2476 N for samples having undergone 1, 3 and 5 freeze–thaw cycles respectively. When compared to the human meniscal tissue tested under the same conditions, an average maximum load of 2467.5 N was observed. This suggests that the PVA/Na_2SO_4 menisci are mechanically comparable to the human meniscus. Biocompatibility analysis of PVA/Na_2SO_4 hydrogels revealed no acute cytotoxicity. The work described herein has innovative potential in load bearing applications, specifically as an alternative to meniscectomy as replacement of critically damaged meniscal tissue in the knee joint where repair is not viable.

1. Introduction

Meniscal lesions are a leading cause of intra-articular knee injury. Overall incidence of meniscal injury is unknown but surgical incidence is 60–70 per 100,000 per year (Antonio et al., 2012; Paringe et al., 2012). Subsequent development of osteoarthritis is also experienced by very many patients (Neyret et al., 1994), and there is considerable clinical and commercial interest in resolving this problem. Meniscal tissue is a unique structural material. Its mechanical properties can be directly correlated to its complex structure and it should therefore be described as a heterogeneous or anisotropic material. In contrast, many man-made polymers have a uniform structure in all directions and can thus be

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considered isotropic materials. Effective meniscal replacements aim to restore the native contact mechanics of the knee. Factors affecting the function of meniscal replacements include: the method of fixation to the tibial plateau the size and material properties of the replacement. The menisci of the human knee act principally to redistribute and alleviate the contact forces experienced in the tibiofemoral articulation. This function is successfully performed by a combination of factors such as the meniscal tissue itself, geometry and to certain extent attaching ligaments. It is generally known that meniscal tissue owes its mechanical strength to the circumferential orientation of tissue fibres and its wedge shape design. However, few attempts have been made to specifically quantify meniscal response in compression. In addition, compressive strength data that are available for meniscal tissue does not fall under any standard testing method and often vary in species and measurements. For example Kobayashi et al. (2003) obtained compressive strength values of approximately 3 Mpa by cutting meniscal samples into small cubes for compression. This particular approach effectively excludes the effect of meniscal geometry. Other reviews of the issue reported compressive values of approximately 0.15 Mpa (Beaufils and Verdonk, 2010). Furthermore, earlier research by Fithian et al. (1990) found the meniscus to be largely inhomogeneous in response to compressive loading in each orientation, with the posterior region of both the medial and lateral meniscus thought to be stiffer overall when compared to the anterior and inner regions. Due to advances made in biomedical polymers, an opportunity now exists to develop a meniscal replacement. A polymeric implant can potentially avoid the traditional partial meniscectomy used on injuries in poorly vascularised areas due to their known biocompatibility properties. The well-established biocompatibility of polyvinyl alcohol (Hassan and Peppas, 2000) has afforded it many opportunities as biomedical polymer, and its use as such has been the focus of much research (Kobayashi and Hyu, 2010; Stasko et al., 2009). PVA's simple chemical structure allows modifications by simple chemical reactions (Hassan and Peppas, 2000; Iwaseya et al., 2005). In recent years, many research groups have focused their attention on the study of PVA films or gels obtained by the simple addition of salts to aqueous PVA solutions. Investigations into the effects of a range of salts on PVA properties by Patachia et al. (2009) determined that PVA solutions combined with sodium sulphate (Na_2SO_4) displayed high crystallinity values with rheological tests showing high storage modulus (G′). This suggested a higher crosslinking density compared to all the other hydrogels analysed, due to the higher interactions of the polymer chains as consequence of the 'salting out' phenomenon. PVA hydrogels may be synthesized to mimic the water content of cartilage and possess a low coefficient of friction, necessary for lubrication of articular joints (Zheng-Qiu et al., 1998). These properties suggest that polyvinyl alcohol modified with Na_2SO_4 would represent an ideal candidate material for the synthesis of load bearing hydrogels. For a more accurate assessment of PVA/Na2SO4 hydrogel as fit for purpose, the mechanical characterisation was necessary with the material resembling a native menisci. This eliminated biases present due to incorrect shape and produced an insight into performance when geometry is considered as a variable. All tests were repeated in triplicate. A comparative biomechanical analysis (compressive strength) of the material with human donor meniscal samples, as well as a cytotoxicological analysis of the material, is described herein.

2. Materials and methods

2.1. Materials

Polyvinyl alcohol (PVA) of molecular weight (M_w) 146,000–186,000 and sodium sulphate (Na_2SO_4) were supplied by (Sigma Aldrich Ireland). All materials were used as received.

2.2. Hydrogel synthesis

A 10% (w/v) solution of PVA was prepared in dH_2O and autoclaved at 121 °C; 103.4 kPa for 15 min. Sodium sulphate, solubilised in 10 ml aliquots of pre-warmed dH_2O, was slowly added to the 50 ml aliquots of 10% (w/v) PVA (final concentration = 6.6% (w/v) Na_2SO_4 in 8.33% (w/v) PVA) and allowed to mix under agitation until the PVA precipitated out of solution. Excess water was poured out; the PVA was kneaded for 10–15 s with a spatula and cast into silicone disk-shaped moulds. The moulds were placed in a −80 °C freezer and subjected to freeze/thaw cycles. Freeze cycles consisted of placing the silicon mould in a −80 °C freezer for 15–20 min. Once frozen, the hydrogels were removed from the mould and allowed to thaw at room temperature for 25–30 min. The samples were then subjected to more cycles of −80 °C for periods between 15 and 20 min, followed by subsequent thawing. Prepared hydrogels were then placed in dH_2O to become swollen until no further weight change was observed. The samples were then transferred to an incubator at 37 °C to dry out. When no weight difference was recorded, the dry samples were then placed in excess dH_2O for seven days, with daily changing of dH_2O, to allow swelling equilibrium and washing out of impurities. Washed hydrogels were then stored in sealable sample bags containing dH_2O at 4 °C. Previous studies (Curley et al., 2014) have shown that there was no discernible difference in the mechanical behaviour of samples that underwent 3 or 5 freeze–thaw cycles.

2.3. Design of multi-functional meniscal mould and tibial plateau

A multi-functional, interactive mould capable of casting lateral and medial menisci was designed to aid in a more comprehensive characterisation of PVA/Na_2SO_4 hydrogel suitability. The mould served multiple purposes including casting of biomaterials, biomechanical evaluation and could easily be adapted to fit onto a mechanical tester. An interactive mould capable of simulating casting PVA meniscus and simulating tibial plateau and femur condyle movements was designed on Pro Engineering Wildfire 5 3D CAD software using parametric surface modelling techniques. Designs were then imported into 3D Lightyear software and setup to run on the 3D Systems Viper rapid prototyper for manufacture using Accura 60™ plastic. Manufacture of the device was carried