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Permeability of human medial collateral ligament in compression transverse to the collagen fiber direction

Jeffrey A. Weiss*, Benjamin J. Maakestad

Department of Bioengineering, The University of Utah, 50 S Central Campus Drive, #2480, Salt Lake City, UT 84112, USA

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Abstract

This study quantified the apparent and intrinsic hydraulic permeability of human medial collateral ligament (MCL) under direct permeation transverse to the collagen fiber direction. A custom permeation device was built to apply flow across cylindrical samples of ligament while monitoring the resulting pressure gradient. MCLs from 5 unpaired human knees were used (donor age 55 ± 16 yr, 4 males, 1 female). Permeability measurements were performed at 3 levels of compressive pre-strain (10%, 20% and 30%) and 5 pressures (0.17, 0.34, 1.03, 1.72 and 2.76 MPa). Apparent permeability was determined from Darcy's law, while intrinsic permeability was determined from the zero-pressure crossing of the pressure–permeability curves at each compressive pre-strain. Resulting data were fit to a finite deformation constitutive law [Journal of Biomechanics 23 (1990) 1145–1156]. The apparent permeability of human MCL ranged from 0.40 ± 0.05 to $8.60 \pm 0.77 \times 10^{-16}\,\mathrm{m}^4/\mathrm{N\,s}$ depending on pre-strain and pressure gradient. There was a significant decrease in apparent permeability with increasing compressive pre-strain ($p = 0.024$) and pressure gradient ($p < 0.001$), and there was a significant interaction between the effects of compressive pre-strain and pressure ($p < 0.001$). Intrinsic permeability was 14.14 ± 0.74, 6.30 ± 2.13 and $4.29 \pm 1.71 \times 10^{-16}\,\mathrm{m}^4/\mathrm{N\,s}$ for compressive pre-strains of 10%, 20% and 30%, respectively. The intrinsic permeability showed a faster decrease with increasing compressive pre-strain than that of bovine articular cartilage. These data provide a baseline for investigating the effects of disease and chemical modification on the permeability of ligament and the data should also be useful for modeling the poroelastic material behavior of ligaments.

Keywords: Permeability; Ligament; Medial collateral ligament; Soft tissue mechanics; Anisotropic

1. Introduction

Ligaments are a biological composite consisting of a ground substance matrix reinforced by collagen and elastin. The ground substance matrix is composed of proteoglycans, glycolipids and fibroblasts and holds large amounts of water, with the total water per wet weight measured as 60–70% (Chimich et al., 1992; Hey et al., 1990). The water content of ligaments has a strong influence on viscoelastic material properties (Chimich et al., 1992; Thornton et al., 2000). Further, it is believed that water movement in/out and within ligament may play an important role in tissue nutrition, transport of metabolites, mechanotransduction and the overall mechanical properties of the tissue.

A number of explanations have been proposed for the mechanisms governing ligament viscoelasticity. These include viscoelasticity of the collagen fibers (Rubin and Bodner, 2002), the extracellular matrix (Weiss et al., 2002), collagen fibril crosslinking (Bailey et al., 1974; Puxkandl et al., 2002; Redaelli et al., 2003) and fluid content (Chimich et al., 1992) and fluid movement within and in/out of the tissue during loading (Atkinson et al., 1997; Butler et al., 1997). However, most proposals have been based on conjecture and there is little experimental data available to support or refute the proposed mechanisms. Thus, the exact origins of ligament viscoelasticity remain controversial.

*Corresponding author. Tel.: +1 801 587 7833; fax: +1 801 585 5361.
E-mail address: jeff.weiss@utah.edu (J.A. Weiss).

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Experimental and modeling studies have suggested that the movement of water within and in/out of ligament may partially or entirely explain the viscoelastic response of ligaments (Atkinson et al., 1997; Butler et al., 1997; Chen et al., 1998; Chimich et al., 1992; Hannafin and Arnoczky, 1994). Exudation of water from ligament occurs under cyclic loading (Hannafin and Arnoczky, 1994). Ligament viscoelastic material behavior is strongly coupled to proteoglycan content (Elliott et al., 2003; Thornton et al., 2000; Yamamoto et al., 2000), and elimination of different proteoglycan species increases the amount of relaxation during stress relaxation testing (Elliott et al., 2003). The flow of water through a tissue in response to mechanical or chemical loading is governed by the apparent permeability, sometimes referred to as the hydraulic permeability (Holmes, 1985; Holmes and Mow, 1990; Mansour and Mow, 1976). In the case of ligaments, it has been suggested that the tissue may exhibit anisotropic permeability due to the highly aligned collagen fiber structure (Atkinson et al., 1997; Butler et al., 1997).

Despite the potential importance of fluid movement in ligaments, data on the permeability of ligament to water are not available. Previous computational simulations of ligaments have used ranges of permeability that were motivated primarily by the range of reported values for articular cartilage (Atkinson et al., 1997; Butler et al., 1997). The direct permeation experiment provides a means to determine tissue permeability directly (Holmes, 1985; Holmes and Mow, 1990; Mansour and Mow, 1976). This experiment requires the measurement of flow across a section of tissue in response to an applied pressure gradient under small to moderate levels of compressive strain. Studies of the other hydrated soft tissues under ultrafiltration have demonstrated that both the pressure gradient and the compressive pre-strain have a strong influence on the apparent permeability (Gu et al., 2003; Holmes, 1985, 1986; Holmes and Mow, 1990; Lai and Mow, 1980; Lai et al., 1981; Mansour and Mow, 1976; Quinn et al., 2001), and the effects of pressure gradient and compressive pre-strain are coupled (Holmes, 1985; Holmes and Mow, 1990; Lai and Mow, 1980; Lai et al., 1981). The coupling of these effects has been attributed to the nonuniform compaction of the tissue along the direction of permeation, and this effect is magnified with increasing pressure gradient. Although direct measurement of the permeability of ligament along the fiber direction presents technical difficulties due to the fibrous nature of the tissue and the aspect ratio, many ligaments are relatively planar, and it is possible to isolate test specimens from these ligaments that are oriented transverse to the collagen fiber direction for measurement of permeability during ultrafiltration. This mode of testing is relevant to physiological loading of ligaments since tensile loading produces lateral contraction and internal pressure via the Poisson effect. The objective of this study was to determine the transverse apparent and intrinsic permeability of human medial collateral ligament (MCL) from a direct permeation experiment. Based on the published reports of the apparent permeability of articular cartilage, it was hypothesized that increasing compressive pre-strain and pressure gradients would result in decreases in apparent permeability and that these effects would be coupled.

2. Materials and methods

2.1. Permeation device

A custom permeation device was designed and built to allow application of small flow rates across cylindrical samples of ligament while monitoring the resulting pressure gradient (Fig. 1). The operation of the device is similar in principle to that described by Gu et al. (1999) in that flow rate is prescribed and the resulting pressure gradient is measured. A syringe pump (SP-101i, WPI, Sarasota, FL) was used with a 500 μl glass syringe (Hamilton 1750, Reno, NV) to apply constant flow rates (0.001–100 μl/min, $<1\%$ error) (Fig. 1, bottom left panel). The area exposed to flow was 3 mm in diameter. Uniaxial compressive pre-strain was applied to the tissue along the direction of permeation by compressing the top piece of a two-piece acrylic loading fixture against the specimen and an O-ring via a micrometer head (Newport, Irvine, CA, ± 1 μm accuracy). The O-ring sealed the specimen between the upper and lower pieces of the loading fixture. Relatively rigid (compressive modulus = 18.7 MPa), highly permeable (hydraulic permeability = 3×10^{-10} m^4/N s) porous polyethylene filters assured free flow to and from the specimen (Porex, Fairburn, GA, 70 μm pore size). The resulting pressure gradient was monitored continuously via a pressure transducer (Setra, Boxborough, MA, accuracy ± 0.004 MPa).

2.2. Tissue harvest

The MCL of the human knee was chosen for testing for several reasons. First, the MCL is an extremely important structure in preventing medial joint opening and external tibial rotation in the human knee (Grood et al., 1981; Monahan et al., 1984; Palmer, 1938; Seering et al., 1980; Warren et al., 1974), and approximately 40% of all severe knee injuries involve the MCL (Miyasaka et al., 1991). Second, because of its planar geometry and size, the MCL is ideal for harvesting transverse samples for direct measurement of permeability. Finally, the results of the present study may compliment existing experimental data on the quasi-static and viscoelastic material properties of the human MCL (Bonifasi-Lista