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Mechanical properties of a novel PVA hydrogel in shear and unconfined compression

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Abstract

Poly(vinyl alcohol) (PVA) hydrogels have been proposed as promising biomaterials to replace diseased or damaged articular cartilage. A critical barrier to their use as load-bearing tissue replacements is a lack of sufficient mechanical properties. The purpose of this study was to characterize the functional compressive and shear mechanical properties of a novel PVA hydrogel. Two formulations of the biomaterial were tested, one with a lower water content (75% water), and the other with higher water content (80% water). The compressive tangent modulus varied with biomaterial formulation and was found to be statistically strain magnitude and rate dependent. Over a strain range of 10–60%, the compressive modulus increased from approximately 1–18 MPa, which is within the range of the modulus of articular cartilage. The shear tangent modulus (0.1–0.4 MPa) was also found to be strain magnitude dependent and within the range of normal human articular cartilage, but it was not statistically dependent on strain rate. This behavior was attributed to the dominance of fluid flow and related frictional drag on the viscoelastic behavior. Compressive failure of the hydrogels was found to occur between 45 and 60% strain, depending on water content. © 2001 Published by Elsevier Science Ltd.

Keywords: Biomaterial; Cartilage; Properties; Compression; Shear; Hydrogel

1. Introduction

In addition to individuals who damage cartilage due to sports or accident-related injuries, approximately 40 million Americans suffer from some form of degenerative joint disease. The estimated annual cost to the economy in lost wages and medical care is nearly 1% of the gross national product [1]. These statistics for the United States alone indicate the critical need for effective clinical treatments to repair debilitating cartilage disorders and injuries. One of the most prevalent approaches to treat severe cartilage degeneration is total joint replacement. Other methods used to treat focal defects include debridement, as well as transplantation of osteochondral allografts or chondrocytes [2]. An alternative approach that has the potential to reduce patient morbidity and recovery time is to arthroscopically replace the damaged cartilage with a synthetic biomaterial that mimics natural tissue behavior.

Natural and synthetic hydrogels retain water within a three-dimensional network of polymer chains [3]. Recent strong interest in the development of novel synthetic hydrogels and hydrogel composites can be attributed to their unique combination of properties, including biocompatibility, permeability, hydrophilicity, and low coefficient of friction. Hydrogel biomaterials have been proposed for a wide range of biomedical applications including drug delivery, contact lenses, corneal implants, and substitutes for skin, tendons, ligaments, cartilage, and bone [4–8]. However, insufficient mechanical

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properties have severely limited the use of hydrogels for load-bearing applications such as the replacement of damaged or diseased tissues.

Polyvinyl alcohol (PVA) hydrogels have been specifically proposed as promising prosthetic biomaterials to replace articular cartilage. Articular cartilage is, in fact, a natural fiber-reinforced hydrogel composed of proteoglycans, type II collagen, and approximately 75% water by weight. PVA hydrogels may be synthesized to mimic the water content of articular cartilage and possess a low coefficient of friction, which is an important characteristic for lubrication of articular joints [9]. The biocompatibility of PVA hydrogels has been studied previously. Oka et al. reported no inflammatory or degenerative changes in the articular cartilage or synovial membrane surrounding PVA hydrogel implants after 8–52 weeks [10].

While PVA hydrogels possess similar water content to articular cartilage, a critical barrier to their use is the lack of sufficient mechanical properties to withstand the severe loading conditions imposed on articular joint surfaces [3,9,11]. Articular joints are subjected to rapidly applied compressive and shear forces up to several times body weight in magnitude for millions of cycles over a lifetime. The properties of hydrogels are determined by the monomer composition, cross-linking density, and polymerization conditions [11]. Attempts to improve hydrogel properties for load-bearing biomedical applications have included the introduction of composite materials such as rubber or glass, the use of cross-linking agents such as glutaraldehyde, and the use of freeze-thawing procedures to induce partial crystallinity [9,12,13]. Clearly, hydrogels intended for orthopedic applications must possess comparable mechanical properties to the native tissue. Previous mechanical testing of hydrogels has focused on tensile testing and dynamic mechanical analysis in tension or shear [11]. For application to articular cartilage, it is critical to evaluate compressive and shear mechanical properties since these are the primary modes of loading in vivo.

One such PVA hydrogel called Salubria™ (Salumedica, Atlanta, GA) displays similarities to natural cartilage tissue in terms of water content and, furthermore, shows promise in terms of its mechanical integrity and biocompatibility. Williams performed burst, tensile, and indentation tests in the initial evaluation of this material [14], and found that the mechanical strength of the hydrogel is potentially sufficient for its use as an artificial vascular graft. Salubria™ biomaterial is made of a freeze–thawed organic polymer containing the poly(vinyl alcohol) (PVA) molecular backbone (CAS Registry Number 9002-89-5, $-CH_2CH(OH)-$) and 0.9% saline [14,15]. The mechanical properties of the Salubria™ biomaterial may be influenced by several factors. These factors include (1) weight percentage of the respective components of the cryogel (water and PVA); (2) the molecular weight of the initial PVA polymer element; (3) the number of freeze/thaw cycles; and (4) the duration of the freeze cycle. The freeze/thaw cycle promotes a mesh entanglement between molecules of PVA to create mechanical strength [15]. This differs from traditional cross-linking methods that include chemicals that inevitably introduce toxic agents and decrease the biocompatibility of the resulting biomaterials [15]. The material is sterilizable, hydrophilic, and nondegradable. In addition, Salubria™ biomaterial can be easily molded into customized anatomic shapes because it is gelatinous prior to the freeze/thaw processing [15]. Since the biomaterial is non-degradable, it is intended to serve as either a permanent replacement for damaged articular cartilage or a temporary solution to improve joint function and delay total joint replacement.

The purpose of this study was to quantify the functional mechanical properties of Salubria™ biomaterial under shear and unconfined compression loading.

Specifically, the compressive tangent modulus and shear tangent modulus were quantified. The strain magnitude and strain rate dependence of the moduli were evaluated since it was expected that the hydrogel would possess nonlinear and time-dependent material behavior. Finally, the compressive failure properties, specifically the failure strain and stress, were determined.

2. Materials and methods

2.1. Specimen preparation and test conditions

Salubria™ biomaterial is thermally crystallized by repeatedly freeze–thawing a solution containing poly(vinyl alcohol) (PVA) and 0.9% saline [14,15]. Water content was determined by weighing samples while hydrated and dehydrated, and dividing the difference in those weights by the hydrated weight. Samples were dehydrated in an oven at 95°C for 24 h, and then weighed with a standard laboratory balance to determine the water content. Two formulations of Salubria™ were tested, one with a lower water content (75% water), designated as formulation A, and the other with higher water content (80% water), designated as formulation B. The two formulations were different in the concentration of PVA used in the process, leading to different amounts of water in the final product. Differences in structure were examined histologically by preparing 50 μm sections of paraffin embedded samples. After the sections were mounted on slides, they were examined under a microscope at 20× magnification, revealing an obvious difference in fiber density between formulations (Fig. 1).

Hydrogel samples were molded to be cylindrical in shape, nominally 6 mm in diameter and 6 mm in height. To more precisely measure the actual dimensions of the samples following removal from the manufacturing

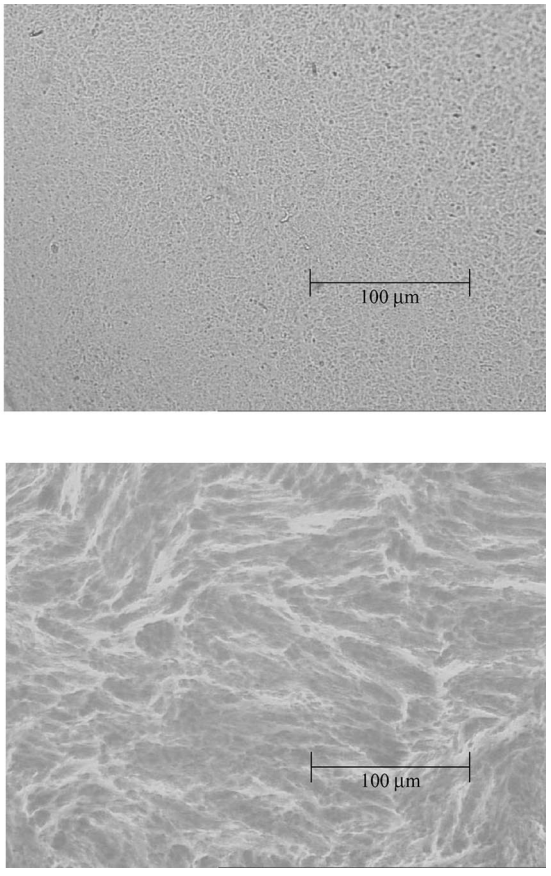

Fig. 1. Unstained histological images of both hydrogel formulations at 20× magnification. (a) Hydrogel formulation A has lower water content (75% water), and thus the fiber density is high; (b) hydrogel formulation B has a higher water content (80% water), as shown by the large pores and low fiber density. The material structure can be changed through parameter modifications during manufacturing.

molds, an optical procedure that combined microscopy software (Northern Eclipse v. 5.0, Empix Imaging, Inc.) and image analysis (PV Wave, Visual Numerics, Inc.) was used. Hydrogel properties are documented as being relatively temperature-dependent [12]. The samples were, therefore, submerged in a deionized water bath and equilibrated at 37°C.

2.2. Strain and strain rate effects on compressive modulus

An electromechanical material testing machine (Info 650R, DDL, Inc., Eden Prairie, MN) was used to test samples in unconfined compression between two impermeable, unlubricated platens. Prior to each test, the samples were preloaded and cyclically preconditioned for 10 cycles between 1 and 10 N to reduce the influence of surface artifacts. Twelve samples were subsequently subjected to a compressive ramp up to 65% strain at a strain rate of $100\%\,\mathrm{min}^{-1}$ (i.e. $0.0167\,\mathrm{s}^{-1}$). A second set of 12 samples was tested at a higher rate of $1000\%\,\mathrm{min}^{-1}$ (i.e. $0.1667\,\mathrm{s}^{-1}$). All given strains and strain rates were referenced to the initial 6 mm length of the specimens. The tangent slope was measured by calculating a line estimate for localized data at 10% increments from 10–60% strain.

2.3. Shear modulus

The flat ends of cylindrical samples were centered and fixed using cyanoacrylate adhesive between two 1 mm thick, square, plexiglass slides. The samples were allowed 15 min for fixation to the slides in air and were subsequently placed in a holding container filled with deionized water until ready for testing. Two aluminum shear platens were machined to facilitate insertion and immobilization of the plexiglass slides in the vertical and horizontal directions. The top platen was coupled to a load cell (SM-5000N, Interface, Inc.) and machine actuator, while the bottom platen was attached to the base of a water bath. Proper alignment was initially assured by measuring the distance across four locations vertically and horizontally, and the sample was preconditioned and subjected to 65% shear strain ($n = 6$) while submerged in deionized water at 37°C. Testing was done for strain rates of $75\%\,\mathrm{min}^{-1}$ (i.e. $0.0125\,\mathrm{s}^{-1}$) and 750% (i.e. $0.125\,\mathrm{s}^{-1}$) min^{-1}. Torsional and horizontal compression effects incurred during loading were neglected, and the shear modulus was calculated according to (1), where F_{parallel} was the recorded load, A was the cross-sectional area of the sample, and ΔL was the recorded displacement.

$$G = \frac{\tau}{\gamma} = \frac{F_{\mathrm{parallel}}}{A[\tan^{-1}\Delta L/L]}. \quad (1)$$

The shear strain rate was calculated according to (2), where $\mathrm{d}\gamma/\mathrm{d}t$ was the shear strain rate and $\mathrm{d}\Delta L/\mathrm{d}t$ was the bulk head speed.

$$\mathrm{d}\gamma/\mathrm{d}t = \tan^{-1}[(\mathrm{d}\Delta L/\mathrm{d}t)/L]. \quad (2)$$

2.4. Time-dependent properties

The time-dependent properties of the Salubria™ biomaterial were assessed by evaluating stress relaxation and creep recovery. Following the previously described preconditioning, a 20% compressive strain was applied and held for a period of 24 h, while monitoring stress relaxation. To assess creep recovery, samples were subjected to increasing strains from 25 to 80% strain at a strain rate of $100\%\,\mathrm{min}^{-1}$, unloaded, and allowed to recover for 24 h in deionized water. These tests also served to identify an approximate strain level resulting in plastic deformation.

2.5. Compressive failure

The first method for determining the point of plastic deformation consisted of subjecting a sample under

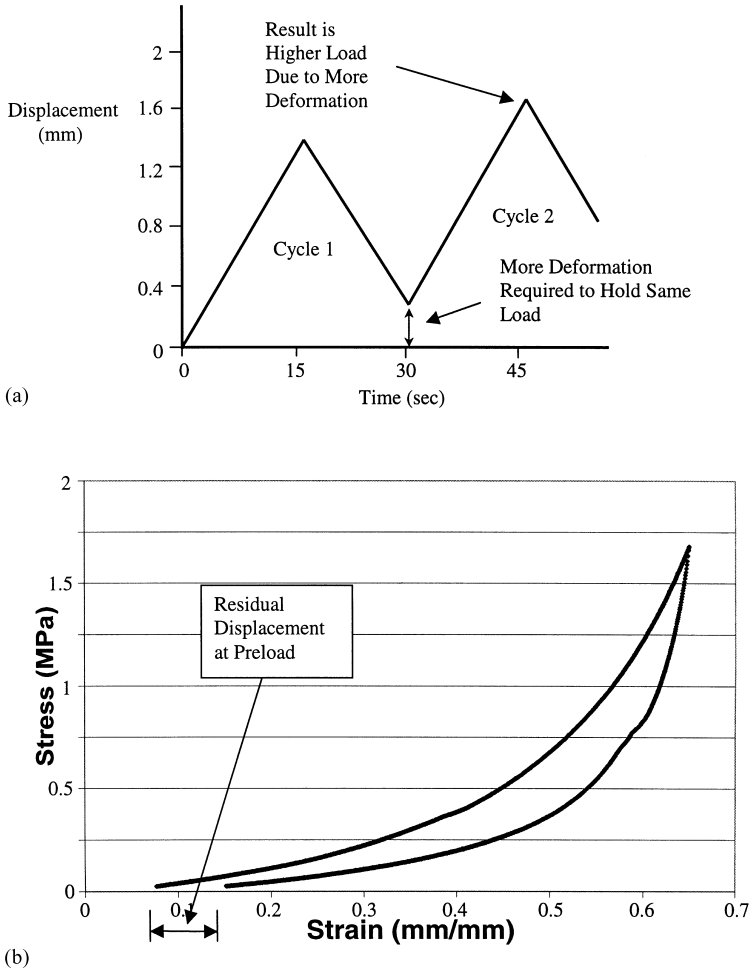

Fig. 2. (a) The first test of compressive failure uses the difference in peak loads of two consecutive cycles as the failure indicator; (b) the second test of failure measures the residual displacement directly after one cycle.

displacement control to 10 preconditioning cycles as described previously. Each sample was subsequently deformed to a specific compressive strain level (25–80%) two consecutive times at a strain rate of 100% min^{-1}, and the peak loads of the two cycles were recorded (Fig. 2). The difference in these peak loads was then plotted versus strain level. One limitation of this approach is that it indirectly measures residual displacement between cycles, which may be due to a combination of both plastic deformation and displacement prior to creep recovery. Therefore, to distinguish between these effects, another experiment was conducted to more directly assess residual displacement.

The second method for evaluating compressive failure included preconditioning, followed by a single compressive cycle in unconfined compression under load control to loads corresponding to the same strain increments used in the first test (25–80% strain). After 1 min of recovery, the residual displacement following compression was measured as being the deviation in position from the initial position at the preload level (Fig. 2). An initial creep recovery region occurring prior to failure was expected, followed by a second mode combining both unrecovered creep displacement and permanent damage [16]. Linear fits were made to both of these modal sets of residual displacement data, and the intersection was taken as the point of damage initiation.

3. Results

The compressive mechanical properties of Salubria™ biomaterial were found to be significantly influenced by both strain magnitude and rate, indicating nonlinear and viscoelastic material behavior (Fig. 3). The tangent modulus increased approximately fivefold between 30 and 60% strain (Fig. 4). Fig. 4 also illustrates the strain rate dependence of the compressive tangent modulus at two different strain levels. At a 30% strain level, an increase in strain rate from 100 to 1000% min^{-1} resulted in a significant increase in modulus for formulation A but not formulation B. At higher strain levels, strain rate

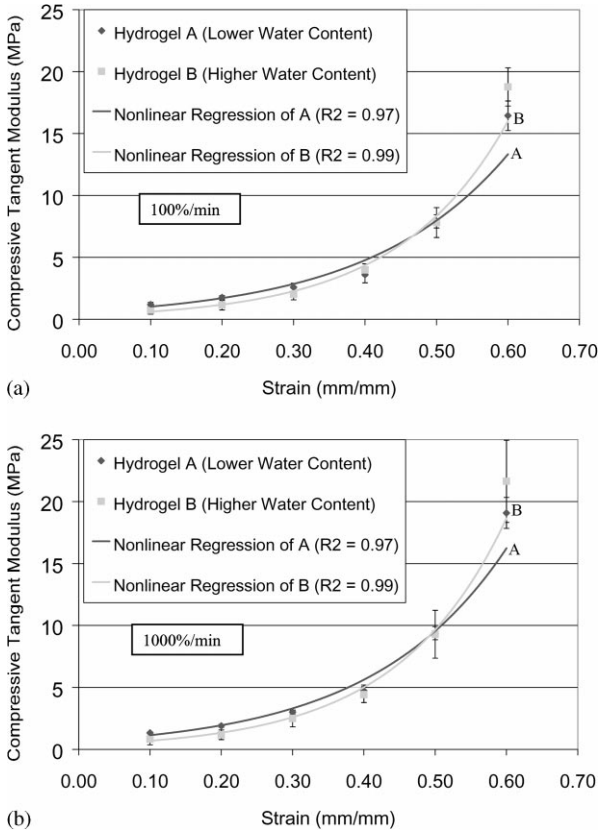

Fig. 3. Compressive tangent modulus versus strain magnitude for both hydrogels at two strain rates of (a) 100% min^{-1} and (b) 1000% min^{-1} ($p < 0.05$).

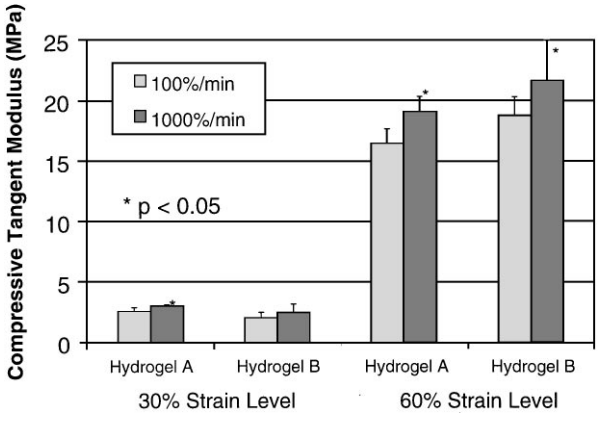

Fig. 4. Strain rate dependence of the compressive tangent modulus for both hydrogel formulations at two strain levels. The difference in moduli for the two formulations is statistically significant at both 30 and 60% strain ($p < 0.05$).

effects were amplified, and significant differences were observed for both cryogel formulations.

Relatively small but statistically significant differences were also observed between the two cryogel formulations tested (Fig. 3). At strain magnitudes less than 40%, the tangent modulus of formulation A was consistently higher than formulation B, independent of strain rate. Interestingly, at 60% strain, formulation B was stiffer than formulation A for both strain rates, despite its higher water content.

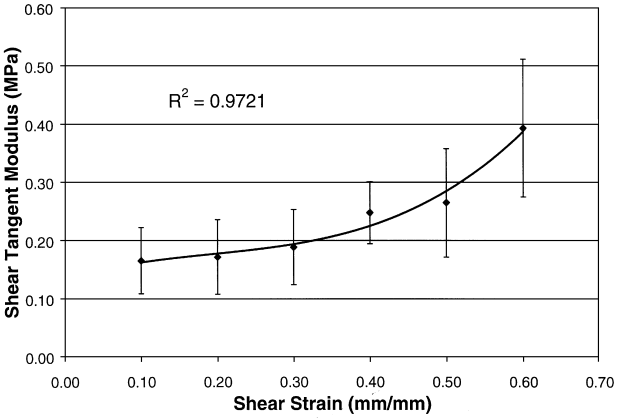

Fig. 5. Shear tangent modulus of hydrogel formulation A at 75% min^{-1} strain rate.

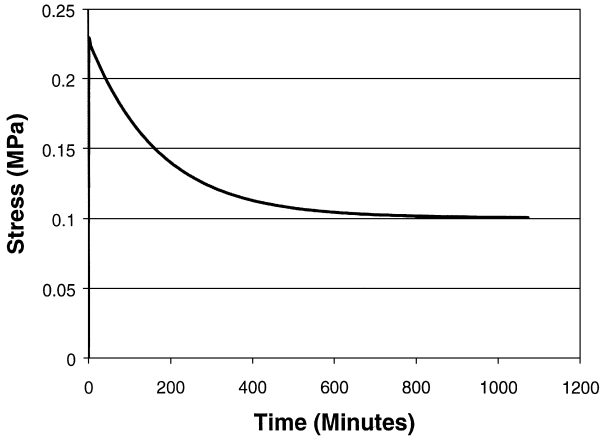

Fig. 6. Stress relaxation behavior of PVA hydrogel formulation A in unconfined compression, indicating equilibrium at 24 h.

The shear tangent modulus of both formulations was also strain magnitude dependent. However, unlike compression, differences in tangent modulus due to strain rate effects were not statistically significant for either formulation. In addition, there was no statistically significant difference between the shear tangent modulus of formulations A and B. The shear tangent modulus for both formulations was consistently between 0.10 MPa at 10% strain and 0.45 MPa at 60% strain (Fig. 5). Due to the consistency of the shear modulus for both strain rates and formulations, only results from one test group (hydrogel A at 75% min^{-1}) are shown (Fig. 5).

The approximate range in which plastic deformation occurred in formulation A was found qualitatively by observing plastic axial deformation and transverse bulging in the samples at strains greater than 65% after 24 h of recovery in solution (Fig. 6). This measurement served

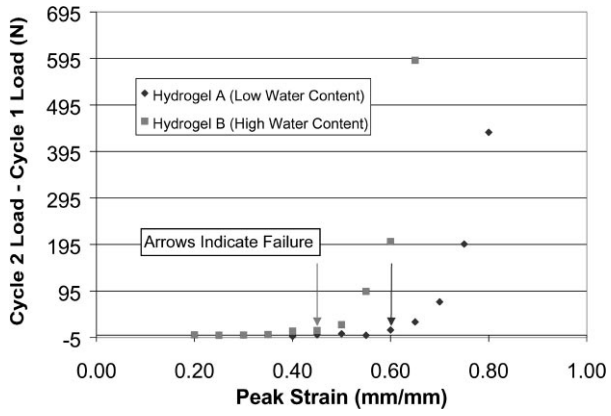

Fig. 7. First test of compressive failure measuring the difference in peak loads of two consecutive cycles. This is an indirect measure of residual displacement. Approximate failure strains for hydrogels A and B are 60 and 45%, respectively.

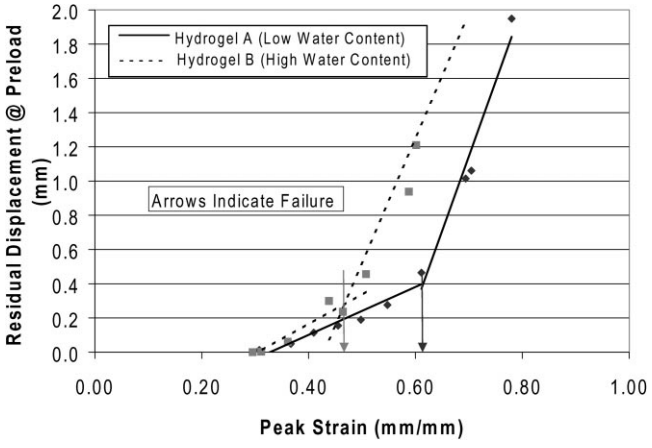

Fig. 8. Second test of compressive failure that directly measures the residual displacement associated with both displacement prior to creep recovery and a combination of this measure and damage. Approximate failure strains for hydrogels A and B are 62 and 47%, respectively.

as a preliminary "ballpark" estimate for quantitatively determining the compressive failure of both formulations.

Irreversible compressive damage was found to occur at a lower strain level for formulation B than for formulation A, and this trend was consistent for both compressive failure test methods. For the first test of compressive failure, the peak load difference was negligible at low strains and then increased rapidly at some higher strain level for both formulations. From this graph, formulation A, which had lower water content (75% water), appeared to fail at around 60% strain and an ultimate stress of 2.1 MPa, while formulation B (80% water) failed near 45% strain and 1.4 MPa stress (Fig. 7). The results acquired from the second test of failure were in agreement with those from the first method. Here, failure occurred at 62% for formulation A and 47% for formulation B (Fig. 8) by taking the intersection of two modal sets of residual displacement data.

4. Discussion

Although hydrogels possess many attractive features for biomedical applications, the mechanical properties of these versatile biomaterials are generally poor [3]. Mechanical testing of hydrogels is therefore an important part of a comprehensive evaluation for load-bearing applications. The particular mechanical testing methodology chosen should be directly relevant to the intended functional loading conditions. With that in mind, the purpose of this study was to quantify the compressive and shear properties of a novel PVA biomaterial intended for use as a synthetic replacement for damaged articular cartilage.

Several studies have compared hydrogels to biological tissues and have identified critical parameters for modifying their mechanical properties. Bray et al. [17] established material selection and design criteria of PVA hydrogels for use as synthetic cartilage replacements and assessed the effect of radiation cross-linking density and temperature on their tensile properties. They observed that the degree of crystallinity and mechanical strength were increased when the gels were subjected to a repeated freeze–thawing process. The behavior of various composite hydrogels in both compression and tension has also been examined, and it was found that glass-reinforced hydrogels possessed mechanical properties similar to those exhibited by canine intervertebral discs [18]. The compressive and tensile mechanical properties of PVA hydrogels have been reported to be similar to those of articular cartilage, although strain and strain rate effects were not tested [7,19]. This study is the first to evaluate the compressive failure properties of a hydrogel biomaterial as well as their strain and strain rate dependence under shear and compressive loading.

Quantitative evaluation of compressive failure in water-containing materials such as cartilage or hydrogels is difficult due to their inherent nonlinear, creep, and stress relaxation behaviors. Kerin et al. reported failure criteria for determining the compressive failure strength of articular cartilage [16]. One of the criteria was a significant increase in hysteresis between two subsequent loading cycles. Hysteresis changes did not, however, conclusively identify failure in the Salubria™ biomaterial tested in this study (data not shown). A second criterion identified an obvious decrease in the gradient of the force-displacement curve as the point of failure. Again, this behavior was not observed in the present study. Finally, an abrupt increase in residual displacement after load removal was found by Kerin et al. to correspond with compressive failure. This criterion, which included an explanation of a low initial region of residual displacement due to "imperfect" recovery, was effectively utilized

Table 1
Comparison of compressive tangent modulus, failure stress and strain, and shear tangent modulus for both PVA hydrogel formulations and human articular cartilage

Material	Compressive modulus, E_{comp} (MPa)	Failure strain, ε_{ult} (%)	Failure stress, σ_{ult} (MPa)	Shear modulus, G (MPa)
Hydrogel formulation A (75% water)	1.1–18.4	60–62[b]	2.1[b]	0.17–0.43
Hydrogel formulation B (80% water)	0.7–6.8	45–47[b]	1.4[b]	0.10–0.40
Human articular cartilage	1.9–14.4[a]	30[c]	—	0.23[d]

[a] Ref. [9].
[b] 100%/min strain rate.
[c] Ref. [17].
[d] Normal human patellar articular cartilage (Ref. [20]).

in the present study to identify compressive failure of the biomaterial. Consistent estimates of failure were achieved from two independent test methodologies that measured residual displacements either indirectly or directly.

The importance of measuring compressive failure was illustrated by the unexpected behavior observed for formulation B at higher strains. At strain levels below 40%, formulation A was consistently stiffer than B; however, the opposite was true at 60% strain. This behavior was most likely due to the fact that, at 60% strain, formulation B was clearly within its failure regime. Because of this complex behavior in compressive failure, the modulus ranges shown in Table 1 are given for the functional (i.e. pre-failure) range of each formulation. This information, along with current efforts to fully evaluate the biomaterial's viscoelastic behavior relative to cartilage, is essential to optimize the material for potential use as an articular cartilage replacement.

Both the compressive modulus and failure stress and strain determined from these experiments on both formulations were within the range of the properties of human articular cartilage tested at nonimpact speeds (Table 1). While other composite or cross-linked hydrogels have been shown to have a higher compressive modulus than Salubria™ biomaterial for other applications [18], the formulations tested here exhibit properties quite similar to those of articular cartilage. Water content and strain rate were found to be significant determinants of compressive modulus. The modulus was also strain magnitude dependent, which is attributed to the inherent nonlinearity of the biomaterial. These compressive properties are also characteristic of articular cartilage. However, further studies investigating fatigue and wear properties are necessary to fully evaluate the potential of Salubria™ to functionally replace damaged articular cartilage in osteoarthritic joints.

Shear tangent modulus was also found to be dependent on strain magnitude. However, unlike compressive modulus, shear modulus was not statistically dependent on strain rate or water content. This observation suggests that the time-dependent behavior of the Salubria™ biomaterial is primarily a consequence of fluid flow through the solid matrix. A volume change occurred due to interstitial fluid flow in compression, whereas little or no such volume change occurred in the pure shear configuration. Since there were no significant rate-induced effects in shear, it is evident that fluid flow, not the intrinsic solid matrix, was predominantly responsible for the viscoelastic behavior of the material. This is consistent with the behavior of articular cartilage, in which interstitial fluid flow and associated frictional drag forces are the principal determinants of the observed time-dependent behavior [20].

This study suggests that the shear, compressive, and failure properties of hydrogels or hydrogel-like biomaterials can be made similar to those of articular cartilage without the use of composite additives or cross-linking chemical agents which may reduce biocompatibility. Future work to further characterize the material behavior of Salubria™ cryogel will include confined compression, fatigue, wear, stress relaxation, and creep testing. The effects of different media such as saline or synovial fluid on the mechanical properties of this PVA hydrogel were not evaluated here and will also need to be addressed in future work. Adherence of the material to host bone and cartilage tissues will be a critical issue, and ongoing studies are exploring the effects of architectural surface modifications on cell adhesion and in vivo integration. The material may be made inert to prevent fibrous scarring, or adhesion sequences can be incorporated into the polymer to enhance attachment between the extracellular matrix produced by chondrocytes and the implant. Bioactive agents such as heparin, thrombin inhibitors, growth factors, and glycosaminoglycans may also be incorporated into Salubria™ cryogel [15]. In addition to this evaluation for use as a cartilage replacement, the biomaterial is being developed for applications such as vascular grafts, ureter stents, and sheaths that promote nerve regeneration.

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