Human and bovine spinal disc mechanics subsequent to trypsin injection

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Abstract  Objective: To investigate the biomechanical effects of injections of a protease on the characteristics of bovine coccygeal and human lumbar disc motion segments.
Methods: Mechanics of treated tissues were measured immediately after injection and 3 h after injection. Motion segments underwent axial rotation and flexion-extension loading.
Results: Stiffness and neutral zone parameters experienced significant changes over time, with bovine tissues more strongly affected than human cadaver tissues. This was true in both axial rotation and flexion-extension. The treatment type significantly affected the neutral zone measurements in axial rotation. Hysteresis parameters were impacted by control injections.
Conclusion: The extrapolation of bovine coccygeal motion testing results to human lumbar disc mechanics is not yet practical. The injected treatment may have a smaller impact on disc mechanics than time in testing. Viscoelasticity of human lumbar discs may be impacted by any damage to the annulus fibrosis induced by needlestick.
The Translational Potential of this Article: Preclinical testing of novel spinal devices is essential to the design validation and regulatory processes, but current testing techniques rely on cadaveric testing of primarily older spines with essentially random amounts of disc degeneration. The present work investigates the viability of using trypsin injections to create a more uniform preclinical model of disc degeneration from a mechanics perspective, for the purpose of testing spinal devices. Such a model would facilitate translation of new spinal technologies to clinical practice.
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Introduction

Chronic low back pain (LBP) is a debilitating condition that affects millions every day, and which has no known cure. LBP has several potential sources, such as osteoarthritis, muscle strains, dysfunctional ligaments, and degenerated intervertebral discs (IVD) [1]. As the disc degrades, annulus fibrosis (AF) and nucleus pulposus (NP) tissues alter their cellular and biochemical characteristics. Early degenerative changes in the NP include breakdown of polar aggregating proteoglycans with subsequent loss of hydration and disc height [2–4]. Changes in the NP are closely correlated with compositional and structural changes in the AF including loss of hydration and proteoglycan content, cracks, delamination, a reduced number of layers, collagen fibre reorientation [5], and increased layer thickness [6]. With advanced disc degeneration, the levels of the majority of matrix molecules are decreased, with the exception of biglycan and fibronectin [3]. Degenerated discs have a more abundant nerve supply than normal discs, and the nerves in discs appear to be capable of conducting pain signals [7–9]. Such changes typically cause a shift in mechanical behaviour of the disc, which in turn affects the clinical stability of the spine [10–12].

Despite the lack of strong clinical correlation between the severity of lumbar pain symptoms and the severity of disc degeneration [13,14], over 90% of surgical spinal procedures are performed consequential to the degenerative process [15]. For clinicians, treating disc degeneration is complicated because of the multifactorial traits of this pathology, including changes in morphology, biochemical composition, and mechanical environment of the disc and surrounding tissue.

In severe cases of chronic LBP, surgical operations can be performed to augment or replace the IVD. Orthopaedic spinal procedures may temporarily reduce pain by removing problematic discs, but do so at the expense of normal functional biomechanics. Current surgical treatments for lumbar related damage, namely spinal fusion and total disc arthroplasty, are problematic in the context of disc degeneration, because they alter the mechanical stress fields experienced by adjacent discs [16–18]. Altered stress fields have been linked to accelerated disc degeneration in adjacent levels, which further complicates the long-term well-being of the patient. Surgical treatments designed to function in a healthy environment are often operating in a degenerate environment.

Cadaver testing of spinal devices is an important part of the design validation process, providing key insights into device functionality and interaction with the surrounding tissue. However, availability and cost issues dictate that most cadaver testing is done on spines from a broad cross-section of degenerative states. Thus, it has heretofore been impractical to experimentally quantify the efficacy of spinal treatments confidently due to progressive degeneration of the surrounding tissue.

Research has shown that protease ingestion of bovine coccygeal disc tissue may serve as a potential degeneration model for cadaveric lumbar discs. Protease activity within animal IVDs has been shown to degrade the cellular integrity of the disc [19–23]. Particularly, Roberts et al. [19] subjected bovine tail discs to different protease solutions for up to 3 weeks. In comparison to disc samples in saline-buffered solutions, trypsin- and papain-treated discs showed extensive damage after testing, with most changes taking place in the NP. Papain caused more extensive damage in less time in comparison to trypsin. A second study completed by Mwale et al. [20] subjected bovine tail segments to trypsin treatment and compressive loading for 16 h to determine the effect on MRI parameters, as well as to determine changes in mechanical and biochemical properties. Trypsin caused greater alterations to mechanical properties than the applied loadings. Proteases such as trypsin digest the proteoglycans found within the cellular matrix of the AF. This loss of glycosaminoglycans is a condition of disc degeneration. The simulation of natural degeneration in animal IVDs via proteolysis has been hypothesized to also model the natural degeneration during the advancement of aging in human IVDs. Improved ability to mechanically mimic the onset of natural disc degeneration can also allow for greater precision in testing treatments in vitro. Biomechanical behaviours of motion segments adjacent to compromised discs which undergo any number of surgical procedures are of particular interest.

This study explores this proteolysis effect on both bovine coccygeal and cadaver lumbar motion segments, with the hypothesis that controlling the timing of the protease action can cause predictable and similar alterations in disc mechanics that can simulate natural degeneration.

Materials and methods

Bovine testing

Twelve bovine coccygeal spines (age 20–25 months) were acquired from a local abattoir and kept frozen at −20 °C until testing. Muscle and adipose tissue were dissected, taking care to preserve each IVD and vertebrae. Discs were screened for testing based on their shape and structural integrity, and irregular or damaged segments were rejected. Twenty functional spinal units (FSUs) [diameter mean = 2.27 cm, standard deviation (SD) = 0.34] were isolated from the spines by cutting through adjacent discs. Hydration was maintained with phosphate-buffered saline (PBS) solution during dissection and a generous coating of petroleum jelly during testing.

Each FSU was potted in custom test fixtures that allowed application of prescribed angular rotations in the flexion-extension (±15°) and axial rotation (±3°) axes. The vertebral endplates of the IVD were embedded in a two-part polyester resin (Bondo, 3M Corp, St. Paul, MN, USA), and care was taken to align the centreline of the disc horizontally with the fixture. A servo-hydraulic testing machine (Instron model 1321, Instron, Norwood, MA, USA) was equipped with a 20N·m torque transducer (Omega Engineering, Stamford, CT, USA) for angular rotation testing.

Each FSU was tested in two modalities: flexion/extension (FE) and axial rotation (AR). Testing order was randomly selected between specimens, but was consistent between subsequent tests on the same specimen. All
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