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ABSTRACT

The objective of this study was to examine the impact of mechanical loading on solute transport in porcine temporomandibular joint (TMJ) discs using the electrical conductivity method. The electrical conductivity, as well as ion diffusivity, of TMJ discs was determined under confined compression with 3 strains in 5 disc regions. The average electrical conductivity over the 5 regions (mean $\pm$ SD) at 0% strain was 3.10 ± 0.68 mS/cm, decreased to 2.76 ± 0.58 mS/cm (-11.0%) at 10% strain, and 2.38 ± 0.55 mS/cm (-22.2%) at 20% compressive strain. Correspondingly, the average relative ion diffusivity (mean $\pm$ SD) at 0% strain was 0.273 ± 0.055 , decreased to 0.253 ± 0.048 (-7.3%) at 10% strain, and 0.231 ± 0.048 (-15.4%) at 20% compressive strain. These results indicated that compressive strain impeded solute transport in the TMJ disc. Furthermore, our results showed that the transport properties of TMJ discs were region-dependent. The electrical conductivity and ion diffusivity in the anterior region were significantly higher than in the posterior region. This regional difference is likely due to the significant differences of tissue hydration between these 2 regions. This study provides important insight into the electrical and solute transport behaviors in TMJ discs under mechanical loading and aids in the understanding of TMJ pathophysiology related to tissue nutrition.

KEY WORDS: temporomandibular joint (TMJ) disc, electrical conductivity, solute diffusivity, cartilaginous tissue, tissue mechanics, solute transport.

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Effect of Mechanical Loading on Electrical Conductivity in Porcine TMJ Discs

INTRODUCTION

The temporomandibular joint (TMJ) is a load-bearing joint with unique articular structure and function (Werner *et al.*, 1991). The TMJ disc, a dense fibrocartilaginous tissue, distributes stress and aids in lubrication of the joint (Nickel and McLachlan, 1994). It is generally believed that pathological mechanical loading (*e.g.*, sustained jaw clenching or traumatic impact) triggers a cascade of molecular events leading to TMJ disc degeneration and derangement, which are central to many TMJ disorders and pathophysiology (Milam, 2005). However, the molecular mechanism through which biomechanical loading at the tissue level initiates remodeling processes at the cellular level is still poorly understood.

The normal adult human TMJ disc is a large avascular structure, and the nutrients required by disc cells are supplied by blood vessels and synovial fluid at the margins of the disc (Rees, 1954; Leonardi *et al.*, 2003). The balance between the rate of nutrient transport through the matrix and the rate of consumption by disc cells establishes a concentration gradient across the disc. The concentration levels of essential nutrients, such as oxygen and glucose, can profoundly affect disc cell viability, matrix synthesis, and response to inflammatory factors (Yamaguchi *et al.*, 2005; Tojyo *et al.*, 2008). This suggests that deviation from physiological nutrient levels in the TMJ disc due to the lack of nutrient supply may initiate tissue remodeling and matrix degradation. Although convection due to interstitial fluid flow induced by mechanical loading may affect large solute transport (O'Hara *et al.*, 1990; Garcia *et al.*, 1996; Evans and Quinn, 2006), the transport of small solutes (*e.g.*, ions, oxygen, and glucose) within avascular cartilaginous tissues depends mainly on diffusion (Evans and Quinn, 2006; Yao and Gu, 2006). The rate of solute diffusion in tissue is governed by solute diffusivities which are affected by the composition and structure of the matrix, as well as by mechanical strains on the tissue. Many studies have been conducted to determine diffusivities of various solutes in articular cartilage and intervertebral discs (IVD) (Jackson and Gu, 2009). However, very few data of solute diffusivities are available for the TMJ disc. Most recently, we measured the solute diffusivities in porcine TMJ discs using the Fluorescence Recovery After Photobleaching (FRAP) technique (Shi *et al.*, 2010). The results showed that the tissue matrix significantly hindered solute diffusion, and that diffusion rates of dextran molecules varied by region. However, the effects of mechanical strains on solute diffusivities have not been investigated in TMJ discs. Such knowledge is important for assessment of the impact of mechanical loading on solute transport and local cell environment in TMJ discs.

Electrical conductivity is a material property of biological tissues and is related to ion diffusivities within the tissue (Maroudas, 1968; Frank *et al.*,

1990). Using an electrical conductivity method, investigators have studied the effects of mechanical strains on ion transport in hydrogels and IVD (Gu *et al.*, 2004; Jackson *et al.*, 2009). In this study, we adopted this method to investigate the impact of mechanical loading on the solute transport in TMJ discs. We hypothesized that the electrical conductivity of the porcine TMJ disc was mechanical-strain-dependent due to changes in tissue porosity caused by tissue compression. We also hypothesized that the electrical conductivity was region-dependent within the TMJ disc, due to its unique composition and structure. Therefore, the objective of this study was to measure the electrical conductivity and tissue porosity of the porcine TMJ disc under 3 compressive strains in 5 disc regions.

MATERIALS & METHODS

Specimen Preparation

Twelve TMJ discs from the right joint were harvested from pig heads (6-8 mos, Yorkshire, male) obtained from a local slaughterhouse within 2 hrs of death. Cylindrical tissue plugs were punched from 5 TMJ disc regions (intermediate, posterior, anterior, lateral, and medial) (Fig. 1a), using a 5-mm corneal trephine. The plugs were trimmed using a microtome to remove the natural tissue concave shape and to allow for a flat surface during electrical conductivity measurements. The prepared disk-shaped specimens ($n = 60$) had a height of 1.693 ± 0.287 mm and a diameter of 5 mm. Three conductivity measurements, corresponding to 3 levels of compressive strain (0%, 10%, and 20%), were performed on each specimen.

Porosity (water volume fraction) Measurement

The porosity or water volume fraction of specimens at the undeformed state (ϕ_0^w) was determined by a buoyancy method (Yao *et al.*, 2002). Briefly, the weight of the specimens in air (W_{wet}) and the weight in phosphate-buffered saline (PBS) solution (W_{PBS}) were measured using the density-determination kit of a Sartorius analytical balance (Sartorius YDK01, Göttingen, Germany). After electrical conductivity was measured, specimens were lyophilized, and the dry weights (W_{dry}) were recorded. According to Archimedes' principle and biphasic assumption, the water volume fraction was determined by:

$$\phi_0^w = \frac{W_{wet} - W_{dry}}{W_{wet} - W_{PBS}} \frac{\rho_{PBS}}{\rho_w} \quad (1)$$

where ρ_{PBS} is the mass density of PBS (1.005 g/mL), and ρ_w is the mass density of water. The water volume fraction of the

Figure 1. Conductivity experimental design. **(A)** Schematic of specimen preparation. The regions and sizes of test specimens are shown. **(B)** Schematic of apparatus for measuring electrical conductivity, consisting of 2 stainless steel current electrodes, 2 Ag/AgCl voltage-sensing electrodes, a non-conductive Plexiglass chamber, a current-sensing micrometer, and a source meter.

specimen at different compression levels (ϕ^w) can be calculated by (Lai *et al.*, 1991):

$$\phi^w = \frac{\phi_0^w + e}{1 + e} \quad (2)$$

where e is the tissue dilatation. Considering the one-dimensional confined compression in this study, the tissue dilatation is equal to the compressive strain.

Electrical Conductivity Measurement

The method and apparatus for measuring electrical conductivity of tissues were reported previously (Gu *et al.*, 2002). Briefly, the conductivity apparatus consists of 2 stainless steel current electrodes coaxial to 2 Teflon-coated Ag/AgCl voltage electrodes placed on the top and bottom of a cylindrical non-conductive Plexiglass chamber (5-mm diameter). Applying the four-wire method and using a source meter (Model 2400, Keithley Instruments, Inc., Cleveland, OH, USA), we measured the resistance (R) values across the specimens at a low, constant current density of 0.015 mA/cm^2 . The height of the specimen was measured with an electrical-current-sensing micrometer. The electrical conductivity (χ) values of the specimens were calculated by:

$$\chi = \frac{h}{RA} \quad (3)$$

where h and A are the height and cross-sectional area of the specimens, respectively.

The electrical conductivity of each specimen was measured at 0%, 10%, and 20% compression levels. The confined compression of the tissue specimen was achieved by lowering the micrometer to the desired height (Fig. 1b), and fluid was allowed to exude from the sample through a small clearance between the chamber and the current electrodes. Following

Figure 2. Effects of compressive strains on regional distribution of electrical conductivity (A), porosity (water volume fraction) (B), and relative ion diffusivity of TMJ disc (C). The symbol (*) indicates significance compared with anterior/posterior regions for the *post hoc* test ($p < 0.05$).

compression, we waited 15 min to allow the specimen to reach equilibrium (*i.e.*, no fluid flow). All electrical conductivity measurements were performed in PBS at room temperature (22°C).

Ion Diffusivity Calculation

Under a zero fluid flow condition, the measured electrical conductivity (χ) of a tissue in NaCl solution is related to intrinsic cation and anion diffusivities (D_i , $i = +, -$) by (Maroudas, 1968; Frank *et al.*, 1990):

$$\chi = F_c^2 \phi^w (c^+ D^+ + c^- D^-) / RT, \quad (4)$$

where F_c is the Faraday constant, R is the gas constant, T is the temperature, c^+ is the cation ion concentration, and c^- is the anion concentration. The TMJ disc was considered as uncharged in this study, since biochemical studies have shown that the GAG content of human and porcine TMJ discs is very low (< 4% dry weight) compared with that of hyaline cartilage and IVD (Almaraz *et al.*, 2006; Kuo *et al.*, 2010). For uncharged tissues in NaCl, the relative diffusivity (D/D_0) of NaCl is simply related to the relative conductivity by (Gu *et al.*, 2004):

$$\frac{D}{D_0} = \frac{\chi}{\phi^w \chi_0}, \quad (5)$$

where D is the mean ion diffusivity of Na⁺ and Cl⁻ in tissue, D_0 is the mean ion diffusivity in the bathing solution, χ is the elec-

trical conductivity of the tissue, and χ_0 is the conductivity of the bathing solution. In our analysis, Na⁺ and Cl⁻ were assumed to carry the electrical current because these ions are the primary ionic components of PBS.

Statistical Analysis

Twelve discs were tested in each of 5 regions (total, 60 specimens), and the porosity, electrical conductivity, and relative ion diffusivity of each specimen were determined under 3 compressive strains. Two-way mixed-effects analysis of variance (ANOVA) and Tukey's *post hoc* tests were performed with SAS software (Cary, NC, USA) to determine if significant differences existed between regions and compressive strains. Linear regression was performed to correlate ion diffusivity with tissue porosity. Both the ANOVA and regression analyses included a random effect for disc to accommodate dependence among measurements obtained from the same disc. Statistical differences were reported at p values < 0.05.

RESULTS

Electrical Conductivity

The effect of compressive strain on electrical conductivity in the 5 disc regions are shown in Fig. 2a. There was a significant decrease in electrical conductivity with increases of compressive strain in all 5 disc regions (ANOVA, $p < 0.0001$). The average electrical conductivity over the 5 regions (mean ± SD) at 0% strain was 3.10 ± 0.68 mS/cm, decreased to 2.76 ± 0.58 mS/cm (-11.0%) at 10% strain (0%/10%, $p = 0.0203$), and 2.38 ± 0.55 mS/cm (-22.2%) at 20% compressive strain (10%/20%, $p = 0.0096$; 0%/20%, $p < 0.0001$). Significant regional variation of electrical conductivities was also detected at all strain levels (ANOVA, $p < 0.0001$). The electrical conductivity in the anterior region was significantly higher than that in the posterior region ($p < 0.0001$). No significant interaction was found between the level of strain and the region of the disc.

Porosity (water volume fraction)

The effect of compressive strain on tissue porosity in the 5 disc regions is shown in Fig. 2b. There was a significant decrease in tissue porosity with increases of compressive strain in all 5 disc regions (ANOVA, $p < 0.0001$). The average porosity over the 5 regions (mean ± SD) at 0% strain was 0.726 ± 0.023 , decreased to 0.696 ± 0.026 (-4.1%) at 10% strain (0%/10%, $p < 0.0001$), and 0.658 ± 0.029 (-9.4%) at 20% compressive strain (10%/20%, $p < 0.0001$; 0%/20%, $p < 0.0001$). Significant regional variation of porosity was also detected at all strain levels (ANOVA, $p < 0.0001$). The porosity in the anterior region was significantly

higher than that in the posterior region ($p < 0.0001$). No significant interaction was found between the level of strain and the region of the disc.

Ion Diffusivity

Electrical conductivities of PBS at 22°C were measured using an Orion conductivity meter (Model 150Aplus, Orion, Beverly, MA, USA). The value of 15.5 mS/cm for solution conductivity was used to normalize the measured conductivity data of tissues in Equation 5. The effect of compressive strain on ion diffusivity in the 5 disc regions is shown in Fig. 2c. There was a significant decrease in ion diffusivity with increases of compressive strain in all 5 disc regions (ANOVA, $p = 0.0002$). The average relative ion diffusivity over the 5 regions (mean $\pm$ SD) at 0% strain was 0.273 ± 0.055 , decreased to 0.253 ± 0.048 (-7.3%) at 10% strain (0%/10%, $p = 0.1103$), and 0.231 ± 0.048 (-15.4%) at 20% compressive strain (10%/20%, $p = 0.0686$; 0%/20%, $p < 0.0001$). Significant regional variation of the ion diffusivity was also detected at all strain levels (ANOVA, $p = 0.0004$). The ion diffusivity in the anterior region was significantly higher than that in the posterior region ($p = 0.0002$). No significant interaction was found between the level of strain and the region of the disc.

DISCUSSION

The objective of this study was to investigate the effect of mechanical strain on small ion diffusivity in porcine TMJ discs using electrical conductivity methods. The measured electrical conductivity and calculated ion diffusivity from this study indicated that compressive mechanical strain impeded solute transport through the disc. Our results also indicated that the solute transport properties of the TMJ disc were region-dependent.

The decrease in electrical conductivity with increasing mechanical strain in the TMJ disc was mainly due to the porosity (water volume fraction) reduction caused by increasing compression. In this study, we confirmed that the ion diffusivity of the TMJ disc positively correlated with the porosity (Fig. 3). Tissue compression caused fluid exudation and a corresponding decrease in tissue porosity. The reduction in porosity resulted in decreased ion diffusivity in the tissue and subsequently decreased electrical conductivity (Gu *et al.*, 2004; Jackson *et al.*, 2009). This is in agreement with previous studies reporting decreasing diffusivity of solutes with increasing static compressive strain in articular cartilage (Quinn *et al.*, 2000, 2001), as well as IVD tissues (Jackson *et al.*, 2008; Yuan *et al.*, 2009). The strain-dependent electrical conductivity and ion diffusivity indicated that mechanical strain impeded solute transport in TMJ discs.

Transport properties of the TMJ disc were region-dependent, with the electrical conductivity and ion diffusivity in the anterior region significantly higher than those in the posterior region. This finding is consistent with the region-dependent solute diffusion of 4 kilodaltons FITC-Dextran in porcine TMJ discs (Shi *et al.*, 2010). The results of this study showed that the water volume fraction in the anterior region (0.749 ± 0.045) was significantly higher than that in the posterior region (0.707 ± 0.017). The correlation between the diffusivity and tissue water volume fraction (porosity) suggests that the diffusive transport

Figure 3. Correlation between the relative ion diffusivity and the water volume fraction (porosity). Significant positive correlation was detected ($R = 0.577$, $p < 0.0001$).

in porcine TMJ discs is dependent upon tissue composition. The inhomogeneous distribution of tissue components results in region-dependent diffusivity.

The electrical conductivity and tissue porosity of cartilaginous tissues were compared and listed in the Table. The electrical conductivity in porcine TMJ discs was the lowest compared with that in human articular cartilage, porcine annulus fibrosis, and human annulus fibrosis. Consequently, the mean relative diffusivity of Na^+ and Cl^- in porcine TMJ discs (0.273 ± 0.055) was lower than that in human articular cartilage (0.35-0.45) (Maroudas, 1968) and human annulus fibrosis (0.35-0.45) (Urban, 1977). The lower solute diffusion in the TMJ disc is likely due to lower tissue porosity compared with that in other cartilaginous tissues. The normal adult TMJ disc is a large avascular structure (Rees, 1954; Leonardi *et al.*, 2003), so the balance between the rate of nutrient diffusion through the matrix and the rate of consumption by disc cells establishes a concentration gradient inside the disc. This study showed that solute diffusivities in the TMJ disc are much lower than the values in other cartilaginous tissues, and compressive mechanical strain can further impede solute diffusion in the TMJ. Moreover, our cell metabolic studies have shown that the TMJ disc has cell density and nutrient consumption rates higher than those in articular cartilage and IVD (Kuo *et al.*, 2011). Therefore, it is likely that a steeper nutrient gradient may exist in TMJ discs and is vulnerable to pathological events which impede nutrient supply, including sustained joint loading due to jaw clenching.

The strain distribution in the TMJ disc *in vivo* is complex and can be determined through finite element analysis (Koolstra and van Eijden, 2005). The strain-dependent diffusivity established in this study needs to be incorporated into finite element models to assess the overall impact of physiological/pathological loading on solute transport in TMJ discs. This study investigated the effect of mechanical strain only on small ion diffusivities. Generally, the mechanical strain has a greater impact on the diffusivity of larger solutes (Jackson and Gu, 2009). Therefore, it

Table. Comparison of Electrical Conductivity and Tissue Porosity in Unstrained State between the TMJ Disc and Other Cartilaginous Tissues

	Electrical Conductivity (mS/cm)	Water Volume Fraction (porosity)	Reference
Porcine TMJ disc	3.10 ± 0.68	0.726 ± 0.023	Present study
Human articular cartilage	6-10	~0.8	Hasegawa <i>et al.</i> , 1983
Porcine annulus fibrosis	5.60 ± 0.89	0.74 ± 0.03	Gu <i>et al.</i> , 2002
Human annulus fibrosis	7.5 ± 0.8	0.80 ± 0.02	Jackson <i>et al.</i> , 2009

is necessary to determine the impact of mechanical strain on the diffusivities of other essential solutes, such as oxygen and glucose. In this study, the electrical conductivity was measured in the superior-inferior direction (the main diffusion route). Considering the tissue structure of the TMJ disc, the relationship between the anisotropic diffusion (Shi *et al.*, 2010) and tissue morphology requires further studies. Although pigs have been considered as a good animal model for the study of human TMJ disc mechanics, it is still necessary to determine the solute diffusivity on human samples.

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