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Coupling plowing of cartilage explants with gene expression in models for synovial joints

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ABSTRACT

Articular cartilage undergoes complex loading modalities generally including sliding, rolling and plowing (i.e. the compression by a condyle normally to the tissue surface under simultaneously tangential displacement, thus generating a tractional force due to tissue deformation). Although in *in vivo* studies it was shown that excessive plowing can lead to osteoarthritis, little quantitative experimental work on this loading modality and its mechanobiological effects is available in the literature. Therefore, a rolling/plowing explant test system has been developed to study the effect on pristine cartilage of plowing at different perpendicular forces.

Cartilage strips harvested from bovine nasal septa of 12-months-old calves were subjected for 2 h to a plowing-regime with indenter normal force of 50 or 100 N and a sliding speed of 10 mm s^{-1}. 50 N produced a tractional force of 1.2 ± 0.3 N, whereas 100 N generated a tractional force of 8.0 ± 1.4 N. Furthermore, quantitative-real-time polymerase chain reaction experiments showed that TIMP-1 was 2.5x up-regulated after 50 N plowing and 2x after 100 N plowing, indicating an ongoing remodeling process. The expression of collagen type-I was not affected after 50 N plowing but it was up-regulated (6.6x) after 100 N plowing, suggesting a possible progression to an injury stage of the cartilage, as previously reported in cartilage of osteoarthritic patients. We conclude that plowing as performed by our mimetic system at the chosen experimental parameters induces changes in gene expression depending on the tractional force, which, in turn, relates to the applied normal force.

1. Introduction

Synovial joints are composed of a mechanical system comprising bones, cartilage, tendons and ligaments. These elements interact and cooperate allowing joint movement, which is also facilitated by synovial fluid—the joint lubricant. Within the mechanical system, each element has a specific function: bones provide support, cartilage—placed on adjacent bones—provides a sliding surface and adsorbs shocks, tendons link muscles and bones, while ligaments stabilize the joint (Cawston and Young, 2010).

It has been demonstrated that in pathological conditions such as in osteoarthritis (OA), elevated expression and activities of proteolytic enzymes cause destruction of articular cartilage and ultimately of the underlying subchondral bone (Goldring and Marcu, 2009; Martel-Pelletier et al., 2008; Williams et al., 2010). Patients affected by this degenerative disease suffer from severe pain and movement impairment with a general decrease in the quality of life (Tellini et al., 2008).

Since injurious mechanical stress has been recognized as one of the causes of OA development, cartilage overloading has been the focus of a number of studies aimed at mimicking unfavorable mechanical conditions that cartilage could experience (Fitzgerald et al., 2006a; Kurz et al., 2005; Lin et al., 2004; Patwari et al., 2001; Torzilli et al., 2010). Although these studies provided insight into the biological response of cartilage to static and cyclic loading of different duration, normal force magnitude and frequency, their uni-axial design presents some limitations.

Drop-tower devices have been built and described by Jeffrey et al. (1995) and Repo and Finlay, (1977). A common disadvantage of these devices was that the strain rate during compression could not be measured. Later, other experiments have been performed using systems with computer-controlled motor-driven plates that were able to control load or displacement during injury (D'Lima et al., 2001; Loening et al., 2000; Quinn et al., 1998; Torzilli et al., 1997).

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