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Review

Magnetic resonance compositional imaging of articular cartilage: What can we expect in veterinary medicine?

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ABSTRACT

Since cartilage has limited ability to repair itself, it is useful to determine its biochemical composition early in clinical cases. It is also important to assess cartilage content in research animals in longitudinal studies in vivo. In recent years, compositional imaging techniques using magnetic resonance imaging (MRI) have been developed to assess the biochemical composition of cartilage. This article describes MR compositional imaging techniques, and discusses their use and interpretation.

Technical concerns still limit the use of some techniques for research and clinical use, especially in veterinary medicine. Glycosaminoglycan chemical-exchange saturation transfer and sodium imaging are better used with high field magnets, which have limited availability. Long acquisition times are sometimes required, for instance in T1rho (ρ) and diffusion-weighted imaging, and necessitate general anaesthesia. Even in human medicine, some techniques such as ultra-short echo T2 are not fully validated, and nearly all techniques require validation for veterinary research and clinical practice. Delayed gadolinium-enhanced MRI of cartilage and T2 mapping appear to be the most applicable methods for compositional imaging of animal cartilage. Combining T2 mapping and T1ρ allows for the assessment of proteoglycans and the collagen network, respectively.

Introduction

Osteoarthritis (OA) is a degenerative process of the joint characterised by progressive degeneration of the articular cartilage and reduced joint function. Articular cartilage has biomechanical properties that are attributable to its extracellular matrix (ECM), which is composed of collagen, proteoglycans (PGs), hyaluronan (HA) and water (Lu and Mow, 2008).

Collagen fibres are organised into three zones (Fig. 1). In the radial zone, the fibres are perpendicular to the articular surface, forming rows; in the transitional zone, they overlap as thin lamellae, and in the superficial zone, they are tangential to the articular surface. This arcade-like orientation is involved in the dynamic behaviour of cartilage, reducing stresses in its deep part during loading and ensuring resistance to shearing forces in its superficial part (Halonen et al., 2013).

PGs are composed of a central core protein linked to hundreds of negatively charged polysaccharide chains called glycosaminoglycans (GAGs) and to HA (Fig. 1). Sulphate and carboxyl groups of GAGs carry negative charges (Maroudas et al., 1969). Each fixed negative charge requires a positive counter-ion (Na^+) for the tissue to maintain overall electroneutrality. The high concentration of Na^+ results in attraction to water.

Water linked to Na^+ is called free water. It exists in two other forms when it is directly linked to collagen or PGs (Maroudas, 1976). When the joint is loaded, water flows through the ECM. Its flow is limited by the frictional resistance of collagen and attraction by ions. Water contributes to the viscoelastic behaviour of cartilage (Lu and Mow, 2008).

With progression of OA, synthesis is insufficient to compensate for the degradation of ECM; biochemical changes, such as a decrease in PGs and the degradation of collagen, occur as a consequence (Bijlsma et al., 2011). The alteration of the collagen network and the associated increase in water content modify the biomechanical properties of cartilage.

Since cartilage has limited ability to repair itself, biochemical changes associated with early OA should be identified as soon as possible in clinical cases. For research purposes, it would be extremely useful to determine the composition of cartilage in longitudinal studies in vivo. In recent years, compositional imaging techniques using magnetic resonance (MR) imaging have been

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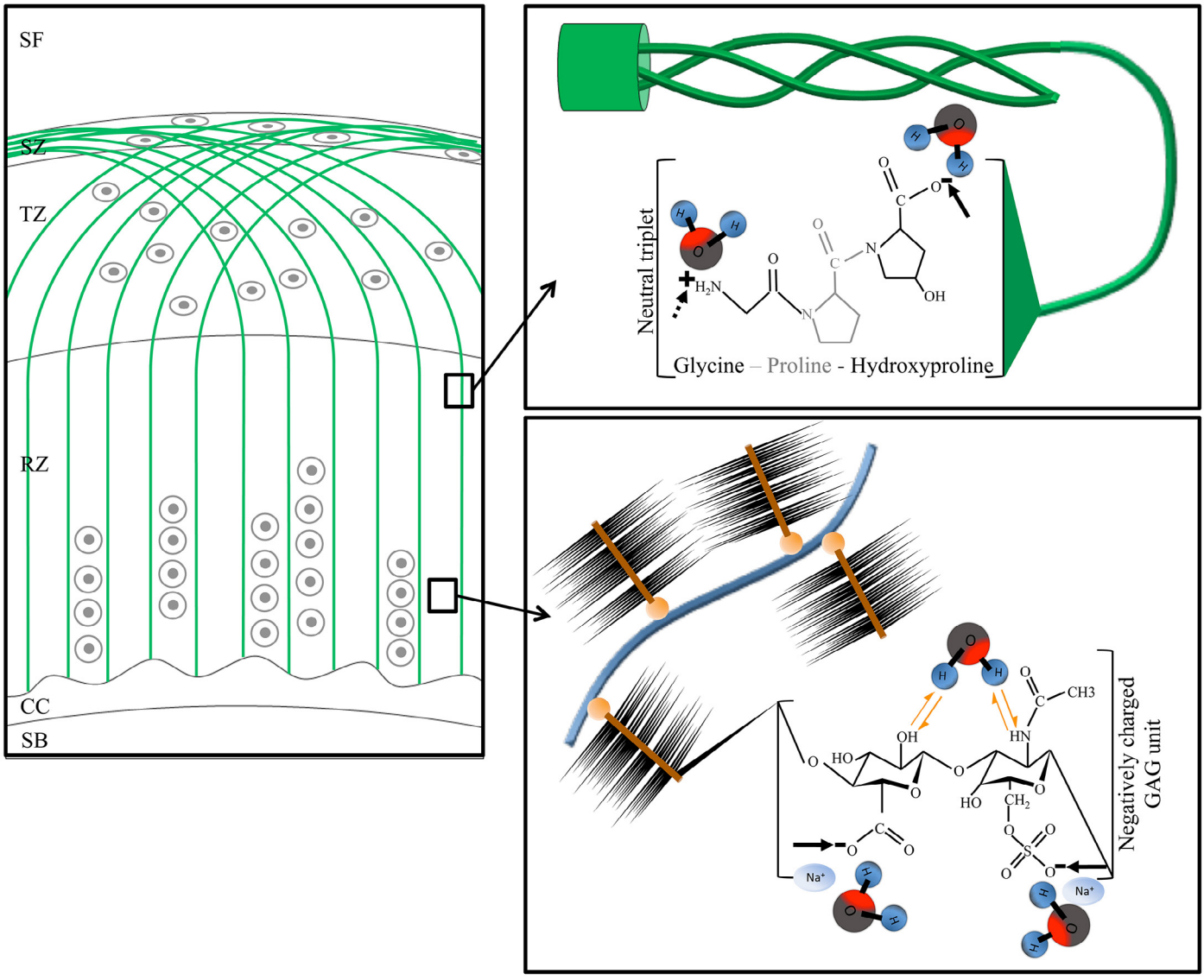

Fig. 1. Biochemical composition of cartilage. Articular cartilage is composed of hyaline cartilage and calcified cartilage (CC) overlying the subchondral bone (SB). Hyaline cartilage is composed of three zones. In the superficial zone (SZ), which is in contact with the synovial fluid (SF), chondrocytes (grey ellipses) are flattened and collagen fibres are parallel to the articular surface. The transitional zone (TZ) is characterised by rounded chondrocytes and arcade-like collagen fibres. In the radial zone (RZ), rounded chondrocytes are aligned in columns and collagen fibres are perpendicular to the articular surface. Collagen fibres are formed by aggregates of tropocollagen subunits. These are composed of a triple helix of polypeptide chains. Although neutral overall, these chains bear a negative (plain arrow) and a positive (dotted arrow) charge. A hydrated gel expands through the collagen network, made of sulphated glycosaminoglycans (GAGs; black pins) linked to a core protein (brown line) to form a proteoglycan (PG). Each PG is connected to HA (woven blue line) by a link protein (orange circle). GAGs are composed of hundreds of negatively charged units, counterbalanced by sodium. Therefore, water exists in three forms: molecular water (linked to the negative [plain arrow] or positive [dotted arrow] charges of collagen and GAG) and free water (attracted by the sodium osmotic pressure; not shown in this figure). In cartilage, protons are found in the hydrogen nucleus (H) of every molecule (collagen, water, GAGs). Orange double arrows illustrate the chemical exchange saturation transfer (CEST) of protons that is possible between amide and hydroxyl groups and is used in a specific compositional imaging technique described in this review.

developed to assess the biochemical composition of cartilage. This article reviews MR compositional imaging techniques and discusses their use and possible applications to veterinary medicine.

T2 mapping

The mobility of water protons varies with tissue type; it is high when protons are in free water and low when they are immobilised in ECM. This influences the transverse (T2) relaxation time, due to spin–spin (neighbouring) interactions (Watrin et al., 2001). In MR imaging (MRI) sequences highlighting T2 (T2 weighted, W), mobile water protons (e.g. in synovial fluid or in damaged collagen networks with increased free water content) give a hypersignal (long T2), whereas water protons immobilised in ECM (short T2) give a hyposignal (David-Vaudey et al., 2004). Since T2 reflects water content and integrity, specialised T2 sequences have been created in an attempt to identify the early stages of OA. In general terms, T2 sequences can demonstrate pathology because they identify changes in water content.

Signals can be plotted in a T2 decay curve, which is used to calculate a mathematical parameter called the T2 relaxation time of the tissue. T2 mapping involves multiple T2 sequences with slightly varying parameters. The differences in T2 relaxation time over all sequences are then combined and a colour map of T2 times is generated. The application of T2 mapping to cartilage assessment was initially reported in 2000 by Mosher et al. and can be performed with a 1.5 Tesla system.