Diffusion MR spectroscopy of extracellular matrix degradation in intervertebral disc degeneration

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Intervertebral disc degeneration (IVDD) is a leading cause of lumbar spine-related low back pain, a disease of wide prevalence causing an enormous societal burden in Hong Kong and worldwide. The principal components of intervertebral discs are the nucleus pulposus (NP) and the annulus fibrosus. In normal discs, ECM in NP is comprised of high concentration of proteoglycans (PGs) intertwined with a well-organized collagen network. PGs are the critical component of ECM and are made of long, aggregated glycosaminoglycan (GAG) chains attached to core and link proteins. ECM degradation begins during early IVDD. PGs and collagen fibers gradually disintegrate, with their fragments then detaching from the ECM and becoming mobile. Over time, these ECM macromolecular fragments slowly leak out of the disc, causing an overall PG reduction in the NP. Eventually, osmotic pressure declines and water absorption diminishes, leading to disc dehydration, morphological changes and impaired biomechanical properties.

Magnetic resonance (MR) provides the most comprehensive means for IVDD assessment. At present, all available MR methods detect pathophysiological changes that develop considerably after the onset of ECM degradation. Although IVDD is a slow process that almost certainly evolves over decades, clinical IVDD diagnoses at present predominantly are made only at a late and irreversible stage. Therefore, there is a pressing clinical need to develop new imaging strategies for early detection of IVDD. Moreover, new IVDD treatments, now in development, will need improved imaging methods that characterize IVDD at molecular and microstructural levels to assess their efficacy in both preclinical and clinical settings.

Diffusion MR is a powerful non-invasive tool for probing tissue microstructure. Molecular diffusion is sensitive to changes in molecule size and microstructural characteristics. As ECM degrades during the early stage of IVDD, PGs and collagen fragments become more mobile. The gel-like NP has low cellular density, providing a relatively unrestricted water space for the diffusion of these macromolecular fragments. GAGs and some collagen degradation components are also highly hydrophilic. Therefore, we hypothesized that diffusion MR spectroscopy (MRS) would allow us to measure the increased mobility of these macromolecular fragments by detecting their increased diffusivities.

In this study, we have developed a new diffusion MRS approach and applied this method to a papain-induced bovine IVDD model at 7T. Our results demonstrate that diffusion MRS can detect the gradual disintegration of collagen and PG in the NP during early IVDD by measuring their increased diffusivities, offering an unprecedented possibility to probe ECM integrity directly and non-invasively. Further development of this new, non-invasive MR method will provide a sensitive imaging capability for both preclinical and clinical investigation of IVDD. It may contribute to early detection and management of clinical IVDD, to better assessment of candidate therapies for IVDD, and to an improved understanding of the molecular and microstructural basis of IVDD.

Acknowledgement: This work is supported in part by Hong Kong Research Grant Council (HKU174314).

Brief CV
Dr. Wu is a Chair and Lam Woo Endowed Professor of Biomedical Engineering, Associate Dean of Engineering (for Research) at University of Hong Kong (HKU). He obtained his BSc in Medical Physics from University of Wisconsin-Madison in 1988, PhD in Radiological Sciences from University of California—Irvine in 1993. From 1990 to 2003, Dr. Wu worked at Columbia University on 3D PET system engineering, high field MRI engineering and biomedical applications. He was an Assistant Professor of Radiology from 1993 and later an Associate Professor of Radiology and Biomedical Engineering from 2000. Dr. Wu joined HKU in 2003. At present, he is the founding Director of Laboratory of Biomedical Imaging and Signal Processing (7T MRI), and Research Director of 3T MRI Unit at HKU. His research focus is the development of high-field MRI methodologies for in vivo microstructural and functional characterization of biological tissues, particularly the CNS systems, using diffusion, spectroscopy and functional approaches. Dr. Wu is an elected Fellow of IEEE (2014), ISMRM (2011) and AIMBE (2010). Presently, Dr. Wu is the Asia-Pacific Regional Editor of NMR in Biomedicine, a journal dedicated to MR imaging and spectroscopy.

Quantitative medical image analysis of musculoskeletal system

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The past decade has witnessed considerable advancements in imaging techniques, developing from structural to functional, from static to dynamic, enabling both individual- and population-based analysis. The speaker will give a brief introduction of advanced computational techniques that enable accurate and efficient extraction of useful information from musculoskeletal images with clinical application, e.g. the etiopathogenesis study of adolescent idiopathic scoliosis, ankylosing spondylitis, and planning of the hearing aid implantation surgery, etc.

Brief CV
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Professor Defeng WANG joined the Chinese University of Hong Kong as an academic staff since 2010. His research interests include medical image analysis, computational radiology and multimodal medical data fusion. Professor Wang won best scientific oral presentation award in annual meeting of the Korean Society of Magnetic Resonance in Medicine in 2012, The Best Young Biomedical Engineer’s Paper Award by The Hong Kong Institution of Engineers in 2012, The Third Prize for Excellent Poster Award in Tianjin International Stroke Conference (TISC) Beijing in 2012 and the IFMBE Best Paper Award in EMBC 2005. Professor Wang has published over 80 papers in renowned journals, and has also contributed to the peer review of 20 journals. He has secured over 10 major competitive research grants. He has also served the editorial boards of four scientific journals.