Student:	Susan Xian
Title:	Determining the health of joint cartilage in osteoarthritis with MARS spectral
Supervisors:	Dr Mohsen Ramyar, Associate Professor Nigel Anderson and Associate Professor Tim Woodfield
Sponsor:	Christchurch Radiology Group

Introduction:

Osteoarthritis (OA) is a common degenerative joint disease and is one of the leading causes of pain and disability around world. The disease is characterised mainly by the degeneration of the cartilage which line the bone ends. However, current imaging techniques used clinically are poor at assessing cartilage.

The main diagnostic imaging technique used for OA are plain radiographs, which are unable to directly visualise the cartilage. Instead, the cartilage thickness is estimated by looking at the joint space width, which is narrowed in OA due to the wearing away of the cartilage. By the time such changes are visible, there has already been substantial loss of cartilage and permanent joint damage.

Early detection and management can help slow the disease process. Thus, there has been increasing interest in developing methods to measure cartilage health before extensive degeneration has occurred.

One way of doing this is by measuring the glycosaminoglycan (GAG) content of the cartilage. GAG are important proteins which give cartilage its compressibility and resilience. GAG can be considered sensitive markers of cartilage health. Non-destructive methods for determining GAG content are particularly valuable, not only for clinical use for detecting early OA changes, but also for research purposes, allowing study of GAG content overtime in response to novel treatment modalities.

GAG are negatively charged proteins and therefore have an inverse relationship to other negatively charged materials, such as a negatively charged (anionic) contrast agent.

MRI techniques for imaging cartilage are in use clinically, but are met with limitations such as poor spatial resolution. This limits its ability to clearly visualise the subtle GAG alterations though the depth of the cartilage. There are also the usual limitations of MRI such as long scan times and inability to use with metal implants.

The MARS spectral CT offers a potential solution. MARS spectral is a new imaging modality being develop in Christchurch. MARS is superior given its higher spatial resolution and ability to distinguish between two similarly dense materials, such as contrast agent and subchondral bone, which has been a limitation of conventional CT.

Previous work has shown that MARS spectral CT used with an anionic, iodine based contrast is able to visualise cartilage and has a quantifiable, inverse relationship with GAG.

In this present study, a Gadolinium contrast agent has been studied as an inverse marker of cartilage health, as it is more suited for use in the energy ranges for human MARS CT scanners and is already FDA approved for injection into the joint space.

Aim:
To map and measure the Gadolinium concentration from MARS images of osteoarthritic tibial plateaux incubated in gadolinium as an inverse marker of cartilage health.

Impact:
Development of a non-destructive method for measuring cartilage health will allow clinicians to detect early osteoarthritic changes for prompt intervention to slow progression to permanent joint damage. Researchers will also be enabled to study the subtle biochemical changes within cartilage overtime to enhance understanding of the disease process of OA, for development of new treatment modalities and a means to evaluate the effect of treatments overtime.

Method:
Nine osteoarthritic human tibial plateaux removed at the time of a total knee joint replacement have been incubated in Gadolinium (Gd) and scanned using the MARS spectral CT. The resulting images were "material decomposed" to separate it into its material make up. The resulting Gd images were analysed with the aid of a computer software to determine the mean Gd concentration in certain regions. These values were then compared to the GAG concentration (as determined by a biochemical assay) in the corresponding volume. Colourmaps visualising and quantifying the Gd concentration through the depth of the cartilage were then generated using MATLAB.

Results:
The MARS spectral CT scans of human tibial plateau samples incubated in Gadolinium (Gd) contrast were able to provide both visual and quantitative data on Gadolinium concentration. Higher concentrations of Gd contrast were present in the surface layer with decreasing concentration through the cartilage depth. These results are inverse to what is known in the literature regarding the GAG distribution within cartilage, where the surface layer has low concentration of GAG with increasing concentration through its depth. This thus supports Gd as an inverse marker of cartilage health.

The bulk Gd concentration in the studied regions held an inverse relationship with the GAG concentration in the corresponding regions as determined by a biochemical assay. Although this was a weak correlation, further analysis of the samples and scans allowed identification of possible confounding factors which may explain the weakening of the association. This will allow refinement of the methodology to aid in future research.

Conclusion:
MARS spectral CT imaging of human osteoarthritic samples incubated in gadolinium contrast was successful and holds promise for use as a measure of cartilage health. Further refinement in the scanning procedures and analysis will aid in future study for the development of protocols and standards for clinical use.