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"Proteoglycan profile" and Level-Specific Biomarker of Lumbar Disc Displacement

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Background

Disc displacement and Disc degeneration

- Disc displacement is defined as herniation, bulge or extrusion of disc material beyond intervertebral disc space (Fig 1) [1], which can result in spinal nerve root compression and clinical symptoms of low back pain and sciatica with lifetime prevalence of 13-40% and 67-84% respectively [2] .
Controversy exists whether disc displacement is associated with disc degeneration. [3]

- Disc degeneration is characterized by a loss of proteoglycan content in disc histologically. However, there is no precise method to measure in-vivo proteoglycan content in disc, which can reflect the severity of disc degeneration in patients. [4]
Therefore, a more precise and quantitative assessment is required to further establish the linkage between two disc pathological entities.

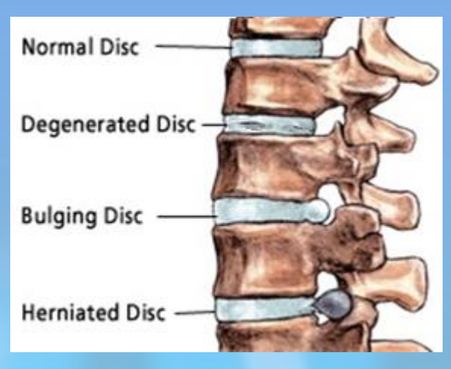

Fig 1 – Graphical illustration comparing a normal intervertebral disc, a disc with degeneration and a disc with displacement (i.e. bulging and herniation)[1]
Disc generation has been proposed to be associated with disc displacement due to its biochemical alteration (i.e. proteoglycan loss) and subsequent mechanical displacement of disc material [3]

MRI : T2-weighted and T1 rho

- Traditionally, **T2-weighted MRI** is used to assess disc degeneration and disc displacement [5].
However, T2-weighted MRI only provides a qualitative snap-shot of disc integrity, which is not precise and lacks quantification. [6]
- On the other hand,**T1-rho MRI** is shown to be capable of providing a precise and quantitative assessment of proteoglycan concentration in disc , and therefore can sensitively detect for any early degenerative changes in the setting of lumbar disc displacement. (Fig 2)[6]

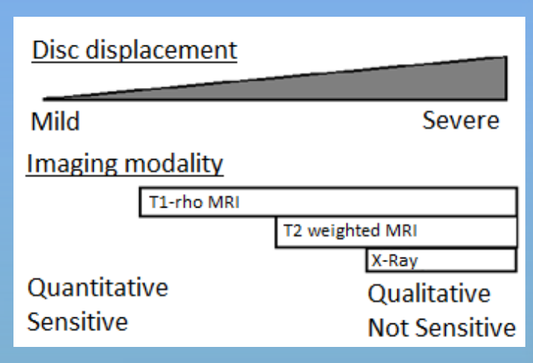

Fig 2 - Comparison between currently used imaging modality for lumbar spine degeneration.
- Conventionally used T2W MRI is superior to X-Ray in determining disc degeneration, [5] but not as sensitive as T1 rho for detecting early disc degeneration.[6] T2W MRI also lacks quantification for precise assessment of disc degeneration

Objective

This is the first study globally aiming to a) generate **"proteoglycan profile"** for lumbar discs (i.e. a quantitative and precise measurement for the degree of disc degeneration) and b) **level specific threshold value** as a predictive biomarker for disc displacement via T1 rho MRI, to address the precise correlation of disc integrity in displacement and degeneration.

Method

i) Study design and Study population

This is a cross-sectional radiological study comprising of 76 Southern Chinese volunteers (mean age: 50.6 years ; 51.3% males) from Hong Kong Degenerative Disc Disease Cohort.[7] Questionnaires based on epidemiology and clinical questions related to low back pain and sciatica was carried out under supervision of research staff in Queen Mary Hospital Orthopedics and Traumatology outpatient clinic.

ii) MR Imaging Acquisition & T2 weighted imaging

All volunteers underwent T2-weighted (T2W) and T1-rho MRI of the lumbar spine from L1-S1 via a clinical 3T MRI scanner in Department of Diagnostic Radiology of University of Hong Kong.
T2-weighted MRI imaging was analyzed using a clinical degenerative score [5], along with other imaging pathological phenotypes (e.g. disc displacement, Schmorl's node, high intensity zone, spondylolisthesis, modic change) (Fig 3 - Left)

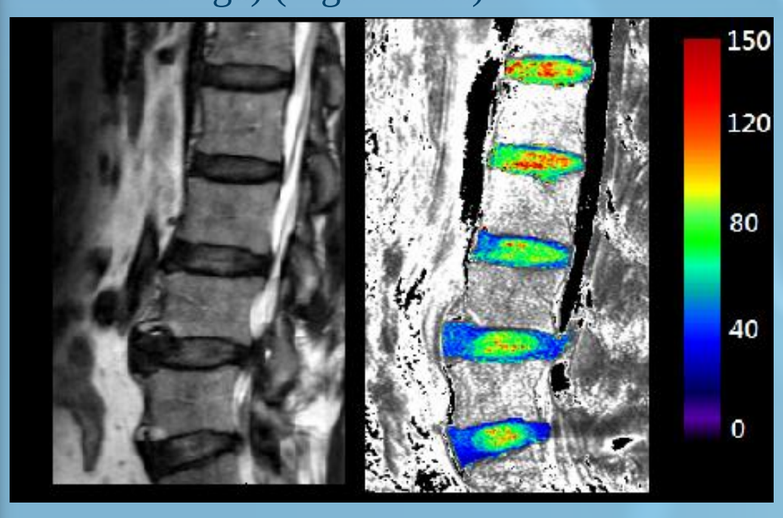

Fig 3. Disc degeneration was detected at lower levels of this patient, who also had disc degeneration at the same levels
(**Left**: Conventional T2-weight MRI on spine
Right : T1 rho MRI mapping on color scale. **Red** / **Yellow** means higher T1 rho value. **Green** / **Blue** means lower value)

iii) T1 rho MRI processing & Data analysis

T1 rho values were calculated on a pixel-by-pixel basis by a linear regression of intensity data to an exponential decay function. Values were used to create 3-dimensional spatial maps of T1 rho (Fig 3 - Right)
Interpretation : lower T1 rho value indicates loss of proteoglycan in disc (i.e. **Green** or **Blue** in Fig 3), which corresponds to disc degeneration in that specific level, and hence risk of displacement
ROC curve analyses were performed to determine a) area under the curve (AUC) (Fig 4) and b) optimal threshold levels for T1-rho values associated with disc displacement. (Fig 5, Table 2)

Result

i) Disc displacement

In total, 380 lumbar discs were assessed.. Overall, 50% of the discs had some degree of disc displacement; whereby, 49.2% had bulging/protrusion and 0.8% had extrusion. Percentage of disc displacement in each lumbar disc level is shown in Table 1 below

Lumbar disc level	L1/2	L2/3	L3/4	L4/5	L5/S1
% of disc with displaced	27.6	51.3	48.7	71.1	51.3

ii) "Proteoglycan profile" in displaced & non-displaced disc

The median T1-rho value for overall non-displaced discs was 77.6ms, compared to 64.5ms for displaced discs ($p<0.001$). The median level-specific T1-rho values for non-displaced discs are all higher than displaced discs, indicating "proteoglycan profile" as a feasible imaging biomarker. (Fig 4)

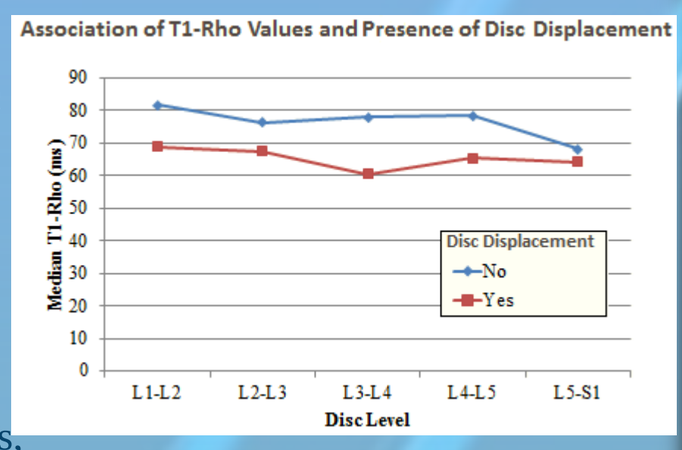

Fig 4. Level specific T1rho values for displaced vs non-displaced disc

iii) Level-specific biomarker

Based on ROC analyses, AUC value for the association of T1-rho values and overall lumbar disc displacement was 0.69 (95% CI: 0.63-0.74),with an optimal threshold value of 54ms.(Fig 5)

Level-specific ROC analyses were also performed based on optimal threshold values for disc degeneration. Result was summarized in Table 2 below

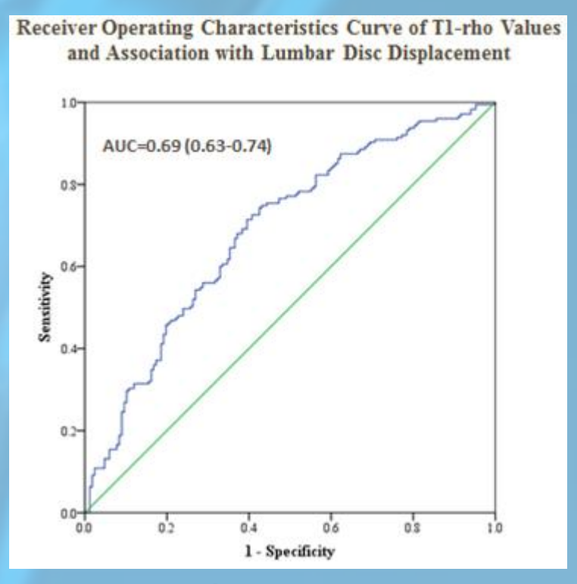

Fig 5. ROC of optimal T1 rho thresholds at 54ms in association with disc displacement. AUC was 0.69.

Lumbar disc level	L1/2	L2/3	L3/4	L4/5	L5/S1
Area under curve	0.74	0.64	0.72	0.63	0.59

Conclusion

This is the **first study** globally to address the correlation between **"proteoglycan profile"** and **disc displacement**. Result from this study has revealed that "Proteoglycan profile" as constructed by T1 rho MRI on intervertebral discs can be a sensitive imaging biomarker to predict disc displacement.
Level-specific biomarker from statistical analyses can provide clinicians and researchers with a more precise and quantitative tool to predict early disc degenerative changes and its associated disc displacement.
With the **"Proteoglycan profile"** and **level-specific biomarker**, further development on the etiology, classification and management strategies of disc degeneration and displacement can be initiated to benefit the great population suffering from the above two common spinal disease entities.

Reference

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