Potential metabolic markers for intervertebral disc pain

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INTRODUCTION:

Conventional imaging methods of assessing the painful, degenerated intervertebral disc focus solely on morphologic criteria. However, it is well-known that there is a poor correlation between morphologic findings and patient symptoms. The goal of this *in vitro* study is to utilize quantitative high-resolution magic angle spinning (HR-MAS) NMR spectroscopy as a tool to accurately characterize biochemical markers in disc specimens harvested from patients undergoing surgery. Spectra from discs obtained from patients that underwent discectomy for back pain and those of a reference population, consisting of patients undergoing surgery for scoliosis, were compared in attempts to identify biochemical signatures of painful disc degeneration.

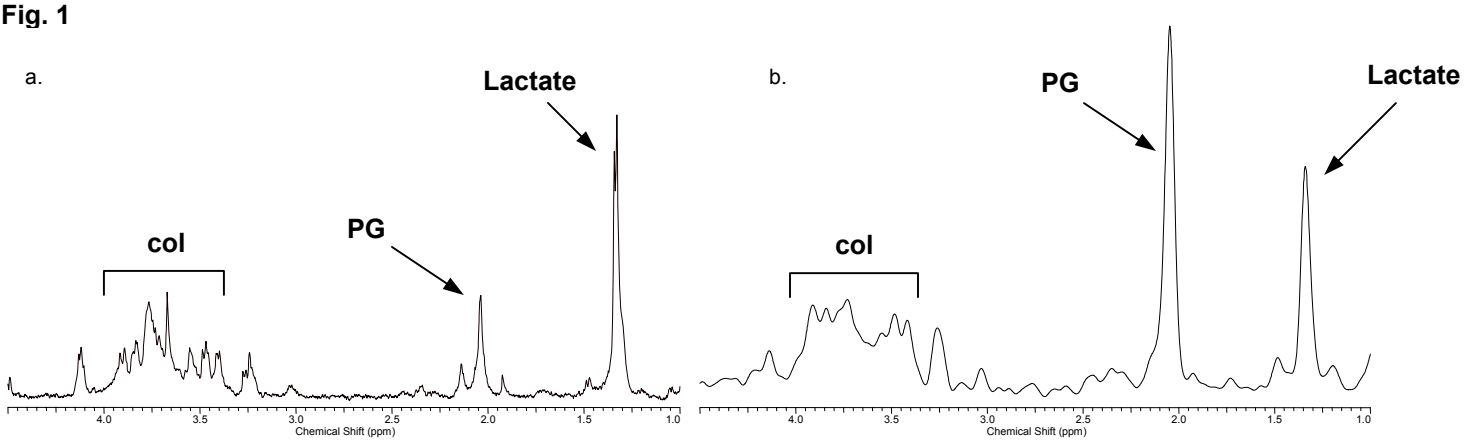
MATERIALS AND METHODS:

Spectral data were acquired at 11.7T (500 MHz), 1°C, and a 2,250 Hz spin rate using a Varian INOVA spectrometer equipped with a 4 mm gHX nanoprobe**.** Disc tissue removed at surgery in patients with discogenic pain (n = 6) and patients with scoliosis undergoing anterior and/or posterior spinal fusion (n = 4) were studied using custom designed 35 ul rotors. Quantitative proton spectra were acquired for tissue samples (mean = 14.28 ± 2.91 mg) with D2O+0.75% TSP as a standard (Sigma-Aldrich, St. Louis, MO). A spin-echo rotor synchronized Carr-Purcell-Meiboom- Gill (CPMG) pulse sequence (nt = 128, at = 2.0 s, TR = 5 s, echo time = 80ms) was acquired for each tissue sample. The lactate resonance (1.31 ppm, doublet), n-Acetyl resonance associated with proteoglycans (PG) (2.04 ppm, singlet), and collagen breakdown region (col) (3.30-4.00ppm) were analyzed to compare disc specimens. These regions are annotated in Fig. 1.

RESULTS:

Relative to deformity patients, those with discogenic back pain demonstrate significantly lower PG/Lactate and PG/col ratios ($p<0.05$; Fig.1, Table 1).

Fig. 1



Above are representative 80ms H1 CPMG spectra of (a) discogenic pain patient and (b) patient with scoliosis. The proteoglycan n-Acetyl resonance (PG), lactate, and collagen breakdown region (col) are indicated.

Table 1 Ratios of PG/Lactate, PG/Col and Lactate/col ± one standard of deviation

	Disc Pain	Scoliosis
PG/Lactate	0.37 ± 0.36	1.72 ± 0.81
PG/col	0.28 ± 0.14	0.66 ± 0.35
Lactate/col	0.70 ± 0.35	0.38 ± 0.08

DISCUSSION AND CONCLUSIONS:

Our results suggest that biochemical markers may characterize processes that correlate with discogenic pain. Previous studies report the influence of pH on proteoglycan synthesis and overall health [1-3]. As lactate concentrations increase, the effective pH of disc material decreases due to the increase in free H+ in solution, which can hinder proteoglycan synthesis. While the direct relationship between lactate concentration and pain is unknown, it may be that increased lactate stimulates nerve fibers in granulation tissue associated with disc healing. Further studies with larger numbers of clinically-relevant samples that are matched for degeneration stage are clearly needed, but the spectroscopic markers for assessing biochemical degeneration and association with discogenic pain appear promising.

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ACKNOWLEDGEMENTS: National Health Institute, R21-AR51048