Letter to the Editor

Towards consistency for magnetic resonance (MR) relaxometry of lumbar intervertebral discs

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Lumber disc degeneration is a potential cause of low back pain (LBP). Though disc degeneration itself is not diagnostic for LBP (1-4), in a recent meta-analysis for adults 50 years of age or younger, Brinjikji *et al*. (5) reported disc degeneration is associated with LBP (OR, 2.24; 95% CI, 1.21–4.15; P=0.01). Many studies on magnetic resonance (MR) relaxometry and disc degeneration have been published (6-8). Novel minimally invasive therapies, such as with injected growth factors or genetic materials, have the potential clinical application to treat pathological disc degeneration (9). MR relaxometry may be useful in clinical trials to evaluate the efficacy of these therapies (9,10).

This issue of *QIMS* published an interesting paper by Menezes-Reis *et al*. (11). It is a prospective, cross-sectional and observational study of 90 asymptomatic volunteers at relatively young age 27.1±4.8 years old (range, 20–40 years), and these subjects had low-level physical activity history. Though the T1rho acquisition approach in the study was suboptimal with spin lock frequency of 250 Hz, a few points in their results deserve attention. There was no T2 relaxometry difference between the anterior and posterior annulus fibrosus for their subjects aged 20 to 40 years; however, in the anterior annulus fibrosus T1rho relaxometry values were higher than in the posterior annulus fibrosus. We did additional analysis for the cohorts we previous reported (12). In our study the T1rho of anterior outer annulus fibrosus (AUAF) and posterior outer annulus fibrosus (PUAF) was 53.6±9.6 and 50.7±9.3 msec respectively (P<0.001), and The T2 of AUAF and PUAF was 44.2±9.1 and 36.9±8.6 msec respectively (P<0.001). These results highlight the necessity and importance of analyzing anterior and posterior annulus fibrosus separately, as recently suggested by Ogon *et al*. (13).

Menezes-Reis *et al*. (11) noted in their subjects there was a negative correlation between age and disc T2 relaxation time of the whole disc, nucleus pulposus (NP) and posterior annulus fibrosus at all lumbar disc levels. They demonstrated T2 relaxometry detected gradual disc dehydration in the first two decades of adulthood. However, they observed no statistical significant correlation between aging and disc T1rho relaxation both for NP and annulus fibrosus for their subjects (age range, 20–40 years). For L1/2–L4/5 discs, we noted that the age associated reduction of T1rho of NP had a slope of –1.06, while that of T2 had a slope of –1.47, and T2 may be more sensitive at looking at age related relaxometry reduction for NP (14). It should be noted that Menezes-Reis *et al*.'s study is small in subject number, and for some parameters such as the association between body mass index (BMI), weight and disc relaxometry, the statistical power might not be satisfied.

A number of potential magnetic resonance imaging (MRI) based disc degeneration technique have been published. However, spine specialists are not particularly impressed by the advance on MR relaxometry contributed by MRI community (6,7). Most of the papers demonstrated MR relaxometry confirms the known physiological phenomenon, but does not seem to be useful for diagnostic practice. For translational research aiming for clinical application, I suggest the following points should be considered:

(I) There is a need to establish age specific and region specific normal ranges of relaxivity values. These

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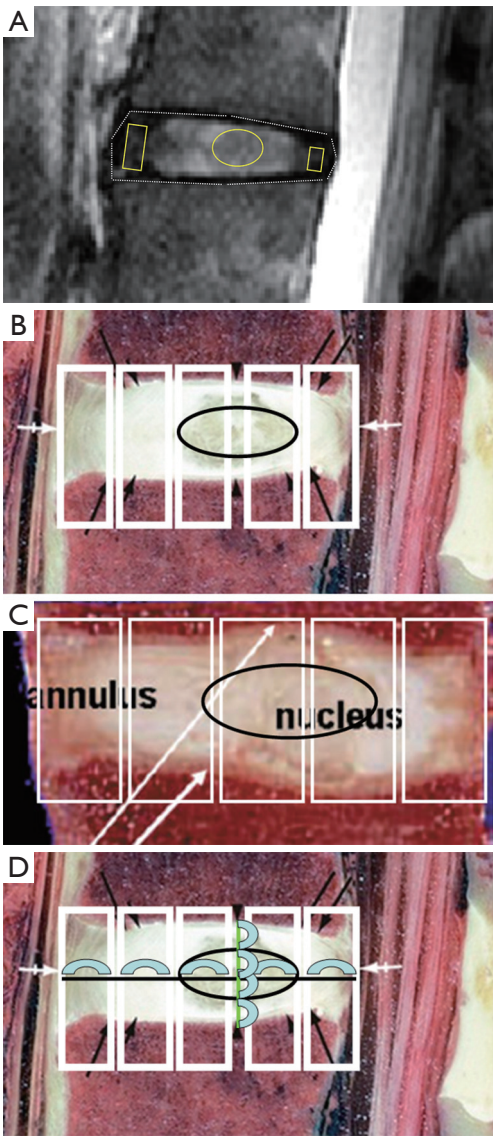

Figure 1 (A) segmentation approach of nucleus pulposus (NP), anterior outer annulus fibrosus (AUAF), and posterior outer annulus fibrosus (PUAF). To accommodate disc degeneration and thereafter NP signal decrease and deformity, the segmentation is anatomical landmark based; ROI for NP will be in oval shape, while AUAF and PUAF will be rectangle shaped with AUAF larger in area than the PUAF. Some spaces were left between ROI for NP and ROIs for AUAF and PUAF. The center of ROI for NP may be located along the 2/5 and 3/5 junction point in the anterior-posterior direction (B,C). In anterior-posterior direction ROI for NP may be approximately 2/5 in length, and in cranial-caudal direction may be approximately 2/4 in length. To avoid partial volume effect, we suggest drawing ROI conservatively, i.e., the ROI area will be a little bit smaller than actually NP or AUAF/PUAF sizes. (B,D) modified and adapted from (19); (C) modified and adapted from (20).

normal ranges should be validated cross sequences and cross MRI vendors. With known sensitivity and specificity value, significant deviation from the normal ranges of disc relaxivity may therefore suggest accelerated aging or pathologies. As a way of example, recently Deng *et al*. (15) and Allkemper *et al*. (16) reported similar mean value for healthy liver parenchyma of 43.2±2.2 msec (at 3.0 Tesla magnet) and 40.9±2.9 msec (at 1.5 Tesla magnet), respectively;

(II) Currently published approaches for anterior and posterior annulus fibrosus, and NP suffer from poor or sub-optimal measurement reproducibility (17). There is a need to establish standardized and reproducible segmentation method. Probably there is a need of acquiring more than a single central slice in the sagittal plane, such as to include three sagittal slices for relaxometry mapping. Segmentation should be based on clear anatomical landmarks, and together with spine size proportionally determined regions of interests (ROI). This is important as accurate segmentation of components is difficult for degenerated discs when the demarcation between annulus fibrosus and NP become fussy, and together with disc space narrowing, portions of NP might protrude into annulus fibrosus (18). A tentative standardized segmentation approach is suggested in *Figure 1*; Due to the differences in the extracellular matrix composition, the annulus fibrosus is divided into an inner annulus fibrosus and outer annulus fibrosus. Till now, in many papers the inner annulus fibrosus is often included as part of NP, instead of annulus fibrosus. The implication of this may need to be further clarified (21). Segmentation of inner annulus fibrosus is certainly difficult for degenerated discs (17,22);

(III) More efforts should be taken to compare and validate novel MR techniques, and to find the complementary roles of each technique (6,7,23). Ideally, MR readouts should be finally validated against clinical readouts (clinical endpoints). MR readouts that characterize intra-discal inflammatory changes remain to be further established (9). Many exploratory MR technically driven studies are being published. However, if a publication of small pilot study was not eventually followed-up by a larger confirmative study (studies); the result of the small study is probably not reproducible. For the later

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case, an open science approach to synthesize data from multiple centers may produce more reliable conclusion.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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