The value of pre-contrast T1 measurement for dGEMRIC

W. Li[1], R. Scheidegger[1], Y. Wu[1], R. R. Edelman[1], and P. V. Prasad[1]

[1]Evanston Hospital and Northwestern University Feinberg School of Medicine, Evanston, IL, United States

INTRODUCTION Delayed gadolinium enhanced MRI of cartilage (dGEMRIC) has been demonstrated as a technique for molecular imaging of proteoglycan in cartilage, in which $Gd(DTPA)^{2-}$ distributes in cartilage in relation to the concentration of the charged gylcosoaminoglycan (GAG) molecules. Currently post-contrast ($Gd\text{-}DTPA^{2-}$) spin-lattice relaxation time (T_{1Gd}) is used as dGEMRIC index to determine relative GAG levels within the joint cartilage. A recent study demonstrated that ΔR_1, *i.e.* the difference between the relaxation rates before (R_{1pre}) and after contrast administration (R_{1post}), showed a better correlation than either R_{1pre} or R_{1post} alone with biopsy determined GAG content in transplanted cartilage (1). On the other hand, in a separate study of native cartilage, a high correlation has been observed between T_{1Gd} and ΔR_1 (2), suggesting that either parameter could be used as dGEMRIC index. The purpose of this study was to evaluate if ΔR_1 compared to T_{1Gd} can provide better characterization of individual subjects as osteoarthritic (OA) or healthy.

MATERIALS & METHODS

Subjects: Thirty-one subjects, including 17 patients with OA (5 men and 12 women, aged 40-86, average age of 61.8 years) and 14 healthy volunteers (HS, 5 men and 9 women, aged 18-40, average age of 29.2 years) participated in this study. **Imaging:** Data were acquired on 1.5T GE Signa short bore twin speed system (GE Healthcare, Milwaukee, WI) using a commercial transmit/receive extremity coil. Pre- and 90 min post-contrast (0.2 mM/kg Gd-DTPA) T_1 measurements were performed. A two dimensional inversion recovery fast spin echo (2D IR-FSE) sequence and/or a three dimensional look locker (3D LL) sequence were used to measure T_1. The parameters of 2D IR-FSE sequence were TR=1.8s (2.2s for pre contrast), TE = 7.4 ms, Matrix = 384x384. TI=1.68, 0.65, 0.35, 0.15, 0.05s (2.9, 2.0, 1.0, 0.5, 0.1s for pre-contrast acquisition). Imaging parameters for 3D LL were: TR=2.2 s (2.8 s for pre contrast), TE=2 ms, flip angle=5°, τ = 5.693 ms, slices prescribed = 32, bandwidth = +/- 62.5 kHz, and matrix = 256•256. Eleven TIs ranged from 20 to 1839 ms (15 TIs ranged from 20 to 2568 ms for pre-contrast) were applied. **Data analysis:** Two ROIs for T_1 mapping were defined in the weight-bearing area of femoral and tibial cartilage, *i.e.* the central region of the femoral cartilage in medial condyle between the outer edges of the meniscus horns and entire tibial cartilage within the slice. T_1 mapping was performed with a custom software analysis routine written in MATLAB (The Mathworks; Natick, MA). Data correction for BMI was performed with a formula: T_1 *(corrected)* $= T_1$ *(measured)* $+3(BMI - 20)$. The averaged T_1 values of the two ROIs were used for data analysis. T_{1pre}, T_{1Gd}, and ΔR_1 ($R_{1Gd} - R_{1pre}$), were calculated with R_{1Gd} and R_{1pre} equal to $1/T_{1pre}$, and $1/T_{1Gd}$. In order to test the effectiveness in separating OA and healthy subjects, a threshold for each parameter was determined based on its mean value (MEAN) and standard deviation (SD). For T_{1Gd}, the threshold was calculated by $[(MEAN + SD)_{OA} + (MEAN - SD)_{HS}]/2$. For T_{1pre} and ΔR_1, the thresholds were determined by $[(MEAN - SD)_{OA} + (MEAN + SD)_{HS}]/2$. Regression analysis and t-test were used for statistical testing.

RESULTS

Compared to healthy subjects (HS), OA group had a slightly higher T_{1pre} (922 ± 76 *vs.* 859 ± 55, p=0.13), significantly higher ΔR_1 (1.31 ± 0.39 *vs.* 0.76 ± 0.21, p=3.53E-5), and significantly lower T_{1Gd} (425 ± 61 *vs.* 524 ± 48, p=2.22E-05). The OA/HS ratios were 1.07, 0.81, and 1.72 respectively (as shown in Figure 1), *i.e.* the differences between the two groups were 7%, 19%, and 72% respectively. But the SDs with ΔR_1 are much larger than those associated with T_{1pre} and T_{1Gd}. High correlation was observed between T_{1Gd} and ΔR_1, with R^2 of 0.93 (Figure 2). When using the calculated thresholds of 880 ms (T_{1pre}), 481 (T1Gd), and 0.95 (ΔR_1), 21, 23, and 26 of the 31 cases respectively could be correctly identified as OA or HS (Figure 3).

DISCUSSION&CONCLUSION

The mean T_{1pre} in the OA group was higher than that for the HS group, probably related to the higher hydration in OA and is consistent with previous reports on T_2 (3). Since the mean T_{1pre} is higher and mean T_{1Gd} is lower in the OA group, ΔR_1 is to be expected to show larger difference between group means for OA and HS (as shown in figure 1). However, figure 3 shows that identification of individual subjects as OA or HS is only slightly better based on ΔR_1 compared to T_{1Gd}. Also figure 2 shows a high level of correlation between T_{1Gd} and ΔR_1 and so either of these parameters could be used as an index of dGEMRIC. In conclusion, we believe that in native cartilage (as opposed to cartilage implants where the hydration differences may be high) T_{1Gd} may be adequate for identifying individuals as OA or HS. However, as shown here, ΔR_1 does provide slightly better ability to distinguish subjects as OA or HS. The relatively modest improvement (given that the difference in mean values was significantly high, 72%) may be due to the higher standard deviation associated with ΔR_1 compared to T_{1Gd}. In practice, one has to also consider the logistics of additional effort and cost involved in acquiring T_{1pre} data.

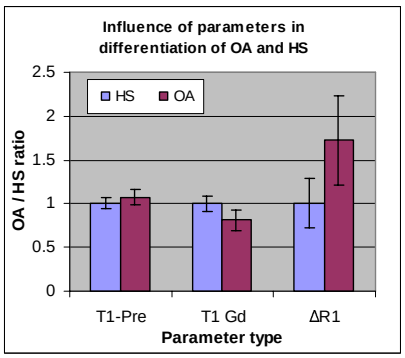

Figure 1 Influence of T_{1pre}, T_{1Gd} and ΔR_1 in differentiation of OA with HS as a group.

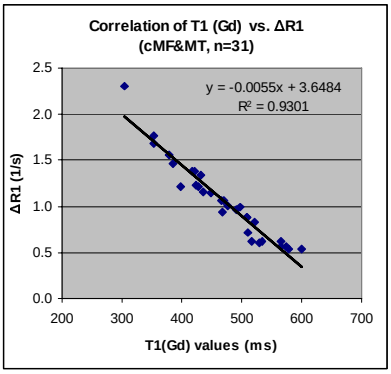

Figure 2 T_{1Gd} is highly correlated with ΔR_1

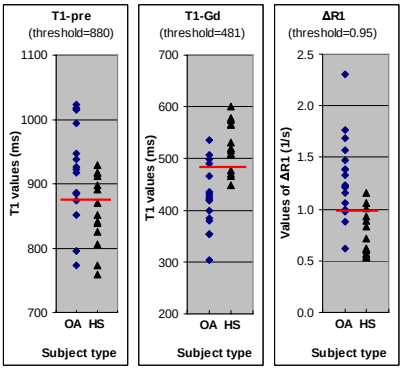

Figure 3 Characterization of individuals as OA or HS based on T_{1pre}, T_{1Gd}, and ΔR_1. Red line indicates threshold value.

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