Published in final edited form as:

Magn Reson Med. 2018 June ; 79(6): 3163–3171. doi:10.1002/mrm.26973.

Compressed Sensing in Quantitative Determination of GAG Concentration in Cartilage by Microscopic MRI

Nian Wang, PhD¹, Farid Badar, BSc², and Yang Xia, PhD^{2,*}

¹Center for In Vivo Microscopy, Department of Radiology, Duke University, Durham, NC 27710

²Department of Physics and Center for Biomedical Research, Oakland University, Rochester, MI 48309

Abstract

Purpose—To evaluate the potentials of compressed sensing (CS) in MRI quantification of glycosaminoglycan (GAG) concentration in articular cartilage at microscopic resolution.

Methods—T1-weighted 2D experiments of cartilage were fully sampled in k-space with five inversion times at 17.6 μm resolution. These fully sampled k-space data were re-processed, by under-sampling at various 1D and 2D CS under-sampling factors (UFs). The under-sampled data were reconstructed individually into 2D images using nonlinear reconstruction, which were used to calculate 2D maps of T1 and GAG concentration. The values of T1 and GAG in cartilage were evaluated at different UFs (up to 16, which used 6.25% of the data). K-space sampling pattern and zonal variations were also investigated.

Results—Using 2D variable density sampling pattern, the T1 images at UFs up to 8 preserved major visual information and produced negligible artifacts. The GAG concentration remained accurate for different sub-tissue zones at various UFs. The variation of the mean GAG concentration through the whole tissue depth was 1.20 %, compared to the fully sampled results. The maximum variation was 2.24 % in the deep zone of cartilage. Using 1D variable density sampling pattern, the quantitative T1 mapping and GAG concentration at UFs up to 4 showed negligible variations.

Conclusion—This study demonstrates that CS could be beneficial in μMRI studies of cartilage by acquiring less data, without losing significant accuracy in the quantification of GAG concentration.

Keywords

compressed sensing; MRI; cartilage; anisotropy; GAG; T1

Introduction

Articular cartilage is a thin layer of load-bearing tissue that covers the bones in synovial joints. The main extracellular components of cartilage are water, collagen fibers, and

*Corresponding Author and Address: Yang Xia, PhD, Department of Physics, Oakland University, Rochester, Michigan 48309, USA, Phone: (248) 370-3420, xia@oakland.edu.

negatively charged glycosaminoglycans (GAG) (1). The orientation of the collagen fibers varies along the thickness of cartilage, which is commonly sub-divided into three histological zones: the superficial zone (SZ) where the fibers are parallel to the tissue surface, the transitional zone (TZ) where the fibers are randomly oriented, and the radial zone (RZ) where the fibers are perpendicular to the tissue surface (2,3). Both collagen and GAG contents in articular cartilage are responsible for the load-bearing property of cartilage (4–6). The reduction of GAG will result in a poor mechanical response and can be regarded as an early sign of the tissue degradation, which eventually leads to arthritis (7–13).

The relaxation parameters in MRI have been used to detect the tissue degradation (14–22). In contrast to the anisotropic and depth-dependent distributions of T2 and T1 ρ , T1 in healthy cartilage is mostly uniform across the tissue depth and isotropic with respect to the specimen orientation in the magnetic field (23–27). In the presence of gadolinium contrast agents (28–30), T1 can become sensitive to the GAG concentration in cartilage (6,31–33). Quantitative mapping of the GAG concentration can be achieved by acquiring two T1 images: T1 before Gd administration (T1b) and T1 after Gd administration (T1a) (6,34).

Since quantitative T1 measurements commonly use the inversion recovery sequence, acquisition time can be long (29,35). Any method to accelerate quantitative T1 experiment is, therefore, highly desirable. In recent years, compressed sensing (CS) has emerged as a new framework that can accelerate image acquisition (36–40). The basic CS theory relies on the inherent sparsity and compressibility of MR data, which allows images to be recovered from randomly under-sampled k-space data using a nonlinear reconstruction algorithm to overcome under-sampling-induced artifacts (36,39). The application of CS to accelerate T1 mapping in the quantification of GAG concentration in cartilage has not yet been investigated. This study aimed to examine the potentials of CS in T1 mapping of cartilage by re-processing the fully sampled T1 data from microscopic MRI (μ MRI), at both 1D and 2D variable density patterns and at different under-sampling factors (UFs). The quantification of GAG in cartilage was used as the criteria for the feasibility investigation (6,41).

Methods

Specimen Preparation

Humeral heads were harvested shortly after the sacrifice of mature and healthy canines that were used for an unrelated research, which were approved by the institutional animal care and use committee (IACUC). The imaging specimen was about $3.5 \times 2.5 \times 6$ mm in size and contained the full-thickness cartilage still attached to the underlying bone (42). The specimens were soaked in physiological saline with 1% protease inhibitor (Sigma, MO). The specimens were never frozen.

Microscopic MRI (μ MRI) Protocols

All experiments were performed at room temperature on a Bruker AVANCE II 300 NMR spectrometer, equipped with a 7T/89mm vertical-bore magnet and microimaging accessory (Billerica, MA). The 2D spin-echo imaging experiments were carried out with an acquisition matrix of 256×128 (which was post-reconstructed into a 256×256 matrix) and a single slice

thickness of 1mm. The Field of View was 0.45cm×0.45cm, resulting in the 2D in-plane pixel size of 17.6μm. The repetition time TR was 2s without Gd immersion and 0.8s with Gd immersion (30).

Quantitative 2D T1 imaging experiments were performed at 55° with respect to the B₀, and followed the previously established protocols (23,30,34). Briefly, T1 contrast used an inversion recovery magnetization-prepared sequence, with five inversion points (0, 0.4, 1.1, 2.2, 4.0 s) prior to Gd solution soaking, and with five inversion points (0, 0.1, 0.3, 0.5, 1.0 s) after immersing in the Gd solution. The scan time for a T1 mapping without and with Gd immersion was about 8 hours and 2 hours, respectively (due to the long delays in the inversion recovery). T1 mapping of cartilage tissue was calculated by a single-component fit on a pixel-by-pixel basis using MATLAB (Natick, MA).

Compressed Sensing Sampling

The varied density k-space sampling pattern (SP_k) generated by a probability density function (PDF) for CS was determined by parameters p_a and p_b using the equation (43,44):

$$SP_k = \exp(-(p_b * k/n)^{p_a}) \quad (1)$$

where n is the k-space matrix size; k = 1, 2, ..., n. SP_k was optimized at different CS under-sampling factors (UF, which is defined by how much data was under-sampled in k-space) using different p_a and p_b values (Fig 1). In essence, the k-space points were fully sampled in the center of k-space, and became gradually sparse to the high frequency area. The sampling patterns then estimated using point spread function (PSF) to measure the incoherence. The optimized k-space sampling pattern was then applied in two sets of the fully sampled k-space data to obtain the various under-sampled k-space data. In comparison, 1D varied density k-space SP_k at different UFs (similar to the 2D k-space SP_k) were also generated. These raw data were randomly selected from over 20 sets of nearly identical data from an unrelated study of cartilage by multi-parametric μMRI project.

Compressed Sensing Reconstruction

Compressed sensing was applied on the k-space of all individual T1-weighted 2D images by minimizing the following function (36):

$$f(x) = \|Fx - y\|_2^2 + \lambda_1 \|\Psi x\|_1 + \lambda_2 TV(x) \quad (2)$$

where x is the image and y is its corresponding k-space, F is the FFT, Ψ is the sparse transform, λ_1 and λ_2 are weighting factors, and TV is the total variation. In this study, λ_1 equals 0.006 for the sparse solution and λ_2 equals 0.0012 for the data consistency. Various CS under-sampling factors (UF = 1, 2, 4, 8, 16, where 1 stands for the fully sampled data and 16 stands for using 1/16 of the fully sampled data) were used to assess the accuracy for quantitative GAG concentration in the cartilage.

GAG quantification by dGEMRIC method

Quantitatively, the GAG concentration can be calculated from the T1 images by a set of three equations based on the Donnan equilibrium theory, which have been documented extensively in the literature (28,41,45). The fully sampled GAG data was considered the ‘ground truth’, since they have been correlated with a number of multidisciplinary imaging and non-imaging techniques (41). The error in the GAG concentration by CS method was calculated based on the GAG concentration map from the fully sampled data:

$$[GAG]_{error}^i = 100 * ([GAG]_{cs}^i - [GAG]_{full}^i) / [GAG]_{full}^i \quad (3)$$

where $[GAG]_{full}$ is the GAG concentration calculated from the fully sampled dataset, $[GAG]_{cs}$ is the GAG concentration calculated from various under-sampled datasets, and i stands for the different histological zones: SZ, TZ, and RZ.

Results

Optimize CS sampling patterns

Figure 1 showed the T1-weighted images at inversion time of 0.0s and 1.1s were compared with the “Ground Truth” using different 2D CS sampling masks, all with an under-sampling factor of 4 (using only 25% of k-space). The CS reconstruction with optimized SP_k (Fig 1b, $p_a = 1.8$; $p_b = 3.6$) demonstrated limited artifacts in the cartilage region (Fig 1j, 1n). The interface between saline and cartilage (black arrows) and the bubble (white arrows) in the reconstructed images at inversion time of 0.0 s (Fig 1j) were largely preserved and showed no visible differences compared to the fully sampled image (Fig 1e, SNR = 59.8). When a different sampling pattern (Fig 1d) was used, the reconstructed image quality was noticeably degraded. Some residual artifacts could be seen in the interface between bone and saline interface (arrowheads). The reconstructed T1-weighted images at inversion time of 1.1 s with relative low SNR (~ 18.1) still showed robust image quality with the optimized sampling pattern in k-space (Fig 1r, 1v).

T1-weighted images at various under-sampling factors

Figure 2 showed the optimized 1D (a–c) and 2D (d–f) k-space sampling patterns, T1b, and the corresponding error maps from the fully sampled k-space data (UF=1), as well as the under-sampled data with UF of 2, 4, 8, and 16. Using the 1D k-space SP_k , the qualities of the reconstructed T1b images were visually comparable with the ground truth at UF up to 4, while the qualities of the constructed images became visibly inferior at UFs of 8 and 16. It is interesting to note that a much higher error was found within the bone region (white arrows) when compared to the limited error in the cartilage area (yellow arrows). Using the 2D k-space SP_k , the reconstructed T1b images were found to be visually comparable with the references (the fully sampled results) at UF up to 8, with major information qualitatively preserved and negligible artifacts. At 2D UF of 16, the image quality diminished to some extent, with exhibition of spatial blurring. (The T1a and their error maps can be found in Supplement Fig 1, which have similar features.)

T1 profiles and mean GAG concentration

Quantitative depth-dependent profiles of T1a, T1b (a) and GAG concentration (b), and mean GAG concentration values at different UF (c), are illustrated in Figure 3. Several conclusions can be reached from this set of data. First, T1b values are always higher than T1a values through the whole tissue depth, regardless of 1D or 2D UFs. T1a profiles showed strong depth-dependent properties throughout the entire cartilage region. In contrast, this depth dependent appearance is much weaker before Gd administration. These observations were consistent with our previous findings (30,34). Second, the GAG profiles also showed a strong depth-dependence profile: lower at the surface zone, and monotonically increased to the deep zone of the tissue. The T1b, T1a, and the GAG concentration profiles by different CS reconstructions were consistent with the fully sampled data even at 2D UF of 16, while the profiles varied significantly at 1D UF of 8 and 16 (arrows). Finally, little variation of the mean values in the GAG concentration was found at the 2D under-sampling SP_k of 16 (Fig 3e), while the variations were larger at the 1D compressed sensing SP_k of 8 and 16 (Fig 3f).

Quantitative T1 and GAG concentration in sub zones

Figure 4 showed the zonal changes of T1b, T1a, and GAG concentration in articular cartilage at various under-sampling factors (1, 2, 4, 8, 16). Since the spatial resolution of cartilage usually is much coarser in clinical MRI, the μ MRI cartilage data was divided to 4 sub-tissue structural zones: SZ, TZ, upper RZ (URZ), and lower RZ (LRZ) in order to investigate the GAG concentration variations in these zones at different UFs and both 1D and 2D patterns. The variation of T1a, T1b, and GAG concentration at each sub tissue zones was found to be small even at 2D UF of 8 or 16, at 1D UF of 4. The maximum variation was found at the LRZ with 2.24 % difference from the ground truth at 2D UF of 16, while the maximum variation was found at the LRZ with 14.18 % at 1D UF of 16. A detailed comparison of the GAG concentrations was summarized in the Table and Supplement Fig 2.

Discussion

It is rare that one has access to the original k-space data from quantitative 2D T1 experiments of cartilage at 17.6 μ m resolution, and also know the statistical correlation between these μ MRI GAG data and the biochemical GAG quantification based on the same specimen (6,41). This study demonstrates that, at high spatial resolution, CS can be applied to the quantitative T1 studies of cartilage to reduce the acquisition time. An under-sampling factor of 16 (i.e., using only 6.25% of the data) could be achieved when a 2D sampling pattern is used, without losing significant accuracy in the GAG quantification in cartilage, based on the zonal analysis.

Effect of Sampling Pattern

While equidistant k-space under-sampling and reconstruction by zero-filling results in coherent aliasing, random k-space under-sampling exhibits incoherent artifacts that behave much like additive random noise. Based on the equation of (1), 2D variable density random under-sampling in Cartesian imaging has been proposed, which was used in this study. As shown in Fig 1, variable density sampling combines with denser sampling near the center of k-space, matching the energy distribution in k-space (concentrated close to the center of k-

space and rapidly decaying towards the periphery). The different combinations of p_a and p_b were further tested using point spread function (Figure 1). For example, the SP_k (UF = 4) was optimized with $p_a = 1.8$ and $p_b = 3.6$, and the reconstructed T1 images preserved major information with few artifacts. This optimized SP_k are likely to differ for different studies, tissues, MRI parameters, and k-space features, which call for the extra caution in CS MRI experiments. Furthermore, since 2D sparsity is fully exploited using 2D variable density SP_k , the images have a sparser representation, thus can achieve to a higher under-sampling factor (UF of 16) than the 1D variable density SP_k (UF up to 4), without introducing major deviation to the quantification T1 and GAG values.

Effect of Gd Administration

Paramagnetic Gd ions can reduce the MRI relaxation times and enhance the MRI image contrast. Whether or not Gd administration would affect the CS reconstruction has not been investigated thoroughly. In this study, the sequences of the 2D T1-weighted images and their calculated T1 mappings maps (prior and post Gd administration) at various under-sampling factors were calculated. No apparent reduction in image quality was found in T1-weighted images, in comparison with the ground truth for different 2D under-sampling factors and each sub regions of the cartilage, once proper k-space sampling patterns were used.

Effect of Under-sampling Factor

Although both T1a and T1b maps exhibited qualitatively good quality even at 2D UF of 16 (using only 6.25 % k-space data), the images began to blur at high under-sampling factors, which may be caused by the significant reduction of high frequency components in k-space, hence, making it more difficult to recover the fine information of the image. Compared to the relatively robust reconstruction in the cartilage area, the bone area showed much larger errors (Fig 2, 3). This can be attributed to the lower SNR in the bone area of the T1-weighted images, where all five inversion times were used in the exponential fitting in the calculation of the T1 maps. In addition, the bone region has more random structure and intensity than the highly structured cartilage, hence, requiring more caution in the CS reconstruction. It may become severe in clinical MRI of bone and joint (46) since the lower resolution and the higher partial volume effect may cause larger errors for T1 or GAG concentration quantification in the RZ of cartilage (close to the bone and cartilage interface).

Difference between Under-sampling Factor and Reduction of Data Acquisition Time

It should be pointed out that the reduction of the data acquisition time at different under-sampling factors depends upon several experimental features in imaging, including the patterns of k-space trajectory and the dimensions of the imaging experiments. In a typical 2D imaging using the Cartesian coordinate, the overall experimental time is limited by the repetition time (TR) in MRI. Since k-space sampling at the read direction is carried out quickly, there is little advantage to under-sample the read dimension. The reduction of the scan time can be achieved by omitting the collection of individual k-space lines in the phase encoding direction. We show in this study that a 1D varied density sampling pattern can be used in the 2D imaging to achieve a factor of 4 time saving without introducing noticeable error (Fig 2). The use of 2D variable density pattern in 2D Cartesian imaging would not be beneficial, since most phase encoding directions cannot be omitted because of the remaining

acquisition points (36). For any 3D imaging, much significant time saving can be achieved when a 2D variable density sampling pattern is applied to the two phase encoding directions (47). The design of novel k-space trajectory pattern can facilitate further reduction on the data acquisition time. In addition, 3D T1 imaging are time-consuming, which warrants the evaluation of the GAG concentration using 2D under-sampling patterns.

In conclusion, to the best of our knowledge, this is the first study that demonstrates the feasibility of implementing CS in μ MRI quantification of GAG. We reveal the challenges of using CS for quantitative imaging of cartilage, especially in the deep RZ of cartilage and the interface between cartilage and bone. We show that 1D and 2D sampling patterns can achieve different time-savings. The calculated GAG concentration did not exhibit major deviation in quantification, even at high under-sampling factors and at different sub tissue zones (SZ, TZ, and RZ). This significant under-sampling could potentially be translated into major reduction in data acquisition time, which would be extremely beneficial to any ex-vivo study of cartilage by MRI. The time saved can be utilized to increase the sample size, to map the topographical variation of the tissue parameters over a joint surface, and to acquire better quality data.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Yang Xia is grateful to the National Institutes of Health for the R01 grants (AR052353 and AR069047). The Center for In Vivo Microscopy is supported through NIH awards P41 EB015897 (to Dr. G Allan Johnson). The authors thank Drs. Cliff Les and Hani Sabbah (Henry Ford Hospital, Detroit) for providing the canine specimens, and Ms. Carol Searight (Department of Physics, Oakland University) for editorial comments on the manuscript.

References

1. Maroudas A. Biophysical chemistry of cartilaginous tissues with special reference to solute and fluid transport. *Biorheology*. 1975; 12:233–248. [PubMed: 1106795]
2. Lechner KB, Rechl HP, Gmeinwieser JK, Heuck AF, Lukas HP, Kohl HP. Structure, function, and degeneration of bovine hyaline cartilage: assessment with MR imaging in vitro. *Radiology*. 1989; 170:495–499. [PubMed: 2911674]
3. Xia Y, Moody JB, Burton-Wurster N, Lust G. Quantitative in situ correlation between microscopic MRI and polarized light microscopy studies of articular cartilage. *Osteoarthritis Cartilage*. 2001; 9:393–406. [PubMed: 11467887]
4. Mow VC, Kuei SC, Lai WM, Armstrong CG. Biphasic creep and stress relaxation of articular cartilage in compression? Theory and experiments. *J Biomech Eng*. 1980; 102:73–84. [PubMed: 7382457]
5. Maroudas A, Venn M. Chemical composition and swelling of normal and osteoarthrotic femoral head cartilage. II. Swelling *Ann Rheum Dis*. 1977; 36:399–406. [PubMed: 200188]
6. Xia Y, Zheng S, Bidthanapally A. Depth-dependent profiles of glycosaminoglycans in articular cartilage by microMRI and histochemistry. *J Magn Reson Imaging*. 2008; 28:151–157. [PubMed: 18581328]
7. Alhadlaq HA, Xia Y. Modifications of orientational dependence of microscopic magnetic resonance imaging T2 anisotropy in compressed articular cartilage. *J Magn Reson Imaging*. 2005; 22:665–673. [PubMed: 16220547]

8. Schiller J, Huster D, Fuchs B, Naji L, Kaufmann J, Arnold K. Evaluation of cartilage composition and degradation by high-resolution magic-angle spinning nuclear magnetic resonance. *Methods Mol Med*. 2004; 101:267–285. [PubMed: 15299220]
9. Tameem HZ, Selva LE, Sinha US. Morphological atlases of knee cartilage: shape indices to analyze cartilage degradation in osteoarthritic and non-osteoarthritic population. *Conf Proc IEEE Eng Med Biol Soc*. 2007; 2007:1310–1313. [PubMed: 18002204]
10. Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, Liang MH, Kremers HM, Mayes MD, Merkel PA, Pillemer SR, Reveille JD, Stone JH. National Arthritis Data W. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I Arthritis Rheum. 2008; 58:15–25. [PubMed: 18163481]
11. Tsushima H, Okazaki K, Takayama Y, Hatakenaka M, Honda H, Izawa T, Nakashima Y, Yamada H, Iwamoto Y. Evaluation of cartilage degradation in arthritis using T1rho magnetic resonance imaging mapping. *Rheumatol Int*. 2012; 32:2867–2875. [PubMed: 21881979]
12. Lee JH, Badar F, Kahn D, Matyas J, Qu X, Xia Y. Loading-induced changes on topographical distributions of the zonal properties of osteoarthritic tibial cartilage--A study by magnetic resonance imaging at microscopic resolution. *J Biomech*. 2015; 48:3625–3633. [PubMed: 26351010]
13. Mittelstaedt D, Kahn D, Xia Y. Topographical and depth-dependent glycosaminoglycan concentration in canine medial tibial cartilage 3 weeks after anterior cruciate ligament transection surgery-a microscopic imaging study. *Quant Imaging Med Surg*. 2016; 6:648–660. [PubMed: 28090443]
14. Duvvuri U, Reddy R, Patel SD, Kaufman JH, Kneeland JB, Leigh JS. T1rho-relaxation in articular cartilage: effects of enzymatic degradation. *Magn Reson Med*. 1997; 38:863–867. [PubMed: 9402184]
15. Akella SV, Regatte RR, Wheaton AJ, Borthakur A, Reddy R. Reduction of residual dipolar interaction in cartilage by spin-lock technique. *Magn Reson Med*. 2004; 52:1103–1109. [PubMed: 15508163]
16. Alhadlaq HA, Xia Y. The structural adaptations in compressed articular cartilage by microscopic MRI (μ MRI) T2 anisotropy. *Osteoarthritis Cartilage*. 2004; 12:887–894. [PubMed: 15501404]
17. Li X, Benjamin Ma C, Link TM, Castillo DD, Blumenkrantz G, Lozano J, Carballido-Gamio J, Ries M, Majumdar S. In vivo T1rho and T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI. *Osteoarthritis Cartilage*. 2007; 15:789–797. [PubMed: 17307365]
18. McCann L, Ingham E, Jin Z, Fisher J. Influence of the meniscus on friction and degradation of cartilage in the natural knee joint. *Osteoarthritis Cartilage*. 2009; 17:995–1000. [PubMed: 19328878]
19. Zheng S, Xia Y. The collagen fibril structure in the superficial zone of articular cartilage by microMRI. *Osteoarthritis Cartilage*. 2009; 17:1519–1528. [PubMed: 19527808]
20. Alizai H, Chang G, Regatte RR. MRI of the Musculoskeletal System: Advanced Applications using High and Ultrahigh Field MRI. *Semin Musculoskelet Radiol*. 2015; 19:363–374. [PubMed: 26583364]
21. Du J, Carl M, Diaz E, Takahashi A, Han E, Szevenyi NM, Chung CB, Bydder GM. Ultrashort TE T1rho (UTE T1rho) imaging of the Achilles tendon and meniscus. *Magn Reson Med*. 2010; 64:834–842. [PubMed: 20535810]
22. Lee JH, Badar F, Matyas J, Qu X, Xia Y. Topographical variations in zonal properties of canine tibial articular cartilage due to early osteoarthritis: a study using 7-T magnetic resonance imaging at microscopic resolution. *MAGMA*. 2016; 29:681–690. [PubMed: 26886872]
23. Xia Y. Relaxation anisotropy in cartilage by NMR microscopy (μ MRI) at 14-microm resolution. *Magn Reson Med*. 1998; 39:941–949. [PubMed: 9621918]
24. Wang N, Xia Y. Depth and orientational dependencies of MRI T2 and T1rho sensitivities towards trypsin degradation and Gd-DTPA(2-) presence in articular cartilage at microscopic resolution. *Magn Reson Imaging*. 2012; 30:361–370. [PubMed: 22244543]
25. Wang N, Xia Y. Experimental issues in the measurement of multi-component relaxation times in articular cartilage by microscopic MRI. *J Magn Reson*. 2013; 235:15–25. [PubMed: 23916991]

26. Zhu Y, Zhang Q, Liu Q, Wang YX, Liu X, Zheng H, Liang D, Yuan J. PANDA-T1rho: Integrating principal component analysis and dictionary learning for fast T1rho mapping. *Magn Reson Med*. 2015; 73:263–272. [PubMed: 24554439]
27. Wang N, Kahn D, Badar F, Xia Y. Molecular origin of a loading-induced black layer in the deep region of articular cartilage at the magic angle. *J Magn Reson Imaging*. 2015; 41:1281–1290. [PubMed: 24833266]
28. Bashir A, Gray ML, Burstein D. Gd-DTPA2- as a measure of cartilage degradation. *Magn Reson Med*. 1996; 36:665–673. [PubMed: 8916016]
29. Mayerhoefer ME, Welsch GH, Mamisch TC, Kainberger F, Weber M, Nemec S, Friedrich KM, Dirisamer A, Trattnig S. The in vivo effects of unloading and compression on T1-Gd (dGEMRIC) relaxation times in healthy articular knee cartilage at 3.0 Tesla. *Eur Radiol*. 2010; 20:443–449. [PubMed: 19727756]
30. Wang N, Chopin E, Xia Y. The effects of mechanical loading and gadolinium concentration on the change of T1 and quantification of glycosaminoglycans in articular cartilage by microscopic MRI. *Phys Med Biol*. 2013; 58:4535–4547. [PubMed: 23760174]
31. Mamisch TC, Dudda M, Hughes T, Burstein D, Kim YJ. Comparison of delayed gadolinium enhanced MRI of cartilage (dGEMRIC) using inversion recovery and fast T1 mapping sequences. *Magn Reson Med*. 2008; 60:768–773. [PubMed: 18816842]
32. Williams A, Shetty SK, Burstein D, Day CS, McKenzie C. Delayed gadolinium enhanced MRI of cartilage (dGEMRIC) of the first carpometacarpal (1CMC) joint: a feasibility study. *Osteoarthritis Cartilage*. 2008; 16:530–532. [PubMed: 18194872]
33. Crema MD, Hunter DJ, Burstein D, Roemer FW, Li L, Eckstein F, Krishnan N, Hellio Le-Graverand MP, Guermazi A. Association of changes in delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) with changes in cartilage thickness in the medial tibiofemoral compartment of the knee: a 2 year follow-up study using 3.0 T. *MRI Ann Rheum Dis*. 2014; 73:1935–1941. [PubMed: 23873880]
34. Xia Y, Wang N, Lee J, Badar F. Strain-dependent T1 relaxation profiles in articular cartilage by MRI at microscopic resolutions. *Magn Reson Med*. 2011; 65:1733–1737. [PubMed: 21452280]
35. Wang N, Badar F, Xia Y. MRI properties of a unique hypo-intense layer in degraded articular cartilage. *Phys Med Biol*. 2015; 60:8709–8721. [PubMed: 26509475]
36. Lustig M, Donoho D, Pauly JM. Sparse MRI: The application of compressed sensing for rapid MR imaging. *Magn Reson Med*. 2007; 58:1182–1195. [PubMed: 17969013]
37. Liang D, Liu B, Wang J, Ying L. Accelerating SENSE using compressed sensing. *Magn Reson Med*. 2009; 62:1574–1584. [PubMed: 19785017]
38. Tariq U, Hsiao A, Alley M, Zhang T, Lustig M, Vasanawala SS. Venous and arterial flow quantification are equally accurate and precise with parallel imaging compressed sensing 4D phase contrast MRI. *J Magn Reson Imaging*. 2013; 37:1419–1426. [PubMed: 23172846]
39. Pandit P, Rivoire J, King K, Li X. Accelerated T1rho acquisition for knee cartilage quantification using compressed sensing and data-driven parallel imaging: A feasibility study. *Magn Reson Med*. 2016; 75:1256–1261. [PubMed: 25885368]
40. Wang HF, Liang D, Ying L. Pseudo 2D Random Sampling for Compressed Sensing MRI. *Ieee Eng Med Bio*. 2009:2672–2675.
41. Zheng S, Xia Y. The impact of the relaxivity definition on the quantitative measurement of glycosaminoglycans in cartilage by the MRI dGEMRIC method. *Magn Reson Med*. 2010; 63:25–32. [PubMed: 19918900]
42. Wang N, Xia Y. Dependencies of multi-component T2 and T1rho relaxation on the anisotropy of collagen fibrils in bovine nasal cartilage. *J Magn Reson*. 2011; 212:124–132. [PubMed: 21788148]
43. Adcock B, Hansen AC, Roman B. A Note on Compressed Sensing of Structured Sparse Wavelet Coefficients From Subsampled Fourier Measurements. *Ieee Signal Proc Let*. 2016; 23:732–736.
44. Adcock B, Hansen A, Roman B, Teschke G. Generalized Sampling: Stable Reconstructions, Inverse Problems and Compressed Sensing over the Continuum. *Adv Imag Elect Phys*. 2014; 182:187–279.

45. Maroudas A, Muir H, Wingham J. The correlation of fixed negative charge with glycosaminoglycan content of human articular cartilage. *Biochim Biophys Acta*. 1969; 177:492–500. [PubMed: 4239606]
46. Zhuang Z, Lee JH, Badar F, Xu J, Xia Y. The influences of different spatial resolutions on the characteristics of T2 relaxation times in articular cartilage: A coarse-graining study of the microscopic magnetic resonance imaging data. *Microsc Res Tech*. 2016; 79:754–765. [PubMed: 27297720]
47. Doneva M, Bornert P, Eggers H, Stehning C, Senegas J, Mertins A. Compressed sensing reconstruction for magnetic resonance parameter mapping. *Magn Reson Med*. 2010; 64:1114–1120. [PubMed: 20564599]

Figure 1.

The reconstructed 2D T1-weighted images using three different 2D sampling patterns at an under-sampling factor of 4, at two different inversion times, (i–p: the inversion time of 0.0 s; q–x: the inversion time of 1.1s, which had lower SNR). The fully sampled images were also shown as the ground truth in a. The point spread function (PSF) images for different sampling patterns were shown in Fig 1e–1h. The quality of the reconstructed T1-weighted images was sensitive to the sampling patterns. The optimized sampling pattern was illustrated in Fig 1b with $p_a = 1.8$, and $p_b = 3.6$. SZ: superficial zone; TZ: transitional zone; RZ: radial zone. “10X” in the figure label means that the display scale (the up limit) has

been reduced to 1/10 to show more clearly the differences between the ground truth and CS reconstructed images.

Figure 2.

The optimized k-space sampling patterns at different under-sampling factors (UF), T1b maps, and the corresponding error maps from the fully sampled k-space data (a–c: 1D k-space sampling patterns; d–f 2D k-space sampling patterns). The reconstructed T1b maps are found to be visually comparable with the references at UF up to 4 (1D patterns) and 8 (2D patterns), with major information qualitatively preserved and negligible artifacts, while the reconstructed relaxation maps have worse quality at UF of 8 and 16 (1D patterns) and 16 (2D patterns). (T1b: T1 mapping before Gd administration; T1a: T1 mapping after Gd administration).

Figure 3.

Quantitative T_{1b} and T_{1a} profiles (a, b), GAG concentration profiles (c, d), and the mean GAG concentration values (e, f) at different under-sampling factors (1, 2, 4, 8, 16) from articular surface (0 μm) to cartilage-bone interface ($\sim 640 \mu\text{m}$). The left half and the right half of the figure used 2D and 1D under-sampling patterns, respectively. T_{1b} , T_{1a} , and the GAG concentration profiles using compressed sensing were very consistent with the fully sampled data using 2D under-sampling pattern, while the profiles varied significantly at 1D under-sampling factors of 8 and 16 (arrows). Little variation of the mean GAG concentration value was found even at a 2D under-sampling factor of 16 (e), while bigger variations were noticeable at 1D under-sampling factors of 8 and 16.

Figure 4. Minimum variations in the T1b, T1a, and GAG concentration in the three histological zones of articular cartilage at various 1D (right) and 2D (left) under-sampling factors (1, 2, 4, 8, 16). Little variation of T1a, T1b, and GAG concentration at any sub-tissue zones was found even at a 2D under-sampling of 16. (SZ: superficial zone; TZ: transitional zone; URZ: upper radial zone; LRZ: lower radial zone.)

Table
GAG concentrations at different zones with different CS under-sampling factors

(a) using 2D sampling patterns					
UF	1	2	4	8	16
K-space Utilization					
SZ (Error)	100%	50%	25%	12.5%	6.25%
	30.90±1.90 (0.0%)	30.86±1.91 (0.13%)	30.92±1.85 (0.06%)	31.19±1.87 (0.93%)	30.63±1.45 (0.87%)
GAG [mg/ml]	TZ (Error)	56.65±2.83 (0.37%)	56.64±2.76 (0.37%)	55.89±2.79 (0.97%)	56.84±2.80 (0.71%)
	URZ (Error)	79.93±2.31 (0.0%)	80.59±2.25 (0.83%)	81.11±2.44 (1.47%)	80.47±2.26 (0.68%)
	LRZ (Error)	108.63±4.00 (0.0%)	110.07±4.48 (1.33%)	109.05±5.74 (0.39%)	111.06±5.21 (2.24%)
(b) using 1D sampling patterns					
UF	1	2	4	8	16
K-space Utilization					
SZ (Error)	100%	50%	25%	12.5%	6.25%
	30.90±1.90 (0.0%)	30.92±1.95 (0.06%)	31.08±1.88 (0.58%)	31.73±1.84 (2.69%)	32.42±1.41 (4.92%)
GAG [mg/ml]	TZ (Error)	56.44±2.94 (0.0%)	56.17±2.65 (0.48%)	54.48±2.56 (3.47%)	52.06±3.13 (7.76%)
	URZ (Error)	79.93±2.31 (0.0%)	79.42±2.51 (0.64%)	81.94±2.14 (2.51%)	77.21±2.54 (3.41%)
	LRZ (Error)	108.63±4.00 (0.0%)	109.99±4.16 (1.25%)	101.37±5.98 (6.68%)	124.03±5.54 (14.18%)

* UF: under-sampling factors; SZ: superficial zone; TZ: transitional zone; URZ: upper radial zone; LRZ: lower radial zone.