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Accelerating 3D- $T_{1\rho}$ Mapping of Cartilage Using Compressed Sensing with Different Sparse and Low Rank Models

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Abstract

Purpose—To evaluate the feasibility of using Compressed Sensing (CS) to accelerate 3D- $T_{1\rho}$ mapping of cartilage and to reduce total scan times without degrading the estimation of $T_{1\rho}$ relaxation times.

Methods—Fully-sampled 3D- $T_{1\rho}$ datasets were retrospectively undersampled by factors 2–10. CS reconstruction using twelve different sparsifying transforms were compared, including finite differences, temporal and spatial wavelets, learned transforms using Principal Component Analysis (PCA) and K-means Singular Value Decomposition (K-SVD), explicit exponential models, low rank and low rank plus sparse models. Spatial filtering prior to $T_{1\rho}$ parameter estimation was also tested. Synthetic phantom ($n=6$) and *in vivo* human knee cartilage datasets ($n=7$) were included.

Results—Most CS methods performed satisfactorily for an acceleration factor (AF) of 2, with relative $T_{1\rho}$ error lower than 4.5%. Some sparsifying transforms, such as spatio-temporal finite difference (STFD), exponential dictionaries (EXP) and low rank combined with spatial finite difference (L+S SFD) significantly improved this performance, reaching average relative $T_{1\rho}$ error below 6.5% on $T_{1\rho}$ relaxation times with AF up to 10, when spatial filtering prior to $T_{1\rho}$ fitting was utilized, at the expense of smoothing the $T_{1\rho}$ maps. The STFD achieved 5.1% error at AF=10 with spatial filtering prior to $T_{1\rho}$ fitting.

Conclusion—Accelerating 3D- $T_{1\rho}$ mapping of cartilage with CS is feasible up to AF of 10 when using STFD, EXP or L+S SFD regularizers. These three best CS methods performed satisfactorily on synthetic phantom and *in vivo* knee cartilage for AFs up to 10, with $T_{1\rho}$ error of 6.5%.

Keywords

$T_{1\rho}$ relaxation; compressed sensing; sparse reconstruction; sparse and low rank models

INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease, affecting more than 27 million people in the United States (1,2). This large affected population and the severe consequent debility of OA leads to significant expenses to the healthcare system (3,4). OA is characterized by biochemical, structural and morphologic degradation of components of the extracellular matrix (ECM) of articular cartilage (5). The ECM is composed of primarily two groups of macromolecules including proteoglycan (PG) and collagen fibers. The relaxation rate $R_{1\rho}$ ($1/T_{1\rho}$) has been shown to increase linearly with the increasing PG content of articular cartilage (6) and several researchers (7,8) have demonstrated that the $T_{1\rho}$ relaxation time is sensitive to proteoglycan content of the cartilage.

Recently, $T_{1\rho}$ has been used as a novel MRI contrast mechanism for many biomedical applications including neurodegenerative, cardiovascular, body and musculoskeletal imaging to assess early macromolecular changes rather than conventional morphological imaging (9–12). This quantitative 3D- $T_{1\rho}$ mapping usually requires the use of multiple images with different spin-lock times (TSLs) to obtain $T_{1\rho}$ maps (13), which demands long scan times for *in vivo* applications. A straightforward way to reduce the image acquisition time of $T_{1\rho}$ mapping is to reduce the numbers of TSLs without compromising the $T_{1\rho}$ quantification accuracy and precision. However, this approach requires high signal-to-noise ratio (SNR) as well as prior knowledge of the true $T_{1\rho}$ range of the cartilage. Fast imaging techniques such as parallel imaging, partial k-space and key-hole approaches have been utilized in order to reduce the acquisition time in $T_{1\rho}$ mapping (14). However, all these approaches have inherent limitations in terms of noise amplification and/or blurring.

Compressed sensing (CS) (15) has emerged as an effective way to overcome the limitations of conventional fast MR imaging. CS relies on the inherent compressibility, or sparsity, of MR images to reconstruct undersampled k-space data (16). Moreover, CS can be combined synergistically with parallel imaging using multiple receiver coils for further increases in speed (17). Recently, several CS methods have been applied to dynamic imaging (18,19) and parametric mapping (20–23), which are particularly suitable for CS due to increased compressibility, which turns into higher accelerations.

Similar studies in (23,24) and (25) have demonstrated that a reduction in acquisition time is possible for $T_{1\rho}$ mapping of knee cartilage, but only a narrow set of CS methods and AFs were compared. Questions such as what regularizers are the most suitable for parametric mapping with least $T_{1\rho}$ error, or how much acceleration can be achieved for $T_{1\rho}$ mapping are still unanswered.

In this paper, we study the feasibility of using CS to accelerate $T_{1\rho}$ mapping by comparing twelve different types of sparsity promoting functions on a synthetic phantom and *in vivo* knee cartilage data. We provide a fair and objective evaluation of these CS methods. Our main aim is to answer the question of what are the best regularization penalties and suitable AFs for CS reconstruction with least relative $T_{1\rho}$ error when the final objective is to reduce image acquisition time in $T_{1\rho}$ mapping of human articular cartilage.

METHODS

MRI Data Acquisition and Standard Reconstruction

Seven datasets of *in vivo* human knee 3D-T1 ρ -weighted images were acquired with different TSLs using a modified 3D Cartesian turbo-Flash sequence (26). The MRI scans were performed using a 3T clinical MRI scanner (Prisma, Siemens Healthcare, Erlangen, Germany) with a 15-channel Tx/Rx knee coil (QED, Cleveland OH). The 3D-T1 ρ acquisition parameters were: TR/TE=7.5ms/4ms, T1 delay=1020ms, k-space lines 64 captured with centric ordering between T1 ρ preparation pulses, flip angle=8°, matrix size 256×128×64, spin-lock frequency=500Hz, slice thickness=2mm, field of view (FOV)=120mm², and receiver bandwidth=515 Hz/pixel.

The T1 ρ -weighted scans of the knee were acquired in sagittal plane from seven healthy volunteers (age=29.6±7.5 years), with 10 TSLs including 2/4/6/8/10/15/25/35/45/55ms, and total acquisition time of 32 minutes. The T1 ρ -protocol was repeated on three volunteers on the same day for repeatability evaluation. This study was approved by the institutional review board (IRB) and all the volunteers were consented before scanning.

For fully-sampled reference reconstruction, a 1D Fourier transform was applied to the 3D k-space data along the frequency encoding direction (k_x). Then, for each slice, the fully-sampled 2D k-space data were reconstructed with SENSE (27,28). The coil maps, required in SENSE, were estimated using ESPIRiT (29) using the central k-space area.

Synthetic Phantom

The synthetic phantom utilized to test the different CS methods is illustrated in Figure 1. It is composed by three areas with T1 ρ relaxation times randomly selected from the ranges 1–25ms, 30–50ms and 50–110ms. At the green areas in the Fig. 1 the selected relaxation time ranges 30–50ms, with only one T1 ρ relaxation time per voxel. The other two areas, the relaxation ranges 1–25ms (blue) and 50–110ms (red), which may intersect generating a bi-exponential model (26). However, only the non-intersecting regions were used in this paper. Large circles, ellipses and small circles compose these three areas. At the large circles, the constant randomly selected T1 ρ is added with a linear gradient of 5% of the selected T1 ρ -time in one circle, and added with a white Gaussian random variation in the other, also with 5% of the selected T1 ρ value. The same variations were added to the magnetization, originally uniform and unitary. At the elliptical and small circular areas only the constant randomly selected T1 ρ was used and the magnitude is unitary and uniform.

K-space dataset was created by multiplying the phantom images by coil sensitivities, 4-coils were utilized, followed by 2D Fourier transform. White Gaussian noise was added to the data in k-space for the noisy experiment, with its standard deviation set to 17% of the mean signal amplitude, resulting in an acquisition SNR¹ of 15dB (5.62 in linear scale).

¹The acquisition SNR is defined as $SNR = 10 \log \frac{\|FCx\|^2}{\|\eta\|^2}$, from the model: $y = FCx + \eta$, not to be confused with image SNR.

Retrospective Undersampling

The 2D ky-kz data, from each slice, were undersampled with 2D Poisson-disk random pattern (30). The AF is defined as the ratio of total k-space samples by the number of captured k-space samples. A central k-space area of 31×15 (for AF=2) or 21×9 (for AF=4) was fully sampled for coil sensitivity estimation. Figure 2 illustrates the acquisition model, including the k-space sampling pattern. In the experiments with the synthetic phantom, the size of the central area is 63×63 (AF=2) or 41×41 (AF=4).

CS Reconstruction

CS reconstructions were performed using twelve different regularization functions to promote sparsity in the solution, as described in Table 1. Most of the regularization penalties use l_1 -norm with different sparsifying transforms. Another type of regularization was the low rank model, where the nuclear-norm (31,32) was utilized. Finally, three regularization penalties utilize the low rank plus sparse (L+S) model, where the nuclear-norm and the l_1 -norm are combined (33). In this case, three different transforms were used with the l_1 -norm.

The CS reconstructions for penalties based on l_1 -norm (15) are posed as:

$$\hat{\mathbf{x}} = \underset{\mathbf{x}}{\operatorname{argmin}} \|\mathbf{y} - \mathbf{SFCx}\|_2^2 + \lambda \|\mathbf{Tx}\|_1, \quad [1]$$

or

$$\hat{\mathbf{x}} = \mathbf{D} \underset{\mathbf{u}}{\operatorname{argmin}} \|\mathbf{y} - \mathbf{SFCDu}\|_2^2 + \lambda \|\mathbf{u}\|_1, \quad [2]$$

where $\mathbf{x}$ is a vector that represents the reconstructed image sequence, originally of size $N_y \times N_z \times N_t$, with N_y being the image size in the y-axis and N_z the size in the z-axis, N_t is the number of TSLs. $\mathbf{y}$ is a vector that represents the captured k-space, with original size of $N_y \times N_z \times N_t \times N_c$, where N_c is the number of coils. The transform $\mathbf{C}$ represents the multiplication with coil sensitivities, and $\mathbf{F}$ represents the Fourier transforms. For retrospective undersampling, the non-sampled k-space points were replaced by zeros as well as their respective positions in the diagonal sampling matrix $\mathbf{S}$. The transform $\mathbf{T}$ or dictionary $\mathbf{D}$ in the regularization term is chosen as one of the possibilities described in Table 1.

The first option in Table 1 is $\mathbf{T}$ as temporal finite differences (FD) transforms of order 1, 2, and 3 (TFD1, 2, or 3). These are one-dimensional high-order total variation (TV) (34–36). The FD of order 1 generates piecewise constant results with temporal discontinuities, similar to standard spatial TV. The order 2 of the FD generates results that look like piecewise lines (37). The FD of order 3 generates piecewise quadratic temporal curves.

Spatio-temporal FD (STFD) (36–38) as $\mathbf{T}$ or 3D wavelet transform (WAV) (39) as $\mathbf{D}$ are general models for 2D+times sequences. These are the only transforms tested that directly impose spatial and temporal models together with l_1 -norm on the reconstructed images.

Temporal principal component analysis (PCA) (40) was also used to construct a sparsifying transform. Applying the PCA analysis, usually using singular value decomposition (SVD), over the Casorati matrix representation of the voxels over time reveals the sparsity, or at least high compressibility, of the singular values of this matrix. This means that left orthogonal matrix of this SVD can be used as a sparsifying transform T or dictionary D , similar to k-t FOCUSS (41). This transform is computed, or learned, for a specific data set or class of data, stored and used later on the reconstruction.

The K-SVD (42) is another possible decomposition applicable to the same Casorati matrix representation (21). In the K-SVD, however, an overcomplete² dictionary D is computed, instead of an orthogonal transform. Therefore, the signal may have a much richer, and consequently sparser, representation. The K-SVD is also trained, or learned, for specific signals of interest.

Note, although, that the expected $T_{1\rho}$ signal is an exponentially decaying signal. In this sense, an overcomplete multiexponential dictionary D is another interesting approach, utilized in NMR relaxation studies (43). This transform also provides a multicomponent decomposition (44), and it is useful for latter analysis of the multicomponent $T_{1\rho}$ imaging.

Different from the l_1 -norm priors, the low rank (LR) CS reconstruction is posed as:

$$\hat{\mathbf{x}} = \underset{\mathbf{x}}{\operatorname{argmin}} \|\mathbf{y} - \mathbf{SFCx}\|_2^2 + \lambda \|\mathbf{x}\|_* . \quad [3]$$

In [3], $\|\mathbf{x}\|_*$ represents the matrix nuclear-norm (31) where $\mathbf{x}$ is reshaped as a $N_y N_z \times N_t$ Casorati matrix, where each row contains the magnetization signal of one particular voxel over TSL.

Computationally speaking, sparsity of the low rank model is related to the one assumed by the PCA model. The main difference is that the PCA is computed once, before the reconstruction, using the SVD on a full data reconstructed images, for example, while in the LR approach, the SVD is applied at each iteration, using the currently available reconstruction (45). This means we do not need to pre-learn any sparsifying transform. In fact, the algorithm learns the best representation while the images are being reconstructed.

The L+S reconstruction (33) is given by:

$$\mathbf{l}, \hat{\mathbf{s}} = \underset{\mathbf{x}}{\operatorname{argmin}} \|\mathbf{y} - \mathbf{SFC}(\mathbf{l} + \mathbf{s})\|_2^2 + \lambda_l \|\mathbf{l}\|_* + \lambda_s \|\mathbf{T}\mathbf{s}\|_1, \quad [4]$$

where $\mathbf{x} = \mathbf{l} + \mathbf{s}$, is a decomposition of $\mathbf{x}$ on a sparse part $\mathbf{s}$ and a low rank $\mathbf{l}$ part. The low rank part is obtained by the use of the nuclear-norm $\|\mathbf{l}\|_*$, while the sparse part is obtained by the use of the l_1 -norm with a specific sparsifying transform T . Table 1 lists the transforms

²An overcomplete dictionary, when represented as a matrix transform, is a matrix with much more columns than rows.

utilized with the L+S reconstruction. This is a very interesting combination with a very rich description of the images to be reconstructed (46). The low rank component usually represents the highly correlated temporal part, while the sparse component represents the more dynamic, less temporally correlated part. A similar combination of low rank and wavelet sparsity was studied in (47) for T_2 mapping.

In all methods, the regularization parameters were adjusted in order to minimize $\|\hat{\mathbf{x}}_{\lambda} - \mathbf{x}_{\text{ref}}\|_2$ where $\hat{\mathbf{x}}_{\lambda}$ is the CS reconstruction and $\mathbf{x}_{\text{ref}}$ the fully-sampled data SENSE reconstruction. While only one regularization parameter needs to be found in l_1 -norm and nuclear-norm minimizations, the L+S requires two parameters to be found.

The CS reconstruction was performed using fast iterative shrinkage-thresholding algorithms (FISTA) (48) and its modification coupled with fast gradient projection (FGP) (49) for the proximal operator. For L+S problems, the same algorithm can be used since the proximal operators are applied independently for s and l vectors. The details of the modified FISTA for nuclear-norm can be found on (50). All methods stopped when the normalized iterative update was lower than 10^{-5} or when the maximum number of 400 iterations³ was reached.

Exponential Models and Fitting Algorithms

The $T_{1\rho}$ relaxation is usually considered an exponential decaying process. The utilized model is described by:

$$|x(t, \mathbf{n})| = a(\mathbf{n}) \exp\left(-\frac{t}{\tau(\mathbf{n})}\right) + b. \quad [5]$$

where $x(t, \mathbf{n})$ is one particular voxel over TSL time t and position $\mathbf{n}$, $a(\mathbf{n})$ is magnitude of the exponential, $\tau(\mathbf{n})$ is the $T_{1\rho}$ relaxation time at position $\mathbf{n}$, and a constant residual noise component b . The $T_{1\rho}$ parameter estimation, or simply fitting process, was done using non-linear least squares, using model [5], where the minimization was done utilizing conjugate gradient Steihaug's trust-region (CGSTR) algorithm (51). The CGSTR algorithm stopped at a maximum of 2000 iterations or normalized parameter update lower than 10^{-4} .

Spatially filtering, used as a denoising over the regions of interest (ROIs), prior to the parameter estimation is sometimes helpful (52) to improve the quality of the estimated parameters. In this paper we compare the non-filtered results with two kinds of filters: standard linear filter of spatially averaging of 3×3 square of voxels, and non-linear filter of median of 5×5 square of voxels (53).

Data Analysis

In this work, we evaluate the quality of the reconstructed images and the quality of the estimated $T_{1\rho}$ parameters. Image reconstruction quality was evaluated using normalized root mean squared error (nRMSE) with respect to SENSE reconstruction of the fully-sampled

³The methods K-SVD and EXP stopped by the maximum number of iterations, but their normalized update value, i.e. $\|\mathbf{x}_{k+1} - \mathbf{x}_k\|_2 / \|\mathbf{x}_{k+1}\|_2$, being k the iteration index, was very close to the stopping value.

data. In the experiments with the synthetic phantom, we also compared against the synthetically produced ground truth. The nRMSE is defined as:

$$nRMSE(\hat{x}, x_{ref}) = \|\hat{x} - x_{ref}\|_2 / \|x_{ref}\|_2. \quad [6]$$

The fitting process was applied only on specific ROI. For *in vivo* knee cartilage 5 ROIs were chosen for evaluation, as shown in (26), including medial femoral and tibial cartilages, lateral femoral and tibial cartilages and patellar cartilage. In those regions, the estimated $T_{1\rho}$ relaxation times from CS reconstructions were compared with the estimated relaxation times from the fully-sampled data with SENSE reconstruction. The quality was evaluated by the normalized absolute deviation (NAD) of the times obtained in each voxel position n . The errors in a ROI or sets of ROIs were quantized by the median of NADs (MNAD):

$$MNAD(\tau, \tau_{ref}) = \text{median}_{n \in ROI} \left(\frac{|\tau(n) - \tau_{ref}(n)|}{(\tau(n) + \tau_{ref}(n))/2} \right). \quad [7]$$

An MNAD of 0.1 corresponds to a median deviation of 10% on the estimated $T_{1\rho}$ relaxation times compared to the reference. The median is more robust than the mean to assess the errors due to the instability of the non-linear least squares. For complete statistics about the NADs box plots are shown, where median evaluates central tendency and quartiles shows variability of the NADs. In the experiments with the synthetic phantom, the $T_{1\rho}$ parameters were also compared with the known ground truth.

Intra-subject repeatability is assessed using the coefficient of variation (CV), defined as $CV=SD/M$, being SD the standard deviation and M the mean of the median times of a ROI of two scans for the same volunteer. Bland-Altman plots were also utilized for selected methods.

RESULTS

Synthetic Phantom

The experiments with synthetic phantom are important to understand how undersampling pattern and noise affect the reconstruction quality and the $T_{1\rho}$ fitting of both, CS and reference methods. This is only possible because a ground truth is available.

Fig. 3(a) shows the reconstruction errors and 3(c) shows the $T_{1\rho}$ relaxation errors for the noiseless case when comparing with the ground truth. Figs. 3(b) and 3(d) show the results when CS is compared with the reference. Note the reference is very close to the ground truth in this case, for both: reconstruction and $T_{1\rho}$ fitting (nRMSE and MNAD, respectively). Box plots for NADs at AF=6 are shown in supporting figures S1(a) and S1(b), where it is shown the median, i.e. MNAD, as a red bar, and central interquartile as a blue box. When comparing the curves in figures. 3(a) with 3(b), 3(c) with 3(d), as well as is in supporting figures S1(a) with S1(b), one can see that curves using reference are very similar to the

curves using ground truth, in the noiseless case. In other words, the fully-sampled SENSE is reliable to be used as reference when there is no noise in the data (see figs. 3(e)–3(h)).

Figures 4(a) and 4(c) show the results when comparing reconstructions with the ground truth for the noisy case, while Figs. 4(b) and 4(d) show the results when the fully-sampled SENSE is utilized as a reference for comparison. Now, the reference is no longer so close to the ground truth, neither for reconstruction nor for $T1\rho$ relaxation. This can also be seen in the box plots for NADs at AF=6 in supporting figures S1(c) and S1(d). In fact, some CS reconstructions such as L+S SFD and STFD are closer to the ground truth than the reference. This means fully-sampled SENSE reconstruction may not be a good reference when data is noisy (Figs. 4(e)–(h)).

When reconstruction results in Fig. 4(a) are compared with $T1\rho$ fitting results in Fig. 4(c), we can notice that some methods that produced small reconstruction error, did not necessarily produced small parameter error. This happened because not only the size of the reconstruction error, measured by nRMSE, is relevant, but the shape of the error is also relevant, and it is different for each regularization penalty, as discussed later in the discussion section. The methods that impose some spatio-temporal smoothness, such as STFD, L+S SFD, and WAV had the best performance in the fitting part of the synthetic experiments.

In Figure 5, the results with pre-filtering before fitting are compared. In general, all methods had some improvement in $T1\rho$ estimation when pre-filtering is utilized. This can be noted by comparing Fig. 5(a) or 5(c) with Fig. 4(c). The reference was the most improved by pre-filtering, moving up together with the best CS methods. The MNAD, originally 0.042 on Fig. 4(c) (meaning 4.2% error), was reduced to 0.019 with 3×3 averaging (1.9%) on Fig. 5(a), and to 0.018 with 5×5 median filtering in Fig. 5(c). The EXP methods gained some positions, ending up very close to WAV. The price for this improvement in the MNAD numbers is the loss of detail in the $T1\rho$ maps and possibly larger errors in the edges of the objects, as seen in Figs. 5(e)–(j).

When comparing the curves that use fully-sampled reconstruction as reference, figures 4(d), 5(b), and 5(d), with the curves that use the ground truth, Figs. 4(c), 5(a), and 5(c) respectively, one can notice the curves with large MNAD behave similarly. However, for the best methods, with small MNAD, the curves may not correspond exactly. This means that appointing one best method among several good methods without a ground truth, using only a (possibly noisy) reference, may be misleading. Precise values from figures 3–5 are available in supporting tables S2–S4

***In Vivo* Knee Cartilage Data**

In vivo knee cartilage is an interesting as well as challenging area since it usually has small artifacts from motion and the cartilage ROI is very thin and curved. However, the results observed here were, in general, consistent with the literature (25,26) in terms of $T1\rho$ error. Since no ground truth is available, CS results were only compared with the reference (fully-sampled SENSE).

Fig. 6 shows the results for reconstruction and $T_{1\rho}$ relaxation times with different pre-filters. Note that the filtering type significantly affects the MNAD values of the methods. Following what was seen with synthetic results, not necessarily the best reconstruction algorithms in terms of nRMSE provided the best $T_{1\rho}$ fitting results in terms of MNAD, since nRMSE does not consider the temporal shape of the error, and this matter for the fitting process.

From Fig. 6, considering the median performance with 7 knee datasets, one can observe that STFD method was the best in all experiments. However, methods such as EXP, KSVD, and L+S SFD, also performed well, not far from STFD⁴.

The best results, in terms of MNAD values, were observed when 3×3 averaging filter was utilized, but 5×5 median filter was almost equally good. However, the lower MNAD (when filtering was utilized) does not translate into a change in the ranking of the methods, as shown in Fig. 6(b)–(d).

Figure 7 shows box plots for some specific AFs. The box plot shows much more information about the statistics of the NADs. Nevertheless, these results give even stronger support to STFD methods for accelerating $T_{1\rho}$ imaging, which shows not only the lowest MNAD, but also much lower variability of the NADs.

Figure 8 shows some intra-subject repeatability by the coefficient of variation and Bland-Altman plots for the best method, the STFD. Basically, almost all CS methods achieved lower or similar CV than the reference, with some exceptions. The CV also had a tendency to reduce with AF for CS methods. If filtering is considered, the 5×5 median filtering provided lowest CVs for almost all methods. Precise values from figures 6 and 8 are available in supporting tables S5 and S6.

Overall Score

In order to have an objective quantification of all results, we compute MNAD for the results with noisy synthetic and *in vivo* together. The first score, in Table 2A, is simply the MNAD of all $T_{1\rho}$ estimation errors (NADs), among 3 noisy synthetic datasets and 7 *in vivo* datasets, for the three filters utilized (no-filter, 3×3 mean, 5×5 median) using comparisons with the reference. The resulting number provides us a median $T_{1\rho}$ error of a particular method for a desired AF. The second score, in Table 2B, the MNAD was obtained only when 3×3 averaging pre-filter was utilized.

From Table 2A, one can notice that a median error below 6.5% is expected when using AFs up to 10 with the method STFD. If we extend the tolerance to 10%, then L+S SFD, EXP, and WAV can be included. According to Table 2B, one can expect an MNAD below 6.5% up to AF of 10 for almost the same methods when 3×3 averaging pre-filter is utilized: STFD, L+S SFD, and EXP. In the literature (54), 5% error is considered acceptable for reproducibility, if one use this limit, we can still use AFs up to 8 with STFD or AF up to 6 with the best three methods.

⁴According to the previous results with synthetic data, the choice of the best method should be taken with care since the reference reconstruction may be noisy. So other good methods should not be immediately discarded.

DISCUSSION

Comparison with a Possibly Noisy Reference

The assumption that fully-sampled data is a good choice to produce a reference should be carefully made, since it is usually perturbed by noise and, possibly, other artifacts. This is, in most practical cases, the only option. However, it is difficult to judge the best CS method by comparing them with a perturbed reference. This is why the synthetic experiments are necessary. Our experiments with synthetic data showed that a noisy reference (15dB) could have a MNAD as high as 4.2% (without filtering, Fig. 4(c)). We can conclude that, under these circumstances, all CS methods with error lower than this should be ranked with care, preferable considered better by other factors than the MNAD alone.

Recommended CS Methods

For AF of 2, almost all methods produced acceptable results, with low MNAD. As the AF is increased, fewer methods kept low MNAD. We marked in bold letters, in tables 2A, 2B some suggested methods for each AF.

Our experimental results indicated that the use of 3×3 averaging filter provided the lowest MNAD for almost all CS methods. However, no matter the pre-filter utilized, we observed that the CS methods STFD, L+S SFD, and EXP appeared among the best methods. This indicates that these three are the most suitable CS methods for accelerating $T_{1\rho}$ mapping of cartilage. However, KSVD and WAV were also good, and should not be discarded.

Performance of the Regularization Penalties and Pre-Filters

Clearly, the choice of the regularization function has significant influence in the success of CS for $T_{1\rho}$ mapping. Simple temporal finite differences, such as TFD1, TFD2, TFD3 did not performed consistently well and their results were extremely unstable. Wavelet transform, represented by WAV, performed better regarding MNAD, close to the best methods.

Even though the reconstruction quality provided by PCA was appropriate, this does not translate into good $T_{1\rho}$ fitting results here. The KSVD performed better in this sense.

The use of fixed overcomplete exponential dictionary, reported as EXP, produced very good results. Surprisingly, this transform is not very popular in the literature, compared for example to PCA. May be the reason is that, as seen in Table 1, it requires much more iterations to converge than PCA. It is very likely that researchers familiarized with relatively quick convergence of PCA have not waited long enough (10 times more iterations) to see the good results provided by EXP.

The LR and L+S methods were also promising approaches, but we observed that the LR part alone provided only limited improvement. The L+S with WAV or no sparsity transform performed equal or worse than LR. However, we notice improvement when combined with SFD, being this last one among the best methods.

The STFD is an improved version of total variation-like regularizers, also not commonly used for parameter estimation problems in MRI in the form utilized here. The standard TV

regularization may generate cartoon-like aspect on the reconstructed images (37). This is undesirable, of course, but it should only happen when the regularization parameter is too large and the results get over-regularized. However, when spatial first order finite difference is combined with temporal second order finite difference, it provides an excellent regularization function for this problem.

We clearly observed that pre-filtering reduced the $T_{1\rho}$ mapping error. In part because it reduced the noise in the reference and in CS reconstructions, resulting in stable fitting and low MNAD. Even though there are better denoising filters (52) than those tested here, we observed that standard 3×3 averaging, which is a simple linear filter, still does a good job in reducing the errors. The median filter is equally good with respect to MAND, but was better with respect to repeatability results with *in vivo* data.

Comparison with Previous Studies

In (25) a combination of CS and autocalibration reconstruction (ARC) was utilized for knee cartilage $T_{1\rho}$ mapping. The AFs of ARC and CS combined reached 2.3. They reported $T_{1\rho}$ mapping errors close to 5%, or lower, for AFs around 2. Note that no filtering was utilized and only spatial finite difference was used in CS. We did observe similar results at these AFs for knee cartilage here, some even lower, as seen in figures 7(b)–7(d).

In (23), three specific CS-like methods: integrating PCA and dictionary learning (PANDA), focal underdetermined system solver with PCA (k-t FOCUSS-PCA) and model-based dictionary learning (MBDL) were compared to accelerate brain and spine $T_{1\rho}$ mapping up to AF of 4. $T_{1\rho}$ relaxation errors between 8.9% and 12% were reported, depending on the CS method⁵ utilized. These resulting errors are very similar to the errors we observed in this paper, but for cartilage.

In (24), a combined reconstruction with locally adaptive iterative support detection (k-t LAISD) and joint image reconstruction and sensitivity estimation in SENSE (JSENSE) method was proposed for knee cartilage $T_{1\rho}$ mapping, with acceleration up to 3 and 3.5. In (24), it was reported significant improvements in the quality of the estimated $T_{1\rho}$ times due to the jointly estimation of the coil sensitivities and local adaptability of the regularization. The reported $T_{1\rho}$ relaxation errors were impressively low due to a different method of evaluation compared to the other papers, with 2.46% error if estimated coil maps were fixed and 0.72% if they were jointly estimated with images in JSENSE. Using the same evaluation as (24), the STFD achieves 0.4% at AF=2, 0.85% at AF=4, and 1.24% at AF=6. This is consistent with reported literature (24).

In (55) blind compressed sensing (BCS) was applied to T_2 and $T_{1\rho}$ mapping of brain. Their reported parameter error was lower than the one we observed but the number are not in the same scale for proper comparison. BCS approaches are also promising, trying to adapt the transform during the reconstruction to increase sparsity and improve the reconstruction. The only adaptable-transform methods tested here are the LR and the L+S methods (including L

⁵The methods PCA and KSVD, tested here, are the most similar to the ones tested in (23).

+S WAV and L+S SFD). However, we did not observe significant superiority of LR and L+S due to the adaptability of the transform; perhaps this would be different with BCS.

One of the novelties of this study, compared with these papers is that we provided much broad evaluations, using AF from 2, up to 10, comparing twelve CS methods, with three different pre-filtering options on 6 synthetic datasets and 7 *in vivo* human knee cartilage datasets. In order to be fair and objective, we are not proposing or claiming here any method of our own. All priors appeared elsewhere in the literature for different applications, in the exact or similar form used here, even though some of them were never used for $T_{1\rho}$ imaging.

Limitations of This Study

In our tests, the regularization parameters were set to have the lowest l_2 -norm of the difference between CS and the fully-sampled reference, essentially minimizing nRMSE. However, the ideal parameter would be the one that makes the reconstruction closer to the ground truth (unknown in practical cases). Therefore, the choice of the regularization parameter is still an open question⁶.

Another aspect is the choice of the minimization algorithms, for reconstruction and for $T_{1\rho}$ fitting, and their respective stopping criteria. These choices affect the reconstruction time and the required number of iterations of each method. See Table 1 for average number of iterations and average time, in seconds, of each method. Note KSVD and EXP provided good results, but with very slow converge, in term of iterations. These are candidates for fast algorithms such as (56).

The number of TSLs and their distribution are also relevant. Our choice was based on previous studies (26), but different distributions are possible. The use of different AFs in each TSL can also be investigated.

Model-based reconstructions are promising approaches (57,58). We did not include them here because they require a specific discussion. Strictly speaking, not all model-based methods belong to the class of CS methods, since sparsity and incoherence are not always included in their models. We hope to discuss these methods in the future.

Finally, studies with prospective data and CS reconstructions for biexponential models (26) for $T_{1\rho}$ mapping of cartilage will be evaluated in the near future.

CONCLUSION

This study shows that CS can significantly accelerate $T_{1\rho}$ mapping of cartilage. Twelve different CS methods were compared, being the most indicated methods: STFD, L+S SFD, and EXP. In addition, the use of pre-filtering prior to $T_{1\rho}$ fitting is recommended. These best CS methods performed satisfactorily for AFs up to 10, with $T_{1\rho}$ error below 6.5%.

⁶See more related to the choice of the regularization parameter in the online supplemental information of this paper.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Synthetic phantom utilized in the experiments, composed by three areas with different $T_{1\rho}$ time ranges. The $T_{1\rho}$ relaxation times were randomly selected from the ranges 1–25ms, 30–50ms and 50–110ms.

Figure 2.

MRI acquisition model used for CS reconstructions, including coil sensitivity C , Fourier transform F , and k-space undersampling pattern S using Poisson disk with central area, also additive white Gaussian noise η .

Figure 3.

Results for synthetic phantom with no noise in the acquisition, including (a) reconstruction error (nRMSE) when compared with ground truth and their counterparts (b) when compared to the reference, also (c) $T_{1\rho}$ relaxation error (MNAD) compared with ground truth and (d) with reference. Representative quantitative accelerated $T_{1\rho}$ maps and corresponding ground truth and reference maps are shown in (e)–(h).

Figure 4.

Results for synthetic phantom with 15dB of noise in the acquisition, including (a) reconstruction error (nRMSE) when compared with ground truth and their counterparts (b) when compared to the reference, also (c) $T_{1\rho}$ relaxation error (MNAD) compared with ground truth and (d) with reference. Representative quantitative accelerated $T_{1\rho}$ maps and corresponding ground truth and reference maps are shown in (e)–(h).

Figure 5.

Parameter fitting using the synthetic phantom with 15dB of noise in the acquisition when prior filtering is utilized, including (a) $T_{1\rho}$ relaxation error (MNAD) compared with ground truth and (b) with reference when 3x3 averaging is used and (c) and (d) when 5x5 median is used with ground truth and reference, respectively. Representative quantitative accelerated $T_{1\rho}$ maps and corresponding ground truth and reference maps are shown in (e)–(j).

Figure 6.

(a) nRMSE for reconstruction and (b) MNAD for $T_{1\rho}$ relaxation parameter fitting of the *in vivo* knee cartilage with no filtering, (c) 3×3 average filtering, and (d) 5×5 median filtering. Representative quantitative accelerated $T_{1\rho}$ maps and corresponding reference maps are shown in (e)–(j).

Figure 7.

Box plot of the NAD for all human knee cartilage datasets with no filtering and (a) AF=2, (b) AF=6, and (c) AF=10, with 3×3 average filtering and (d) AF=2, (e) AF=6 and (f) AF=10, and also with 5×5 median filtering with (g) AF=2, (h) AF=6 and (i) AF=10. The box plot shows more information about the NADs than only the MNAD. The horizontal red bars represent the median of NAD (or NMAD), the blue box represent the central interquartile, where 50% of the MAD values are into. The dashed dark lines represent the range of the data.

Figure 8.

Coefficient of variation of the different methods and acceleration factors with (a) no filtering, (b) 3×3 average filter and (c) 5×5 median filter considering two repetitions with each of the three volunteers. Bland-Altman plots for the STFD method with (d) no filtering, (e) 3×3 average filter and (f) 5×5 median filter considered the best in the previous experiment.

Table 1

Priors utilized with compressed sensing methods:

Prior Model	Penalty	Transform	Number of parameter	Minimization algorithm	Avg. iterations	Avg. Time
TFD 1,2, or 3	l_1 -norm	Temporal finite difference, order 1, 2 or 3	1	FISTA-FGP	40,60,80	514, 684, 691 sec
STFD	l_1 -norm	Spatial and temporal finite difference, spatial order 1 and temporal order 2	1	FISTA-FGP	120	1298 sec
WAV	l_1 -norm	3D Wavelet transform (2D+time) Daubechies 4, with 4 levels of decomposition.	1	FISTA	43	1005 sec
PCA	l_1 -norm	Unitary transform from temporal principal component analysis from fully-sampled data	1	FISTA	43	121 sec
KSVD	l_1 -norm	Overcomplete temporal dictionary computed from fully-sampled data using KSVD	1	FISTA	400	249 sec
EXP	l_1 -norm	Overcomplete temporal dictionary of exponentials with 100 relaxation times between 1 and 150 ms	1	FISTA	400	1240 sec
LR	nuclear-norm	Applied to a $N_y N_z \times N_t$ matrix formed with the reshaped $N_y \times N_z \times N_t \times 1$ vector.	1	Modified FISTA	38	194 sec
L+S	nuclear-norm and l_1 -norm	Same as low rank, plus identity for l_1 -norm	2	Modified FISTA	80	218 sec
L+S SFD	nuclear-norm and l_1 -norm	Same as low rank, plus spatial finite difference for l_1 -norm	2	Modified FISTA-FGP	120	837 sec
L+S WAV	nuclear-norm and l_1 -norm	Same as low rank, plus 2D spatial wavelet for l_1 -norm, also Daubechies 4, with 4 levels.	2	Modified FISTA	55	1052 sec

Table 2

A) Ranking the methods using its expected $T_{1\rho}$ parameter error up to certain acceleration factor, for synthetic and *in vivo* datasets and all three pre-filters. Values lower than 0.065 (error of 6.5%) are bold-marked. B) Ranking the methods by its expected $T_{1\rho}$ parameter error, when 3×3 averaging pre-filter is utilized, up to certain acceleration factor, for synthetic and *in vivo* datasets. Values lower than 0.065 (error of 6.5%) are bold-marked.

A. Expected $T_{1\rho}$ error for synthetic and <i>in vivo</i> datasets and all three pre-filters									
AF 2		AF 4		AF 6		AF 8		AF 10	
STFD	0.025	STFD	0.040	STFD	0.049	STFD	0.057	STFD	0.064
L+S SFD	0.028	L+S SFD	0.048	L+S SFD	0.060	L+S SFD	0.066	L+S SFD	0.072
EXP	0.030	EXP	0.048	EXP	0.061	EXP	0.072	EXP	0.081
WAV	0.031	WAV	0.056	WAV	0.072	WAV	0.085	WAV	0.096
TFD2	0.031	KSVD	0.060	KSVD	0.076	KSVD	0.091	LR	0.106
TFD3	0.031	TFD3	0.064	TFD2	0.086	LR	0.099	L+S WAV	0.106
KSVD	0.035	TFD2	0.066	PCA	0.088	L+S WAV	0.099	KSVD	0.107
PCA	0.037	PCA	0.067	LR	0.089	L+S	0.102	L+S	0.110
TFD1	0.040	L+S WAV	0.071	L+S WAV	0.090	PCA	0.104	PCA	0.122
LR	0.042	L+S	0.072	L+S	0.091	TFD2	0.108	TFD3	0.136
L+S WAV	0.042	LR	0.072	TFD3	0.096	TFD3	0.126	TFD2	0.143
L+S	0.045	TFD1	0.079	TFD1	0.123	TFD1	0.154	TFD1	0.247
B. Expected $T_{1\rho}$ error for synthetic and <i>in vivo</i> datasets and 3×3 averaging pre-filter									
AF 2		AF 4		AF 6		AF 8		AF 10	
STFD	0.017	STFD	0.030	STFD	0.038	STFD	0.045	STFD	0.051
TFD2	0.021	EXP	0.037	EXP	0.047	L+S SFD	0.056	L+S SFD	0.059
L+S SFD	0.021	L+S SFD	0.039	L+S SFD	0.049	EXP	0.056	EXP	0.061
EXP	0.021	WAV	0.044	KSVD	0.058	KSVD	0.071	WAV	0.081
TFD3	0.021	KSVD	0.045	WAV	0.058	WAV	0.071	KSVD	0.084
WAV	0.022	TFD3	0.048	TFD2	0.067	TFD2	0.086	LR	0.093
KSVD	0.024	TFD2	0.051	PCA	0.072	PCA	0.086	L+S WAV	0.094
PCA	0.028	PCA	0.054	TFD3	0.072	LR	0.087	L+S	0.097
TFD1	0.029	L+S WAV	0.060	LR	0.077	L+S WAV	0.088	PCA	0.101

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A. Expected T_p error for synthetic and <i>in vivo</i> datasets and all three pre-filters									
	AF 2	AF 4	AF 6	AF 8	AF 10				
LR	0.033	L+S	0.061	L+S WAV	0.078	L+S	0.090	TFD3	0.111
L+S WAV	0.033	LR	0.061	L+S	0.079	TFD3	0.098	TFD2	0.119
L+S	0.035	TFD1	0.067	TFD1	0.108	TFD1	0.140	TFD1	0.231