High Spatio-Temporal Resolution Dynamic Contrast-Enhnaced MRI using Compressed Sensing

Kyunghyun Sung^{*†}, Manoj Saranathan[†], Bruce L Daniel[†] and Brian A Hargreaves[†]

University of California, Los Angeles, CA, USA

[†] Stanford University, Stanford, CA, USA

E-mail: kyunghsu@gmail.com Tel: 310-267-6842

Abstract—Iterative thresholding methods have been extensively studied as faster alternatives to convex optimization methods for solving large-sized problems in compressed sensing MRI. A novel iterative thresholding method, called LCAMP (Location Constrained Approximate Message Passing), is presented for reducing computational complexity and improving reconstruction accuracy when a non-zero location (or sparse support) constraint can be obtained from view shared images in dynamic contrast-enhanced MRI (DCE-MRI). LCAMP modifies the existing approximate message passing algorithm by replacing the thresholding stage with a location constraint, which avoids adjusting regularization parameters or thresholding levels. This work is applied to breast DCE-MRI to demonstrate the excellent reconstruction accuracy and low computation time with highly undersampled data.

I. INTRODUCTION

Cancer is the second most common cause of death in the United States. In 2012, about 577,190 Americans are expected to die of cancer, more than 1,500 people a day [1]. Non-invasive detection of cancer continues to be one of the primary goals of medical imaging, and magnetic resonance imaging (MRI) has great potential to become a major imaging modality for cancer imaging as it is non-invasive, non-toxic, and involves no ionizing radiation [2]. Compared to other imaging modalities such as X-ray, computed tomography or ultrasound, MRI has the unique ability to achieve several different types of soft tissue image contrast and can provide a means of resolving blood flow alterations associated with tumoral, vascular, and infectious diseases.

Dynamic contrast-enhanced MRI (DCE-MRI) is a widely used method in the diagnosis of cancer in abdominal, pelvic, and breast imaging [3], [4]. A common approach is to acquire T1-weighted reference images, inject a low molecular-weight paramagnetic contrast agent, and acquire a time series of T1weighted images as the contrast agent circulates through the tissue microvasculature. We can extract quantitative microvascular properties by either fitting the uptake of contrast to a pharmacokinetic model [5] or computing the initial area under the gadolinium concentration curve [6]. Both high spatial and high temporal resolution are required to accurately estimate these microvascular properties, which can provide not only a non-invasive method for tumor detection but also predictive and prognostic biomarkers for cancers [7]–[9].

MRI remains limited by tradeoffs between spatial resolution, temporal resolution, and signal-to-noise ratio (SNR).

Multiple rapid MRI techniques have been developed for accelerating MR imaging, including non-Cartesian sampling (e.g., spiral [10] and radial [11]), spatio-temporal undersampling [12] and parallel imaging [13], [14]. In addition, compressed sensing (CS) is an emerging technique that can allow accurate reconstruction of images from a reduced amount of acquired data [15], [16], and its promise to improve the speed of MRI has been successfully demonstrated [17], [18]. However, depending on implementation and application, conventional CS-MRI is limited in some cases by practical and fundamental issues, depending on implementation and application.

One of the major issues in CS-MRI is high computational complexity for the reconstruction [19], [20]. The CS reconstruction typically finds an optimal sparse solution among all possible candidates by minimizing the L1-norm, defined by a sum of absolute values of sparse coefficients [15], [16]. Since the L1-norm is convex, many standard convex optimization techniques [21] can be directly applied to solve the problem. However, solving the L1 problem using convex optimization is substantially more computationally expensive than using traditional gradient-based algorithms [19], [22]. This high computational complexity often precludes the further use of CS in many MR applications where the problems are considerably larger scale such as DCE-MRI.

Fast iterative thresholding methods have been widely studied as alternatives to convex optimization due to their low computational complexity [19], [23]-[26]. We have developed a variation of the iterative thresholding algorithm that incorporates both an approximate message passing (AMP) term and a non-zero location (or sparse support) constraint, called Location Constrained Approximate Message Passing (LCAMP) [27]. The AMP term was recently developed to correct a residual bias in the iterative thresholding methods, and the AMP algorithm has been shown to improve reconstruction performance over iterative thresholding methods [20]. We have expanded the AMP algorithm by replacing the thresholding operation with the location constraint, masking out insignificant sparse coefficients based on the sparse support. This can further increase reconstruction accuracy while retaining low computational complexity.

The overall purpose of this work is to offer high spatiotemporal resolution of 3D volumetric DCE-MRI. We hypothesize that the spatial and temporal resolution of DCE-MRI can be substantially increased by our proposed LCAMP algorithm and expect that the enhanced spatial and temporal resolution can improve quantitative features of DCE-MRI, which can enable identification and characterization of smaller tumors.

II. THEORY

We first explain the standard convex optimization method that is most commonly used in CS-MRI and later describe three faster alternatives to the convex optimization (iterative thresholding methods, AMP and LCAMP), which have equivalent computational complexity at each iteration.

A. L1-Regularized Least Squares Program (L1 LSP)

Assuming an N-point image x is sufficiently sparse (or compressible) and the undersampled Fourier transform Φ ($n \times N$; $n \ll N$) possesses incoherence, CS can allow accurate reconstruction of x from a reduced set of measurements [15], [16]. The reconstruction can be achieved by solving the following L1 minimization:

$$\min \|y - \Phi x\|_2^2 + \lambda \|\Psi x\|_1, \tag{1}$$

where y consists of the acquired k-space samples Φx , Ψ is a sparse transformation, and $\lambda > 0$ is the regularization parameter. This unconstrained minimization problem, called an L1-regularized least-squares program (LSP), has been used in many ways and yields a sparse solution due to the L1 norm when λ is chosen appropriately.

The optimal solution to the L1-regularized LSP must be computed numerically due to its non-differentiable (or nonsmooth) objective function. One common way is to transform Eq. 1 to a convex quadratic program or a second-order cone program with linear inequality constraints and to use a standard interior point method. The interior point method has high computational complexity, approximately $O(N^3)$, and various methods have been proposed to reduce the computation time using a truncated Newton method [22], [28], [29]. However, the general computation time is still not practical for largesized problems, and the ability to choose the regularization parameter (λ) sometimes limits the reconstruction reliability.

B. Iterative Soft/Hard Thresholding (IST/IHT)

Fast iterative thresholding methods have been extensively studied as alternatives to solve Eq. 1 [23]–[26], [30] and mostly fall into two groups: iterative soft thresholding (IST) and iterative hard thresholding (IHT), depending on the choice of the non-linear thresholding operators. These approaches are known to be extremely fast, especially if they use efficient algorithms for the matrix-vector operations, such as the fast Fourier transform. [23], [25], [30]. The generic form of the iterative thresholding methods can be simply written as:

$$z_k = y - \Phi \Psi^* w_k,$$

$$w_{k+1} = \eta (w_k + \Psi \Phi^* z_k; \theta_k),$$
(2)

where z_k is the residual of the estimate in k-space at the kth iteration, w_k is the current estimate of the sparse vector and $\eta(x; \theta_k)$ is either the soft- or hard-thresholding function. Φ^*



Fig. 1. Illustration of three iterative thresholding-based methods (IST/IHT, AMP and LCAMP) for one iteration. Note that all three methods share the same matrix-vector operations ($\Phi\Psi^*$ and $\Psi\Phi^*$), which are the main computational load, and the differences between each methods are highlighted in the gray box.

and Ψ^* denote the transpose of Φ and Ψ , and the solution x can finally be found as $x = \Psi^* w$.

Although there are many extensions to IST/IHT, the selection of θ_k is the major challenge in achieving high reconstruction accuracy and stability and is very difficult to optimize since it can vary iteration-by-iteration. In practice, the thresholding levels can be sub-optimally tuned by using precomputed values based on a comprehensive study of parameter variations and options [31]. More importantly, non-linear thresholding creates a bias in noise contribution, potentially making the reconstruction unstable. Iterative thresholding methods are known to perform worse than conventional L1 minimization methods [20], [31].

C. Approximate Message Passing (AMP)

Donoho *et al.* recently presented an algorithm, called firstorder approximate message passing (AMP) [20], that extends IST by adding a new term. The main idea of AMP is to fix the bias in the residual z_k , making the thresholding operation more effective. Due to its improved residual, the overall reconstruction accuracy is equivalent to conventional L1 minimization and better than iterative thresholding methods [20]. The idea is inspired by belief propagation in graphical models and a more detailed derivation of the extra term can be found here [32].

The general iteration steps of the AMP algorithm can be

written as:

$$b_{k} = \frac{1}{n} \sum_{i=1}^{N} \eta'(w_{k-1} + \Psi \Phi^{*} z_{k-1}; \theta_{k}),$$

$$z_{k} = y - \Phi \Psi^{*} w_{k} + b_{k} z_{k-1},$$

$$w_{k+1} = \eta(w_{k} + \Psi \Phi^{*} z_{k}; \theta_{k}),$$
(3)

where $\eta(x; \theta_k)$ is the soft-thresholding function and $\eta'(s; \theta_k)$ is defined as $\frac{\partial}{\partial s}\eta(s; \theta_k)$. The only difference between the iterative thresholding methods and AMP is the extra term $b_k z_{k-1}$ in the calculation of z_k . This extra term, often called an "Onsager term," has a significant impact on the reconstruction by correcting the noise component of $w_k + \Psi \Phi^* z_k$ to follow a Gaussian distribution at every iteration.

Figure 1 illustrates a simplified diagram of IST/IHT and AMP for one iteration. Both methods share the same main computational load, the matrix-vector operations ($\Phi\Psi^*$ and $\Psi\Phi^*$), and the main difference between two is the AMP term (dotted box, labeled **C** in Fig 1). The AMP term typically adds minimal computational effort, and the computational complexity of AMP remains similar to that of IST/IHT. The computation time is proportional to the number of iterations required to achieve convergence, and the AMP algorithm has been extensively tested by both simulation and mathematical analysis to show equivalent reconstruction accuracy to the conventional L1 minimization but with lower computation time [20]. Therefore, the AMP algorithm is a suitable choice for CS MRI, especially when the problem size is large.

D. Location Constrained Approximate Message Passing (LCAMP)

An important operation for both AMP and IST/IHT is the thresholding step, where sparsity is enforced by choosing only significant sparse coefficients. Careful choice of θ_k is essential but difficult in practice, especially when measurements are noisy. In our new method, we replace thresholding with a location (or sparse support) constraint, which forces some sparse coefficients to be zero at every iteration. This selection operation completely removes the need for a threshold and is guaranteed to be near-optimal since the decision between significant and insignificant coefficients is not made by a current proxy ($w_k + \Psi \Phi^* z_k$) but instead by the location constraint. Note that the operation becomes similar if the thresholding level is near-optimal and the proxy is good enough (e.g., measurements $\Phi \Psi^*$ satisfy the restricted isometry property condition [33]).

The location constraint can be performed by multiplying a non-zero location mask M (one for non-zeros and zero for zeros), and b_k in Eq. 3 becomes simply supp(M)/n where supp(M) is the sparsity of M. By introducing a reduction factor r = N/n and a sparsity level c = supp(M)/N, LCAMP has simpler iteration steps than AMP:

$$z_k = y - \Phi \Psi^* w_k + r \cdot c \cdot z_{k-1},$$

$$w_{k+1} = M \cdot (w_k + \Psi \Phi^* z_k).$$
(4)

We assume M is available prior to the reconstruction and will discuss how to obtain this information later. Figure 1 describes the differences among all three iterative thresholdingbased methods. LCAMP is implemented by replacing soft/hard



Fig. 2. Pseudorandom undersampling pattern used for LCAMP. View-shared (time-averaged) composite images are used as a sparse location constraint to reconstruct each individual frame with LCAMP.

thresholding, labeled **A**, with the location constraint, labeled **B** in Fig 1. All three methods share the same core operations $(\Phi\Psi^* \text{ and } \Psi\Phi^*)$, and the computational complexity for one iteration is similar.

III. METHODS AND MATERIALS

In DCE-MRI, a set of images is repeatedly acquired on a same object to capture dynamic signal uptake, and the location constraint M can be estimated using the fact the underlying sparsity may not be changed across the measurements. Figure 2 describes the generation of k-space undersampling patterns $(k_y - k_z - t)$ for LCAMP. The undersampling patterns contained four sampling densities: a fully sampled region and three randomly sampled regions with different acceleration factors. The pseudo random sampling is generated by randomly selecting k-space locations among all unselected ones so that each region becomes fully sampled when combined over R frames (e.g., the smallest region becomes fully sampled when combined over 3 frames, and the largest region becomes fully sampled when combined over 12 frames). Note that many other methods including different random undersampling can be explored to generate composite images, depending on implementation and applications.

We used the wavelet transform Ψ as the sparse transformation due to its ability to sparsely represent natural images, and the non-zero location mask M for each time frame was estimated by thresholding the wavelet coefficients of the composite image, constructed from a time-averaged full data set. Any wavelet coefficients above the threshold were considered to be significant, and a binary image (non-zero location mask M) was set to be one at locations that contained significant wavelet coefficients. An outline of the LCAMP algorithm is in Algorithm 1.

Algorithm 1: LCAMP Algorithm

Input

- y measured k-space data $(n \times 1)$
- Φ undersampled Fourier transform $(n \times N)$
- Ψ wavelet transform ($N \times N$) M - non-zero location mask

Initial Estimate: w_0 - initial estimation $(N \times 1)$

Initialization

r = N/n;c = supp(M)/N $w_k = w_0;$ $z_{k-1} = y - \Phi \Psi^* w_0;$ k = 0;

while halting criterion false do

 $\begin{bmatrix} z_k \leftarrow y - \Phi \Psi^* w_k + r \cdot c \cdot z_{k-1}; \\ w_{k+1} \leftarrow M \cdot (w_k + \Psi \Phi^* z_k); \\ k \leftarrow k+1; \\ w \leftarrow w_k; \end{bmatrix}$

Output : w - wavelet coefficients $(N \times 1)$

As a stopping criterion, the algorithm employed the difference in the data fidelity term $(y - \Phi \Psi^* w_k)$ divided by the norm of measured data. The data fidelity becomes more relaxed when the measurements are noisier and/or the underlying signal is more sparse because the contribution from insignificant coefficients (masked-out components) becomes more prominent, but the amount of relaxation tends to become stable (i.e., difference in the data fidelity term per iteration becomes small) when approaching to the solution. Here, we monitored the data fidelity at each iteration and stopped the reconstruction when it does not change considerably:

$$\frac{\|y - \Phi \Psi^* w_k\|_2 - \|y - \Phi \Psi^* w_{k-1}\|_2}{\|y\|_2} < \epsilon, \tag{5}$$

where ϵ is a tolerance factor, which must be set by the user. In general, small values (10^{-2} to 10^{-4}) are sufficient to generate stable results.

All reconstructions were implemented in Matlab (R2010b; The MathWorks Inc., USA) and run on a Linux PC equipped with a dual six-core 2.66 GHz CPU (Intel Xeon) and 64 GB of memory. The matrix size for DCE-MRI data was 244 × 128 × 48 ($N_x \times N_y \times N_z$) with 20 time frames, and we used a 3D dual-tree wavelet transform. We used the DCE analysis software (OsiriX Plug-in) to calculate the kinetic behavior of the contrast uptake, which can be analyzed on user-defined regions or a per-pixel basis. The plug-in can generate pixelby-pixel quantitative maps such as an initial slope of the signal enhancement.



Fig. 3. DCE breast images at selected slice locations: (a) original, (b) LCAMP and (c) the absolute difference between original and LCAMP. The absolute difference is scaled to be 10% of the maximum signal and was typically less than 2% of the maximum.

IV. RESULTS

Figure 3 shows representative volumetric images reconstructed with a high acceleration factor ($R_{net} = 10$). Magnitude images at the eighth time frame (23 seconds after contrast injection) are shown at different slice locations. The absolute difference images are also shown on the right to accentuate the differences. Compared with the original images, the LCAMP reconstruction is able to recover almost all the features and the absolute difference remains small. The absolute difference images are scaled to be 10% of the maximum signal and the average over the largest 5% of errors is 1.2 - 1.8% of the maximum signal over the breast.

Figure 4 shows an example of reconstructed images at different time frames (t = 2, 6, 10 and 14). The original and LCAMP images are qualitatively similar and the absolute



Fig. 4. DCE breast images at selected time frames: (a) original, (b) LCAMP and (c) the absolute difference between original and LCAMP. The absolute difference is scaled to be 10% of the maximum signal, and the absolute difference was typically less than 2% of the maximum.



Fig. 5. Maps of initial slope of contrast enhancement generated using (a) original, (b) view sharing and (c) LCAMP. Magnitude images are shown for the anatomical reference, and a region containing a tumor, indicated by the arrows, is zoomed-in to show the difference between view sharing and LCAMP. Different colors in the initial slope map indicate various degrees of line slope, computed by a linear regression of initial enhancement signals in arbitrary units and typically expresses the steepness of initial signal uptake.

difference images confirm the excellent reconstruction performance (the average over the largest 5% of errors is 1.7 - 2.4% of the maximum signal over the breast). Note that the absolute differences are relatively large in the heart because the location constraint is inaccurate due to the heart motion, resulting in a loss of spatial resolution. Note that by acquiring the data with a high undersampling factor, the temporal resolution can be significantly reduced. For example, the data shown was acquired with an 11-second temporal resolution, which could be reduced to 1 second with R_{net} =10 undersampling.

Figure 5 shows initial slope maps computed by reconstructed DCE images using view sharing and LCAMP. The initial slope maps, computed using a linear regression from three time frames, show the slopes of initial signal enhancement (red: highest and blue: lowest). Selected initial slope maps containing tumor regions (arrows) are overlaid on the magnitude images for anatomical references. When the view sharing method is used, signal dynamics are temporally blurred, which results in underestimation of the initial slopes. In contrast, the LCAMP method maintains similar signal enhancement information on a per-pixel basis.

V. DISCUSSION

We have presented a novel CS reconstruction method that quickly and accurately finds a sparse solution when a location (or sparse support) constraint is provided as prior knowledge. The LCAMP algorithm fundamentally shares similar operations with other iterative thresholding methods and therefore retains their extremely low computational complexity. More importantly, the AMP term corrects the residual bias, while the location constraint assures a near-optimal selection of sparse coefficients at every iteration, which collectively improve the accuracy of the reconstruction.

A location constraint is stronger prior knowledge on the signal than conventional sparsity as the sparsity assumes no

knowledge of the non-zero locations in a sparse representation of a signal. The existence of the location constraint can create a reduced sparse transform consisting of only a vector of non-zero locations. The problem then can become an overdetermined system using the reduced sparse transform (i.e., more measurements than unknowns), and least-squares can be applied to find a solution. In our numerical simulation, the least-squares with the reduced sparse transform worked perfectly when the measurements have no or very little noise but diverged quickly when the measurements are noisy or any incorrect location constraints are included. This has suggested to use an iterative approach with the location constraint for more stable reconstruction results.

Accurate estimation of the location constraint is important for enforcing the correct constraint. When there is motion between dynamic images or measurements are too noisy, the time-averaged composite images may not represent correct sparsity locations, which mainly result in a loss of spatial resolution. We may be able to make the location constraint more immune to small motion by performing soft thresholding within only the known support, while forcing the signal outside the support to be zero. Low SNR composite images tend to underestimate the underlying sparsity level because any small wavelet coefficients less than the background noise level will be ignored. We may be able to overcome this SNR issue by averaging more temporal images.

LCAMP replaces the thresholding operation with a location constraint. This removes the ambiguity of manually selecting the threshold levels, enables faster convergence and makes the reconstruction more stable. This was shown as a more consistent reconstruction performance with different reduction factors while other reconstruction methods rapidly degraded as the reduction factors increased. In addition, the LCAMP reconstruction is free of many user-defined values (regularization/relaxation parameters and threshold levels), and only the stopping criterion remains to be determined. This may make the reconstruction more reproducible in practice.

VI. CONCLUSIONS

We have presented a novel CS reconstruction method called LCAMP (Location Constrained Approximate Message Passing) to achieve both accurate and fast reconstruction. The location constraint was estimated from the temporally averaged composite image in DCE-MRI and used to replace conventional thresholding. LCAMP was shown to preserve qualitative and quantitative features in DCE MRI. This fast reconstruction can also be easily implemented as an automated reconstruction since there are no regularization parameters that need to be manually selected.

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