Iterative Projection Reconstruction of Time-Resolved Images Using Highly-Constrained Back-Projection (HYPR)

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Highly-constrained back-projection (HYPR) is a technique for the reconstruction of sparse, highly-undersampled time-resolved image data. A novel iterative HYPR (I-HYPR) algorithm is presented and validated in computer simulations. The reconstruction method is then applied to cerebral perfusion MRI simulated as a radial acquisition and contrast-enhanced angiography of the head to assess feasibility in accelerating acquisitions requiring high temporal resolution and accurate representation of contrast kinetics. The I-HYPR algorithm is shown to be more robust than standard HYPR in these applications in which the sparsity condition is not met or in which quantitative information is required. Specifically, iterative reconstruction of undersampled perfusion and contrast-enhanced angiography data improved accuracy of the representation of contrast kinetics and increased the temporal separation of arterial and venous contrast kinetics. The I-HYPR reconstruction may have important diagnostic applications in settings requiring high temporal resolution and quantitative signal dynamics. Because I-HYPR allows relaxation of the sparsity requirements for the composite frame, the iterative reconstruction can enable novel acquisition strategies that independently optimize the quality of the composite and temporal resolution of the dynamic frames. Magn Reson Med 59:132–139, 2008. © 2007 Wiley-Liss, Inc.

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In time-resolved imaging, the classic tradeoff between temporal and spatial resolution motivates the investigation of faster acquisition methods. One such method that has recently gained popularity is undersampled projection imaging. Angular undersampling decreases acquisition time in projection imaging while maintaining image resolution by varying the sample density in k-space (1). However, in standard projection reconstruction methods, large undersampling factors lead to streak artifacts that may render the reconstructed images unsuitable for quantitative analysis.

One recently-developed reconstruction method for undersampled time-resolved images is the highly-constrained back-projection (HYPR) reconstruction (2). In the HYPR method, a priori information from an image, known as the composite, is used to constrain the reconstruction to locations with signal. The composite is typically reconstructed from sufficiently-sampled time-averaged data using conventional filtered back-projection (FBP) or regridding. In conventional noniterative HYPR, unfiltered back-projection of highly-undersampled projection data is used to apply the temporal signal changes to the composite image. In the absence of motion and for sufficiently sparse data sets, this approach has been shown to mitigate the problem of streak artifacts while depicting temporal dynamics with good fidelity. For example, HYPR has been shown to perform well in time-resolved angiography in which the data generally meet these conditions (2). However, it has been shown that HYPR reconstruction results in inaccurate representation of signal changes in more spatially- and temporally-complex data (3). These errors would be particularly problematic in perfusion and diffusion data in which highly-accurate reconstructions of each time-point are essential for accurate measurement of quantitative functional maps. In addition, angiographic applications that demand high temporal resolution in circumstances in which blood vessels nearly overlap, such as arteriovenous malformations (AVM), may also be challenging.

To address the sparsity limitation of the standard HYPR implementation, the present work introduces a unique iterative HYPR (I-HYPR) algorithm that is conceptually related to the non-I-HYPR algorithm in that it repeatedly uses the result of the HYPR reconstruction as the composite image for the next iteration. An I-HYPR algorithm using the method of conjugate gradient minimization has recently been presented by Griswold et al. (4). However, the algorithm presented in this work is mathematically similar to ordered subset expectation maximization (OSEM) (5,6) in which the seed image is the HYPR composite image itself and requires similar assumptions of nonnegativity and compact support for convergence. The principal advantage of the I-HYPR algorithm compared to the conjugate gradient method includes robust monotonic convergence for a wide range of data sparsity and signal-to-noise conditions under the assumption of an inherent positivity constraint. Therefore, the I-HYPR method does not require an empirical convergence or regularization parameter to control the rate of convergence to enforce stability for different applications.

Because of its robustness to noise and favorable convergence properties, OSEM has been applied to emission tomography, where FBP performs poorly (7,8). OSEM has been applied with good results to undersampled projection MR angiography as a method to reduce streak artifacts (9). However, the approach taken here starts with a streak-free estimate of the time-point (i.e., HYPR reconstructed image), and the iterative algorithm, I-HYPR, is used to more accurately represent the temporal kinetics at the desired time-point, rather than simply to remove undersampling artifacts.
The purpose of this work is to demonstrate the feasibility of a novel I-HYPR algorithm to improve the accuracy of time-resolved images using computer simulations and specific applications in nonsparsel data sets, including cerebral perfusion MRI and contrast-enhanced MR angiography of the foot. It is hypothesized that the iterative algorithm will converge to a temporally-accurate depiction of the desired dynamic time-point while preserving spatial resolution.

THEORY
In time-resolved projection imaging, the experiment is as follows: at \( t \) time-points, a series of sinograms, \( s_t \), are acquired of an object by measuring projections at sets of angles \( \phi_t \) (note that each \( \phi_t \) represents a set of angles covering 180°, which, in general, do not satisfy the Nyquist criterion and change with \( t \)). The objective is to reconstruct a set of images, \( I_t \), that closely approximate the ideal images, \( I_t^* \) related to \( s_t \) by the Radon transform,

\[
s_t = R_{\phi_t}(I_t),
\]

where \( R_{\phi_t} \) denotes the Radon transform over the sets of angles \( \phi_t \). Equation [1] can be inverted using FBP. However, it is well known that artifacts result when the set of projection angles does not meet the Nyquist criterion. One approach used to reduce these undersampling artifacts is the HYPR reconstruction.

HYPR
In the HYPR reconstruction some or all of the measured time-point sinograms, \( s_t \), are combined to create a series of composite sinograms, \( c_t \). In general the composite sinograms are required to be sufficiently sampled to allow reconstruction by conventional methods such as FBP. The composite images for each time frame, \( t \), are defined as,

\[
c_t = FBP[c_t],
\]

where FBP is the filtered back-projection operator and the composite may be centered about the desired time frame. Following this formalism the HYPR reconstruction is shown in Eq. [3], in which the reconstruction of a single time-point is depicted and the subscript \( t \) is dropped for clarity:

\[
J = C \cdot R_{\phi}^{-1}\left(\frac{s}{R_{\phi}(C)}\right)
\]

where \( R_{\phi} \) and \( R_{\phi}^{-1} \) are the Radon and inverse Radon transforms, respectively. The inverse Radon transform here is performed without a filter and is equivalent to unfiltered back-projection. Also, note that the Radon transform is performed using the set of angles at which the projections were actually measured in \( s \).

While HYPR reconstruction works well for spatially- or temporally-sparse datasets, the reconstruction can result in errors for structures that have different time dynamics because of overlap in the projection data.

I-HYPR
The iterative approach is motivated by the observation that data acquired at certain specific projection angles may distinguish signal changes for overlapping objects better than data acquired at other angles. Note that two or more structures will overlap for only some of the projection angles. The projection angles in which they do not overlap can then be used to estimate the correct time dynamics for each structure. By repeating the HYPR reconstruction iteratively such that the result of the previous iteration serves as the composite image for the next iteration, the errors caused by structural overlap can be progressively reduced.

Therefore, the iterative algorithm presented here repeats the HYPR reconstruction over \( N \) iterations. This iterative procedure is mathematically equivalent to expectation maximization (EM) using undersampled data as has been applied more commonly to single-photon emission computed tomography (SPECT) and positron emission tomography (PET) data (8). However, this work is to be distinguished from conventional applications of EM by its use of the time-averaged composite image. An iteration loop is inserted around Eq. [3] as follows,

\[
\begin{align*}
C_{n+1} &= C_n \cdot R_{\phi}^{-1}\left(\frac{s}{R_{\phi}(C_n)}\right) \\
J &= C_{nM}
\end{align*}
\]

where Eq. [4b] simply assigns the final composite image to be the estimate of the time-point image, \( J \). The present implementation terminates the loop after an empirically predetermined number of iterations. Alternative stopping criteria are explored in the discussion section.

Motivated by the similarity between the I-HYPR reconstruction and the expectation maximization reconstruction (8), a further modification is made by adding an inner loop over subsets of the measured projections, \( s \), as in OSEM (5,6). The inclusion of an additional loop over subsets of the projection angles has been shown to speed convergence in OSEM (6). Including a loop over \( M \) subsets of the measured projections to the algorithm given in Eq. [4] gives,

\[
\begin{align*}
C_{n+1} &= C_{n,m} \cdot R_{\phi}^{-1}\left(\frac{s_m}{R_{\phi}(C_{n,m})}\right) \\
J &= C_{NM}
\end{align*}
\]

where the Radon operators, \( R_{\phi} \) and \( R_{\phi}^{-1} \), operate only on the subset \( m \) of the measured angles. This allows the estimate
of the time-point to be updated more often than in the algorithm as represented by Eq. [4a,b], resulting in more rapid convergence. Note that because of Eq. [5a], if a pixel in the composite is zero at any point in the algorithm, it will remain zero and may result in divide-by-zero errors. Therefore, in the practical implementation of the algorithm, if a zero appears in the denominator of Eq. [5a], that pixel is set to zero, avoiding errors due to division by zero. This most commonly occurs in the image background, i.e., outside of the region of support of the image where there is no significant signal.

MATERIALS AND METHODS

To evaluate the feasibility and convergence of I-HYPR for nonsparse data sets, the reconstruction was applied to computer simulations with known temporal signal variations. After establishing feasibility in computer simulations, the performance of I-HYPR was compared to non-I-HYPR in specific applications. I-HYPR was tested in contrast-enhanced angiography of the head, an application in which the data are sparse and HYPR is expected to perform well. The I-HYPR reconstruction was also applied to a cerebral perfusion simulation without mask subtraction, an application in which HYPR would likely be challenged because the data are not sparse by definition. The cerebral perfusion simulation was specifically constructed to test the I-HYPR algorithm in a spatially nonsparse data set known to demonstrate complex temporal dynamics.

Computer Simulation 1

For illustrative purposes, a simple example was constructed using a $256 \times 256$ composite image of two $16 \times 16$ pixel square objects and a single time-point image in which only one of the objects exhibits signal (Fig. 1a). I-HYPR was performed on three equally-spaced projections of the time-point, one vertical and two diagonal. Zero mean Gaussian noise was added in quadrature to the sinogram data. Four trials were conducted in which the added noise varied with standard deviations (SDs) of 0%, 1%, 5%, and 10% of the maximum signal in the sinogram data. For all the trials the mean signal value measured in an region of interest (ROI) placed in the upper object was calculated and plotted for the first seven iterations.

Computer Simulation 2

A second, more realistic example was constructed consisting of a $256 \times 256$ pixel composite image containing three point-like circular objects (Fig. 2a), each with a radius of eight pixels, one positioned in the upper region, distant from two nearly-overlapping objects in the lower region. Each of the three objects had a signal intensity that varied over 32 time-points according to three unique gamma-variate functions (Fig. 2b). The undersampled time-point sinograms were generated from each ideal (i.e., fully-sampled) time-point image by applying the Radon transform at 16 unique angles interleaved within a total of 256 projections. The composite images were reconstructed using FBP and a centered sliding window that was six time-points wide—equivalent to $6 \times 16 = 96$ unique projection angles per image. Reconstruction of each individual time-point was performed with HYPR and I-HYPR. For this simulation, the I-HYPR reconstruction used four subsets and one iteration. These values were selected empirically based on convergence rates observed in computer simulation 1. For comparison the data were also simulated at 400 projections per time frame (i.e., fully-sampled) and reconstructed using FBP. Zero mean Gaussian noise was added in quadrature to the sinogram data. Three trials were conducted in which the added noise varied with SDs of 0%, 5%, and 10% of the maximum signal in the sinogram data. Time curves were calculated from both the HYPR and the I-HYPR reconstructed data and compared to the curves from the fully-sampled FBP reconstruction.

Contrast-Enhanced Angiography of the Head

In vivo results were obtained in a healthy human subject (male, age = 32 years) who underwent MRI using a highly-undersampled three-dimensional (3D) “stack-of-stars” acquisition using a GE 1.5T scanner (Signa HPx, GE Healthcare,
Milwaukee, WI, USA). Imaging was done with a spoiled gradient-recalled echo sequence (SPGR) sequence with TR/TE = 8.8 ms/1.4 ms, field of view (FOV) = 22 cm, BW = ±62.5 kHz, flip angle = 30°, and 28 slices at 2.6 mm per slice and interpolated using zero-filling up to 56 slices overlapped by 1.3 mm. A readout of 256 points was used with 256 projection angles and 32 interleaves for a reconstructed matrix size of 256 x 256. At eight projection angles per time-point and a 256 image matrix, the undersampling factor relative to a fully-sampled Cartesian acquisition was 32. HYPR and I-HYPR reconstructions were performed without using mask subtraction and a moving composite window 8-s wide. In the I-HYPR reconstruction, eight subsets and two iterations were used, based on the relatively high SNR in these data.

In each case, MTT maps were calculated using block circulant singular value decomposition (10) with an arterial input function obtained from the original fully-sampled data. The fully-sampled arterial input function was chosen to focus the simulation on the effects of the low data sparsity in the perfused tissues. For each of the HYPR, I-HYPR, and fully-sampled data sets, the mean and SD of the MTT were calculated and compared for ROIs in gray and white matter in normal and affected regions.

RESULTS

Computer Simulation 1

The composite and ideal time-point images are given in Fig. 1a. Enlarged and cropped versions of the I-HYPR reconstructed time-point images for the first five iterations of the 0% noise trial are shown in Fig. 1b. Note that the window and level differs from that in Fig. 1a to allow better visualization of the residual error. After a single iteration (i.e., standard HYPR reconstruction), a substantial amount of residual signal error remains in the reconstructed time-point (Fig. 1b); however, after each iteration the mean value in the upper object becomes progressively closer to the ideal value of zero. Since no subsets were used in this case, the first iteration represents the result obtained with standard noniterative HYPR. Plots of the mean signal value in the upper object vs. iteration number for the first seven iterations are shown (Fig. 1c) for each of the four trials with varying noise levels. In each trial the value converges after about four or five iterations. Note that while the ideal signal value for the object is zero, the reconstructed values converge to a higher value that increases with the level of added noise, which is consistent with expectations using EM-based methods.

Computer Simulation 2

The signal variations measured using the HYPR (dotted black lines) and I-HYPR (solid black lines) reconstructions are...
shown in Fig. 3 compared with the fully-sampled FBP time curves (gray lines). Results are shown for each of the three point-like objects used in the phantom described in Fig. 2 and for the three levels of added noise. In each case the curve from I-HYPR-reconstructed images is a better estimate of the actual curve compared to HYPR. I-HYPR especially shows improved agreement at the peak of the curves. Interference of object 2 with object 3 in the HYPR reconstruction can also be seen as a slight depression in the HYPR curve for object 2 at the arrival time of object 3 (Fig. 3). While the I-HYPR curve is very close to the FBP curve in each case, an increasing degradation in the peak of the curve can be seen as the noise increases. Images from the three noise levels at a single time-point are compared using cropped images depicting only objects 2 and 3 in time-point 15 for FBP, HYPR, and I-HYPR reconstructions at each noise level (Fig. 4). This depicts the early enhancement of object 3 in the HYPR image (Fig. 4, second row), which is not present in either the FBP or I-HYPR images, as well as the empirical effects of increased noise level.

**Contrast-Enhanced Angiography of the Head**

A maximum intensity projection (MIP) is shown in Fig. 5a from the time-point 30 s into the scan reconstructed with I-HYPR with the carotid artery (arrow labeled, “ca.”), the vertebral artery (arrow labeled, “v.”), and the jugular vein (arrow labeled, “j.”). Time curves for ROIs placed in the carotid are given in Fig. 5b for both the HYPR (gray line) and the I-HYPR (black line) reconstructed time series. The I-HYPR curve exhibits a more well-defined peak than the HYPR curve, suggesting better depiction of the passage of the contrast bolus. This is consistent with the results of computer simulation 2 (Fig. 3). The peak SNR obtained in the carotid with HYPR and I-HYPR was 75 and 100, respectively, reflecting both the increase in signal intensity and the substantial reduction in background noise using the I-HYPR reconstruction. Time curves for ROIs placed in the vertebral artery and the jugular vein are given in Fig. 5c. The HYPR curve for the vertebral artery (solid gray line) is biased toward the HYPR curve for the jugular vein (dashed gray curve) indicating interference caused by the vessels’ close proximity. This is consistent with previously observed work (3) and the results for object 2 in Fig. 3. The influence of the jugular vein (dashed black line) on the vertebral artery (solid black vs. solid gray lines) for the I-HYPR curve is substantially less than in the HYPR case, as evidenced by the vessels’ greater separation and the steeper rise time of the vertebral artery enhancement.

This is reflected in improved arterial-venous separation in specific images from time-points 20 s and 24 s into the scan (Fig. 6). The HYPR image from 20 s into the scan (Fig. 6a) exhibits early enhancement in the sagittal sinus (white arrow), which is not present in the I-HYPR image (Fig. 6b). Importantly, in the HYPR image from 24 s into the scan (Fig. 6c) the jugular vein (white arrow) enhances early in comparison to the I-HYPR image from the same time-point.
The higher level of background suppression of the I-HYPR images as compared to the HYPR images is also visible, particularly in the images at 24 s into the scan. Note that the images have been scaled so that in each time point the HYPR and I-HYPR images have the same dynamic range.

Cerebral Perfusion Simulation

Three examples of I-HYPR reconstructed images in simulated data from a stroke patient are shown in Fig. 7a–f. In Fig. 7g, time courses obtained from fully-sampled “true” images are compared to those obtained from HYPR and I-HYPR reconstructed images for ROIs placed in the gray matter of the normal right hemisphere and the affected left hemisphere. In both normal and affected tissue, the HYPR curves (dotted black lines) underestimate the peak while the I-HYPR curves (solid black lines) show good agreement with the true curves (gray lines). The effect of the differences in the HYPR curves from the true curve manifest themselves as significant overestimation of the MTT as can be seen in both the comparison of the MTT maps (Fig. 8) and specific ROIs (Table 1). It can be seen in Table 1 that the MTT values obtained from the I-HYPR reconstruction are within the standard error (SEM) of the true value for all four ROIs.

DISCUSSION

This work extends the significant improvements in temporal and spatial resolution afforded by the HYPR reconstruction of projection acquisition data to situations where data are nonsparse in space and time. Many applications in perfusion MRI, diffusion MRI, and contrast-enhanced MR angiography demand either high temporal or spatial resolution or both. While the a priori information in the composite image allows HYPR to significantly improve the spatial and temporal resolution in these studies, regional variations in the contrast kinetics of the structures in the composite images can lead to errors in the measured signal values. The I-HYPR reconstruction is more robust than HYPR to nonsparse data because it allows projections from multiple view angles to modify or update the a priori information in the composite image and thus improve the accuracy of the kinetic information at a given time-point. In computer simulations using models of reduced sparsity, I-HYPR consistently provided a more accurate quantitative
depiction of contrast kinetics and was robust to degraded SNR. Moreover, the overall image quality is robust to noise as demonstrated in similar simulations, with SNR levels as low as 10.

In addition, it was shown in simulated cerebral perfusion data that robust convergence is achieved even when the signal changes in the composite images differ markedly from the signal changes in the time-point images or mask subtraction is not used to increase the sparsity of the data. Quantitative measures of cerebral perfusion and MTT derived from contrast curves were also shown to be more accurate using the I-HYPR reconstruction relative to HYPR alone.

By allowing the relaxation of the sparsity requirements of the composite image in the HYPR reconstruction, the I-HYPR reconstruction can potentially extend the capability of MRI to measure dynamic processes with very rapid kinetics or to achieve more rapid quantitative diffusion measurements. Potential applications include depiction of contrast kinetics in applications with very short artery–vein separation such as AVMs, functional MRI of the BOLD activation response in the brain, and diffusion tensor imaging (11).

The iterative portion of the I-HYPR reconstruction is related to OSEM techniques and thus is similar in sensitivity to data with low SNR (6). This imposes a practical limit on the number of achievable iterations before the reconstruction begins to converge to the noise in the data. This limitation is mitigated relative to conventional OSEM by the use of a composite image with a high SNR, but the

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<td><strong>MTT Comparison</strong></td>
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<tr>
<td>White matter (s)</td>
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<td>Normal</td>
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<tr>
<td>True</td>
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<td>HYPR</td>
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*Comparison of MTTs (in seconds) obtained with HYPR and I-HYPR to those obtained from ideal data for both normal and affected regions in gray and white matter.
SNR of the individual projection will still limit the achievable number of useful iterations. The empirical SNR threshold for robust image quality and contrast kinetics with I-HYPR based on simulations was found to be approximately 10. However, more work needs to be done to evaluate the dependence of the number of achievable iterations as a function of SNR and for a given MRI application. Unlike nuclear imaging implementations of OSEM, the MR signal in the current implementation of I-HYPR was assumed to have equal probability of detection throughout the FOV. In future implementations, the spatial sensitivity profiles of the MR coil could be used to weight the signal intensities to further improve accuracy and robustness to noise.

The number of subsets and iterations used in the present implementation of the I-HYPR algorithm is determined empirically. It is known from previous work on OSEM that higher numbers of subsets lead to faster convergence, while increasing the number of subsets can produce artifacts in the reconstruction when SNR is low (6). In the case of the angiography exam, the SNR of the individual images was very low so only one subset was used. In the cerebral perfusion study, the SNR was substantially better so more subsets were used. Iteration in all cases was continued until the image quality ceased to improve. It should be noted that the use of subsets effectively increases the number of iterations without significantly increasing computation time by updating the composite image more frequently. So, in the case of computer simulation 2, in which four subsets and one iteration were used, the composite was updated four times. An obvious improvement over this would be an automated stopping criterion in which the differences between the projections of the reconstructed image and the measured data are forced below a predetermined threshold.

Because the I-HYPR reconstruction allows the relaxation of the sparsity constraints on the composite image, the I-HYPR reconstruction may allow the data for the composite image and dynamic frames to be independently optimized. For example, it may no longer be required to use a “moving composite” reconstruction (2), in which the composite is chosen from a finite time aperture centered about the time-frame of interest. It may be preferable to acquire a high-SNR composite image separately before or after the dynamic process. The dynamic phases of the process could then be further undersampled to improve temporal resolution without the requirement of sufficient sampling to construct a local composite.

The results of the cerebral perfusion simulation presented here demonstrate that small errors in the representation of the signal changes can manifest themselves as significant errors in quantitative functional maps. Furthermore, the results of the contrast-enhanced angiography experiment indicate that I-HYPR reconstruction can improve the accuracy of signal representation compared to standard HYPR. While these improvements may not be needed in standard angiographic applications, quantitative applications such as perfusion and diffusion imaging require accurate signal representation and are areas of future work.

The present implementation of the algorithm in Matlab on a 2.8 GHz desktop computer has a reconstruction time of about 1.5 h per iteration for 32 time-points of a 256³ volume with 16 angles per time-point, which is prohibitively long for practical application. The most time-consuming steps are the Radon and inverse Radon steps. However, a particular strength of the I-HYPR approach is that existing hardware implementations of the Radon transforms could significantly accelerate reconstruction time in clinical applications.

In summary, a new I-HYPR algorithm has been presented and validated in computer simulations and in several MRI applications. Feasibility for quantitative perfusion measurement in a non-sparse data set was also shown using a simulation derived from cerebral perfusion data in a human stroke patient. In all cases, I-HYPR improved the accuracy compared to the known contrast kinetics of the reconstruction over the original HYPR reconstruction. However, the number of supported iterations and subsets for I-HYPR appears to depend highly on the SNR of the projections. Good results were also obtained in an undersampled acquisition of contrast-enhanced angiography of the peripheral vessels in the foot, although more study is needed to better characterize robustness of the technique to noise, motion, and off-resonance conditions. Future work will be directed at further validating the technique and optimizing the selection of iteration and subset number based on a priori information in the projection data.

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