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Rapid Dual-RF, Dual-Echo, Three-Dimensional Ultrashort Echo Time Craniofacial Imaging: A Feasibility Study

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Abstract

Purpose: To develop a dual-RF, dual-echo, three-dimensional ultrashort echo-time (UTE) pulse sequence and bone-selective image reconstruction for rapid high-resolution craniofacial MRI.

Methods: The proposed pulse sequence builds on recently introduced dual-RF UTE imaging [Johnson et al, MRM, 2017]. While yielding enhanced bone specificity by exploiting high sensitivity of short T_2 signals to variable RF pulse widths, the parent technique exacts a two-fold scan time penalty relative to standard dual-echo UTE. In the proposed method, the parent sequence's dual-RF scheme was incorporated into dual-echo acquisitions while radial view angles are varied every pulse-to-pulse repetition period. The resulting four echoes (two for each RF) were combined via view-sharing to construct two sets of k-space datasets, corresponding to short and long TEs, respectively, leading to a two-fold increase in imaging efficiency. Further, by exploiting the sparsity of bone signals in echo-difference images, acceleration was achieved by solving a bone-sparsity constrained image reconstruction problem. In vivo studies were performed to evaluate the effectiveness of the proposed acceleration approaches in comparison to the parent method.

Results: The proposed technique achieves 1.1 millimeter isotropic skull imaging in 3 min without visual loss of image quality, compared to the parent technique (scan time = 12 min). Bone-specific images and corresponding 3D renderings of the skull were found to depict the expected craniofacial anatomy over the entire head.

Conclusion: The proposed method is able to achieve high-resolution volumetric craniofacial images in a clinically practical imaging time, and thus may prove useful as a potential alternative to computed tomography.

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Keywords

Bone-specific imaging; magnetic resonance imaging (MRI); solid-state MRI; short T_2 ; ultrashort echo time (UTE)

1. INTRODUCTION

Recent developments in solid-state MRI via ultrashort echo-time (UTE) (1, 2) or zero TE (3, 4) methods have enabled detection and quantification of very short T_2 (ranging from tens of microseconds to a few milliseconds) species of the human body such as cortical bone water (5–7), myelin in white matter (8), lung tissue (1, 9), and phosphorus in bone mineral (10, 11). In particular, MR-based bone imaging, as a potential, noninvasive alternative to computed tomography (CT), has gained growing interest in many applications requiring information of bone structure and composition, e.g., the attenuation correction of positron emission tomography (PET) signals in MR/PET imaging (12) and MR-guided focused ultrasound (13).

In both UTE and ZTE imaging methods, signal reception begins immediately after transmit-receive switching (requiring a dead-time of tens of microseconds in modern clinical scanners). Typically, a center-out trajectory is employed for k-space sampling, thereby allowing capture of signals from sub-millisecond T_2 constituents, such as those from protons in water bound to the bone's organic matrix. Nevertheless, long T_2 components (i.e., water in soft tissue or residing in the bone pore spaces), unless suppressed, also exhibit high signal intensities, which would obscure short T_2 contrast. To enhance short- T_2 conspicuity in reconstructed images, various approaches have previously been explored, generally falling into two categories: inversion recovery (IR)-based long T_2 signal attenuation (6, 14–16), and acquisition of two or more images at different TEs, with subsequent post-processing to filter out long T_2 components (12, 17–20). While the former, typically using adiabatic IR pulses, has been shown to be very effective for long T_2 suppression (21), it may result in impractically long imaging times, which may limit its clinical utility. On the other hand, there is some evidence to suggest the dual-echo subtraction method to yield higher SNR efficiency in short- T_2 imaging than IR-prepared UTE (21, 22).

It is well known that once the RF pulse duration approaches T_2 , there is increasing damping of the resulting transverse magnetization (23). Recently, a method that exploits the sensitivity of bone proton magnetization to both, T_2 and RF pulse duration, has been reported (24). In that method, two hard RF pulses differing in duration and amplitude are applied alternately, and two sets of data are acquired, one from short RF at short TE and one from long RF at long TE. Compared to standard dual-echo based UTE, the technique enhances discrimination of bone signals between the two datasets, thus yielding a higher level of bone specificity in echo difference images. However, the two RF interleaves, obtained with identical k-space coverage, result in an inevitable two-fold increase in scan time.

In this work, we propose a rapid bone MR imaging method by developing a three-dimensional (3D) DUAL-RAdiofrequency aNd Dual-Echo (DURANDE) UTE pulse sequence

along with bone-selective image reconstruction. Similar to the parent method, dual echoes are acquired following short and long RF pulses. However, in distinction to the method described in (24), encoding gradients are varied continuously along the entire pulse train, leading to a reduction of imaging time by a factor of two. During image reconstruction, two independent k-space datasets are generated by combining the four echoes via a view-sharing (VS) approach. Further, the sparsity of bone voxels in the corresponding difference images was exploited, thereby enabling substantially accelerated UTE bone imaging. In vivo studies were performed at 3 T to evaluate the feasibility of the proposed technique in achieving isotropic high-resolution volumetric craniofacial images within 3 min.

2. METHODS

2.1. Dual-RF, Dual-Echo UTE with View-Sharing (VS-DURANDE UTE)

Figure 1a shows a diagram of 3D VS-DURANDE UTE. Two hard RF pulses (RF_1 , RF_2) differing in duration and amplitude for the same nominal flip angle are applied alternately in successive TR periods along the entire pulse train, while within each TR two echoes are collected at short TE (TE_1) and long TE (TE_2), from the beginning of gradient ramp-up. Thus, four echoes are acquired: $ECHO_{11}$, $ECHO_{12}$, $ECHO_{21}$, and $ECHO_{22}$. Here, the subscripts represent the corresponding RF and TE indices (Fig. 1a).

Bone proton magnetization, due to its very short T_2 relaxation time, exhibits a substantial level of signal decay during the relatively long duration of RF_2 , while soft-tissue and pore water magnetizations remain nearly intact during nutation. Figure 2 provides numerical simulations for T_2 relaxation times (0.01 – 100 ms) versus transverse magnetization with varying RF durations (0.04, 0.25, 0.5, and 1 ms; flip angle fixed at 12°) under different off-resonance conditions (0 – ± 300 Hz). With varying RF pulse durations, transverse magnetization of bone proton (T_2 : 0.1 – 0.5 ms) is gradually saturated while that of soft-tissue (T_2 : 50 – 100 ms) is nearly unaltered (Fig. 2a). However, in the presence of magnetic field inhomogeneities, longer RF_2 pulses result in undesirably elevated soft-tissue signals in the difference (Fig. 2b), which potentially leads to ambiguities in bone identification. Given the simulation results, a RF_2 duration of ~ 0.5 ms was chosen in this work.

It has also been demonstrated in (24) that the dual-RF based technique with subtraction of $ECHO_{22}$ from $ECHO_{11}$, as opposed to merely subtracting $ECHO_{12}$ from $ECHO_{11}$, further enhances bone contrast. However, in the parent method all four echoes undergo identical spatial encoding over every two TR cycles, resulting in doubling of total imaging time compared to conventional single-RF, dual-echo UTE imaging. Furthermore, since $ECHO_{12}$ and $ECHO_{21}$ are not utilized in the subtraction process, acquisition of those two signals may be redundant.

To improve imaging efficiency in the method of (24), in the present work a VS scheme is integrated into the DURANDE UTE scheme. To this end, radial view angles are varied every TR period (Fig. 1a) to make $ECHO_{11,12}$ and $ECHO_{21,22}$ traverse distinct k-space portions. Bone proton signal intensities in each echo follow the order: $ECHO_{11} > ECHO_{21} >> ECHO_{12} > ECHO_{22}$. Thus, the first two and last two echoes are combined, respectively, to construct two independent k-space sets (k_1 , k_2). Specifically, central regions of k_1 and k_2 in

which intrinsic oversampling is performed, are composed only of ECHO₁₁ and ECHO₂₂ (Fig. 1b) to retain the highest and lowest bone signals, respectively, thereby maximizing bone signal specificity upon subtraction.

2.2. Bone-Selective Image Reconstruction

Since soft-tissue signals remain at a similar level over the four echoes while bone signals appear only at short TE echoes, subtraction of images pertaining to k_1 and k_2 highlights bone voxels. Given the sparse bone signals in the difference image, VS-DURANDE UTE scanning is further accelerated with fewer radial views by exploiting such sparsity during image reconstruction (25–27). The following sparse signal recovery problem can then be formulated:

$$\min_{I_1, I_2} \frac{1}{2} \sum_{j=1}^{N_c} \left\{ \|k_{1,j} - F_{NU}(\mathbf{S}_j I_1)\|_2^2 + \|k_{2,j} - F_{NU}(\mathbf{S}_j I_2)\|_2^2 \right\} + \lambda \|I_1 - I_2 e^{-i\varphi}\|_1 \quad [1]$$

where I_1 and I_2 are complex signals ($\in \mathbb{C}^{N \times 1}$; $N = N_x N_y N_z$) to be solved for images (size: $N_x \times N_y \times N_z$) at TE₁ and TE₂, $\mathbf{S}_j$ is the receiver sensitivity matrix for the j -th coil ($\in \mathbb{C}^{N \times N}$), N_c is the number of receive coil elements, $\mathcal{F}_{NU}(\cdot): \mathbb{C}^{N \times 1} \rightarrow \mathbb{C}^{N_r N_p \times 1}$ is the non-uniform fast Fourier transform (NUFFT) operator that performs FFT on its argument and subsequent mapping onto prescribed radial coordinates with the size, N_r (number of readout points in each radial view) $\times$ N_p (number of projection lines), λ is the regularization parameter that balances data consistency with residual sparsity, φ is the phase accrual during TE ($=\text{TE}_2 - \text{TE}_1$), and $\|\cdot\|_1$ and $\|\cdot\|_2$ are l_1 - and l_2 -norms. It is noted that as I_1 and I_2 are complex, phase correction with φ in the last term of Eq. [1] is essential, which otherwise potentially disrupts residual sparsity. Both $\mathbf{S}$ and φ are spatially smooth and thus can be estimated using over-sampled central low spatial frequency data. The solutions (I_1 , I_2) can be found by employing an alternating minimization approach (28) that splits Eq. [1] into the following two sub-problems with respect to I_1 and I_2 :

$$\begin{cases} \min_{I_1} \frac{1}{2} \sum_{j=1}^{N_c} \|k_{1,j} - \mathcal{F}_{NU}(\mathbf{S}_j I_1)\|_2^2 + \lambda \|I_1 - I_2 e^{-i\varphi}\|_1 \\ \min_{I_2} \frac{1}{2} \sum_{j=1}^{N_c} \|k_{2,j} - \mathcal{F}_{NU}(\mathbf{S}_j I_2)\|_2^2 + \lambda \|I_2 - I_1 e^{i\varphi}\|_1 \end{cases} \quad \text{Eq.[2a] Eq.[2b]}$$

Each sub-problem is then solved by alternately applying the two operations: 1) sensitivity-encoding based projection to enforce data consistency (29, 30) and 2) soft-thresholding to control the sparsity of image difference (31). The two solutions are iteratively updated until convergence is reached. Implementation details of the above procedures are provided in the Appendix.

Given the two solutions, I_1 and I_2 , a bone-specific image (I_{Bone}) is finally generated as in (24):

$$I_{\text{Bone}} = \frac{|I_1| - |I_2|}{|I_1| + |I_2|} \quad [3]$$

The normalization in Eq. [3] removes proton-density weighting in the difference image while correcting for spatial variations of signal intensities due to transmit/receive field inhomogeneities.

2.3. Human Subject Studies

All human subject studies performed in this work were approved by the local Institutional Review Board. Informed written consent was obtained from all study participants ($n = 5$; 3 females, 2 males; ages = 32 ± 8 years) prior to imaging.

The VS-DURANDE UTE pulse sequence was implemented in the SequenceTree pulse programming environment (32). Unless otherwise stated, the following parameters were used: TR = 7 ms, TE₁/TE₂ = 0.06/2.36 ms, RF₁/RF₂ durations = 0.04/0.52 ms, flip angle = 12°, readout bandwidth = ± 125 kHz, gradient ramp-up duration = 0.24 ms, N_r = 158, matrix size = $256 \times 256 \times 256$, and field-of-view = $280 \times 280 \times 280$ mm³. Additionally, a calibration scan was performed using the method in (33) to measure the gradient timing delay to correct for k-space trajectory mismatches.

To evaluate the effectiveness of the proposed VS approach and sparsity-constrained image reconstruction, a set of data was acquired in one subject at 3 T (TIM Trio; Siemens Medical Solutions, Erlangen, Germany) using the parent method (24) serving as reference. Here, 50,000 radial views were collected for each echo, resulting in 12 minutes of imaging time. A 12-channel head coil was used for signal reception. The acquired data was retrospectively undersampled by a factor of two by removing every other half projection lines, and subsequently processed with and without the VS scheme (Fig. 1b). Corresponding images were reconstructed directly by applying inverse NUFFT (iNUFFT) to each dataset. Furthermore, the reference data was decimated by a factor of four by retaining every fourth radial views only. Subsequently, images were reconstructed in three different ways for comparison: iNUFFT on k_1 and k_2 , constructed with and without VS, respectively, and solving Eq. [1] for the view-shared data. In both cases (with and without VS), the k-space data contain 12,500 views each of ECHO₁₁ (k_1) and ECHO₂₂ (k_2), while in the former 12,500 views of ECHO₂₁ (k_1) and ECHO₁₂ (k_2) each were additionally utilized to fill peripheral k-space regions.

To investigate feasibility of the VS-DURANDE UTE with bone-selective image reconstruction method, four healthy subjects were scanned at 3 T (Prisma; Siemens Medical Solutions, Erlangen, Germany) for 3 minutes (N_p = 12,500 for each echo) using a 20-channel head/neck receiver coil. All I_{Bone} images obtained via Eqs. [1–3] were displayed in sagittal, coronal, and axial orientations using multi-planar reformatting. Furthermore, 3D renderings of the skull were produced in two study subjects, derived from the three image

sets (I_1 , I_2 , and I_{Bone}). To this end, segmentation of bone voxels was performed using the ITK-SNAP software package (34, 35) in a semi-automatic fashion as follows: 1) manual labeling of representative voxels belonging to background, soft-tissue, and cortical bone, respectively (approximately 500 – 1000 voxels for each group), 2) training each group based on signal intensities of those voxels and their neighborhood, 3) generation of a classification-based probability map for cortical bone, and 4) automatic identification of bone voxels using an active contour segmentation pipeline.

3. RESULTS

Figures 3a-c compare three sets of images ($|I_1|$, $|I_2|$, and I_{Bone}) in one study subject obtained by the parent technique for reference (Fig. 3a; $N_p = 50,000$ each for ECHO₁₁ and ECHO₂₂, respectively, imaging time = 12 min), and its accelerated version with an undersampling factor of two without (Fig. 3b; $N_p = 25,000$ each for ECHO₁₁ and ECHO₂₂, 6 min scan time) and with (Fig. 3c; $N_p = 25,000$ each for all four echoes, 6 min scan time) the view-shared k-space ordering. A line profile of I_{Bone} in each method is plotted in Fig. 3d. Supporting Information Figure S1 shows I_{Bone} images of the whole-head in sagittal, coronal, and axial planes. When compared with the reference, the proposed VS scheme yields visually similar quality of images by effectively suppressing noise amplifications resulting from data undersampling.

Figure 4 shows three sets of images ($|I_1|$, $|I_2|$, and I_{Bone}) reconstructed from 12,500 radial half projections (simulating 3 min imaging time) of the reference data above using direct iNUFFT on k-space data constructed without (Fig. 4a) and with (Fig. 4b) the VS scheme, and the sparsity-constrained reconstruction (Fig. 4c), along with I_{Bone} signal intensity profiles for the three methods (Figs. 4d,e) in comparison to the reference (Fig. 3a). Corresponding I_{Bone} images of the whole-head in the three methods are provided in Supporting Figure S2. Amplified noise due to high undersampling in Fig. 3a impairs bone contrast, thus leading to ambiguity in identifying bone voxels (Fig. 4d). The VS method partially remedies the problem (Fig. 4b), while its combination with the sparsity constrained reconstruction yields significantly noise-reduced images (Fig. 4c) with the desired I_{Bone} signal profile retained (i.e., separation of inner and outer tables of cranial bone with diploe; Fig. 4e).

Figure 5 displays I_{Bone} images for the four additional subjects examined using the VS-DURANDE UTE with prospective undersampling ($N_p = 12,500$; imaging time = 3 min). All the bone-specific images in the sagittal, coronal, and axial orientations exhibit clear depiction of anatomic features of the skull over the entire head (e.g., mandible, sphenoid bone, zygomatic bone, and upper cervical spine), thus demonstrating feasibility of the proposed method in craniofacial imaging. Figure 6 displays 3D renderings of the skull in two subjects (Subjects 1 and 2 of Fig. 5), exhibiting the expected anatomic structures such as those mentioned above.

4. DISCUSSION AND CONCLUSIONS

VS-DURANDE UTE in combination with the bone-selective image reconstruction enables isotropic high-resolution (~ 1.1 mm) skull imaging of the whole head in a clinically practical scan time (~ 3 min). While building on the dual-RF based UTE bone imaging method (24) to enhance differentiation of cortical bone from long T_2 species, the proposed technique efficiently utilizes data redundancy both during signal acquisition (via VS) and image reconstruction (by solving the sparse recovery problem). The two acceleration strategies are synergistically combined, leading to four times higher imaging efficiency without visual loss of image quality when compared to the parent technique.

In the proposed method, there exists signal discontinuity around the boundary of the central portion of view-shared k-space. Although not prominent in the reconstructed images shown in this article, image artifacts and noise amplification can potentially result from the VS-related high-pass filter. Nevertheless, the level of such undesirable effects is minimized with the sparsity-constrained reconstruction, which is evident from the smoothly varying soft-tissue signals in the bone-specific image, obtained with the sparse prior (Fig. 4e). On the other hand, in order to completely avoid VS-induced artifacts, full readout samples of $ECHO_{21}$ and $ECHO_{12}$ could be employed to fill even the central portions of k-space. In this case, however, bone contrast in the difference image would be sacrificed because of signal averaging between $ECHO_{11}$ and $ECHO_{21}$, in which signal intensities of bone protons differ substantially (Fig. 2). Given the above considerations, the VS and sparse reconstruction approaches in this work are complementary to each other in reducing residual noise and artifacts while achieving optimal bone contrast.

The enhanced imaging speed should render the proposed technique useful as a potential alternative to CT. One possible clinical application is the evaluation and diagnosis of craniofacial abnormalities, including craniosynostosis, a relatively common disorder involving premature fusion of cranial sutures, in infants and young children (6, 36). In order to be a viable alternative to CT, the new MRI method would still need to be optimized for scan time, spatial resolution, minimizing number of views while preserving bone-specificity, and other image quality metrics. In particular, the receive bandwidth per pixel needs to be carefully chosen so as to exceed the spectral linewidth of the bone proton signal (~ 0.82 kHz at $T_2^* = 390$ μ s (6)), otherwise potentially resulting in loss of actual spatial resolution for bone voxels. Further investigation is also needed for quantitative inter-modality comparison.

Another potential application of the new method is attenuation correction in PET- MRI. It has been demonstrated that classification of bone, adipose tissue, and brain regions on UTE multi-echo images leads to accurate maps of γ -photon attenuation correction in PET imaging (12, 37). The flexibility of DURANDE UTE in adjusting TEs of $ECHO_{12}$ and $ECHO_{21}$ would enable water/fat separation based on the multi-point Dixon method (38). In this case, imaging efficiency should be maintained if the VS scheme were employed to construct an additional set of k-space data, in which low spatial frequency regions are occupied only by those echoes reflecting water/fat phase offset while high spatial frequency areas are filled with all four echo signals.

The normalized image via Eq. [3] provides adequate contrast between soft-tissues and bone voxels, facilitating skull segmentation. Nevertheless, a close look at the signal profiles of I_{Bone} in Figs. 3d and 4e suggests that soft-tissues are not completely suppressed because of T_2^* weighting in I_2 . A weighted subtraction of soft-tissue signals could be envisioned as an alternative with the following steps: 1) estimating a T_2^* map using I_1 and I_2 , 2) applying a T_2^* threshold (e.g. 10 ms) to obtain rough segmentation of soft-tissue voxels, and 3) computing $I_1 - I_2 e^{\frac{\Delta TE}{T_2^*}}$ for the nominator of Eq. [3]. While this T_2^* correction would further enhance the bone contrast in normalized images, it may also result in locally amplified noise in the presence of errors in T_2^* estimation.

Various solid-state MRI methods with short TR and small flip angles have recently demonstrated their potential for skull bone identification by means of ZTE (39, 40) and also UTE (41). In that work, bone segmentation was performed involving the following steps: 1) correction for intensity variations in proton-density weighted images, 2) inverse-log transformation, 3) search for optimal values of thresholding on Gaussian distribution models in a heuristic (39, 40) or analytic (41) manner, and 4) successive application of morphological refinements such as connected component analysis. In this process, ambiguities may arise from overlap of the histogram comprising either bone/air or bone/soft-tissue, resulting in falsely classified bone voxels. The method presented in this study produces self-normalized bone images with virtually complete elimination of soft-tissue signals via Eq. [3], allowing for simplification of post-processing. One limitation of DURANDE UTE, in combining data with different TEs, is that certain subregions are susceptible to errors caused by induced frequency shifts. Areas near air-tissue interfaces are particularly prone to errors, given the 9 ppm difference in magnetic susceptibility between air and tissue water.

In conclusion, the results demonstrate the feasibility of the presented bone-selective MRI technique for whole-skull imaging at isotropic high spatial resolution in a clinically practical scan time. Further work is required to examine the accuracy of the method relative to CT imaging, and comparison to alternative MR approaches.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX

The following describes implementation steps to solve the sparsity-constrained linear inverse problems in Eq. [2] using the iterative soft-thresholding algorithm (31):

- Step 0: Iteration $n = 0$, $I_1^0 = \sum_{j=1}^{N_c} \mathbf{S}_j^H \mathcal{F}_{NU}^{-1}(\mathbf{D}k_{1,j})$ and $I_2^0 = \sum_{j=1}^{N_c} \mathbf{S}_j^H \mathcal{F}_{NU}^{-1}(\mathbf{D}k_{2,j})$
- Step 1: Enforce data consistency between measured k-space data and sensitivity-encoded images at current iteration by updating the solution as:

$$\tilde{I}_1^n = I_1^n + \frac{1}{\alpha_n} \sum_{j=1}^{N_c} \mathbf{S}_j^H \mathcal{F}_{NU}^{-1}(\mathbf{D}(k_{1,j} - \mathcal{F}_{NU}(\mathbf{S}_j I_1^n)))$$

- Step 2: Control the sparsity of the difference image vector $(I_1 - I_2 e^{-i\varphi})$ by solving:

$$\begin{aligned} I_1^{n+1} &= \min_{I_1} \frac{1}{2} \|I_1 - \tilde{I}_1^n\|_2^2 + \frac{\lambda}{\alpha_n} \|I_1 - I_2 e^{-i\varphi}\|_1 \\ &= \mathcal{T}\left(\tilde{I}_1^n - I_2 e^{-i\varphi}, \frac{\lambda}{\alpha_n}\right) + I_2 e^{-i\varphi} \end{aligned}$$

- Step 3: Repeat Steps 1 and 2 for Eq. [2b] with $I_1 = I_1^{n+1}$.
- Step 4: Repeat Steps 1 – 3 with $I_2 = I_2^{n+1}$ and $n = n + 1$, if $n < N_{\text{iter}}$.

Here, the $\mathbf{S}_j^H$ represents the Hermitian transpose of $\mathbf{S}_j$, $\mathbf{D}$ is the sampling density compensation matrix, $\mathcal{T}$ is the soft-thresholding operator: $\mathcal{T}(z, \beta) = \max(|z| - \beta, 0) \cdot z / |z|$, and N_{iter} is the maximum number of iteration. In the present implementation, the step size α_n at each iteration was determined by $\alpha_n = \sum_{j=1}^{N_c} \|\mathcal{F}_{NU}(\mathbf{S}_j d^n)\|_2^2 / \|d^n\|_2^2$ where $d^n = I^n - I^{n-1}$ as suggested by (42). Convergence of the solutions was reached within $N_{\text{iter}} = 20$. Figure A1 provides a flow diagram of the above computation steps, implemented in Matlab (MathWorks Inc., Natick, MA) with the nfft software library (43) included for forward and inverse NUFFT operations.

Figure A1.

A flow diagram of the computation steps to solve Eqs. [2a] and [2b] in an iterative framework.

REFERENCES

1. Bergin C, Pauly J, Macovski A. Lung parenchyma: projection reconstruction MR imaging. *Radiology* 1991;179(3):777–781. [PubMed: 2027991]
2. Robson MD, Gatehouse PD, Bydder M, Bydder GM. Magnetic resonance: An introduction to ultrashort TE (UTE) imaging. *J Comput Assist Tomogr* 2003;27:825–846. [PubMed: 14600447]
3. Madio DP, Lowe IJ. Ultra-fast imaging using low flip angles and FIDs. *Magn Reson Med* 1995;34(4):525–529. [PubMed: 8524019]
4. Weiger M, Pruessmann KP, Hennel F. MRI with zero echo time: hard versus sweep pulse excitation. *Magn Reson Med* 2011;66(2):379–389. [PubMed: 21381099]
5. Techawiboonwong A, Song HK, Wehrli FW. In vivo MRI of submillisecond T2 species with two-dimensional and three-dimensional radial sequences and applications to the measurement of cortical bone water. *NMR Biomed* 2008;21:59–70. [PubMed: 17506113]
6. Du J, Carl M, Bydder M, Takahashi A, Chung CB, Bydder GM. Qualitative and quantitative ultrashort echo time (UTE) imaging of cortical bone. *J Mag Reson* 2010;207(2):304–311.
7. Wu Y, Hrovat MI, Ackerman JL, Reese TG, Cao H, Ecklund K, Glimcher MJ. Bone matrix imaged in vivo by water- and fat-suppressed proton projection MRI (WASPI) of animal and human subjects. *J Magn Reson Imaging* 2010;31:954–963. [PubMed: 20373441]
8. Wilhelm MJ, Ong HH, Wehrli SL, Li C, Tsai PH, Hackney DB, Wehrli FW. Direct magnetic resonance detection of myelin and prospects for quantitative imaging of myelin density. *Proc Natl Acad Sci U S A* 2012;109(24):9605–9610. [PubMed: 22628562]
9. Togao O, Tsuji R, Ohno Y, Dimitrov I, Takahashi M. Ultrashort echo time (UTE) MRI of the lung: assessment of tissue density in the lung parenchyma. *Magn Reson Med* 2010;64(5):1491–1498. [PubMed: 20574988]
10. Wu Y, Chesler DA, Glimcher MJ, Garrido L, Wang J, Jiang HJ, Ackerman JL. Multinuclear solid-state three-dimensional MRI of bone and synthetic calcium phosphates. *Proc Natl Acad Sci USA* 1999;96:1574–1578. [PubMed: 9990066]
11. Seifert AC, Li C, Rajapakse CS, Bashoor-Zadeh M, Bhagat YA, Wright AC, Zemel BS, Zavaliangos A, Wehrli FW. Bone mineral ^{31}P and matrix-bound water densities measured by solid-state ^{31}P and ^1H MRI. *NMR Biomed* 2014;27(7):739–748. [PubMed: 24846186]

12. Keereman V, Fierens Y, Broux T, De Deene Y, Lonnew M, Vandenberghe S. MRI-based attenuation correction for PET/MRI using ultrashort echo time sequences. *J Nuc Med* 2010;51(5): 812.
13. Miller GW, Eames M, Snell J, Aubry JF. Ultrashort echo-time MRI versus CT for skull aberration correction in MR-guided transcranial focused ultrasound: In vitro comparison on human calvaria. *Med Phys* 2015;42(5):2223–2233. [PubMed: 25979016]
14. Larson PE, Conolly SM, Pauly JM, Nishimura DG. Using adiabatic inversion pulses for long-T2 suppression in ultrashort echo time (UTE) imaging. *Magn Reson Med* 2007;58(5):952–961. [PubMed: 17969119]
15. Horch RA, Gochberg DF, Nyman JS, Does MD. Clinically compatible MRI strategies for discriminating bound and pore water in cortical bone. *Magn Reson Med* 2012; 68(6):1774–1784. [PubMed: 22294340]
16. Li C, Magland JF, Zhao X, Seifert AC, Wehrli FW. Selective in vivo bone imaging with long-T suppressed PETRA MRI. *Magn Reson Med* 2016;77(3):989–997. [PubMed: 26914767]
17. Robson MD, Bydder GM. Clinical ultrashort echo time imaging of bone and other connective tissues. *NMR Biomed* 2006;19(7):765–780. [PubMed: 17075960]
18. Gatehouse PD, Bydder GM. Magnetic resonance imaging of short T2 components in tissue. *Clin Radiol* 2003;58:1–19. [PubMed: 12565203]
19. Du J, Bydder M, Takahashi AM, Carl M, Chung CB, Bydder GM. Short T2 contrast with three-dimensional ultrashort echo time imaging. *Magn Reson Imaging* 2011;29:470–482. [PubMed: 21440400]
20. Du J, Diaz E, Carl M, Bae W, Chung CB, Bydder GM. Ultrashort echo time imaging with bicomponent analysis. *Magn Reson Med* 2012;67(3):645–649. [PubMed: 22034242]
21. Li C, Magland JF, Rad HS, Song HK, Wehrli FW. Comparison of optimized soft-tissue suppression schemes for ultrashort echo time MRI. *Magn Reson Med* 2012;68(3):680–689. [PubMed: 22161636]
22. Rahmer J, Blume U, Börnert P. Selective 3D ultrashort TE imaging: comparison of “dual-echo” acquisition and magnetization preparation for improving short-T2 contrast. *Magn Reson Mater Phy* 2007;20(2):83.
23. Sussman MS, Pauly JM, Wright GA. Design of practical T2-selective RF excitation (TELEX) pulses. *Magn Reson Med* 1998;40:890–899.
24. Johnson EM, Vyas U, Ghanouni P, Pauly KB, Pauly JM. Improved cortical bone specificity in UTE MR Imaging. *Magn Reson Med* 2017;77(2):684–695. [PubMed: 26972442]
25. Lustig M, Donoho D, Pauly JM. Sparse MRI: The application of compressed sensing for rapid MR imaging. *Magn Reson Med* 2007;58(6):1182–1195. [PubMed: 17969013]
26. Nam S, Akcakaya M, Basha T, Stehning C, Manning WJ, Tarokh V, Nezafat R. Compressed sensing reconstruction for whole-heart imaging with 3D radial trajectories: a graphics processing unit implementation. *Magn Reson Med* 2013;69(1):91–102. [PubMed: 22392604]
27. Zhou Z, Han F, Yu S, Yu D, Rapacchi S, Song HK, Wang DJ, Hu P, Yan L. Accelerated noncontrast-enhanced 4-dimensional intracranial MR angiography using golden-angle stack-of-stars trajectory and compressed sensing with magnitude subtraction. *Magn Reson Med* 2018;79(2): 867–878. [PubMed: 28480537]
28. Wang Y, Yang J, Yin W, Zhang Y. A new alternating minimization algorithm for total variation image reconstruction. *SIAM J Imaging Sci* 2008;1(3):248–272.
29. Pruessmann KP, Weiger M, Börnert P, Boesiger P. Advances in sensitivity encoding with arbitrary k-space trajectories. *Magn Reson Med* 2001;46(4):638–651. [PubMed: 11590639]
30. Samsonov AA, Kholmovski EG, Parker DL, Johnson CR. POCSENSE: POCS-based reconstruction for sensitivity encoded magnetic resonance imaging. *Magn Reson Med* 2004;52(6): 1397–1406. [PubMed: 15562485]
31. Daubechies I, DeFrise M, De Mol C. An iterative thresholding algorithm for linear inverse problems with a sparsity constraint. *Commun Pure Applied Math* 2004;57:1413–1457.
32. Magland JF, Li C, Langham MC, Wehrli FW. Pulse sequence programming in a dynamic visual environment: SequenceTree. *Magn Reson Med* 2016;75(1):257–265. [PubMed: 25754837]

33. Herrmann KH, Kramer M, Reichenbach JR. Time Efficient 3D Radial UTE Sampling with Fully Automatic Delay Compensation on a Clinical 3T MR Scanner. *PLoS One* 2016;11(3):e0150371. [PubMed: 26975051]
34. Yushkevich PA, Piven J, Hazlett HC, Smith RG, Ho S, Gee JC, Gerig G. User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. *Neuroimage* 2006;31(3):1116–1128. [PubMed: 16545965]
35. Yushkevich PA, Yang G, Gerig G. ITK-SNAP: An interactive tool for semi-automatic segmentation of multi-modality biomedical images. *Conf Proc IEEE Eng Med Biol Soc* 2016;2016:3342–3345. [PubMed: 28269019]
36. Johnson D, Wilkie AO. Craniosynostosis. *Eur J Hum Genet* 2011;19(4):369–376. [PubMed: 21248745]
37. Berker Y, Franke J, Salomon A, Palmowski M, Donker HC, Temur Y, Mottaghy FM, Kuhl C, Izquierdo-Garcia D, Fayad ZA. MRI-based attenuation correction for hybrid PET/MRI systems: a 4-class tissue segmentation technique using a combined ultrashort-echo-time/Dixon MRI sequence. *J Nuc Med* 2012;53(5):796.
38. Glover GH. Multipoint Dixon technique for water and fat proton and susceptibility imaging. *J Magn Reson Imaging* 1991;1(5):521–530. [PubMed: 1790376]
39. Wiesinger F, Bylund M, Yang J, Kaushik S, Shanbhag D, Ahn S, Jonsson JH, Lundman JA, Hope T, Nyholm T. Zero TE-based pseudo-CT image conversion in the head and its application in PET/MR attenuation correction and MR-guided radiation therapy planning. *Magn Reson Med* 2018;80(4):1440–1451. [PubMed: 29457287]
40. Wiesinger F, Sacolick LI, Menini A, Kaushik SS, Ahn S, Veit-Haibach P, Delso G, Shanbhag DD. Zero TE MR bone imaging in the head. *Magn Reson Med* 2016;75(1):107–114. [PubMed: 25639956]
41. Jang H, Liu F, Bradshaw T, McMillan AB. Rapid dual-echo ramped hybrid encoding MR-based attenuation correction (d RHE-MRAC) for PET/MR. *Magn Reson Med* 2018;79(6):2912–2922. [PubMed: 28971513]
42. Wright SJ, Nowak RD, Figueiredo MA. Sparse reconstruction by separable approximation. *IEEE T Signal Proces* 2009;57(7):2479–2493.
43. Keiner J, Kunis S, Potts D. Using NFFT 3-A Software Library for Various Nonequispaced Fast Fourier Transforms. *Acm T Math Software* 2009;36(4):19.

Figure 1.

a: Diagram of the VS-DURANDE UTE pulse sequence, in which RF₁ (short ~ 40μs) and RF₂ (long ~ 520μs) are alternately played out and four independent datasets are produced: ECHO₁₁, ECHO₁₂, ECHO₂₁, and ECHO₂₂. b: A schematic of k-space construction with VS between ECHO₁₁ and ECHO₂₁ (k₁) and between ECHO₁₂ and ECHO₂₂ (k₂). Note that varying gradients (radial view angles) on a TR basis (a) makes it possible to employ the VS approach (b), thus enabling scan time reduction by two-fold. Note also that the central portions of k₁ and k₂ are composed only of ECHO₁₁ and ECHO₂₂, respectively, to maximally differentiate bone signals between two corresponding images.

Figure 2.

a: Excitation profile (transverse magnetization) for a range of T_2 species (0.01 – 100 ms) in response to various RF pulses differing in durations (0.04, 0.25, 0.5, and 1 ms) but employing the same flip angle (12°). b: $(S_1 - S_2)/S_1$; (S_1 , S_2 : transverse magnetization produced by RF₁, RF₂) with varying the duration of RF₂ (0.1 – 2 ms) while keeping that of RF₁ fixed to 0.04 ms, under different off-resonance conditions (0 – ± 300 Hz). In b, T_2 values of 0.5, 100, and 100 ms were used for bone, fat, and soft-tissue, respectively. One could expect from the simulation a that in dual-RF based UTE with longer RF₂ pulse, short T_2 species are better discriminated from long T_2 tissues in the difference between S_1 and S_2 . However, in the presence of off-resonance frequencies long RF₂ pulses result in elevated long T_2 signals in the difference, thus making it difficult to differentiate between bone and soft-tissues.

Figure 3.

a-c: Three sets of images ($|I_1|$, $|I_2|$, I_{Bone}), acquired using the 3D DURANDE UTE pulse sequence and reconstruction based on the parent technique (using only ECHO_{11} and ECHO_{22}) with 50,000 (a; 12 min) and 25,000 (b; 6 min) radial views for each echo, and the proposed technique with the VS scheme that utilizes all four echoes (Fig. 1b) with 25,000 views each (c; 6 min). d: Signal profiles of I_{Bone} , corresponding to the colored lines in a-c. Note that VS-DURANDE (c), when compared with the reference (a), suffers no appreciable loss in image quality with undersampling-induced noise amplifications (b and arrows in d) suppressed. Note further that in I_{Bone} the posteriorly positioned foam pad is also visible due to short proton T_2 of the polymeric material from which it is made.

Figure 4.

a-c: I_1 , I_2 , and I_{Bone} images for retrospectively decimated data (12,500 views, 3 min), produced without (a) and with (b) the VS scheme, and by its combination with the bone-sparsity constrained reconstruction (c). d,e: Signal intensity profiles of I_{Bone} (horizontal colored lines in a-c) plotted together with the data from the reference scan (Fig. 3a). Note that image reconstruction using the VS + sparse prior (c) effectively suppresses amplified noise signals (a, arrow in d) resulting from data subsampling, thus leading to clear depiction of bone signals representing outer and inner table of the skull, comparable to those in the reference (e).

Figure 5. Whole-skull bone images in four subjects, acquired and reconstructed using the proposed technique with prospective undersampling by a factor of four (imaging time = 3 min), displayed in sagittal, coronal, and axial planes. Note that diploe and separation of inner and outer layers of cranium are well visualized in all subjects. Note also clear demonstration of anatomic features such as mandible (yellow arrows), zygomatic bone (blue), sphenoid bone (red), and upper portion of cervical spine (green).

Figure 6. 3D renderings of the skull in two subjects (#1 and 2 in Fig. 4) in anterior, lateral, posterior, and superior views. Note the expected anatomic structures including mandible and upper portion of cervical spine. More subtle structures including zygomatic arch and mastoid process (blue and yellow arrows) are pointed out as well.