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A Method for Unwrapping Highly Wrapped Multi-echo Phase Images at Very High Field: UMPIRE

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Abstract

Purpose—To develop a method of unwrapping phase images from multi-echo scans that works even where there are several wraps between echoes, and which generates unwrapped phase images in addition to phase difference (PD) images.

Theory—The difference between the echo spacings in an acquisition with three unevenly spaced echoes (an imposed delay) can be selected such that the phase evolution in that time is in the range $-\pi$ to $+\pi$ in all voxels of interest. Under this condition, an image of the difference between the phase evolutions in the two inter-echo periods, an estimate of B_0 , is free of wraps. This B_0 estimate can be used to identify and remove receiver phase offsets and wraps in phase images.

Methods—The approach was tested on simulated data and high-resolution in vivo brain data acquired from six subjects at 7 Tesla.

Results—The method generated wrap-free phase images. It was able to remove more wraps than is possible with PD imaging and was faster and more reliable than spatial unwrapping.

Conclusion—Unwrapping Multi-echo Phase Images with iRegular Echo spacings (UMPIRE) is conceptually simple, fast, reliable, and requires no fitting, thresholds, or operator intervention.

Keywords

phase imaging; high field; phase wraps; unwrapping; multi-echo; UMPIRE

INTRODUCTION

Enhanced susceptibility effects at high field have led to the rapid development of methods which use the phase of the MR signal, particularly in neuroimaging. These include mapping local deviations from the static magnetic field (B_0) (1,2), high-resolution phase imaging (3,4), susceptibility-weighted imaging (SWI) (5,6) and quantitative susceptibility mapping (7-9). B_0 mapping is widely used to correct distortions in echo-planar imaging (1), and high-resolution gradient-echo (GE) phase imaging has been applied in the assessment of

vascular malformations such as cavernomas (10) and iron stores in pathologies including dementia (11), Huntington's, and Alzheimer's disease (12).

The phase of the MR signal has both time-independent and time-dependent components. The time-independent components, frequently referred to cumulatively as the "receiver phase offset" comprise contributions arising from the path length of the MR signal from a particular location in the object to the receiver coil in question given a finite MR wavelength (13,14), a linear phase gradient in the readout direction introduced by the readout gradient (15), the cable length from the coil to the receiver and artifacts in the receiver chain including frequency synthesizer drift and imperfectly centered k-space (16). The time-dependent component is dominated by deviation from the static magnetic field, B_0 , which evolves linearly over time. This contribution reflects physiologically interesting tissue properties such as local iron content.

Because the range of phase values which can be measured in MRI is limited to 2π , phase aliasing occurs, leading to discontinuities in phase images which are known as "wraps." Well-behaved wraps are isocontours that either form closed loops within the object or begin and terminate at the object boundary. A wrap which ends within the object is known as a "non-terminating fringe line," and indicates a nonphysical infinite gradient in the phase, and generally belies a point at which there is no signal in the corresponding magnitude image. Wraps obscure interesting phase features in the object and, in most applications, need to be removed.

In this study, we classify unwrapping methods as either "spatial" or "temporal." Spatial methods are image-based, and use some regional characteristics of phase or complex values at a single echo time, usually abrupt change, to identify wraps. Temporal methods, on the other hand, are based on identifying wraps by means of the evolution of the phase in each voxel at two or more echo times. Temporal phase unwrapping should not be confused with the unwrapping of a time-series of data (as in, e.g., (17)). Spatial methods usually use region-growing algorithms which begin in a region of stable phase (as defined, e.g., by local phase coherence (18) and proceed either in two dimensions (2D) or 3D, identifying a wrap when the phase difference (PD) between adjacent voxels exceeds π . The main disadvantages of spatial unwrapping are that it tends to be computationally intensive and, in most implementations, needs to distinguish the object (which should be unwrapped) from the background (which should not be unwrapped). This requires a threshold relating to the local phase coherence (19) or signal level in the corresponding magnitude image (19,20) to be set, which generally entails operator intervention. Spatial unwrapping also leaves an integer number of 2π phase jumps between slices (in 2D unwrapping) and echoes (2), if applied to multi-echo data. As a result of these problems, spatial methods have proven too slow and fragile to be implemented on the scanner console. Instead, homodyne filtering (21)—complex division by a low-pass filtered version of the data—is often used. This fails if images are highly wrapped, and modifies phase values so they cannot be used quantitatively (19).

Temporal methods require phase images acquired at two or more echo times. Where the phase evolution between two measurements is between $+\pi$ and $-\pi$, a wrap-free image can be

created by calculating the difference between the two images from the angle of the complex difference, by means of a conditional phase difference or using the Hermitian inner product method (19). This is a simple and robust approach. At high field, however, with B_0 values up to approximately 1300 rad s^{-1} at 3 Tesla (T) and 3000 rad s^{-1} at 7T in the head (2) (down to a level of $z = -14$ in the ICBM152 template of the Montreal Neurological Institute (MNI) (22)), echo spacings would have to be approximately 2.4 ms at 3T and 1 ms at 7T to avoid wraps developing in the inter-echo period. While using such a short echo spacing has been demonstrated to be feasible for SWI at 3T (15), dB/dt limitations mean that this cannot be achieved in a high-resolution multi-echo acquisition at 7T or higher field strengths. A very recent method by Dagher et al has shown one way in which this limit may be overcome in a triple-echo acquisition with unevenly spaced echoes (23), although this involves calculating and comparing several feasible wrap scenarios. The second problem with temporal methods is that most have been developed to yield unwrapped PD images and not unwrapped individual phase images. This limitation arises as receiver offset contributions to the phase, which can also cause wraps, have generally not been isolated and resolved. PD images have lower gray–white matter contrast than phase images (14).

The aim of this study was to develop a fast and simple method of unwrapping phase images from multi-echo acquisitions with widely spaced echoes, corresponding to low bandwidth, high signal to noise ratio (SNR) scans, at ultra-high field, in which several wraps occur between echoes, and to generate unwrapped phase images rather than PD images. The method we present (24,25) achieves this by using unequal echo spacings, chosen such that no wraps occur in the time difference between the echo spacings, and by calculating and removing receiver phase offsets.

THEORY

The fact that the measured phase of the MR signal, θ , can only be defined over a range spanning 2π rad means that values of the true phase, Φ , outside this range, become aliased. If θ is defined in the range $0 \rightarrow 2\pi$, the relationship between θ and Φ is:

$$\theta = \Phi - n2\pi \quad [1]$$

where

$$n = \left\lfloor \frac{\Phi}{2\pi} \right\rfloor \quad [2]$$

brackets denoting rounding down to the nearest integer (the floor function). Unwrapping is the process of identifying n , the number of wraps which have occurred, so that the true phase, Φ , may be restored.

In the following explanation of the steps in Unwrapping Multi-echo Phase Images with iRegular Echo spacings (UMPIRE), we consider a multi-echo GE acquisition with three echoes, acquired at echo times T_{E1} , T_{E2} , and T_{E3} , in which the time between T_{E2} and T_{E3} is longer than that between T_{E1} and T_{E2} (see Fig. 1). The acquisition yields three phase images; θ_1 , θ_2 , and θ_3 . We define the spacing between the first two echoes as:

$$\Delta T_E = T_{E2} - T_{E1} \quad [3]$$

and the short additional delay between θ_2 and θ_3 , δT_E , as:

$$\delta T_E = T_{E3} - T_{E2} - \Delta T_E \quad [4]$$

No wraps occur in the time δT_E , which can be chosen at will, for $\delta T_E < \frac{\pi}{\gamma |\Delta B_0|}$. δT_E can be selected on the basis of knowledge of the typical range of B_0 values encountered at the field strength in question, or can be set on the basis of B_0 values measured in the subject under study in a prior fast, low-resolution field map. Steps in the following description correspond to the images in Figure 2. Calculations are carried out on all voxels in images; voxel indices are omitted for simplicity.

Step 1: Phase images θ_i are reconstructed for each echo time T_{Ei} .

Step 2: PD images, with values ranging from $-\pi$ to $+\pi$, are calculated between neighboring pairs of phase images. These can be calculated by means of (a) the angle of the complex difference:

$$\theta_{i+1,i} = \angle \exp(i(\theta_{i+1} - \theta_i)) \quad [5]$$

in which $\angle$ denotes the angle (the four-quadrant inverse tangent) of the complex vector, (b) the Hermitian inner product (19)

$$\theta_{i+1,i} = \angle S_{i+1} S_i^* \quad [6]$$

where S_i is the complex-valued signal for image i , or (c) a simple subtraction of the second angle from the first, with 0 , 2π or -2π being added to the difference, depending on the relative sizes of the two angles:

$$\theta_{i+1,i} = \begin{cases} \theta_{i+1} - \theta_i, & \text{if } -\pi \leq \theta_{i+1} - \theta_i \leq \pi \\ \theta_{i+1} - \theta_i - 2\pi, & \text{if } \theta_{i+1} - \theta_i > \pi \\ \theta_{i+1} - \theta_i + 2\pi, & \text{if } \theta_{i+1} - \theta_i < -\pi \end{cases} \quad [7]$$

PD images reflect phase changes that evolve in the echo spacings T_{Ei} . They contain values in the range $-\pi$ to π , and are subject to residual wraps if $|\gamma \Delta B_0 \Delta T_{Ei+1,i}| > \pi$, where γ is the gyromagnetic ratio. This is frequently the case in high-resolution measurements at very high field.

Step 3: A difference between PD (DPD) images is calculated:

$$\theta_{i+2,i+1,i+1,i} = \angle \exp(i(\theta_{i+2} - 2\theta_{i+1} + \theta_i)) \quad [8]$$

(or by means of one of the other methods for calculating PD detailed in step 2). The DPD image reflects phase changes that evolve in the additional delay, δT_E , which can be chosen

to be as small as desired. Optimally, it should be set to $\frac{\pi}{\gamma|\Delta B_{0max}|}$, where B_{0max} is the highest value occurring in the object for which the phase should be unwrapped. For this value of δT_E (and all lower values), the DPD image contains no wraps.

Step 4: For convenience, the DPD image is converted to an angular frequency shift (ω), which is proportional to the local deviation from the static magnetic field, B_0 :

$$\omega = \frac{\theta_{i+2,i+1,i+1,i}}{\delta T_E} \quad [9]$$

Step 5: Wraps in PD images are identified by comparison with the expected phase evolution in the inter-echo interval, on the basis of ω . The number of wraps in the PD image for echoes i and $i+1$ is given by

$$n_{i+1,i} = \left\lfloor \frac{\theta_{i+1,i} - (T_{Ei+1} - T_{Ei}) \cdot \omega}{2\pi} \right\rfloor \quad [10]$$

Step 6: The value of $2\pi \cdot n_{i+1,i}$ is subtracted pixelwise from PD images, unwrapping them. The unwrapped PD images are labeled with a prime:

$$\theta'_{i+1,i} = \theta_{i+1,i} - 2\pi n_{i+1,i} \quad [11]$$

The original phase images are unwrapped in the following steps.

Step 7: The PD images are used to obtain a higher SNR estimate of ω , which we label ω^* , as follows:

$$\omega^* = \frac{\theta'_{i+1,i}}{\Delta T_E} \quad [12]$$

A magnitude-weighted average of $\theta'_{3,2}$ and $\theta'_{2,1}$ could be used here.

Step 8: This map of ω^* is used to identify wraps in individual phase images. Analogous to step 5, the number of wraps that occur between time 0 and T_{Ei} due to B_0 is given by:

$$n_i = \left\lfloor \frac{\theta_i - T_{Ei} \cdot \omega^*}{2\pi} \right\rfloor \quad [13]$$

Step 9: The wraps that occurred in the time T_{Ei} are removed, thus:

$$\theta'_i = \theta_i - 2\pi n_i \quad [14]$$

Step 10: These images still contain phase variation due to the receiver offset, R , which can leave some remaining wraps. The phase offset term is calculated according to reference (14) using, for example, the first two echoes:

$$R = \frac{T_{E1} \cdot \theta'_2 - T_{E2} \cdot \theta'_1}{T_{E1} - T_{E2}} \quad [15]$$

Step 11: The receiver offset is subtracted from each phase image:

$$\theta_{i0} = \angle \exp(i(\theta_i - R)) \quad [16]$$

(the zero in the subscript denoting the removal of the phase at time zero). This removes time-independent sources of phase but re-introduces wraps due to B_0 .

Step 12: Analogous to step 8, the number of wraps that occurred between time 0 and T_{Ei} is re-estimated:

$$n'_i = \left\lfloor \frac{\theta_{i0} - T_{Ei} \cdot \omega^*}{2\pi} \right\rfloor \quad [17]$$

Step 13: Finally, phase images that are free of wraps due to both receiver offset and B_0 variations, are yielded thus:

$$\theta''_i = \theta_{i0} - 2\pi n'_i \quad [18]$$

This approach can be extended to more echoes, which may be separated by several different echo spacings, and the additional delay can be inserted between any pair of echoes. Modest smoothing of the DPD image can lead to a reduction of errors in the calculation of n . Steps 10–13 are not needed if receiver offsets are removed in combining the phase images from the individual channels in a phased array (14). In that case, the images are fully unwrapped after step 9.

METHODS

The characteristics and performance of UMPIRE were investigated in unwrapping simulated data and in vivo MR data acquired at 7 Tesla. UMPIRE was compared with conventional temporal phase unwrapping and the most commonly used spatial unwrapping implementations PRELUDE (20) (in both 2D and 3D mode) and PHUN (19).

Simulated data, created with MATLAB (Mathworks Inc, Natick, MA), allowed the features of UMPIRE to be explored and the performance of all unwrapping methods to be compared against the ground truth.

Simulated Data 1: Linear Gradients in B_0 and Receiver Phase Offset

These data were simulated to illustrate the properties of UMPIRE compared with conventional temporal phase unwrapping. Simulated phase images consisted of a time-dependent gradient in the x direction G_x (simulating a range of B_0 values) and a time-independent linear gradient in phase offset in the y direction, G_y (simulating a range of receiver phase offsets). G_x varied from $-\pi$ to $+\pi$ rad ms⁻¹ and G_y from 0 to 6π . Phase images were generated at $T_E = 5, 10$, and 16 ms. The simulated phase Φ was given by $\Phi(x, y, T_E) = G_x \times x \times T_E + G_y \times y$, (column A in Fig 3). Wrapped phase images $\theta(x, y, T_E)$ were generated according to Eqs. [1] and [2] (column B in Fig. 3).

Simulated Data 2: Complex Topographies

The accuracy and processing time of UMPIRE was compared with spatial methods in unwrapping complex topographies. These were $256 \times 256 \times 256$ voxels in size and were labeled Complexity 1–6, with 6 being the most difficult to unwrap. Complexity 1 consisted of a single 3D Gaussian distribution, centered in the centre of the matrix, with a full width half maximum (FWHM) (W_1) of 128 voxels. Complexity 2 was the sum of the Complexity 1 topography and a second 3D matrix of the same dimensions which was formed from the $2 \times 2 \times 2$ arrangement of eight narrower Gaussian distributions (width $W_2 = 64$ voxels) each occupying a matrix of $128 \times 128 \times 128$ voxels. Each more complex topography was formed by adding (Complexity 3) Gaussian distributions occupying a matrix of size $256 / (2^{\text{Complexity}-3})$, of width $W_1 / (2^{\text{Complexity}-3})$ to the previous one (first column in Fig. 4). The wrapping operator (Eqs. [1] and [2]) was applied to generate wrapped phase images (second column in Fig. 4).

Simulated Data 3: Noisy Objects

The accuracy and processing time of UMPIRE in unwrapping in the context of noise was compared with spatial methods. The data set was $128 \times 128 \times 128$ voxels in size, and the object to unwrap was a sphere 90 voxels in diameter, which contained a 3D Gaussian distribution with FWHM of 128 voxels. The phase distribution was such that there were four wraps to remove at the third echo time. Magnitude data are required by the spatial methods. The magnitude signal was taken to decay with a T_2^* time of 20 ms, and data were simulated at echo time = 5, 10, and 16 ms. Gaussian distributed white noise of between 0 and 60% of the value at time zero (in 5% increment), was added to both the magnitude and phase before applying the wrapping operator to the phase.

Measurements

Measurements were made with a 7T MR whole-body system (Magnetom, Siemens Healthcare, Erlangen, Germany) using a 32-channel head coil (Nova Medical, Wilmington, MA) consisting of a birdcage transceiver coil and 32 receive-only elements. The study was approved by the Ethics Committee of the Medical University of Vienna. Six healthy subjects (two females), aged 33.9 ± 7.8 years, participated in the study with written, informed consent. A high-resolution 3D multi-echo GE (NE = 3) scan was acquired with a matrix size of $320 \times 320 \times 160$ (isometric voxels of 0.65 mm side length), monopolar readout, and $T_E = [3.9, 9.0, 15.1]$ ms, i.e., with an additional delay (δT_E) of 1 ms between the second and third

echo. The bandwidth (BW) was 240 Hz/pixel and the total acquisition time (TA) was 10 min 57 s. The first echo was flow compensated in all directions. To allow the performance of UMPIRE to be assessed in very inferior regions, the same sequence was acquired with more extensive coverage in the head-foot direction (17.2 cm) in an acquisition with $320 \times 320 \times 265$ voxels in one subject (TA = 22 min 27 s). A low-resolution 2D dual-echo GE scan was also acquired for all subjects for the purpose of phase combination (14)), with $T_E/T_R = (4.6, 9.3)/606$ ms, GRAPPA factor 4, TA = 42 s, with a 128×128 matrix, 50 slices of 3.0-mm thickness, and a 230×230 field of view.

Analysis

The steps in UMPIRE, which are outlined in Figure 2 and Eqs. [3–18], were implemented in C using standard NIfTI libraries (<http://nifti.nimh.nih.gov/>). When applied to Simulated Data 3 and for in vivo data, DPD images were median filtered using a $3 \times 3 \times 3$ voxel kernel to reduce noise.

Analysis of Simulated Data—Simulated Data 1 were unwrapped with UMPIRE, including steps for removing receiver phase offsets. Conventional temporal phase unwrapping was also used both to create PD images and to attempt to unwrap individual phase images, using the PD between the images at 5 ms and 10 ms to extrapolate and identify wraps that had occurred between $T_E = 0$ and each echo time. Simulated Data 2 and 3 were unwrapped with UMPIRE, PRELUDE (in 2D and 3D mode), and PHUN. For Simulated Data 2 (complex topographies) threshold values in PRELUDE and PHUN were set so as to unwrap all voxels (in PRELUDE, by setting t , the intensity threshold for masking, to 0, and in PHUN, using the -phaseOnly option). For Simulated Data 3 (noisy objects) PRELUDE and PHUN were set to unwrap only the object by fixing the intensity threshold for masking to 5 in PRELUDE, and in PHUN, setting - tqmin, the lower limit for pixel quality (19)), to 0.05, where these values were determined empirically. There were residual inter-slice and inter-echo phase jumps of $n2\pi$ (where n is an integer) in PRELUDE and PHUN, arising from the fact that seed voxels can be located on different sides of isophase contours in different slices and/or echoes. These jumps were identified and removed using a MATLAB program that compared the mean in-brain phase in adjacent slices (2). Unwrapped phase values in all the methods were compared with simulated values. For each method, the percentage accuracy was calculated as the mean over all voxels of

$$100 \times \left(1 - \left| \frac{\theta_{gt} - \theta_{uw}}{\theta_{gt}} \right| \right), \text{ where } \theta_{gt} \text{ is the ground truth (the simulation value) and } \theta_{uw} \text{ is the unwrapped phase value.}$$

Analysis of In Vivo Data—In vivo phase data from the 32 surface coils were combined using MCPC-3D-II (14)), in the process of which receiver phase offsets are calculated and removed from the phase information from each channel. In unwrapping with UMPIRE, steps for the subtraction of receiver phase offsets (steps 10–13 in Fig. 2) were, therefore, omitted as redundant. Average processing times for all methods were calculated from six executions on a desktop computer with a quad-core 2.67 GHz Intel Xeon processor and 12 GB RAM, running Ubuntu 12.04. In the spatial methods, the additional time required to remove inter-slice and inter-echo phase jumps was not included in the calculation time.

To allow methods to be compared in data with spatially variable SNR, in vivo phase images from individual radiofrequency (RF) coils were also unwrapped with UMPIRE (including the removal of receiver phase offsets), PRELUDE, and PHUN.

RESULTS

Simulated Data 1

The characteristics of conventional temporal phase unwrapping were compared with those of UMPIRE over a range of simulated local field deviations (x direction in “A”) and phase offsets (y direction in “A”) (Fig. 3). Conventional temporal phase unwrapping, or PD imaging, failed when the magnitude of the phase change in the time interval T_E exceeded π (Fig. 3C). This corresponds to the vertical wraps, the first of which are indicated by red arrows. If unwrapping of individual phase images was attempted with the conventional method, these phase images also contain phase wraps due to phase offsets (Fig. 3D). The first of these is indicated by green arrows. As a result of these deficits, phase values are only correct in the region bounded by arrows. The range of phase values over which UMPIRE can unwrap was limited only by δT_E , which was 1 ms in this simulation, and phase offsets were removed in a separate step. The resulting images (Fig. 3E), therefore, contained no wraps and only phase arising from B_0 [note the lack of phase variation in the y direction, and the reduced phase range of $-15\pi \rightarrow +15\pi$ compared with $-15\pi \rightarrow +21\pi$ in the original images (Fig. 3A)].

Simulated Data 2

PRELUDE and PHUN both made errors in unwrapping complex topographies. PHUN made errors in unwrapping difficulty levels 4, 5, and 6 and PRELUDE (2D) in unwrapping difficulty levels 5 and 6 (see examples in Fig. 4). These unwrapping errors are quantified in Figure 5 (top). UMPIRE made no unwrapping errors in any difficulty levels. The time taken by UMPIRE to unwrap complex topographies was independent of the complexity, and was approximately 10 times faster than the fastest spatial unwrapping method, PHUN, which was approximately 50 times faster than PRELUDE 2D. PRELUDE 3D only completed difficulty level 1 (in 11.6 days), with more complex topographies not completing in under 20 days. Unwrapping times are plotted in Figure 5 (bottom).

Simulated Data 3

The accuracy and time taken to unwrap noisy spheres are shown in Figure 6. Prelude (2D) showed the best performance, maintaining an accuracy of 98% up to 50% noise fraction. Prelude (3D) performed well at low noise levels, but no assessment was performed above 20%, where unwrapping times exceeded 36 h. The performance of PHUN reduced sharply at 35%. UMPIRE performed similarly to the spatial methods up to 20% noise, after which the accuracy dropped sharply. A comparison of SNR between in vivo and simulated data indicates that typical in vivo data correspond with 10% noise in simulations. Unwrapping times in UMPIRE were independent of noise and were the shortest of all methods tested (at 0.5 s). UMPIRE was 5–10 times faster than PHUN and 3–600 times faster than PRELUDE 2D (where the unwrapping time was more strongly dependent on noise). Unwrapping times

in PRELUDE 3D were heavily dependent on noise, with the unwrapping time for no noise being 1 s and over 5 h for 20% noise, with higher noise levels not completing.

In Vivo Results

Conventional temporal phase unwrapping showed residual wraps where $\Delta T_E < \frac{\pi}{\gamma|\Delta B_0|}$ (Fig. 7, red arrows). PRELUDE (2D) failed to unwrap phase in a large vein (Fig. 7, red arrow) but otherwise yielded good results within the brain. There were phase jumps between disconnected regions of scalp signal. PRELUDE (3D) did not complete processing, although the threshold was appropriate. PHUN made the same error in the large vein as PRELUDE 2D, and additionally showed several “tear” artifacts: regions beginning at a voxel with a large difference in phase to the surrounding region, which propagated over a region to the image periphery. UMPIRE showed no phase errors and yielded plausible results for the skull and eyeballs as well as brain. Results from all six subjects (Fig. 8) demonstrate UMPIRE’s ability to unwrap highly wrapped phase images consistently over subjects, generating phase images with circa 60 rad phase range.

UMPIRE successfully unwrapped phase in highly wrapped ventral regions and cerebellum (Fig. 9), and even the eyes and scalp (Fig. 9, arrows).

In single-channel data, difficulty choosing a threshold level appropriate for the whole image in the spatial unwrapping methods led to unwrapping noise close to the coil (green arrows in Fig. 10) and neglecting brain regions distant from the coil (blue arrows in Fig. 10). There were also unwrapping errors with PHUN (red arrows in Fig. 10). UMPIRE unwrapped the entirety of the image without apparent errors.

The time taken for UMPIRE to unwrap all three echoes of the high resolution in vivo data (of $320 \times 320 \times 160$ voxels, a total of circa 5×10^7 voxels) was 20.76 ± 0.04 s. The corresponding times for PHUN and PRELUDE (2D) were 103.3 ± 6.5 s and 2091.2 ± 1.7 s (approx. 35 min), respectively.

DISCUSSION

We have presented a method for unwrapping multi-echo GE phase images that is based on an acquisition with at least three unevenly spaced echoes. The timing and spacing of one pair of echoes is selected at will, according to SNR requirements, dB/dt limitations, and the desired T_2^* weighting. An additional delay δT_E is added between the other pair of echoes

such that $\delta T_E < \frac{\pi}{\gamma|\Delta B_0|}$. Under this condition, the phase evolution in the time δT_E is in the range $-\pi \rightarrow +\pi$ in all voxels of interest. Calculating the difference between the phase evolution in the two inter-echo periods allows a wrap-free field map to be calculated. This is used to unwrap PD images (by comparison) and ultimately, after receiver offsets have been calculated and removed, to unwrap the original phase images. The approach is conceptually simple, computationally fast, and works even when there are several wraps between pairs of echoes.

The dominant phase unwrapping approaches in current use are Homodyne filtering (10) and spatial phase unwrapping (26). Both require only one echo. Homodyne filtering is fast and simple, and removes many phase wraps. The fact that it also removes receiver phase offsets (as low-frequency features) means that, if it is applied to phase data from each channel, these data can be combined. The removal of low-frequency phase information makes it inappropriate for quantitative methods such as quantitative susceptibility mapping; however, and the ability of this approach to remove wraps is dependent on the filter width. As such, wraps in regions of high B_0 remain, and, if further processed in SWI, have the potential to be misconstrued as pathologies, such as microhemorrhages (27). Spatial unwrapping is capable of removing wraps more effectively than Homodyne filtering, but is inherently slow and subject, in both calculation time and unwrapping quality, to specification of the threshold that defines which parts of images to unwrap. In addition, there needs to be continuity of signal in the image and the approach works poorly where there is inhomogeneous SNR, such as in the single-channel phase images that need to be unwrapped in the unwrap-and-high-pass-filter phase combination method (2,28). Problems also occur if there are rapid phase changes within images, as can occur in large veins such as the sagittal sinus. Phase jumps between echoes and slices (in the case of 2D spatial unwrapping) also need to be removed after unwrapping (2). These constraints make it unsuitable for implementation on the scanner console, and were evident in this study.

UMPIRE was 5 times faster than PHUN, which showed several gross unwrapping errors, and 100 times faster than PRELUDE (in the faster 2D mode). The voxel-by-voxel nature of UMPIRE would allow further speed improvement if parallelization to multiple processors were to be used (29). Both PHUN and PRELUDE performed poorly in unwrapping single-channel data in which there was inhomogeneous SNR. Thresholds had to be set carefully in the spatial methods, necessitating repeated executions. UMPIRE uses no thresholds or user-defined parameters.

Temporal phase unwrapping avoids many of the problems of spatial unwrapping by treating each voxel independently, meaning the object does not need to be defined by means of a threshold and there need not be continuity of signal between objects; an advantage in breast imaging, ophthalmological applications, and the assessment of in vitro samples. Temporal phase unwrapping has historically suffered from three significant disadvantages, however, which have seen it underused. First, images at more than one echo time are required.

Second, the echo spacing must satisfy $\Delta T_E < \frac{\pi}{\gamma|\Delta B_0|}$ in order for phase wraps to be resolvable, and third, temporal approaches generally yield unwrapped PD images rather than phase images. We consider these problems in turn, particularly in relation to the inroads offered by UMPIRE.

A minimum of two echoes are required for temporal phase unwrapping, although many temporal approaches require three (23,30) or more echoes (15,31). Acquiring echoes in separate or interleaved acquisitions is too time-consuming to be practical for high-resolution imaging, and is not considered further. Instead, we consider multi-echo approaches. An increasing number of phase-related applications use multi-echo sequences. In SWI, multi-echo acquisitions have been shown to offer increased contrast to noise ratio and SNR over

single-echo acquisitions (32-34), as well as to improve the possibilities for noise reduction (33,35). In imaging with multi-channel coils at high field, measurements of phase at two or more echo times can also be used to calculate the phase offsets for each channel, allowing phase images from several RF coils to be combined without a reference volume coil measurement (14). Multi-echo GE images also allow T_2^* mapping, and field maps derived from the series of echoes can be used to correct for macroscopic dephasing effects (36). Acquiring more than one echo within the desired TR is feasible even for high-resolution, low-bandwidth acquisition at ultra-high field. The advantages of multi-echo acquisitions and the additional information they provide demonstrate that the requirement that two or three echoes be acquired rarely constitutes a drawback of temporal phase unwrapping.

The usual restriction in temporal phase unwrapping is that $\Delta T_E < \frac{\pi}{\gamma |\Delta B_0|}$ in all voxels to be unwrapped. In high-resolution phase imaging and SWI in the brain, the echo times will generally be chosen to achieve a set of desired T_2^* weightings, conditional on the minimum echo spacing. This is in turn determined, for a particular imaging resolution, by both the receiver BW (RBW) and gradient switching rate. RBW is inversely proportional to SNR squared, so phase images become noisy for high RBW. Ultimately, the limiting factor on

T_E is not SNR, however, but the gradient switching rate. High dB/dt can cause peripheral nerve stimulation, gradient heating, high levels of acoustic noise, and image degradation due to eddy currents. Feng et al have shown that the echo spacing condition above can be met at 3T even in quite ventral brain regions and for a relatively high resolution of 0.5 mm in-plane (with an RBW of 465 Hz/pixel and echo spacings down to 2.63 ms) (15). It is not feasible with high-resolution measurements at 7T, however. Both UMPIRE and the method recently described by Dagher et al (23) overcome the echo spacing limitation. The method of Dagher et al also uses triple-echo scans with unequal echo spacings to calculate PD images over a range larger than the conventional limitation ($\gamma T_E B_0$). This method is based on the principle that, if all feasible wrap possibilities are considered for each pair of echoes, then the best agreement between B_0 calculated from each scenario will be for the number of wraps that actually occurred. The authors demonstrated a dynamic unwrapping range in vivo of 91% more than would be expected from the shortest echo spacing, which is $1/T_E$ (in Hz) (37). In UMPIRE, all echoes can be very widely spaced, and we demonstrate unwrapping corresponding to 510% of the range expected from the shortest echo spacing. Compared with the Dagher method, UMPIRE offers the advantages that an unwrapped map of B_0 is generated in a single step (step 3 in Fig. 2), without the need to calculate and compare alternative possibilities. Additionally, by calculating and subtracting receiver offsets, UMPIRE generates unwrapped phase images from each echo time in addition to field maps. In challenging SNR conditions, the echo times selected by means of the Dagher T_E optimization procedure (23) will lead to the fewest unwrapping errors, whether unwrapping is under-taken by means of the authors' Closest L2-Distance Estimation or UMPIRE.

The final restriction of temporal unwrapping methods to date has been that they generally yield PD images rather than phase images. PD images are noisier and inferior in contrast to phase images (14). Temporal phase unwrapping methods are generally not able to generate phase images, because they calculate B_0 contributions to the phase but not other, temporally invariant, sources, which can also lead to wraps. As far as we are aware, the only

other temporal phase unwrapping method that yields unwrapped phase images is the recent CAMPUS method of Feng et al (15). In this, the user defines a strip region of interest along the readout direction in a homogeneous background region, which is used to calculate the phase induced by the readout gradients, which is subtracted from the phase at each echo time. This was shown to be effective, although it has the disadvantage of requiring operator intervention. Also, other contributions to the receiver phase offset are assumed to be constant throughout the image in CAMPUS. The authors demonstrate that this does not lead to phase wraps in 3T phase images. At 7T, however, where the RF wavelength is shorter, and the variation in receiver phase offset exceeds 2π over the brain (14), it would be expected to lead to residual wraps. In UMPIRE, phase unwrapping can be applied to phase images in which the receiver phase offset has been subtracted in the reconstruction process or these can be calculated and subtracted from phase images in the steps outlined. This allows phase images to be reconstructed regardless of how large receiver phase offsets are. As such, it can be expected to work at higher field strength, with shorter RF wavelength.

UMPIRE isolates receiver phase offset information. Although this contribution to the phase has generally been viewed as uninteresting, recent work has shown that receiver phase offsets can be used to calculate tissue conductivity (38), a property which can be modified in pathologies including stroke (39) and brain tumors (40).

An appropriate value for the additional delay to be used, δT_E , can be determined from measurements of the range of B_0 values encountered in a group of subjects at the field strength in question, or can be set on the basis of B_0 values measured in the subject under study in a prior fast, low-resolution field map. In the first approach, some margin should be left for outlier subjects, but this should be kept modest, as very short δT_E values lead to low SNR in DPD images, which are the starting point of the unwrapping.

As a method based on the difference between phase images, UMPIRE is more sensitive to noise than spatial approaches. This was reflected in its relatively poor performance in simulations with high noise levels. With the SNR typical of in vivo images and the appropriate additional echo spacing, however, excellent results were achieved, even in the temporal poles, the cerebellum, the scalp, and eyes. Regarding noise, UMPIRE has the advantage over spatial methods that unwrapping time is independent of noise level (as well as topographical complexity), a feature that would be valuable in on-console use.

A limitation of the sequence used in this study was that only the first echo was fully flow-compensated. This leads to vessel displacement artifact in later echoes, and velocity-induced (rather than susceptibility-induced) phase changes (28,41). This can be greatly reduced by using a bipolar flow compensation gradient before each echo (41).

Phase changes have been assumed to be linear over echo time in our approach. Phase has been shown to have a quadratic component in vessels with significant flow, however, even when bipolar flow compensation is used. This could lead to UMPIRE failing to correctly unwrap phase in large vessels, although that was not apparent in our results. Nonlinear behavior also arises in voxels containing multiple water compartments (42), an effect that has been used to image myelin. The frequency shifts involved are small, however. At less

than 5 Hz at 7T (42), δT_E would have to be exceed 100 ms for them to cause a phase wrap. As such, it is difficult to conceive of a situation in which they would jeopardize the approach outlined here.

In the current description, the steps in UMPIRE have been outlined for a multi-echo GE acquisition with three echoes. UMPIRE can be extended, without substantial modification to the method, to any number of echoes. In the simplest case, there would, as for three echoes, only be one additional delay between one pair of echoes, with all other echo spacings being equal. To optimize SNR in the DPD image, the starting point for unwrapping, the additional delay should be between either of the first two pairs of echoes, and the DPD image should be calculated from the first three echoes, to minimize T_2^* degradation of SNR.

CONCLUSIONS

The UMPIRE method allows phase images to be unwrapped even where the phase evolution between echo times is much greater than π . Only three, unequally spaced echoes are required. Phase images, rather than PD images, are generated by means of the calculation and subtraction of time-invariant contributions to the phase. As such, the method is suited to widely spaced, highly wrapped phase images acquired at very high field. The speed and simplicity of the approach make it ideally suited to implementation on the scanner console.

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FIG. 1. Data acquisition in UMPIRE (illustrated for three echoes).

The true phase and wrapped phase are plotted for a hypothetical voxel in which the phase evolution between a pair of echoes is slightly larger than 2π . Shaded bars indicate periods of echo acquisition. Central to the UMPIRE method is the additional echo delay, δT_E , between one of the pair of echoes.

FIG. 2. Steps in the UMPIRE unwrapping process.

PD images (2.) and DPD images (3.) are calculated from phase images at the three echo times (1.). The additional delay between T_{E2} and T_{E3} is chosen so that DPD is free of wraps. DPD is rescaled to the angular frequency offset ω (4.). Comparison of ω and PD images allows the number of wraps in PD images to be identified (5.) and removed (6.). A higher SNR estimation of ω (ω^*) is calculated from these (7.). Comparison of phase images (1.) with ω^* allows the number of wraps occurring in the respective echo times to be calculated (8.) and removed. These phase images are used to calculate the receiver phase offset R (10.), which is subtracted from phase images, removing wraps originating from R but reintroducing those arising from B_0 . The number of wraps in these phase images is re-estimated (12.) and removed (13.) to yield unwrapped phase images at each echo time. Steps are detailed mathematically in full in the Theory section.

FIG. 3. Comparison of phase images unwrapped with conventional temporal phase unwrapping and UMPIRE.

A: Simulated phase images have both linear echo-time dependent phase variation in the x direction (mimicking B_0) and a time-invariant phase variation in the y direction (mimicking receiver phase offset). **B:** The wrapping operator was applied to yield the phase images to be unwrapped. **C:** Conventional temporal phase unwrapping of B yields unwrapped PD images which are correct only in the region between the red arrows. **D:** If conventional temporal phase unwrapping is applied to phase images, wraps due to receiver phase offsets are also present (the arrows are explained in the main text). **E:** UMPIRE unwraps the entirety of the image. UMPIRE also removes variation in the y direction due to phase offsets. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIG. 4. Example results achieved by PRELUDE (2D), PHUN, and UMPIRE in unwrapping complex topographies (Difficulty 5, echo 3, sample slices).

FIG. 5. A comparison of the accuracy (top) and processing times (bottom) for PRELUDE (2D), PRELUDE (3D), PHUN, and UMPIRE in unwrapping complex topographies.

FIG. 6. A comparison of the accuracy (top) and processing times (bottom) for PRELUDE (2D), PRELUDE (3D), PHUN, and UMPIRE in unwrapping spheres with a range of noise.

FIG. 7. In vivo unwrapping results of a single subject comparing conventional temporal phase unwrapping and the spatial methods PRELUDE (2D) and PHUN with UMPIRE. Magnitude and phase images, and unwrapping results, are illustrated for echo 3. Unwrapping errors are marked with red arrows. Phase image scales are in radians.

FIG. 8. Demonstration of unwrapping with UMPIRE in six subjects in both a relatively inferior slice (left) and a more superior slice (right).

The third echo image is shown. Wrapped phase images are scaled between $0 \rightarrow 2\pi$ rad and unwrapped phase images $-4\pi \rightarrow +4\pi$ rad. The highest positive phase values (in inferior slices) exceed 10π rad.

FIG. 9. Triplanar view of the magnitude (top) and wrapped phase (middle) at the third echo time in a single subject (Sub5 in Fig. 8; measurement with more extensive slice coverage). UMPIRE unwraps phase in disconnected and highly wrapped regions, including the temporal lobes and cerebellum (axial section), eyes, and scalp signal (at arrows). Phase image scales are in radians. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIG. 10. Comparison of unwrapping single-channel data with the spatial methods PRELUDE (2D), PHUN, and UMPIRE.

At this threshold, PRELUDE and PHUN attempt to unwrap skull and noise (green arrows), while areas of the object are neglected (blue arrows). Unwrapping errors within the object in PHUN are indicated in red. Phase image scales are in radians. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]