

## Application of Laplacian-based Methods to Multi-echo Phase Data for Accurate Susceptibility Mapping

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## Synopsis

**In Susceptibility Mapping (SM) using multi-echo gradient-echo phase data, unwrapping and/or background-field removal is often performed using Laplacian-based methods. However, SM pipelines in the literature have applied these methods at different stages. Here, using simulated and acquired images, we compared the performance of three pipelines that apply Laplacian-based methods at different stages. We showed that Laplacian-based methods alter the linearity of the phase over time. We demonstrated that only a processing pipeline that takes this into account, i.e. by fitting the multi-echo data over time to correctly estimate a field map before applying Laplacian-based methods, gives accurate susceptibility values.**

## Introduction

In Susceptibility Mapping (SM), Laplacian-based techniques, e.g. SHARP<sup>1,2</sup>, have been used to perform unwrapping and/or background-field removal of multi-echo gradient-echo phase data. The unwrapped gradient-echo phase at time  $t$  and location  $\mathbf{r}$  is

$$n(t, \mathbf{r}) = V \cdot \Delta B(\mathbf{r}) \cdot t + n_0(0, \mathbf{r}) \quad (1),$$

where  $V$  is the proton gyromagnetic ratio,  $n_0$  the  $t = 0$  phase offset and  $\Delta B$  the total field variation from local ( $\Delta B_{loc}$ ) and background ( $\Delta B_{bg}$ ) sources. In SM, multi-echo acquisitions are preferable because they allow fitting to Equation (1) to give  $n_0$  and increase the accuracy of  $\Delta B$  estimates<sup>3</sup>.

Several studies<sup>4-6</sup> have used Laplacian unwrapping at each echo time (TE) as an initial step. Assuming  $n_0 = 0$ , a field map has then been calculated by scaling the Laplacian-unwrapped phase according to (1) at each TE and averaging the results. Similarly, other studies<sup>7,8</sup> have used simultaneous Laplacian unwrapping and background-field removal at each TE followed by scaling according to (1), again assuming  $n_0 = 0$ . However, averaging the processed phase images assumes that Laplacian-based methods preserve the linear phase-time dependence (1). In contrast, others<sup>2,9</sup> have fitted the unwrapped phase over TEs to calculate  $\Delta B$  (and  $n_0 = 0$ ) and have then removed  $\Delta B_{bg}$  from the fitted  $\Delta B$  using a Laplacian-based technique.

## Purpose

Here, we applied three processing pipelines<sup>2,4-9</sup> to phase images of a numerical phantom and a healthy volunteer. We investigated the effect of using Laplacian-based methods at different stages of the SM pipeline on the phase-time linearity (1) and the accuracy of  $\mathbf{j}$  estimation.

## Methods

Laplacian-based phase unwrapping (*Lap-Unw*) or background-field removal (*Lap-Bg*) were implemented with SHARP<sup>1,2</sup> and a 3x3x3 Laplacian kernel<sup>2</sup>. For *Lap-Unw*, non-eroded brain mask (FSL BET<sup>10</sup> for the volunteer) and threshold<sup>11</sup>  $f = 10^{-10}$  were used. For *Lap-Bg*, the same brain mask with 2-voxel<sup>12</sup> erosion and threshold<sup>2</sup>  $f = 0.05$  were used.

## Phantom

Wrapped phase ( $n_0 = 0$ ) was simulated at five echoes ( $TE_1/\Delta TE = 10/10$  ms) from a ground-truth susceptibility distribution<sup>13,14</sup> (Zubal phantom<sup>15</sup>, Figure 1), using a Fourier-based forward model<sup>16</sup>. Background-field free field maps were then calculated using three distinct pipelines:

- **Avg-Unw**: *Lap-Unw*<sup>1</sup> on the phase at each TE; field map calculation:<sup>5</sup>

$$\Delta B = \frac{\sum_{\text{echo}=1}^5 n_{\text{echo}}(TE_{\text{echo}}, \mathbf{r})}{V \sum_{\text{echo}=1}^5 TE_{\text{echo}}} \quad (2)$$

then  $Lap-Bg^1$  on  $\Delta B$ .

- **Avg-Bg**:  $Lap-Bg^2$  on the phase at each TE; field map calculation:<sup>7</sup>

$$\Delta B = \frac{1}{5} \sum_{\text{echo}=1}^5 \frac{n(TE_{\text{echo}}, \mathbf{r})}{V \cdot TE_{\text{echo}}} \quad (3).$$

- **Fit**: linear fit of the simulated (non-wrapped) phase over TEs;  $Lap-Bg^2$  on the fitted  $\Delta B^{2,9}$ .

$J$  maps were calculated (TKD<sup>17</sup> with correction for underestimation<sup>2</sup> and  $W=2/3$ ) to assess the effect of each pipeline on the  $J$  values.  $J$  mean, standard deviation (SD) and Root Mean Square Error (RMSE) were calculated in all the regions of interest (ROIs) shown in Figure 1.

### Volunteer

3D gradient-echo brain images of a healthy volunteer were acquired on a Philips Achieva 3T scanner with a 32-channel head coil, 1-mm isotropic resolution, 7 echoes ( $TE_1/\Delta TE = 3.7/6.9$  ms), TR = 50 ms, SENSE factor = 2 and flip angle = 10°.

The effect of  $Lap-Unw$  and  $Lap-Bg$  was tested. For comparison, the phase at each TE was also unwrapped with PRELUDE<sup>18</sup>. The mean and SD of the processed phase were calculated in three ROIs (Figure 3a) drawn on the fifth-echo magnitude image.

### Results and Discussion

Laplacian-based processing altered the linearity of the phase-time relationship (1) in both the numerical phantom (Figure 2) and the volunteer (Figure 3). Such alterations of (1) were expected, because SHARP<sup>2</sup> involves non-linear operations. These findings suggest that Laplacian unwrapping does not only unwrap the phase but also removes some  $\Delta B_{bg}$  from  $\Delta B$ , even with a very small  $\tau$ .

In the phantom, scaling and averaging the SHARP-processed phase caused inaccuracies in the estimated field maps (Figure 4) and, therefore, errors in  $J_{Avg-Unw}$  and  $J_{Avg-Bg}$  versus  $J_{Fit}$  (Figure 5). Unlike  $J_{Fit}$ ,  $J_{Avg-Unw}$  and  $J_{Avg-Bg}$  underestimated  $J_{True}$  in the caudate nucleus and globus pallidus, whereas all mean  $J$  estimates were similar in the thalamus and white matter.  $J_{Fit}$  had the lowest SDs or the smallest RMSE values in all ROIs except the globus pallidus, in which, however,  $J_{Fit}$  had the lowest RMSE as a percentage of  $J_{Fit}$ .

### Conclusions

We demonstrated that Laplacian-based techniques alter the phase-time linearity (1). We also showed that **Fit**, therefore, gave the most accurate  $J$  results, suggesting that **Fit**, or analogous pipelines<sup>13</sup> that fit the phase over multiple echoes, should be used before applying Laplacian-based methods.

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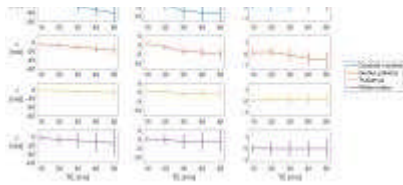
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Figures

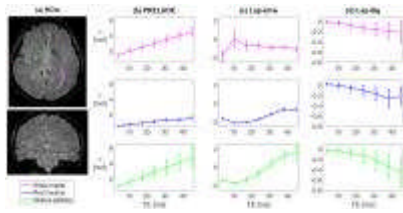


**Figure 1.** Susceptibility phantom and J values. J values were taken from Ref. 13 for white matter, caudate nucleus, putamen, globus pallidus, thalamus, superior sagittal sinus and other brain regions and from Ref. 14 for air/non-brain regions.

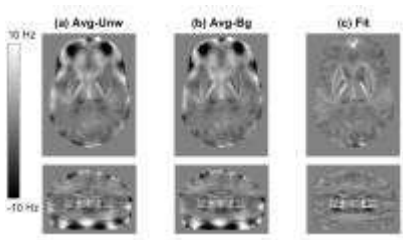




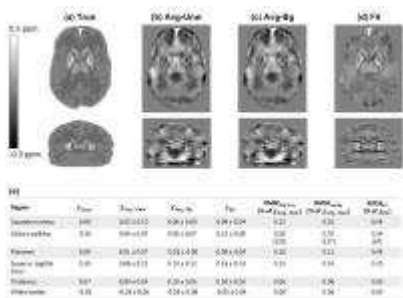
**Figure 2. Phantom:** effect of **Avg-Unw** (b) and **Avg-Bg** (c) on the phase simulated from the ground-truth  $j$  distribution (a). Mean and SD of the phase in four ROIs (caudate nucleus, thalamus, globus pallidus and white matter) are plotted against TEs.



**Figure 3. Healthy volunteer:** effect of PRELUDE unwrapping (b), *Lap-Unw* (c) and *Lap-Bg* (d) on the measured phase. Mean and SD of the phase in three ROIs drawn on the fifth-echo magnitude image (a) are plotted against TEs.



**Figure 4. Phantom:** transverse and coronal slices of field maps calculated with **Avg-Unw** (a), **Avg-Bg** (b) and **Fit** (c).



**Figure 5. Phantom:** transverse and coronal slices of  $j$  maps calculated with **Avg-Unw** (b), **Avg-Bg** (c) and **Fit** (d) versus the true  $j$  (a).

The table (e) shows the true and calculated  $j$  [ppm] (mean  $\pm$  SD) and the RMSEs [ppm] for each method in all ROIs.