

# iHARPERELLA: an improved method for integrated 3D phase unwrapping and background phase removal

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**TARGET AUDIENCE:** Clinicians and scientists interested in the application of quantitative susceptibility mapping (QSM).

**PURPOSE:** QSM is a recently developed MRI technique that provides a quantitative measure of tissue magnetic susceptibility, and has demonstrated promising applications in many neurological diseases with demyelination and iron overload. Although QSM itself required sophisticated steps for the inversion, the quality of phase pre-processing, i.e. 3D phase unwrapping and background phase removal, also plays very important roles in determining the final quality of the QSM reconstruction. Previously, we have developed a method for integrated method for phase unwrapping and harmonic background phase removal using Laplacian, namely the HARPERELLA method (1). In this abstract, we introduced an improved version of this HARPERELLA method, which allows more robust suppression of the low frequency background phase and allowed the input of unwrapped phase by other methods. This iHARPERELLA method is provided in the software package of “STI Suite”, which is available online at <http://people.duke.edu/~c1160/>.

**METHODS:** *Brain Imaging:* In vivo brain imaging of a healthy adult volunteer was conducted on a GE MR750 3.0T scanner (GE Healthcare, Waukesha, WI) equipped with an 8-channel head coil. High-resolution phase images with whole-brain coverage were acquired using a standard flow-compensated 3D spoiled-gradient-recalled (SPGR) sequence with the following parameters: TE = 42 ms, TR = 60 ms, flip angle = 20°, FOV = 256x256x180 mm<sup>3</sup>, matrix size = 256x256x180. This protocol resulted in an isotropic resolution with a voxel size of 1x1x1 mm<sup>3</sup>.

*Data Analysis:* The previous HARPERELLA method essentially solved a boundary problem for inverse Laplacian by estimating the phase Laplacian outside the brain to compensate the background phase from the phase Laplacian inside the brain. In this study, we improved this method with a more robust implementation.

For raw phase, the phase Laplacian  $\nabla^2\varphi$  is also calculated using the sine and cosine functions of the brain:

$$\nabla^2\varphi = \cos\varphi \cdot \nabla^2 \sin\varphi - \sin\varphi \cdot \nabla^2 \cos\varphi \quad [1]$$

Alternatively, unwrapped phase obtained by the traditional path-based phase unwrapping method, e.g. the method described in (2), can also be used as the input. In that case, the Laplacian is obtained as:

$$\nabla^2\varphi = -4\pi^2 FT^{-1} \left[ k^2 FT(\varphi) \right] \quad [2]$$

It is important to note that this operation is implemented using Fourier transforms and zero padding the phase maps to improve the calculation accuracy. The phase outside the brain tissue is obtained from the following minimization:

$$\min_{\nabla^2\varphi_{out}} \left\| W_{Brain} \cdot FT^{-1} \left\{ \frac{1}{k^2} \cdot FT \left[ \nabla^2\varphi \cdot M_{Brain} + \nabla^2\varphi_{out} (1 - M_{Brain}) \right] \right\} \right\|_2 \quad [3]$$

Here  $M_{Brain}$  is brain mask,  $W_{Brain}$  is a weighing function defined according to the brain geometry. This equation is solved using the LSQR method in Matlab. The final tissue phase can be determined as follows:

$$\varphi = M_{Brain} \cdot FT^{-1} \left\{ \frac{1}{k^2} \cdot FT(\nabla^2\varphi \cdot M_{Brain} + \nabla^2\varphi_{out} (1 - M_{Brain})) \right\} \quad [4]$$

**RESULTS:** Fig. 1 illustrated the main steps for iHARPERELLA. From the raw phase (Fig. 1A), the Laplacian of the brain tissue can be calculated (Fig. 1B). Subsequently, the optimal Laplacian outside the brain can be obtained using Eq. 3 (Fig. 1C). By combining the Laplacians, the brain tissue phase can be obtained using the inverse Laplacian as described in Eq. 4 (Fig. 1D).

iHARPERELLA allows two types of inputs: (1) the raw phase, and (2) the unwrapped phase obtained by traditional path-based phase unwrapping. Their differences are shown in Fig. 2. If raw phase is used as the input, the Laplacian-based phase unwrapping is used, which will NOT affect local gray-white matter contrast, but will lead to local differences around the veins from the raw phase (Fig. 2E). In this case, the comparison is made with V-SHARP [1] filtered phase to avoid the contamination of large background phase (Fig. 2D). In contrast, if the unwrapped phase by path-based phase unwrapping is used as the input, the local phase contrast around the veins will not be altered.

**DISCUSSION:** There are two differences between the iHARPERELLA and HARPERELLA: (1) iHARPERELLA provides more robust suppression of low frequency background phase that has been tested using many datasets; and (2) iHARPERELLA allows the use of unwrapped phase obtained by the traditional path-based phase unwrapping to preserve the local phase contrast around the venous networks. Both HARPERELLA and iHARPERELLA share the same feature that they do not require any regularization.

**CONCLUSION:** iHARPERELLA is a significantly improved integrated 3D phase unwrapping and background phase removal method, which provides a useful tool for routine phase processing for QSM and susceptibility tensor imaging.

**REFERENCES:** (1) Li et al, NMR Biomed 2014; 27:219. (2) Abdul-Rahman et al, Int. Soc. Opt. Photonics. 2005:32-40.

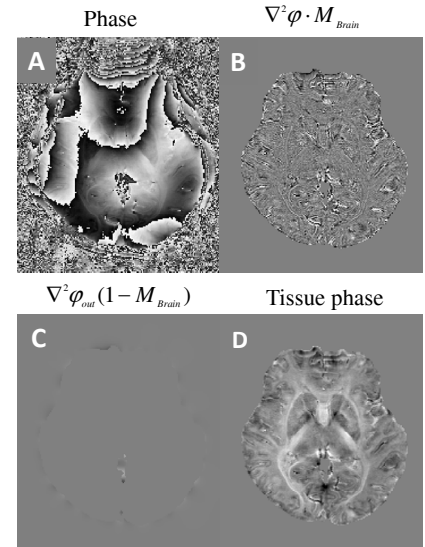


Fig. 1. Main steps of iHARPERELLA. A: raw phase. B: Tissue Laplacian. C: Optimized Laplacian outside the brain. D: Brain phase.

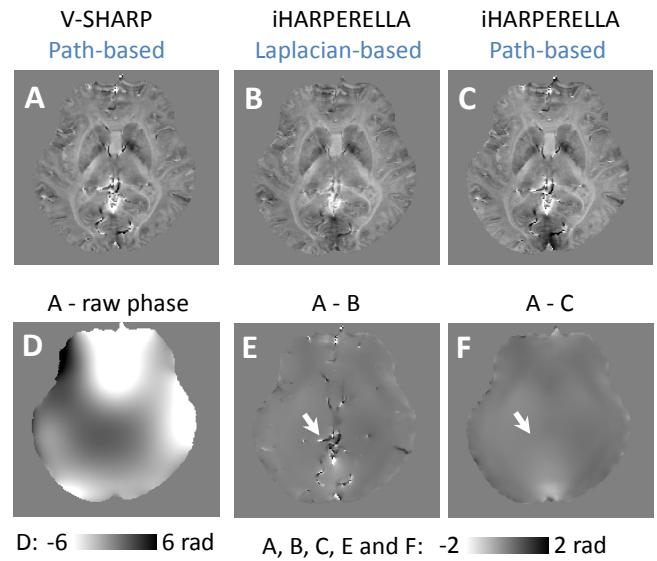


Fig. 2. Differences between phase processing methods. A-C: phase processed with V-SHARP or iHARPERELLA with path-based or Laplacian-based phase unwrapping. D: the difference between A and raw phase. E and F: the difference between A and B, and between A and C.