

# ADJUSTED NONLINEAR REGISTRATION IN SPATIAL NORMALIZATION FOR REAL-TIME fMRI

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## PURPOSE

Real-time functional magnetic resonance imaging (rtfMRI) is a novel neurofeedback technique that permits simultaneous measurement and observation of brain activity during an ongoing task [1]. In rtfMRI, the entire data processing has to be completed within a single repetition time (TR). In consideration of the real-time requirement, the data preprocessing in rtfMRI mainly includes head motion correction and spatial smoothing. As a common data preprocessing procedure in offline processing of fMRI data, spatial normalization can provide abundant referential information for the brain region recognition in rtfMRI [2]. Generally, spatial normalization consists of the affine registration (AR) and nonlinear registration (NR) [3, 4], and NR is a time-consuming process that make spatial normalization can not be finished within one TR. The NR, which is normally modeled by the combination of a series of discrete cosine transform (DCT) basis functions, is used to estimate the nonlinear deformation parameters by optimizing the cost function. The cutoff frequency of DCT basis function determines the number of basis functions, which extremely affects the accuracy and runtime of spatial normalization. In this paper, we discussed the cutoff frequency and iteration number using bisection method, which were two key conditions of NR, and then proposed an adjusted NR method to meet the real-time requirement of rtfMRI.

## METHODS

Based on the NR of spatial normalization in SPM, the cutoff frequency of DCT basis function determines the number of basis functions and the number ( $N$ ) of coefficients describing the deformations. The cutoff frequency can be termed as  $L_c$ , which is measured in millimeters and proportional to  $N^{1/3}$ . In SPM, the default  $L_c$  of 25 mm and the default iteration number ( $DIN$ ) of sixteen, which are also sufficient for the structural MRI spatial normalization, make the runtime much longer than a TR. Therefore, for fMRI image with lower spatial resolution than the structural MRI image, appropriately increasing  $L_c$  to reduce  $N$  and decreasing iteration number is reasonable and necessary for the online process. Using the bisection method, the value of  $N$  with the default  $L_c$  of 25 mm is reduced by half of the previous value over three instances. The corresponding  $L_c$ s are 31 mm, 40 mm, 50 mm. The detailed process to achieve an adjusted NR method that meets the real-time requirement is described as follows: Firstly, the mean cost functions with the series of  $L_c$ s are computed along the iteration number, by which the adjusted iteration number ( $AIN$ ) is defined. Secondly, the runtime of NR with a series of  $L_c$ s under the iteration number  $AIN$  and  $DIN$  are computed and compared. Then, the least  $L_c$  that meets the real-time requirement is acquired. Thirdly, the mean squared errors (MSE) [5] between the EPI template and the normalized images by NR without any adjustments and with a series of  $L_c$ s under the iteration number  $AIN$  are summarized. To some degree, the MSE could reflect the accuracy of spatial normalization. The larger MSE means lower accuracy. The paired t-test is used to test the difference between the MSE by NR without any adjustments and the MSEs by NR with a series of  $L_c$ s under the iteration number  $AIN$ . Then, the largest  $L_c$  that keeps the moderate accuracy is obtained.

## RESULTS

The fMRI data, from twenty subjects (age  $22.3 \pm 1.6$ , 8 females), was scanned using a 3.0-T Siemens MRI scanner. A single-shot T2\*-weighted gradient-echo echo-planar imaging (EPI) sequence (TR/TE/flip angle = 2000 ms/40 ms/90°, matrix size =  $64 \times 64$ , voxel size =  $3.1 \times 3.1 \times 4.8$  mm<sup>3</sup>, slice thickness = 4 mm, slice gap = 0.8 mm) was used to acquire each volume with 32 axial slices in the interleaved order. The fMRI data was normalized to the EPI template provided by SPM using spatial normalization with different NR methods. After ten iterations, the cost function got plane and could not be reduced in a large amount, so the  $AIN$  was set to ten (Fig. 1). The runtime with  $L_c$ s of more than 31 mm under the iteration number  $AIN$  was less than half a TR, which might meet the real-time requirement (Fig. 2). There was a significant difference between the MSE by NR without any adjustments and the MSE by NR with the  $L_c$  of 50 mm under the iteration number  $AIN$  (Fig. 3). In addition, the results of suggested  $L_c$  of 35 mm were also provided in the figures.

## DISCUSSION

The  $L_c$  (or cutoff frequency) and iteration number affects the runtime and accuracy of spatial normalization in a large amount. There are mainly three rules that could be derived or presented by the results. Firstly, the iteration number can be limited to reduce the runtime, because the change of cost function will be plane after ten iterations (Fig. 1). Secondly, the runtime can be reduced by increasing the  $L_c$ . It can be observed from Fig. 2 that the runtime is nearly proportional to the  $L_c^3$ , because the runtime is proportional to  $N$  that is proportional to the  $L_c^3$ . Thirdly, the MSE increases along with the rising  $L_c$ , which is almost linear related to the  $L_c$  (Fig. 3). It means that the accuracy decreases with the  $L_c$  growing. Therefore, the NR method, which can keep moderate accuracy and meet the real-time requirement, could be achieved by properly adjusting the  $L_c$  and iteration number.

## CONCLUSION

Considering the entire data processing of rtfMRI, the runtime of NR should be at least less than half a TR to reserve time for other processing procedures. When the  $L_c$  is more than 31 mm and less than 40 mm and the iteration number is set to ten, the adjusted NR can keep the moderate accuracy and meet the real-time requirement of rtfMRI. The proposed NR method could also provide a reference for further improvements of real-time spatial normalization.

## REFERENCES

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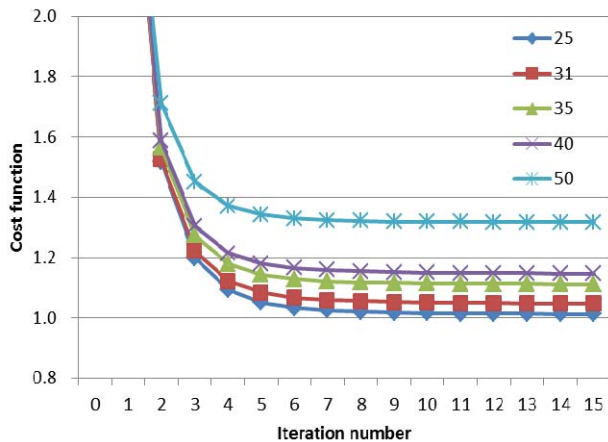


Fig. 1. The mean cost function of NR along with the iteration number, with different  $L_c$ s of 25 mm, 31 mm, 35 mm, 40 mm, and 50 mm.

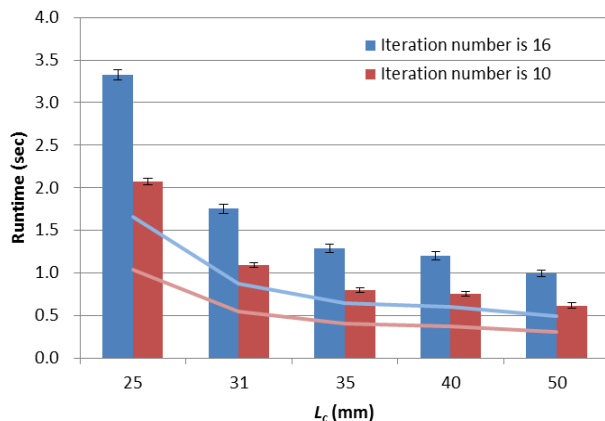


Fig. 2. The runtime of NR along with different  $L_c$ s of 25 mm, 31 mm, 35 mm, 40 mm, and 50 mm, under adjusted 10 iterations and default 16

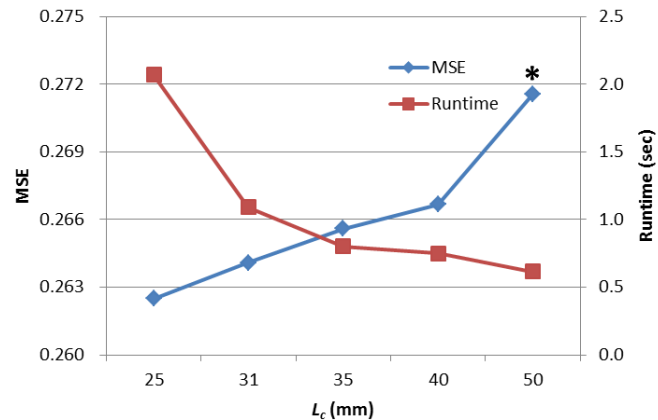


Fig. 3. The MSE and runtime along with different  $L_c$ s of 25 mm, 31 mm, 35 mm, 40 mm, and 50 mm, under adjusted 10 iterations. By paired t-test, the difference with the  $L_c$  of 50 mm shows significance (\*).