Improving Quantitative CT Perfusion Parameter Measurements Using Principal Component Analysis

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Rationale and Objectives: To evaluate the improvements in measurements of blood flow (BF), blood volume (BV), and permeability–surface area product (PS) after principal component analysis (PCA) filtering of computed tomography (CT) perfusion images. To evaluate the improvement in CT perfusion image quality with poor contrast-to-noise ratio (CNR) in vivo.

Materials and Methods: A digital phantom with CT perfusion images reflecting known values of BF, BV, and PS was created and was filtered using PCA. Intraclass correlation coefficients and Bland–Altman analysis were used to assess reliability of measurements and reduction in measurement errors, respectively. Rats with C6 gliomas were imaged using CT perfusion, and the raw CT perfusion images were filtered using PCA. Differences in CNR, BF, BV, and PS before and after PCA filtering were assessed using repeated measures analysis of variance.

Results: From simulation, mean errors decreased from 12.8 (95% confidence interval [CI] = −19.5 to 45.0) to 1.4 mL/min/100 g (CI = −27.6 to 30.4), 0.2 (CI = −1.1 to 1.4) to −0.1 mL/100 g (CI = −1.1 to 0.8), and 2.9 (CI = −2.4 to 8.1) to 0.2 mL/min/100 g (CI = −3.5 to 3.9) for BF, BV, and PS, respectively. Map noise in BF, BV, and PS were decreased from 51.0 (CI = −3.5 to 105.5) to 11.6 mL/min/100 g (CI = −7.9 to 31.2), 2.0 (CI = 0.7 to 3.3) to 0.5 mL/100 g (CI = 0.1 to 1.0), and 8.3 (CI = −0.8 to 17.5) to 1.4 mL/min/100 g (CI = −0.4 to 3.1), respectively. For experiments, CNR significantly improved with PCA filtering in normal brain ($P < .05$) and tumor ($P < .05$). Tumor and brain BFs were significantly different from each other after PCA filtering with four principal components ($P < .05$).

Conclusions: PCA improved image CNR in vivo and reduced the measurement errors of BF, BV, and PS from simulation. A minimum of four principal components is recommended.

Key Words: CT perfusion; principal component analysis; image noise; brain tumor; blood flow.

Computed tomography (CT) perfusion is a diagnostic tool for the evaluation of acute ischemic stroke, and it is becoming increasingly used for measuring blood flow (BF), blood volume (BV), and permeability–surface area product (PS) in malignant brain tumors (1). The measurements of BF, BV, and PS in tumors are affected by CT perfusion image contrast-to-noise ratio (CNR). Recently, Balvay et al. (2) showed that filtering CT perfusion images with principal component analysis (PCA) improved CNR in CT perfusion images of patients with ovarian and metastatic renal tumors. It is not known whether PCA can improve CNR of CT perfusion images of patients with malignant brain tumors, which have a lower CNR because of lower tumor blood flow in the brain compared to other malignancies such as metastatic renal tumors (3–6). In preclinical imaging of cancer models with a clinical CT scanner, a high spatial resolution is desirable to detect small tumors. However, CNR from scanning small animals is low because: (1) image noise increases with higher spatial resolution (ie, smaller pixel size); and (2) the effect of partial volume averaging is more prominent in small animals than in humans. Therefore, we hypothesized that CT perfusion images of a preclinical model of malignant glioma are useful to evaluate the ability of PCA in improving image quality under low-CNR condition. It has not been demonstrated that an increase in CNR after PCA filtering improves the measurements of BF, BV, and PS. Accurate and precise measurements of these parameters are important because they have been shown to be

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valuable for grading gliomas (1,6) and for distinguishing recurrent tumor from treatment-induced necrosis (7).

In this study, we first designed a digital phantom to validate PCA image filtering by comparing the accuracies and precisions of BF, BV, and PS without and with PCA filtering of simulated CT perfusion images. We then evaluated the improvement in CNR and changes in BF, BV, and PS measurements after PCA filtering CT perfusion images of a malignant rat glioma model.

MATERIALS AND METHODS

Validation of PCA by Simulation

A digital phantom of CT perfusion images with time-attenuation curves (TAC) reflecting known values of BF, BV, and PS was developed. The phantom consisted of 16 CT slices and 44 sequential images for each slice simulating a two-phase CT perfusion protocol. Images were simulated at 1.4-second intervals during the first phase of 30-seconds and then at 15-second intervals during the second phase of 300-seconds. Each image contained 3 × 4 tiles of 10 × 10 pixels, which resembled the number of pixels in an axial rat brain CT image. Pixels in each tile had the same TAC simulating known values of BF, BV, and PS. Each tile was assigned with increasing mean transit times (MTTs; 4, 4.5, 5.0, …, 9.5 s) and extraction fraction (E; 0.05, 0.06, …, 0.14, 0.3, 0.4). Each slice was assigned to two different BV values, the range of values were 0.5, 1.0, 1.5, …, 8 mL/100 g. BF values (3.2–120 mL/min/100 g) were calculated as BV/MTT, and PS values (0.4–25.8 mL/min/100 g) were obtained using $-BF \times \ln(1-E)$ (8). Based on the Johnson–Wilson model, these values were used to simulate different impulse residue functions for each tile (9). A population-averaged arterial TAC was generated by averaging TACs from carotid arteries of nine Wistar rats. Each impulse residue function was convolved with the population-averaged arterial TAC to generate a tissue TAC. The values of the TACs at different time points were embedded into the corresponding pixels to generate CT perfusion images of the digital phantom. Appendix 1 describes the mathematical details on how the tissue TACs were simulated. In total, the set of noise-free CT perfusion images in the digital phantom gave rise to 192 different TACs with different combinations of BF, BV, and PS values. This phantom reflected values of BF, BV, and PS in the physiological range of a rat. The design of this phantom is illustrated in Figure 1.

To add image noise to the set of noise-free CT perfusion images, a rat was scanned *without* contrast injection in high-resolution mode with a clinical CT scanner (Discovery 750 HD; GE Healthcare, Waukesha, WI) using the same two-phase CT perfusion protocol as the simulation. The scanning parameters were 80 kVp, 120 mAs, 0.4 s/rotation, 10 cm field of view, 16 slices, and 1.25 mm slice thickness (voxel size is 0.2 × 0.2 × 1.25 mm). A high-definition bone filter with a limiting in-plane resolution of 0.33 mm was used to

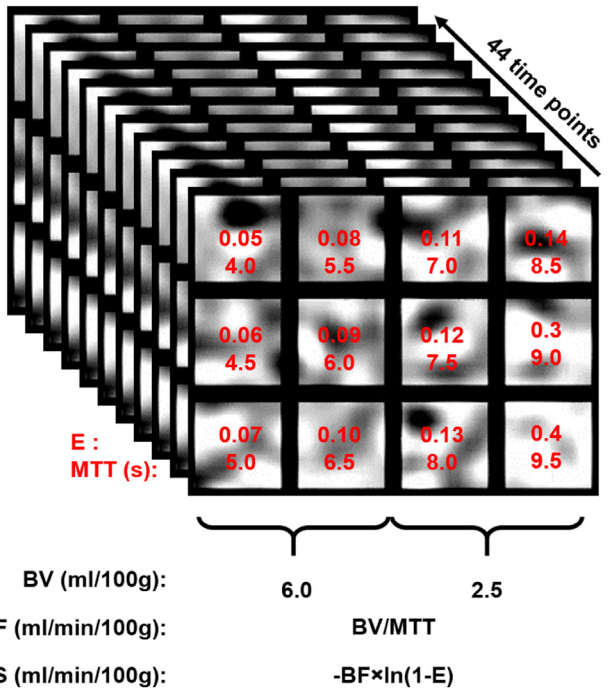

Figure 1. An example of one slice (out of 16 slices) of the digital computed tomography perfusion phantom with image noise. Each tile contains tissue-enhancement curves reflecting a combination of extraction fraction (E), mean transit time (MTT), blood volume (BV), blood flow (BF), and permeability–surface area product (PS).

reconstruct the images. Adaptive statistical iterative reconstruction (ASIR) was used to reconstruct the images. The skull was used to rigidly register the images using the prototype version of CT Perfusion 4D (GE Healthcare) to minimize misregistration due to motion in the axial plane. A "noiseless" CT image for each slice was generated by averaging the series of noncontrast CT images of the same slice. The set of noise *only* images of each slice was obtained by subtracting the average CT image from each CT image of the same slice. This set of noise images was added one by one to the set of noise-free CT perfusion images. The final set of noisy images was designated as the unfiltered CT perfusion images of the digital phantom, and they were then filtered using PCA.

Principal Component Analysis

PCA is a statistical technique that transforms a set of multidimensional observations into principal components that describe the variance of the original set of observations (2). In the context of a series of m dynamic images from a CT perfusion study, attenuation in each pixel as a function of time was measured as a TAC. If one interprets each TAC as m numbers of observations, PCA linearly transforms the possibly correlated m variables into a set of principal components that are uncorrelated with each other. The linear transformations are defined so that the first principal component has the largest variance, which describes the most informative part of the data. Each subsequent principal component