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Perfusion CT in Acute Stroke: A Comprehensive Analysis of Infarct and Penumbra

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Appendix E1

Maximum Slope (Peters) Model

Under the assumption of no venous outflow, CBF can be calculated as the maximum initial slope of the time-enhancement curve in tissue divided by the maximum enhancement within the brain-supplying artery (20).

CBV is defined as the fractional vascular volume within a tissue voxel. The CBV is calculated as the maximum enhancement of the time-enhancement curve in tissue divided by the maximum enhancement in blood (21).

MTT is calculated as the ratio of CBV to CBF for each pixel according to the central volume principle.

Time to peak is calculated in seconds as the time from the start of contrast material arrival in the AIF to the peak of the time-enhancement curve for each voxel.

Partial Deconvolution

The MTT map is calculated by using a closed-form (noniterative) deconvolution approach (22). A box-shaped residue function of a certain width can be convolved with the AIF to produce a simulated time-enhancement curve. A series of width values are evaluated by means of least-mean-squares fitting of the simulated curves against the measured time-enhancement curve, and the MTT is determined as the width value corresponding to the best fit.

The CBV map is calculated by dividing the AUC by the AUC of the scaled AIF. To remove the effect of contrast material recirculation on the calculation of CBV, a gamma-variate curve fitting is applied to the time-attenuation curves of tissue and AIF respectively. The gamma-variated fitted curves are used for CBV calculation in this study.

CBF is calculated as the ratio of CBV to MTT for each pixel according to the central volume principle.

Time to peak is calculated in the same way as with the maximum slope method. That is, the time to peak is calculated in seconds as the time from the start of contrast material arrival in the AIF to the peak of the time-enhancement curve for each voxel.

SVD

The tissue time-enhancement curves are deconvolved with the AIF by using the SVD method (23) to produce an impulse residue function (IRF), and various perfusion maps can be calculated from this IRF. CBF is calculated from the peak height of the IRF curve, CBV is calculated from the area under the IRF curve, and MTT is calculated as the ratio of CBV to CBF according to the central volume principle.

In addition, the peak of the IRF curve may not always occur at zero time point, particularly for pixels with abnormal perfusion. T_{max} is calculated from the time to peak of the IRF curve, where T_{max} = 0 reflects normal blood supply in normal tissue without delay. Conversely, T_{max} > 0 is often associated with an acute ischemic lesion owing to arterial delay and dispersion effect. A global SVD threshold of Psvd (partial SVD) = 0.2 was used in this study.

SVD with Delay Correction

To compensate for arterial delay and dispersion effects, a vascular transport model involving an arterial transport function with a delay time and a relative dispersion has been proposed (24). The effect of the arterial transport function is to shift and broaden the AIF profile in an attempt to more realistically model the physiology of acute stroke. This method uses a delay-corrected SVD deconvolution approach by applying a series of delay time values, DTi, ranging from 0 to T_{max}. For each delay time, a modeled arterial transport function is convolved with the measured global AIF to produce an AIFi, which is used for SVD of the tissue curve to generate an IRFi with its maximum appearing at T_{max}(i). The actual delay time, DT, is determined as the minimum DTi value, which produces T_{max}(i) = 0. Subsequently, CBF and CBV can be determined by the peak height and AUC of IRFi, respectively, with MTT calculated as the ratio of CBV to CBF. A constant relative dispersion value of 0.35 is used in this study. It should be pointed out that delay time is different from T_{max}.

Block-Circulant Deconvolution

In the case of major vessel disease, such as acute stroke or carotid artery stenosis, the measured AIF is often associated with a delay and dispersion before it reaches the tissue of interest and causes overestimation of the MTT and underestimation of the CBF (13). The block-circulant deconvolution method (12) was proposed as a delay-insensitive deconvolution technique to avoid CBF underestimation. This approach extends the conventional SVD method by using a block-circulant matrix. Because the block-circulant method may produce spurious oscillations dominating the deconvolved IRF, it uses an optimization approach by minimizing an oscillation index with adjustable pixel-dependent global SVD threshold. Use of a delay time calculated with block-circulant deconvolution was labeled as dT_{max} to reduce confusion with other measures of time to peak, T_{max}, or delay.

Stroke-Stenosis Model

In contrast to the delay-corrected SVD method, this model is based on a forward-deconvolution method using least-square-fitting deconvolution involving the vascular transport model as described above. Because all model-free deconvolution methods (eg, SVD) are sensitive to noise, some mathematic cut-off threshold (global SVD threshold) has to be assumed to derive meaningful tissue IRF. Conversely, the least-square-fitting deconvolution method uses the distributed-parameters model to attempt to describe a more realistic tissue IRF, where all perfusion parameters (CBV, CBF, MTT, delay time, arterial dispersion, and tissue dispersion) can be determined with least-square fitting (20). For the purpose of comparison in this study, a constant arterial relative dispersion value of 0.35 is used (not a fitting parameter).

To minimize the noise effect from CT perfusion imaging data, the time-enhancement curve is smoothed with a gamma-variate least-mean-square fitting method. The fitted curves are used for the calculation of the perfusion maps.

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Table E1. Details of Best Thresholds for Infarct Core and Perfusion Lesion for Maximum Slope Model							
Parameter	AUC*	Sensitivity	Specificity	PPV	NPV	Mean Volume Error (mL ⁻¹)†	‡
Infarct core definition							
CBF ≤40%	0.69	0.4	0.91	0.47	0.88	-5.8 (-1.5, -9.3)	0.61
CBF ≤45%	0.69	0.46	0.89	0.45	0.89	-0.8 (-5.1, 7.3)	0.65
CBF ≤50%	0.69	0.52	0.86	0.42	0.9	4 (-0.9, 8.3)	0.64
Perfusion lesion definition							
MTT ≥140%	0.71 (0.05)	0.67	0.74	0.62	0.78	1.5 (-2.4, 5.2)	0.73
MTT ≥145%	0.71 (0.05)	0.63	0.78	0.65	0.77	0.1 (-4.3, 4.5)	0.76‡
MTT ≥150%	0.71 (0.05)	0.6	0.81	0.66	0.76	-1.4 (-5.3, 6.5)	0.73
Double core threshold							
MTT ≥145% and CBF ≤40%	0.67	0.53	0.77	0.96	0.088	-3.9 (-6.4, 2.5)	0.69‡
MTT ≥145% and CBV ≤30%	0.63	0.32	0.92	0.98	0.8	2.8 (2, 3.6)	0.64

Note.—Data are results for the detection of the acute infarct core and perfusion lesion and the combination of results required for an effective mismatch to improve the accuracy of acute infarct core detection. An MTT of ≥145% is the most accurate when defining the acute perfusion lesion. The infarct core is best defined by a CBF of ≤45%. When combined with the perfusion lesion threshold of MTT ≥145%, a CBF of ≤40% is the most accurate for defining the acute infarct core. NPV = negative predictive value, PPV = positive predictive value.

* Numbers in parentheses are standard deviations.

† Numbers in parentheses are 95% CIs.

‡ P = .05.

Table E2. Details of Best Thresholds for Infarct Core and Perfusion Lesion for Partial Deconvolution							
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Note.—Data are results for the detection of the acute infarct core and perfusion lesion and the combination of results required for an effective mismatch to improve the accuracy of acute infarct core detection. An MTT of ≥155% is the most accurate when defining the acute perfusion lesion. The infarct core is best defined by a CBF of ≤20%. When combined with the perfusion lesion threshold, a CBF of ≤20% is the most accurate for defining the acute infarct core. NPV = negative predictive value, PPV = positive predictive value, TTP = time to peak.

* Numbers in parentheses are 95% CIs.

† P = .05.

Table E3. Details of Best Thresholds for Infarct Core and Perfusion Lesion for SVD							
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Note.—Data are results for the detection of the acute infarct core, perfusion lesion, and the combination of results required for an effective mismatch to improve the accuracy of acute infarct core detection. A T_{max} of ≥6 seconds is the most accurate when defining the acute perfusion lesion. The infarct core is best defined by a CBF of ≤25%. When combined with the perfusion lesion threshold, a CBF of ≤7.5 mL/100 g/min is the most accurate for defining the acute infarct core. NPV = negative predictive value, PPV = positive predictive value.

* Numbers in parentheses are 95% CIs.

† P = .05.

Table E4. Details of Best Thresholds for Infarct Core and Perfusion Lesion for SVD with Delay Correction							
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Note.—Data are results for the detection of the acute infarct core and perfusion lesion and the combination of results required for an effective mismatch to improve the accuracy of acute infarct core detection. A relative delay of ≥2 seconds is the most accurate when defining the acute perfusion lesion. The infarct core is best defined by a CBF of ≤45%. When combined with the perfusion lesion threshold, a CBF of ≤40% is the most accurate for defining the acute infarct core. NPV = negative predictive value, PPV = positive predictive value.

* Numbers in parentheses are 95% CIs.

† P = .05.

Table E5. Details of Best Thresholds for Infarct Core and Perfusion Lesion for Block-Circulant Deconvolution							
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Note.—Data are results for the detection of the acute infarct core and perfusion lesion and the combination of results required for an effective mismatch to improve the accuracy of acute infarct core detection. A relative T_{max} of ±4 seconds is the most accurate when defining the acute perfusion lesion. The infarct core is best defined by a CBF of ≤15 mL/100 g/min. When combined with the perfusion lesion threshold, a CBF of ≤15 mL/100 g/min is the most accurate for defining the acute infarct core. NPV = negative predictive value, PPV = positive predictive value.

* Numbers in parentheses are 95% CIs.

† P = .05.

Table E6. Details of Best Thresholds for Infarct Core and Perfusion Lesion for the Stroke-Stenosis Model							
Click to view table							

Note.—Data are results for the detection of the acute infarct core and perfusion lesion and the combination of results required for an effective mismatch to improve the accuracy of acute infarct core detection. A CBF of 20 mL/100 g/min is the most accurate for defining the acute perfusion lesion. The infarct core is best defined by a CBF of 10 mL/100 g/min. When combined with the perfusion lesion threshold, a CBF of 10 mL/100 g/min is the most accurate to define the acute infarct core. NPV = negative predictive value, PPV = positive predictive value.

* Numbers in parentheses are 95% CIs.

FiguresReferencesRelatedDetails

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Abbreviations

AIF	arterial input function
AUC	area under the ROC curve
CBF	cerebral blood flow
CBV	cerebral blood volume
CI	confidence interval
MTT	mean transit time
ROC	receiver operating characteristic
SVD	singular value deconvolution
T _{max}	time to peak of the residual function

Metrics

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