

Introduction:

The severity and duration of hypoperfusion are essential determinants of the severity of damage resulting from ischemic stroke and the potential tissue outcome.

Imaging of perfusion and related hemodynamic parameters is possible using bolus injection of an intravascular tracer and repeated MRI or CT scanning.

Quantification of perfusion and tissue Mean Transit Time rely upon detecting the increased width of the bolus as it passes through the tissue relative to the width of the bolus in a feeding artery(1,2).

Stenosis or collateral flow can broaden the arterial bolus in the immediate feeding artery relative to arterial concentration in large arteries at the base of the brain.

This broadening, or dispersion, causes overestimation of MTT and underestimation of perfusion when the arterial concentration at a single location is used to determine the arterial bolus width from the entire brain(3,4).

MTT is a desirable target for quantitative evaluation of stroke both because absolute MTT measurement does not require a measure of absolute arterial concentration, which can be problematic with MRI, and because normal gray and white matter MTTs are similar, potentially permitting a single threshold without segmentation of tissue.

Objectives:

To compare a new technique for quantifying cerebral hemodynamics from bolus passage that employs a local measurement of the width of the arterial input concentration with the traditional global arterial input concentration approach.

To determine the optimum thresholds for defining the volume of MTT abnormality to maximize correlation with brain dysfunction at acute presentation as measured by the National Institutes of Health Stroke Scale.

To determine the optimum thresholds for defining the volume of MTT abnormality to maximize correlation with eventual tissue outcome as determined on T2 weighted MRI scans in the chronic phase

Methods: Imaging

32 patients presenting with acute stroke symptoms less than 24 hours after onset (16 less than 6 hours) were studied.

MR Imaging

Gradient Echo Echoplanar imaging was performed every 2 seconds within 12 7mm slices during the bolus injection of Gd-DTPA, 0.1 mmol/kg. Diffusion weighted imaging from the entire brain was also acquired.

A followup scan at >72 hours was used to define the final stroke lesion volume.

Methods: Perfusion and MTT Analysis

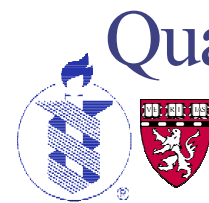
Images were converted to concentration vs. time curves.

The integral and first moment of the concentration time curve was calculated for each voxel.

The voxel with the lowest first moment, subject to a minimum integral, or blood volume, cutoff, within a region centered on each voxel, was labeled as an arterial voxel.

Local input functions for all the voxels were calculated by gaussian interpolation from a collection of the nearby arterial voxels. The input function at the location with the shortest first moment in the entire brain was used as a global input function.

Relative perfusion and blood volume, and absolute MTT were calculated using a least squares fit to a gamma variate tissue response function



Quantitative Mean Transit Time for Tissue Assessment in Acute Stroke

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Methods: Optimal Threshold Determination

Semiautomatic masking of choroid plexus, noncerebral tissues, and motion artifact was performed using baseline signal intensity and goodness of model fit criteria. Additional manual masking of particular artifacts and regions was necessary in some subjects, especially to remove the eyes.

Volume of MTT abnormality was determined for both global and local input function analysis results for a large number of thresholds.

MTT volumes were correlated separately with acute NIHSS and chronic lesion volume using Pearson's r.

Thresholds which produced the best correlation were determined.

Results

Both global and local input functions analyses demonstrated volumes of MTT abnormality consistent in location and severity with the clinical evaluation

Local input function MTT values were shorter and volumes of abnormality were generally reduced relative to the global input function.

The best correlation between acute NIHSS and acute MTT lesion volume was for an MTT threshold of 5.0s ($r = 0.58$) for the local input function and 7.5s for the global input function ($r=0.33$). These were both higher than the correlation between NIHSS and diffusion lesion volume ($r=0.22$).

The best correlation between chronic lesion volume and acute MTT lesion volume was for an MTT threshold of 7.5s ($r = 0.44$) for the local input function and 7.5s for the global input function ($r=0.52$). Mean MTT volumes for these thresholds were 81% of the T2 volume for the local input function and 55% of the T2 volume for the global input function. These were both lower than the correlation between acute diffusion and chronic T2 volume ($r=0.57$).

Conclusions

MTT with the local input function had a higher correlation with acute neurologic impairment than the global input function or diffusion lesion volume. An increased number of subjects will help to improve the statistical significance of the higher correlation.

These results support the hypothesis that broadening of the arterial input during transit through stenotic or collateral vessels is an important source of systematic error in MTT and perfusion quantification with intravascular contrast agents.

Quantitative MTT is not superior to diffusion lesion volume in predicting chronic lesion volume. This likely reflects interindividual differences in the time dependence of hypoperfusion and additional tissue risk factors yet to be determined.

Quantitative MTT will be useful for the objective determination of the diffusion-perfusion mismatch and thus may assist the decision to treat in an extended time window.

References:

1. Rempp et al. Radiology 193 637-641 (1994)
2. Ostergaard et al. Magn Reson Med 36:715-725 (1996)
3. Calamante et al. Magn Reson Med 44:466-473 (2000)
4. Lythgoe et al. Magn Reson Imaging 19:1-11 (2000)

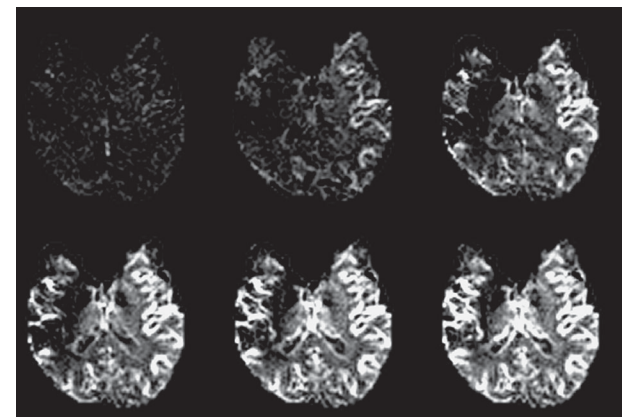


Figure 1.

An example highlighting the problem of nonuniform arterial input to tissue. Concentration vs. time is shown for one slice from a patient with abnormal supply to the right MCA distribution. Arterial signal is delayed and prolonged relative to the contralateral side. Images were acquired every 2 seconds.

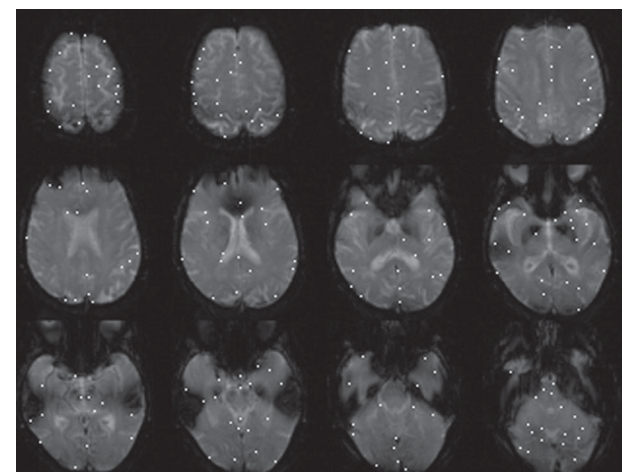


Figure 2.

Locations selected for local input function determination throughout the brain of a normal volunteer. Selected voxels are shown as bright points on the darker background image.

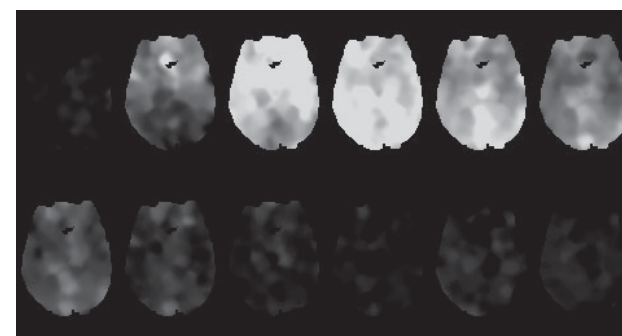


Figure 3.

The local input function determined for a normal volunteer. Delayed arrival and slight broadening of the bolus is apparent in the posterior circulation relative to the anterior circulation.

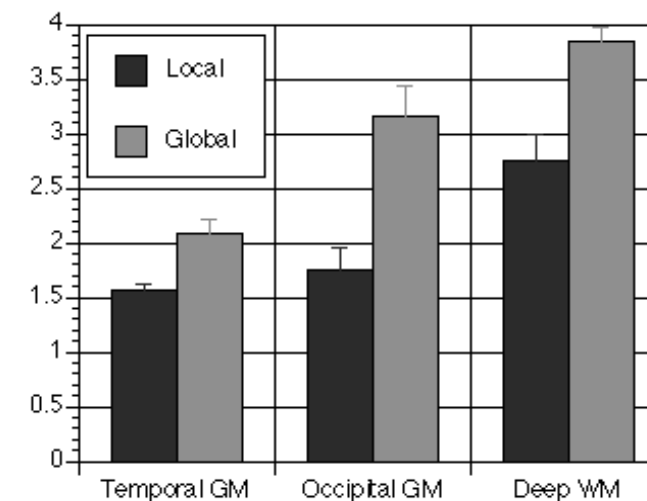


Figure 4.

Regional values for absolute MTT across 5 normal volunteers using both the local and global input function analysis. MTT is shorter for the local input function and the discrepancy between the local and global results is greatest for the posterior circulation.

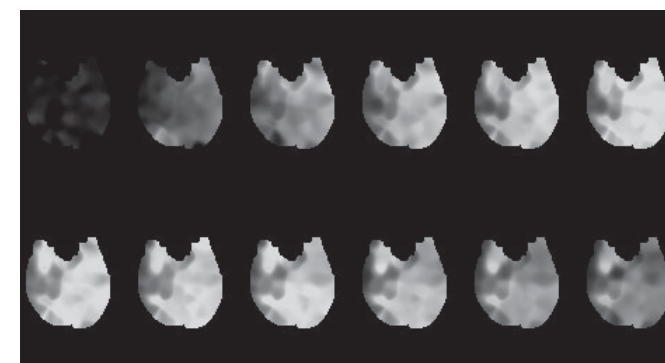


Figure 5.

Local input function vs. time calculated for the patient in figure 1. Delayed arrival in the right MCA distribution is apparent.

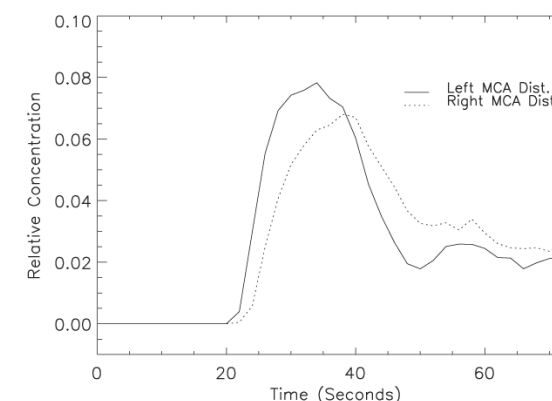


Figure 6.

Average of the local input function for the patient of figure 1 from the contralateral and ipsilateral MCA distribution showing the delayed and broader input function for the ipsilateral side.

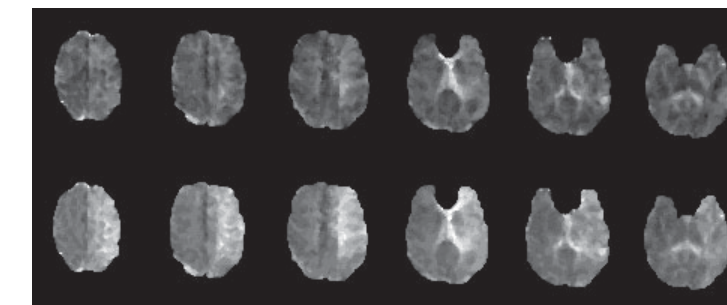


Figure 7.

Comparison of MTT maps calculated using a local input function, top, and a global input function, bottom, for a patient 4 hours after onset. Prolonged MTT throughout much of the left MCA distribution in the global input function map is removed by the local input function analysis.

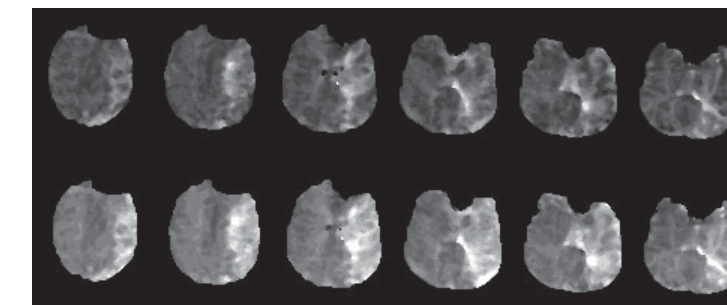


Figure 8.

Comparison of MTT maps calculated using a local input function, top, and a global input function, bottom, for a patient six hours after onset. In this case, the local input function reduces the volume of abnormality but a large region of MTT abnormality is still apparent.

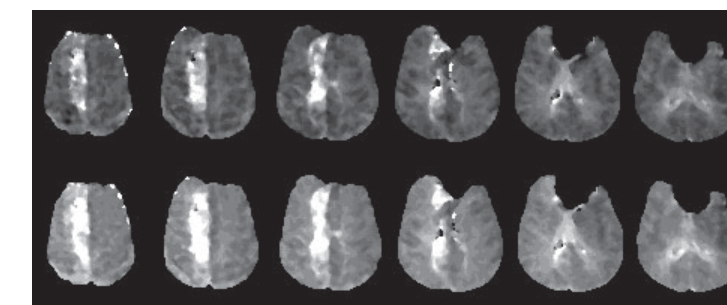


Figure 9.

Comparison of MTT maps calculated using a local input function, top, and a global input function, bottom, for a patient more than 24 hours after onset. In this case both methods describe similar regions of abnormality.