A New Model For Characterizing the Temporal Progression of the Ischemic Penumbra in Acute Ischemic Stroke

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Introduction

Determining the progression of the ischemic penumbra, the hypoperfused but potentially salvageable brain tissue around an area of infarct, is important in acute stroke care. Current paradigms that describe the penumbral region include 1) the use of "penumbral brain volumes" as thresholds of hypoperfusion that are thought to represent the ischemic region and 2) the perfusion- and diffusion-weighted imaging (PWI/DWI) mismatch in lesion size. The "penumbral brain volume" approach uses threshold values on functional perfusion maps such as T_{max}, MTT, TTP, or CBF/CVB, to delineate threshold volumes thought to correspond to the 1) ischemic core, 2) penumbra, and 3) benign oligemia.[1] The PWI/DWI mismatch paradigm assesses the discrepancy in lesion volume between PWI and DWI in order to represent the volume of tissue that is potentially salvageable.[2] The DWI lesion volume is suggested to represent the infarct core, while the lesion volume seen on PWI is regarded as encompassing all of the hypoperfused regions, thus the mismatch region should give an estimate of the volume of tissue that is at-risk but may be reperfused with timely clinical intervention.[3] A drawback inherent to both of these paradigms is that while they may provide an accurate assessment of the size of the ischemic penumbra, they are limited by two factors: 1) a need for pre-defined threshold values which are not personalized to each patient, nor widely agreed upon, and 2) an inability to predict the temporal course of the ischemic penumbra. This last point is especially important as knowledge about the speed at which penumbral tissue will die may allow treatment of patients who present beyond a pre-defined time window for treatment and will therefore assist in triage of acute stroke patients. We propose a model of the ischemic region based on a series of "balloon volumes" expanding outwards from the occluded artery, with each volume corresponding to a certain T_{max} (time-to-maximum of the residue function) threshold. Our hypothesis is that infarct expansion will be minimum when the series of "balloon volumes" are spread out more in the periphery of the ischemic region than centrally, thus suggesting better leptomeningeal collateral status (Fig. 1). By plotting these volume ratios for each patient at one time point serially and analyzing the slope of the line thus obtained, a graphical representation of the potential temporal course of the ischemic tissue beyond the already infarcted core may be produced. Most importantly, this plot is not limited by biologically derived perfusion thresholds.

Fig. 1: Example schematic of "balloon volumes" in two acute ischemic stroke patients.

Methods

Our model was tested using serial PWI and DWI data obtained in a canine stroke model.[4] Five animals were studied, with all animals undergoing single-shot gradient-echo echo-planar imaging (EPI) at 3 T (Signa VH/i; GE Healthcare, WI) at baseline and set intervals after the onset of stroke. The EPI sequence had a TR/TE/flip angle = 2000 ms/ 30 ms/4 5°, FOV = 24 cm × 14.4 cm, acquired matrix of 144 × 144 reconstructed to 256 × 256, and 5 mm slice thickness. Raw perfusion images were then exported from the scanner, and offline workstations were used with quantitative perfusion analysis software to produce functional maps.[5] Cross-calibrated maps were generated by selecting an arterial input function from the middle cerebral artery contralateral to the affected hemisphere, performing deconvolution, and then calibrating regions of normal white matter for each set of maps. Volumetric analysis was performed on each slice where the lesion was present, and at each T_{max} threshold. We were then able to calculate the serial volume ratios for each set of T_{max} thresholds, which when plotted provided a graphical representation with upward and downward slopes to test our hypothesis. We determined infarct expansion by calculating the ratio of DWI lesion volumes soon after stroke onset with volumes 2 h later. Smaller diffusion volume ratios indicated more infarct growth over the 2 h interval.

Results

Fig. 2 shows the results of our "balloon volume" analysis and the associated infarct expansion ratios. Canines with upward sloping lines at lower T_{max} thresholds (Canine 3 and 5) had more infarct expansion than those with downward sloping balloon volume ratios (Canines 1,2 and 4).

Conclusions

We have created an easily understandable, visually appealing, perfusion paradigm in acute ischemic stroke, which is based on biological principles, is not limited by pre-specified thresholds, and which has the ability to potentially predict infarct expansion.

References:

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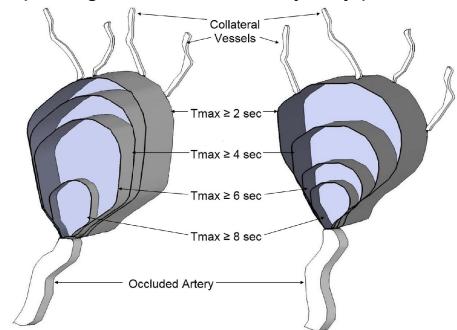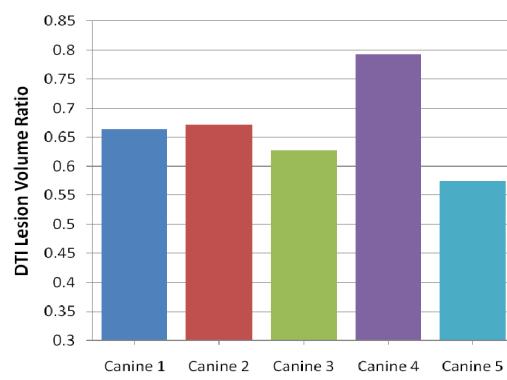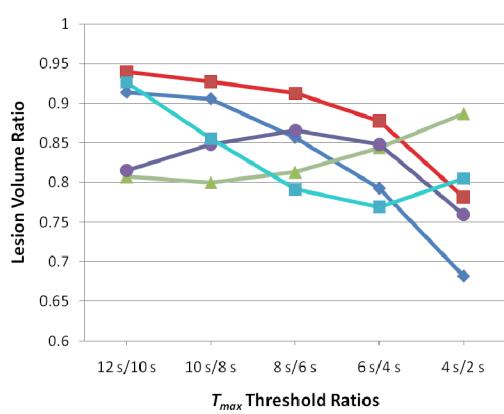
Fig. 2: "Balloon volume" analysis plots for five canine stroke models (left). Corresponding DWI lesion volume ratios for each canine (right).