Time Course of Diffusion Kurtosis in Cerebral Infarctions of Transient Middle Cerebral Artery Occlusion Rat Model

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Objective: To evaluate the relationship between fiber bundle direction and changes in diffusion kurtosis, we evaluated the apparent diffusion kurtosis coefficients (AKCs) that were perpendicular to and parallel to the principal diffusion tensor eigenvector. *Materials and Methods:* Adult male Wistar rats were subjected to 30 or 60 minutes of middle cerebral artery occlusion and imaged with a 7T Magnetic Resonance Imager System (Varian MRI System 7T/210: Agilent Technologies, CA). Diffusion kurtosis images were obtained before middle cerebral artery (MCA) reperfusion and 3, 6, and 24 hours after reperfusion to generate the apparent diffusion coefficient (ADC), fractional anisotropy (FA), mean apparent diffusion kurtosis coefficient (mAKC), AKC axial to the eigenvector (axAKC), and AKC radial to the eigenvector (radAKC) images. The time course of the region/normal ratio was evaluated for the above parameters in the caudoputamen and white matter. *Results:* Relative FA and relative ADC values decreased 3 hours after MCA reperfusion and remained decreased until 24 hours. Relative mAKC, axAKC, and radAKC values were increased 3 hours after MCA reperfusion, peaked after 6 hours, and slightly decreased after 24 hours. In the white matter, axAKC showed larger changes than radAKC. *Conclusion:* The time course of the diffusion kurtosis value showed earlier pseudonormalization than the ADC value of the lesions. For white matter lesions, the increase in axAKC was larger than that in radAKC, suggesting that the tissue changes after infarction mainly produce reduced diffusivity along the fibers and lead to increased inhomogeneity of the diffusion.
Key Words: Rat—infarction—middle cerebral artery occulusion—MRI—diffusion—kurtosis.

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Introduction

Since the introduction of imaging methods to visualize the diffusion phenomenon of water molecules within tissues,[1] diffusion imaging has become one of the most important imaging techniques in clinical practice. The most useful application of diffusion imaging is the finding that decreased diffusion can be used to detect brain ischemia at an early stage.[2] Although the underlying mechanisms for the decreased diffusion are not fully understood, cell swelling, changes in cell membrane permeability, decreased cytoplasmic streaming, and increased intracellular viscosity have been proposed.[3-5] The major hypothesis for the conventional diffusion imaging method or diffusion tensor method is that "Water diffusion shows a Gaussian distribution." Although this hypothesis sufficiently reflects tissue characteristics as required for most clinical requirements, the conventional model or the diffusion tensor model is not applicable for understanding the complicated microstructure of the tissue including multiple barrier structures in which diffusion deviates from a Gaussian distribution.[6,7]

To overcome the limitations of the Gaussian model for diffusion imaging, acquiring the probability distribution of water molecules can provide information about complicated barrier structures. Dedicated model-free methods for diffusion have been introduced, including *q*-space imaging,[8] Q-ball imaging,[9] and diffusion spectrum imaging,[10] which place high demands on scanner hardware and require long acquisition times. Diffusion kurtosis imaging (DKI) is a method for analyzing the non-Gaussian distribution of water molecules within tissues.[11,12] Higher kurtosis means that the distribution has a distinct peak near the mean and has heavy tails and is closely associated with diffusional heterogeneity.[11,12] DKI provides better characterization of normal and pathological tissues and is less susceptible to free fluid contamination than mean diffusivity or fractional anisotropy (FA) provided by the diffusion tensor method.[13] In contrast to model-free diffusion methods such as diffusion spectrum imaging, diffusion kurtosis can be calculated by combining more than 3 different strengths of motion probing gradient by using cumulant expansion within clinically feasible imaging times.[12]

The purpose of the current study was to determine the time course after cerebral infarction using DKI in rats with transient middle cerebral artery occlusion (MCAO). To evaluate the relationship between fiber bundle direction and changes in diffusion kurtosis, we evaluated the apparent diffusion kurtosis coefficient (AKC) that was perpendicular to the principal diffusion tensor eigenvector (AKC radial to the eigenvector [radAKC]) and parallel to the principal diffusion tensor eigenvector (AKC axial to the eigenvector [axAKC]).

Materials and Methods

Animal Experiment

Adult male Wistar rats weighing 270-320 g (n = 12) were subjected to MCAO. The rats were divided into a group with 30 minutes' MCAO (n = 6: $MCAO_{30}$) and a group with 60 minutes' MCAO (n = 6: $MCAO_{60}$). All MCAO experiments were performed according to reported methods[14,15] in accordance with our institutional guidelines. The rats were anesthetized with a gas mixture of 98% air and 2% isoflurane. After a median incision of the neck skin was made, the left common carotid artery and the left external carotid artery were exposed. A 4-0 monofilament nylon suture coated with silicon was inserted via the common carotid artery into the internal carotid artery. The suture was inserted 20-22 mm from the bifurcation of the common carotid artery, according to the animal's body weight, to occlude the origin of the

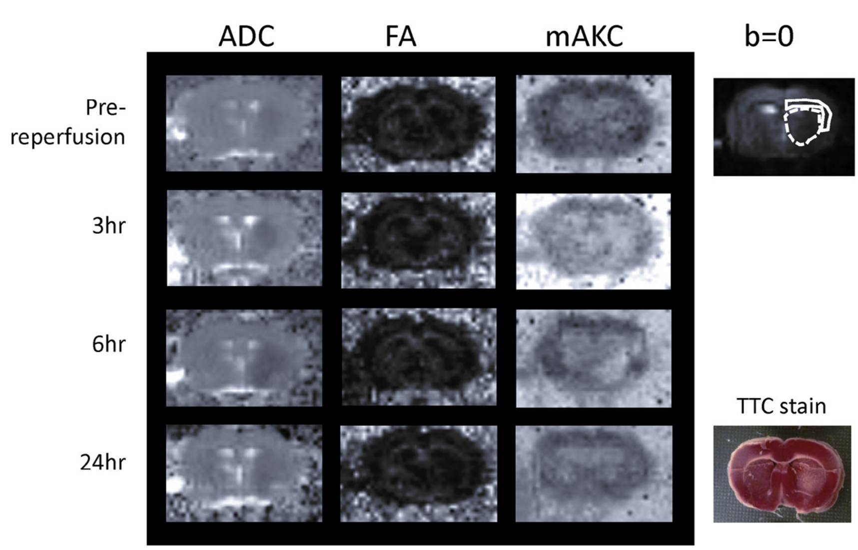

Figure 1. *ADC, FA, and mAKC of a rat brain after MCAO for 60 minutes. ROIs were set in the caudoputamen (dotted line) and white matter (solid line) on the* b = 0 *image and were coregistered into metric images. Histopathological study using TTC stain following imaging studies 24 hours after the reperfusion indicates cerebral infarction was successfully inducted. Abbreviations: ADC, apparent diffusion coefficient; FA, fractional anisotropy; mAKC, mean apparent diffusion kurtosis coefficient; MCAO, middle cerebral artery occlusion; ROI, region of interest; TTC, triphenyl tetrazolium chloride.*