# HIGH ORDER DIFFUSION IMAGING USED TO DIFFERENTIATE CYTOTOXIC AND VASOGENIC EDEMA IN HUMANS

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**Introduction:** Diffusion weighted imaging (DWI) has been effectively used to detect ischemic stroke [1,2]. Although its underlying physical mechanism remains unknown, the restricted diffusion at the early stage is likely caused by cytotoxic edema, and the subsequent escalated diffusion might arise from the vasogenic edema [2, 3]. The diffusion in water compartments during cytotoxic edema was validated in animal model [4], and the results were consistent with the study in ischemic human brain using the bi-exponential model [5]. However, the physical assumption of bi-exponential model is questionable [6,7]. Recently, stretched exponential (αDWI) [8,9] and second-order cumulant (DKI) [10,11] models were developed to characterize the intra-voxel heterogeneity in diffusion rate. In this work, we studied the feasibility of identifying cytotoxic and vasogenic edema using above two high order diffusion models. This was accomplished by fitting the data of suggestive cases of cytotoxic (n=3) and vasogenic edema (n=2) through stretched exponential and second-order cumulant fits. The measured parameters were compared with those from the control areas to further understand the physical underpinnings of pathological changes of ischemic stroke.

**Methods:** Subjects were four patients within 7 to 14 days after the onset of the neurologic deficit. Echo planar imaging (EPI) sequences were implemented on a GE 3T scanner with 40 mT/m gradients. DWI images were acquired with three gradient directions (X, Y, and Z axes) and six b-values (0, 500, 1000, 1500, 2000, 2500 s/mm$^2$). Other imaging parameters were: TR/TE = 4000/104 ms, NEX = 6, and slice thickness = 5mm, FOV = 240 × 240 mm$^2$, and matrix = 128 × 128. Two regions of interest (ROI) were selected for each analysis; one was placed on the edema area, and the other was placed on the normal area as a control. Stretched exponential and second-order cumulant models were fitted to the data using the Levenberg-Marquardt algorithm in MATLAB (Mathworks, Inc.). Data below the noise floor were excluded from the data fitting.

**Results:** DDC distinctly differentiated the edema from the control areas in all cases, and its values reduced in cytotoxic edema and increased in vasogenic edema (second row of Fig. 1 and 2). The values of α of the edema greatly overlapped with those of control area in all cases of two edema types (second row of Fig. 1 and 2). $D_{app}$ and $K_{app}$ generally could differentiate the edema for the control areas, except for the case 2 of cytotoxic edema (Third row of Fig. 1 and 2). $D_{app}$ decreased in cytotoxic edema, but increased in vasogenic edema. However, $K_{app}$ increased in cytotoxic edema, but decreased vasogenic edema (Third row of Fig. 1 and 2).

**Discussion:** Our results showed that both DDC and $D_{app}$ reflected the decreased and increased diffusion in cytotoxic and vasogenic edema respectively. The values of $K_{app}$ tended to increase in cytotoxic edema, consistent with the results by Jensen et al. [10], and the alternations of $K_{app}$ was related to the changes in permeability of membrane [10]. The scatter plots of $D_{app}$ and $K_{app}$ basically suggested their inverse relationship, as expected from the model definition [10]. However, the poor correlations between DDC and α may support the hypothesis made by Bennett et al. [9] that αDWI could detect the changes in mean diffusion rate and heterogeneity separately. The large overlap of α value between the edema and control areas indicated the diffusional heterogeneity were mostly unchanged in two types of edema. In conclusion, αDWI and DKI could be used to identify the cytotoxic and vasogenic edema, and the information they provided beyond conventional DWI may improve the understanding of the underlying physical mechanisms.

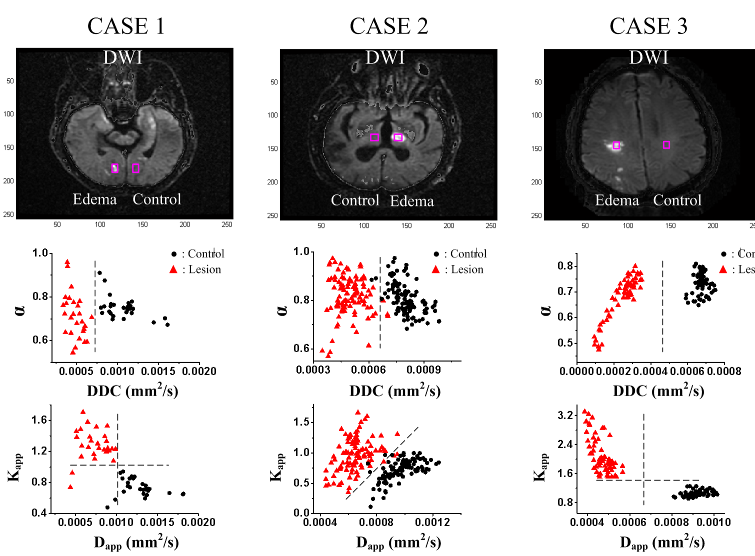


*Fig. 1 Suggested cases of cytotoxic edema: stretched exponential and second-order cumulant fits were fitted to the data of ROI (marked by the squares; .the α versus DDC (**second row**) and $K_{app}$ versus $D_{app}$ (**third row**).*

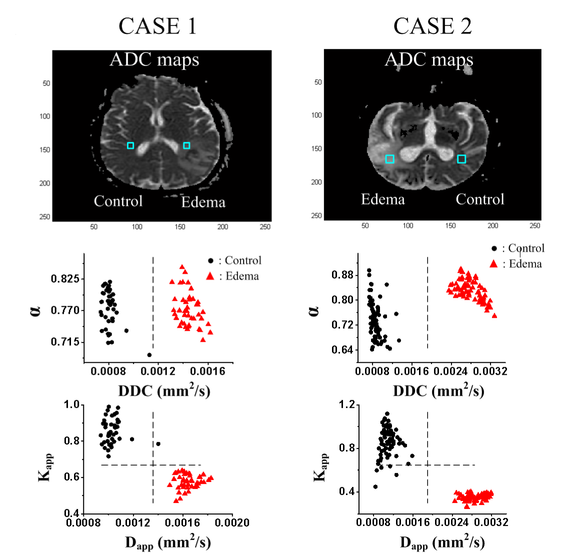


*Fig. 2 Suggested cases of vasogenic edema: stretched exponential and second-order cumulant fits were fitted to the data of ROI (marked by the squares; .the α versus DDC (**second row**) and $K_{app}$ versus $D_{app}$ (**third row**).*

**Reference:** [1] Lovblad KO et al. AJNR 19(6), 1998. [2] Schaefer PW et al. Radiology 217(2), 2000. [3] Knight RA et al. Stroke 22(6), 1991. [4] Niendorf T et al. MRM 36(6), 1996. [5] Brugières P et al. AJNR 25(5), 2004. [6] Sehy JV et al. MRM 48(5), 2002. [7] Kiselev VG et al. MRM 57(3), 2007. [8] Bennett KM et al. MRM. 50(4), 2003. [9] Bennett KM et al. MRM. 52(5), 2004. [10] Jensen JH et al. MRM. 53(6), 2005. [11] Lu H et al. NMR Biomed. 19(2), 2006.