Apparent kurtosis and fractional anisotropy potentially predicts tissue outcome in sub-acute stroke

D. van Westen[1,2], M. Nilsson[3], H. Sjunnesson[1,2], F. Ståhlberg[2,3], S. Brockstedt[4], R. Wirestam[3], and J. Lätt[1,3]
[1]Center for Medical Imaging and Physiology, Lund University Hospital, Lund, Sweden, [2]Department of Diagnostic Radiology, Lund University, Lund, Sweden,
[3]Department of Medical Radiation Physics, Lund University, Lund, Sweden, [4]Radiation Physics, Lund University Hospital, Lund, Sweden

Introduction

In acute to early subacute middle cerebral arterial stroke, the mean diffusivity (*MD*) is more reduced in white matter (WM) than in gray matter (GM) [1]. Moreover, the temporal evolution of *MD* and fractional anisotropy (*FA*) is different for WM and GM with varying degree of WM damage at three months [2]. The apparent diffusion kurtosis (*ADK*) has previously been proposed for visualization of non-Gaussian diffusion [3]. Changes in kurtosis, determined in repeated diffusion weighted (DW) measurements using different diffusion times (T_D), reflect altered micro-structural tissue properties in subacute stroke [4].

Our aim was to evaluate the potential of *MD*, *FA* and *ADK* to predict tissue outcome in WM and GM immediately after stroke onset with measurements performed three months after stroke onset used as reference.

Method

Two patients were studied, both with subacute ischemic stroke involving WM and GM, with WM involvement encompassing the deep white matter (Fig 1a, 1c, 1d, shown by small white arrows) as well as the subcortical U-fibres (Fig 1a, 1c, 1d, shown by the large white arrow). Measurements were performed 2, 9 and 90 days after stroke onset at a Philips 3T Achieva scanner, using six diffusion encoding directions. Signal-versus-*b* curves were acquired for T_d = 30 ms and T_d = 60 ms, using a constant TE/TR of 109/2000 ms. For each T_d, the signal curve was sampled with 16 *b*-values with b_{max} = 9000 s/mm^2. Images were eddy-current and motion corrected using FLIRT [5]. Diffusion tensor imaging (DTI) analysis was performed for both diffusion times (data only shown for T_d = 30 ms) using *b*-values less than or equal to 1500 s/mm^2 and parametrical maps of *MD* and *FA* were calculated, and *ADK* maps was calculated from the geometric mean of the six encoding directions [4].

Under guidance of T2-weighted (T2W) images acquired day 2 after stroke onset, tissue in the infarcted area was labelled WM or GM. Tissue outcome was determined using T2W images from day 90; WM was either appearingly normal WM (WM*normal*) or showed increased signal intensity as in gliosis (WM*gliosis*), while GM showed gliosis in all parts of the infracted area.. For each time point of investigation, twelve regions of interest (ROI) were placed in each tissue type. For comparison T2-values were obtained from the same ROIs as well as from ROIs placed in the contralateral hemisphere and the ratio of lesion to contralateral normal tissue T2W signal intensity was determined. The difference in parameters estimated in WM*normal* and WM*gliosis* was calculated for each time point and expressed in percent.

Result

At day 90, normal appearing WM was found in deep white matter (Fig 1a, 1c, 1d, shown by small white arrows), while development of gliosis was seen in the subcortical U-fibers (Fig 1a, 1c, 1d, shown by the large white arrow). The T2-ratios differed between tissue types at day 2 after stroke onset, at day 9 as well at day 90 ($p < 0.0001$) (Table 1). *MD* was similar in WM*normal* and WM*gliosis* at day 2 after stroke onset, while *FA* and *ADK* for both T_d depended on tissue outcome (Table 1). The difference between WM*normal* and WM*gliosis* in *FA*, *ADK* T_d30 and *ADK* T_d60 was 40% or more and persisted, although somewhat smaller, at day 90.

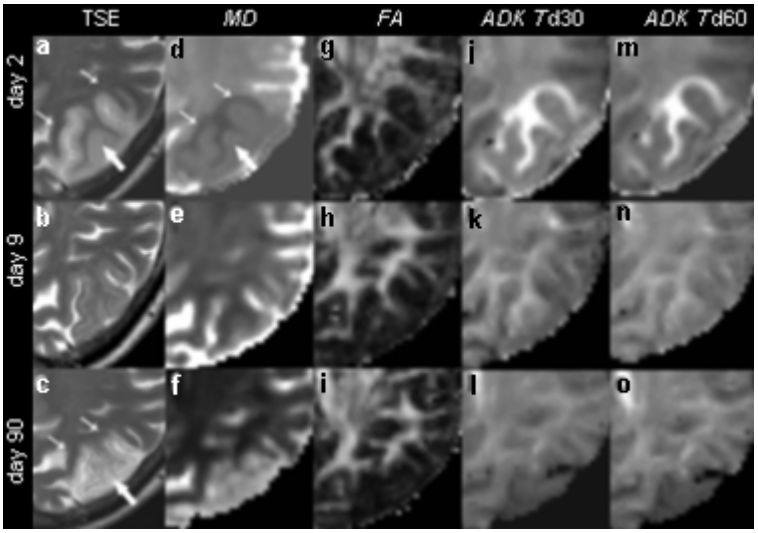
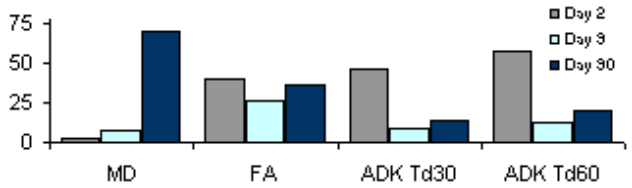


Fig 1 (above). Image set from one patient showing *T2-TSE* (a, b, c), *MD* (d, e, f), *FA* (g, h, i), *ADK*(T_d30) (j, k, l) and *ADK*(T_d60) (m, n, o) at day 2 (top row), day 9 (middle row) and day 90 (bottom row) after stroke onset. In the T2W image WM in the subcortical U-fibers (large white arrow) has a normal appearance at day 90, while WM in deep white matter (small white arrows) shows gliosis.

Fig 2 (right). Difference between WM*normal* and WM*gliosis* for both patients at day 2, 9, and 90 after the stroke onset (percentage). *FA* and *ADK* predict the tissue outcome at day 2 with a percentage contrast change of 40% or more.

Table 1. Average values for each parameter, obtained from the patient shown in Fig 1. *ADK* and *FA* differed between WM*normal* and WM*gliosis* at day 2, while *MD* did not.

param WM	T2-ratio normal /gliosis	*MD* T_d30 normal /gliosis	*FA* T_d30 normal /gliosis	*ADK* T_d30 normal /gliosis	*ADK* T_d60 normal /gliosis
Day 2	1.06 / 1.35	0.24 / 0.25	0.46 / 0.33	1.13 / 1.69	1.15 / 1.87
Day 9	1.15 / 1.35	0.67 / 0.59	0.29 / 0.17	0.71 / 0.75	0.70 / 0.72
Day 90	1.31 / 2.25	0.80 / 1.57	0.24 / 0.08	0.79 / 0.59	0.76 / 0.55
param	T2	*MD* T_d30	*FA* T_d30	*ADK* T_d30	*ADK* T_d60
GM	ratio	gliosis	gliosis	gliosis	gliosis
Day 2	1.54	0.43	0.11	0.73	0.65
Day 9	1.47	0.69	0.16	0.73	0.71
Day 90	2.47	1.86	0.07	0.47	0.48



Discussion and conclusion

Tissue outcome in acute stroke is dependent not only on tissue type (WM or GM), but in WM also on location (deep WM versus subcortical U-fibres). In the subacute stage, *MD* cannot distinguish between WM that will pseudo normalize and WM that will progress to gliosis, but *FA* and *ADK* can. Furthermore, kurtosis obtained from two diffusion times shows an increase in non-Gaussian diffusion at day 2 in WM*gliosis* and GM, that becomes more Gaussian later, indicating tissue degeneration.

References

[1] Mukherjee P, *et al*. Radiology;2000; 215:211–20
[2] Muñoz M, *et al*. JNNP;2004:75:1714-18
[3] Jensen JH *et al*. MRM;2005;53:1432-40
[4] Lätt J, *et al*. In Proc. ISMRM;2008 p40
[5] Jenkinson M, Smith S. Med. Image Anal;2001;5:143-58