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<特別講演 I>

Imaging Examinations of Cerebrovascular Disease

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Introduction

There is a need to stage and predict the evolution of stroke on the occasion of first investigation. The challenge is to reduce 1) the time methods and 2) identify the most critically important measures for the diagnosis, staging and prediction of outcome of stroke. We believe this challenge can be met by a signature model of tissue histopathology which employs DWI in combination with conventional T₂-weighted imaging (T₂WI). With this tissue signature model there is the potential to characterize cerebral ischemic histopathology in experimental and clinical stroke, independent of time at the cost of only a few minutes delay in stroke assessment.

Model

We have examined the relationships of MR measures to tissue histopathology in a rat model of permanent and transient focal cerebral ischemia¹⁾²⁾. The relationships of ADC_w and T₂ changes in a core of the ischemic focus are depicted diagrammatically in Figure 1. To these changes we can assign six different MR signatures (A-F) to tissue histopathology, ranging from normal to cell death. Briefly, the model assumes that normal tissue corresponds to normal ADC_w and normal T₂ (designated "A"); that low ADC_w with normal T₂ (designated "B") signifies either compromised tissue which

Fig. 1

may either recover or eventually die; that low ADC_w with high T_2 (designated "C") predicts progression to cell death; that normal (pseudonormal) ADC_w with high T_2 (designated "D") signifies transition to cell death; and that high ADC_w with high T_2 (designated "E") or high ADC_w with normal T_2 (designated "F") identifies cell death. Using these combinations we generated maps of the different proportions of each of the tissue signatures in ischemic stroke. Details of the complete model of experimentally derived tissue signatures of ischemic histopathology applied to human stroke have been previously published³⁾.

Methods

DWI and T2WI studies were performed with a 3 Tesla, 80 cm bore magnet with actively shielded gradients of 20 mT/m interfaced to a SMIS imaging and spectroscopy console. DWI echo-planar imaging (DWI-EPI) or DWI-FLASH were used to acquire a complete 2D image set following a single excitation and application of diffusion gradients.

ADC_w maps were generated and combined with T_2 maps for cluster analysis using image analysis techniques³⁾. Normal gray and white matter clusters and the total ischemic lesion were identified. Theme maps of the distribution of each tissue signature in the stroke focus were constructed.

All patients studied suffered focal cortical ischemic stroke due to occlusion of a single intracranial large or branch artery supplying anterior or posterior brain cortex. Patients were studied whenever possible on three occasions during the acute (up to 24 hours), subacute (from 24 to 72 hours), intermediate (7–10 days) and chronic (2–3 months) stages after onset of symptoms. We first sought to confirm the presence of the tissue signatures in individual clinical cases. A small number of the cases which were serially studied had stroke volumes measured together with calculation of the proportions of the signatures within the volume of the lesion.

To test the sensitivity of the tissue signature model to rapidly accelerating brain tissue necrosis we studied a separate group of nineteen focal ischemic stroke patients who underwent DWI- T_2 studies performed within 48 hours poststroke and diagnostic evaluation of the stroke mechanism. The specific hypothesis of this study was that during the subacute period of stroke, an embolic mechanism, because it may generate a more rapidly maturing ischemic lesion, should contain a majority (>60%) of E + F signatures. Alternatively, a non-embolic mechanism should contain >40% of D, the signature of transition to cell death. Blinded observers classified the strokes as embolic or non-embolic using clinical (TOAST) and radiologic criteria (Ringelstein).

Results

All five signatures of ischemic histopathology were identified in human stroke foci. In the group of 19 patients, according to the signature model, 14 lesions (74%) had more than 60% of E + F and therefore were considered as embolic stroke and 5 (26%) had more than 40% of D and so were

Fig. 2

considered as non-embolic stroke. According to radiologic criteria 13 strokes (68%) were considered as embolic stroke and 6 (32%) as non-embolic stroke. According to TOAST.2 15 cases (79%) were considered embolic stroke and 4 cases (21%) non-embolic stroke. Agreement between the signature model and neuroradiological criteria, and between neuroradiological criteria and TOAST was substantial ($.80 < k < .90$), and moderate between the signature model and TOAST.2 ($.60 < k < .80$).

In five separate patients we had the opportunity to serially study the volume of the ischemic lesion as it progressed to infarction (Fig. 2). When the maximum size attained by the lesion was calculated and expressed as 100%, it can be seen that the volume enlarged in the early days after onset of ischemia.

Discussion

In clinical practice, stroke patients cannot be studied at the precise time of stroke onset or serially over prolonged time periods. Instead a "snapshot" of events is obtained at the earliest possible time and on one or two other occasions during a stroke evaluation. Nevertheless in clinical stroke patients studied in the present series we are able to identify the MR tissue signatures that we believe on the basis of our model, have the potential to characterize ischemic tissue damage and stage the evolution of ischemia towards infarction. We were able to test the sensitivity of the signature model by identifying accelerated ischemic cell death which occurs in cerebral embolism. Thus the signature model appears sensitive to the accelerated necrosis that is characteristic of the histopathology of cerebral embolism.

The significance of an available predictor and marker of cell death cannot be overemphasized. Imaging T_2 in combination with DWI opens the possibility to identify tissue which may respond to cytoprotective therapy, and perhaps extend the therapeutic window or open it for those cases in whom the time of stroke onset cannot be determined with certainty. At the least, such MR tissue signatures as we have derived might indicate, at subacute stages of stroke, whether the total lesion is beyond recovery by identifying irreversible components of ischemic tissue. The volume measurements that we carried out in a selected but small number of patients seem to suggest that the volume of damaged tissue enlarges over days after onset of ischemia and incorporates tissue not predicted by either DWI or T2WI at very early times of study. Thus it appears that a three, possibly four, parameter signature model may be needed to predict the evolution of cell death and the eventual volume of infarction at the earliest times available for human study. The utility of perfusion imaging has been emphasized in this regard. We are currently exploring magnetization transfer imaging, especially the forward rate constant of bound water to macromolecules, for its potential to provide this information. Whatever, we believe the tissue histopathology MR signature assessment of clinical stroke appears worthy of further study.

References

- 1) Knight RA, Dereski MO, Helpert JA, Ordidge RJ, Chopp M: MRI assessment of evolving focal cerebral ischemia: comparison with histopathology in rats. *Stroke* 25: 1252-1262, 1994.
- 2) Jiang Q, Zhang ZG, Chopp M, Helpert JA, Ordidge RJ, Garcia JH, Marchese BA, Qing ZX, Knight RA: Temporal evolution and spatial distribution of the diffusion constant of water in rat brain after transient middle cerebral artery occlusion. *J Neurol Sci* 120: 112-130, 1993.
- 3) Welch KMA, Windham J, Knight RA, Nagesh V, Hugg JW, Jacobs M, Peck D, Booker P, Dereski MO, Levine SR: A model to predict the histopathology of human stroke using diffusion and T_2 -weighted magnetic resonance imaging. *Stroke* 26: 1983-1989, 1995.