DEVELOPMENT OF NON-INVASIVE DIAGNOSTIC AND MONITORING SYSTEMS FOR HYPERACUTE ISCHEMIC STROKE

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In several western countries (USA, Canada, Australia, Germany), thrombolytic therapy has been established as the treatment of choice within three hours of onset of ischemic stroke. Intravenous administration of recombinant-tissue plasminogen activator significantly improved patients' outcome at 90 days after onset. Increase in mortality rate after thrombolytic therapy due to massive intracerebral hemorrhage, however, was also noted in the clinical trials. In order to avoid such fatal side effects of hyperacute thrombolytic therapy, the ischemic stroke patients expected to benefit from the therapy should be carefully selected. Brain imaging is a potential to provide methods to evaluate location and severity of brain damages, pathogenesis of stroke (hemorrhagic or ischemic, embolic or thrombotic), and effect of therapy (occluded or recanalized). The aim of the present study was to establish a non-invasive diagnostic and monitoring system applicable for patients with acute stroke in the emergency setting to improve clinical outcome of stroke victims.

In Japan, the X-ray computed tomography (CT) has been the choice of imaging modalities for decision making of stroke. Hirano demonstrated that early ischemic change in CT is comparable with severe hypoperfusion (50% or less of cerebral blood flow in unaffected hemisphere), indicating irreversible brain damages. Although CT is available 24-hours a day, the sensitivity to early ischemic change of brain is not high enough. Hatazawa et al. investigated an accuracy of early ischemic change on emergency CT. It was around 70% even in experienced radiologists. Takahashi and Nogawa revealed that higher-voltage scanning can improve a detectability of faint reduction of Hounsfield' unit (which would correspond to early ischemic change) in the phantom study. Feasibility of cerebral perfusion measurement by means of CT with intravenous administration of contrast medium or cold-Xe inhalation was tested in emergency setting. CT based perfusion imagings were applicable and increased a detectability. Further investigation should be conducted to guide a specific decision-making for thrombolytic therapy by CT.

Magnetic resonance imaging (MR) has higher sensitivity of detecting ischemic brain damages. Diffusion-weighted MR (DWI) combined with perfusion-weighted MR (PWI) and angiography (MRA) visualized the site of arterial occlusion, extension of abnormal perfusion, and extension of cytotoxic brain edema. Hatazawa demonstrated that diffusion-perfusion mismatch (normal DWI with disturbed PWI) diminished during the first three days and that diffusion-perfusion mismatch showed 50% reduction of cerebral oxygen metabolism. Ohnishi indicated in their animal experiments that mild DWI abnormality (less than 30% change in apparent diffusion coefficient of water) was reversible. These studies indicated that DWI-PWI mismatch and mild DWI abnormality is a target of reperfusion therapy. Limited availability of MR and standardization of imaging methods should be improved.

The application of ultrasound sonography (US) was intensively studied in ischemic stroke patients. Nagatsuka demonstrated a nature of thrombi formed in the carotid artery. Their technique makes possible a diagnosis of potential risk of thrombi as embolic sources. Kimura visualized “Willis ring” by transcranial Doppler US, which also made possible flow velocity measurement. Bed-side monitoring of cerebral perfusion, recanalization or re-occlusion, micro-emboli is possible by US.

Preliminary studies indicated measurement of cerebral oxygen metabolism (Inubuse) and cerebral blood flow by PWI (Nishimura, Kuwabara, Matsuda), differential diagnosis between emboli and thrombi (Furui), improvement of MRA (Araki, Shirane), and evaluation of white matter damage (Ishikawa). These imaging modalities will play an important role in the near future.

Takahashi tried to rescue patients with internal carotid artery occlusion by intraarterial thrombolytic therapy with urkinase within 2 hours of onset. The candidates were selected based on the CT and MR findings (no ischemic findings) as well as their age, collateral circulation, and clinical signs. The results in embolic patients were favorable (100% recanalization, clinical improvement in 73% of patients, hemorrhagic transformation in 18%). The study indicated that imaging-based decision-making for thrombolysis was important to treat effectively and safely.

In conclusion, the CT and MR are key imaging modalities for hyperacute ischemic stroke. Ultrasound sonography is useful for bed-side and repeated evaluation. In CT, increasing sensitivity to ischemia and training of emergency physicians is necessary. In MR improvement of availability in emergency setting is essential.

Key words; brain infarction, computed tomography, magnetic resonance imaging, ultrasound sonography