Imaging techniques for acute ischemic stroke: nice gadgets or essential tools for effective treatment?

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In this issue of Neuroradiology, two papers present a state of the art on computed tomography (CT) and magnetic resonance (MR) imaging of acute ischemic stroke [1, 2]. These papers provide an excellent overview for the general neurologist and radiologist on established and newer imaging modalities available with MRI and CT that can be used in stroke imaging. The authors eloquently describe established early findings on CT or diffusion-weighted imaging, as well as newer techniques like susceptibility weighted MRI or perfusion imaging with CT.

These papers also address several important issues that are the object of current stroke imaging research. A burning question is which imaging modality is best suited for use in acute stroke, advanced CT, or MRI. Clearly, CT and MRI have their own advantages and disadvantages as described in Table 1. Still, with the increased sophistication of CT and MRI, we have to keep in mind that plain CT was used as the sole imaging modality in the only universally accepted treatment modality that we have available right now, intravenous tissue plasminogen activator [3, 4]. Even in the most recent successful trial of thrombolysis, CT was used as the imaging modality of choice [5]. At the same time, I think we have exhausted the way we can treat stroke using plain CT in many of the other treatment needs in acute stroke, as painfully illustrated by the abciximab in Emergency Treatment of Stroke Trial [6]. In this trial, reliance on CT to treat the patients who woke up with symptoms, led to disaster. Even relying on the concept of a “clinical CT mismatch”, in which salvageable brain tissue

is thought to be present based on a discrepancy between the severity of the clinical deficit and the relative absence of early imaging findings on CT, did not lead to improved outcomes [7].

Probably, a direct comparison of advanced CT versus advanced MRI as the sole purpose of a randomized controlled clinical trial will never be performed. I would propose that this is also not the heart of the matter in stroke imaging. The most important question now is whether advanced imaging, be it CT- or MRI-based, will make a difference in how we treat acute ischemic stroke. Indeed, we still have to answer an important question: does our better diagnostic ability lead to better clinical outcomes?

Let us first examine what the current treatment needs are in acute ischemic stroke. At present, there is no established treatment option for the 20–30% of patients who wake up with stroke, yet we often suspect that these patients could benefit from acute recanalization be it by medication or by thrombectomy [8]. Even though intravenous thrombolysis is a successful treatment with a high average benefit compared to other treatments, there are a large number of patients who fail to respond or who suffer from reocclusion in the first hours after successful treatment [9]. Newer and safer thrombolytic agents are needed [10]. There is no established treatment option for patients who fall outside the accepted time window for thrombolysis and we have only limited ways of predicting treatment response for individual patients. There is weak evidence for supporting invasive stroke treatment, but this occurs at the cost of a high risk of intracerebral hemorrhage [11]. Even though recanalization with thrombectomy is a strong predictor of good outcome it does not always lead to improvement in all patients. Finally, there is a need for a neuroprotective strategy that can be used hand-in-hand with the current ‘plumbing’ approach. Clearly, the current treatment needs require a more sophisticated

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Table 1 Comparison of CT and MRI based techniques.

	CT	MRI
Sensitivity	–	+
Exclusion of acute intracerebral hemorrhage	+	+
Exclusion of old intracerebral hemorrhage	–	+
Exposure to radiation	+	–
Availability	+	–
Speed	+	–
Imaging of vessels	+	+
Imaging of vessel wall hematoma	–	+
Imaging of “penumbra”	+	+
Coverage of perfusion	–	+
Reliability of absolute perfusion values	+	+/-
Claustrophobia inducing	–	+

approach than the information offered by “time since stroke onset” and results of plain CT can answer. Each of these preliminary studies has shown that advanced neuroimaging can be powerful adjuncts in treatment decisions. For wake-up stroke, simple fluid-attenuated inversion recovery combined with diffusion-weighted imaging may indicate whether stroke falls within the current 3- or 4.5-h time window or not [12]. For the poor responders to intravenous thrombolysis, both MR and CT are able to provide information on the persistence or reappearance of vessel occlusion and the presence of salvageable tissue that is potentially aided by intra-arterial thrombolysis. MR and CT are potentially able to extend the time window by generating individualized imaging patterns that help stratify risk benefit [13, 14]. This allows for more accurate prediction of intracerebral hemorrhage and poor or excellent treatment response to revascularization [15, 16]. Novel neuroprotective agents can be tested in homogeneous patient groups with prespecified imaging characteristics, rather than the mix of patients typically tested in CT based trials, an approach which led to a graveyard of once promising neuroprotective agents.

If we want to convince health authorities that these tools are more than nice imaging gadgets, clinical trials that test these concepts and show actual clinical benefit for patients will be eventually required. The first steps in this direction were taken with studies like Diffusion-Weighted Imaging Evaluation for Understanding Stroke Evolution or Echoplanar Imaging Thrombolysis Evaluation Trial [13, 14]. However, they need to be replicated, expanded, and refined. These studies will require intimate cooperation between neurologists, neuroradiologists, and neurointerventionists. Too often in the past, these disciplines have lived side by side and did not listen to each other's needs. These studies will require standardization of definitions, image processing, and analysis that are accurate, but also feasible in the context of

multicenter trials. They will probably require relatively large numbers of patients and will be quite costly given the advanced technology required. On the other hand, the numbers of strokes are so vast, and treatment needs so dramatic that the societal “return on investment” can be huge if we can prove that this approach is successful.

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