



Published in final edited form as:

Stroke. 2010 October ; 41(10 Suppl): S152–S153. doi:10.1161/STROKEAHA.110.595116.

The Future of Stroke Imaging: What We Need and How to Get to It

Carlos Leiva-Salinas, MD and Max Wintermark, MD

University of Virginia, Department of Radiology, Neuroradiology Division

Abstract

Clinical trials of reperfusion therapies for acute ischemic stroke patients in an extended time window have shown mixed results. Advanced neuroimaging for stroke, more specifically vascular imaging and perfusion/penumbra imaging, have been hypothesized to be powerful selection tools in this setting. However, a number of improvements and validation steps are needed to make these imaging techniques operational and accurate in the stroke community in general. This article briefly describes the needs in this field and recommends future steps to achieve them.

Keywords

Brain infarction; brain ischemia; cerebral infarct; CT; magnetic resonance; reperfusion therapies

Although imaging remains a mainstay of stroke diagnosis and treatment, variable results in a number of clinical trials where imaging has been used as a selection tool for acute ischemic stroke patients in an extended time window have left many unanswered questions 1-2. Overall, the two main barriers to the implementation of advanced imaging in the broad stroke community are the lack of standardization and the lack of validation, especially for perfusion/penumbra imaging.

There are a number of perfusion/penumbra software/models available in the community, some developed at academic centers and others commercially available. All published models of ischemic penumbra have demonstrated moderately good predictive performance in small samples 3. These models, however, have not been systematically compared to one another; none has been validated in a large series. As a result, it is impossible to determine the relative value of these models in terms of accuracy 4-5. One of the recommendations of the STroke Imaging Repository - STIR - Consortium is to systematically compare and harmonize the perfusion/penumbra imaging software packages developed by individual academic centers and imaging companies in a large series of patients 5. The goal of this project is to achieve the harmonization of the perfusion software packages so that a stroke patient, scanned on any type of CT or MRI scanner, with the data processed using any type of post-processing software package, will be diagnosed with similar values in terms of the volumes of infarct core and penumbra.

Corresponding author for proof and reprint requests: Max Wintermark, MD, University of Virginia Medical Center, Department of Radiology, Neuroradiology Division. 1215 Lee Street-New Hospital, 1st Floor, Room 1011. PO Box 800170. Charlottesville, VA. 22908, 434-243-9312 (phone), 434-982-5753 (fax), Max.Wintermark@virginia.edu.

The authors have nothing to disclose.

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Two cornerstones in the standardization of perfusion processing are automation and quantification. Automation eliminates the variability that is created by implementing the same software at different sites or by users with variable degrees of expertise. The practicality and advantages of automation are currently being demonstrated in two ongoing trials: Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evaluation 2 (DEFUSE 2) and MR and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE). These two trials use fully automated implementation of perfusion/penumbral models to assess the brain perfusion in candidates for the trial. These automated packages perform apparent diffusion coefficient (ADC) computation, brain segmentation, determination of arterial input function, computation of perfusion measures, co-registration of DWI and PWI images, and prediction of the infarct size and tissue at risk in less than 5 minutes. By ensuring reproducible results independently of the user, automation enables quantification, with the use of optimized quantitative thresholds to determine the infarct core and the penumbra.

Yet, the greatest challenge is to show that advanced neuroimaging, used as a biomarker to select patients for reperfusion therapy in an extended time window, improves patient outcome. This would represent a critical advance in the field of stroke imaging. Although MRI has been used in several randomized studies 2-6-8, there are as yet no published prospective multicenter perfusion-CT trials that can help define how to best use this technique in acute ischemic stroke patients. After the key step of standardization of perfusion-CT packages, a clinical trial using a validated perfusion-CT software package to select acute ischemic stroke patients for reperfusion therapy in an extended time window will be required. The wide availability of CT scanners in medical centers will facilitate site and patient enrolment, and hopefully lead to a successful trial in a short period of time, provided standardization holds when implementation involves a large number of sites. In this regard, automation will again play a decisive role.

All the steps listed above, standardization, automation and validation, will require access to large series of data, collected either prospectively or retrospectively. The STIR consortium has a large set of patient cases and images that are available for research studies and is continuously looking for contributors to accrue this dataset. Rules to access or contribute data to the STIR repository are detailed on the STIR website (<https://stir.ninds.nih.gov/html/index.html>).

In conclusion, advanced stroke imaging has made significant progress in the last 5 years. However, additional efforts are needed so that the role of these techniques in the management of acute ischemic stroke patients can be defined precisely. This needs to happen quickly. Indeed, there is a risk that, if used inappropriately, these techniques can be potentially harmful (cf. recent episodes of overradiation delivered to patients by technically inadequate perfusion-CT studies) 9. Such unfortunate events can damage the reputation of technologies that have the potential to significantly improve patient outcome. Large studies are needed to validate advanced neuroimaging techniques and to provide guidance on their use in acute ischemic stroke patients.

Acknowledgments

No other persons have made substantial contributions to this manuscript

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