

**TITLE: Acute Stroke Triage & Management: Physics Perspective**

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**HIGHLIGHTS**

- Importance of clinical translation of advanced MRI techniques for acute stroke triage
- Examples of new approaches for stroke therapy triage
- Practical study design considerations for translation of advanced techniques from research to clinical settings

**TARGET AUDIENCE:** Clinician research scientists and translational neuroimaging researchers

**OBJECTIVES:**

Discuss recent technical advances and promising new approaches with the goal to ultimately address unanswered clinical needs.

**PURPOSE:**

“Penumbral” imaging techniques have stimulated stroke imaging research by offering the possibility of focusing treatment decisions on likelihood of tissue salvage<sup>1,2</sup> rather than an oft ill-defined time when a patient was last seen well.<sup>3</sup> Brain tissue, vessel and perfusion imaging may lead to substantial insights in the understanding and therefore the treatment of stroke.<sup>4</sup> Beyond “penumbral” imaging, sophisticated imaging approaches have the potential of providing greater insight into the underlying pathophysiological mechanisms of injury and recovery after stroke. Advanced imaging techniques can also potentially be used to identify which patients are at high risk of stroke and therefore candidates for stroke prevention trials and interventions. Furthermore, new imaging approaches have also been posited to be helpful for monitoring brain recovery and therefore may be used to tailor physical and neurocognitive therapy after stroke.

**METHODS:**

Promising emerging imaging techniques for providing greater understanding into stroke sequelae include non-invasive measurement of cerebral blood flow (e.g. arterial spin labeling [ASL] MRI<sup>5,6</sup>), oxygen extraction fraction-weighted<sup>7,8</sup> MRI<sup>9,10</sup>, pH-weighted MRI,<sup>11</sup> glucose chemical exchange saturation transfer MRI (Gluco-CEST),<sup>12</sup> cerebrovascular reactivity measured with MRI,<sup>13</sup> diffusion kurtosis MRI<sup>14</sup>, diffusion-tractography<sup>15,16</sup>, resting-state functional MRI<sup>17,18</sup>, vessel-size imaging<sup>19,20</sup>, and blood-brain barrier permeability imaging<sup>21-23</sup>. New imaging approaches offer practical benefits such as less invasive techniques that allow for repeat assessments or faster<sup>24</sup> or less motion sensitive<sup>25</sup> methods which are critical for imaging agitated and non-compliant subjects whom make up most acute stroke subjects.

**RESULTS:**

Although advanced neuroimaging techniques have the potential to have widespread impact on stroke prevention, acute stroke treatment and recovery after stroke, the practical translation of these potentially transformative techniques from research to clinical settings faces many challenges. Some of these include limited support for developing advanced imaging techniques in clinical environments and criticisms regarding their feasibility in acute settings. Pragmatic issues such as scan duration are important especially in the acute stage since many patients are non-responsive to instructions to not move during the scan. In addition, short scan durations are needed for acute studies of patients who may be eligible for

interventions for which there exists a therapeutic time window. For evaluating patients without pressing time constraints, e.g. patients with chronic stroke, transient ischemic attack (TIA), or asymptomatic carotid stenosis, longer acquisitions may be feasible. But, automatic motion correction will likely be required as many of the advanced techniques tend to require longer data acquisition times.

### **DISCUSSION:**

The question remains on the best means of translating novel techniques that will move the field forward, while taking into consideration practical considerations such as clinical feasibility along with long-term research possibilities. For translating new techniques from research settings to clinical bedside, several study designs are possible. The consensus is that multi-center, multi-vendor studies would be the most practical and receive the most support from industry, critical for successful translation of new techniques into non-academic hospital centers.<sup>2</sup> There is still debate on whether to limit evaluation of new techniques to current state of the art technology, e.g. 3 Tesla scanners, or to prefer generalizability, e.g. include 1.5 Tesla scanners. The choice will likely depend on the imaging method being tested, i.e. the technique can work only on specialized equipment. For evaluating the clinical utility of these sequences, both acquisition and processing techniques will need to be standardized by expert panels, such as what is being done for ASL and dynamic susceptibility contrast perfusion-weighted imaging by the Perfusion Study Group of the International Society for Magnetic Resonance in Medicine (ISMRM). Mechanisms are needed to translate and test advanced imaging methods across sites, to encourage the use of advanced imaging in acute settings, to stimulate closer academic-industry collaborations and to promote the prospective collection and pooling of imaging data.<sup>2</sup>

### **CONCLUSION:**

Critical to the acceptance of new techniques will be their performance. Depending on the patient population under investigation, from patients at-risk of stroke (e.g. TIA patients) to chronic stroke patients (e.g. recovery research), there are many possible criteria by which new imaging techniques can be evaluated. For acute stroke patients, imaging techniques are typically evaluated using lesion volumes on follow-up imaging as a reference standard or by correlation with clinical stroke symptoms at time of imaging. The equivalent for at-risk patients would be prediction of future strokes. For acute stroke or at-risk patients, additional evaluation criteria could include prediction or measurement of response to intervention or medication. For chronic stroke patients, techniques could be evaluated against neurocognitive testing<sup>26</sup> and prediction of response to rehabilitation therapy<sup>27</sup>. Ultimately, new techniques will need to impact clinical management of these patients, whether by making the imaging study less invasive (e.g. ASL) or providing additional information on potential tissue salvage or tissue at risk or risk of complication with treatment.

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