

# Innovations in Endovascular Treatment of Acute Ischemic Stroke and Cerebral Aneurysms

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## A B S T R A C T

Technological innovations are optimizing endovascular treatment of patients with acute ischemic stroke (AIS) and cerebral aneurysms. At the 10<sup>th</sup> Congress of the European Society of Minimally Invasive Neurological Therapy (ESMINT), a symposium dedicated to state-of-the-art approaches to AIS provided insight into the use of RAPID, an imaging analysis software, to triage patients for mechanical thrombectomy in stroke networks. The symposium also examined the effect of the first pass of a clot retrieval device on AIS outcomes and identified procedural characteristics associated with the ability to complete the procedure with a single pass. In addition, a new feature of the Sim&Size modulation software, which is used to optimize selection of a Pipeline Embolization Device (PED), was introduced. This new feature, metallic surface coverage (MSC), may enhance occlusion at the aneurysmal neck.

**Key words:** acute ischemic stroke, mechanical thrombectomy, cerebral aneurysm, Pipeline Embolization Device

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## INTRODUCTION

*Time is Brain: Acute Ischemic Stroke (AIS) State-of-the-Art Approaches to Improve Outcomes* was a symposium held at the 10<sup>th</sup> Congress of the European Society of Minimally Invasive Neurological Therapy (ESMINT) in Nice, France. The symposium included a presentation on use of RAPID, an automated imaging analysis tool, in hub-and-spoke stroke centers to facilitate endovascular treatment in patients with AIS. The symposium also included discussion of characteristics associated with good clinical outcomes, such as number of passes. An update on Sim & Size, a modular software that optimizes size selection of flow-diverting stents for the treatment of cerebral aneurysms, was also presented at ESMINT 2018.

### IMPROVING OUTCOMES IN AIS: USE OF “RAPID” IN A STROKE NETWORK

RAPID is an automated imaging analysis tool that offers a fast, objective method for determining eligibility for mechanical thrombectomy and quickly assesses computed tomographic perfusion (CTP) or magnetic resonance diffusion imaging in a stroke network. University Hospital Graz (UHG), which has been performing mechanical thrombectomies since 2011, is a comprehensive stroke center (CSC) that works closely with four primary stroke centers (PSCs) in southeastern Austria. In 2012, UHG began to use the RAPID automated imaging analysis tool to improve patient selection for mechanical thrombectomy. RAPID interprets CTP imaging or diffusion weighted magnetic resonance imaging of the infarction core and assesses mismatch between the perfusion lesion and the critically hypoperfused brain tissue (penumbra). It also generates an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) to expedite patient selection. A recent iteration of RAPID enables clinicians to apply evidence from the DAWN and DEFUSE 3 trials to cases to assist in decision-making. Images and information from CT/MR can be downloaded onto mobile phones or emailed to an on-call neuro-radiologist or neuro-interventionalist, or from a PSC to a CSC.

Although RAPID can be integrated into a stroke network, not all PSCs have the technology, expertise, and experience to adopt RAPID. Requisites for a PSC to adopt RAPID include: CTP or MR perfusion systems, neuroradiologists, and experience. For these PSCs, RAPID offers three key advantages:

1. In the event a patient is not eligible for mechanical thrombectomy, the individual will not undergo unnecessary facility transfer;

2. Duplicate imaging may not need to be performed at the CSC after eligibility has been determined at the PSC; and
3. In many instances, the patient can be directly transferred to the interventional suite at the CSC.

RAPID helps stroke systems achieve puncture times <90 minutes from the time of the first image. For instance, results from a study at Baptist Medical Center (BMC) demonstrated that patients triaged at a PSC with RAPID significantly reduced door-to-puncture time ( $P<0.001$ ) compared to patients transferred from a PSC without CTP.<sup>1</sup> However, algorithms in any automated software have arbitrary definitions and thresholds. In RAPID, these include designations for the apparent diffusion coefficient (ADC) threshold in diffusion weighted imaging and the Tmax threshold for the delay of the bolus. The algorithm may also pre-determine the location of the arterial inflow and venous outflow. It may automatically correct for motion artifacts. In addition, RAPID’s criteria for mismatch may be different than what is used internally at the PSC. These may result in miscalculations by RAPID. In certain cases, clinicians should view the source images and always pay close attention to the patient’s clinical status.

RAPID is an impressive technology that speeds the transfer of information between centers and specialists and improves stroke care. This technology provides quantified data regarding the core, penumbra, and mismatch and generates an ASPECTS score. RAPID enables clinicians to make decisions regarding mechanical thrombectomy and may be particularly valuable in patients who have surpassed the six-hour window or had stroke symptoms upon waking.

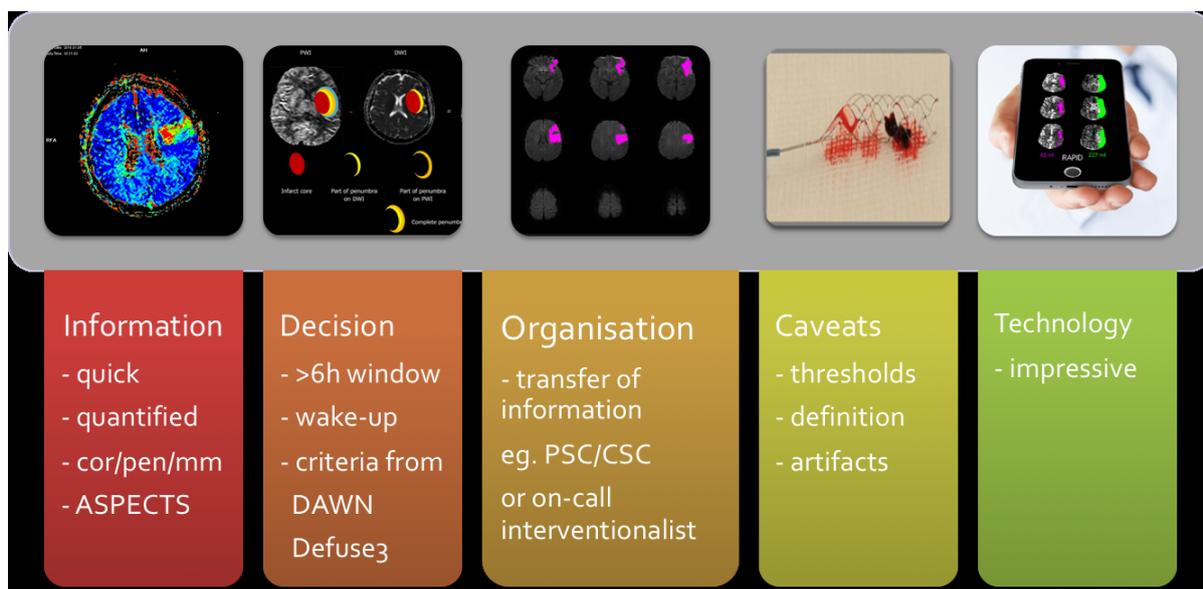


Figure 1. Summary of RAPID Use in Assessment of Patient Eligibility for Mechanical Thrombectomy

**A GOOD FIRST PASS IS BETTER THAN MULTIPLE ATTEMPTS**

There has been increasing attention on variables that influence outcomes. Thrombolysis in Cerebral Infarction (TICI) scores were developed to assess cerebral perfusion before and after endovascular treatment. It is now understood that full reperfusion, denoted by TICI 3, is associated with better outcomes than TICI 2b.<sup>2</sup> Recently, there has been increasing recognition that the number of passes has an effect on outcomes.

The North American Solitaire Acute Stroke Registry (NASA Stroke Registry) showed that about 40% of patients had TICI 3 after mechanical thrombectomy; however, only 25% of those were achieved on the first pass.<sup>3</sup> Indeed, not all TICI 3 outcomes were the same. First-pass TICI 3 had lower mortality rates compared to any TICI 3 at 16.3% and 20.5%, respectively (Table 1). Any TICI 2 was associated with a mortality rate of 30.2%.<sup>3</sup> Morbidity, as denoted by modified Rankin scale (mRS) was also better with first-pass TICI 3 compared to any TICI 3 or any TICI 2.<sup>3</sup>

**Table 1. NASA Stroke Registry: First-Pass TICI 3 vs TICI 3 or TICI 2<sup>3</sup>**

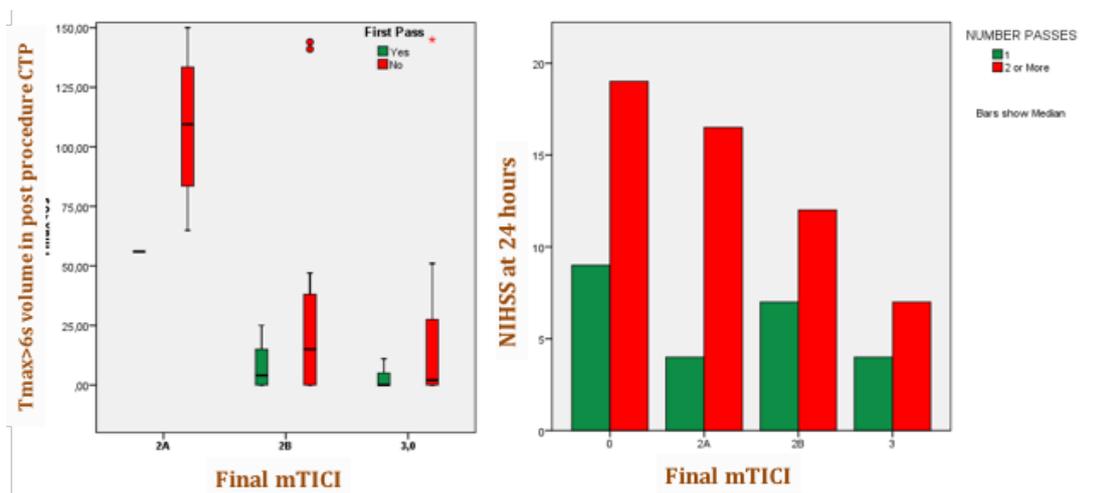
	mRS ≤2 (%)	Mortality (%)
First-Pass TICI 3	61.3	16.3
Any TICI 3	55.0	20.5
Any TICI 2	44.3	30.2

mRS – modified Rankin scale.

A study at Hospital Vall d’Hebron in Barcelona, Spain is currently underway to investigate the effect of the first pass, or single use of the retrieval device, in mechanical thrombectomy. According to the study protocol, CTP is performed before and after mechanical thrombectomies. In general, patients with better post-procedure perfusion had a more dramatic clinical recovery at 24 hours compared to patients with larger hypoperfused areas after thrombectomy. Moreover, smaller areas of hypoperfusion post-procedure were a better predictor than TICI score in terms of predicting clinical outcome; data show that a lesion <6cc is likely to have a good recovery even if the case is a TICI 2b or even TICI 2a. Looking at the number of passes and post-procedure perfusion, cases with a single pass had better perfusion, denoted by smaller areas of

hypoperfused brain, than cases for which multiple passes were used.

These two analyses combined suggest that it is better to achieve any TICI score with a single pass than with multiple passes. Data from this study also suggest that patient outcomes will be better even if the first pass results in TICI 2a, than if multiple passes are attempted. First pass was associated with better National Institutes of Health Stroke Scale (NIHSS) and mRS scores. A single pass was also associated with shorter procedure time, which itself was correlated with lower NIHSS score. For the overall cohort, short procedure time with a single pass was associated with a lower NIHSS score compared to short procedure time with multiple passes (Figure 2).



**Figure 2. Correlation of Passes and a) post-procedure hypoperfused volume, b) 24-Hour NIHSS Score in Short Procedures**

Although it remains unknown why multiple passes impair recovery, it is possible that multiple passes cause greater disruption to the clot or there may be incremental damage to the vessel wall with each pass. It is proposed that the target for each procedure should be to achieve the highest recanalization possible on the first pass.

The 4S study (N=193) assessed procedural characteristics of first-pass mechanical thrombectomies and outcomes performed at five institutions in Spain. Over one third (38.8%) of cases achieve TICI 2c or TICI 3 after the first pass. Variables that were significantly correlated with success after first pass included:

- Push & fluff stent during deployment versus standard unsheathing (P=0.02)
- Size the stent according to the vessel diameter vs. oversizing (P=0.03)
- Balloon guide catheter vs. no balloon (P=0.03)
- High placement of balloon versus low placement (P=0.05)
- Clot protrusion vs no protrusion (P=0.01)

Differences between <i>in vivo</i> measurements and simulations			
Localisation	N	Mean	SD
Proximal	26	3,3%	3,0%
Distal	31	0,4%	1,8%
Ext. curv.	19	0,2%	1,4%
Neck	15	0,6%	4,1%
Other	5	-0,1%	1,8%
<b>All</b>	<b>97</b>	<b>1,1%</b>	<b>2,8%</b>

### METALLIC SURFACE COVERAGE AND OPTIMIZING PIPELINE DEVICE OUTCOMES

Sim&Size is a modular software system used to optimize procedures involving the Pipeline Embolization Device (PED). A stack of 2D images (3DRA) are imported and post-processed into the Sim&Size module, and the user defines the desired landing zone. Sim&Size then constructs the final stent length after deployment as well as wall apposition. This process usually takes < 5 minutes. Sim&Size’s newest feature shows variation of metallic surface coverage (MSC) on the stent. A recent *in vivo* validation study was based on several measurements taken after PED placement. An MSC calculation was taken for three different measurements of rhombi designated along various locations of the PED (distal, proximal, etc). The MSC calculations were then compared to the MSC proposed by Sim&Size prior to the procedure. The average agreement between the *in vivo* measurement and Sim&Size was about 1%, with a standard deviation of 2.8% (Figure 3).

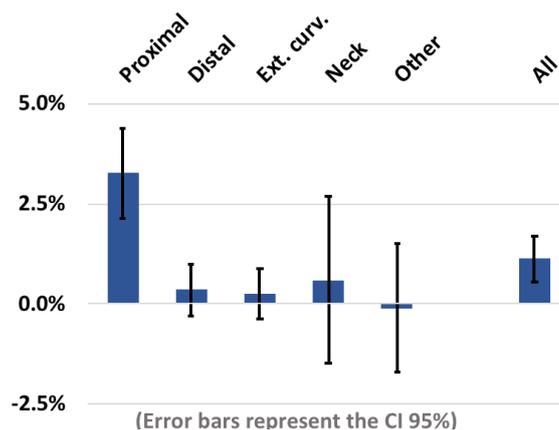
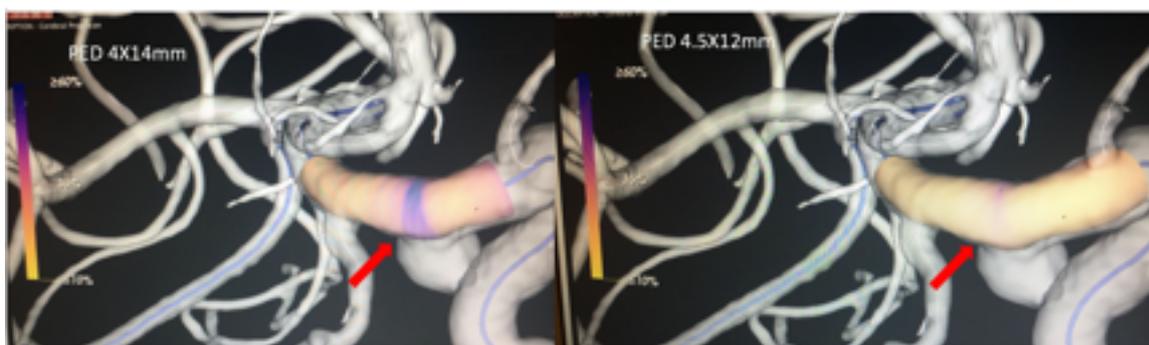


Figure 3. In Vivo MSC Calculations Compared to Sim&Size Simulations

MSC can be used to optimize stent selection. For example, in a patient for whom two PED sizes might be appropriate based on length and wall apposition (PED 4x14mm and PED 4.5x12mm), MSC calculations for the stent selection parameters indicate that the 4x14mm would result in more metal at the neck. The mesh of a braided device,

such as PED, can be adversely affected when the device is oversized too much. A post-procedure CT image of the implanted 4X14mm PED showed high-density coverage at the aneurysmal neck.



Note: Purplish area denotes degree of MSC.

Figure 4. Comparison of MSC for PED 4x14mm and PED 4.5X12mm in Case Patient

This new feature of Sim&Size provides incremental pre-procedural data to avoid excessive sizing and to optimize PED procedures. After defining the landing zones, Sim&Size shows the optimal length, wall apposition, and MSC. This also has the benefit of shortening the deployment time. MSC was slated to be launched, in collaboration with Medtronic, in Europe, the Middle East, and Africa in October 2018. A study assessing whether MSC improves aneurysm occlusion is planned.

## **CONCLUSION**

Technological innovations and understanding of procedural techniques are improving outcomes for patients with AIS. RAPID, an automated imaging analysis tool, can provide a fast, objective assessment of whether patients are eligible for mechanical thrombectomy and facilitates communication between a PSC and the CSC. It may eliminate duplicate imaging at the CSC, and some patients can be transferred directly to the interventional suite. New research suggests that patients undergoing mechanical thrombectomy will have better outcomes if only a single pass of the clot retriever is used. Related to endovascular treatment of aneurysms, MSC, a new feature of Sim&Size, can inform size selection of PED to optimize density at the aneurysmal neck, which may enhance occlusion.

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