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# NeuroNews

EDUCATIONAL SUPPLEMENT


## Siemens' Unique Imaging Technologies:

# Tailored to Enhance Your Stroke Workflow

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In this supplement:



# Siemens' unique imaging technologies support a one-stop-shop stroke workflow

The presentation of a groundbreaking trial in October 2014 hailed the dawn of a new era in the field of interventional neuroradiology. Presented by Diederik Dippel at the World Stroke Congress (17-21 October 2014, Istanbul, Turkey) the MR CLEAN trial initiated a domino effect, causing at least four other similar trials, including EXTEND-IA, ESCAPE, SWIFT PRIME and REVASCAT, to be stopped early.

MR CLEAN, a pragmatic, phase 3 clinical trial, compared intra-arterial treatment (intra-arterial thrombolysis, mechanical treatment, or both) plus usual care (which could include intravenous administration of alteplase) with usual care alone (control group) in patients with acute ischaemic stroke and a proximal intracranial arterial occlusion of the anterior circulation that was confirmed by vessel imaging. In the study published in the *New England Journal of Medicine*, Dippel *et al* concluded: "Our results show that patients with acute ischaemic stroke caused by a proximal intracranial arterial occlusion of the anterior circulation have a benefit with respect to functional recovery when intra-arterial treatment is administered within six hours after stroke onset. This treatment leads to a clinically significant increase in functional independence in daily life by three months, without an increase in mortality. Our findings stand in clear distinction to those of recent randomised, controlled trials that failed to show a benefit of intra-arterial treatment."

In MR CLEAN and in all subsequent trials, the overwhelming efficacy of intra-arterial treatment for acute ischaemic stroke was shown.

Now that the efficacy of mechanical inta-arterial treatment has been firmly established, the question is how the workflow can be improved, and the procedure made faster to ensure better outcomes for the patients. In that vein, much emphasis is now being placed on the imaging that is used to select patients, and how this in turn can contribute to improved outcomes. This educational supplement will highlight the importance of improved stroke workflow in clinical practice and explore the benefits of faster pathways.

***Endovascular thrombectomy leads to a clinically significant increase in functional independence in daily life by three months, without an increase in mortality.***

# The evolution of stroke workflow

While the most recent trials in favour of endovascular treatment for acute ischaemic stroke are considered satisfactory, there is the general consensus in the field that there remains room for improvement. Much emphasis is being placed on the time it takes from symptom onset to reperfusion of the brain, and where along the stroke workflow this time can be reduced (60 minutes or less: Time to reperfusion in acute stroke therapy must be reduced. *NeuroNews* Issue 19, September 2015).

Today's **standard** stroke workflow consists of a neurological exam upon arrival at the hospital, followed by patient transfer to either computed tomography (CT) or magnetic resonance imaging (MRI) facilities for a diagnostic brain scan. Depending on the results, the patient, if appropriate, is sent to the angiography suite for treatment. These steps, although highly dependent on multiple factors at the clinic, typically translate into ~130 minutes of elapse between the patient's arrival at the hospital and reperfusion of the brain.

In order to save time, the first logical step is to bring diagnosis (CT/MRI) and treatment (angio) closer together; optimally in one room. This **combined solution** is already available at selected comprehensive stroke centres across the world. In order to reduce transfer time, which constitutes a large percentage of the overall time from onset to reperfusion, diagnosis (CT/MRI) and treatment (angio) 'meet each other' in one room. The beauty of the Siemens solution lies in its independence: Both modalities can be used together, but also independently of each other in different rooms. This means that in addition to the emergency stroke scenario, the CT scanner can be used as a regular diagnostic scanner, optimising the usage profile and speeding up return on investment.

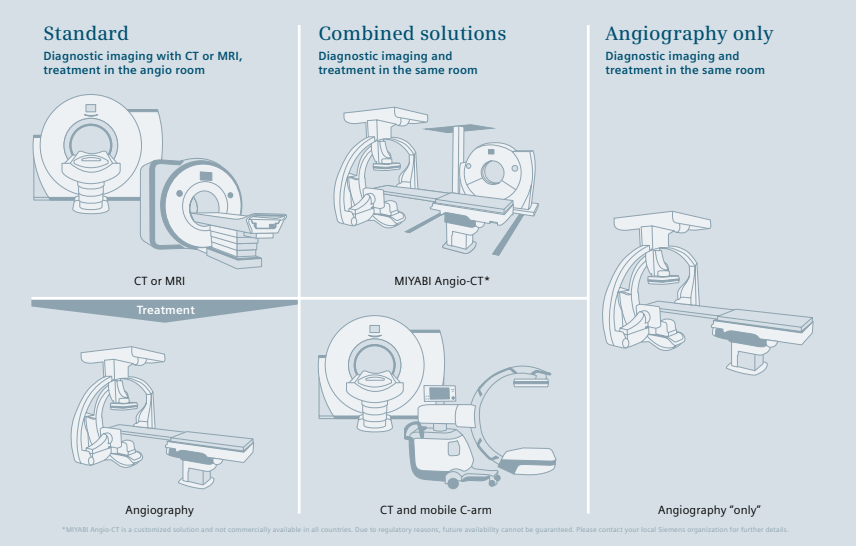


**Figure 1:** Siemens' pathways for optimising stroke workflow

Moreover, **Siemens' angio-only one-stop-shop stroke workflow** opens up a new and exciting potential pathway to shorten door-to-groin time by ~60 minutes. In essence, the angio-only one-stop-shop stroke workflow saves time by specifying that patients with a high National Institute of Health Stroke Scale (NIHSS) score should be taken directly to the angio suite for diagnosis with a DynaCT (cone-beam CT) and receive immediate endovascular treatment, if necessary. According to Meretoja *et al* (*Stroke*. 2014 Apr;45(4):1053-8. doi: 10.1161/STROKEAHA.113.002910. Epub 2014 Mar 13), this accelerated care path can potentially translate into 108 days of additional disability-free life for the patient (95% prediction interval, 0.9–2.7), respectively 20% higher chance (see Figure 2) of good outcome (mRS≤2).

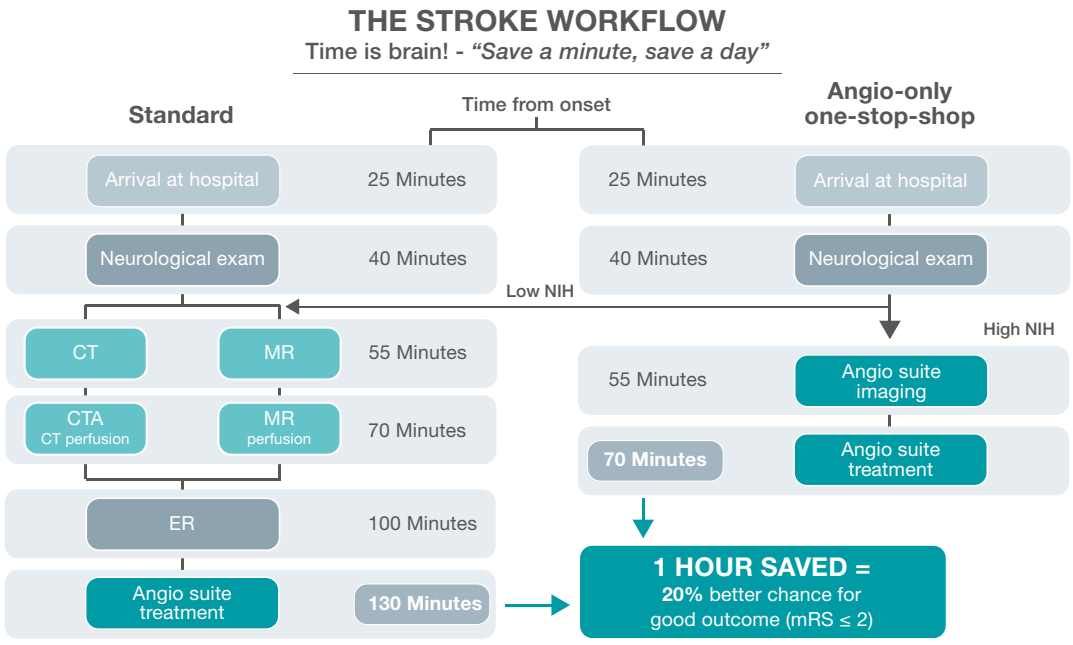


**Figure 2:** Comparing "standard workflow" and "angio-only one-stop-shop" workflow

# Interview

Tudor Jovin, MD, University of Pittsburgh School of Medicine, Pittsburgh, USA, speaks to *NeuroNews* about his experience treating acute stroke patients and his thoughts on the future of stroke therapy. He also explains the potential benefits of incorporating the "one-stop-shop" stroke workflow.

Tudor Jovin, MD

### Which angiography system are you currently using at your institution?

At the moment we have two biplane systems: a Siemens AXIOM Artis and a GE Innova. Soon we will be using the Siemens Artis Q biplane system.

### What is the most critical piece of diagnostic information for patient selection in the stroke workflow?

In my opinion, it is the presence of vessel occlusion and size of the ischaemic core.

### Do you believe that this information can be provided by the "one-stop-shop" workflow?

Yes! The combination of DynaCT Angio and DynaPBV has great potential for being capable of providing this important information with sufficient accuracy for clinical decision making.

### What are the clinical benefits of the "one-stop-shop" workflow?

First and foremost I would mention the substantial time savings, accompanied by potential cost savings by avoiding additional imaging.

### Do you also anticipate benefits for clinics in the "one-stop-shop" workflow?

Yes. I would expect to see benefits through a reduction in unnecessary imaging. Subsequently, I would see improved outcomes through faster recanalisation which translates into lower costs for the hospital by reduced length of stay, reduced ICU care, or fewer additional procedures such as feeding tubes, and many more.

### What are the prerequisites for the realisation of the "one-stop-shop" workflow?

Currently, these are adequate angiographic equipment and adequate in-hospital infrastructure: 24/7 in-house available emergency medicine, stroke neurology support, technologists and an appropriate level of nursing and anaesthesia, plus the immediate availability of neuro-interventionalists.

### Recent studies have shown that the time from symptom onset to reperfusion must be reduced. How can the "one-stop-shop" workflow help with this?

The most time-consuming steps from arrival at the hospital to groin puncture are transportation to and from imaging, as well as the imaging itself. Imaging in the angio suite would help to save precious time.

### Do you expect many new centres to offer interventional stroke treatment in the near future?

Yes. But acute stroke interventions need to be streamlined to centres that have the adequate volumes and infrastructure.

### What needs to be considered for these new centres? How should these centres be equipped?

A modern endovascular stroke centre should have all the available imaging modalities including CT angiography, CT perfusion and MRI capabilities 24/7—not necessarily for routine patient selection, but for more challenging selection questions and also for peri-procedural management.

> ***"The combination of DynaCT Angio and DynaPBV has great potential for being capable of providing this important information with sufficient accuracy for clinical decision making."***

# Time is brain

The phrase "time is brain" is one that has been linked to the treatment of stroke for a number of years. It has never been truer, however, than in the current climate where multiple trials have shown that the previous gold standard of care (IV t-PA) can be significantly improved with new treatment. Not only did these trials prove that a new treatment could drastically improve outcomes for stroke patients—they also helped stroke teams to determine that there is still room for even more improvement. The value of the "time is brain" concept is made clear when comparing the older generation of negative endovascular stroke trials, with the newer, positive trials.

In the Merci Registry (a dataset that shows the efficiency of the treatment of US hospitals treating endovascular stroke at the time the IMS III trial was ongoing), the door-to-groin time was a median of 2.7 hours, which largely explains why all the previous trials (IMS III, MR RESCUE) were negative. Since then, and thanks to the additional data collected in the new wave of trials, it has been established that every 30 minutes saved translates into a 10% higher chance of a good outcome.

Looking at the times in the more recent trials, ESCAPE (the most efficient trial) had a median door-to-groin time of 90

minutes, while in SWIFT PRIME it was 95 minutes and in REVASCAT it was 109 minutes. Picture-to-puncture time was 50 minutes in ESCAPE, 63 minutes in SWIFT PRIME and 68 minutes in REVASCAT. It is clear that in the later trials, the investigators recognised the importance of efficiency and planned accordingly.

The minutes saved between symptom onset and reperfusion directly affect the patient outcome. The faster patients receive treatment, the better their chances of leading a disability-free life, and the lower the long-term financial burden. Meretoja *et al* (*Stroke*. 2014 Apr;45(4):1053-8. doi: 10.1161/STROKEAHA.113.002910. Epub 2014 Mar 13) found that each minute of symptom onset-to-treatment time saved, granted an extra 1.8 days of healthy life on average. In the cohort studied, each 15 minute decrease in treatment delay provided an average equivalent to one month of additional disability-free life.

***Each minute of symptom onset-to-treatment time saved, granted an extra 1.8 days of healthy life on average. In the cohort studied, each 15 minute decrease in treatment delay provided an average equivalent to one month of additional disability-free life.***

Implementing the new angio-only one-stop-shop stroke pathway has the potential to significantly shorten the door-to-treatment time by merging diagnostics and therapy steps. This new care path (see Figure 2) specifies that clinically pre-selected patients with a high NIHSS score could be taken directly to the angiography suite. As all patients are given an NIHSS score when they arrive at the hospital, this pre-selection method only sends those patients to the angiography suite who either have larger bleed (~10-15%) or a severe ischaemic stroke (~85-90%). The latter subgroup of patients has the highest probability of having a large vessel occlusion and thus strongly benefits from endovascular treatment.

Siemens' unique imaging technologies optimally support the new one-stop-shop stroke workflow, combining diagnostic and therapy steps in the angio suite, and therefore help to reduce door-to-treatment time.

# The faster the endovascular treatment, the lower the Rankin score

The year 2015 saw the presentation of data and the publication of what have become the most ground-breaking stroke trials in recent history. These historical trials proved one indisputable fact: The faster the endovascular treatment, the lower the Rankin score.

## MR CLEAN

MR CLEAN, a pragmatic, phase 3 clinical trial, compared intra-arterial treatment (intra-arterial thrombolysis, mechanical treatment, or both) plus usual care (which could include intravenous administration of alteplase) with usual care alone (control group) in patients with acute ischaemic stroke and a proximal intracranial arterial occlusion of the anterior circulation that was confirmed by vessel imaging.

Study authors, Diederik Dippel *et al*, report that between December 2010 and March 2014, 500 patients were randomised in 16 Dutch centres. Initiation of intra-arterial treatment had to be possible within six hours after stroke onset. Eligible patients were those with an occlusion of the distal intracranial carotid artery (M1 or M2), or anterior cerebral artery (A1 or A2)—established with computed tomography angiography (CTA), magnetic resonance angiography (MRA), or digital-subtraction angiography (DSA)—and a score of 2 or higher on the National Institutes of Health Stroke Scale (NIHSS). All patients underwent clinical assessment at baseline, after 24 hours, and at five to seven days or at discharge if earlier.

In the study, 233 patients (46.6%) were assigned to the intervention group and 267 patients (53.4%) were assigned to the control group. The authors report that the results show a shift in the distribution of the primary-outcome scores in favour of the intervention. "The shift toward better outcomes in favour of the intervention was consistent for all categories of the modified Rankin scale, except death. The absolute between-group difference in the proportion of patients who were functionally independent (modified Rankin score, 0 to 2) was 13.5 percentage points (95% CI, 5.9 to 21.2) in favour of the intervention (32.6% vs. 19.1%), with an adjusted odds ratio of 2.16 (95% CI, 1.39 to 3.38)."

Dippel *et al* conclude, "our results show that patients with acute ischaemic stroke caused by a proximal intracranial arterial occlusion of the anterior circulation have a benefit with respect to functional recovery when intra-arterial treatment is administered within six hours after stroke onset. This treatment leads to a clinically significant increase in functional independence in daily life by three months, without an increase in mortality. Our findings stand in clear distinction to those of recent randomised controlled trials that failed to show a benefit of intra-arterial treatment."

Commenting on the results, Dippel told *NeuroNews* that going forward, "the challenge for the future will be to identify all patients who are eligible for this treatment: Those with an occlusion who can be treated within six hours, and transfer them quickly to an intervention centre."

## EXTEND IA

Following the presentation of the MR CLEAN data, the Australia/New Zealand-based EXTEND-IA trial was stopped early due to efficacy after 70 patients had undergone randomisation (35 patients in each group—alteplase plus endovascular thrombectomy vs. alteplase alone).

Patients with ischaemic stroke who were receiving 0.9mg of alteplase per kilogram of body weight fewer than 4.5 hours after onset were randomised to undergo endovascular thrombectomy with

the Solitaire stent retriever (Covidien/Medtronic) or to continue receiving alteplase alone. The authors report that all the patients had occlusion of the internal carotid or middle cerebral artery and evidence of salvageable brain tissue, and an ischaemic core of less than 70ml on computed tomographic (CT) perfusion imaging. The co-primary outcomes were reperfusion at 24 hours and early neurological improvement (≥8-point reduction on the NIHSS or a score of 0 or 1 at day three).

The study authors reported that patients in the endovascular therapy group had significant improvements in both co-primary endpoints compared with the alteplase-only group. "Endovascular therapy resulted in increased reperfusion at 24 hours and a probability of reperfusion of more than 90% without symptomatic intracerebral haemorrhage, as compared with the alteplase only group (89% vs. 34%, p<0.001)," they wrote.

Further, Bruce Campbell *et al* found that endovascular therapy led to greater early neurological recovery at three days, and improved functional outcome in an ordinal analysis of the score on the modified Rankin scale at 90 days.

Comparing EXTEND-IA to MR CLEAN, the authors note in the discussion that, "the interval between the initiation of alteplase and randomisation was 30 minutes in our study, as compared with 100 minutes in the MR CLEAN trial, because of our approach of identifying patients with the greatest potential to benefit from reperfusion and then maximising early reperfusion with the use of combined alteplase and endovascular therapy, rather than waiting to assess clinical response to alteplase." They add that as a result, the EXTEND-IA trial had a median of 50 minutes less in the time from stroke onset to the initiation of the endovascular procedure, which may have contributed to the substantially higher proportion of patients with independent functional outcomes observed in the Australia/New Zealand-based study.

## ESCAPE

Similarly to EXTEND-IA, the ESCAPE trial was stopped early following an unplanned interim analysis that was conducted after the initial release of the MR CLEAN results. The halting of the trial was announced for the first time at the Society of Vascular and Interventional Neurology meeting (SVIN, 6–9 November, Hollywood, USA) by co-principal investigator Michael Hill (University of Calgary, Canada). The final data were published in the *New England Journal of Medicine*.

ESCAPE investigators enrolled 316 participants at 22 centres worldwide, of whom 238 received intravenous alteplase (120 in the endovascular treatment group and 118 in the standard care control group). Patients with a proximal intracranial occlusion in the anterior circulation were included up to 12 hours after symptom onset. Patients with a large infarct core or poor collateral circulation revealed by CT and CT angiography were excluded. The primary outcome was the score on the modified Rankin scale at 90 days.

In the endovascular treatment group, the median time from the study CT of the head to first reperfusion was 84 minutes. The rate of functional independence (90-day modified Rankin score of 0 to 2) was increased with the intervention (53% vs. 29.3% in the control group; p<0.001). The primary outcome favoured the intervention, and the intervention was associated with reduced mortality (10.4% vs. 19% in the control group).

Hill *et al* conclude that the ESCAPE trial provides evidence of the benefit of endovascular treatment in patients with moderate to severe ischaemic stroke who were selected using imaging.

In the ESCAPE trial, compared with the MR CLEAN trial, the investigators note that there was a pre-specified efficiency target for the time from non-contrast CT to reperfusion which encouraged fast image acquisition and interpretation and fast decision-making. They comment that, "critical to the achievement of rapid treatment was parallel decision-making and action. For example, participants in the intervention group underwent groin puncture while alteplase was being infused, and complete reperfusion was achieved in some participants before the alteplase infusion was finished. The primary emphasis was on achieving early reperfusion."

Based on the results from these trials, it is clear that there are three pillars that support these positive outcomes: 1) imaging selection to identify patients with a small core, proximal blocked artery and good collaterals; 2) very fast treatment; and 3) use of this new technology to open arteries safely and completely.

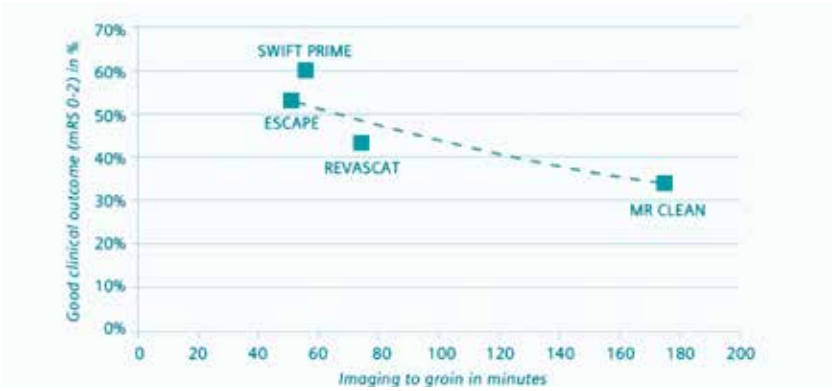


Figure 3: Faster access to endovascular treatment associated with better outcomes

# Siemens' unique imaging technologies – the one-stop-shop idea

Siemens' unique technology optimally supports a one-stop-shop workflow. After clinical NIHSS-based pre-selection, the imaging technologies provided by Siemens help to detect rare cases of bleedings (haemorrhagic stroke) in the angio suite. In the case of an ischaemic stroke, the collateral supply and infarct core can be evaluated, helping the stroke team to decide whether the patient should be treated or not.

The Artis Q with its 16-bit detector and the true 16-bit image chain with its dedicated cone-beam CT reconstruction create 3D reconstructions that allow clinicians to detect haemorrhages in the angiography suite.

According to the latest guidelines, knowledge about the infarct core and penumbra (potentially salvageable brain tissue) is crucial for non-invasive image-based patient selection. Using Siemens' unique *syngo* DynaPBV Neuro software with integrated bolus-watching phase,

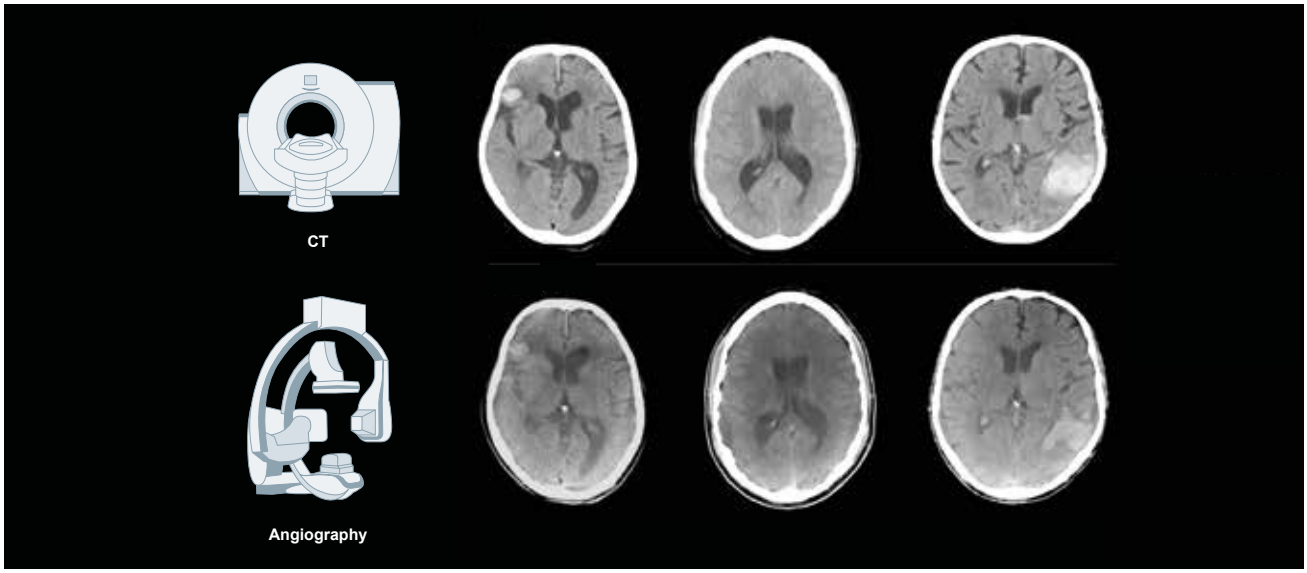


**Figure 4:** CT vs *syngo* DynaCT to determine whether stroke is haemorrhagic or ischaemic: One step ahead with Artis Q. Images courtesy of Prof. Skalej, Neuroradiology, Magdeburg, Germany.

both the core infarct area and the tissue at risk can be evaluated.

Siemens *syngo* DynaPBV is the only technology on the market which enables functional imaging in the angiography suite. Hence, after validation of an ischaemic stroke, clinicians can immediately verify the location of the occlusion (tissue at risk), analyse the status of collateral networks, and evaluate the core infarct area (shown as hypo-perfusion in the *syngo* DynaPBV map). This information is used to determine how much brain tissue is potentially salvageable and to decide on a treatment plan.

With the Siemens algorithms, the physician gains three volumes with one *syngo* DynaPBV Neuro acquisition (only 60cc of contrast agent). Optimal timing for the scan is accomplished by Siemens' unique integrated bolus-watching phase.

To summarise, the three volumes from the *syngo* DynaPBV acquisition (see Figure 5) have the following advantages:

1. The native *syngo* DynaCT can be used to check for bleedings (→haemorrhagic stroke).
2. The *syngo* DynaCT in angiography helps detect the occlusion and thereby allows evaluation of location and extent of tissue at risk.
3. The *syngo* DynaPBV Neuro reconstruction itself provides information comparable to cerebral blood volume (CBV) data conventionally acquired, among others, with CT perfusion imaging concerning the location and extent of the core infarct.

With a mismatch analysis of tissue at risk and core infarct, the physician can determine if the patient will benefit from endovascular therapy and decide to treat or not to treat. What is more, with *syngo* DynaPBV Neuro, contrast is given intravenously. The decision to treat or not to treat can be made non-invasively before the groin puncture avoiding additional risk for patients not indicated for endovascular therapy.

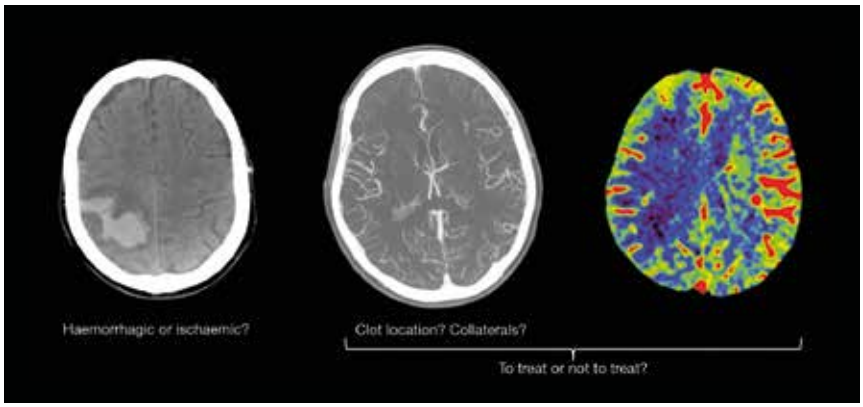


**Figure 5:** *syngo* DynaPBV Neuro: Gain three volumes with one *syngo* DynaPBV Neuro acquisition (only 60cc of contrast agent). Images on the left: courtesy of Prof. Skalej, Neuroradiology, Magdeburg, Germany; image on the right: courtesy of Prof. Dörfler, Dr Struffert, Neuroradiology, Erlangen, Germany.

## Conclusion

The success of the MR CLEAN, EXTEND-IA, ESCAPE, SWIFT PRIME and REVASCAT trials have validated the use of mechanical thrombectomy for patients with acute ischaemic stroke with large vessel occlusion in the anterior circulation. These results will have a tremendous impact on the management of acute ischaemic patients and will likely revolutionise the organisation of stroke care.

Such results call for a new care path which can significantly reduce door-to-treatment time by combining diagnostics and therapy steps.

When it comes to finding the optimal solution concerning stroke management to meet your needs, Siemens offers the broadest range of imaging solutions for stroke management, including solutions for the one-stop-shop treatment in the angio suite, that can be perfectly tailored to the demands of each site.

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# Can you afford to only have the 2nd best solution for your stroke patients?


Thanks to most recent studies (as MR CLEAN,ESCAPE, EXTEND IA, etc), interventional treatment has proven to be the treatment of choice for many stroke patients. Excellent imaging for patient selection and during intervention is indispensable for safe and efficient vascular therapy. Inter ventional angiography systems have to provide uncompromising image quality while interfering as little as possible with interventional procedures.

Siemens' Artis systems fulfill these requirements by offering comprehensive imaging capabilities such as *syngo* DynaCT to check for bleedings. The unique combination of *syngo* DynaCT in Angiography (to check for clot location and collateral status) and perfusion analysis by *syngo* DynaPBV Neuro (to evaluate size and location of the infarct core) further on helps the physician to decide whether an interventional treatment is advised or not. All that can be done in the angio suite by only one intravenous contrast injection, and thereby saves time and enhances outcome.

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