

# Ideas and Innovations in Acute Ischaemic Stroke Treatment

Jens Fiehler<sup>(1)</sup>, Sam Zaidat<sup>(2)</sup>, Marc Ribó<sup>(3)</sup>, Jan Gralla<sup>(4)</sup>, Mayank Goyal<sup>(5)</sup>, Vincent Costalat<sup>(6)</sup>

<sup>1</sup> Director of the Department of Diagnostic and Interventional Neuroradiology, University Medical Center, Hamburg-Eppendorf, Germany

<sup>2</sup> Director of the Mercy Neuroscience and Stroke Center, Toledo, Ohio, USA

<sup>3</sup> Assistant Professor, Stroke Unit, Department of Neurology, Hospital Vall d'Hebron, Barcelona, Spain

<sup>4</sup> Director of the Institute of Diagnostic and Interventional Neurology, Inselspital of the University Hospital, Berne, Switzerland

<sup>5</sup> University of Calgary, Director of Research, Department of Diagnostic Imaging, Calgary, Canada

<sup>6</sup> Department of Neuroradiology, Hospital Centre University of Montpellier, France

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## A B S T R A C T

The effectiveness and safety of endovascular thrombectomy for the treatment of large vessel occlusion (LVO) have been demonstrated in landmark randomized controlled trials. However, patients in these studies were pre-selected and recruited using stringent inclusion and exclusion criteria. The STRATIS registry has evaluated almost 1,000 US patients, with acute stroke, who received endovascular thrombectomy treatment for LVO with a Medtronic stent retriever device in a less stringent “real world” hospital setting. STRATIS data demonstrate that the outcomes and level of safety achieved in RCTs can also be achieved in a non-selective cohort of acute stroke patients, with higher mean baseline NIHSS scores, and with more risk factors than patients in the SEER collaboration database. Patients in STRATIS who were routed directly to a comprehensive stroke centre, compared with patients who were transferred from a peripheral community hospital, to an endovascular centre, had better clinical outcomes and a shorter onset to puncture time.

Two randomized controlled trials are in progress to address the questions of whether acute stroke patients with LVO should bypass local community hospitals in favour of direct transfer to a comprehensive stroke centre, and whether direct mechanical thrombectomy is non-inferior to IV t-PA plus mechanical thrombectomy. The ongoing RACECAT trial has been designed to compare the **T**RANSfer to the **C**losest local stroke centre vs. direct transfer to **E**ndovascular stroke **C**entre of **A**cute stroke patients with suspected large vessel occlusion in the Catalan **T**erritory. This study will provide specific randomized data that will help decide which transportation option provides the best outcome for acute stroke patients.

The SWIFT Direct study is: **S**olitaire™ **W**ith the **I**ntention **F**or **T**hrombectomy plus intravenous t-PA versus **D**IRECT Solitaire™ stent-retriever thrombectomy in acute anterior circulation stroke. The focus of this trial is to determine whether subjects, in Canada and Europe, with an acute ischaemic stroke in the anterior circulation, who are referred to a stroke centre with endovascular facilities, and who are candidates for IV t-PA, will have a non-inferior functional outcome at 90 days when treated with direct mechanical thrombectomy, compared with subjects treated with combined IV t-PA and mechanical thrombectomy.

SIM & SIZE™ is a new simulation software that helps interventional neurologists to optimize and validate their choice of endovascular flow diverter devices for the treatment of intracranial aneurysms. Clinical benefits associated with this software include the successful deployment of shorter devices, and the need for significantly less secondary implants per procedure.

**Key words:** STRATIS, RACECAT, SWIFT Direct, acute stroke, large vessel occlusion, endovascular thrombectomy, SIM & SIZE, simulation software.

**Corresponding author:** Marc Ribó - marcriboj@hotmail.com

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## THE STRATIS REGISTRY

### Introduction and background to STRATIS

This recent symposium was held at the European Society of Minimally Invasive Neurological Therapy Conference (ESMINT) 9th Congress in September 2017, in Nice, and moderated by Professor Jens Fiehler. The purpose of this symposium was to review primary outcome results of the Medtronic-sponsored STRATIS registry. This is a multicenter registry of acute stroke patients with large vessel occlusion (LVO) who have received mechanical thrombectomy intervention with Medtronic devices (Solitaire™, Mindframe Capture™). STRATIS is the **S**ystematic Evaluation of Patients **T**reated with Neurothrombectomy Devices for **A**cu**T**e **I**schemic **S**troke.

Dr Zaidat explained that following positive outcomes with mechanical thrombectomy in published randomized controlled trials (RCTs)<sup>1-5</sup>, mechanical thrombectomy with stent retriever devices has become the accepted global standard of care for acute ischemic stroke patients with LVO. However, the patient populations studies in these

trials were highly selected, with restrictive inclusion and exclusion criteria, and the question of whether the same process timelines and patient outcomes can be achieved with mechanical thrombectomy in a “real-world” setting is a pertinent one. STRATIS is a prospective, multi-center, observational, single-arm registry designed to capture a real-world experience without the requirement of specialized triage imaging, age limits or technique exclusions at academic and non-academic centers in the USA.

### Overall Key STRATIS Results

The methodology, entry criteria and key assessments for STRATIS are summarized below. Imaging, event and technique adjudication, laboratory and statistical analyses were conducted independently by individuals blinded to the study results. Primary performance-related outcomes were the time from puncture to revascularization, and revascularization assessment at end of procedure. Clinical efficacy was based on mRS assessment at 90 days.

## OVERALL STRATIS KEY RESULTS

### METHODS

<b>Design/Objective</b>	<ul style="list-style-type: none"> <li>▪ Independent Steering Committee, imaging and core lab, &amp; statistician</li> <li>▪ Prospective, multi-center, observational, single-arm registry designed to capture a “real world experience” without requirement of specialized triage imaging, age limits or technique exclusions at academic and non-academic centers in the USA.</li> <li>▪ Patients with large vessel occlusion (LVO) acute ischemic stroke (AIS) were enrolled within 8 hours from symptom onset.</li> </ul>
<b>Endpoints &amp; Evaluations</b>	<p><u>Performance</u></p> <ul style="list-style-type: none"> <li>▪ Time from puncture to revascularization (mTICI ≥ 2b)</li> <li>▪ Revascularization assessment at the end of the procedure using TICI score</li> </ul> <p><u>Clinical Efficacy</u></p> <ul style="list-style-type: none"> <li>▪ mRS at 90 days</li> </ul> <p><u>Safety</u></p> <ul style="list-style-type: none"> <li>▪ All-cause mortality (up to 90 days post procedure)</li> <li>▪ Incidence of symptomatic ICH</li> </ul> <p><u>Reproducibility:</u></p> <ul style="list-style-type: none"> <li>▪ A patient-level comparison with SEER database was performed</li> </ul>
<b>Devices</b>	<ul style="list-style-type: none"> <li>▪ First neurothrombectomy device use must be:                             <ul style="list-style-type: none"> <li>▪ Solitaire™ Revascularization Device</li> <li>▪ MindFrame Capture™ LP Device</li> </ul> </li> </ul>

Stratis Registry Key Primary Results

Abbreviations: mRS = Modified Rankin Scale; ICH = Intracranial haemorrhage. mTICI = Modified Treatment in Cerebral Infarction Score.

Over the period August 2014 to June 2016, 1,000 patients were enrolled and the recruitment picture is summarised

in the figure below. A total of 984 eligible patients contributed data for analysis.

## OVERALL STRATIS KEY RESULTS

### PRIMARY RESULTS

- **AUGUST 2014 TO JUNE 2016**
  - 1,000 PATIENTS WERE ENROLLED AT 55 US CENTERS
  - **16 PATIENTS WERE IDENTIFIED TO BE SCREEN FAILURES AND EXCLUDED FROM THE ANALYSIS**
  - TOTAL OF **984** PATIENTS
- **DEVICES USED**
  - SOLITAIRE™ WAS THE FIRST MT DEVICE USED IN 954 PTS (96.9%)
  - MINDFRAME CAPTURE™ LP IN 30 PTS (3.1%)

Stratis Registry Key Primary Results

Primary baseline demographic data and workflow characteristics of patients enrolled in the STRATIS study,

compared with SEER collaboration intervention data, are summarized in the table below.

## OVERALL STRATIS KEY RESULTS

### COMPARISON OF BASELINE & WORKFLOW CHARACTERISTICS, CONTINUED

Characteristic	SEER Intervention	STRATIS	P
Initial Qualifying NIHSS Score	16.6 ± 4.9 (398) [17] (13,20)	17.3 ± 5.5 (984) [17] (13,22)	<b>0.042</b>
IV t-PA delivered	80.5% (323/401)	64.0% (628/982)	<b>&lt;0.001</b>
ASPECTS – per imaging core lab†	8.3 ± 1.7 (388) [9] (7,10)	8.2 ± 1.6 (763) [8] (8,9)	0.091
<b>Target Intracranial Occlusion Location‡</b>			<b>&lt;0.001</b>
Not reported	2.5% (10/401)	0.8% (8/984)	
Internal Carotid Artery Terminus	18.2% (73/401)	22.6% (222/984)	
MCA – First segment (M1)	71.1% (285/401)	54.7% (538/984)	
MCA – Second segment (M2)	8.2% (33/401)	17.3% (170/984)	
MCA – Third segment (M3)	0.0% (0/401)	0.2% (2/984)	
Posterior Circulation	0.0% (0/401)	4.5% (44/984)	

Data are % (n/N), or mean ± SD (N), [median] (IQR). Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale. The protocol was amended to restrict enrollment to mRS 0-1 to ensure consistency with SWIFT PRIME enrollment criteria. †Baseline imaging received for 835 patients, of whom 72 were not evaluated for ASPECTS (38 Posterior stroke, 30 no non-contrast CT, 4 not evaluable), resulting in 763 patients evaluable for ASPECTS. ‡For STRATIS, assessed by the Techniques Core Lab based on operative reports.

Stratis Registry Key Primary Results

Abbreviations: NIHSS = National Institutes of Health Stroke Scale; MCA = Middle cerebral artery; ASPECTS = Alberta Stroke Program Early CT Score; t-PA = tissue plasminogen activator

Of note, initial NIHSS scores were higher in STRATIS patents (i.e. slightly sicker) compared with SEER patients. Intravenous t-PA usage was understandably higher in the SEER data, where a narrow 4.5-hour time window for intervention was enforced in the RCTs vs. STRATIS patients. Internal carotid artery terminus occlusions were

higher in STRATIS vs. SEER patients, and more posterior circulation stroke was evident in STRATIS patients. The process metrics in the STRATIS study, compared with SEER interventions, at different time points are summarized in the table below.

### OVERALL STRATIS KEY RESULTS

COMPARISON OF BASELINE & WORKFLOW CHARACTERISTICS, CONTINUED

Characteristic	SEER Intervention	STRATIS	P
<b>Process Metrics</b>			
Stroke onset to enrolling hospital arrival (door)	143.5 ± 122.2 (400)	149.3 ± 101.0 (907)	0.030
Stroke onset to alteplase initiation	122.9 ± 49.2 (322)	113.3 ± 50.5 (622)	0.001
Hospital arrival to alteplase initiation	28.7 ± 66.0 (265)	42.1 ± 26.5 (336)	0.503
Stroke onset to puncture	263.1 ± 194.7 (394)	226.4 ± 100.0 (976)	0.011
Hospital arrival to puncture	122.0 ± 173.7 (392)	80.1 ± 49.4 (901)	<0.001
Imaging to puncture	68.9 ± 34.7 (394)	71.2 ± 46.4 (824)	0.642
Alteplase to puncture	107.2 ± 206.5 (259)	102.0 ± 73.5 (613)	0.001
Puncture to TICI 2b/3 or completion	45.9 ± 31.0 (348)	45.6 ± 29.0 (939)	0.740
Stroke onset to TICI 2b/3 or completion	293.6 ± 126.5 (349)	271.1 ± 105.7 (945)	0.020

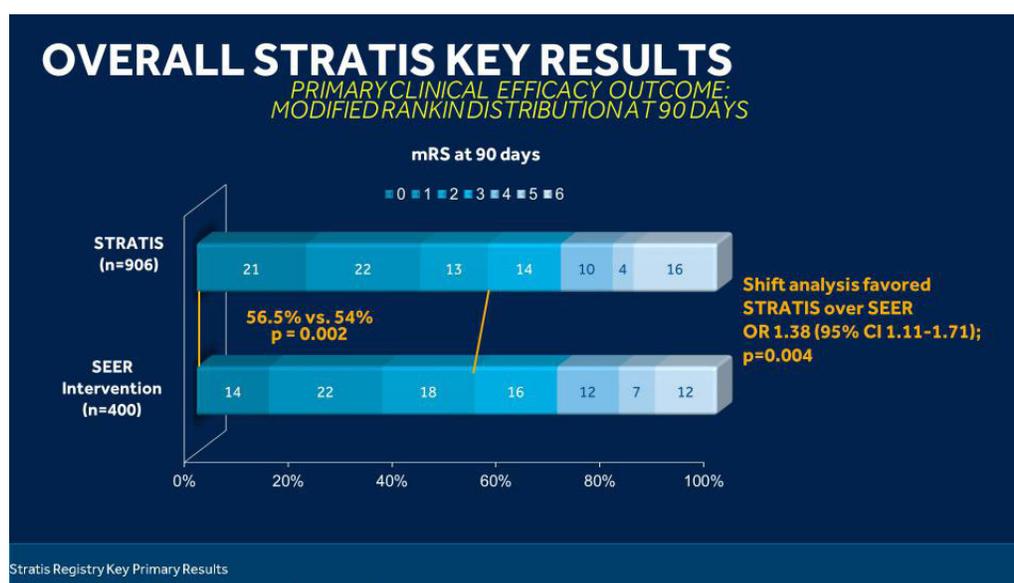
Data are % (n/N), or mean±SD (N). Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale. The protocol was amended to restrict enrollment to mRS 0-1 to ensure consistency with SWIFT PRIME enrollment criteria.

Stratis Registry Key Primary Results

Stroke onset to hospital arrival was 5.8 minutes shorter for SEER compared with STRATIS patients. Time taken from hospital arrival to alteplase initiation was also shorter with SEER intervention compared with STRATIS patients; however, the times from stroke onset to puncture, from hospital arrival to puncture, and from alteplase administration to puncture, were all significantly shorter for STRATIS patients compared with the SEER population. Intervention procedure time, i.e. from puncture to TICI 2b/3 completion, was almost identical for each patient population, but notably, the time from stroke onset to TICI 2b/3 completion was significantly shorted in the STRATIS study. Dr Zaidat suggested two factors were probably contributing to the shorter process metrics recoded in STRATIS; these are: (1) workflow efficiency with

mechanical thrombectomy has improved in stroke centres since this intervention was adopted as the standard of care for LVO, and (2) patient entry to STRATIS is less time consuming than is the case for RCT patient enrolment.

Analysis of the primary efficacy outcome, mRS assessment at 90 days, showed that STRATIS patients scored significantly better on this scale than patients in the SEER database. Significantly more STRATIS patients scored 0 (no disability), or 1 (no significant disability), or 2 (slight disability but can manage own affairs without assistance) on the mRS (56.5%) compared with the SEER population (54%; p = 0.002). This comparison, showing Shift analysis was in favour of STRATIS over SEER, is shown below.



Dr Zaidat summarized the key results and outcomes from the STRATIS study. He stressed that STRATIS enrolled a non-selective population of acute stroke patients, who, compared with SEER RCT populations, had or included:

- significantly higher NIHSS scores;
- a higher percentage of Internal Carotid Artery Terminus (ICAT) occlusion;
- patients with posterior selection strokes;
- a longer median stroke onset to hospital arrival time.

Despite these patient characteristics, which would suggest outcomes favouring the SEER patient cohorts, STRATIS achieved similar technical, safety, and clinical outcomes to those reported in SEER patients. The primary efficacy outcomes achieved in STRATIS, compared with SEER patients, and the incidence of symptomatic intracranial haemorrhage (sICH reported in the two patient populations are summarized in the following table.

Outcome	SEER	STRATIS
Core Lab mTICI 2b-3	76.6%	87.9%; p<0.001
sICH	2.5%	1.4%
mRS 0-2 at 90 days	54%	56.5%

The mean time from stroke onset to puncture was 36.7 minutes shorter in STRATIS compared with SEER; this was primarily driven by a 41.9-minute shorter mean door to puncture time achieved in STRATIS patients. These promising results indicate that the use of Solitaire™ and Mindframe Capture™ for mechanical thrombectomy in LVO, in real-world hospital environment, results in comparable angiographic and mRS-assessed efficacy outcomes, and a level of safety, comparable to that achieved in RCTs.

**STRATIS system of care – transfer vs. direct**

The STRATIS study provided an opportunity to compare outcomes and metrics associated with US acute stroke

patients who are transferred from a peripheral hospital to a comprehensive stroke centre (45%) vs. patients who are transferred directly to comprehensive stroke centres for thrombectomy (55%). Inter-hospital transfer prior to thrombectomy is associated with delayed treatment and worse outcome in the STRATIS registry.

Dr Zaidat highlighted three key differences between transfer and directly received patients. Transfer patients are more likely to have severe stroke score ratings, worse ASPECT assessments, and a greater likelihood of having received IV t-PA. These key differences (yellow text) are summarized in the following table.

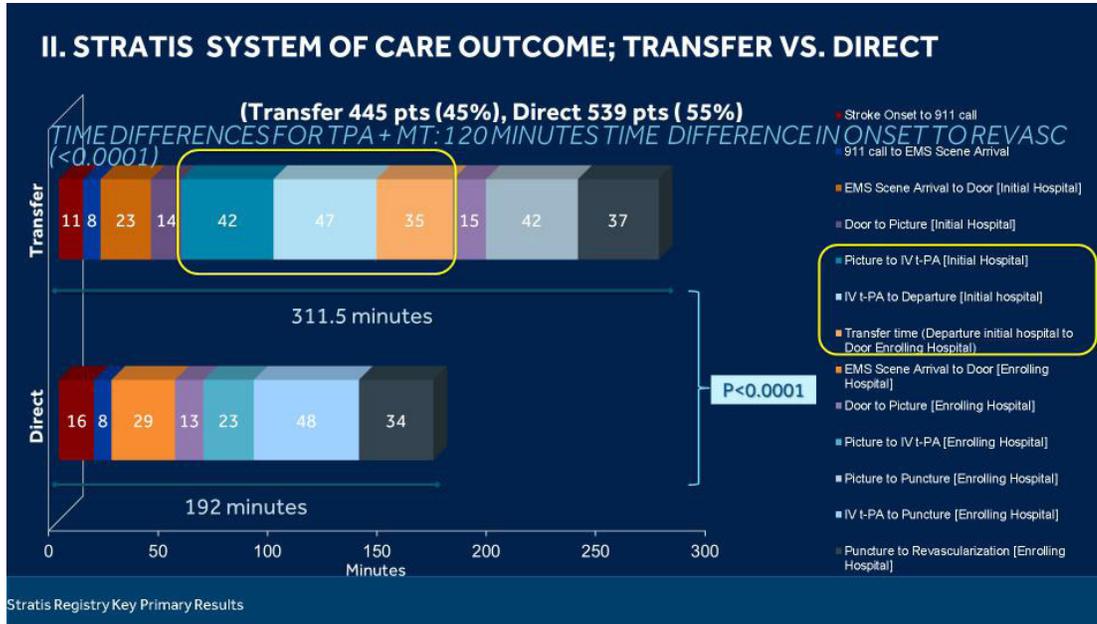
<b>II. STRATIS SYSTEM OF CARE OUTCOME; TRANSFER VS. DIRECT</b>				
<i>DEMOGRAPHICS: DIRECT 539/984 (55%) TRANSFER 445/984 (45%)</i>				
Characteristic	ALL (984)	Transfer (445)	Direct (539)	P
Age, mean (SD), y	67.8 (14.7)	66.9 (14.6)	68.5 (14.8)	0.10
Atrial flutter/Atrial fibrillation	369 (37.5)	165 (37.1)	204 (37.8)	0.80
Systemic Hypertension	712 (72.4)	321 (72.1)	391 (72.5)	0.89
Diabetes mellitus	252 (25.6)	108 (24.3)	144 (26.7)	0.38
Hyperlipidemia	414 (42.1)	184 (41.3)	230 (42.7)	0.68
Current or former tobacco use	465 (47.3)	222 (49.9)	243 (45.1)	0.13
Baseline mRS 0	748 (76.0)	326 (73.3)	422 (78.3)	
Baseline mRS 1	209 (21.2)	104 (23.4)	105 (19.5)	
Initial Qualifying NIHSS Score, mean (SD), median (IQR)	17.3 (5.5), 17.0 (13-22)	18.0 (5.5), 18.0 (13-22)	16.7 (5.5), 17.0 (12-21)	<0.001
Baseline ASPECTS – per core lab*	N=763	N=306	N=457	
Mean (SD), median (IQR)	8.2±1.6, 8.0 (8-9)	7.9 (1.8), 8.0 (7-9)	8.4 (1.4), 9.0 (8-9)	<0.001
Treatment with IV-tPA, No. (%)	628 (63.8)	299 (67.2)	329 (61.0)	0.044

\*Baseline imaging received for 835 pts, of which 72 were not evaluated for ASPECTS (38 Posterior stroke, 3 CT not available, 4 not evaluable), resulting in 763 pts evaluable for ASPECTS.

Stratis Registry Key Primary Results

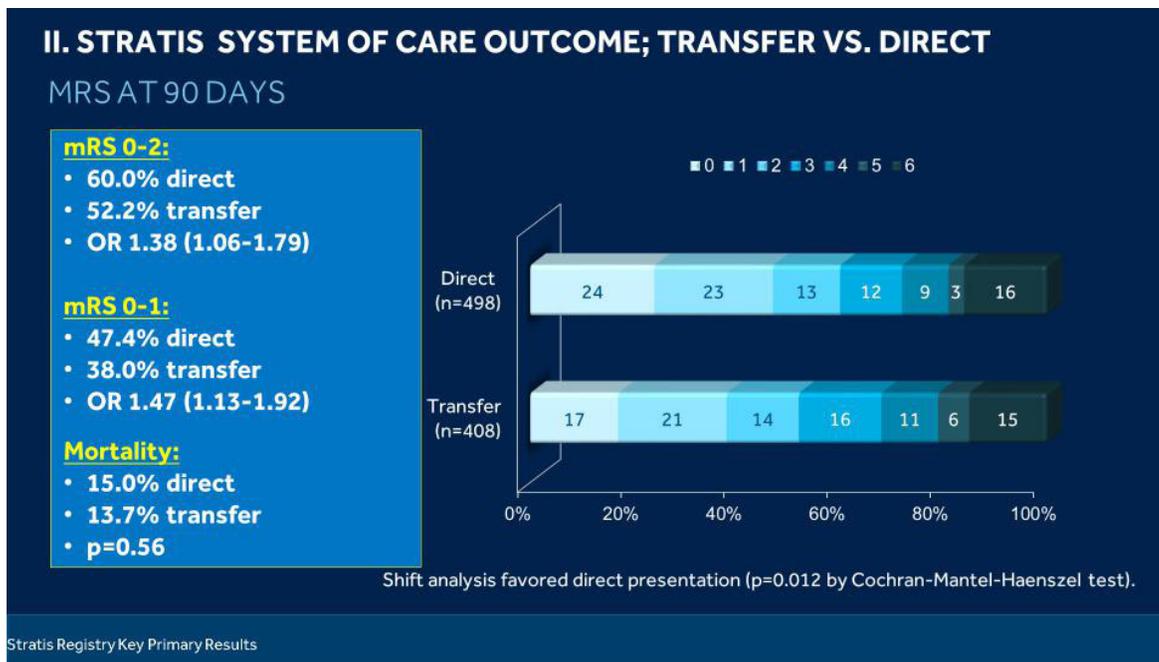
Patients who were transferred in STRATIS were subject to a 120-minute delay in time of stroke onset to revascularization compared with directly transferred patients. This significant delay ( $p < 0.0001$ ) was due to

transferred patients undergoing initial CT scanning, IV t-PA administration, preparation for departure, and transfer time to the comprehensive stroke centre. These delays are highlighted in the figure below.



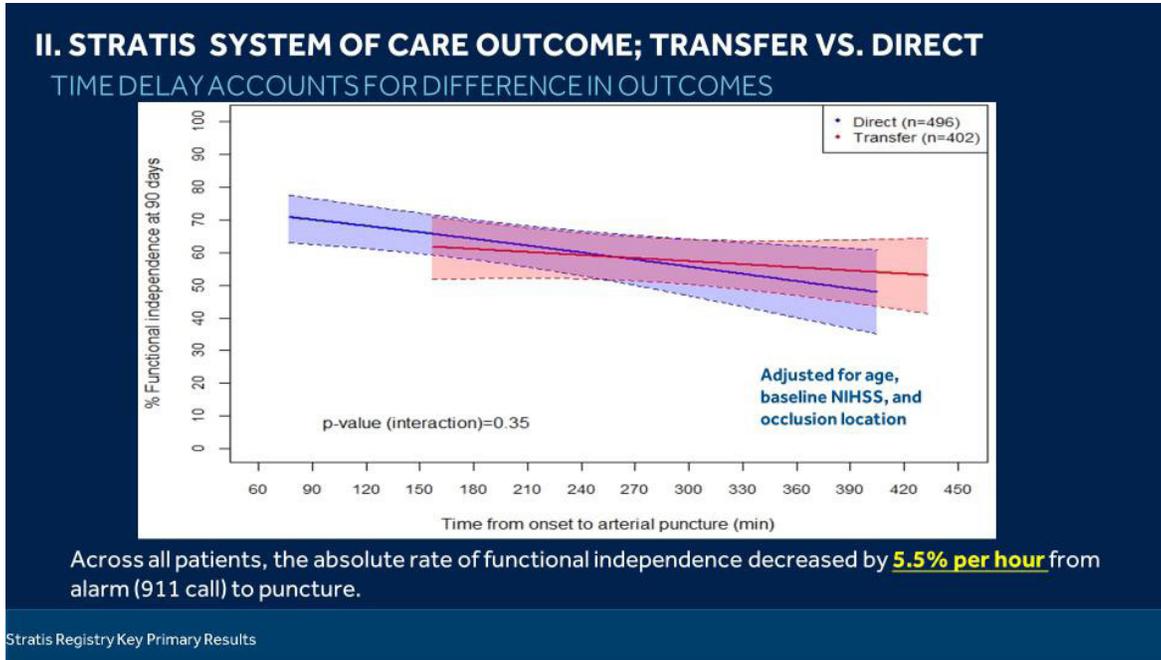
For patients who did not receive IV t-PA, and were transferred from a peripheral community hospital to a comprehensive stroke centre for mechanical thrombectomy alone, these patients were delayed by 82.5 minutes compared with patients routed directly to the comprehensive stroke centre (311.5 vs. 192 minutes;  $p < 0.0001$ ). The events responsible for this delay were CT scanning at the initial hospital, and transfer time to the second hospital with comprehensive endovascular facilities.

The delays associated with transferring patients in STRATIS were associated with poorer outcomes, as determined by mRS assessments; however, there was no significant difference in mortality rate between transferred and directly routed patients. The outcomes achieved with transferred vs, directly routed patients are summarized below.



Using data from all STRATIS patients adjusted for age, stroke scale, and occlusion location, Dr Zaidat emphasized that there is a likelihood of a 5.5% decline in the patient’s functional independence at 90 days post-stroke for

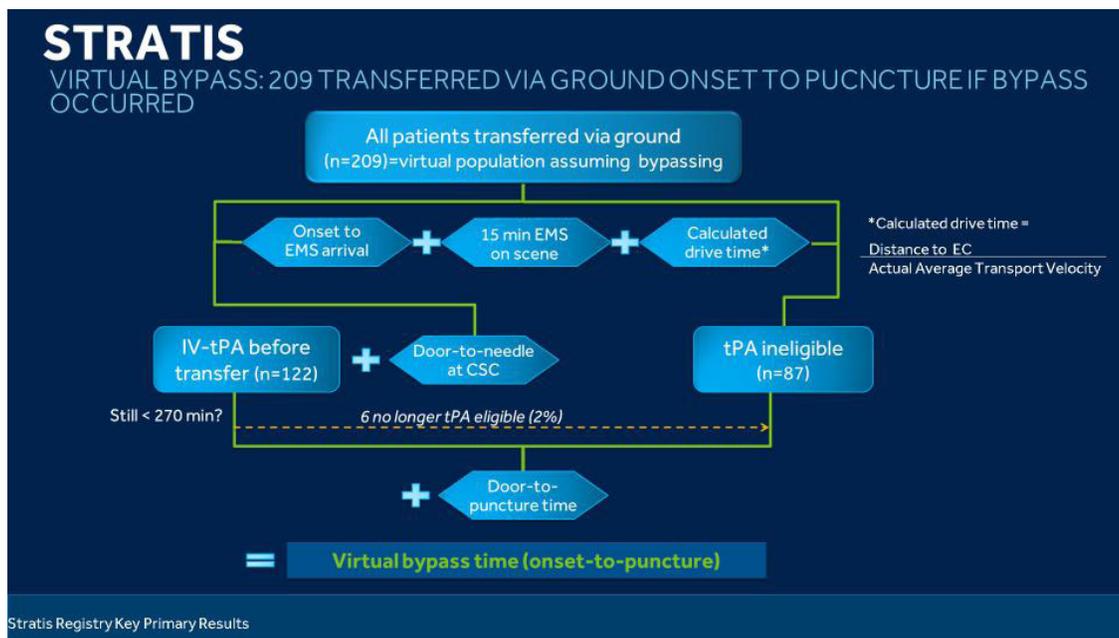
every hour of delay during the period from stroke onset to puncture. This time-related loss of functional independence is illustrated in the figure below.



After accounting for differences in outcome related to time to endovascular treatment, the administration of IV-tPA did not have a significant effect on outcome, either overall, or in interaction with time. The principal driver for difference in outcomes between transferred and direct patients in STRATIS is the extent of the time delay between onset and groin puncture for thrombectomy.

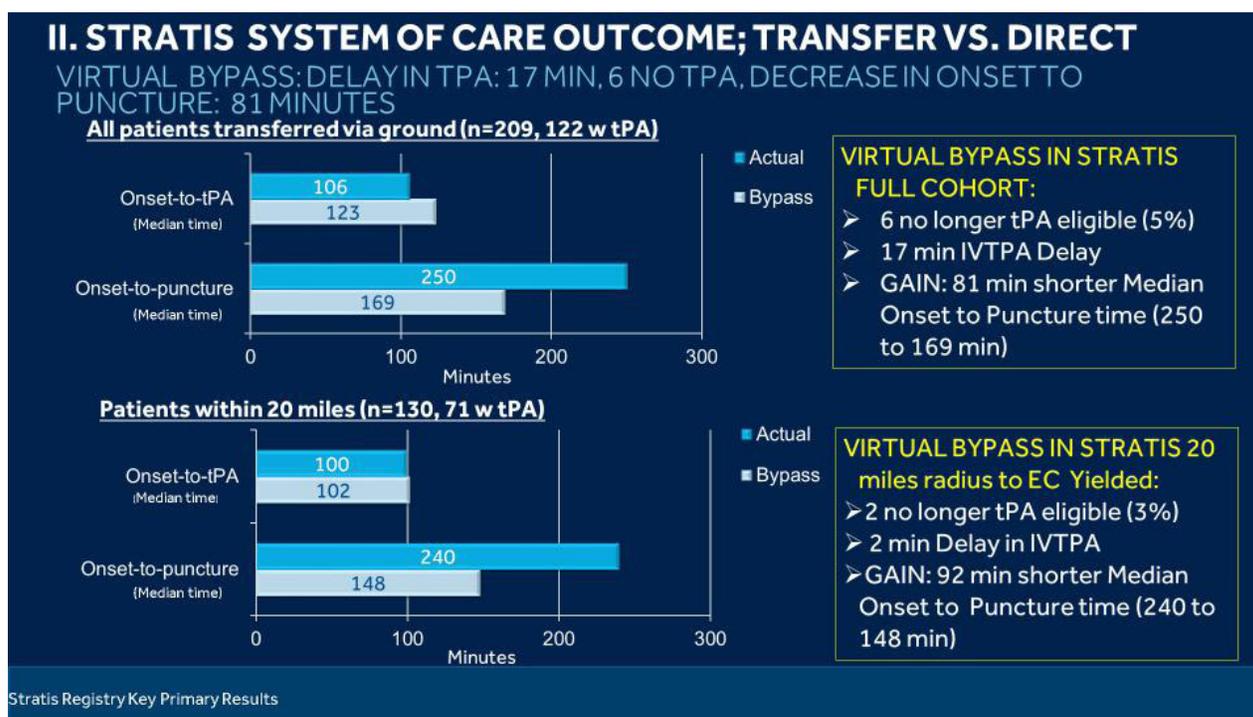
thrombectomy, concerns would remain regarding potential delay in the provision of IV t-PA, or that some patients might miss receiving IV t-PA altogether. To address these concerns, a virtual simulation was conducted with STRATIS data using only those patients who initially were routed to a community hospital, and hospitalized using ground transfers only. The simulation was designed to answer the question: what would happen if these patients did not stop at the peripheral community hospital? The virtual simulation algorithm for the 209 transferred STRATIS patients is shown below.

Dr Zaidat raised the question of whether bypassing the community hospital would be a good strategic decision. Although bypassing may reduce time to mechanical



The virtual simulation bypass was run on all transferred patients (n = 209) and those patients who were transferred to an endovascular centre (EC) within a 20-mile radius of the peripheral community hospital (n = 130). For the all-transferred patient cohort, the simulation showed that six patients would be no longer eligible for t-PA, and that the median time delay in stroke onset to IV t-PA administration would be 17 minutes; however, an 81-minute gain (from 250 to 169 minutes) in stroke onset to puncture time

would be achieved. For patients within 20 miles of an endovascular centre, the simulation indicated that two patients would be t-PA ineligible, a 2-minute delay in IV t-PA would occur, and a gain in stroke onset to puncture time of 92 minutes (from 240 to 148 minutes) would be expected. The summary outcomes from actual (transferred patients) data vs. the virtual bypass simulation data are shown in the figure below.



This analysis shows that 3-5% of transferred patients, if they were to be bypassed, would be ineligible for IV t-PA. However, Dr Zaidat stressed if t-PA is missed, due to bypassing a nearer hospital in favour of direct routing to more specialist endovascular care, there is no predicted difference in outcome. Outcome remains dependent on the key determining driver of time from stroke onset to treatment.

**STRATIS adjunctive technique evaluation and outcomes**

The STRATIS registry, via available procedural reports, has allowed comparative evaluation of adjunctive aspiration techniques used in mechanical thrombectomy with stent retrievers, the extent of use of these adjunctive techniques, and measurement of the associated outcomes achieved with different adjunctive techniques. The objectives for, and the methodology used in STRATIS to evaluate adjunctive techniques, and to quantify outcomes achieved are summarized in the following table.

### III. STRATIS ADJUNCTIVE TECHNIQUE OUTCOMES

METHODS

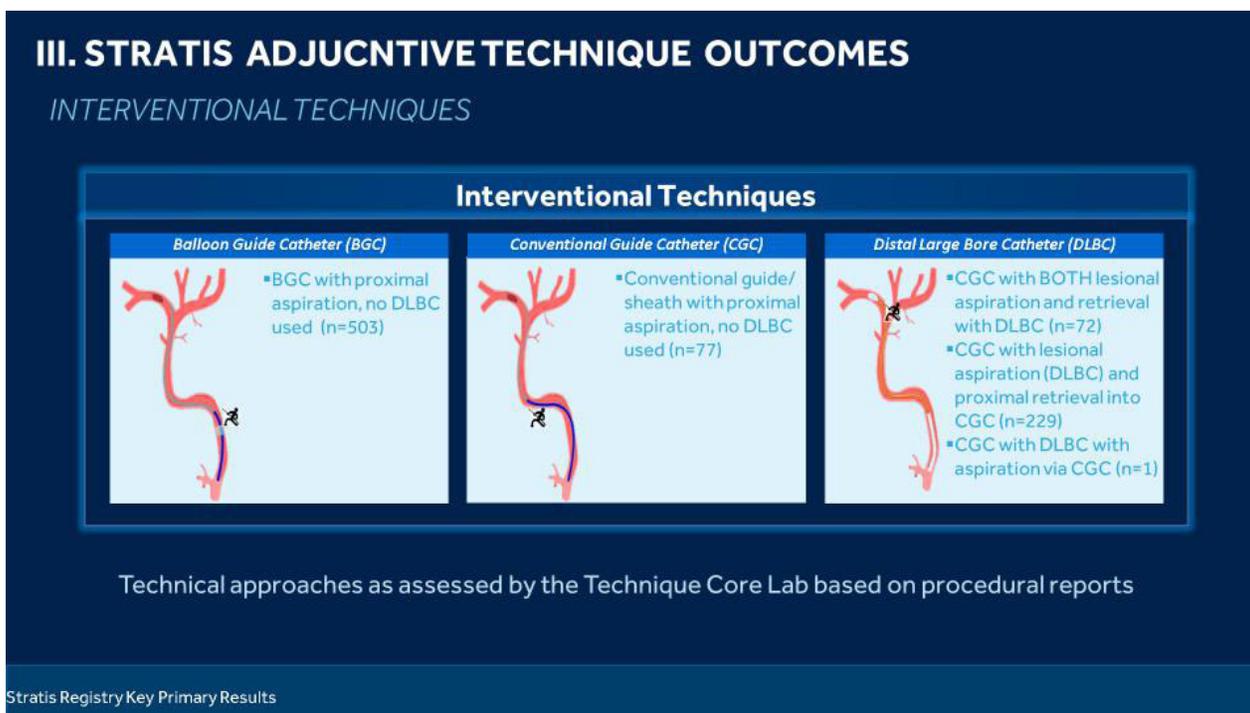
<b>Objective</b>	<ul style="list-style-type: none"> <li>To evaluate the influence of thrombectomy adjunctive devices/techniques on angiographic and clinical outcomes from the STRATIS Registry: BGC+SR, DLBC with local or lesional aspiration, CGC</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>Modified First pass effect (FPE) defined as successful reperfusion of <math>\geq</math>TICI2b after first device pass</li> <li>True FPE defined as TICI 2c or 3 after first pass</li> <li>Number of passes</li> <li>Rate of good clinical outcome defined as mRS 0-2 at 90 days</li> </ul>
<b>Independent Evaluation</b>	<ul style="list-style-type: none"> <li>A Technique Core Lab blinded to clinical outcome extrapolated the techniques and assessed FPE and True FPE based on procedural reports.</li> <li>An Image Core Lab blinded to clinical outcome assessed final angiographic reperfusion status.</li> </ul>
<b>Analysis Population</b>	<ul style="list-style-type: none"> <li>Included anterior circulation target vessel occlusion</li> <li>Excluded subjects in whom combined BGC and DLBC approach was used</li> </ul>

Stratis Registry Key Primary Results

**Abbreviations:** BGC = balloon guide catheter; SR = stent retriever; DLBC = distal large bore catheter; CGC = conventional guide catheter; TICI = Thrombolysis in Cerebral Infarction Scale.

Technical adjunctive approaches, based on STRATIS procedural reports, were broadly categorized into three types of adjunctive intervention techniques i.e. use of a balloon guide catheter (BGC; n = 503), conventional guide

catheter (CGC; n = 77), or distal large bore catheter (DLBC) use (including combined DLBC and CGC use n = 302) as illustrated below.



Baseline patient characteristics were generally well matched (except for current or previous tobacco use) across the three groups. Patient pre-procedure

characteristics and the location of the intracranial vessel, treated at first pass, were not significantly different across the three groups, as illustrated in the following table.

### III. STRATIS ADJUNCTIVE TECHNIQUE OUTCOMES

STUDY POPULATION & BASELINE CHARACTERISTICS, CONTINUED.

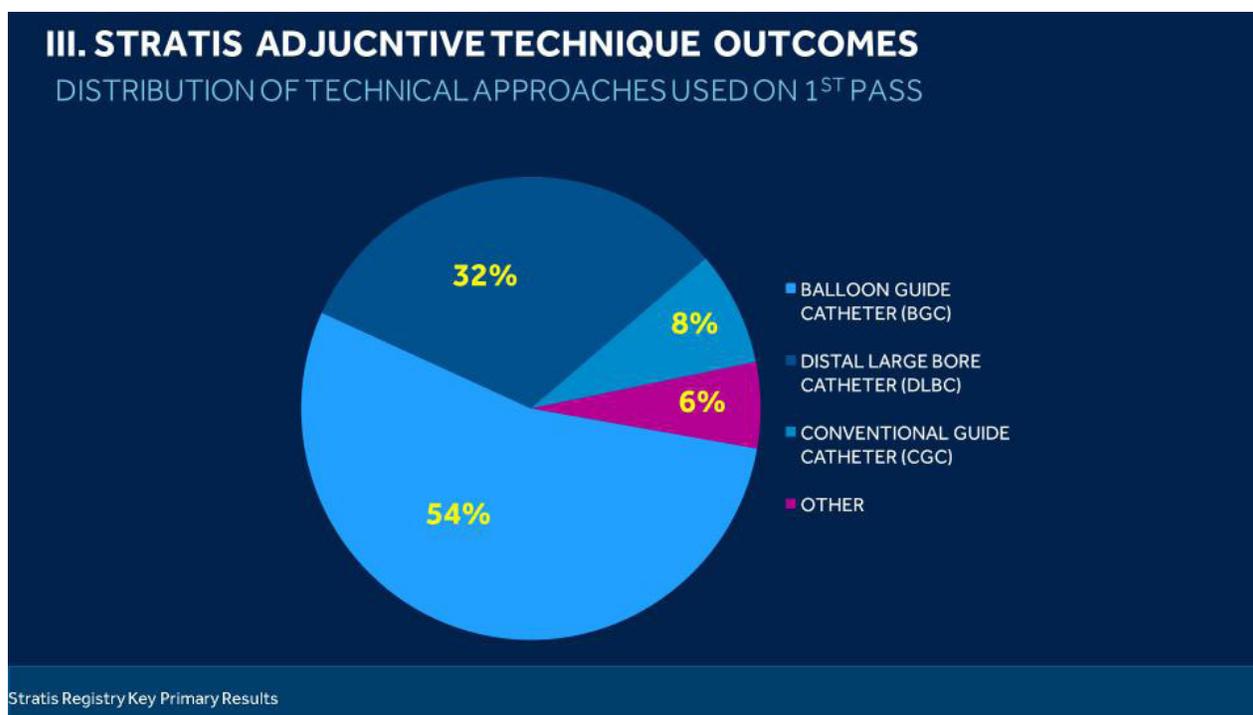
Characteristic	BGC (503, 54%)	CGC (77, 8%)	DLBC (302, 32%)	P-value
<b>Pre-Procedure</b>				
Initial Qualifying NIHSS Score	17.1±5.34 (503)	17.5±5.73 (77)	17.5±5.50 (302)	0.7489
IV t-PA delivered	328/503 (65.2%)	51/77 (66.2%)	195/302 (64.6%)	0.9489
ASPECTS – per imaging core lab†	8.3±1.59 (415)	8.5±1.28 (66)	8.1±1.59 (235)	0.0685
<b>Intracranial Vessel treated on First Pass‡</b>				
Internal Carotid Artery Terminus	105/503 (20.9%)	18/77 (23.4%)	89/302 (29.5%)	0.1967
Middle Cerebral Artery – First segment (M1)	300/503 (59.6%)	43/77 (55.8%)	164/302 (54.3%)	
Middle Cerebral Artery – Second segment (M2)	97/503 (19.3%)	16/77 (20.8%)	48/302 (15.9%)	
Middle Cerebral Artery – Third segment (M3)	1/503 (0.2%)	0	1/302 (0.3%)	

Data are % (n/N), or mean±SD (N). Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale. The protocol was amended to restrict enrollment to mRS 0-1 to ensure consistency with SWIFT PRIME enrollment criteria. †759 patients evaluable for ASPECTS. ‡Assessed by the Techniques Core Lab based on operative reports.

Stratis Registry Key Primary Results

Of the three categories of adjunctive aspiration techniques used in STRATIS, the most frequently used was the balloon guide catheter (54%). The distribution of the technical

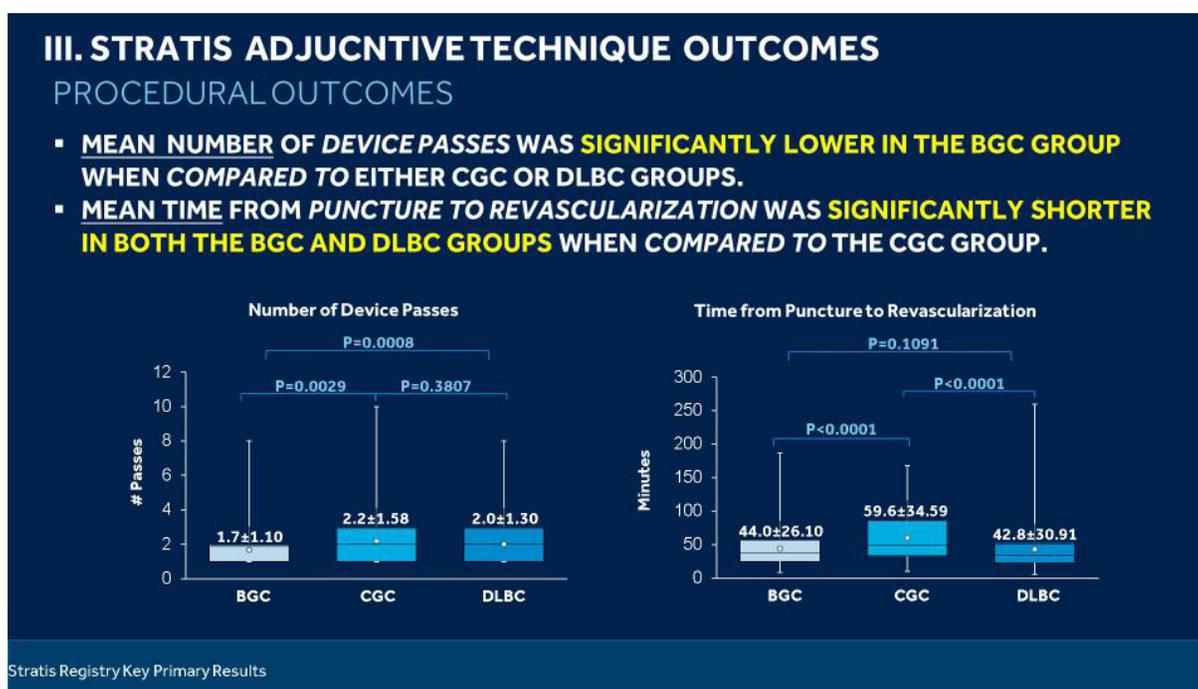
approaches used on first pass in STRATIS is illustrated in the following figure.



Two clear key procedural outcomes emerged from this analysis:

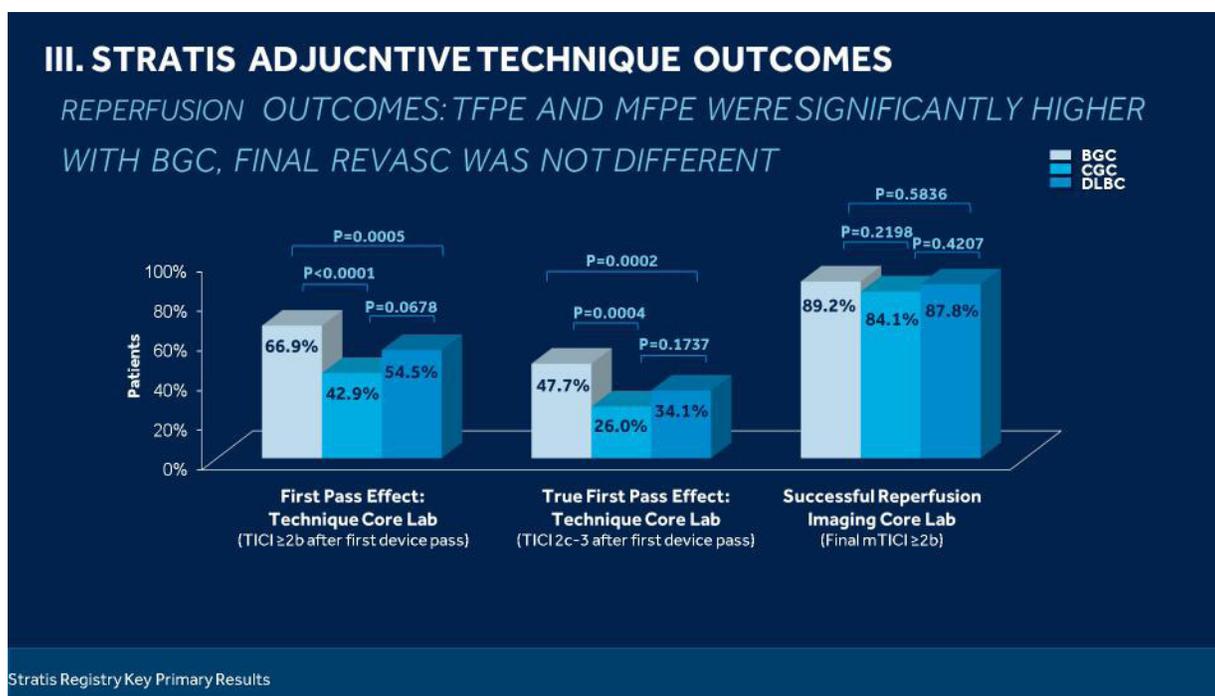
- The significantly lower number of device passes in the balloon guide catheter group (BGC), potentially resulting in less endothelial damage, compared with either the conventional guide catheter (CGC) group, or the distal large bore catheter (DLCB) group.

- The mean time from puncture to revascularization was significantly shorter in both the balloon guide catheter group (BGC) and distal large bore catheter (DLCB) groups compared the conventional guide catheter (CGC) group. These comparisons, with their associated levels of statistical significance, are shown in the figure below.



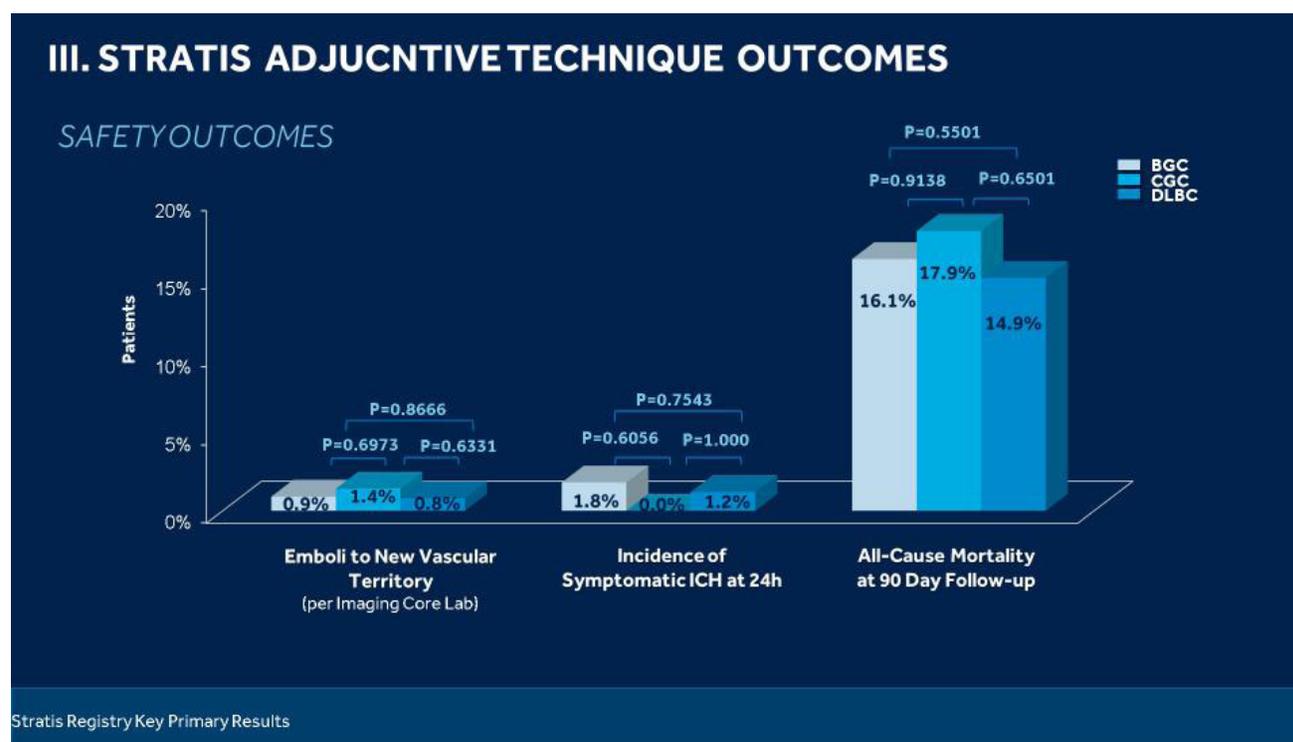
With respect to revascularization, the balloon guide catheter group (BGC) was associated with significantly higher first pass performance (i.e. TICI ≥2b after first device pass), and true first pass effect performance (i.e. TICI 2c-3 after first device pass), compared with the other

two groups. However, there were no significant differences in the rates of final successful reperfusion between the three groups. These comparisons, with their associated levels of statistical significance, are shown in the figure below.



Notably, the highest rate of good clinical outcome, defined as patients who achieved scores of 0-2 on the modified Rankin Scale (mRS) at 90-day follow-up, was achieved with the balloon guide catheter group (61.8% of patients). This outcome was significantly better than the percentage of patients who achieved a good clinical outcome in the conventional guide catheter group (44.8%;  $p = 0.0079$ ), and in the distal large bore catheter group (50.2%;  $p = 0.002$ ).

Safety outcomes were similar in all three groups of adjunctive interventions. All safety assessments were blindly adjudicated. There were no statistically significant differences between the three groups with respect to emergence of emboli in new vascular territory, the incidence of symptomatic intracranial haemorrhage (sICH) at 24 hours, or in all-cause mortality at 90 days. These safety comparisons, with their associated levels of statistical significance, are shown in the figure below.



### STRATIS – conclusions

The STRATIS study provides compelling evidence, based on a large population of US patients, that the technical and clinical outcomes achieved in landmark randomized clinical trials, investigating mechanical thrombectomy with stent retriever devices<sup>1-5</sup>, can be reproduced in a less restrictive real-world setting. Despite enrolling a population with higher mean baseline NIHSS, and with more risk factors than patients in the SEER collaboration database, STRATIS results demonstrate that mechanical thrombectomy with a Medtronic stent retriever is both safe and effective.

Shorter door to puncture intervals were documented in STRATIS. This may suggest an increasing awareness of the importance of rapid hospital workflow since publication of the SEER trials that has led to improved timing. Patients in STRATIS who were routed directly to a comprehensive stroke centre, compared with patients who were transferred from a peripheral community hospital, to an endovascular centre, had better clinical outcomes and a shorter onset to puncture time. A virtual by pass simulation illustrated a higher gain in shortening stroke onset to puncture time,

with a 3-5% loss of patient eligibility for IV t-PA, and a less than 17 min delay in administration of IV t-PA.

STRATIS data were used to compare adjunctive aspiration techniques deployed during mechanical thrombectomy. Final successful recanalization rates were similar in all three categories of adjunctive technique; however, balloon guide catheter (BGC) use as the first approach in STRATIS demonstrated higher rates of first pass effect (FPE) and resulted in a higher percentage of patients achieving good clinical outcome at 90 days (mRS 0-2) compared with conventional guide catheter (CGC) and distal large bore catheter (DLBC) use.

### TO BYPASS OR NOT TO BYPASS FOR INTERVENTION

#### Introduction and background

This is a summary of an evening symposium held at the ESMINT 9<sup>th</sup> Congress, Nice, in September 2017; it was sponsored by Medtronic and moderated by Professor Mayank Goyal. The symposium was opened by Dan Raffi, Senior Director of Neurovascular at Medtronic, who gave a brief presentation outlining the company's

history of innovation in the development and provision of successful devices for neurovascular interventions. Mr Raffi emphasized that Medtronic are committed to continued investment in the delivery of future devices and services that will help interventional neurologists to improve outcomes for their patients. In particular, new developments highlighted included the recent Medtronic partnership with Rapide, to provide novel software for the rapid analysis of CT scans; the development of innovative digital apps to capture long-term follow-up data from patients following endovascular interventions, and the availability of REVEAL LINQ™, a minimally invasive insertable cardiac monitoring system for the diagnosis of atrial fibrillation. Mr Raffi also announced that Medtronic were now supporting the ANGELS initiative in collaboration with Boehringer Ingelheim and ESO.

This symposium featured three presentations:

- The STRATIS registry – delivered by Dr Sam Zaidat;
- The RACECAT study: progress and update – delivered by Dr Marc Ribó;
- The SWIFT DIRECT study: progress and update – delivered by Professor Jan Gralla.

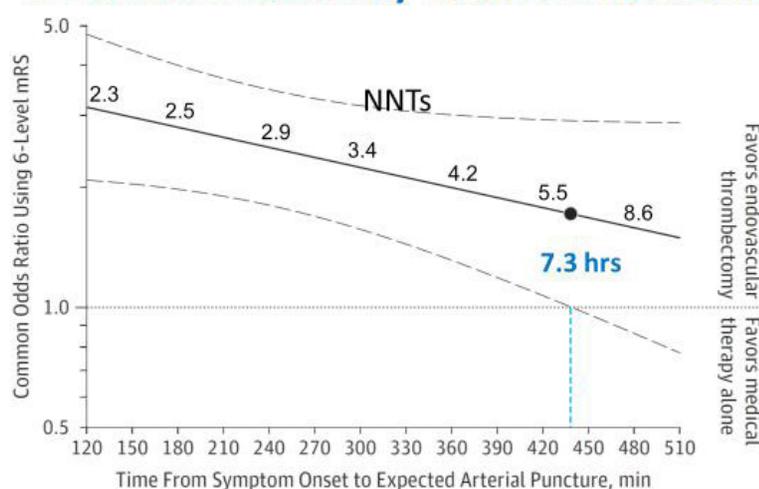
Each of these presentations include findings and data pertinent to the question of whether acute stroke patients with large vessel occlusion should by pass local community hospitals in favour of direct transfer to a comprehensive stroke centre. Dr Zaidat also presented on the STRATIS registry separately in the congress, and this has already been covered in this article. Accordingly, summaries of the RACECAT study and SWIFT DIRECT study are presented in the following sections.

#### Where are we now? – Professor Mayank Goyal

Professor Goyal gave a brief summary describing the current landscape of endovascular treatment. He stressed endovascular treatment for anterior circulation, proximal vessel occlusion is now the standard of care, and this position is supported by five pivotal endovascular thrombectomy RCTs<sup>1-5</sup>. Meta-analysis based on data from these five trials has revealed an impressive overall treatment effect, with the number needed to treat (NNT) calculated at 2.6. Professor Goyal stated the endovascular thrombectomy works well in a wide spectrum of acute stroke patients, including patients eligible for IV t-PA and ineligible patients. Time from stroke onset to effective treatment remains the biggest challenge. A recent JAMA publication<sup>6</sup> indicates the “window of opportunity” for endovascular thrombectomy closes at around 7.3 hours



### Time from Onset to Expected Puncture Odds of Reduced Disability with EVT vs Medical



JAMA. 2016;316(12):1279-1288. doi:10.1001/jama.2016.13647

15/09/2017



25

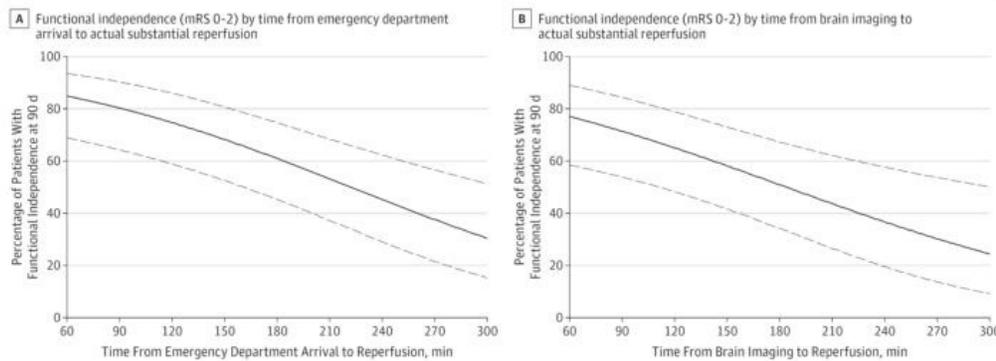
This meta-analysis underlines the “time is brain” reality faced by interventional neurologists and their patients. Furthermore, under the “Ship and Drip” transfer model, Professor Goyal emphasized the tremendous amount of

time that can be lost if the patient is sent to the wrong hospital, with increasing loss of patients’ functional independence as time to revascularization increases. This is illustrated in the following figure.



## Process Efficiencies Matter after Arrival at Endovascular Hospital

Figure 3. Relation Between In-Hospital Treatment Speeds and Functional Independence (mRS 0-2) at 3 Months Among Direct Arrival Patients in the Endovascular Thrombectomy Group Achieving Substantial Reperfusion (mTICI score, 2b or 3)



JAMA. 2016;316(12):1279-1288. doi:10.1001/jama.2016.13647

19/09/2017



27

The role of general anaesthetic vs. no general anaesthetic during endovascular thrombectomy remains controversial; however, a recent meta-analysis of RCT data from the Hermes collaborators indicates that patients who receive general anaesthetic have poorer outcomes, as assessed by mRS at 90 days, than their counterparts who received no general anaesthetic.

Professor Goyal reviewed imaging predictors as treatment effect modifiers and the prognostic and treatment impact of penumbral imaging in pooled HERMES analysis of randomized trials of endovascular stent thrombectomy. He stressed that even in the Alberta Stroke Program Early CT Score (ASPECTS) 0-4 grouping, there is a benefit of

treatment; additionally, penumbral imaging confirms that even when ischaemic core volume is >70 mL a treatment benefit is evident. A clear relationship has been established between the quality of recanalization and reperfusion achieved with endovascular thrombectomy and patient outcome. Professor Goyal felt that this relationship will drive further device innovation in industry, and the training of future generations of interventional neurologists to improve revascularization techniques.

Professor Goyal listed important research directions that can be expected to shape future endovascular thrombectomy technique, work flow and outcomes. These are presented in the following figure.

## Future research directions

- How is the community performing at large after the trial results: what is real world experience?
- How low of an ASPECTS should be treated (or how big of a core can be treated)
- What about low NIH with LVO
- Rebirth of neuroprotection
- Big M2, A2, P2 with disabling deficit
- tPA/no tPA
- Drip and ship vs. mother ship

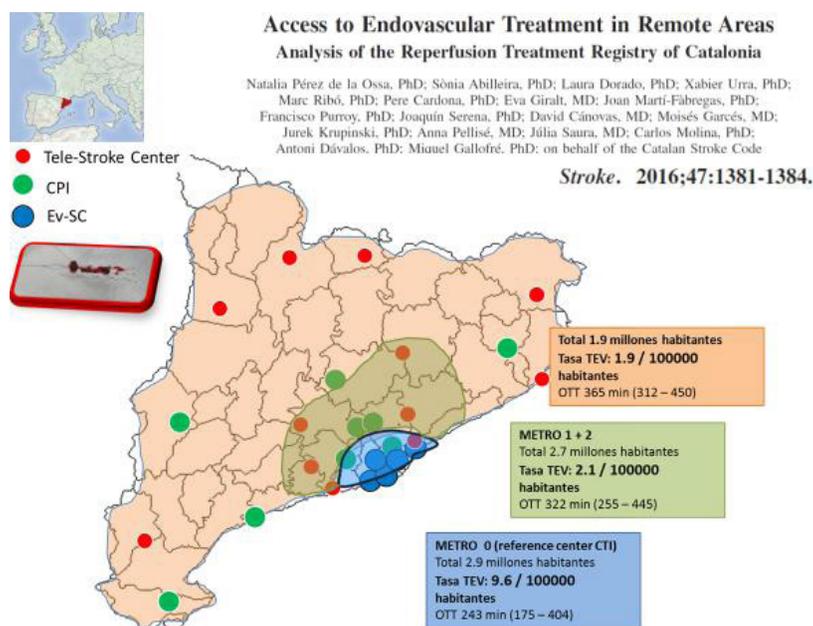
Of these research directions, the main area of uncertainty is the best way for patients outside of endovascular-capable or Comprehensive Stroke Centres (CSCs) to access treatment for acute ischaemic stroke. The role of nonendovascular-capable primary stroke centres that can offer thrombolysis, and a “drip and ship” transfer, but not mechanical thrombectomy, is still unclear. Hence, the presentations by Dr Ribó on the RACECAT study, and Professor Gralla on the SWIFT Direct study, may offer further insights into this difficult treatment dilemma.

thrombectomy depending on where patients lived in Catalonia. Where patients lived within an area with close access to a comprehensive stroke centre, the recent (2015) rate of thrombectomy is around 10 per 100,000; this is close to an accepted “ideal” rate of between 10-20 per 100,000 of the population. By comparison, there is a markedly 5-fold lower rate of endovascular thrombectomy for patients who were initially hospitalized in more remotely situated peripheral community hospitals, as illustrated in the following figure. Furthermore, those patients who did receive a thrombectomy after initial routing to a local community hospital were delayed by around two hours compared with directly transferred patients.

### TO BYPASS OR NOT TO BYPASS FOR INTERVENTION

#### RACECAT study– Dr Mark Ribó

Dr Ribó gave an overview of access to endovascular treatment in Catalonia, Spain, based on 2016 data.<sup>7</sup> This analysis identified the likelihood of receiving a



Reviewing the results from the MR CLEAN study<sup>8</sup>, Dr Ribó highlighted that inter-hospital transfer prolonged the time to emergency department (ED) arrival significantly, by 140 minutes; however, a reduction in time from ED arrival, to treatment, of 77 minutes was achieved with transferred patients. These timings are shown in the following

ORIGINAL RESEARCH  
**Workflow and factors associated with delay in the delivery of intra-arterial treatment for acute ischemic stroke in the MR CLEAN trial**

Esmee Venema,<sup>1,2</sup> Nikki Boodt,<sup>3</sup> Olvert A Berkhemer,<sup>3,4,5</sup> Pleunie P M Rood,<sup>6</sup> Wim H van Zwam,<sup>4</sup> Robert J van Oostenbrugge,<sup>7</sup> Aad van der Lugt,<sup>8</sup> Yvo B W E M Roos,<sup>8</sup> Charles B L M Majoie,<sup>2</sup> Hester F Lingsma,<sup>1</sup> Diederik W J Dippel,<sup>2</sup> on behalf of the MR CLEAN investigators

*J NeuroIntervent Surg* 2017;**0**:1–6. doi:10.1136/neurintsurg-2017-013198

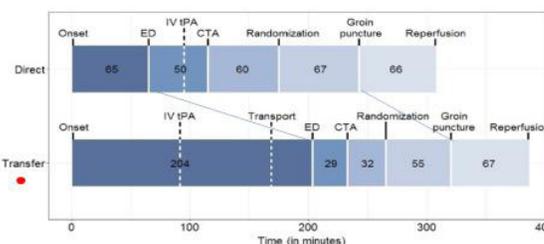
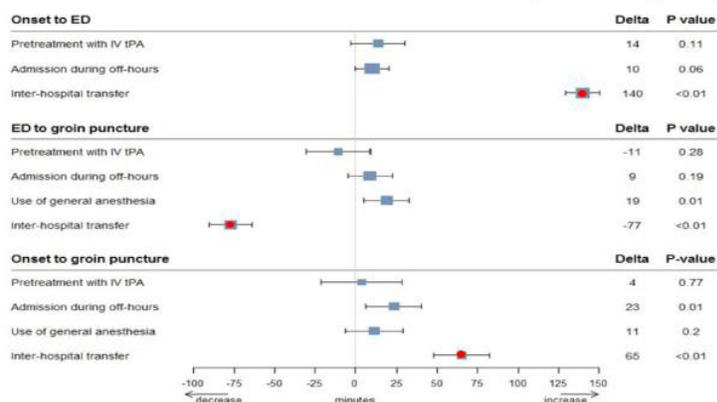


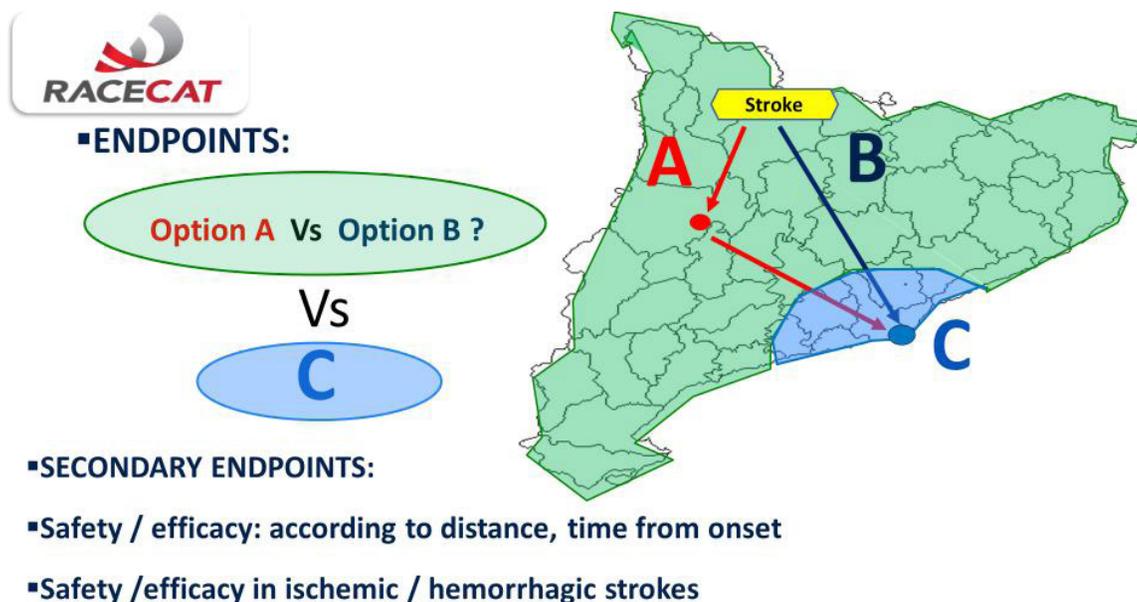
figure. Dr Ribó argued that if the same improvements in work flow metrics can be achieved with non-transferred, directly routed patients, outcomes can be improved for all patients who need intra-arterial treatment for acute ischaemic stroke.

Dr Ribó reviewed a number of concerns associated with bypassing acute stroke patients from primary stroke centres (PSCs) in favour of directly routing patients to a comprehensive stroke centre (CSC) with endovascular treatment facilities. Identification by paramedics of large vessel occlusion vs. e.g. distal occlusions is a difficult task, and improved diagnostic tools are required. Dr Ribó highlighted instances where patients had been transferred to a CSC, after having received t-PA at a PSC, and on examination, the patient had responded well to the t-PA and a thrombectomy was deemed unnecessary. Complications during secondary transfers may occur, particularly over long distances in ambulances with rudimentary support facilities for patients with acute stroke; accordingly, transport capability and safety considerations should be factored in when making the decision to transfer. Performance at individual centres is another important factor: a PSC with good door-to-needle and door-in-door-out times may only take 30-40 minutes for t-PA administration, but this good performance may be negated if e.g. door to groin puncture takes two hours at the CSC. The logistics of CT scanning raises the question: is a CTA scan at a primary centre always necessary, and if performed, is a second CT/CTA scan necessary following transfer to the CSC? Finally, Dr Ribó drew attention to organizational consequences that may arise if bypassing becomes a more widespread practice. Under these changed circumstances, the role and necessity for PSCs will be questioned, especially those close to a CSC, and bypassing will inevitably lead to a loss of expertise at any marginalized PSCs.

The American Heart Association has proposed a severity-based stroke triage algorithm for EMS when large vessel occlusion is suspected. Bypassing primary stroke centres is recommended if direct transport to a comprehensive stroke centre (CSC) adds a  $\leq 15$  minutes delay, and transport to the CSC will not preclude use of IV Alteplase. Dr Ribó felt this approach was relatively simplistic and does not take into account the concerns associated with bypassing that he had raised.

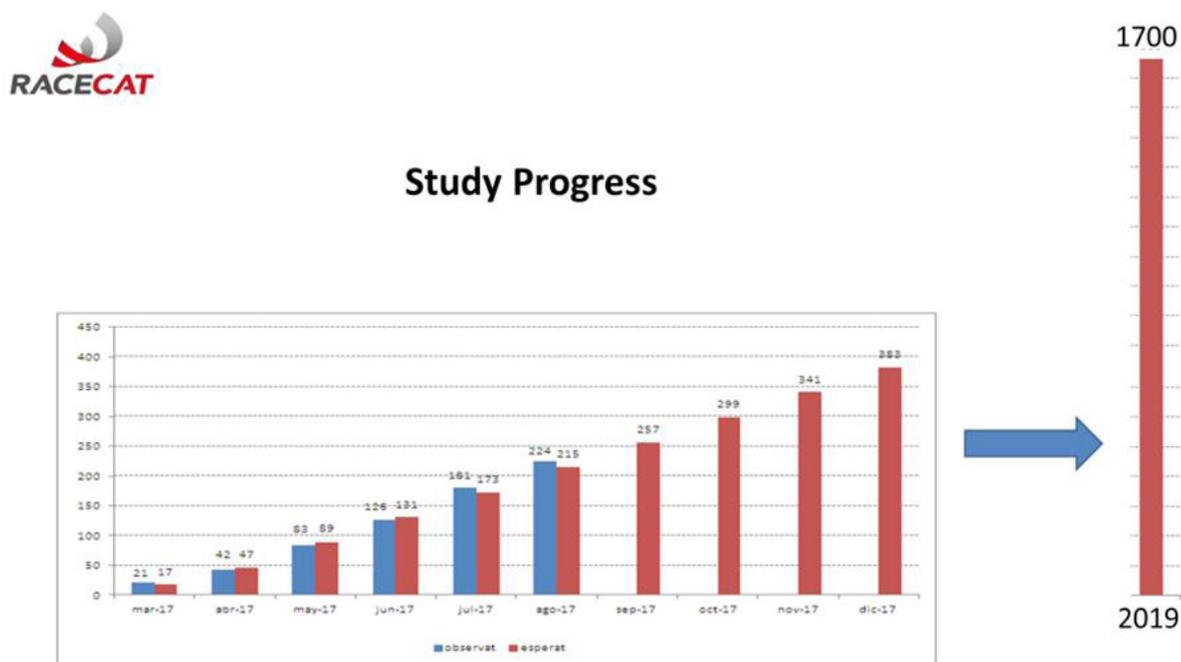
Dr Ribó explained that modelling methodology is available that allows comparisons to be made between transfer (“Drip ‘n Ship”) and transporting patients direct to CSC (“mothership”) options.<sup>9</sup> Modelling for the best transportation options for optimal outcomes for acute stroke patients is based on assumptions; however, in the absence of randomized data, modelling provides a useful tool for exploring transportation options, and entering anticipated work flow metrics to define the best option for individual patients with suspected LVO.

The ongoing RACECAT trial has been designed to compare the TRansfer to the Closest local stroke Centre vs. direct transfer to Endovascular stroke Centre of Acute stroke patients with suspected large vessel occlusion in the Catalan Territory. This study will provide specific randomized data that will help decide which transportation option provides the best outcome for acute stroke patients.



Dr Ribó summarized the progress achieved to date with the RACECAT study. Recruitment commenced in March 2017, and as at 7<sup>th</sup> September 2017, 233 patients have

been entered. The study is planned to complete with a total of 1,700 patients in 2019. The recruitment picture is summarized in the following figure.



Until RACECAT data are available to provide guidance on optimal hospitalization and treatment strategy, emergency services and interventional neurologists will continue with difficult decision making on the question of whether to bypass acute stroke patients with suspected LVO, or not. A further possible option of referring the patient back to the PSC, after transfer and mechanical thrombectomy at a CSC (the “drip, ship, ship” model), may also prove to be valuable. This would help preserve and retain expertise

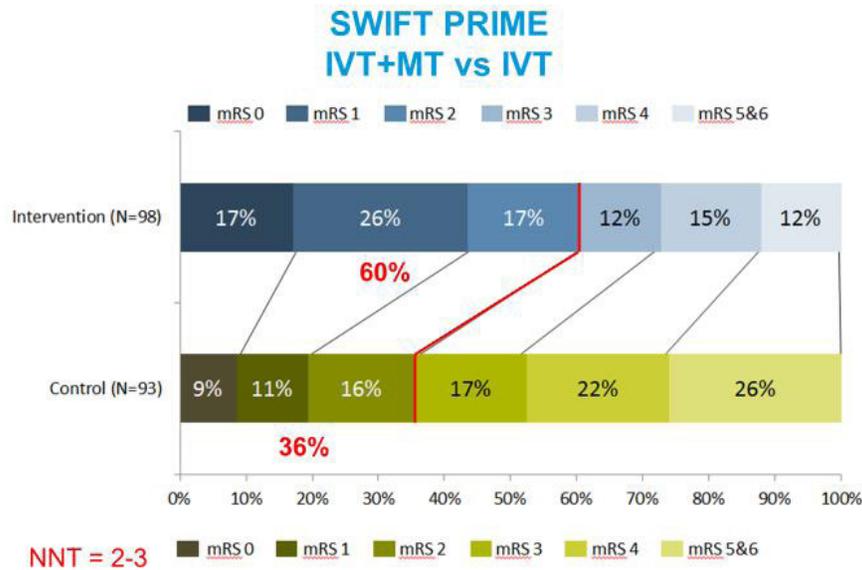
at PSCs and, Professor Goyal noted, is being evaluated in Ireland.

**SWIFT DIRECT study - Professor Jan Gralla**

Professor Gralla explained that initial RCTs had demonstrated no benefit of endovascular treatment on top of IV treatment. In retrospect, he felt this performance can be explained by their use of less well-developed devices

available at the time, and incorrect patient selection. More recently, data emerging from five RCTs investigating endovascular treatment have been positive. As an example, the SWIFT PRIME study<sup>4</sup> showed that IVT plus mechanical

thrombectomy (MT) led to more patients having a good outcome compared with patients receiving IVT only. This is illustrated in the following figure.

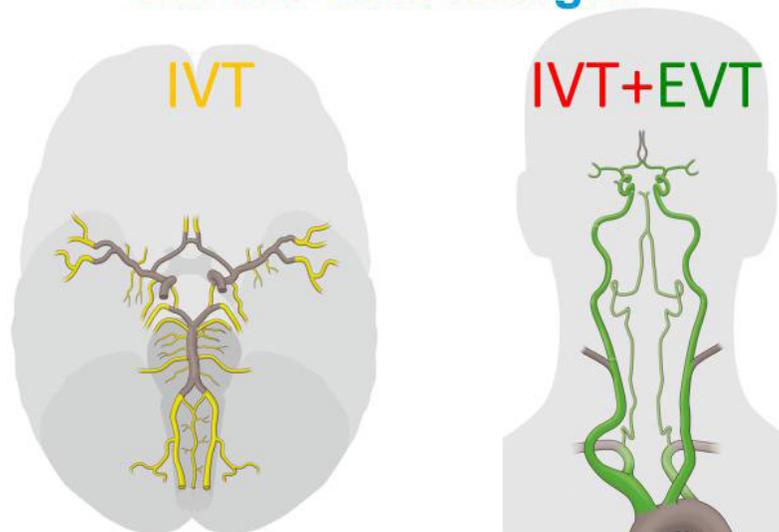


Saver J et al., NEJM 2015

89

Currently, IVT tends to be used to treat distal occlusions and IVT plus MT for large proximal vessel occlusions.

### For the time being...



90

Pooled analysis of intravenous alteplase vs. control studies (ECASS, ATLANTIS, NINDS, EPITHET and IST-3 trials)<sup>10</sup> confirms the effectiveness of IV thrombolysis. Notably, patients with low NIHSS scores are likely to receive greatest benefit with IV tPA compared with patients with high NIHSS scores. Referring to a study conducted by Riedel et al. (2011)<sup>11</sup>, Professor Gralla noted that the thrombus size determines the likelihood of successful recanalization with IV tPA. If the thrombus is below 8 mm (small thrombus burden) there is a high chance of successful revascularization. IV thrombolysis is very effective on small clots, and mechanical thrombectomy allows for treatment of LVOs. These treatments should therefore not be seen as competitive but as complementary treatments.

In trying to define the role of IVT in proximal vessel occlusion, Professor Gralla acknowledged the difficulty imposed by historical trial data where all patients received IVT as the standard of care at that time, with some patients

subsequently receiving mechanical thrombectomy. However, it is possible to take a theoretical approach and examine the benefits of IVT. These include: the low infrastructure requirements; IVT can be initiated easily, quickly, and earlier than endovascular treatment; IVT may facilitate recanalization, and may improve reperfusion in small vessels. With respect to the disadvantages associated with IVT, these can be listed as: the narrow time window for treatment, with decreasing efficacy as time from stroke onset increases; poor recanalization rates in large vessel occlusion; the possibility of life-threatening complications with IVT; IVT may increase the rate of haemorrhage, IVT may limit dual antiplatelet medication (stenting), and IVT may delay endovascular treatment. Analysis of work flow metrics from the STAR<sup>12</sup> study revealed that IVT conducted within the Mothership treatment model added an additional 32 minutes. This is illustrated in the following figure.

### Workflow performance measures

#### Optimal Workflow and Process-Based Performance Measures for Endovascular Therapy in Acute Ischemic Stroke Analysis of the Solitaire FR Thrombectomy for Acute Revascularization Study

Table 1. Final Multivariable Linear Regression Models Reporting Characteristics Associated With Delay in Each Prespecified Interval Time

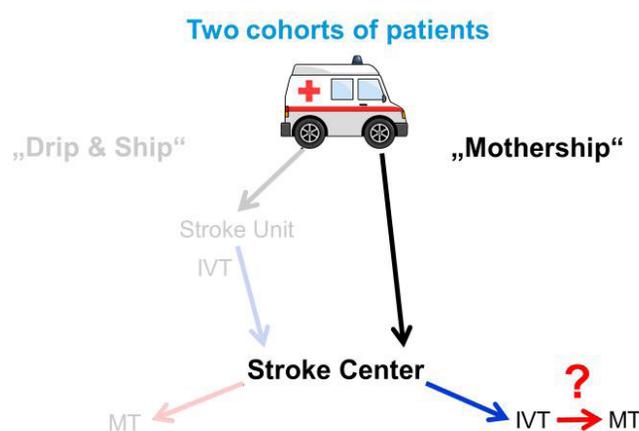
Interval Times	Significant Variable	Parameter Estimate (Multivariable)	SE	P Value
Hospital arrival to baseline imaging	Female sex	-10.75	4.25	0.013
	Time from stroke onset to hospital arrival (in hours)	-2.44	1.22	0.047
Baseline imaging to groin puncture	Warfarin use	-53.68	16.76	0.002
	Intravenous tissue-type plasminogen activator use	31.88	8.73	<0.001
	CT=CTP (vs MRI)	-18.06	8.86	0.043
Groin puncture to first stent deployment	Female sex	-4.92	2.25	0.031
	Extracranial carotid disease	24.53	9.99	0.015
	Prestroke mRS	3.37	1.54	0.031
Groin puncture to final DSA (or TICI 2b/3)	GA use	12.54	5.68	0.029

Menon et al Stroke 2014

96

Professor Gralla raised the question of what is the direct role of mechanical thrombectomy in patients who are eligible

for IVT? The “Mothership” versus “Drip & Ship” treatment paradigms are shown in the following illustration.



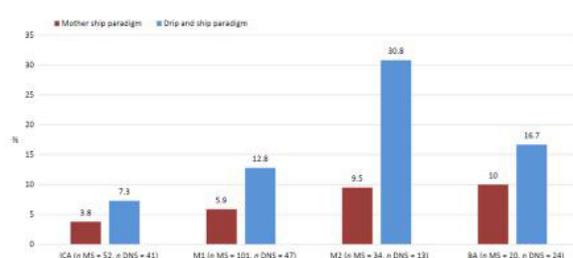
104

For Mothership patients, where the interventional neurologist has control of all initial and subsequent treatments, a key question is: following initial IVT, and prior to deciding on mechanical thrombectomy, what impact on recanalization is seen in the angiography suite? Limited data are available; however, rates of relevant recanalization have been measured in a recent published study conducted by Professor Gralla and colleagues<sup>13</sup>. This study showed that bridging IVT, within a Mothership

treatment concept, led to a recanalization rate of less than 4% in patients with an internal carotid artery (ICA) occlusion. For occlusions in the middle cerebral artery segment 1, middle cerebral artery segment 2, and basilar artery (BA), the corresponding percentages were 5.9%, 9.5%, and 10%, respectively. These recanalization rates indicate the effect of IVT within the work flow for Mothership patients is not extensive. These recorded rates of recanalization are illustrated in the following figure.

## Bridging in mothership concept

Bernese population: Intention to bridge (319 patients)



**Figure 2** Rate of relevant recanalization before endovascular therapy, dependent on occlusion location and treatment paradigm. DNS, drip-and-ship paradigm (■); MS, mother-ship paradigm (■). BA, basilar artery; ICA, internal carotid artery; M1, middle cerebral artery segment M1; M2, middle cerebral artery segment M2. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)].

## Rate of relevant recanalization

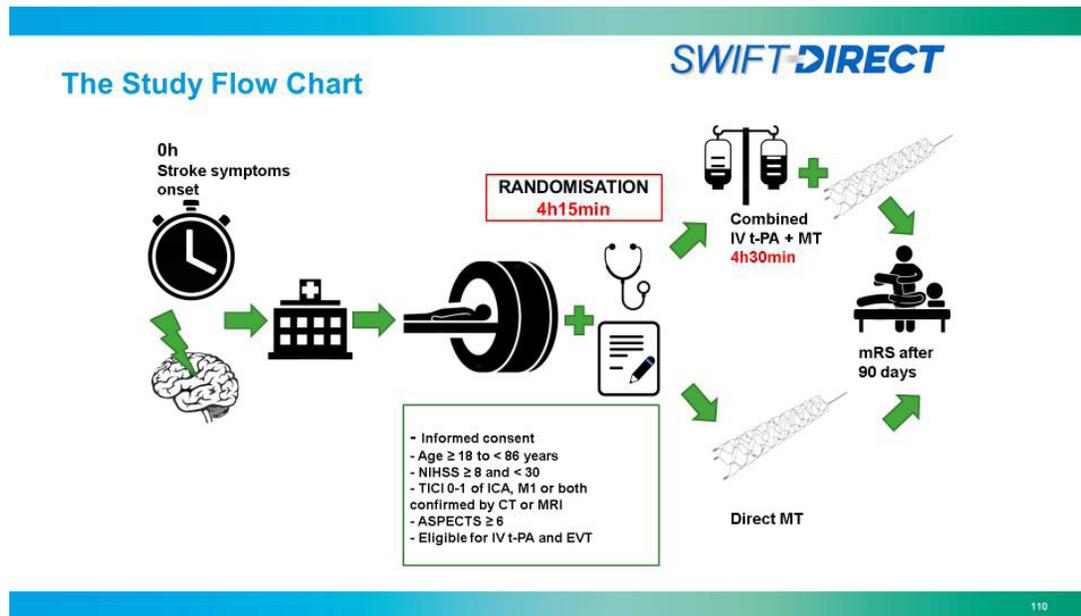
Mueller L et al, Eur J Neurol. 2017

105

Professor Gralla noted that the rates of recanalization in Drip & Ship patients, particularly in M2 patients, will be higher (approximately 30%), indicating an effect of time especially in small vessels and with longer time for the drug to act.

This question will be addressed by the SWIFT Direct study i.e. **S**olitaire™ **W**ith the **I**ntention **F**or **T**hrombectomy Plus Intravenous t-PA Versus **D**IRECT Solitaire™ Stent-retriever Thrombectomy in Acute Anterior Circulation Stroke. The primary objective of this trial is to determine whether subjects experiencing an acute ischaemic stroke in the anterior circulation, who are referred to a stroke centre with endovascular facilities, and who are candidates for IV t-PA, will have a non-inferior functional outcome at 90 days when treated with direct mechanical thrombectomy compared with subjects treated with combined IV t-PA and mechanical thrombectomy. The secondary objectives of the trial are to study the causes of mortality, and assess the quality of life of subjects in each treatment group.

SWIFT Direct will be conducted in European countries and Canada. The planned study recruitment is 404 mothership patients eligible for IVT, with proximal vessel occlusions (M1-MCA and ICA) including tandem occlusions. All patients will be randomized on a 1:1 basis to their allocated treatment, and this will be administered within a 4.5 hour time window at comprehensive stroke centres. The study will investigate IVT as a bridging concept plus MT versus direct MT, and only stent retriever thrombectomy will be performed. A non-inferiority design will be utilised, and the primary outcome will be modified Rankin Scale assessment at 90 days. Recruitment will involve 30 high volume centres (>80-100 patients/year), with well-established fast in-hospital workflows. An illustration of the SWIFT Direct study design is shown in the flow chart presented below.



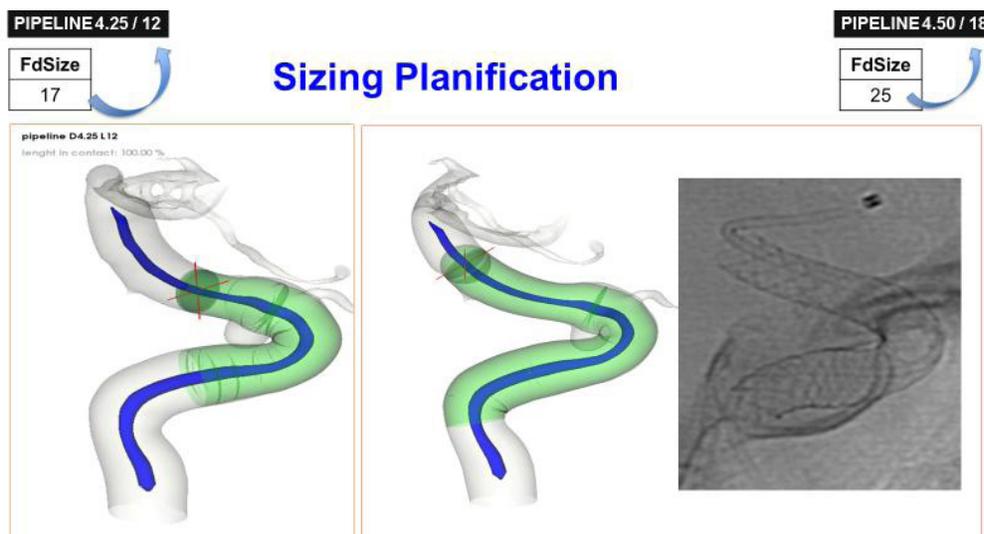
Professor Gralla summarized key regulatory milestones and timings for SWIFT Direct. The study protocol has been finalised; trail registration (ClinicalTrials.gov) has been achieved; Clinical Events Committee (CEC) approval in Switzerland has been achieved, and the CEC for EU/Canada has been submitted. Consequently, the first patient should be enrolled in September/October 2017, and the planned completion date for the study is July 2020.

**SIM & SIZE™: A new generation of software for patient-specific sizing – Professor Vincent Costalat**

Professor Costalat explained that SIM & SIZE™ is a new simulation software that helps to optimize the choice of endovascular flow diverter devices for the treatment of intracranial aneurysms. The development of SIM & SIZE™ has followed a paradigm shift in simulation as an assessment tool in neuroradiology. Initially, simulations were based on purely haemodynamic considerations;

however, SIM & SIZE™ simulations are based on a more recent mechanical approach. Biomechanical simulation now offers practical assistance to questions raised in the angiograph suite regarding most appropriate size of flow diverters and where to start deployment from.

Deciding on the correct size of pipeline device is not straightforward. A flow diverter may change markedly during deployment, depending on the choice of diameter selected. The extent of elongation and foreshortening that can occur during deployment is difficult to predict. Professor Costalat provided the following example, where pipeline embolization devices (PEDs) with dimensions of 4.25 mm x12 mm and 4.50 x18 mm, when deployed in patients, would assumed lengths of 17 and 25 mm, respectively. The extent of PED elongation can vary between 0 and 80%. This is illustrated in the following figure.

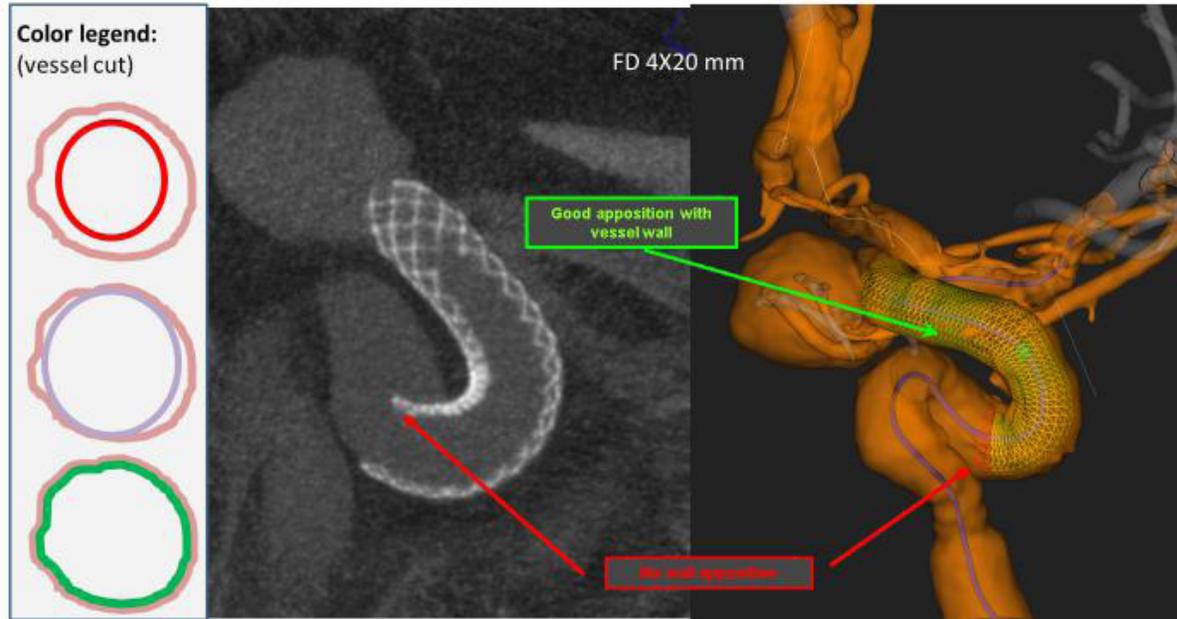


Sim&Size by Sim&Cure. Is pending CE Mark approval

During deployment of the PED, foreshortening or less than expected elongation is possible, and incomplete or

loss of vessel wall apposition may occur, as shown in the following image.

### FDsize: LINNC Case....



Sim&Size by Sim&Cure is pending CE Mark approval

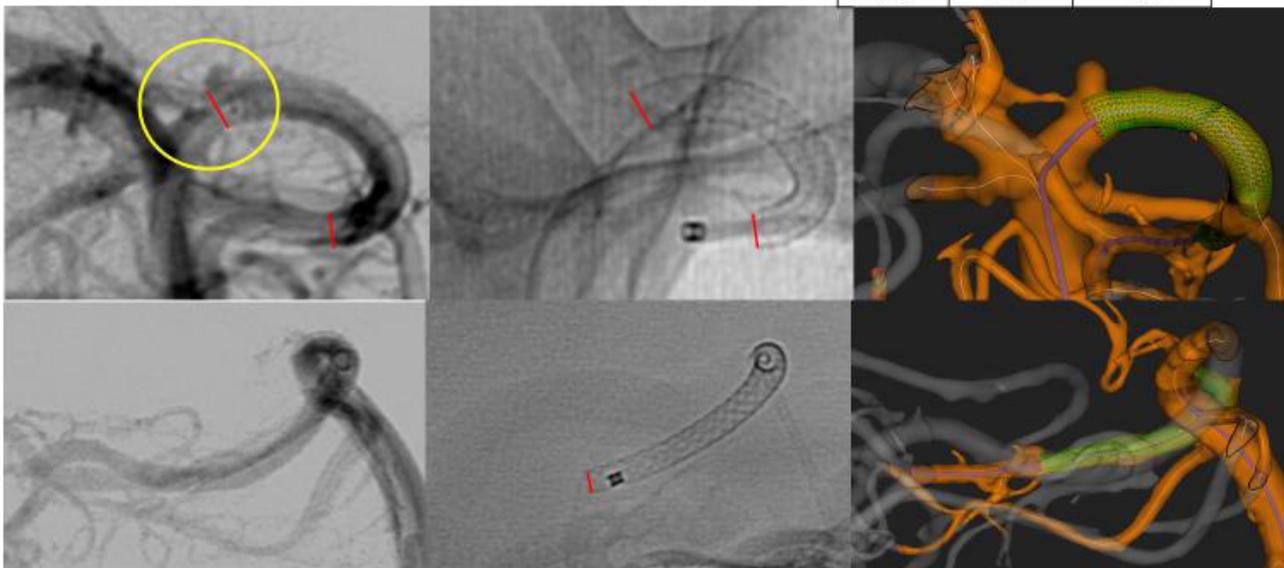
Professor Costalat stressed the SIM & SIZE™ software is based on retrospective validation of over 400 cases, and it allows interventional neurologists to validate their choice of PED and its dimensions. The following images show

measurement of the proximal and distal landing of the PED and simulated deployment of the PED from the distal to proximal positions.



ID: 37 PIPELINE 2.75 / 16

FdSize	Image	error
25	26	-1%

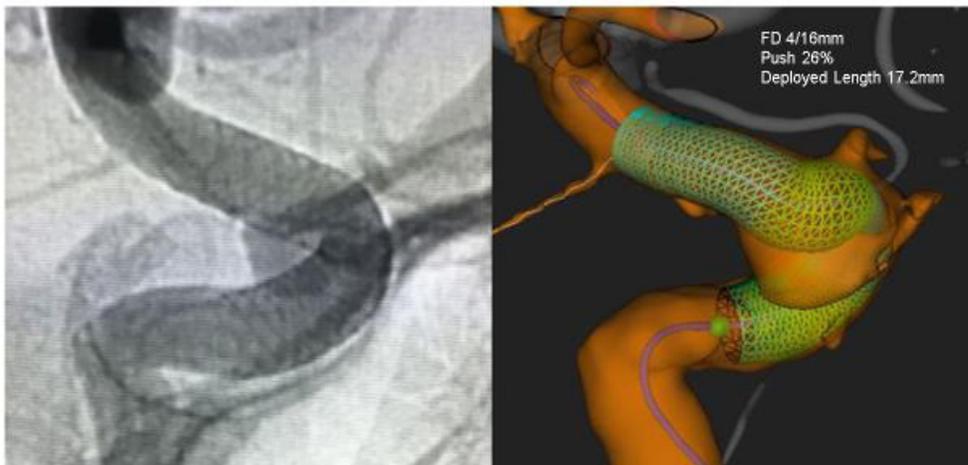


Sim&Size by Sim&Cure is pending CE Mark approval

In this case, a pipeline device of 16 mm was under consideration, but the simulation reveals a 26 mm actual requirement for deployment in the patient. The timing associated with using the SIM & SIZE™ software is rapid; usually less than 10 minutes. The 3D data from

the angiography suite are transferred by USB upload to a laptop, and processing the data takes approximately 2-5 minutes. The following example images illustrate how simulated device sizing can be used to select pipeline device dimensions with an appropriate margin of safety.

## FDsize: In Courtesy of Dr Mario Galdamez, Madrid



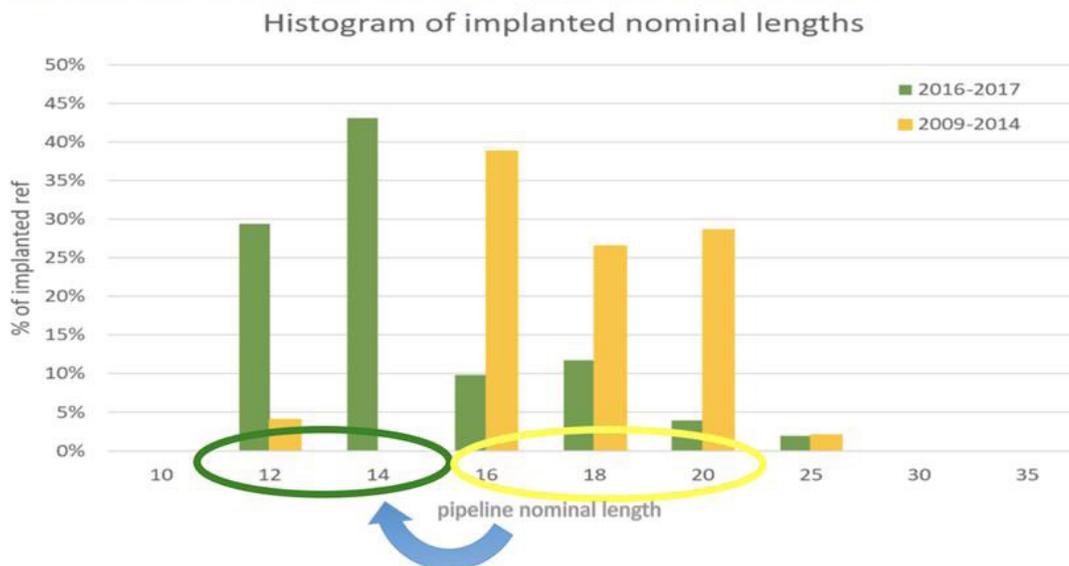
In this case,, according to the 2D and 3D measurements, the Pipeline chosen was a 4.25/18mm. The software showed the best option to cover the target zone was a 4/14 or 4/16 mm. To take a margin of safety, the FD 4/16mm was selected.

Sim&Size by Sim&Cure is pending CE Mark approval

Professor Costalat outlined the considerable clinical impact that simulated device sizing using the SIM & SIZE™ software has had in his hospital department. Most notably, this has been the routine use of dramatically shorter devices, often with a reduced diameter compared with previous use. There has also been a measurable deployment of less

implants per procedure. The most frequently used length of pipeline device used at Montpellier is now 12 mm, and this marked shift towards shorter implants is illustrated in the following histogram.

### Shorter Devices..... 12 Now most Famous PED !



Sim&Size by Sim&Cure is pending CE Mark approval

Up until 2015, the second stent implant rate at Montpellier was 12%. Following the routine use of SIM & SIZE™ simulation as a basis for making sizing PED sizing

decisions, the second implant rate has been reduced to 3.7%. These statistics are summarized in the table below.

## CLINICAL : Less Implant per procedure

Year	Implanted PED	Not Implanted	Procedures	PED number per Procedure	Second Implant Rate
2015	77	9	59	1.305	12%
2016	90	5	80	1.125	5.5%
Last 6 months of 2016*	53	2	49	1.08	3.7%
2017 Based on first 6 months*	110	4	100	1.1	3.7%



\* With Fdsize Being used in clinical routine

Sim&Size by Sim&Cure is pending CE Mark approval

The SIM & SIZE™ software has a 100% focus on neuro-interventional devices and provides simulations for sizing stent, intrasaccular, and flow diverter implants. Use of this simulation software may help reduce the time to endovascular treatment prevent, by speeding up implant sizing decisions, and reduces the possibility of having to repeat an implant procedure, should an initial implanted device prove to be less than optimal in its dimensions.

### CONCLUSIONS

Data from the STRATIS registry demonstrate that the efficacy and safety outcomes achieved in seminal published randomized controlled trials of mechanical thrombectomy with stent retriever devices<sup>1-5</sup> can be replicated, using Medtronic devices, in the more diverse population of acute stroke patients with LVO faced by interventional neurologists in current “real world” hospital settings. Presentations at the recent September 2017 ESMINT Congress explored the question: Is it better to bypass the local community hospital and transfer acute stroke patients directly to a comprehensive stroke centre with endovascular treatment facilities?

Patients in STRATIS who were routed directly to a comprehensive stroke centre, compared with patients who were transferred from a peripheral community hospital, to an endovascular centre, had better clinical outcomes and a shorter onset to puncture time. In addition, the SWIFT PRIME study<sup>4</sup> has shown that IVT plus

mechanical thrombectomy led to more patients having a good outcome compared with patients receiving IVT treatment only. However, definitive randomized controlled trial data, to guide strategic decisions on best practice patient transfer and treatment interventions are currently lacking. Consequently, the outcomes from the RACECAT trial, due to complete in 2019, and SWIFT Direct trial due to complete in 2020, are eagerly awaited. Outcomes from these studies are anticipated to provide a basis for optimal hospitalization and treatment strategy for acute stroke patients.

In parallel with the conduct of these studies, the accuracy of fit and the efficiency of pipeline embolization device deployment (PED) is being enhanced by the availability of SIM & SIZE™ simulation software. This software now allows device deployment simulation to be undertaken, to help verify device sizing decisions, and ensure greater implant precision. Use of SIM&SIZE™ is allowing shorter devices to be deployed and significantly reduces the requirement for secondary implants.

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