Mobile Stroke Unit News

News magazine of the PRE-hospital Stroke Treatment Organization

Volume 2, No. 2

A Year of Accomplishments for Mobile Stroke Treatment

By Jim Grotta, MD
President

If you are like me, I am sure you are tired of hearing the platitudes about how awful 2020 has been and in particular how the misery isn't over yet. So, at risk of being labelled a "Pollyanna", I'm not going to mention anything about COVID and instead highlight PRESTO's awesome accomplishments of this past year and our plans for 2021.

In March, PRESTO took the big step in formalizing as a member-driven organization. We are now managed by a professional association management company, Global Management Partners LLC, and with that we were able to apply for and were granted status from the Internal Revenue Service as a charitable non-profit. This means that your membership and any other contributions to PRESTO are tax deductible. With the help of GMP, and in particular Leslie Thomas, PRESTO's Executive Director and Robert Kowalski from the Colorado MSU, we overhauled the PRESTO website and formalized this newsletter.

With the help of Leslie and Margaret Hilger, PRESTO's Member Engagement Specialist, we developed a membership database, formed a Membership Committee, and began our first membership drive. Importantly, we created a menu of membership benefits—a list which will hopefully multiply during 2021. We have developed several other committees that represent the priorities of the membership. This includes a Reimbursement Committee which has sent out and compiled the results of a reimbursement survey. Anne Alexandrov and co-committee members will be presenting an abstract of their findings at the upcoming International Stroke Conference in March, 2021. The Dispatch Committee, led by Dr Audebert, also circulated a survey, with the recognition that understanding how to make the dispatch process more accurate is a challenge faced by all MSUs.

Finally, we formed a Research Committee led by Drs Bache and Saqqur charged with formulating a policy and template for fostering collaborative research projects among PRESTO membership. We hosted two educational webinars that pertained to the effects of COVID (uh oh—I broke my promise!) on MSU activities worldwide.

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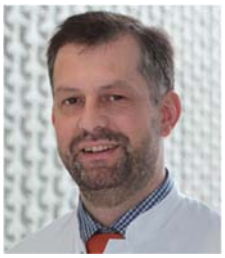
RACECAT and Prehospital Stroke Care



By Heinrich J. Audebert, MD

RACECAT was a trial comparing the drip-and-ship and the mothership model for patients with high probability of intracranial large artery occlusion living in rural Catalonia, Spain. Patients with suspected stroke during pre-hospital EMS care were included in the trial if they had their stroke in a geographical area not covered by endovascular therapy capable stroke centers (EVT-SC), had more than 4 points on the previously validated RACE Scale, and had a time of estimated arrival of less than 7 hours in case of direct transfer to an EVT-SC. In a cluster randomized design, they were either assigned to primary transport to a local SC with CT/CTA imaging and start of thrombolysis onsite and – if indicated secondary transfer to an EVT-SC, or to direct transport to an EVT_SC. Local SC could be Neurology based or Telestroke Units.

The primary outcome was the full

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Field LVO Tests and MSU Approach Compared

By Klaus Fassbender, MD
Immediate Past President

Currently, stroke management guidelines recommend the transport of all patients to the nearest stroke-ready hospital, which in most cases is a primary stroke center (PSC). In such cases, patients with large-vessel occlusion (LVO) may require secondary transport to a comprehensive stroke center (CSC) for thrombectomy. Importantly, compared with direct referral to a CSC, such inter-hospital transfers cause pronounced treatment delays that, consistent with the "time is brain" concept, significantly worsen clinical outcomes.

Researchers have proposed the use of stroke severity scales aimed at detecting LVO in the field; patients with LVO could then profit from direct transfer to a CSC. Of the many proposed LVO scales, the Los Angeles Motor Scale (LAMS), the Rapid Arterial Occlusion Evaluation (RACE),

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Mobile Stroke Unit News

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Note From the Editor

By Robert G. Kowalski, MD, MS

With this, the second 2020 newsletter for the PRE-hospital Stroke Treatment Organization, or PRESTO, we bring the year to a close. In this issue we present articles describing important research developments with implications for the mobile stroke paradigm of stroke care, as well as the maturing of the organization as it has grown to include members in six nations worldwide.

In his column, PRESTO President Jim Grotta, MD, encapsulates the steps PRESTO took during the year to advance as a professional organization, with the hiring of a professional management company, launching of a new website, and establishment of membership, dispatch, research and reimbursement committees. Dr. Grotta also previews anticipated presentation and publication of important efficacy studies on mobile stroke, the B-PROUD and BEST-MSU trials.

Heinrich J. Audebert, MD, Professor of Neurology at Charité University, in Berlin, Germany, describes the results of the RACECAT stroke trial, comparing direct transfer of patients with a suspected large vessel occlusion (LVO) to an endovascular center with transfer to the closest stroke center. Prof. Audebert is also Principal Investigator on the B_PROUD trial.

Klaus Fassbender, MD, Professor and Chairman of Neurology, Saarland University Medical Center, Homburg, Germany, describes research comparing clinical instruments such as LAMS (Los Angeles Motor Scale) administered in the field, with mobile stroke, for accuracy of stroke triage decisions. Prof Fassbender was the PRESTO organization's first President, and the founder of the mobile stroke concept.

The featured program for this issue of the newsletter is the Melbourne Mobile Stroke Unit. Stephen M. Davis, MD, Melbourne Brain Centre at Royal Melbourne Hospital, and colleagues, describe the birth of the first MSU service in the Australian and Oceania region, and the hurdles it overcame funding and instituting the service.

Finally, Henry Zhao, MBBS; Bruce Campbell, MBBS, PhD; Andrew Bivard, PhD; and Mark Parsons, PhD – all of the Department of Neurology and Department of Medicine, Melbourne Brain Centre at the Royal Melbourne Hospital, The University of Melbourne, Australia – describe advantages of tenecteplase vs. tPA, on mobile stroke unit. Their report provides a thorough and fascinating comparison of the two treatments.

We anticipate another newsletter to accompany the International Stroke Conference in March 2021, being conducted 100% virtually this year due to the COVID-19 environment. At that time we will provide updates on the status of important and anticipated clinical efficacy stroke trials involving mobile stroke.

As the newsletter continues to chronicle developments and advances in the still-nascent field of mobile stroke care, we welcome any ideas and contributions for future issues of the Mobile Stroke Unit News.

Robert G. Kowalski, MD, MS is Clinical Research Instructor at the University of Colorado School of Medicine, Department of Neurology, and is leading research on the university's Mobile Stroke Unit.

PREHOSPITAL STROKE TREATMENT ORGANIZATION
PRESTO

The Melbourne Mobile Stroke Unit and the New Frontier

Stephen M. Davis[1], Geoffrey A. Donnan[1]*, Henry Zhao[1,2], Bruce C. V. Campbell[1,2], Shane Foster[2], Michael Stephenson[2,3], Skye Coote[1], Francesca Langenberg[1], Dominique A. Cadilhac[3,4], Leonid Churilov[1], Christopher F. Bladin[2], Bernard Yan[1], Nawaf Yassi[1,5], Mark Parsons[6], Damien Easton[1] for the Melbourne MSU collaboration*

Professors Stephen Davis and Geoff Donnan established the Melbourne Mobile Stroke Unit (MSU) as the first MSU service in the Australian and Oceania region following a successful commonwealth government research grant in 2015. We saw that pre-hospital stroke care was a critical part of the stroke treatment pathway and also an exciting platform for hyperacute stroke research. Gratifyingly, the MSU was enthusiastically endorsed by key partners, particularly Ambulance Victoria (CEO Tony Walker and Executive Clinical Director Michael Stephenson) and a plan rapidly evolved to develop and implement a pilot prehospital clinical service. The vehicle would be based at the Royal Melbourne Hospital (RMH) and operate in partnership with Ambulance Victoria.

We were very fortunate to obtain philanthropic support for the vehicle purchase and build costs from generous donors who wished to remain anonymous. Our national Stroke Foundation (CEO Sharon McGowan) agreed to fund the AUD$500,000 CT scanner. Our Victorian State Government then committed to fund the operational costs of AUD$2 million/year pilot for 4 years. The plans included clinical and independent economic analysis to determine whether it would become an ongoing clinical service at the end of the pilot.

We assembled a multidisciplinary team to then plan and build our MSU within 12 months (Project Lead Damien Easton). We considered many design options but elected to have an ambulance that was familiar to our Ambulance Victoria colleagues, relatively compact and able to access ED transit bays in metropolitan hospitals. We used a long wheelbase Mercedes 519 Sprinter and a specially designed rear cabin, incorporating the CereTom® CT scanner, used in most MSU's around the world. We also incorporated telemedicine capability and seating for 3 crew members in the rear cabin: a stroke physician, stroke nurse and CT radiographer. The front cabin seats two highly skilled paramedics, one ALS (advanced life support) and one MICA (mobile intensive care specialist). Henry Zhao is Medical Lead, Skye Coote is Nursing Lead, Francesca Langenberg is CT Lead and the MSU Paramedic Lead is a critical rotational role.

Figure 1. Melbourne Mobile Stroke Unit exterior (A) and interior hardware comprising monitors for viewing and sending imaging in real-time (B), contrast injector (C), storage compartments for medications (D), CereTom® CT scanner (E) and contrast warmer (F).

Melbourne is home to over 5 million people. Stroke services in Melbourne comprise 2 statewide endovascular centres and several other centres equipped for endovascular thrombectomy. The Melbourne MSU is housed in a specially designed bay at the RMH from which it is deployed via the central Ambulance Victoria dispatch system. The MSU operates primarily in a 20-kilometer radius and transports patients to the nearest appropriate hospital, including triage to a comprehensive center if necessary. This region serves around 1.5 -2 million people.

A dual dispatch protocol is used where a first responder ambulance usually arrives at the scene first and may stand down the

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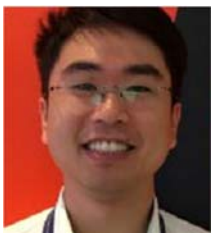
Tenecteplase in the Mobile Stroke Unit: Access and Clinical Outcomes

By Henry Zhao, MBBS; Bruce Campbell, MBBS, PhD; Andrew Bivard, PhD; and Mark Parsons, PhD


Henry Zhao, MBBS


Bruce Campbell, MBBS, PhD


Andrew Bivard, PhD


Mark Parsons, PhD

Intravenous alteplase (rtPA) has been the standard thrombolytic agent since the NINDS trial published in 1995. Since then, desmoteplase appeared initially promising as a superior drug, but interest waned after six trials failed to show improved functional outcomes. Therefore, it is not surprising that much hope has fallen on tenecteplase (TNK) to progress intravenous reperfusion therapy. In this article we will summarize the evidence of TNK so far and the practical advantages of using TNK in the mobile stroke unit setting.

The Evidence for Tenecteplase

TNK has greater fibrin affinity than rtPA and is used as the standard thrombolytic agent in ST-elevated myocardial infarction. The first clinical trial in ischaemic stroke was a dose ranging study that found acceptable rates of symptomatic hemorrhagic transformation for doses up to 0.4mg/kg,(1) but a subsequent clinical efficacy phase was terminated due to poor recruitment and did not demonstrate improved outcomes compared to rtPA.(2) The Australian TNK phase II trial compared TNK at 0.1mg/kg and 0.25mg/kg to rtPA 0.9mg/kg in n=75 patients (25 in each arm) selected by CT-perfusion up to 6 hours from onset.(3) The pooled TNK arms showed greater reperfusion (p=0.0004) and return to independence (modified Rankin Score 0-2, 72% vs 44%, p=0.02).(3) Additionally, the higher TNK dose at 0.25mg/kg improved reperfusion and clinical outcomes vs 0.1mg/kg. In contrast, the phase II ATTEST trial compared TNK 0.25mg/kg to rtPA 0.9mg/kg in n=104 patients within the standard 4.5-hour thrombolysis window and did not show superiority in the primary endpoint of tissue salvage (p=0.81).(4) Subsequent pooling of the Australian TNK and ATTEST trials (n=146), however, showed that patients with significant penumbral tissue on CT perfusion had significantly better clinical outcomes with TNK 0.25mg/kg, with the greatest benefit seen in those with large vessel occlusion.(5, 6)

The Norwegian NORTEST phase III trial of TNK enrolled n=1,107 patients <4.5 hours of onset or wake from sleep and compared TNK 0.4mg/kg to rtPA 0.9mg/kg.(7) Despite the higher dose, TNK did not show superiority in improving excellent outcome (modified Rankin Scale 0-1, 64% vs 63%, odds ratio 1.08 [95% CI 0.84-1.38, p=0.52]). However, there are significant issues with this trial including the unusually high number of patients diagnosed with stroke mimics enrolled (17%) and the low median baseline severity (NIHSS 4), reducing the power to detect a meaningful difference.

Subsequently, the Australian-led EXTEND-IA TNK trial compared TNK 0.25mg/kg to rtPA in n=202 patients with large vessel occlusion intended for endovascular thrombectomy.(8) This showed a doubling of vessel recanalization prior to any need for mechanical intervention (22% vs 10%, non-inferiority p=0.002, superiority

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PRESTO Executive Committee and Working Groups

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Developments in 2020 for PRESTO and Mobile Stroke Treatment

Continued from *Grotta*, p. 1

We are happy to report that, at the end of 2020, we have over 120 members with six countries represented. This has enabled us to balance our budget for the year. We are looking forward to seeing that number grow, and to welcome all MSUs worldwide into our membership.

2021 promises to be a banner year for MSUs and PRESTO. We look forward to the publication of two pivotal controlled trials testing the effect of MSU management on stroke outcome. The positive results of the B_PROUD study have already been presented and the soon-forthcoming publication will provide the stroke community with a more in-depth understanding of the study methodology, results, and impact on improving disability. The BEST-MSU study has completed enrollment and publication of the results is expected in the first quarter of 2021. Additional data are also expected this next year from other MSU centers in the U.S., Norway and Australia. Together, these anxiously awaited results should provide PRESTO membership and the entire stroke community the data to enable us to put the contribution of MSUs into the larger perspective of stroke management.

How much do we help patients? How does this compare to other treatments? How generalizable are the results? What are the MSU processes that have the greatest impact on the results? Where are the opportunities for further improvement? What are the next studies that need to be done? Can the Research committee help PRESTO membership approach some of these questions collaboratively? How can the Reimbursement and Dispatch committees leverage the data to help achieve appropriate reimbursement and more accurate dispatch? And finally, depending on the results, we might see worldwide interest in MSUs substantially expand (or not). If it does, PRESTO needs to continue to encompass and represent the MSU "community", and will need to be nimble in being a useful resource for new MSUs starting up worldwide.

In closing, on behalf of the PRESTO Board of Directors, let me wish all of you a happy, healthy, productive, and exciting 2021.

James C. Grotta, MD, is Director of Stroke Research and Director, Mobile Stroke Unit Consortium, Memorial Hermann-Texas Medical Center, Houston, TX.

Mobile Stroke vs. Prehospital LAMS Clinical Score Evaluation

Continued from *Fassbender*, p. 1

and the A2L2 test (A, arm; L, leg) have been studied in the field by emergency medical services (EMS) personnel. However, so far, sensitivities and specificities lie between 70% and 80% (Turc G, et al, Stroke 2016; 47: 1466–72) (Noorian AR et al. Stroke 2018; 49: 565–72). The use of such instruments may nevertheless be superior to the current practice of using no instrument for LVO identification but rather transferring all patients to the nearest stroke-treating hospital.

However, a recent randomized study examined whether such optimized prehospital management featuring a clinical score can compare with management in a Mobile Stroke Unit (MSU) in terms of triaging stroke patients to hospitals providing or not providing neurointerventional treatment. This randomized trial, involving 116 patients and using a protocol including evaluation with the LAMS, resulted in accurate triage decisions for 69.8% of patients, whereas an MSU with imaging capability enabled accurate triage decisions for 100% of patients, a statistically significant difference (Helwig et al., JAMA Neurology 2019;76:1484-92).

Moreover, MSUs offer additional beneficial effects for acute stroke management, such as earlier thrombolysis, the option of etiology-specific measures such as prehospital blood pressure management, or reversal of anticoagulant medication.

Therefore, the use of either clinical scores or an MSU may be better than the current practice of transferring all patients to the next stroke center. The optimal triage concept would, however, be the deployment of an MSU, which depends on the specific health care setting and available resources.

Klaus Fassbender, MD, is Professor and Chairman of Neurology, Saarland University Medical Center, Homburg, Germany. He is the founding President of the PRE-hospital Stroke Treatment Organization (PRESTO).

Drip-and-ship and mothership models compared in RACECAT Trial

Continued from *Audebert*, p. 1

range of the modified Rankin Scale (mRS) at 3 months in patients with ischemic stroke (modified intention to treat analysis, mITT). Safety outcomes consisted of 90-days mortality in the entire study population and in patients with intracerebral hemorrhage as well as need of intubation during transport.

Of 7,475 patients with EMS stroke code activation, a total of 1,401 patients were randomized in a 1:1 ratio, yielding 676 allocated to local SC and 670 to EVT-SC primary transport (467 vs 482 in the mITT). Four-hundred-twenty patients (31%) had a diagnosis other than ischemic stroke.

As expected, thrombolysis rate (60.4 vs 47.5%) was higher with shorter median onset-to-needle time (120, IQR: 89-168 vs 155, IQR: 120-195min) in patients primarily transported to a local-SC compared to patients with direct transport to EVT-SC. Reversely, thrombectomy rate was lower (40.9 vs. 50.0%) and time to groin puncture was longer (270, 215-348 vs 214, 172-230min, respectively) in patients in the local-SC group. There were no significant differences in the primary outcome with an adjusted common odds ratio for worse outcome on the mRS of 0.99 (95%-CI: 0.78-1.43) nor in the overall mortality (adjusted HR 0.97, 95%-CI: 0.79-1.18) or mortality in patients with intracerebral hemorrhage (adjusted HR: 1.22, 95%-CI: 0.86-1.71).

The investigators summarize that under the particular conditions of the highly coordinated and monitored stroke care system of Catalonia, a mothership transfer protocol in patients with suspected LVO was not superior over the drip-and-ship protocol.

Why is the trial important for the Mobile Stroke Unit concept?

The RACECAT trial sought to resolve the dilemma of routing patients possibly eligible for two different time-critical treatments to the nearest stroke-ready hospital or to a more distant EVT-capable stroke center.

Even in a region with a well-established network of primary and comprehensive stroke centers and ambulance crews trained to detect patients with high probability of large artery occlusion, there was no advantage of direct transport to EVT-capable centers. Apart from a 35-min longer onset-to-needle time in the direct EVT transport group, the main reason was that only 47% of patients with suspected large vessel occlusion according to the RACE scale had a confirmed large- artery occlusion, which makes any transport decision without definite intracranial vessel status very challenging. The currently best solution therefore remains pre-hospital imaging as realized on Mobile Stroke Units. This approach secures immediate brain imaging to exclude intracranial hemorrhage before starting intravenous thrombolysis at the scene[1,2] and offers vessel imaging via CTA before transport decision, allowing transport to the most appropriate stroke center with pre-notification of the endovascular team[3,4].

However, most of the MSU services are established in metropolitan areas in order to guarantee frequent activation. For rural areas with also wider differences in distance to primary and comprehensive stroke centers, innovative technologies for large artery occlusion diagnosis based on ultrasound, microwave, near-infrared spectroscopy or blood bio-markers are currently being developed and should be investigated in the near future.

Prof. Heinrich J. Audebert, M.D. is Professor of Neurology at Charité Universitätsmedizin, Berlin, Germany.

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PRE-HOSPITAL STROKE TREATMENT ORGANIZATION (PRESTO)

PRESTO was formed in 2016 as an international consortium of medical practitioners involved in pre-hospital treatment of patients with acute stroke. PRESTO exists for and is dedicated to the following purposes:

PRESTO's Mission is to improve stroke outcomes by supporting research for pre-hospital stroke treatment in Mobile Stroke Units (MSUs).

PRESTO will provide a platform to enhance collaborative research across the spectrum of acute stroke management in the pre-hospital setting.

PRESTO will facilitate the appropriate proliferation and distribution of MSUs by providing a forum for professional communication, resource for public education, and stimulus for government, industry, and philanthropic support.

Melbourne MSU: Prehospital Stroke Care in Australia and Oceania

Continued from *Davis et al*, p. 3

attendance by the MSU (cancellation in about 60% of dispatches).

The Melbourne MSU operates 10 hours per day, 5 days a week, designed to capture approximately around 64% of all suspected stroke dispatches within the primary co-dispatch radius. However, there is some flexibility and there is opportunity to rendezvous with an ambulance crew far beyond this radius, particularly if the MSU is requested for patients with a severe stroke syndrome. As part of the program, we have included a process and economic evaluation to support translation to other settings, as well as research on the clinical effectiveness. Very few programs have reported on the factors that have led to the success and or challenges of implementing a new, first-ever MSU service from an inter-disciplinary perspective.

The Melbourne MSU was launched at the end of 2017 and has been a clinical and economic success[1, 2]. Over the past 3 years, we have been dispatched to 4,381 patients and attended 1,649 patients (38%). As a result, the Victorian State Government has just refunded the program as an ongoing service. There are also provisional plans for a second MSU (MSU-2) in our Eastern and Southern suburbs of Melbourne. The New South Wales (NSW) government has just announced plans for an MSU in Sydney. The MSU-2 development will occur in close collaboration with our NSW colleagues to ensure uniformity of design and implementation.

Faster thrombolysis

A principal aim of MSUs is the ability to provide faster pre-hospital thrombolysis. We have treated 172 patients to date. We showed that we cut the time to treatment by 42.5 minutes (95% CI 36.0-49.0).[1] In the first "Golden Hour" after stroke onset, we increased the proportion treated 10-fold from 1.5% in Melbourne acute stroke centers to 15% on the MSU. We treated about 50% of our patients in the first 90 minutes (the "Silver 90 minutes") compared to around 12% of our controls. The MSU is truly a mobile treatment service and able to treat seizures, administer antihypertensive agents pre- and post-thrombolysis, or intravenous idarucizumab to reverse dabigatran prior to thrombolysis.[3]

Faster endovascular thrombectomy

To date, we have triaged 136 patients for endovascular thrombectomy (EVT). In Melbourne, we widely use the ACT-FAST triage algorithm on standard ambulances to screen patients for large vessel occlusion.[4] However, the CTA capability on the MSU allows specific diagnosis of large vessel occlusion. This results in substantial time savings with a median time saving of 51 minutes (95% CI 30-72). This is substantially due to time avoidance of secondary transfers. In addition, the MSU pre-screening resulted in a further 17 minutes (95% CI 8-26) time saving from hospital arrival to EVT commencement.[1]

Faster treatment of intracerebral hemorrhage

We treated 42% of our MSU ICH patients with acute intravenous anti-hypertensive therapy. Pre-hospital imaging and management allows faster blood pressure reduction and potentially greater stabilization of hematoma growth. We use anticoagulant reversal with intravenous vitamin K and 3-factor prothrombin concentrate for warfarin-related ICH and intravenous idarucizumab for dabigatran-associated ICH. Pre-hospital diagnosis facilitates triage of patients directly to a neurosurgical center.

Our MSU is a clinical trials platform, with

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The New Frontier – Lightweight brain imaging

Figure 2. Micro-X scanner concept

Australia is a vast continent. About one third of Australians live in rural and remote regions and have little access to modern stroke therapies.[5] Not surprisingly, stroke outcomes for rural, remote and Indigenous Australian communities are significantly worse.[5, 6] The main barrier is the lack of access to acute brain imaging and expertise. The current scanner used in most mobile stroke units weighs over 500 kg. We have formed the Australian Stroke Alliance (Co-Chairs Donnan & Davis; CEO Easton) with over 30 State and National partners, to address the current unacceptable inequity in access to modern acute stroke therapies (https://austrokealliance.org.au/).

The development of lightweight, portable and affordable brain imaging is therefore a key goal and then embedding these in rural ambulances and aircraft, linked with digital telemedicine. Hence, the plan is to bring the hospital to the patient, wherever they live in Australia, with disruptive technologies. Prototype imaging devices under development will weigh under 100kg.

Melbourne Center Explores Australian Air-MSU

Continued from *Davis et al*, p. 7

the majority of treated patients enrolled into one of several intervention trials. Around one third of all MSU diagnosed ICH patients were recruited into STOP-MSU (CI Zhao, Yassi, Donnan, Davis, Clinicaltrials.gov registration: NCT0338-5928), a clinical trial of tranexamic acid administered within 2 hours of onset, placebo-controlled and with the primary aim of attenuation of hematoma growth at 24 hours. We are also investigating the utility of acute stroke blood biomarkers in the prehospital environment (CI Yan). There are a range of other clinical trials such as TASTE-A (CI Parsons, Bivard; NCT04071613) which is comparing tenecteplase with tPA and DIRECT SAFE, testing rapid thrombectomy without bridging thrombolysis (CI Mitchell, Yan; NCT03494920).

One prototype lightweight imaging device is using a microwave technique, which can detect changes in the electrical properties of brain tissue due to change in blood flow, water content and temperature with a high sensitivity. In early clinical tests, there is encouraging ability of microwaves to differentiate haemorrhagic stroke from ischaemic stroke. Another approach uses ultra- lightweight CT scanning using novel, non-thermionic nanotube technology. This allows miniaturization of the scanner and has no moving parts.

Cost benefit of the Melbourne MSU

Preliminary health economic analyses confirmed that the Melbourne MSU is cost-effective, recently reported by Kim and Cadilhac.[2] The overall cost to save one disability-adjusted life year was estimated to be between AUD$19,003-$44,255 in 95% of model iterations, below the general AUD$50,000 threshold for approval of subsidy by the Australian Government. We are partnering with many national organizations such the Royal Flying Doctor Service (the largest aeromedical retrieval service worldwide) to develop an Air-MSU[7] to access the vast distances in Australia and serve rural, remote and Indigenous populations. The outcomes of this research program could transform the model of pre-hospital stroke care across Australia with global implications. This will lay the foundations for extensive international collaborations with our PRESTO colleagues.

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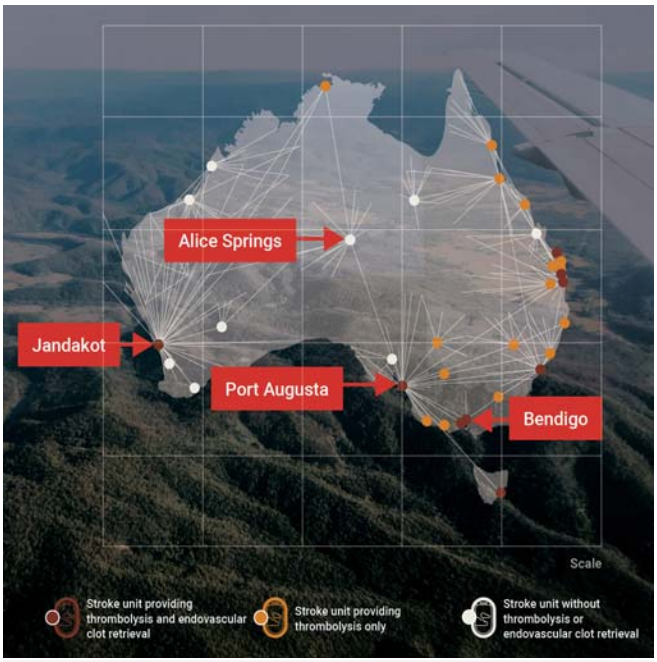

Figure 3. Map of Royal Flying Doctor Service flight paths and potential test beds for Air-MSU validation studies.

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Tenecteplase Presents Practical Advantages for Mobile Stroke Care

Continued from *Zhao et al*, p. 4

p=0.03) and also improved overall 3-month functional outcomes (ordinal analysis of the modified Rankin Scale, common odds ratio 1.7 [95% CI 1.0-2.8, p=0.04]).(8) A follow-on trial compared TNK 0.25mg/kg with 0.4mg/kg and did not find any further benefit with the higher dose for vessel recanalization or improved outcomes.(9)

A recent meta-analysis of TNK was conducted comparing TNK versus rtPA.(10) Using non-inferiority margin of 6.5%, the study found that TNK was non-inferior for all clinical efficacy measures (modified Rankin Scale 0-1, 0-2 and ordinal analysis) as well as symptomatic hemorrhagic transformation.(10) This effect did not appear modified by dosage (although the study noted that TNK 0.1mg/kg was underpowered) or need for endovascular thrombectomy for large vessel occlusion.(10)

Advantages of Tenecteplase on the Mobile Stroke Unit

Even if we accept that TNK is simply non-inferior, there are many practical advantages of using TNK vs rtPA in a MSU setting. The first is ease of administration, with TNK only requiring one vial given as a single bolus. This is compared to rtPA which, depending on administration method, requires separate drawing up of bolus and the one-hour infusion. TNK may therefore facilitate shorter scene to needle time and higher rates of golden hour thrombolysis. Furthermore, the simplicity reduces the risk of administration error, reduces need for infusion equipment and potentially allows other staff like paramedics/EMTs to give the drug.

Another advantage is the potential costs of the thrombolytic, with TNK having a set cost with one vial per patient, compared to potentially several rtPA vials for patients with higher body weight. Storage space is often more limited in the MSU setting and the single vials allow more doses to be stored at once (as well as less need for infusion pumps).

In our experience on the Melbourne MSU we have had many cases where intravenous access is difficult, with only one IV cannula possible, yet patients require both thrombolysis and hypertensive management. In these cases, we prefer TNK such that the thrombolytic can be pushed in quickly and intravenous anti-hypertensives started thereafter. This would be extremely difficult with a rtPA infusion, making safe pre-hospital thrombolysis virtually impossible.

On the Melbourne MSU, we are also currently running the TASTE-A trial (Clinicaltrials.gov NCT04071613) comparing TNK 0.25mg/kg to rtPA on pre-hospital thrombolysis-eligible patients. The primary endpoint of the trial will be CT-perfusion lesion on hospital arrival and clinical efficacy measures as a secondary outcome. This is expected to finish in 2021.

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