

Mobile Stroke Unit News

News magazine of the PRE-hospital Stroke Treatment Organization

Volume 4, No. 1

Research Expanding in Mobile Stroke Paradigm It is Time to Walk Together on The Road of Prehospital Stroke



*By Heinrich J. Audebert, MD
President*

In this PRESTO newsletter, there are three contributions from MSU groups around the world that report on their current research projects including development and implementation of new stroke imaging technologies, bio-

markers and a multicenter trial investigating the use of tenecteplase as an alternative to alteplase. This is an evident expression of the high level of research activities on Mobile Stroke Units that is gaining more and more momentum.

After the publication of the three prospective controlled studies in 2021¹⁻³ showing that prehospital diagnosis and immediate start of thrombolytic treatment improves functional outcome in acute ischemic stroke and systematic meta-analysis of all available MSU studies⁴, the first international guideline has been released recommending MSU to improve prehospital management of suspected stroke patients.⁵

Based on this body of evidence, we need to make MSU care sustainable, which will require regular reimbursement from health insurers or federal healthcare services. PRESTO is

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TASTE-A for Multi-centre Phase III MSU Trial: Are You With Us?

By Mark Parsons MBBS, FRACP, PhD; Andrew Bivard, PhD and Henry Zhao MBBS (Hons) PhD

At the 8th European Stroke Organisation Conference on the 4th of May 2022 (and more importantly, International Star Wars Day), we presented the results of the Tenecteplase vs Alteplase Stroke Evaluation Ambulance trial from the Melbourne Mobile Stroke Unit (TASTE-A). In this phase II randomised controlled trial, we were able to show that pre-hospital treatment with the intravenous thrombolytic agent Tenecteplase leads to faster time to treatment, better early clinical recovery, and much smaller post-lysis perfusion lesions than with intravenous alteplase. There was no serious brain haemorrhage with either Tenecteplase or Alteplase. The trial enrolled 104 patients in little over a year, demonstrating the immense potential for clinical trials on MSUs where an expert



Andrew Bivard, PhD (L) and Mark Parsons, PhD, on the mobile stroke unit in Melbourne, Australia

clinical group are present and can enroll patients into trials in the acute setting. Although pre-hospital thrombolysis for Myocardial Infarction is now widespread in rural Australia, TASTE-A was the first trial of pre-hospital Tenecteplase for stroke.

Despite these impressive results,

TASTE-A was a phase II study and not powered to show a difference in 3-month outcomes. Thus, we would caution against prematurely switching to Tenecteplase for pre-hospital stroke thrombolysis until a multi-centre phase III MSU RCT is performed. Indeed, despite cautioning against this more than two years ago we have unfortunately seen a premature change to Guidelines and consequent flood of off-label use of Tenecteplase for in-hospital stroke without the requisite level I (phase III RCT) evidence. This has led to a global shortage in Tenecteplase and anxiety in the Australian system about supply of Tenecteplase for Myocardial Infarction as well as stroke.

So, where to now? At the recent PRESTO meeting there was strong consensus that we should push ahead with a phase III randomised controlled trial of Tenecteplase versus Alteplase

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TreatNASPP, MSU biomarkers, CT for AirMSU Story, p. 3

Mobile Stroke Care with Blood-based Biomarkers for Prehospital Diagnosis

Research on alternatives to cerebral imaging. Story, p. 4

Mobile Stroke Unit News

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Note From the Editor

By Robert G. Kowalski, MD, MS



This issue of the newsletter for the PRESTO group provides a glimpse into the depth and breadth of the research efforts under way, and planned, in medical institutions op-

erating mobile stroke units and other modes of prehospital stroke care.

In his letter on the front page, President Heinrich Audebert, Professor of Neurology at Charité Universitätsmedizin, Berlin, Germany, summarizes the remarkable number of clinical and basic science research efforts now being undertaken in the prehospital stroke field.

Also on the first page, Mark Parsons, MBBS, FRACP, PhD; Andrew Bivard, PhD and Henry Zhao MBBS (Hons) PhD FRACP –with the University of Melbourne and Royal Melbourne Hospital, discuss the findings of the Tenecteplase vs Alteplase Stroke Evaluation Ambulance (TASTE-A) trial. That study, with results, presented at the 8th European Stroke Organisation Conference in May 2022, was a Phase II comparison of conventional thrombolytic stroke therapy involving alteplase, with Tenecteplase, as is rapidly becoming standard of care at many stroke centers in the U.S. and elsewhere.

The concept of the mobile stroke unit as a rolling laboratory is explored by Maximilian Kaffes, MD and Joachim E. Weber, MD, both of Charité Universitätsmedizin, Berlin, Germany. Their article discusses the potential for blood-based biomarkers in stroke care, and blood sampling on an MSU. Of particular interest on both sides of the Atlantic, has been glial fibrillary acidic protein (GFAP) and its potential utility as a marker of

intracranial hemorrhage. The authors note the opportunity that discoveries related to such biomarkers might provide not only in the prehospital setting on MSUs, but also in traditional ambulances used to transport acute stroke patients.

Biomarkers are also being explored at the Norwegian Air Ambulance Foundation and the University of Oslo, as is described in the “featured program” in this issue of the newsletter. Karianne Larsen, MD; Else C. Sandset, MD, PhD; and Maren R. Hov, MD, PhD of the Norwegian program, explore in great depth the wealth of prehospital research endeavors taking place in Norway. Included are the TreatNASPP study, assessing parameters of mobile stroke delivery; the ParaNASPP study which evaluated administration of the NIHSS in the field; and development of a modified, lightweight CT scanner for use in helicopters.

The field of mobile stroke continues to expand as is depicted in the updated world map of existing and planned MSU centers on page 5 of this newsletter issue.

We are grateful for the articles contributed on these important research developments in mobile stroke. The newsletter will continue to monitor these studies, and those in the pipeline, in the field of mobile stroke and airborne pre-hospital 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, Departments of Neurology and Neurosurgery, and is leading research on the university's Mobile Stroke Unit.



International Stroke Conference 2023

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Featured Program

Norwegian Prehospital Stroke Research Experience and Future Plans

By Karianne Larsen, MD; Else C. Sandset, MD, PhD; and Maren R. Hov, MD, PhD

In 2012 the idea of a Norwegian mobile stroke unit (MSU) was formed based on the pioneering studies in Germany. Prehospital stroke care proved to save time to treatment by moving stroke expertise out in the field, closer to the patients.

However, Norway has vast distances, sparsely populated areas and few neurology specialists which resulted in the need of an alternative model to the independently run prehospital stroke unit. Instead of moving in-hospital specialists into the field, the Norwegian model is based on the existing pre-hospital physician-staffed emergency medical services (EMS). The Norwegian MSU was staffed like the helicopter emergency medical service (HEMS) with an anesthesiologist trained in pre-hospital critical care (air ambulance physician), a paramedic (pilot) and a nurse with special training as a paramedic (rescuer).

The Norwegian MSU implemented advanced stroke assessment to the worklist of trained prehospital personnel rather than development of a model based on neurologist care in a prehospital unit.

The first study completed in the Norwegian MSU was the Norwegian Acute Stroke Prehospital Project (NASPP) which explored if trained non-neurologist MSU personnel could perform clinical stroke diagnostics using The National Institutes of Health Stroke Scale (NIHSS) and identify radiological contraindications to thrombolytic treatment on prehospital CT scans. The NASPP study showed that anesthesiologists trained in prehospital critical care working in an MSU could do clinical and radiological stroke diagnostics in the field with a high inter-rater agreement

compared to the in-hospital stroke team. Further development of the Norwegian MSU model was explored in the Treat NASPP study, in which prehospital thrombolytic therapy was added to

the procedure. The study showed that thrombolysis was given around 20 minutes earlier in the MSU, 13 times more often within the golden hour and 22% more patients were treated compared to the conventional in-hospital pathway. A health economic analysis conducted based on the TreatNASPP results, proved the model to be potentially cost-effective if more than 125-260 ischemic stroke patients are treated with thrombolysis per MSU per year. TreatNASPP was finished in March 2020 in the beginning of the Covid pandemic, and due to these circumstances, plans for new MSU projects were delayed.

Biomarkers in acute stroke

As part of NASPP and TreatNASPP, a biomarker study was developed. Blood samples were drawn from suspected stroke patients in the prehospital environment, in ambulances and the MSU, within 4.5 hours from symptom onset. The main aim



Karianne Larsen, MD



Else C. Sandset, MD, PhD



Maren R. Hov, MD, PhD

was to test if biomarkers could differentiate between ischemic and hemorrhagic strokes. Glial Fibrillary Acidic Protein (GFAP) can identify large intracerebral hemorrhages (ICH) with a high degree of accuracy. The biomarker study explores the diagnostic accuracy of GFAP in combination with Ubiquitin C-Terminal Hydrolase-L1 (UCH-L1) and a stroke score. The role of Factor Seven Activation Protease (FSAP) in the early phase of acute stroke are also investigated and plasma samples are screened for microRNA to identify microRNAs with differential diagnostic potential.

Even though biomarkers, especially GFAP, can rule out larger cerebral bleedings, the CT scanner is still superior. If biomarkers can be used as a diagnostic tool in the field, it will have great influence on the availability of prehospital stroke identification and treatment.

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The Norwegian MSU. Photo: Fredrik Naumann/Felix Features

New Perspectives for an Established Concept

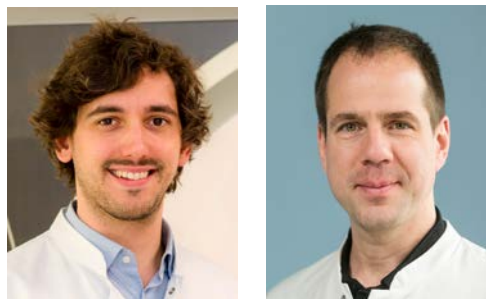
Mobile Stroke Care with Blood-based Biomarkers

By Maximilian Kaffes, MD
and Joachim E. Weber, MD

Mobile stroke units (MSUs) have been established as an evidence-based stroke intervention that not only leads to earlier and more frequent treatment with intravenous thrombolysis (IVT), but in particular also to an improvement in functional outcomes by bringing diagnostics and therapy directly to the patient. Thereby, a relevant proportion of treatments takes place in the first hour after the event, the so-called golden hour [1-3].

Future efforts to improve the prognosis of patients with acute stroke must focus on facilitating earlier diagnosis and thus enabling the initiation of specific therapies both in urban and rural areas. The current setup of MSUs is based on the transfer of established diagnostics and expertise, particularly cerebral imaging using computed tomography, from the hospital to the prehospital setting. However, the use of computed tomography is associated with increased protective measures (radiation protection), increased vehicle weight, and increased costs compared with standard ambulances, resulting in decreased cost-effectiveness, particularly in sparsely populated areas with low absolute stroke incidence [4].

While there are a variety of concepts to bypass these limitations, including research on alternative point-of-care stroke imaging technologies (for a review, see [5]), blood biomarkers have recently advanced as a potentially promising alternative to cerebral imaging. Point-of-care measurements could potentially offer cost-effective support for the introduction of prehospital stroke treatment. An ideal blood biomarker (or a combination of different biomar-



Maximilian Kaffes, MD Joachim E. Weber, MD

kers) should be able to differentiate between acute ischemic stroke (AIS) and intracerebral hemorrhage (ICH) and distinguish them from stroke mimics (SM), as well as give an indication of time of stroke onset and stroke severity, i.e. detection of large vessel occlusion (LVO), see also figure 1.

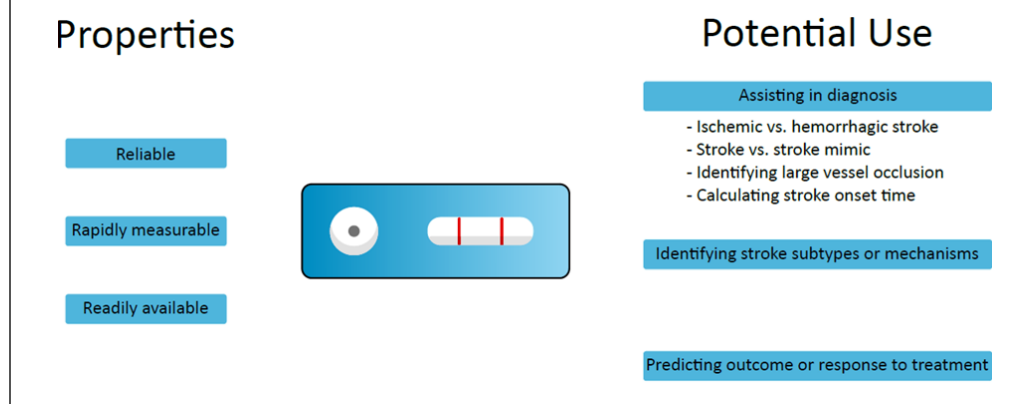
Reliable exclusion of ICH constitutes one major benefit of an effective biomarker, allowing for ultra-early prehospital thrombolysis in patients with AIS without

transport to comprehensive stroke centers with endovascular treatment capability. Furthermore, biomarkers could be used to anticipate complication risks of IVT or serve as an early prognostic marker.

The overall advantage of blood biomarkers lies in the opportunity to use them in regular ambulances, resulting in a much larger proportion of stroke patients benefiting from acute stroke treatment than is currently possible.

Various promising blood-based biomarkers have been increasingly identified in both animal models and early intrahospital clinical trials, focusing on the distinction between AIS and ICH and between stroke and SM. One candidate biomarker that has recently demonstrated high diagnostic sensitivity and specificity in patients admit-

Fig. 1: Properties and potential use of an ideal blood based biomarker (or a combination of biomarkers) in acute stroke care



prior neuroimaging. On the other hand, detection of ICH would enable targeted blood pressure management. Repeated measurements could be used to extrapolate time of onset, if the respective biomarker shows comprehensible dynamics over time.

Biomarkers sensitive to stroke severity and thus indicating LVO could facilitate

ted with acute stroke within 4.5 hours of stroke onset is GFAP (glial fibrillary acidic plasma protein) a glial protein found in astrocytes. GFAP is brain-specific, detectable at very low concentrations in plasma under physiological conditions, and not elevated in most neurological diseases

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Diagnostic Utility of Blood-based Biomarkers Studied in Mobile Stroke

Continued from *Kaffes and Weber*, p. 4
other than stroke.

On the Berlin MSUs (Stroke Emergency Mobile, STEMO), we conducted a study using prehospital blood sampling to determine the diagnostic accuracy of plasma GFAP in the prehospital diagnosis of ICH [6]. GFAP levels of >0.29 ng/mL were detected only in ICH and not in AIS. The sensitivity and specificity of GFAP for differentiating between ICH and AIS were 36.0 and 100%. In a recent prehospital study performed by Mattila et al [7], using the short-term kinetics of GFAP, ICH could be excluded with a high degree of certainty (negative predictive value 98.4%) in 68% of patients with AIS (sensitivity for ICH 96.6%, specificity 68%, positive predictive value 50%).

MSUs provide an optimal platform for biomarker research because 1) they enable ultra-early post stroke sampling, 2) they reach the targeted patient pop-

ulation and 3) many MSUs are actively involved in research projects and thus experienced in obtaining informed consent and collecting study-related data. The implementation of such projects usually requires a centrifuge, a workplace for pre-processing of biosamples, and capacity for interim storage of processed samples. On the STEMO, we are currently running a number of biomarker studies in cooperation with different partners from science and industry.

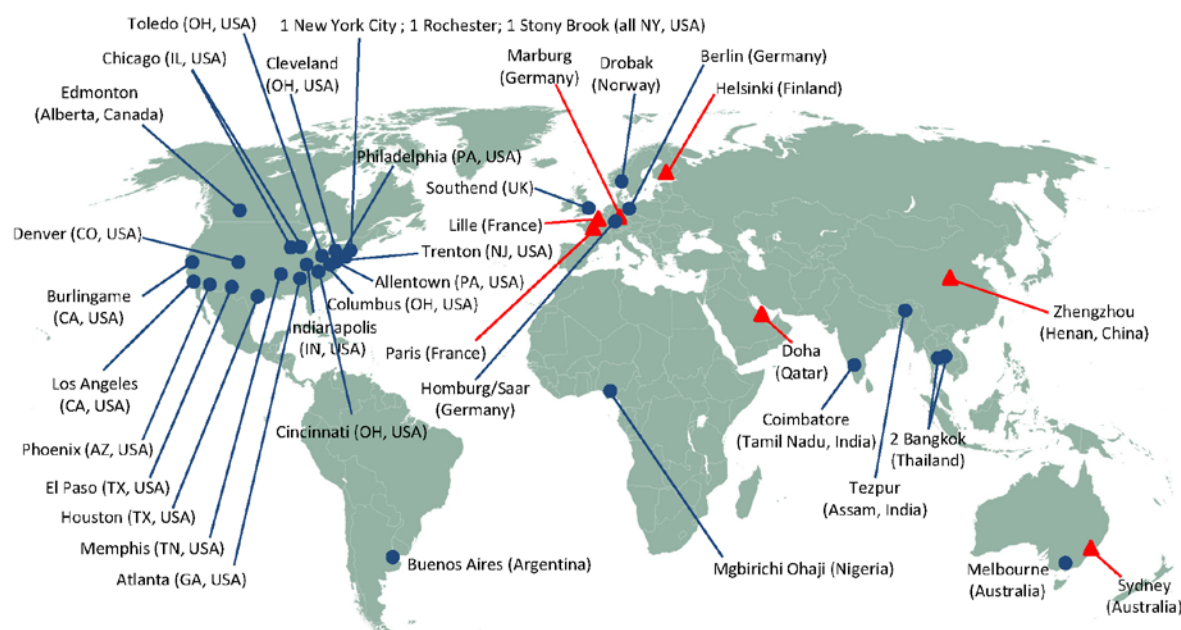
On the one hand, we are aiming to identify new blood-based biomarker candidates for the above-mentioned applications using a discovery approach, on the other hand, we are evaluating a set of different biomarkers in a very application-oriented project aiming to use it as a point-of-care tool for the identification of LVOs.

Maximilian Kaffes, M.D. is Neurology resident and research fellow and Joachim E. Weber is Senior Physician, Neurology, at Charité Universitätsmedizin, Berlin, Germany.

References

1. Turc, G., et al., Comparison of Mobile Stroke Unit With Usual Care for Acute Ischemic Stroke Management: A Systematic Review and Meta-analysis. *JAMA Neurol*, 2022. 79(3): p. 281-290.
2. Ebinger, M., et al., Association Between Dispatch of Mobile Stroke Units and Functional Outcomes Among Patients With Acute Ischemic Stroke in Berlin. *JAMA*, 2021. 325(5): p. 454-466.
3. Grotta, J.C., et al., Prospective, Multicenter, Controlled Trial of Mobile Stroke Units. *N Engl J Med*, 2021. 385(11): p. 971-981.
4. Lund, U.H., et al., Cost-Effectiveness of Mobile Stroke Unit Care in Norway. *Stroke*, 2022. 53(10): p. 3173-3181.
5. Chennareddy, S., et al., Portable stroke detection devices: a systematic scoping review of prehospital applications. *BMC Emerg Med*, 2022. 22(1): p. 111.
6. Rozanski, M., et al., Glial Fibrillary Acidic Protein for Prehospital Diagnosis of Intracerebral Hemorrhage. *Cerebrovasc Dis*, 2017. 43(1-2): p. 76-81.
7. Mattila, O.S., et al., Ultra-Early Differential Diagnosis of Acute Cerebral Ischemia and Hemorrhagic Stroke by Measuring the Prehospital Release Rate of GFAP. *Clin Chem*, 2021. 67(10): p. 1361-1372.

Mobile Stroke Global Distribution 2022



Lesmeister/Fassbender 2022

GFAP, microRNA and NIHSS in Field Studied in Norwegian MSUs

Continued from *Larsen et al*, p. 3

Future projects will further validate microRNA candidates to explore the diagnostic potential.

Training prehospital personnel in performing NIHSS

ParaNASPP was a cluster randomized study in the EMS in Oslo that was ongoing from 2019 until 2021. The main aim was to explore if NIHSS performed by ambulance personnel in the field could increase the positive predictive value of the discharge diagnosis stroke. The participating paramedics were trained using a standardized e-learning program. They were trained to use a mobile application to register NIHSS parameters in addition to other vital information that could be directly and digitally transferred to the in-hospital stroke physician. Preliminary results were presented at ESOC 2021. The intervention group identified more subtle stroke symptoms, reduced in-hospital time, and created a common language in the chain of acute stroke survival. The main results from the study are expected to be published by the end of 2022.

Based on the experiences from ParaNASPP with NIHSS training, a new project, GameStroke, tested gamification as a platform for digital simulation training. GameStroke was designed as an app and was developed by NAAF in collaboration with stroke researchers, stroke clinicians and paramedics. The game shows an animated paramedic character performing NIHSS on an animated patient.



Prehospital blood samples are analyzed in the biomarker study. Photo: Fredrik Naumann/Felix Features

GameStroke can be played anywhere and at all times, more than 1000 variations of symptom presentations are available, and scores and leaderboards are presented at the end of each game. The GameStroke study tested the paramedic students' performance and accuracy in scoring NIHSS after digital game-based simulation training compared to standard in-person simulation training. The results will be published in 2022. Gamification has become popular in educational settings due to its engaging nature and availability, and we believe that gamification can play an

important role in training health care personnel in the future.

Prehospital Mobile CT – AirMSU

NAAF has in the recent years worked with new solutions to both improve the standard air ambulance (helicopter) cabin to optimize and improve the work environment for air ambulance physicians. During these years the opportunities for integrating a CT scanner into the helicopter ambulance have been explored by an innovation team including engineers, industrial designers, and medical physicists, in close collaboration with the medical crew.

The team disassembled a CereTom scanner and removed “unnecessary” parts and lightened the structure, to explore if was possible to integrate the scanner into the helicopter cabin. The project concluded that the CereTom scanner could be reduced by around 160 kg (353 lbs) reaching a minimum weight of 240 kg (529 lbs). Further weight reductions would be very difficult and

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The ParaNASPP model of communication and competence in the chain of stroke survival. Photo: Marius Svaleng Andresen



Lightweight CT Scanner Designed for AirMSU in Norwegian Prehospital Air Stroke Care System

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costly. Together with high complexity and many moving and fragile parts, the conventional CT technology was discarded.

The project started to explore new diagnostic devices and innovative technology that could be plausible alternatives to the traditional CT scanner. As of mid-2022, the most promising product is a head-scanner based on carbon nanotube technology developed by the Australian company Micro-X, with funding from the Australian Stroke Association (ASA). This technology opens for a lightweight robust construction weighing 60-80 kg, no moving parts and with low energy consumption. While still being in the prototype phase this product may be possible to integrate into the helicopter cabin in a not-too-distant future.

In 2021 NAAF invested in a new 5-bladed Airbus H145 helicopter dedicated to research and development purposes. At the AirMed conference 2022 in Salzburg, Austria, NAAF presented the Airbus H145 with a concept model of a CT scanner aimed to trigger the industry to recognize that there is a market for prehospital lightweight CT scanners. This was presented together with NAAF's full-size mock-up of the H145 showcasing a new Medical Cockpit. In the helicopter mock-up, Micro-X displayed a model of their head CT scanner. The ideas gained great interest from other air ambulance operators, industrial partners, and air ambulance personnel.

With this new evolving technology, we hope to test this new scanner in the research helicopter within the next 3 to



Morten Evensmo, industrial designer and project manager, showing the future vision of a full body CT scanner in the H145 helicopter. Developed by NAAF based on principles from Micro-X's head CT scanner. Photo: Marianne Wennesland



Demo version of a Micro-X head CT scanner displayed in the helicopter mock up model. Photo: NAAF

5 years. The AirMSU concept is closer to reality than ever.

New research program and future plans

The Norwegian Prehospital Acute Brain (PAB) Program is a research program established by NAAF's Department of Research and Development in 2021. The PAB program is led by Maren R. Hov, MD, PhD with Else C. Sandset MD, PhD and Karianne Larsen, MD and the re-

search is performed in collaboration with Department of Neurology, Oslo University and Oslo Metropolitan University. NAAF is the program funder and the preliminary budget for 2023 is 1.5 mill USD. Currently, the program has 4 PhD candidates.

Several prehospital projects are planned for the coming years with the aim to

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New Mobile Stroke Concept Planned for Oslo

Continued from *Larsen et al*, p. 7

organize prehospital research and development in acute brain disease and brain trauma. The main project will be the new OsloMSU study.

OsloMSU study

Based on TreatNASPP study results and future perspectives for implementation of prehospital stroke diagnostics in the Norwegian EMS, we are planning a new MSU version with the newest technology. A technical evaluation was done of both the MSU vehicle and the CereTom CT scanner used in the NASPP studies. The vehicle is 10 years old, which is beyond the normal lifetime of an operative ambulance, and it was concluded that if the MSU was to be implemented and fully operative, a new vehicle was needed. The CereTom had technical defects with a broken x-ray tube and generator, and it is reaching “end of life” in 2023 which means no guarantee for spare parts and no available service agreement.

Considering this, the best alternative was to replace the old scanner with a new one. We therefore plan for a new MSU study in the Oslo-area with a new vehicle and CT scanner. The coming year will be used to develop and build the new MSU in close collaboration with the hospital and involved departments. Geospatial analysis will prepare the optimal location for the MSU in the Oslo area, and this will also be explored for other regions. The aim is that the MSU gradually will be implemented as an operative part of the health care system including governmental funding and reimbursement. The MSU will have the same setup as validated in the NASPP studies and the objective is that the MSU will be integrated in the physician-staffed EMS in a 24-hour operative service.

Using the existing prehospital system and staffing allows the MSU to dispatch to other emergency medical and trau-

matic conditions in addition to stroke.

The study will explore prehospital communication, standardized clinical assessment including prehospital NIHSS, use of CT angiography, treatment with Tenecteplase, acute prehospital treatment of cerebral hemorrhages, pre-hospital triage of large vessel occlusions and hemorrhages, and treatment and triage of head trauma. A new cost-effectiveness analyses incorporating these new aspects of MSU care will also be performed.

Exploring the differential diagnostic potential of microRNAs

Plasma from TreatNASPP patients have been analyzed using next generation sequencing (NGS) to identify microRNAs with differential diagnostic potential. We will test different machine learning methods to identify microRNA candidates and thereafter validate these microRNAs in a large population of suspected stroke patients, recruited in Denmark. The study will explore if a “fingerprint” of microRNAs can rule out hemorrhages or holds the potential to differentiate between stroke and mimic which is another very important aspect of prehospital stroke identification.

Implementation of NIHSS in the EMS

In 2023 it is planned to implement NIHSS in the EMS in Oslo University Hospital in southeastern Norway and Nordland Hospital in north of Norway, following the ParaNASPP model. The aim is to develop a digital platform integrated in the hospital’s IT system for using the ParaNASPP educational platform and system for seamless transfer of prehospital data to the hospital’s journal system (DIPS). In addition, info registered in the ParaNASPP application will be stored in a local quality registry. We believe that introducing NIHSS in the EMS will improve prehospital stroke assessment, improve the communication between pre- and in-hospital

personnel as it creates a “common language” along the stroke care chain.

Training in a virtual reality

The next step for GameStroke and gamification of stroke simulation training will involve virtual reality (VR). VR allows for realistic and accurate simulation training within a controlled environment. Many remote learners can train simultaneously over various locations where exercises can be repeated numerous times to quickly improve skills at reduced costs. Gamification can be helpful in the training of all personnel handling acute stroke patients, but it is also relevant in educational settings for other health personnel.

Prehospital mobile CT

NAAF is planning stroke-related research projects in the research helicopter together with development of new and optimized interior layout of medical and technical devices, and we are interested in collaboration with other stroke research groups regarding this. The research helicopter is a unique laboratory for research and development and the first studies will explore in which scenarios AirMSUs will save time to diagnostics and treatment and testing the feasibility of using new diagnostic devices in the helicopter. The studies will not involve patients as the research helicopter is not operative.

Karianne Larsen, MD, is a specialist in neurology and PhD scholar at the Department of Research and Development, Norwegian Air Ambulance Foundation and the Institute of Basic Medical Sciences, University of Oslo. Else C. Sandset MD, PhD is senior consultant and senior researcher at the Department of Neurology, Oslo University Hospital, and Department for Research and Development, Norwegian Air Ambulance Foundation. Maren R. Hov, MD, PhD, is associate professor in the training programme for paramedics at Oslo Metropolitan University, doctor and senior researcher at the Department of Neurology, Oslo University Hospital and Department of Research and Development, Norwegian Air Ambulance Foundation.

Nanotube CT Scanning, Robotic Assisted Ultrasound Tested in MSUs

Continued from *Audebert*, p. 1

working on this challenge in different healthcare systems.

At the same time, we see an increased awareness in our stroke community that the prehospital time window is most promising for any therapeutic interventions, not only in ischemic but also in hemorrhagic stroke. As a consequence, several MSU groups in the U.S. and Europe are participating in the FASTEST trial investigating the effects of Factor VIIa on clinical outcomes in acute intracerebral hemorrhage.⁶

We all share the vision that specific stroke treatment should ideally be offered to all acute stroke patients already before hospital arrival. Over the last years, several approaches have been pushed forward in order to make this vision real. It starts with biomarker research, includes new nanotube CT scanner technologies and is the driver of new technological advances like microwave or robotic assisted ultrasound applications. If one of these approaches or a combination of new technologies proves to reliably differentiate ischemic and hemorrhagic stroke at the scene, adds exclusion of stroke mimics and identification of large vessel occlusions, this will really change

the field of acute stroke management and improve outcomes of millions of stroke patients. As all these innovations have to be tested against the Gold Standard - hence CT-based diagnosis and treatment during prehospital management - MSUs will be indispensable for many years even if we can finally switch to smaller, lighter and less expensive diagnostics.

For now, we should exploit the exciting

opportunities to move the field forward by joining our forces in prehospital stroke research. I would like to encourage all PRESTO groups to participate in multicenter studies as this will dramatically increase the speed and power of prehospital science in acute stroke.

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

References

1. Larsen K, Jaeger HS, Tveit LH, Hov MR, Thorsen K, Roislien J, Solyga V, Lund CG, Bache KG. Ultraearly thrombolysis by an anesthesiologist in a mobile stroke unit: A prospective, controlled intervention study. *Eur J Neurol*. 2021;28:2488-2496. doi: 10.1111/ene.14877
 2. Ebinger M, Siegerink B, Kunz A, Wendt M, Weber JE, Schwabauer E, Geisler F, Freitag E, Lange J, Behrens J, et al. Association Between Dispatch of Mobile Stroke Units and Functional Outcomes Among Patients With Acute Ischemic Stroke in Berlin. *JAMA*. 2021;325:454-466. doi: 10.1001/jama.2020.26345
 3. Grotta J, Parker S, Bowry R, Gonzales NR, Alexandrov A, Navi B, al. e. BEST-MSU Study- Benefits of Stroke Treatment Delivered by a Mobile Stroke Unit Compared to Standard Management by Emergency Medical Services. https://professional.heart.org/-/media/phd-files/meetings/isc/2021/science-news/isc21_best_msu_summary_slide.pdf?la=en. 2021. Accessed 30.04.2021.
 4. Turc G, Hadziahmetovic M, Walter S, Churilov L, Larsen K, Grotta JC, Yamal JM, Bowry R, Katsanos AH, Zhao H, et al. Comparison of Mobile Stroke Unit With Usual Care for Acute Ischemic Stroke Management: A Systematic Review and Meta-analysis. *JAMA Neurol*. 2022. doi: 10.1001/jamaneurol.2021.5321
 5. Walter S, Audebert HJ, Katsanos AH, Larsen K, Sacco S, Steiner T, Turc G, Tsivgoulis G. European Stroke Organisation (ESO) guidelines on mobile stroke units for prehospital stroke management. *Eur Stroke J*. 2022;7:XXVII-LIX. doi: 10.1177/23969873221079413
 6. Naidech AM, Grotta J, Elm J, Janis S, Dowlatshahi D, Toyoda K, Steiner T, Mayer SA, Khanolkar P, Denlinger J, et al. Recombinant factor VIIa for hemorrhagic stroke treatment at earliest possible time (FASTEST): Protocol for a phase III, double-blind, randomized, placebo-controlled trial. *Int J Stroke*. 2022;17:806-809. doi: 10.1177/17474930211042700
- Functional Outcomes among Patients with Acute Ischemic Stroke in Berlin. *JAMA*. 2021.

Researchers Envision TASTE-A Phase III Trial

Continued from *Parsons et al*, p. 1

on the MSU. The TASTE-A team suggest that that we should now undertake a multi-centre phase 3 Randomised Controlled Trial of Tenecteplase vs Alteplase on multiple MSUs with 3 month disability (modified Rankin Score) as the primary outcome. Given there was a 10% increase in mRS 0-2 with Tenecteplase we would estimate a sample size of around 700 patients. Given we enrolled 100 patients in a year, we could easily knock over the study

with 10 MSUs worldwide in one year! Importantly, we can secure clinical trial stock that may be a bonus during the global shortage of Tenecteplase. Are you with us? Let's do this together!

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i Andrew Bivard, Henry Zhao, Leonid Churilov, Bruce Campbell, Skye Coote, Nawaf Yassi, Bernard Yan, Michael Valente, Angelos Sharobeam, Anna H Balabanski, Angela Dos Santos, Jo Lyn Ng, Vignan Yogendrakumar, Felix Ng, Francesca Langenberg, Damien Easton, Alex Warwick, Elizabeth Mackey, Amy MacDonald, Gagan Sharma, Michael Stephenson, Professor Karen Smith, David Anderson, Philip Choi, Vincent Thijs, Henry Ma, Geoffrey C Cloud, Tissa Wijeratne, Liudmyla Olenko, Dominic Italiano, Stephen M. Davis, Geoffrey A. Donnan, and Mark W. Parsons, on behalf of the TASTE-A collaborators Comparison of tenecteplase versus alteplase for the early treatment of ischaemic stroke in the Melbourne Mobile Stroke Unit (TASTE-A): a phase 2, randomised, open-label, superiority trial. *The Lancet Neurology* 2022 Jun;21(6):520-527.

ii Mark Parsons, Leonid Churilov, Aletta E Schutte and Christopher Levi. Tenecteplase (and common sense) in short supply during the COVID-19 pandemic. *Med J Aust* 2020; 213 (10): 442-443