Issue 42 Nov - Dec 2020

A Newsletter For The Research Community In Singapore

National Healthcare Group

Adding years of healthy life

e-catalyst

ACCELERATING **RESEARCH**

SPECIAL FEATURE: *INNOVATION PROJECTS*

This series of special edition articles shifts the Innovation & Research Corridor to an online experience, allowing e-Catalyst readers to still be updated on some of the projects that would have been exhibited as part of the IRC 2020 had SHBC 2020 gone ahead as planned.

Calf Circumference as a Case-Finding Tool for Sarcopenia

Click **here** to view more

NTU Singapore Researchers Speed Up Gold-Standard COVID-19 Diagnostic Test

Click **here** to view more

Outcomes of the NMRC November 2019 Call for Applications

Congratulations to the NHG clinicans who have received the National Medical Research Council (NMRC) Talent Development Awards and Research Grants during the November 2019 NMRC calls for applications.

Name	Institution	Project Title	Award
Dr Joseph Lo Zhiwen	TTSH	Evaluating and Decreasing the Socio-Economical Burden of Wound Care in Singapore through Health Systems Innovations and Health Literacy	Research Training Fellowship (RTF)
Asst Prof Yew Yik Weng	NSC	Investigating the effect of adiposity on skin barrier function in a general population cohort	Transition Award (TA)
Assoc Prof Rupesh Agrawal	TTSH	To establish a predictive artificial intelligence (AI) based model using immune-phenotype correlation for disease stratification and prognosis in patients with ocular tuberculosis (OTB)	Clinician Scientist Award - Investigator (CSA-INV)
Dr Kalisvar Marimuthu	NCID / TTSH	Oral capsule-administered faecal microbiota transplantation for intestinal carbapenemase-producing Enterobacteriaceae decolonisation	Clinician Scientist/ Clinician Investigator Salary Support Programme (CS/CISSP)
Dr Kalisvar Marimuthu	NCID / TTSH	Household transmission of carbapenemase-producing Enterobacteriaceae Singapore: A cohort study	Clinician Scientist/ Clinician Investigator Salary Support Programme (CS/CISSP)
Dr Sapna Sadarangani	NCID / TTSH	Probing the Immunometabolic Factors of Influenza Vaccine Immune Response in Singapore Elderly	Clinician Scientist/ Clinician Investigator Salary Support Programme (CS/CISSP)
Assoc Prof David Lye	NCID / TTSH	A Randomised Controlled Trial Evaluating a Novel Individualised Treatment Strategy for Carbapenem-Resistant Gram-Negative	Clinician Scientist/ Clinician Investigator Salary Support Programme (CS/CISSP)
Dr Allen Liu Yan Lun	KTPH	Novel genetic and non-genetic risk factors for endothelial dysfunction and diabetic micro-angiopathies - meeting future challenges	Clinician Scientist/ Clinician Investigator Salary Support Programme (CS/CISSP)

To find out more about the NMRC Talent Development Awards and Research Grants, please click *here*.

GOOD TO READ!

NTU Singapore Researchers Speed Up Gold-Standard COVID-19 Diagnostic Test

Clinician-scientists at Nanyang Technological University, Singapore's (NTU Singapore) Lee Kong Chian School of Medicine (LKCMedicine) have demonstrated a way to improve the speed, handling time and cost of COVID-19 laboratory tests. The improved testing method yields results in 36 minutes – a quarter of the time required by existing gold-standard tests.

Their new approach could enable the wider adoption of COVID-19 testing for diagnosis in academic or research laboratories, and allow for screening and research, especially in countries and regions with limited laboratory capabilities. The test, which can be done with portable equipment, could also be deployed in the community as a screening tool.

Click *here* to read more.

A Neuroscience Approach To Understanding Response To Cognitive Treatments

Cognitive impairments are found in many psychiatric disorders. When patients have problems paying attention, processing information and remembering, they cannot carry out daily activities, or go back to school or work. They fail to remember or understand why they have to take medications or undergo psychosocial rehabilitation.

No drug has yet to satisfactorily treat cognitive impairment in psychosis. **Cognitive remediation (CR) is a behavioural training-based intervention with modest effects in improving global cognitive deficits.**

Like all clinical interventions, response to CR treatment will be most robust if it can be personalised to each individual. **This preliminary study sought to find out whether CR response can be detected using non-invasive measures of DNA patterns and brain activity.**

Scrapings from insides of the cheeks were used to sample for DNA methylation patterns, specifically that of Reelin, a gene responsible for neuroplasticity.

Brain activity was collected while at-rest i.e. lying quietly for 8 minutes in an MRI scanner. After that, measures of functional connectivity (how synchronised one region of the brain is to another) and global efficiency (how integrated information transfer is across the circuitries in the brain) were calculated (Figure 1).

The study team examined the measures in patient volunteers with schizophrenia before and after they participated in an intensive 32 session personalised CR programme called NEAR (Medalia, 2017) over 5-7 weeks that targeted a range of higher cognitive skills using restorative and compensatory techniques. They were compared with schizophrenia patients who chose not to participate in CR, and healthy volunteers over the same time period.

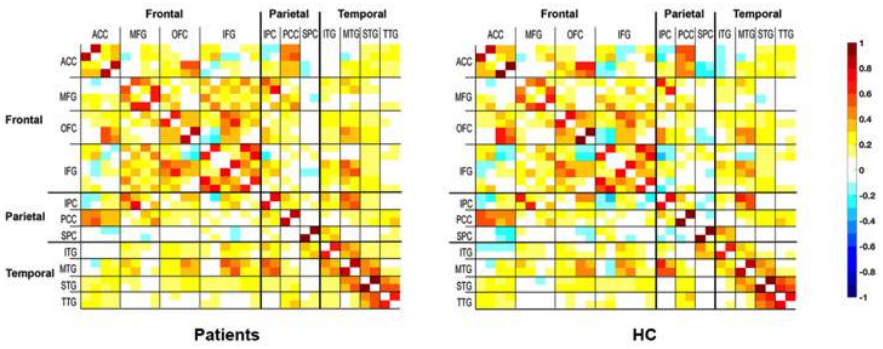


Figure 1: Brain functional connectivity in patients and healthy controls are different

Abnormal functional connectivity between the frontal and temporal parts of the brain were found in patients with schizophrenia, before CR (Figure 2). **CR led to changes in Reelin methylation patterns. CR also led to modified within-frontal and frontal-temporal connectivity, and increased global efficiency of the brain in schizophrenia, which were associated with improvements in their cognitive performance.** The study team was the first to report concomitant modifications across the spectrum of molecular to behavioural manifestations — epigenetic modification, brain connectivity reconfiguration and network efficiency and amelioration of cognitive deficits. **Findings from this proof-of-concept study suggest that a neuroscience-informed approach to measuring outcomes from behavioural-training interventions is possible.** Future larger randomised controlled trials can build on findings of this study to ask more questions e.g. are the neuroplastic effects through CR durable? Besides schizophrenia, are they generalisable across our local patient community?

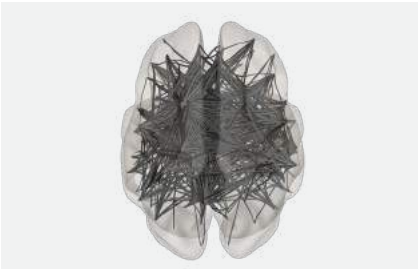


Figure 2: Patterns of functional connectivity in a representative brain

This study included researchers and clinicians from various institutes such as IMH, NUS, Duke-NUS, NTU and Columbia University and was made possible with funding from the NHG Small Innovative Grant SIG/15014.

Please click here to read the full publication.

Contributed by:
Dr Ho New Fei (First Author)
Former Research Fellow
IMH

Adj. A/Prof Sim Kang
Senior Consultant, West Region
IMH

Calf Circumference as a Case-Finding Tool for Sarcopenia

Sarcopenia refers to the age-related loss of skeletal muscle mass plus loss of muscle strength and/or reduced physical performance. It is associated with adverse health outcomes including frailty, disability, falls, hospitalisation and even mortality.

The 2019 Asian Working Group for Sarcopenia (AWGS) consensus update aims to promote greater integration of sarcopenia in clinical practice through efficient community case finding. One of the recommended screening tools is calf circumference (CC). Earlier Asian studies did not compare CC with other validated tools such as the SARC-F, nor examine the influence of body composition phenotypes such as Sarcopenia Obesity (SO), where CC may not reflect muscle mass, due to fat infiltration in calf muscle. We thus aimed to compare the diagnostic performance of CC with SARC-F for sarcopenia diagnosis in SO and sarcopenic non-obesity (S-NO).

We studied 230 community-dwelling older adults recruited in the Longitudinal Assessment

of Biomarkers for Characterisation of early Sarcopenia and Osteosarcopenic Obesity (GeriLABS2). Sixty-two (27%) participants (28 SO and 34 S-NO) fulfilled AWGS 2019 criteria for sarcopenia. **CC had superior diagnostic performance [AUC (95% CI): 0.735 (0.663 – 0.806) vs. 0.571 (0.486 – 0.656), P<0.01] and sensitivity (64.5% vs. 43.5%) than SARC-F for sarcopenia diagnosis, particularly in the S-NO subgroup [AUC (95% CI): 0.799 (0.716 – 0.881) vs. 0.539 (0.432 – 0.645), P<0.001; Sensitivity: 58.8% vs. 38.2%].**

However, the diagnostic performance of CC was attenuated in SO due to decreased sensitivity with under-detection in female participants. The cost of missing a diagnosis of SO is arguably higher in older women, as SO is more prevalent due to female predisposition for abdominal adiposity in middle to late age.

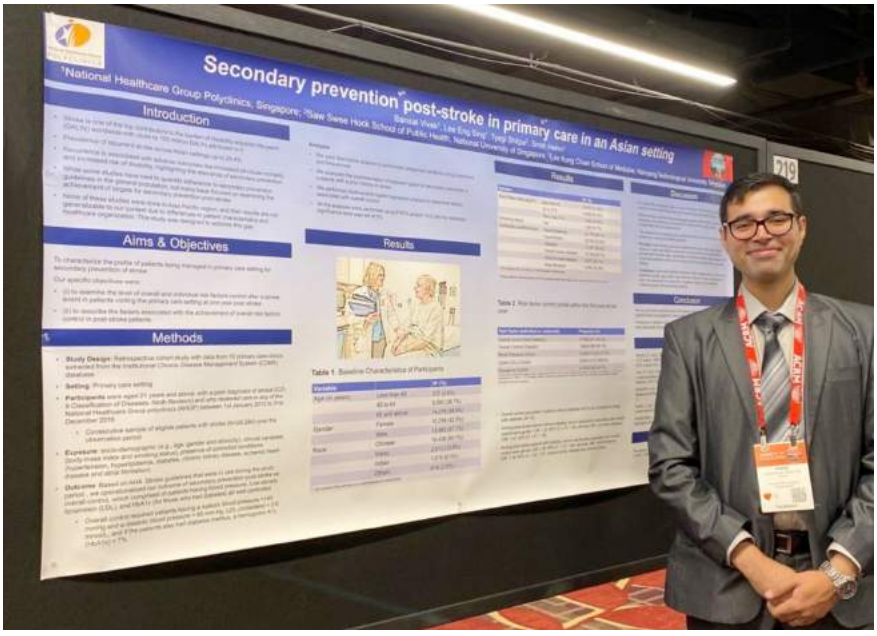
In summary, **the diagnostic performance of CC is influenced by body composition phenotypes, being worse in SO compared with S-NO**. Taken together, although AWGS 2019 represents a step forward through the inclusion of CC, the influence of obesity on diagnostic performance of CC for the detection of sarcopenia merits further study.

Contributed by:
Ms Audrey Yeo
Research Executive
Institute of Geriatrics and Active Ageing (IGA)
TTSH

Research in Primary Care

After completing my residency in Family Medicine, I got to know of the NHG-LKCMedicine Clinician-Scientist Preparatory Programme (CSPP) while undergoing further training in the Fellowship in the College of Family Medicine Course (FCFP). As a firm believer of lifelong learning, pursuing FCFP and CSPP in tandem helped me find synergies across both endeavours. **The CSPP, in particular, has been a great opportunity for me to gain hands-on research experience.**

Considering the significant burden of stroke on our healthcare system, we conceptualised our research project around secondary prevention post-stroke. **Our study aimed to quantify the overall control of risk factors post-stroke, describe the profile of patients managed in primary care setting for secondary prevention post-stroke, and to describe the factors associated with the achievement of overall control in post-stroke patients.**



I believe in the core principles of conducting research with responsibility, accuracy and translatability. Responsibility relates to differentiating good, bad and unnecessary research along with avoiding practices like data dredging. Accuracy aligns with keeping our research skills current and relevant. **During the CSPP program, I had the opportunity to attend various courses, which not only helped me with my research project, but also helped me appreciate different study designs and critically evaluate medical literature.** Finally, translatability implies incorporating our research findings into clinical practice, which can be facilitated by the use of local population data. Based on my experience, I feel that while coming up with a good research question and equally strong methodology is no easy feat, focusing on these increases the integrity and quality of our work which is more important than chasing a publication.

My hope after completing CSPP is to translate the skills learnt into answering questions that arise in my clinic/work settings and be able to juggle my duties as a clinician, educator and researcher, finding synergies across these roles.

Dr Vivek Bansal is an FY2018 awardee of NHG-LKCMedicine CSPP. Click here to find out more about the programme.

Contributed by:
Dr Vivek Bansal
Family Physician - Associate Consultant
Woodlands Polyclinic
NHGP

The Innovation and Research Corridor (IRC) is part of the Singapore Health & Biomedical Congress (SHBC), the largest annual medical congress in Singapore which attracts an average of 3000-4000 delegates a year. The IRC showcases some of the exciting new technologies and innovations that clinician innovators and clinician scientists/researchers from the National Healthcare Group have developed. This series of special edition articles shifts the IRC to an online experience, allowing e-Catalyst readers to still be updated on some of the projects that would have been exhibited as part of the IRC 2020 had SHBC 2020 gone ahead as planned.

Rapid Development of the Face Shield

Problems/Challenges

Donning personal protective equipment (PPE) conscientiously minimises the risk of infection to healthcare workers (HCWs). However, the prolonged use of goggles (a PPE for the eyes) can cause pain and discomfort to the wearer. The lenses also tend to fog up, obstructing the wearer's vision and sometimes resulting in giddiness. Due to the discomfort, HCWs may adjust the goggles, exposing themselves to the risk of contamination with bodily fluids and other potentially infectious materials.

Visor masks offer a more comfortable alternative. However concerns have emerged that its stock level might be insufficient to fulfil demand timely during a crisis (such as the COVID-19 outbreak), due to global supply-chain disruptions. This situation presented an opportunity to swiftly design and develop a face shield for HCWs. The prototype should provide robust protection with better fit and comfort. For ease of use and viability, it should also be disposable and low-cost.

Findings/Solutions

Within a three-week period from 1 February 2020, an interdisciplinary team – comprising a design team from Centre for Healthcare Innovation (CHI), along with Infectious Disease physicians and Infection Control nurses from National Centre for Infectious Diseases (NCID) and Tan Tock Seng Hospital (TTSH) – collectively developed and tested the product. They did this through a user-centric process, adapted from the United Kingdom Design Council's "Double Diamond" design approach, which employs divergent and convergent thinking over four phases – "Discover", "Define", "Develop" and "Deliver".

The team conceptualised, produced and iteratively refined 10 prototypes, through close engagement with clinical end users. Two of these prototypes – the "Disposable Face Shield" (Design 1) and "Spectacle Face Shield" (Design 2) – were piloted with staff at inpatient wards and NCID Screening Centre, as they met the criteria of desirability (met users' needs), feasibility, viability and sustainability. From the responses of these staff (n=75), 78.5% rated "likely" and "very likely" to recommend these two prototypes to their colleagues using the Net Promoter Score. Some staff commented that light reflection and refraction obstructed their vision. The nature and duration of tasks, along with environmental factors (such as lighting), were identified as key influencers. Measures were then taken to mitigate the effects of light reflection and refraction.

Disposed after attending to each patient, Design 1 is deemed more suitable for HCWs performing routine clinical care in inpatient settings. Design 2 is more suited for HCWs in ambulatory settings, e.g. NCID Screening Centre, where extended use of the face shield is desired.

Current Status/Future Plans

User feedback from the pilot has indicated that both designs are comparable to commercially available goggles and visor masks for splash protection. Furthermore they provide greater comfort and better fit. Based on users' feedback and preferences, alongside consideration of usage needs, both designs have been sent for production and use within defined areas in TTSH and NCID. The designs have been patented and are in the midst of being commercialised.

Contributed by:
Mr Tan Ghim Meng (TTSH) and
Mr Chua Jia Xiang TTSH

Study team
Mr Chua Jia Xiang (TTSH),
Ms Lynette Ong (TTSH),
Mr Thian Kun Ming (TTSH),
Mr Chung Kai Siang (TTSH),
Mr Wilson Chin (TTSH),
Adj. Assoc Prof Shawn Vasoo (NCID/TTSH),
Adj Assoc Prof Brenda Ang (NCID/TTSH) and
DDN Poh Bee Fong (TTSH)

The Prototypes Selected for Pilot and Internal Use

Development of a Transparent Medical Mask to Enhance (Healthcare Worker) HCW–Patient Communication

Problems/Challenges

Verbal communication is a complex cognitive function that goes beyond just hearing. The cognitive encoding of auditory signals is greatly enhanced by non-auditory cues which includes posture, limb gesturing, facial expression, and lip movements. Being able to see a speaker's face aids speech understanding, especially for communication vulnerable persons like those with hearing loss or language difficulties. Studies have found that the contribution of face and lip reading towards speech understanding is proportional to the degree of hearing loss, though persons with normal hearing also benefitted, especially where there is significant background noise.

The COVID-19 `new normal' currently mandates face masks be worn by healthcare workers (HCWs) and patients in all healthcare and community settings in many countries including Singapore. Inadvertently, the mask covers the lower half of the face, obscuring visual cues from lip movements and facial expressions. These masks can also attenuate the level of speech output and negatively impact speech understanding, particularly in noisy healthcare environments like clinic counters, the pharmacy, and in the Intensive Care Unit. In the community, noise levels may be even higher, especially in environments like hawker centres and markets.

Additionally, reduced facial visibility may compromise conveyance of emotions like concern, kindness and empathy, affecting the quality of therapeutic relationships HCWs can build with our patients.

Findings/Solutions

Notably, our survey of both staff and patients had both groups reporting that mandatory face mask-wearing compromised communication, understanding and emotional aspects of patient-HCW relationships. Many HCWs found it especially difficult to communicate effectively with communication vulnerable patients, who typically benefitted from visual cues or lip reading.

To overcome this issue, there needs to be a paradigm shift to disposable medical masks that feature a "transparent" window to allow clear visualisation of the mouth while maintaining existing Health Sciences Authority (HSA) safety standards. It is vital that this redesigned mask provide adequate respiratory protection against droplets, maintain bacterial filtration efficiency of ≥ 95% and fulfil all other safety and performance requirements. Importantly, the clear window must be fog-resistant whilst maintaining breathability.

Current Status/Future Plans

In collaboration with our engineering collaborator, RacerTech, we have already gone through multiple iterations of early prototypes. A Human Factor Engineering process will be incorporated to ensure that this mask meets end user needs i.e. be comfortable, durable, and acceptable. We have recently been awarded the Ng Teng Fong Innovation Grant to support this R&D process with the end point being a commercialisable, HSA-certified disposable medical mask that can be a viable alternative to the current default medical mask.

Concurrent collaborative efforts will be made to develop a reusable version for community use. We will also explore a version with clear window magnification as a novel countermeasure to enhance lip visibility whilst complying with safe distancing requirements. This enhanced visibility version will further aid communications, for e.g. for speech rehabilitation sessions, auditory-visual therapies, voice trainings, and communications with deaf persons. The recent inventions of high performance `transparent' filter fabrics hold exciting possibilities for a fully transparent mask in future.

Contributed by:
Principal Investigators
Dr Ho Eu Chin (TTSH),
Dr William Go Teck Wah (TTSH),
Ms Florence Tang Mei Ai (TTSH),
Dr Brenda Ang (NCID/TTSH) and
Ms Poh Bee Fong (TTSH)

Formulation of a Safe and Economical Ceramide Moisturiser for Dermatological Patients in Public Healthcare Institutions

Problems/Challenges

There are currently no safe and economical ceramide moisturisers appropriate for dermatological patients in public healthcare institutions in Singapore. Ideally, moisturisers meant for dermatological patients in public healthcare institutions should possess these features:

a) Effective ingredients, including to contain sufficient concentration of ceramides
b) Safe for patients with skin barrier defects
c) Economical

a) Effective ingredients

Ceramides have been shown to be essential for skin barrier function. However, the 'ceramide' moisturisers in the market generally contain very low to negligible amounts and variety of ceramides. Many other marketed 'ceramide moisturisers' contain pseudo-ceramides rather than true ceramides. These moisturisers are typically priced highly, leveraging on their 'ceramide' property.

In addition, a healthy skin surface pH is known to be essential for the physiological functions of the epidermis. However, the pH of most of the available moisturisers is not known.

b) Safety

Currently in the market, moisturisers, even those specifically marketed for sensitive skin, tend to have features that are not optimal for patients with skin barrier dysfunction. Atopic dermatitis (AD) is the most common cause of skin barrier dysfunction and its prevalence in Singapore's population is 10-20%. The moisturisers in the market often:

- Contain ingredients not suitable for sensitive skin. Our survey of the commonly-used moisturisers currently available in the market revealed that most contained prominent allergens, such as parabens, Methylisothiazolinone/Methylchloroisothiazolinone (MI/MCI), and Benzyl alcohol.
- Have a pH much higher than that of healthy skin, which is not suitable for sensitive skin, or do not state their pH, leaving a doubt as to suitability for eczema skin.

Multiple studies have shown that AD patients have higher prevalence of contact sensitization compared to healthy people with normal skin barriers.[1,2] In a systematic review and meta-analysis we have conducted (yet-to-be published data), we identified the 10 most common allergens in moisturisers, cleansers and topical medicaments used by individuals with AD and found that individuals with AD have increased risk of contact sensitisation to two of these allergens, namely MCI/MI and myroxylon pereirae (Balsam of Peru). Our recommendation is for individuals with AD to avoid these allergens; however, these ingredients are ubiquitous in many of the products in the market. In addition to contact dermatitis, there are concerns of systematic contact dermatitis subsequent to frequent exposure to these sensitisers.[3] In this phenomenon, individuals who were previously sensitised to these allergens through application subsequently develop generalised rashes after ingesting food containing these allergens.

During this Covid-19 pandemic, another problem that surfaced in an epidemic proportion is hand eczema. Frequent handwashing and use of hand sanitisers have resulted in skin dryness and hand dermatitis in the general population, especially amongst healthcare workers.[4] The increased frequency of handwashing (>10 times daily) has been found to increase the risk of hand skin damage by at least two-fold[4]. Frequent use of a safe moisturiser is required to repair the damaged skin and to avoid risk of contact dermatitis through the defective skin barrier.

Doctors find it difficult to recommend safe and effective moisturisers for their patients to use on a daily basis, as many patients have previously been sensitised to certain ingredients that are commonly found in existing products. We therefore decided to formulate our own products that are safe and appropriate for our dermatological patients.

c) Economical

The currently-available ceramide-containing moisturisers in the market are generally too pricy for patients in our public healthcare system. The higher prices also discourage patients from frequently applying moisturisers, which result in suboptimal control of their skin condition.

Solutions

To address the problems delineated above, we formulated a moisturiser with the following features:

a) Containing effective ingredients
- High concentration and a range of ceramides
- Filaggrin breakdown product (sodium pyrrolidone carboxylic acid), which acts as a natural moisturising factor
- Having pH 5.5 that matches that of healthy skin

b) Safe
- Devoid of common allergens and irritants, including being 'preservative-free', 'fragrance-free' and 'colouring-free'

c) Economical
- We aim to make quality products affordable and within reach of patients who are not well-off. Cost savings can be achieved through sourcing of economical ingredients, simplification of design, and omission of marketing.

Current Status

The formulation has passed the laboratory stability test, and the shelf-life of the product is 3 years.

NSC has exclusively licenced the formulation to Good Pharmaceuticals Pte Ltd., which has an established distribution network and a good track for commercialisation. The product is expected to be available to NSC patients by early 2021.

Future Plans

The product will further undergo the following tests:

(1) Irritancy tests in sensitive skin human subjects
  a. Testing on intact skin
    i. 21-day continuous repetitive patch test
  b. Testing on comprised skin
    i. 48-hour patch test after removal of stratum corneum using a needle
    ii. 48-hour patch test after applying 3% sodium lauryl sulfate to reduce skin barrier function

(2) Hypoallergenicity tests in sensitive individuals
  - Performing patch tests repetitively for three times, after a period of sensitisation

Contributed by:
Principal Investigator
Asst. Prof Tey Hong Liang
Head of Research Division and
Senior Consultant, NSC
Adj. Assoc Prof,
LKCMedicine
Adj. Assoc Prof,
Yong Loo Lim School of Medicine, NUS

Study team
Dr John O'Shea
(Co-founder, Good Pharm Dermatogy Pte. Ltd)

References

1. Skin absorption through atopic dermatitis skin: a systematic review. Br J Dermatol. 2017 Jul;177(1):84-106.
2. Both children and adult patients with difficult-to-treat atopic dermatitis have high prevalences of concomitant allergic contact dermatitis and are frequently polysensitized. J Eur Acad Dermatol Venereol. 2018 Sep;32(9):1554-1561.
3. Allergic and systemic contact dermatitis to methylparaben. Contact Dermatitis. 2006 Feb;54(2):117-8.
4. Lan J, Song Z, Miao X, et al. Skin damage among health care workers managing coronavirus disease-2019. J Am Acad Dermatol. 2020;82:1215-1216.

AI System Enables Early Flag-Up of Abnormal Chest X-Rays with Sharp Accuracy for COVID-19 Screening in Singapore

Problems/Challenges

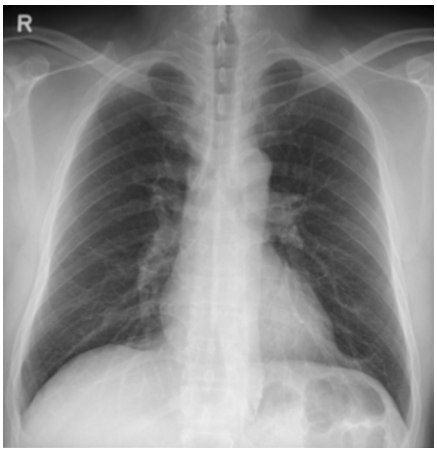
An artificial intelligence (AI) powered diagnostic tool has been developed to allow for rapid flag-up of abnormal chest X-ray findings in individuals being tested for COVID-19 at the National Centre for Infectious Diseases (NCID) Screening Centre, so that appropriate care can begin sooner and more accurately for those patients with pneumonia.

The AI system, named *RadiLogic*, uses a machine (deep) learning technology that has been programmed to classify images of normal and abnormal chest X-rays, specifically, those that show signs of pneumonia, in a patient. Pneumonia on chest X-rays has been classified as one of the admission criteria for suspected COVID-19 at NCID. The research team in TTSH and NCID has shown that more severe findings on chest X-rays correlate with an increased need for supplemental oxygen therapy and mechanical ventilation in ICU.

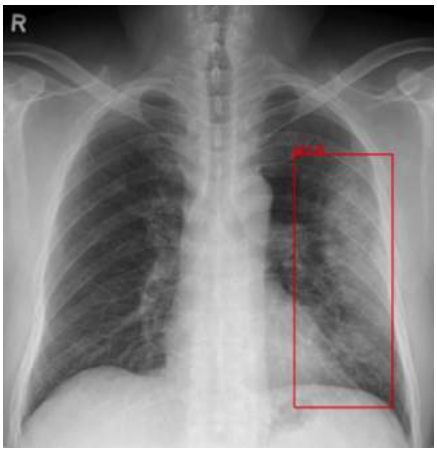
This system will be most useful in times of a surge in number of people reporting to the NCID Screening Centre for testing. NCID itself sees about 60 to 70% of hospitalisations for COVID-19 patients in Singapore and to date, everyone at NCID Screening Centre who undergoes a chest X-ray will have that reviewed by a radiologist, typically within an hour.

Previously, radiologists had to read each radiograph in order of their occurrence in time. With this AI technology, the system is now able to automatically prioritise and flag-up an abnormal chest X-ray, thus allowing the on-call radiologists to more expediently report such cases. This provides greater confidence to radiologists in analysing chest X-rays. *RadiLogic* is able to provide a result within a few seconds, and flagged onto the system within a minute with a high level of accuracy. This provides our radiologists with the opportunity to enhance their operational efficiency.

During surge circumstances in April, the NCID Screening Centre received an average of 200-300 X-ray images each day. This influx of chest X-rays from the NCID was also a golden opportunity for the research team to develop the database set, as *RadiLogic* is now able to classify abnormal chest X-rays with accuracy of up to 96.1%.



A) Normal chest radiograph with clear lungs



B) Abnormal chest radiograph with haziness in the left lung indicative of pneumonia

The clinical team at Tan Tock Seng Hospital's Department of Diagnostic Radiology put in long hours over two months to painstakingly label suitable X-ray images for the *RadiLogic* database.

One challenge in working with models is that chest x-rays are two-dimensional projections of the three-dimensional lungs, heart and chest anatomy. With limited training samples, especially positive COVID-19 chest x-rays, the developed AI model would need to be sensitive to the changes in pneumonia features.

For this project, the Diagnostic Radiology team at TTSH ensured clinical relevance and reliability of the datasets. Concurrently, Dr Cui's and Dr Huang's teams at IHPC and I²R respectively, ensured the AI models churned out an accurate output while working to ensure that the AI system would work reliably and securely on the hospital's intranet network.

Current Status/Future Plans

This collaboration is the result of an Open Innovation Challenge jointly held by NHG Centre for Medical Technologies and Innovation, Enterprise Singapore and A*STAR's arm for technology translation and commercialisation, A*ccelerate. The team pivoted towards the diagnosis of COVID-19 as a response to the pandemic.

The joint team is seeking to further develop the clinical application as an audit tool, and wider implementation of the AI model through industry partnership.

Contributed by:

Principal Investigators

Assoc Prof Tan Cher Heng (TTSH),
Dr Huang Weimin (A*STAR I²R) and
Dr Cui Yingnan (A*STAR IHPC)

Collaborators

Dr Ting Yonghan (TTSH),
Dr Jordan Sim (MOHH) and
Mr Chen Wen Xiang (TTSH)

Study team

Dr Ting Yonghan (TTSH),
Dr Jordan Sim (MOHH),
Mr Chen Wenxiang (TTSH),
Dr Cui Yingnan (A*STAR IHPC),
Dr Teo Soo Kng (A*STAR IHPC),
Dr Wong Sum Thai (A*STAR IHPC),
Dr Huang Weimin (A*STAR I²R) and
Ms Zhou Nina (A*STAR I²R)

Odourless and Tasteless Thickener for Pureed Food

Problems/Challenges

Improving the quality of life for patients with dysphagia (swallowing impairment) is important. While most commercially available thickeners are used to thicken beverages, there remains a gap in having thickeners that are both effective and affordable in thickening up pureed foods. For inpatient care, these patients are currently served with pureed diets prepared with the addition of thickeners such as corn flour, arrowroot powder, and potato flakes in order to avoid the watery textures that may be unsafe to swallow. While these ingredients may be cost-effective, they often do not provide good taste, texture, mouthfeel and visually appealing meals.

Solutions

KTPH Dietitians were awarded with a $10,700 Rapid Prototyping Grant and teamed up with KTPH Chefs and a Singapore based food technology company, Faesol Pte Ltd, to develop an odourless and tasteless thickener that can be used to thicken pureed food. Apart from intended use in inpatient settings, the thickener will be commercially available for easier home use when the patients are discharged.

KTPH team and Faesol CEO, taken together during the food tasting session. Photo taken in 2019, pre-COVID-19

Pureed food made from KTPH kitchen using the Odourless and Tasteless Food Thickener, iLite Requol™ TS1

By making the thickener easier to use, the carer of patients with dysphagia can essentially puree the same foods they have prepared for the family and thicken accordingly for safe consumption. Thus allowing these patients to better enjoy the pureed food with the rest of the family.

These thickeners will be marketed as iLite Requol™ TS1 (Food thickener). The Requol™ series of products from Faesol aims to help patients to “Regain Quality Of Life”. CEO of Faesol Pte Ltd, Dr Saw Lin Kiat commented that it has been a meaningful experience working with multiple stakeholders of the KTPH team, from dietitians to speech therapists and the Food Services team. He is thankful for the supportive and open nature of the collaboration.

Current Status/Future Plans

KTPH Food Services team is now exploring adopting Requol Food thickener for inpatient use.The Dieticians will also be exploring making this thickener available at KTPH pharmacy for public purchase to help improve and provide a better quality of care at home. Separately, the team is working with Singpoare Institute of Technology (SIT) to develop other thickeners, including thickeners to make the thickened food products moldable, which will also complement the ongoing 3D printed foods research.

Contributed by:
Study Lead – Chow Pek Yee (KTPH)
Study Team Members –
Wong Hooi Chuan Gladys (KTPH),
Ghazali Bin Mohamad (KTPH),
Puah Hong Lam Simon (KTPH) and
Angeline Tan Lay Ting (KTPH)

A Secure Digital Platform for Managing Customised (Including 3D Printed) Medical Parts and Devices

Problems/Challenges

There has been increasing interest in the adoption and application of customised parts in clinical medicine. An area of recent interest arising from both the industry and clinicians is in the application of customised parts through additive manufacturing. There have been positive benefits of additive manufacturing (3D printing) seen in healthcare. However, the whole process beginning from a clinical need, to the design, and then to manufacturing is not clearly developed. Support is needed in terms of standards in file processing, data security, encryption/de-encryption, database management and the handling of end to end integrated workflows to connect Customers, Designers/intellectual property (IP) owners and additive manufacturing companies (AMCs)/Manufacturers on one platform. Typically to make a customised part, clinicians will need to perform 3D scanning of a body part. The image is then passed to the additive manufacturers for processing, which includes refinement and designing before printing. One major challenge in this process is the manual transfer of scanned images while protecting the personal data of patients. There is also a lack of a database library and records of the parts that were previously printed. This database could serve as a good stepping stone to wider adoption of additive manufacturing through suggested parts that clinicians can potentially select and print.

Findings/Solutions

In order to connect and facilitate the manufacturing of customised parts, a platform is essential to close the gap between clinicians and the AMCs.

The platform consists of five key modules:

1. The blockchain-enabled encryption system allows all AM activities to be performed in a secure and traceable environment.
2. Integrated workflow to handle the additive manufacturing process and to track completely from customer order to fulfillment.
3. The marketplace (library/ database) is a catalogue system comprising of parts approved for clinical use and parts used for research only.
4. The quality management system (QMS) comprises modules and systems to document and track processes and procedures for achieving and monitoring of quality policies and objectives.
5. The artificial intelligence module includes an artificial intelligence/ machine learning algorithm installed thereon to provide 'learning capabilities' to various aspects of the platform so that the system can perform learning over time, based on data collected.

Future Plans

Currently the base platform is constructed by Secure3DP+ together with inputs from NHG clinicians. The next phase of the project will be to conduct usability tests on a wider pool of clinicians to provide feedback on the platform. The input will be used to further refine the system in the next phase. The final goal of this platform is to scale up and function as a marketplace for customisation of medical parts and devices, to be widely used by clinicians (in both public and private healthcare systems), as well as a network of validated additive manufacturers.

Contributed by:
Principal Investigators
Mr Khalid Anuar
Head,
Foot Care & Limb Design Centre
(TTSH)

Ms Tabitha Quake
Assistant Head of Prosthetic
& Orthotic Services (TTSH)

Asst Prof Pua Uei
Senior Consultant
Diagnostic Radiography
(TTSH)

Mr Low Eng Kiat (Secure 3DP+),
Mr Kaylan Balasubramanian (Secure 3DP+)

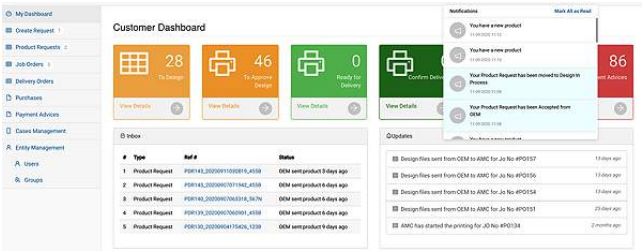


Figure 1: Customer Dashboard

Figure 2: Growing database of objects to be 3D Printed

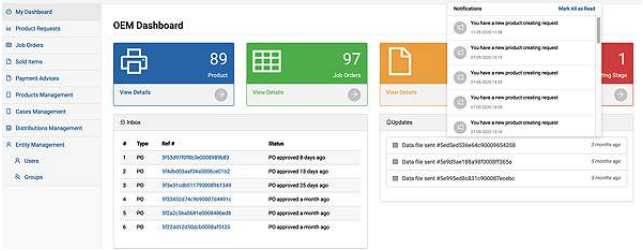


Figure 3: Original Equipment Manufacturer (OEM) Dashboard

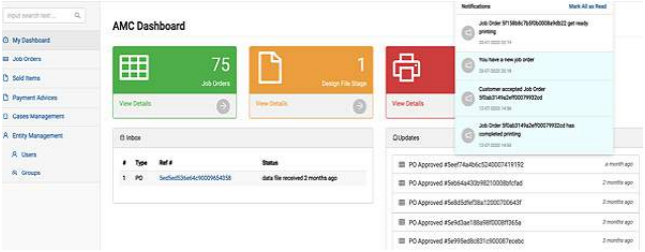


Figure 4: Additive Manufacturing Company (AMC) Dashboard

Clinical Validation and Improvement of WoundAide Imaging System

Problems/Challenges

Wounds present a substantial clinical and economic burden to healthcare systems globally with significant reductions in quality of life for those affected. From 2013 to 2017, there was a 95.1% increase in wound episodes per 1000 inpatient admissions (142/1000 to 277/1000) at Tan Tock Seng Hospital (TTSH), with the average length of stay for each wound episode 2.4 times that of an average acute admission (17.7 days versus 7.4 days) and average gross charge per wound episode at SGD$17,558 in 2017[1]. The ability to characterise and document wounds accurately is crucial and serves as a critical first step in assessing severity, healing potential, determining the optimal treatment and monitoring subsequent clinical progress. Although most wound imaging systems are anecdotally deemed superior to traditional wound assessment measurements, the majority of commercially available wound assessment systems have not been academically reviewed within the literature for measurement accuracy[2]. In 2017, Konica-Minolta collaborated with TTSH to develop a contactless hand-held wound measurement device (WoundAide), which allows clinicians to capture 3-dimensional wound data and use machine learning algorithms to automatically detect and measure wound boundaries. In our current study, we aim to prospectively validate WoundAide measurements against traditional assessments by trained wound nurses on patients with venous leg ulcers (VLU) and improve the WoundAide imaging system via clinical feedback.

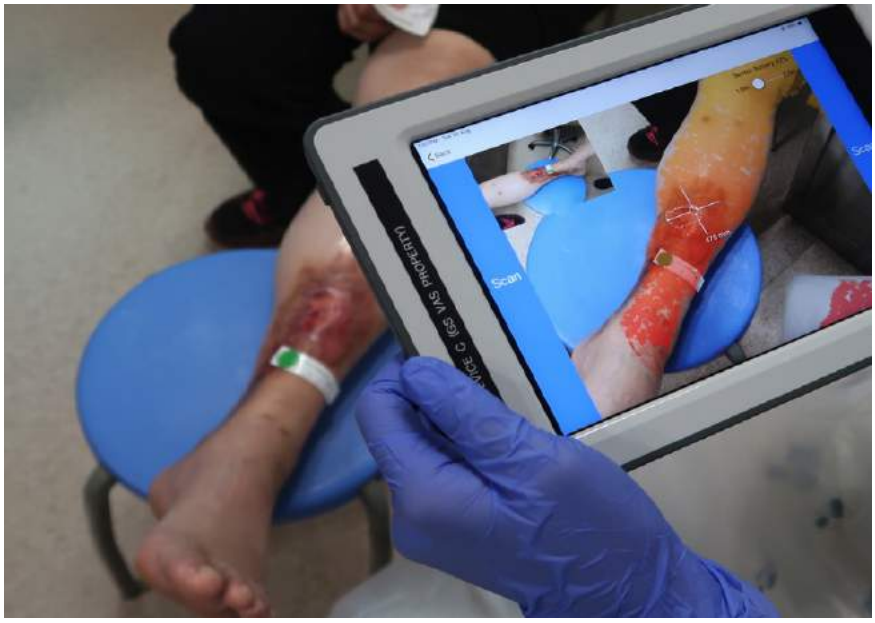
Findings

Based on WoundAide's 2017 pilot analysis of 30 patients and 60 data points, the baseline mean accuracy ranges from 85% to 95%. Based on correlation and reliability statistics (Power 90%, Alpha 0.05), the overall sample size required was 341 wound images. Accounting for average recruitment rates, drop-out and average healing rates, we aim to prospectively study 100 patients over 5 clinic visits (500 wound images expected). Since study commencement in September 2019, a total of 54 subjects have been recruited into the study. For statistical analysis, Pearson's correlation coefficient is being used to evaluate inter-rater reliability between devices and traditional nurse clinician's measurements, while intraclass correlation statistics are being selected to evaluate intra-rater reliability between three separate devices against the same wound.

We present here our interim analysis of 30 patients who had completed the study. There is high intra-rater reliability of each device, with intra-class correlation statistics (ICC) ranging between 0.957-0.991 for breadth, length and area across all three devices ($p<0.001$). There is high inter-rater reliability (ICC ranging 0.953-0.997) across all three devices for breadth, length and area ($p<0.001$). There is also high inter-rater reliability (ICC ranging 0.879-0.924) between each device and measurements taken by trained wound nurses for breadth, length and area ($p<0.001$). To date, a total of 42 clinical feedback points had been provided to aid in the improvement of the WoundAide imaging system.

Future Plans

Interim analysis clinically validates the inter-rater and intra-rater reliability of the WoundAide imaging system across devices and also with measurements taken by trained wound nurses, for patients with VLU. Further clinical feedback will be provided to help improve the user interface and user experience (UI/UX) of the system. WoundAide imaging system is an accurate and useful adjunct in wound care. We aim to complete the study in 2021 and assist in the digitisation of wound imaging, documentation and monitoring within National Healthcare Group, in conjunction with Wounds iCare Collaborative (WiCC) Research and Clinical Workgroup.



Usage of WoundAide imaging system in documenting a venous leg ulcer in a clinical setting

Contributed by:
Dr Joseph Lo Zhiwen (TTSH),
Dr Chan Kai Siang (MOHH),
Ms Liang Shanying (TTSH),
Ms Neo Shufen (TTSH),
Dr Hong Qiantai (TTSH),
Dr Yong Enming (TTSH),
Dr Zhang Li (TTSH),
Dr Lester Chong (MOHH),
Dr Pravin Lingam (WHC),
Dr Sadhana Chandrasekar (TTSH),
Dr Glenn Tan Wei Leong (TTSH),
Ms Lai Peiting (TTSH),
Mr Sivakami Muthuveerappa (TTSH),
Ms Goh Cheng Cheng (TTSH),
Ms Audrey Tan (TTSH) and
Ms Diane Eng (TTSH)

References:

1. Lo ZJ, Lim X, Eng D, et al. Clinical and economic burden of wound care in the tropics: a 5-year institutional population health review. Int Wound J. 2020; 17:790-803
2. Chan KS, Lo ZJ. Wound assessment, imaging and monitoring systems in diabetic foot ulcers: A systematic review. Int Wound J. 2020; doi:10.1111/iwj.13481

Collaborative Model of Care between Orthopaedics and Allied Healthcare Professionals Trial (CONNACT) for Knee Osteoarthritis: Pilot Study

Problems/Challenges

Osteoarthritis is a leading cause of global disability resulting in significant morbidity and costs to the healthcare system[1]. Current guidelines recommend lifestyle changes such as exercises and weight loss as a first line treatment prior to surgical consideration. A local study in 2017 showed that almost half the patients who were prescribed with physiotherapy (PT) did not receive any PT. This is consistent with international literature which reports that almost two-thirds of patients receive suboptimal non-pharmacological treatment for osteoarthritis[2]. **The reality is that our current model of care is inefficient with suboptimal allied health intervention for effective behavior changes.**

CONNACT Program

The multidisciplinary intervention program was developed jointly with the departments of Orthopaedic Surgery, Psychology, Physiotherapy and Nutrition in conjunction with our community partner, St Luke Eldercare. Expert guidance was provided locally by Professor Julian Thumboo from SingHealth and internationally from Professor Soren Skou and Professor David Hunter, founders of the Good Life with Arthritis: Denmark (GLA:D) and Osteoarthritis Chronic Care Program Australia (OACCP) respectively during program conceptualisation. The target population were patients who were suffering from knee osteoarthritis. The intervention consisted of a 12-week community based, individualised, multidisciplinary model of care for knee osteoarthritis based on the following key principles and consisted of these components.

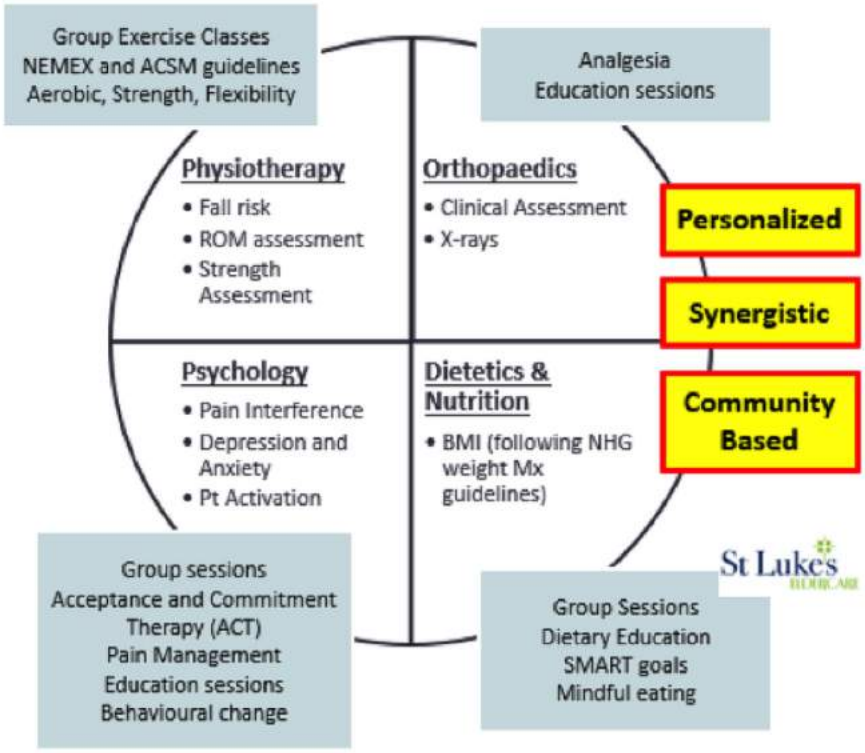


Figure 1: Summary of the CONNACT program

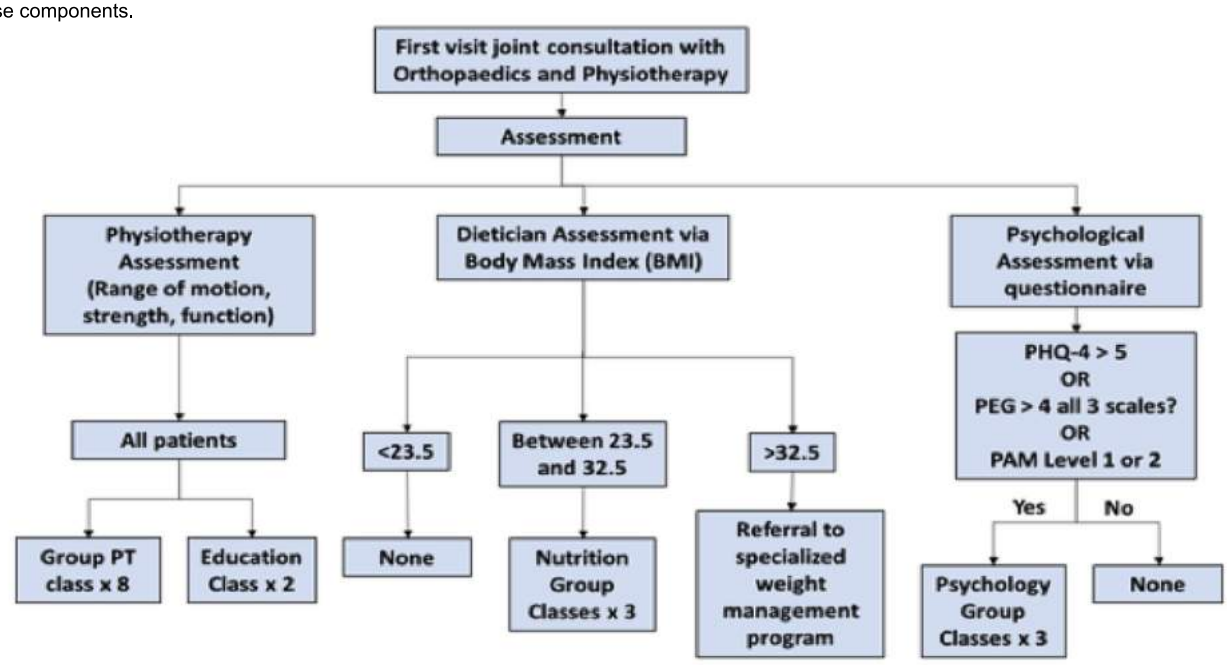


Figure 2: Personalised Patient Assessment Protocol

Solutions

The primary aim was to conduct a pilot study to evaluate the clinical effectiveness of the new proposed model of care for knee osteoarthritis compared to usual care. The secondary aim was to conduct a process evaluation[3] to evaluate the feasibility for a full randomised control trial (RCT) and to guide future wider scale application. The study design was an effectiveness-implementation hybrid randomised control trial utilising a mixed method approach[4]. Semi-structured interviews focusing on intervention feasibility and design optimisation were conducted with both the patients and healthcare providers at 12-weeks as part of a process evaluation. In addition, progression criteria for a full RCT was developed to guide RCT feasibility[5]. The primary outcome measure is the Knee Injury and Osteoarthritis Outcome Score (KOOS)[6] at baseline and 12-weeks. Secondary outcomes included quality of life, functional and psychological assessments. A total of 20 patients (3 males, 17 females) were randomised. Results are summarised in the table below. Semi-structured interviews revealed several themes pertaining to intervention optimisation and study design feasibility. Results from the pilot met the proposed progression criteria for a full RCT.

Table 1: Summary of Pilot Results

	Outcome Measure	Intervention	Control
Physiotherapy	KOOS4	Mean improvement of 21.38	Mean improvement on 9.46
	EQ5D	VAS mean improvement of 15	VAS mean improvement of 10
	Functional Assessment	Equivocal – confounded by concomitant MSK issues	
Dietetics	BMI	Mean weight loss of 0.3kg	Mean weight gain of 1.8kg
	FFQ	All patients demonstrated positive change in diet	57.1% demonstrated negative change in diet
Psychology	PEG	Mean improvement of 2.33	Mean improvement of 1.5
	PHQ-4	No difference	No difference

Table 2: Progression Criteria for full RCT

Proceed with RCT	Proceed, but changes to the protocol need to be discussed	Do not proceed with main trial unless the problem can be solved
Recruitment of 30 participants with osteoarthritis within 3 months	Recruitment of 30 participants with osteoarthritis within 3-6 months	30 participants with osteoarthritis are not recruited within 6 months
At least 75% retention of participants through follow up	At least 50% retention of participants through follow up	Less than 50% retention of participants through follow up
At least 75% complete more than half of the exercise therapy sessions	At least 50% complete more than half of the exercise therapy sessions	Less than 50% complete more than half of the exercise therapy sessions
At least 80% of participants do not find the outcomes so burdensome that they would not participate in the study again	At least 70% of participants do not find the outcomes so burdensome that they would not participate in the study again	Less than 70% of participants do not find the outcomes so burdensome that they would not participate in the study again
Improvements in function and quality of life found clinically relevant by at least 50% of the participants	Improvements in function and quality of life found clinically relevant by at least 25% of the participants	Improvements in function and quality of life found clinically relevant by less than 25% of the participants
No serious care-related adverse events during follow up	Less than five serious care-related adverse events during follow up	Five or more serious care-related adverse events during follow up

Table 1: Success criteria to proceed with the randomized controlled trial (RCT)

Future Plans

The pilot demonstrated the potential effectiveness of this new model of care, and the results were used to improve the intervention content, delivery model and study design for a larger effectiveness-implementation hybrid randomised trial that is currently underway. The main trial includes a 1-year follow up, economic evaluation and the RE-AIM[7] and Global Alliance for Musculoskeletal Health (GMUSC)[8] implementation framework to guide large scale implementation.

Multidisciplinary collaborations, community **partnership and engaging key stakeholders can be tough but potentially result in a more effective, robust and sustainable program.** Starting with a well-designed pilot with an embedded process evaluation to optimise intervention and inform feasibility is key. Recognising the ultimate goal is effective wide scale implementation, beginning with the end in mind by including appropriate implementation models early is crucial to ensuring success.

This project won the Health Services Research (Gold) award during SHBC 2019 and was recently award the NHG Population Health Grant to upscale the CONNACT program to the NHG Cluster.

Contributed by:
Principal Investigator
Dr Bryan Tan Yijia
Associate Consultant
Orthopaedic Surgery
WHC

Study team
Dr Lee Theng Kiam (TTSH),
Dr Yang Su Yin (TTSH),
Dr Madelynn Chan (TTSH),
Ms Ngo Xueting (TTSH),
Dr Lim Yen Peng (TTSH),
Ms Quek Wei Lin (TTSH),
Ms Vicky Chan (TTSH),
Dr Michelle Pereira (HSOR, NHGHQ),
Prof Josip Car (LKCMedicine),
Prof Julian Thumboo (SGH),
Dr Kenny Tan (SLEC),
Dr Lestor Leong (SLEC),
Ms Jennifer Goh (SLEC) and
Ms Jennifer Vitualla (SLEC)

References:

1. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Annals of the rheumatic diseases. 2014 Jul;73(7):1323-30. Epub 2014/02/21.
2. Basedow M, Esterman A. Assessing appropriateness of osteoarthritis care using quality indicators: a systematic review. Journal of evaluation in clinical practice. 2015 Oct;21(5):782-9.Epub 2015/06/18.
3. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ (Clinical research ed). 2015 Mar 19;350:h1258. Epub 2015/03/21.
4. Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Medical care. 2012 Mar;50(3):217-26. Epub 2012/02/09.
5. Avery KNL, Williamson PR, Gamble C, O'Connell Francischetto E, Metcalfe C, Davidson P, et al. Informing efficient randomised controlled trials: exploration of challenges in developing progression criteria for internal pilot studies. BMJ open. 2017;7(2):e013537.
6. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. Health and quality of life outcomes. 2003 Nov 3;1:64. Epub 2003/11/14.
7. Glasgow RE, McKay HG, Piette JD, Reynolds KD. The RE-AIM framework for evaluating interventions: what can it tell us about approaches to chronic illness management? Patient education and counseling. 2001 Aug;44(2):119-27. Epub 2001/08/02.
8. Briggs AM, Jordan JE, Jennings M, Speerin R, Bragge P, Chua J, et al. Supporting the Evaluation and Implementation of Musculoskeletal Models of Care: A Globally Informed Framework for Judging Readiness and Success. Arthritis Care Res (Hoboken). 2017 Apr;69(4):567-77. Epub 2016/06/09.

An Exploratory Study on the Development of a Customised Head Protection Prototype Device (HPPD) for Post-Decompression Craniectomy Patients

Problems/Challenges

Life-saving decompressive craniectomy (DC) following malignant stroke or traumatic brain injury (TBI) results in a cranial defect. The optimal timing of cranioplasty remains controversial and variable[1]. DC patients are at increased risk of secondary brain injury from falls, seizures, physical and cognitive disability. Head protection devices have been recommended, however, recommended standards and acceptance are unclear.[2,3,4] (Figure 1)

Figure 1. Standard head protection post decompression craniectomy

Solutions

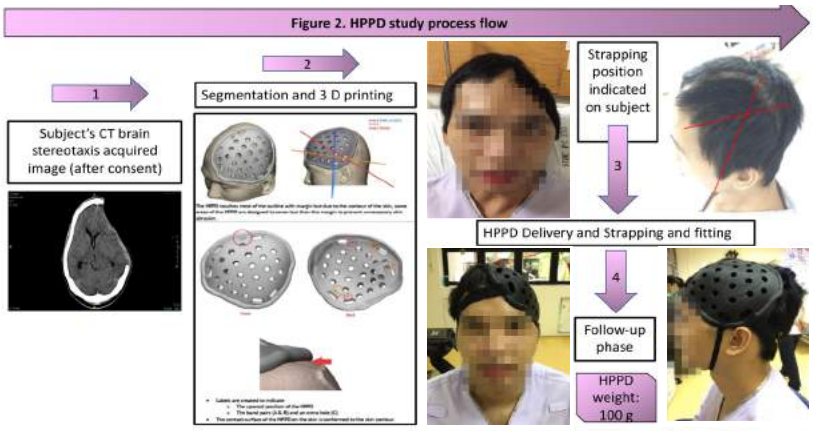
An exploratory feasibility clinical trial by TTSH Rehabilitation Centre, NNI Neurosurgery, and Creatz3D was conducted from 1 April 2019 to 30 October 2020. Medical additive manufacturing techniques (3 D printing) using Nylon12 were used to fabricate a customisable externally-applied Head Protection Prototype Device (HPPD) for post-DC patients. The primary outcome was safe fitting of HPPD within 30 minutes of wear without wound changes or pain. Ethics board approvals were granted by NHG and informed consent from all subjects / next-of-kin (NOK) was obtained. (NHG-DSRB 2019/00155, Trial registry: www.clinicaltrials.gov; NCT04021095)

Study protocol

Subjects with unilateral DC, > 30 days post-surgery with healed and stable cranial flaps who were able to obey simple commands, without active sepsis or agitation; and had a caregiver were enrolled.

The study work process is shown in Figure 2. Following HPPD fabrication using Nylon12 material, integration with customised straps, carers' instruction on HPPD wearing and activities, rest periods and device logging. Subjects were then followed up (FU) over 8 weeks; via physical visits at 1, 2, 4 ,6 and 8 weeks and phone FU at days 1,3 and week 6. Outcomes assessed included hours worn per day, subject-reported side effects of pain, pressure, itch, dislodgement; cosmesis ratings and assessor ratings of wound changes.

Figure 2. HPPD study process flow



Findings

Of 31 subjects screened, 13 were eligible and 10 were enrolled. A total of 12 HPPDs were fabricated; 2 patients each received > 1 HPPD fitting due to misplacement and incorrect fit. All 10 (100%) subjects were then fitted without immediate wound changes or complaints of pain. One drop-out (10%) occurred at week 4 FU due to an unrelated medical hospitalisation.

Of 10 enrolled subjects, 50% were male (5/10), 80% (8/10) had right-sided DC, mean (SD) age 45.8 (14.3) years and 90% (9/10) were inpatients. Aetiologies included; TBI (4), intracerebral haemorrhage (3), malignant cerebral infarction (2), and subarachnoid haemorrhage (1). The mean (SD) duration post-DC to HPPD fitting was 110.2 (SD 76.2 days), range 45-311 days; mean (SD) mass of HPPD was 62.8g (SD 20.3); range: 37 - 100g.

During FU, there were no HPPD-related wound infections or dehiscence; and 2 (20%) subjects received cranioplasty within 8 weeks of FU. The remaining subjects (8/10), including 1 drop-out retained their HPPDs.

Side events related to HPPD occurred in 6/10 of subjects (60%) including, pressure (4/10) associated with > 3 hours of wear, pruritus (3/10), pain (1/10), all to mild-moderate degrees; and transient skin imprints (2/10).

In conclusion, findings from this exploratory study showed preliminary feasibility and safety in application of 3 D printing to provide head protection options post-DC, without serious adverse events during the 8-week FU period. Supervision and regular rest breaks during HPPD wear were important to prevent discomfort.

Future Plans

Future work involves improving HPPD comfort,

Contributed by:
Principal Investigator
Dr Chua, Sui Geok Karen
Senior Consultant
Department of Rehabilitation Medicine
TTSH

Study team/ authors:
Karen Chua[1] (PI), Rathi Krishnan[1], Jia Min Yen[1], Tegan K Plunkett[1], Yan Ming Soh[1], Chien Joo Lim[3], Catherine Chia[4], Sean Looi[4], Suan Gek Ng[2] and Jai Rao[2]

Institutional Affiliations:
1. TTSH Rehabilitation Centre
2. NNI, Department of Neurosurgery
3. CRIO, TTSH
4. Creatz 3D, Singapore

References:

1. De Cola MC, Corallo F, Pria D, Lo Buono V, Calabrò RS. Timing for cranioplasty to improve neurological outcome: A systematic review. Brain Behav. 2018;8(11). doi:10.1002/brb3.1106
2. Livesay S, Moser H. Evidence-based nursing review of craniectomy care. Stroke. 2014;45(11):e217-9. doi: 10.1161/STROKEAHA.114.006355
3. Honeybul S. Decompressive craniectomy: A new complication. J Clin Neurosci. 2009;16(5):727-729.doi:10.1016/j.jocn.2008.06.015
4. Honeybul S. Neurological dysfunction due to large skull defect: Implications for physiotherapists. J Rehabil Med. 2017;49(3):204-207. doi:10.2340/16501977-2209

Real-time Ultrasound Guidance Lumbar Puncture Device

Problems/Challenges

Current Clinical ChallengeLumbar Puncture (LP), also known as the spinal tap, can be done either as a diagnostic or therapeutic procedure that extracts cerebrospinal fluid (CSF), or through the administration of treatments through the lower lumbar region (L3-L4). In developed countries, LP is considered an established procedure and ultrasound-guided LP has been strongly recommended to improve the success rates. However, the current way of using an ultrasound probe to guide LP is not always efficient since the probe blocks the direct needle-in-plane entry. As a result, the use of ultrasound to guide LP has been reduced.

Physicians have relied on palpation methods and "blind" lumbar punctures which resulted in a high procedural failure of 20-35%. The failure rates are further elevated in difficult cases including obese patients and patients with spinal deformities. Even for experienced doctors, LP can be difficult when they must deal with patients with deformed spines, particularly in elderly patients or obese patients that represent increasing patient demographics globally.

Solutions

Medulla Pro Technology ("Medulla Pro"), a portfolio company under Trendlines Medical Singapore, has developed a device that can be attached to ultrasound probes to provide real-time ultrasound guidance LP. This device enables real-time imaging and tracking of the needle during insertion through the deflection of ultrasound waves. The methodology of accurately deflecting ultrasound waves also made needle-in-plane entry possible without affecting the resolution of the ultrasound images. Medulla Pro's device was designed to be a single-use disposable device per patient to eliminate cross-contamination and is compatible with most commercially available low-frequency ultrasound probes. In a series of bench tests performed, the device successfully achieved a 90% success rate for "first-attempt" needle entry in successfully extracting CSF on the first attempt.

Future Plans

Medulla Pro is preparing for its first pilot build of the device before embarking on a first-in-human (FIH) study with Khoo Teck Puat Hospital (KTPH) for safety studies.

Contributed by:
Principal Investigators
Dr Bin Wern Hsien (KTPH) and
Dr Eugene Fan (TTSH)

Principal Investigators
Dr Darryl Heng (KTPH)

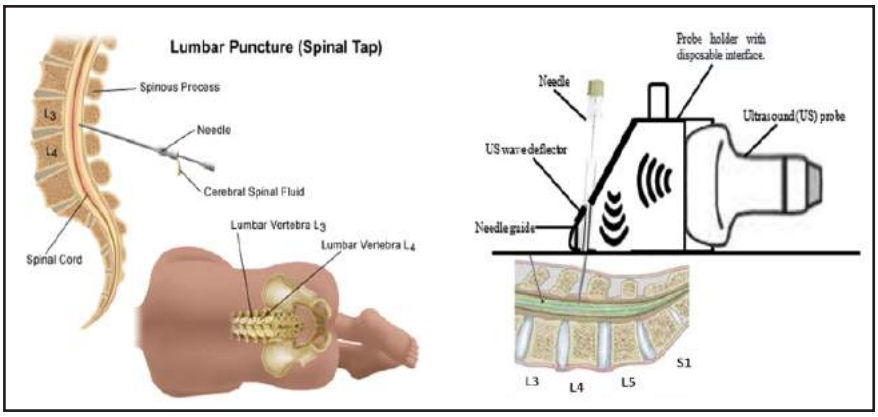


Figure 1: Illustration on Medulla Pro's concept for lumbar puncture

Figure 2: Medulla Pro's concept & functional prototype

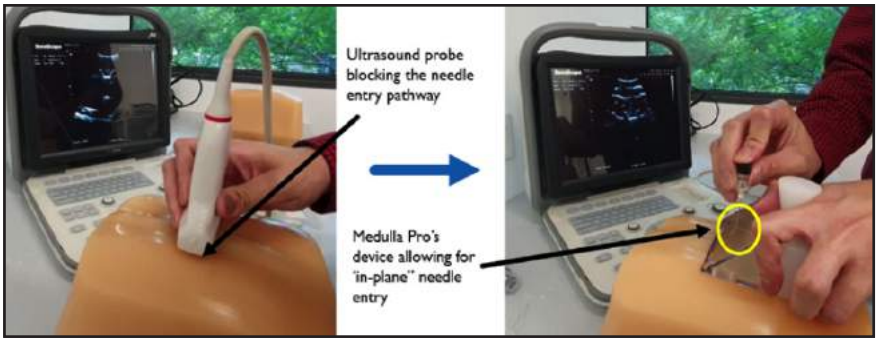


Figure 3: Illustration of ultrasound guidance procedure using conventional (left) versus Medulla Pro's device (right).

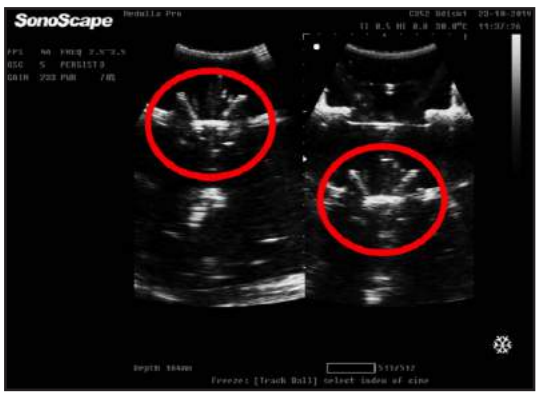


Figure 4: Original image (left) clarity maintained with use of Medulla Pro's device.

References

1. Ageing. (n.d.). Retrieved August 10, 2020, from https://www.un.org/en/sections/issues-depth/ageing/

Ultrasound Based Location Tracker to Verify Nasogastric Tube Placement

Problems/Challenges

Nasogastric Tubes (NGTs) are used to provide nutrition, administer medication or decompress/irrigate the gastric tubes of patients with difficulties in ingestion[1]. Incorrect placement of the NGTs can often lead to catastrophic outcomes including death.

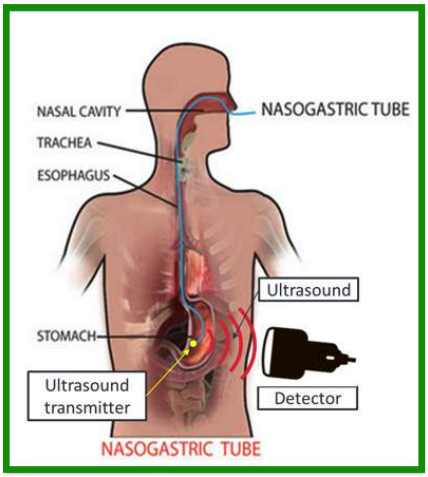


Figure 1: Nasotrak's ultrasound detection concept

Well-established methods of determining the correct position of the NGTs, such as X-rays or the pH aspirate test have severe limitations[2], resulting in unacceptably high rates of 2-4% of NGT misplacements yearly.

Globally about 40 million NGTs being are being used every year[3]. This translates to the potential of at least 1.6 million NG tube misplacements that can be prevented if there is a more efficient system that can detect the correct NG tube placement. The clinical unmet need is evident and there is a need for better solutions to determine the position of NGTs before feeding. Whilst new methods of detection have been introduced in recent years, these methods are often expensive and difficult to operate.

Solutions

Nasotrak is developing an ultrasound-based NGT positioning system in partnership with clinicians from the National Healthcare Group. NasoTrak's NGT system, as illustrated in the diagram below, comprises a proprietary NGT and a separate hand-held, portable detector. The NGT is designed such that it is able to transmit ultrasound from within the body, which will be picked up by the hand-held detector. This helps the user to determine the location of the distal end of the NGT to give a real-time, accurate and safe means of tube placement before feeding.

Future Plans

Nasotrak has performed bench tests on the prototype in various mediums including water and an ex-vivo test on animal tissue to simulate conditions to detect the NGT, and has achieved positive results with >90% accuracy in the detection of the NGT. The company has planned for an upcoming pre-clinical study and will also be working with our clinicians to plan for first-in-human trials.

Contributed by:
Principal Investigators
Dr Leong Khai Pang (TTSH),
Dr Ravinder Singh Sachdev (TTSH) and
Dr Bin Wern Hsien (KTPH)

Collaborators
TTSH, KTPH and Trendlines Medical Singapore

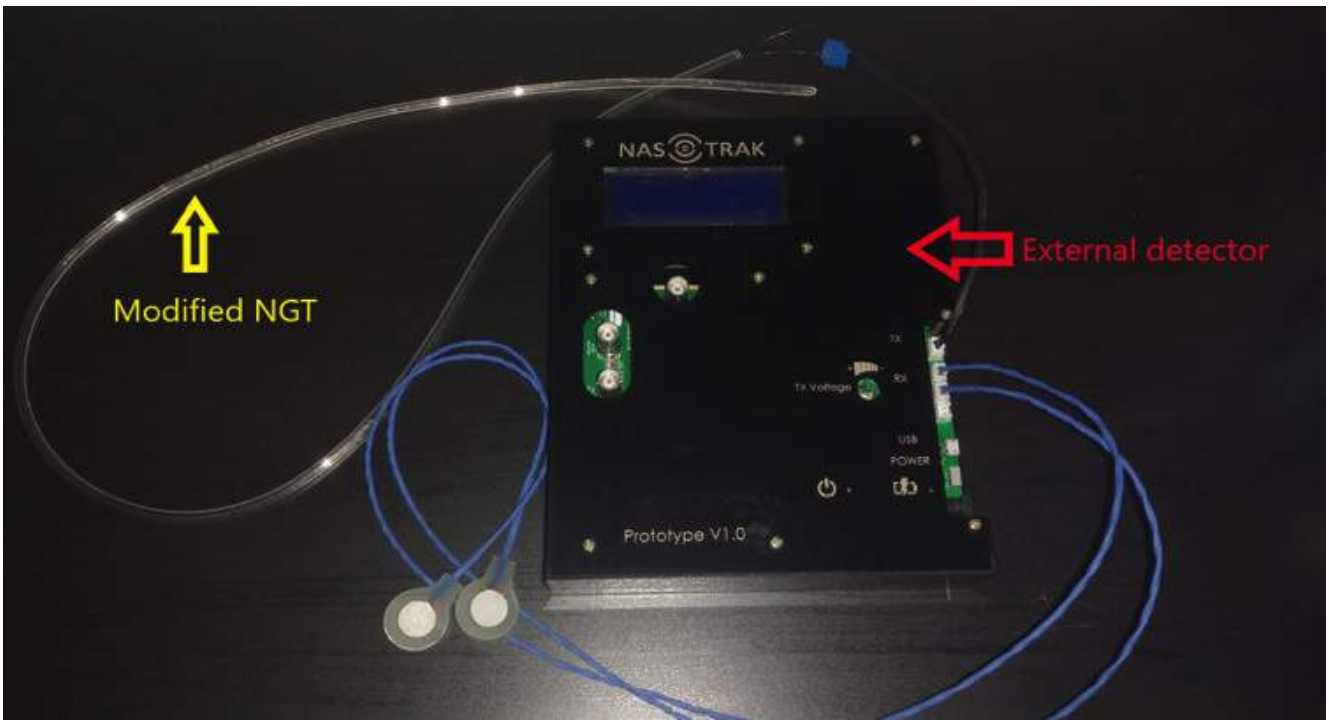


Figure 2: Nasotrak's prototype assembly

References:

1 Ministry of Health, Singapore (2010): Nursing Management of Nasogastric Tube Feeding in Adult Patients
2 Esther Monica Peijin Fan, Singapore General Hospital, Proceedings of Singapore Healthcare (2017): Nasogastric tube placement confirmation: where we are and where we should be heading
3 Details of the Global Market Insights

Hydration Monitoring through Novel Tongue Bioimpedance Measurement Device

Challenges

Heart Failure (HF) affects 26 million people worldwide, while close to 80 million American adults are at risk of Chronic Kidney Disease (CKD).

Fluid management is an important concern in patients with HF and CKD, with both groups of patients suffering from frequent switching between hypovolaemia and hypervolaemia. Fluid volume depletion causes discomfort and cramps, while fluid overload, particularly sustained over longer periods of time, is linked to poor prognosis.

Fluid overload control is considered an unmet clinical need. Conventional fluid management methods such as fluid restriction and dry weight measurement are often subjective and inaccurate. The healthcare burden from inadequate fluid management has been estimated at $9.1 billion per year in the United States, further highlighting the need of a practical hydration monitoring solution. The market for hydration monitoring devices is expected to see a growth rate of 8.9% annually.

Findings

Szone Medical, a portfolio company of Trendlines Medical Singapore, has developed a device that quantifies the user's hydration levels through tongue bioimpedance. The device is easy-to-use and provides accurate, real-time levels of hydration measurement in a non-invasive manner. The initial clinical study conducted at Rambam Hospital, Israel, had found significant correlations between tongue bioimpedance and blood osmolality, a reliable marker of hydration status.

Future Plans

Szone is currently working with Tan Tock Seng Hospital on a clinical study to further develop correlations with hypervolaemia clinical signs and B-type natriuretic peptide, a heart attack risk marker. The device can also potentially quantify dry weight and edema index, a promising prognostic tool among HF and CKD patients. Following the clinical studies on cardiac patients, the company plans to embark on additional studies for renal patients.

With these correlations, the device is anticipated to enable interventions before the serious onset of disease repercussions and improve clinical outcomes. The untapped value of this device is to guide the physician's care – the readings can potentially help titrate diuretic prescription and fluid restriction.

As part of future developments and improvements to the device, Szone aims to augment the measurement capabilities with wireless features to allow for remote monitoring and better management of patient conditions. The adoption of such technologies can potentially reduce the overall burden on the healthcare system while improving patient outcomes.

Contributed by:
Principal Investigator
Dr Hoon Hui Qing Violet
Consultant
Cardiology
TTSH

Study team
Dr Loh Seet Young (TTSH),
Dr Claude J. Renaud (KPTH),
Dr Lim Eng Kuang (KPTH),
Dr Allen Liu Yan Lun (KPTH) and
Asst Prof Tey Hong Liang (NSCH)

Figure 1. Szone Portable Bioimpedance Measurement Device

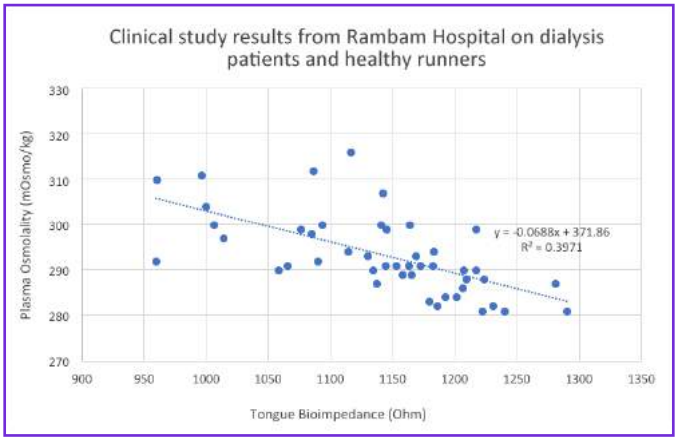


Figure 2. Clinical study results from Rambam Hospital on dialysis patients and healthy runners

National Paramedic Termination of Resuscitation (TOR) Studies 1 & 2

There are approximately 1800 out-of-hospital cardiac arrests (OHCAs) in Singapore every year. Based on robust scientific evidence, following a period of resuscitation, it is possible to identify patients have no chance of survival. This proportion ranges from 21.7% to 74.8% of all cases. **Transport of futile OHCA patients result in prolonged futile resuscitation, high-risk ambulance transports, increased consumption of limited Emergency Department (ED) resources and worsens ED overcrowding.**

While prehospital termination of resuscitation (TOR) protocols have been successfully implemented in Western countries, few Asian countries have reported applying such protocols. Success in implementing TOR protocols has, in part, been attributed to practicable protocols, positive paramedic attitudes and formal paramedic training to shape mindsets towards TOR.

We aimed to successfully implement a TOR protocol in Singapore by firstly, **understanding factors associated with local paramedic acceptance and adoption and secondly, evaluate the effectiveness of a structured training program.**

We undertook a prospective, national, longitudinal study of all practicing paramedics in Singapore. The study took place from 2016 to 2018. We administered an anonymous questionnaire before and after formal TOR training was conducted. **Overall psychological comfort scores and domain-specific scores were obtained.** A 3-hour training session was conducted. Pre-training and post-training scores were compared.

This is the first Asian study to look at paramedic psychological comfort factors which we found is associated with personal and external factors. Training should target not only knowledge of TOR protocols, but also public arena management, communication skills for engaging families and help paramedics resolve prior personal loss.

Our findings have revealed gaps that have allowed us to improve training and improve protocol structure, especially with respect to tackling cognitive overload in application of the protocol. This research translated to the successful nationwide launch of the prehospital TOR protocol on 1 Jan 2019.

Contributed by:
Dr Desmond Mao *(Left)*
Consultant

Dr Bang Chungli *(Right)*
Resident Physician
Department of Acute and Emergency Care
KTPH

Training Calendar

Date	Training Courses	Course Provider
Monthly	Good Clinical Practice (Online)	NHG Group Research
	(PCR100) Study Start-Up: Budgeting, Case Report Form Design and Database Design*	
	(PCR200) Study Conduct I: Subject Recruitment and Informed Consent*	
	(PCR300) Study Conduct II: Documentation, Safety Reporting and Investigational Products*	
	(PCR400) Monitoring, Audits and Inspections*	
6 - 8 Jan 2021	Biostatistics	
19 Jan 2021	Questionnaire Design	
5 Feb 2021	Evidence-Based Medicine Core Skills for Protocol Development	
5 Mar 2021	Basic SPSS Workshop	TTSH CRIO
9 Mar 2021	Basic Grant Writing	

*Blended learning courses involve Online Lectures coupled with a Classroom Workshop on a stipulated date.

Dates are subject to changes without prior notice.

For registration and full details on courses by:

~ NHG Group Research, please visit www.research.nhg.com.sg
(Training & Education → Register for Courses and Other Events)

~ TTSH CRIO, please contact Ms Siti Aisha Binte Jaffar Siti_Aisha_JAFFAR@ttsh.com.sg

CHICKEN SOUP FOR THE BUSY COORDINATOR

Education to facilitate high standards of research conduct

1. **Jun 2020: Performing Subject Eligibility Assessment & Documentation**
2. **Jul 2020: Ensuring Data Integrity With Principles Of Good Documentation**
3. **Aug 2020: Ensuring Data Integrity With Principles Of Good Documentation**
4. **Sep 2020: Remote Source Document Verification (SDV) Requirements**
5. **Oct 2020: Documentation for Pre-Screening and Screening Process of Research Subjects**

Click on the respective issues to find out more!