




MTP Connect
MedTech and Pharma Growth Centre

BMTH BioMedTech Horizons PROGRAM

SUPPORTING TRANSLATION OF AUSTRALIAN MEDICAL TECHNOLOGY INNOVATION

A summary of the progress and impact of new Australian medical technologies supported by the BMTH Program (2017–2023)

BMTH Rounds 2, 3 & 4
August 2023

Contents

Australian Government
Department of Industry, Science and Resources

Front Cover images: top line from left, WearOptimo, Miniprobes and Atmo Biosciences; lower line from left, Inventia Life Science, Synchron Australia and ResusRight.
Photo credit Synchron Australia: Peter Cassamento for the European Patent Office 2023.

MTPCONNECT CEO FOREWORD

I am delighted to report that MTPConnect has successfully completed all four funding rounds of the BioMedTech Horizons (BMTH) program for the Medical Research Future Fund (MRFF).

Stuart Dignam
Chief Executive Officer

This report captures the outcomes of 38 projects awarded $30.3 million funding in the second, third and fourth rounds and builds on the successes of round one, which were detailed in the BMTH1 Impact report published in November 2021.

It has been an immense achievement from awardee companies who delivered much of their work during COVID-19 pandemic restrictions – the first lockdowns occurring within weeks of BMTH2 commencing. And while the pandemic certainly had impacts on access to facilities, hospitals, patients and supply chains, it did not define the outcomes of this program.

MTPConnect designed the BMTH program to address gaps in early biomedical and medical technology product development. Its aim was to increase the number of promising innovations reaching proof-of-concept stages or beyond.

It is pleasing to outline in this report that companies in the BMTH program have been able to develop their product ideas substantially, clearly increasing product maturity and with several achieving commercial outcomes.

With a significant shift to private funding, the report demonstrates success in nurturing companies through the first 'valley of death' and de-risking product development to increase the appeal to private investment.

Companies supported through BMTH have really captured the interest of investors, taking our $30.3 million in funding and going on to secure at least $479 million of further flow-on and external investment.

This shows what can be achieved by backing start-ups, entrepreneurs and SMEs to bring life-saving medical products from research labs to market: stronger companies, a more resilient economy and healthier communities.

The BMTH program would not have been possible without the involvement of industry leaders and clinical, commercialisation and medical device experts with deep national and international networks. They have reviewed, assessed and recommended commercially viable applications into the program with independence, skill and rigor and contributed to these significant outcomes.

I would like to thank fellow members of the BMTH Steering Committee for providing robust governance, expertise and guidance during the last four years: Ian Burgess – CEO of the Medical Technology Association of Australia, Paul Grand – CEO of MedTech Innovator, and Frank Jaskulke – Head of Medical Alley Starts at the Medical Alley Association.

Thanks also to the MTPConnect program team of Dr Gerard Gibbs, Elizabeth Stares, Dr Vishal Srivastava and Dr Erin McAllum, who built strong relationships with funded companies and helped guide and support their progress to success.

As Australia's life sciences industry accelerator, we understand the challenges involved in taking ideas and turning them into medical products.

Enjoy reading about these exciting new medtech innovations led by start-ups and SMEs that have seized the MRFF opportunity to progress their research and commercialisation activities, some of which are now launched as products.

Stuart Dignam
Chief Executive Officer
MTPConnect

A MESSAGE FROM THE CEO OF THE MEDICAL TECHNOLOGY ASSOCIATION OF AUSTRALIA

The Medical Technology Association of Australia (MTAA) is the national association representing companies in the medical technology industry. It aims to ensure the benefits of modern, innovative and reliable medical technology are delivered effectively to provide better health outcomes to the Australian community.

Ian Burgess
Chief Executive Officer

With this as its foundation and recognising the transformative opportunity that new technologies can offer patients, MTAA was a strong advocate for the usage of the MRFF commercialisation initiative funding to support the translation of promising, transformative medical technologies. MTAA is proud to have initiated discussions that led to the development of the BioMedTech Horizons (BMTH) program. With my role as an advocate for the medical technologies sector in Australia, I was pleased to be a founding member of the Steering Committee that provided direction for BMTH and provide advice and governance support through each of the four rounds of funding.

Advances in medtech are critical to our nation's efforts to improve the health and wellbeing of every Australian and reduce the burden of disease that significantly impacts patients, their families, our healthcare system and our nation's production. We see these advances daily, with more coming and as evident through this report – driving improvements to ensure we capture disease earlier and putting new tools in the hands of patients and their healthcare professionals.

MTAA recently released the *Value of Medtech Report* to highlight the value of medical technology in Australia along the whole value chain, from idea to patient. The report, prepared by Nous Group with support from MTPConnect, is a major economic study that outlines and quantifies the positive contributions the Australian medtech industry makes to the Australian healthcare system and its economy, and to the health of Australians each and every day.

The role that driven innovators, clinicians, research and technology play in supporting the healthcare innovation system is significant and increasing. Commercialisation-focused programs such as the MRFF-supported BMTH program have proven to be of value to the development of the sector in Australia and will have national and global impact in treating patients. I am a strong advocate for the ongoing delivery of such programs – leveraging leaders in business and medical device commercialisation to independently assess, recommend and support projects.

It is for these reasons that MTAA has been so pleased to support BMTH from its conception and is so excited to see the results from this MRFF program. I offer my congratulations to each of the teams awarded funding in this program and I am pleased to see the significant advancements they have achieved in developing their projects.

Finally, I offer my congratulations to the team at MTPConnect for delivering a highly effective program that engaged closely with applicants and the awardees and selected the projects to be funded through a rigorous application and selection process.

Ian Burgess
Chief Executive Officer
Medical Technology Association of Australia

EXECUTIVE SUMMARY

The $45 million BioMedTech Horizons (BMTH) program is an initiative of the Medical Research Future Fund (MRFF) delivered by MTPConnect to support early-stage medical device developments to move towards commercialisation. The BMTH program comprises four funding rounds, with the first phase – BMTH1 – concluding on 29 October 2021 and the second phase – covering rounds 2, 3 and 4 – concluding on 30 June 2023.

The MRFF Act requires a focus on translation and commercialisation, and as such the objective of the BMTH funding opportunity was to address the gap in early biomedical and medical technology product development and increase the number of viable, new health technologies reaching proof-of-concept stage that are attractive for private capital investment and have potential to benefit the health and wellbeing of Australians.

With Phase II grant funding of $30.3 million backing 38 projects, leveraging $36 million in industry contributions and a further $479 million in flow-on and external investment, the BMTH program has been a vast – and successful – undertaking. This report details how the program's objective has been met – and more.

Program anatomy

Phase II of the BMTH program, covering rounds 2, 3 and 4 and supporting 38 projects in 36 companies, is the focus of this report.

Funding of up to $1 million per project was provided in rounds 2 and 3. While matched funding was not required, it was often offered by awarded companies. Round 4 supported companies with $800,000 in funding with a requirement to provide matched contributions.

All funds provided were non-diluting investments, allowing companies to retain equity and ownership and support future growth.

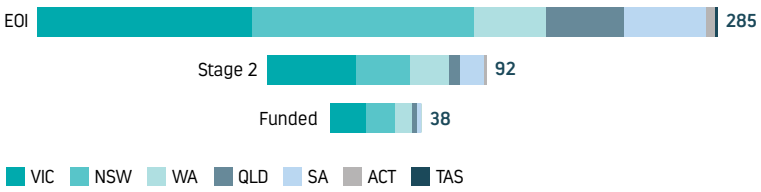
The funding rounds were open and contestable, with successful applicants passing through Expression of Interest (EOI) and full application stages. Applications were reviewed by independent assessment panels involving a pool of 31 national and international medical device commercialisation leaders, with deep expertise across regulatory, reimbursement, commercial and clinical areas.

Over the course of this second phase, 285 EOIs were received and reviewed, resulting in 92 full applications and 38 projects being funded.

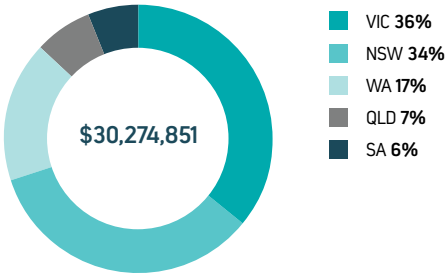
Funding rounds targeted projects being delivered within SMEs building medical device products, where the funding support would provide a meaningful boost to product development. Funding prioritised innovations where the foundational research had been completed and a solid market case was developed, with the aim of assisting companies to mature their products to demonstrate proof of value or validation of their solution so that further funding could be secured.

BMTH funding was distributed nationally in a manner consistent with historical trends and with the numbers of applications received. A standout in this regard was the overall performance of Western Australia, with the state coming in third position for funding awarded but excelling in successfully converting EOIs submitted to receiving funding. Applicants from Western Australia had the highest success rate.

Numbers of applications per stage with distribution by state



BMTH cash expenditure for funded projects

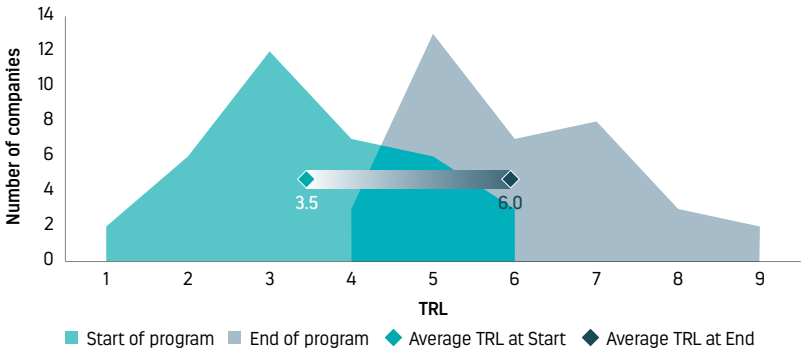


Technology Readiness

Using CIMIT's Guidance and Impact Tracking System (GAITS) Technology Readiness Levels (TRLs) as an indicator, the target was to mature a product from a fully evaluated idea with robust market research and technical foundations established (TRL2), or an early-stage proof-of-concept (TRL3), up to validation in a relevant environment (TRL5) or beyond.

A self-assessment conducted by funded companies shows the shift in TRLs from the starting point through to the end point, with an overall average change in product maturity of 2.5 TRL points, from 3.5 to 6.0.

Progress against TRLs



MTPConnect furthered its analysis of publicly available information with data collected by Health Horizon up to 30 June 2023. Published information was analysed comparing companies that had received BMTH funding to those that had submitted full applications into the program but were unsuccessful – companies selected were at a similar stage at the time of application and were all medical device companies meeting the same eligibility criteria. This demonstrated accelerated progress across a range of metrics of the BMTH cohort compared to the control group. BMTH companies:

- communicated news about research and strategic collaborations 3.2 times more
- have planned, started and completed 5 times more clinical trials/studies
- have achieved 1.8 times more regulatory and protection milestones
- received 6.3 times more funding (not including BMTH funds).

Accelerated performance was related to technical areas where funding was vital to progress the technology development, whereas no difference was observed in other activities that did not require funding, such as participation in accelerator programs. While this analysis seems obvious in many ways – receiving funding accelerated growth – the significant message is the value of targeted funding to support acceleration of technical research activities for SMEs.

The COVID-19 pandemic and related restrictions had a significant impact on the program. With the first restrictions initiated within three weeks of Round 2 activities commencing, it represented a significant time of adjustment and uncertainty.

While every company and individual were impacted in different ways, the systemic impacts for the program – which mirrored the situation globally – meant that clinical trial activities were stopped and production of prototypes requiring electronic components became challenging. Lack of access to facilities and loss of staff played a significant role in delaying projects' progress across the board.

These delays had ongoing downstream impacts and took time to be resolved. In three cases, it became apparent that projects could not be completed within the timeframe of the BMTH program or priorities had shifted, and they were concluded early. While the original objectives were not met, valuable work was still completed that will have lasting benefit.

Despite challenges, and with project management support from MTPConnect, companies were able to pivot or recover and deliver on originally planned objectives and project success.

Value-add opportunities

In addition to grant funding, tailored value-add opportunities were offered to further support development of projects aligned to the needs of each company.

These commercialisation-focused activities included engagement with Intellectual Property and valuation experts, market access consultants and communication specialists to hone investor pitching strategies.

Access was also provided to bootcamp training opportunities to deepen understanding of requirements to commercialise medical device products.

De-risking Innovation Investment

Funding of $30.3 million through rounds 2, 3 and 4 of the BMTH program has supported 38 projects in 36 companies. It leveraged further cash and in-kind industry contributions of $36 million and a further $1.7 million in tailored value-add initiatives were deployed for the direct benefit of awardees.

This investment has supported 306 jobs, 87 medical technologies have been progressed toward commercialisation, 27 human clinical studies and trials have been initiated or completed, and eight technologies have received marketing approval and are commercialised.

Awardees in the program have captured the interest of investors, with public information indicating more than $479 million in flow-on and external investment has been secured after receipt of BMTH funding.

Seventy-nine per cent – or 30 of 38 companies – have been successful in securing flow-on funding and 92 per cent of that has been secured from non-grant funds such as seed, angel, private investments or series A, B or C financing.

Jobs supported (FT or PT)	New technologies invented or progressed	New patent, trademark applications and licences	Clinical studies or trials initiated or completed	New products launched	Total sector investment
306	87	117	27	8	$66M

Notable achievements

Products developed spanned a broad range of therapeutic areas and technology types including ophthalmology, cardiovascular disease, orthopaedics, neonatal care, oncology and trauma. They include rehabilitation, diagnostic, digitally enabled and implanted medical devices, used in hospital environments and at home.

Five companies successfully achieved regulatory approval for eight products that are currently in use:

- **3DMorphic** makes patient-specific 3D-printed titanium implants for spinal fusion. 3DMorphic has achieved a world-leading turn-around time of five days to design and manufacture patient-specific implant devices, achieving TGA regulatory approval and ARTG listing for three products. These products have been used in more than 100 patient cases.
- **Artrya** secured regulatory approval in Australia, New Zealand, the UK and Europe for its cloud-based, AI-driven Salix software product used to identify high-risk vulnerable plaque formation in patients with coronary heart disease at risk of heart attack.
- **Neuromersiv** received TGA approval of its Ulysses virtual reality rehabilitation system for upper limb rehabilitation following stroke, acquired brain injury or spinal cord injury. The system is in use in rehabilitation clinics in Australia and the UK.
- **ZiP Diagnostics** received TGA approval for the export of the ZiP-CoVx-P2 assay test and export of the ZiP-P2 instrument, and 'Manufacturers' Evidence' approval, which supports the export of the ZiP Diagnostics test to the EU. ZiP Diagnostics also received European registration/approval of the ZIP-CoV-2 assay. The ZiP Diagnostics platform has comparable sensitivity to lab-based PCR tests, but the tests can be done in a fraction of the time and cost, and at the point of care. The instrument and the diagnostic assay are manufactured in Australia but are currently not available or approved for use in Australia.
- **Seer Medical** launched the Seer Health App, a digital diary that tracks historical epilepsy seizure events and interventions such as medication usage and can forecast epilepsy seizure risk profiles for users incorporating physiological signals from the FitBit smart watch. It is the first epilepsy risk forecasting tool available to patients.

Improving health and the economy

The BMTH program is all about supporting the development of the Australian medical device sector. That means backing start-ups, entrepreneurs and smaller companies to bring life-saving medical products from an idea to patients.

The outcomes detailed in this report build on the success of BMTH1 and mean the $45 million BMTH program (rounds 1–4) has contributed to more than $590 million flowing into Australia's medical technology sector.

This result reinforces the potential of medical research commercialisation programs to improve the health and wellbeing of Australians and build stronger companies and a more resilient economy.

COMPANY NAME	THERAPEUTIC AREA	BMTH ROUND
Ferronova	Oncology	Round 3
OncoRes Medical	Oncology	Round 3
Optiscan	Oncology	Round 3
Miniprobes	Oncology	Round 3
Seer Medical	Epilepsy	Round 3
ZiP Diagnostics	Infectious disease diagnostics	Round 3
ClearDrum	Hearing	Round 3
Hemideina	Hearing	Round 3
ResusRight	Neonatal care	Round 4
VitalTrace	Neonatal care/Obstetrics	Round 4
Atmo Biosciences	Gut health	Round 3 Round 4
Advanced Genetic Diagnostics	Cardiovascular	Round 2
WearOptimo	Cardiovascular	Round 2
Apollo Medical Imaging Technology	Cardiovascular	Round 3
Artrya	Cardiovascular	Round 3
Northern Research	Cardiovascular	Round 3
Seer Medical	Cardiovascular	Round 3
VenstraMedical	Cardiovascular	Round 3
Enlighten Imaging	Vision	Round 2
IDE Group	Vision	Round 2
Macuject	Vision	Round 2
PolyActiva	Vision	Round 2
Bionic Vision Technologies	Vision	Round 3
ARIA Research	Vision	Round 4
Proteomics International	Chronic disease diagnostics	Round 4
Cyban	Brain	Round 2
Carbon Cybernetics	Brain	Round 3
Synchron Australia	Brain	Round 3
Anatomics	Brain	Round 3
Cortical Dynamics	Brain	Round 4
Neuromersiv	Upper limb rehabilitation	Round 3
Inventia Life Science	Skin regeneration	Round 3
IntelliDesign	MRI Clinical Imaging	Round 2
Kunovus Technologies	Orthopaedics	Round 2
Anisop Holdings	Orthopaedics	Round 3
Merunova	Orthopaedics	Round 3
3DMorphic	Orthopaedics	Round 4

ASSISTIVE OR REHABILITATION DEVICES

IN THIS SECTION:

- ARIA Research
- Bionic Vision Technologies
- Inventia Life Science
- Neuromersiv

Developing bionic vision glasses to deliver a sense of sight via sound

PROJECT:
ARIA Research Pty Ltd

THERAPEUTIC AREA:
Vision

ARIA

START DATE: 1 October 2021	TOTAL BMTH GRANT: $800,000
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $800,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $800,503
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $0
	TOTAL PROGRAM: $1,600,503

Jobs within the project budget	6
Number of trademark applications	1
Number of patent applications	1
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	12

Blindness and moderate-to-severe vision impairment impacted over 338 million people worldwide and 687,000 Australians in 2020[1]. In Australia there has been an 18 per cent increase since 2010, with the prevalence expected to double again by 2050.

Any vision loss can understandably impact quality of life – often leading to lower rates of workforce participation and productivity and higher rates of depression and anxiety, not to mention social isolation and increased risk of falls and fractures, particularly among older adult populations. The annual economic cost in 2010 was estimated to be $16 billion[2,3], and, importantly, there is anecdotal evidence that people who receive specialist services can maintain employment, live independently and require less government assistance.

ARIA Research, a Sydney-based start-up, has developed a world-first solution for people living with blindness and low vision – conceiving bionic glasses that deliver a sense of sight via sound, and consequently engender life-changing agency and independence.

The ARIA technology is non-surgical, non-invasive and provides immediate benefit with minimal training. It is also non-fatiguing and able to be worn as an all-day, everyday device. It provides a vision-analogous sense to blind users via their natural sense of hearing – enabling them, within seconds of putting on the glasses, to experience an intuitive, detailed, real-time spatial perception of the layout of a space and objects, so they may identify, locate, move among and reach for or grasp objects within it. The ARIA solution offers the potential to achieve things many take for granted, like walking

Image: ARIA Development Prototype.

1. International Agency for the Prevention of Blindness (IAPB).
2. The Economic Impact and Cost of Vision Loss in Australia (2010), Access Economics.
3. A Snapshot of Blindness and Low Vision Services in Australia (2015).

through a room and avoiding collisions, reaching for a door handle without fumbling or finding an empty seat. ARIA is already in daily use by completely blind users and, to date, has undergone more than 100 preliminary small-scale trials in a wide variety of everyday indoor and outdoor environments.

ARIA is being developed as a Class IIa (Therapeutic Goods Administration) and Class I (US Food and Drug Administration) medical device – an electronic vision aid – that delivers benefit to users, regardless of the underlying pathology of their vision loss.

Developed in close collaboration with the blind community, ARIA's design and functionality are direct distillations of the needs and desires expressed in hundreds of hours of ongoing consultations with leaders of peak blind organisations and members of the global blind community. The project's Australia-based team has expanded from the two founders in 2021 – at the time of receiving BioMedTech Horizons (BMTH) funding – to 18-people from 12 countries and consequently generates broad global perspectives. Over one third of ARIA Research's design team is blind, bringing deep lived experience and subject matter expertise to ARIA's engineering, training development, industrial design and overall company philosophy.

For Principal Clinical Trials Investigator at ARIA Research, Dr Lil Deverell, it is this commitment to creating a product by and for the blind community that sets the company apart. "Co-design runs through the culture of the company, which means plenty of power-share and 360-degree feedback," she said. "We're all keen to learn more about the blind world: what matters, what works and what is frustrating. We come from such different professional backgrounds; everyone is keen to learn, and everyone has something unique to offer the team."

In February 2021, the ARIA system exceeded the real-world performance of implanted bionic eye systems, which have been under development for more than 30 years but have yet to clear clinical trials and become a commercial product. ARIA is notable for directly addressing the challenges faced in commercialisation and scale adoption of implanted bionics.

The BMTH program allowed ARIA to develop its first functional prototypes that validated its solution with blind users, supported comprehensive design development and documentation resulting in the manufacture of its first devices to be used in a clinical trial. The prototypes validated safety measures appropriate to test under clinical trial conditions, explored system capabilities that demonstrate efficacy of proposed medical device claims, and tested the usability of the solution.

ARIA is Australian conceived, developed and owned, with a road map to manufacture, undertake clinical trials and launch to NDIS participants within three years. Thanks to the BMTH program, ARIA secured the capital and specialist resources needed to remain in Australia and move from proof of concept to prototype with a degree of validation. Without BMTH, the company would have been forced to move to California to attain the early-stage, high-risk capital needed to advance to the next stage. BMTH has allowed ARIA to significantly de-risk the venture, gather proof points necessary to gain investment interest as an Australian-based innovator focused on export potential, and for the executive team to gain experience in medical device commercialisation. The result is a successful and blossoming project that is growing significant value, a pathway for Australia-first clinical trials and manufacture, and in the process finding and growing mutual benefit to the medtech ecosystem that the team interacts with (including the development of the Human Augmentation Laboratory [HAL]).

With respect to medical devices, the project has established the potential of ARIA through its successful execution to date, with the team and technology capable of delivering the first commercially scalable solution to vision disability. This includes health economic development for compelling benefits to the launch market payer (NDIS); socialisation of the solution with leading eyecare professionals; preliminary validation of the ARIA system with potential payers in a key overseas market; and engagement of the state and federal policymakers on using ARIA as a practical case study, on contemporary medtech innovation commercialisation strategies.

Managing Director of World Access for the Blind Australia, Julee-Anne Bell, began with the project as a Research Partner (blind subject matter expert), and has since joined the company, leading blind community engagement and product development. "It's refreshing to work for a company with a true heart for their consumers," she said. "ARIA really wants to create a solution to a problem, and, with their deeply customer-centred attitude, they will change lives.

"So many tech companies create problems to solve rather than listening to the target consumer and working to solve the tough problems. ARIA is in the trenches with us, the blind users, and we are all working together to create something magnificent."

Julee-Anne Bell, Director, World Access for the Blind Australia (now, ARIA team member, leading community relations, and product/clinical trial codesign), sporting the ARIA Development Prototype.

Groundbreaking bionic eye system connects blind people to the world around them

PROJECT:
Bionic Vision Technologies Pty Ltd

THERAPEUTIC AREA:
Vision

BIONIC VISION TECHNOLOGIES

START DATE: 1 October 2020	TOTAL BMTH GRANT: $1,000,000
END DATE: 31 December 2022	TOTAL BMTH EXPENDITURE: $1,000,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $269,423
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $1,288,076
	TOTAL PROGRAM: $2,557,499

Jobs within the project budget	23
Number of trademark applications	1
Number of patent applications	1
Number of licenses	1
Number of new technology(ies) invented/progressed	3
Number of clinical trials commenced	2
Number of patients to clinical trial recruitment	4

Most people take the ability to find an empty chair in a crowded room for granted, or to know if a person is looking in your direction when you are talking to them.

For those suffering severe vision loss or blindness these are daily challenges that are known to result in increased isolation, lower rates of workforce participation, significant negative impact on mental health and a decrease in quality of life. For many blind people, restoring an ability to socially engage without embarrassment is identified as the most important factor of any potential therapy.

Inherited retinal dystrophies (IRDs) are the most common form of blindness in working-age adults in Australia[1] and globally[2], and with no cure or current treatment option there is a significant unmet need.

Retinitis pigmentosa (RP) is incurable and the most common form of IRD in working-age adults, affecting approximately 1.5 million people worldwide. The condition presents as an initial loss of night vision, leading to a further loss of peripheral vision and eventually, in most cases, severe vision loss or blindness. Age of onset can vary from childhood to adulthood, with a decline in visual field of approximately nine per cent per year.

Reports by Deloitte Access Economics for Retina International[3,4] show that RP contributed to an estimated economic burden of between $4 billion and $11 billion across North America, UK and Ireland in 2019. Wellbeing costs (the value attributed to loss of disability-adjusted life years), loss of productivity, informal carer costs and healthcare system costs were key contributors to the overall economic burden. Much of this cost is absorbed by the patient or their carer(s).

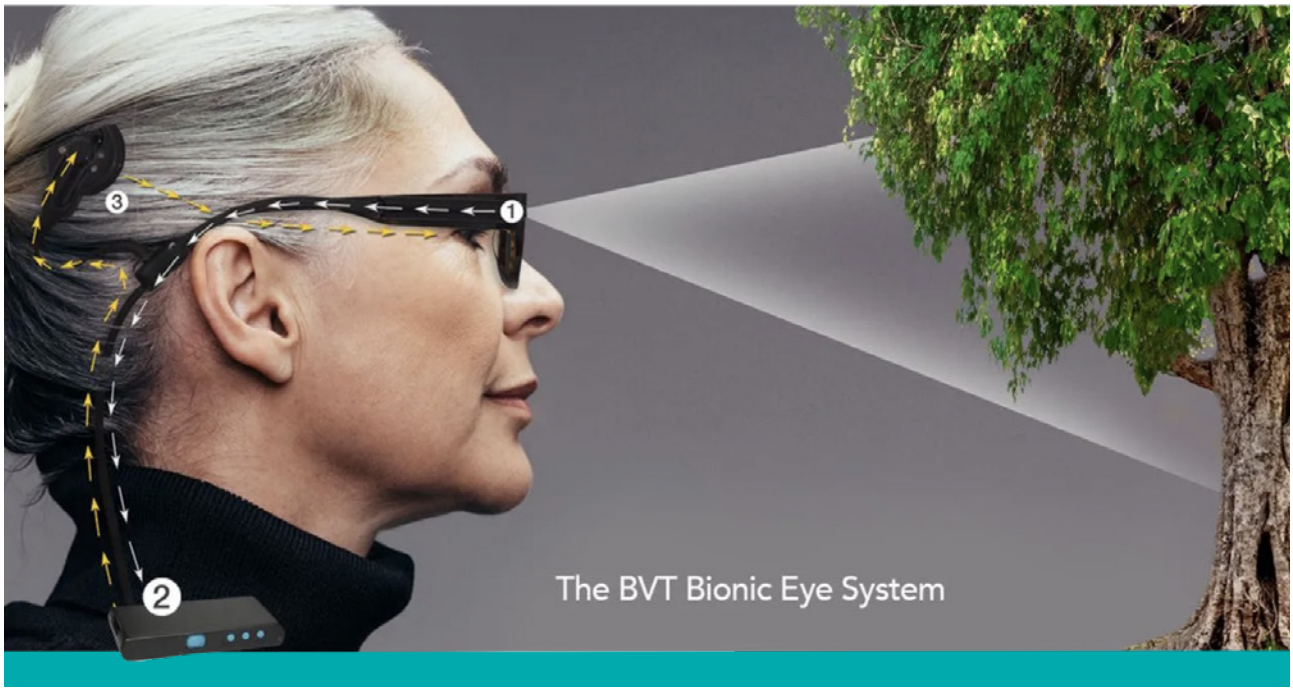
Hoping to reduce these costs and, more importantly, provide a system that helps patients living with RP to actively engage in real-world activities, Bionic Vision Technologies (BVT) and its research partners at the Centre for Eye Research Australia and the Bionics Institute have developed a pioneering bionic eye system.

The approach had been proven with seven patients safely receiving the transformational technology, that consists of eyeglasses fitted with cameras to capture images that are sent to a computational processing unit[5]. There, images are filtered and translated into electrical signals and conveyed to a retinal implant uniquely located at the back of the patient's retina, known as the suprachoroidal space. Electrodes within the implant stimulate remaining retinal cells to portray a sense of vision.

Building on the earlier generation bionic eye systems, and with support from BioMedTech Horizons (BMTH) funding, BVT set out to upgrade the system's headset, processing unit and algorithms, so it could be taken home by severely blind RP patients and tested in their day-to-day lives.

Their earlier patients indicated that they had a strong desire to identify the presence of people within their vicinity, so they could actively establish contact and engage in social interaction, rather than passively waiting for someone to approach and initiate contact – to connect to the world

1. Inherited retinal diseases are the most common cause of blindness in the working-age population in Australia, 2021.
2. Retinitis Pigmentosa: Burden of Disease and Current Unmet Needs, 2022.
3. The socioeconomic impact of inherited retinal dystrophies in the UK and Republic of Ireland, 2019.
4. IRD Cost of Illness Study: US & Canada.
5. Ten-year safety and stability results of a suprachoroidal retinal prosthesis, 2023.



around them. To address this, BVT developed a new algorithm that used artificial intelligence (AI) face detection and presented this to patients as a visual stimulus via the implant.

In addition, a simulation system was developed that allowed normally sighted individuals to experience what it would be like for someone with prosthetic vision. This system supported the rapid development of algorithms related to finding an empty chair, and an alternative depth algorithm for judging the distance to objects.

BVT designed and built its next generation take-home system which included a depth-sensing module, a sophisticated image processing chip and a battery integrated into a custom design with all the necessary peripheral components. Multiple rounds of testing and optimisation with Tekt Industries and Tricycle Developments addressed key design and manufacture issues, such as thermal management of the glasses and controller to ensure they stayed within safe limits for the patient wearing the device.

User testing demonstrated that patients were able to use the system to perform previously challenging tasks related to daily life and visual orientation. Being able to detect people's faces, especially family and friends, find an empty chair in a cafe or better judge the distance of objects has already had a positive impact on their quality of life, allowing them to live more independently and confidently.

Future enhancements will be built off this platform and likely come from software enhancements, AI learning, patient comfort and usability feedback. With robust clinical information, a product that can be manufactured to the required medical device standards and underpinned by extensive intellectual property, the BVT bionic eye is now proceeding to its next exciting phase – commercialisation within Australia and in markets worldwide.

An earlier retinal implant product, the Argus II, had been developed and approved for use, however, this is no longer available as the cost/benefit for the patients was marginal and the surgical approach introduced some complications. A key advantage of the approach by BVT is use of the suprachoroidal space for the implant, making the surgical process simpler to perform and possible to reverse, if required.

These early surgical and design decisions informed by clinicians contribute to BVT's bionic eye system being granted designation as a Breakthrough Device by the Food and Drug Administration (FDA) in the US. This recognition will help accelerate its development and, as in the hearing space for Cochlear, take another Australian company onto the global stage.

BVT's former Director (R&D) Hardware and Technology and Computer Vision Engineer, Sam Stefopoulos, said the BMTH project supported the company to progress its commercial system.

"Not only have we developed hardware, software and algorithms that are being used for our current clinical trial and can be used for future clinical trials, but we've also established important partnerships and business relationships that will make the path to commercialisation and future improvements a lot smoother," he said.

Once brought to market, the system has the potential to benefit thousands of people, added former Director (R&D) Software and Artificial Intelligence at BVT, Xerxes Battiwalla.

"This project has made significant strides in advancing the bionic eye system from the realm of research into directly addressing real-world patient needs," he said.

3D bioprinting device transforming treatment for skin injuries

PROJECT:
Inventia Life Science Pty Ltd

THERAPEUTIC AREA:
Skin Regeneration

INVENTIA LIFE SCIENCE

START DATE: 1 October 2020	TOTAL BMTH GRANT: $1,000,000
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $1,000,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $401,284
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $1,013,802
	TOTAL PROGRAM: $2,415,086

Jobs within the project budget	7
Number of trademark applications	1
Number of patent applications	2
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	7

Many people would have seen sci-fi movies with a robotic arm in an operating theatre treating a patient. That is the future Inventia has in store for patients experiencing skin trauma such as burns, cancer, and other chronic conditions such as ulcers.

Inadequate healing after skin trauma is a major health problem that presents a high risk of scarring, long-term debilitation and significant healthcare costs. The global wound care management market is expected to total $38.3 billion in 2030, and the tissue engineered skin substitutes segment of this market is expected to grow from $2 billion per annum in 2022 to almost $3 billion in 2033[1]. In Australia, the cost of managing wounds from ulcers was estimated to be $3.5 billion in 2018[2].

Australia's first bioprinting start-up, Inventia Life Science, has developed a device aiming to improve outcomes for the millions of skin trauma patients worldwide. Ligō is a world-first technology: a 3D bioprinting surgical robotic platform that prints a patient's own cells, embedded in an optimised matrix material, directly onto a wound site. This is expected to accelerate and improve healing after skin injury, with the potential to reduce the length of stay in hospital, reduce infection rates, reduce severity of scarring and reduce the likelihood of follow-up scar revision surgery.

The technology behind Ligō is a fundamentally novel approach to regenerative medicine that has the potential to enable a shift in clinical practice. It allows for unparalleled scalability across indications and clinical requirements – building towards creating a scar-free and fully functioning skin-replacement technology.

Image: Advanced prototype concept design.

1. Global Data. Wound Care Management, Tissue Engineered Skin Substitutes, 2023.
2. Chronic wounds in Australia: A systematic review of key epidemiological and clinical parameters, 2018.

Ligō is being developed as a collaboration between cell biology industry leaders Inventia, leading research groups at The University of Western Australia and University of Wollongong, and clinicians, including Professor Fiona Wood, a world-leading burns wound specialist and plastic and reconstructive surgeon.

Ligō utilises the company's core drop-on-demand bioprinting technology and adds to intellectual property (IP) from five different patent families, developed in partnership with the University of New South Wales, Professor Justin Gooding and Professor Maria Kavallaris. This core technology is making an impact in Inventia's RASTRUM instrument, used for accelerating drug discovery by enabling cells to be studied in 3D structures more similar to that found naturally in the human body. RASTRUM has already won the Good Design Award, Eureka Prize and Frontiers Research Award, and is currently in market and being sold to pharmaceutical and academic customers globally.

Developed under the subsidiary Inventia Skin and supported by BioMedTech Horizons (BMTH), Ligō is Inventia's first medical device product in development. The Ligō project team sought to take the platform from a functional proof-of-concept with initial preclinical studies to an advanced prototype ready for use in clinical trials.

The Ligō team iterated through at least seven *in vitro/in vivo* experimental cycles to investigate, screen and refine the system and biomaterial formulation, which was especially challenging when faced with a variable skin-wound environment in a completely novel system.

Through the project, Ligō progressed from a proof-of-concept to an advanced prototype that has de-risked the technical challenges of printing cells directly onto a patient's wound in a clinical setting, with strong preclinical validation data to support commencement of a first-in-human trial.

Inventia developed a novel proprietary disposable printhead for Ligō that enables the sub-millimetre precision required for *in situ* drop-on-demand bioprinting, while supporting an efficient and sterile clinical workflow.

The printhead was designed to be installed and removed in an operating theatre without tools, using a simple mechanism and integrated onto the medical device certified KUKA LBR Med robotic arm and built as a self-contained system, capable of being wheeled into the operating theatre by a single person. Professor Wood explained, "The robotic 3D printing system delivers a level of precision that facilitates regeneration in a way that we haven't seen previously by manual application."

In parallel, Inventia developed a biomaterials pipeline to refine the "bioink", the formulation containing growth factors and cells from the patient that were included in the disposable printheads to allow printing of specific cell types in a way to allow re-formation of the various layers of skin. With these formulations, the safety profile and surgical workflow was established across six preclinical studies and a final longer-term study. These validated that the printing process was completed in a clinically relevant timeframe, achieved sufficient engraftment of cells, cell retention and stimulation of regeneration to be suited for clinical application.

Existing methods of treatment and the current standard of medical care include using dermal matrix products followed by coverage with split thickness skin grafts at a follow up surgery once the neo-dermis is vascularised. Wounds treated using Ligō achieved complete re-epithellialisation and a configuration of the dermal network equivalent to that which results from dermal matrix products. The outcome is an optimised biomaterial formulation that can be translated to the first-in-human clinical trial.

In preparation for commencement of these human trials, work was also completed during the BMTH project to mature documentation under an ISO 13485-compliant Quality Management System (QMS), identify well-characterised primary and secondary clinical trial indications, and develop the clinical investigation protocol for the first-in-human study. Regulatory and commercial strategies were developed to map the path to clinic, including regulatory and reimbursement requirements in relevant markets.

The rapid progress in development of Ligō during the BMTH program was recognised through an invitation to MEDICA 2022 – one of the largest international medical device conferences – where Inventia featured in KUKA's 'Robotics in Healthcare Challenge'.

Future development of Ligō will involve completing a first-in-human study in early 2024, with further clinical studies to validate performance of the technology in clinical indications.

The funding provided by BMTH and progress achieved during the program contributed to Inventia raising $35 million as a Series B in 2021, for the acceleration of the delivery of RASTRUM to market and ongoing development of Ligō. Additionally, Inventia received $3.6 million from the NSW Medical Devices Fund to continue development of Ligō beyond this project.

CEO and Founder of Inventia, Dr Julio Ribeiro, said, "Once Ligō is released onto the market, burns, skin cancer, ulcer and other victims of skin damage and their clinicians will benefit from receiving a better standard of care. The options available today for patients with a deep burn or wound, such as skin grafts, still result in a lot of scarring," he said. "New treatment paradigms focus on regeneration – it's a new wave of medicine and there are now ways to do it accurately with Ligō, a world-first technology being developed right here in Australia."

Ligō Advanced Engineering (Beta) Prototype and the team that built it.
Photo Credit: Jason Leavens.

VR-based upper-limb rehabilitation system improves functional mobility for people recovering from stroke, brain or spinal cord injury

PROJECT:
Neuromersiv

THERAPEUTIC AREA:
Upper limb rehabilitation

NEUROMERSIV

START DATE: 1 October 2020	**TOTAL BMTH GRANT:** $994,000
END DATE: 31 March 2023	**TOTAL BMTH EXPENDITURE:** $994,000
STATUS: Completed	**TOTAL CASH CO-CONTRIBUTION:** $536,071
DELIVERABLES COMPLETED: 100 per cent	**TOTAL IN-KIND:** $105,000
	TOTAL PROGRAM: $1,635,071

Jobs within the project budget	11
Number of trademark applications	2
Number of patent applications	1
New products launched	1
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	5

Unlike many other forms of neurorehabilitation, standard therapy for upper limb rehabilitation has not progressed significantly in the past 30 years. As such, it is globally estimated that 66 per cent of stroke patients alone do not regain functional use of their paralysed upper limb. This results in limited independence with daily life activities, reduced participation in society, reduced quality of life, and a large economic and social burden on the healthcare system, caregivers, and families.

Deloitte Access Economics estimates that in 2020[1] there were 27,428 new strokes and 445,087 patients living with stroke in Australia, with a direct cost exceeding $6.2 billion and a further $26 billion in lost wellbeing.

To empower stroke, spinal cord and acquired brain injury survivors to regain their independence and improve their quality of life, Sydney-based medtech company Neuromersiv is developing a novel and data-driven approach to rehabilitation therapy.

Combining a next-generation commercial virtual reality (VR) headset with a hand and arm wearable device offering combined haptics and Functional Electrical Stimulation (FES) feedback, Neuromersiv's 'Ulysses' therapy system will represent a new technology-based therapy that is highly accessible, portable, and effective.

With the Ulysses VR upper-limb therapy system, patients can enjoy performing reward-based Activities of Daily Living (ADLs) in immersive, realistic environments. For example, users can practice activities such as washing hands, brushing teeth and cleaning the basin in an immersive virtual bathroom; making and drinking a cup of tea, chopping fruit and vegetables, or blending a smoothie in a virtual kitchen; and testing their fine motor skills by filling in a shape on a virtual whiteboard.

Image: The Ulysses VR upper-limb therapy system being tried out by a patient.

1. Deloitte Access Economics: Perspectives – The economic impact of stroke in Australia.

Each ADL task has been clinically designed according to recognised standard therapies with the goal to enhance engagement, motor recovery and a sense of achievement. All tasks have been carefully integrated with a unique 'avatar system' that gently guides the user to successfully perform tasks using text and auditory prompts.

Supported by BioMedTech Horizons (BMTH) funding, Neuromersiv aimed to determine the technical design, commercial viability, and clinical efficacy of its VR upper-limb therapy system. As part of these key objectives, the company aimed to achieve significant advancement as a commercial organisation, including developing a robust intellectual property (IP) strategy, business model and venture investment readiness.

During the project, Neuromersiv conducted a pilot clinical trial, in which five participants completed a total of 15 sessions each using early prototypes of the Ulysses system over the course of a five-week study. The results were highly positive: three out of five participants demonstrated improved functional mobility, as measured by the Motor Assessment Scale, while four out of five participants showed improved functional mobility, as measured by the Fugl-Meyer Assessment. These two tests are the recognised standard clinical tests for testing different elements of motor function in stroke patients.

Even for an early-stage design and preliminary trial, likability and comfort scores were extremely high at 80 per cent and 79 per cent, respectively. This feedback and the remarkably high rate of users indicating they would like to keep using the product, 76 per cent, were highly encouraging for Neuromersiv.

With the beta-prototype now designed and built based on users' inputs from the alpha trial, extensive health economics insights and deepening understanding of clinician needs from a global set of opinion leaders, Neuromersiv is now gearing up for its next stage of growth. Overall, it has acquired the confidence to develop and execute a successful pivotal clinical trial directly as a result of undertaking the alpha prototype feasibility trial during the BMTH project.

The BMTH project was also essential in helping Neuromersiv achieve critical commercialisation milestones, said the company's CEO, Anshul Dayal.

"The BioMedTech Horizons program has been instrumental in not only helping us successfully develop our groundbreaking technology, but also in achieving pivotal commercialisation milestones that mean Ulysses VR, Neuromersiv's first product, is now available for sale in Australia and the UK having received regulatory approval," he explained.

The company has also now established a clear pathway for first sales in India. Furthermore, the project has created significant intangible asset wealth through the design and development of pioneering new technology, that will provide the company with greater assurance of the capital raising pathway into the future. Likewise, the company has strengthened its IP position with trademark filings for both the 'Neuromersiv' company brand name and 'Ulysses' product brand name in Australia.

A planned pivotal clinical trial with a sample size of approximately 60 subjects will endeavour to provide greater evidence as to the efficacy of the therapy system to improve quality of life, the cost savings to be made by the health system and the increased productivity of using the system. Subsequently, this will also endeavour to mount a strong case for multiple reimbursement pathways in Australia and in foreign markets.

Enhancing therapy adoption by offering multiple clinical-grade rehabilitation modalities into one portable, easy-to-use system will allow more patients access to regular and effective therapy in clinical environments, or in their homes, while being remotely managed in line with the current trend towards telehealth adoption. Users will be more motivated to undertake therapy, due to the system's enjoyable, motivating and practical 'daily living' skill re-acquisition focus. This will empower stroke, brain and spinal cord injury survivors to reach their rehabilitation goals sooner, compared to conventional upper limb therapy alone.

Having seen the therapy system in action with patients, Sara Neaves, a physiotherapist and Clinical Lead at Askham Rehab in the UK, said: "What Ulysses offers on top of the functional learning elements, is to use gamified therapy to engage and motivate the patient to continue to practice, while engaging them in both physical and cognitive rehabilitation. I think the system holds great benefit in giving the patient the ability to maintain a regular therapy protocol, which is critical particularly during the subacute stage of stroke."

Likewise, patients at Sydney's Enable Exercise have engaged with the device as part of their rehabilitation and have enjoyed a range of benefits, said the company's CEO, Kwan Leung.

"We have been able to witness a remarkable level of client engagement using the Ulysses virtual reality-based rehabilitation," he said. "The innovative approach has effectively challenged our clients' functional capacity and developed promising outcomes in their rehabilitation journey."

Neuromersiv gained a wealth of knowledge and experience from working with all its partners on the BMTH project, especially with our clinical research partners, designers and engineers, and through the development and global regulatory requirements. Neuromersiv is committed to a commercialisation strategy that continues to base operations in Australia, creating job opportunities and contributing to greater workforce skill and knowledge acquisition.

From a technical perspective, the project represents the world-first development of a wearable device that administers FES and haptic feedback based on interactions in VR environments. To the best of Neuromersiv's knowledge, it is the first time all three modalities have been combined into one integrated therapy system. While only the VR component is commercially available at this time, using all three components together will be the focus of the company's next trial, and subsequent regulatory approval.

DIAGNOSTICS AND MONITORING DEVICES

IN THIS SECTION:

- Advanced Genetic Diagnostics
- Atmo Biosciences
- Cortical Dynamics
- Cyban
- Enlighten Imaging
- Ferronova
- IntelliDesign
- Miniprobes
- OncoRes Medical
- Optiscan
- Proteomics International
- ResusRight
- Seer Medical – Epilepsy Forecasting
- Seer Medical – Cardiac Monitoring
- VitalTrace
- WearOptimo
- ZiP Diagnostics

World-first genetic testing to identify risk of cardiovascular disease

PROJECT:
Advanced Genetic Diagnostics Pty Ltd

THERAPEUTIC AREA:
Cardiovascular

AGD

START DATE: 1 April 2020	TOTAL BMTH GRANT: $998,802
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $967,208
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $0
DELIVERABLES COMPLETED: 98 per cent	TOTAL IN-KIND: $561,165
	TOTAL PROGRAM: $1,528,373

Jobs within the project budget	4
Number of new technology(ies) invented/progressed	9

Cardiovascular disease (CVD) accounts for 12 per cent of the total burden of disease in Australia, ranking third behind all cancers and musculoskeletal conditions. In 2020, CVD was the underlying cause of 25 per cent of all deaths and the cost to the healthcare system exceeded $12.5 billion[1]. New ways to identify people at risk would provide an enormous opportunity to improve the health and welfare of Australians.

Stroke occurs when a blood vessel supplying blood to the brain becomes blocked or ruptures and is one of the five leading causes of death in Australia. Coronary Heart Disease (CHD) occurs when there is a narrowing or blockage in the vessels that supply blood to the heart. It can result in angina and heart attack and was the leading single cause of death in Australia in 2020.

Currently, identification of CVD risk is based on various clinical factors such as age, high blood pressure, smoking status and cholesterol levels. But by the time these signs appear, the processes leading to CVD are underway, meaning damage to the body has already occurred and can be difficult to reverse.

Advanced Genetic Diagnostics (AGD) is working to identify CVD risk sooner than current methods allow, to enable earlier management and potentially disease prevention.

Based in Western Australia, AGD is applying its breakthrough genetic technology to develop tests that can predict a person's individual risk of suffering various cardiovascular conditions. These genetic tests can identify people at risk of disease years – and even decades – earlier than current practices, because they rely only on an individual's genetics with no other clinical risk factors needed.

Image: AGD is working to identify CVD risk sooner than current methods allow.

1. Data from the Australian Institute of Health and Welfare.

Family history plays a role in CVD risk, meaning that it has a genetic basis. In fact, CVD is known as a complex genetic disease, in which multiple genetic variants interact with each other and with environmental factors to cause disease. Genetic variants are inherited differences between individuals in a population, with the most common type of variant known as a single nucleotide polymorphism (SNP). Each SNP is a difference in one single 'letter' of the billions that make up a person's genetic inheritance. Most SNPs have no individual impact on disease risk. AGD's novel method finds groups of SNPs whose interactions bring about diseases. The company is the first in the world to design and use these methods, and to apply them to CVD.

Supported by the BioMedTech Horizons (BMTH) program, AGD set out to create and confirm genetic tests that could identify people at highest risk of the most common CVDs: coronary atherosclerosis (CAD), heart failure (HF), heart attack (also known as myocardial infarction or [MI]) stroke and angina. The team combined its expertise with leading cardiologists at the Baker Heart and Diabetes Institute, the Harry Perkins Institute of Medical Research and Fiona Stanley Hospital to recruit patients and test their DNA.

When designing the project, AGD assigned an expected 4,300 samples from the Baker Institute Biobank with known clinical outcomes as its training set, and 2,073 validation samples from the Fiona Stanley Hospital, the Carotid Ultrasound in Patients with Ischaemic Heart Disease (CUPID) study conducted by The University of Western Australia, and the Diabetes Clinic Survey (DSC) run by Royal Perth Hospital.

Using genetic information from these samples, AGD not only succeeded in creating genetic tests for the four main CVDs (MI, CAD, HF and stroke), but also showed that its genetic tests had higher predictive power than the most used medical tests. AGD validated each of its genetics tests in at least three other independent datasets, confirming that they were successful in assigning risk to patients.

AGD is now focused on commercialising its prognostic test and plans to obtain Therapeutic Goods Administration (TGA) regulatory approval for usage in the Australian market. The team estimates that the project will achieve better patient outcomes as early as the first year after gaining TGA approval.

AGD's goal is to allow members of the public, and the doctors who treat them, to know their risk of disease, so they can take proactive changes to limit the progression of disease by modifying other known risk factors, either by lifestyle changes or appropriate medical treatment.

Many people stand to gain from this non-invasive, inexpensive and fast procedure. First, those at high risk of CVD could be managed with treatments (pharmacological and/or lifestyle) to prevent emergence of symptoms; or, where these are already present, reduce them by more targeted treatment. Second, identifying people with low risk and without signs of disease is also important, as this can avoid unwarranted intervention, avoiding stress as well as costs and possible side effects of potentially unnecessary medications. Thus, the tests could improve quality of life for both high- and low-risk groups. It could also ease demand on Australia's health system.

Delaying or even preventing just 10 per cent of cases could save Australia's healthcare system over $1 billion every year. In the longer term, treatments could be developed against the molecular pathways of disease that AGD has identified.

According to AGD's Managing Director, Professor Grant Morahan, the BMTH-funded project has advanced the team's innovative technology on the pathway towards commercialisation.

"The support from MTPConnect allowed us to develop tests that can identify people at highest risk of having a heart attack, a stroke, or developing heart failure," he said. "These tests require only a small saliva sample yet are more powerful than existing clinical tests in predicting likelihood of disease in the future. They have the potential to save lives and save the Australian economy billions of dollars each year."

The BMTH project allowed AGD to support employment of three people at the Harry Perkins Institute of Medical Research and one person at Fiona Stanley Hospital. It also streamlined the company's test development process and improved outcomes in terms of faster development of tests and their improved power.

Importantly, AGD can now use the knowledge gained from the BMTH project to develop tests that predict a person's risk of other diseases, such as diabetic complications or dementia. Others in the research community are aware of the team's work and are collaborating to investigate how these tests can impact their own research projects.

For now, in terms of its impact on CVD sufferers, once TGA approval is secured, AGD's genetic tests have the potential to change – and save – lives, said Director and Secretary at AGD, William Coleman AM. He added: "The results AGD obtained from this program could make personalised healthcare for heart diseases a reality."

Ingestible capsule set to revolutionise gut health diagnosis

PROJECT:
Atmo Biosciences

THERAPEUTIC AREA:
Gut health

Atmo Biosciences was funded twice within the BMTH program. Details of each project below:

Round 3 funding

START DATE: 1 October 2020	TOTAL BMTH GRANT: $620,000
END DATE: 31 March 2022	TOTAL BMTH EXPENDITURE: $620,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $844,411
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $317,001
	TOTAL PROGRAM: $1,781,412

Round 4 funding

START DATE: 6 May 2022	TOTAL BMTH GRANT: $343,310
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $343,310
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $676,403
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $0
	TOTAL PROGRAM: $1,019,713

	Round 3/Round 4
Jobs within the project budget	13/14
Number of trademark applications	1/0
Number of patent applications	2/3
Number of new technology(ies) invented/progressed	1/1
Number of clinical trials commenced	2/1
Number of patients to clinical trial recruitment	126/260

Many individuals worldwide suffer from gastrointestinal (GI) disorders, which incur debilitating symptoms, significant morbidity and high healthcare costs.

Irritable bowel syndrome (IBS), for example, affects 25 to 45 million people in the US and two to five million people in Australia[1,2]. Other common disorders include motility abnormalities, small intestinal bacterial overgrowth (SIBO), which is often associated with IBS, and inflammatory bowel disease (IBD).

Yet such conditions often remain undiagnosed and untreated. Gases are important biomarkers of disease, dysfunction and dysbiosis, but current diagnostic methods for GI disorders are normally highly invasive or rely on subjective symptomatology and questionnaires. Diagnostic methods such as aspiration, biopsy, endoscopy, motility pills, imaging pills and breath testing all have limitations. Even with these limitations, the current SIBO diagnostics market is growing rapidly with increased awareness and is estimated to reach US$194 million in 2028[3].

Gas sensing from within the gut offers an accurate method for diagnosing common GI conditions, but to date there have been no convenient tools available to clinicians.

Seeking to create an accurate, cost-effective and user-friendly diagnostic solution for common GI disorders, Melbourne-based biotech company Atmo Biosciences is developing the world's first single-use, ingestible motility and gas-sensing capsule. While previous ingestible pills had been developed and are useful for motility assessment only, they do not offer the same breadth of measurement and diagnostic capability as the Atmo Biosciences solution.

1. International Foundation for Gastrointestinal Disorders, 'IBS Facts and Statistics'.
2. Dietitians Australia, Irritable Bowel Syndrome.
3. Global Small Intestinal Bacterial Overgrowth Diagnostics Market Report 2021.

The capsule, when swallowed, can electronically report important data about the human GI system by detecting gases in real time from known locations within the gut. Clinicians can use these biomarkers to diagnose conditions such as SIBO, and consequently provide targeted treatment to patients – which, in turn, leads to earlier relief of symptoms and reduced healthcare costs.

The Atmo capsule leverages technology initially licensed from RMIT University in 2018 and has been in development since. Measurement of motility in transit was the first test case and that product was substantially developed but still under clinical trial when they received BioMedTech Horizons (BMTH) funding in 2020 through BMTH Round 3. With this new funding Atmo set out to demonstrate proof of concept for its gas-sensing technology to be incorporated into the same capsule, and to develop algorithms to correlate gas composition measured from the capsule to gut health issues, including IBS and SIBO.

Atmo's goals were to scale up the manufacturing process to ensure production of capsules for testing purposes; evaluate and select a diagnosis method; develop machine learning and artificial intelligence (AI) tools; analyse signals from the capsule; and run a clinical study to assess the diagnostic method.

Atmo completed the planned clinical studies validating gas sensing in the capsule during transit through the gut with IBS with more than 120 capsules administered. The team benchmarked its diagnostic criterion against the two existing diagnostic methods: hydrogen breath testing and the gold-standard jejunal aspirate. The pilot-study results showed a good correlation to the latter, while emphasising the poor outcomes offered by breath testing.

According to Atmo CEO, Malcolm Hebblewhite, the BMTH project enabled the team to take its first steps towards identifying a large target group of patients living with SIBO globally.

"This evidence helps to strengthen our investment thesis to target conditions with unmet clinical needs such as GI motility disorders and SIBO," he said. "This program has allowed us to accelerate the development of our technology in a short period of time. The project has also increased our engagement with global key opinion leaders and clinicians, which facilitated the establishment of an international medical advisory committee."

Atmo scaled up manufacturing from 150 capsules per year to 500, to support the needs of the subsequent testing and validation studies and achieved ISO 13485 accreditation at its facility in Melbourne to ensure it could manufacture the product for clinical use. This produced flow-on benefits to other aspects of company activities, including the ability to engage with functional food companies to investigate gut gas composition upon change in diet.

In May 2022, Atmo received additional BMTH funding through the fourth round of the program with the aim to have all technical requirements in place to initiate the final clinical validation – a pivotal trial – in preparation for regulatory approval and market launch.

This project resulted in the successful completion of product verification and significant progress towards regulatory and commercial readiness. Key achievements included IEC 60601 certification for electrical safety, ISO 10993 certification for biocompatibility, along with the preparation of a Human Factors Summative Evaluation Protocol. Hardware readiness was also achieved, and the final labelling and packaging were designed, critical achievements in commercialising a medical device.

Atmo commenced participant recruitment in a multi-site pivotal study which will support an initial US Food and Drug Administration (FDA) submission around the use of the Atmo Gas Capsule to assess GI transit, which is relevant to the assessment of motility disorders such as gastroparesis and slow transit constipation.

Through the two projects, the company significantly strengthened its intellectual property (IP) position to support its commercial plan. One provisional patent moved to PCT stage, and three more provisional patent applications were lodged. The European Patent Office and IP Australia granted key patents that will provide coverage until 2037. The US Patent and Trademark Office also granted a patent for Atmo's ingestible gas-sensor capsule.

Hebblewhite said: "The patent is an important cornerstone of Atmo's IP strategy for protection of the Atmo Gas Capsule System and the Atmo future product pipeline. Grant of the patent in the US is particularly satisfying, as it supports our commercial plans, which prioritise this large and important market."

Data generated from the BMTH-supported activities has supported Atmo to significantly advance its commercial goals, including raising $9.6 million in private capital and raising $8 million in a fully subscribed Series B funding round.

Successful completion of the project activities has taken Atmo several steps closer to market entry, said Atmo's Head of Clinical Affairs, Dr Kyle Berean.

"It has been an incredible journey from our initial research on the underlying capsule technology to these final stages of product development," he said. "During this project, we have taken many crucial steps forward towards realising our goals of addressing unmet clinical needs and improving quality of life for many patients suffering from common gut disorders."

Atmo's Head of Commercial, Sue Dafnias, said support from the BMTH program has been critical in achieving several key milestones in the final verification, validation and commercialisation of the Atmo Gas Capsule.

"The successful completion of this project has facilitated product readiness for our pivotal study, which will ultimately support an initial FDA 510(k) regulatory submission to aid the diagnosis of gastroparesis and slow transit constipation," she said. "These are both debilitating gastrointestinal motility disorders impacting millions of individuals worldwide."

Image: Atmo Biosciences is developing the world's first single-use, ingestible motility and gas-sensing capsule.

Better understanding of the brain's response to anaesthesia to improve patient outcomes

PROJECT:
Cortical Dynamics Ltd

THERAPEUTIC AREA:
Brain

CORTICAL DYNAMICS
ADVANCED BRAIN MONITORING

START DATE: 6 May 2022	TOTAL BMTH GRANT: $137,000
END DATE: 30 October 2022	TOTAL BMTH EXPENDITURE: $137,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $174,762
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $0
	TOTAL PROGRAM: $311,762

Jobs within the project budget	3
Number of trademark applications	1
Number of patent applications	3
Number of new technology(ies) invented/progressed	2

In the USA alone, up to 43,000 patients per year remain aware of their surroundings during surgery while under general anaesthetic. Anaesthetists will try to minimise the occurrence of this highly traumatic event by evaluating response to various stimuli, monitoring brain activity, and using combination drugs. Overdosing of anaesthetic can sometimes result during surgery which brings its own set of complications and impacts on the patient, as well as increasing the cost of healthcare. In the US, post-operative delirium is the most common complication of hospitalisation among people aged over 65, and the cost of severe post-operative delirium resulting from elective surgery has been estimated at $32.9 billion USD annually[1] and rivals the cost of diabetes and cardiovascular disease.

Cortical Dynamics, a medical device technology company headquartered in Western Australia, has developed a next-generation medical brain monitor. Its core product, the Brain Anaesthesia Response Monitor (BARM™), is used in surgical theatres to provide anaesthesiologists with an objective measure of the depth of anaesthesia and, for the first time, an objective measure of pain – enabling them to keep patients optimally anaesthetised and pain free.

The depth of anaesthesia or composite cortical state (CCS) capable BARM™ has been available for limited clinical use for a few years. However, the Cortical Input (CI) pain response is a new measure developed by Cortical Dynamics planned for use in the second-generation of BARM™ post trials, and regulatory approval is attracting significant global interest.

Image: Cortical Dynamics deep learning app and cloud-based analytical tool aims to improve patient outcomes.

1. One-Year Medicare Costs Associated with Delirium in Older Patients Undergoing Major Elective Surgery.

The BARM™ improves on currently used electroencephalogram (EEG) technologies by incorporating the latest advances in how the brain's rhythmic electrical activity, the EEG, is produced. The approach is fundamentally different from all other devices currently available in the market, in that its underlying algorithm produces an EEG index that is directly related to the physiological state of the patient's brain, meaning that anaesthesiologists can offer improved patient-specific treatment.

Each time the BARM™ is used, highly valuable data is generated, which can be a great source of information to fuel better understanding of a patient's brain activity when under general anaesthetic. These insights could potentially assist clinicians not only to monitor brain anaesthesia response trends, but also enable them to understand, generate prognosis and gain early warnings of potential risks associated with various types of anomalies, by learning from the experiences of previously treated patients. However, the BARM™ data is currently not captured in any system to store, compute and further analyse for enhanced decision-making.

Supported by BioMedTech Horizons (BMTH) funding, Cortical Dynamics set out to leverage this opportunity, developing a unique and specific deep learning app and cloud-based analytic tool focused on anaesthesia that would help clinicians to better manage their patients during an operation and therefore lower interoperative and post-operative issues. Through the project, the team partnered with Lorgan – an Australian-based artificial Intelligence (AI), Internet of Things (IoT) and digital organisation – to implement a rich brain-monitoring data lake.

The platform built as part of this project, Cortical Dynamics Analytics (CORDYAN™), consists of two main components: a mobile app, which captures the patient data required to generate analytics, insights and machine-learning models, and a data visualisation and analysis 'self-service' toolkit for healthcare professionals to analyse patient data, BARM™ data and associated analytics and insights.

Multiple interviews, reviews, evaluations and brainstorming sessions were held with practising anaesthesiologists, clinical nurses and key opinion leaders from all over the world. Multiple influencing factors covering both the clinical and economic side of the anaesthesia-based treatments offered to patients were discovered and analysed. Eighty attributes that play an important role during the anaesthesia procedures performed on patients were reviewed, with all incorporated into a 'deep dive' mobile app. The most important factors were prioritised into a simplified 'light' version of the user interface which matches the needs of the clinicians.

As a result of the project, the foundation of the CORDYAN™ platform was successfully developed and tested with clinician feedback. Two new permanent roles at Cortical Dynamics were created: a Project Manager and a Data Scientist, who will continue to work on the product. As a result of the BMTH funding, Cortical Dynamics was able to secure additional direct private investment.

Cortical Dynamics CEO Ashley Zimpel said that the developments made under the BMTH project have been critical to the team's planned clinical trial for pain monitoring and eventual commercial rollout.

"For some time now, it has been our objective to build a deep learning and AI analytical capacity associated with our BARM™ brain monitoring technology to help us better understand the patient experience and help clinicians to provide better outcomes for patients undergoing a general anaesthetic," he explained. "The BMTH funding has enabled us to achieve this."

Looking ahead, the new CORDYAN™ analytical capacity will lay the foundation for Cortical Dynamics to develop second- and third-generation BARM™ monitors and allow the team to carry out far more extensive and comprehensive analytics of the CI or pain index, it has developed.

The CORDYAN project will give Cortical Dynamics major points of differentiation to its competitors when it begins the commercial phase of its technologies. According to the company's Chief Technical Officer, Nicholas Sinclair, the technology is poised to provide the sector with a completely new and unique analytic tool that can make a positive difference in helping clinicians achieve better patient outcomes.

"The deep learning capacity we have developed focused on anaesthesia will have extensive applications for clinicians, researchers, the conducting of clinical trials and hospitals in a way not available before in our view," he said.

The World Health Organization estimates there are 312 million major surgical procedures each year, with many requiring general anaesthetics. Given these very large numbers of patients, this project will have significant implications for patients, hospitals and the healthcare system. As a deep learning system, CORDYAN™ will be a dynamic tool, and will also provide numerous points of commercial and research interest synergies from collaborators across the industry, on a global scale.

For now, new datasets and information relating to anaesthesia will continuously be collated from future operations, while data from existing and historical BARM™ datasets will be reassessed. Cortical Dynamics will continue this work as these datasets are compiled and added to the data lake – eventually building out a very extensive database that will enable a much more comprehensive understanding of the impact of anaesthetic drugs on patients.

World-first non-invasive brain pulse monitor helping clinicians assess brain injuries

PROJECT:
Cyban Pty Ltd

THERAPEUTIC AREA:
Brain

CYBAN

START DATE: 1 April 2020	TOTAL BMTH GRANT: $960,000
END DATE: 31 October 2022	TOTAL BMTH EXPENDITURE: $960,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $750,679
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $0
	TOTAL PROGRAM: $1,710,679

Jobs within the project budget	15
Number of patent applications	10
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	4
Number of clinical trials commenced	7
Number of patients to clinical trial recruitment	104

The incidence of traumatic brain injury (TBI) is rising globally, showing a 28 per cent increase since 2,000[1], and a 50 per cent mortality rate with 67 per cent of survivors suffering from long-term disability. It has the second highest economic cost of any health condition. From 2013-15, TBI accounted for 23,445 hospital admissions, 2,605 admissions to Intensive Care Units (ICUs) and 856 deaths in Australia, with total costs estimated at $8.6 billion annually[2,3].

Patients with an acquired brain injury (ABI) or TBI often develop a secondary brain injury, which can lead to severe neurological impairment or death. Secondary brain injuries develop in five per cent of mild[4], 10.8 per cent of moderate and 55 per cent of severe TBI cases[5] and in 47 per cent of these cases the cause is attributed to brain hypoxia, whereby brain cells die within minutes if deprived of sufficient oxygen[5].

When brain hypoxia is detected, treatments to maintain adequate brain oxygen levels and prevent secondary brain injury are straightforward and effective. Evidence confirms that with early detection and treatment of hypoxia, patient outcomes are improved, and the risk of long-term disability and death is reduced.

The existing standard of care for brain oxygen monitoring involves physical examination and often the surgical insertion of monitoring probes into the brain through the skull. Physical exams are subjective and point-in-time assessments, and the use of invasive monitoring, is complex, costly and risks further

Image: Cyban's next generation brain pulse monitor.

1. Institute for Health Metrics and Evaluation, Global Burden of Disease 2019
2. Australian Institute of Health and Welfare, Health service use for patients with traumatic brain injury. 2021, AIHW: Canberra.
3. Limited, A.E.P., The economic cost of spinal cord injury and traumatic brain injury in Australia. 2009.
4. Chojak, R., et al., Deterioration After Mild Traumatic Brain Injury: A Single-Center Experience With Cost Analysis. Front Neurol, 2021. 12: p. 588429.
5. Maloney-Wilensky, E., et al., Brain tissue oxygen and outcome after severe traumatic brain injury: a systematic review. Crit Care Med, 2009. 37(6): p. 2057-63.

injury; as such, only 10 per cent of patients with TBI receive brain oxygen monitoring, and even those are only monitored for a relatively short part of the at-risk period.

Frustrated by the limitations of existing techniques, Dr Barry Dixon – a practicing ICU Clinician – founded Cyban to create a next-generation brain pulse monitor that would advance the treatment of brain injuries by accelerating detection, diagnosis accuracy and treatment times.

Supported by BioMedTech Horizons (BMTH) program funding, the Melbourne-based company set out to develop and prove the efficacy of its Brain Pulse Monitor, designed for non-invasive brain oxygen and intracranial pressure monitoring of acutely injured and critically ill patients in emergency departments (EDs) and ICUs, or those at risk of a brain injury in operating theatres.

Using a proprietary sensor design, Cyban's innovative technology is placed onto the head and measures through the skin and skull, providing access to the brain's unique pulsatile waveform, which is then used to provide a measure of brain blood oxygen, intracranial pressure (ICP) and cerebral perfusion. The goal of the BMTH project was to demonstrate via clinical trial that the sensor and algorithms correlate with the current gold standard of invasive monitoring used in ICUs, and to undertake significant commercialisation planning.

Cyban's Chief Scientific Officer and Principal Investigator, Dr Barry Dixon, said the project achieved all its objectives.

"We were able to demonstrate a strong signal from the brain pulse monitor, that enabled us to non-invasively measure intracranial pressure reliably from patients with acute brain injury," he said.

As part of the project, an ABI study of critically ill patients at St Vincent's Hospital Melbourne was completed. It showed that ICP, as estimated via the Brain Pulse Monitor, correlated to the gold standard invasive intracranial pressure. The positive results from this study led to the initiation of a study with a similar design, which will be undertaken with a key opinion leader at Cleveland Clinic in the US.

An acute hypoxia study involving 21 healthy volunteers was likewise completed at Duke University in the US. The objective of this pivotal study (for clearance by the US Food and Drug Administration [FDA]) was to demonstrate that oxygen levels, as estimated by the BPOx device, correlated with venous and arterial blood gas samples. The results were positive, and correlation was shown paving the way to premarket clearance and extended clinical trials.

Armed with a robust clinical dataset, health economic case and market research from 230 anaesthesiologists, neurosurgeons, neurologists, neuro-intensivists, nurses and nurse practitioners in the US, Cyban validated that its first-generation product will address the key needs of clinicians, giving a clear path for its product roadmap and commercial launch.

During the BMTH project, Cyban substantially progressed regulatory, market access and IP activities, laying the foundation to successfully close a Series A capital raise in July 2022 exceeding the $5 million target.

At the time of the project's completion, the technology had progressed from Technology Readiness Level (TRL) 4 to TRL 7, with TRL 9 and product launch anticipated by mid-2024. In January 2022, Cyban's PCT/AU2020/050695 moved to national phase registration.

Once commercialised, Cyban's simple, low-cost and non-invasive method of brain oxygen monitoring will meet a major unmet clinical need – allowing all patients with acquired or traumatic brain injury, or those at risk of a brain injury, to be monitored using a continuous and non-invasive alternative.

This technology represents a world first. No solution exists today that can capture a pulsatile brain signal non-invasively and, therefore, address the key needs of clinicians, that is, to enable early detection of patient complications from brain hypoxia and early intervention, resulting in improved patient outcomes and reduced cost of patient care.

With Brain Pulse Monitoring throughout the care pathway, comprehensive prevention of brain hypoxia is possible, and Cyban estimates that long-term disability and death would be reduced by ~10 per cent, equating to ~$427 million AUD annually in the Australian market alone. The potential impact on healthcare outcomes is compelling and the reduction in the cost of TBI would far exceed the cost of implementation.

Significant export income and investment is anticipated – meaning many patients could benefit from the company's proprietary pulse oximetry products and services globally.

Excitingly, Cyban technology will provide multiple opportunities for growth over time, including new user segments and geographies for brain monitoring and the monitoring of new large organ indications, said ICU Clinical Research Manager at Cyban, Dr Elliot Teo.

"We have demonstrated this technology can benefit many more patients than first thought; expanding from the ICU into the operating theatre, emergency department, interventional radiology, and outpatient clinics," he said. "It's really made it clear to me that we are just scratching the surface."

Advanced hyperspectral retinal imaging to transform the diagnosis of eye and central nervous system diseases

PROJECT:
Enlighten Imaging

THERAPEUTIC AREA:
Vision

enlighten imaging

START DATE: 1 April 2020	TOTAL BMTH GRANT: $1,000,000
END DATE: 30 September 2022	TOTAL BMTH EXPENDITURE: $1,000,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $74,317
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $1,650,000
	TOTAL PROGRAM: $2,724,317

Number of trademark applications	1
Number of patent applications	2
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	2

Vision impairment and blindness are major public health issues in Australia, with over 13 million people experiencing at least one long-term vision disorder in 2017–18[1]. Older people are particularly at risk; about 444,400 people aged 55 or older (almost 10 per cent of that age group) are visually impaired. By 2050, the prevalence of vision loss in people aged greater than 50 is forecast to exceed one million[2]. By 2050, vision loss will impact 7.5 per cent of the entire population.

The major causes of visual impairment are age-related macular degeneration (AMD), cataract, glaucoma, and diabetic retinopathy, and together with uncorrected refractive error, they contribute to over 90 per cent of visual impairment among older Australians. Early detection of these and other eye and central nervous system diseases remain a challenge, as patients often have no symptoms.

Imaging the retina, the inner layer of the eye, presents two diagnostic opportunities, firstly the diagnosis of a range of ocular conditions, as well as the identification of biomarkers of neurological conditions, including Alzheimer's disease. Early detection of retinal and central nervous system diseases is important to enable treatment before irreversible impairment occurs.

Hyperspectral imaging, imaging across many discrete wavelengths simultaneously in every pixel, is opening new windows into the diagnosis of both vision and central nervous system conditions.

Enlighten Imaging – a medical technology company spun-out of the Centre for Eye Research Australia – has developed a novel eye imaging method inspired by NASA satellite technology. Instead of imaging the eye with a single white flash of light, the company has developed a camera

Image: Enlighten Imaging's state-of-the-art hyperspectral retinal imaging camera.

1. Australian Institute of Health and Welfare.
2. Future burden of vision loss in Australia: Projections from the National Eye Health Survey.

capable of rapidly capturing many images of the eye with different colours (wavelengths) of light. The resulting 'cube' of image data is interrogated with machine learning algorithms to detect signs of disease that cannot be seen using other imaging methods. This 'hyperspectral' imaging platform is poised to transform the detection of a wide range of retinal and brain diseases including diabetic retinopathy, age-related macular degeneration, glaucoma, and Alzheimer's disease.

With the support of BioMedTech Horizons (BMTH) program funding, Enlighten Imaging set out to transform its prototype hyperspectral retinal camera into a regulated medical device for advanced retinal imaging. While there is one other hyperspectral retinal imaging camera on the market, its substantial size and cost, coupled with the requirement for pupil dilating eye drops mean that application and benefit to patients is likely to be limited. The Enlighten Imaging platform overcomes these limitations and has potential to become the new standard in optical imaging.

The team partnered with a leading Australian product development company, Ingenuity Design Group, whose expertise, and quality management systems were instrumental in developing the device. Additional support was provided by experienced regulatory consultancy Blue Curve, as well as Entech Electronics, an Australian electronic board manufacturer.

During the project, the team designed and fully assembled a state-of-the-art hyperspectral retinal imaging camera under ISO 13485 – a significant achievement, particularly given that there was a global shortage of electronic components at the time. These cameras are critical for the next phase of clinical studies and are to be used by clinical trial centres globally.

While some of the project's planned clinical activities were impacted by COVID-19, preliminary biomarker findings for the detection of diabetic retinopathy and glaucoma have been validated, including contrast-free retinal angiography to detect areas of the retina that are not receiving sufficient blood (ischemia) and estimating the thickness of the retinal nerve fibre layer in glaucoma.

Throughout the project, all aspects of product development were addressed, from specification to risk assessment, user needs evaluation and extensive verification and validation processes, explained Enlighten Imaging's Lead Software Engineer, Maxime Jannaud.

"Building the software to control all aspects of the camera, while keeping user and patient needs at the forefront, has made this a challenging and rewarding experience," he said.

The first patent has now progressed from Patent Cooperation Treaty (PCT) stage to national phase in 10 jurisdictions, which is integral to the commercial value of the device. A patent application related to the camera design has also been submitted, which will soon enter national phase in 10 jurisdictions, having received favourable review on patentability.

As part of the BMTH project, Enlighten Imaging held a positive pre-submission meeting with the US Food and Drug Administration (FDA), gaining valuable clarification on the data needed for regulatory approval of the camera. Technical development and validation through the BMTH project have placed the company in a strong position for eventual marketing approval by the FDA and has primed the team to seek external investments for the next stage of its commercialisation journey.

The team is now actively engaged in fundraising to gain FDA clearance of its camera, develop a cloud analytical platform, advance a pipeline of novel imaging biomarkers for clinical validation and scale device manufacture.

Enlighten Imaging is developing an end-to-end imaging and analytics platform that utilises advanced artificial intelligence (AI) methods. This could lead to substantially improved AI-based decision support in retinal imaging, with the potential to transform clinical workflows and facilitate more accurate and earlier diagnosis of diseases.

As the team's Product Development Lead, Dr Francis Labrecque, explained, participation in the BMTH program has enabled Enlighten Imaging to transform a promising research project into a state-of-the-art medical device. "It has been quite a journey over the past two years, and it has involved a lot of learning," he said. "We have come a long way and the device has exceeded our expectations."

Enlighten Imaging is now at a pivotal point for investment and partnership opportunities. Over time, the company hopes to make its technology available to people around the world in eye clinics, optometry practices and hospitals. Realising these objectives will involve national capacity development, as well as local and international partnerships.

According to Enlighten Imaging's CEO and Co-Founder, Associate Professor Peter van Wijngaarden, this innovative technology is set to disrupt the provision of primary eyecare and may prove transformational in the early-stage diagnosis of neurological conditions such as Alzheimer's disease.

"I am tremendously proud of what our team has managed to achieve with support from MTPConnect, funding from the MRFF through the BMTH program and expert assistance from leading Australian product development, IP and regulatory specialists," he said. "In this process we have evolved as a company and are excited to take the next steps to bring this remarkable technology to the clinic for the advancement of human health."

Sources

https://www.aihw.gov.au/reports/eye-health/vision-problems-in-older-australians/summary

Transforming colorectal cancer outcomes with more accurate micro-metastases identification

PROJECT:
Ferronova Pty Ltd

THERAPEUTIC AREA:
Oncology

START DATE:
1 October 2020

END DATE:
31 March 2023

STATUS:
Completed

DELIVERABLES COMPLETED:
95 per cent

TOTAL BMTH GRANT:
$826,000

TOTAL BMTH EXPENDITURE:
$826,000

TOTAL CASH CO-CONTRIBUTION:
$826,000

TOTAL IN-KIND:
$844,000

TOTAL PROGRAM:
$2,496,000

Jobs within the project budget	5
Number of trademark applications	2
Number of patent applications	7
Number of licenses	1
Number of new technology(ies) invented/progressed	2
Number of preclinical trials commenced	2
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	16

Colorectal (bowel) cancer is the third most common cancer worldwide. In 2020, more than 1.9 million new cases were diagnosed and over 930,000 deaths were attributed globally to this disease[1]. In Australia, colorectal cancer causes the second highest number of cancer deaths per annum and has its greatest impact on those aged between 60 and 79 years of age. While early screening programs have significantly improved outcomes with a 71 per cent five-year survival rate, challenges remain.

Colorectal surgery involves removing the primary tumour and a large block of surrounding tissue containing lymph nodes, which are then analysed by pathology. If no cancer is found in the sampled lymph nodes, the patient is considered cured, yet up to 31 per cent of Stage II patients have recurrence of the cancer in less than five years and up to 10 per cent die[2].

The problem with this current standard of care is that pathologists may miss an important lymph node – and due to the large number of nodes they find, they only undertake a limited assessment. Several researchers have shown that when pathologists do a more thorough analysis of lymph nodes, approximately 25 per cent of patients have undetected cancer cells. Past research suggests these patients have a poor prognosis, yet patients that truly have no cancer in their lymph nodes are cured.

A solution to overcome the limitations of this existing process is to map the lymph system from the primary tumour to the direct draining lymph node (the sentinel lymph node or SLN) and perform a detailed assessment of this node only.

Supported by BioMedTech Horizons (BMTH) program funding, South Australian biotechnology company Ferronova set out to develop and test in a clinical trial a surgical oncology tracer system – designed to improve the treatment guidance and staging of complex cancers and help increase survival rates.

Ferronova's unique patented technology, FerroTrace®, is a new-generation, polymer-coated magnetic nanoparticle. This nanoparticle is detected on MRI for radiotherapy and surgical planning. It also drives a magnetically guided imaging system to precisely identify the SLNs, to assist surgeons and pathologists to more accurately stage solid tumours and locate and address micro-metastases that may otherwise go undetected.

Preclinical activity including optimisation of the FerroTrace composition, development, and refinement of the surgical procedures, testing of the localisation of the imaging markers to lymph nodes, and optimisation of the MRI parameters, created the foundation for the design and setup of the first-in-human clinical study.

Despite the challenges of conducting a clinical trial during the COVID-19 pandemic, the safety and feasibility of the system was demonstrated in 16 patients. The trial has since been expanded and will continue to enrol up to 40 patients.

Excitingly, Ferronova has transferred nanoparticle synthesis from an academic environment at The University of Sydney to Ferronova's premises, developed new analytical methods for nanoparticles, and is well positioned for the next stage of manufacturing development in 2023–24, up-scaling of the manufacturing process.

1. WHO International Agency for Research on Cancer.
2. Breast and colorectal cancer recurrence-free survival estimates in the US: Modeling versus active data collection, 2023.

Ferronova's unique patented technology, FerroTrace®, is a new-generation, polymer-coated magnetic nanoparticle.

With a detailed assessment of the regulatory and reimbursement pathways completed and establishing highly efficient in-house manufacturing capability under GMP conditions, and under the control of a quality management system, Ferronova has made significant progress toward setting up for larger scale trials, regulatory approval, and eventual commercialisation.

The BMTH program delivered significant value to Ferronova, helping it progress its innovative system along its journey towards commercialisation, said the company's CEO Stewart Bartlett.

"This project has supported the establishment of infrastructure and systems required to transfer outstanding academic research in nanoparticles to a commercial setting and a first-in-human gastrointestinal clinical trial," he explained.

The project was a collaborative effort involving Ferronova, scientists from The University of Sydney and University of South Australia (UniSA), as well as clinicians from the Ingham Institute for Applied Medical Research and surgeons/researchers from the Royal Adelaide Hospital. The preclinical testing was conducted at the SAHMRI Preclinical, Imaging and Research Laboratories (PIRL), with support through the loan of equipment from industry, including KARL STORZ Endoscopy Australia, Stryker, and Device Technologies (Intuitive Surgical).

The impact of these relationships has already been felt, with Ferronova and UniSA establishing new research and clinical collaborations with other partners including the Australian Bragg Centre for Proton Therapy and Research, Siemens, and the Olivia Newton-John Cancer Wellness and Research Centre.

These collaborations have resulted in Ferronova, UniSA and the new partners receiving grant funding of approximately $5 million to bring to the clinic a second variation of the FerroTrace technology, for use in brain and pancreatic cancer.

Director of the Key Centre for Polymers and Colloids at The University of Sydney, Associate Professor Brian Hawkett, said that the collaborations established through the BMTH project have proved beneficial for all parties.

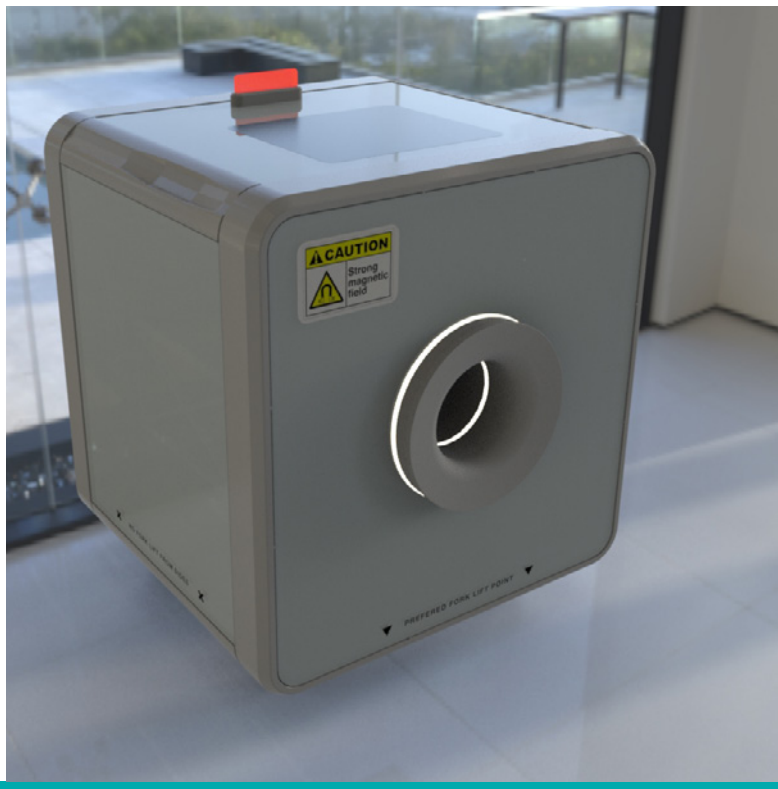
"The University of Sydney has been developing unique polymer chemistry for nanoparticles for over 20 years and investigating the application in medicine for almost as long," he said. "The collaboration with Ferronova, UniSA and the Ingham Institute has been one we are proud to be associated with and is the first time our technology has been applied in human trials. We look forward to continuing our collaboration into the future."

With the progress made in the first-in-human trial, new IP, and a promising pipeline of projects, Ferronova recently secured an equity investment of $8 million led by industry partner Renew Pharmaceuticals: the leader in infrared dyes for image-guided surgery.

Over time, the project will lead to larger trials, where anticipated success is expected to create lasting impact and change for patients with early-stage gastrointestinal cancers – increasing their odds of becoming truly cancer free.

Nanoparticles and nanomedicines are part of a growing industry with broad potential. Ferronova's experience in this project is identifying pathways for other researchers to transition their own academic research to the clinic and commercialisation.

Developing portable low-field MRI technology for bedside imaging to improve patient outcomes



PROJECT:
IntelliDesign Pty Ltd

THERAPEUTIC AREA:
MRI Clinical Imaging

intellidesign smart solutions®

START DATE:
1 April 2020

END DATE:
31 December 2022

STATUS:
Completed

DELIVERABLES COMPLETED:
100 per cent

TOTAL BMTH GRANT:
$1,000,000

TOTAL BMTH EXPENDITURE:
$1,000,000

TOTAL CASH CO-CONTRIBUTION:
$74,615

TOTAL IN-KIND:
$668,396

TOTAL PROGRAM:
$1,743,011

Jobs within the project budget	8
Number of patent applications	2
Number of new technology(ies) invented/progressed	4

Magnetic resonance imaging (MRI) has had a powerful impact on medical diagnosis, supplanting other imaging modalities for many disorders. MRIs are now a critical part in many clinical workflows, yet they have several limitations.

Conventional MRI scanners rely on strong magnetic fields (>1 Tesla) produced using cryogenically cooled superconducting magnets. Higher magnetic fields mean higher imaging resolution and the trend has been for progressively increasing field strength, with 3 Tesla MRI's now common in clinical environments.

The strong magnetic fields necessitate tightly controlled, specially constructed and dedicated facilities to provide for patient and staff safety. MRI scanners are very expensive to purchase, operate and maintain, putting MRI imaging beyond the reach of much of the world's population.

With one in three ICU patients experiencing an adverse event during transport, the risk to move them to the facility can be too high, or it is simply not practical, with between two and six ICU staff being required depending on the patient; or the usage of other medical equipment or devices containing metal parts cannot be removed, meaning that for many patients MRI imaging cannot be undertaken.

Yet, evidence suggests that early imaging enhances outcomes and reduces length of stay[1]. While other imaging modalities such as X-ray or Computed Tomography are useful, MRI's have a distinct capability and offer value in the clinical diagnosis. A portable MRI instrument for bedside deployment has the potential to overcome many limitations and offer patient and clinician benefit.

Image: Rendered image of the low-field MRI device.

1. Patients imaged early during admission demonstrate reduced length of hospital stay: a retrospective cohort study of patients undergoing cross-sectional imaging, 2010.

Brisbane-based design and manufacturing company IntelliDesign, in partnership with the Centre for Advanced Imaging (CAI) at The University of Queensland, is working to develop a low-field portable MRI (LF-MRI) technology for imaging with field strengths in the less than 0.2 – 0.5 Tesla. Such an instrument could be appropriate for smaller regional hospitals or used at the bedside in areas like the ICU, to sit alongside other life-supporting devices, such as pacemakers and ventilators, so that the most critically ill patients will be able to access the benefits of MRI technology.

Switching to a configuration with negligible in-bore and external magnetic fields allows it to run off standard mains electricity and standard air supply commonly available in small hospitals and clinics. As it does not use superconducting magnets it does not require cooling agents like liquid helium, reducing risk to staff and patients; it is compact and light and can be moved safely. Unlike conventional MRI, the low magnetic field allows the scanner to be used for imaging in the presence of metal.

The main objective of IntelliDesign's BioMedTech Horizons (BMTH) project was to build the first functional prototype of its LF-MRI instrument and the operating console. This required construction and testing of the dynamic permanent magnet arrays (dPMAs) for magnetic field production and switching; the development of extremely sensitive room temperature signal detectors; a novel spatial encoding method; and a novel machine learning method for noise correction.

Components were progressively built and tested with changes to the design required along the way to accommodate for observed performance characteristics. Additional refinements and changes were required upon first testing of the full prototype LF-MRI, but these were resolved and proved to be highly informative regarding the avenues for future design development. With a functional LF-MRI prototype built, and with development of data acquisition and control software and hardware in place, the CAI team tested its first imaging sequences and achieved a significant milestone.

The BMTH project was highly successful, leading to the creation of novel intellectual property (IP) and detailed understanding of the market conditions and opportunities, which allow IntelliDesign and CAI to proceed the instrument to the next stage of development. Significantly, the images produced by the team were the first ever captured using a system with an operating field strength as low as a 1.92 mT field. This is a remarkable achievement for the project and provides a platform to build upon. The fact that some structure can be seen in these images suggests potential for such devices; however, several improvements are still required.

This is a developing field and a small number of groups around the world have recognised the gap in patient care due to the existing MRI instrument form factor, and the opportunity that low-field MRI might bring. IntelliDesign and the CAI are at the leading edge and the BMTH project was an exciting initiative to be part of, said IntelliDesign's Lead Mechanical Engineer, Jeff Turner.

"The LF-MRI is a really rewarding project; it is innovative and mechanically ambitious. I feel very proud and satisfied that the mechanical design achieved its tough specifications," he said.

Alongside the development of a working prototype (Prototype 2) instrument, a strong ongoing relationship was formed between IntelliDesign, The University of Queensland and UniQuest – the commercialisation arm of the latter institution.

As Head of the Centre for Advanced Imaging, Emeritus Professor David Reutens, explained: "BMTH funding has been crucial in moving from an idea to a reality, allowing us to work with a strong team from IntelliDesign with complementary skills to ours."

IntelliDesign and the CAI focused on continued enhancements and development for the LF-MRI, including streamlining components, modularising electronics, simplification of mechanical components, improved generation of the switched polarising magnetic fields to boost signal-to-noise ratio, and optimise how the machine learning-based noise suppression framework works when the device is moved from one place to the next.

The Prototype 2 LF-MRI system provides a new way of testing novel ideas and componentry and designing new data acquisition sequences and image reconstruction methods. It forms a platform to build upon which can be directed towards producing a marketable product.

Smart brain biopsy needle to provide real-time image guidance to neurosurgeons

PROJECT:
Miniprobes

THERAPEUTIC AREA:
Oncology

MINIPROBES

START DATE: 1 October 2020	TOTAL BMTH GRANT: $1,000,000
END DATE: 30 September 2022	TOTAL BMTH EXPENDITURE: $1,000,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $59,035
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $1,295,002
	TOTAL PROGRAM: $2,354,037

Jobs within the project budget	5
Number of new technology(ies) invented/progressed	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	5

Each year over 1,900 Australians are diagnosed with brain tumours[1] – the leading cause of cancer-related death in children aged up to 14[2]. Surgical complications can be debilitating, or fatal, and accurate diagnosis is essential to minimising collateral damage. Needle brain biopsies are a standard part of the diagnosis, with over 37,000 brain biopsies performed each year in the US and Europe[3].

A needle brain biopsy involves inserting a needle into the patient's brain to take a small sample of tissue. This tissue is examined, which enables surgeons to accurately diagnose the type of cancer and choose the best treatment. However, inserting a needle into a patient's brain carries significant risk; two to three per cent of patients suffer permanent disability and one per cent die as a result of this procedure[4,5].

Typically, several needle biopsies will be performed to ensure that the surgeon has successfully taken a sample of the cancerous tissue. Each additional insertion increases the risk to the patient.

To help neurosurgeons perform safer, faster brain biopsies, Miniprobes – a high-tech spin-out from The University of Adelaide that produces fibre-optic imaging devices – is developing a smart needle that can detect when it is correctly positioned in cancerous tissue.

Image: Miniprobes smart needle being used in surgery.

1. Cancer in Australia 2021, Australian Institute of Health and Welfare.
2. Cancer in adolescents and young adults in Australia, 2023. Australian Institute of Health and Welfare.
3. Estimate based on reported incidence from the Centers for Disease Control and Prevention National Center for Health Statistics, National Hospital Discharge Survey, 2010.
4. Comprehensive assessment of haemorrhage risks and outcomes after stereotactic brain biopsy. 2001.
5. Factors affecting diagnostic yield in needle biopsy for brain lesions. British Journal of Neurosurgery, 2013.

As a recipient of BMTH funding, Miniprobes set out to evaluate two imaging technologies that could be incorporated individually or in combination into a brain biopsy needle, establish the feasibility of a minimal viable product including manufacturing feasibility, and define a clear way forward to clinical release.

Two technologies were investigated that could be suitable for use in neurosurgery and incorporated into the biopsy needle, optical coherence tomography and fluorescence. This project allowed Miniprobes to build close relationships with surgeons, understand the impact that each technology could have, identify the device that would have the most significant impact in practice, and then build and validate a working prototype.

Through the project, Miniprobes identified that the most clinically compelling device would include the single technology of fluorescence detection to identify when the brain biopsy needle was correctly positioned in cancerous brain tissue. The other technology, optical coherence tomography to identify blood vessels, was less important for the minimum viable product.

The intended use of the Miniprobes device is to integrate a fluorescence detecting fibre-optic probe into a brain biopsy needle to provide real-time image guidance to neurosurgeons. The patient will be administered a drug that causes the cancerous tissues to fluoresce when the probe is nearby and this will allow accurate positioning of the biopsy needle into the cancerous tissue, which should reduce the risk of taking unnecessary, non-diagnostic biopsies and may remove the need for intraoperative histopathological assessment.

As part of the BMTH project, Miniprobes developed a prototype device to establish the feasibility of manufacturing its smart needle. The team tested this prototype device with brain tissue taken from five patients undergoing brain surgery and working closely with pathologists at the Royal Adelaide Hospital, analysed the tissue and demonstrated that the smart needle could reliably detect when it was inserted into cancerous tissue. The results were shown to correlate well with histopathological gold standard results.

The Miniprobes product development matured through the project with a minimum viable product developed which comprised of a single-use consumable smart biopsy needle and a scanner console comprising optical scanner, computer workstation and display.

Managing Director of Miniprobes, Professor Robert McLaughlin said the team had accomplished the objectives of its BMTH project – creating a device that has the potential to improve outcomes for brain tumour patients and enable surgeons to deliver a higher quality of care.

"Our smart needle can see when it is in cancerous tissue. It helps the surgeon do their job more safely," explained Professor McLaughlin.

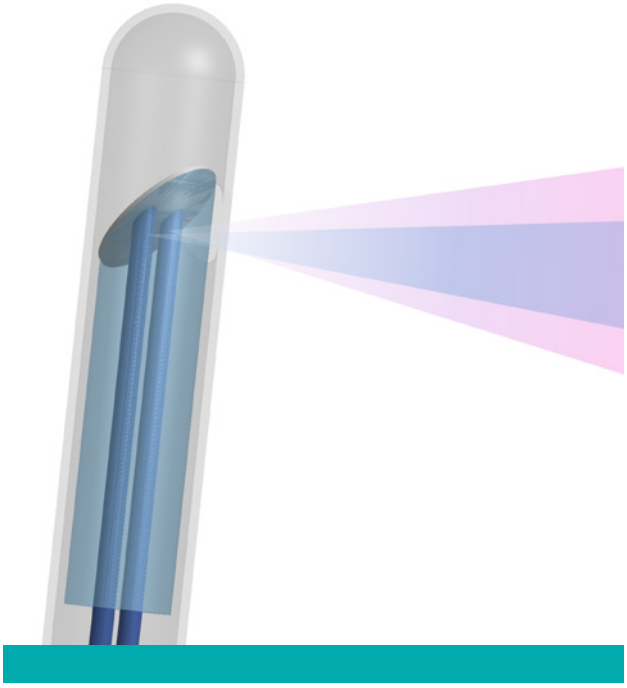
As a result of work undertaken through the BMTH project, Miniprobes has established the requirements for the minimal viable product for its market, as well as technical feasibility of its technology. Importantly, it has also significantly improved its manufacturing capabilities, empowering the team to mature manufacturing processes in fibre-optic technologies.

The company has now established the regulatory, quality assurance and commercial paths that will be pursued to take its smart needle device towards regulatory approval and commercial release.

In other exciting news, Miniprobes has received an AUD$1.5 million Cooperative Research Centres Project (CRC-P) grant from the Department of Industry, Science and Resources, which will fund a related project that builds upon the expertise developed within the BMTH project. This new grant will be used to develop a comparable smart needle device for a different application in the livestock industry, which Miniprobes anticipates will be released commercially by the end of 2023.

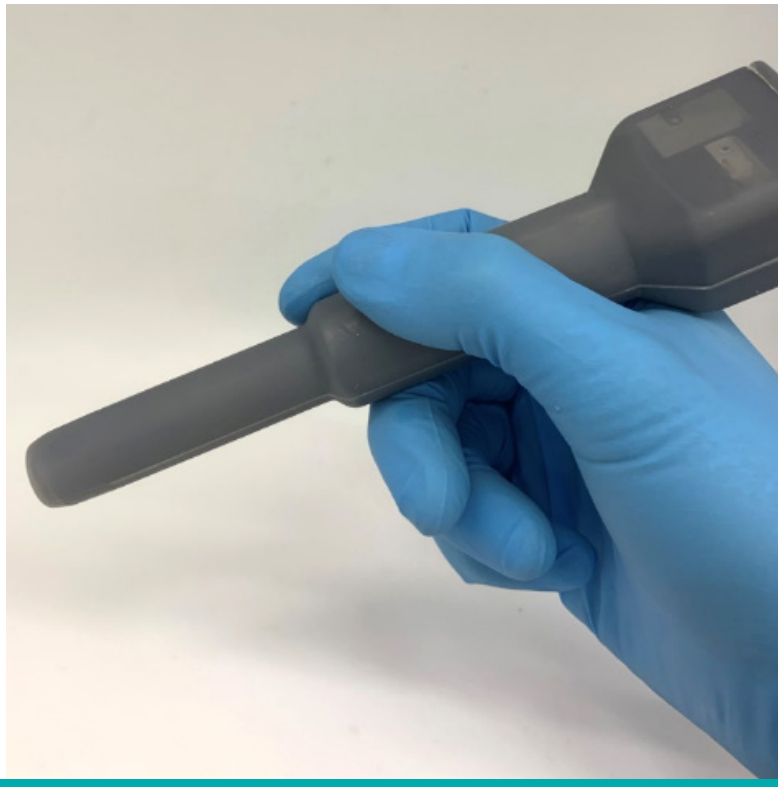
According to Professor McLaughlin, the BMTH project allowed Miniprobes the resources and time to understand the clinical need and workflow and identify the best solution with a compelling business case. As a result, the company is much more likely to successfully develop a device that will have impact.

"The BioMedTech Horizons program allowed our company to build critical relationships and validate our technology," he said. "It allowed us to take the next steps in medical device development."



Schematic of the Miniprobes Smart Needle.

Novel diagnostic imaging system aims to identify residual cancer during surgery



PROJECT:
OncoRes Medical

THERAPEUTIC AREA:
Oncology

OncoRes Medical

START DATE: 1 October 2020	TOTAL BMTH GRANT: $1,000,000
END DATE: 30 September 2022	TOTAL BMTH EXPENDITURE: $1,000,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $0
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $149,883
	TOTAL PROGRAM: $1,149,883

Jobs within the project budget	2
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	1
Number of patients to clinical trial recruitment	56

Surgeons will often plan a cancer removal informed by Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) images. However, once surgery begins, most often, they are required to identify and assess cancerous tissue based on their anatomical knowledge, visual differences in tissue structure and importantly, their sense of touch. Cancerous tissue has an elasticity difference compared to surrounding normal tissue, and during surgery this is assessed by the surgeon with their sense of touch, through one or more pairs of surgical gloves which dampens their sense of touch significantly.

Breast cancer is the most prevalent form of cancer worldwide, with around 2.3 million people diagnosed with the disease in 2019[1]. In Australia, breast cancer is the most diagnosed cancer with 20,428 women receiving a diagnosis in 2022[2], and in females aged between 30 and 59, breast cancer has the highest mortality rate of all cancers[3].

Most women with breast cancer have breast conserving surgery (BCS) (a lumpectomy), rather than a mastectomy which have equivalent survival rates, but BCS is less invasive, minimises recovery time and preserves the appearance and function of the breast. However, due to the limitations of technologies available to oncology surgeons today, the cancer will not be completely removed in many of these patients, committing one in five to a repeat operation. Lacking an intraoperative tool, surgeons must rely on their sense of touch to ensure that the entire tumour has been removed and as a result, cancer is often left behind.

Image: OncoRes Medical prototype probe.

1. Union for International Cancer Control, GLOBOCAN 2020.
2. Cancer Australia Breast Cancer Statistics.
3. Australian Institute of Health and Welfare; Cancer Data in Australia 2022.
4. Beyond the Margins—Economic Costs and Complications Associated with Repeated Breast-Conserving Surgeries, 2017.

A 2017 report found that repeated BCS surgeries cost an additional $16,072 per patient[4]. Scaled globally, this billion-dollar burden on healthcare systems as well as the immeasurable and significant time, cost and distress for patients and families can be reduced with improved outcomes from the first surgical intervention.

Consequently, Perth-based medical device company OncoRes Medical is developing a novel diagnostic imaging system to increase the opportunity for complete clearance of cancer during breast conserving surgery.

As a BioMedTech Horizons (BMTH) program funding recipient, OncoRes Medical proposed to develop proof of concept for a novel technology platform capable of detecting changes in tissue elasticity that are characteristic of cancerous tissues. This, in turn, translates a surgeon's sense of touch into a microscale image, which will improve the likelihood of complete cancer clearance during the initial surgery and reduce complication rates.

The goals of the BMTH project were to understand the market opportunity for the company's novel technologies and implement a clinical benchtop device suitable for use on clinical breast cancer surgery specimens, integrate the sensor into a handheld probe form factor suitable for use by a surgeon, and conduct a pilot study on lumpectomy specimens and compare results to pathology.

During the project, OncoRes Medical achieved its objectives, progressing its novel, early-stage technology platform to technology proof of concept and defining additional market opportunities and use cases.

The team demonstrated proof of concept of its technology by applying benchtop implementation of Stereoscopic Optical Palpation (SOP) imaging, achieving visualisation of microscale stiffness to depths greater than 1 mm in excised breast cancer tissue. The *ex vivo* benchtop SOP study demonstrated the diagnostic accuracy of SOP images for the detection of cancer within 1 mm of the margins of excised breast tissue specimens, with assessments validated through complimentary histological examination.

The team also achieved proof of technical product feasibility and incorporated the technology into a handheld SOP device intended to be operated by surgeons during breast conserving surgery.

Surgeon engagement and use of early-stage prototypes carried out during the project provided important information to inform user requirements and product specifications. Feedback informed development decisions taken during this project to progress the development of the handheld prototype device.

Sourcing of a highly valuable burden of illness (BOI) dataset from US-based hospitals proved critical in informing the product development and commercialisation path. Detailed analyses were performed to understand the size and accessibility of the US breast conserving surgery market and competitor activity in breast cancer surgical imaging technologies. Recognising significant opportunity from the BOI dataset, some changes in the commercial and technical direction of the BMTH program were made.

Surgeon interviews conducted during the project, enabled the identification of expansion opportunities into other solid cancers. These opportunities were further investigated using the BOI dataset, accessed as part of the BMTH project. Clinical protocols for proof-of-concept studies in additional cancer indications were drafted as part of the project rescoping to realise greater commercial opportunity. Through the BMTH program, OncoRes was able to scope these market opportunities more fully than would otherwise be possible and develop commercialisation plans for these, and positions OncoRes in the broader cancer surgery market.

Major achievements were reached encompassing commercial and technical aspects of the project, advancing product development towards market, and progressing from Technology Readiness Level (TRL) 2 to 4.

The new SOP platform technology is complementary to OncoRes Medical's existing and more advanced Quantitative Micro-Elastography (QME) technologies and may enable the company to present a pipeline of products that best meet the needs of specific clinical-use cases.

Since commencing the BMTH project, OncoRes Medical has secured $22.5 million in funding to support the development of its QME Imaging System, which the company's CEO and Managing Director, Dr Katharine Giles, has said is validation of the system's potential to improve outcomes in breast conserving surgery.

"At OncoRes Medical we believe that all women deserve the opportunity to move beyond their initial breast cancer surgery knowing that all of the cancer has been removed, the first time," she said.

"Continued support of our technology has helped us progress through the path from a university research project to a standalone company with FDA breakthrough device designation. This continued support takes us closer to providing a game-changing solution for cancer surgeons, so we can bring these benefits to the people at the centre of our mission, patients."

Intra-oral digital microscope set to revolutionise oral cancer detection

PROJECT:
Optiscan Imaging Ltd

THERAPEUTIC AREA:
Oncology

OptiScan

START DATE: 1 October 2020	TOTAL BMTH GRANT: $971,000
END DATE: 30 September 2022	TOTAL BMTH EXPENDITURE: $971,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $0
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $587,323
	TOTAL PROGRAM: $1,558,323

Jobs within the project budget	4
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	71

Oral cancer is a devastating condition that carries high mortality and morbidity rates when not detected and treated early. Of the 28 specific cancer types reported by the Institute for Health Metrics and Evaluation[1] oral cancer ranks in the middle in terms of disability adjusted life years (DALY), years of life lost (YLL) and deaths, with 199,397 deaths reported in 2019.

Many oral cancers are preceded by changes to the oral mucous membrane, appearing as painless white or red areas of the skin, collectively termed oral potentially malignant disorders (OPMDs). The current standard of care for monitoring these lesions is macroscopic visualisation and assessment, with physical biopsies undertaken as required. However, biopsies can only sample parts of lesions and have associated risks, morbidities and costs.

As the global leader in real-time non-destructive digital microscopic imaging for medical applications, Melbourne-based Optiscan Imaging Ltd has developed an intra-oral digital microscope that can distinguish between normal, precancerous and cancerous oral tissue – a promising alternative to current testing methods for oral potentially malignant disorders. InVivage®, built with the company's unique patented 3D imaging technology, performs a live, non-invasive 'digital biopsies' of the oral cavity, which enables clinicians to make immediate informed decisions relating to patient care.

Image: Optiscan Invivage device and handpiece.

1. IHME Global Burden of Disease 2019.
2. Acquisition and annotation in high resolution in vivo digital biopsy by confocal microscopy for diagnosis in oral precancer and cancer.
3. Malignant transformation in 1,458 patients with potentially malignant oral mucosal disorders: a follow-up study based in a Taiwanese hospital, 2007.
4. Malignant transformation in 5,071 southern Taiwanese patients with potentially malignant oral mucosal disorders, 2014.

The goal of Optiscan's BioMedTech Horizons (BMTH) program project was to generate the clinical evidence needed to support the use of the InVivage® device for monitoring oral potentially malignant disorders. If successful, this could enable routine monitoring of early-stage disease and significantly earlier detection of malignant tissue, accompanied by a revolutionary reduction in physical biopsies.

Through the BMTH project, the team also aimed to provide evidence that the technology could be used in telemedicine by remote capture and digital reporting by oral medicine and pathology specialists. Likewise, it set out to determine whether the device could be used in an outpatient setting in oral precancerous mucosal conditions with acceptability from both patients and clinicians.

This project initiated an exciting new collaboration between Optiscan and Melbourne Dental School at the University of Melbourne, supported by Dental Health Services Victoria and clinicians within the Victorian Comprehensive Cancer Centre Alliance (VCCC Alliance).

Despite delays and challenges associated with COVID-19 during the project's execution, through a clinical study conducted at Melbourne Dental School, the team collected sufficient data to show effective oral mucosal disease imaging. The study outcomes were published in Frontiers in Oncology in July 2023[2], and the data is being used by Optiscan to pursue US Food and Drug Administration (FDA) clearance for InVivage® through the De Novo pathway.

More than 250 image sets were analysed to test a developed categorical scoring template with two observers, with important image interpretation challenges resolved. It was concluded, *in vivo* acquired confocal fluorescence microscopy can be used to indicate the presence of oral mucosal dysplasia and/or neoplasia.

The ability to rapidly collect hundreds of images demonstrated the clinical potential of non-invasive tissue level assessment at microscopic resolution. This offers the potential to increase the diagnostic precision, allows opportunity for monitoring of the same location within a patient's mouth over time and reduces the number of times that scalpel biopsy is required.

These findings provide a strong foundation for demonstrating the utility of the device in real time in expert hands, as well as tele-reporting following acquisition remotely by a trained imaging technician. The data collected can now be used to seek resources for a population-level study.

Three to five per cent of people who present with OPMD will develop an oral cancer[3,4], and in 2019 up to 7 million cases of OPMD presented globally. These cases could have benefited from Optiscan's non-invasive image-based biopsy. The significant numbers of OPMD assessments that are performed each year will mean the InVivage® by Optiscan will have an important role in supporting clinicians and patients alike worldwide.

According to Senior Lecturer at Melbourne Dental School, Dr Tami Yap, this technology stands to disrupt oral cavity screening, with obvious prospects for screening in other tissues.

"We can now take painless, digital biopsies of our patients' mouths," she said, adding that InVivage® could be a game changer for healthcare systems. Given that oral cancer is the 16th most common cancer globally and imposes significant personal and financial costs across society, InVivage's ability to provide accurate, immediate feedback to clinicians about the status of oral lesions could save lives and money by enabling early identification of problematic lesions, so they can be treated before they become cancerous.

Applications and Customer Support Manager at Optiscan, Dr Lindsay Bussau, explained that support from the BMTH program was instrumental in advancing the device along the pathway to commercialisation.

"Optiscan Imaging Ltd is proud to partner with MTPConnect on this BioMedTech Horizons project," he said. "The aims of the study using InVivage® for the monitoring of oral precancerous mucosal conditions were achieved. Specifically, its utility for identification of characteristic features of various OPMD conditions was demonstrated, indicating the potential of the technology for non-invasive early detection of premalignant and malignant tissue.

"The results of this study will play a key role in the regulatory submission for clearance of InVivage® by the US Food and Drug Administration through the De Novo pathway. It has also fostered ongoing collaborative translational work with clinicians and researchers at the University of Melbourne Dental School, the Walter and Eliza Hall Institute, and the Peter MacCallum Cancer Centre.

"Publication of this work will further validate the use of the technology in monitoring oral lesions and detection of cancer. Data collected during this project will be used to further enhance the usability of this technology."

New predictive test will save lives and reduce economic burden of diabetic kidney disease

PROJECT:
Proteomics International Ltd

THERAPEUTIC AREA:
Chronic disease diagnostics

Proteomics International

START DATE: 11 May 2022	TOTAL BMTH GRANT: $413,516
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $413,516
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $924,716
DELIVERABLES COMPLETED: 95 per cent	TOTAL IN-KIND: $433,816
	TOTAL PROGRAM: $1,772,048

Jobs within the project budget	10
Number of new technology(ies) invented progressed	1

Diabetes is the primary cause of chronic kidney disease (CKD). Globally, 537 million adults have diabetes[1] and one-third have diabetic kidney disease (DKD). In 2019 there were 460,000 DKD deaths caused by diabetes[2].

Current testing for CKD is based on urine or blood tests that measure products indicating poor kidney function. By the time these tests indicate disease, the damage is done and is irreversible. If detected too late or untreated, patients can require lifelong dialysis or a kidney transplant.

Treatments are available to slow or stop the onset of disease, but early detection is critical to a patient's management and treatment trajectory.

Aiming to provide a solution for earlier detection of DKD, Proteomics International, a Perth-based medical technology company, has developed the PromarkerD test. This *in vitro* diagnostic (IVD) test predicts the onset of DKD by measuring the levels of three plasma protein biomarkers, combined with three routinely available clinical variables (age, HDL cholesterol and estimated glomerular filtration rate). These inputs are entered into an advanced cloud-based software algorithm, which then calculates a patient's risk score for DKD as low, moderate or high.

Extensive clinical testing has shown that PromarkerD predicted 86 per cent of otherwise 'healthy patients' who went on to develop kidney disease within four years. These patients were all missed by current standard testing. Being a first-in-class and cost-effective prognostic test of DKD, the PromarkerD test has the potential to offer a life-changing outcome for patients.

Image: Proteomics International Managing Director Dr Richard Lipscombe holding the PromarkerD predictive test.

1. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045.
2. WHO Diabetes Fact Sheet, 2023.
3. Australian Institute of Health and Welfare. Diabetes: Australian facts. 2023.
4. Australian Institute of Health and Welfare. Chronic kidney disease: Australian facts.

Patients identified as being at high risk of DKD, who receive proactive early intervention, have lower risk of developing DKD after treatment, thereby reducing the likelihood of invasive and expensive dialysis and transplants. Meanwhile, those identified as low risk could avoid the unnecessary adoption of therapeutic treatments.

More broadly, PromarkerD could save the Australian healthcare system hundreds of millions of dollars. It is estimated that 1.3 million people have diabetes nationwide[3] and that 37 per cent of kidney failure cases are caused by diabetes. With CKD costing the healthcare system $1.8 billion annually[4], it is estimated about $666 million is attributed to diabetic causes – a figure that could no doubt be significantly reduced through earlier detection and intervention.

Immunoassays have underpinned diagnostic testing for decades, yet medical device companies wishing to manufacture to Australian and international standards must currently seek overseas partners. For its BioMedTech Horizons (BMTH) program project, Proteomics International set out to establish local manufacturing supply chains, quality assurance procedures and support the PromarkerD application for Australian Therapeutic Goods Administration (TGA) approval.

During the project, Proteomics International sourced new raw reagents from suppliers, enabling greater quality control, batch consistency and enhancing supply chain security for PromarkerD manufacturing. These raw reagents are of a high standard and have been validated and approved according to the company's internal quality control and quality assurance acceptance criteria.

Additionally, Proteomics International developed a successful partnership with local start-up Proteowa to produce recombinant antibodies at small scale. This partnership leverages Proteowa's affiliation with the Western Australian State Agricultural Biotechnology Centre (SABC) at Murdoch University and is a huge win for both parties, said Managing Director of Proteomics International, Dr Richard Lipscombe.

"Establishing this highly specialised production capability for reagents for the PromarkerD test, locally, is a significant achievement. This has strengthened and de-risked our supply chains and provides a strong platform to launch future tests under development by Proteomics International."

Founder and Director of Proteowa, Dr Reza Zareie, added: "This partnership with Proteomics International has enhanced Proteowa's capabilities, and we are delighted to be in a position to supply the high-quality antibodies for PromarkerD."

The BMTH-funded project also saw Proteomics International obtain a renewal in ISO 13485 certification and submit a request to the TGA for inclusion of PromarkerD in the Australian Register of Therapeutic Goods (ARTG), to enable the sale and clinical use of the test in Australia. The Company is likewise undergoing consultation for approval, in addition to having commenced the reimbursement pathway for Medicare.

In early 2023, Proteomics International achieved a major milestone with the American Medical Association (AMA) approving a unique US Proprietary Laboratory Analyses reimbursement code for PromarkerD. This code is key to reimbursement coverage of PromarkerD by Medicare and private health insurers in the US. Excitingly, in May 2023 Proteomics International signed an exclusive license agreement for the use and commercialisation of PromarkerD with Sonic Healthcare USA to take the test to the US market.

Overall, the project achieved its main purpose of de-risking the supply chains for key reagents such as antibodies and providing a solid platform for scaling up future manufacture in Australia. The Proteomics International team was also exposed to and addressed issues that could have arisen in the commercial production phase, developing knowledge that will be critical to production going forward.

Ultimately, the BMTH project has set the foundation for the manufacture, sale and clinical use of the PromarkerD test in Australia. Its success will have positive flow-on effects for other diagnostics that the company currently has in its pipeline; most advanced through the R&D pipeline is its diagnostic test for endometriosis. The knowledge gained by the team from the process of commercialising and manufacturing PromarkerD will equip Proteomics International with the skill set and know-how to accelerate the progress of other diagnostics in the future.

PromarkerD has had extensive clinical testing.

Novel monitor advancing the standard of care for neonatal resuscitation

PROJECT:
ResusRight Pty Ltd

THERAPEUTIC AREA:
Neonatal care

ResusRight
FOR SAFER BIRTH

START DATE: 28 September 2021	TOTAL BMTH GRANT: $800,000
END DATE: 30 May 2023	TOTAL BMTH EXPENDITURE: $800,000
STATUS: Complete	TOTAL CASH CO-CONTRIBUTION: $830,344
DELIVERABLES COMPLETED: 96 per cent	TOTAL IN-KIND: $30,000
	TOTAL PROGRAM: $1,660,344

Jobs within the project budget	7
Number of trademark applications	1
Number of patent applications	1
Number of new technology(ies) invented/progressed	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	12

Each year, three to six per cent of babies require positive pressure ventilation (PPV) at birth to begin breathing[1]. With 134 million births in 2021[2], there were up to eight million babies requiring PPV including around 17,000 babies in Australia[3].

If a baby requires ventilation at birth, this is provided manually by the clinician with a mask that covers the babies' mouth and nose. The major cause of variation is leakage from around the edge of the mask, or variations in volume and rate from the healthcare provider providing the care.

Alarmingly, excessive gas volumes delivered during resuscitation can lead to acute lung injury and life-threatening lung collapse (pneumothorax in one per cent of newborns), or lifelong lung damage in preterm babies (60 per cent of very preterm newborns). Meanwhile, insufficient volumes can result in asphyxia. These babies carry a lifelong disease burden that impacts their health, family and the healthcare system. Despite these outcomes, gas volumes and mask leak are not routinely measured during resuscitation.

Hoping to ease this burden and advance the standard of care for neonatal resuscitation, Sydney-based ResusRight has developed the NEMO Clinical Monitor. The NEMO attaches to neonatal resuscitation equipment and guides clinical care through objective feedback on the quality of resuscitation. This feedback enables clinicians to optimise support for each infant to reduce the risk of mortality or morbidities associated with manual ventilation.

Image: ResusRight monitor.

1. Neonatal resuscitation in low-resource settings, 2010.
2. Our World in Data.
3. Australian Institute of Health and Welfare: Mothers and Babies.

The company's BioMedTech Horizons (BMTH) funded project set out to progress the NEMO Clinical Monitor along the medical technology commercialisation pathway. It funded a first-in-human clinical trial to evaluate the safety and feasibility of using the NEMO Clinical Monitor during manual resuscitation, as well as production and verification of advanced prototypes. Channel development and market exploration activities were also funded to build out the commercial strategy in the local Australian market, as well as in the US and Europe. Several key Australian manufacturing partners were identified to develop all pre-commercial prototypes.

During the project, ResusRight implemented a fit-for-purpose quality management system (QMS), alongside the clinical trial planning and approvals, to ensure all future development will take place under relevant standard operating procedures. Following manufacture of prototype devices for use in the trial and for technical validation, the team performed a comprehensive design review and identified a range of improvements that will assist in future manufacturing, and ensure it is optimised to improve care during the resuscitation process.

The project achieved all its objectives. The 'Neonatal Monitoring Trial' (NeMo Trial), ResusRight's first-in-human trial run at Westmead Hospital in Sydney, successfully recruited 12 infants. Data analysis demonstrated that the monitor safely and effectively assisted with all resuscitations, with no safety issues related to the investigational device reported. Qualitative and quantitative data collected supported the conclusion that the monitor was used – and functioned – as intended in 100 per cent of resuscitations. Beyond the technical achievement, the team now has invaluable firsthand experience in sponsoring a trial that will be beneficial as NEMO moves toward its pre-market pivotal trial.

Progress made during the BMTH project has positioned the NEMO Clinical Monitor for US Food and Drug Administration (FDA) clearance through the 510(k) pathway within the next 18 months, and Therapeutic Goods Administration (TGA) and Conformité Européenne (CE) clearance after a pre-market pivotal trial, which will evaluate efficacy outcomes, explained CEO of ResusRight, Matt Boustred.

"Seeing the Clinical Monitor being used to help babies during actual resuscitations is a massive step for the company and exciting validation of the work the team has done to date," he said. "Completing the feasibility study puts us in a great position to conduct a pivotal trial, gain regulatory clearance, and get this technology into the real world, where it can begin to help clinicians care for babies in their first few moments of life."

ResusRight established key partnerships on the commercialisation pathway including with clinical teams at leading national and international tertiary hospital centres with interest to partake in the pre-market pivotal trial. The company also signed a distribution agreement with Laerdal Global Health, a major multinational corporation and one of the largest medical device manufacturers in the neonatal space. ResusRight's intangible intellectual property (IP) protection strategy has been established, with one provisional patent application filed.

Off the back of milestones achieved during the BMTH project, ResusRight is raising a $3 million Series A round to fund further commercialisation activities and FDA clearance. Meanwhile, the team is planning to publish the results of the NeMo Trial in a peer-reviewed journal and is currently drafting a manuscript.

Given the start-up nature of ResusRight and the novel nature of the product it is developing, the BMTH project has played a critical role in progressing the NEMO Clinical Monitor closer to market and de-risking the technology.

According to ResusRight's Chief Clinical Advisor Dr Mark Tracy, the BMTH program's support has enabled the team to accelerate progress of the NEMO Clinical Monitor through the development and clinical validation phase – enabling the company to get this technology onto the market sooner.

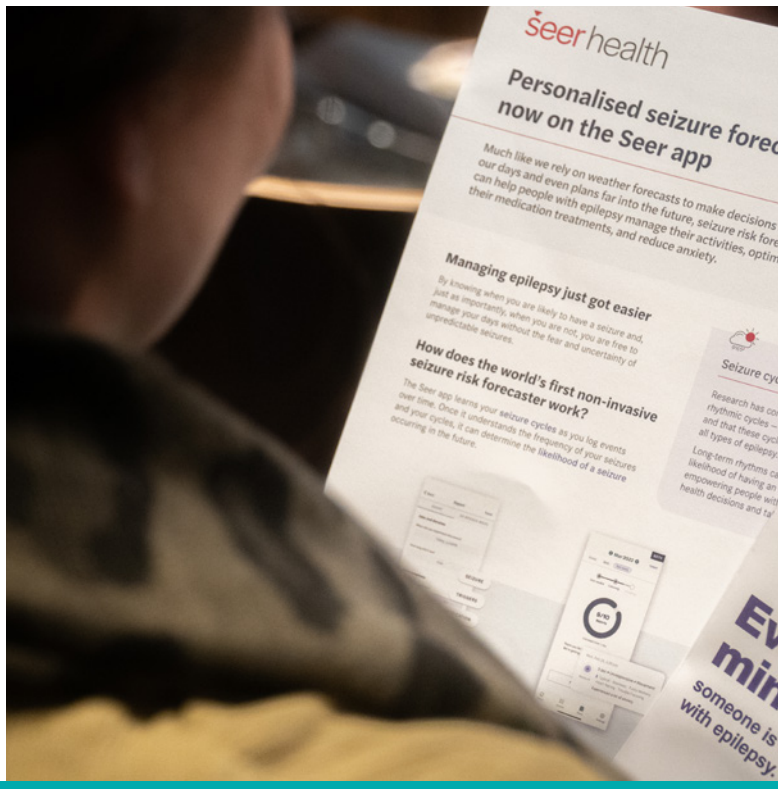
This was critical to securing partnerships with world-leading hospitals, paving the way for the upcoming multi-centre trials both in Australia and globally.

"For millions of babies born across the world each year, resuscitation is performed with little or no feedback on the quality of the ventilation process," Dr Tracy said.

"We recognise that the first few minutes of life are essential to both save lives and prevent lifelong brain damage for millions of babies. It was very exciting through this project to provide practitioners in the birthing suite with feedback through the ResusRight monitor for the first time. These first-in-human studies are incredibly difficult to run, and it was remarkable that the team was able to meet the recruitment numbers to demonstrate the feasibility of this technology during resuscitation and gratifying to see the positive clinical feedback collected."

Once the NEMO Clinical Monitor is commercialised, ResusRight hopes resuscitation monitoring will become the new standard of care for every baby that needs help to start breathing – just as pulse oximetry has become standard of care at every resuscitation over the past decade. This type of volume monitoring is standard if a baby is moved to the neonatal intensive care unit; however, a lack of technology developed for the birthing suite has prevented its adoption in this environment. There is already evidence demonstrating the potential effectiveness of respiratory monitors for guiding clinical care, by helping clinicians improve the effectiveness of mask ventilation and, consequently, reducing the burden of inaccurate PPV on so many lives.

Seizure forecasting app to empower people with epilepsy



PROJECT:
Seer Medical Holdings Ltd

THERAPEUTIC AREA:
Epilepsy

START DATE: 1 October 2020	TOTAL BMTH GRANT: $1,000,000
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $926,690
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $27,110
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $448,708
	TOTAL PROGRAM: $1,402,508

Jobs within the project budget	1
Number of patent applications	4
New products launched	1
Number of new technology(ies) invented/progressed	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	50

In 2019 there were approximately 150,000 patients diagnosed with epilepsy resulting in $12.3 billion of direct and indirect costs[1,2]. It is now estimated that up to 200,000 Australians face the daily prospect of debilitating epileptic seizures that interrupt normal brain function and can lead to loss of bodily control, consciousness, and even life. The constant uncertainty surrounding when these events will occur limits people's ability to participate in everyday experiences like working, exercising, and driving.

Discoveries made during clinical trials conducted in Melbourne from 2010 to 2012 by Professor Mark Cook[3], indicated the existence of strong patient-specific cycles in neural activity that modulate seizure risk.

Diagnostics company Seer Medical, which specialises in the diagnosis and management of epilepsy, has hypothesised that these cycles are driven by naturally occurring physiological changes, which could be detected using wearables.

The ability to track and forecast cycles of seizure risk via non-invasive wearable devices could radically transform the management of epilepsy, empowering individuals to make informed decisions about their health. It stands to reduce the burden of lifelong medication, by allowing administration of fast-acting anti-seizure medication only when required. Meanwhile, the objective and actionable data these devices gather could improve mortality and the economic costs associated with unpredictable seizures.

1. Deloitte Access Economics, 2020.
2. Australian Institute of Health and Welfare. Epilepsy in Australia.
3. Prediction of seizure likelihood with a long-term, implanted seizure advisory system in patients with drug-resistant epilepsy: a first-in-man study, 2013.

Working towards these objectives with collaborators at The University of Melbourne, Melbourne-based Seer Medical set out to develop a real-time seizure forecasting system leveraging the inbuilt sensors of smart watches such as the Fitbit, a strategic partner in this project. Bolstered by BioMedTech Horizons (BMTH) funding, the team set out to determine the system's validity.

Seizure diaries have been a recommended practice by many organisations globally but for some people they can be unreliable. So, the team wanted to validate its predictive forecasts using Seer Medical's own gold-standard video EEG (brain wave) recordings via the Seer Sense product and understand which signals from the wearable would successfully forecast seizures for most people.

Establishing secure data transfer from a consumer grade wearable product to the Seer Medical's patient data secure (HIPPA compliant) servers, database and analysis tools was a significant undertaking and laid the foundation for the clinical study to be coordinated with the University of Melbourne. The seizure forecasting app moved from a simple proof-of-concept design to a fully functioning mobile app validated through extensive testing.

With all the parts in place, the clinical study team demonstrated for the first time that seizure forecasting is possible with non-invasive digital health tools. This is a first-in-class device for epilepsy and has potential applications to grow into other episodic disorders, such as syncope or functional neurological disorders.

During the project, Seer Medical launched the world's first risk forecasting mobile app, at no cost to users. Listed as a Class 1 medical device on the Australian Register of Therapeutic Goods, the Seer app requires people to log seizure events through the app diary, including details to help identify their triggers.

Over time with additional input from the Fitbit wearable, the app delivers insights about their seizure cycles, so they can see when they are more or less likely to experience seizure activity and can plan accordingly.

Seer Medical's General Manager in Australia Marguerite Wintle added that when using seizure forecasts to book Seer Sense diagnosis more optimally, prior use of the app was found to improve the yield of seizures by 63 per cent in adults and 93 per cent in children. This has the potential to greatly reduce both the direct and indirect costs of undertaking EEG monitoring, by improving the yield of these studies.

"We hope to one day utilise each patient's individual risk forecast when scheduling home-based video EEG-ECG studies to increase the likelihood of capturing the events under investigation. This is particularly useful in patients who have infrequent seizures, who would otherwise potentially require repeat monitoring."

Over the life of the BMTH project, Seer Medical strengthened collaborations with academics at the Mayo Clinic, King's College London, the Epilepsy Foundation of America, and many tertiary epilepsy centres in Melbourne, broadened its field of play through expansion to the US, the UK and Germany; grew its workforce significantly; and demonstrated scientific leadership and ability to translate research ideas into patient and clinician-facing products and services.

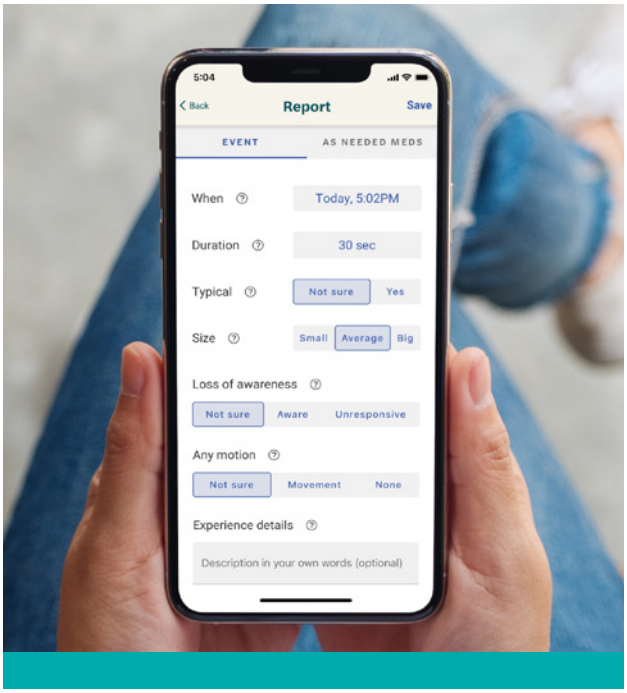
Seer Medical's seizure forecasting system offers numerous benefits to people with epilepsy. The uncertainty around future seizure events is widely considered one of the most disabling aspects of epilepsy, and the potential to manage medication dose in line with seizure forecasts could save both direct pharmaceutical cost and minimise side effects. The Seer app product launched with support of the BMTH program represents a great step towards alleviating this disability.

About two-thirds of the 50 million diagnosed people with epilepsy achieve seizure freedom on medications once properly diagnosed. That leaves one-third of people with epilepsy that could potentially benefit from ongoing use of seizure management tools, including the Seer app, and seizure risk forecasting.

According to Seer Medical's CEO and Co-Founder Dr Dean Freestone, the BMTH project has enabled the company to significantly advance the suite of tools available to patients for capturing data related to their epilepsy and alleviating the burden of ongoing seizures.

"The BioMedTech Horizons funding has been transformational for Seer," he said. "Being able to translate our seizure forecasting IP into a patient-facing feature has cemented Seer as global scientific leaders in epilepsy. This leadership greatly improves our relationships with external stakeholders such as foundations, leading hospitals, and key opinion leaders.

"Most importantly, seizure risk forecasting is already improving the lives of people with epilepsy and reducing the social and economic costs of the disease," said Dr Freestone.



Seer app in use on a mobile phone.

Advancing cardiac monitoring wearable for at-home use

PROJECT:
Seer Medical Holdings Ltd

THERAPEUTIC AREA:
Cardiovascular

START DATE: 1 October 2021	TOTAL BMTH GRANT: $800,000
END DATE: 28 November 2022	TOTAL BMTH EXPENDITURE: $435,397
STATUS: Terminated	TOTAL CASH CO-CONTRIBUTION: $435,440
DELIVERABLES COMPLETED: 78 per cent	TOTAL IN-KIND: $364,541
	TOTAL PROGRAM: $1,235,378

Jobs within the project budget	3
Number of new technology(ies) invented/progressed	1
Number of pre-clinical trials commenced	1

Cardiac monitoring via ECG is common and there are well established tools to conduct this in the clinic, for short duration 24/48hr monitoring at home with a Holter monitor, or through implanted loop recorder devices for longer term monitoring over many months.

Frequently the Halter monitors do not record for long enough to capture an event, and the longer duration implant is normally used for people who have infrequent events or an unexplained cause. For many patients, events occur over a seven to 14-day period, yet no device is available to capture events over that period.

Diagnostics company Seer Medical is hoping to fill the gap in medium-term monitoring by leveraging its existing combined EEG/ECG wireless monitor, Seer Sense: a revolutionary wireless brain and heart-monitoring wearable that takes gold standard week-long epilepsy diagnostics out of the hospital and into the home.

With funding from the BioMedTech Horizons (BMTH) program, Seer Medical sought to diversify its high-quality real-time and Artificial Intelligence-supported event identification technology for use beyond epilepsy, into cardiac monitoring. Sense Cardiac aimed to offer a new level of sophistication to at-home cardiac monitoring, delivering a step change in patient comfort and freedom, while giving doctors the data they need to make a conclusive diagnosis.

The project team established an advisory group of diverse cardiac experts from around the country, who were enthusiastic about the prospect of a superior ambulatory ECG monitor. They provided valuable insights into current practices and the industry needs and wants of a new device, which were supported by survey data gathered from more than 100 GPs and patients. This helped to define the product development road map through to market adoption.

Substantial headway was made with the company's cloud-based reporting capabilities for cardiac monitoring, and six prototype Sense Cardiac devices were manufactured for patient trials. The team assessed the usability of the Sense Cardiac and the data quality compared to an industry standard device, and the user experience for multi-week studies (ranging from one to four weeks) from the first pilot study, which involved 50 participants. This study identified data quality, usability, and comfort issues, which reduced long-term satisfaction and compliance.

With these challenges identified through the trial, and with Seer Medical focused on the international expansion of its epilepsy monitoring products, a decision was made to pause development of the cardiac monitoring device. Though Seer Medical did not complete all the objectives of its BMTH project, the company remains excited about the possibility of improving diagnostic offerings in the ambulatory ECG space.

Seer Sense cardiac wearable device.

Lead Cardiac Scientist at Seer Medical, Livia Cucuzza, explained that the BMTH project accelerated Seer Medical towards its goal of delivering the fastest path to diagnosis for patients with cardiac arrhythmias.

"In Australia, access to quality non-invasive long-term ECG monitoring is limited. The BMTH funding provided an opportunity to harness the technology suite at Seer and significantly progressed our understanding of the future work required to bring a superior standalone ambulatory ECG service to market," Cucuzza said.

"Our cloud-based, AI reporting methods will increase access to long-term ECG monitoring by collecting continuous ECG data for arrhythmia detection in real time. This will improve cardiac reporting workflows and reduce reporting turnaround times, ultimately improving access to monitoring and providing a faster pathway to diagnosis."

Seer Medical's Chief Operations Officer, George Kenley, agreed, adding that the BMTH project allowed the team to make important progress with its cardiac-focused technology.

"Involvement in any BMTH project is a fantastic opportunity that allows businesses like ours to investigate and progress our early-stage commercialisation endeavours," she said. "Participation in the BMTH-supported project allowed us to make significant headway into better understanding industry needs and design centred around usability and patient experience."

For now, more research and development will be required before the market launch of Sense Cardiac, but it remains an important target. Delivering high-quality diagnostic data over longer durations will mean fewer inconclusive ambulatory ECG studies undertaken, as well as less repeat testing and conditions going undetected or treated incorrectly.

On a mission to prevent childbirth complications by developing a real-time fetal biosensor

PROJECT:
VitalTrace Pty Ltd

THERAPEUTIC AREA:
Neonatal care/Obstetrics

VitalTrace

START DATE: 5 October 2021	TOTAL BMTH GRANT: $800,000
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $800,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $1,123,629
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $0
	TOTAL PROGRAM: $1,923,629

Jobs within the project budget	7
Number of patent applications	2
Number of new technology(ies) invented/progressed	2
Number of preclinical trials commenced	1

Childbirth remains a comparatively high-risk period for both mother and child, and delivery complications, most seriously an interruption of oxygen to the baby and its brain, can result in disability with lifelong consequences.

There were 134 million births[1] and 2.3 million neonatal deaths in 2021[2]. While neonatal death rates have fallen approximately 50 per cent in 30 years, they still ranked fifth overall in terms of deaths globally[3] with main causes being birth asphyxia (inadequate oxygen) and birth trauma, neonatal sepsis and infections, and preterm birth complications.

Such devastating outcomes from asphyxia drive the obvious interest for monitoring babies' wellbeing during pregnancy and childbirth. The current gold standard for real-time monitoring during birth is cardiotocography (CTG) developed in Australia in 1981. While transformational, it is now recognised, including by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, that it can be inaccurate and prone to subjective interpretation.

CTG monitors are attached to the mother's stomach during birth and indirectly measure the fetal heart rate. When signs of distress are observed through an increased heart rate a blood sample from the baby may be taken and analysed for lactate levels to indicate hypoxia. Blood sampling is an invasive and time-intensive lab-based test and having a real-time monitor may have benefits in detecting hypoxia

Image: Leg plate for VitalTrace biosensor.

1. Our World in Data.
2. World Health Organisation, The Global Health Observatory.
3. World Health Organisation, The Top 10 Causes of Death.
4. Electronic fetal monitoring, cerebral palsy, and caesarean section: assumptions versus evidence, 2016.
5. World Health Organisation, Newborn Health.
6. Australian Bureau of Statistics.
7. Australian Institute of Health and Welfare. Health of Mothers and Babies.
8. Australian Institute of Health and Welfare. MyHospitals procedures data.

much earlier than currently possible. In addition, each year, emergency C-sections are performed on thousands of healthy mothers and babies because of a 50 per cent false-positive rate associated with CTG monitoring[4].

Western Australian medical device company VitalTrace was founded to improve safety for mothers and babies during childbirth and eliminate the unnecessary health, psychological and economic burdens from inaccurate childbirth monitoring.

The aim of VitalTrace's BioMedTech Horizons (BMTH) program project was to progress the development of a precision real-time fetal biosensor – DelivAssure™ – for the prevention of fetal complications during childbirth.

Specifically supported by BMTH funding, the company set out to develop manufacturing methods and establish facilities and capabilities in Australia to produce pre-commercial prototypes of the biosensor suitable for use in its intended environment.

With birth asphyxia causing 900,000 deaths annually[5] and many more babies suffering lifelong impacts, the combined factors of the risk of these complications and inadequate monitoring have contributed to an increasing rate of caesarean sections in many Western countries including Australia. Of the 310,000 births in Australia in 2021[6], 37 per cent were by caesarean section[7] and 47 per cent of those were unplanned emergency interventions[8].

The health economics model developed by VitalTrace indicates unnecessary C-sections and fetal hypoxia triggered by unclear data from current monitoring devices impose a healthcare burden of US$6.4 billion annually in the US and Australia.

During the BMTH project, VitalTrace achieved far more than its original objectives. The team designed a manufacturable product, developed manufacturing methods with potential for scale-up manufacturing, established two manufacturing facilities in Perth, successfully produced pre-commercial prototypes, and performed animal studies to gain insights on performance, safety and usability.

This progress has been critical to support VitalTrace's engagement with regulators, including the US Food and Drug Administration (FDA) who granted a breakthrough designation in 2021, and with new intellectual property generated supporting one granted patent and two patents filed.

With the initial phase being a tech-transfer process from an outsourced international contract manufacturer, the team established new in-house capabilities in formulation, microfabrication and manufacturing that gave an improved ability to rapidly iterate through design and quality challenges and resulted in a significant increase in production yield.

VitalTrace Head of Manufacturing Ana Fonseca said: "Achieving extremely reproducible sensors through precise manufacturing has been a great outcome of the project, generating scalable capabilities as we enter global markets."

VitalTrace CEO and Co-Founder Dr Arjun Kaushik explained further: "With input from our Australian research partners and local parts suppliers, the creation of an Australian-first advanced biosensor manufacturing capability is an achievement the team is particularly proud of. This feat has enabled the company to de-risk itself significantly in the eyes of investors.

"The BMTH grant was able to bring forward our manufacturing timeline by at least two years, accelerate research and development and increase the reliability of our novel biosensors. The flow-on effect of this has been massive for VitalTrace, allowing us to secure funding from investors, who looked favourably on our progress in a short span of time.

"Our valuation has tripled since the last raise, mainly due to the value of our unique manufacturing capability resulting from the BMTH program. This has resulted in the company's ability to raise funds that will help it progress towards human trials and regulatory approval," said Dr Kaushik.

VitalTrace has recently secured further funding for a commercial launch from the Western Australian government and MTPConnect's Clinical Translation and Commercialisation Medtech (CTCM) program, to support a human clinical trial. A second funding, from the Western Australian government, has also been secured (Investment Attraction Fund) to progress manufacturing facilities towards commercial prototypes.

When DelivAssure™ receives regulatory approval, it has the potential to ensure the dynamic process of labour is safer for mothers and babies. Once obstetricians have access to real-time lactate values, they will be able to assess whether there is fetal distress and quickly determine whether an emergency C-section is required.

The impact of this project is likely to extend beyond VitalTrace and its immediate stakeholders, to future mothers and babies, obstetricians, midwives, clinicians and hospitals around the world, who stand to benefit the most.

Pictured, front left, Dr Michael Challenor Co-Founder and Chief Technical Officer; middle, Nadia Rahman Scientist; right, Dr Shaghraf Javid Electrochemist; rear, Robert Atkinson Research Chemist and Patent Officer.

‘Micro’-Wearable sensor delivers real-time biomarker sensing for improved personal healthcare

PROJECT:
WearOptimo

THERAPEUTIC AREA:
Cardiovascular

WearOptimo

START DATE: 1 April 2020	TOTAL BMTH GRANT: $983,127
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $983,127
STATUS: Complete	TOTAL CASH CO-CONTRIBUTION: $1,468,000
DELIVERABLES COMPLETED: 97 per cent	TOTAL IN-KIND: $984,000
	TOTAL PROGRAM: $3,435, 127

Jobs within the project budget	12
Number of patent applications	9
Number of new technology(ies) invented/progressed	2
Number of preclinical trials commenced	2
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	9

Wearable health sensors that measure biomarkers in real-time and over an extended period offer the potential to impact on healthcare practice and outcomes by rapidly measuring clinically relevant indicators of disease, in real-time. Real-time biomarker monitoring can indicate progression toward a specific condition, or the effect of a therapeutic intervention, and is known to be effective in cases like real-time glucose monitoring.

Existing clinical practice for measurement of blood-based biomarkers requires taking a sample and sending it to a pathology lab for diagnosis, or measurement in a point-of-care device in the clinician’s office. These can take a long time and collect information relating to a single point in time, as well as requiring a visit to a clinician or pathology lab. While they are informative in cases such as in critical care scenarios, they do not indicate a trend which is vitally important.

Consumers have become accustomed to the idea of real-time health monitoring – with the proliferation of rapid-antigen testing for COVID-19, and the advent of wearable technology such as smart watches incorporating EEG monitoring and temperature sensing, among other things. While wearables are in the main consumer products and not medical devices, there is a gradual shift in this direction, which consumers seem ready to adopt.

Taking wearables to the next level and tackling a significant challenge in management of critical healthcare conditions, Brisbane-based healthtech company WearOptimo is developing a Microwearable patch that will measure hydration and biomarkers such as Troponin I, a protein that is released into the bloodstream when there is damage to the heart muscle, in real time. The level of Troponin I rises within a few hours of a heart attack and remains elevated for several days.

Image: WearOptimo Microwearable and monitoring App.

1. Our World in Data.
2. Australian Institute of Health and Welfare (AIHW): Disease expenditure in Australia 2019–20.
3. Australian Institute of Health and Welfare (AIHW): Heart, stroke & vascular diseases.

The company's minimally invasive, user-friendly device has been designed to continuously monitor wearers for the detection of events such as heart attacks. It forms part of WearOptimo's suite of Microwearable products that seek to address major health challenges by measuring changes in the interstitial fluid just below the surface of the skin. The sensor is integrated into an electronic device that transmits information to a phone or other device.

The first chronic condition that WearOptimo is targeting is cardiovascular disease, the leading cause of death globally[1]. It accounts for an estimated 9.1 per cent of disease-specific expenditure in the Australian health system, that is $12.7 billion[2], and 12 per cent of the total burden of disease[3].

The WearOptimo project specifically focuses on the early detection of cardiac biomarkers associated with heart-related conditions. The goals were to establish the Cardiac Microwearable technology as a clinically relevant measurement device and to use the Microwearable in a first-in-human study to demonstrate safety and tolerability of the platform. This outcome would provide the foundation for future commercial and clinical deployment.

Having optimised the sensor fabrication process, the measurement parameters and the Microwearable geometry for optimal signal generation, the prototype Microwearable sensors were manufactured for the feasibility study. While an *in-vivo* animal study was initially planned for the cardiac sensing, COVID-19 related impacts meant this was delayed and instead a robust microfluidic model was generated.

The sensors demonstrated utility in 100 per cent human serum for over 40 hours of continuous monitoring. They were able to detect clinically relevant concentrations of Troponin I, with a dynamic range spanning four orders of magnitude. The sensitivity demonstrated the capability of the sensor for rapid, real-time detection of the occurrence of heart injury, which will be fully validated in subsequent animal and human trials.

The proprietary DNA-based aptamer-sensing chemistry is now protected by three patent filings, contributing to the company's patent portfolio across all aspects of the sensor, which currently sits at 35 filings across 13 families.

In parallel to the development of the aptamer Microwearable, all the requirements to set up for first-in-human studies of Microwearables were undertaken and completed, and the trial was initiated. Human clinical trials have now been conducted on 19 occasions, and for each trial the participant has worn four Microwearable sensors, recording over 380 hours of continuous sensor data.

During these trials, the sensors were applied without pain to the wearer and were highly tolerable. The human clinical evidence of safety and tolerability will form a core component of WearOptimo's Design History File and will inform regulatory (Therapeutic Goods Administration and US Food and Drug Administration) pre-submissions, as the Microwearable regulatory strategy and pivotal study design is finalised.

The BioMedTech Horizons (BMTH) project has been instrumental in driving the progression of WearOptimo's Microwearable platform and will serve as a catalyst for future growth, said the company's CEO and Founder, Professor Mark Kendall.

"The vision for WearOptimo is to develop affordable wearable technology that offers early intervention and personalised monitoring to help people stay well and productive in their day-to-day lives," he said. "The human clinical trials that commenced in this project are a huge milestone for WearOptimo, they are critical on our path to rapidly advance our Microwearable sensor products, helping to address key health challenges."

To date, the company has secured over $20 million of funding. In addition, it has signed a commercialisation deal with Aspen Medical – a global healthcare company based in Australia that provides a range of healthcare solutions.

Unanticipated yet highly promising outcomes have emerged from the project including an expansion of the market opportunity in measuring hydration. This may have application in areas as diverse as aged care, mining, and high-performance sports, as the impact of dehydration is very significant in cognitive and physical performance.

Today, WearOptimo continues to progress its unique Microwearable monitoring sensor platform to access key health signals that today's surface wearables are unable to reach.

According to Dr Anthony Brewer, WearOptimo's Chief Technology Officer, the company's Microwearable sensor for measuring cardiac Troponin could revolutionise health practices – enabling personalised monitoring, improved disease management and prevention of cardiac events. Importantly, it has the potential to empower individuals to take charge of their cardiac health and enhance patient outcomes, reduce healthcare costs, and contribute to a more proactive and preventive approach to cardiovascular care.

"I am privileged to showcase the outstanding work undertaken by our passionate team in developing Microwearable sensors," he said. "The research in this successful BMTH-funded project represents a convergence of deep tech, novel data science and transformative engineering, unlocking invaluable insights into human health and wellness. With clinical trials commenced in the development of WearOptimo's Hydration Index, a new digital biomarker, we stand at the forefront of a new era where wearable health sensors enhance personal wellbeing, revolutionise healthcare and unlock untapped potential in human performance."

Australian-made high quality rapid point of care test for infectious diseases

PROJECT:
ZiP Diagnostics

THERAPEUTIC AREA:
Infectious disease diagnostics

START DATE:
1 October 2020

END DATE:
30 June 2022

STATUS:
Complete

DELIVERABLES COMPLETED:
100 per cent

TOTAL BMTH GRANT:
$600,000

TOTAL BMTH EXPENDITURE:
$600,000

TOTAL CASH CO-CONTRIBUTION:
$1,831,363

TOTAL IN-KIND:
$1,750,954

TOTAL PROGRAM:
$4,182,317

Jobs within the project budget	25
Number of trademark applications	2
Number of licenses	1
New products launched	2
Number of new technology(ies) invented/progressed	8
Number of preclinical trials commenced	2
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	100

Launched in 2019, ZiP Diagnostics is an Australian-owned, Melbourne-based company that develops and manufactures point-of-care (POC) diagnostics for infectious diseases, such as COVID-19, for use in remote locations or in workplaces including hospital ICUs, GP clinics, and aged-care homes that need accurate test results to remain safe from these infections.

The ZiP Diagnostics test is not another Rapid Antigen Test, but a DNA/RNA-based molecular diagnostic that can rapidly identify symptomatic and asymptomatic people with a sensitivity comparable to lab-based PCR.

In 2020, the company secured funding through MTPConnect's BioMedTech Horizons (BMTH) program. The focus of this work was to establish core requirements of DNA polymerase protein production and validate its function, to establish a quality manufacturing system (QMS), to achieve ISO-13485 certification; and to develop and validate two tests including test cartridge integration, one for SARS-CoV-2, the virus which causes COVID-19, and another for sexually transmitted diseases, Chlamydia trachomatous and Neisseria gonorrhoea (CT-NG).

At the time of the award, the COVID-19 pandemic lockdowns in Australia were 195 days old and it quickly became apparent that access to samples and progress of the SARS-CoV-2 assay should be prioritised ahead of the CT-NG assay, so, changes were made to the program to accommodate this need.

Image: ZiP Diagnostic point-of-care test in action.

The company's commitment to scaled-up manufacturing in Australia, led the engineering team to design and assemble a range of cellular production units to perform the various functions required for assay dispensing, cartridge assembly, packing and quality control. Given the regulatory requirements associated with the manufacture of human *in vitro* diagnostics, ZiP established an ISO-13485-certified QMS, and assembled an in-house team to conduct high-quality clinical trials and regulatory submissions.

The pandemic accelerated progress of the SARS-CoV-2 assay for ZiP-Diagnostics and reinforced the need for accessible, high-quality, rapid POC tests and diagnostic options that were not confined to centralised laboratories. To ensure the tests performed using the wide heterogeneity seen with human samples, the ZiP team established clinical studies to enable collection of samples from test-negative individuals and systems to spike in controlled doses of microorganisms.

ZiP Diagnostics was already on its way to becoming the first Australian company to manufacture novel molecular POC tests that would meet domestic and international needs and, with the support of BMTH funding, it has now developed fundamental platform technologies that can be applied to SARS-CoV-2, as well as other existing and emerging infectious diseases.

According to infectious disease physician and ZiP Diagnostics' Founder, Dr Jack Richards, the company's capacity to locally produce rapid POC diagnostic tests will have a radical impact on the emerging market and will deliver dramatic health improvements and cost savings.

"Hospital ICUs, GP clinics and aged-care homes need highly accurate COVID-19 testing, which is low cost, easy and quick to administer, so they can keep people safe and their services operational. This is not something that was available in Australia before ZiP," Dr Richards said. "Rapid Antigen Tests, have their place, but they are not usually designed to screen asymptomatic people and do not deliver the accuracy these workplaces need to ensure they remain COVID-safe."

Though ZiP Diagnostics faced several pandemic-imposed disruptions during its early days, it managed to expand from eight employees at the start of the BMTH project to more than 30 highly skilled medtech development and manufacturing staff. It also built and commissioned a new PC2 laboratory and clean room manufacturing facility in Collingwood, near Melbourne's CBD. Here, the team can manufacture up to one million tests per year and produce good manufacturing practice (GMP) grade proteins to service this volume of production, with scope for further increases in scale.

Establishing such an operation understandably presented its share of technical challenges – many of which stemmed from the diversity of technologies required to bring a new POC molecular diagnostic test to market. For example, the need to track and respond to changes in microbial strains required ZiP Diagnostics to develop unique bioinformatic solutions to ensure new microbial variants would be detected by its tests.

Having overcome these and other obstacles, ZiP Diagnostics obtained CE mark* regulatory registration for the use of its SARS-CoV-2 test in Europe and its ZiP-P2 instrument, and also received Therapeutic Goods Administration (TGA) export approval in February of 2022.

As the company's Co-Founder and Director, Bill Hopper, said: "ZiP Diagnostics is an example of great Australian innovation with a focus on community need. Australia has a need to manufacture more effective COVID test alternatives, which deliver speed and accuracy outside of labs. We have the opportunity to bring PCR-grade testing to the people and facilities that need it most, including people who have COVID but are asymptomatic. For people who work in healthcare with high-risk patients – it will be a game changer.

"This is where the BMTH program funding proved to be extremely important for us; it provided direct support for many of these crucial activities to help our technology and business develop the momentum we needed," Mr Hopper said.

Yet the future of ZiP Diagnostics is not dependent on SARS-CoV-2 alone. The team is directing its platform technologies to a wide range of other applications that have key clinical and public health needs in Australia and overseas. The CT-NG test that was removed from the BMTH program has continued development.

More recently, ZiP Diagnostics announced new studies with the WEHI (Walter and Eliza Hall Institute) focused on rapid tests for malaria, and has also progressed work for viral hepatitis and initiated work for detection of priority pathogens in the Indo-Pacific region. ZiP Diagnostics continues to demonstrate the importance of local capability and capacity to manufacture high-quality and high-sensitivity POC tests, to support the specific needs for Australia and low to middle-income countries globally.

**The letters 'CE' appear on many products that are traded on the single market in the European Economic Area (EEA). The CE mark shows that the manufacturer has checked that these products meet European Union (EU) safety, health, or environmental requirements.*

DECISION SUPPORT DEVICES

IN THIS SECTION:

- Apollo Medical Imaging Technology
- Artrya
- Macuject
- Merunova

AI-fuelled software guiding treatment decisions for stroke

PROJECT:
Apollo Medical Imaging Technology

THERAPEUTIC AREA:
Cardiovascular

Apollo Medical Imaging Technology

START DATE: 1 October 2020	TOTAL BMTH GRANT: $346,500
END DATE: 30 September 2022	TOTAL BMTH EXPENDITURE: $346,500
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $0
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $505,000
	TOTAL PROGRAM: $851,500

Jobs within the project budget	4
Number of new technology(ies) invented/progressed	1

Stroke is a leading cause of adult disability worldwide and is also one of Australia's biggest killers, with one stroke occurring every 19 minutes. In 2020, the estimated national cost of stroke exceeded $6.2 billion in direct financial impact, and a further $26 billion in lost wellbeing due to short- and long-term disability and premature death.

Ischaemic stroke, the most common type of stroke, occurs when a clot blocks blood flow to the brain; consequently, identifying and removing the clot is the key component of acute stroke therapy. Data from the Australian Institute of Health and Welfare (AIHW) estimate there were 33,704 new acute ischaemic stroke cases in people aged 18+ in 2022, with 329,463 diagnosed prevalent cases.

There are two treatment approaches currently available, including intravenous thrombolysis (IVT, clot dissolving) and endovascular thrombectomy (EVT, clot retrieval). The choice of treatment carries potentially life-changing consequences. Multiple studies and clinical trials have shown early thrombolysis to be a powerful and highly cost-effective intervention for appropriately selected patients. However, thrombolysis carries a significant risk of major intracranial haemorrhage (ICH).

For the most severe strokes, recent clinical trials have shown that successful reperfusion with EVT can double the odds of a patient's disability-free survival. However, EVT is a high-cost intervention requiring rapid identification and patient transfer to a limited number of major hospitals with appropriate infrastructure. EVT also carries risk of possible complications including hematoma, vascular occlusion, or perforation, and more.

Image: CT scanner in use.

Making the decision about which of these options will be best for a patient is a challenging task. Current clinical guidelines provide limited assistance to clinicians, who lack effective tools to predict how an individual patient will respond to each therapy.

Seeking to rectify this unmet clinical need, Apollo Medical Imaging Technology is developing a clinical decision support system (CDSS), fuelled by artificial intelligence (AI), that will predict good and poor patient outcomes for stroke patients if treated by different therapies. The Melbourne-based company, which specialises in the creation of advanced image processing software for clinical and research applications, is developing the software in partnership with the Ingham Institute for Applied Medical Research and The University of Newcastle, with the support of BioMedTech Horizons (BMTH) program funding.

Apollo had established and commercialised a software tool (AutoMIStar) to automate processing, analysis, and visualisation of computed tomography (CT)/magnetic resonance imaging (MRI) scans, including CT perfusion (CTP), CT angiography (CTA), non-contrast head CT (NCCT) and diffusion-weighted imaging (DWI). The device provides quantitative perfusion- and diffusion-related parameter maps, together with characteristic threshold maps and volumes reflecting tissue pathophysiological status.

Through the BMTH project, Apollo succeeded in creating CDSS models based on data from around 2,000 patients to train the models. The CDSS tool has now been incorporated within AutoMIStar as a research option. Subsequent validation using historical data sets has shown that decisions made by a human assisted by the CDSS will not have resulted in an increase of adverse outcomes and could even potentially result in better patient outcomes.

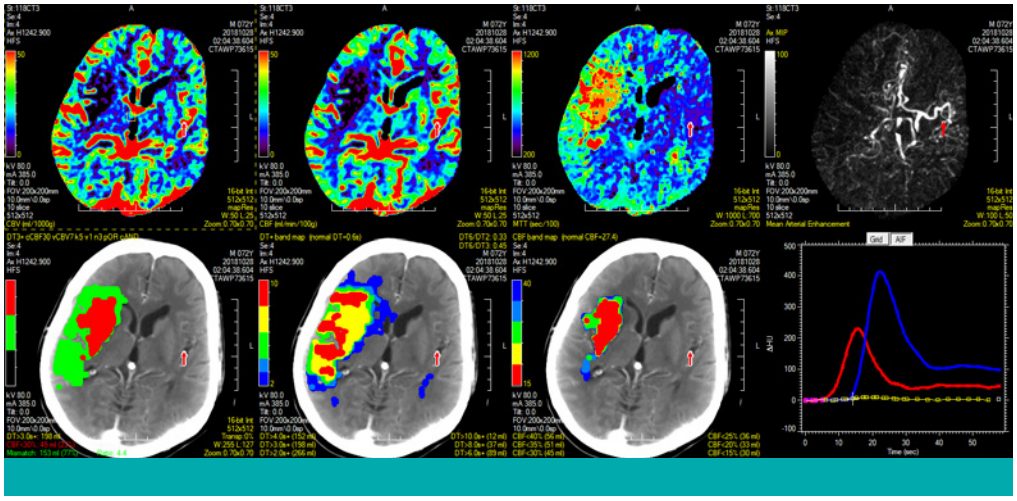
These results met the expectations of Stroke Specialist and Director of the neurology department at China's Ningbo First Hospital, Dr Jianhong Yang, who said the software will have significant implications for a specific cohort of stroke patients, in particular.

"In clinical practice, my treatment decision relies on CTP," he said. "It is relatively easy to make a treatment decision for patients with large core and small penumbra (no to treatment) or those with small core and large penumbra (yes to treatment). However, it is often quite challenging to make treatment decisions on patients with similar size of core and penumbra, such as patients with 30 ml penumbra and 30 ml core. Patients in this 'middle' group often vary in their responses to IVT or EVT treatment. Therefore, this CDSS tool is of most use to make individual treatment decisions in this 'middle' group."

While the results are promising and the BMTH project has provided a critical foundation for the Apollo Medical team, recent research indicates that relying on derived characteristics like lesion volume sets a hard limit on what AI models can achieve. Recent studies have started using 3D imaging-based deep learning models to explore advanced CT imaging data and demonstrate the potential for imaging-based outcome prediction models to achieve significantly higher accuracy than volume-based outcome prediction models.

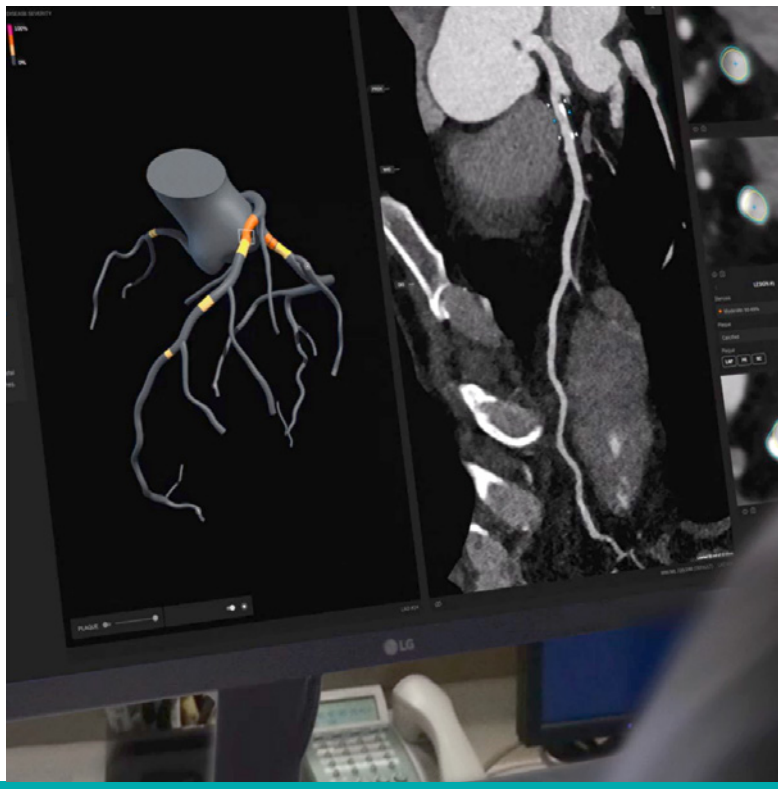
Apollo, in partnership with Ingham and other research and industry partners, has recently been awarded a Commonwealth-supported grant for research and development of AI models for automatic detection and analysis of ischaemic injury, and imaging-based outcome prediction models for stroke patients.

Once commercialised, the software's value will be particularly felt by rural and remote hospitals, where lack of access to expert stroke assessment contributes to two times the likelihood of lifelong disability. Additionally, the software should help lessen the financial burden of stroke, given that existing clot-retrieval treatments cost up to $20,000 per patient. Most importantly, the software should help improve patient outcomes as it enables treatment options to be more accurately assessed.



CT Perfusion scan of a patient's brain.

Leveraging AI to accurately identify patients at risk of coronary artery disease



PROJECT:
Artrya

THERAPEUTIC AREA:
Cardiovascular

ARTRYA

START DATE:
1 October 2020

END DATE:
31 March 2023

STATUS:
Completed

DELIVERABLES COMPLETED:
91 per cent

TOTAL BMTH GRANT:
$987,428

TOTAL BMTH EXPENDITURE:
$987,428

TOTAL CASH CO-CONTRIBUTION:
$831,903

TOTAL IN-KIND:
$250,000

TOTAL PROGRAM:
$2,069,331

Jobs within the project budget	41
Number of trademark applications	12
Number of patent applications	8
New products launched	1
Number of new technology(ies) invented/progressed	9
Number of preclinical trials commenced	4

Artrya, a Perth-based digital health company, is set on improving clinical outcomes for those at risk of heart attack through its Artificial Intelligence-based tools to analyse coronary computed tomography angiography (CCTA) images. Artrya's approach is to minimise requirements for highly invasive tests and to extend the insight available through the non-invasive CCTA.

Coronary heart disease (CHD) is the leading cause of death in Australia, accounting for 17,300 deaths in 2021 – representing 10 per cent of all deaths and 41 per cent of cardiovascular disease deaths[1]. In 2020, the estimated direct health expenditure on CHD in Australia was $2.4 billion[1] and in 2022, CHD remained the leading specific cause of burden in Australia, with 306,000 years of healthy life lost.

CHD occurs when the major blood vessels that supply the heart (coronary arteries) struggle to send enough blood, oxygen and nutrients to the heart muscle. Atherosclerotic plaques (cholesterol deposits) in the arteries and inflammation are typically the cause.

Heart attack risk and the benefits of coronary revascularisation are determined by the susceptibility of atherosclerotic plaque to rupture and the burden of restricted blood flow (ischaemia).

An invasive coronary angiography (ICA) is the most common test to detect CHD, yet it provides no direct assessment of ischaemic burden, is associated with considerable cost, and exposes patients to potentially serious complications. Assessing ischaemia requires an additional invasive test, the fractional flow reserve (FFR).

Image: An onscreen image of a Salix assessment of a patient's coronary arteries.

1. Australian Institute of Health and Welfare. Heart, stroke and vascular disease: Australian facts.
2. Understanding the predictive value and methods of risk assessment based on coronary computed tomographic angiography in populations with coronary artery disease: a review, 2021.
3. Economic Cost of Acute Coronary Syndrome in Australia, 2018.

To reduce ICA risks and costs, non-invasive stress tests (treadmill, stress echocardiogram, myocardial perfusion imaging [MPI] and coronary computed tomography angiography [CCTA]) are used. Except for CCTA, these tests have limited accuracy and provide no information about coronary plaque characteristics.

CCTA has greater than 95 per cent predictive value in excluding the presence of CHD[2], but is unable to assess ischaemia, which requires an additional test. Recent advances in computational fluid dynamics (CFD) address this limitation by estimating FFR non-invasively from a standard CCTA scan. However, the only commercially available non-invasive CCTA-based FFR assessment is costly and requires offsite analysis for up to two days, severely limiting its use.

Artrya's non-invasive point-of-care software solution uses its custom AI to analyse CCTA for blockages and build-up of high-risk plaque in blood vessels. The cloud-based tool's assessment process is completed within 15 minutes, offering substantial time and cost savings compared to competing technologies and current industry practices, which often take 45 minutes or longer for complex cases.

The software can identify two forms of plaques: those that limit blood flow, causing ischemia, and those not presently hemodynamically significant, but prone to rupture and consequently cause heart attack – vulnerable plaques that will evolve and eventually lead to acute coronary syndrome (ACS). Accurately identifying the former could reduce the healthcare costs associated with the management of symptomatic patients, while the latter could reduce both the economic and societal costs of ACS, which The Heart Foundation estimated to be $6.8 billion in 2017–18[3].

The BioMedTech Horizons (BMTH) funding enabled Artrya to refine its beta product, clinically validate its solution for regulatory approval and complete commercialisation. Additionally, it supported the development of a novel method to measure blood flow non-invasively off the same CCTA scan. This method helps clinicians identify areas where there is not enough blood reaching the heart due to blockages, using the principles of fluid dynamics to pinpoint these blockages without the need for invasive procedures like angiograms.

Artrya's Chief Scientific Officer, Professor Girish Dwivedi, said of the project's success: "Our work through the BMTH program has led to the development of 'Salix', an advanced AI-powered solution that assesses heart CT scans. This remarkable technology not only identifies arterial narrowings, but also targets challenging imaging biomarkers that often go unnoticed and aren't reported. Our internal studies have demonstrated Salix's immense promise, positioning it as a true game changer in the field of cardiac CT scans."

Once in market, Salix has the potential to deliver significant value – empowering clinicians and patients to improve diagnosis in a more time-efficient manner and with greater accuracy and precision. It will also enhance understanding for all stakeholders in the care pathway, guide personalised treatment (whether lifestyle or medical therapy) and track therapeutic success by assessing disease progression and plaque transformation.

To drive approval and adoption of its solution, Artrya has assembled a highly skilled global team with impressive credentials, leveraging Salix's unique value proposition to improve outcomes and productivity for patients, providers and payers.

For the BMTH project, a key objective was to refine and validate the underlying algorithms. Artrya forged strategic partnerships with prominent institutions in Australia and internationally. The Harry Perkins Institute of Medical Research in Western Australia played a vital role, by offering invaluable clinical insights and subject matter expertise for the development and evaluation of the vulnerable plaque algorithm. Canada's University of Ottawa Heart Institute played a key role in providing valuable clinical expertise, and also granted access to a substantial CCTA dataset.

Several distinguished key opinion leaders from Stanford University, Mayo Clinic and the Huntsville Hospital Heart Center in the US participated in various studies. Their involvement contributed significantly to validating Artrya's algorithms' efficacy. These partnerships also played a crucial role in providing insights and feedback for the refinement and development of the company's software products.

As part of the BMTH project, Artrya conducted an extensive market assessment and sizing, segmentation, competitors' analysis and pricing strategies for Australia, the US, the European Union (EU), the UK and Canada, utilising the services of EVERSANA. This analysis has further solidified and validated the company's business case for Salix, while also revealing additional opportunities for Artrya's products.

The funding also allowed Artrya to develop unique intellectual property, differentiating its solution from competitors, safeguarding the software and establishing a competitive advantage in key areas. This achievement included the submission of eight patents currently under review by patent offices, as well as the approval of 12 trademarks. To ensure adherence to quality standards and software development as a medical device, Artrya obtained several essential ISO certifications.

The company also gained several regulatory approvals, including Therapeutic Goods Administration (TGA), UK Conformity Assessed (UKCA) and Conformité Européenne (CE). Additionally, Artrya initiated the regulatory approval process with the US Food and Drug Administration (FDA).

During the project period, Artrya progressed through a pre-initial public offering (IPO) fundraising round of $15 million and an IPO round of $40 million and was successfully listed on the Australian Securities Exchange (ASX:AYA) in 2021.

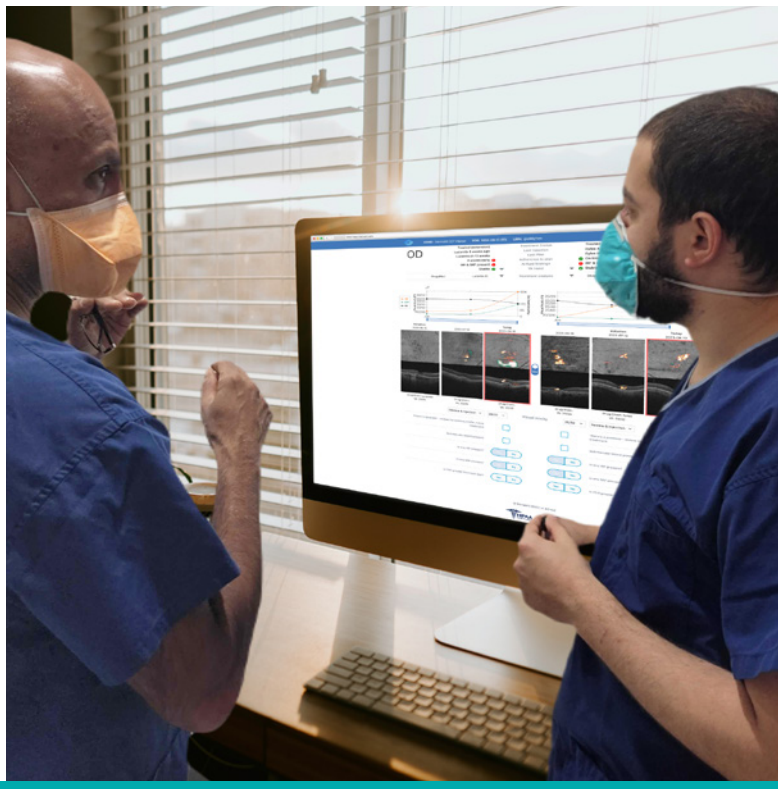
As Artrya CEO Mathew Regan explained: "Artrya is very focused on saving lives using our breakthrough AI technology. The BMTH program has provided important support to our dedicated team as they have developed the product. We are moving rapidly to the commercialisation phase of our development here in Australia and working hard to secure FDA approval."

AI-based clinical decision support software to help prevent blindness in age-related macular degeneration

PROJECT:
Macuject

THERAPEUTIC AREA:
Vision

MACUJECT



START DATE: 1 April 2020	TOTAL BMTH GRANT: $948,000
END DATE: 30 March 2023	TOTAL BMTH EXPENDITURE: $944,613
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $471,508
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $623,240
	TOTAL PROGRAM: $2,039,361

Jobs within the project budget	10
Number of trademark applications	1
Number of patent applications	3
Number of licenses	2
Number of new technology(ies) invented/progressed	2
Number of preclinical trials commenced	2

Age-related macular degeneration (AMD) results in a progressive loss of vision caused by either fluid build-up or cellular degeneration in the retina. Disease prevalence grows from two per cent of people aged in their 50s, up to nearly 30 per cent of over-75s. Advanced disease stages often result in legal blindness, making AMD the most common cause of irreversible blindness in developed countries.

In 2020, there was an estimated 198 million people suffering from AMD worldwide, with estimates up to 288 million in 2040[1]. The dry form of the disease, in which the light-sensitive cells of the macula slowly break down, accounts for 90 per cent of diagnosed cases. Meanwhile, the wet form of the disease, in which fluid leaks into the macula, accounts for only 10 per cent of cases.

Estimates of the global cost of visual impairment due to AMD in 2010 were US$343 billion, including US$255 billion in direct healthcare costs[2]. Highly effective anti-VEGF treatment exists for wet AMD; however, most AMD sufferers are unable to access optimal treatment, even in wealthy countries. New dry AMD therapies have received regulatory approval in 2023, which will generate a large increase in the number of patients eligible for treatment, further exacerbating the already critical shortage of treatment capacity by retinal specialists.

Melbourne-based digital health company Macuject is striving to address this shortfall by developing clinical decision support software for AMD.

Image: Macuject Clinic.

1. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis, 2014.
2. Global Cost of Vision Loss. Access Economics 2010.

The Macuject software platform comprises both artificial intelligence (AI) based image analysis and decision tree components. The tool has been designed to be used throughout the patient journey and will guide monitoring and tracking of early-stage AMD in optometry clinics, and then recommend optimised treatment protocols and facilitate monitoring of advanced AMD progression by ophthalmologists. The software will increase the volume of patients that can be monitored for early disease in optometry, and improve decision-making and workflow in ophthalmology, resulting in larger numbers of patients receiving optimal treatment.

With support from the BioMedTech Horizons (BMTH) program, Macuject set out to establish the design of the application, complete minimum viable product (MVP) development, complete a retrospective clinical trial and establish commercial partners with a validated protocol to support regulatory approval. The BMTH support helped Macuject move from an identified clinical problem and unmet need with a proposed solution, through to a functional product validated in market with input from a range of national and international key opinion leaders and companies.

The project saw successful development of the wet AMD platform and real-world utilisation in 10 Australian clinics, gathering over 27,000 life years of wet AMD data, including treatment with more than 190,000 intravitreal injections for over 4,700 patients. This dataset provided completely novel insights into real-world clinical practice and was the basis of five pharma-sponsored analytics projects. Macuject completed two De Novo Food and Drug Administration (FDA) pre-submission meetings to finalise the design of a validation study, and now has two patent families.

Macuject's wet AMD project put the company in an ideal position to capitalise on the emergence of the first therapies to treat dry AMD. The team has now pivoted to focus on this large market opportunity, which will place new demands on optometrists and ophthalmologists from late 2023.

Looking ahead, the company expects to commence beta-testing of the platform in the US in late 2023, with support from both large pharma and global retinal imaging companies. The regulatory approval process with the FDA will then begin in 2024.

The BMTH funding enabled Macuject to expand its internal development team and secure two US patents for AI-based technologies. The real-world clinical data generated by this work also enabled Macuject to generate revenue by providing analytics to pharma and obtain additional seed funding – of more than $800,000 – from private business angels and the Australian Medical Angels investor syndicate. Follow-on funding from US investors is expected in 2023, leading to a Series A in 2024.

Once in market, the Macuject platform has the potential to improve patient outcomes for sufferers of wet AMD by facilitating detection of the disease in OCT images, optimising treatment protocols based on personal medical history, and minimising undertreatment through clinical decision support that aligns with the gold-standard treatment protocols.

Meanwhile for dry AMD patients, Macuject will deliver earlier diagnosis in primary care, triage referral to retinal specialists at the optimal time, and encourage treatment persistence via personalised education and messaging to avert injection fatigue, a common reason for sub-optimal outcomes.

These developments are an important breakthrough for patients and clinicians alike, said Macuject's Clinical Success Lead Stephanie Mauger.

"I have seen the benefits that a clear dashboard showing the complete clinical history can bring to both doctors and patients," she said. "Decision-making is easier, and patients have a much better understanding of how the treatments are working and the benefits of continuing therapy."

Real-world beta-testing of the wet AMD platform in Australian clinics has confirmed increased clinician adherence to gold-standard treatment protocols, and a reduction in undertreatment. Plus, Macuject has facilitated increases in clinic workflow, resulting in 10 to 30 per cent more patients seen, associated with shorter waiting times for patients.

Overall, this platform will increase the capacity of both primary and secondary care providers to handle a very large number of AMD patients, resulting in less preventable blindness and lower socioeconomic cost to society.

According to ophthalmologist and Macuject Founder and CEO, Dr Devinder Chauhan, the software delivers significant benefits to all stakeholders involved in preventing blindness caused by AMD, helping the company achieve the best clinical outcomes for patients more confidently, consistently and efficiently.

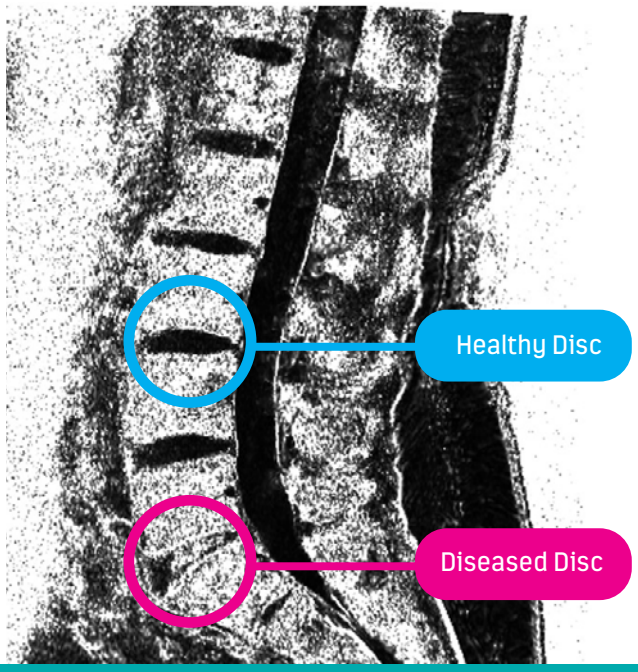
"The Macuject platform has significantly boosted the efficiency and consistency of my clinical decision-making, and the AI tools provide an excellent back-up to detect unidentified disease and refine treatment decisions," he said. "It is a valuable aid and will help me prevent blindness in more patients."

Digital 'add-on' software for MRI scanners to revolutionise how back pain is diagnosed and treated

PROJECT:
Merunova

THERAPEUTIC AREA:
Orthopaedics

Merunova



START DATE: 1 October 2020	TOTAL BMTH GRANT: $975,350
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $877,815
STATUS: Complete	TOTAL CASH CO-CONTRIBUTION: $20,664
DELIVERABLES COMPLETED: 98 per cent	TOTAL IN-KIND: $4,500
	TOTAL PROGRAM: $902,979

Jobs within the project budget	9
Number of patent applications	3
Number of new technology(ies) invented/progressed	1
Number of clinical trials commenced	2
Number of patients to clinical trial recruitment	27

Image: Annotated image of a new scan using this technique, it shows a massive difference between the bottom disc which is clearly diseased and the others which are clearly healthy.

Back pain affects one in six Australians, or about four million people, and is the third-largest cause of disease burden – costing the health system an estimated $3.4 billion in 2019–20; 2.4 per cent of all health expenditure and the third leading burden, accounting for 4.2 per cent of all burden of disease in Australia[1]. Despite this, almost 90 per cent of cases have no diagnosable cause. There is reduced participation in the workforce and an approximate 16 per cent increase in mental health and behavioural issues reported, compared to those with no back problems.

Most back pain issues are diagnosed with magnetic resonance imaging (MRI) and computerised tomography (CT) imaging, with MRIs better able to distinguish soft tissues such as muscle, cartilage, and nerves. In many cases clinicians can identify the problem from these imaging tools but cannot identify the underlying cause to better direct an intervention.

Better diagnostic techniques would allow personalised treatment based on underlying cause and allow existing treatments to be better targeted to individual patients. Yet techniques for diagnosing potential causes of back pain have made little progress in the past 20 years.

Hoping to fill this void, Sydney-based digital health start-up Merunova has developed a digital 'add-on' software device named DeVa™ that can be used with existing MRI scanners. Its purpose is to gather more meaningful information about degeneration of the spinal disc: a shock absorber between the bones of the spine that can wear out or become damaged with age, leading to chronic back pain.

Prior to receiving BioMedTech Horizons (BMTH) funding, Merunova had completed preclinical animal testing, showing its device significantly outperformed the main current technique in clinical practice – T2 weighted imaging – and the gold standard MRI technique used in research – quantitative T2 relaxometry.

1. Australian Institute of Health and Welfare (AIHW): Chronic musculoskeletal conditions.

One reason that other techniques have failed to gain traction is that radiographers acquiring scans are already overloaded, and other techniques were complicated and took too much time. Other products that worked well in a research environment failed to translate to practice. With insights from their practicing clinical backgrounds the founders of Merunova sought to create a highly automated 'low friction' solution, which allows radiographers to take a scan with one button push.

The focus of Merunova's project was translating the validated research imaging protocols to those which will work in a regular clinical setting, using a range of clinical MRI instruments having a lower field strength than high-field research instruments, with imaging times limited by established regular clinical workflow and the patient's ability to stay still.

The BMTH project was a collaborative effort between Merunova, Healthcare Imaging Services (one of Australia's largest medical imaging providers) and the University of New South Wales. It aimed to complete human validation to prove value in clinical decision-making, and to define the role of the device in shifting to a personalised medicine approach to back pain from the current paradigm of non-specific treatment. Secondary objectives were market definition, referrer education and price setting.

The software was redeveloped to meet regulatory requirements (IEC62304 and ISO-134845) and fulfill requirements according to the Software As A Medical Device guidelines. A key technical achievement was to reduce the time it takes to acquire a scan to about eight minutes – a fraction of the time required for existing scans and a critical commercial advantage. In addition, wide-ranging clinician feedback was sought to ensure reported information fulfilled the requirements of the referring doctor.

With technical development progressed to a functional product, ethics clearances received and imaging facilities recovered after COVID-19 restrictions, the team was ready to undertake the critical test – imaging real patients on clinical MRI instruments.

The team performed its DeVa™ scans on humans as part of this project, using multiple different MRI scanners at different sites operated by different companies. The outcome offered the radiographer and clinician additional insight, even when applied to 'basic' everyday scanners available in suburban radiology practices and not just very high-strength scanners that are available in research institutes.

This very promising result means the software is likely to be readily integrated into existing facilities and clinical practice, with no change in MRI instrument required – a critical advantage to support commercial implementation.

And with these tests completed, Merunova has been undertaking its pivotal clinical trial recruiting participants that are undergoing expensive and invasive spinal fusion operations. The unblinded results for this will be available in mid-2024, paving the way for submission of the regulatory documentation. This regulatory quality observational study is aiming to better quantify how well the technique predicts response to spinal fusion, with definitive results expected in 2024. This will set the scientific basis for pricing the technology and related products.

Merunova has been awarded a US patent and a Japanese patent covering critical processes. It has prepared a market analysis supporting commercialisation plans and developed safety and regulatory documents for submission to the Therapeutic Goods Administration (TGA) for approval as a Class IIa medical device, a critical milestone and precursor to its commercialisation globally.

Merunova is currently fundraising and seeking strategic alliances simultaneously. The work funded through the BMTH program places the company on a global footing, allowing investors and partners to consider its technology as an almost-ready-for-market medical device.

Ultimately, the software offers hope to millions of people with undiagnosable back pain. It will lead to better targeted spinal surgery, less unnecessary surgery, and better patient outcomes. This will save millions of dollars in Australia and billions worldwide in direct health expenditure – not to mention avoid significant patient harm.

According to Dr Ashish Diwan, Merunova Co-Founder and Project Lead, hundreds of thousands of Australians who are currently told 'we don't know where your pain is coming from' will probably now be told 'your pain is coming from here and not there'.

"This technology fills a gap that clinicians have been complaining about for decades," he said. "This has a ready audience all around Australia and across the world. It will be a game changer in the management of chronic low back pain."

Expedited by the BMTH project, the device is on track to revolutionise how back pain is diagnosed and treated, added Dr Brian Hsu, a spinal and scoliosis surgeon, and Director of Community Development on the AO Spine Asia-Pacific Board.

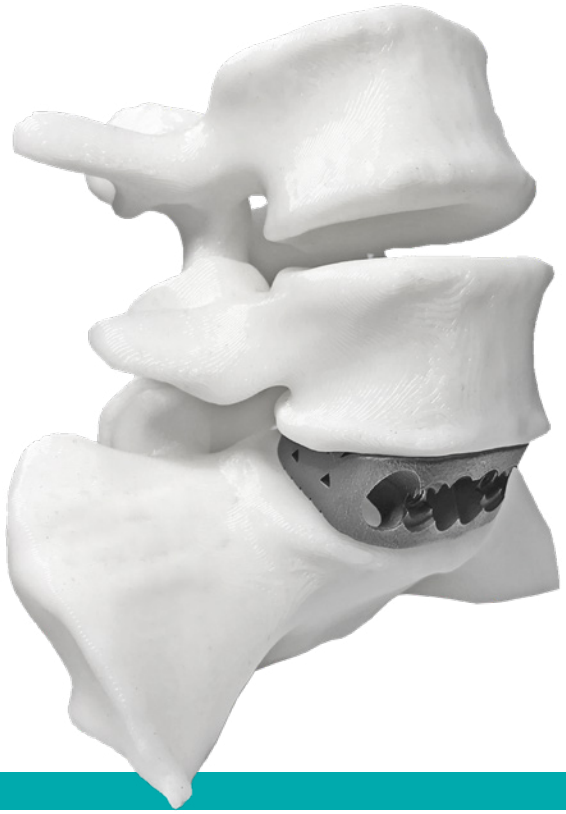
"This is the most promising diagnostic advance I've seen in a generation for back pain," he said. "Patients and doctors are crying out for technology like this and translating this discovery to a serious product for use, it would not have been possible without the funding Merunova received."

IMPLANTED MEDICAL DEVICES

IN THIS SECTION:

- 3DMorphic
- Anatomics
- Anisop Holdings
- Carbon Cybernetics
- Ear Science Institute Australia/ClearDrum
- Hemideina
- IDE Group
- Kunovus Technologies
- Synchron Australia
- VenstraMedical
- PolyActiva

Revolutionising spinal fusion outcomes with world's fastest patient-specific systems



PROJECT:
3DMorphic Pty Ltd

THERAPEUTIC AREA:
Orthopaedics

START DATE: 29 September 2021	TOTAL BMTH GRANT: $800,000
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $800,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $955,446
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $0
	TOTAL PROGRAM: $1,755,446

Jobs within the project budget	10
Number of trademark applications	2
Number of patent applications	3
New products launched	3
Number of new technologies invented/progressed	11
Number of preclinical trials commenced	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	122

About four million, or one in six, Australians are afflicted with back problems. Back pain can have a significant impact on quality of life, including the sufferer's ability to work.

Around 15,000 spinal fusion surgeries were performed in Australia in 2022 with a forecast compound annual growth rate of 10 per cent. These surgeries aimed to reduce pain, restore normal function, and allow patients to get back to work. These procedures have been under the spotlight in recent years, with the government making changes to the Medicare Benefits Schedule (MBS) items for spinal surgery in 2018. This is because spinal fusion surgery is currently less successful than various other procedures in terms of reoperation rates. For example, in New South Wales (NSW), spinal surgery has a 23 per cent reoperation rate within two years of the initial procedure, compared with less than two per cent for hips and knees. Reoperation can lead to problems for patients, as revision surgeries have lower success rates than primary surgeries and are costly.

The established practice has been to use standard 'off-the-shelf' device designs that are intended to work for most people. As each person has variations in vertebral shape, this means that the devices are not tailored to any one person or their specific needs. During surgery, the bone is shaped as best as possible to fit the device. This results in extended surgery and recovery times and can cause pain hot spots due to mismatched shape between the spine and the implanted device. Mismatch in shape also leads to instability in the fusion construct, which can lead to failed fusion. This is a significant contributor to the reoperation rates.

While patient specific devices have been produced previously, their design and manufacture has taken about six weeks which is unacceptable for the patient, increases the cost of healthcare, and is not a viable approach for manufacturers. In contrast, the standardised design devices

Image: 3DMorphic spinal fusion device.

can be held in stock by the hospital and used immediately; however, the poor outcomes mean that this is also unacceptable for the patient and increases the cost of healthcare as well.

Clearly, there is an urgent need, in terms of both patient outcomes and maintaining an economically sustainable health system, for improvement in spinal fusion procedures.

NSW-based 3DMorphic is on a mission to fill this gap by revolutionising spinal surgery with patient-specific systems in quick turn around with a target of five days. The company designs and manufactures 3D-printed medical devices in-house, specific to a patient's anatomy, using state-of-the-art additive manufacturing.

With support from the BioMedTech Horizons (BMTH) program funding in 2021, 3DMorphic commenced a world-first clinical trial into patient-specific spinal fusion devices. The aim of the project was to provide clinical, radiographic, functional, and cost evidence that the company's products can be delivered within the target timeframe, and deliver better outcomes to patients, healthcare providers and payers than traditional 'off-the-shelf' device alternatives.

During the trial, 122 patients were treated with 147 devices. Highly positive outcomes have been demonstrated by the first 72 patients, with post-operative follow-up data indicating that those treated with 3DMorphic devices are both clinically and statistically significantly better than those treated with alternative devices.

The Visual Analogue Scale (VAS) is a current 'gold standard' in patient-reported outcome measures, requiring patients to rate their pain on a scale of 1-10. The clinical improvement in terms of VAS pain scores for patients treated with 3DMorphic devices took patients from severe/intolerable pain (>7) to mild/tolerable pain (<3). These results have remained stable, while becoming statistically more powerful with the addition of more patient post-operative follow-up scores. The 3DMorphic team expects this trend to continue, as it monitors patients into the future.

Currently, none of the trial patients treated with the 3DMorphic devices have had revision surgeries. While this may not remain the case, if the trend of lower reoperation rates for 3DMorphic's BMTH patients continues as patients pass the two-year post-operative time point, this would demonstrate a significant reduction in spinal fusion reoperation rates.

Excitingly, production time for the spinal devices exceeded expectation, with printing and post-processing improvements meaning that through the course of the clinical trial, it became apparent that 3DMorphic's production methods were capable of true 'just-in-time' manufacturing. The nominal pre-trial target of 10 days for manufacture was considered ambitious, as other manufacturers of custom-made devices usually state six weeks. However, during the first part of the trial, 3DMorphic was designing, manufacturing and delivering devices with a 5.4-day average turnaround. By the end of the trial, a 48-hour turnaround had become standard, with several sub-24 hour (emergency cases) being achieved. This demonstrates the value of 3DMorphic's technology, which is powered by innovative, patent-protected methods embodied in the company's proprietary software. Speed of turnaround is key to the value and scalability of the technology. The clinical trial has proven 3DMorphic's technology on both fronts.

3DMorphic's Quality Assurance and Regulatory Engineer, Chloe Amaro, said that the project achieved its objective.

"This project has allowed us to gather the data and give weight to the notion that patient-specific implants really do perform better than off-the-shelf devices," she explained. "It's something that hasn't really been done before in the industry, and that's really exciting to be part of."

Early clinical outcomes of the first 50 patients from the BMTH-funded trial were used as part of the clinical data submitted to the Therapeutic Goods Administration (TGA) for regulatory assessment. Notably, 3DMorphic is now the first and only company to have patient-specific spinal devices listed on the Australian Register of Therapeutic Goods (ARTG).

Additionally, during the BMTH project, 3DMorphic had six patents granted (national and international) and published two further international patents, along with two Patent Cooperation Treaty (PCT) applications. These patents aim to protect technologies core to 3DMorphic's commercial spinal devices and intellectual property (IP) portfolio. Results from the clinical trial have likewise been used in a Prostheses List application. If successful, this will have a direct impact on the commercialisation of 3DMorphic's technology, as well as set a precedent and define a pathway for other manufacturers to transition to patient-specific devices, which should benefit patients and the healthcare economy.

Now, 3DMorphic aims to continue expanding its team, Australian production capabilities and product lines – creating job opportunities for skilled STEM graduates.

One such graduate is Jack Hill, who joined 3DMorphic as an intern in 2021, and is now the team's Clinical Trial Coordinator and Production Engineer.

"Working on 3DMorphic's clinical trial has been an incredibly rewarding experience for me," Hill said. "It provided a great opportunity to apply my skills outside of university and further deepen my understanding of the medical device industry. It has been exciting to see the years of work from everyone on the team translate into impressive results that we expect to advance spine surgery and ultimately improve outcomes for patients."

Critically, the impact of the project for the general public has been increased access to new and improved spinal fusion technology, that is benefiting patients' lives through reduction in pain and improvement of function compared to off-the-shelf alternative treatments.

3DMorphic will continue the project into the future, with the aim of collecting definitive evidence of the benefits of its technology. The team hopes this will ultimately lead to the changes in clinical practice necessary to ensure that this transformative technology reaches any patient that needs it.

World-first smart wearable for neurosurgery patients set to deliver remote monitoring capability

PROJECT:
Anatomics Pty Ltd

THERAPEUTIC AREA:
Brain

Anatomics

START DATE:
1 October 2020

END DATE:
14 July 2023

STATUS:
Completed

DELIVERABLES COMPLETED:
100 per cent

TOTAL BMTH GRANT:
$997,920

TOTAL BMTH EXPENDITURE:
$997,918

TOTAL CASH CO-CONTRIBUTION:
$0

TOTAL IN-KIND:
$371,693

TOTAL PROGRAM:
$1,369,611

Jobs within the project budget	2
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	1

People that have suffered from stroke or traumatic head injury can experience potentially fatal brain swelling that may require a craniectomy – an operation to remove a section of the skull, to allow the brain to swell and expand, reduce intracranial pressure and reduce the risk of death and permanent brain damage. This swelling can take months to subside and during this time, the patient will normally wear a helmet to protect the brain and conceal the craniectomy defect.

Currently, neurosurgeons determine the timing for skull reconstruction through direct examination of the patient at arbitrarily scheduled consultations. This can result in surgery being performed when the brain is not the optimal size, sometimes resulting in complications that necessitate further surgery or cause additional brain injury.

Aiming to make a fit-for-purpose solution, Melbourne-based medical device company Anatomics has developed the SkullPro®, which is a patient matched, 3D-printed protective nylon casing that is placed within a fabric cap that looks like a beanie – a significant step forward from the previous common approach of wearing a sport helmet. This product has been available since 2020, and Anatomics saw opportunities to use SkullPro as a platform to incorporate devices that will enable clinicians to remotely monitor patients that have undergone decompressive craniectomy to better time the reconstructive surgery.

SkullPro® 2.0 is the latest iteration of the company's original SkullPro® device. The new model builds upon the SkullPro® 1.0 by measuring, recording and exporting environmental, anatomical and physiological data including cranial motion, brain swelling, scalp temperature, ambient temperature and barometric pressure.

Image: SkullPro® 2.0 Remote monitoring smart wearable device.
Photo credit: Sam Miatke, Anatomics Pty Ltd.

For its BioMedTech Horizons (BMTH) project, Anatomics set out to develop and validate the SkullPro® 2.0 to remotely capture this data, while leveraging CSIRO's Embedded Intelligence Platform (EIP) to provide a foundation for secure data transfer and interpretation.

The project resulted in the development of two SkullPro® 2.0 prototype designs, and the manufacture of five prototypes with a secure encrypted data pipeline and a clinician dashboard that collects environmental and patient physiological data.

Key stages of the program were the comprehensive market literature search ensuring Freedom to Operate (FTO), updated review of the competitor landscape and understanding of the regulatory requirements in key markets. These informed the detailed technical design and selection of sensing modalities, which would enable the device to meet the established clinical requirements. With hardware requirements established, software and firmware were developed to support secure data transfer and storage of information to present to the clinician dashboard.

With technical elements in place and having validated the secure flow of information from the SkullPro® 2.0, approval to run a first-in-human trial was granted. Anatomics and its collaboration partners at CSIRO initiated the first-in-human trial with a positive outcome on their first patient and have successfully set up for ongoing trials of SkullPro® 2.0.

Sharing these exciting outcomes, Anatomics Vice President of Process Automation, Mark Owbridge, said: "By successfully delivering both the functional prototypes and the accompanying data pipeline for the SkullPro® 2.0 device, Anatomics has been able to demonstrate the feasibility for remotely monitoring patients to determine appropriate timing for reconstructive surgery following decompressive craniectomy.

"Monitoring patients' environmental and physiological data remotely is a monumental shift in patient care and allows surgeons to objectively assess patient data to facilitate key decision-making processes."

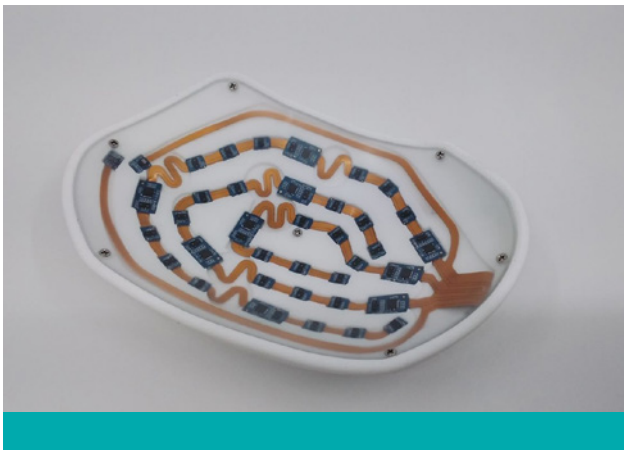
To advance SkullPro® 2.0 towards commercialisation, the team is collaborating with the Florey Institute, its commercial partner B. Braun/Aesculap, and academic neurosurgical units in Australia, Spain, the UK and Israel. Through the BMTH project, the technology readiness level for the device increased from level one to five, and Anatomics has discussed the possibility of developing follow-on technology for SkullPro® in a continuing partnership with CSIRO.

The partnership between Anatomics and CSIRO has brought together some of the best minds, software and manufacturing capabilities Australia has to offer, establishing a framework for collecting, transmitting and securing patient data for smart, wearable medical devices. This project will enable future manufacturing and assembly capabilities to take place within Australia, securing and establishing high-tech manufacturing jobs and research/development opportunities.

The company has a vision to deliver a neuroscience portfolio of 'smart products' that provides surgeons and patients with an end-to-end neuro-care pathway, from the ICU, as outpatients or at home. This will ensure patients can get the best possible treatment and decisions can be made based on objective data, thereby improving patient outcomes, increasing efficiency, and reducing waste and complications. Remote patient monitoring will alleviate the need for clinical visits and reduce the burden on people who have recently experienced a significant traumatic event.

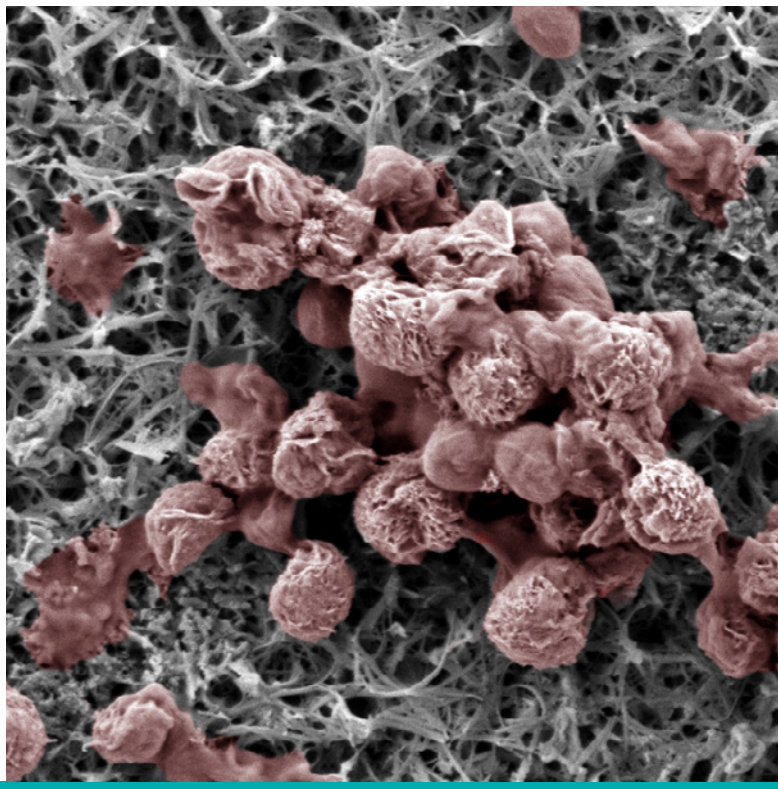
Anatomics can now proudly showcase the SkullPro® 2.0 system, including prototypes, software capabilities and a clinician dashboard, to surgeons and partners across the globe.

As neurosurgeon and Anatomics Executive Chairman Professor Paul D'Urso explained: "The development of the SkullPro® 2.0 system has provided Anatomics with a secure platform for clinicians to remotely monitor patients after brain surgery, providing an additional level of care not previously possible. The framework allows Anatomics to develop next-generation smart, neuromonitoring devices for remote patient imaging, diagnosis and treatment via an Industry 4.0 connected device."



SkullPro® 2.0 printed circuit board array.
Photo credit: Sam Miatke, Anatomics Pty Ltd.

Pioneering transformational antibiotic-free infection control medical implants



PROJECT:
Anisop Holdings Pty Ltd

THERAPEUTIC AREA:
Orthopaedics

ANISOP

START DATE: 1 October 2020	TOTAL BMTH GRANT: $1,000,000
END DATE: 31 December 2022	TOTAL BMTH EXPENDITURE: $950,907
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $250,015
DELIVERABLES COMPLETED: 99 per cent	TOTAL IN-KIND: $511,250
	TOTAL PROGRAM: $1,712,172

Jobs within the project budget	10
Number of new technology(ies) invented/progressed	1

Infection control is a huge and growing problem with the rise of antimicrobial resistance and the relative absence of new antibiotic treatments. Infection control for implanted medical device products, such as dental implants and joint replacements, represent a particular problem because if an infection establishes and biofilm forms after surgery, a repeated (revision) surgery is often required to remove the device and install a replacement.

Orthopaedic implants such as knee and hip joint replacements are among the most common elective surgical procedures globally. Estimates vary depending upon the surgical procedure, but revision surgery of orthopaedic implants associated with bacterial infection or biofilm formation are between one and nine per cent[1], resulting in billions of dollars of cost to the global healthcare system and significant burden on patients.

There has been a huge investment in sterilisation and surface treatment methods for implants to improve integration with the surrounding tissues, to ensure the devices are not toxic to surrounding tissues and to prevent microbial growth or biofilm formation. Yet the problems of infection and subsequent biofilm formation have not been resolved and the challenge is increasing.

Recognising these challenges and the persistent and growing problem of antimicrobial resistance, Adelaide-based Anisop Holdings, with its partners at the University of South Australia, is focused on developing antimicrobial implant materials that maintain antimicrobial properties of their surface over their entire life because of the unique nanostructure of the surface, having no requirement for the usage of antimicrobial drugs.

Image: Scanning electron microscopy showing bacteria being killed on the Anisop Holdings optimised and treated surface.

1. Diagnosis and management of orthopedic implant-associated infection: a comprehensive review of the literature, 2017.

Inspired by research that demonstrated the inherently antimicrobial properties of the dragonfly wing, which has minuscule protrusions that kill bacteria, solid data showing inhibition of biofilm formation, and patents in Australia and the European Union, Anisop has sought to scale up, validate and commercialise its surface treatment technologies to introduce inherently antibacterial properties to titanium medical implants.

Anisop was awarded funding through the BioMedTech Horizons (BMTH) program to advance the commercial pathway for a novel antimicrobial surface for dental and orthopaedic implants. Key objectives were the *in-vitro* and *in-vivo* validation of the antibacterial and antibiofilm forming properties of surface treated titanium, to demonstrate the biocompatibility of the surface, perform engineering tests to show it had the same mechanical and performance properties, and to scale up and standardise the surface treatment steps.

Using a range of clinically relevant bacteria for periodontal disease, Anisop showed sustained inhibition of bacterial growth in culture and ability to maintain normal growth of human cell lines on the treated surface. When implanted into an animal model the outcomes were similarly promising, with no signs of biofilm formation on the treated devices and, importantly, signs of integration of bone cells equivalent to levels of titanium products already used in orthopaedic implant devices. This integration is a desired characteristic improving long-term stability of the implant and improved outcomes for patients.

Mechanical joints and implants can undergo substantial stress and fatigue in the body. With testing under ISO 14801:2016 conditions for dental implants, Anisop showed its surface treatment retained mechanical properties similar to untreated materials, clearing another significant hurdle in the development path.

Armed with robust mechanical and functional data, Anisop sought to make its pilot scale production facilities more robust and develop methods considering future regulatory requirements.

Anisop's Chief Medical and Technology Officer, Dr Dan Barker, said the BMTH project has been critical in advancing the commercialisation of this pioneering surface for dental and orthopaedic implants. Likewise, the team established expertise in producing the surface locally so it can now scale, which is important for moving towards models of mass production.

"This project has developed local expertise that will enable us to make antimicrobial implants in Australia," Mr Barker said.

Another benefit of the BMTH project is that it has enabled Anisop to expand its team, said Professor Krasimir Vasilev, a key academic collaborator at the University of South Australia and a world leader in nano-surfaces for medical devices.

"This project enabled the hiring and funding of up to 10 local scientists and has spawned research projects into the future," Professor Vasilev said.

A key success factor in this technology is that there are no antibiotics or novel biomaterials introduced, which present major regulatory hurdles. Rather, the optimisation of the surface architecture at the nano-level is all that is required to kill bacteria but leave the host cells safely intact. While the treated surface appears rough under an electron microscopy, the surface feels the same to touch as regular polished metal surfaces.

With infection control becoming a more significant issue, the possibility of extending the market for Anisop's product to other metal products like hospital trolleys, or high-touch areas in public spaces such as handrails, or to veterinary applications, means the future looks promising for this groundbreaking optimised surface.

Moving forward, the team hopes to continue the commercialisation pathway for dental and orthopaedic implants, having established a pilot facility in Sydney in conjunction with the Corin Group, one of the fastest growing orthopaedics companies in Australia.

Anisop Holdings optimised surface is inspired by research of the dragonfly wing.

Diamond and carbon fibre brain implant aims to stop epileptic seizures before they begin

PROJECT:
Carbon Cybernetics

THERAPEUTIC AREA:
Brain

Carbon Cybernetics

START DATE: 1 October 2020	TOTAL BMTH GRANT: $999,676
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $999,676
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $30,970
DELIVERABLES COMPLETED: 97 per cent	TOTAL IN-KIND: $353,000
	TOTAL PROGRAM: $1,383,646

Jobs within the project budget	3
Number of licenses	4
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	2

Approximately 30 per cent of the 50 million people worldwide living with epilepsy are drug resistant[1]. For this cohort, treatment options are limited. Resective surgery helps some patients, but for many, the anxiety associated with the unpredictability of seizures represents one of the primary burdens of the disease.

In 2018–19, 151,000 people in Australia were living with epilepsy[2], resulting in $557 million of direct health system costs and a combined economic burden of $12.3 billion[3]. A significant portion of the economic burden is from those people who cannot control seizures through medication, meaning that alternate interventions offer a substantial opportunity to address unmet need and lower the overall economic burden.

Implantable devices that record neural activity to predict seizure risk offers a highly promising seizure-management strategy. By providing warning of an impending seizure preventative measures can be taken to avoid injury. Equally important, with such a device, a patient would gain confidence knowing that a seizure is extremely unlikely to occur within a specific timeframe.

To achieve this objective, Carbon Cybernetics – a medtech start-up based at The University of Melbourne – has developed a miniaturised research prototype carbon brain interface, with the end goal being that it can capture high-fidelity neural activity over an extended period. Constructed from diamond and carbon fibre, it is highly resistant to degradation in the body and can record neuronal action potentials from 100 channels from mm scale implants.

Image: The Carbon Cybernetics 2 mm wide device featuring 25 carbon fibre electrodes, each 1/10th the width of a human hair. Photo credit: Dynamic Visuals, Melbourne.

1. World Health Organisation.
2. Australian Institute of Health and Welfare. Epilepsy in Australia.
3. Deloitte Access Economics, 2020.

Unlike other implantable devices that require invasive craniotomies, the Carbon Cybernetics electrode arrays can be inserted using a burr hole of less than 10 mm in diameter.

Supported by BioMedTech Horizons (BMTH) funding, Carbon Cybernetics set out to conduct pivotal preclinical experiments to demonstrate that the device is safe and can record with high signal quality, to operate as the recording component of an eventual functional cure for epilepsy. This research would give the team the minimum necessary data to attract investment to undertake future larger preclinical and clinical trials.

While carbon fibres have previously been shown to be quite inert when inserted into brain tissues, carbon fibres embedded in diamond in the format by Carbon Cybernetics has not been tested; so, initial experiments were conducted to prove that they did not induce a significant immune response or scarring. These results showed almost undetectable impact, much lower than existing penetrating electrode types and were highly encouraging.

Carbon fibres are very small and flexible, which is good news for the brain, because they cause no damage when inserted. Yet their flexibility also causes problems, as they sometimes bend and don't penetrate the brain. To solve this, Carbon Cybernetics developed several techniques including a smart robotic insertion method to gently guide the electrodes into place, avoiding blood vessels on the surface of the brain.

With early technical validations completed, Carbon Cybernetics engaged national and international consultants to develop a comprehensive market and competitor analysis, conducted an intellectual property (IP) landscape report, developed a detailed understanding of the reimbursement landscape in the US and Food and Drug Administration (FDA) regulatory requirements for its device and established a quality management system (QMS).

Each of these contributed to the delivery of a robust business plan resulting in success in pre-seed funding, through the Genesis fund, and will guide Carbon Cybernetics activities as it actively pursues Series A funding to support the development of a human-ready implant.

Ultimately, the BMTH project was highly successful. The team confirmed that carbon fibre electrodes coexist safely with the brain. No scar tissue formed around the electrodes after six months, indicating that the immune system does not recognise the electrode as a foreign body. The team also found that the electrodes recorded from the same neuron without signal degradation for at least three months. This level of safety and stability is required for permanent implantation into people living with epilepsy.

Upon sharing these exciting results during an interview with ABC's Drive Melbourne radio program, Carbon Cybernetics' Co-Founder and Chairman, Professor Steven Prawer, explained: "The body loves carbon. Carbon fibre and diamond are both types of pure carbon. As you know, diamonds are forever – we have to make sure anything we put in the body is safe and can last a long time."

Once brought to market, the Carbon Cybernetics device has the potential not just to improve the lives of people living with epilepsy, but also offer significant economic savings.

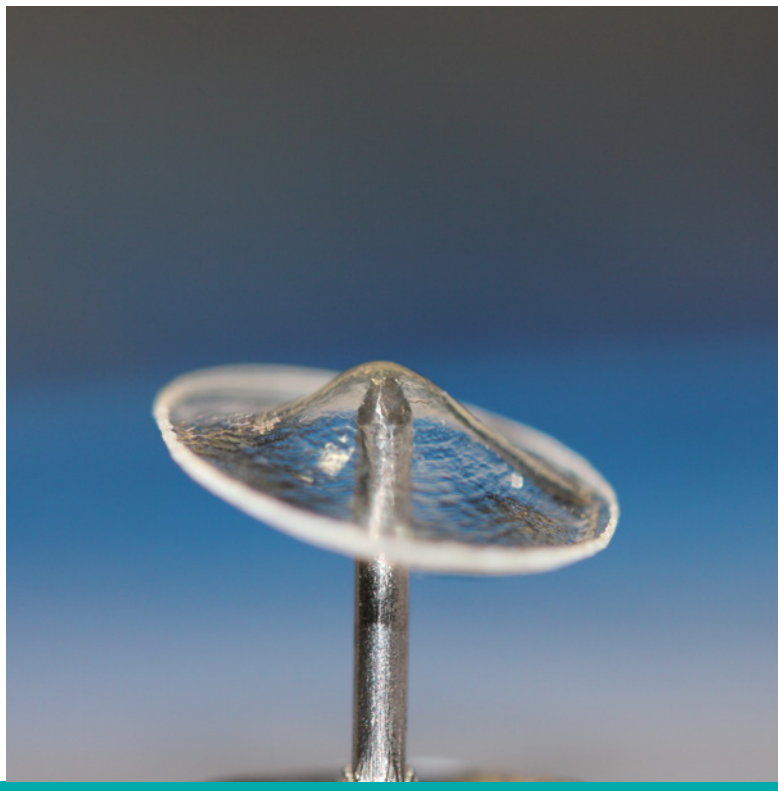
Direct neural monitoring, forecasting of epilepsy, and feedback intervention as planned to be delivered by the device, would provide healthcare systems with a more accurate diagnosis, much more effective feedback on disease progression or regression, and would permit a more holistic and proactive approach to patient care.

Carbon Cybernetics is the first in the world to be developing a permanent solution for recording from single neurons in the brain. Beyond offering the potential of better treatment of epilepsy, the level of information that the device can extract could be used to treat or monitor a wide range of other neurological conditions.

But for now, Carbon Cybernetics Founder and Chief Technical Officer Associate Professor David Garrett said in his TEDx presentation: "We want people living with epilepsy to have the confidence to climb a mountain, ride a skateboard or bath a newborn infant. We want people to be seizure free for so long that they forget the fear of having a seizure."

Carbon Cybernetics PhD Student, Simon Higham, aligning delivery equipment during a surgery. Photo credit: Dynamic Visuals, Melbourne.

World-first prosthetic device to replace a damaged ear drum and repair chronic middle ear disease



PROJECT:
Ear Science Institute Australia/ ClearDrum Pty Ltd

THERAPEUTIC AREA:
Hearing

EAR SCIENCE Institute Australia

ClearDrum

START DATE: 1 October 2020	TOTAL BMTH GRANT: $993,500
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $935,791
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $144,114
DELIVERABLES COMPLETED: 98 per cent	TOTAL IN-KIND: $160,721
	TOTAL PROGRAM: $1,240,626

Jobs within the project budget	6
Number of licenses	1
Number of new technology(ies) invented/progressed	3
Number of preclinical trials commenced	3

Image: The ClearDrum® device – similar in appearance and size to a contact lens.

Chronic middle ear disease (CMED) is a common condition that affects the space between the ear drum (tympanic membrane) and the inner ear. It can be caused by a long-lasting infection, an injury to the ear, or repeated ear infections. It can lead to pain, hearing loss, discharge, or ringing in the ear.

CMED is especially prevalent among Indigenous Australians, impacting 12 per cent of the population and three per cent of children under 14[1], with numbers increasing significantly depending upon the degree of remoteness. The most common reason for hearing related hospitalisation was CMED, at 73 per cent of all cases[2].

Chronic suppurative otitis media (CSOM) is a serious type of CMED that involves a persistent perforation of the tympanic membrane (TM) and recurrent ear discharge. The World Health Organization estimates that CSOM impacts 65–330 million individuals, 60 per cent of whom suffer from significant hearing impairment, with Australian Aboriginals having the highest prevalence of perforation[3]. The total direct health cost of hearing loss in Australia exceeds $400 million per annum[4], with estimates up to $33.3 billion per annum in combined financial and lost wellbeing costs[5].

About half of all CMED patients are children under five years of age and treatment failure can have a long-term detrimental impact on their speech, language, intellectual, psychological and social development, and education. In adults, it can contribute to long-lasting social stigma and reduced employment opportunities.

1. Australian Aboriginal and Torres Strait Islander Health Survey: First Results, Australia, 2012-13.
2. Overview of Aboriginal and Torres Strait Islander health status 2022.
3. Chronic suppurative otitis media: burden of illness and management options, 2004.
4. Australian Institute of Health and Welfare. Disease expenditure in Australia 2019–20.
5. Hearing Care Industry Association. Social and Economic Cost of Hearing Loss, 2017.

While some perforations from CMED heal naturally, many require surgery to correct the perforation. It is estimated there are more than 300,000 surgeries per year, with 30 per cent requiring revision. In serious cases of CMED, the surgical procedure replaces the TM with grafted tissue, but this often has a poor outcome requiring repeated surgery or fails completely.

The ClearDrum® device developed by the Ear Science Institute Australia (Ear Science) aims to provide the world's first off-the-shelf, near-permanent implant to resolve these difficulties in a single, straightforward surgical procedure. Over the past eight years, Ear Science has partnered with Deakin University's Future Fibres Hub to develop a device prototype: a mechanically and acoustically optimised silk-based implant that is the first of its kind to mimic the real properties of a natural eardrum.

Similar in appearance and size to a contact lens, ClearDrum is biocompatible and strong enough to resist negative middle ear pressure. Its transparency allows surgeons to easily monitor the healing process, during surgical follow-up.

The BioMedTech Horizons (BMTH) program funding allowed the ClearDrum team to advance significantly with the development of its innovative product and to commence its commercialisation.

Prior to the BMTH project, the team developed a working prototype. This process required the exploration of many design variations, including changes to formulation, manufacturing method and shape. The team tested these extensively for mechanical properties *in vitro*, and in simulations with surgeons, to arrive at an optimal design.

During the project, key preclinical studies were completed. They first investigated the implantation of the ClearDrum® device in the middle ear of an animal model and tested for any adverse effects or hearing loss. The results were very positive with no significant ototoxic effect (loss of hearing) and no other adverse effect observed at four and 12 weeks post-implantation.

A biofilm study sought to show that the manufactured silk membrane did not degrade or support the formation of a biofilm when challenged with bacteria. As the eardrum (and this synthetic ear drum) acts as a barrier between the inner and outer ear, the likelihood of an ear infection occurring in everyday life cannot be ruled out, and so stability in the presence of bacteria was tested. Results showed that ClearDrum is not a good substrate for bacteria growth – a good starting point for future *in-vivo* testing.

The ClearDrum team took the important steps of establishing an ISO-9001 compliant quality management system (QMS) and operating to the ISO-13485 standard, creating a solid foundation for eventual product registration, manufacturing, and market launch.

A regulatory and reimbursement strategy was developed and validated with consultants in the US, the company's first target market. A 510(k)-class II regulatory category was chosen for ClearDrum® and a suitable predicate device was selected. Several existing codes for the surgical procedure involving ClearDrum were identified giving a clear strategy to obtain reimbursement in the US.

Freedom to Operate was reviewed and new technical work initiated to remove future risk. A thorough intellectual property (IP) plan was implemented, including expansion of the international patent portfolio to align with commercial goals, with the aim to launch in multiple markets including the US, the EU and Australia. A new commercial entity, ClearDrum Pty Ltd was created, with the new structure offering advantages for access to rebate programs and future investment.

Leveraging Ear Science's international network of hearing companies, and through the new connections established during this project, the team contacted numerous international medical device companies to discuss opportunities. The team is currently negotiating with a US commercial distributor of ear, nose, and throat (ENT) products with an established network of hospitals and surgeons, with a view to allowing ClearDrum to be incorporated into clinical practice quickly.

The BMTH program's impact in progressing ClearDrum towards commercialisation cannot be overstated, with the product's launch onto the US market anticipated for 2025, said ClearDrum's Chief Technology Officer, Dr Filippo Valente. "This project is a major step for the advancement of our product as we move to translate our research science to the world," he said.

The ClearDrum® device will significantly impact patients, surgeons, and healthcare systems by simplifying surgery, reducing hospital stays and the rate of recurrent operations. Removing the need for harvesting autologous grafts, reducing surgical errors during graft preparation, operating time, and allowing monitoring of the healing process in the middle ear. This will lessen the economic burden for patients with CMED by cutting costs associated with hospital stays, outpatient procedures, long-term care, radiology requirements and pharmaceuticals.

Creating a stable, dry ear after surgery and improving the patient's hearing has direct economic and quality of life benefits, such as improved cognitive and mental health, enhanced education outcomes, employment opportunities and higher levels of social participation.

Over time, Ear Science's newly established spinout company, ClearDrum, aims to become a global developer and producer of ENT surgical devices as it grows and develops a pipeline of products. Based in Western Australia, it will support the state's innovation strategy and vision of being a renowned global hub of invention, investment, innovation, and impact.

State-of-the-art wireless cochlear implant system aims to enhance hearing implants for profoundly deaf patients

PROJECT:
Hemideina

THERAPEUTIC AREA:
Hearing

HEMIDEINA
MAKING WAVES IN SOUND

START DATE: 1 October 2020	TOTAL BMTH GRANT: $660,520
END DATE: 30 September 2022	TOTAL BMTH EXPENDITURE: $660,520
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $594,832
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $0
	TOTAL PROGRAM: $1,255,352

Jobs within the project budget	3
Number of patent applications	3
Number of new technology(ies) invented/progressed	3
Number of preclinical trials commenced	3

The World Health Organization reported that over 60 million people worldwide suffer from severe-to-profound sensorineural hearing loss[1]. This condition occurs when a patient's inner ear is damaged to the point where sounds are no longer transmitted to – or are only partially transmitted to – the auditory nerve from the cochlea. This is due to lost or damaged hair cells in the cochlea, which in normal hearing would stimulate the auditory nerve.

Less than five per cent[2] of the world's severe-to-profoundly deaf population has received treatment, highlighting a clear, unmet medical need. Even for those who do receive treatment, the standard of care is a cochlear implant, which has technical limitations that preclude a natural sound quality and the ability to hear in noisy environments. This is because contemporary devices use low fidelity digital sound processing to restore human hearing, not conveying critical timing information which is needed for hearing in noisy environments and when appreciating music. Existing devices are also large, which can leave some wearers feeling self-conscious and creates a visible indicator of their hearing loss – a barrier to adopting this treatment.

Adding to these issues, a challenge associated with all implantable medical devices is how to provide a wireless link that will send sufficient power and maximum data to the implant from the external component. Contemporary cochlear implant sound processors (the external component) have a limited wireless transfer efficiency because they use a single link for data and power. This also reduces the data bandwidth available for transferring information to the implant.

Image: Hemideina's in-ear design for its wireless cochlear system provides a discreet alternative to existing and much larger hearing devices.

1. WHO Report: Deafness and hearing loss. February 2023.
2. Cochlear Limited Annual Report 2022.

Hoping to tackle these challenges, Melbourne-based hearing technology company Hemideina is adopting a unique approach to power and data transfer with its Hera Cochlear Implant System – a device that aims to maximise the benefits of higher fidelity mechanical sound processing and provide improved power transfer efficiency. This innovation will have profound benefits for the broad array of implantable medical devices that need wireless data and power transfer and create a paradigm shift in cochlear implant treatment.

Co-Founder and CEO Dr Liz Williams said that Hemideina set out to improve on the existing technologies in three main ways: a revolutionary in-ear design to provide a discreet alternative; a magnet-free implant and alternative implant placement to reduce clinical risk and Nature Inspired Sound Processing to improve sound quality, hearing in noisy environments and to allow music appreciation. These benefits need to be proven in future clinical trials.

Supported by BioMedTech Horizons (BMTH) funding, Hemideina set out to determine whether a miniaturised wireless power and data transfer system could power a cochlear implant. The goal was to produce a small in-ear sound processor that would replace the external sound processor currently worn behind the ear by people with cochlear implants.

As part of the BMTH project, Hemideina built a benchtop prototype wireless system with custom printed circuit boards and coil designs that could fit in the ear canal and deliver simultaneous power and communications. The team demonstrated technical feasibility of the Hera wireless link with communications and power measurements to enable power and data transfer across the ear canal wall.

The prototype achieved 56 per cent coupling efficiency between coils – this means it is theoretically able to achieve 40 per cent power transfer efficiency when an integrated circuit is implemented. Meanwhile, it delivered up to 60-megawatts of power transfer and transferred data with fidelity to deliver stimulation data to a cochlear implant, achieving a six-millisecond transfer delay. Although not hitting the target three-millisecond transfer delay, future design improvements will address this.

Successfully transmitting power and data across a transcutaneous link within such a small volume is an excellent technical achievement, said Head of Engineering at Hemideina Pierre Vancaillie.

"The transmission of both power and data across the skin is critical to Hemideina's device, and this project has allowed us to show that we are able to adequately do this even when constrained to the very small space within the ear canal," he said.

Excitingly, through the BMTH project, Hemideina discovered and patented a method to reduce unwanted coil coupling interactions in their power and data transfer, to ensure only the paired coils interacted. Hemideina was granted Australian and US patents to protect its multi-coil approach for the simultaneous transfer of multiple analogue data channels.

Hemideina also identified a theoretical implant site and procedure, based on the size of the wireless power and data receiver coils to fit within the mastoid cavity, and tested this with surgeons globally. This has enabled the team to refine its surgical assumptions and develop design inputs for the next stage of development to deliver a clinical prototype for use in humans.

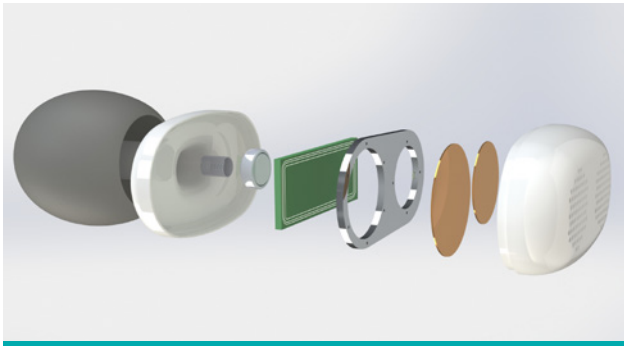
Another major achievement of the project was that Hemideina realised these outcomes without needing magnets to keep the coils aligned. This means that the Hera Cochlear Implant System could be the first cochlear implant system that is magnet-free and therefore avoids the complications that arise from implantable magnets. For example, when users undergo MRI procedures, they wouldn't need to have the magnet surgically removed, as they might with current systems.

The positive results achieved through the BMTH project have enabled Hemideina to progress its system from Technology Readiness Level (TRL) 3 to 5 and complete a Series A funding round, raising $10 million in equity capital.

Having fast-tracked the development of Hemideina's ground-breaking technology, the BMTH initiative has made a significant impact on the company's mission to improve clinical outcomes and enhance the user experience for people who are profoundly deaf.

As Senior Electrical Engineer at Hemideina Dr Simon Kennedy explained, the device will be the smallest of its kind on the market – a feature that will likely increase treatment adoption and restore hearing to a larger proportion of the population with severe-to-profound hearing loss.

"This project has delivered Hemideina a state-of-the-art wireless design that enables us to disrupt the cochlear implant market through our revolutionary form factor," he said.



Components of Hemideina's prototype wireless system.

New drug delivery system to improve treatment and outcomes for retinal disease

PROJECT:
IDE Group

THERAPEUTIC AREA:
Vision

START DATE: 1 April 2020	TOTAL BMTH GRANT: $1,000,000
END DATE: 30 September 2022	TOTAL BMTH EXPENDITURE: $1,000,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $1,412,065
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $0
	TOTAL PROGRAM: $2,412,065

Jobs within the project budget	9
Number of licenses	1
Number of new technology(ies) invented/progressed	4

Age-related macular degeneration (AMD) is the leading cause of blindness in Australia, afflicting one in seven people over the age of 50, and diabetic retinopathy (DR) – a complication of diabetes – is the leading cause of avoidable vision loss in working aged Australians aged 16-65[1]. Early detection and ongoing treatment for both conditions are critical to minimising the chance of irreversible vision loss and blindness.

Current treatment for AMD involves ongoing monthly injections of anti-vascular endothelial growth factor (anti-VEGF) drugs into the eye, which is highly effective, but both costly and invasive. This, in turn, leads to patient non-compliance and consequential vision loss. Numerous studies have indicated the compliance rates drop significantly in the first year[2], and these issues can be compounded in regional and remote areas where patients are often required to travel for long distances to see an ophthalmologist at a regular interval.

There are also challenges for clinicians treating patients with anti-VEGF drugs. The injections are highly repetitive and labour intensive, plus the procedure carries the risk of complications including retinal detachment and vitreous haemorrhage. With the increasing rates of AMD and DR, and the frequency of injections required, ophthalmologists are under pressure to keep up with the required volumes despite the compliance issue.

Drug delivery to the eye is challenging due to the eye's anatomical structure, with the ocular barrier preventing topical or systemic routes for delivery of the therapeutic drug. Additionally, protein-based therapeutics such as anti-VEGFs are prone to degradation, so need to be injected frequently to be effective.

IDE Group, in partnership with CSIRO, is working to develop a combination drug delivery-device system to improve the treatment process and clinical outcomes of retinal diseases, such as AMD and DR. It will achieve this by developing a product that utilises an innovative syringe platform to deliver an injectable gel that can be photo activated for a controlled release of the therapeutic to the eye. The syringe device addresses user needs of improved stability, visibility, positioning, safety and control. Meanwhile, the drug delivery gel will provide for the controlled release of the anti-VEGF drug using light activation, instead of through ongoing monthly injections.

Supported by the BioMedTech Horizons (BMTH) program, IDE Group and CSIRO, in collaboration with pharmaceutical industry partners, sought to identify a target drug, design and develop a prototype, and demonstrate effectiveness via an *in vivo* animal study.

Despite delays and challenges brought on by the COVID-19 pandemic, the project achieved its aim of de-risking technical and commercial uncertainties surrounding the drug delivery system being developed.

With the expertise of its existing team – alongside three new team members supporting the project – IDE signed a licensing agreement with CSIRO, developed and validated the technology, and undertook significant commercialisation work to define the path to market. This included regulatory, clinical, manufacturing, risk management and funding, facilitating opportunities for commercial partnerships to further develop and commercialise the technology.

1. Macular Disease Foundation Australia.
2. Long-Term Outcomes of Anti-VEGF Therapy, 2021.

Rendered image of IDE's prototype ocular injector.

In addition, new technologies and intellectual property were discovered during the project in the form of a sustained-release implant technology and an advanced auto-injector, which have broad application both within ophthalmology and beyond – ultimately having the potential to improve the standard of care through better drug delivery in numerous indications.

Significant market research with stakeholders and key opinion leaders led to the development of user and stakeholder needs, underpinning the business plan and product development plan. The impact of these findings was to uncover areas of opportunity, both from a usability perspective for the product and in identifying areas of unmet need. Addressing these needs will increase clinician adoption of the technology, improve patient compliance, and ultimately deliver better patient outcomes for people with AMD and DR.

Moving forward with production-equivalent prototypes manufactured and all subsystems designed, IDE Group will focus on advancing commercial partnerships to fund and facilitate ongoing development of the technology, to ensure that its full potential to improve the standard of care and vision outcomes is reached.

Managing Director of IDE Group, George Sidis, said the BMTH program provided integral funding and support to the company as it set out to invest in its intellectual property portfolio.

"This support specifically allowed IDE to license and further develop a novel implantable drug delivery technology from CSIRO, and create a new intravitreal injection system," he said. "IDE has leveraged this growing intellectual property portfolio to expand its business, creating a new Drug Delivery Systems Business unit that provides innovation and drug delivery technology development services to pharmaceutical companies around the world."

The success of the BMTH project lies in the development and eventual commercialisation of a product that sets a new standard of care for patients suffering from AMD and DR. The product will remove barriers to patient compliance, such as fear of injections and inconvenience of frequent visits to the clinic, enabling more effective treatment and leading to better treatment outcomes. Ultimately, this will help more patients retain their sight, which not only is a significant benefit for patients, but also reduces the societal and economic costs of blindness.

In addition, the use of photo-mediated release means that the intervals of drug release – after the initial gel implant – do not require an ophthalmologist and can be done by a nurse, optometrist or eventually perhaps by the patient at home. This will likely have a positive impact on compliance rates and has the potential to make a significant difference at the clinic level.

Eliminating the need for regular, in-clinic injections for AMD patients will improve workflows and reduce the burden on ophthalmologists to administer injections, which typically represents a significant proportion of their clinical time. Instead, the ophthalmologist will be able to spend more time diagnosing and monitoring disease progression, improving practice efficiencies and treating more patients.

In addition, the potential to move treatment away from the clinic and into the home will enable patients living in regional and remote areas to gain greater access to the care they need to manage their condition – making healthcare delivery more equitable in Australia and other underserved areas globally.

Australian made novel medical device for early-stage back pain intervention set to become reality

PROJECT:
Kunovus Technologies Pty Ltd

THERAPEUTIC AREA:
Orthopaedics

Kunovus

START DATE: 1 April 2020	TOTAL BMTH GRANT: $998,600
END DATE: 30 September 2022	TOTAL BMTH EXPENDITURE: $998,600
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $1,201,576
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $329,163
	TOTAL PROGRAM: $2,529,339

Jobs within the project budget	5
Number of patent applications	2
Number of licenses	1
Number of new technology(ies) invented/progressed	2
Number of preclinical trials commenced	1
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	10

Low back pain is among the leading causes of disability worldwide, ranking number two or three in Europe, Australasia and America[1]. Back pain cost the Australian health system $3.4 billion in 2019-2020[2] ranking 10th overall in terms of economic burden and is the top reason for lost work productivity and early retirement[3] and a decline in living standards[4]. With the direct cost being 10-15 per cent of the indirect costs, the overall cost of low back pain to the economy is significant[5].

Lumbar spine osteoarthritis is a common cause of low back pain, initiated by degenerative changes in the spinal disc. The surgical standard of care is discectomy, during which surgeons remove loose nuclear fragments in the spinal canal and clear the nuclear cavity. However, this option is only available for advanced stages of disc degeneration and, even then, nearly 20 per cent of all spinal operations fail. Close to 40 per cent of patients remain unhappy with the results.

Kunovus Technologies is aiming to solve this vexing problem with its patent-protected novel and unique Australian-designed Kunovus™ System – developed for early-stage intervention in disc degeneration patients, who would otherwise have to wait for osteoarthritis to deteriorate to warrant a more invasive and expensive spinal surgery.

With support from BioMedTech Horizons (BMTH) funding, the Kunovus team – led by internationally renowned spinal surgeon and Chief Scientific Advisor Dr Ashish Diwan – designed, manufactured and trialled an elastomeric cushion to replace lost disc tissue for patients suffering from lumbar disc prolapse. The Kunovus System delivers the silicone elastomer to the inner core of a patient's spinal disc, which cures in situ and forms a bespoke prosthetic, restoring the biomechanical integrity of the disc without the need for spinal fusion.

Project areas supported by BMTH included prototype development, product testing and regulatory support, as well as preclinical and clinical trial activities. As part of the work required for regulatory approvals, Kunovus also developed a functioning and ISO-compliant quality management system.

The main aim of the BMTH project was to achieve a first-in-human implantation trial of the Kunovus™ Disc Device in 10 lumbar disc herniation patients scheduled for discectomy, and then collect follow-up data on the safety and effectiveness of the device. The realisation of this objective marked the first time a novel spinal device with a novel material was manufactured in Australia. During the BMTH project, Kunovus also successfully manufactured, assembled, sterilised and packaged 120 clinical cupboard kits of the Kunovus System, transferring 98 per cent of manufacturing and assembly from international suppliers to New South Wales-based contracting partners. Kits were used for manufacturing validation studies, cadaveric training and clinical trials.

1. Institute for Health Metrics and Evaluation, Global Burden of Disease Study 2019.
2. Australian Institute of Health and Welfare, Disease Expenditure 2019-2020.
3. Lost productive life years caused by chronic conditions in Australians aged 45-64 years, 2010-2030.
4. Labor force participation and the influence of having back problems on income poverty in Australia, 2012.
5. Low back pain in Australian adults: the economic burden, 2003.
6. Australian Atlas of Healthcare Variation 2015 – Chapter 3.3 – Lumbar spine surgery hospital admissions 18 years and over.

Kunovus Technologies' medical device for early-stage back pain intervention.

Kunovus conducted three cadaver workshops to develop and assess surgical techniques for the implantation of the Kunovus Disc Device, as well as examine the ease of use of various components of the system. Overall, it was deemed an effective system in being able to carry out the implant procedure in a minimally invasive manner.

One particularly positive outcome of the BMTH project was that Kunovus was able to attract the topmost medical distributor in Australia and New Zealand as a strategic investor, raising $1.9 million in external investment from an ASX entity and a strategic family office.

Having completed the project, Kunovus has matured its technology from Technology Readiness Level (TRL) 5 to 6, and the team has now commenced preparations for regulatory approvals of the device. The organisation has likewise taken the critical first step towards commercialisation by completing Phase I studies and a Phase IIa clinical trial.

Once introduced into the public hospital system and/or work cover cases in Australia (and later in private hospitals, pending listing on the Prostheses List), this technology is well placed to have a significant economic impact. Currently, diagnosis and surgical management of recurrent lumbar disc herniation results in an average additional direct cost of approximately $38,000 per operated patient. With 12,000 decompression-discectomies and 17,280 fusion surgeries performed in Australia each year on patients above 18 years of age a failure rate of 20 per cent[6] in the decompression group incurs a $91 million expense. Kunovus expects uptake of its device to lower the failure rate by 50 per cent, leading to a $45 million annual saving in direct healthcare costs.

Yet the economy won't be the only beneficiary of this innovative technology, which has the potential to improve quality of life for people with low back pain and, as a direct result, boost the nation's workforce and productivity. The team's research indicates that on a global scale, the prevalence rate of back pain that could be alleviated by this novel device could be approximately three per cent among the entire population, and as high as 10 per cent among the growing elderly population.

Additionally, the system presents an appealing option to spinal surgeons. The 20-minute procedure for implantation of the Kunovus Disc Device is designed to significantly minimise the occurrence of accelerated disc degeneration, segmental instability and recurrent herniation. Not only will the device revolutionise and standardise surgical care for discectomy patients, but it will also reduce variability and improve clinical outcomes.

For Kunovus Technologies' Dr Diwan, this BMTH project will disrupt the world of spinal surgeries: "It's filling a big gap in managing with a 'small shaving of the spur' type of operation to a 'big and maiming in spinal fusion' operation," he said.

Dr Brian Hsu, an Adult and Paediatric Spine Surgeon in Sydney, agreed, stating that Kunovus' elastomeric technology will change the field of spinal surgery for the better.

"Dr Diwan's early trials of the Kunovus Device for microdiscectomy patients is promising," he said. "I believe that when available in the market it will fill a major gap in the spectrum of treatment for common spinal disorders with great benefit to our patients. I am fully supportive of further trials. My hospital, Norwest Private, will be participating in the multi-centre trial."

Minimally invasive device allows people to operate computers with their mind

PROJECT:
Synchron Australia

THERAPEUTIC AREA:
Brain

START DATE: 1 October 2020	TOTAL BMTH GRANT: $989,175
END DATE: 28 November 2022	TOTAL BMTH EXPENDITURE: $815,461
STATUS: Terminated	TOTAL CASH CO-CONTRIBUTION: $1,140,461
DELIVERABLES COMPLETED: 77 per cent	TOTAL IN-KIND: $240,000
	TOTAL PROGRAM: $2,195,922

Jobs within the project budget	5
Number of patent applications	3
Number of clinical trials commenced	1
Number of patients to clinical trial recruitment	1

Paralysis occurring through accidental causes or degenerative neuromuscular disorders, like motor neuron disease, is irreversible and affects more than 30 million people worldwide. While available, there have been very few ways to support these individuals to engage with their surroundings or with other people.

However, the emerging field of brain computer interface (BCI) technology offers great hope in allowing impacted individuals to engage in a more meaningful way.

To this end, clinical stage medtech company Synchron has created a tiny, minimally invasive device that reads brain signals, allowing patients with paralysis to operate computers and phones with their minds. Originating from The University of Melbourne, with offices in Melbourne and New York, Synchron is recognised as a global leader in BCI technologies and is attracting significant public attention with regular news, interviews, and keynote presentations.

The company's platform is built on the Stentrode™, an endovascular electrode array, which is designed to record or stimulate the brain or nerves from within the blood vessels. While other companies are also racing to develop BCI's, the advantage of the Synchron approach is the surgical technique which uses a minimally invasive standard interventional neurologist technique of inserting a stent though the jugular vein up into the relevant part of the brain. Other companies require invasive insertion through the skull which can result in bleeding and inflammation.

Once implanted, the device becomes incorporated into the wall of the blood vessel in the same way as a stent does and can receive and input electrical signals from a device implanted into the chest.

Image: Synchron's Professor Nick Opie holding the Stentrode™.
Photo credit: Peter Cassamento for the European Patent Office 2023.

In 2020, the company was granted a breakthrough device designation from the US Food and Drug Administration (FDA) and, in addition to its first-in-human trial conducted in Australia, was granted approval in 2022 to conduct an early feasibility study in the US.

With the support of BioMedTech Horizons (BMTH) program funding, Synchron sought to further develop its computer interface technologies, to allow patients to control a cursor and make selections on a screen, continue their SWITCH1 clinical trial and patient-monitoring activity, and initiate the SWITCH2 trial.

One additional patient was recruited into SWITCH1 which was enough to complete the trial, with outcomes published in January 2023. Further planned recruitment was impacted by COVID-19 closures and further compounded by the fact that with just one trial site there was only a small pool of candidate patients. Synchron broadened the number of clinical trial sites to expand recruitment, with five sites being established across Queensland, New South Wales, and Victoria through the first half of 2022.

However, after having done all the required preparation, Synchron made the decision to defer the SWITCH2 Australian trial as new technology iterations were being developed and the company had received approval by the FDA for a trial in the US. While everything was in place, technically the project could not be completed in the BMTH program timeframe, and this part was ended early.

The second part of the project focused on the user interface and the decoder performance, which was continued in parallel with other studies and was highly successful. The switch output is now robust, meaning it does not make a switch during 'rest' periods and is able to produce a 'click' in 0.6 ± 0.15 seconds. The improved usability of the switch enabled Synchron to focus on how participants use its switch.

A custom Windows application that supports participants to use core computer functions with a single switch was created. The BCI switch can be used to select the active application and the software allows participants to easily send emails, search the web, join Zoom meetings, and communicate via predefined phrase boards. Numerous patents were progressed specifically covering the application interface and technologies developed during the project.

Despite not achieving all the objectives of its BMTH project, the SWITCH1 study and the development of software and interfaces laid an essential foundation for the initiation of the US trial. Synchron continues its mission to enable patients afflicted with paralysis to achieve digital device control and to engage with the world using multiple commands, including typing text (word), and navigating web browsers.

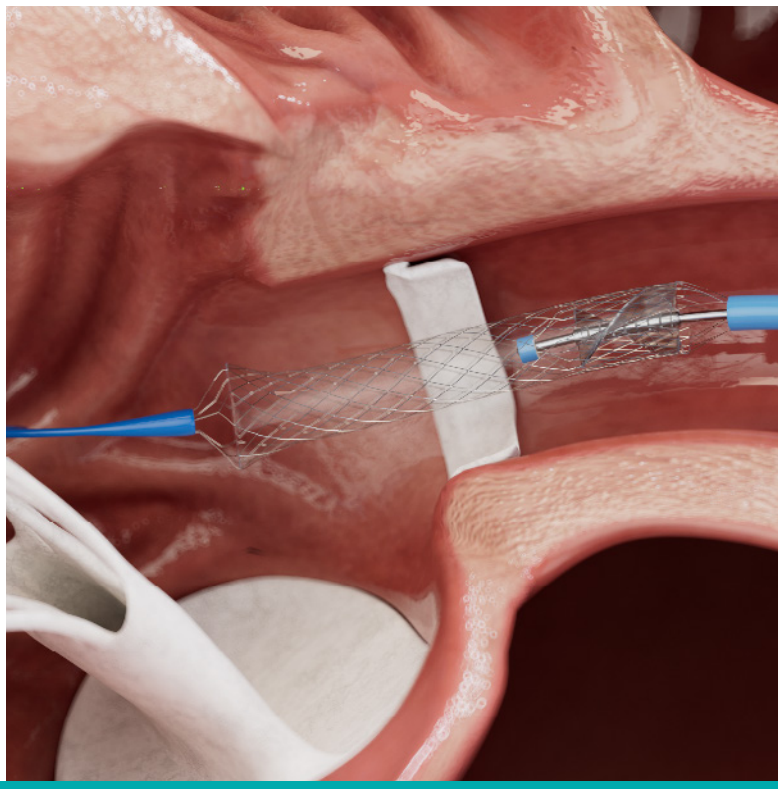
Impressively, it is the first company to achieve this feat and it has captured the attention of the world. The US trials are currently underway, marking a major milestone towards gaining FDA approval.

Synchron Co-Founder and Chief Innovation Officer Professor Nick Opie said that BMTH support had helped the company conduct and complete successful clinical trials in Australia, with all patients able to safely control a computer with their minds.

"The developments supported through the BMTH program played an important part at an important time and contributed to our future growth. Shortly following our BMTH program, Synchron completed a Series B investment round that provided us with the necessary capital to expand internationally. Synchron is now the world's leading brain computer interface company, and I am sure that were it not for the support from MTPConnect (and others), this would not have been possible," Professor Opie said.

Synchron Australia's team with Co-Founder and Chief Innovation Officer Professor Nick Opie front row centre.

Development of a Transcatheter Blood Pump System



PROJECT:
VenstraMedical

THERAPEUTIC AREA:
Cardiovascular

START DATE: 1 October 2020	TOTAL BMTH GRANT: $850,000
END DATE: 31 March 2023	TOTAL BMTH EXPENDITURE: $850,000
STATUS: Completed	TOTAL CASH CO-CONTRIBUTION: $127,000
DELIVERABLES COMPLETED: 100 per cent	TOTAL IN-KIND: $44,000
	TOTAL PROGRAM: $1,021,000

Jobs within the project budget	2
Number of patent applications	2
Number of new technology(ies) invented/progressed	1
Number of preclinical trials commenced	1

Each year in Australia approximately 57,000 people experience acute coronary events including heart attacks or unstable angina, with around 12 per cent of those being fatal[1]. It remains the leading single cause of death in Australia[2].

Three to 10 per cent of heart attack victims develop cardiogenic shock – the top cause of death for those who have a heart attack – and may benefit from use of a circulatory support device, such as a stent or a pump to help circulate blood, reducing the pressure on the heart.

Patients admitted to Intensive Care Unit (ICU) for cardiogenic shock in Australia have a mortality rate of 40 per cent, which is five times higher than other causes of ICU admission[3,4]. Mortality rates have not significantly improved for these patients in over 20 years, despite the introduction of a range of new treatments and devices. Venoarterial extracorporeal membrane oxygenation (VA-ECMO), for which there is a state-wide referral system in New South Wales, only services the sickest one per cent of patients experiencing cardiogenic shock.

There remains an unmet need for interventions supporting heart attack patients that are more effective, more accessible, and reduce patient trauma.

Aiming to fill this void, Newcastle-based cardiovascular medical device company VenstraMedical has acquired an intellectual property (IP) portfolio and rights to all technical proof-of-concept development efforts for a percutaneous ventricular assist device (pVAD).

Image: The SAVA Device and its deployment across the Aortic valve.

1. Australian Institute of Health and Welfare. Heart, stroke and vascular disease: Australian facts.
2. Australian Bureau of Statistics.
3. Acute Heart Failure – The AU and NZ Experience, 2018.
4. Temporal trends in incidence and patient characteristics in cardiogenic shock following acute myocardial infarction from 2010 to 2017: a Danish cohort study, 2019.

A pVAD is a small blood pump placed at a catheter tip, implanted by a cardiologist into the patient's heart to provide temporary cardiac support. Though the pVAD market is well established in the US and growing, next-generation devices that are small enough for rapid non-surgical implantation are required to provide full cardiac support.

The Venstra system is designed to be the world's smallest and most powerful catheter-based heart pump compared to existing approved pVADs. It will be used to treat patients at high risk due to cardiogenic shock, or those undergoing high-risk coronary interventions – enabling clinicians to alter the disease course at an earlier stage, thereby potentially transforming outcomes.

The Venstra system is unique due to the collapsibility of the pump, which is expanded upon deployment – allowing for a minimally invasive insertion process and reduced trauma to the patient. It can be implanted quickly on an emergency basis and still provide full cardiac unloading. The system includes an external software-controlled power unit that drives the pump via a magnetic coupling and allows the clinician to monitor and set operational parameters.

The objective of VenstraMedical's BioMedTech Horizons (BMTH)' project was to develop and technically de-risk the Venstra system. In particular, the team aimed to develop the pump and external console parts to further assess the feasibility of the patented collapsible/expandable pVAD. It also planned to mature the company with the addition of key people and processes.

With input from a medical advisory board that included Australian and US cardiology key opinion leaders the team developed comprehensive user needs for the implantable pVAD pump, the drive system and fluid purge system that are part of the external console.

An iterative design and computational testing process were conducted with project collaborators at The University of Queensland, enabling rapid prototyping and validation. Subsequent *in vitro* validation on assembled prototypes showed performance met expectations as set by the medical advisory board, giving great confidence for the team to move ahead.

The team completed multiple Freedom to Operate studies and formulated three new patents, two of which were lodged during the project period. With new IP and existing IP in multiple jurisdictions, extensive market research completed through the development phase and a clear understanding from the US Food and Drug Administration (FDA) of the clinical and regulatory requirements to validate its product, VenstraMedical made significant strides in the commercialisation of its product.

As a result of the work completed through the BMTH-supported project, VenstraMedical raised both a seed round ($2.4 million, June 2021) and, based on development progress, a Series A round ($11.4 million, January 2023) with the Australian Unity Future of Healthcare Fund being an investor co-leading the round.

Though the Venstra system still requires further development, a major milestone will be achieved with first-in-human clinical use in Australia. It is anticipated that clinical studies will be required for both key indications of use, high-risk percutaneous coronary intervention [PCI] and cardiogenic shock.

VenstraMedical's Co-Founder and Chief Medical Officer, Dr Suku Thambar, added that the company's work will advance the view that Australians are at the cutting edge of medical device innovation and development.

"By developing the world's smallest and most powerful catheter-based heart pump, compared with existing approved pVADs, VenstraMedical will save lives and healthcare costs and will put Australia on the map for medical device innovation," he said. This will result not only in thousands of lives saved, but also reduce infarct size and heart damage, resulting in less heart failure in the community. This will in turn lead to fewer hospitalisations, lower hospital costs and a reduced burden on the healthcare budget.

Excitingly, because of the work undertaken to develop the pump during the BMTH project, VenstraMedical has now commenced the console development with the world-class Design+Industry (D+I) team in Sydney, which will lead to increased manufacturing jobs in Australia and millions of dollars in income.

According to D+I's Project Manager Paul Scopes, the Venstra system represents a ground-breaking advancement in the field of cardiac support.

"It is a remarkable technological leap and we do not know of any other approved device with this capability in the market," he said. "Once introduced, the device has the potential to make a global impact. The project itself will demonstrate the ability for a highly complex Class III medical device to be developed in collaboration with multiple parties across Sydney, Newcastle and the US, highlighting the fantastic capabilities Australia, and in particular New South Wales, has to offer."

VenstraMedical's SAVA Device.

Drug release ocular implants for macular oedema

PROJECT:
PolyActiva Pty Ltd

THERAPEUTIC AREA:
Vision

START DATE:
1 April 2020

END DATE:
27 October 2022

STATUS:
Terminated

DELIVERABLES COMPLETED:
74 per cent

TOTAL BMTH GRANT:
$829,147

TOTAL BMTH EXPENDITURE:
$363,185

TOTAL CASH CO-CONTRIBUTION:
$676,590

TOTAL IN-KIND:
$187,116

TOTAL PROGRAM:
$1,226,891

Jobs within the project budget	2
Number of new technology(ies) invented progressed	1

Macular oedema is a retinal disease that arises from progressive build-up of fluid in the macular, the part of the retina that is important for central vision. This can result from inflammation associated with ocular surgery or diabetic retinopathy. Affected people will experience blurry vision that gets progressively worse over time if not treated. For people with diabetic retinopathy, macular oedema affects about half of all people and is the most common cause of lost vision.

After ocular surgery, for example cataract surgery, ophthalmologists prescribe patients steroids, Non-Steroidal Anti-Inflammatory Drugs (NSAID) and antibiotic eye drops to reduce inflammation and prevent infection. Treatment is often compromised by poor drop competence, associated with patient age and adherence to the course of treatment.

There is a significant unmet need for alternatives to drop therapy, such as ocular implants that can be administered at the point of surgery that release the therapeutic in a controlled way for defined periods of time. While injectable slow-release technologies exist, they will often have a multi-year drug release profile and several leave remnants of the capsule in the eye.

Hoping to bridge this gap, PolyActiva – a Melbourne-based clinical-stage ophthalmology company – set out to develop both steroidal and non-steroidal anti-inflammatory ocular implants for short-term and long-term prevention and treatment of macular oedema. The products are based on PolyActiva's proprietary polymer-based drug release chemistry, that biodegrades in a controlled way after release of the drug and leaves no remnant within the eye.

Along with its research partners, at Monash University Department of Pharmacology in Parkville, PolyActiva's BioMedTech Horizons (BMTH) project focused on developing up to three products for the target indication of diabetic macular oedema, as well as reducing pain and inflammation following cataract surgery. Two of the products were steroid implants delivering short-term therapy – six weeks, and longer-term therapy – six months. In addition, the program was to develop a NSAID implant as an alternative to steroid treatment.

The project was initially delayed by a range of factors relating to the COVID-19 pandemic, including closure of PolyActiva's collaborator laboratories and loss of key staff. In addition to causing a delayed start to the project, this had a significant ongoing impact, and the team was unable to substantially progress the project deliverables within the timeframe, which were further complicated by technical challenges.

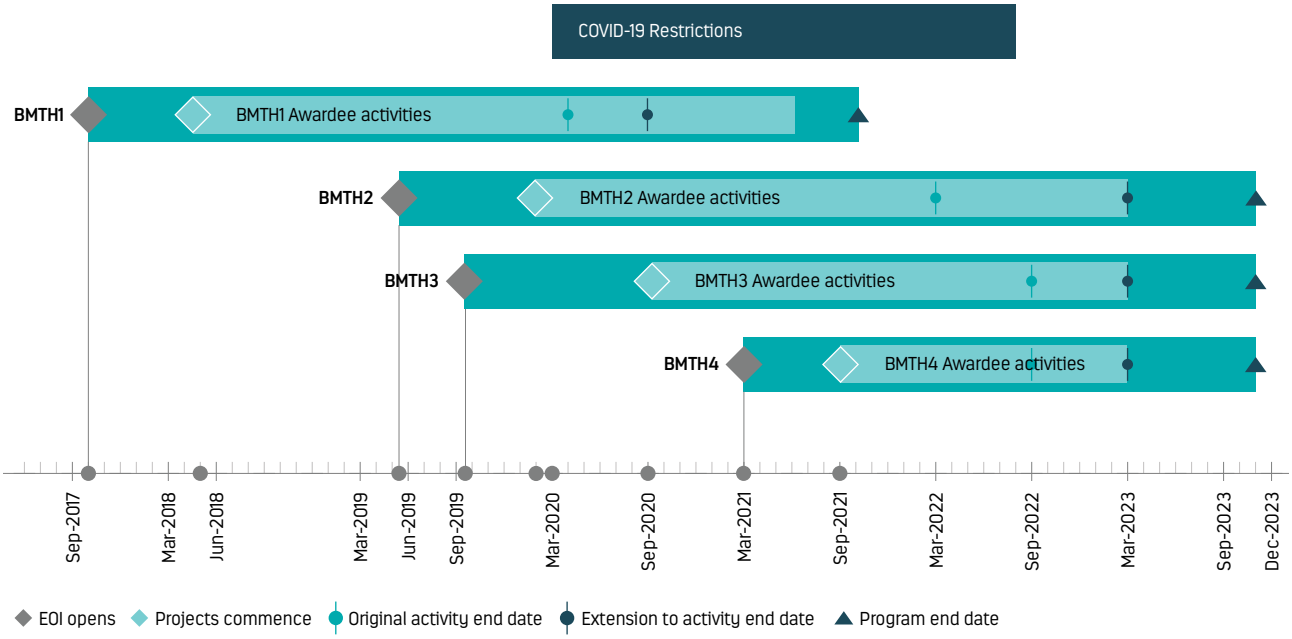
However, PolyActiva was able to conduct some important market validation studies including engaging with leading ophthalmologists, which assessed the three formulations being developed. This important feedback, combined with downstream consequences of the COVID-19 pandemic, resulted in a change in activities. Two streams of the formulation development were ended in May 2022, because of limited market enthusiasm for the steroid only product, or due to persistent technical challenges in the NSAID drug release profile, meaning the project could not be delivered in the program timeframe.

The third stream including the blended steroid product for use after cataract surgery progressed for a period with promising technical outcome. However, simultaneous investigation of the market opportunity and reimbursement path in the US indicated that the landscape was uncertain and may limit revenue opportunity. As a result, the decision was made by the company to end the final stream of research activity until greater certainty could be achieved. Consequently, the project ended prematurely in October 2022.

While this outcome did not meet the initial stated goal, it did reinforce the value of conducting robust market investigations in the early stages to inform product development and priorities.

Since the project ended, the research has continued and some of the earlier challenges have been resolved. Despite the setbacks encountered during the BMTH project, PolyActiva's pipeline of next-generation ocular implants remain on track to one day offer safe and effective therapies for patients with a wide range of ocular diseases.

BioMedTech Horizons Program Timeline 2017–2023



BMTH BioMedTech Horizons PROGRAM

SUPPORTING TRANSLATION OF AUSTRALIAN MEDICAL TECHNOLOGY INNOVATION

MTPConnect
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