BELUGABAND

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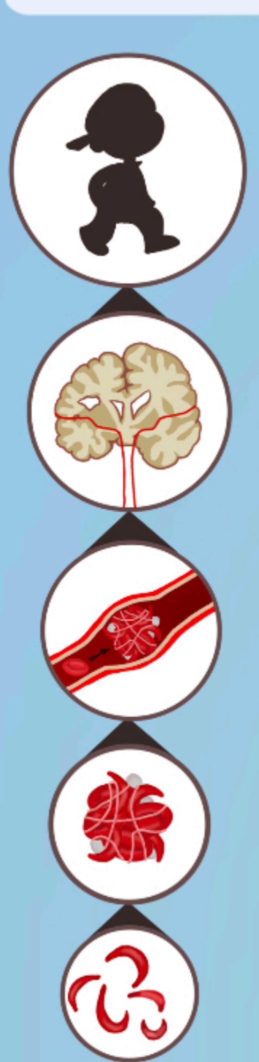
Bibliography

impington international college

Sickle cell anaemia and ischemic stroke

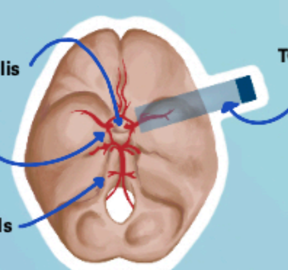
Sickle cell anaemia is a genetic disease affecting haemoglobin, causing red blood cells to become sickle shaped. Sickle cell disease is a significant risk factor for ischemic stroke as abnormal red blood cells easily clump together in arteries, obstructing the flow of blood to the brain. Ischemic stroke, if not detected rapidly, will cause permanent brain damage or death.



Silent strokes are ischemic strokes where patients experience no physical symptoms. Currently, silent strokes are not typically detected unless the patient undergoes MRI or CT scanning for an unrelated condition. However, silent strokes do cause permanent brain damage; neurological symptoms are likely to manifest in the long term. As the true cause is not known, these symptoms are often harmfully misattributed to psychological disorders, meaning patients receive incorrect care and treatments.
Early detection is crucial to identifying both symptomatic and asymptomatic strokes. Identifying potential ischaemic strokes before they occur would play a vital role in improving prevention and immediate treatment for severe brain damage, and detection of silent strokes would provide a far clearer basis for accurate and effective treatment of their long-lasting effects.

Patient specificity

TCD is typically used in major arteries as they are straighter so the angle of incidence of the ultrasound transmission and the angle of blood flow are known and therefore accounted for. It is more difficult to measure blood flow velocity in the vessels of the brain as they are often smaller, branched, and more curved, requiring individual adjustment as the angle of incidence will vary significantly between patients.
To ensure accurate results, Belugaband requires an initial set-up appointment where TCD and MRI scans are carried out for the patient by healthcare professionals using established hospital technology. This will allow doctors to adjust the band to make sure that the transducers are at their optimum before the patient wears the device at home. These initial readings will be used by the AI to predict a safe range for the patient. As such, the AI app tailors itself to the patient, providing patient-specific monitoring.



Belugaband as a medical device should comply with Medicine and Healthcare products Regulatory Agency (MHRA) regulation and guidance on good machine learning practice, which is regulated by the UK's Information Commissioner's Office (ICO). This includes only transferring sensitive patient information between the hospital and patient's device. These measures will maximise patient safety and confidentiality.

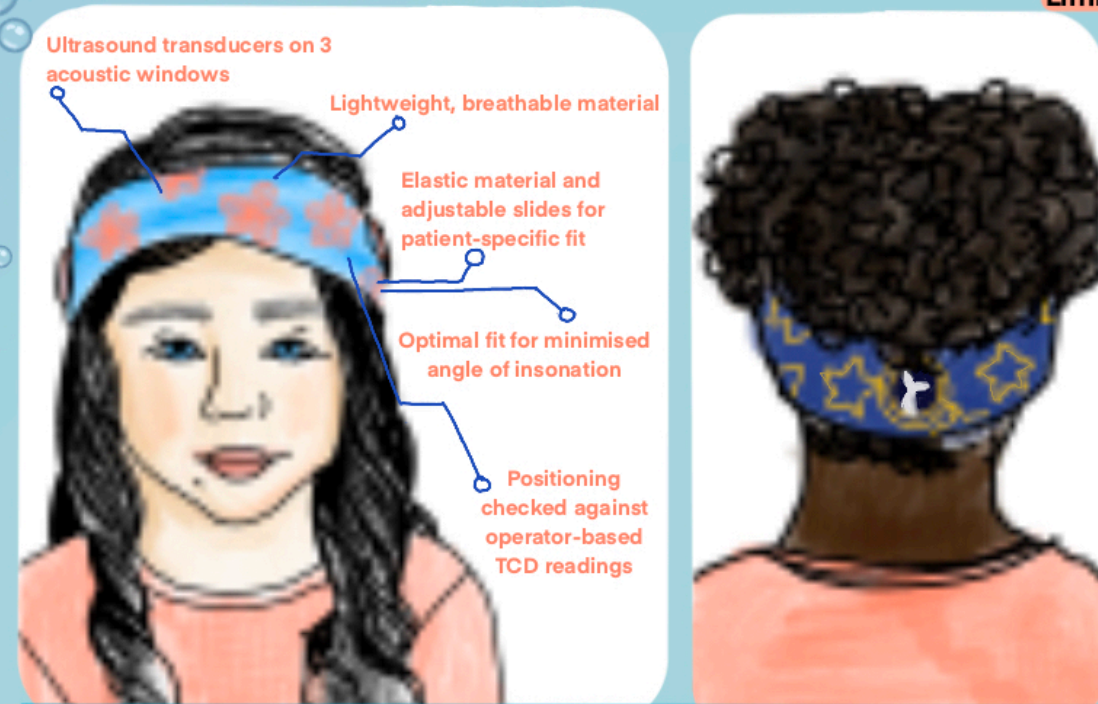
Ethics and feasibility

In the UK, children under 16 cannot consent to medical procedures, therefore their legal guardians will decide whether a procedure is right for their child. However, it is important that the child is still involved in decision making to ensure that patient-centred care is delivered. Belugaband must be accompanied with easy-to-understand accessible information and explanations for young people.

Once clinical studies are successful, Belugaband will be submitted to NICE for a Single Technology Appraisal.
Belugaband will likely be expensive for private buyers, making the device unavailable to patients in countries like Nigeria or India where SCD has the highest prevelance. This could lead to increased disparity between affluent and non-affluent countries. Once the patent of Belugaband expires, we would sell the product at cost to these countries to maximise the global outreach of the device.

Our device

We have designed Belugaband, a pragmatic, agile, robust, and adaptable headband which uses transcranial Doppler (TCD) ultrasound technology for continuous remote monitoring of blood flow velocity in the brain. TCD ultrasound is a painless, non-invasive test that uses ultrasound waves to detect abnormal blood flow velocity in the brain, providing rapid, inexpensive, real-time measurements of cerebrovascular function.
TCD ultrasound can detect many crises such as stroke in the brain before they cause lasting damage. This is because abnormal cerebral blood flow velocity can indicate the presence of blood clots, narrowed sections of blood vessels, and vasospasm due to a subarachnoid haemorrhage in the brain.



Belugaband comes in a range of colours, patterns, and styles, making healthcare fun and personalised

Limitations of current TCD devices

Currently, TCD treatment is highly operator dependent; the operator must have a detailed knowledge of cerebrovascular anatomy and be able to interpret ranges of blood flow velocity.
Additionally, treatment is psychologically taxing on children because regular TCD requires regular hospital visits, which can put unnecessary strain on family life.
Current TCD appointments can last for up to an hour, during which the child is required to stay still. This is particularly difficult for young children, meaning that a compromise must be made between accurate measurements and comfort for the child.
Our device addresses these problems as it is created for remote monitoring, meaning it has the benefit of being small and discreet, and causes minimal interference with children's lives. The less active role of radiologists reduces the burden on the healthcare system and makes management of chronic conditions such as sickle cell anaemia less demanding for the family.

Medical imaging techniques comparison

	Invasiveness	Resolution	Applications	Advantages	Limitations	Suitability for children
Transcranial Doppler Ultrasound	Non-invasive	High temporal resolution Moderate spatial resolution	Cerebral blood flow assessment, stroke detection	Bedside (continuous), real-time monitoring, no radiation	Operator dependent, limited to accessible areas	High as non-invasive and safe
Magnetic Resonance Angiography	Non-invasive	High spatial resolution	Blood vessel imaging, aneurysm, stenosis	Detailed vessel images, no radiation	Expensive, less available, longer procedure time	Low Long duration May require general anaesthetic
Position Emission Tomography	Minimally invasive (requires injection of radioactive tracers)	High spatial resolution	Brain metabolism, blood flow, functional imaging	Detailed functional and metabolic information	Expensive, radiation exposure	Low due to long duration, radiation exposure, and injection

Clinical trials

Pilot stage
- Small group (10-30) of healthy adult human volunteers
- Preliminary safety and device performance data in humans
- Assesses safety and efficacy of detecting stroke in humans

Pivotal stage
- Large group (100s) of children with SCD
- Study to confirm clinical effectiveness, safety, and risks
- Compare Belugaband readings with standard operator monitoring TCD (product development and testing)
- Statistical analysis with Bland-Altman plot

Post-market stage (1000s of participants)
- Monitors long-term effectiveness, safety, and usage of the device in the general population
- Testing whether Belugaband can detect silent strokes - we hypothesise that it could as it monitors continuously
- Investigate if other areas of the brain more commonly affected by silent stroke could be monitored using Belugaband
- Tests specificity and sensitivity to out of range readings

Preventing stroke in children with SCD

Belugaband is designed specifically for children because the adult skull is too thick for TCD to take accurate measurements (as the bone absorbs most of the ultrasound wave). Specifically, Belugaband will be aimed at children with sickle cell disease (SCD) who have a heightened risk of ischaemic stroke. In 1996, an estimated 11% of patients with SCD had a stroke with clear physical symptoms before age 20, and silent strokes (which do not have any physical signs) may occur in up to 39% of children with SCD. Belugaband will be able to detect abnormal blood flow velocity, indicating a potential stroke.
The data from Belugaband will be sent via a mobile app, which uses AI and Bluetooth, to the patient's healthcare team, who will be alerted to abnormal readings and can initiate rapid referral and treatment such as chronic transfusion. Combined TCD and chronic transfusion has been shown to lower the occurance of pediatric stroke by up to 10 times. Because of this, we predict that Belugaband will improve patient outcomes by ensuring that children with SCD at risk of stroke can be identified and offered preventative chronic transfusion.

How Belugaband works

The Doppler effect describes the change in frequency of a wave due to the relative motion of the source of the wave in comparison to the observer. When the source starts to move towards the observer, the wavelength shortens so that the sound appears to be at a higher frequency to the observer. TCD ultrasound exploits the Doppler effect to measure blood flow velocity in cerebral vessels.

This equation (right) means that if we know:

- the frequency (f0) the ultrasound is emitted at
- the difference between f0 and the reflected ultrasound frequency (Δ)
- the velocity of ultrasound in blood ($c = 1570 ms^{-1}$)
- the angle between the transducer and the vessel (θ)

$$\frac{\Delta f}{f_0} = \frac{2v\cos\theta}{c}$$

Assumptions:
- Angle of insonation = 0
- The diameter of the insonated vessel remains constant

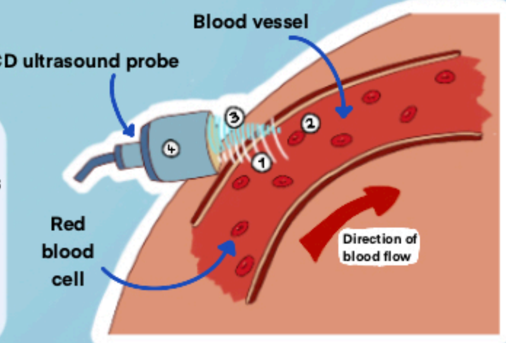
... we can find out the blood flow velocity (v) by inputting these parameters into the equation and rearranging for v.
Furthermore, as the angle approaches 0, cosθ approaches 1 and therefore can be removed from the equation.
Since c is a constant (speed of sound in blood) we can assume that the change in frequency is equal to 2v/c.
Belugaband's transducers will record this change in frequency, and then use this to calculate blood flow velocity.

Belugaband app

App template for remote patient monitoring. We will train AI on normal and abnormal readings using Class A IEC 62034 technology.

Process

1. Ultrasound pulses emitted from transducer into blood vessel
2. Ultrasound wave is reflected by moving blood cells
3. The moving blood causes a shift in the frequency of the reflected ultrasound
4. The transducer detects an increase in frequency if the blood is moving towards the transducer and a decrease if it is moving away.



Next steps

In the future, Belugaband may be used as a tool to research the relationship between cerebral blood flow and silent stroke (or silent cerebral infarct [SCI]) in children with SCD. SCIs affect up to 39% of people with SCD by age 18 causing cognitive and neurological impairments, with long-term impacts on quality-of-life due to difficulties with attention, executive function, processing speed and memory.
Children with SCD, who have had an SCI, may find learning more difficult and require additional support in educational settings. Their SCI may also affect their psychological and social development into independent responsible citizens. Because of this, it is incredibly important to research the warning signs of SCIs so that they can be prevented. We hypothesize that there may be a positive correlation between elevated cerebral blood flow and SCIs in SCD. Combined with regular MRI screening for SCIs, Belugaband could be used to continuously measure cerebral blood flow in children with SCD and investigate whether increased cerebral blood flow correlates with damage to the brain by SCIs.