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Biomedical Device Design

Feasibility report

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1 Introduction

This report comprises the process of arriving at a solution to the problem previously identified. We go through the steps of ideation and concept screening as specified in the book [I].

2 Need statement

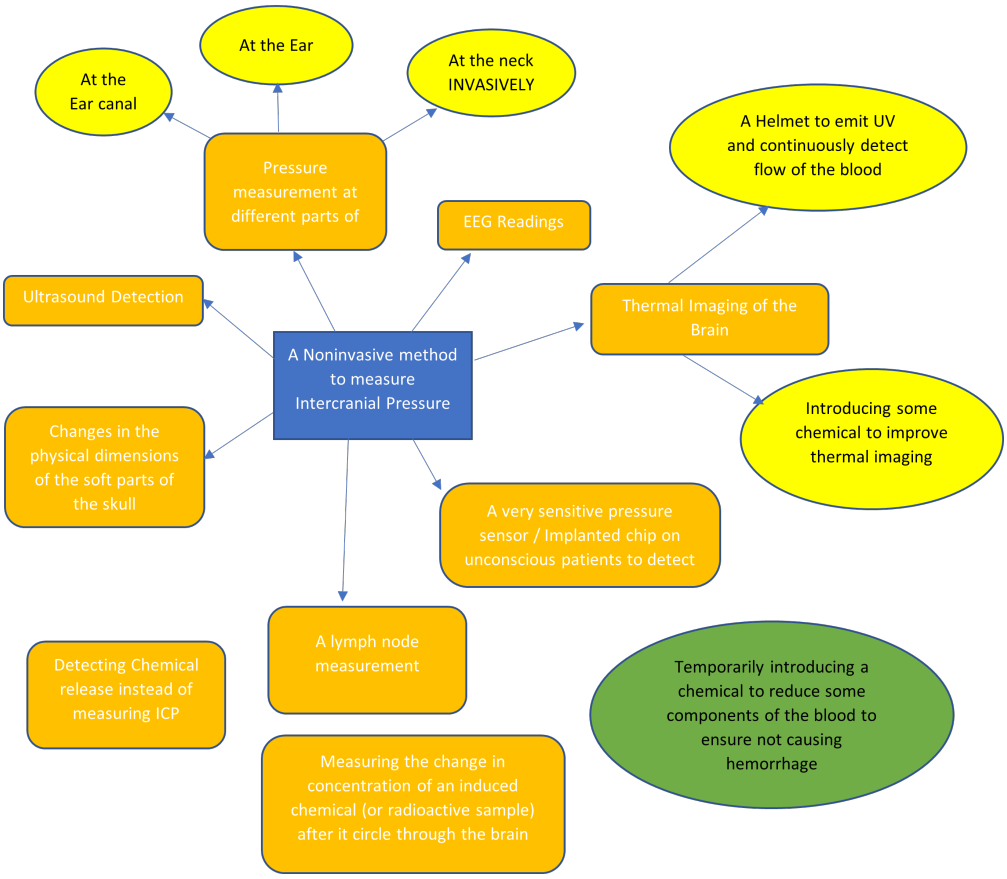
"The way to address Non-invasive Neurovascular monitoring of the head in Patients who underwent trauma/head surgery to Real-time detection of hemorrhages before any complications"

The rupture of blood vessels in the brain leads to a hemorrhage. Hematomas result in damage to the functional tissues, which results in the loss of cognitive functions and would be fatal if the brain stem got affected. The existing effective method is to use the change in intracranial pressure by using an intravascular catheter, which will be very invasive and has only been done in high-level trauma centers and severe cases. CT and MRI have also been used to detect slowly progressing hematomas, but they cannot detect drastic ruptures as patients are not under continuous scanning. EEG could also warn, but it will be somewhat late.

The detection method should be quick and continuous to minimize and prevent the damage caused by hematomas.

3 Ideation

In the process of finding solutions, a brainstorming session was conducted on 08/12/2022 to generate ideas to tackle the need, and the proposed ideas are given below.



4 Initial concept selection

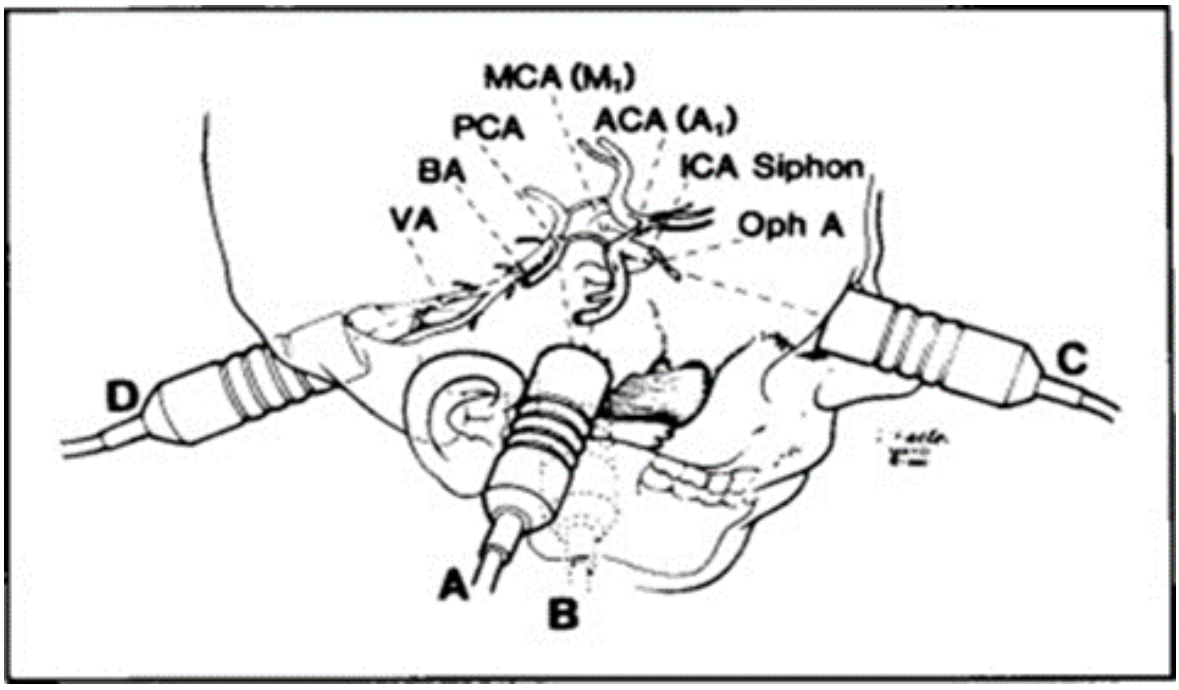
From the above-proposed ideas, we selected a few concepts that we could move forward with, and those that were not feasible were removed. EEG is one of the most commonly used methods to detect hemorrhage, but at the time of EEG detection, there is some significant damage to the tissues and optical nerves. The effect of hematoma inferior to the head is negligible and undetectable, making neck measurement difficult. Also, the idea of introducing chemicals to reduce the blood flow in post-surgery patients is unorthodox and outside our engineering scope. Apart from those previously rejected, we have chosen the three ideas below to analyze and select the most feasible one.

4.1 Measuring acoustic properties of the inner ear

The idea is to measure the acoustic properties of the inner ear, as they are directly correlated to the intracranial pressure. Implementation of the device would include transmitting a sound wave into the ear canal and analyzing the echo signal using signal processing algorithms. This method has been used in studies to measure ICP in pilots and astronauts performing microgravity parabolic flights. An implanted device can be used to get these readings continuously. [II]

4.2 Doppler Ultra Sound

Transcranial Doppler could directly monitor vascular activities and give many vital details related to flow patterns. But unlike other parts of the body, the brain is covered by a thick skull, and ultrasound could not penetrate it at every point. We can peer through specific windows (orbital, occipital, and terminal), and different arteries can be seen from different windows. We could analyze these flow patterns using machine learning algorithms and detect any abnormalities.



4.3 Introducing a radioactive isotope to the brain arteries and observe it's behavior.

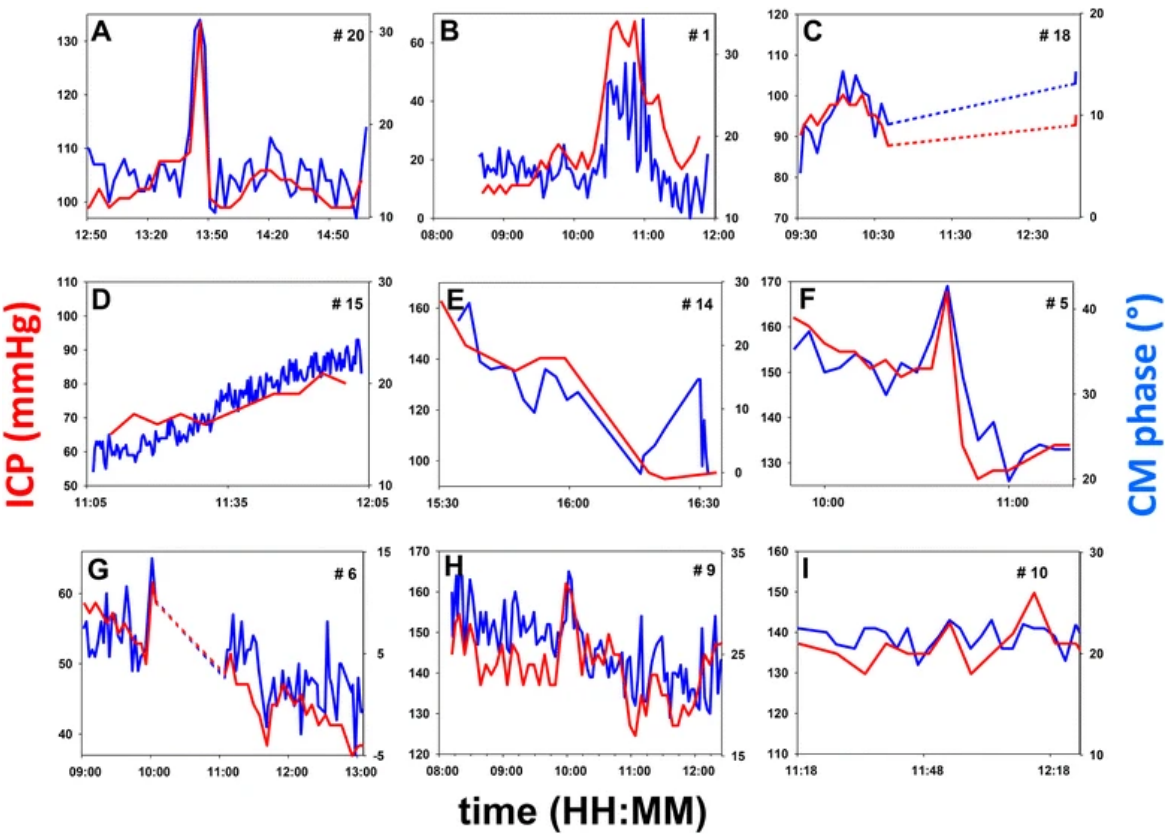
First, we introduce a radioactive isotope to an artery going towards the brain and observe its behavior to identify potential hemorrhages. A special sensor array will be placed around the head to intercept the radiation. Spatial processing algorithms could be used to identify the place where the abnormality has occurred.

5 Concept screening

5.1 Intellectual Property(IP)

5.1.1 Measuring acoustic properties of the inner ear

Inner-ear fluids are directly connected to the cerebrum fluids. ICP changes make subtle changes in the physiology of the inner ear, which can be detected by the phase of the cochlear microphonic potential(CM). [III]



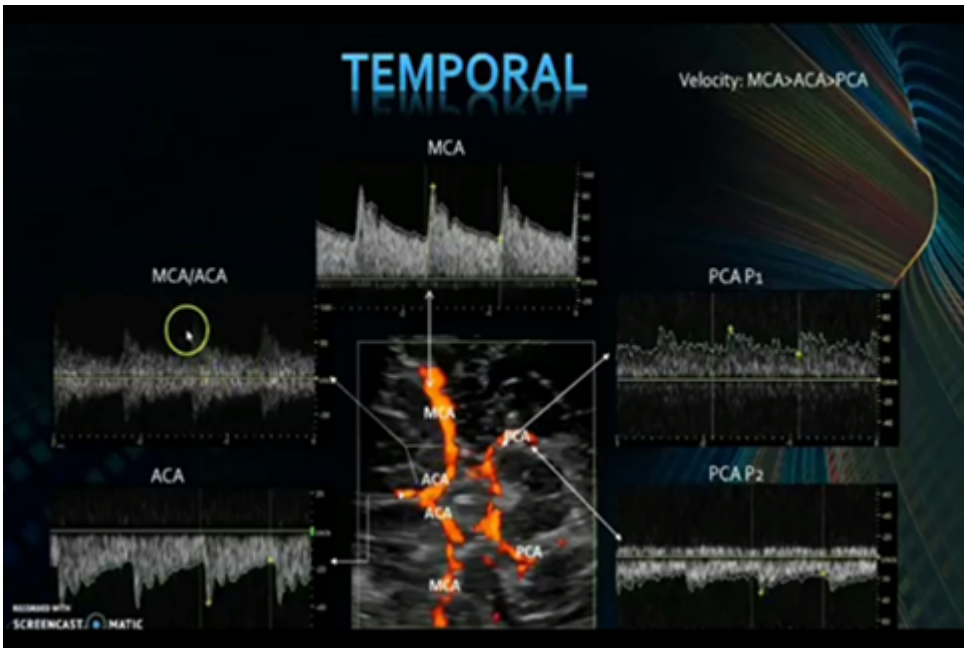
The above picture shows various measurements taken on different patients. Dotted lines: interruptions in data collections. ICP-slope and CM-phase are interconnected, and we could develop a relationship. The researchers are conducting studies to improve on this concept.

[Patent 01] WO2007118092A2 - Method and system for monitoring intracranial pressure - Google Patents, 3 April 2007, https://patents.google.com/patent/WO2007118092A2/en

5.1.2 Doppler Ultra Sound

Transcranial Cerebral hemodynamics can be easily evaluated using a TCCS (transcranial color-coded sonography), which provides data to evaluate brain anatomy and ICP. We can choose an appropriate and reliable window (orbital, occipital, or terminal) and calibrate a doppler to obtain the ICP as an output. This is a method found to be a very effective substitute for an invasive ICP catheter. [IV]

[Patent 02] US20050015009A1 - Systems and methods for determining intracranial pressure noninvasively and acoustic transducer assemblies for use in such systems - Google Patents, 3 Jun. 2004, https://patents.google.com/patent/US20050015009A1/en



5.1.3 Introducing a radioactive isotope to the brain arteries and observe it's behavior

A common method that is the oldest but is still in use to scan the brain is by using a radioactive isotope (such as technetium or iodine). There is currently no invention that combines injection and detection. A CAT scanner can be used to detect the emissions of the radioactive sample. But the accuracy and response time are yet to be identified to determine if this method is effective.

5.2 Regulatory

All three require class II FDA approval and can be marketed via the 510(k) procedure. Depending on the in-ear device that is used to detect ICP, it might fall under class III; in that case, the PMA regulatory pathway must be taken.1

5.3 Reimbursement

In Sri Lanka, the majority of the patients do not have insurance, Most hospitals are run with government funds. Only about a quarter of Sri Lanka's hospitals are private. Out of the three ideas, the doppler ultra sound will have a lower reimbursement than the other two because it will be more costly.

5.4 Buisiness Model

Since we plan to first implement our solution in Sri Lanka, the product should be in the affordable range of something similar to an ICP catheter. And the solution should be best suited to the current state of the country's resources and economy. With the suggested method, it will be easier for the medical staff to get these readings, reducing the risk factor and mortality due to complications that could occur with the current method of ICP measuring.

5.4.1 Measuring acoustic properties of the inner ear

In-ear scanners are already available in the country, but they are equipped only to detect hearing disabilities. Innovating the existing device to take records of CM phase change and calibrating it to show the ICP can reimburse the government on many levels. Due to the familiarity of the already existing in-ear scanners, it will be easier to familiarize the medical staff with the newly implemented features and components. Most low-income countries that cannot afford the current ICP catheter would find this a great substitute.

5.4.2 Doppler Ultra Sound

Other than the cost and time reduction of what it takes to do the usual ICP reading technique, the easily accessible nature of the device makes it easier for patients to even take readings on their own, saving hospital accommodations and man hours and eventually saving the government money. Though the technology is a bit advanced and costly, it has been found to provide more accurate detection of probable hemorrhage to some extent than others.

5.4.3 Introducing a radioactive isotope to the brain arteries and observe it's behavior

In Sri Lanka, radioiodine therapy and newborn screening for congenital hypothyroidism are performed, with approximately 30,000 tests performed each year. With the available resources, we could implement this device and save the government funds that go into replacing ICP catheters. There are radiation risks, and it may be necessary to be isolated for a while, but this will reduce the risks and costs involved in drilling and the invasiveness of the older method.

5.5 Screeening matrix

With the above analysis, the feasibility of the products is analyzed. The following screening matrices explains the process. The abbreviations used in the matrix are as follows:

IP - Intellectual Property
RR - Regulatory Requirements
RI - Reimbursement
BM - Business Model

The objective and concept abbreviations are given below:

(01) : Measuring acoustic properties of the inner ear

Idea	IP	RR	RI	BM
(01). Acoustic properties of the inner ear				
(02). Doppler Ultra Sound				
(03). Introducing a radioactive isotope				

Table 1: Risk analysis

(02) : Doppler Ultra Sound
(03) : Introducing a radioactive isotope to the brain arteries and observe it's behavior

Accuracy : capable of providing the required accuracy
Non-invasive : able to take measurements uninvasively
Continuous : provide a continuous diagnosis for the patient
Accessibility : easy to use by the patient or the medical staff

Objectives	Weight	Invasive ICP (baseline)	(01)	(02)	(03)
Accuracy	5	0	+1	+1	0
Non-invasive	4	0	+1	+1	0
Continuous	3	0	+1	+1	0
Accessibility	5	0	0	+1	-1
Final score		0	12	17	-5

Table 2: Objectives and concept screening

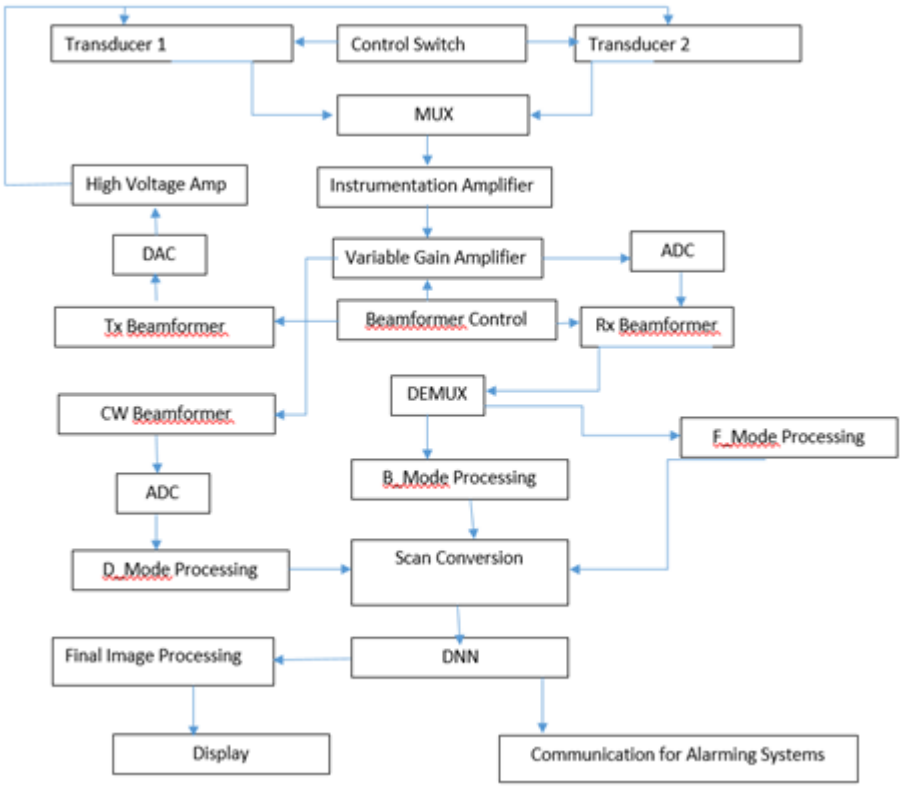
6 Final concept selection

According to the screening analysis, the **Doppler ultra sound** method is found to be the most feasible among the three. And it also carried the fewest risks.

6.1 Concept exploration and testing

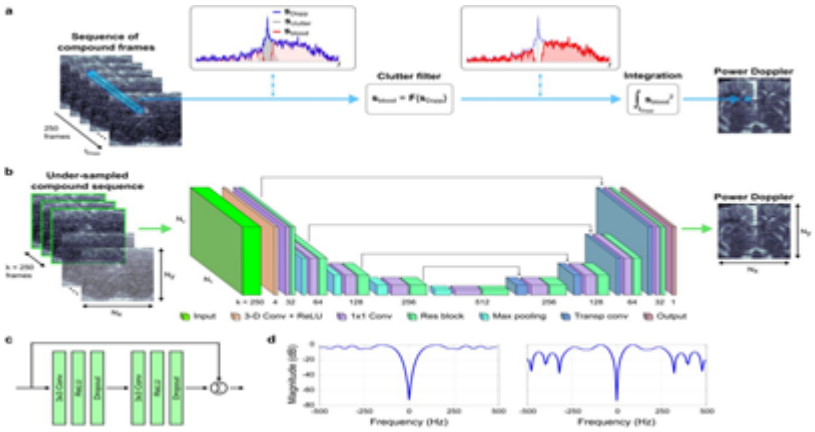
6.1.1 Prototyping

The doppler design prototype consists of two transducers that we place at two selected windows to the cranium. These transducer arrays are connected to a multiplexer to reduce the amount of wiring, as each transducer array may contain nearly 200 sensors. Then this signal goes through an instrumentation amplifier, which would eliminate any common-mode noise added to it. After that, it passes through a variable-gain amplifier to reduce the effect of the exponential decay of the signal with time. [V]



A beamformer is used to create the waves in the necessary direction with the desired shape of the wavefront. Then these data go through image processing, in which B mode produces the image of time elapsed and the strength of the returning signal. F-mode color doppler produces the image that corresponds to blood flows inside the brain. We also require D-mode processing, which converts the signal of the frequency shift into blood velocities.It is necessary to mention that these velocities are also dependent on the angle of incidence. Thus, the deep neural network should be trained to interpret velocity variations rather than the absolute value.

Then the neural network would detect any abnormalities in the neurovascular states of the brain and would trigger an alarm if a specific abnormality was detected.

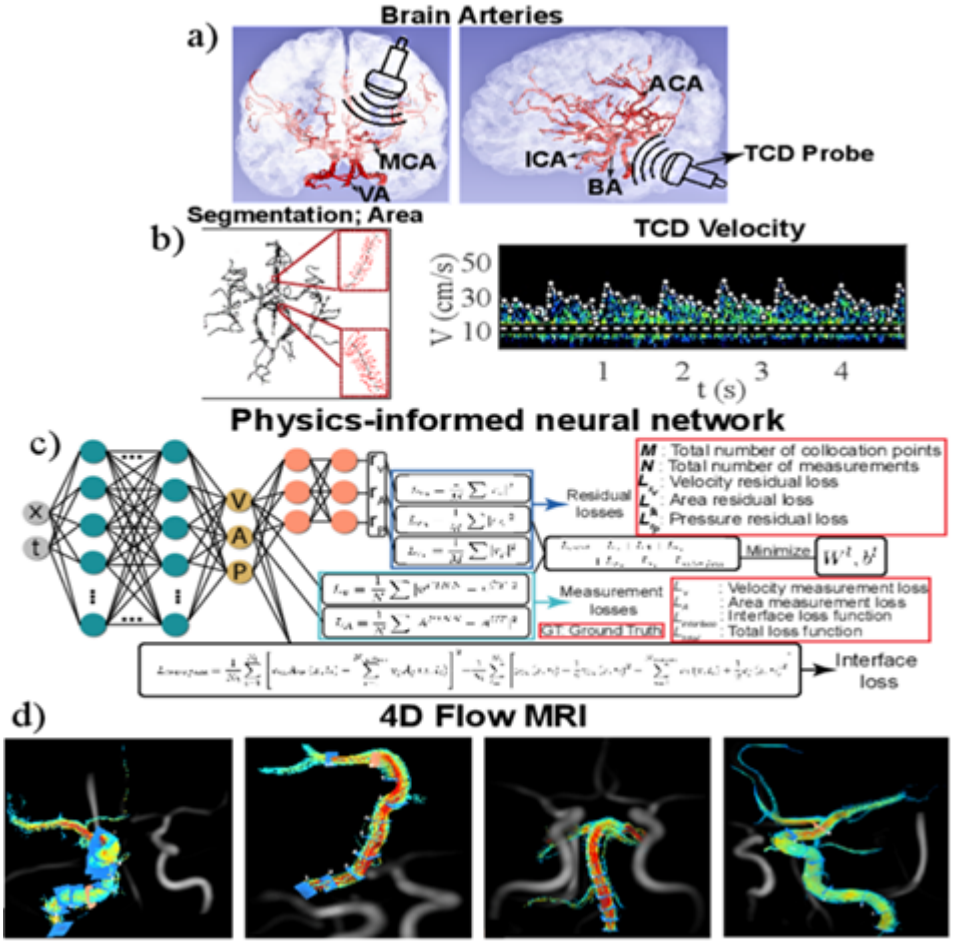


6.2 Technical Feasibility

Most of the components mentioned above are basic building blocks that are being used by many ultrasound scanner manufacturers. So designing the electronics would not require a strenuous R&D effort. However, neural networks are still in their early stages and would require significant R&D resources to be allocated.

6.3 Testing

Data obtained from MRI scans could be used to test the functionality. In practice, we could not continuously take an MRI of a patient, but for the testing prototype, we could use a 4D flow MRI to collect data continuously, train the neural network, and then again use an MRI to evaluate and measure the performance.



7 Conclusion

To summarize, Doppler ultrasound is the most appropriate and feasible substitute for invasive intracranial pressure measurement, and it would meet the primary goals of our requirement, which are accurate and continuous non-invasive detection of ICP.

References

[I] Paul g. yock, stefanos zenios, josh makower, todd j. brinton, uday n. kumar, f. t. jay watkins, lyn denend, thomas m. krummel, christine q. kurihara, "biodesign: The process of innovating medical technologies", 2nd edition, cambridge university press, new york, 2009.

[II] Avan P, Normand H, Giraudet F, Gerenton G, Denise P. Noninvasive inear monitoring of intracranial pressure during micro gravity in parabolic flights. J Appl Physiol 125: 353–361, 2018. First published May 3, 2018; doi:10.1152/japplphysiol.00032.2018.

[III] Giraudet, F., Longeras, F., Mulliez, A. et al. Noninvasive detection of alarming intracranial pressure changes by auditory monitoring in early management of brain injury: a prospective invasive versus noninvasive study. Crit Care 21, 35 (2017). https://doi.org/10.1186/s13054-017-1616-2.

[IV] Robba, C., Taccone, F.S. How I use Transcranial Doppler. Crit Care 23, 420 (2019). https://doi.org/10.1186/s13054-019-2700-6.

[V] Mohammad Sarabian, Hessam Babaee, Kaveh Laksari, Physics-informed neural networks for improving cerebral hemodynamics predictions,https://www.catalyzex.com/paper/arxiv:2108.11498.

Appendix: Brainstorm canvas

The original image taken from the brainstorming session is given below.

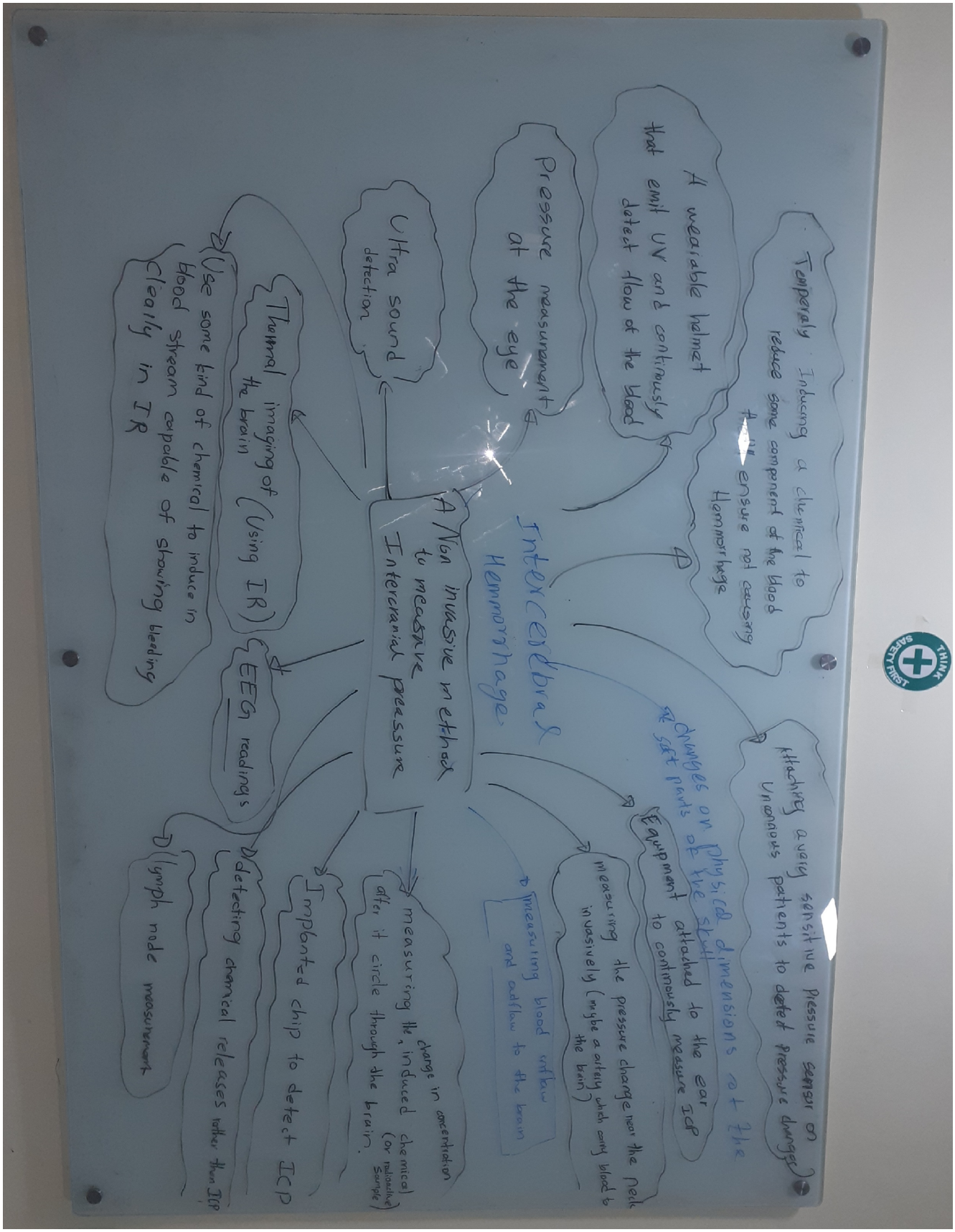


Table 4.2.1 Device classification has direct implications on the number and complexity of the requirements imposed by the FDA.

Class	Examples	Description	FDA requirements
I	Bandages, tongue depressors, bedpans, examination gloves, hand-held surgical instruments	Class I devices present minimal potential harm to the person they are being used on and are typically simple in design.	With Class I devices, most are exempt from premarket clearance. There is no need for **clinical trials** or proof of safety and/or efficacy since adequate predicate experience exists with similar devices. However, they must meet the following "general controls": • Registration of the establishment with the FDA. • Medical device listing. • General FDA labeling requirements. • Compliance with quality system regulation (**QSR**), with the exception of design controls, unless specifically called out in the regulation.
II	X-ray machines, powered wheelchairs, surgical needles, infusion pumps, suture materials	**Class II** devices are often non-invasive, but tend to be more complicated in design than Class I devices and, therefore, must demonstrate that they will perform as expected and will not cause injury or harm to their **users**.	Class II devices are generally cleared to market via the **510(k)** process, unless exempt by regulation. They must meet all Class I requirements, in addition to the "special controls" which may include: • Special labeling requirements. • Mandatory performance standards. • Design controls. • Post-market surveillance.
III	Replacement heart valves, silicone breast implants, implanted cerebellar stimulators, implantable pacemakers	Class III devices are high-risk devices. These are typically implantable, therapeutic, or life-sustaining devices, or high-risk devices for which a predicate does not exist.	Class III devices must generally be approved by the **PMA** regulatory pathway, although a small number are still eligible for 510(k) clearance. (FDA has begun the process of requiring PMAs for all of these.) Class III devices must meet all Class I and II requirements, in addition to stringent regulatory approval requirements that necessitate valid scientific evidence to demonstrate their safety and effectiveness, before they can be used in humans.

Figure 1: Source : "Biodesign: The Process of Innovating Medical Technologies" [I]