# Phase 2: Project Detailed Summary

## Project Title

**Reliability of a Novel Deep Learning System for Optic Nerve Sheath Diameter Measurement.**

## Existing Knowledge

The bedside diagnosis of raised intracranial pressure (ICP) is challenging as the symptoms lack sensitivity and fundoscopic examination is associated with clinician diffidence [1-7]. Elevated ICP requires timely recognition and management as it is associated with significant morbidity and mortality [4-6]. In South Africa, there is limited access to specialised diagnostic imaging modalities [8] necessitating innovative adaptations to existing infrastructure to achieve the required diagnostic accuracy. One such potential opportunity is to leverage a Deep Learning System (DLS) to assist clinicians in assessing the Optic Nerve Sheath Diameter (ONSD), a surrogate marker for ICP [9-12].

The optic nerve can be structurally visualised at the bedside using non-invasive techniques which include Fundoscopy, Optical Coherence Tomography (OCT), and Ocular Ultrasound [6, 13-14]. Papilloedema is a clinical sign and is defined as swelling of the optic disc secondary to raised ICP [15].

The gold standard for the diagnosis of raised ICP are intraventricular or intraparenchymal catheters [6]. These methods require anaesthesia and are invasive, expensive, and associated with infection, haemorrhage, and malposition [16-20]. The non-invasive modalities for detecting raised ICP are classified as structural or functional [6]. Structural modalities include CT, MRI, Fundoscopy, Optical Coherence Tomography (OCT), and Ocular Ultrasound [6]. Functional modalities include Transcranial Doppler Ultrasound, Near-Infrared Spectroscopy, and Visual Evoked Potentials [6, 21].

Bedside fundoscopy is readily available due to the low cost and portability of the ophthalmoscope but its use is limited due to its poor diagnostic accuracy and clinician diffidence [6-7, 22-24].

OCT parameters show good sensitivity for raised ICP [6]. The machine is portable and used in the primary care setting. Access at present is the major limitation.

Point-of-care ultrasound (POCUS) is an attractive alternative given the limitations of fundoscopy and OCT in South Africa. For suspected raised ICP, ocular ultrasound is used to measure the Optic Disc Elevation (ODE), a surrogate for papilledema, and ONSD, which is a measure of CSF in the subarachnoid space around the optic nerve. [25, 26]

The proposed cut-off for ODE ranges from 0.3mm to 1mm and has a sensitivity in diagnosing raised ICP that ranges from 70% to 90% and a specificity close to 100% [13]. ONSD has a sensitivity of 95.6% and specificity of 92.3% when 5mm is taken as the cut-off and it is measured 3mm posterior to the globe [14]. There is however poor standardisation of this cut-off in clinical practice. A South African population-based study recommended a cut-off value of 5.6mm when screening for raised ICP [27].

Ocular ultrasound’s major limitation lies in the significant inter-operator variability and as such, reliability is inconstant and it is used inconsistently [6]. It does however pose little risk to patients, is relatively inexpensive, portable, quick, and correlates well with ICP measurements [6, 28]. Point of Care Ultrasound use is gaining momentum and as such there is an established infrastructure of usable devices within sub-Saharan Africa [29].

There is an emerging trend in medical imaging where Artificial Intelligence (AI) is making significant strides, particularly in the field of DLS based on Convolutional Neural Networks (CNN). DLS can diminish discrepancies that arise from different observers interpreting the same image, known as inter-observer variability [9]. While rule-based systems face challenges in generalizing across different observers and equipment, DLS offers a promising solution to this limitation, leading to its increasing relevance and growth in the medical imaging field.

AI has been successfully applied to medical image segmentation and diagnosis, improving work efficiency and accuracy [9]. By leveraging AI algorithms, accurate and automated measurements of ONSD can be obtained [10, 11], reducing the reliance on subjective assessments and enhancing diagnostic accuracy.

## Hypothesis

A dataset of transorbital ultrasound images can be used to train a DLS to reliably measure the ONSD.

## Aim

* Accumulate a dataset of defined ocular ultrasound images.
* Use these curated images to fine-tune a Deep Learning System (DLS), aiming for precision in measuring the ONSD.
* Evaluate the DLS’s reliability using a method comparison test

## Methodology

A retrospective cross-sectional study to train and test the reliability of a novel DLS against a defined internal dataset of ONSD measurements taken by a trained and experienced ultrasound provider. This is the first step in determining the feasibility of a DLS capable of assisting in clinical practice.

Retrospective de-identified, ocular ultrasound images will be collected from a database of previously defined images taken as part of a study carried out on healthy black South African adults [27]. This study received approval from the Human Research Ethics Committee of the University of the Witwatersrand (ethics clearance number M191159) and adhered to the tenets of the Declaration of Helsinki. Additional approval will be sought from the Human Research Ethics Committee of the University of the Witwatersrand to use these images in this study prior to data collection. There are approximately 198 ocular ultrasound images available through the study that were captured between March and December 2022.

The images will be captured on a secure electronic Case Report Form (eCRF). Age, gender, co-morbidities and intraocular pressure (IOP) will be captured with the image when available. Inclusion will be based on image quality and age >18 years. Pre-processing will be used to standardize images to a consistent size and format and enhance the images if needed to improve the visibility of structures.

The chosen platform for model development and verification is Google Colab, a top-tier Jupyter Notebook hosting service [29]. Google Colab provides an optimal environment for executing Python code efficiently, making it highly suitable for sophisticated machine-learning tasks [30].

Regression analysis will be conducted to predict the continuous measures of ONSD. A CNN will be trained using the pre-processed and augmented ultrasound images to achieve this.

To assess the reliability of the Deep Learning System (DLS), a distinct dataset of images that were not used during the training phase will be leveraged [31]. This will therefore be an agreement study looking at method comparison between the pre-defined study-based images and the novel DLS. Interclass Correlation Coefficients (ICC) and Bland-Altman Plots will be used to assess the reliability. [32-34]

Sample size calculation:

The reliability of the novel DLS will give insight into the feasibility of further research potential.

## Achievability

Protocol submission was made to the Witwatersrand’s Human Research Ethics Committee (Wits HREC) on 03 November 2023. Feedback from this submission is expected in late January 2024.

Local sponsorship through the University of the Witwatersrand will be implemented for the study.

Of notable concern is the delay in feedback from Wits HREC. Given the nature of the proposed study, it is conceivable that there will be possible changes required to the protocol, which would require further local ethics approval before data can be collected. This could ultimately lead to delays in the project timeline.

The following project timeline is proposed:

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Sep-23 | Oct-23 | Nov-23 | Dec-23 | Jan-24 | Feb-24 | Mar-24 | Apr-24 | May-24 | Jun-24 |
| Literature Review |  |  |  |  |  |  |  |  |  |  |
| Project Outline Summary |  |  |  |  |  |  |  |  |  |  |
| Ethics WHREC Submission |  |  |  |  |  |  |  |  |  |  |
| Detailed Summary |  |  |  |  |  |  |  |  |  |  |
| Data Collection |  |  |  |  |  |  |  |  |  |  |
| DLS Training/Validation |  |  |  |  |  |  |  |  |  |  |
| e-Poster |  |  |  |  |  |  |  |  |  |  |
| Completed Project Report |  |  |  |  |  |  |  |  |  |  |

Figure 1. *Gantt chart*

## Novelty

There is a need to assist clinicians working across various settings, in the diagnosis of elevated ICP. Traditionally, the assessment for raised ICP has been available to select specialised and experienced physicians using fundoscopic examination and more recently ocular ultrasound. With the advent of AI, there is now an opportunity to leverage existing infrastructure to assist clinicians at all levels in the diagnosis of raised ICP. Several studies look at AI in medical imaging but none focuses on the use of a DLS in assessing the ONSD in a South African population. If successful, this may have the potential to aid healthcare services across varied settings.

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