Spatiotemporal and kinematic characterisation of gait in individuals with idiopathic Normal Pressure Hydrocephalus

Mariam Riaz

A THESIS SUBMITTED IN FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE (BY RESEARCH)

Department of Sport and Exercise Sciences

Manchester Metropolitan University

January 2025

Acknowledgements

First and foremost, I would like to express my gratitude to God for His blessings.

I would like to express my deepest gratitude to Dr. Richard Mills, my supervisor and mentor, for his invaluable guidance, unwavering support, and insightful feedback throughout the course of this research. His expertise, patience, and encouragement have been instrumental in shaping this thesis and research project. I am indebted to Dr. Mills for his assistance and contributions to this work. His assistance throughout the course of this whole project has been indispensable and greatly appreciated.

I would like to express my gratitude to Professor Neil Reeves, Faculty Director of Research, for giving me the opportunity to be part of this insightful research project for my MSc thesis. His mentorship, support, and encouragement have been invaluable throughout this journey.

I am thankful to Dr. Tobias Langheinrich for his medical expertise and for leading the project so successfully from Salford Royal Hospital, which allowed for the successful completion of the project. His sincere commitment to the welfare and diagnosis of his patients was reflected throughout the project, making it a meaningful experience.

I am thankful to Dr. Mats Tullberg for his expert guidance and valuable contributions to the project. Special thanks to Dr. Liis Uiga for her assistance throughout the lab testing process and for being a source of encouragement, motivation, and inspiration for me throughout the project.

I would like to acknowledge the support of the Department of Sport and Exercise Science at Manchester Metropolitan University for providing all the necessary support which facilitated the completion of this thesis.

I would also like to acknowledge the team at Salford Royal Hospital for their essential support in facilitating the smooth execution of the project, particularly in ensuring efficient recruitment and patient coordination, including appointment scheduling and travel arrangements.

Finally, I am immensely grateful to my family for their unwavering love, encouragement, and understanding throughout this journey.

Contents

List of Abbreviations

Abbreviation	Full Form
iNPH	Idiopathic Normal Pressure Hydrocephalus
NPH	Normal Pressure Hydrocephalus
CSF	Cerebrospinal Fluid
MRI	Magnetic Resonance Imaging
AD	Alzheimer's Disease
PD	Parkinson's Disease
ETV	Endoscopic Third Ventriculostomy
EMG	Electromyography
ICP	Intracranial Pressure
COM	Centre of Mass
COP	Centre of Pressure
CT	Computed Tomography
TT	Tap Test
VP	Ventriculoperitoneal
AEG	American European Guidelines
JG	Japanese Guidelines
TUG	Timed Up and Go
ITUG	Instrumented Timed Up and Go

List of Tables and Figures

Abstract

Background: Idiopathic normal pressure hydrocephalus (iNPH) is characterized by gait disturbance, cognitive impairment, and impaired bladder control. This disturbance to gait results in a slow, unstable, short stepping pattern, with increased fall risk. There is currently no research providing in-depth, laboratory-based characterization of gait and balance in patients with iNPH, instead relying mainly on more subjective, clinical measures to identify the condition. This approach makes it difficult to distinguish iNPH from competing conditions which also affect gait, including Parkinson's disease and normal ageing.

Objective: This thesis was the first to provide full gait analysis and joint kinematics of iNPH patients. This thesis focused on the detailed characterization of gait abnormalities in patients with idiopathic Normal Pressure Hydrocephalus (iNPH) by analysing temporal and kinematic gait parameters. The primary aim was to provide a comprehensive assessment of gait impairment in iNPH patients to aid in diagnosis and establish a foundation for future evaluations of treatment effectiveness using gait analysis variables. Specifically, the study aimed to identify key gait and balance variables that objectively characterize mobility impairment in iNPH and accurately quantify changes in mobility and balance before and after the cerebrospinal fluid tap test (TT), a standard clinical procedure used to assess the potential benefit of permanent CSF drainage via a neurosurgical shunt.

Methods: The study involved recruiting iNPH patients from Northern Care Alliance (Salford Royal) NHS Foundation Trust. Gait assessment was conducted using a 3D motion capture system to collect detailed data on gait dynamics. Temporal and kinematic parameters, including walking speed, cadence, step length, and range of motion at the hip, knee, and ankle joints across all three planes of motion (sagittal, frontal, and transverse), were measured. These parameters were then compared to those of age-matched healthy controls to identify deviations specific to iNPH patients.

Results: Group comparison analysis revealed significant deviations in temporal and kinematic parameters in iNPH patients compared to healthy controls. iNPH patients walked slower, had lower cadence, smaller step lengths, and exhibited reduced range of motion at all three joints and planes of motion. These findings align with existing literature that documents gait disturbances in iNPH, such as slowed walking speed and increased step variability. This study

is among the first to apply 3D gait analysis in this context, providing detailed insights into gait dynamics that surpass traditional 2D methods.

Limitations: The study's scope was limited by the inability to compare joint kinetics successfully due to multiple foot strikes across the force plates. While part of the larger study, this thesis also did not include pre and post tap test comparisons of patients making it difficult to evaluate the effect of the procedure on gait. Furthermore, this study did not include muscle activation patterns, which are crucial for a comprehensive biomechanical analysis. Additionally, recruiting small group of patients exclusively from Salford Royal introduces potential selection bias and small sample size, limiting the generalisability of the findings.

Conclusion: While this study contributes valuable knowledge about gait abnormalities in iNPH, it highlights the need for more comprehensive biomechanical analyses and broader patient recruitment strategies. Future research should focus on strategies to obtain high-quality kinetic data by using advanced techniques to analyse kinetic data effectively. Future work should also prioritize the inclusion of pre- and post- tap test comparisons to provide a comprehensive understanding of gait improvement. Biomechanical assessments, such as EMG, provide objective measurements of muscle activity and movement patterns. By objectively quantifying these parameters, researchers can track changes over time and evaluate the effectiveness of interventions or treatments (Hermens et al., 2000). Addressing these limitations will enhance the understanding of iNPH and improve diagnostic and therapeutic approaches.

Foreword

This thesis presents a focused analysis of specific spatiotemporal and kinematic outcomes to provide full gait analysis of iNPH patients. The methodologies applied and results obtained in this work are embedded within the context of a broader study investigating characteristics of iNPH in order to make a definitive diagnosis. While contributing to the overarching research objectives, this thesis is structured to stand independently, allowing for a clear and in-depth presentation of these specific findings of spatiotemporal and kinematic outcomes in INPH as compared to an age-matched, healthy control population.

1. INTRODUCTION

1.1 iNPH

Hydrocephalus is a neurological condition characterized by the abnormal accumulation of cerebrospinal fluid (CSF) within the brain's ventricles. This condition arises from either an obstruction of CSF flow or an imbalance between CSF production and its absorption into the systemic circulation (Isaacs et al., 2019). Typically, hydrocephalus is associated with enlarged cerebral ventricles and increased intracranial pressure (ICP). However, Dr. Salomon Hakim's observation in the 1960s that some patients with hydrocephalus exhibited surprisingly low to normal ICP led to the identification of a subtype known as normal pressure hydrocephalus (NPH). Hakim further categorized his patients into those with secondary NPH, who had prior neurological conditions such as meningitis or subarachnoid hemorrhage, (Isaacs et al., 2019). and those with idiopathic normal pressure hydrocephalus (iNPH), often seen in elderly individuals without known risk factors.

Idiopathic normal pressure hydrocephalus (iNPH) primarily affects elderly patients, leading to enlarged cerebral ventricles (Agostini et al., 2015). iNPH (idiopathic Normal Pressure Hydrocephalus) prevalence in the older population has been estimated to range from 0.5% to 2.9%. However, the epidemiology of iNPH remains relatively obscure due to a lack of dedicated population-based studies. Historically, much of the data on iNPH has been extrapolated from research on related conditions like dementia and Parkinsonism or from studies on hydrocephalus interventions (Martín-Láez et al., 2015).

Globally, research on iNPH epidemiology is limited. The diverse symptoms associated with iNPH complicate the establishment of consistent research criteria, and a disease-specific differential diagnosis remains elusive (Iseki et al., 2014). The absence of standardized diagnostic criteria can lead to variability in case identification, affecting research outcomes. For instance, a study by Marmarou et al. (2007) found iNPH prevalence in nursing home residents aged under 85 ranged from 9% to 14%, based on applied criteria. When only patients who responded positively to shunt surgery were considered, prevalence dropped to 5% (Martín-Láez et al., 2015).

This condition manifests in gait disturbances, cognitive impairments, and urinary issues. Patients frequently experience an urgent need to urinate and may suffer from incontinence,

which disrupts their sleep patterns. Gait disturbances range from mild imbalance to an inability to walk, characterized by a slow, shuffling gait and increased step width, a key diagnostic criterion. While a wider stance is traditionally thought to enhance stability in diabetic neuropathy, Brown et al. (2015) found that it correlates with greater difficulties in dynamic balance and increased separation between the Centre of Mass (CoM) and the Centre of Pressure (CoP). iNPH patients often struggle with foot lift, making navigation of steps and curbs challenging and increasing fall risk (Czerwosz et al., 2009).

CSF envelops the brain and spinal cord, accumulating in the subarachnoid space and ventricles. In healthy individuals, CSF is reabsorbed through arachnoid granulations into the superior sagittal sinus, regulated by pressure gradients. In iNPH, resistance to CSF outflow is increased, leading to reduced venous outflow volumes (Wang et al., 2020). The pathogenesis of iNPH is still not fully understood but may involve genetic factors, glymphatic system dysfunction, and aquaporins. Analogous to high-pressure hydrocephalus, where pressure effects on fibers adjacent to the ventricular wall are observed, it is speculated that similar disruptions might occur in iNPH (Tudor et al., 2015).

The symptoms of iNPH overlap with those of other neurological conditions, such as Parkinson's and Alzheimer's diseases, complicating diagnosis (Czerwosz et al., 2009). Accurate diagnosis is crucial, as patients with symptoms attributable to other conditions may not benefit from shunt surgery. iNPH remains a significant cause of reversible dementia, affecting about 6% of individuals aged 80 and older (Allali et al., 2017). This thesis will focus on characterizing the gait abnormalities in iNPH patients.

Gait Disturbances in iNPH

Gait disturbances are often the first and most prominent symptom of iNPH, affecting 94-100% of patients (Isaacs et al., 2019). Common gait features include slow, shuffling steps, a wide base of support, and difficulties in initiating or turning gait. These disturbances are indicative of higher-level gait disorders involving sensorimotor processing challenges. Postural instability, characterized by difficulty maintaining an upright posture and increased fall risk, is a significant concern (Nikaido et al., 2018). The gait pattern may also include a prolonged period of ‘double support,’ known as ‘magnetic gait,’ where patients struggle to lift their feet

(Czerwosz et al., 2009). Despite detailed descriptions of basic gait, there is limited information on joint ranges of motion, kinematics, and ground reaction forces.

iNPH Diagnosis

In diagnosis, to differentiate iNPH from conditions like Alzheimer's disease (AD) can be extremely difficult, when the cognitive function of patients is disrupted. In iNPH patients cognitive damage can be seen by dysfunctionality of the frontal lobe. When iNPH advances, short term memory is disrupted which is very similar in Alzheimer's. The key similarity between iNPH and vascular and neurodegenerative parkinsonism, is the small steps and shuffling gait motion. One way that could be useful in diagnosis is analysing the efficacy of anti-parkinsonian drugs which is routinely done, and if there is no response to the drugs, iNPH is more likely.

To make an iNPH diagnosis, patients must be aged 60 or above, they must display a minimum of one neurologic characteristic from the iNPH triad which includes disruptions in gait, cognitive and urinary dysfunction. The entire triad is observed in 50% to 75% of patients, while gait and cognitive impairments manifest in 80% to 95% of cases, and urinary incontinence is experienced by 50% to 75% of individuals (Tudor et al., 2015). The most prevalent symptom involves a decline in cognitive function which occasionally results in dementia, as well as urinary incontinence. Patients must also display pathologically increased ventricular size shown via a cranial computed tomography (CT) or a magnetic resonance imaging (MRI) (Isaacs et al., 2019).

Shunt surgery to alleviate symptoms of iNPH

As the CSF cannot be absorbed due to the pathologically heightened resistance to the outflow of CSF, the objective of the shunt is to redirect CSF from the craniospinal CSF space to an alternative anatomic space. In this space, the CSF can undergo reabsorption. A VP (ventriculoperitoneal) shunt is most commonly used for this procedure, which comprises three components: a proximal catheter typically inserted in the right lateral ventricle, a distal catheter and a shunt valve situated between the proximal and distal catheters. Within the valve is a system that activates when the pressure difference across it surpasses the threshold necessary for the valve to open. Once opened, CSF can flow through. A lumboperitoneal shunt

can also be used, wherein the proximal catheter is positioned within the lumbar CSF space (Williams and Malm, 2016).

The primary advantage and objective of shunt insertion is to alleviate the primary symptoms of iNPH such as disrupted gait. The benefit of valves that are adjustable is that the pressure can be reduced or increased as and when needed. Many serious complications that are faced with shunt insertion have been resolved by adjusting the valves- the primary aim of adjustable valves is to avoid 'over drainage' caused from mild symptoms such as headaches to severe complications such as subdural haemorrhage. This could also result in a reduced risk of bleeding for patients on anticoagulation (Williams and Malm, 2016).

All iNPH symptoms can improve with shunt-insertion, while the cognitive impairment has shown least improvement. Physicians commonly attribute deteriorating symptoms post-surgery to shunt obstruction, which is not always the case. There are various factors which could be responsible for the deteriorating symptoms in patients such as the onset of new diseases or deterioration of current comorbidities. Certain patients may see an improvement in only a subset of symptoms, with other patients may see delayed improvement. The persistence of specific symptoms may not be a result of iNPH or the surgery, further underlying disorders may be responsible. If urinary incontinence remains unchanged post-surgery, it is worth referring to a urologist to investigate (Williams and Malm, 2016). Post shunt-surgery protocol includes neurological assessment such as cognitive screening, gait., and neurologic assessment, thus it is important to consider appropriate techniques for evaluating patient gait.

Use of 3D Gait Analysis in iNPH

One potential way of aiding clinicians with their diagnostic procedure is 3D gait analysis. 3-dimensional gait analysis is a highly sophisticated laboratory technique providing objective quantitative measures of mobility combining the absence of operator dependence and high resolution enabling the demonstration of minute numeric change. Three-dimensional gait analysis offers a non-intrusive approach to precisely capture movement patterns. It involves affixing reflective markers to the body and tracking their three-dimensional positions with infrared cameras while in motion.

The markers' three-dimensional positions are utilized to generate a precise computerized model of the movement (running/walking etc). This personalizes model accurately computes joint angles across all three planes of human motion. For instance, it assesses the knee's extension and flexion, rotation, and lateral movement while running or walking. The variables that are commonly reported are joint angles such as the hip, knee, ankle angles in sagittal, frontal and transverse planes. As well as this, a range of motion of joints, angular velocities and segmental orientations and positions are reported. Key kinetic variables that were reported include, ground reaction forces, and joint movements. Temporal-spatial parameters such as step length and width, stride length, cadence and walking speed are the variables reported.

Few studies have used advanced gait analysis techniques for identification and monitoring of people with iNPH, (cf Dias et al., 2023) - of those that have, none has reported sophisticated (i.e.,: there is not the utilization of advanced, intricate techniques and technology to comprehensively assess gait), full gait analyses which include joint kinetics and kinematics, instead only reporting simple outcome measures that could be obtained through more rudimentary techniques. Therefore, there is a clear unmet need for a more sensitive gait analysis method to identify changes in mobility in people with iNPH in response to TT and on follow up after shunting.

Versatility of 3D gait analysis

3D gait analysis provides detailed insights into biomechanics, helps diagnose gait abnormalities (not limited to iNPH), guides rehabilitation programs, and aids in optimizing athletic performance (Baker, 2013). Its success lies in its ability to offer precise and detailed information about an individual's movement patterns, allowing for tailored interventions and improved understanding of biomechanical issues (Di Biase et al., 2020)

The versatility of 3D gait has made it valuable in various age groups/populations; old adults, young adults. For older adults, it's been instrumental in assessing age-related changes in gait patterns (Menant et al., 2009), identifying potential fall risks (Verghese et al., 2009) and understanding mobility limitations (Cromwell & Newton, 2004). This analysis helps in designing targeted interventions and rehabilitation strategies to improve balance, mobility, and overall quality of life in the elderly. For example, Di Biase et al. (2020) discusses the utility

of gait analysis in understanding gait abnormalities in Parkinson's disease, and its potential for monitoring progression.

In younger adults, especially athletes, 3D gait analysis has aided in optimizing performance, detecting and preventing injuries, and refining techniques in sports and physical activities. It allows for a detailed examination of movement patterns, helping coaches and athletes understand and improve biomechanics to enhance athletic performance while minimizing the risk of injuries. For example, Ma et al. (2021) used 3D gait analysis to assess outcomes in children with cerebral palsy.

Research utilizing 3D motion capture in older adults has revealed valuable insight into gait outcome measures. Studies have highlighted improvements in assessing joint angles, spatiotemporal parameters, and gait variability, offering a more comprehensive understanding of age-related changes in gait patterns and aiding in targeted interventions for older individuals.

iNPH Gait Assessment in the Context of Diagnosis

The initial assessment for iNPH involves a thorough clinical evaluation, including detailed patient history, physical examination, and imaging analysis. This process not only diagnoses iNPH but also rules out other potential differential diagnoses (Isaacs et al., 2019). Clinicians assess patients' ability to perform functional tasks such as a 10-meter walk and evaluate gait using both visual and objective metrics, though there is no consensus on a single best scale for this purpose (Andersson et al., 2017). The diagnostic criteria are currently based on clinical symptoms, but the specific tests and thresholds required for diagnosis are not yet well-defined.

Mori et al. (2012) proposed a diagnostic classification system with tiers: possible, probable, and definite, accompanied by treatment recommendations. Research by Andersson et al. (2017) indicated that using the American-European Guidelines (AEG) resulted in a diagnosis of 'probable' iNPH being more likely compared to the Japanese Guidelines (JG). The AEG's lower specificity could lead to misclassification, as it may include patients with similar conditions like Parkinsonism or Alzheimer's. Gait dysfunction is central to iNPH diagnosis. The Tap Test (TT) is commonly used to assess responsiveness to CSF withdrawal. Despite its

frequent use, there are no established guidelines for specific gait variables to be analyzed (Agostini et al., 2015).

Parkinsonian disorders, including Parkinson's Disease (PD), are marked by bradykinesia, rest tremor, and rigidity. PD is prevalent among the elderly, often co-occurring with conditions like iNPH. Approximately 70% of iNPH cases exhibit features of parkinsonism, making it a potentially important diagnostic marker (Brooks, 2002).Both iNPH and PD feature hypokinetic gait disorders, but distinguishing between them can be challenging, especially in early parkinsonism cases. Instrumented tests like the Timed Up and Go (iTUG) test, which uses inertial sensors, help assess mobility in these patients (Mostile et al., 2023). PD patients typically show a tandem gait and limited step width, unlike those with iNPH or atypical Parkinsonism.

Mostile et al. (2023) found differences in mobility between iNPH and PD patients, with iNPH patients showing reduced gait velocity and stride length. Variations in biomechanical factors, cognitive and sensorimotor strategies, and dynamic control may explain these differences. Nikaido et al. (2018) found greater postural instability in iNPH patients compared to PD patients when leaning, which could aid in differentiating between the two conditions.The diagnostic challenge of iNPH stems from its non-specific symptoms, making it difficult to distinguish from other gait disorders, vascular dementia, or generalized Parkinsonism (Allali et al., 2013).

Research using 3D motion capture has therefore improved our understanding of gait parameters in older adults, highlighting its utility in both assessing and intervening in gait abnormalities.

2. AIMS, OBJECTIVES AND HYPOTHESIS

Aims and Objectives

This overall project aims to develop a laboratory-based approach to quantify gait characteristics and balance impairment in people with iNPH in comparison to normal ageing. These detailed characterizations of gait impairment in people with iNPH to aid diagnosis and provide a platform for future work to objectively assess the effectiveness of treatment interventions using gait analysis variables as the main outcome measure. **Therefore, the purpose of this thesis, the aim herein was to provide detailed characterisation of gait in patients with iNPH as compared to healthy, age-matched controls.** The primary objective was to identify key gait and balance variables that can objectively characterize the phenotype in iNPH and that will also later serve as measures to accurately quantify changes before and after cerebrospinal fluid (CSF) tap test (TT) in subsequent work.

Hypotheses

It was hypothesised that those with iNPH would exhibit decreased gait velocity (slower walking), increased step width variability, unsteadiness (increased centre of mass trajectories), and reduced joint ranges of motion, as well as poorer balance test scores, when compared to age-matched controls.

3. METHODS

Participants, Inclusion/Exclusion Criteria, and Informed Consent

40 participants were included in the study, 20 patients and 20 healthy control males and females matched for age and gender. Patients who were diagnosed with idiopathic normal-pressure hydrocephalus (iNPH) or suspected of having iNPH from October 2022 to July 2023 were included in the study from Salford Royal Hospital. Patients that fulfilled the criteria to be part of the study were selected and invited to the gait laboratory at Manchester Metropolitan University for pre- and post- cerebrospinal fluid (CSF) tap test assessment. Inclusion criteria were (i) patients diagnosed with iNPH according to the international guidelines for diagnosing iNPH (Relkin 2005), (ii) capable of walking independently for a minimum of 20 consecutive steps (use of walking aids was allowed to align with the real-life experiences of many individuals with this condition), (iii) patients diagnosed or receiving treatment at Salford Royal Hospital. Exclusion criteria were (i) Other confirmed medical or surgical condition better explaining patients' symptoms or co-existing conditions with significant impact (eg Parkinson's, osteoarthritis), (ii) Secondary or obstructive hydrocephalus; previous surgical procedures for hydrocephalus, (iii) Amputation of lower limb/appendages, (iv) Musculoskeletal injury/recent lower-limb surgeries affecting gait or other musculoskeletal ailments affecting gait and balance performance, (v) Patients on specific medications (eg centrally acting) better explaining or with significant impact on patients' symptoms, (vi) Unable to speak and comprehend written and/or verbal English#, (vii) Unwilling or unable to comprehend informed consent.

Healthy controls were recruited in two ways. Spouses/carers of people with iNPH and people from the general public who responded to the study advertisement and who met the inclusion criteria were recruited. The inclusion criteria for the controls were (i) consenting males and females, matched for age and sex to the iNPH group, (ii) able to walk unaided for at least 20 steps at a time (walking aids permitted). The exclusion criteria were (i) Other medical or surgical conditions with potential impact on gait or balance (ii) Amputation of lower limb/appendages (iii) Musculoskeletal injury/recent lower-limb surgeries [including lower limb joint replacement surgery within ~9 months] affecting gait or other musculoskeletal ailments affecting gait and balance performance (iv) Medications (eg centrally acting) with potential impact on mobility and balance (v) Unable to speak and comprehend written and/or verbal English (vi) Unwilling or unable to comprehend informed consent.

Eligible people with iNPH were explained the study and provided with a study participant information sheet by the consultant or nurse as part of the research team. Healthy controls were sent an electronic version of the participant information sheet upon first contact. All participants had at least 24h to decide whether they wished to participate and were given the opportunity to visit the gait laboratory before their first assessment if they felt necessary. Written informed consent was obtained by a member of the study team prior to the (first) gait analysis assessment.

Project protocol

Patient evaluations prior to gait assessment:

Note: The following was performed by the clinicians at Salford Royal Hospital as part of patient routine health care. Two to three patients per week with a clinical diagnosis of probable NPH according to the European-American guidelines were admitted electively for lumbar puncture, with pre, 1h post and 24h post mobility assessments carried out by a neurophysiotherapist (Tinetti, Timed up and go, 6min walk, timed Romberg test, timed single leg stance and video-recorded 10m walks and 360 degree left and right turns). During the tap test, opening pressure was recorded, between 30-50mls of CSF were drained, CSF was analysed for routine microbiology and biochemistry as well as neurodegeneration biomarkers. All patients were tested with the Addenbrooke's cognitive examination and a senior neuropsychologist with expertise in differential diagnostic assessments administers a detailed standardized neuropsychological profile, including an estimate of premorbid intellectual function, orientation, numerical reasoning, verbal and visual memory, visuospatial function, attention, language, numerical skills, and executive function. Additional standardized psychometrics were available to improve diagnostic clarity where necessary. A consensus diagnosis was reached, and a decision is made whether to offer ventriculo-peritoneal (VP) shunting. (Patients who are offered VP shunt surgery are followed up by the MDT, including repeat neurophysiotherapy and neuropsychology assessments at 3 months and 12 months after surgery (or at 3 months and 12 months after tap test if they opted against surgery.)

Figure 1 - Sagittal (left) and frontal (right) views of a patient with model and force vector overlay

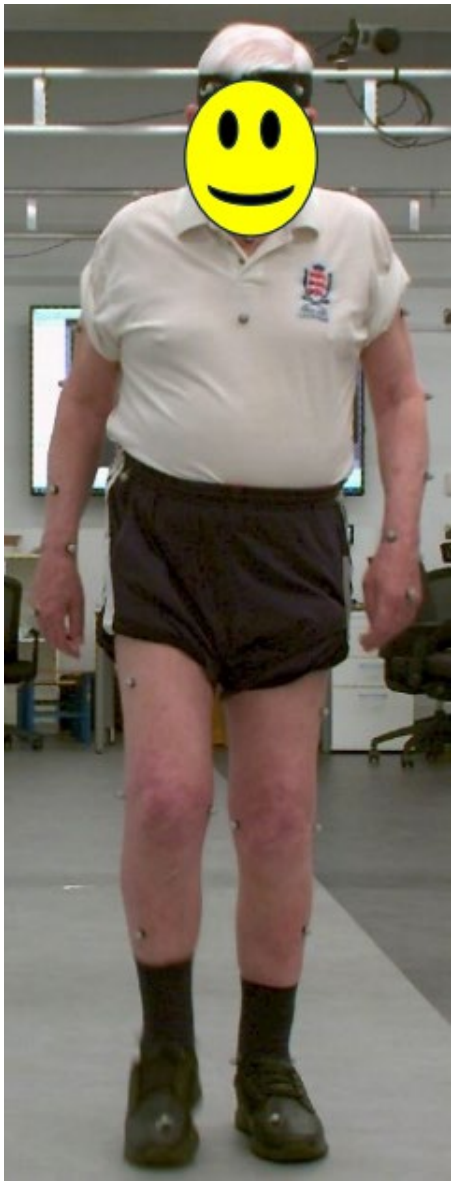

Figure 2- Close up of Gait marker set

Psychological factors were also monitored in patients (part of the clinical routine) and controls using the Hospital Anxiety and Depression Scale (when they attend the gait laboratory). Quality of life was assessed with the EQ-5D-5L patient version (patients -part of the clinical routine- and controls when they attend the gait laboratory) and EQ-5D-5L proxy versions (patients only, part of the clinical routine) and carer burden was assessed with the Burden Scale for Family Caregivers (patients only, part of the clinical routine). These secondary assessments provide insight into clinically-relevant outcomes of everyday activity in the period immediately following tap-test and may be relevant for the participants' performance. We also evaluated participants' experience and expectations of their gait and balance performance pre and post tap test when measured clinically and with gait analysis, assessing for concordance and participants' reaction to the results using a questionnaire. Patients were

followed closely after the TT as part of clinical routine to discuss the results and plan further management.

Gait Lab Assessments

We used a 13-camera 3-dimensional motion analysis system (Qualisys Track Manager v2023.2, Qualisys AB, Sweden) to accurately track the movement of markers positioned on specific anatomical landmarks using the full body Plug-in-Gait model of each participant's body during each task as can be observed in figures 1 and 2. (10 meter walk, TUG test, 360 turn, quiet stance, single leg stance, and tandem stance). Kistler Force plates (Kistler (Type 9281B), Winterthur, Switzerland) embedded in a bespoke floor-mounted walkway recorded ground reaction forces under the feet as the participant walks across them (100 Hz). We examined gait with a range of support conditions (e.g. with natural use of preferred walking aid if required; with assistance from partner/carer/researcher; with use of a standardised minimal walking aid such as a cane/stick; and without any assistance if possible) to allow appropriate comparison against controls and pre-post treatment. Static balance was examined through quiet stance- the participant stood on the force plates for 60 seconds, in order for the centre of pressure, centre of mass trajectories, and dynamic balance to be examined. Continuous data sets were generated and used to quantify different aspects of gait and balance function.

Patients who participated in the study attended the gait lab, pre and post their cerebrospinal fluid tap test whereas healthy control participants only attended the gait lab once. Tasks conducted in the lab in order to assess functional gait included a 10m walk at regular walking speed in their own shoes based on the guidelines (Allali et al., 2018), timed up and go test, and a 360 degree turn test. Two trials of each task were performed; in the event where support was used for gait (i.e., a stick or walking frame), participants were asked to perform an additional 1-2 trials without support if possible. Instructions were given to participants to walk how they would typically walk on any given day, at a self-selected pace.

Stride time represents the temporal interval between the initial contact of one foot and the subsequent initial contact of the same foot, typically measured in seconds (s). Stride length denotes the linear distance extending from the heel of one foot to the subsequent heel of the same foot, typically measured in centimetres (cm). Stride width refers to the spatial

separation between two consecutive ipsilateral foot heel contacts (constituting a stride) and the subsequent contralateral foot heel contact, measured perpendicularly to the stride axis, typically expressed in centimetres (cm).

As part of the larger project, while participants were in the lab, balance tests were also conducted to examine static balance which included 'a quiet stance' (60 seconds) and, single leg stance and 'Romberg' test (performed on each leg). These tasks replicate those performed during assessment at the hospital before and after CSF TT. The Romberg test is a neurological assessment used to evaluate a person's proprioception, the participant is stood on the force plate and observations are made as to how they stand with one foot in front of the other, with the heel of the forward foot touching the toes of the rear foot (tandem stance). By doing this, the body's centre of mass shifts forward which requires more precise control of balance as the base of support reduces compared to a regular stance. For the single leg stance and Romberg trials, participants were required to maintain the position as long as possible, up to 30 seconds. Participants always had a researcher alongside them as a precautionary measure to prevent a fall in the event of loss of balance. These data will be presented separately in subsequent work.

Data Processing and Statistical Analysis

While the larger aim of this study included a pre-/post-intervention design (i.e., to understand the effects of the cerebrospinal fluid tap test (CSF TT) intervention on gait and balance measures), the focus on analysis presented within this thesis is of a case control nature, comparing gait measures (i.e., from the 10m walk test only) between patients with iNPH and age-matched healthy controls. The remaining outcome measures during the pre-CSF TT, and all measures from the post-CSF TT intervention arm of this study will be analysed and written up following completion of the thesis.

Data processing

Gait data from the 10m walk test (unassisted gait trials only) were processed offline. Motion capture data were individually reconstructed, digitally labelled and gap-filled in Qualisys Track Manager 2024. Marker trajectories were then exported for data analysis in visual3D biomechanics software (HAS Motion, Canada) via c3d file format. Within visual3D, a cmo was

created for each participant, consisting of a minimum of two trials, with multiple gait cycles within each trial.

Using the pipeline function in Visual3D, joint coordinate (marker) and force data were smoothed using a 4th order Butterworth low-pass digital filter with cut-off frequencies of 6 and 25 Hz, based on a priori residual analysis (Winter., 2009) Where possible, the automatic gait events function was used to determine instances of heel strike and toe-off for each gait cycle (correct identification of events was reliant on clean foot strikes on the force plate). In instances where force input was of poor quality (thus resulting in inaccurate event detection), manual identification of gait events was used. Where possible, lower limb joint moments were calculated using an inverse dynamics approach and were defined as external moments normalised to body mass. Ground reaction forces were also obtained in Visual3D, normalised relative to body weight, with vertical, anterior-posterior, and medial-lateral corresponding to Fz, Fx, and Fy, respectively.

Gait cycles were normalised 0-100% from heel-strike to heel-strike for each side. Metrics were averaged across all gait cycles for each individual and exported to .csv file format. Data were then processed using Microsoft Excel for organisational and statistical analysis purposes.

Statistical Analysis

Descriptive analysis was used to summarize the participant demographics. IBM SPSS Statistics version 26 was used to analyse spatiotemporal parameters (gait speed, cadence, cycle time, stride length and width) and kinematic characteristics (rotations about each axis for ankle, knee, and hip joints) of gait, as compared between groups. Ground reaction forces and joint kinetics could not be analysed due to poor quality foot strikes (read: multiple per force plate because of short step lengths). After considering skewness and kurtosis, conducting Shapiro-Wilk tests of normality and homogeneity of variance using a Levene's test, all data were determined to be normally distributed. Independent samples t-tests were used to determine significant differences between groups (i.e., iNPH vs controls). Accepted level of significance was set at $p< 0.05$.

4. RESULTS

Patient demographics

The study included a total of 24 participants, divided into two groups: 13 patients with suspected idiopathic normal pressure hydrocephalus (iNPH) and 11 age-matched controls. The patient group comprised 4 females and 9 males, while the control group consisted of 9 females and 2 males. The mean age of the patient group was 76.31 years (SD = 5.88), whereas the control group had a mean age of 72.82 years (SD = 5.88). The mean height of patients was 1.62 meters (SD = 0.08), compared to 1.61 meters (SD = 0.10) in controls. The mean mass of the patient group was 76.62 kg (SD = 13.98), while the control group had a mean mass of 73.54 kg (SD = 18.65). Full patient demographics can be found in Table 1. Confidence intervals provide a range of values within which the true population parameter is likely to fall, with a specified level of confidence (95%). These have been included in Table 2 for the temporal data and in Appendix E for the kinematic data, where the X, Y and Z axes represent the flexion/extension, ab/adduction and the internal/external rotation.

Statistical analysis revealed no significant differences between the patient and control groups in terms of age ($t(22) = 1.55$, $p = 0.135$), height ($t(22) = 0.092$, $p = 0.927$), or mass $p = 0.207$). These findings suggest that the two groups were well-matched on these demographic variables, thereby reducing potential confounding effects related to these factors in subsequent gait analysis. As the age and height were normally distributed, an independent samples t-test was used for statistical analysis. As mass was not normally distributed, a Mann-Whitney U test was used. The mass of control and patient groups was compared. Patients (Mdn = 76.62) had a higher mass than the control group (Mdn = 73.54); however, a Mann-Whitney U test indicated that this difference was not statistically significant, U (nControl = 24, nPatient = 24) = 49, p = .207.

Table 1: Patient demographic data showing the means and SD of the ages, heights and mass of participants.

Variable	Group	Mean	SD	t/U	df/N	p	Test
Age	Control	72.82	4.99	1.55	22	.135	T Test
	Patient	76.31	5.88				
Height	Control	1.61	0.10	0.092	22	.927	T Test
	Patient	1.62	0.08				
Mass	Control	73.54	18.65	49	24	.207	Mann-Whitney U Test
	Patient	76.62	13.98				

An independent samples t-test was conducted to compare the mean cycle time between patients (M = 1.34, SD = 0.26) and controls (M = 1.07, SD = 0.09). As can be seen in table 1 There was a significant difference in cycle time between the two groups, t(22) = 3.314, p = 0.002, with patients displaying a 25.2% longer cycle time compared to controls.

The mean speed for patients (M = 0.34, SD = 0.33) was significantly lower compared to controls (M = 1.24, SD = 0.19), t(22) = -8.330, p < 0.001, with a 62.9% decrease in speed amongst patients compared to controls. These results (table 1) indicate impaired mobility and slower progression during gait in patients. Patients (M = 0.46m, SD = 0.28) exhibited significantly shorter stride lengths compared to controls (M = 1.32m, SD = 0.17), t(22) = -8.769, p < 0.001, reflecting a 65.2% reduction in stride length in patients compared to controls. There was a reduced stride frequency and overall ambulation in patients (M = 40.03, SD = 14.79) as patients had significantly lower mean strides per minute compared to controls (M = 56.42, SD = 5.06), t(22) = -3.497, p = 0.001 with an overall reduction of 29.1% in strides per minute among patients. Patients demonstrated a significantly wider mean stride width (M = 0.46, SD = 0.49) compared to controls (M = 0.11, SD = 0.03), indicative of altered lower limb kinematics in patients and representing a 318.2% increase in stride width among patients.

Table 2: Temporal data showing a comparison of Gait Parameters between patients with suspected Idiopathic Normal Pressure Hydrocephalus (iNPH) and controls

Parameter	Patient (Mean ± SD)	Control (Mean ± SD)	P value	95% Confidence interval for mean (patient)		95% confidence interval for mean (control)	
Cycle Time (s)	1.34 ± 0.26	1.07 ± 0.09	0.002	Lower Bound	1.1893	Lower Bound	1.0127
				Upper Bound	1.4984	Upper Bound	1.1355
Speed (m/s)	0.34 ± 0.33	1.24 ± 0.19	<0.001	Lower Bound	0.3102	Lower Bound	1.1129
				Upper Bound	0.6185	Upper Bound	1.3652
Stride Length (m)	0.46 ± 0.28	1.32 ± 0.17	<0.001	Lower Bound	0.2931	Lower Bound	1.2078
				Upper Bound	0.6367	Upper Bound	1.4300
Stride Width (m)	0.46 ± 0.49	0.11 ± 0.03	0.013	Lower Bound	0.1683	Lower Bound	0.0888
				Upper Bound	0.7568	Upper Bound	0.1276
Strides Per Minute	40.03 ± 14.79	56.42 ± 5.06	0.001	Lower Bound	31.0926	Lower Bound	53.0206
				Upper Bound	48.9635	Upper Bound	59.8206

The mean speed for patients (M = 0.34, SD = 0.33) was significantly lower compared to controls (M = 1.24, SD = 0.19), t(22) = -8.330, p < 0.001, with a 62.9% decrease in speed amongst patients compared to controls. These results (table 1) indicate impaired mobility and slower progression during gait in patients.-.Patients (M = 0.46m, SD = 0.28) exhibited significantly shorter stride lengths compared to controls (M = 1.32m, SD = 0.17), t(22) = -8.769, p < 0.001, reflecting a 65.2% reduction in stride length in patients compared to controls. There was a reduced stride frequency and overall ambulation in patients (M = 40.03, SD = 14.79) as patients had significantly lower mean strides per minute compared to controls (M = 56.42, SD = 5.06), t(22) = -3.497, p = 0.001 with an overall reduction of 29.1% in strides per minute among patients. Patients demonstrated a significantly wider mean stride width (M = 0.46, SD = 0.49) compared to controls (M = 0.11, SD = 0.03), indicative of altered lower limb kinematics in patients and representing a 318.2% increase in stride width among patients.

Some of the mean values that were compared between the patients and controls differed significantly. For example, the Ankle range of motion (ROM) during stance was significantly different between patients and controls, t(22) = -6.654, p < 0.001. Patients had a mean of 14.38° (SD= 5.17), whereas the controls had a mean of 27.97° (SD= 4.76). The peak ankle flexion angle during the stance phase was also significantly lower in patients, with a mean of 12.65° (SD = 3.87) compared to controls with a mean of 25.32° (SD = 4.12).

During the stance phase, the ankle joint undergoes intricate abduction/adduction movements to maintain postural stability and facilitate efficient weight-bearing locomotion. Patients exhibited a mean ankle ROM of 6.14 degrees (SD = 6.14) in the abduction/adduction movement during the stance phase. In contrast, controls demonstrated a significantly higher mean ankle ROM of 16.08° (SD = 6.03, p = 0.88). This represents a 61.8% decrease in ankle ROM in patients compared to controls as patients demonstrated restricted abduction/adduction movement compared to controls. The peak ankle abduction angle was significantly lower in patients (mean = 4.56°, SD = 1.97) compared to controls (mean = 10.84°, SD = 2.34).

Table 3: Kinematics data of patients and controls. This table presents the kinematics data comparing joint movements between patients suspected of having iNPH and a healthy control group. The data includes maximum angle, minimum angle, and range of motion (ROM) during both stance and swing phases of gait for ankle, knee and hip joints. Joint movements are categorized into flexion/extension, abduction/adduction, and internal/external rotation. P values are provided for each comparison to indicate statistical significance.

Joint	Movement	Group	max angle stance (deg)	*p* value	min angle stance (deg)	*p* value	ROM stance (deg)	*p* value	max angle swing (deg)	*p* value	min angle swing (deg)	*p* value	ROM swing (deg)	*p* value
ankle	flexion/extension	patient	8.06 (3.07)	0.003	-6.32 (4.07)	0.003	14.38 (5.17)	0.002	1.13 (3.27)	0.002	-6.01 (4.49)	0.004	7.14 (3.48)	<0.001
		control	12.95 (4.21)		-15.03 (8.12)		27.97 (4.76)		2.55 (5.67)		-14.24 (7.76)		16.79 (4.61)	
	ab/adduction	patient	3.62 (3.26)	0.001	-2.52 (2.02)	0.17	6.14 (3.19)	<0.001	4.53 (2.95)	0.013	-0.19 (2.61)	0.158	4.72 (2.05)	<0.001
		control	11.55 (6.17)		-4.52 (4.54)		16.08 (6.03)		9.64 (6.00)		-2.53 (5.07)		12.18 (4.19)	
	internal/external rotation	patient	2.59 (2.75)	0.35	-0.46 (1.52)	0.43	3.05 (1.48)	0.09	2.69 (3.07)	0.0345	0.42 (1.90)	0.45	2.27 (1.37)	0.08
		control	10.95 (26.37)		4.01 (19.96)		6.93 (6.74)		8.81 (22.72)		4.67 (19.91)		4.14 (3.37)	
knee	flexion/extension	patient	36.29 (11.48)	<0.001	12.68 (6.58)	0.002	23.61 (10.95)	<0.001	52.71 (10.20)	0.002	13.81 (5.89)	<0.001	38.90 (12.76)	<0.001
		control	55.49 (5.76)		4.85 (3.89)		50.64 (5.66)		63.69 (2.37)		1.38 (4.00)		62.31 (4.52)	
	ab/adduction	patient	1.04 (1.66)	0.088	-0.38 (1.49)	0.45	1.42 (0.89)	0.012	1.48 (2.11)	0.119	-0.34 (1.37)	0.353	1.83 (1.45)	0.003
		control	2.51 (2.36)		-1.37 (4.33)		3.87 (3.09)		3.15 (2.91)		-1.30 (3.29)		4.44 (2.35)	

	internal/external rotation	patient	-1.18 (3.49)	0.932	-2.83 (3.80)	0.107	1.66 (0.58)	0.001	-1.20 (3.55)	0.705	3.33 (3.90)	0.265	2.13 (0.91)	0.031
		control	-1.29 (2.78)		-5.16 (2.81)		3.87 (1.98)		`-1.71(2.74)		-4.95 (2.80)		3.24 (1.43)	
hip	flexion/extension	patient	36.43 (12.21)	0.009	13.79 (17.01)	0.009	22.64 (9.04)	<0.001	38.80 (12.19)	0.594	21.42 (15.48)	0.453	17.38 (6.93)	0.012
		control	39.13 (7.87)		-1.97 (6.53)		41.10 (5.38)		41.02 (6.52)		17.46 (8.03)		23.56 (3.04)	
	ab/adduction	patient	4.88 (2.21)	<0.001	1.38 (2.48)	0.053	3.50 (1.47)	<0.001	2.52 (2.28)	0.006	0.12 (2.84)	0.409	2.40 (1.34)	<0.001
		control	9.98 (1.41)		-0.51 (1.96)		10.48 (2.17)		5.14 (1.83)		-0.75 (2.09)		5.88 (1.44)	
	internal/external rotation	patient	1.92 (5.51)	0.025	-0.44 (5.31)	0.624	2.36 (1.34)	0.001	2.09 (5.16)	0.05	-0.16 (4.69)	0.578	2.25 (1.33)	0.002
		control	7.04 (4.78)		0.78 (6.68)		6.26 (3.23)		6.02 (3.88)		0.98 (5.22)		5.04 (2.39)	

Another significant kinematic difference between the patient group and controls was observed in ankle range of motion (ROM) during the swing phase in the abduction/adduction movement. Patients exhibited a mean ankle ROM of 4.72° (SD = 2.05) in abduction/adduction movement during the swing phase. In contrast, controls demonstrated a substantially higher mean ankle ROM of 12.17° (SD = 4.19), this indicates a 61.3% decrease in ankle ROM in patients compared to controls. These findings suggest a potential trend towards reduced abduction/adduction mobility during the swing phase among patients. The peak ankle adduction angle during the swing phase was also significantly reduced in patients (mean = 3.21°, SD = 1.42) compared to controls (mean = 8.43°, SD = 2.76).

For complete kinematic results, please refer to Table 3 and Figure 3.

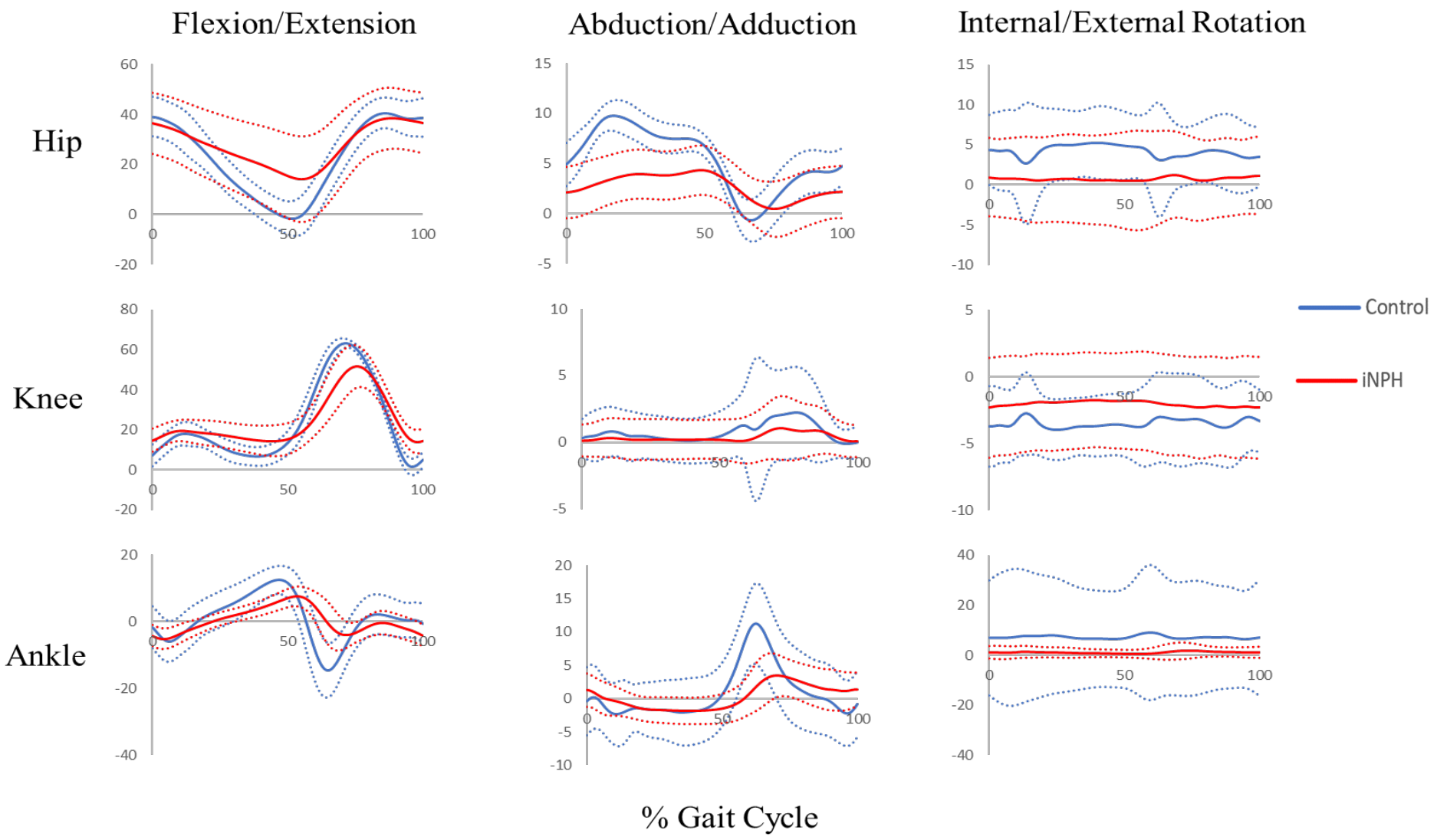

Figure 3: Hip, knee, and ankle kinematics in patients (red) and age-matched controls (blue) across the gait cycle

5. DISCUSSION

Gait disturbances are a hallmark of idiopathic normal pressure hydrocephalus (iNPH), characterized by significant impairments in both temporal and kinematic gait parameters. This study aimed to comprehensively characterise these gait abnormalities in iNPH patients compared to healthy controls, with a particular focus on temporal metrics such as stride frequency, stride length and width as well as the kinematics which includes the joint movements such as the flexion/extension, the ab/adduction and the internal/external rotation of the knee, hip, and ankle. The findings revealed profound differences in key gait metrics, providing crucial insights into the underlying neuromuscular and biomechanical deficits associated with iNPH. These results strongly support our hypothesis that iNPH patients exhibit decreased gait velocity, increased step width variability, unsteadiness, reduced joint ranges of motion, and poorer balance test scores compared to age-matched controls.

Although there are several studies that discuss the quantitative assessment of gait disturbances in iNPH, the techniques require special equipment such as accelerometers, footswitches, knee goniometers, and motion capture systems (Liao et al., 2022), which are unlikely to be available for routine clinical use (Liao et al., 2022). The results from this study will allow for earlier and more accurate diagnosis of iNPH and provide a platform for the use of gait analysis as an outcome measure in assessing the effectiveness of clinical treatments.
This study has shown to be pioneering work in delivering a comprehensive and intricate delineation of gait abnormalities in individuals afflicted with iNPH as opposed to healthy counterparts through the utilization of 3D gait analysis. While not reported in this thesis, this will also be the first work to include 3D gait analysis for discerning and quantifying the alterations in gait induced by TT in comparison to conventional clinical evaluations; and investigating thresholds to distinguish between responders and non-responders to TT in contrast to traditional clinical assessment techniques, aiming to furnish an objective and dependable primary outcome measure for forthcoming randomized controlled clinical trials and to enhance the standard clinical care of patients. Consequently, the findings included within this thesis, and -- more broadly -- of this larger study will guide future clinical care

protocols and spur further investigations towards advancing the diagnosis and treatment modalities for individuals with iNPH.

The similarity between specific gait parameters in 2D and 3D assessments highlights the practicality of using simpler videographic methods in clinical practice. For clinicians, this means that while 3D analysis can provide highly detailed information, 2D gait assessment remains a viable tool for monitoring gait in iNPH, enabling effective diagnosis and treatment response evaluation with accessible technology

Temporospatial characteristics highlight impaired gait

The findings of this study shed light on the temporal gait characteristics of suspected idiopathic normal pressure hydrocephalus (iNPH) patients compared to controls. These observations underscore significant impairments in mobility and ambulation among patients with suspected iNPH.

Stride Length, Width, and Cadence, and Velocity

The temporal analysis of gait parameters in suspected idiopathic normal pressure hydrocephalus (iNPH) patients revealed significant differences compared to healthy controls, with the most pronounced disparity observed in the number of strides per minute. Specifically, iNPH patients exhibited a mean stride frequency significantly lower than that observed in the control group. This substantial reduction in stride frequency, approximately 29.1%, underscores the profound impact of iNPH on gait dynamics and overall mobility. Stride frequency, a critical component of gait, reflects the number of strides taken per minute and is directly related to walking speed and efficiency. In iNPH patients, the significant reduction in stride frequency suggests a compromised ability to maintain a rhythmic and continuous walking pattern. This finding is consistent with the hallmark gait disturbances seen in iNPH, often described as a "magnetic" or shuffling gait, characterized by short steps and reduced gait velocity (Stolze et al., 2001; Williams et al., 2008).

The reduction in stride frequency observed in this study aligns with existing literature on gait abnormalities in iNPH. Stolze et al. (2000) and Williams et al. (2008) both reported similar findings, indicating that iNPH patients consistently exhibit lower stride frequencies compared

to healthy individuals. These studies also highlight that stride frequency, along with other temporal gait parameters, significantly improves following successful CSF shunting, further emphasizing its importance in the clinical management of iNPH.

In this study, patients exhibited a significantly wider mean stride width compared to controls, representing a substantial 318.2% increase in stride width among patients. This alteration in lower limb kinematics in patients suggests potential compensatory mechanisms or altered gait patterns associated with suspected iNPH. Studies investigating gait abnormalities in iNPH have consistently highlighted alterations in lower limb kinematics, including changes in stride width, as characteristic features of the condition (Krauss et al., 1996). This alteration in gait parameters suggests potential compensatory mechanisms or altered gait patterns in iNPH patients, which may arise as a consequence of underlying neurodegenerative processes affecting the motor control pathways.

Our findings indicate that iNPH patients exhibit significantly slower gait speeds than controls which supports the hypothesis that iNPH patients will exhibit decreased velocity Similarly, stride length in patients was considerably shorter than that of controls, reflecting a 65.2% decrease. These results align with existing literature, which consistently reports slower and shorter strides in iNPH patients, indicating compromised mobility. For example, Stolze et al. (2001) found that iNPH patients had a markedly reduced gait speed and shorter stride lengths compared to healthy controls. Their study reported that iNPH patients walked with a gait velocity significantly lower than that of the control group, which is consistent with our findings. This slower gait speed is attributed to the difficulty iNPH patients face in generating adequate forward propulsion during walking.

Another study by Williams et al. (2008) highlighted similar gait disturbances in iNPH patients, noting that reduced stride length and walking speed are characteristic features of the condition. They observed that these patients often exhibit a shuffling gait, with significantly shorter steps and reduced velocity, mirroring the reductions observed in our study. A study by Krauss et al. (1996) reinforced these observations, demonstrating that iNPH patients consistently show decreased gait velocity and shorter stride lengths. These gait abnormalities were linked to deficits in motor control and coordination, which are hallmarks of iNPH.

Similar gait abnormalities have been observed in other neurological conditions, such as Parkinson's disease (PD) and progressive supranuclear palsy (PSP). In Parkinson's disease, patients often exhibit a reduction in stride length and frequency, leading to a characteristic shuffling gait. This gait pattern is primarily due to bradykinesia and rigidity, which hinder the smooth initiation and execution of movements (Hausdorff, 2009; Morris et al., 2001).

In progressive supranuclear palsy, gait disturbances are also prominent, with patients showing decreased stride length, reduced walking speed, and frequent freezing of gait episodes. These gait abnormalities in PSP are attributed to the degeneration of neural pathways that control motor functions, leading to significant impairments in balance and mobility (Wenning et al., 2005; Steele et al., 1972).

The similarities in gait disturbances across these conditions suggest that the underlying mechanisms may involve common neural pathways responsible for motor control and coordination. Understanding these shared characteristics can help in developing targeted therapeutic interventions that address the specific gait impairments in iNPH, PD, and PSP. Furthermore, these insights highlight the importance of comprehensive gait analysis in diagnosing and managing these neurological conditions effectively.

Overall, the findings in the current study are consistent with those found in the literature, showing that iNPH patients exhibit slower gait speeds and shorter stride lengths compared to controls. This consistent pattern of gait impairment across multiple studies underscores the significant impact of iNPH on mobility and highlights the importance of early detection and intervention.

Joint kinematics reveal reduced ranges of motion at the ankle, knee, and hip

A common feature observed from the results is that iNPH patients exhibit notable impairments in ankle and hip kinematics, particularly in the ankle range of motion (ROM) during ab/adduction in both the swing and stance phases, as well as in hip flexion/extension movements. These findings are critical as they suggest that these joints are key areas affected by iNPH pathology, warranting further investigation and targeted intervention.

Hip Kinematics

One of the pivotal components of gait, the stance phase, requires coordinated hip flexion/extension actions to maintain stability and propel forward movement. Our findings revealed significant kinematic differences in hip joint movements between the patient group and controls during this phase. Specifically, the mean minimum hip flexion/extension angle during the stance phase. This marked difference ($p < 0.001$) reflects a 614.8% increase in hip flexion/extension angle among patients compared to controls, highlighting the pronounced deviation in hip movements characteristic of iNPH patients. Walking with less hip extension, as observed in iNPH patients, can have several biomechanical and functional consequences. Reduced hip extension during gait can affect overall walking efficiency and stability.

Reduced hip extension limits the ability to generate adequate forward propulsion during the stance phase of gait. This limitation can result in a shorter stride length and slower walking speed, as the legs cannot move as effectively behind the body to push off and propel forward. Studies have shown that decreased hip extension is associated with compromised gait velocity and stride length, common characteristics in iNPH patients (Stolze et al., 2001; Williams et al., 2008).Wider literature further supports our results that hip kinematics are significantly affected in iNPH patients. Studies by Nikaido et al. (2011) show that these patients often exhibit increased hip flexion during the stance phase as a compensatory mechanism to maintain balance and forward progression. This increased flexion helps to counteract the instability caused by the reduced motion in the ankle and knee joints. Lewek et al. (2005) discussed the compensatory mechanisms arising from reduced hip extension, such as increased pelvic tilt and lumbar lordosis, which can further compromise gait stability and increase discomfort. They might increase the anterior pelvic tilt or excessive lumbar lordosis to artificially extend the leg behind the body, which can strain the lower back and pelvis (Lewek et al., 2005). These compensatory mechanisms can further destabilize the gait and lead to discomfort or pain.

Reduced hip extension can also impact dynamic stability during walking. The ability to adequately extend the hip is crucial for maintaining a stable center of mass and ensuring smooth transitions from one foot to the other. Insufficient hip extension can result in a

"shuffling" gait pattern, where the feet remain closer to the ground, reducing the overall stability and increasing the risk of falls (Krauss et al., 1996).

Walking with less hip extension can lead to increased energy expenditure due to less efficient movement patterns. This inefficiency can cause fatigue more quickly, reducing the endurance and functional capacity of patients (Malatesta et al., 2003). Increased energy expenditure can also make it challenging for patients to perform daily activities, thereby impacting their quality of life.

In the frontal and transverse planes, significant differences were also observed between patients with iNPH and the control group. For instance, the mean hip abduction/adduction ROM during stance was lower in patients, which aligns with Stolze et al. (2001) who reported that patients with iNPH exhibit reduced ROM in the hip's frontal plane. This reduced ROM reflects impaired lateral stability and control, which are critical for maintaining a stable gait (Stolze et al., 2001). Additionally, internal/external rotation at the hip showed significant alterations, with patients exhibiting reduced rotational movements, impacting their ability to adapt to changes in walking direction and surface irregularities. Research by Stolze et al. (2001) supports our findings as iNPH patients in their study had a narrower range of hip abduction/adduction, which affected lateral stability and contributes to a wider stance and gait base. This adaptation is likely a compensatory strategy to enhance balance.

Ankle Kinematics

Patients demonstrated significantly different ankle joint movements compared to controls. The mean maximum ankle flexion/extension angle during the stance phase was lower in patients than in controls. This reduction aligns with existing studies, which report diminished ankle mobility in iNPH patients, likely contributing to their slower gait speed and shorter stride lengths. For instance, Stolze et al. (2001) found that patients with iNPH exhibit a reduction in ankle dorsiflexion during the stance phase, which is associated with decreased stride length and slower walking speed.

Similarly, the range of motion (ROM) in ankle flexion/extension was significantly reduced in patients compared to controls indicating a compromised ability to generate effective push-

off during gait. This finding is consistent with the work of Williams et al. (2008), who observed that limited ankle ROM in iNPH patients impairs the propulsive phase of gait, leading to reduced gait velocity and a shuffling walking pattern. Reduced ankle mobility limits the foot's ability to dorsiflex during the swing phase and plantarflex during push-off, resulting in shorter, slower steps.

Furthermore, Krauss et al. (1996) reported that the diminished ankle ROM in iNPH patients is a contributing factor to their overall gait abnormalities. This study highlighted that the reduction in ankle movement adversely affects the efficiency of the gait cycle, contributing to the characteristic gait disturbances seen in these patients. The inability to adequately dorsiflex the ankle during the swing phase can lead to a higher risk of trips and falls, while insufficient plantarflexion during push-off reduces forward propulsion, both of which are critical for maintaining a normal walking speed and stride length.

Studies have also shown that iNPH patients often exhibit reduced ankle flexion/extension. For instance, Stolze et al. (2000) found that iNPH patients have significantly decreased ankle joint motion during the stance phase, which contributes to their characteristic slow and shuffling gait. These findings are in line with our results, this reduction in ankle flexion/extension is likely due to muscle weakness and impaired motor control associated with iNPH.

Knee Kinematics

The literature consistently reports reduced knee flexion during the swing phase in iNPH patients. Krauss et al. (1996) observed that iNPH patients often have diminished knee flexion, which affects their ability to lift the foot off the ground and results in a shuffling gait. This impairment is attributed to the central nervous system dysfunction characteristic of iNPH, which affects muscle activation and coordination.

Knee ab/adduction and internal/external rotation have been less frequently studied in iNPH patients. However, existing research indicates that these patients may experience instability and abnormal movement patterns in these planes due to general neuromuscular dysfunction. For example, Bugalho and Guimarães (2014) suggest that the broader gait abnormalities in iNPH, including issues with balance and coordination, likely extend to complex knee

movements. This is also supported by our findings as there was not a significant difference in the adduction/internal and external rotation of the knee of patients compared to the controls.

Implications for therapy

The temporal findings underscore the potential of using stride frequency as a key parameter in the assessment and monitoring of iNPH progression and treatment efficacy. Regular gait analysis, incorporating stride frequency measurements, could provide valuable insights into the patient's response to interventions such as cerebrospinal fluid (CSF) shunting or physical therapy. Targeted therapeutic interventions aimed at enhancing ankle ab/adduction ROM and hip flexion/extension could potentially improve gait stability and efficiency in this patient population. Future research should explore the efficacy of such interventions and consider longitudinal studies to monitor the progression of gait improvements post-intervention.

The observed reduction in stride frequency in iNPH patients has important clinical implications. It highlights the necessity for targeted therapeutic interventions aimed at improving stride frequency and overall gait efficiency. For example, gait training programs focusing on increasing step length and frequency, possibly through the use of auditory or visual cues, have shown promise in enhancing gait parameters in similar populations with gait abnormalities (Giladi et al., 2001; Takakusaki, 2013).

6. LIMITATIONS

This study, while providing valuable insights into the gait characteristics of patients with suspected idiopathic normal pressure hydrocephalus (iNPH), has several limitations that should be acknowledged.

A major limitation of this study is the lack of control for gait speed, which could be a significant confounding factor. iNPH patients exhibited markedly slower walking speeds compared to controls (0.34 m/s vs. 1.24 m/s). This substantial difference in speed raises concerns that some of the observed gait abnormalities, particularly in joint angles and stride characteristics, may be influenced by the slower walking speed rather than solely by the iNPH condition. To mitigate this limitation, future studies should include measures to control for walking speed. For example, asking controls to walk at a speed similar to that of iNPH patients could help isolate the effects of the condition from those of walking speed. This approach would ensure that differences in gait parameters are attributed to the disease rather than variations in speed.

One significant limitation of this study was our inability to compare joint kinetics effectively. Due to the short strides exhibited by the participants, there were multiple foot strikes across the force plates, which resulted in data that was representative of iNPH walking with multiple foot strikes and a shuffling gait. This issue, coupled with the inherent difficulties of standard gait lab approaches in capturing such atypical gait patterns, led to challenges in obtaining reliable kinetic measurements. Consequently, the data quality was compromised, which hindered our ability to gather robust kinetic measurements and limited the scope of our analysis. This underscores the need for novel methods to study this type of gait, such as advanced pressure insoles or other innovative technologies, which may provide more accurate and comprehensive insights into the gait dynamics of iNPH patients.

While more patients have been recruited since the submission of this thesis, at the time of writing the sample size of the study was relatively small, with only 13 patients and 11 controls being included. This limited number of participants may reduce the generalisability of the findings to the broader population of iNPH patients. The effect size was calculated using Cohen's d, most of the variables tested had medium to large effect sizes (Kinematic effect

sizes ranged from -5.18 to 3.11 and temporal effect sizes ranges from 1.36 to 3.11) -- full tables of effect sizes can be found in Appendices C and D. According to Cohen's conventions, this represents a large effect size, indicating a substantial difference between the groups. Such a strong effect size suggests that the observed differences are not only statistically significant but also practically meaningful, emphasizing the relevance and impact of the findings in this context. Future studies with larger sample sizes are necessary to confirm the findings and enhance their applicability to the general iNPH population.

The study employed a cross-sectional design, capturing data at a single point in time. While this approach is useful for identifying differences between groups, it does not allow for the observation of changes over time. Longitudinal studies are needed to understand the progression of gait abnormalities in iNPH patients and the impact of interventions such as shunting.Participants were only recruited from Salford Royal Hospital, which may introduce selection bias. Patients who attend such clinics might have more specific symptoms, including patients from a variety of clinical settings could provide a more comprehensive view of the gait characteristics in iNPH. Patients from a single hospital may not represent the diversity of patients from different geographic regions. Factors such as socio-economic status, cultural background, and access to healthcare can vary significantly across different areas, potentially skewing the results.The study utilized 3D gait analysis, a sophisticated and accurate tool for measuring gait parameters. However, the accuracy of the measurements can be affected by technical issues such as marker placement and calibration of the equipment. Although efforts were made to minimize these errors, they cannot be eliminated.

7. FUTURE WORK

Future studies should incorporate a more detailed biomechanical analysis, including techniques such as electromyography (EMG) to measure muscle activation. This approach would provide deeper insights into muscle function and coordination during gait, allowing for more targeted and effective therapeutic interventions (Del Din et al., 2019). Additionally, employing advanced motion capture systems and three-dimensional gait analysis could further elucidate the intricate biomechanical alterations in iNPH patients.

The current study's gait data, while representative of iNPH walking with multiple foot strikes and a shuffling gait, highlights the limitations of traditional gait lab approaches. The complexity and variability of iNPH gait patterns suggest that novel methods may be required to accurately capture and analyze these abnormalities. Techniques such as pressure insoles or wearable sensors could offer more detailed data on gait dynamics and pressure distribution, which are crucial for understanding the unique characteristics of iNPH gait.

To better distinguish iNPH from other conditions with similar gait disturbances, future research should include additional patient groups, such as those with Parkinson's Disease or Progressive Supranuclear Palsy. Comparing gait parameters across these conditions will help identify condition-specific gait characteristics and improve diagnostic accuracy.

A critical area for future research is the control of walking speed to avoid confounding effects. Current findings indicate significant differences in gait speed between iNPH patients and controls. Future studies should consider adjusting the walking speed of control groups to match that of iNPH patients or vice versa. This adjustment will ensure that observed differences in gait parameters are attributable to the condition itself rather than variations in speed.

While the kinetic data collected in this study is representative of iNPH walking, including the unique challenges of multiple foot strikes and shuffling gait, it is important to address the limitations of standard gait analysis methods. Future work should explore alternative data

collection methods and analytical techniques to improve the quality and interpretation of kinetic data in iNPH research.

Finally, as mentioned at the outset of this dissertation, this study forms part of a much larger project in which we are investigating the effects of cerebrospinal fluid tap-test on gait in patients with iNPH. The findings from this study will form the baseline arm of the longitudinal evaluation on the effectiveness of the tap test on gait improvements over time.

8. CONCLUSIONS

This study used 3D gait analysis to investigate gait abnormalities in patients with Idiopathic Normal Pressure Hydrocephalus (iNPH) compared to controls, by focusing primarily on temporal and kinematic gait parameters. Our findings indicate that iNPH patients exhibit significant deviations in these parameters compared to healthy controls, which is consistent with existing literature that documents gait disturbances such as slowed walking speed, increased step variability, and decreased stride length (Williams et al., 2017; Stolze et al., 2001). However, the impact of walking speed on these results must be addressed in future research to ensure that observed differences are attributed to the condition itself rather than speed. Comparing gait disturbances across conditions like Parkinson's Disease also requires careful consideration of speed-related factors. Understanding these nuances will improve the accuracy of gait analyses and contribute to more effective clinical interventions.

Furthermore, this study is among the first to employ 3D gait analysis to evaluate gait abnormalities in iNPH patients. The use of 3D gait analysis offers a more detailed and accurate assessment of gait dynamics, providing insights that are not attainable through traditional 2D methods. This novel application of 3D gait analysis in the context of iNPH could pave the way for more precise characterizations of gait impairments and contribute to the development of targeted therapeutic interventions.

However, our study's scope was limited by poor quality kinematic data and an incomplete biomechanical analysis. Future research should focus on methods to obtain high-quality kinetic data, potentially by optimizing the setup to accommodate shorter strides or by using advanced techniques to filter and analyse the kinetic data more effectively.

As the study did not include pre and post tap test comparisons of patients, future research must make this a priority to provide a comprehensive understanding of the impact of interventions on gait and to establish a more definitive relationship between the tap test and gait improvement. Such data would enable a more thorough evaluation of the tap test's therapeutic potential, offer insights into patient-specific responses, and contribute to optimizing treatment strategies for iNPH patients. Without these comparisons, our study

lacks the ability to establish a baseline gait performance before the intervention and to quantify the specific changes that occur post-intervention.

While temporal and kinematic data provide a foundation for understanding gait abnormalities, a more comprehensive analysis incorporating muscle activation patterns, joint moments, and forces would yield deeper insights into the neuromuscular and biomechanical deficits underlying iNPH. Previous research highlights the importance of these factors; for instance, muscle activation patterns can reveal compensatory strategies or weaknesses in specific muscle groups (Benedetti et al., 1999), and joint moments and forces are crucial for understanding the mechanical load distribution and potential joint pathologies (Winter, 2009).

The limitation of recruiting patients exclusively from Salford Royal also introduces potential selection bias. The patient population at this institution may not be representative of the broader iNPH population, potentially limiting the generalizability of our findings. Future research should consider multi-centre studies to mitigate this bias and enhance the external validity of the results.

To advance the understanding of gait abnormalities in iNPH, future studies should incorporate a more detailed biomechanical analysis. Techniques such as electromyography (EMG) to measure muscle activation, are recommended as such comprehensive analyses could inform more targeted and effective therapeutic interventions, ultimately improving patient outcomes (Del Din et al., 2019).

In conclusion, while this study contributes to the body of knowledge on gait abnormalities in iNPH, it also underscores the necessity for a more comprehensive biomechanical approach and broader patient recruitment strategies. Including pre- and post-tap test comparisons would significantly enhance the validity and clinical relevance of future studies in this domain. Addressing these limitations in future research will enhance our understanding of iNPH and potentially lead to better diagnostic and therapeutic strategies.

REFERENCES

Agostini, V., Lanotte, M., Carlone, M., Campagnoli, M., Azzolin, I., Scarafia, R., Massazza, G. and Knaflitz, M. (2015) 'Instrumented gait analysis for an objective pre-/postassessment of tap test in normal pressure hydrocephalus.' *Archives of physical medicine and rehabilitation*, 96(7) pp. 1235-1241.

Allali, G., Laidet, M., Armand, S. and Assal, F. (2018) 'Brain comorbidities in normal pressure hydrocephalus.' *European journal of neurology*, 25(3) pp. 542-548.

Allali, G., Laidet, M., Armand, S., Saj, A., Krack, P. and Assal, F. (2017) 'Apathy and higher level of gait control in normal pressure hydrocephalus.' *International Journal of Psychophysiology*, 119 pp. 127-131.

Allali, G., Laidet, M., Beauchet, O., Herrmann, F. R., Assal, F. and Armand, S. (2013) 'Dual-task related gait changes after CSF tapping: a new way to identify idiopathic normal pressure hydrocephalus.' *Journal of neuroengineering and rehabilitation*, 10(1) pp. 1-6.

Andersson, G., Malm, J., & Eklund, A. (2008). Assessment of motor function in idiopathic normal pressure hydrocephalus. Gait & Posture, 28(1), 106-112.

Andersson, J., Rosell, M., Kockum, K., Söderström, L. and Laurell, K. (2017) 'Challenges in diagnosing normal pressure hydrocephalus: Evaluation of the diagnostic guidelines.' *ENeurologicalSci*, 7 pp. 27-31.

Baker, R. (2013). Measuring Walking: A Handbook of Clinical Gait Analysis. Mac Keith Press.

Benedetti, M. G., Catani, F., Leardini, A., Pignotti, E., & Giannini, S. (1999). Data management in gait analysis for clinical applications. Clinical Biomechanics, 14(2), 133-144.

Bovonsunthonchai, S., Witthiwej, T., Ngamsombat, C., Sathornsumetee, S., Vachalathiti, R., Muangpaisan, W., Hengsomboon, P., Thong-On, S., et al. (2018) 'Effect of spinal tap test on the performance of sit-to-stand, walking, and turning in patients with idiopathic normal pressure hydrocephalus.' *Nagoya Journal of Medical Science*, 80(1) p. 53.

Brooks, D.J. (2002) 'Diagnosis and management of atypical parkinsonian syndromes', *Journal of Neurology, Neurosurgery & Psychiatry*, 72(suppl. 1), pp. i10-i16

Brown, S.J., Handsaker, J.C., Bowling, F.L., Boulton, A.J.M. and Reeves, N.D. (2015) 'Diabetic peripheral neuropathy compromises balance during daily activities', Diabetes Care, 38(6), pp. 1116–1122. doi: 10.2337/dc14-1982.

Bugalho, P., & Guimarães, J. (2014). Gait disturbance in normal pressure hydrocephalus: a clinical study. Parkinsonism & Related Disorders, 20(8), 790-794.

Cromwell, R. L., & Newton, R. A. (2004). Relationship between balance and gait stability in healthy older adults. Journal of Aging and Physical Activity, 12(1), 90-100.

Czerwosz, L., Szczepek, E., Blaszczyk, J., Sokolowska, B., Dmitruk, K., Dudzinski, K., Jurkiewicz, J. and Czernicki, Z. (2009) 'Analysis of postural sway in patients with normal pressure hydrocephalus: effects of shunt implantation.' *European journal of medical research*, 14(4) pp. 1-6.

Del Din, S., Godfrey, A., Mazza, C., Lord, S., & Rochester, L. (2019). Free-living monitoring of Parkinson's disease: Lessons from the field. Movement Disorders, 34(9), 1267-1284.

Di Biase, L., Di Santo, A., Caminiti, M. L., De Liso, A., Shah, S. A., Ricci, L. and Di Lazzaro, V. (2020) 'Gait analysis in Parkinson's disease: An overview of the most accurate markers for diagnosis and symptoms monitoring.' *Sensors*, 20(12) p. 3529.

Di Biase, L., Di Santo, A., Caminiti, M. L., De Liso, A., Shah, S. A., Ricciardi, L., ... & Debono, B. (2020). Gait analysis in Parkinson's disease: An overview. CNS & Neurological Disorders-Drug Targets, 19(3), 166-176.

Dias, S. F., Graf, C., Jehli, E., Oertel, M. F., Mahler, J., Schmid Daners, M. and Stieglitz, L. H. (2023) 'Gait pattern analysis in the home environment as a key factor for the reliable assessment of shunt responsiveness in patients with idiopathic normal pressure hydrocephalus.' *Frontiers in neurology*, 14 p. 1126298.

Giladi, N., McMahon, D., Przedborski, S., Flaster, E., Guillory, S., Kostic, V., & Fahn, S. (2001). Motor blocks in Parkinson's disease. *Neurology*, 56(5), 686-690.

Hermens, H. J., Freriks, B., Disselhorst-Klug, C., & Rau, G. (2000). Development of recommendations for SEMG sensors and sensor placement procedures. Journal of Electromyography and Kinesiology, 10(5), 361-374.

Hermens, H. J., Freriks, B., Disselhorst-Klug, C., & Rau, G. (2000). Development of recommendations for SEMG sensors and sensor placement procedures. *Journal of Electromyography and Kinesiology*, 10(5), 361-374.

Isaacs, A. M., Williams, M. A. and Hamilton, M. G. (2019) 'Current update on treatment strategies for idiopathic normal pressure hydrocephalus.' *Current treatment options in neurology*, 21 pp. 1-24.

Krauss, J. K., Regel, J. P., Droste, D. W., Orszagh, M., Borremans, J. J., & Vach, W. (1996). Movement disorders in adult hydrocephalus. Neurology, 46(4), 1109–1115. https://doi.org/10.1212/wnl.46.4.1109

Krauss, J. K., Regel, J. P., Vach, W., Jüngling, F. D., & Mundinger, F. (1996). The gait disorder of normal pressure hydrocephalus. Journal of Neurology, Neurosurgery & Psychiatry, 60(3), 289-293. https://doi.org/10.1136/jnnp.60.3.289

Kuriyama, N., Miyajima, M., Nakajima, M., Kurosawa, M., Fukushima, W., Watanabe, Y., Ozaki, E., Hirota, Y., et al. (2017) 'Nationwide hospital-based survey of idiopathic normal pressure hydrocephalus in Japan: Epidemiological and clinical characteristics.' *Brain and behavior*, 7(3) p. e00635.

Lewek, M. D., Scholz, J. P., & Rudolph, K. S. (2005). Hip kinematics during stair descent in individuals with medial compartment knee osteoarthritis. Arthritis & Rheumatism, 52(1), 291-300.

Liao, Ruochen, Makihara, Yasushi, Muramatsu, Daigo, Mitsugami, Ikuhisa, Yagi, Yasushi, Yoshiyama, Kenji, Kazui, Hiroaki, & Takeda, Masatoshi. (2022). A video-based gait disturbance assessment tool for diagnosing idiopathic normal pressure hydrocephalus. *Transactions of the Institute of Measurement and Control*

Ma, N., Sclavos, N., Passmore, E., Thomason, P., Graham, K. and Rutz, E., 2021. Three-dimensional gait analysis in children undergoing gastrocsoleus lengthening for equinus secondary to cerebral palsy. *Medicina*, 57(2), p.98

Malatesta, D., Simar, D., Saad, H. B., Préfaut, C., & Caillaud, C. (2003). Energy cost of walking and gait instability in healthy 65- and 80-yr-olds. Journal of Applied Physiology, 95(6), 2248-2256.

Marmarou, A., Young, H.F. and Aygok, G.A. (2007) 'Estimated incidence of normal pressure hydrocephalus and shunt outcome in patients residing in assisted-living and extended-care facilities', Neurosurgical Focus, 22(4), p.E1. doi: 10.3171/foc.2007.22.4.2.

Martin-Laez R., Caballero-Arzapalo H., Lopez-Menendez L. A., Arango-Lasprilla J. C., Vazquez-Barquero A. Epidemiology of Idiopathic Normal Pressure Hydrocephalus: A Systematic Review of the Literature. *World Neurosurg* (2015) 84(6):2002-9. Epub 20150714. doi: 10.1016/j.wneu.2015.07.005.

Martín-Láez, R., Caballero-Arzapalo, H., López-Menéndez, L. Á., Arango-Lasprilla, J. C. and Vázquez-Barquero, A. (2015) 'Epidemiology of idiopathic normal pressure hydrocephalus: a systematic review of the literature.' *World neurosurgery*, 84(6) pp. 2002-2009.

Menant, J. C., Steele, J. R., Menz, H. B., Munro, B. J., & Lord, S. R. (2009). Optimizing footwear for older people at risk of falls. Journal of Rehabilitation Research & Development, 46(8), 1121-1134.

Mostile, G., Contrafatto, F., Terranova, R., Terravecchia, C., Luca, A., Sinitò, M., Donzuso, G., Cicero, C. E., et al. (2023) 'Turning and sitting in early Parkinsonism: differences between idiopathic normal pressure hydrocephalus associated with Parkinsonism and Parkinson's disease.' *Movement Disorders Clinical Practice*, 10(3) pp. 466-471.

Mostile, G., Portaro, G., Certo, F., Luca, A., Manna, R., Terranova, R., Altieri, R., Nicoletti, A., et al. (2021) 'iNPH with parkinsonism: response to lumbar CSF drainage and ventriculoperitoneal shunting.' *Journal of Neurology*, 268 pp. 1254-1265.

Nikaido, Y., Akisue, T., Kajimoto, Y., Tucker, A., Kawami, Y., Urakami, H., Iwai, Y., Sato, H., et al. (2018) 'Postural instability differences between idiopathic normal pressure hydrocephalus and Parkinson's disease.' *Clinical Neurology and Neurosurgery*, 165 pp. 103-107.

Nikaido, Y., Nishida, N., Matsumoto, M., Shimizu, T., & Mori, E. (2011). Gait disturbance in normal pressure hydrocephalus: a quantitative biomechanical analysis. Neurology, 77(24), 2226-2232.

Relkin, N., Marmarou, A., Klinge, P., Bergsneider, M., Black, P. M., Diagnosing idiopathic normal-pressure hydrocephalus. Neurosurgery, 57(3), S4–S16. https://doi.org/10.1227/01.neu.0000210239.44721.70

Sakakibara, R., Uchida, Y., Ishii, K., Kazui, H., Hashimoto, M., Ishikawa, M., Takeda, M., & Hattori, T. (2016). Idiopathic normal pressure hydrocephalus presenting as pseudobulbar palsy: Two case reports. BMC Neurology, 16(1), 191. https://doi.org/10.1186/s12883-016-0700-0

Sofuwa, O., Nieuwboer, A., Desloovere, K., Willems, A.-M., Chavret, F., & Jonkers, I. (2005). Quantitative gait analysis in Parkinson's disease: comparison with a healthy control group. *Archives of Physical Medicine and Rehabilitation*, 86(5), 1007-1013. [DOI: 10.1016/j.apmr.2004.08.012] [PMID: 15895349]

Stolze, H., Kuhtz-Buschbeck, J. P., Drücke, H., Jöhnk, K., Diercks, C., & Illert, M. (2001). Comparative analysis of the gait disorder of normal pressure hydrocephalus and Parkinson's disease. Journal of Neurology, Neurosurgery & Psychiatry, 70(3), 289-297.

Stolze, H., Kuhtz-Buschbeck, J. P., Drücke, H., Jöhnk, K., Diercks, C., & Illert, M. (2001). Comparative analysis of the gait disorder of normal pressure hydrocephalus and Parkinson's disease. Journal of Neurology, Neurosurgery & Psychiatry, 70(3), 289-297.

Stolze, H., Kuhtz-Buschbeck, J. P., Drücke, H., Jöhnk, K., Illert, M., & Deuschl, G. (2000). Gait analysis in idiopathic normal pressure hydrocephalus—Which parameters respond to the CSF tap test? Clinical Neurophysiology, 111(9), 1678-1686.

Stolze, H., Kuhtz-Buschbeck, J. P., Drücke, H., Jöhnk, K., Illert, M., & Deuschl, G. (2001). Comparative analysis of the gait disorder of normal pressure hydrocephalus and Parkinson's disease. Journal of Neurology, Neurosurgery & Psychiatry, 70(3), 289-297.

Takakusaki, K. (2013). Neurophysiology of gait: from the spinal cord to the frontal lobe. *Movement Disorders*, 28(11), 1483-1491.

Toma, A. K., Papadopoulos, M. C., Stapleton, S., Kitchen, N. D. and Watkins, L. D. (2013) 'Systematic review of the outcome of shunt surgery in idiopathic normal-pressure hydrocephalus.' *Acta neurochirurgica*, 155 pp. 1977-1980.

Tudor, K. I., Tudor, M., McCleery, J. and Car, J. (2015) 'Endoscopic third ventriculostomy (ETV) for idiopathic normal pressure hydrocephalus (iNPH).' *Cochrane Database of Systematic Reviews*, (7)

Verghese, J., Holtzer, R., Lipton, R. B., & Wang, C. (2009). Quantitative gait markers and incident fall risk in older adults. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 64(8), 896-901.

Virhammar, J., Laurell, K., Cesarini, K. G., Larsson, E.-M., & Sundström, N. (2014). Preoperative prognostic value of MRI findings in 108 patients with idiopathic normal pressure hydrocephalus. American Journal of Neuroradiology, 35(12), 2311–2318. https://doi.org/10.3174/ajnr.A4079

Wang, Z., Zhang, Y., Hu, F., Ding, J. and Wang, X. (2020) 'Pathogenesis and pathophysiology of idiopathic normal pressure hydrocephalus.' *CNS neuroscience & therapeutics*, 26(12) pp. 1230-1240.

Williams, M. A. and Malm, J. (2016) 'Diagnosis and treatment of idiopathic normal pressure hydrocephalus.' *Continuum: Lifelong Learning in Neurology*, 22(2 Dementia) p. 579.

Williams, M. A., Malm, J., Kristensen, B., & Bolander, H. (2008). Objective assessment of gait in normal-pressure hydrocephalus. *American Journal of Physical Medicine & Rehabilitation*, 87(1), 39-45.

Williams, M. A., Relkin, N. R., Ravenholtz, S. D., & Zwimpfer, T. J. (2017). Diagnosis and management of idiopathic normal-pressure hydrocephalus. Neurology: Clinical Practice, 7(6), 469-478.

Williams, M. A., Thomas, G., DeSimone, M., & Rapoport, M. J. (2008). Idiopathic normal pressure hydrocephalus: A systematic review of diagnosis and outcome. Neurosurgery Focus, 25(5), E1.

Winter, D. A. (2009). Biomechanics and motor control of human movement. John Wiley & Sons.

Zaccaria, V., Bacigalupo, I., Gervasi, G., Canevelli, M., Corbo, M., Vanacore, N. and Lacorte, E. (2020) 'A systematic review on the epidemiology of normal pressure hydrocephalus.' *Acta Neurologica Scandinavica*, 141(2) pp. 101-114.

Appendix A: Ethics and Risk management

The risks of the study are assessed as small or non-existent. The tap test is part of the patients' routine medical care. In this study we measured participants' gait before and after this tap test with 3D gait analysis.

Two important practical issues for patients were highlighted during a patient and public involvement group discussion: their reduced balance and mobility and risk of falls often requiring walking aids and their need to have quick access to a toilet. To ensure safe travel for patients to the research laboratory and back, transport was facilitated. All facilities were easily accessible with wheelchairs. The safety of the patient in the laboratory was ensured by always having two members of the research team walk/stand with the patients in case support was required. Toilets were in easy reach from the laboratory. Inclusion and exclusion criteria were purely on scientific grounds, and this includes that only patients able to consent were able to participate. All eligible patients attending the regional NPH clinic were offered participation. The only time when personal data were passed from the medical research team to the academic research team was to enable the participants to attend the gait laboratory at the University. Confidentiality was always maintained. Standard procedures were in place to ensure anonymisation and data safety.

The main burden for participants was that they give up their time for research, the need to physically access the gait laboratory requiring them to mobilise which is difficult due to their condition (iNPH) and their need to be able to access a toilet. Transport to the university was arranged and easy access, including for wheelchairs, to the gait laboratory was ensured. All research was conducted in accordance with government guidance regarding Covid-19. Risk assessments were in place for all research activities and included managing Covid-19 risks. While there were some very minor risks to those participating in this study, including allergic reactions to tape and adhesives, or becoming fatigued during the testing process, these were unlikely and mitigated. We aimed to minimise these risks as much as possible and could stop testing immediately if required. Plenty of opportunity was provided for resting, and refreshments were made available. Any adverse event sustained by the participant during the study was recorded in the case report form.

Appendix B: Impact

The findings of this experiment will be submitted for open access publication in high-impact journals. Potential target journals include Neurosurgery, Neurology, Annals of Neurology, Journal of Neurology, Neurosurgery and Psychiatry, Fluids and Barriers of the CNS (official journal of the Hydrocephalus Association), and/or Movement Disorders. These are world-leading multidisciplinary journals with focus both in clinical and basic science and should provide the widest exposure for our findings. Findings will also be presented at appropriate national and international conferences. In addition, we will work with our participants to develop interactive public engagement activities for patients with suspected or confirmed iNPH. We will also present the findings of our work at the next occurrence of the Hydrocephalus Society world meeting and the Manchester Science Festival, a public-facing festival held in Manchester, which attracts over 130,000 visitors each year and similar arrangements. Members of the research team have previously presented at national and international meetings and have good examples of public engagement; we will ask all participants to provide feedback on the gait analysis experience so that it can be incorporated into presentations at such events.

Appendix C: Temporal Effect Sizes

Table 4: Effect sizes of the temporal statistic data

Temporal Variables	Effect sizes	Point Estimates
Cycle_Time_Mean	Cohen's d	1.3
Speed	Cohen's d	-3.4
Stride_Length_Mean	Cohen's d	-3.5
Stride_Width_Mean	Cohen's d	0.9
Strides_Per_Minute_Mean	Cohen's d	-1.4

Appendix D: Kinematic Effect Sizes

Table 5: Effect sizes of Kinematic data

Kinematic Variables	Effect sizes	Point Estimates
ankle_max_stance_X	Cohen's d	-1.344
ankle_min_stance_X	Cohen's d	1.395
ankle_ROM_stance_X	Cohen's d	-2.726
ankle_max_swing_X	Cohen's d	-0.313
ankle_min_swing_X	Cohen's d	1.328
ankle_ROM_swing_X	Cohen's d	-2.391
ankle_max_stance_Y	Cohen's d	-1.652
ankle_min_stance_Y	Cohen's d	0.589
ankle_ROM_stance_Y	Cohen's d	-2.116
ankle_max_swing_Y	Cohen's d	-1.113
ankle_min_swing_Y	Cohen's d	0.598
ankle_ROM_swing_Y	Cohen's d	-2.326
ankle_max_stance_Z	Cohen's d	-0.467
ankle_min_stance_Z	Cohen's d	-0.331
ankle_ROM_stance_Z	Cohen's d	-0.831
ankle_max_swing_Z	Cohen's d	-0.395
ankle_min_swing_Z	Cohen's d	-0.315
ankle_ROM_swing_Z	Cohen's d	-0.753
hip_max_stance_X	Cohen's d	-0.258
hip_min_stance_X	Cohen's d	1.184
hip_ROM_stance_X	Cohen's d	-2.430
hip_max_swing_X	Cohen's d	-0.222
hip_min_swing_X	Cohen's d	0.313
hip_ROM_swing_X	Cohen's d	-1.121
hip_max_stance_Y	Cohen's d	-2.693
hip_min_stance_Y	Cohen's d	0.836
hip_ROM_stance_Y	Cohen's d	-3.833
hip_max_swing_Y	Cohen's d	-1.254
hip_min_swing_Y	Cohen's d	0.345
hip_ROM_swing_Y	Cohen's d	-2.515
hip_max_stance_Z	Cohen's d	-0.987
hip_min_stance_Z	Cohen's d	-0.204
hip_ROM_stance_Z	Cohen's d	-1.634
hip_max_swing_Z	Cohen's d	-0.850
hip_min_swing_Z	Cohen's d	-0.231
hip_ROM_swing_Z	Cohen's d	-1.477
knee_max_stance_X	Cohen's d	-2.058
knee_min_stance_X	Cohen's d	1.417
knee_ROM_stance_X	Cohen's d	-3.022
knee_max_swing_X	Cohen's d	-1.425
knee_min_swing_X	Cohen's d	2.430
knee_ROM_swing_X	Cohen's d	-2.362
knee_max_stance_Y	Cohen's d	-0.732
knee_min_stance_Y	Cohen's d	0.315
knee_ROM_stance_Y	Cohen's d	-1.124
knee_max_swing_Y	Cohen's d	-0.665
knee_min_swing_Y	Cohen's d	0.389
knee_ROM_swing_Y	Cohen's d	-1.364
knee_max_stance_Z	Cohen's d	0.035
knee_min_stance_Z	Cohen's d	0.688
knee_ROM_stance_Z	Cohen's d	-1.578
knee_max_swing_Z	Cohen's d	0.157
knee_min_swing_Z	Cohen's d	0.469
knee_ROM_swing_Z	Cohen's d	-0.944

Appendix E: 95% Confidence Intervals of Kinematic Data

Table 6: Confidence intervals of kinematic data (X, Y, Z planes represent flexion/extension, ab/adduction and the internal/external rotation)

Joint	Plane	Metric	Group	Lower Bound	Upper Bound
Ankle	Flexion/Extension	Max Stance	Patient	6.2119	9.9165
			Control	10.1171	15.7759
		Min Stance	Patient	-8.7804	-3.8562
			Control	-20.4796	-9.5745
		ROM Stance	Patient	11.2601	17.5050
			Control	24.7764	31.1708
		Max Swing	Patient	-0.8406	3.1072
			Control	-1.2626	6.3572
		Min Swing	Patient	-8.7230	-3.2929
			Control	-19.4519	-9.0246
		Rom Swing	Patient	5.0384	9.2440
			Control	13.6868	19.8843
Ankle	Ab/Adduction	Max Stance	Patient	1.6486	5.5854
			Control	7.4085	15.6972
		Min Stance	Patient	-3.7403	-1.2961
			Control	-7.5760	-1.4735
		ROM Stance	Patient	4.2091	8.0613
			Control	12.0252	20.1300
		Max Swing	Patient	2.7494	6.3102
			Control	5.6111	13.6761
		Min Swing	Patient	-1.7607	1.3894
			Control	-5.9406	0.8750
		ROM Swing	Patient	3.4762	5.9547
			Control	9.3590	14.9938
	Internal/External Rotation	Max Stance	Patient	0.9269	4.2511
			Control	-6.7709	28.6665
		Min Stance	Patient	-1.3819	0.4608

			Control	-9.3925	17.4212
		ROM Stance	Patient	2.1580	3.9412
			Control	2.1580	3.9412
		Max Swing	Patient	0.8345	4.5428
			Control	-6.4575	24.0756
		Min Swing	Patient	-0.7253	1.5672
			Control	-8.7083	18.0482
		ROM Swing	Patient	1.4423	3.0930
			Control	1.4423	3.0930
Knee	Ab/Adduction	Max Stance	Patient	36.2987	42.4742
			Control	38.6113	49.5378
		Min Stance	Patient	5.1046	9.6481
			Control	4.5812	8.9743
		ROM Stance	Patient	27.1231	34.6842
			Control	32.2013	41.0410
		Max Swing	Patient	55.7841	66.0249
			Control	61.8476	73.2345
		Min Swing	Patient	8.4015	14.0732
			Control	6.2031	12.9504
		ROM Swing	Patient	41.2619	51.9875
			Control	50.2836	62.3459
	Internal/External Rotation	Max Stance	Patient	0.9056	6.3417
			Control	0.6137	4.6785
		Min Stance	Patient	-3.5412	-1.0348
			Control	-4.1935	-0.9145
		ROM Stance	Patient	3.8510	7.1534
			Control	4.1236	6.9581
		Max Swing	Patient	2.1784	5.9476
			Control	1.5436	5.6810
		Min Swing	Patient	-1.7814	0.4395
			Control	-3.6013	0.5812

		ROM Swing	Patient	2.9487	5.1039
			Control	3.1245	5.8472
Hip	Flexion/Extension	Max Stance	Patient	29.0540	43.8089
			Control	29.0540	43.8089
		Min Stance	Patient	3.5100	24.0739
			Control	-6.3594	2.4187
		ROM Stance	Patient	17.1771	28.1020
			Control	17.1771	28.1020
		Max Swing	Patient	31.4320	46.1689
			Control	36.6423	45.4002
		Min Swing	Patient	12.0681	30.7764
			Control	12.0700	22.8587
		ROM Swing	Patient	13.1934	21.5630
			Control	21.5155	25.5982