Caracterización de la Parálisis Cerebral mediante la Estimación del Movimiento Ocular

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Cerebral Palsy Characterization by Estimating Ocular Motion

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To my family because of their constant support, patience and understanding gave to me in starting and finishing this great project in my life. To whom is my rock and in whom I have always trusted.

*The man who moves a mountain begins by carrying away small stones.*

Confucius
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Abstract

Cerebral Palsy (CP) is considered as a public health problem and the most common cause of motor illness in children with an incidence of 2 to 2.5 cases per 1,000 live births. Between 50-90% of the patients with this condition present visual problems, reason why this population exhibits visual sensory and motor abnormalities at rates exceeding those detected in neurologically normal children. This work proposes an automatic characterization of cerebral palsy by estimating the ocular motion during a gaze pursuit task. For this, an estimation of the eye movement is performed using an optical flow approach, at a dataset organized in two groups: cerebral palsy children and controls. From the motion field obtained, a quantitative characterization of the eye movement is carried out through velocity histograms of magnitude and orientation. The temporal result is accumulated in a histogram and a correlation distance between histograms quantifies the differences between groups. The proposed approach was evaluated with an experimental group of 16 cerebral palsy patients and 16 control subjects. When evaluating with the Wilcoxon statistical test, results show significant differences between cerebral palsy patients and controls, obtaining a \( p \)-value < 0.01 for the orientation distances in both visual tasks and a \( p \)-value < 0.05 for the magnitude distances in the smooth pursuit task. Making this strategy a way to characterize ocular movement patterns in children with cerebral palsy.

Keywords: Cerebral Palsy, characterization of the ocular motion, optical flow approach, ocular motion patterns.
Resumen

La Parálisis Cerebral (PC) se considera un problema de salud pública y la causa más común de discapacidad motora en niños, con una incidencia de 2 a 2.5 casos por 1,000 nacidos vivos. Entre el 50-90 % de los pacientes con esta condición presentan problemas visuales, por lo que esta población exhibe anomalías visuales sensoriales y motoras a tasas que superan las detectadas en niños neurológicamente normales. Este trabajo propone una caracterización automática de la parálisis cerebral mediante la estimación del movimiento ocular durante una tarea de búsqueda de la mirada. Para esto, se realiza una estimación del movimiento del ojo utilizando un enfoque del flujo óptico, en un conjunto de datos organizado en dos grupos: niños con parálisis cerebral y controles. A partir del campo de movimiento obtenido, se lleva a cabo una caracterización cuantitativa del movimiento del ojo a través de histogramas de orientación y magnitud. El resultado temporal se acumula en un histograma y una distancia de correlación entre histogramas cuantifica las diferencias entre grupos. El enfoque propuesto fue evaluado con un grupo experimental de 16 pacientes con parálisis cerebral y 16 sujetos controles. Al evaluar con la prueba estadística de Wilcoxon, los resultados muestran diferencias significativas entre los pacientes con parálisis cerebral y los controles, obteniendo un valor de $p < 0.01$ para las distancias de orientación en ambas tareas visuales y un valor de $p < 0.05$ para las distancias de magnitud en la tarea de búsqueda suave. Haciendo de esta estrategia una forma de caracterizar los patrones del movimiento ocular en los niños con parálisis cerebral.

Palabras clave: Parálisis Cerebral, Caracterización del Movimiento Ocular, Enfoque de Flujo Óptico, Patrones de Movimiento Ocular.
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1 Introduction

1.1. Cerebral Palsy

Cerebral palsy (CP) is the most common cause of disability in childhood\cite{48} with an incidence of around 2 to 2.5 cases per 1,000 live births\cite{82}, being a public health problem worldwide\cite{18, 51}. Cerebral Palsy is defined as a 'large group of permanent disorders of the development of movement and posture, causing limitations of physical activities'\cite{17, 8} that are attributed to non-progressive alterations in the developing fetal or infant brain\cite{78}. Although the brain lesion is static or non-progressive, its manifestations are progressive. The primary manifestations include loss of selective motor control, alteration in balance and muscle tone abnormalities; which results in secondary manifestations of abnormal growth and development of the musculoskeletal system. It significantly affects a child’s function, including abnormalities in gait and ambulation\cite{22}.

Abnormalities of reflexes are also included as principal signs in CP, which affect the achieving developmental milestones and control of balance and movements. Advanced postural reactions and equilibrium that are required for sitting and walking are delayed or non-existent. Moreover, the inability to plan and execute motor function (apraxia) is presented and cortical sensation, proprioception, and sensation of movement may be impaired\cite{11}.

The range of disorders that can arise with CP is wide. Depending on the extent and topography of the damage, in addition to motor impairments, deficits in perception, reading, language, and cognition can occur, leading to limitations in daily activities\cite{49}. In particular, visual impairments are frequent in CP, affecting between 40-75\% of these children\cite{12}.

1.1.1. Etiology

Currently, there has been an increase in the number of children with CP\cite{74}, in whom the brain abnormality can occur pre, peri or postnatally\cite{6, 9}. Among the most well-known prenatal risk factors are: congenital brain malformations, vascular events and maternal infections; and the least common include metabolic disorders, maternal ingestion of toxins and rare genetic syndromes. Perinatal risk factors include problems during labor such as obstetric emergencies of obstructed labor, antepartum hemorrhage, cord prolapse, and neonatal encephalopathy can compromise the fetus causing cerebral hypoxia\cite{63}. Approximately 10 to 20 percent of patients acquire cerebral palsy after birth, mainly due to brain damage from
bacterial meningitis, viral encephalitis, hyperbilirubinemia, motor vehicle collisions, falls or child abuse[48].

Prematurity is considered the increased risk of CP, and both the presence and grade of periventricular leukomalacia (PVL) increase that risk[96]. CP rate rises considerably with decreasing gestation age to odds of 70% if born before 32 weeks. If born before 26 weeks, 16–28% of children will develop CP. Even, children born between 32 and 36 weeks of gestation still have higher odds of developing CP than those born after 36 weeks[27].

Intrauterine infection or inflammation and prolonged rupture of membranes are important antecedents of preterm birth, and also of CP in prematurely born children. In addition, risk factors for premature birth include previous preterm birth, black race, low maternal body mass index, vascular disease, and multiple gestation[77]. Medical indications for preterm delivery include preeclampsia or eclampsia and fetal growth restriction[57].

Birth weight is also included as a risk factor for cerebral palsy since the small infant for gestational age presents more likely to be affected by hypoxic ischaemic events in labour. The neonate with symmetrical growth retarded (low head circumference, underweight and short height) is also at risk of developmental delay even in the absence of birth asphyxia. And the large for gestational age infant has a higher risk related to maternal diabetes and obstructed labour[27].

Finally, multiple births such as twin and higher multiple births are strong risk factors for CP. The risks increase as the number of babies increases and if the twins are identical. Among the factors related to these risks are twin-to-twin transfusions, vascular anomalies of the placenta, death-in utero of a twin, prematurity, small for gestation age, premature rupture of membranes and hypoxia during labour[27].

1.1.2. CP Diagnosis

Some clinical practice guidelines recommend that the diagnosis of CP or high risk of CP be made within the first 6 months post-term age and other studies such as Spittle et al.[89] and Voss et al. suggested that CP could be confirmed at the age of 2 years with sufficient reliability. However, recent studies [66] document stability in the Gross Motor Function Classification System longitudinal curves around 5 years of age supporting the choice of this age as the most appropriate to ensure that the condition is nonprogressive.[98] It confirms the importance of ongoing clinical assessment for children with CP, in that the motor signs of children with CP can change over time[34].

This has led to finding cases where children were misdiagnosed. For instance, Gupta et al. found that some neurodegenerative and metabolic disorders may present with similar symptoms and signs of CP, particularly in infancy and early childhood, being misdiagnosed as CP. Likewise, Zarrinkalam et al. examined the accuracy of the diagnoses in a CP, reporting a CP diagnostic misclassification rate of 5.2%. These findings support the importance of undertaking a complete clinical assessment based on analysis of evidence and recommend
practice parameters at the time of diagnosis.

In clinical practice, the CP diagnosis is based on a balanced combination of the following items to make an early accurate diagnosis of CP: the anamnesis of the risk factors and the psychomotor development of the child (clinical history), the neuromotor examination, functional assessments, and complementary tests.

**Clinical history**

To determine the diagnosis of the CP, clinicians begin by performing an interview with the child’s parents, obtaining information related to the clinical history. This medical history includes a collection of information on birth history, developmental milestones, medical problems, surgical history, current physical therapy treatment, and current medication [59]. Birth history offers important information for accurate diagnosis, future prognosis, treatment, and goal setting. Developmental milestones give information regarding the maturity of skills and the child’s future capacity [59]. Among the important gross motor milestones to be evaluated in cerebral palsy are: control of the head at 2 months, rolling at 4 months, sitting at 6 months and walking at 1 year of age [2]. Likewise, reports of previous surgeries are included in clinical history, which allows evaluating the current deformities and compensations and carrying out their therapeutic follow-up [59].

Children with cerebral palsy may be prescribed a variety of different medications [96], reason why it is essential for clinicians to be aware of any possible side effects that these medications may have [90].

**Neuromotor examination**

CP palsy becomes evident when the child reaches the age of 6 to 9 months and initiates extremity mobilization. Clinicians perform neuromotor examination based on the observation of the child’s motor skills. The preferential use of limbs, asymmetry or gross motor developmental delay, growth delay, persistent primitive reflexes may be seen in this clinical assessment. Regarding bigger children examination, clinicians evaluate spasticities, spasms, involuntary movements, unsteady gait, joint and bone deformities and contractures and problems with balance. However, previous to this examination, the observation also allows revealing the abnormal tone of the neck or trunk (floppy or very stiff), asymmetric posture, strength, gait or abnormal coordination [2].

**Functional assessments**

In clinical practice, some tools have been used to evaluate the functional performance of the CP child. Among the gait measures of children with CP is the FAQ (Functional Assessment Questionnaire), which is a report of a child’s ambulation obtained with the information given by the parents using a scale of 10-level. This tool assesses the functional skills related to ambulation such as stair climbing, running, and encountering obstacles in the community.
such as curbs. A child who is typically able to keep up without limitations is scored at level 10, and the scale decreases with decreasing ability for ambulation[59].

Another measure of ambulatory performance is the Functional Mobility Scale (FMS) designed by Graham and colleagues[67], which demonstrates different ambulatory abilities and includes the use of different assistive devices to walk various distances. This assessment is administered via parent/patient interview and categorizes the assistance needed (none, canes, crutches, walker, wheelchair) for a child to walk three distances (5, 50, and 500 yards, or 5, 50, and 500 m). By each distance category, the following ratings are given (Fig. 1-1): 1, uses a wheelchair; 2, uses walker or frame; 3, uses crutches; 4, uses sticks (canes); 5, independent on level surfaces; 6, independent on all surfaces. At last, a rating of C is given if the child crawls the designated distance, and an N is given if the child is unable to move through a given distance. The FMS is an evaluative measure of functional mobility in children with CP aged 4 to 18 years.

![Functional Mobility Scale](image)

**Figure 1-1**: Functional Mobility Scale. (Courtesy of Kerr Graham.)

Regarding the upper limb evaluation, the Manual Ability Classification System (MACS) is frequently used by the clinicians where upper-extremity performance in activities of daily living for children with CP is described[87]. MACS levels are based on children’s ability to initiate handling objects and their need for assistance or adaptation to perform manual daily life activities according to their age. This assessment is applied to CP children between 4 and 18 years and was designed as a five-category scale[75]:

- Level I: handles objects easily.
- Level II: handles most objects but with a little-reduced quality or speed.
- Level III: handles objects with difficulty and need help to prepare or change activities.
- Level IV: handles a limited quantity of objects and requires continuous support to partially conclude the activities.
- Level V: does not handle objects and has severely limited ability to perform even simple actions.

The muscle tone assessment is also commonly used in the physical evaluation in CP children. The Modified Ashworth Scale (MAS) measures spasticity and is applied manually to determine the resistance of the muscles to passive movement. However, the reliability of this scale is poor in children with CP, and it is recommended that the interpretation of scores be used with caution[3].

Scores:

- 0 : No increase in tone.
- 1 : Slight increase in tone giving catch when the limb is moved in flexion and extension.
- 2 : A more marked increase in tone, but the limb is easily flexed.
- 3 : Considerable increases in tone, passive movement difficult.
- 4 : Limb rigid in flexion or extension.

Complementary tests

In the diagnostic evaluation of a child with CP certain tests that contribute in the evaluation of the degree of motor functional limitation, the level of global disability and the associated alterations are also necessary, such as:

- **Neuroimaging techniques**

Neuroimaging plays an important role in characterizing the non-progressive lesion of the developing brain, causing CP[89]. Neuroimaging studies can help to evaluate brain damage and to identify children who are at risk of developing cerebral palsy[2]. Ultrasonography has been extensively used in very preterm born infants, in whom periventricular white matter injury is common. However, early ultrasonography has not proved very specific in predicting CP due to it is not well suited to imaging the cortical and cerebellar structures[14]. On the other hand, computed tomography (CT) scanning of the brain helps to identify congenital malformations, intracranial hemorrhage, and periventricular leukomalacia more clearly than
ultrasonography. Likewise, electroencephalography (EEG) is useful to evaluate the severe hypoxic-ischemic injury, being important in the diagnosis of seizure disorders[2]. Magnetic Resonance Imaging (MRI) of the brain is currently the evaluation of choice for the vast majority of children with suspected cerebral palsy, showing an abnormality in about 90% of cases[39]. This technique provides information about the location and extent of brain injuries such as the major and minor brain malformations, in utero strokes, and white matter loss which is strongly associated with CP[23].

- Tests of accompanying conditions

Some tests are applied according to the associated alterations that each CP patient presents. In the sensory and perceptive disorders, of touch and pain, the FACES Pain Rating Scale of Wong-Baker is used to assess the intensity of pain. In cases with findings in the history or physical examination suggestive of epilepsy or epileptic syndromes, is recommended to perform an electroencephalogram. The ophthalmological damage is assessed through guidelines for visual screening in children with CP. Speech and language disorders are also evaluated to detect anarthria and dysarthria and distinguish them from language disorders associated with mental retardation since both can occur in patients with CP.[32]

The investigation of cognitive and sensory alterations should be part of the initial evaluation of the patients with CP, taking into account the frequency with which they occur.[32]

1.1.3. Classification of CP

From the determination of the diagnosis, several classifications have been proposed to determine the heterogeneity of the conditions in the patients.

Topographic Classification

This classification describes the CP regarding the localization or topography of the abnormal motor function. Monoplegia describes one extremity involved. Hemiplegia is presented in almost 30% of the CP cases, where both extremities on the same side are involved, and usually, upper extremity is involved more than lower extremity. Paraplegia is considered when both lower extremities are equally involved. Diplegia is presented in the 50% of the cases where bilateral lower extremities are involved, and fine-motor/sensory abnormalities are presented in the upper extremity. In the triplegia, three extremities (typically both lower and one upper extremity) are affected. And, quadriplegia refers to severe four-extremity involvement but, normal head/neck control is presented[2, 63].

Physiological Classification

According to this classification, CP is divided into 2 main physiologic groups, the pyramidal (cases in which spasticity is prominent) and the extrapyramidal types (dyskinetic and ataxia), shown in Fig. 1-2[63].
1.1 Cerebral Palsy

Spasticity is a common sign in children with CP where the velocity-dependency increases with muscle tone. This is detected by using a passive stretch[2]. This motor disorder is generated due to an injury in the central nervous system that produces an upper motor neuron lesion[22], which is characterized by hyperreflexia, clonus, extensor plantar responses, and primitive responses[11].

The second most common type of CP is the dyskinetic representing approximately 10% to 15% of all CP cases. It is characterized by abnormal postures or movements associated with impaired muscle tone regulation, movement control, and coordination. Athetosis, dystonia, and chorea are the main movement disorders seen in dyskinetic children.

This condition includes two movement disorder patterns: dystonia and choreoathetosis [56]. In dystonia, sustained or intermittent muscle contractions generate abnormal postures, repetitive movements, and involuntary twisting are present[81]. Dystonia affects posture, mobility, hand and oral-motor function, and non-verbal communication[55] and it can be exacerbated by stimuli such as emotion, cognitive tasks, stress, pain, and the intention to move, and is relieved by sleep[56]. On the other hand, choreoathetosis is characterized by hyperkinesia and muscle tone fluctuation and can be divided in two physical signs: chorea that refers to rapid, involuntary, jerky, and often fragmented movements, and athetosis is a slow, continuous, involuntary writhing movement that affects the posture stability[81].

By last, ataxia is characterized by the abnormal pattern of posture and/or movement and loss of orderly muscular coordination so that movements are performed with abnormal force, rhythm, and accuracy[19]. Ataxia is usually associated with cerebellar lesions and becomes apparent toward the age of 2 to 3 years[11].

**Functional classification**
Looking for standardizing the severity of the disability for the movement, the Gross Motor Function Classification System (GMFCS) was proposed. Its last version is the GMFCS-Expanded and Revised (GMFCS-ER) at 2007[67], which has been widely used internationally for clinical, research, and administrative purposes[79]. It allows to evaluate the gross motor function, based on the use of mobility aids and performance in sitting, standing, and walking activities. Thus, the classification of a patient’s gross motor function level is given according to his or her typical performance, rather than their best capability [75]. This classification separates the gross motor function characteristics of children into five different levels of severity (Fig. 1-3) with descriptions of skills provided for 5 age groups: less than 2 years of age, 2 to 4 years of age, 4 to 6 years of age, 6 to 12 years of age, and finally 12 to 18 years of age[67]. The distinctions between GMFCS levels are based on functional limitations, the need for assistive mobility devices (walkers, crutches, canes) or mobility with a wheelchair[64] where level I indicates the level of least motor difficulty and level V presents a greater functional limitation.

- In GMFCS I level children walk inside and outside and climb the stairs without limitations; however, balance and coordination skills are limited.

- Children in level II walk in most settings and climb stairs holding onto a railing. They may experience difficulty walking long distances and balancing on uneven terrain, inclines, in crowded areas or confined spaces. Children may walk with physical assistance, a hand-held mobility device or used wheeled mobility over long distances. Children have only minimal ability to perform gross motor skills such as running and jumping.

- In level III Children walk using a hand-held mobility device in most indoor settings. They may climb stairs holding onto a railing with supervision or assistance. Children use wheeled mobility when traveling long distances and may self-propel for shorter distances.

- Children in level IV use methods of mobility that require physical assistance or powered mobility in most settings. They may walk for short distances at home with physical assistance or use powered mobility or a body support walker when positioned. At school, outdoors and in the community, children are transported in a manual wheelchair or use powered mobility.

- Children in level V are transported in a manual wheelchair in all settings. Children are limited in their ability to maintain antigravity head and trunk postures and control leg and arm movements.

1.1.4. Treatment

Currently there is no cure for cerebral palsy; as a result, various therapeutic interventions with interdisciplinary approaches have been used to control CP [86]. Appropriate interven-
tions for cerebral palsy are dictated by the patient’s functional ability, severity, the pattern of motor disorder, associated pain and discomfort, and age [10]. Thus, treatment options change with the age and developmental stage of the child[46].

A combination of physical, developmental, medical, chemical, surgical and technical procedures are used to help prevent secondary deficiencies and improve the child’s development capabilities[86].

Nonoperative treatment in CP includes several modalities such as medication, therapeutic modalities, and rehabilitation therapies, which are commonly used as a primary treatment or in conjunction with other forms of treatment (surgery)[2]. These modalities reduce the effect of increased muscle tone, improving the fluidity of motor control[10].

A wide variety of medications have been used in CP treatment. Dantrolene drug decreases abnormal muscle stretch reflexes and tone. Botulinum toxin type A (BTX-A) is a neurotoxin that has been used to weaken muscles selectively in patients with CP. It is injected directly
into the muscle blocking the release of the neurotransmitter acetylcholine and inhibiting muscle contraction. It is also used as an adjuvant to a bracing, casting, or physical therapy treatment program[2]. Spasticity is also treated with oral medications such as diazepam, baclofen, dantrolene sodium, and tizanidine, which are commonly prescribed[22]. Therapeutic modalities are used to facilitate the range of motion, to delay or prevent deformity, to provide joint stability, to maximize activity, and to encourage adaptive mechanisms. Among the most used modalities in CP are: electrical stimulation, splinting, casting, and orthotics. Therapeutic electrical stimulation uses daily low exposure of spastic muscles producing a visible muscle contraction [46]. Orthotics are common devices used in CP to provide stability, to prevent or delay contractures, to maintain range of motion, and to normalize function[46]. Indications of these devices differ according to the age, type of deformity, selective motor control level, and functional prognosis of the child[20, 11].

Rehabilitation therapies play an important role in CP treatment[2]. Among the main rehabilitation therapies are physiotherapy and occupational therapy which are considered highly effective in improving the functional capabilities of children with cerebral palsy[70]. These therapeutic measures are in charge of improving mobility, preventing deformity, and helping the child in her or his independence in daily life activities[11]. In CP cases where contractures or deformities decrease function, cause pain or interfere with activities of daily living, operative treatment is indicated. These procedures allow to correct static or dynamic deformity, to balance muscle power across a joint, to reduce spasticity, and to stabilize uncontrollable joints[2]. Likewise, these operative treatments should be individually adjusted according to the patient’s age, disease severity, underlying pathology (spastic, dystonic, or mixed), comorbidities, and overall well-being[46]. Approximately 80% of CP children need orthopedic surgery in childhood or adolescence[11].

1.1.5. Prognosis

CP is not a progressive disorder but the symptoms can become more severe over time due to subdural damage[1]. The clinical picture in CP ranges depending on the extent of the CNS lesion. Approximately 85% of partially involved children have the potential to become independent ambulators compared with only 15% of severely involved children[85]. Spastic hemiplegic and diplegic children with good cognitive function generally reach independence in their ambulation. Children who have mildly affected use assistive devices and mobility aids to ambulate and severely involved children remain totally dependent[11]. The life span of the child with cerebral palsy is curtailed by the presence of certain key disabilities such as: the presence and severity of mental retardation, inability to speak intelligible words, inability to recognize voices, inability to interact with peers, physical disability, limitations on mobility, inability to propel wheelchair, inability to roll over, inability to creep/crawl/scoot, lack of upper extremity function, inability to eat without assistance, tube feeding, incontinence, cortical blindness and presence and severity of seizures[45].
From this factors, it was found in the literature that children with mild cerebral palsy have a normal or near-normal life expectancy, children with the most profound cerebral palsy have a life expectancy of 19 to 21 years and intermediate degrees of severity of neurologic deficit are associated with an intermediate life expectancy[45].

1.2. Visual impairment

The diagnosis of CP is usually performed on the basis of uncoordinated muscle movements and delays in reaching developmental milestones. Moreover, computerized tomography and/or magnetic resonance imaging of the child’s brain to look for brain insults and abnormalities, help to diagnose the condition[58]. However, the characterization of the clinical picture of CP can be based not only on the characteristics of the motor deficit and topography but also on neuro-ophthalmological aspects[28].

Vision plays an essential role in motor development, being the main sensory modality available to normal infants[35]. Indeed, children with CP tend to rely more on visual feedback than children with typical development[73] and visual problems can interfere with motor learning and may be responsible for some of their deterioration in manual and locomotive skills[25]. Moreover, the CP patient’s classification of cognitive style can be affected by the eye movements exhibited [43], and oculomotor abilities can also be linked to visual-perceptual impairment in these children [29].

CP population presents anomalies of the sensory and visual motor pathways at rates exceeding than those detected in neurologically normal children[33], evidencing that between 40-75 percent of children with cerebral palsy have some type of problem or visual disability[12]. Disorders of visual function in cerebral palsy are often due to damage to central visual pathway[35], where chronic hypoxia to the brain usually causes damage to the visual cortex. Among the most common visual damages in CP are strabismus, refractive anomalies, optic atrophy, disorders of eye movement, nystagmus, ptosis, and accommodative dysfunctions. Neurological vision loss, also called cerebral/cortical visual impairment (CVI) can result from visual neural processing dysfunctions commonly co-occurring with CP[21].

Many of the patients with CP are born prematurely, so they are at risk for visual-perceptual dysfunction. Likewise, CP primarily involves the motor system, any task that engages motor input and/or output will be affected[83]. Thus, cerebral palsied children who present any visual problem must be referred to ophthalmologists at an early stage for visual rehabilitation which is one of the important parameters in increasing the physical and intellectual capacity of them[61]. Moreover, the rehabilitation of children with cerebral palsy depends, in large part, on visual stimulation, and the identification of visual defects in an early state, these facts are important for the prognosis and treatment[26].

On the whole, visual exploration seems to be crucial in the rehabilitation of affected children, contributing to their motor improvement and to a better overall prognosis. So, early and careful neuro-ophthalmological assessment of CP children is essential for an accurate
1.2.1. Ocular movement strategies in Cerebral Palsy

Eye movement abnormalities are common in CP[44, 13, 35], affecting almost 50% of these children[49]. Although there is an importance in the research of these alterations, there is a lack of objective research to describe the oculomotor function in children with CP[5]. For this reason, some objective strategies have been proposed in the state-of-art to quantify the oculomotor function in this population by analyzing specific visual functions.

One of the first quantitative analyses of eye movements in children with CP was proposed by Katayama et al.[44]. In this work, CP subjects were evaluated maintaining their heads mechanically fixed and looking to 13 target lights that appear on a screen. Horizontal saccades were evaluated and measured by standard electrooculography and, after amplification and filtering, were recorded on magnetic tape. Data analysis was performed off-line and included measurements of reaction times and saccade velocities. Although they found abnormalities of saccadic eye-movements in the majority of CP children with lower velocities, a small cohort of patients was used, the results were not compared with control subjects using the same experimentation and there was also a lack of statistical analysis to support their conclusions and to make their results comparable with other studies.

Likewise, there are some approaches that have tried to measure and quantify the performance evaluation of Functional Vision Assessments for CP children using diagnostic techniques. For instance, Illavarason et al.[41] analyzed the visual acuity through an ophthalmological device Visually Evoked Potential (VEP) in 25 patients with CP. This approach used the parameter measurement of mean latency and mean amplitudes, finding significant differences with a p-value < 0.05 in the VEP for the CP children and controls analyzed. However, although VEP is considered the only clinically objective test that evaluates the functional status of the visual system, this procedure presents some disadvantages: tests are long and tedious for patients, the risk of technical error, therefore the likelihood of repeating the test, is high.

Eye tracking technology is commonly used to register eye movements[36], allowing fast and quick acquisition of records from clinical patients[41]. Currently, this method has been applied in medicine to research the nature of diseases, therapy or improvement of medical education.

Head-mounted systems are one of the first types of eye tracking systems implemented in Cerebral Palsy as presented by Lee et. al[50]. This work develops an analysis of binocular movements in adults with CP, using a head-mounted, infrared corneal reflection instrument - 7000S was used to measure the smooth pursuit and saccadic eye movements. However, this approach presented limitations due to the small sample of patients tested and the displacement information is not enough to perform a reliable analysis of the eye movement.

On the other hand, remote systems have also been used for eye tracking analysis. This technology uses infrared light to detect the center of the pupil and then estimate a gaze
1.3 Contribution and academic products

The main contribution of this work is an automatic characterization method of the ocular motion in cerebral palsy, performing an estimation of the movement using simply a camera. The device used allows capturing the eye movement without the need to perform a calibration per user and without presenting restriction on head movement. Likewise, being a device attached to the head, it improves the gaze accuracy due to the distance from the subject to the camera is the same during the video recording. Therefore, this method gives a reliable quantification of the ocular movements during a gaze pursuing task. The main advantage of this method is the analysis of the ocular movement patterns through the used of a head-mounted system during the evaluation of two visual tasks that allow assessing the smooth pursuit and saccadic eye movements. These movements describe the oculomotor system function[5], due to these are used to stabilize the image of selected objects on the fovea (region of the retina with the highest acuity), being crucial to getting a clear vision of the environment[25]. This method gives a characterization of the development of cerebral palsy children through an objective and quantitative assessment of ocular motion. It provides a support tool to the clinicians to perform a follow-up of the patients and establish a treatment according to the condition of each patient. The results of this work were presented in:

1.4. Thesis outline

Following chapters are presented in this manner:

- **Chapter 2: Cerebral Palsy Characterization by Estimating Ocular Motion.** This chapter presents an exploratory approach to the estimation of ocular motion in a small sample of patients, performing a pattern identification in ocular movement through the use of phase planes to relate the velocity and acceleration of the eye movement during the evaluation of two visual tasks. This strategy allowed us to quantify the differences between subjects.

- **Chapter 3: Ocular Control Characterization of Motor Disabilities: the Cerebral Palsy Case.** In this chapter, the methodology of the previous approach was used and it was extended towards quantitative analysis of the ocular motion, taking as an advantage the quantification of the visual tracking performance along the time of each visual task. This approach is validated with a greater number of data and showed a reliable and objective method to assess the oculomotor function in patients with Cerebral Palsy.

- **Chapter 4: Conclusions and Future Work.** This chapter presents the main conclusions of the proposed work. Likewise, it describes some of the future perspectives promoted by this thesis.
2 Cerebral Palsy Characterization by Estimating Ocular Motion

This chapter presents an automatic characterization of the cerebral palsy is herein presented by estimating the ocular motion during a gaze pursuing task. Specifically, after automatically detecting the eye location, an optical flow algorithm tracks the eye motion following a pre-established visual assignment. Subsequently, the optical flow trajectories are characterized in the velocity-acceleration phase plane. Differences are quantified in a small set of patients between four to ten years. A version of this chapter has been accepted for publication as a research article in the proceedings of 13th International Seminar on Medical Information Processing and Analysis - SIPAIM 2017.
2.1. Introduction

Cerebral palsy (CP) is a public health problem and the most common cause of motor dysfunction in children worldwide, reaching an incidence of 3 per 1000 live births[18]. CP limits many physical activities and is caused by fetal or infant brain development non-progressive alterations. [8] Sensorial impairment is also commonly found in children with CP[35] since this population presents abnormalities of the visual sensory and motor pathways [33] [71], between 40-75 percent of cerebral palsy children have some form of vision problems or disabilities[12].

Usual clinic evaluation protocols are hardly standardized by the large intra and interexaminer variability. Patients with cerebral palsy are more dependent on visual information than unaffected ones [25]. Barca, et al. [7] applied a battery of tests for examining visuo-perceptual and visuospatial domains but observations resulted quite subjective and hardly comparable. Similarly, Dufresne et al.[24] introduced an statistical analysis based on parents’ interview, clinical history, interpretation of neuroimaging data and visual observation of the patient stage. Although prenatal antecedents and visual dysfunction were correlated, the resulting profile of visual impairment still provides a subjective appreciation.

Other studies in contrast, have attempted a quantitative visual analysis. Kooiker et al.[47] proposed visual examination by measuring ocular orientation responses to visual stimuli with an integrated 60 Hz sampling infrared eye tracking system (Tobii T60-XL). Ego et al.[25] used an Eyelink 1000 infrared eyetracker to record horizontal eye movements at 1000 Hz. However this approach limits the binocular movement that is altered in CP. Current cerebral palsy diagnosis is based on clinical observations and qualitative motor evaluation. In consequence, evidence based on medical results are hard to support since diagnoses are hardly repeatable and fully dependent on the examiner[62].

A main contribution of this study is an automatic characterization of the cerebral palsy by estimating the ocular motion during a gaze pursuing task. This evaluation is devised to interact with children between four to ten years. A simple emoticon draws the patient’s attention while this figure is moving horizontally in a laptop screening. The ocular response is recorded by an independent video camera placed on the patient’s forehead. After eye automated detection, a simple optical flow algorithm tracks the eye motion, which is characterized by finding the attractors in the velocity-acceleration phase plane.

2.2. Materials and methods

A main aim of the present work is to perform an objective characterization of cerebral palsy. Yet the ocular system is not part of the usual examination, a core of evidence demonstrates many patients develop ocular alterations. The approach herein proposed records the ocular motion during a specific task and tracks the eye by an optical flow algorithm. Motion patterns are further analyzed in the velocity-acceleration space phase.
2.2 Materials and methods

2.2.1. Experimental setup

One subject with cerebral palsy and three control patients participated in this study, these experimental subjects are presented in the table 2-1. A complete description of the procedure was given to child’s parents and an it was obtained an informed consent from them, following the Helsinki convention [97]. Selection criteria were: the patient must be able to sit in a chair, to maintain trunk and head straight, to have cognitive skills and follow instructions.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral Palsy</td>
<td>9 years</td>
</tr>
<tr>
<td>Control 1</td>
<td>4 years</td>
</tr>
<tr>
<td>Control 2</td>
<td>6 years</td>
</tr>
<tr>
<td>Control 3</td>
<td>9 years</td>
</tr>
</tbody>
</table>

Table 2-1: Experimental population

The experimental setup consisted of a 32-inch TV screen, a child helmet and a speed camera. During the experiment, the patient tracks two visual horizontal stimuli with an emoticon shown in figure 2-1: the smooth and the saccadic tasks, being the former a motion in 30 s and the later in 17 s. In addition, the helmet holds a camera Gopro hero session 5 which records the ocular motion at 120 frames s⁻¹.

2.2.2. Experimental protocol

Anthropometric measures define the environment setup during the video capture as illustrated in figure 2-2.

The patient performs the task in front of the TV screen. The sit is placed 80 cm far from the screen, aligning the eyes and mid-line of the screen, as shown in the left panel of figure 2-2. An extension arm, attached to the helmet, maintains the camera out of the visual field, as illustrated in the left panel of figure 2-2. The video capture was synchronized according to the different tasks.

2.2.3. ROI extraction

The region where eyes are located, the Region of Interest (ROI) (figure 2-3), is found using the Viola Jones Algorithm. This method provides an efficient selection of features for the present investigation since it has been reported as a scale-position invariant detector [54].
The Viola-Jones algorithm has been widely used to scan a given input image and detect faces across sub-windows previously set [80]. Briefly, this algorithm classifies input images by computing a set of Haar-like features directly from an intermediate representation, the integral image. The whole processing can be described as a band-pass filtering where the integral image is the low-pass part and the Haar-processing the high-pass processing. Afterwards, given a feature set and a training set of positive and negative examples, a variant of AdaBoost is used to both select the features and to train the classifier [93]. Finally, the cascaded classifier is applied to determine whether or not a given sub-window is an eye.

The Viola Jones method was used to automatically separate the region with eyes, the Region of Interest (RoI), from the face (see Figure 2-3). Nevertheless, this method is sensitive to lighting conditions to capture images and is most effective on frontal images to detect both eyes as well. Taking these drawbacks into account, the experimental procedure is designed to perform video-capture in front of the patient and with adequate illumination.

### 2.2.4. Feature extraction

Once the ROI is obtained, the eye motion is tracked using the Horn-Schunck optical flow algorithm. This optical flow models the apparent motion as the independent motion per pixel between two consecutive frames at times $t$ and $t + \Delta t$, as follows

$$ f(x + \Delta x, y + \Delta y, t + \Delta t) \approx f(x, y, t) $$

where $f(x, y, t)$ is the intensity of the image at position $(x, y)$ and at time $t$, and $(\Delta x, \Delta y)$ is the pixel displacement in the time interval $\Delta t$. The optical flow equation: $\nabla I \cdot P + I_t = 0$, where $\nabla I = (I_x, I_y)$ is the spatial gradient, $P = (z, w) = (\Delta x, \Delta y)$ is the displacement field.

---

1 Each pixel equals the entire sum of the pixel values located to the left and above the pixel.
2.2 Materials and methods

Figure 2-3: Region of interest. (a) Eyes’s patient location and delimitation mask. (b) Eye delimitation and region of interest detection.

and $I_t$ is the temporal derivative [60]. In this work, the Horn Schunck approach perform an optical flow estimation for consecutive frames and the obtained apparent motion presents an oriented pixel-to-pixel and neighbor variation, case in which flow distortions are minimal and the smoothest solutions can be selected[38].

In addition, this method yields a high density of flow vectors, obtaining the flow information from the motion boundaries. Consequently, this algorithm captures small motion details, providing information about slow and rapid eye movements, expected movements to analyze in the children population.

2.2.5. Characterization

From the estimation of velocity vectors resulting from the optical flow method, a calculation of the acceleration vectors is performed, $\mathbf{a} = \frac{d\mathbf{v}}{dt}$. Obtaining in this way an estimation of the tangent velocity and acceleration.

Velocity $\mathbf{v}$ and acceleration $\mathbf{a}$ vectors for each time interval $t$ describe main characteristics of the eye motion during this specific task. Then, the analysis of motion patterns was performed by a metric in the phase plane ($\mathbf{v}, \mathbf{a}$), which represent a vectorial field and the main direction was accumulated in a directional histogram.

The subjects’ histograms were obtained and a quantification of the experiment was performed by measuring differences between histograms with the Chi-Squared $\chi^2$ distance, obtaining the number differences in the eye movement behavior of CP and control subjects.
2.3. Results

This study presents an ocular motion analysis of a group of four patients, three control and one patient in stage 3 according to the GMFCS classification [65]. Since the visual tasks and the video capture were synchronized, the phase planes hereafter presented correspond to the comparison of the same one frame in which the greatest change in velocity is presented in saccadic and smooth pursuit tasks for the whole experimental group.

![Phase planes of one frame corresponding at the end of the smooth task for the whole experimental group. Panel (a) shows the phase plane for the patient with CP while the other three display the three control patients.](image)

**Figure 2-4**: Phase planes of one frame corresponding at the end of the smooth task for the whole experimental group. Panel (a) shows the phase plane for the patient with CP while the other three display the three control patients.

Observe in figure 2-4 how vectorial trajectories are different for the CP patient when compared with the three control patients. This is of course a single observation but the patterns definitely look quite different, while the CP patient evidences a dissociated pattern between both eyes, control patients follow similar trajectories in the plane. This difference may be
attributed to three factors; first, in the detected frame was generated a change in velocity of the eye movement; second, patient attention decreases at the end of the task and third, the strabismus is more notorious when the task demands the oculo-motor system.

Figure 2-5: Phase planes of one frame in the saccadic movement task for different subjects (a) Cerebral Palsy (CP) patient. (b) control patient with four years old. (c) and (d) correspond to the other control patients.

Figure 2-5 illustrates a similar result for a different experimental condition. In this case the task is more rapid and the purpose is to reach a greater exigence level of the oculo-motor system. Observe how the patient with CP presents dissociated trajectories when comparing both eyes, even more dissociated than the previous experiment. Interestingly, one of the subjects is four years, an age in which the oculo-cephalic dissociation has not occurred and his pattern is not different from the others, likely because the saccade movement is quite independent from the central control.

The final analysis with the phase planes was performed by summarizing the main direction run over by the child gaze during the experiment. For so doing, the vectorial field was vector
per vector taken and the main direction was cumulated in a directional histogram. This procedure was repeated along the planes generated at each time and the final histogram summed then up the main directions during the experimental time.

A quantification of the whole experiment was obtained by measuring differences between histograms with the Chi-Squared $\chi^2$ distance. This distance is taken herein from the $\chi^2$ test-statistic where it is used to test how well a distribution fit the observed frequencies[72].

The following tables show this $\chi^2$ metrics during smooth pursuit and saccade tasks.

<table>
<thead>
<tr>
<th>Patient</th>
<th>CP</th>
<th>C1</th>
<th>C2</th>
<th>C3</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP</td>
<td>0</td>
<td>0.3113</td>
<td>0.1338</td>
<td>0.3113</td>
</tr>
<tr>
<td>C1</td>
<td>0.3113</td>
<td>0</td>
<td>0.0527</td>
<td>0</td>
</tr>
<tr>
<td>C2</td>
<td>0.1338</td>
<td>0.0527</td>
<td>0</td>
<td>0.0527</td>
</tr>
<tr>
<td>C3</td>
<td>0.3113</td>
<td>0</td>
<td>0.0527</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2-2: Chi-Square-Right eye during smooth pursuit

<table>
<thead>
<tr>
<th>Patient</th>
<th>CP</th>
<th>C1</th>
<th>C2</th>
<th>C3</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP</td>
<td>0</td>
<td>0.6335</td>
<td>0.7585</td>
<td>0.6335</td>
</tr>
<tr>
<td>C1</td>
<td>0.6335</td>
<td>0</td>
<td>0.1695</td>
<td>0</td>
</tr>
<tr>
<td>C2</td>
<td>0.7585</td>
<td>0.1695</td>
<td>0</td>
<td>0.1695</td>
</tr>
<tr>
<td>C3</td>
<td>0.6335</td>
<td>0</td>
<td>0.1695</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2-3: Chi-Square-Left eye during smooth pursuit

For smooth pursuit task, the histogram distances values are presented in tables 2-2 and 2-3 for both eyes. The distances for saccadic visual task are shown in tables 2-4 and 2-5. The results in both tasks exhibit high distances values between CP and controls. In contrast to low distances values are found among controls.

<table>
<thead>
<tr>
<th>Patient</th>
<th>CP</th>
<th>C1</th>
<th>C2</th>
<th>C3</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP</td>
<td>0</td>
<td>0.1484</td>
<td>0.0878</td>
<td>0.1484</td>
</tr>
<tr>
<td>C1</td>
<td>0.1484</td>
<td>0</td>
<td>0.0089</td>
<td>0</td>
</tr>
<tr>
<td>C2</td>
<td>0.0878</td>
<td>0.0089</td>
<td>0</td>
<td>0.0089</td>
</tr>
<tr>
<td>C3</td>
<td>0.1484</td>
<td>0</td>
<td>0.0089</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2-4: Chi-Square. Right eye during saccades

<table>
<thead>
<tr>
<th>Patient</th>
<th>CP</th>
<th>C1</th>
<th>C2</th>
<th>C3</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP</td>
<td>0</td>
<td>0.5447</td>
<td>0.5210</td>
<td>0.5056</td>
</tr>
<tr>
<td>C1</td>
<td>0.5447</td>
<td>0</td>
<td>0.0013</td>
<td>0.0022</td>
</tr>
<tr>
<td>C2</td>
<td>0.5210</td>
<td>0.0013</td>
<td>0</td>
<td>0.0005</td>
</tr>
<tr>
<td>C3</td>
<td>0.5060</td>
<td>0.0022</td>
<td>0.0005</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2-5: Chi-Square. Left eye during saccades

These number data show the differences between the eye movement behavior in both tasks for subjects. From these results a qualitative and quantitative difference is presented in the CP patient ocular movement behavior compared to controls during experiments, where an unstable eye movement behavior is identified in cerebral palsy by analyzing ocular motion characterized in the velocity-acceleration phase plane.
2.4. Conclusions

In this exploratory work, an automatic characterization of cerebral palsy is proposed. This method performs an analysis of ocular movement patterns through phase planes describing ocular motion velocity and acceleration. In the clinical context, a better ocular motor control is characterized by trajectories defined and parallel to each other in the direction of the visual objective. Therefore, they would become indicators of the quality of movement and the fulfillment of the visual task. Future work will be performed on a larger sample of patients with CP and controls.
3 Ocular Control Characterization of Motor Disabilities: the Cerebral Palsy Case

This chapter presents an automatic estimation of the ocular motion, an evaluation that might be extended to any kind of motor disorder. Visual patterns are quantified when challenging the ocular motor system by smooth and saccadic gaze tasks. The motion field obtained by a customized optical flow is characterized by velocity histograms of magnitude and orientation. The temporal result is accumulated in a histogram and a correlation distance between histograms quantifies the differences between subjects. Evaluation results showed significant differences between two CP and control groups constituted by 16 subjects each. This work introduces actual quantification of a prevalent disease whose evaluation and treatment so far if fully dependent on the examiner expertise. A complete version of this chapter has been accepted for publication as a research article in the SaMBa: Sipaim - Miccai Biomedical Workshop, September 2018.
3.1. Introduction

According to the World Health Organization, 10% of the population has some type of disability and 80% lives in developing countries. In Latin America and the Caribbean, that figure would correspond to 85 million people [91]. In Colombia, there are about two and a half million people (6.3% of the population) with some permanent limitation [52]. Cerebral palsy (CP) describes a group of permanent disorders characterized by some kind of movement and posture abnormality, causing an activity limitation attributed to fetal or infant brain non-progressive disturbances [78]. CP is considered the most common cause of physical disability in childhood [33, 4, 52, 52]. CP is a highly cost disease, e.g., according to the Center of Disease Control and Prevention (CDC) a patient lifetime expenses may reach US 1.000.000 per CP patient [30].

This disease often presents dysfunction of the visual system [73]. Between 50-90% of patients with this condition shows visual problems, including refractive errors, strabismus, nystagmus, and amblyopia as well as cortical visual impairment [68], at rates far exceeding those detected in neurologically normal children [33][15][73]. CP diagnosis is currently based on both clinical observation and qualitative assessment of the degree of motor development [48].

Treatment for Cerebral Palsy based on qualitative assessments entails therapeutic challenges as formulating an individualized treatment plan according to the needs of each child [42]. Qualitative assessment generates variability among the experts to determine the best treatment for the patient; likewise the treatment is also evaluated subjectively, which may vary evaluation of the patient’s evolution.

For this reason, there is a need to optimize treatment strategies for individual patients in order to lead to lifelong improvements in function and capabilities [62]. Quantification of clinical assessment could support treatment strategies for individual patients.

3.2. State of the art

Few studies have tried to measure CP visual impairment because of the large intra and inter-examiner variability. There exists a limited number of works that quantify the ocular movement in CP.

Several studies have been devoted to characterize CP eye movements. Ghasia et al. [33] carried out an observational study by performing ophthalmic and neurologic examinations, finding that visual deficits differ between mild and severe CP. Barca et al. [7] evaluated oculomotor function in children with CP by ophthalmological and orthoptic assessments. These authors reported most children (97%) showed visual disturbances. Black et al. [12] clinically examined visual defects in various types of CP and informed children with this condition show higher incidence of ocular abnormalities. Dufresne et al. [24] introduced an statistical analysis based on parents’ interview, clinical history, interpretation of neuroimaging data and visual observation of the patient stage. These studies agree about most CP patients
present some degree of visual disturbances but none of them somehow quantify it.

On the other hand, some investigations have tried to quantify eye motion. Illavarason et al. [41] report improvement of Visual Evoked Potentials (VEP) in a group of 25 CP patients before and after therapy, yet their results were not compared with a control group. Ego et al. [25] recorded horizontal eye movements of the dominant eye using an infrared eye tracker (Eyelink 1000). Different smooth and saccadic visual tasks determined the performance of the CP patients and the control subjects. This work demonstrated CP ocular control improves with age. Nevertheless, this study failed at analyzing the binocular movement which is usually altered in CP. Kooiker et al. [47] proposed a method to quantify visual information by measuring visual orienting responses with an integrated infrared eye-tracking system (Tobii T60-XL). They evaluated the evolution in two different sessions and reported improvement in 80% of the CP children.

Other studies characterize the disease using eye tracking technologies. For example, Wong et al. [95] explore correlations between eye movement parameters with cognitive functions in Parkinson patients using an eye tracking device, obtaining ocular patterns in specific tests such as mean saccadic amplitude and mean fixation duration, both highly correlated with the cognitive decline in Parkinson's disease. Likewise, different studies perform ocular quantification using this type of technology. For example Schmidt et al. [84] and Hunt et al. [40] present a study of ocular motion in Parkinson's disease. Hong et al. [37] analyzed the eye gaze and pupillary response. A complete review of it can be found in Harezlak et al. [36]. However, these studies present a high susceptibility to the calibration process that is required to control the position of the eyes and calculate the direction of the gaze on a visual stimulus.

The main contribution of this work is an automatic characterization of the ocular motion that might be extended to any kind of motor disorder, performing an reliable quantification of a prevalent disease. This method gives a quantitative assessment that may contribute clinicians to perform a follow-up of the patient to provide a treatment according to the condition of each patient - personalized treatment.

### 3.3. Materials and Methods

#### 3.3.1. Participants

Thirty two participants were involved in this research. Sixteen patients with CP and sixteen control children aged between 2 and 15 years. Participants were selected to constitute a study cohort depicted in the table 3-1. They were compared by age and gender, with twenty males and twelve females, showing a homogeneous group. Some characteristics of the CP group can be seen in table 3-2 including the GMFCS (Gross Motor Function Classification System) [65] level, which is used to characterize the functional severity of CP patients.
3.3 Materials and Methods

<table>
<thead>
<tr>
<th></th>
<th>CP group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td><strong>Num. participants</strong></td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td><strong>Age[years]</strong></td>
<td>6.9 ± 3.4</td>
<td>9.4 ± 3.2</td>
</tr>
</tbody>
</table>

Table 3-1: Experimental population

<table>
<thead>
<tr>
<th>GMFCS</th>
<th># CP patients</th>
<th>Age[years]</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>1</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Level 2</td>
<td>1</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>Level 3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Level 4</td>
<td>4</td>
<td>9.7 ± 3.4</td>
<td>1</td>
</tr>
<tr>
<td>Level 5</td>
<td>10</td>
<td>6.9 ± 3.5</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 3-2: CP group general characteristics

Selection process for CP cohort was performed taking into account following criteria: the patient must be able to sit in a chair, to maintain trunk and head with or without support, to follow instructions and to have cognitive skills.

CP participants belong to RIIE Rehabilitation Center in Bogotá, Colombia. Informed consents were obtained from the volunteers during the research, following the Helsinky convention [97], in which a complete description of the procedure was given to child’s parents.

3.3.2. Acquisition

Two horizontal visual tasks were designed to attract patient’s visual attention with the help of moving emoji as object in Fig. 3-1. A video capture of ocular motion is recorded with a medium speed camera (120fps) hold in a helmet.

As studied population were children, a simple emoji was used to attract patient’s attention by moving it over a black background (Fig. 3-1). Two tasks were evaluated: for the pursuing task, the emoji moved smoothly and horizontally over the background in a video of 30 s. While for the saccadic task, the emoji changed its position spontaneously in a video of 17 s. The horizontal ocular movement was chosen being this the easiest eye movement to control due to from the anatomical base the medial and lateral rectus muscles form an antagonistic pair that controls the horizontal position of each eye[76]. From which visual tasks were designed to evaluate the saccadic and smooth pursuit systems in the horizontal direction of the eye movement. These systems constitute most gaze-shifting mechanisms, where the smooth pursuit system allows the fovea to track a moving target as it slides across a stationary background and in the saccadic system gaze rapidly shifts from one point to another[76].
Performing the analysis of the ocular movement behavior of these two visual tasks, it is possible to find distinctive patterns for each experimental group (CP and Control).

### 3.3.3. Experimental setup

A 32-inch screen, a child helmet and a speed camera were used for the experimentation. The helmet hold a GoPro Hero Session 5 camera which recorded the ocular motion at 120 fps. Anthropometric measures were taken into account to define the environment setup parameters during the video capture.

The patient was located in front of the screen to perform the task. The sit was placed 80 cm far from the screen, aligning the eyes and mid-line of the screen. An extension arm, attached to the helmet, maintained the camera out of the visual field. In the experimental protocol, video capture and the visual tasks were synchronized for the ocular motion evaluation with all the participants.

### 3.3.4. Preprocessing

Viola Jones’ Algorithm [93], is automatic detection system[94] widely used in facial and eye detection[92]. We used it to detect and get a ROI associated to the eyes. Then, a morphological reconstruction method [53] is applied on each ROI to automatically delimit the eye and thus obtain the ROI to be analyzed (Fig. 3-2). This is performed just in one frame in the video (where subject has both eyes opened) and then applied to the rest of the video; this given that as the camera is fixed the ROI does not change over the rest of the video.

### 3.3.5. Motion description

From the detected region, the ocular motion is tracked using the optical flow approach. This method models the apparent motion as an independent per pixel motion between two consecutive frames at times $t$ and $t + \Delta t$, as follows: $f(x, y, t) \approx f(x + \Delta x, y + \Delta y, t + \Delta t)$
3.4 Results

Figure 3-2: Face and eye detection is performed by using Viola Jone’s algorithm (a). Morphological reconstruction allows to refine the ROI (b).

where $f(x, y, t)$ is the intensity of the image at position $(x, y)$ and at time $t$, and $(\Delta x, \Delta y)$ is the pixel displacement in the time interval $\Delta t$. Optical flow equation is then obtained:

$$\nabla I \bullet P + I_t = 0$$

where $\nabla I = (I_x, I_y)$ is the spatial gradient, $P = (\Delta x, \Delta y)$ is the displacement field and $I_t$ is the temporal derivative. [60] This equation relates the velocity to the space-time image derivatives at one image location [31]. The Lucas-Kanade method [69] solves the basic optical flow equations by a least squares criterion. This algorithm provides an estimate of the movement of interesting features in successive images of a scene.

3.3.6. Motion histogram

Magnitude and orientation histograms are computed from the obtained velocity vectors along the time for each visual task. Histograms display the relative frequency of velocity data values and its temporal distribution. Blinks that correspond to velocity vectors between $75^\circ$ to $105^\circ$ and $255^\circ$ to $285^\circ$ were discarded from the analysis since their characteristics are very similar to those of saccadic eye movements and can affect a robust eye movement analysis.[16]

3.4. Results

Velocity histograms characterized the ocular movement during the smooth pursuit and saccadic visual tasks in all participants. Estimation of relative ocular motion among the participants was performed by measuring the distance between velocity histograms using the cosine distance [88] as a measure of similarity. This measure indicates how close two histograms in the same direction are by performing a dot product between the two histograms. Velocity magnitudes are hereafter shown for the two pursuit task:
Figure 3-3: Box plots of the velocity magnitude for the CP group (blue boxes) and Control group (red boxes). Panels (a) and (b) show the box plots for smooth pursuit and saccadic tasks.

Fig. 3-3 shows the obtained histogram distances corresponding to the velocity magnitude during both tracking tasks: smooth and saccadic for the CP and control groups (R and L conventions stand for right and left eye). Basically, this plot is showing how variable the velocity is during the particular task. It is observable the largest variability of the CP group for the smooth task, probably meaning that this pursuit task requires a more exigent control which starts to be lost by the CP group. In contrast, these differences are less clear for the saccadic task, likely because the level of control required in such situation is much less important.

Likewise, the distance between orientation histograms is plotted in fig. 3-4 for both visual tasks. In each figure, the experimental groups are referred by their abbreviation: CPR - Right eye in Cerebral Palsy group, CPL - Left eye in Cerebral Palsy group, ConR - Right eye in control group and ConL - Left eye in control group.

On the other hand, figure 5a the box plots of the distances between histograms of orientations. A first remarkable observation is that the CP group shows a largest data scattering, an observation attributed to the lose of visual control in this patient. In contrast with the magnitude estimation, this difference is also observed for the saccadic task.

Wilcoxon test was applied to compare the two experimental groups: CP and control. Magnitude comparison (right and left eyes) using this test shows statistically significant differences ($p < 0.05$) in the smooth pursuit task. These statistical differences were not obtained for the saccadic task (both eyes). Likewise, orientation distances were also evaluated and they showed to be significant ($p < 0.01$) for both visual tasks.
3.4.1. Discussion

This work has introduced an automatic ocular motion characterization of the Cerebral Palsy. Our results demonstrate it was possible to identify quantifiable differences between CP and control groups during eye tracking of two visual tasks. These results also showed significant differences between the CP and Control groups. They were however more evident in the smooth pursuit visual task. In contrast, the saccadic task limited the expression of the control system since the fixation mechanism was challenged during few moments of the visual task, basically a couple of acceleration and decelerations to track the target. The orientation evaluation showed larger differences between the two groups. It is very likely this type of tasks is more challenging for the control system and eventually a quantitative scale that objectively can follow-up the treatment for each patient with CP.

3.5. Conclusions

This work presents an automatic ocular motion characterization of Cerebral Palsy. The proposed method employs the optical flow and challenges the ocular control system with gaze pursuing tasks. The results show oculomotor control limitations in CP children. This quantitative and objective measurement may support clinicians to perform a follow-up of the patient and provide a personalized treatment.
4 Conclusions and future work

4.1. Conclusions

This thesis work develops a method to automatically characterize the ocular motion during a gaze pursuing task in the cerebral palsy population. It has been established under two approximations. In the first one, it was performed a pattern identification in ocular motion. In this, an analysis of eye motion is characterized through velocity-acceleration phase planes, finding differences between the subjects. Howbeit, this approach presented some limitations such as the small sample of patients evaluated and the lack of analysis along the time of each visual task, to carry out a reliable assessment of the ocular motion. A second approximation was developed applying the same video capture and processing images steps as the first approximation. Considering the preceding approach, some improvements are made: it is employed a greater sample of patients, and visual patterns are quantified through by velocity histograms of magnitude and orientation. Finally, these histograms were computed along the time for each visual task, finding quantitative differences between subjects. The results obtained in this work demonstrated that it was possible to identify quantifiable differences between CP and control groups during eye tracking of two visual tasks, evidencing oculomotor limitations in the CP children.

In this way, our approach aimed to study two specific visual eye movements accepting the magnitude and orientation information to characterize cerebral palsy. This study presents some limitations such as the reduce sample size, the necessity of other clinical assessments, such as cognitive assessments, to better characterize the sample and which could have influenced the results. However, the strength of our study include that may serve as a quantitative and objective clinical assessment, providing to the clinicians valuable information about the follow-up of the treatment in CP children, being a complementary tool to comprehend the clinical picture of CP. Likewise, in this study, the use of eye movement recordings could bypass the use of affected limbs in characterizing the development of these children.

Finally, this is a reliable tool due to it allows an objective measurement of the oculomotor function which reduces the subjectivity, and the implementation of this evaluation is accessible to the clinical setting.
4.2 Future Work

This work thesis has contributed to the construction of a quantitative tool for measuring the oculomotor function in Cerebral Palsy, providing a reliable assessment that could support the construction of an optimal management plan in the treatment of each patient. A quantitative clinical tool for CP children decreases the subjectivity when monitoring the improvement during the rehabilitation process. In this sense, as future work, a longitudinal study will be carried out to perform a follow-up of the same patients with Cerebral Palsy in order to measure and quantify their performance improvement during the therapeutic treatment. In addition, a different metric will be employed to analyze as the oculomotor control of the patients as to quantify their improvement. Likewise, it could contribute to the research of the relationship between oculomotor control with motor impairments and generate a tool table to contribute to the early and timely CP diagnosis.

In the other hand, our work presents an analysis based on binocular recordings. Nevertheless, the study of the conjugate eye movements could also be explored, due to ocular abnormalities, such as strabismus and nystagmus, that are also altered in Cerebral Palsy[35, 21, 41].
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Glossary

**Accommodative dysfunction:** condition in which the amplitude of accommodation is less than expected for a non presbyopic patient’s age. Associated signs and symptoms are usually related to reading and other close work activities and include blurred vision at near, intermittent blurred vision when looking up from near work, headaches, watering or burning of the eyes, tired eyes, loss of concentration, and avoidance of near activities.

**Accommodation:** mechanism by which the eye changes focus from distant to near images, is produced by a change in lens shape resulting from the action of the ciliary muscle on the zonular fibers.

**Anamnesis:** information (subjective data: family and personal history, signs and symptoms of the health problem, experiences, memories) provided by the patient to the health professional during a clinical interview, to analyze their clinical situation and shape the clinical history.

**Ballistic:** has properties similar to the trajectory of a thrown projectile. It is applied to the saccades movements and to the rapid phase of the movements of vergence.

**Convergence:** simultaneous inward movement of eyes toward each other.

**Developmental milestones:** set of functional skills or age-specific tasks that most children can do at a certain age range.

**Encephalopathy:** any diffuse disease of the brain that alters brain function or structure. Encephalopathy may be caused by infectious agent (bacteria, virus, or prion), metabolic or mitochondrial dysfunction, brain tumor or increased pressure in the skull, prolonged exposure to toxic elements (including solvents, drugs, radiation, paints, industrial chemicals, and certain metals), chronic progressive trauma, poor nutrition, or lack of oxygen or blood flow to the brain.

**Electro-oculography:** electrophysiological test based on the principle of variations of the corneo-retinal rest potential in the displacements of the eyeball. These variations give rise to an electrical current of weak intensity, which, after its amplification, can proceed to its graphic recording. The result is the generation of permanent potentials by the activity of the chorioretina.

**Fixation:** maintaining of the visual gaze on a single location. To maintain visibility, the nervous system carries out a mechanism called fixational eye movement, which continuously stimulates neurons in the early visual areas of the brain responding to transient stimuli. Ocular fixation is
a dynamic process that is actively controlled by many of the same brain structures involved in the control of eye movements, including the superior colliculus, cerebellum and reticular formation.

**Fovea:** tiny depression located in the center of the macula. It has an extension of 0.4 mm in diameter, in equivalence with central 1.5°. This depression mirrors in youth, and this phenomenon is known as foveolar reflex. It is the thinnest part of the macula because there are no internal layers of the retina (internal nuclear, internal plexiform, ganglion cells and optical fiber layer).

**Gaze:** sum of eye and head movements, whereas target movement in space has to be reconstructed by adding retinal image movement, eye and head movements.

**Hyperbilirubinemia:** an elevated level of the pigment bilirubin in the blood. A sufficient elevation of bilirubin produces jaundice. Some degree of hyperbilirubinemia is very common right after birth, especially in premature babies.

**Microsaccades:** saccades, involuntarily produced during fixation periods. They are the largest and fastest of the fixational eye movements. Like saccades, microsaccades are usually binocular, and conjugate movements with comparable amplitudes and directions in both eyes.

**Nystagmus:** Syndrome pertaining to alteration of the ocular statics, characterized by rhythmic, repetitive movements, and conjugates of the eyes, of opposite direction, with a phase of going and another of return, realized of involuntary and, normally, bilateral form, that, without altering nor disturb the ocular physiological movements, make it difficult in a remarkable way the foveolar fixation capacity of the objects that we look at in space.

**Optic atrophy:** death of the retinal ganglion cell axons that comprise the optic nerve with the resulting picture of a pale optic nerve on funduscopy. Optic atrophy is an end-stage that arises from myriad causes of optic nerve damage anywhere along the path from the retina to the lateral geniculate. Since the optic nerve transmits retinal information to the brain, optic atrophy is associated with vision loss.

**Periventricular leukomalacia (PVL):** represents a major precursor for neurological and intellectual impairment, and cerebral palsy in later life. The disorder is characterized by multifocal areas of necrosis found deep in the cortical white matter, which are often symmetrical and occur adjacent to the lateral ventricles.

**Ptosis:** medical name for the drooping of the upper eyelid, which can happen in one or both eyes. Ptosis can either be present at birth (congenital), or appears later in life (acquired), following long-term contact lens wear, trauma, after cataract surgery or other eye operations.
Refractive anomalies: disorders of shape and size determined by inheritance and growth. Correct refraction depends on the distance between the cornea and the retina and its relation with the curvatures of both the cornea and the lens. The three common disorders of refraction are hypermetropia (long sight), myopia (short sight), and astigmatism - which may exist on its own or in combination with either myopia or hypermetropia.

Saccades: quick, ballistic, simultaneous movements of both eyes between two or more phases of fixation in the same direction. Controlled cortically by the frontal eye fields (FEF), or subcortically by the superior colliculus, saccades serve as a mechanism for fixation, rapid eye movement, and the fast phase of optokinetic nystagmus. The largest saccades (excluding the contributions of head movements) can be up to 100 degrees, with a duration of up to 300 milliseconds and a maximum velocity of about 500–700 degrees per second.

Smooth pursuit eye movements: slower tracking movements of the eyes designed to keep a moving stimulus on the fovea. Such movements are under voluntary control in the sense that the observer can choose whether or not to track a moving stimulus. The pursuit of targets moving with velocities of greater than 30°/s tends to require catch-up saccades.

Vergence: disconnected or disjunctive binocular movement, induced exclusively by visual stimuli, in which the ocular axes deviate in the opposite direction to be able to fix the inductive stimulus at different distances, matching the images of the two eyes to avoid diplopia.

Visual field: total area of the space that covers the vision of an eye staring at a specific point. The normal limits are: 60th nasal, 100th temporal, 60th higher, 75th lower.

Visual evoked potential: evoked potential caused by a visual stimulus, such as an alternating checkerboard pattern on a computer screen. Responses are recorded from electrodes that are placed on the back of your head and are observed as a reading on an electroencephalogram (EEG). These responses usually originate from the occipital cortex, the area of the brain involved in receiving and interpreting visual signals.