Ocular Metrics in Concussion: An Analytical Prospective Cohort Study to Establish Normative Ocular Metrics in a Healthy Sporting Population

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List of Abbreviations

SRC   Sports Related Concussion

CISG   Concussion in Sport Group

IOC   International Olympic Committee

FIFA   Federation Internationale de Football Association

F-MARC   Federation Internationale de Football Research Centre

IIHF   International Ice Hockey Federation

SIS   Second Impact Syndrome

CTE   Chronic Traumatic Encephalopathy

OCT   Optical Coherence Tomography

AE   Athlete Exposure

AFL   Australian Rules Football

GAA   Gaelic Athletic Association

EAAs   Exititatory Amino Acids

NMDA   N-Methyl-D-Aspartate

AMPA   D-amino-3-Hydroxy-5-Methyl-4-Isoxazoleproprionic Acid

ATP   Adenosine Triphosphate

CBF   Cerebral Blood Flow

mTBI	Mild Traumatic Brain Injury
MRI	Magnetic Resonance Imaging
DTI	Diffusion Tensor Imaging
DAI	Diffuse Axonal Injury
FA	Fractional Anistrophy
CNS	Central Nervous System
M.S.	Multiple Sclerosis
cSP	Cortical Silent Period
CANTAB	Cambridge Neurophysiological Test Automated Battery
SCAT	Sport Concussion Assessment Tool
ImPACT	Immediate Post-Concussion Assessment and Cognitive Test
VOMS	Vestibular/Ocular Motor Screening
WHO	World Health Organisation
CT	Computed Tomography
KD	King Devick
MMA	Mixed Martial Arts
NPC	Near Point Convergence

VOR   Visual Ocular Reflex

VMS   Visual Motion Sensitivity

FEI   International Federation for Equestrian Sports

SAC   Standardised Assessment of Concussion

PCSS   Post Concussion Symptom Scale

GCS   Glasgow Coma Scale

mBESS   Modified Balance Error Scoring System

SSS   Symptom Severity Score

fMRI   Functional Magnetic Resonance Imaging

SS-OCT   Swept Source OCT

RNFL   Retinal Nerve Fibre Layer

GCL++   Ganglion Cell Layer ++

ILM   Inner Limiting Membrane

INL   Inner Nuclear Layer

IPL   Inner Plexiform Layer

SD-OCT   Spectral domain Optical Coherence Tomography

ROC   Receiver Operating Characteristic

HIA	Head Injury Assessment
GCC	Ganglion Cell Complex
OPP	Ocular Perfusion Pressure
HR	Heart Rate
mBP	Mean Blood Pressure
IOP	Intra-Ocular Pressure
GAT	Goldmann Applanation Tonometer
RBT	iCARE Pro Rebound Tonometer
SPSS	Statistical Package for Social Sciences
SEM	Standard Error of the Mean
MDC	Minimal Detectable Change
ICC	Intra-Class Correlation Coeffiicient
MSS	Maximal Sprint Speed
NMT	Non-Motorised Treadmill
ETDRS	Early Treatment Diabetic Retinopathy Study

Abstract

Title: Ocular Metrics in Concussion: An Analytical Prospective Cohort Study to Establish Normative Ocular Metrics in a Healthy Sporting Population.

Introduction: Concussion diagnosis is a clinical challenge for healthcare providers. Identification of concussion is presently aided by tools such as the Sport Concussion Assessment Tool (SCAT3); such tools remain largely subjective in nature. There is currently no objective gold standard for concussion diagnosis. The overall aim of this study was to investigate potential objective ocular bio-markers for the purpose of concussion diagnosis. The ocular tools employed in this study were the iCare Pro rebound tonomoter (RBT), which measures intraocular pressure (IOP), Topcon OCT-DRI triton plus, which measures thickness of various retinal layers, and the SCAT3. The research was split into 3 component, complimentary studies. 1. iCare pro rebound tonometer reliability study. 2. Effects of Exercise on ocular metrics. 3. The effects of concussion on ocular metrics.

Methods: Intra-rater reliability of the RBT was established in a single session in a standing position in 31 male and female particpants. Mean IOP±SD(mmHg), standard error of the mean (SEM), minimum detectable change (MDC) and Intra-class correlation coefficients (ICC's) were calculated for both left and right eyes. The effects of exercise on IOP and OCT values were established using a simulated team-sport running protocol in 11 male and female participants. Mean±SD values of IOP(mmHg) and OCT measures of RNFL, GCL++ and Choroidal thickness(μm) were established pre-exercise and follow up measures taken 2-minutes and 10-minutes following exercise. Normative values for SCAT3 measures and OCT measures of RNFL and GCL++ thickness(μm) were established for 151 male and female team sport athletes. The effects of concussive injury on these measures were established in 3 individual case studies.

Results: Fair/Acceptable intra-rater reliability of the RBT was established (ICC's 0.771 and 0.753 in left and right eyes respectively). There was a minimal thinning effect of exercise on RNFL, there was a thickening effect of exercise on GCL++, there was an initial thinning effect of exercise on the choroid, followed by a return toward baseline thickness. There was a similar response in IOP. IOP and choroidal responses to exercise were positively and strongly correlated (R = 0.948 and R = 0.786 in left and right eyes respectively). There were some gender differences with regard to the subjective SCAT3 elements. There were no significant differences in RNFL with regard to gender, sport or history of concussion. Males displayed a significantly thicker superior temporal GCL++ sector in the left (P = 0.012) and right eyes (P = 0.007). SCAT-3 symptom scores increased following concussive injury and improved in the days following injury. There were minimal OCT findings in the small number of case studies observed.

Conclusion: A sports medicine professional with minimal ophthalmic training can obtain acceptable reliability with the RBT. Further research is needed to establish reliability over a number of days. This is the first study to establish the effects of exercise on ocular metrics in team sport athletes, further research is warranted with an increased sample size. Gender must be taken into account when interpreting SCAT-3 symptom scores. SCAT-3 scores of SAC and mBESS along with RNFL and GCL++ thickness are interchangeable within this cohort. The study was limited by the lack of follow-up data, future research is needed with an increased sample size.

CHAPTER ONE:
Introduction

The word concussion originates from the Latin word *concutere,* which means to 'shake violently' (Maroon *et al.*, 2000). Sports related concussion (SRC) has garnered attention in the sporting, media and scientific communities in recent years. In 2001, the concussion in sport group (CISG) was formed, it was made up of an expert panel appointed by the International Olympic Committee (IOC), Federation Internationale de Football Association and Reseach Centre (FIFA, F-MARC) and the International Ice Hockey Federation (IIHF). The CISG held its' first meeting in Vienna, 2001. The CISG produced a consensus statement with the aim of informing and providing recommendations for healthcare professionals with regard to concussion in the sporting environment. This statement encompassed the evaluation, management, prevention, education and future directions for concussion management (Aubry *et al.*, 2002). Since the inaugural consensus statement in 2001, subsequent CISG meetings have been held every 4-years. Following the 2nd CISG meeting, a 'Sport Concussion Assessment Tool' (SCAT) has been developed from each meeting. The latest consensus meeting in Berlin 2016 updated the definition of concussion, stating that a SRC is "a traumatic brain injury, caused by biomechanical forces", as such, the injury may be induced by a direct blow to the head or by an impact to another body part, from which the resultant forces are transferred to the brain (McCrory *et al.*, 2017a). SRC involves short-term neurological dysfunction immediately following the inciting incident with some signs and symptoms often taking minutes to hours to manifest (McCrory *et al.*, 2017a). Symptoms of concussion include, headache, nausea, memory and attention impairments, behavioural changes, unsteadiness and irritability to name a few (Barkhoudarian *et al.* 2011). It is now acknowledged that repeated concussive insults and an accumulation of sub-concussive blows may lead to devastating, long-term and potentially fatal health complications such as second impact syndrome (SIS) and chronic traumatic encephalopathy (CTE) (Bowen 2003; Omalu 2014).

Concussion diagnosis remains a clinical decision for healthcare providers, and is guided by predominantly subjective and performance-based tools such as the SCAT, VOMS, King Devick and ImPACT (Maroon *et al.,* 2000; McCrory *et al.*, 2017b; Mucha *et al.,* 2014, Leong *et al.,* 2015). The World Health Organisation (WHO) define a biomarker as "any substance, structure or process that can be measured in the body or its' products and influence or predict the incidence or outcome of disease" (WHO, 2001). There is currently no accepted diagnostic biomarker for concussion (Makdissi *et al.*, 2015). It is evident that such a biomarker would be of huge benefit to the wellbeing of athletes of all ages with regard to concussion diagnosis.

Neuro-ophthalmic findings such as photosensitivity (sensitivity to light), as well as abnormalities in vestibular-ocular reflex (the maintenance of stable vision during head movmement), saccadic eye movement (quick, concurrent movement of both eyes between two or more points) and smooth pursuit (smooth, continuous movement of both eyes between points) have emerged as manifestations of concussion in recent years (Ventura et al. 2015). These findings clearly warrant the eye as a potential site for objective concussion manifestation. Optical Coherence Tomography (OCT) is a technology that allows for *in vivo* subjective and objective analysis of the structures of the eye, specifcally the various layers of the retina. Due to the fact that there are neuro-ophthalmic findings in concussion, it is logical to explore the possibility of acquired structural changes *via* OCT analysis. However, if such a measure is to be utilised in a team sport scenario, the effects of the demands of team sport activity on such metrics must be established. Intra Ocular Pressure (IOP) is another ocular metric, defined as the pressure of the contents inside the eyeball (Murgatroyd and Bembridge, 2008). It has previously been postulated that the autonomic nervous system may have a regulatory effect on IOP (Najmanova *et al.*, 2018), changes in which may manifest as a result of concussive injury. The effects of exercise on IOP have been previously reported, with conflicting findings depending on the type of exercise (Roddy *et al.,* 2014; Huang, 2015). The effects of team sport running demands on OCT or IOP have not yet been established. The reliability of various devices that measure IOP has previously been well

established in a seated posture as measured by ophthalmic professionals (Kim *et al.*, 2013; Martinez-De-La-Casa *et al.*, 2005; Sahin *et al.*, 2007; Salim *et al.*, 2013) however, the reliabillity of this device in a standing posture, which is more applicable to a sporting scenario has not yet been established.

The symptoms of concussion are numerous, varied, often subtle and may evolve over time. This poses a difficult challenge to healthcare providers regarding the accurate recognition, diagnosis and management of concussion. A validated and reliable objective outcome measure that could identify concussion would be invaluable to both healthcare providers and athletes.

CHAPTER TWO:
Literature Review

2.1 – Prevalence and Incidence of Concussion

The prevalence of concussion has risen in recent years. According to the England Rugby Injury Surveillance Project 2013 - 2014 the prevalence of concussion doubled from 5.2/1000 match hours between the 2002 and 2013 seasons to 10.5/1000 match hours in the 2013 - 2014 season (England Professional Rugby Injury Surveillance Project Steering Group 2015). Interestingly, although the concussion prevalence rate increased over this period, the overall injury prevalence has remained relatively stable according to the same report (England Professional Rugby Injury Surveillance Project Steering Group 2015). This disparity between concussion and overall injury rates may be attributed to an increase in media attention, concussion awareness campaigns and an increased availability of clinical and pitch-side tools in recent years, causing an increase in recognition of the injury rather than due to a true increase in rates of concussion. Lincoln *et al.,* (2011) carried out a study examining the trends in concussion in 12 high-school sports in the USA over an 11-year period from 1997 – 2008. Over the course of the study, the overall concussion incidence per 1000 athlete exposures (AEs) increased 4.2 fold from 0.12/1000 AEs to 0.49/1000 (Lincoln *et al.,* 2011). One AE was defined as 1 athlete's participation in either training or competition (Lincoln *et al.,* 2011) These findings are similar to the results from the England Rugby Surveillance Project. Lincoln *et al.,* (2011) suggest that an increased awareness and improved concussion guidelines may be the reason for the increased reported incidence of concussion over the course of the study. In light of the above, it may be possible that historically, incidence rates of concussion may have been underreported. It is vital to the health of sportspeople that concussion is recognised, reported and managed appropriately across all sporting disciplines.

Table 2.1 below outlines the concussion incidence rates documented over the past 7 decades for Rugby, Boxing, Soccer and Austrailian-rules football (AFL) among others. The incidence rates per 1000 hours in each respective sport outlined in table 2.1 range from 0.2/1000 hours in soccer (Koh *et al.,* 2003) to 13.8/1000 hours in Rugby (Moore *et al.*, 2015), a considerable difference, which is unsurprising considering the high impact nature of rugby.

One study reported the incidence rates as per 1000 AEs, american football (0.5/1000 AEs); Ice Hockey (1.2/1000 AEs); Lacrosse and Wrestling (0.2/1000 AEs); Basketball, Field Hockey, Softball, Baseball and Cheerleading all (0.1/1000 AEs) and Volleyball (0.05/1000 AEs) [Pfister *et al.,* 2016]. The main finding from the studies represented in table 2.1 below is that rugby consistently displays the highest incidence rate when compared with other sports.

Table 2.1 – Concussion Incidence Rates in Sport

Author	Number of Studies/Participants Included	Study Type	Sport	Timeframe (Years Duration)	Incidence Rate/1000 Hours	Incidence Rate/1000 Athlete Exposures (AEs) or Alternate unit of measure
Koh *et al.*, (2003)	23 Studies	Systematic Review	Boxing	1982 - 1984 (2)		0.8/10 Rounds
				1983 – 1985 (2)	2.4	
				1992 – 1993 (1)		7.9/1000 Man-Minutes
			Rugby	1950-1979 (29)	1.0	
				1979 (1)	2.9	
				1979, 1980, 1982 (3)	2.5	
				1979 (1)	2.9	
				1989 – 1991 (2)	1.6	
				1990 – 1994 (4)	8	
				1996 (1)	9	
			Soccer	1995 – 1997 (2)	0.2	
Gardner *et al.*, (2014)	96 Systematic Review 37 Meta-Analysis	Systematic Review and Meta-Analysis	Rugby Union	Up to 2014	4.7 – Men	
					0.6 - Women	

Table 2.1 Continued

Author & Year	Number of Studies/Participants Included	Study Type	Sport	Timeframe (Years Duration)	Incidence Rate/1000 Hours	Incidence Rate/1000 Athlete Exposures (AEs) or Alternate unit of measure
Fuller *et al.*, (2015)	Not Stated (included all players in tournaments)	Prospective Cohort Study	Rugby Union	2007 – 2010 English Premiership (4)	4.6	
			Rugby 7's	2007, 2011 Rugby World Cup (2)	5.2	
				2012, 2013 Pacific Nations Cup (2)	5.4	
				2008, 2010 - 2013 Junior World Championship (3)	3.3	
				2008, 2010 -2013 Junior World Rugby Trophy (5)	4.8	
				2008 -2013 World Series (6)	8.3	
Fortington *et al.*, (2015)	132 Participants	Secondary Analysis of Injury Data	Community Australian Rules Football (AFL)	2007-2008 (2)	1.2	
Moore *et al.*, (2015)	78 Participants	Descriptive Epidemiology Study	Welsh Rugby Union National Team	2011 – RWC* 2012 - 2014 – 6 Nations 2012 – 2014 – Summer Tournaments 2012, 2013 – Autumn Tournaments	13.8	

Table 2.1 Continued

Author & Year	Number of Studies/Participants Included	Study Type	Sport	Timeframe (Years Duration)	Incidence Rate/1000 Hours	Incidence Rate/1000 Athlete Exposures (AEs) or Alternate unit of measure
Mc Fie *et al.*, (2016)	7216 Participants	Prosepective Cohort Study	Youth Rugby Union	2011 – 2014 (4 Youth Week Tournaments)	6.8	
Pfister *et al.*, (2016)	23 Systematic Review 13 Meta-Analysis	Systematic Review and Meta-Analysis	Youth Sports - 12 Sports	1980 – 2014 (34)		0.2
			Rugby			4.2
			American Football			0.5
			Soccer			0.2
			Hockey			1.2
			Lacrosse			0.2
			Wrestling			0.2
			Basketball			0.1
			Softball			0.1
			Baseball			0.1
			Field Hockey			0.1
			Cheerleading			0.1
			Volleyball			0.05
Roberts *et al.*, (2017)	Not Stated (Inluded Numerous Clubs over a Number of Seasons)	Descriptive Epidemiology Study	Community Rugby Union	2009 – 2015 (7)	1.5	
Archbold *et al.*, (2017)	825 Participants	Prospective Injury Surveillance Study	Schoolboy Rugby Union	2014-15 (1)	6.0	

* = Rugby World Cup

2.1.1 – G.A.A. sports

Hurling (males), Camogie (female equivalent of hurling), and Gaelic Football (male and female) are field sports that are predominantly played in Ireland. These sports are played on a field, which is between 130m and 145m long and between 80m and 90m wide, each team is made up of 15 players. Teams aim to score goals in a net (similar to soccer) and points above the crossbar and in between the posts (similar to rugby) [Croke Park, 2017] . Hurling is played with an ash stick called a 'Hurley'. The stick is used to strike a small ball called a 'Sliotar' and all players are required to wear a regulation helmet (Croke Park, 2017). Players can tackle an opponent by making shoulder to shoulder charge on a person who is in possession of the ball, or while in contest with another player to win possession of the ball (Croke Park, 2017). Gaelic football is governed by the same rules as hurling, with the exception that it is played with a football, there is no 'hurley' involved and the players do not wear helmets (Croke Park, 2017). To date there is a lack of specific concussion incidence data with regard to GAA in the literature. However there are a number of studies that report injury incidence relative to the body part injured rather than specifically reporting on the exact injury, these are outlined below.

2.1.2 – Incidence of Head Injury in Hurling

Blake *et al.,* (2014) conducted a prospective cohort study on the injury incidence and injury type sustained by elite male inter-county hurlers over 5 seasons (2007 – 2011). Overall there were 61.8 injuries/1000 match hours reported with 4.1% of the total injuries being attributable to the head and neck region (Blake *et al.*, 2014). Similarly, Murphy *et al.,* (2012) examined the incidence and prevalence of injuries in 4 inter-county teams over the course of the 2007 season. During this season, 102.5 injuries/1000 match hours were reported. In total there were 204 injuries sustained by 104 players. 5.4% of these were attributable to the head and neck region, of which there was one reported concussion, accounting for 0.5% of total injuries (Murphy *et al.,* 2012). However, this figure may not be representative of the actual concussion incidence rate, due to the possibility of under-

reporting and potential mis-diagnosis as mentioned above (Lincoln *et al.* 2011). With regard to camogie, to the best knowledge of the author there has only been one published epidemiological study on injury in camogie. Buckley and Blake, (2018) reported an overall injury incidence of 26.4/1000 match hours, in total there were 21 injuries observed over the course of the study 2 of these injuries (9.5%) were to the head, but a specific concussion incidence rate was not reported. Lacrosse is the most comparable sport to hurling, for which specific concussion incidence data has previously been reported. As outlined in table 2.1 there was a concussion incidence rate of 0.2/1000 AEs (Pfister *et al.*, 2016).

2.1.3 – Incidence of Head Injury in Gaelic Football

Murphy *et al.,* (2012) examined the incidence and type of injuries sustained in 851 inter-county Gaelic football players between 2007 and 2010. There was a total of 61.9 injuries/1000 match hours reported (Murphy *et al.*, 2012). This finding is remarkably similar to the figure reported by Blake *et al.*, (2014) in hurling, which is outlined above, indicating a similar overall injury incidence rate between hurling and Gaelic football. There were a total of 1014 injuries reported for the 841 Gaelic football players over the course of the study, with 37 head and neck injuries, accounting for 3.6% of the total injuries (Murphy *et al.*, (2012). These findings are lower in comparison to the figures reported in hurling, 4.1% and 5.4% by Blake *et al.,* (2014) and Murphy *et al.,* (2012) respectively. Thus demonstrating a marginally higher incidence of head and neck injuries in hurling despite the requirement to wear a helmet in this discipline. However, it must be noted that these injury percentages do not specifically account for concussion incidence and further epidemiological studies specifically reporting concussion in the GAA are recommended. Gaelic football and AFL share many similarities with regard to the physical demands and mechanics.

There is a link between the GAA and AFL, manifesting in an annual match in which GAA players compete against AFL players in a 'compromised' or 'international' rules match (Murphy *et al.*, 2012). Thus, the most comparable

sport to Gaelic football for which concussion incidence rates have been directly reported in the literature is AFL. Fortington *et al.,* (2015) reported a concussion incidence rate of 1.2/1000 playing hours in community AFL over the course of 2-seasons. The sole mention of concussion in the GAA epidemiological studies outlined above is that of Murphy *et al.,* (2012), reporting 1 concussion out of 127 players over the course of the 2007 season. This is surprising considering that an average Gaelic football game is 60 minutes in duration, there are 15 players (not including substitutions), a single game therefore equates to 15 playing hours. In future, GAA epidemiological studies specifically reporting concussion incidence rates would be highly recommended to afford a direct comparison to other international contact sports. The results of such studies would better inform healthcare professionals and governing bodies as to the correct incidence rates of concussion, which would lead to improved healthcare and safety for athletes across sporting disciplines.

2.1.4 – Incidence of Concussion in Rugby

According to the data presented above in table 2.1, concussion incidence rates are highest in rugby, notably in more recent years, in the professional game and in youth tournaments. The systematic review carried out by Koh *et al.,* (2003) reported rugby incidence rates between 1.0/1000 and 2.9/1000 match hours spanning from years 1951 – 1991. The same review included two rugby studies, which reported on data collected between 1990 – 1994 and 1996. Both of these studies reported considerably higher incidence rates of 8.0/1000 and 9.0/1000 match hours respectively (Koh *et al.,* 2003). These findings suggest that historically concussion may have been under-reported and under-recognised. It must be noted that these studies were conducted on single teams and may be more representative of the reporting ability of a single group of players and medical staff. Moore *et al.,* (2015) reported on the concussion incidence rate in the Welsh men's national rugby team over a number of tournaments between 2011 and 2014. This study reported an incidence rate of 13.8/1000 match hours, again suggesting and increase in incidence rates in recent times, again, this study only followed a single

team/group of players. In comparison, a systematic review (96 studies) and meta-analysis (37 studies) conducted by Gardner *et al.,* (2014) reported a concussion incidence rate of 4.9/1000 match hours, which may be a more representative figure of the overall reported incidence rate rather than that of a single team. These figures are consistent with rugby union figures reported by Fuller *et al.,* (2015), which ranged from 3.3/1000 to 5.4/1000 match hours, this study included players competing in multiple top-level professional tournaments between 2007 and 2013. Concussion incidence rates appear to be lower in the amateur game. Roberts *et al.,* (2017) conducted a descriptive epidemiological study on community rugby union using data from 2009 to 2015. This study reported an incidence rate of 1.5/1000 match hours (Roberts *et al.*, 2017). This figure is consistent with figures reported in community AFL, which were 1.2/1000 match hours (Fortington *et al.,* 2015). The lower incidence rates in the amateur game may be attributed to community and amateur sport not have the same medical reporting strategies in place, pressure from the media to remove players from play or simply less concussions occuring at this level of the sport.

Interestingly, with regard to Rugby 7's, Fuller *et al.,* (2015) reported a discrepancy with regard to incidence rates depending if there was a tournament the following week. When there was a tournament the following week there was an incidence rate of 4.9/1000 playing hours, however when there was no tournament the following week the incidence rate increased substantially to 11.6/1000 playing hours. Fuller *et al.,* (2015) suggest that the reason for this increase in incidence rate may be due to accumulated fatigue following the first tournament, or potentially due to underreporting by some players or medical personnel. If a player was concussed during the first tournament they may not be medically cleared to play in the subsequent tournament. This is a concerning possibility, it must be ensured that there is correct reporting and diagnosis of concussion for the well-being of athletes.

2.1.5 – Self-reporting of Concussion

The responsibility and role of reporting a suspected concussion or the presence of concussive symptoms falls not only on the medical personnel but also with the players themselves and indeed all stakeholders in sport. Fraas *et al.*, (2014) examined the self-reporting of concussion in 4 professional Irish rugby union teams during the 2010-2011 season. Results of the study found that 45% of players sustained at least 1 concussion over the course of the season, however, only 46.6% of these players actually reported the incident to medical personnel (Fraas *et al.* 2014). The reasons given by the players for not reporting concussion were that they did not want to be taken out of the game and that they didn't think the injury was severe enough (Fraas *et al.* 2014). These findings are consistent with the suggestions of under-reporting by both players and medical personnel outlined above by Fuller *et al.*, (2017). Rugby, however, is not the only sporting discipline, for which there is evidence of under-reporting of concussion. Sullivan *et al.,* (2017) investigated GAA players' (13-25 ±3.54 years) attitudes to concussion, and in particular, their approach to reporting the injury. The study found that 25% of participants admitted to having played on whilst they believed that they were suffering from a potential concussion (Sullivan *et al.,* 2017). It is clear that athletes are also under external pressures to continue playing following injury, Kroshus *et al.*, (2016) conducted a study to measure the pressure from coaches, team-mates, parents and fans that players are under to continue playing following concussive injury. Findings of the study were that ¼ of players (328 males and females across 7 sports) had experienced pressure from at least one of the 4 measured sources, furthermore, it was revealed that players who experienced pressure from all 4 sources were more likely to continue playing in the future following injury than those who were under less pressure (Kroshus *et al.*, 2016). These findings clearly demonstrate the need for multi-disciplinary concussion educational campaigns aimed at all stakeholders in sport, a policy which is advocated in the research (Guskiewicz *et al.*, 2014). Such educational campaigns and resources do exist (IRFU, 2009; Gómez and Hergenroeder, 2013; ABI Ireland, 2014; Sport Scotland, 2015; GAA Medical, 2016), and it is recommended that research be conducted to

establish their impact on attitudes of stakeholders toward concussion. If potential concussive injury is not recognised or reported correctly there is potential for underdiagnosis and potential health implications for the athlete. These findings support the need for further exploration of an non-biased, validated and reliable objective outcome measure to facilitate the identification and diagnosis of concussion, and furthermore to monitor and guide the recovery period and return to play. Effectively shifting the paradigm away from a subjective laden assessment and toward a more objective based approach. This would potentially eliminate some of the subjectivity and uncertainty surrounding concussion diagnosis by providing a more definitive and measureable metric for assessment. In order to identify such a metric, it is necessary to understand the underlying anatomy and pathophysiological mechanisms associated with concussion.

2.2 – Pathophysiology of Concussion

Unfortunately, in the past, pathophysiological studies have been confined to the examination of autopsy tissue, however in recent years advances in science, medicine and neuroimaging have allowed microstructural and neurochemical changes to be identified in living tissue (Choe, 2016). These advances in imaging and other investigative methods have provided vital insights into the underlying physiological mechanisms involved with concussive brain injury. Such insights will pave the way for improved *in vivo* diagnostic tools and potentially even treatments for concussion.

2.2.1 – Neuro-Physiological Cascade/Neurotransmitter Release

Concussion results from the biomechanical forces that are imposed upon the brain caused by the acceleration/deceleration forces following an impact, thereby provoking the onset of a complex cascade of neuro-chemical and neuro-metabolic events (Signoretti *et al.*, 2011). These biomechanical forces cause an ionic flux in the cerebrum involving an efflux of potassium, which is concurrent with an influx of sodium and calcium as a result of deformation of lipid membranes due to trauma at the cellular level (Giza and Hovda, 2015).

The same mechanical insult causes the release of excitatory amino acids (EAAs), mainly glutamate, which binds to the kaintine N-methyl-D-aspartate (NMDA) and D-amino-3-hydroxy-5-methyl-4-isoxazoleproprionic acid (AMPA) ionic channels, causing further ionic flux and depolarisation (Barkhoudarian *et al.* 2011). Many of the acute post-concussive signs and symptoms may be attributable to this depolarisation and flux, which both create a spreading depression-like state (Giza and Hovda, 2015). This cascade is graphically presented in figure 2.1 below. A summary of some of the pathophysiological mechanisms discussed above and their suggested symptom and clinical correlations are presented below in table 2.2.
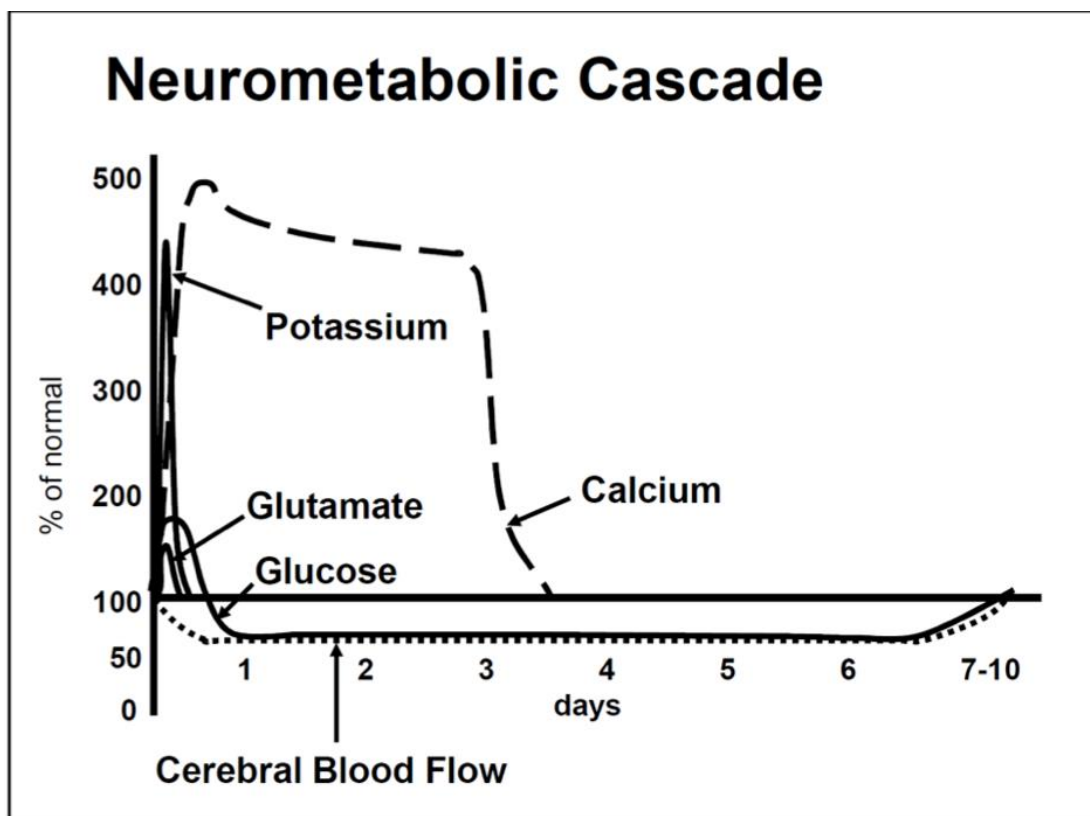
Figure 2.1 – Neurometabolic Cascade of Concussion (Giza and Hovda 2015)

Table 2.2 – Post-TBI pathophysiology and Clinical Correlates (Giza and Hovda 2015)

Post-TBI Pathophysiology	Acute Symptom/Clinical Correlate
Ionic Flux	Migrane headache, photophobia, phonophobia
Energy Crisis	Vulnerability to second injury
Axonal Injury	Impaired cognition, slowed processing, slowed reaction time
Impaired Neurotransmission	Impaired cognition, slowed processing, slowed reaction time
Protease Activation, Altered Cytoskeletal Proteins, Cell Death	Chronic Atrophy, Development of Persistent Impairments

In an effort to replenish homeostatic balance following the metabolic disruption outlined above, the mitochondria increase energy production of the cell. The sodium/potassium adenosine triphosphate (ATP) dependant pumps work in overdrive in an effort to restore ionic homeostasis to pre-injury levels, such activity requires a high level of glucose oxidation in order to provide for the increased energy needs (Signoretti *et al.*, 2011). The ionic imbalance compromises the ability of the mitochondria to maintain normal phosphorylation, causing an overall reduction in high-energy metabolites in the cell and an inverse increase of their low-energy counterparts (Signoretti *et al.*, 2011). This cascade of events, therefore creates an energy crisis as a result of the biomechanical forces being imparted upon the brain. These pathophysiological processes may explain the initial acute symptomatic and cognitive responses experienced by concussed individuals followed by a resolution in most cases within 10-14 days (McCrory *et al.*, 2017b). Future research should consider investigating potential objectives measures for concussion in conjunction with one or more of the well established concussion assessment tools such as the SCAT.

2.2.2 – Cerebral Blood Flow

Another pathophysiological mechanism proposed in the literature is decreased cerebral blood flow (CBF). The cerebral vasculature regulates the level of oxygenated blood that reaches the brain by quickly responding to changes in arterial CO_2 (Choe, 2016). Therefore, any alterations in the control of this mechanism could have profound effects with potential health implications depending on the length of time that the CBF is compromised. There is some evidence to suggest that a reduction in CBF following mild traumatic brain injury (mTBI) may be present despite the absence of structural abnormalities on Magnetic Resonance Imaging (MRI) Using arterial spin labelling, Wang *et al.,* (2015) investigated CBF in paediatric participants who had sustained a mTBI 3 -12 prior to participation in the study, Wang's study demonstrated that CBF was lower in participants who had suffered mTBI in comparison to healthy controls. Furthermore, there were no abnormalities found on MRI or neuropsychological testing (Wang *et al.*, 2015). Another study investigated the effects of paediatric mTBI on neuropsychological testing, susceptibility weighted MRI, Difussion Tensor Imaging (DTI), proton magnetic resonance spectroscopy and phase contrast angiography (Maugans *et al.*, 2012). Measures were taken <72-hours, 14-days and 30 days or greater following concussion, gender matched controls were evaluated at one time point. Results of this study demonstrated significantly lower CBF at the <72-hour follow up in concussed participants when compared to the control group (38ml/100g/min *vs* 48ml/100g/min, P = 0.027). CBF measures improved in 27% of concussed individuals at 14-days and in 64% at >30-days post injury, once again despite any structural abnormalities on MRI (Maugans *et al.*, 2012). Both of the studies outlined above used separate gender and age-matched healthy control groups. However, future research should consider using participants acting as their own controls by establishing baseline normative data for a cohort population, thereby affording a more reliable comparable measure in the event of suspected concussive injury.

2.2.3 – Traumatic/Diffuse Axonal Injury

Traumatic Diffuse axonal injury (DAI) is also considered to be a pathological process associated with concussion. DAI is characterised by multi-focal white matter lesions (Choe, 2016). DAI is more commonly described following severe traumatic brain injury, in comparison concussion is generally accepted as being a mild traumatic brain injury (mTBI) on the spectrum of brain injury (Vos *et al.,* 2012; Young *et al.,* 2016). Nonetheless, there is evidence suggesting that some level of axonal damage occurs following mTBI in both animal and human populations. DTI can be used to assess white matter fibre structure by tracking the movement of water molecules in the brain (Collins *et al.*, 2014). A study carried out by Niogi *et al.,* (2008) used DTI measures of fractional anistrophy (FA) to quantify damaged white matter tracts along with conventional magnetic resonance imaging (MRI) to quantify traumatic microbleeds. The findings were significantly correlated with a simple cognitive reaction time test (R = 0.49, P = 0.012), conversely, the MRI findings were not significantly correlated with reaction time (R = -0.08, P = 0.701), these findings suggest that DTI may be an effective biomarker for mTBI and concussion (Niogi *et al.*, 2008). Similarly, Wilde *et al.,* (2008) demonstrated that patients suffering from mTBI displayed a significant correlation of increased FA with higher post-concussive symptoms (rho = 0.76, P = 0.01) when compared to a control group (rho = 0.17, P = 0.78). Niogi *et al.,* (2008) studied participants at least 1-month post-injury (range: 1 - 65 months), whereas Wilde *et al.,* (2008) studied participants 1 – 6 days post injury. The findings from both studies suggest that white matter changes are identifiable by DTI in both the days, months and potentially years following concussive injury, such changes are also significantly correlated to concussion symptom scores and cognitive reaction times. DTI may not be easily accessable and therefore, more readily available, time and cost effective neurological imagiing modalities such as OCT retinal imaging warrant investigation for potential concussion diagnosis. OCT allows for, but is not confined to imaging the neurological structures of the eye. There is evidence to suggest axonal damage to the neurological white matter tissue following concussive injury, as such, it is logical to explore the possibility that there may be identifiable structural changes to the the neurological structures

(Retinal Nerve Fibre Layer and Ganglion Cell Complex) of the neighbouring retina also. Furthermore, OCT allows for direct objective measurement which can be followed up and compared to baseline or previous measures in the days, weeks and months following injury.

The neurological and vascular structures of both the eye and the brain lie in close proximity to each other. The retina is considered to the an extension of the central nervous system (CNS), during embryonic development the optic nerve and the retina both stem from the diencephalon (London *et al.,* 2013). Furthermore, it has been demonstrated that there are retinal structural findings in other neurological conditions such as Alzheimer's disease, Parkinson's disease and Multiple Sclerosis (M.S) (London *et al.,* 2013; Javaid *et al.,* 2016). Therefore, it is logical to observe the effects of suspected concussion on the neurological structures of the retina.

2.3 – Health Implications of Concussion

The symptoms and short-term effects of concussion are well documented with public awareness being targeted *via* educational campaigns and management guidelines that have been rolled out in recent years (IRFU, 2009; Gómez and Hergenroeder, 2013; ABI Ireland, 2014; Sport Scotland, 2015; GAA Medical, 2016). In the majority of cases, most symptoms associated with concussion resolve within the first 2-weeks post injury. However, there are also some potentially devastating effects and conditions such as second impact syndrome (SIS), chronic traumatic encephalopathy (CTE), and mental health problems which have also been associated with concussive injury and an accumulation of multiple sub-concussive blows (Covassin and Elbin, 2010; Bowen 2003; Manley *et al.,* 2017; Omalu 2014). SIS is defined as a rapid cerebral edema and accompanying herniation of the brain that occurs when an athlete, who has sustained a concussive injury, experiences a subsequent blow while still suffering from the acute symptoms of the initial impact (Bowen, 2003). SIS is a catastrophic occurrence and often results in fatality. The secondary impact may be

relatively minor and the blow does not necessarily have to be to the head, but the resultant forces are nonetheless transferred to the brain. Evidently, it is imperative that an individual suffering from concussion or displaying concussive symptoms is removed from play and does not return to play unless symptom free and cleared by a medical professional. An objective assessment of concussion has the potential to better identify the condition, thereby potentially avoiding cases of SIS or other unnecessary sequelae in the future as a result of under-diagnosis. Such sequelae may not necessarily be confined to the brain itself, interestingly, it has been shown that sustaining a recent concussion predisposes athletes to a higher risk of sustaining a subsequent lower extremity musculoskeletal injury during a 90-day period following return to play when compared to sport, position and gender-matched controls (odds ratio, 2.48, P = 0.04) (Brooks *et al.* 2016). Further investigations into the potential physiological, cognitive and motor control deficits that may outlast clinical recovery from concussion are required.

Repeated concussive injury is associated with potential cumulative long-term effects on cerebral function, which can cause memory impairment and dementia-like symptoms (Barkhoudarian *et al.*, 2011). CTE is a progressive neuro-degenerative syndrome caused by a single or repeated blows to the cranium or indirectly transferred forces transmitted to the brain (Omalu 2014). CTE is typically charaterised by an accumulation of hyper-phosphorylated tau protein (Choe, 2016). Tau protein is an axonal protein, its function is to stabilise axonal microtubules, however when it becomes hyper-phosphorylated these microtubules become unstable, causing axonal dysfunction and negatively effecting neuronal function (Choe, 2016). Historically, CTE was known as *dementia pugilistica* or boxers dementia, suggesting boxers were the only sportspeople to suffer this neurodegenerative condition secondary to multiple blows to the head (Gavett *et al.*, 2010). However it has garnered much attention in recent years, particularly with regard to American football (Omalu *et al.*, 2005; Omalu *et al.*, 2006). These findings suggest that CTE can occur as a result of repeated concussive blows and perhaps an accumulation of sub-concussive blows

sustained over the course of a sporting career in; American football, American wrestling, boxing and potentially any field sports which involve repetitive head impact such as the heading of the ball in soccer.

A recent study has shown that sub-concussive impacts from a single session of heading the ball in soccer leads to transient decrements in memory function along with an increase in corticomotor inhibition (Di Virgilio *et al.*, 2016). The participants of this study headed 20 soccer balls over 10-minutes, which were released at a standardised speed from a machine, corticomotor inhibition was measured as cortical silent period (cSP) and cognition was measured using the Cambridge neuropsychological test automated battery (CANTAB) (Di Virgilio *et al.*, 2016). There was a significant increase in cSP in 74% of participants following the protocol ($p = 0.049$) and a significant increase in errors on both the spatial working memory ($P = 0.03$) and paired associate learning ($P = 0.007$) elements of the CANTAB, however these decrements were transient and returned to normal after 24hrs (Di Virgilio *et al. 2016)*. If this rate of headed balls is extrapolated to a full 90-minute game of soccer it would equate to 180 total headed balls per player in a match, which is unrealistic, however, such a figure could be attainted in a specific heading drill in training. Tysvaer and Storli, (1981) reported the frequency of heading the ball in 10 Norwegian first division games, 6 English games and 4 international games, there was an average of 111 total headings per game for all players combined, which may be considered a more accurate representation of actual match heading frequency. Nonetheless, the accumulated sum of headers over the course of a playing career could have potential long-term health implications. Further research incorporating both objective physiological and functional measures is needed on this topic. This potential risk has been the genesis of some rule changes and recommendations in youth soccer. According to U.S. Soccer (2018) children aged ≤10 years should not head the ball in practice or games and for children aged 11-13 years should be limited to 30-minutes and a maximum of 15-20 headers per week.

The literature suggests that incorrect management of concussion, multiple concussions and indeed even an accumulation of sub-concussive blows may contribute to the development of catastrophic conditions such as SIS, CTE, mental health problems and even less severe sequelae such as an increased risk of musculoskeletal injury. An *in vivo* method to proactively and objectively hallmark any physiological changes as a result of concussion or repeated sub-concussive blows would be invaluable in improving the diagnostic capabilities for concussive injury.

2.4 – Current Concepts in Concussion Diagnosis

There are currently a number of predominantly subjective and performance-based tools, which are used to aid in the recognition and clinical diagnosis of concussion. These tools incorporate a combination of neuropsychological elements, performance measures and symptom reporting tools. These include; the Sport Concussion Assessment Tool (SCAT-5) (McCrory *et al.*, 2017b) and its' predecessors (SCAT, SCAT-2, and SCAT-3), computer-based neurocognitive tests such as the Immediate post-concussion assessment and Cognitive Test (ImPACT) [Maroon *et al.*, 2000],the vestibular/ocular motor screening (VOMS) assessment (Mucha *et al.*, 2014) and the King-Devick (KD) test (Leong *et al.*, 2015). These tools provide an indication as to whether a person is demonstrating the signs and symptoms of concussion. However, the general consensus remains that diagnosis and the time of return to play for any athlete is a medical decision determined by clinical judgement (McCrory *et al.*, 2017). There are some biomarkers proposed in the literature as suggested above in sections 2.2 – 2.2.3 e.g. DTI and other neurological imaging techniques such as computed tomography (CT). Furthermore, there are numerous fluid biomarkers postulated in the literature such as S100B, neuron-specific enolase, protein breakdown products, glial fibrillary acidic protein as well as certain metabolites, many of which have conflicting findings with regard to identifying concussion and therefore require further research (Jeter *et al.*, 2013). As such, there is currently no accepted diagnostic biomarker for concussion (Makdissi *et al.*, 2015). It is clear that a valid and reliable objective marker to facilitate the

diagnosis of concussion would be advantageous to the decision making process of the healthcare professional. However, for the moment, concussion diagnosis remains a clinical judgement that is guided by predominantly subjective tools, some of which will be discussed further in the following sections. Table 2.3 below outlines the currently utilised subjective and performance measures along with some of the potential objective biomarkers for concussion diagnosis.

Table 2.3 – Outline of Current Performance Measures, Subjective Tools and Potential Objective Biomarkers in Concussion

Type	Name of Measure	Author
Performance Measures	Impact	Maroon *et al.,* 2000
	King Devick	Leong *et al.,* 2015
	SCAT (currently SCAT-5)	McCrory *et al.,* 2017b
Subjective Measures	VOMS (Symptom Provocation)	Mucha *et al.,* 2014
	SCAT (Symptom Reporting)	McCrory *et al.,* 2017b
Objective Biomarkers	CBF (Arterial Spin Labelling/Phase contrast Angiography)	Wang *et al.,* 2015; Maugans *et al.,* 2012
	Susceptibility Weighted MRI	Maugans *et al.,* 2012
	Proton Magnetic Resonance Spectroscopy	Maugans *et al.,* 2012
	Diffusion Tensor Imaging (DTI)	Niogi *et al.,* 2008
	Fluid Biomarkers (SB100, Neuron-specific Enolase, Protein Breakdown Products, Glial Fibriliary Acidic Protein)	Jeter *et al.,* 2013

2.4.1 – ImPACT

ImPACT or 'immediate measurement of performance and cognitive testing' is comprised of a battery of performance and cognitive tests which were designed to assess neuropsychological performance levels of athletes (Maroon *et al.*, 2000). Included in the ImPACT assessment are; detailed symptom inventory, a questionnaire, along with 7 modules, which are designed to assess neuro-cognitive function such as memory tests, processing speed, reaction time and impulse control (Collins *et al.*, 2003). Maerlender *et al.,* (2010) investigated the validity of the various domains of ImPACT by comparing them to a battery of traditional neuropsychological measures and experimental measures in a healthy population. The findings revealed that 4 out of the 5 imPACT domains demonstrated convergent validity, however 2 cognitive areas that are often affected following mTBI (sustained memory and auditory working memory) were not identified by impact, the study concluded that ImPACT is a useful screening tool, but it is not a comprehensive examination (Maerlender *et al.*, 2010). The test re-test reliability of ImPACT has been established in healthy participants between baseline, 45-day follow up and 50-day follow up, the ICC's for the 7 imPACT modules ranged from 0.15 to 0.39 between baseline and 45-day and from 0.39 to 0.61 between the 45-day and 50-day follow up, demonstrating a relatively poor level of reliability (Broglio *et al.*, 2007). Thus, imPACT may be a useful adjunct tool to assist in the clinical decision that is concussion diagnosis, but should be used as part of a multi-modal battery of tests.

2.4.2 – King-Devick Test

The KD test is a sideline assessment tool that involves the participant quickly reading a series of numbers from 3 cards (Leong *et al.*, 2015). The test involves an example card and 3-test cards of varying format (Figure 2.2), where participants must read the numbers as quick as possible from left to right, the time taken to do so is recorded along with the number of errors for each test, the scores are then compared to pre-established baseline values (Leong *et al.*, 2015). The KD allows the level of cognitive visual processing and performance to be established, which can be done quickly on the

sideline (Tjarks *et al.*, 2013). Deficits in visual function such as saccades/antisaccades, smooth pursuit and convergence are common in concussion (Ventura *et al.*, 2015). The King-Devick test provides a valuable functional performance assessment, which can be readily utilised in a pitch-side scenario, to further aid the clinical decision making process of concussion.
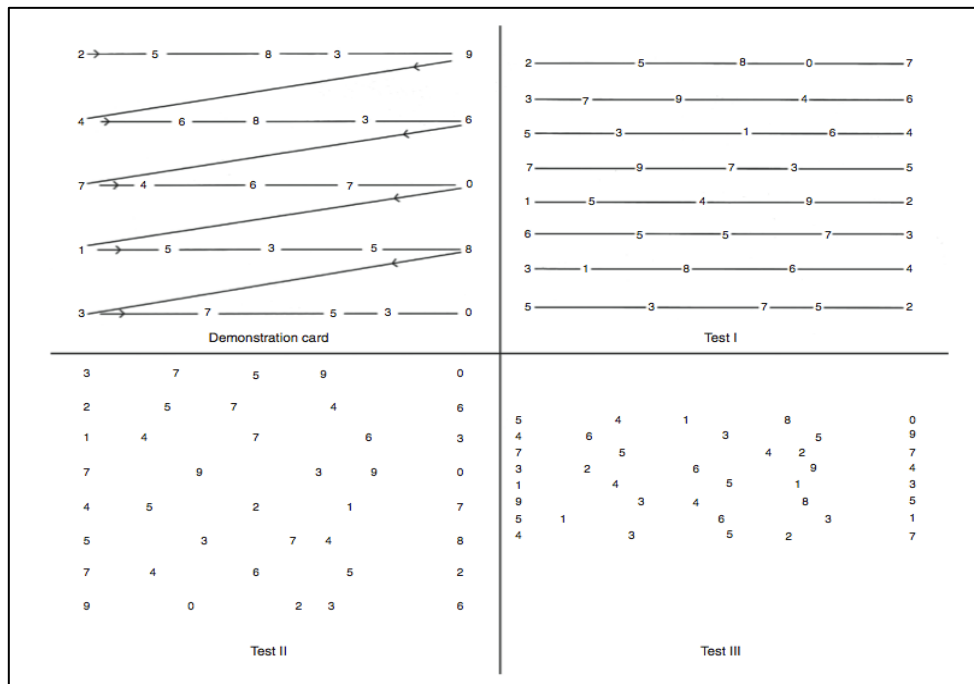
Figure 2.2 King-Devick Test Cards (Leong *et al.*, 2015)

The KD test has been shown to be a reliable and accurate tool for identifying athletes with head trauma and concussion. Galetta *et al.,* (2011) examined KD scores pre and post-fight in a cohort of Boxers and mixed martial arts (MMA) fighters and compared those who sustained head trauma vs those who did not along with test-retest reliability for 2 pre-fight measures taken within 15-minutes of each other. There was high test-retest reliability established for pre-fight measures (ICC: 0.97 [95% confidence interval [CI] 0.90 – 1.0]). For those who suffered head trauma during the bout, KD scores were significantly higher compared to those who did not suffer head trauma (59.1±7.4 vs 41.0±6.7 seconds, $p < 0.0001$) (Galetta *et al.,* 2011). These results indicate that the KD test is a reliable and valid tool for identifying martial artists with head trauma. Leong *et al.,* (2015) conducted pre and

post-season KD testing on collegiate football men's and women's basketball teams, KD testing was also conducted immediately on the sideline in the event of suspected concussive injury during the season. Players who sustained concussion had significantly higher scores than their baselines (36.5 ± 5.6 vs 31.3 ± 4.5 seconds, p < 0.005), furthermore there was a high test-retest reliability from pre to post-season in non-concussed athletes (ICC: 0.95) [CI: 0.85-1.05) although there was a slight learning effect from pre to post season (Leong *et al.*, 2015). The KD test has also been shown to aid in the identification of concussion in rugby. King *et al.,* (2015) carried out a prospective observational cohort study on an amateur rugby union team over 3-seasons (2012 – 2014). Baselines were established prior to the start of the season, over the course of the study there were 44 unwitnessed and 5 witnessed concussive injuries, significant differences were found in KD test scores post-concussion displaying a 4.6 second decrement in the overall concussed group (p < 0.05) (King *et al.*, 2015). Therefore, the KD is a useful tool to aid in the clinical decision making process of concussion through saccadic visual assessment, nonetheless it is still a performance measure and does not provide healthcare professionals with an objective biomarker to confirm or refute diagnosis of concussion.

2.4.3 – Visual Ocular Motor Screening (VOMS)

It is well established that athletes can present with vestibular and ocular dysfunction following concussion and both of these elements, along with symptomatic behaviour, cognitive function and mental status and the potential need for neuro-imaging should all be part of a multi-modal assessment (McCrory *et al.*, 2017a). A further screening tool to aid in the clinical decision making process of concussion is known as the VOMS assessment. The VOMS includes 5 domains; smooth pursuit, horizontal and vertical saccades, near point convergence (NPC), visual ocular reflex (VOR) and visual motion sensitivity (VMS) (Mucha *et al.*, 2014). Rather than just assessing the ability of an individual to rapidly read numbers from a chart as is the case with the KD test, the VOMS incorporates both a vestibular and an ocular motor assessment. The VOMS takes about 5-minutes to complete,

participants subjectively report their symptomatic response on a scale of 0 (none) to 10 (severe) and the results are compared with the pre-test symptom rating and the NPC measurement (cm) (Collins *et al.*, 2013). It has been demonstrated that a positive VOMS screen in all domains except eye accommodation and near point convergence is associated with an increased recovery time following sports related concussion (Anzalone *et al.*, 2017). These findings support the use of VOMS and add to the currently available tools which can guide a healthcare provider to making a decision regarding concussion diagnosis. (Mucha *et al.*, 2014) examined 64 concussed individuals (13.9 ±2.5 years) using the VOMS. It was demonstrated that 61% of participants reported symptoms after at least 1 VOMS item, all VOMS items were positively correlated to PCSS total symptom score and a NPC distance of ≥5cm and any VOMS item symptom score ≥2 increase the possibility of correctly identifying concussion by 38% and 50% respectively (Mucha *et al.*, 2014).

There are therefore many tools to aid in the diagnosis of concussion, however, such tools can demonstrate a learning effect, furthermore athletes with a learning difficulty may be presented with anxiety or undue pressure when having to read out lists of numbers and remember words which is precipitated by already being in a potentially injured state. As discussed above in section 2.3, physiological recovery may indeed outlast clinical/functional recovery. Therefore a normal VOMS, King-Devick, ImPACT or other test may not represent full physiological recovery. A validated and reliable objective examination for concussion may have the potential to identify physiological recovery and even potentially identify subtle structural changes caused by sub-concussive blows. Such an objective tool would provide a valuable addition to the battery of tools that are already available to practicitioners. These subjective and objective markers could then be utilised in conjunction to identify concussion and guide full clinical and physiological recovery. The tool that is currently endorsed by the IOC, International Federation for Equestrian Sports (FEI), World Rugby, and FIFA is the SCAT.

2.5 – Sport Concussion Assessment Tool (SCAT)

There have been 4 versions of the SCAT to date which are the culmination and end product of the CISG meetings outlined above in chapter 1. The first edition of the SCAT was the consensus derived from the 2nd CISG meeting that was held in Prague 2004. The main goal of the SCAT was to develop a standardised tool for concussion, serving the dual purpose of the medical assessment of the condition, along with patient/parent education (McCrory *et al., 2005)*. The SCAT incorporated various elements of existing concussion assessment tools including; The standardised assessment of concussion (SAC) (McCrea *et al.*, 1997; M McCrea *et al.*, 1998), a post-concussion symptom scale (PCSS) and modified maddocks questions (Maddocks *et al.*, 1995). The SCAT also incorporated recommendations from the UK Jockey Club, the University of Pittsburgh Medical Centre, Thinksafe, Sports Medicine New Zealand, the Brain Injury Association and the American Academy of Neurology (McCrory *et al.*, 2005).

The 2nd edition of the tool, the 'SCAT-2' was the product of the 3rd CISG meeting, which was held in Zurich in 2008 (McCrory *et al.,* 2009). Elements added to this edition included; the Glasgow Coma Scale (GCS) (Teasdale and Jennett 1974), additional lists of words for the memory component of the SAC and a balance component, which incorporated a modified version of the Balance Error Scoring System (mBESS) (Guskiewicz 2003; McCrory *et al.,* 2009).

The 3rd incarnation of the tool, the 'SCAT-3' was developed at the 4th CISG meeting in Zurich, 2012. Once again, there were some slight changes and additions in the form of a cervical spine assessment and further testing options for the mBESS (McCrory *et al.*, 2013). Furthermore, a child SCAT-3 was developed following this meeting, which is intended for use with 5 -12 year olds (McCrory *et al.*, 2013). The SCAT-3 consists of 2 main component sections. The first section includes the sideline/immediate assessment of concussion, which comprises the GCS and the Maddocks questions. The

second section includes a brief background information of the injured individual, the PCSS, SAC and the mBESS. A full copy of the SCAT-3 can be found in appendix A.

The most recent version of the tool is the SCAT-5, which was developed at the 5th CISG meeting held in Berlin, 2016 (McCrory *et al.*, 2017a). There was no SCAT-4, the reason for this was seemingly to numerically synchronise the edition of the SCAT with its relevant CISG meeting number (i.e. the 5th CISG meeting produced the 'SCAT-5). Additions and changes to the SCAT for the 5th edition included; the inclusion of red flags, which if present, warrant the immediate medical referral, the cervical spine assessment was also moved to be included in the on-field/immediate section of the tool (McCrory *et al.*, 2017b). The PCSS section previously allowed for different rating options (i.e. Self-rated or Clinician Interview), in contrast, the SCAT-5 states that the symptom scale should be self-rated by the athlete themselves (McCrory *et al.*, 2017b), for the purpose of this study the number of symptoms and symptom severity score (SSS) will be self-reported by the athlete. Further additions included in the SCAT-5 were; extra number and word lists for the immediate memory and concentration sections, along with the addition of new sections for neurological screening and final descision documentation (McCrory *et al.*, 2017b).

Previously, studies have reported on the reliability and validity of the SCAT-3 (Chin *et al.*, 2016), normative values for its component parts (Hänninen *et al.* 2016; Zimmer *et al.*, 2015) as well as a systematic review which commented on the effects of gender and history of concussion on SCAT-3 component scores (Yengo-Kahn *et al.*, 2016).

2.5.1 – Post Concussion Symptom Scale (PCSS)
The PCSS is one of many concussion symptom checklists/scales that exist. Alla *et al.,* (2009) conducted a systematic review to identify such scales, there were 6 main scales identified with numerous derivative scales. The majority of these scales use a 7-point Likert scale. There are some

differences between scales with regard to the number of symptoms that a scale consists of, furthermore some scales are computer based such as ImPACT while others are paper-based (Alla *et al.*, 2009). The PCSS was initially devised as part of the first SCAT by the second CISG meeting in 2004 (McCrory *et al.*, 2005), this scale contained 18 possible symptoms. The current scale, which is an evolution of the original PCSS contains 22 possible symptoms, with the same 7-point Likert scale as the previous edition, therefore an athlete can report a maximum of 22 symptoms with a score ranging from 0 – 6 for each one (figure 2.3). The number of symptoms and the combined symptom severity score (Maximum score of 122) are then documented on the SCAT-3 (McCrory *et al.*, 2013).

Figure 2.3 – SCAT-3 PCSS

The inter-day reliability of the PCSS was established in a group of 52 healthy adults over a 7-day period who had not suffered a concussion in the 6-months prior to testing (Robinson and Mc Elhiney 2017). ICC's reported were 0.496 (95% C.I. = 0.382 – 0.620) and 0.438 (95% C.I. = 0.325 – 0.568) for the number of symptoms and SSS respectively. Robinson and McElhiney (2017) state that these figures suggest a moderate inter-day reliability of both component parts of the PCSS, however these figures may be viewed as representing poor reliability according to other classification systems as used by Currier (1990), for which values <0.69 are considered poor. This must be taken into account when interpreting baseline/follow up data for the PCSS

The PCSS, has been validated as part of the assessment of concussion by using cognitive testing and functional MRI (fMRI) (Chen *et al.*, 2007). 28 males were included in the study, there was a low PCSS group (N = 9), a moderate PCSS group (N = 9) and a control group (N = 10). The moderate PCSS group displayed significantly lower scores than the control group on two of the cognitive tests ($P < 0.05$), furthermore, the fMRI displayed reduced task-related activation patterns in both the low and moderate groups (Chen *et al.*, 2007). However it must be noted that a subjective-based symptom scale such as the PCSS may be influenced by factors such as gender. Hunt *et al.,* (2016) displayed both age and gender differences in youth (13-17 years old) athletes with regard to concussion symptoms. Hunt *et al.,* (2016) broke the symptoms down into physical, cognitive, emotional and fatigue domains, findings of this study demonstrated that females reported more symptoms than males in total ($P = 0.009$) emotional ($P < 0.001$) and fatigue ($P <0.001$) symptoms. Shehata *et al.,* (2009) examined the PCSS in 260 male and female university football (American), ice hockey and wrestling athletes. It was reported that females scored higher than males on the SSS (6.39 *vs* 3.52) but no statistical significance testing was reported (Shehata *et al.,* 2009). Snyder and Bauer, (2014) compared gender with regard to PCSS in 656 participants (14.77 ±2.3 years) from 20 different sporting disciplines. Snyder and Bauer (2014) demonstrated that females reported a significantly higher number of symptoms ($P < 0.001$) and a higher SSS ($P < 0.001$) than

males. Therefore it is well established that there are gender differences in symptom reporting, with females generally reporting more than males. The current study will examine gender differences in an older age group (16 – 40 years old) from a rugby, GAA and soccer cohort. Another potential influencing factor outlined in the systematic review by Yengo-Kahn *et al.*, (2016) was a previous history of concussion. Shehata *et al.*, (2009) reported that participants with a previous history of concussion reported a higher SSS than those without a previous history of the injury (5.25 *vs* 3.75), however, similarly to the gender comparison no statistical significance testing was reported. Hunt *et al.,* (2016) reported that a previous concussion was significantly associated with self-reported cognitive symptoms ($P = 0.034$), participants who reported having sustained a previous concussion reported more cognitive symptoms. This is in agreement with the findings of Valovich McLeod *et al.*, (2012), who also reported that those with a previous history of concussion reported more symptoms than those without a previous history ($P < 0.001$).

Therefore both gender and history of concussion have been previously shown to have an effect on PCSS, however, these factors have not yet been studied within the sports of rugby, GAA and soccer.

2.5.2 - SAC

The SAC was developed in 1997, in response to a call for a standardised concussion examination that could be carried out on the side-line (McCrea *et al.*, 1997). The SAC contains 4 components; orientation, immediate memory, concentration and delayed recall (figure 2.4). The maximum (perfect) score an individual can attain on the SAC is 30 points (McCrea *et al.*, 1997). The SAC was combined with the PCSS mentioned above at the second CISG meeting, forming the first edition of the SCAT (McCrory *et al.*, 2005). Since then it has been ever-present in each subsequent version of the SCAT, with some minor changes to word and number lists over time.

COGNITIVE & PHYSICAL EVALUATION

4

Cognitive assessment
Standardized Assessment of Concussion (SAC)[4]

Orientation (1 point for each correct answer)

	0	1
What month is it?	0	1
What is the date today?	0	1
What is the day of the week?	0	1
What year is it?	0	1
What time is it right now? (within 1 hour)	0	1
Orientation score		of 5

Immediate memory

List	Trial 1		Trial 2		Trial 3		Alternative word list		
elbow	0	1	0	1	0	1	candle	baby	finger
apple	0	1	0	1	0	1	paper	monkey	penny
carpet	0	1	0	1	0	1	sugar	perfume	blanket
saddle	0	1	0	1	0	1	sandwich	sunset	lemon
bubble	0	1	0	1	0	1	wagon	iron	insect
Total									
Immediate memory score total								of 15	

Concentration: Digits Backward

List	Trial 1		Alternative digit list		
4-9-3	0	1	6-2-9	5-2-6	4-1-5
3-8-1-4	0	1	3-2-7-9	1-7-9-5	4-9-6-8
6-2-9-7-1	0	1	1-5-2-8-6	3-8-5-2-7	6-1-8-4-3
7-1-8-4-6-2	0	1	5-3-9-1-4-8	8-3-1-9-6-4	7-2-4-8-5-6
Total of 4					

Concentration: Month in Reverse Order (1 pt. for entire sequence correct)

	0	1
Dec-Nov-Oct-Sept-Aug-Jul-Jun-May-Apr-Mar-Feb-Jan	0	1
Concentration score		of 5

8

SAC Delayed Recall[4]

Delayed recall score	of 5

Figure 2.4 – SCAT-3 Standardised assessment of Concussion (SAC)

35

The first study to examine the clinical utility and validity of the SAC was carried out by McCrea *et al.,* (1998), this study baseline tested 568 healthy high school and collegiate athlete football players, of which 33 sustained a subsequent concussion and were re-tested immediately post-concussion, 28 of these underwent further testing 48-hrs post-injury (McCrea *et al.*, 1998). Results of the study found that concussed athletes performed significantly lower than non-concussed athletes in total SAC score as well as orientation, memory and delayed recall (P < 0.0001) and concentration (P < 0.0007). Athletes were also compared to their own total SAC baseline scores, which were significantly lower following concussion (P < 0.001), furthermore, 48hr follow up testing found that all 28 athletes returned to their baseline levels (McCrea *et al.*, 1998). These findings demonstrate that SAC is a useful tool to aid in the clinical decision making process of concussion immediately following concussion. However it is well known that many concussive symptoms can be present longer than 48-hrs, furthermore, the current minimum stand down time from sport is 1-week for adults and 2-weeks for children (McCrory *et al.*, 2017a). Therefore, results from the SAC alone may be applicable in the acute assessment of the condition but not sufficient past 48-hrs.

The systematic review carried out by Yengo-Kahn *et al.,* (2016) states that the majority of literature reports that females outperform males in the SAC, however there remains some inconsistency in the literature with regard to gender differences in SAC. With two studies by the same author reporting no gender differences in SAC scores (Zimmer *et al.*, 2013; Zimmer *et al.*, 2015). Furthermore, Zimmer *et al.*, (2015) found no differences in SAC scores in participants across different sporting disciplines and also in those with a history of concussion *versus* those without. No study has previously compared the sporting disciplines of rugby, GAA and Soccer with regard to the SCAT.

2.5.3 – mBESS

For many years, balance examination has been included in neurological assessment, maintaining posture and balance is dependent on the input of the somatosensory, visual and vestibular systems (Guskiewicz, 2003). These systems can all be implicated in concussive injury (Ventura *et al.*, 2015; Choe, 2016). The mBESS component of the SCAT has been in use since the 2nd iteration of the tool (McCrory *et al.*, 2009). It is a modified version of the Balance Error Scoring System (BESS) (Guskiewicz, 2003). The BESS is somewhat an evolution of the Romberg test, first introduced by Mortiz Henrich Romberg in 1853, for which the purpose was to assess somatosensory impairment by removing the sensory input of vision and asking a participant to stand in various stances (Riemann *et al.*, 1999). The mBESS employed by both the SCAT-2 and the SCAT-3 are identical with the only difference being the optional addition of a 'tandem gait' test in the SCAT-3 (McCrory *et al.*, 2013). The examination consists of 3 stances; double leg, single leg (on non-dominant foot) and tandem (non-dominant foot at the back). Each stance is tested for a duration of 20-seconds with a standardised set of instructions explained to the participant prior to each stance. The number of errors are recorded by the tester (figure 2.5). The maximum number of errors a participant can make for any single stance is 10 (McCrory *et al.*, 2013). The stances can optionally be performed on a less stable surface of medium density foam to make the exam more challenging (McCrory *et al.*, 2013).

6 Balance examination

Do one or both of the following tests.
Footwear (shoes, barefoot, braces, tape, etc.) _____

Modified Balance Error Scoring System (BESS) testing[5]
Which foot was tested (i.e. which is the **non-dominant** foot)   ☐ Left ☐ Right
Testing surface (hard floor, field, etc.) _____
Condition

Double leg stance:	Errors
Single leg stance (non-dominant foot):	Errors
Tandem stance (non-dominant foot at back):	Errors

And/Or

Tandem gait[6,7]
Time (best of 4 trials): _____ seconds

Figure 2.5 – SCAT-3 Modified Balance Error Scoring System (mBESS)

Riemann *et al.*, (1999) conducted a study to compare a computerised force plate platform with the 3 stances that are today known as the mBESS. Participants performed the testing with eyes open and eyes closed on both the firm and foam surfaces while standing on a force platform. There were no errors observed in the double stance for either measure (foam or firm) and therefore statistical analysis was not possible, however, significant, weak to moderate correlations were observed between force plate and mBESS measures for both the single leg stance (r = 0.421, P = 0.00) and tandem stance (r = 0.589, P = 0.00) (Riemann *et al.*, 1999). Thus, the mBESS is a suitable method for assessing balance and postural stability when computerised methods are not available, which is the case in most sports medicine settings. A study carried out by Putukian *et al.*, (2015) showed that in 32 concussed athletes mBESS scores were significantly worse than pre-injury baseline levels (P < 0.05), demonstrating that concussion has an impact on postural stability. With regard to gender differences, it has been shown in high school athletes that females outperformed males on the mBESS (P = 0.01) (Jinguji *et al.*, 2012), this is in agreement with the findings of Valovich McLeod *et al.*, (2012) who found that females outperformed males on the mBESS (P < 0.001). Both studies by Jinguji *et al.*, (2012) and Valovich McLeod *et al.*, (2012) used adolescent participants, future research should include a wider age-group. With regard to previous history of concussion, Valovich McLeod *et al.*, (2012) found no significant difference in mBESS scores (P = 0.551).

According to the literature above, it is clear that the SCAT-3 is a useful tool in the multi-factorial assessment of concussion, however it can be influenced by factors such as gender and history of concussion which were examined in this study. There is clearly a need for a reliable, validated objective-based assessment of concussion. While there are some preliminary findings with regard to state of the art brain imaging modalities such as susceptibility weighted Imaging, gradient echo, fMRI and DTI (Choe, 2016) there remains much more research to be conducted on such modalities. Furthermore, these methods are expensive and often inacceessable. Considering that the

neurological and vascular structures of the brain and the eye are in close proximity to each other and the retina is considered to be an extension of the CNS (London *et al.,* 2013) the investigation of potential effects of concussion on the retina is warranted.

2.6 – Optical Coherence Tomography

Optical Coherence Tomography (OCT) is a non-invasive diagnostic imaging technology that can produce both micron resolution 3D images and 2D cross sectional images of the retina (Podoleanu, 2012; Duker *et al.,* 2014). The operation of OCT is relatively straight forward with image acquisition only taking a few seconds, ensuring minimal patient discomfort (Thomson *et al.*, 2015). The principle of OCT is similar to that of ultrasound, with two main differences; the first being that OCT uses light instead of sound, the speed of light is approximately 1-million times faster than sound and therefore OCT can image structures with a resolution of ≤10µm as opposed to a 100µm scale available with ultrasound. Secondly, ultrasound requires tissue contact for imaging while OCT does not (Gupta *et al.,* 2005). Swept source OCT (SS-OCT) is a relatively new form of OCT. The developments in technology associated with SS-OCT allow for an improved image penetration, which uses a wavelength of 1050nm, an axial resolution of 5.3µm and an axial scan rate of 100,000 scans per second (Lavinsky and Lavinsky 2016). The high scan speeds of SS-OCT allow for a denser sampling and improved registration, maintaining a higher sensitivity with an increased depth of scan compared to other iterations of OCT, this facilitates improved visualisation of the retina and structures posterior to the retina (Duker *et al.,* 2014). Evidently, OCT is primarily utilised in ophthalmic practice for diagnosis and monitoring of ocular disease such as glaucoma (Bussel *et al.,* 2014; Hood, 2016; Hammel *et al.,* 2017), diabetic retinopathy (Hwang *et al.*, 2015) and age related macular degeneration (Jia *et al.*, 2015) among others. Structural OCT changes have been correlated with presence of neurological conditions such as Parkinson's disease, Alzheimer's, M.S. and stroke (London *et al.,* 2013; Thomson *et al.,* 2015). Considering that concussion is a neurological injury, an investigation of its effects on the retina using OCT is warranted.

The retina is made up of various layers containing specialised neurons that are interconnected *via* synapses (London *et al.,* 2013). The retinal layers, specifically, the retinal nerve fibre layer (RNFL) [labelled 'nerve fibre layer in fig. 2.6] and the ganglion cell layer ++ (GCL++) are depicted in figure 2.6 below. Furthermore, the vascular, sub-retinal choroidal layer can be seen at the bottom of figure 2.6 below as the mottled black and grey area.
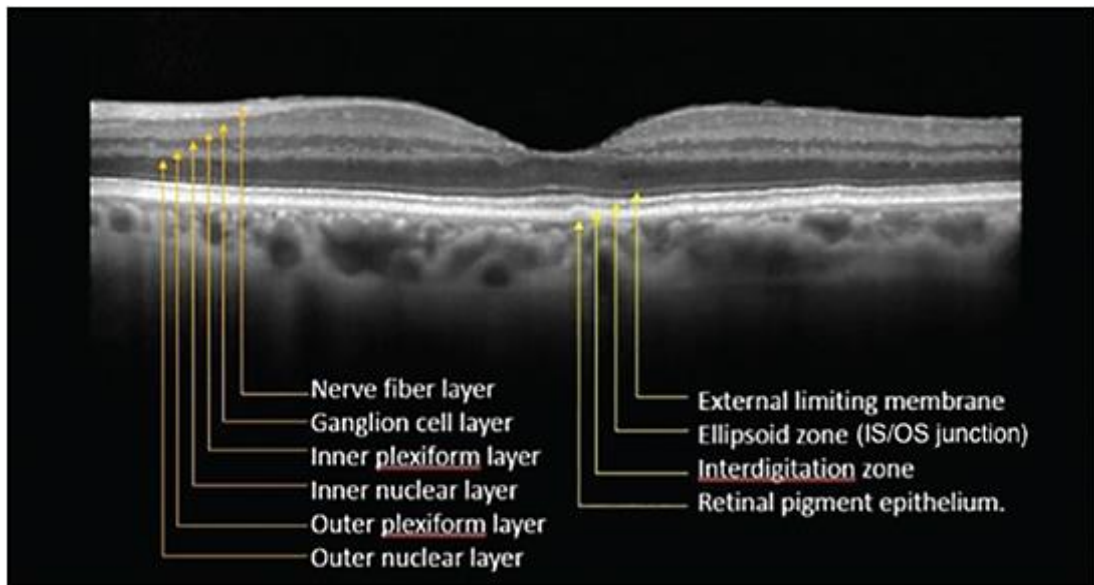
Figure 2.6 – Layers of the Retina (PentaVision 2015)

With regard to OCT examination, it is commonplace to use drug induced pupillary dilation, however it has been demonstrated that there is no difference between OCT scans in participants with and without 1% tropicamide-induced pupillary dilation (Tanga *et al.*, 2015). Therefore, drug-induced pupillary dilation is not required for the purpose of OCT scanning.

2.6.1 – Retinal Nerve Fibre Layer (RNFL)

The RNFL is the inner-most layer of the retina, an OCT device calculates the RNFL thickness by determining the distance between the internal limiting membrane and the outer aspect of the RNFL (Duker *et al.,* 2014). This is depicted below in figure 2.7.
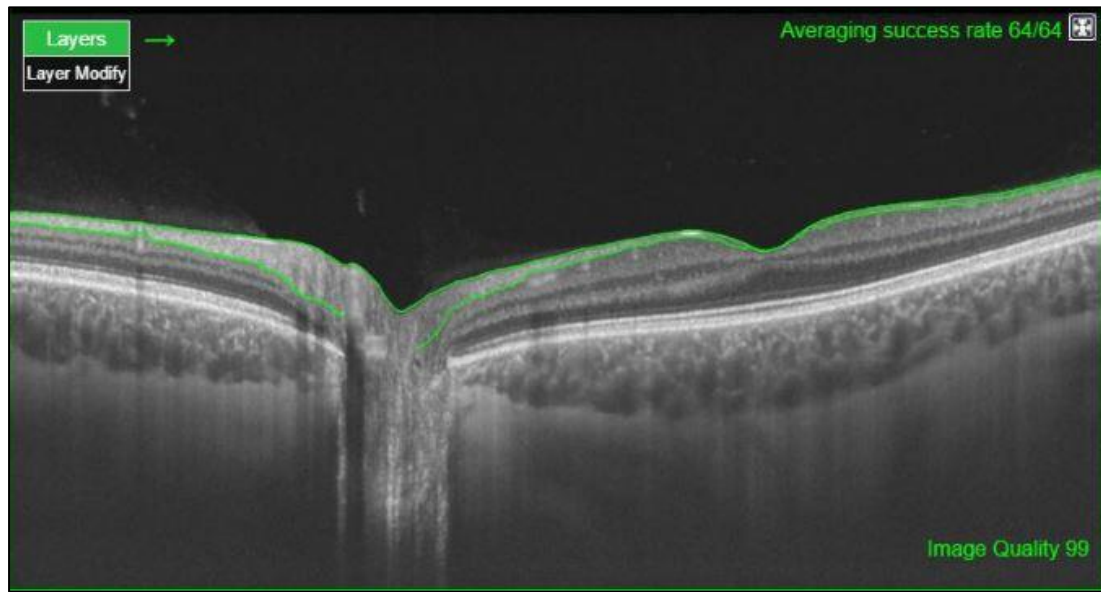
Figure 2.7 – Inner and Outer Limiting Lines of the RNFL (Authors own work)

The RNFL is made up of unmyelinated ganglionic axons making it a suitable structure to investigate neurodegeneration and potentially neuro-repair (Kristin M. Galetta *et al.*, 2011). These ganglionic axons travel in the direction of the optic nerve head where they merge together on the optic disc, as a result the RNFL is thicker and easier to measure around the optic disc, this area is known as the peripapillary area (Reynolds and Olitsky, 2011) The peripapillary area is depicted below in figure 2.8.
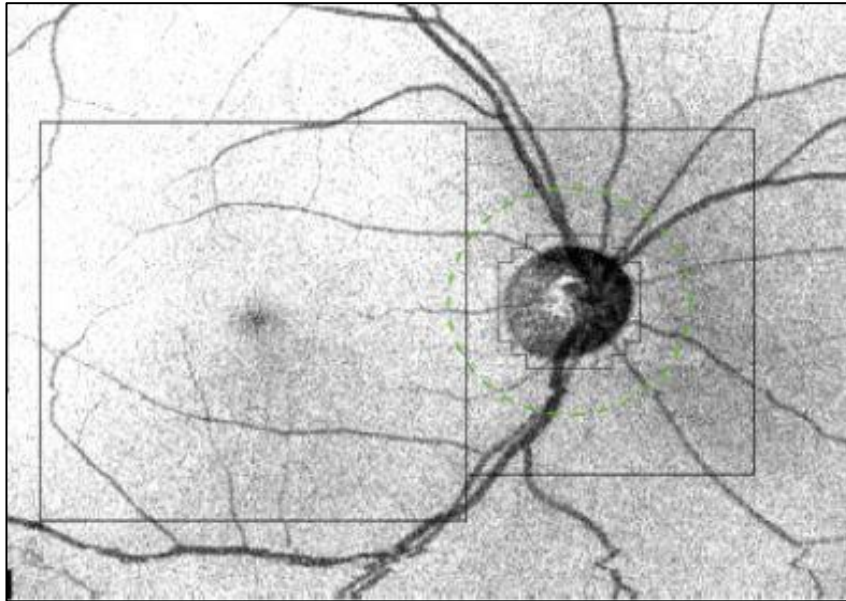
Figure 2.8 – Macular area with the fovea located in the centre (left square) and peripapillary area (right square) of the retina (Authors own work)

2.6.2– Ganglion Cell Layer ++ (GCL++)

The GCL++ complex is comprised of the tissues between the inner limiting membrane (ILM) to the Inner Nuclear Layer (INL) boundaries (Satue *et al.*, 2017), i.e. the RNFL, Ganglion Cell Layer (GCL), Inner Plexiform Layer (IPL) and INL layers. These layers are depicted individually above in Figure 2.6 and together as the GCL++ below in figure 2.9
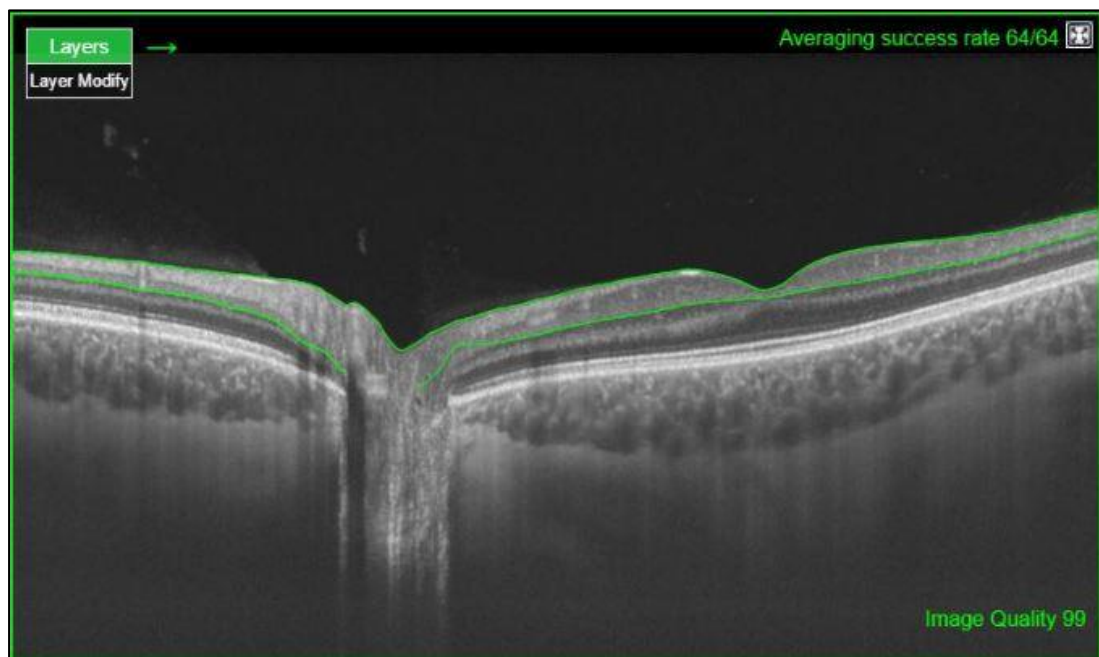
Figure 2.9 – Inner and Outer Limiting Lines of the GCL++ (Authors own work)

Retinal ganglion cells possess the same properties of CNS neurons, they contain a cell body (which makes up the GCL itself), dendrites, and axons (which make up the RNFL) (London *et al.,* 2013). The GCL is thickest around the perifoveal macular area (depicted above in figure 2.8), the surrounding 10⁰ of the centre of the macula (known as the fovea) contains approximately 50% of all retinal ganglion cells (Curcio and Allen, 1990). The fovea is depicted above in figure 2.8 as the small darkened area located at the centre of the left square.

The Topcon DRI OCT Triton Plus (SS-OCT) allows for concomitant scanning of both the peripapillary and macula areas, therefore allowing for examination of both peripapillary RNFL thickness and the macular GCL++ thickness at their optimal scanning sites, furthermore this allows for examination of the ganglion nerve axons, as well as the cell bodies themselves together with the remaining layers that make up the GCL++. This provides an opportunity for comprehensive analysis of the neurological structures of the retina. However it is vital that the OCT measures being utilised are of a high reliability and accuracy. The reliability of both the peripapillary RNFL and macular GCL++ measured by SS-OCT have previously been established. Hong *et al.,* (2018) examined both glaucomatous and healthy eyes of 122 participants in a single day and reported ICC's for RNFL and GCL++ thickness ranging from 0.994 – 0.998 depending on the sector, demonstrating an almost perfect test-retest reliability for the measures being employed in the current study. The diagnostic accuracy of SS-OCT to detect glaucoma has also previously been established. Yang *et al.,* (2015) examined the RNFL of 144 glaucomatous eyes and 66 healthy eyes with both SS-OCT and spectral domain OCT (SD-OCT), areas under the receiver operating characteristic (ROC) curve were used to establish the accuracy of the SS-OCT and SS-OCT measures in differentiating between glaucomatous and healthy eyes. Area under the ROC for peripapillary RNFL measured by the SS-OCT and SD-OCT were 0.89 and 0.90 respectively (1.0 indicates perfect discrimination) (Yang *et al.*, 2015).

2.6.3 – Choroid

The choroid comprises the primary vascular layer of the eye, providing up to 70% of its blood supply (Spaide 2010). The limiting lines of the choroid are outlined below in figure 2.10.
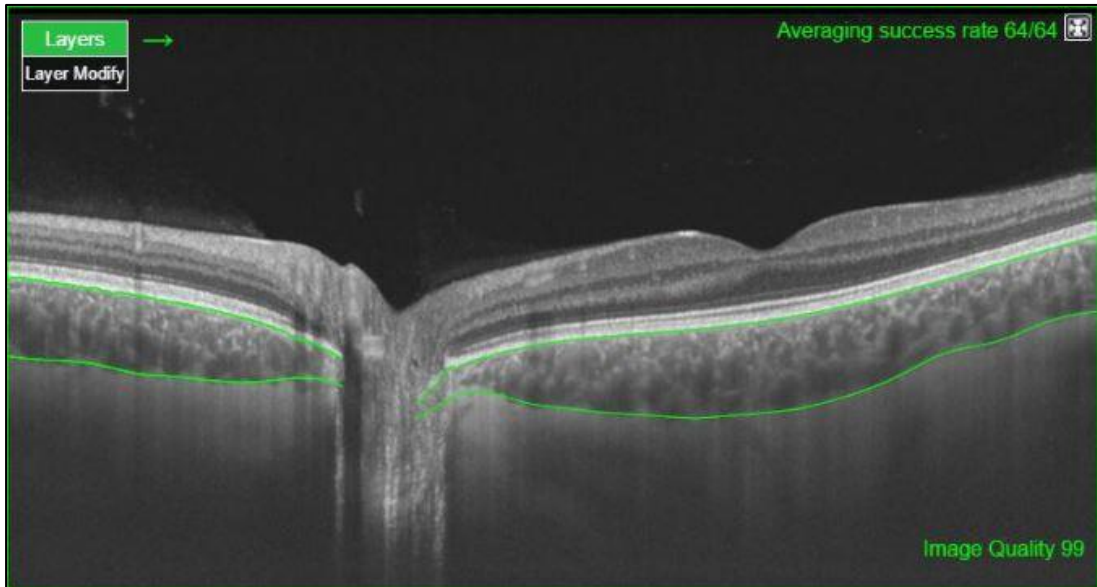
Figure 2.10 – Inner and Outer Limiting Lines of the Choroid (Authors own work)

The choroid possesses the highest blood flow per unit weight of any tissue in the human body (Gupta *et al*., 2005). Due to the high vascularity of the choroid, changes in this layer may manifest themselves during and after exercise due to the dynamic nature of blood flow during exercise. If there were significant findings with regard to the effects of concussion on the retina, it is necessary to explore the potential effects of exercise on the retinal and sub-retinal structures. Particularly if OCT was to be used as part of a head injury assessment (HIA) or for diagnostic purposes immediately post-injury during exercise.

2.6.4 – Concussive Injury and OCT

There is a sparsity of research with regard to suspected concussive injury and OCT investigation. RNFL changes have been reported in university football players with a remote history of concussion in the U.S.A. (Bixenmann *et al.*, 2014). This study compared RNFL thickness and ganglion cell complex (GCC) thickness with OCT in participants with a self-reported history of concussion against those with no self-reported history. Findings of the study displayed a significantly thicker RNFL in players with a history of concussion compared to those with no history (106.8µm, SEM = 0.96 *vs* 103.7µm, SEM = 0.65, $P < 0.01$). The significant difference between groups equates to 3.1µm. The GCC layer demonstrated similar findings, however it was not found to be significantly significant between those with and without a previous history of concussion (98.1µm, SEM = 0.78 *vs* 96.7µm, SEM = 0.54, $P = 0.15$ respectively). RNFL thinning rather than thickening is a common finding in other neurological conditions such as M.S. Stroke, Parkinsons' and Alzeimers' disease (London *et al.,* 2013). These contrasting OCT findings may contribute to the differential diagnosis between concussion history and other neurological diseases. In contrast to the study carried out by (Bixenmann *et al.*, 2014), Mohan *et al.,* (2013) conducted an animal study on mice examining the effects of blast-mediated head trauma on OCT metrics, the study demonstrated a significant superior-temporal peripapillary RNFL thinning 3-months post-injury when compared with controls (56.4 ± 1.7 µm *vs* 61.1 ± 0.9µm, $P = 0.0217$). However it must be noted that there were no other significant differences found in the other quadrants of the peripapillary retina. In light of the above, there are conflicting findings with regard to concussion/head trauma and the RNFL and there is a clear need for further research involving human participants.

2.6.5 - Exercise and OCT

Previously there have been a number of studies carried out with regard to the effects of different types of exercise on retinal and choroidal thickness (Sayin *et al.*, 2015; Alwassia *et al.*, 2013; Balk *et al.*, 2013). Furthermore choroidal blood flow has also been studied in this regard (Zhang *et al.*, 2012; Schmidl *et al.*, 2016; Iester *et al.*, 2007).

Sayin *et al.*, (2015) conducted a study to examine the effects of moderate-intensity aerobic exercise (10-minutes on a bicycle ergometer) on choroidal thickness, retinal thickness, ocular perfusion pressure (OPP), heart rate (HR) and mean blood pressure (mBP), measures were taken before exercise, 5-minutes and 15-minutes post exercise. There was a significant increase in choroidal thickness from baseline to 5-minutes post ($344.00 \pm 64.71\mu m$ *vs* $370.63 \pm 63.58\mu m$, $P < 0.001$) while measurements at 15-minutes had almost returned to baseline levels ($345.31 \pm 63.58\mu m$). In contrast, there were no significant differences observed in retinal thickness or IOP at any time point ($P > 0.05$) (Sayin *et al.*, 2015). The study by Sayin *et al.*, (2015) was limited by the fact that the inner and outer limiting lines of the choroid were measured manually, SS-OCT measured by the triton, however, employs automatic segmentation therefore addressing this limitation. In contrast to the findings of Sayin *et al.*, (2015), a study carried out by Alwassia *et al.*, (2013) found no significant differences in choroidal or retinal thickness following exercise. The age of participants and the type of exercise differed between both studies. The participants in the study by Sayin *et al.*, (2015) had a mean age of 27 ± 4.08 years *vs* 60.6 ± 10.4 years in the study by Alwassia *et al.*, (2013). Furthermore, Sayin *et al.*, (2015) used a 10-minute bicycle ergometer as the exercise intervention *vs* a cardiac exercise stress test however the exact procedure was not described.

Another similar study examined the effects of a 10km run on the thickness of retinal layers in 27 runners (mean age: 44 years) compared with 15 controls (mean age 28 years) (Balk *et al*., 2013). OCT measures were taken pre-race, immediately post-race and 1.5 hours post-race. There was a significant increase observed in RNFL (P = 0.018), the combined inner plexiform/ganglion cell layer (P = 0.038) and the outer nuclear layer (P = 0.018) immediately post-race. All of these changes in thickness, with the exception of the RNFL returned to normal following the 1.5 hour rest/rehydration period. Balk *et al.,* (2013) propose that these changes in thickness may be attributable to a shift in cellular volume due to hydration changes. According to the current research, there is conflicting evidence with regard to the effects of exercise on OCT measures. There are varying forms of both OCT examination and types of exercise used. The exercise protocol being used in the current study replicates the running demands of a team sport scenario and has been shown to be reliable for various physiological and performance measures (Sirotic and Coutts 2007; Sirotic and Coutts 2008) therefore affording a direct investigation to the effects of team sport demands on retinal and choroidal structures. Another ocular metric associated with the vascular supply to the eye and which changes as a result of exercise is intra ocular pressure (IOP).

2.7 – Intra Ocular Pressure

Intraocular pressure (IOP) is defined as the pressure of the contents inside the eyeball (Murgatroyd and Bembridge 2008). There are many physiological factors that can influence IOP. These include intra-global factors such as aqueous humour volume, blood volume, foreign bodies, vitreous humour volume as well as extra-global factors such as tumour, abscess, anaesthesia, and extra-ocular muscle tone, among others (Murgatroyd and Bembridge 2008). Furthermore, it has been shown that posture has an effect on IOP, with the literature showing that IOP increases from seated to supine positions (Jorge *et al.*, 2010; Sawada and Yamamoto 2013; Lam *et al.*, 2013; Prata *et al.*, 2010). IOP is currently the only modifiable risk factor (*via* surgery, laser or medication) for the management of glaucoma (Stamper 2011). Therefore the majority of research concerning IOP is centred on glaucoma. Due to the fact that IOP is closely associated with both systemic blood pressure (Singleton *et al.*, 2003), it is logical to study this metric in conjunction with the choroid.

The method by which IOP is measured is known as tonometry, of which there are various forms, such as applanation/Goldmann tomometry, non-contact (air-puff) tonometry and rebound tonometry among others, which incorporate combinations of the above (Stamper, 2011). The current accepted clinical gold standard for the measurement of IOP is the Goldmann applanation tonometer (GAT), which requires a slit lamp, administration of both fluorescein dye and topical anaesthetic to the eye (Murgatroyd and Bembridge, 2008). In an effort to increase the practical availability of IOP measurements, without the necessity for dye and anaesthetics other types of tonometer have been developed. One such type of tonometer, and the type of tonometer used in the current study is known as a rebound tonometer. The first model of rebound tonometry was proposed by Konitola, (1997). The principle of rebound tonometry involves a small probe being propelled from a handheld device, once the probe makes contact with the cornea the contact and deceleration time of the probe is then recorded *via* an acceleration sensor and converted to a voltage measurement *via* a capacitance meter (Konitola, 1997). The iCare Pro rebound tonometer (RBT) (*ICare, Tiolat, Oy,*

Helsinki, Finland) was introduced in 2005, it is a handheld, portable instrument, which does not require the use or application of topical anaesthesia (Dahlmann-Noor *et al.*, 2013). This is a clear advantage when measuring IOP in a more dynamic environment such as a sport settting, or with more vulnerable young or elderly populations as it may be impractical to use dye or anaesthetic. However it is imperative that other forms of tonometry produce reliable measures, which are also comparable to the accepted clincial gold standard of GAT.

2.7.1 – Validity and Reliability of the iCare Rebound Tonometer

The validity of the RBT has been established by comparing it to the clinical gold standard of GAT. Martinez-De-La-Casa *et al.,* (2005) and Kim *et al.,* (2013) correlated RBT measures with GAT (gold standard) measures. There was a good correlation, which was significant, found between the two devices ($r = 0.6995$, $P < 0.001$) reported by Kim *et al.,* (2013). Furthermore, Martinez-De-La-Casa *et al.,* (2005) reported a higher correlation, which was also significant ($r = 0.865$, $P < 0.0001$). Both studies also reported that RBT over estimates IOP slightly by 1.92 ± 3.29mmHg (Kim *et al.*, 2013) and 1.8 ± 2.8mmHg (Martinez-De-La-Casa *et al.*, 2005). Therefore RBT is a good substitute for GAT, but it must be taken into account that it slightly over-estimates IOP.

There are two forms of reliability in clinical research; intra-rater reliability, which concerns a single rater/tester or measurement tool and inter-rater reliability, which concerns two or more raters (Batterham and George 2003). Reliability can range from 0 to 1, the closer an ICC value is to 1, the higher the observed reliability (Bruton *et al.,* 2000). Test-retest reliability provides a clinician with a degree of confidence that a tool measures an outcome measure in the same way each time it is used, providing the client/participant is stable (Vaz *et al.*, 2013). The reliability of the RBT has been well established in the literature (Kim *et al.*, 2013; Martinez-De-La-Casa *et al.*, 2005; Sahin *et al.*, 2007; Salim *et al.*, 2013), reporting intra-rater reliability ranging from fair to excellent (ICC: 0.730 – 0.981). However the testing

position/posture was only described in the study by Kim *et al.,* (2013) in which all measures were taken in a seated position. The studies by Martinez-De-La-Casa *et al.,* (2005); Sahin *et al.,* (2007) and Salim *et al.*, (2013) did not specify the testing posture, however the normal testing posture used for the gold standard of GAT, to which the RBT was compared to in each of these studies, therefore these studies presumably used a seated posture for all measures. To the best knowledge of the author, the reliability of the RBT has not yet been established in a standing posture, which may be more applicable in a sporting setting.

2.7.2– Effects of Exercise on IOP

The effects of different types of exercise (isometric and dynamic) on IOP have been well documented in the literature with varying results (Qureshi, 1996; Huang, 2015; Gale *et al.*, 2009; Roddy *et al.*, 2014; McMonnies, 2016). An isometric exercise refers to a muscle action where the contractile force is equal to the resistive force (Baechle and Earle, 2008), an example of such an exercise (a static squat with the knees flexed to 90º) was used by (Huang, 2015).

The study by Huang, (2015) examined the effects of both isometric (static squat) and dynamic (10-minutes on a stair climber) on IOP, the tonometer used was a handheld tonopen (Huang 2015). Findings of the study revealed no significant differences pre to post exercise for either type of exercise ($P > 0.05$), however there was a significant difference observed during the isometric exercise ($P < 0.0001$), which may be attributed to an increase in blood volume in the choroidal vessels during the exercise, thereby increasing IOP (Huang, 2015). The relatively short duration (10-minutes) of aerobic exercise used by Huang, (2015) may not have been sufficient to cause changes in IOP. Another study carried out by Qureshi, (1996) examined the effects of aerobic exercise on IOP using GAT, the exercise protocol consisted of cycling a bike ergometer for 60-mins at 50 cycles/min. IOP was measured in the last 30-seconds of the 5th, 20th, 40th and 60th minutes of the test, furthermore during a cool down period following the protocol, IOP was

measured every 10-minutes until IOP returned to baseline levels in two groups of males (N =16 in each group) (Qureshi, 1996). Results of the study revealed that IOP decreased over the course of the study in both groups, significant differences were found between each time point in both groups ($P < 0.05$) with a 27.65% decrease in IOP from baseline in one group and 28.72% in the other. Furthermore IOP returned to normal levels after an average of 48:13 minutes in one group and 49:38 minutes in the other (Qureshi 1996). A meta-analysis was conducted by Roddy *et al.,* (2014) on the effects of aerobic exercise on IOP, findings of the study reported that there is a clear effect (decrease) of aerobic exercise on IOP, interestingly the effect size was almost double that in a sedentary population (ES = 4.198mmHg) in comparison to an active population (ES = 2.340mmHg). The differences in effect size between these populations are also not attributable to either exercise intensity or duration. Therefore it is generally accepted in the literature that aerobic exercise decreases IOP, however these decrements are relatively transient. The effects of a team sport running protocol on IOP have not yet been established.

2.8 – Summary

Concussion remains a clinical challenge for healthcare professionals. This decision is difficult and predominantly guided by subjective and sub-optimal tools. There is no validated, objective bio-marker for concussion diagnosis. The most widely used tool to guide concussion diagnosis and management is inarguably the SCAT (Currently SCAT5). However, this tool is influenced by many confounding factors. Therefore, a more reliable objective tool is warranted. The eye, specifically the retina, is an extension of the C.N.S. There are structural findings in the retina which are associated with various neurological conditions. It is therefore logical to investigate for potential structural changes in the retina following suspected concussive injury *via* OCT. If such a measure was to be used in a sporting environment then it is necessary to first establish the effects of exercise on these measures. IOP has been postulated to be associated with certain OCT (choroidal) measures. The effects of exercise on IOP have been well established. However there is a gap in the literature with regard to the effects of a simulated team sports running protocol on IOP.

The review of literature has identified a number of aims and hypotheses, listed below according to their individual studies these will be presented again at the beginning of each component study in order to provide context.

Study 1

Aim:

- The aim of this study was to establish the intra-rater reliability of the iCare® PRO rebound tonometer (RBT) in a standing posture in a single testing session.

Hypothesis:

- There will be fair to excellent intra-rater reliability of the iCare rebound tonometer measured in a standing position in a single session.

- IOP will significantly decrease following exercise.

- There will be a significant increase in peripapillary RNFL, Macular GCL++ and Choroidal thickness following exercise.

- There will be a significant negative correlation between IOP and choroidal thickness changes following exercise.

Study 3 - Hypotheses:

SCAT-3 Baselines

- Females will report significantly higher symptom scoring than males on baseline testing, and will significantly outperform males on the SAC and mBESS

- Participants with a history of previous concussion will report significantly higher symptom scoring than those without a history of concussion

OCT Baselines

- Males will have a significantly thicker GCL++ than females on baseline testing

- Participants with a history of concussion will display a significantly thicker peripapillary RNFL and Macular GCL++ than participants without a previous history of concussion.

Follow-up Measures

- There will be a significant increase in symptom number and SSS following concussive injury

- There will be a significant decline in cognitive function (SAC) and postural control (mBESS) following concussive injury

- There will be a significant thickening of peripapillary RNFL and Macular GCL++ thickness following concussive injury

CHAPTER THREE:

Study 1: Intra-Rater Reliability of the ICare Pro Rebound Tonometer

Abstract

Title: Intra-rater reliability of the ICare® Pro Rebound tonometer

Introduction: The aim of this study was to establish intra-rater reliability of the Icare® PRO rebound tonometer (*Icare*, tiolat, oy, Helsinki, Finland) in team sport athletes measured in a standing posture. The rebound tonometer measures Intra-ocular pressure (IOP) by releasing a small, sterile plastic probe that rebounds off the cornea and provides a measure of the pressure inside the eye. Fair to high intra-rater reliability of the Icare® PRO rebound tonometer has been well established in previous studies (Martinez-de-la-Casa *et al.*, 2005, Sahin *et al.,* 2007), the common posture of testing is in a seated position. Reliability in a standing position has not yet been established. The standing posture is more applicable to a sporting situation such as a head injury assessment (HIA) in team sports.

Methods: To examine intra-rater reliability and agreement 62 eyes of 31 male (N=17) and female (N=14) participants were examined using the Icare® PRO rebound tonometer. There was a single session of testing. Participants were tested in a rested state following 5 minutes of static stance. Three consecutive measures were taken in alternating eyes with 2 minutes between each measure. Intra-class correlation coefficients (ICC's) were calculated for both eyes to establish reliability.

Results: Fair intra-rater reliability was observed for both eyes, ICC = 0.771(CI: 0.63-0.87) and 0.753 (CI: 0.60 – 0.86) for the left and right eyes respectively. Standard error of the mean (SEM) was calculated as 0.17mmHg and 0.16mmHg for the left and right eyes respectively. Minimal detectable change (MDC) was calculated as 2.15mmHg and 2.11mmHg for left and right eyes respectively

Conclusions: The Icare Pro rebound tonometer is a reliable device with regard to intra-rater reliability when tested in a standing posture at rest in a single testing session. This portable device could be effective in a sporting setting, possibly as part of a HIA assessment and as a screening tool for intraocular pressure in team sports. However, the effects of team sport exercise demands on IOP must first be established. Further research could be carried out in determining the effects of the reliability of the device over a number of days.

3.1 - Introduction

The review of literature has established that there is fair to excellent intra-rater reliability of iCare® PRO rebound tonometer (RBT), the testing position of these studies is however, either not specified or is in the seated position. Therefore there is a gap in the literature with regard to establishing the reliability of this device in a standing position, which may be more applicable to a sporting setting. The RBT and it's relevant component parts are represented in figure 3.1 below.

1. Forehead support adjustment wheel
2. Forehead support
3. Collar
4. Probe base
5. Navigation buttons: Up, Down, Left and Right
6. Display
7. Main button
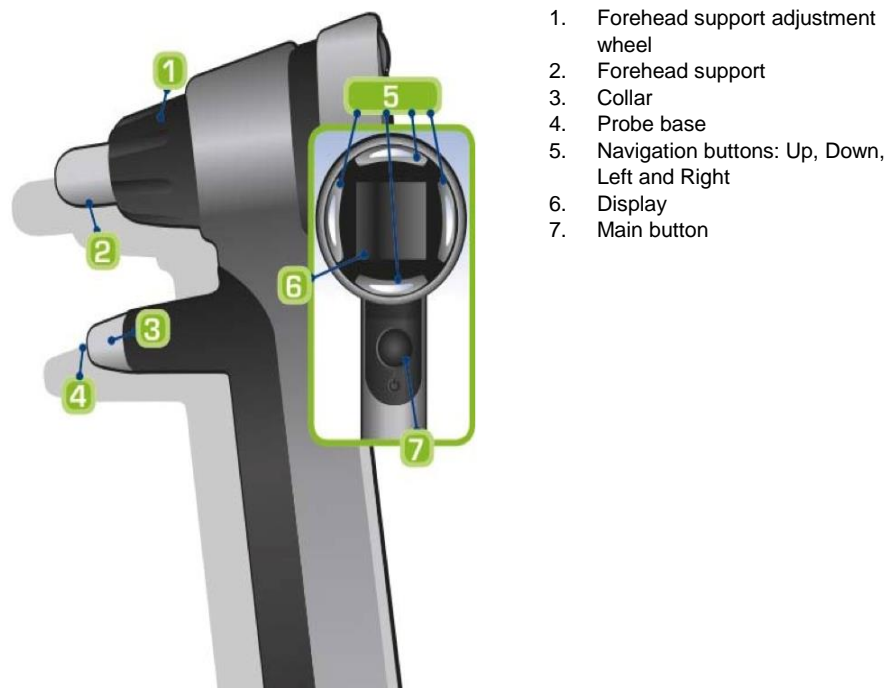
Figure 3.1: iCare Pro Rebound Tonometer (iCare, 2017)

Hypothesis:

- There will be fair to excellent intra-rater reliability of the iCare rebound tonometer measured in a standing position in a single session.

3.2 – Methodology

<u>Participants</u>

Ethical approval was obtained from the Institute of Technology Carlow (ITC) ethics committee prior to recruitment of any participant. The sample size sought was based on a similar study carried out by Martinez-De-La-Casa *et al.*, (2005) in which a sample of 12 participants were used. For the current study, 31 participants (17 male and 14 female) were recruited verbally from the ITC department of science and health student population. Participants were initially approached during class time, the purpose procedures and exclusion criteria were explained at this time. Exclusion criteria comprised any active eye infection or a previous history of eye surgery, diabetes, glaucoma, or keratoconus. The inclusion criteria for this study were; being generally active, which for the purpose of this study was defined as partaking in some form of sporting activity 2-3 times per week and to be aged between 18 and 31 years old. A health screening form was completed and written consent obtained prior to any procedure (Appendix B). Participants were asked to refrain from exercising on the day of testing and to not wear contact lenses.

<u>Procedure</u>

The procedure is represented below as a flow chart (figure 3.2). The RBT (Figure 3.1) was used to take all measurements throughout the study. The same device was used for every measurement, which was conducted by a single rater. The rater underwent training, (1-hour in duration) in the operation and maintenance of the RBT under the guidance of a professional in the area of ophthalmology prior to commencement of the study. This training invloved correct handling of the device, loading of probe and multiple repeated measurements to the satisfaction of the professional, the rater then undertook approximately 2-hours of practice measures on 15-20 volunteers from the ITC Department of Science and Health prior to capturing any recorded study data. Testing took place in a single session. Full explanation and verbal instruction was given to each participant during the testing procedure. Participants were asked to stand for 5-minutes prior to obtaining

the measurement, allowing pressure to stabilise in the eye, as it is well established that postural changes can have an initial effect of IOP (Jorge *et al.*, 2010; Sawada and Yamamoto 2013; Lam *et al.*, 2013; Prata *et al.*, 2010). All measures were taken at rest in a standing position. Operation of the tonometer was carried out in accordance with the iCare® PRO instruction manual (iCare 2017). An individually packaged, sterile probe was used for each participant. The sterile probe package was partially opened and the probe was inserted into the RBT by pushing it into position with the sterile package until a slight click was felt (Figure 3.3). This confirmed that the probe was in place. The RBT then calibrated itself. The device was moved into position at a 90° angle to the cornea, the distance from the tip of the probe to the cornea was 3-7mm (Figure 3.3). This distance was achieved by adjusting the forehead support appropriately according to the depth of each individual participants' eye. Each participant was instructed to look over the shoulder of the rater during measurement and to breathe normally. The RBT takes 6 individual readings, the device automatically discards the highest and lowest reading and calculates an average of the remaining 4 readings. Furthermore, the RBT calculates the standard deviation between measures and alerts the tester if it is not acceptable. The average IOP (mmHg) was recorded and the procedure repeated for the other eye. This procedure was repeated 3 times for each eye with a 2-minute interval in between measures this interval time was chosen as some previous studies carried out consecutive measures (Sahin *et al.*, 2007; Salim *et al.,* 2013), wheras another study allowed a 5-minute interval between measures (Martinez-De-La-Casa *et al.*, 2005). It was deemed that a 2-minute interval would improve participant comfort rather than having 36 consecutive measures taken. If there was an obvious error caused by either the rater or the participant then the reading would be discarded and re-measured. Examples of errors included; the participant moving the eye or squinting during the measurement and incorrect positioning of the tonometer causing the probe to either come in contact with the eyelid or to not make contact with the centre of the cornea.
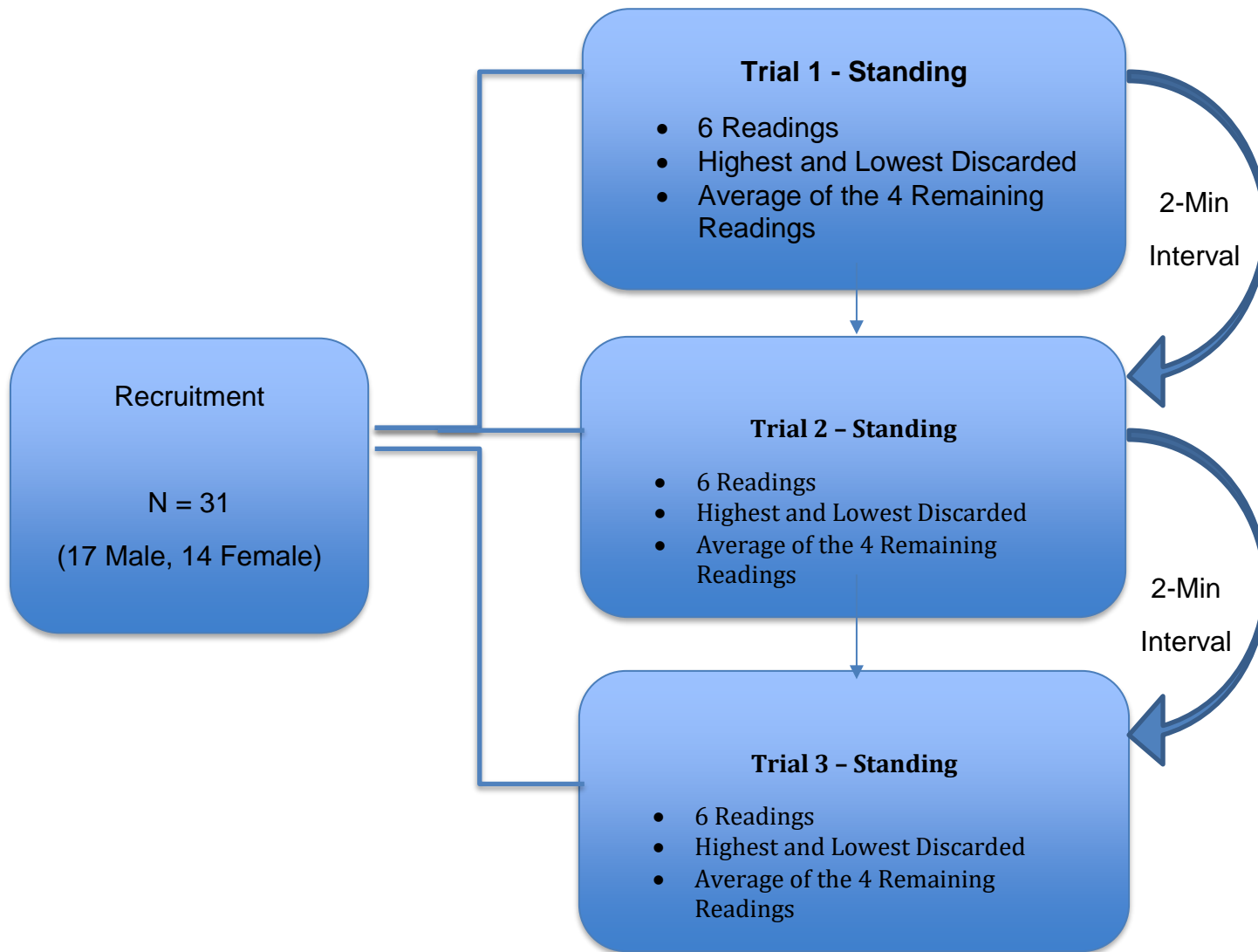
Figure 3.2 – Reliability Methodology Flow Chart
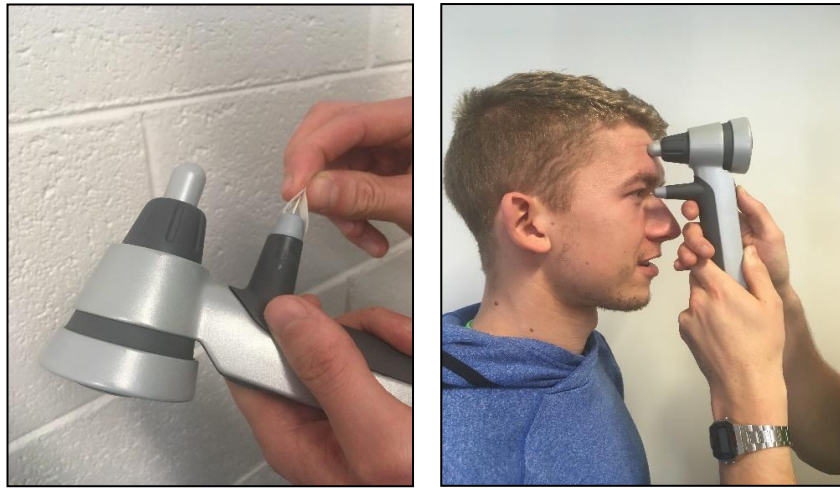
Figure 3.3 – Insertion of Sterile Probe (Left) and Measurement of IOP (Right)

Data Analysis

IBM SPSS (Statistical Package for Social Sciences) version 23 was used to analyse the data. Measures of both relative and absolute relaibility were used for analysis. Relative reliability represents the degree to which participants keep their rank in a sample population over repeated measures, correlation coeffiecients (such as ICC's) are an example of a measure of relative reliability (Bruton *et al.*, 2000). Absolute reliability is associated with the amount that repeated measures vary for individuals, an example of absolute variability is SEM, (Bruton *et al.*, 2000). 2-way fixed (3,1) Intra-Class Correlation Coefficient's (ICC) and Mean and Standard Error of the Mean (SEM) were calculated for both the left and right eyes respectively over the 3 trials. Minimal detectable change (MDC) was calculated by using the following equation (Koo *et al.*, 2013), where SD = standard deviation.

$$MDC = (SD \sqrt{(1-ICC)}) \times 1.96 \times \sqrt{2}$$

According to Haley and Fragala-Pinkham (2006) the minimal detectable change is the smallest amount of change that is not attributed to normal variation in measurement. Therefore any change greater than this is due to an actual change caused by a treatment, intervention or condition. ICC's were interpreted according to the classification system (figure 3.4) used by (Currier 1990).
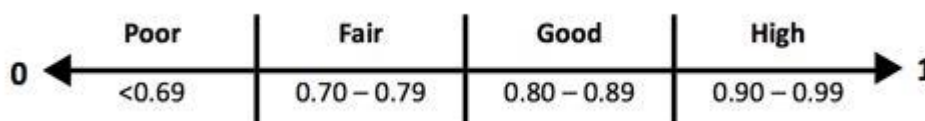
Figure 3.4 - Classification of Reliability (Currier, 1990)

3.3 – Results

Thirty one participants (17 male, 14 female). Participants had mean age of 20.97 ±3.30 years.

The Mean ±Standard Deviation IOP for each of the 3 trials in the left and right eyes are displayed in table 3.1 below. Individual IOP values ranged from 13.8 mmHg to 21.9 mmHg in the left eye and from 13.3 mmHg to 20.7 mmHg in the right eye. Figure 3.5 displays the correlation of the measures over the 3 trials in both the left and right eyes.

Table 3.1 – Mean ± SD of IOP(mmHg) for Each Trial

Eye	Trial 1 (mmHg)	Trial 2 (mmHg)	Trial 3 (mmHg)
Left Eye	17.23 ±1.60	16.82 ±1.48	16.71 ±1.77
Right Eye	16.88 ±1.59	16.68 ±1.59	16.39 ±1.42
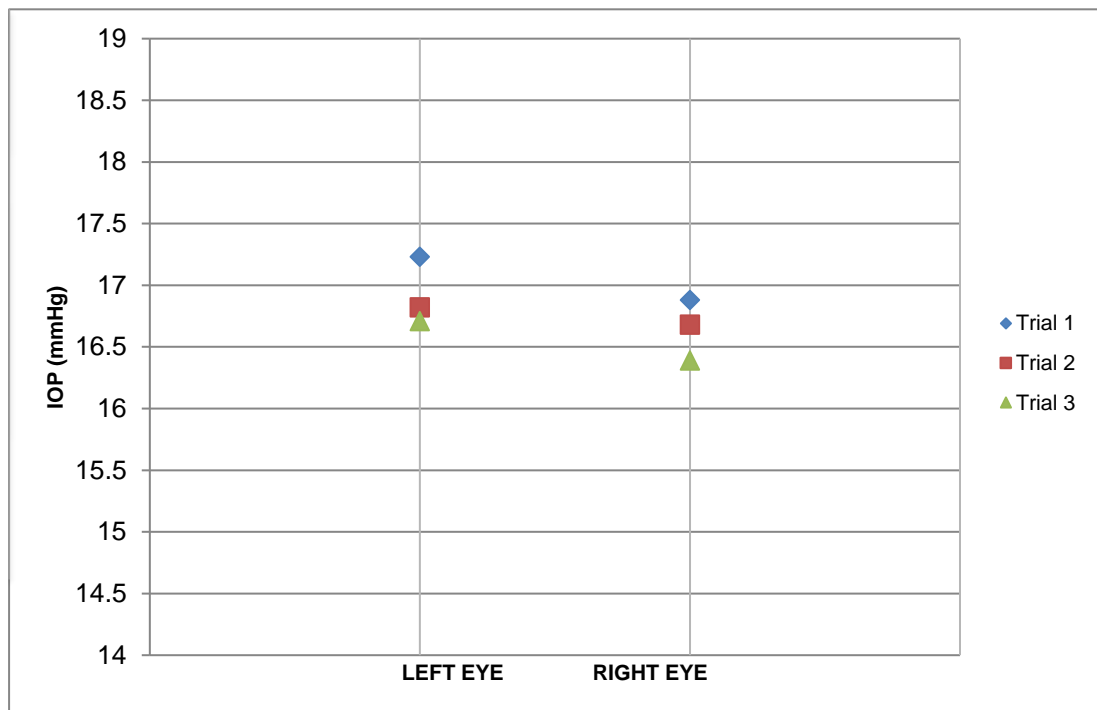
Figure 3.5 – Correlation Scatter Plot for the Means of 3 Trials of Left and Right Eyes

Overall Mean ± SD, SEM, MDC and ICC (95% C.I) values are displayed in table 3.2. Mean IOP was 16.92 ±1.62 mmHg and 16.65 ±1.53 mmHg for the left and right eyes respectively. The SEM was 0.17 mmHg for the left eye and 0.16 mmHg for the right eye. MDC was calculated as 2.15 mmHg and 2.11 mmHg for the left and right eyes respectively. Fair/Acceptable Intra-rater reliability was calculated for both eyes, an ICC (3,1) of 0.77 (95% C.I: 0.63 – 0.87) was calculated for the left eye and 0.75 (95% C.I: 0.60 – 0.86) was calculated for the right eye.

Table 3.2 – Mean IOP, SEM, MDC and ICC for Left and Right Eyes

Eye	Mean IOP ±SD (mmHg)	SEM (mmHg)	MDC (mmHg)	ICC (95% C.I)
Left	16.92 ±1.62	0.17	2.15	0.77 (0.63 - 0.87)
Right	16.65 ±1.53	0.16	2.11	0.75 (0.60 - 0.86)

3.4 – Discussion

As mentioned in the methodology, measures of both relative and absolute reliability were employed in this study, the general consensus is that reliability studies should use a mixed approach with regard to estimates of reliability (Bruton *et al.*, 2000). Therefore the utilisation of both ICC's and SEM provided a more global representation of reliability in this study. Fair/acceptable intra-rater reliability has been established for the RBT in the current study. Reliability of the RBT has been previously established in the literature. Kim *et al.*, (2013) reported an ICC of 0.778 for the RBT. These findings are consistent with ICC values established in the current study, which established ICC's of 0.771 for the left eye and 0.753 for the right eye (Table 3.2). Martinez-de-la-casa *et al.*, (2005) calculated ICC's for 3 separate raters, which were reported as 0.73, 0.82 and 0.87. Salim *et al.*, (2013) investigated the intra-rater reliability of the RBT using 2 raters and found excellent ICC's of 0.981 and 0.979, similarly, Sahin *et al.*, (2007) reported ICC's of 0.974 and 0.970 for left and right eyes respectively for one rater and 0.970 and 0.963 for the other. The previous literature, including results from the current study report intra-rater reliability ranging from 0.730 to 0.981. Confirming that the RBT is a reliable device for the measurement of IOP in multiple postural positions.

The ICC's calculated in the current study are slightly lower than those reported by Salim *et al.*, (2013) and Sahin *et al.*, (2007). This may be attributable to the standing posture used in the current study and the greater amount of free movement available to the participant while in a standing position when compared with the traditional sitting posture used in the majority of previous studies. Future research could modify the posture of the patient by having them stand with their back against a wall to promote a more stable testing position. A further explanation for the slightly lower ICC calculated in the current study may be the fact that previous studies used experienced professional ophthalmologists as raters whereas the rater in the current study was a sports medicine professional, inexperienced in the field of ophthalmology. Nonetheless the results of this study suggest that a

healthcare professional with a limited experience of tonometry can quickly produce an acceptable level of reliability with the iCare Pro rebound tonometer with just 1 hour of training with a professional in the area of opthalmology and approximately 2 hours practice prior to data collection.Employing a longer training and rater-familiarisation period could potentially further improve these already acceptable reliability meaures. The measures for both right and left eyes decreased from trial 1 to trial 2 and again from trial 2 to trial 3 (Table 3.1), a possible explanation for this decreasing trend in IOP over the three trials may be attributable to the fact that the patient stood in the testing posture for only 5-minutes prior to the first trial and the postural effects on IOP were still ongoing. In a future reliability study it may be appropriate to extend the initial time in the testing posture to 10 or 15 minutes, which is comparable to a study carried out by Lam *et al*., (2012) that examined the variations of IOP from sitting to standing with the iCare Pro. Sahin *et al*., (2007) displayed a similar trend to the current study showing that IOP decreased over the 3 trials for one rater in both left and right eyes. Sahin *et al*., (2007) allowed for a 5-minute interval between tests compared with the 2-minute interval used in the current study. The slightly longer interval use by Sahin *et al*., (2007) may have attenuated the postural effects on IOP.

The SEM calculated was 0.17 mmHg and 0.16 mmHg for the left and right eyes respectively (Table 3.2). The SEM is a measure that shows how representative a sample is of the whole population (Field 2009). A large SEM would suggest there is a high level of variability between the means of different samples and a small SEM would suggest the opposite, suggesting a low level of variability between various samples (Field 2009). In the current study, a low SEM was calculated for both the left and right eyes, therefore displaying that there is a low level of variability between the means of different samples of the population.

The MDC calculated was 2.15 mmHg for the left eye and 2.11 mmHg for the right eye (Table 3.2). MDC is the amount of change that a particular measure must alter to ensure that the change is greater than measurement error (Donoghue *et al.,* 2009). Therefore, according to the sample employed, this data provides clinicians with a certain amount of assurance that a change within the MDC (< 2.2mmHg) could possibly be due to normal measurement error. Any change outside the MDC (> 2.2mmHg) could be attributable to the influence of an intervention or change in a patients' condition such as an exercise or postural induced alteration of IOP. An ideal sample size was calculated using G*Power software (Faul *et al.*, 2009) With an expected medium effect size of $p = 0.3$ and significance level set to 0.05, it was calculated that an ideal sample size of 111 participants would be necessary to obtain a power of 0.95. Therefore future research should include a larger sample size. MDC is a valuable and worthwhile measure to establish, with particular utility in clinical practice. To the best knowledge of the author the MDC for the RBT has not previously been reported. It is recommended that future research take this measure into account.

Conclusion

In light of these findings, the hypothesis that there is fair-excellent intra-rater reliability of the RBT measured in a standing position in a single session is accepted. The portability and practicality of this tonometer would be useful as a screening tool in a sporting setting. Furthermore, this study has demonstrated that a healthcare professional inexperienced in the area of ophthalmology can attain an acceptable level of reliability with a minimal amount of training. Future reliability studies should include exercise of different intensities and carry out trials on multiple days. If this device were to be used in a sporting environment then it is imperative that the effects of exercise on IOP are established. This will be one of the primary aims of study 2.

CHAPTER FOUR:

Study 2: The Effects of Exercise on Ocular Metrics

Abstract

Title: The Effects of Exercise on Ocular Metrics

Introduction: This study was a component part of a larger study investigating the effects of concussive injury on the retina. The objective of this study was to examine the effects of exercise on ocular metrics utilising Optical Coherence Tomography (OCT) measures of the retinal nerve fibre layer (RNFL), Ganlgion Cell Layer++ (GCL++), Choroidal thickness and intraocular pressure (IOP).

Methods: The exercise intervention used in this study was the protocol described by Sirotic and Coutts, (2008), and has been proven reliable for numerous physiological and performance measures. All running was carried out on the Woodway Curve 2.1 non-motorised treadmill (NMT) (Woodway, Weil Am Rhein, Germany). 11 male (N = 7) and female (N =4) active team-sport participants (21.2 ±1.3 years) were recruited for this study. Testing consisted of 3 laboratory visits over the course of 1-week with 48hrs in between visits. Day 1 of testing consisted of, collection of anthropometric data, maximum sprint speed (MSS) familarisation on the NMT and a 10-minute self-paced familiarisation. Day 2 of testing consisted of MSS calculation *via* three 6-second sprints and a 10-minute self-paced familiarisation. Day 3 of testing consisted of baseline IOP and OCT measures, followed by a 30-minute simulated team sport running protocol (running speeds were determined on an individual basis according to the MSS achieved on day 2). Follow up IOP and OCT measures were taken 2-mins post-exercise and 10-mins post exercise. One way repeated measures ANOVA and Bonferronni post-hoc analysis was used to examine for differences pre-post exercise in IOP and OCT measures. Pearsons' R was used to correlate mean IOP with mean choroidal thickness.

Results: There was minimal thinning of the RNFL following exercise, this was only found to be significant in the inferior sector of the left eye between baseline and 2-mins post ($P < 0.05$, $P = 0.013$) and baseline to 10-mins post ($P < 0.05$, $P = 0.025$). There was an overall thickening effect post exercise observed for total GCL++ thickness in the left eye between baseline and 10-mins post ($P < 0.05$, $P = 0.018$) and in the right eye between baseline and 10-mins post ($P < 0.05$, $P = 0.003$) and 2-mins post to 10-mins post ($P < 0.05$, $P = 0.0001$). There was an initial thinning effect observed on choroidal thickness immediately following exercise, thickness returned toward baseline levels in the left eye. IOP followed a similar trend. There was a strong correlation observed between mean choroidal thickness and IOP ($R = 0.948$ and $R = 0.786$ in left and right eyes respectively).

Conclusion: The effects of a simulated team sport running protocol on ocular metrics were established in this study, however it is recommended that future research include more participant numbers and examine the effects of more sports specific exercise such as heading of the ball in soccer or tackling technique in rugby, and how ocular metrics respond beyond 10-minutes post-exercise.

4.1 – Introduction

This exploratory study was a single arm, pre-post intervention trial design. The review of literature has revealed that the effects of exercise on ocular metrics have previously been studied, however, a standardised exercise protocol has not been employed throughout the literature leading to heterogeneity of findings. There has been no previous research on the effects of a simulated team sport running protocol on ocular metrics. The objective of this study was to investigate the acute effects of exercise on ocular metrics (IOP and OCT measures of RNFL, GCL++ and Choroidal thickness) in team sport athletes. If the ocular metrics being employed in this study were to be used in a sporting setting, it would be necessary to identify the normal ocular and retinal responses to exercise. Particularly if these measures had the potential to contribute to part of a pitch-side or head injury assessment. In the event of a concussive episode during exercise, if the normal ocular responses to exercise are known then any change in ocular metrics may then be attributed to the concussive impact. However it must also be noted that there may be other potential influencing factors on ocular metrics, which are beyond the scope of this study.

Hypotheses:

- IOP will significantly decrease following exercise.

- There will be a significant increase in peripapillary RNFL, Macular GCL++ and Choroidal thickness following exercise.

- There will be a significant negative correlation between IOP and choroidal thickness changes following exercise.

4.2 – Methodology

Participants:

Prior to the recruitment of any participant ethical approval for the study was obtained from the ITC ethics in research committee. For the purpose of this exploratory study, 11 participants (7 male, 4 female) were recruited. Inclusion criteria for the study consisted of: age between 18 and 31 years old and actively partaking weekly (either recreationally or competitatively) in sport with a physical contact element. Sample size was not calculated for this study as it was intended to inform secondary future research by utilising a small sample which was representative of the participants included in the main study. Exclusion criteria consisted of; currently suffering from suspected concussion, history of refractive (laser) eye surgery, history of keratoconus (abnormal curvature of the cornea), history of glaucoma, photosensitive epilepsy, history of severe eye trauma, history of diabetes and any musculoskeletal or any other injury that would hinder participation in the running protocol.

Recruitment Process:

Participants were recruited in person during class time with all procedures fully explained to them. Participants were then contacted *via* mobile phone to arrange a suitable testing schedule for them. It was communicated that the participants could not partake in any other form of exercise over the proposed 1-week time course of the study. Participants were provided with an information sheet, and completed a health-screening questionnaire and informed consent prior to taking part in any procedure (Appendix C).

<u>Procedures:</u>

Testing consisted of 3 laboratory visits for each participant over a 1-week time course with 48hrs between sessions (figure 4.1). The first visit consisted of collection of anthropometric data and a maximal sprint speed (MSS) familiarisation session. Weight was recorded using a SECA digital weighing scales (Seca, Hamburg, Germany). Height was recorded using a SECA stadiometer (SECA, Hamburg, Germany). The treadmill used was the Woodway Curve 2.1 non-motorised treadmill (NMT) (Woodway, Weil Am Rhein, Germany). The MSS familiarisation was followed by a 10-minute self-paced jog on the treadmill to become familiar with the technique required to run on the NMT. The second session consisted of the MSS calculation followed by additional 10-minute self-paced jog to facilitate further familiarisation. The third and final session consisted of pre-exercise IOP and OCT measures. This was followed by the simulated team sport running protocol. Finally, repeat measures were taken 2-minutes and 10-minutes post-exercise to explore the effects of exercise on ocular metrics in team sport athletes. IOP was taken first, followed by OCT measures.

IOP data was collected using the same procedures described in study 1. Pre-exercise IOP was taken at rest in a standing position prior to measurement it was ensured that each participant did not take part in exercise on the day of testing and that they were not wearing contact lenses. Participants were asked to stand for 5-minutes at rest prior to baseline measures. Each participant was asked to look over the raters' shoulder and breathe normally during measurement.
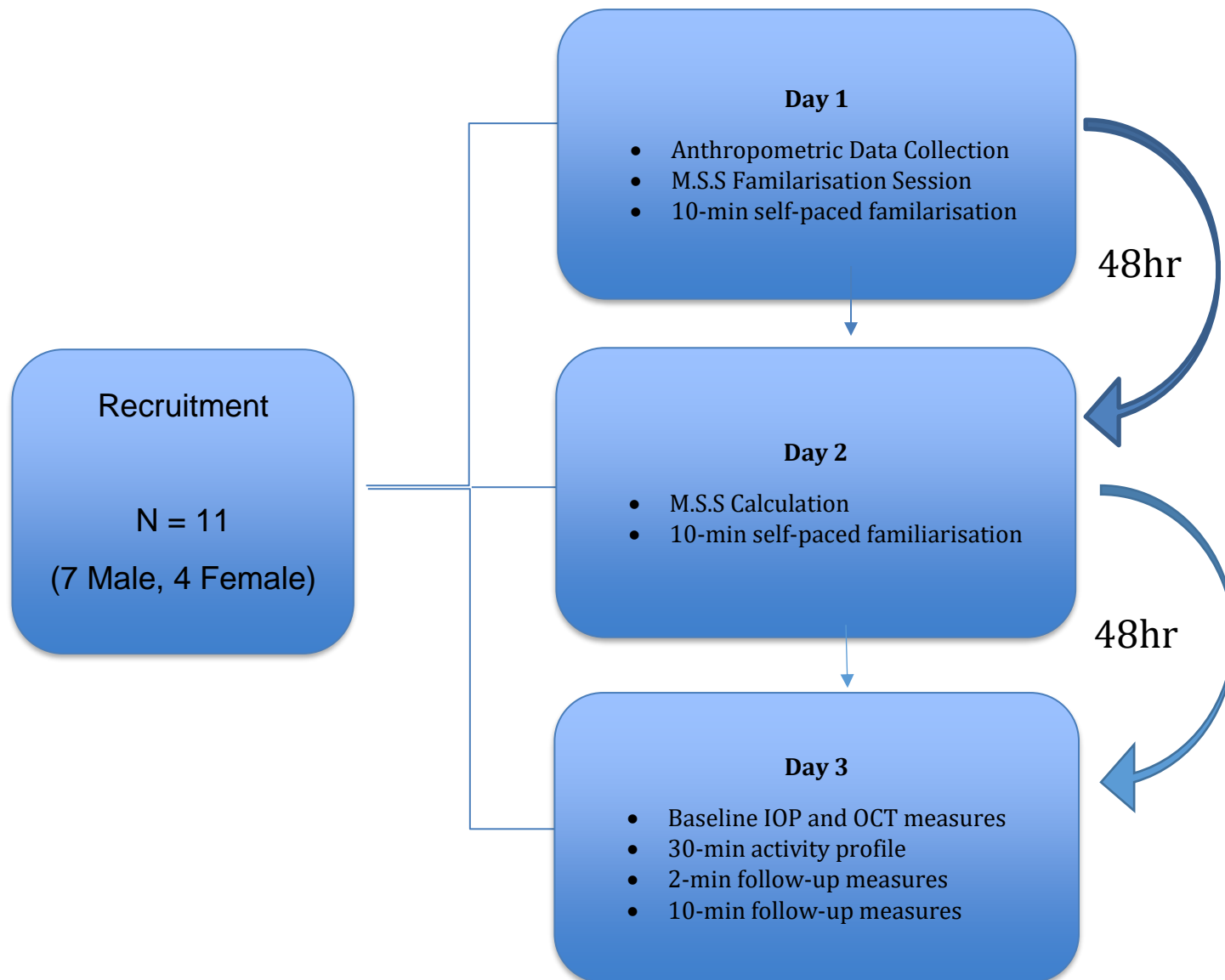
Figure 4.1 – Methodology Flow chart

The OCT used for the duration of the research was a 3D optical coherence tomography DRI OCT Triton Plus (*Topcon Corporation, Hasunuma-cho, Itabashi-ku, Tokyo, Japan*) [figure 4.2]**.** The principal investigator carried out all OCT scans, post completion of full training from a consultant ophthalmologist, a medical photographer and company technician prior to recruitment. The OCT apparatus was located in a darkened room to allow for sufficient pupil dilation, facilitating a larger aperture of the pupil and thereby improving image quality. IMAGEnet6 ophthalmic data system was the complimentary software used to generate OCT reports, interpret and view the scans.
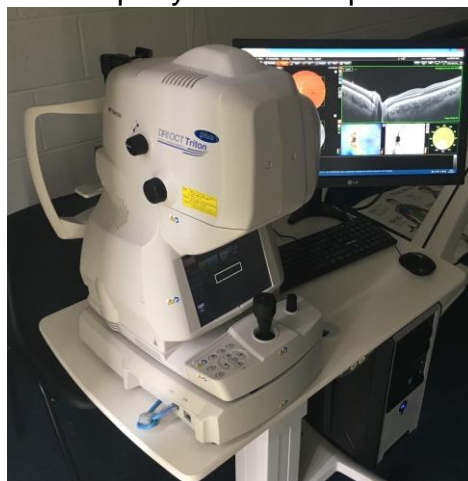
Figure 4.2– OCT Apparatus

The participant was instructed to sit down in front of the OCT. Prior to capturing an image, participants were made aware that the principal investigator was going to take 2 images, one of each eye and there would be a small flash each time an image was captured. Participants were given an opportunity to ask any questions they might have with regard to the procedure. The type of scan taken was 3D (H) + Line (H) 12.0mm X 9.0mm with a wide fixation. This scan-type was chosen as it allows simultaneous examination of both macular and peripapillary areas of the retina. A scan of the left eye was captured first followed by the right eye in all participants.

Firstly, the type of scan was selected on the touch display of the OCT. The participant was asked to place their chin and forehead onto their respective rests. The height of the OCT table was then adjusted to suit the specific height of the participant and to ensure a comfortable testing position. Following this, the height of the chin rest was adjusted so the small marks on either side of the forehead rest lined up with the apex of the canthus (lateral corner) of the participant's eyes. The brackets on the OCT display were then moved into position so they were located on either side of the pupil. The

moveable camera section of the OCT was then positioned in closer to the eye. Gross movements were controlled by moving the adjustable platform and fine movements were achieved with the joystick. The OCT guides the practitioner to the optimal distance and positioning of the lens by using colour-coded circles. When the circles align and are displayed as green the optimal position for image acquisition has been achieved (Figure 4.3). The OCT incorporates a fixation point for the participant to focus on, which ensures the desired section of the eye is scanned, the participant was asked to concentrate their vision on this point (in this case a single black square in the middle of 4 green squares). Once the satisfactory alignment was achieved, the participant was asked to blink if they wished and to then re-focus on the fixation point without blinking until the scan was complete. The scan was then taken by pressing the trigger on the joysick of the OCT. The 3D (H) + Line (H) scan takes approximately 5-10 seconds to acquire. During the scan, the participant was verbally encouraged to keep staring at the fixation point at all times. The OCT provided a measure of the image quality and previewed an image of each scan. If the participant blinked during the scan, had excessive eye movement or the image quality was poor or if there was presence of any artifact then the scan was repeated. The IMAGEnet6 ophthalmic data system manual states that if the image quality is 30 or more (arbitrary units out of 100) there is proper image quality, if the quality is lower than 30 the reliability of the data is compromised (Topcon 2014). To further ensure the quality of the data captured, any scan with an image quality of less than 50 was discarded and the scan was repeated until satisfactory image quality was attained.

Figure 4.3 – OCT Optimal positioning guide – Orange Cirlces (Left) = Not Close enough. Yellow Circles (Right) = Too Close. Green Circles aligned (Center) = Optimal position for scan.

OCT Outcome Measures

The 'Glaucoma report' was generated for each individual scan and exported in the form of an image file to be incorporated into an excel spreadsheet and stored on a password-protected laptop. The OCT outcome measures used in this study were the Retinal Nerve Fibre Layer (RNFL) measured around the peripapillary area and the GCL++ measured around the macula. Average values for superior, temporal, inferior and nasal sectors were calculated as well as average overall thickness of the RNFL. The 6-sector grid was used to document GCL++ thickness, which was measured around the macula (Figure 4.4). The 6 GCL++ sectors were defined as superior (S), superior temporal (ST), inferior temporal (IT), inferior (I), inferior nasal (IN) and superior nasal (SN). All OCT measures were in microns (µm).

Figure 4.4 – Glaucoma Report - Peripapillary RNFL measures (Yellow Circle) and Macular GCL++ measures (Blue Circle)

Macular choroidal thickness was also selected for analysis in this study as outlined in the review of literature. The thickness of the choroid was analysed from the retinal thickness screen using the 9-sector early treatment diabetic retinopathy study (ETDRS) format. The ETDRS splits the sectors into a central 1mm ring, an inner 3mm ring and outer 6mm ring, centered at the fovea. (Figure 4.5). The 9-sectors of the ETDRS were; central (C), inner superior (IS), inner temporal (IT), inner inferior (II), inner nasal (IN), outer superior (OS), outer temporal (OT), outer inferior (OI) and outer nasal (ON). (Figure 4.6 and 4.7). Overall mean choroidal thickness was also manually calculated.
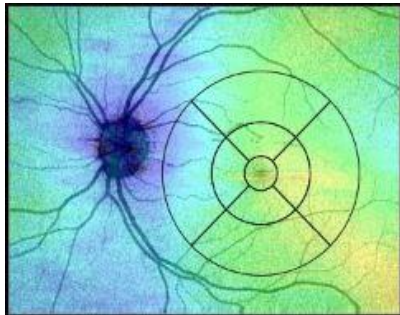
Figure 4.5 - 9-sectors of the choroid (ETDRS) format with thickness map
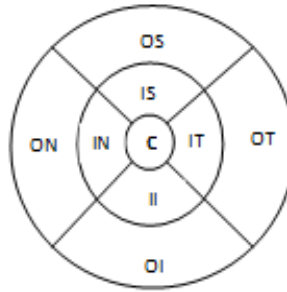
Figure 4.6 – Breakdown of the 9-sectors of the choroid (ETDRS) format

Figure 4.7 - 9-sectors of the choroidal thickness (µm)

Maximal Sprint Speed (MSS)

The research by (Sirotic and Coutts 2008) used both 3-second and 6-second sprints to evaluate MSS, however they found the 6-second method to have a lower coefficient of variance and concluded that this method should be used instead of the 3-second method. Therefore the 6-second method was used for the purpose of this study. The participant first performed a standardised 5-minute warm up on the NMT. The participant then completed three maximal 6-second sprints with a 2-minute active recovery in between. The maximum speed (km/hr) achieved by the participant over the course of the 3 sprints was then plugged into 6 speed categories, which determined the individual speed for each category (Table 4.1). These speeds were then combined with the activity profile (Figure 4.8) to create an individualised activity profile for each participant relative to their MSS achieved.

Table 4.1 – Speed Categories for a participant with a 20 km/hr MSS

Speed Category	% MSS	Speed (km/hr)
Standing	0%	0
Walking	20%	4
Jogging	35%	7
Running	45%	9
Fast Running	65%	13
Sprinting	100%	20
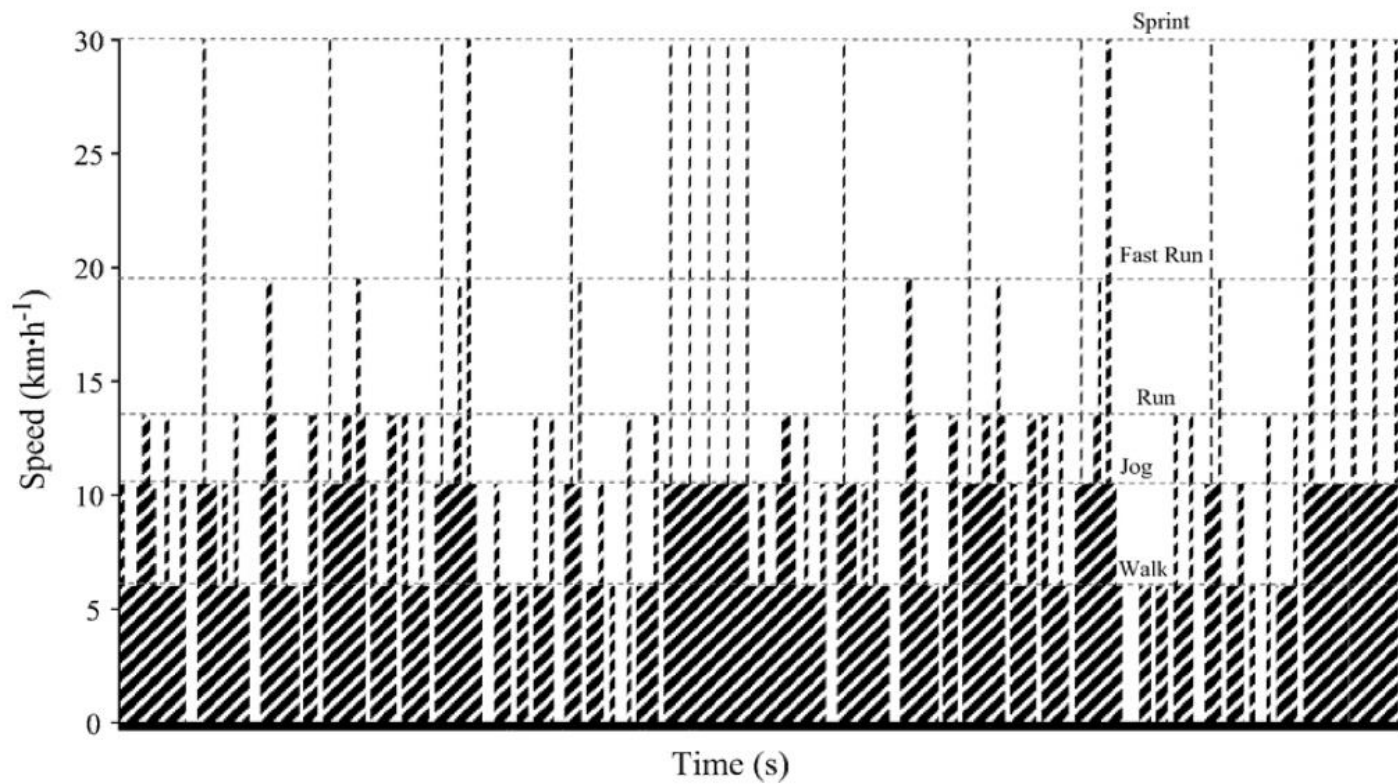
Figure 4.8 – 30 minute activity profile for a subject with MSS of 30km/hr used by (Sirotic and Coutts, 2008)

Simulated Team Sport Running Protocol

The simulated team sport running protocol consisted of two, identical 14-minute and 20 second activity profiles with a 2-minute active recovery in between. The protocol incorporated the 6 speed categories assigned to each individual participant. The duration and frequency of each speed category was based on time-motion analysis of soccer, rugby league, rugby union and Australian-rules football (Bangsbo *et al.*, 1991; Meir *et al.*, 1993; Appleby and Dawson, 2002; Duthie *et al.*, 2003). A 14-minute, 20-second activity profile was constructed based on the first half of the model used by Sirotic and Coutts, (2008). Once the first half of the activity profile was complete, the participant completed a 2-minute self-paced active recovery. This was followed by the second activity profile (identical to the first). During the running protocol each participant had a speed chart positioned at eye level (Appendix D), this was used in conjunction with the NMT speed display to attain the necessary speeds. The activity profile was programmed into an online interval timer, this protocol is available at (http://www.intervaltimer.com/timers/7709637-simulated-team-sport-protocol-ben). The online interval timer was displayed on a laptop at eye-level for the tester and participant. Each speed of the protocol was programmed a different colour, this colour corresponded to the speed chart for each participant. The interval timer provided both visual and audio countdown cues for each speed change. The tester informed the participant of the changes in the activity profile which involved the announcement of the next speed category and then a 3….2….1 countdown followed by the name of the speed category once more. Full and equal verbal encouragement was given to all participants throughout the protocol. Once the full activity protocol was complete, follow-up IOP and OCT measures were taken 2-minutes, 10-minutes and 20-minutes post-exercise. The participant was allowed to drink water *ad libitum* and rest in a standing, but not any other position or posture during this time. This was to avoid any potential postural effects on IOP (Jorge *et al.*, 2010; Sawada and Yamamoto 2013; Lam *et al.*, 2013; Prata *et al.*, 2010).

Data Analysis:

IBM SPSS (Statistical Package for Social Sciences) version 23 was used to analyse the data. Statistical significance was set at $P < 0.05$. Cohen's classification was used to determine of effect size (0.2 = small, 0.5 = medium and 0.8 is large) (Cohen, 1988). Effect size was reported as partial eta^2. Descriptive statistics were used to report mean values ± standard deviations at each time point in the study. Dependant variables included for analysis were RNFL, GCL++ and choroidal thickness along with IOP. Independent variables were the relative sectors for each OCT measure and the left and right eye for IOP. Data was screened for normality using a Shapiro-Wilk test. Mauchly's test for sphericity was used to test for equality of variance between each combination of related groups.

A one-way repeated measures ANOVA was used to test for differences pre to post intervention. In the case of a significant difference, a Bonferroni post-hoc test was used to examine where the difference lay. In the event that the assumption of normality was violated, a non-parametric Freidman's test was used to analyse the data. In the event that the assumption of sphericity was violated a Greenhouse-Geisser test was used to analyse data. Pearson's correlation was used to examine the relationship between changes in the choroidal layer and IOP in both eyes.

4.3 - Results

The primary aim of this study was to investigate the effects of a simulated team sport running protocol on the retinal structures of peripapillary RNFL and Macular GCL++ layers, the sub-retinal vascular macular choroid layer and IOP in young, healthy male and female team sport athletes. The secondary aim of the study was to explore the relationship between any changes in the choroidal layer and IOP. The mean age of participants was 21.2 ±1.3 years. The mean weight and height of participants was 74.3 ±12.1kg and 175.4 ±9.8cm respectively.

Retinal Nerve Fibre Layer

Left eye - All data was found to be normally distributed (P > 0.05). The assumption of sphericity was satisfied in the superior and inferior sectors (P > 0.05) but not in the temporal, nasal sectors or mean total RNFL thickness (P < 0.05). A repeated measures ANOVA revealed no significant difference in RNFL thickness across time points in the superior sector (P > 0.05). There was a significant difference revealed in the inferior sector (F [2,20] = 10.53, P = 0.001 with a medium effect size of 0.51 and an observed power of 0.97), a Bonferroni post-hoc analysis revealed a significant difference between baseline and 2-minutes post exercise (P = 0.013) and between baseline and 10-minutes post exercise (P = 0.025). A Greenhouse-Geisser test revealed no significant difference across time points in the temporal and nasal sectors as well as total RNFL thickness (P > 0.05). Means ± SD and significant differences are represented below in table 4.2 and figure 4.9.

Table 4.2 – Mean ±SD Left RNFL Thickness (μm) Response to Exercise

Sector	Baseline	2-Min Post	10-Min Post	Effect size (Eta^2)
Superior	131 ±16.9	131 ±16.6	131 ±17.5	0.01
Temporal	73 ±11.2	75 ±9.4	75 ±9.0	0.08
Inferior	141 ±21.3	138 ±20.8(*)	138 ±21.7(**)	0.51
Nasal	92 ±18.1	88 ±21.2	88 ±20.4	0.09
Total Thickness	109 ±12.0	108 ±13.2	108 ±13.3	0.24

* = Significant Difference (P < 0.05) Between Baseline and 2-Min Post. ** = Significant Difference (P < 0.05) Between Baseline and 10-Min Post.
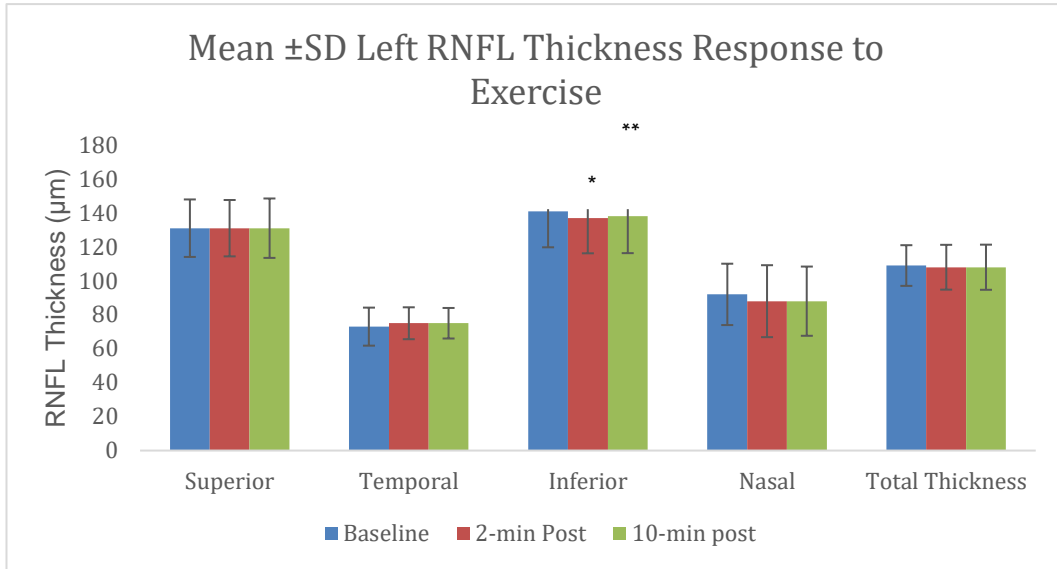
Figure 4.9 – Left RNFL Thickness Response to Exercise. * = Significant difference (P < 0.05) between baseline and 2-min post ** = Significant difference (P < 0.05) between baseline and 10-min post.

Right eye - All data was normally distributed (P > 0.05). The assumption of sphericity was satisfied in the superior, inferior and nasal sectors (P > 0.05) but not in the temporal sector or total RNFL thickness (P < 0.05). A repeated measures ANOVA test revealed no significant difference across time points in the superior, inferior or nasal sectors (P > 0.05). A Greenhouse-Geisser test revealed no significant difference across time points in the temporal sector as well as total RNFL thickness (P > 0.05). Means ± SD, significant differences and effect sizes are represented below in table 4.3 and figure 4.10.

Table 4.3 – Mean ±SD Right RNFL Thickness (μm) Response to Exercise

Sector	Baseline	2-Min Post	10-Min Post	Effect size (Eta^2)
Superior	127 ±22.7	128 ±19.0	128 ±20.2	0.03
Temporal	80 ±11.5	77 ±9.5	77 ±9.7	0.12
Inferior	136 ±22.2	135 ±20.7	136 ±22.0	0.04
Nasal	86 ±22.7	87 ±20.5	87 ±21.4	0.11
Total Thickness	109 ±15.9	107 ±12.3	107 ±13.3	0.06
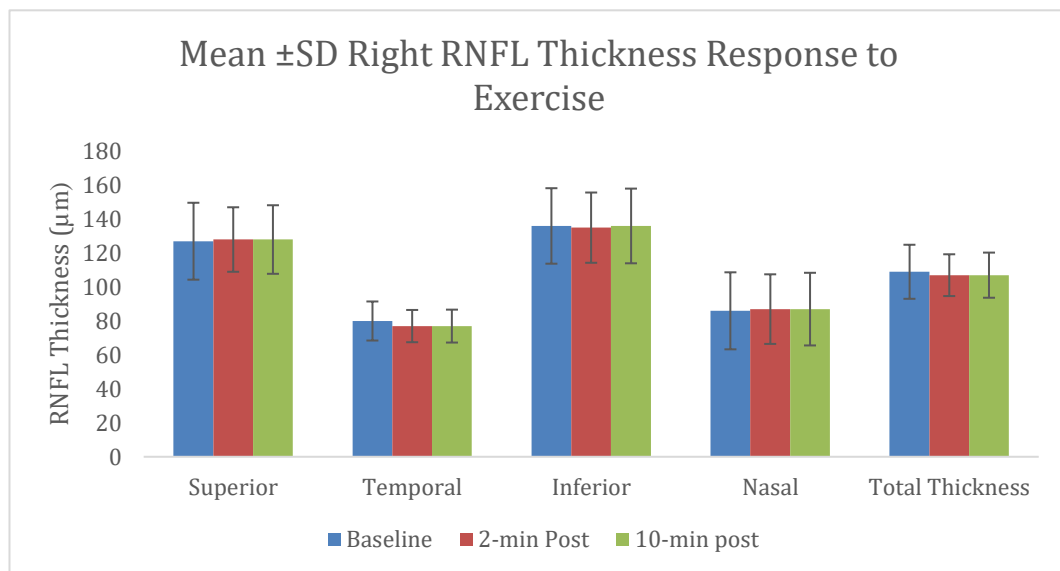
Figure 4.10 – Right RNFL Thickness Response to Exercise.

Ganglion Cell Layer ++

<u>Left Eye</u> - All data was normally distributed (P > 0.05). The assumption of sphericity was satisfied in all sectors as well as for total GCL++ thickness according to Mauchly's test (P > 0.05). Repeated measures ANOVA and a Bonferroni post-hoc analysis where indicated were used to analyse all data. Significant differences are represented below in table 4.4. There was a significant difference observed in the superior sector (F [2,20] = 7.74, P = 0.003) with a small effect size of 0.44 and an observed power of 0.91. Bonferroni post-hoc revealed a significant difference between 2-minutes and 10-minutes post (P = 0.012). A significant difference was observed in the inferior temporal sector (F [2,20] = 3.895, P = 0.37 with a small effect size of 0.28 and an observed power of 0.63), however a Bonferroni post-hoc test failed to identify where the significance lay. There was a significant difference observed in the inferior nasal sector (F [2,20] = 7.410, P = 0.004) with a small effect size of 0.43 an observed power of 0.90. Bonferroni post-hoc test revealed a significant difference between baseline and 10-minutes post exercise (P = 0.038). There was a significant difference observed in the superior nasal sector (F [2,20] = 10.43, P = 0.001) with a medium effect size of 0.51 and an observed power of 0.973. Bonferroni post-hoc analysis revealed a significant difference between baseline and 10-minutes post (P = 0.012) and between 2-minutes and 10-minutes post (P = 0.014). There was a significant difference observed for total left GCL++ thickness (F [2,20] = 20.250, P = 0.001) with a medium effect size of 0.70 and an observed power of 1.0). Bonferroni post-hoc analysis revealed a sgnificant difference between baseline and 10-minutes post (P = 0.003) and between 2-minutes and 10-minutes post (P = 0.001). Means ± SD, significant differences and effect sizes are represented below in table 4.4 and figure 4.11.

Table 4.4 – Mean ±SD Left GCL++ Thickness (µm) Response to Exercise

Sector	Baseline	2-Min Post	10-Min Post	Effect size (Eta^2)
Superior	107 ±6.8	107 ±6.6	108 ±6.4$^{(***)}$	0.44
Superior Temporal	94 ±6.5	94 ±6.0	95 ±7.1	0.18
Inferior Temporal	97 ±7.1	97 ±7.2	98 ±7.3	0.28
Inferior	105 ±8.0	105 ±7.9	106 ±7.6	0.15
Inferior Nasal	119 ±8.9	119 ±8.8	121 ±8.4$^{(**)}$	0.43
Superior Nasal	119 ±7.3	119 ±7.2	121 ±6.7$^{(**)}$	0.51
Total Thickness	107 ±6.8	107 ±6.7	108 ±6.5$^{(**)(***)}$	0.67

** = Significant Difference Between Baseline and 10-Min Post. *** = Significant Difference between 2-Min Post and 10-Min post.
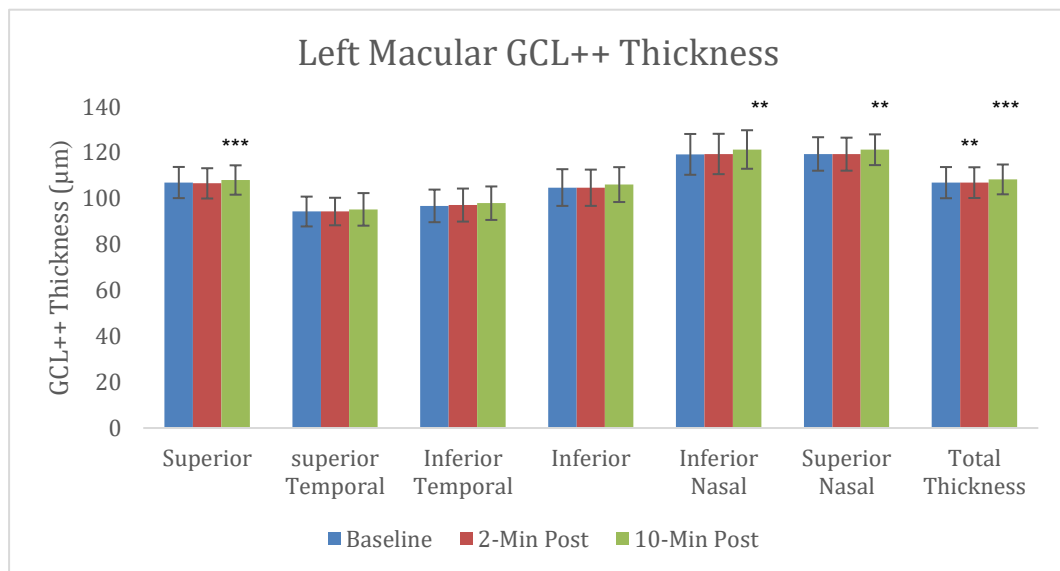
Figure 4.11 – Left Macular GCL++ Thickness Response to Exercise. ** = significant difference between baseline and 10-Min Post.   * = Significant Difference between 2-Min Post and 10-Min Post.**

Right Eye - All data was normally distributed (P > 0.05). The assumption of sphericity was satisfied in all sectors according to Mauchly's test (P > 0.05). Repeated measures ANOVA and Bonferroni post-hoc analysis, where indicated were used to analyse the data. There was a significant difference observed in the superior sector (F [2,20] = 4.698, P = 0.021) with a small effect size of 0.32 and an observed power of 0.721. Bonferroni post-hoc analysis revealed a significant difference between 2-minutes and 10-minutes post (P = 0.043). There was a significant difference in the inferior sector (F [2,20] = 9.494, P = 0.001) with a small effect size of 0.49 and an observed power of 0.96. Bonferroni post-hoc analysis revealed a significant difference between baseline and 10-minutes post (P = 0.005) and between 2-minutes and 10-minutes post (P = 0.049). There was a significant difference in total GCL++ thickness (F [2,20] = 4.831, P = 0.019) with a small effect size of 0.33 and an observed power of 0.734. Bonferroni post-hoc analysis revealed a significant difference between baseline and 10-minutes post (P = 0.018). Means ± SD, significant differences and effect sizes are represented below in table 4.5 and figure 4.12.

Table 4.5 – Mean ±SD Right GCL++ Thickness Response to Exercise (μm)

Sector	Baseline	2-Min Post	10-Min Post	Effect size (Eta^2)
Superior	109 ±7.2	109 ±7.0	111 ±6.6[(***)]	0.32
Superior Temporal	96 ±6.4	96 ±5.9	98 ±5.9	0.22
Inferior Temporal	99 ±7.4	99 ±7.0	100 ±6.7	0.01
Inferior	106 ±8.1	106 ±8.3	107 ±8.3[(**)(***)]	0.49
Inferior Nasal	119 ±7.7	119 ±7.5	121 ±7.7	0.13
Superior Nasal	121 ±6.8	120 ±6.3	122 ±6.6	0.14
Total Thickness	108 ±6.9	108 ±6.6	110 ±6.5[(**)]	0.33

** = Significant difference (P < 0.05) (ANOVA + Bonferroni) between baseline and 10-Min Post.
*** = Significant difference (P < 0.05) (ANOVA + Bonferrroni) between 2-Min Post and 10-Min post.
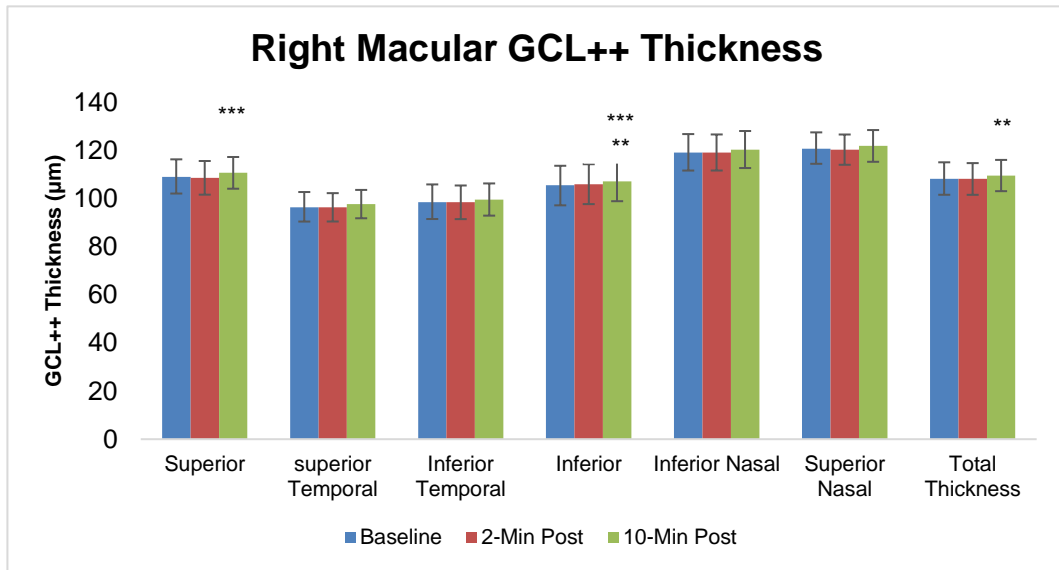
Figure 4.12 – Right Macular GCL++ Thickness Response to Exercise. ** = Significant difference (P < 0.05) between baseline and 10-Min Post.   * = Significant Difference (P < 0.05) between 2-Min Post and 10-Min Post.**

Choroid

<u>Left eye</u> - All data was normally distributed (P > 0.05) with the exception of the inner-inferior sector 2-min post and 10-min post (P < 0.05). The assumption of sphericity was satisfied in central, inner temporal, outer superior, outer temporal, outer inferior,outer nasal sectors as well as total choroid thickness according to Mauchly's test (P > 0.05), but not in the inner superior or inner nasal sectors (P < 0.05). Repeated measures ANOVA and Bonferroni post-hoc analysis (where indicated) were used to analyse central, inner temporal, outer superior, outer temporal, outer inferior, outer nasal and total thickness sectors. Friedman's test was used to analyse the non-parametric inner inferior sector. A Greenhouse-Geisser test was used to analyse the inner superior and inner nasal sectors. A Repeated measures ANOVA revealed a significant difference in the central (F [2,20] = 4.161, P = 0.031) with a small effect size of 0.29 and an observed power of 0.67, however bonferroni post-hoc analysis failed to identify where the significance lay. There was a significant difference in the outer superior sector (F [2,20] =

6.615, P = 0.006) with a small effect size of 0.40 and an observed power of 0.86. Bonferroni post-hoc analysis revealed a significant difference between baseline and 2-minutes post (P = 0.023). There was a significant difference in the outer temporal sector (F [2,20] = 5.544, P = 0.012) with a small effect size of 0.36 and an observed power of 0.79. Bonferroni post-hoc analysis revealed a significant difference between baseline and 2-minutes post (P = 0.032). There was a significant difference in the outer inferior sector (F [2,20] = 4.402, P = 0.026) with a small effect size of 0.31 and an observed power of 0.69, however Bonferroni post-hoc analysis failed to identify where the difference lay. There was a significant difference observed in the outer nasal sector (F [2,20] = 5.171, P = 0.015) with a small effect size of 0.34 and an observed power of 0.76. Bonferroni post-hoc analysis revealed a significant difference between baseline and 2-minutes post (P = 0.022). There was a significant difference in total left choroidal thickness (F [2,20] = 6.043, P = 0.009) with a small effect size of 0.38 and an observed power of 0.83. Bonferroni post-hoc analysis revealed a significant difference between baseline and 2-minutes post (0.023). Means ± SD and significant differences are represented below in table 4.6 and figure 4.13.

Table 4.6 – Mean ±SD Left Macular Choroidal Thickness (µm) Reponse to Exercise

Sector	Baseline	2-Min Post	10-Min Post	Effect size (Eta^2)
Central[^]	314 ± 80.8	308 ± 82.8	310 ± 79.1	0.29
Inner Superior	299 ± 71.0	291 ± 72.0	292 ± 67.2	0.12
Inner Temporal	307 ± 73.0	301 ± 74.2	304 ± 70.0	0.21
Inner Inferior	316 ± 89.6	310 ± 89.1	310 ± 86.6	0.40
Inner Nasal	285 ± 82.7	273 ± 84.2	280 ± 83.4	0.23
Outer Superior	291 ± 77.5	283 ± 77.0[^*]	285 ± 73.4	0.40
Outer Temporal	284 ± 63.4	277 ± 63.0[^*]	281 ± 60.4	0.36
Outer Inferior[^]	302 ± 86.1	297 ± 85.7	298 ± 82.9	0.31
Outer Nasal	216 ± 76.1	211 ± 75.2[^*]	214 ± 75.6	0.34
Total Thickness	290 ± 73.7	283 ± 74.6[^*]	286 ± 71.5	0.38

* = Significant difference (P < 0.05) (ANOVA + Bonferroni) between baseline and 2-Min Post.
** = Significant difference (P < 0.05) (ANOVA + Bonferroni) between baseline and 10-Min Post.
^ = Significant difference (P < 0.05) (ANOVA)
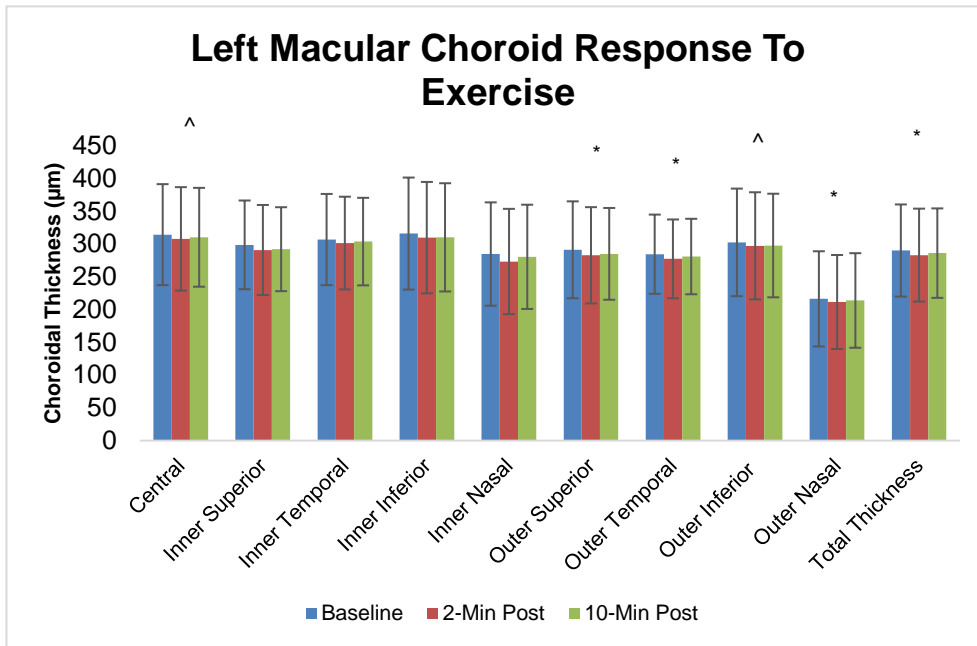
Figure 4.13 – Left Macular Choroidal Thickness Response to Exercise.
* = Significant Difference (P < 0.05) (ANOVA + Bonferroni) between baseline and 2-min post
** = Significant Difference (P < 0.05) (ANOVA + Bonferroni) between baseline and 10-min post
^ - Significant Difference (P < 0.05) (ANOVA)

Right eye - All data was normally distributed ($P > 0.05$) with the exception of outer temporal sector 10-min post ($P < 0.05$). The assumption of sphericity was satisfied in central, inner superior, inner temporal, inner inferior, outer superior, outer inferior, outer nasal sectors as well as total choroidal thickness ($P > 0.05$) but not in the inner nasal sector. Repeated measures ANOVA revealed a significant difference in the inner superior sector ($F_{[2,20]} = 6.204$, $P = 0.008$) with a small effect size of 0.38 and an observed power of 0.84, however the Bonferroni post-hoc analysis failed to identify where the significant difference lay. There was a significant difference in the inner nasal sector ($F_{[1.31,13.14]} = 4.356$, $P = .0.048$) with a small effect size of 0.30 and an observed power of 0.55, however the Bonferroni post-hoc test failed to reveal where the significant difference lay. There was a significant difference in the outer inferior sector ($F_{[2,20]} = 5.247$, $P = 0.015$) with a small effect size of 0.34 and an observed power of 0.77. Means ± SD, significant differences and effect sizes are represented below in table 4.7 and figure 4.14.

Table 4.7 – Mean Right Macular Choroidal Thickness ±SD (µm)During Exercise

Sector	Baseline	2-Min Post	10-Min Post	Effect size (Eta^2)
Central	303 ± 69.3	297 ± 71.9	294 ± 67.0	0.18
Inner Superior[^]	302 ± 68.5	294 ± 67.9	295 ± 65.9	0.38
Inner Temporal	298 ± 55.3	296 ± 55.6	294 ± 50.2	0.11
Inner Inferior	311 ± 72.5	306 ± 72.8	306 ± 70.3	0.26
Inner Nasal[+]	284 ± 76.0	276 ± 74.0	276 ± 72.1	0.30
Outer Superior	289 ± 79.9	284 ± 78.0	285 ± 75.8	0.22
Outer Temporal	278 ± 48.6	277 ± 89.4	262 ± 89.4	0.10
Outer Inferior	292 ± 81.6	286 ± 81.9[*]	287 ± 80.8	0.34
Outer Nasal	220 ± 73.7	223 ± 82.9	223 ± 85.3	0.01
Total	286 ± 64.5	282 ± 64.6	280 ± 63.8	0.21

* = Significant difference ($P < 0.05$) (ANOVA + Bonferroni) between baseline and 2-Min Post.
^ = Significant difference ($P < 0.05$) (ANOVA)
+ = Significant difference (Greenhouse-Geisser)
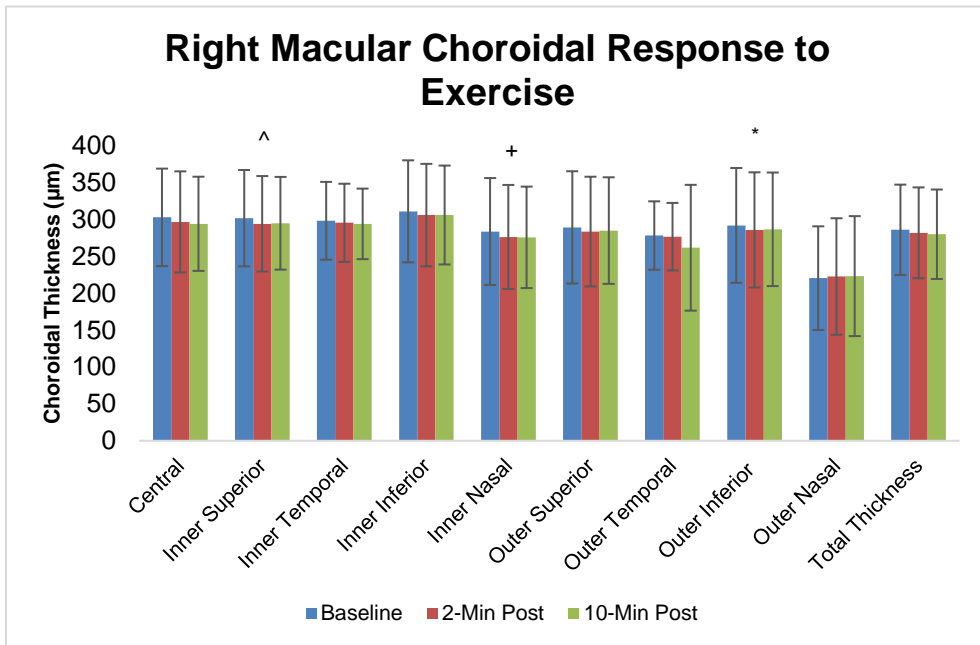
Figure 4.14 – Right Macular Choroidal Thickness Response to Exercise.
* = Significant difference (P < 0.05) (ANOVA + Bonferroni) between baseline and 2-min post
+ = Significant difference (P < 0.05) (Greenhouse-Geisser + Bonferroni) between baseline and 2-Min post
^ = Significant difference (P < 0.05) (ANOVA)

Intra-Ocular Pressure

Left IOP data was not found to be normally distributed (P < 0.05). A Friedman's test revealed a significant difference across time points (X^2 (2) = 8.909, P = 0.012) with a medium effect size of 0.54 and an observed power of 0.99. Pairwise comparison revealed that there was a significant difference between baseline and 2-min post (P = 0.006) and between 2-min post and 10-min post (P < 0.05, P = 0.019) but not between baseline and 10-min post (P = 0.670). Means ± SD, significant differences and effect sizes are represented below in table 4.8 and figure 4.15.

Right IOP data was not found to be normally distributed (P < 0.05). A Friedman's test revealed a significant difference across time points (X^2 (2) = 13.273, P = 0.001). Pairwise comparison revealed that there was a significant difference between baseline and 2-Min post (P = 0.0001) and between 2-min post and 10-min post (P = 0.033) but not between baseline and 10-min post (P > 0.05, P = 0.136). Means ± SD and significant differences are represented below in table 4.8 and figure 4.15.

Table 4.8 - Mean IOP Measures ±SD (mmHg) Response to Exercise

	Baseline	2-Min Post	10-Min Post	Effect size (Eta^2)
Left Eye	16.9 ± 2.5	14.8 ± 1.9$^{(*)}$	16.3 ± 2.8$^{(***)}$	0.54
Right Eye	17.5 ± 2.6	15.1 ± 2.1$^{(*)}$	15.9 ± 1.8$^{(***)}$	0.40

* = Significant difference (P < 0.05) (Friedman + Pairwise) between baseline and 2-min post.
*** = Significant difference (P < 0.05) (Friedman + Pairwise) between 2min post and 10-min post.

Figure 4.15 – IOP Response to Exercise
* = Significant difference (P < 0.05) (Friedman + Pairwise) between baseline and 2-min post.
*** = Significant difference (P < 0.05) (Friedman + Pairwise) between 2min post and 10-min post.

Relationship of Intra-Ocular Pressure and Choroid Thickness

In order to explore the possible relationship between IOP and choroidal thickness responses to exercise a Pearson's R correlation was run on the means of IOP and choroidal thickness in both the right and left eyes. The results are represented below in figures 4.16 and 4.17.
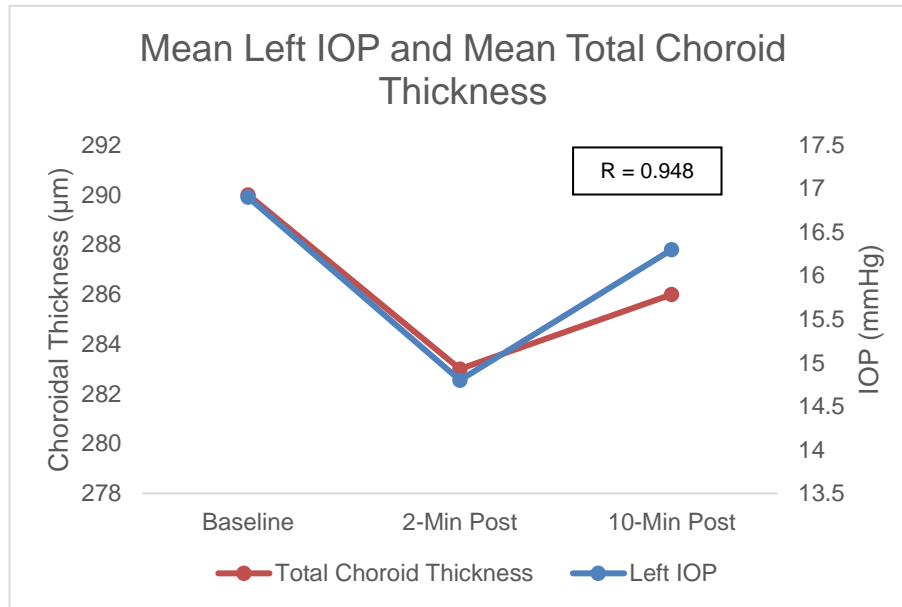
Figure 4.16 – Correlation of Mean Total Left Choroidal Thickness vs Left IOP.   Figure 4.17 – Correlation of Mean Total Right Choroidal Thickness vs Right IOP.
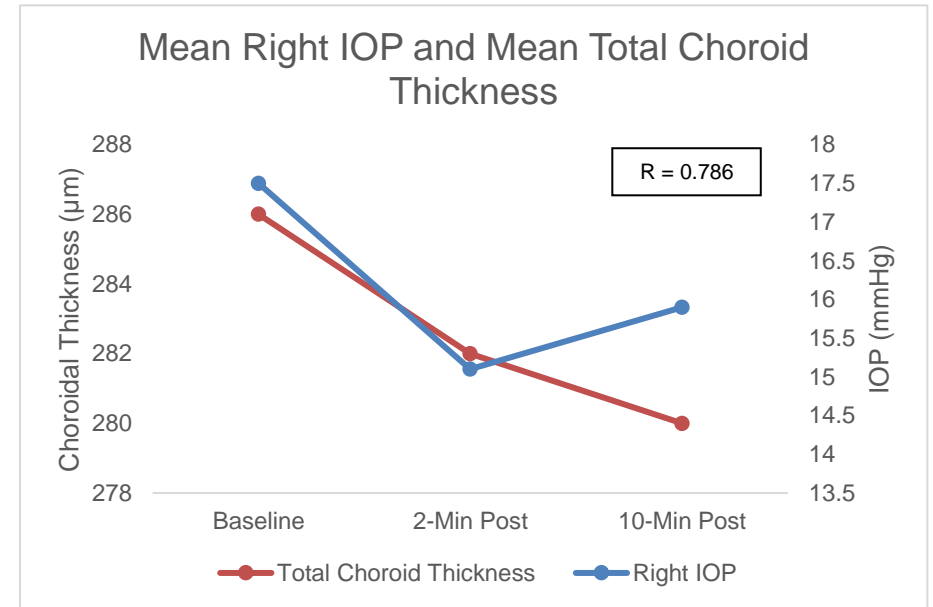
A Pearsons' R correlation revealed that the mean values for total left choroid thickness and left IOP demonstrated a non-significant (P = 0.257), but positive strong correlation (R = 0.948). [Figure 4.13]. A Pearsons' R correlation revealed that the mean values for total right choroidal thickness and right IOP demonstrated a non-significant (P = 0.425), but positive strong correlation (R = 0.786) [Figure 4.14].

4.4 – Discussion

The results of the current study demonstrated an overall thinning trend of the RNFL, therefore the hypothesis that there is a significant increase in RNFL thickness following exercise is rejected. With regard to GCL++, there was an overall thickening trend observed, which was most apparent between the 2-minute and 10-minute follow up, therefore the hypothesis that there is a significant thickneing of the GCL++ following exercise is accepted. Choroidal thickness demonstrated an overall thinning trend, therefore the hypothesis that choroidal thickness increases significantly following exercise is rejected, however, the decreases in thickness that were observed are not uniform in both eyes and a larger sample size is needed to consolidate these findings. There were a number of choroidal sectors, for which repeated measures ANOVA revelaed a significant difference, however the Bonferroni post-hoc analysis failed to reveal where the significance lay, this may be attributable to the small sample size employed in the current study. With regard to IOP, there was an initial significant decrease observed in both eyes immediately following exercise, the hypothesis that there is a significant decrease in IOP following exercise is accepted. IOP levels were also found to significantly increase back toward baseline levels 10-minutes following exercise. There was a strong, positive correlation observed between IOP and choroidal thickness in the current study, the hypothesis that there is a significant negative correlation between IOP and choroid thickness following exercise is rejected. Further research with increased participant numbers is recommended.

There is a paucity of research with regard to the effects of exercise on individually segmented retinal and sub retinal layers, the current study has investigated the effects of a team sport running protocol on the RNFL and GCL++ retinal layers as well as the sub-retinal vascular choroid layer and IOP. This protocol been proven reliable for various performance and physiological measures (Sirotic and Coutts 2008).

The findings of this study revealed a significant decrease in the thickness of the inferior RNFL sector of the left eye from baseline to 2-minutes post exercise (P = 0.013) and from baseline to 10-minutes post exercise (P =0.025), which equated to a 3μm decrease. The temporal sector in the right eye also displayed a 3μm decrease in thickness from baseline to both 2-mins and 10-mins post exercise, however this was not found to be significant. Furthermore, the nasal sector of the right eye revealed a thinning of 4μm which was the largest difference in any sector of both eyes, however this was not found to be statistically significant. Other sectors displayed a slight thickening of between 1-2μm, but overall there was a thinning trend observed. These findings are in contrast with those of Balk *et al.*, (2013) who reported a small but significant (P = 0.018) overall thickening of the RNFL pre to post 10km run (exact μm change not specified). Balk *et al.*, (2013) proposed two possible mechanisms for an increase in thickness observed in their study; the first was hyperaemia, whereby an increase of blood in the vessels would translate to an increased thickness. The second mechanism proposed by Balk *et al.*, (2013) is associated with changes in the osmotic gradient caused by intravascular hyponatremia as a result of re-hydration during exercise. This would equate to H_2O moving with the osmotic gradient out of the blood vessels and into the intracellular compartment thereby increasing cellular volume, with the polar opposite occurring in a dehydration situation (Balk *et al.* 2013). The overall thinning trend observed in the current study may be due to the level of exercise that was performed which involved sprinting and changes in speed, causing more fluctuations in heart rate and possibly blood pressure than the steady-state exercise in the study by Balk *et al.*, (2013). Other previous studies have examined the effects of exercise on retinal thickness as a whole (encompassing both RNFL, GCL++ and the other layers of the retina). One such study carried out by Alwassia *et al.*, (2013) reported no significant differences in retinal thickness following a cardiac stress test, but reported small 1-2μm changes in individual sectors (both thickening and thinning) which is in agreement with the RNFL findings of the current study. Sayin *et al.*, (2015) also found no significant difference in retinal thickness following exercise (10-minutes on a bicycle ergometer).

Overall, there was a thinning trend observed, which was found to be statistically significant in just the inferior sector of the left eye.

In contrast, the GCL++ findings of the current study, revealed an overall thickening trend post-exercise. There was minimal change in GCL++ thickness from baseline to 2-minutes post exercise, with a non-significant 1μm thinning observed in the superior nasal sector, all other sectors demonstrated the exact same values to the micron between baseline 2-minute follow up, in contrast, there was a thickening trend of 1-2μm across the board in all sectors for both eyes between the 2-minute follow up and 10-minute follow up.

The right eye demonstrated a significant thickening of the GCL++ superior sector between 2-minutes and 10-minutes post exercise ($P = 0.043$), this increase in thickness, however equated to 2μm. There was also a significant thickening observed between baseline and 10-mins post ($P = 0.005$) and 2-minutes and 10-minutes post ($P = 0.049$) in the inferior sector (1μm) and between baseline and 10-minutes ($P = 0.018$) for total average GCL++ thickness (2μm). Similar to the right eye, the left eye demonstrated a significant thickening ($P = 0.012$) in the superior sector (1μm) from 2-minutes to 10-minutes post exercise. There was also a statistically significant thickening between 2-minutes to 10-minutes post exercise in the inferior sector ($P = 0.049$) (1μm), the superior nasal sector ($P = 0.014$) (2μm) and for total thickness ($P = 0.0001$). There was a statistically significant thickening observed between baseline and 10-mins post exercise in the inferior nasal ($P = 0.038$) and superior nasal ($P = 0.012$) sectors and for total thickness ($P = 0.003$). The overall thickening trend demonstrated in the current study is in agreement with the findings of Balk *et al.*, (2013) who reported a significant increase in thickness in the ganglion cell layer to the Inner plexiform layer (which is the GCL++ without the RNFL). Balk *et al.*, (2013) reported that the thickness returned to baseline following a 1.5hr resting period. The current study demonstrated a thickening trend at 10-minutes post exercise but further follow up measures were not recorded and as a result the timeframe to which these metrics return to baseline levels cannot be commented on from the resuts of this study. Therefore, there is a slight thickening of the

GCL++ following exercise. This thickening was more apparent between the 2-minute and 10-minute follow up. There is a lack of literature regarding how long it takes for these metrics to return to baseline levels, this warrants further investigation.

Previously the effects of exercise on choroidal thickness have been reported (Alwassia *et al.*, 2013; Sayin *et al.,* 2015). With regard to the choroid findings in the current study there was a thinning effect of exercise observed across the board in both eyes at 2-minutes following exercise (with the exception of the outer nasal sector in the right eye). The central, outer superior, outer temporal outer inferior, outer nasal sectors, as well as total choroidal thickness were found to be significant decreases in the left eye. This equated to a 7µm decrease in mean total thickness. The right eye displayed the same trend in the 2-minute follow up with a decrease in thickness across the board, there were significant decreases in the inner superior, inner nasal and outer inferior sectors. The right eye demonstrated a slightly lower total choroid thinning than the left eye at the 2-minute follow (4µm).

At the 10-minute follow up, 9 of the 10 sectors in the left eye demonstrated a thickening trend from baseline values compared to the 2-minute follow up, but no sector returned to baseline levels. The right eye in comparison did not display the same uniform trend, with a slight thinning, thickening or no change being observed in the various sectors. Only one sector in the right eye returned to baseline levels at 10-minutes post exercise. There was a significant decrease from baseline to 10-minutes post exercise in choroidal thickness observed in the left outer inferior and right inner superior sectors. The difference in trends between eyes may be attributable to individual variations which transpired as differences between responses in eyes due to the relatively small sample size employed.

The choroidal findings of the current study are in contrast to that of Sayin *et al.,* (2015) who reported a significant increase in mean choroidal thickness at 5-minutes post exercise compared to baseline measures, these measures were not found to be significantly thicker than baseline at 15-minutes post exercise. Sayin *et al.,* (2015) demonstrated an initial thickening following

exercise followed by a thinning trend returning toward baseline levels at 15-minutes post exercise. In contrast, the current study found this effect to be the opposite in the left eye with an initial thinning followed by a thickening back toward baseline after 10-minutes. Alwassia *et al.*, (2013) demonstrated no changes in choroidal thickness following exercise, however it must be noted that the exercise protocol used was a cardiac stress test (exact procedure was not described). This exercise would not be as strenuous as the 10km run in the study by Sayin *et al.*, (2015) or the simulated team sport running protocol used in the current study. Furthermore, the age of the sample may have been a factor. Participants were aged 60.6 ±10.4 years in the study by Alwassia *et al.*, (2013) as opposed to 21.2 ±1.3 years in the current study and the comparable 27 ±4.08 years in the study by Sayin *et al.*, (2015). The mechanism of hyperaemia (an increase of blood in the vessels) by Balk *et al.*, (2013) somewhat conflicts the the thinning effect that was observed in the choroid in the current study. However, it is theorised that some of the alterations in thickness are due to changes in osmotic gradients due changes in hydration status following exercise as suggested by Balk *et al.,* (2013) may explain some of the changes in thickness observed in the current study. Participants were free to drink water *ad libitum* upon completion of the exercise protocol in the current study, however follow-up testing took place directly (2-minutes and 10-minutes) post exercise therefore the mechanism of intravascular hyponatremia would have minimal influence in this brief time-frame. Therefore, future studies should examine hydration status and further control fluid intake, which would help to confirm or refute the potential influence of osmotic gradient on specific retinal layer thickness. Furthermore, a standardised exercise protocol used across future studies may address the heterogeneity that is apparent in the current literature and lend to a better comparison between studies, ultimately contributing to a consensus.

The findings of this study have clearly demonstrated that there is an initial significant decrease in IOP at 2-minutes follow up post completion of a simulated team sport running protocol in young, healthy team sport athletes; with an increase back towards resting values at 10-minutes post exercise.

The results revealed a 2.1mmHg decrease in the left eye and a 2.4mmHg decrease in the right eye at the 2-minute follow up, both of these decrements were found to be significant ($P < 0.05$, $P = 0.06$ and $P = 0.000$ for left and right eyes respectively). Between the 2-minute and 10-minute follow up there were increases of 1.5mmHg and 0.8mmHg in the left and right eyes respectively, again these increases were found to be statistically significant ($P = 0.019$ and $P = 0.033$ for left and right eyes respectively) . There was no significant difference observed between baseline and 10-minute follow up, indicating that IOP had approximately returned to baseline levels, this trend was more obvious in the left eye. This results concur with previous research, Qureshi (1996) reported a statistically significant decrease in IOP measurements at each time point in 2 groups of sedentary males participants (21-30 years) following a 60-minute bicycle ergometer trial, measures were taken at 5, 20, 40 and 60-minutes during the exercise protocol. Furthermore, Qureshi, (1996) demonstrated that IOP returned to baseline levels following 48:13 minutes of rest in one group and 49:38 minutes in the other, the current study in comparison, revealed that IOP levels were returning toward, but had not reached baseline values, following 10-minutes of rest. Conversely, Huang (2015) demonstrated no significant difference in IOP following either aerobic (10-minutes on a stair climber) or isometric exercise (2-minutes static squat). Interestingly there was a significant increase in IOP from 14.6mmhg to 19.1mmhg ($P < 0.0001$) observed during the isometric exercise but not post exercise, demonstrating that there is an increase during isometric exercise but this effect quickly diminishes after exercise. If IOP could be continuously monitored during exercise (both aerobic and/or isometric) this would provide a better insight into the dynamics of IOP with regard to exercise. It must be noted that the aerobic exercise employed by Huang, (2015) was only 10-minutes in duration compared with the 60-minutes used in the study by Qureshi, (1996) and approximately 30-minutes used in the current study. Although there was not a significant decrease in IOP reported by Huang, (2015) there was a slight decrease in IOP from pre (16.8mmHg) to post (16.4mmHg) following aerobic exercise, therefore this duration and indeed intensity of exercise may have not been sufficient to cause a significant decrease in IOP but it did nonetheless decrease from

baseline levels. The systematic review conducted by Roddy *et al.,* (2014) concluded that although the vast majority of studies demonstrate a decrease in IOP following exercise there is a large amount of heterogeneity across studies and therefore calling for a standardised protocol to be established. This study has utilised a simulated team sport running exercise protocol which employs speeds relative to each individuals' speed capability and furthermore has been previously proven to be reliable for various performance and physiological outcome measures (Sirotic and Coutts 2008; Sirotic and Coutts 2007). Therefore, it is recommended that this protocol be used in future research regarding team sport athletes.

With regard to the relationships between the mean IOP and mean choroidal thickness, the left eye demonstrated an almost perfect positive correlation between mean choroidal thickness and mean IOP (R = 0.948), in comparison, the right eye also demonstrated a strong positive correlation between mean choroidal thickness and mean IOP (R = 0.786) but did not display the same choroidal rebound effect that was observed between the 2-minute follow up and 10-minute follow up in the left eye. Both of these correlations were not found to be significant. Nonetheless, these findings depict a clear relationship between IOP and choroidal responses to exercise. Suggesting that there may be a causal or associated relationship between both metrics which may be influenced by the same mechanism(s). It must be noted that there may be individualised responses between IOP and choroidal thickness following exercise, future research should take this into account.

There are many mechanisms associated with IOP regulation during exercise, that are beyond the scope of the current research. Some of the mechanisms suggested in the literature are; valsalva manoeuvre, changes in posture, changes in intracranial pressure, respiratory effort (McMonnies, 2016). Decreased blood PH levels, elevated blood plasma molarity and elevated blood lactate have also been postulated as being associated with the immediate decrease in IOP following exercise (McMonnies, 2016). Furthermore there is research that suggests retinal blood flow is controlled by autoregulation of local arterioles during exercise (Iester *et al.*, 2007). It has also been suggested that during strenuous exercise, ocular perfusion

pressure (OPP) can increase by 40 – 60%, where the limits of autoregulation are surpassed and blood flow increases in a linear fashion (Gale *et al.*, 2009). The findings observed in the current study, a decrease in choroidal thickness however could not be attributable to the limit of autoregulation being surpassed and blood flow increasing linearly. However, it may explain for the increases in thickness observed in the previous literature (Sayin *et al.*, 2015). Nonetheless it is clear from these findings that both IOP and choroidal thickness are dynamic with regard to the running demands of team sport.

Conclusion

In conclusion, this exploratory study provides the first insight into the effects of team sport demands on the retinal and sub-retinal structures as well as IOP. The findings of this study are limited by the small sample size, are inconclusive and therefore recommendations cannot yet be made in a clinical sense. An ideal sample size was calculated using Gpower software. With a small estimated effect size (similar to the effect sizes observed in the current study) of F = 0.25 and significance level set to 0.05 it was calculated that an ideal sample of 43 participants would provide a power of 0.95 for future research. If such measures are to be used in a team sport setting, potentially for the assessment of concussion, it is vital that the effects of the demands of team sport on these metrics are known, the protocol employed in the current study has been proven to be reliable for measuring both physiological and performance measures, furthermore, it is individualised for each participant according to their abilities. Therefore making the protocol applicable to a global sporting population, both elite and sub-elite. The existing evidence, including the findings from the current study, suggest that there is conflicting evidence for changes in the RNFL pre to post-exercise. Although some of these changes were found to be significant, they were minimal in the current study. With regard to the GCL++ there is a slight thickening trend following exercise, but again, these changes are minimal. Mean IOP and mean choroidal thickness display similar responses to exercise. It is vital that these

responses are well established if such metrics are to be used to potentially diagnose concussive injury in a sporting setting.

CHAPTER FIVE:

Study 3: Prospective Cohort Study – The Effects of Concussion on Ocular Metrics

Abstract

Title:Prospective Cohort Study: The Effects of Concussion on Ocular Metrics

Introduction: Concussion diagnosis is a clinical challenge for healthcare providers. Identification of concussion is presently aided by tools such as the Sport Concussion Assessment Tool (SCAT3); such tools remain largely subjective in nature, allowing for interpretation bias affected by multiple confounders. There is currently no objective gold standard for concussion diagnosis. The retina is an extension of the brain, therefore it is a potential structure that can be investigated in context to concussion manifestation. Structural retinal findings have been identified in other central neurological conditions such as dementia using Optical Coherence Tomography (OCT). It is therefore logical to explore the effects of concussion on the retina. The primary aim of this study was to establish baselines for SCAT-3 and OCT and to compare these measures with regard to gender, sport and history of concussion. The secondary aim of this study was to examine the effects of concussive injury on these measures.

Methods: 154 male (N =111) and female (N = 43) team-sport participants (20.9 ±4.5 years) were recruited. Baseline SCAT-3 and OCT measures of retinal nerve fibre layer (RNFL) and ganglion cell layer (GCL++) were taken using a Topcon DRI OCT Triton plus (Tokyo, Japan). Following suspected concussion, individuals reported for a follow-up 48hrs, 14-days and 2-months post-injury to investigate effects of concussion on the retina. Independent samples t-test was used to test for significant differences with regard to gender and history of concussion. One-way ANOVA was used to test for significant differences with regard to sport. Repeated measures ANOVA was used to test for significant differences between baseline and suspected concussion follow up measures.

Results: Males reported statistically more symptoms (P = 0.0001) and higher symptom severity score (P = 0.0001) than females on the SCAT-3. There were no other significant differences in SCAT-3 measures with regard to gender, sport or history of concussion. There were no significant differences observed in RNFL with regard to gender sport or history of concussion. Males displayed a significantly thicker superior temporal GCL++ sector in the left (P = 0.012) and right eyes (P = 0.007). Due to the small amount of follow up measures statistical testing was not possible. SCAT-3 symptom scores increased following concussive injury and improved in the days following injury.

Conclusion: Gender must be taken into account when interpreting SCAT-3 symptom scores, the findings of this study demonstrated males to report more than females. This is not consistent with previous literature, however there was a large difference in the male and female representation within the study and across the sporting disciplines. It is recommended that future research recruit equal male and female participants within each sporting discipline. SCAT-3 scores of SAC and mBESS along with RNFL and GCL++ thickness are interchangeable within this cohort. The study was limited by the lack of follow-up data. It is recommended that future research be carried out in conjunction with a hospital and/or neurological consultant to ensure more follow-up data is collected.

5.1 – Introduction

This study was an observational prospective cohort design. The review of literature has highlighted that the potential effects of concussion on the eye and specifically the retina, warrants investigation. The primary objective of this study was to establish normative values of ocular metrics along with the already accepted and utilised SCAT-3 assessment tool in male and female team sport athletes (Rugby, Hurling, Camogie, Gaelic Football and Soccer). The secondary objective of this study was to examine the effects of suspected concussive injury on the retina and SCAT-3 scores. The establishment of healthy baseline values would provide the opportunity to compare these measures pre-post suspected concussion. Thereby affording an insight into the potential retinal manifestations of concussion.

Hypotheses:

SCAT-3 Baselines

- Females will report significantly higher symptom scoring than males on baseline testing, and will significantly outperform males on the SAC and mBESS

- Participants with a history of previous concussion will report significantly higher symptom scoring than those without a history of concussion

OCT Baselines

- Males will have a significantly thicker GCL++ than females on baseline testing

- Participants with a history of concussion will display a significantly thicker peripapillary RNFL and Macular GCL++ than participants without a previous history of concussion.

Follow-up Measures

- There will be a significant increase in symptom number and SSS following concussive injury

- There will be a significant decline in cognitive function (SAC) and postural control (mBESS) following concussive injury

- There will be a significant thickening of peripapillary RNFL and Macular GCL++ thickness following concussive injury

5.2 – Methodology

Participants

Prior to recruitment, ethical approval was received from the ITC ethics
committee. Inclusion criteria for the study consisted of: age between 15 and
40 years old and actively partaking in sport with a physical contact element
on a weekly basis. Exclusion criteria consisted of; currently suffering from
suspected concussion (previous history of concussion was not an exclusion
criterion), history of refractive (laser) eye surgery, history of keratoconus
(abnormal curvature of the cornea), history of glaucoma, photosensitive
epilepsy, history of severe eye trauma and history of diabetes. There were
154 participants included in this study, 111 males and 43 females, mean age
20.9 ±4.5 years. There were 76 Rugby players (72 male, 4 female), 44 GAA
players (10 male, 34 female) and 34 soccer players (29 male and 5 female)
this is represented below in figure 5.1.
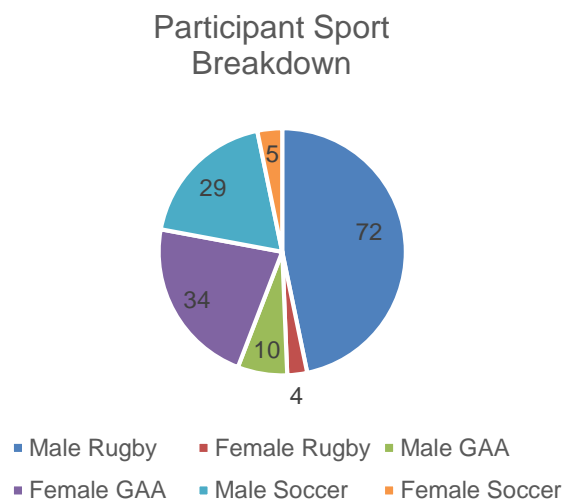
Figure 5.1 – Participant Demographic Breakdown

Recruitment Process:

With the assistance ITC Director of Sport, three ITC sports course directors (Rugby, G.A.A and, Soccer) were approached initially with email, and a subsequent meeting in person, participants were then recruited in person during class time with all procedures fully explained to them. Three external sports teams around the province of Leinster were also contacted *via* email and/or telephone for recruitment to the individual team management, medical personnel and coaches were initially approached to explain the purpose, procedures and aims of the current study, this information was initially communicated *via* email. Once the team agreed to partake in the study, the information sheet, health-screening questionnaire and informed consent (and assent to minors (<18 years) were made available to the management (Appendix E). This documentation was then distributed to potential participants and their parents, where applicable Following recruitment, a suitable date and time was agreed for baseline testing to take place.

Procedures:

Participating teams and groups were tested over either one or two days depending on the size and availability of each group. All teams were tested on site at ITC with the exception of one school team who were tested off-site at their training grounds. Once inclusion/exclusion criteria and the health-screening questionnaire were satisfied, along with written informed consent and assent, participants and management/coaches were sent a structured timetable allowing approximately 30-minutes for every 5 participants to undergo baseline testing. In order to operate on a more practical timescale for testing large numbers of participants, additional manpower was recruited in the form of a post-graduate sport-scientist and a post-graduate athletic rehabilitation therapist, both of whom were responsible for carrying out all SCAT-3 testing, both of whom under-went 1 on 1 training on the specific implementation of the tool and the standardised specific language (according to the SCAT-3 instructions) to be used for all participants. This training was delivered by the main researcher for 1-hour in duration. Multiple practice-runs were then carried out to ensure competency. In the event of a follow-up

measure, the same rater was used. Two testing stations were set up and each participant followed the same order for baseline testing, which was: SCAT3 testing followed by OCT scans. Players, coaching staff and medical personnel agreed that in the event of a suspected concussion, diagnosed by their own or another medical professional, that they would alert the principal investigator by email or phone. Subsequently the player would return to ITC for follow-up measures 48hrs, 2 weeks and 2 months post suspected concussion. The procedure is outlined below in figure 5.2.

Baseline Testing
- 1: SCAT-3
- 2: OCT (RNFL + GCL++)

Suspected Concussive Injury

1st Follow-up
- 1: SCAT-3
- 2: OCT (RNFL + GCL++)

48-Hours Post Injury

2nd Follow-up
- 1: SCAT-3
- 2: OCT (RNFL + GCL++)

14-Days Post Injury

3rd Follow-up
- 1: SCAT-3
- 2: OCT (RNFL + GCL++)

2-Months Post Injury

Recruitment

N = 154

(111 Male, 43 Female)

76 – Rugby

44 – GAA

34 -Soccer
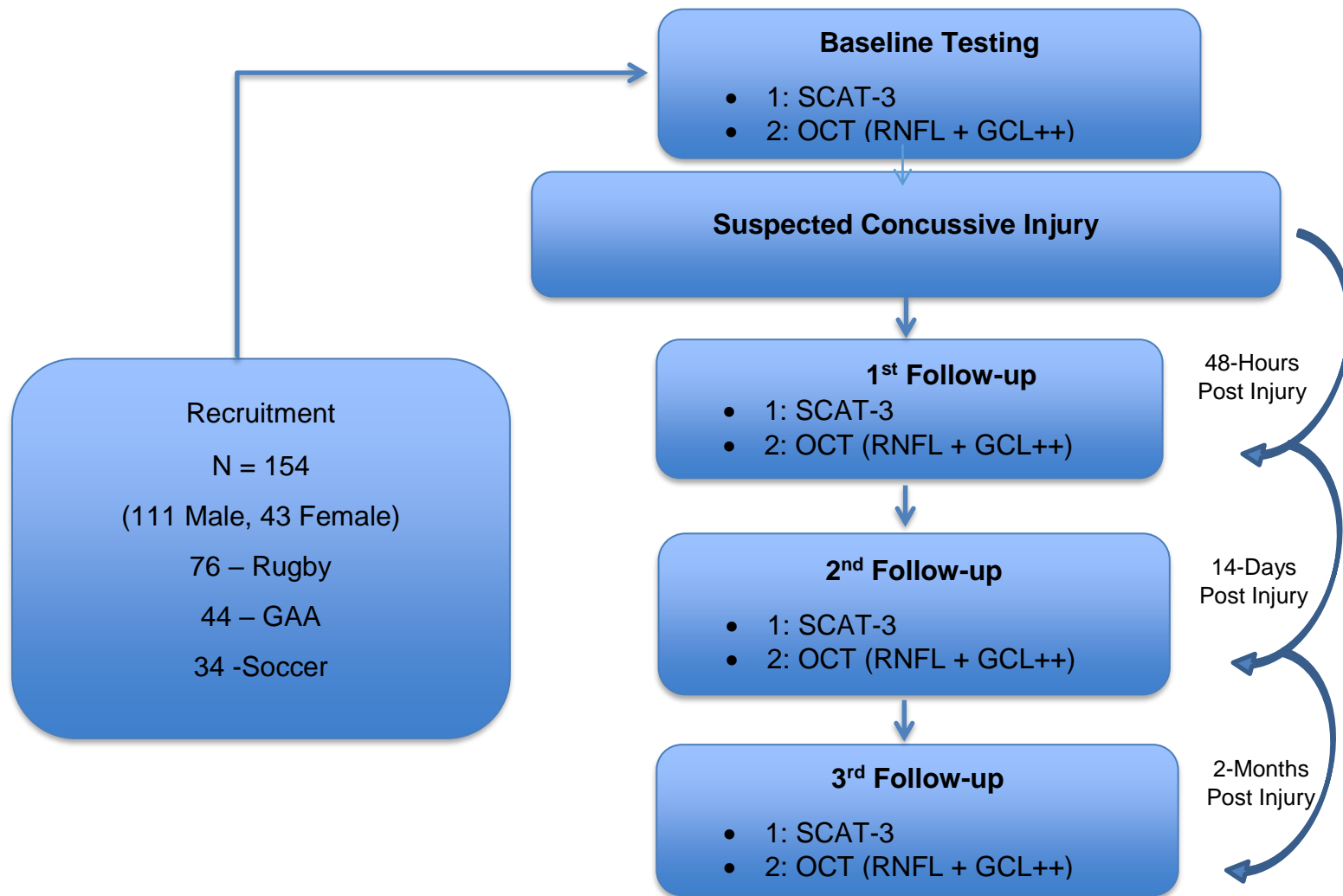
Figure 5.2 – Methodology Flow Chart

Sport Concussion Assessment Tool (SCAT3)

The outcome measures taken from the SCAT-3 comprised of: Number of symptoms, symptom severity score (SSS), SAC score, and Modified Balance Error Scoring System (BESS).

The sports scientist and athletic rehabilitation therapist were the sole raters for all SCAT3 measures, both raters were trained and familiarised with the standardised procedures and instructions of the SCAT3 (Appendix A). In the case of a follow-up, the same rater was used for baseline and follow-up measure to negate any possible inter-rater variations. Each participant filled out the background (with the date, name of examiner and date of injury blocked out) (Figure 5.3) the current date are questions in the cognitive assessment element of the SCAT3. Therefore filling out the date on the background section may have confounded results in the cognitive section. The participant also filled out the symptom evaluation section of the SCAT3. Following the standardised SCAT3 instructions, the rater then completed Standardised Assessment of Concussion (SAC) (Michael McCrea *et al.*, 1998). The SAC incorporates cognitive assessment (orientation, immediate memory, concentration – 'digits backward', concentration - 'months in reverse' and delayed recall). Prior to the delayed recall assessment, the balance examination of the SCAT3 was performed. The total SAC score (out of a maximum of 30) was then calculated. Once the SCAT3 was complete, the participant was directed to the OCT testing station.

A history of previous suspected concussion was reported on the background portion of the SCAT-3. This provided the opportunity to examine the potential variances in baseline/normative data between participants with and without a history of suspected concussion.

BACKGROUND

Name: _____ ████████████████

████████████████████████████

Sport/team/school: _____ ████████████████

Age: _____ Gender: ☐ M ☐ F

Years of education completed: _____

Dominant hand: ☐ right ☐ left ☐ neither

How many concussions do you think you have had in the past? _____

When was the most recent concussion? _____

How long was your recovery from the most recent concussion? _____

Have you ever been hospitalized or had medical imaging done for a head injury? ☐ Y ☐ N

Have you ever been diagnosed with headaches or migraines? ☐ Y ☐ N

Do you have a learning disability, dyslexia, ADD/ADHD? ☐ Y ☐ N

Have you ever been diagnosed with depression, anxiety or other psychiatric disorder? ☐ Y ☐ N

Has anyone in your family ever been diagnosed with any of these problems? ☐ Y ☐ N

Are you on any medications? If yes, please list: ☐ Y ☐ N

SCAT3 to be done in resting state. Best done 10 or more minutes post excercise.

SYMPTOM EVALUATION

3 How do you feel?

"You should score yourself on the following symptoms, based on how you feel now".

	none	mild		moderate		severe	
Headache	0	1	2	3	4	5	6
"Pressure in head"	0	1	2	3	4	5	6
Neck Pain	0	1	2	3	4	5	6
Nausea or vomiting	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Blurred vision	0	1	2	3	4	5	6
Balance problems	0	1	2	3	4	5	6
Sensitivity to light	0	1	2	3	4	5	6
Sensitivity to noise	0	1	2	3	4	5	6
Feeling slowed down	0	1	2	3	4	5	6
Feeling like "in a fog"	0	1	2	3	4	5	6
"Don't feel right"	0	1	2	3	4	5	6
Difficulty concentrating	0	1	2	3	4	5	6
Difficulty remembering	0	1	2	3	4	5	6
Fatigue or low energy	0	1	2	3	4	5	6
Confusion	0	1	2	3	4	5	6
Drowsiness	0	1	2	3	4	5	6
Trouble falling asleep	0	1	2	3	4	5	6
More emotional	0	1	2	3	4	5	6
Irritability	0	1	2	3	4	5	6
Sadness	0	1	2	3	4	5	6
Nervous or Anxious	0	1	2	3	4	5	6

Figure 5.3 – Adjusted SCAT3 – Self-Reported Background and Symptom Evaluation

Optical Coherence Tomography (OCT)

Peripapillary and macular OCT measures were taken using the same scan-type that was used in study 2 (3D (H) + Line (H) 12.0mm X 9.0mm - wide fixation). Peripapillary RNFL and macular GCL++ were recorded in the same way as described in study 2

<u>Follow-up measures</u>

In the event that any participant sustained a suspected concussion it was agreed upon that the coaching/medical staff of each team would contact the principle investigator to arrange for follow up testing. Regular monthly contact was maintained by either email, telephone call or meeting in person. In the unfortunate event that any participant enrolled in the study sustained a suspected concussion, follow up measures were taken 48hrs, 2-weeks and 2-months post-concussive incident where possible, using the same procedures as outlined above. This comprised of SCAT-3 testing, followed by OCT scans. The participant was free to ask any questions they wished throughout the testing procedures. Participant who underwent follow-up testing were asked a few brief questions regarding their injury. This would provide some additional information with regard to the impact area, situation and the main symptomatic complaints of the participant (Figure 5.4).

```
┌─────────────────────────────────────────────────────────────────────┐
│                  Concussion Follow-up Examination                     │
│                                                                       │
│                                                                       │
│  Name: _____Date of Birth: _____   │
│                                                                       │
│                                                                       │
│  Position: _____                           │
│                                                                       │
│                                                                       │
│  Loss of consciousness: _____                            │
│                                                                       │
│                                                                       │
│  If yes, how long: _____                              │
│                                                                       │
│                                                                       │
│  Impact Area: _____ Impact Situation: _____  │
│                                                                       │
│                                                                       │
│  Vision problems:                                                     │
│  _____  │
│                                                                       │
│                                                                       │
│  Primary Complaint:                                                   │
│  _____  │
│  _____  │
└─────────────────────────────────────────────────────────────────────┘
```

Figure 5.4 – Concussion Follow-up questionnaire

Data analysis:

IBM SPSS (Statistical Package for Social Sciences) version 23 was used to analyse the data. Statistical significance was set at $P < 0.05$. Descriptive statistics were used to report mean values ± standard deviations for the SCAT-3 and OCT measures for each sport and gender included in this study. All data was screened for normality using a Shapiro-Wilk test. Levene's test was used to screen data for homogeneity of variance. Independent samples or Mann-Whitney U tests (where normality was violated) were used to test for significant differences with regard to gender and history of concussion effect size was calculated for independent samples using the following formula (Ellis, 2009). Where M = mean and SD = Standard Deviation.

$$Cohen's\ d = \frac{M1 - M2}{SD\ Pooled}$$

One-way ANOVA tests were used to test for a significant difference between sports. In the case of a significant difference, a Bonferroni post-hoc test was used to determine where the difference lay. Effect Sizes (Eta^2) and observed power were also calculated using SPSS. Cohen's classification was used to determine of effect size (0.2 = small, 0.5 = medium and 0.8 is large) [Cohen 1988]. There was not sufficient data to conduct statistical analysis on follow-up data, these measures are represented below as individual case studies.

5.3 – Results

The primary purpose of this study was to establish baseline/normative values of SCAT-3 and OCT measures (RNFL and GCL++) in young, healthy male and female team sport athletes. The secondary aim was to draw comparisons and explore for significant differences in these aforementioned measures with regard to gender, sporting discipline, and history of concussion in a young, healthy team-sport population. The tertiary aim was to explore the effects of a suspected concussion on the baseline SCAT-3 and OCT measures established in this cohort. 47% (n=73) of participants reported a lifetime prevalence of concussion. All data was tested for normality using Shapiro-Wilks test. Homogeneity of variance was tested where appropriate using Levene's test.

SCAT-3

Gender Comparison

SAC in the female group was found to be normally distributed ($P < 0.05$). Number of symptoms, SSS, mBESS in both male and female groups and SAC in the male group were found to be non-normally distributed ($P > 0.05$). All data with regard to gender comparison is presented in table 5.1 below. Baseline values were higher for all SCAT3 measures in males with the exception of the mBESS, which was marginally higher in the female group. A Mann-Whitney U test revealed a significant difference between groups for the self-reported subjective SCAT3 elements; number of symptoms ($U = 1521$, $P = 0.0001$) with a medium effect size of 0.52 and SSS ($U = 1501.5$, $P = 0.0001$) with a small effect size of 0.38. There was no significant difference between groups for the SAC and mBESS elements ($P > 0.05$) all with small effect sizes.

Table 5.1 –Baseline SCAT-3 Gender Comparison

	Mean±SD		Difference±SD	P-Value	Effect size (d)
	Male(N = 111)	Female (N = 43)			
Number of Symptoms	3.2 ± 3.7	1.5 ± 2.8	1.7 ± 0.9	0.0001*	0.52
SSS	5.8 ± 8.0	3.0 ± 6.7	2.8 ± 1.3	0.0001*	0.38
SAC	26.5 ± 2.1	26.1 ± 1.7	0.4 ± 0.4	0.268	0.21
mBESS	4.1 ± 3.6	4.3 ± 3.6	0.2 ± 0.0	0.895	0.06

SSS = Symptom Severity Score, SAC = Standardised Assessment of Concussion, mBESS = Modified Balance Error Scoring System. * Denotes Significant Difference (P < 0.05) (Mann-Whitney U)

Sport comparision

Number of Symptoms, SSS, SAC and mBESS were all found to be non-normally distributed (P < 0.05) with the exception of SAC in the soccer group, which was normally distributed (P > 0.05). All elements displayed homogeneity of variance accoring to Levene's test (P > 0.05) with the exception of the number of symptoms element (P < 0.05). A Kruskal-Wallis test revealed no significant difference between groups for any of the SCAT3 elements (P > 0.05) all with small effect sizes. All data with regard to sport comparison is represented below in table 5.2.

Table 5.2 – Baseline SCAT-3 Sport Comparison

	Mean ±SD			P-Value	Effect Size (eta^2)
	Rugby (N = 76)	GAA (N = 44)	Soccer (N = 34)		
Number of Symptoms	3.1 ± 3.5	1.8 ± 2.5	3.1 ± 4.5	0.069	0.03
SSS	5.7 ± 7.7	3.2 ± 5.2	5.9 ± 10.0	0.051	0.02
SAC	26.4 ± 2.1	26.1 ± 1.9	26.8 ± 2.0	0.256	0.02
mBESS	4.2 ± 3.6	4.6 ± 4.1	3.5 ± 2.6	0.769	0.01

SSS = Symptom Severity Score, SAC = Standardised Assessment of Concussion, mBESS = Modified Balance Error Scoring System.

History of Concussion Comparison

Number of Symptoms, SSS, SAC and mBESS were all found to be non-normally distributed ($P < 0.05$). A Mann-Whitney U test revealed no significant difference between groups for any of the SCAT3 elements ($P > 0.05$), all with small effect sizes. All data regarding history of concussion comparison is represented below in table 5.3.

Table 5.3 – Baseline SCAT3 History of Concussion Comparison

	Mean ±SD		Difference	P-Value	Effect Size (d)
	P.C (N = 73)	N.C (N = 81)			
Number of Symptoms	2.9 ± 3.5	2.5 ± 3.6	0.4 ± 0.1	0.133	0.11
SSS	5.4 ± 7.5	4.6 ± 8.0	0.8 ± 0.5	0.079	0.10
SAC	26.4 ± 2.1	26.3 ± 1.9	0.1 ± 0.2	0.859	0.05
mBESS	4.2 ± 3.7	4.1 ± 3.4	0.1 ± 0.3	0.891	0.03

SSS = Symptom Severity Score, SAC = Standardised Assessment of Concussion, mBESS = Modified Balance Error Scoring System. P.C = Previous History of Concussion. N.C = No Previous History of Concussion.

RNFL

<u>Gender Comparison</u>

<u>Left eye</u>

All sectors for both male and female groups were found to be normally distributed ($P > 0.05$) with the exception of the nasal sector in the male group, which was non-normally distributed ($P < 0.05$). All sectors displayed homogeneity of variance according to Levene's test ($P > 0.05$). Independent samples t-tests revealed no significant difference between gender in the superior, temporal and inferior sectors as well as Total RNFL thickness ($P > 0.05$). Mann-Whitney U test revealed no significant difference in the Nasal sector ($P > 0.05$). Small effect sizes were observed in all sectors. All data with regard to RNFL gender comparison are represented below in table 5.4.

<u>Right eye</u>

All sectors for both male and female groups were found to be normally distributed ($P > 0.05$) with the exception of the superior sector in the female group and the temporal sector in the male group, which were both found to be non-normally distributed ($P < 0.05$). All sectors displayed homogeneity of variance according to Levene's test ($P > 0.05$). Mann-Whitney U tests revealed no significant difference between male and females in either superior or temporal sectors ($P > 0.05$). Independent sample T-tests revealed no significant difference between males and females in inferior and nasal sectors as well as total RNFL thickness ($P > 0.05$). Small effect sizes were observed in all sectors.

Table 5.4 – Baseline RNFL Thickness (µm) Gender Comparison

	Left Eye						Right Eye				
Sector	**Mean ±SD**		**Difference**	**P-Value**	**Effect size (d)**		**Mean ±SD**		**Difference**	**P-Value**	**Effect size (d)**
	Male (N = 111)	Female (N = 43)					Male (N = 111)	Female (N = 43)			
Superior	136.3 ± 17.0	136.4 ± 16.5	0.1 ± 0.5	0.973	0.01		129.6 ± 15.6	134.3 ± 16.9	4.7 ± 1.3	0.221	0.29
Temporal	75.7 ± 10.7	76.9 ± 8.2	1.2 ± 2.5	0.533	0.13		78.9 ± 12.0	80.7 ± 8.8	1.8 ± 3.2	0.334	0.17
Inferior	140.4 ± 16.5	143.9 ± 17.7	3.5 ± 1.2	0.242	0.20		138.2 ± 17.7	140.6 ± 15.7	2.4 ± 2.0	0.483	0.14
Nasal	88.2 ± 14.4	90.7 ± 13.9	2.5 ± 0.5	0.247	0.18		87.1 ± 14.9	88.4 ± 13.4	1.3 ± 1.5	0.632	0.01
Total	110.2 ± 10.3	111.9 ± 10.4	1.7 ± 0.1	0.374	0.17		108.9 ± 10.5	111.0 ± 9.7	2.1 ± 0.8	0.247	0.20

<u>Sport Comparison</u>

<u>Left eye</u>

All data was normally distributed (P > 0.05) with the exception of the temporal sector in the GAA group (P < 0.05). All data displayed homogeneity of variance according to Levene's test (P > 0.05). A one-way ANOVA test revealed no significant difference across groups for superior, inferior, nasal sectors as well as total RNFL thickness (P > 0.05). A Kruskal-Wallis test revealed no significant difference across sports for the temporal sector (P > 0.05). Small effect sizes were observed in all sectors. All data with regard to RNFL sport comparison is represented below in table 5.5.

<u>Right eye</u>

All data was normally distributed (P > 0.05) with the exception of the temporal sector in the GAA group. All data displayed homogeneity of variance according to Levene's test (P > 0.05). A one-way ANOVA test revealed no significant difference between groups in the superior, inferior and nasal sectors as well as total RNFL thickness (P > 0.05). A Kruskal-Wallis test revealed no significant difference between groups in the temporal sector (P > 0.05). Small effect sizes were observed in all sectors.

Table 5.5 – Baseline RNFL Thickness (µm) Sport Comparison

	Left Eye					Right Eye				
Sector	**Mean ±SD**			**P-Value**	**Effect Size (eta^2)**	**Mean ±SD**			**P-Value**	**Effect Size (eta^2)**
	Rugby (N = 76)	GAA (N = 44)	Soccer (N = 34)			Rugby (N = 76)	GAA (N = 44)	Soccer (N = 34)		
Superior	138.1 ± 17.5	134.8 ± 16.0	134.1 ± 16.2	0.404	0.01	131.7 ± 15.6	132.6 ± 16.9	127.0 ± 16.0	0.262	0.02
Temporal	75.7 ± 9.5	76.2 ± 9.5	76.6 ± 12.0	0.882	0.00	79.4 ± 11.8	79.4 ± 8.8	79.6 ± 12.8	0.969	0.00
Inferior	141.0 ± 16.6	145.4 ± 18.7	136.9 ± 13.9	0.084	0.03	139.6 ± 17.3	141.8 ± 18.0	133.4 ± 14.6	0.087	0.03
Nasal	87.6 ± 12.9	92.0 ± 14.7	87.6 ± 16.3	0.220	0.02	86.6 ± 12.8	90.6 ± 14.4	85.6 ± 17.7	0.232	0.02
Total	110.7 ± 10.4	112.1 ± 10.5	108.8 ± 10.0	0.391	0.01	109.6 ± 10.1	111.0 ± 10.6	107.2 ± 10.2	0.276	0.02

Left eye

All data was normally distributed (P > 0.05) with the exception of the superior sector for the previous concussion group and the temporal sector for the no previous concussion group (P < 0.05). A Mann-Whitney U test revealed no significant difference between groups in the superior and temporal sectors (P > 0.05). An independent samples t-test revealed no significant difference between groups in the inferior and nasal sectors as well as total RNFL thickness (P > 0.05). Small effect sizes were observed in all sectors. All data with regard to RNFL history of concussion comparison is represented below in table 5.6.

Right eye

All data was normally distributed (P > 0.05) with the exception of the temporal sector in the previous concussion group. All data displayed homogeneity of variance (P > 0.05) according to Levene's test with the exception of the Nasal sector (P < 0.05). An Independent samples T-test revealed no significant difference between groups for superior and inferior sectors as well as total RNFL thickness (P > 0.05). A Mann-Whitney U test revealed no significant difference between groups for the Temporal and Nasal sectors (P > 0.05). Small effect sizes were observed in all sectors.

Table 5.6 – Baseline RNFL Thickness (µm) History of Concussion Comparison

	Left Eye					Right Eye				
Sector	**Mean ±SD**		**Difference**	**P-Value**	**Effect Size (d)**	**Mean ±SD**		**Difference**	**P-Value**	**Effect Size (d)**
	P.C (N = 73)	N.C (N = 81)				P.C (N =73)	N.C (N = 81)			
Superior	137.8 ± 16.7	134.9 ± 16.9	2.9 ± 0.2	0.461	0.17	130.5 ± 15.2	131.3 ± 16.9	0.8 ± 1.7	0.781	0.05
Temporal	76.3 ± 9.5	75.8 ± 10.6	0.5 ± 1.1	0.622	0.05	80.2 ± 11.8	78.7 ± 10.6	1.5 ± 1.2	0.535	0.13
Inferior	140.5 ± 16.0	142.1 ± 17.6	1.6 ± 1.6	0.535	0.01	138.4 ± 15.4	139.3 ± 18.6	0.9 ± 3.2	0.764	0.05
Nasal	88.8 ± 12.6	89.0 ± 15.8	0.2 ± 3.2	0.942	0.01	87.8 ± 12.2	87.2 ± 16.3	0.6 ± 4.1	0.821	0.04
Total	110.9 ± 9.8	110.5 ± 10.9	0.4 ± 1.1	0.843	0.04	109.9 ± 9.1	109.0 ± 11.3	0.9 ± 2.2	0.586	0.09

P.C = Previous History of Concussion. N.C = No Previous History of Concussion

In summary, with regard to RNFL there were no significant differences observed between gender for any sector in either left or right eyes. There were no significant differences observed between sporting disciplines for any sector in either left or right eyes. There were no signiicant differences observed between participants with a history of concussion *vs* participants with no history of concussion.

GCL++

<u>Gender Comparision</u>

<u>Left eye</u>

All data was normally distributed (P > 0.05) with the exception of the inferior nasal sector in the female group (P < 0.05). All data displayed homogeneity of variance according to Levene's test. An Independent samples T-test revealed a significant difference in the superior temporal sector (t(152) = 2.54, P = 0.012) with a small effect size of 0.48, the male sector was 3.0 μm thicker. Independent samples T-test revealed no significant difference between groups in Superior, Inferior temporal, Inferior, and Superior Nasal sectors, as well as total GCL++ thickness (P > 0.05) all with small effect sizes. A Mann-Whitney U test revealed no significant difference between groups for the Inferior-Nasal sector.

<u>Right Eye</u>

All data was normally distributed (P > 0.05) with the exception of superior temporal and inferior temporal in the male group and superior nasal in the female group (P < 0.05). All data displayed homogeneity of variance (P > 0.05) according to Levene's test. An independent samples T-test revealed no significant difference between groups in the superior, inferior, inferior nasal sectors, as well as total GCL++ thickness (P > 0.05). A Mann-Whitney U test revealed a significant difference between groups in the superior temporal group (U = 1717.5, P = 0.007) but not in the inferior temporal or superior nasal groups (P > 0.05). All sectors displayed a small effect size.

Table 5.7 – Baseline GCL++ Thickness (µm) Gender Comparison

		Left Eye						Right Eye			
Sector	**Mean ±SD**		**Difference**	**P-Value**	**Effect Size (d)**		**Mean ±SD**		**Difference**	**P-Value**	**Effect Size (d)**
	Male	Female					Male	Female			
Superior	111.7 ± 7.1	111.1 ± 8.4	0.6 ± 1.3	0.680	0.08		113.2 ± 7.5	112.3 ± 8.4	0.9 ± 0.9	0.547	0.11
Superior Temporal	100.3 ± 6.6	97.3 ± 5.8	3.0 ± 0.8	**0.012***	0.48		102.1 ± 6.8	99.1 ± 5.9	3.0 ± 0.9	**0.007***	0.47
Inferior Temporal	102.4 ± 6.5	100.3 ± 6.0	2.1 ± 0.5	0.073	0.34		104.5 ± 6.9	102.1 ± 7.1	2.4 ± 0.2	0.059	0.35
Inferior	109.7 ± 7.8	109.9 ± 7.0	0.2 ± 0.8	0.894	0.03		111.0 ± 7.7	111.6 ± 7.8	0.6 ± 0.1	0.681	0.08
Inferior Nasal	124.9 ± 9.1	124.0 ± 8.8	0.9 ± 0.3	0.351	0.03		124.4 ± 8.6	124.1 ± 7.9	0.3 ± 0.7	0.822	0.04
Superior Nasal	124.4 ± 7.9	121.8 ± 8.2	2.6 ± 0.3	0.070	0.32		125.3 ± 7.9	123.6 ± 8.2	1.7 ± 0.3	0.116	0.21
Total	112.3 ± 6.9	110.9 ± 6.8	1.4 ± 0.1	0.243	0.20		113.5 ± 6.8	112.2 ± 6.7	1.3 ± 0.1	0.276	0.19

* = Significant difference (P < 0.05) Independent Samples t-test
** = Significant difference (P < 0.05) Mann-Whitney U test

<u>Sport Comparison</u>

<u>Left eye</u>

All data was normally distributed (P > 0.05) with the exception of the inferior temporal sector in the rugby group, the inferior sector in the soccer group and the inferior nasal group in the GAA group. All data displayed homogeneity of variance (P > 0.05) according to Levene's test. A one-way ANOVA test revealed no significant difference between sports in the superior, superior temporal and superior nasal sectors as well as total GCL++ thickness (P > 0.05). A Kruskal-Wallis test revealed no significant difference between sports in the inferior temporal, inferior, and inferior nasal sectors (P > 0.05). All sectors dislayed a small effect size. Data with regard to GCL++ sport comparision is represented below in table 5.8.

<u>Right eye</u>

All data was normally distributed (P > 0.05) with the exception of the superior temporal, inferior temporal and superior nasal sectors in the rugby group (P < 0.05). All data displayed homogeneity of variance (P > 0.05) according to Levene's test. A one-way ANOVA test revealed no significant difference across sports for the superior, inferior, inferior nasal sectors as well as total GCL++ thickness (P > 0.05). A Kruskal-Wallis test revealed no significant difference between sports for the superior temporal, inferior temporal and superior nasal sectors (P > 0.05). All sectors dislayed a small effect size.

Table 5.8 – Baseline GCL++ Thickness (µm) Sport Comparison

Sector	Left Eye					Right Eye				
	Mean ±SD			P-Value	Effect Size (Eta^2)	Mean ±SD			P-Value	Effect Size (Eta^2)
	Rugby	GAA	Soccer			Rugby	GAA	Soccer		
Superior	112.2 ± 6.9	111.0 ± 8.1	110.8 ± 7.8	0.543	0.01	113.6 ± 7.2	112.5 ± 8.4	112.1 ± 8.2	0.576	0.01
Superior Temporal	100.4 ± 6.2	97.7 ± 6.3	99.6 ± 7.2	0.099	0.03	101.9 ± 5.9	100.2 ± 7.9	101.1 ± 6.6	0.122	0.01
Inferior Temporal	102.4 ± 6.3	100.8 ± 6.4	101.8 ± 6.8	0.428	0.01	104.4 ± 6.2	102.5 ± 8.6	104.2 ± 6.7	0.120	0.02
Inferior	109.6 ± 7.8	110.4 ± 7.3	109.2 ± 7.5	0.933	0.00	111.1 ± 7.6	111.8 ± 7.9	110.5 ± 7.7	0.754	0.00
Inferior Nasal	124.8 ± 8.7	124.7 ± 9.4	124.2 ± 7.6	0.914	0.00	124.7 ± 7.9	123.9 ± 7.9	124.1 ± 9.1	0.868	0.00
Superior Nasal	124.9 ± 7.6	122.6 ± 8.4	122.6 ± 8.3	0.197	0.02	125.8 ± 7.4	123.6 ± 8.7	124.2 ± 8.4	0.226	0.01
Total	112.5 ± 6.6	111.3 ± 7.1	111.4 ± 7.3	0.584	0.01	113.7 ± 6.4	112.5 ± 7.1	112.8 ± 7.4	0.633	0.01

Left eye

All data was normally distributed (P > 0.05) with the exception of the inferior temporal sector in the concussion group. All data displayed homogeneity of variance (P > 0.05) according to Levene's test. An Independent samples T-test revealed no significant difference between groups in superior, superior temporal, inferior, inferior nasal, superior nasal sectors as well as total GCL++ thickness (P > 0.05). A Mann-Whitney U test revealed no significant difference between groups in the inferior temporal sector (P > 0.05). Small effect sizes were observed in all sectors. All data regarding GCL++ history of concussion comparison is represented below in table 5.9.

Right eye

All data was normally distributed (P > 0.05) with the exception of the superior temporal and inferior temporal sectors in the concussion group (P < 0.05). All data displayed homogeneity of variance (P > 0.05) according to Levene's test. An Independent samples T-test revealed no significant difference between groups in superior, inferior, inferior nasal, superior nasal sectors as well as total GCL++ thickness (P > 0.05). Mann-Whitney U tests revealed no significant difference between groups in the superior temporal and inferior temporal sectors (P > 0.05). Small effect sizes were observed in all sectors.

Table 5.9 –Baseline GCL++ Thickness (μm) History of Concussion Comparison

Sector	Left Eye		Difference	P-Value	Effect Size (d)	Right Eye		Difference	P-Value	Effect Size (d)
	Mean ±SD					Mean ±SD				
	P.C (N = 73)	N.C (N = 81)				P.C (N = 73)	N.C (N = 81)			
Superior	112.3 ± 7.7	110.8 ± 8.0	1.5 ± 0.3	0.212	0.19	113.2 ± 7.2	112.7 ± 8.3	0.5 ± 1.1	0.714	0.06
Superior Temporal	100.0 ± 5.7	98.9 ± 7.2	1.1 ± 1.5	0.310	0.17	101.9 ± 6.9	100.7 ± 6.5	1.2 ± 0.4	0.409	0.18
Inferior Temporal	102.4 ± 5.9	101.3 ± 6.8	1.1 ± 0.9	0.371	0.17	104.7 ± 6.8	103.0 ± 7.2	1.7 ± 0.4	0.227	0.24
Inferior	110.5 ± 7.0	109.0 ± 8.0	1.5 ±1.0	0.216	0.20	111.7 ± 7.2	110.8 ± 8.1	0.9 ± 0.9	0.479	0.12
Inferior Nasal	125.5 ± 8.9	123.9 ± 8.9	1.6 ± 0.0	0.261	0.18	124.4 ± 8.1	124.3 ± 8.6	0.1 ± 0.5	0.903	0.01
Superior Nasal	123.9 ± 7.4	123.6 ± 8.6	0.3 ± 1.2	0.797	0.04	124.5 ± 7.5	125.1 ± 8.5	0.6 ± 1.0	0.599	0.07
Total	112.6 ± 6.4	111.3 ± 7.3	1.3 ± 0.9	0.251	0.19	113.5 ± 6.3	112.9 ± 7.2	0.6 ± 0.9	0.602	0.09

In summary, with regard to GCL++, there were significant differences observed between gender in the superior-temporal sector of both left and right eyes, with males displaying significantly thicker superior-temporal than females. There were no significant differences observed between sporting disciplines for any sector in either the left or right eye. There were no significant differences observed between participants with a history of concussion *vs* participants with no history of concussion.

Concussion Case Studies

During the course of the study there were 2 reported concussions for which follow up measures were taken. The follow-up measure was 14-days post-concussion. There was also another reported concussion, however this participant was absent for baseline testing. Therefore, a comparison was made on this participants' 48-hr post-concussion measures followed by a 14-day follow up. There were too few reported concussions to perform statistical analysis, and as such, data is represented below as individual case studies. Furthermore % changes have been calculated and tabulated below.

Case Study 1:
The athlete was a 16 year-old male 2nd row rugby player. He sustained a trauma to the posterior right side of his head while in a ruck situation. He had no loss of consciousness. The player was not taken off and the concussion was diagnosed by the teams' medical staff following the game. The primary complaint reported by the player was that he had difficulty concentrating for the rest of the game and felt "50% there". The athlete reported no previous concussions prior to this. SCAT-3, and OCT measures are reported below in tables 5.10, 5.11 and 5.12.

Table 5.10 – Case Study 1: SCAT-3 Measures and % Change

	Baseline	14-Day	% Change
Number of Symptoms	16	19	19
SSS	38	56	47
SAC	28	30	7
mBESS	3	8	167

The athlete reported 19% more symptoms and a 47% higher symptom severity score in the 14-day follow up when compared to the baseline testing. SAC score improved by 7% in the same time-frame. The biggest % increase (more errors made) for any SCAT-3 element was in the mBESS, for which there were 167% more errors made at the 14-day follow up.

Table 5.11 – Case Study 1: RNFL Measures (μm) and % Change

Left Eye	Baseline	14-day	% change	Right Eye	Baseline	14-day	% change
Superior	100	96	-4.0	Superior	100	101	1.0
Temporal	50	50	0.0	Temporal	49	52	6.1
Inferior	89	90	1.1	Inferior	84	82	-2.4
Nasal	76	77	1.3	Nasal	76	75	-1.3
Total Thickness	79	78	-1.3	Total	77	78	1.3

The % changes in RNFL thickness ranged from -4.0% (-4μm) in the superior sector of the left eye to +6.1% (+3μm) in the right eye between baseline and 14-day follow up. There was a total thinning of -1.3% in the left eye equating to a change of 1μm and a thickening of 1.3% in the right eye, equating to a change of 1μm in the right eye.

Table 5.12 – Case Study 1: GCL++ Measures (μm) and % Change

Left Eye	Baseline	14-Day	%Change	Right Eye	Baseline	14-Day	%Change
Superior	104	104	0.0	Superior	102	103	1.0
Superio-Temporal	95	95	0.0	Superio-Temporal	93	95	2.2
Inferio-Temporal	91	92	1.1	Inferio-Temporal	93	94	1.1
Inferior	91	93	2.2	Inferior	94	95	1.1
Inferio-Nasal	118	119	0.8	Inferio-Nasal	118	120	1.7
Superio-Nasal	122	123	0.8	Superio-Nasal	121	122	0.8
Total Thickness	104	104	0.0	Total	104	105	0.8

The % changes in GCL++ thickness ranged from 0.0% to 2.2%. There was no thinning observed in any sector in either eye. The largest thickening was between baseline and the 14-day follow up was 2μm in the inferior sector of the left eye and the superio-temporal and inferio-nasal sectors of the right eye.

Case Study 2:

Athlete was an 18 year-old male back-row rugby player. He sustained a trauma to the right side of his head in a tackle situation. He had loss of consciousness for 20-30 seconds. He was removed from play. His primary complaints reported were a slight sensitivity to light and difficulty concentrating. The athlete reported no previous concussions prior to this. SCAT-3 and OCT measures are reported below in tables 5.13, 5.14 and 5.15.

Table 5.13 – Case Study 2: SCAT-3 Measures and % Change

	Baseline	14-Day	% Change
Number of Symptoms	5	6	20.0
SSS	8	12	50.0
SAC	26	27	3.8
mBESS	4	4	0.0

The athlete reported 20% more symptoms and a 50% increase in symptom severity score at the 14-day follow up. The SAC score imporved by 3.8% from baseline to 14-day follow up and there was no change in errors made on the mBESS.

Table 5.14 – Case Study 2: RNFL Measures (μm) and % Change

Left Eye	Baseline	14-day	% change	Right Eye	Baseline	14-day	% change
Superior	154	153	-0.6	Superior	147	145	-1.4
Temporal	82	82	0.0	Temporal	86	85	-1.2
Inferior	136	137	0.7	Inferior	131	133	1.5
Nasal	83	85	2.4	Nasal	82	81	-1.2
Total Thickness	113	114	0.9	Total	111	111	0.0

The % changes in RNFL thickness ranged from -1.4%(-2μm) in the superior sector of the right eye to +2.4%(+2μm) in the nasal sector of the left eye. There was an overall total thickening of 0.9% observed in the left eye and there was no total change in thickness in the right eye.

Table 5.15 – Case Study 2: GCL++ Measures (μm) and % Change

Left Eye	Baseline	14-Day	%Change	Right Eye	Baseline	14-Day	%Change
Superior	108	109	0.9	Superior	113	114	0.9
Superio-Temporal	95	95	0.0	Superio-Temporal	100	101	1.0
Inferio-Temporal	98	99	1.0	Inferio-Temporal	100	100	0.0
Inferior	107	108	0.9	Inferior	106	105	-0.9
Inferio-Nasal	127	125	-1.6	Inferio-Nasal	122	121	-0.8
Superio-Nasal	123	125	1.6	Superio-Nasal	123	122	-0.8
Total Thickness	110	110	0.0	Total	111	111	0.0

The % changes in GCL++ thickness ranged from -1.6%(-2μm) in the inferio-nasal sector of the left eye to +1.0%(+1μm) in the superio-temporal sector of the right eye. There was no total change in thickness observed in both the left and right eye.

Case Study 3:

Athlete was a 20 year old male soccer player. He sustained a trauma to the posterior of his head by hitting it off the pitch surface following a tackle. He had no loss of consciousness. The player was removed from play. His primary complaint was nausea. The player reported 2 previous concussions prior to this. SCAT-3 and OCT results are reporesented below in tables 5.16, 5.17, and 5.18.

Table 5.16 – Case Study 3: SCAT-3 Measures and % Change

	48hr	14-Day	% Change
Number of Symptoms	7	1	-85.7
SSS	12	1	-91.7
SAC	27	29	7.4
mBESS	7	6	-14.3

The athlete reported a 85.7% reduction in number of symptoms and a 91.7% reduction in symptom severity score between 48hrs pos-concussion and the 14-day follow up. SAC scores improved by 7.4%. There was a reduction of 14.3% in mBESS errors between 48hrs post concussion and the 14-day follow up.

Table 5.17 – Case Study 3: RNFL Measures (µm) and % Change

Left Eye	48hr	14-day	% change	Right Eye	48hr	14-day	% change
Superior	163	160	-1.8	Superior	153	148	-3.3
Temporal	86	86	0.0	Temporal	85	86	1.2
Inferior	158	157	-0.6	Inferior	163	166	1.8
Nasal	109	103	-5.5	Nasal	113	115	1.8
Total Thickness	129	126	-2.3	Total	128	129	0.8

The % changes in thickness for RNFL ranged from -5.5%(-6µm) in the nasal sector of the left eye to +1.8%(+3µm) in the nasal sector of the right eye and +2µm in the inferior sector of the right eye. There was a total thinning of -2.3% in the left eye, equating to -3µm, there was a total thickening of 0.8% in the right eye, equating to +1µm.

Table 5.18 – Case Study 3: GCL++ Measures (µm) and % Change

Left Eye	48hr	14-Day	%Change	Right Eye	48hr	14-Day	%Change
Superior	128	127	-0.8	Superior	129	128	-0.8
Superio-Temporal	114	114	0.0	Superio-Temporal	111	111	0.0
Inferio-Temporal	119	117	-1.7	Inferio-Temporal	117	118	0.9
Inferior	126	125	-0.8	Inferior	126	127	0.8
Inferio-Nasal	143	142	-0.7	Inferio-Nasal	139	139	0.0
Superio-Nasal	142	141	-0.7	Superio-Nasal	141	141	0.0
Total Thickness	129	128	0.0	Total	127	127	0.0

The % changes in thickness for GCL++ ranged fro -1.7%(2µm) in the inferior-temporal sector of the left eye to +0.9% (1µm) in the inferior temporal sector of the right eye. There was no total change in thickness in either left or right eyes between measures.

5.4 – Discussion

This research has established baseline/normative values for SCAT-3 and OCT measures for both male and female team sport participants. Furthermore, comparisons of these measures have been drawn between gender, type of sport (G.A.A, Soccer and Rugby) and history of concussion. Finally, 3 separate case-studies examining the effects of concussion on the individuals' respective established baseline measures of the SCAT-3 and OCT measures have been presented. Accoring to the findings of the current study, there is more variation between gender in the more subjective elements of the SCAT-3 such as the self-reported PCSS when compared to the more cognitive and performance-based elements in the form of the SAC and mBESS. Thus further advocating the need for a shift in the paradigm toward a more objective-based assessment criteria for which the potential gender variances are established. Males were found to report significanlty more symptoms and also a higher symptom severity score (SSS). Therefore, the hypothesis that females report significantly more symptoms on the SCAT-3 than males is therefore rejected. There were no significant differences between gender in SAC or mBESS observed in the current study. The hypothesis that females would significantly out-perform males on both the mBESS and SAC elements of the SCAT-3 is therefore rejected. With regard to comparison of SCAT-3 elements across sporting discipline, there were no significant differences found for PCSS, SAC or mBESS. With regard to previous history of concussion, there were no significant differences observed for any SCAT-3 components when comparing those reporting a history of concussion *versus* no history of concussion. Although previously concussed particiapnts reported marginally higher symptom scoring, the hypothesis that participants with a previous history of concussion would report significantly higher SCAT-3 symptom scoring is therefore rejected. There were no significant differences observed in RNFL when comparing gender, sporting discipline or previous history of concussion. The hypothesis that previously concussed athletes have a significantly thicker RNFL than athletes with no previous history of concussion is therefore rejected. For GCL++ analysis, there was a significant difference observed in the superior temporal sector between males and females in both left and right eyes, there

was no significant differences observed in any other sector. The hypothesis that males have a significantly thicker GCL++ than females is therefore rejected. There were no significant differences observed in the current study with regard to GCL++ thickness comparison between sports or with regard to history of concussion. In relation to the 3 case-studies, athlete symptom reporting was clearly affected by concussive injury, worsening following injury and demonstrating a resolution in the days following injury. There were unexpected findings with regard to SAC findings and mixed findings in the mBESS element. In relation to OCT findings in the case studies, there were minimal changes (both thickening and thinning) observed in both peripapillary RNFL and Macular GCL++ thickness. Clearly, a larger sample size is needed to further explore both SCAT and OCT responses to concussive injury.

SCAT-3

Gender Comparison

A significant difference was found between male and female participants in both elements of the PCSS comprising of; number of symptoms ($P < 0.05$, $P = 0.0001$) and SSS ($P < 0.05$, $P = 0.0001$), with males reporting more symptoms than females (3.2 ±3.7 *vs* 1.5 ±2.8) and also demonstrating a higher SSS (5.8 ±8.0 *vs* 3.0 ±6.7). In contrast to these findings, the vast majority of previous research on SCAT symptom reporting has demonstrated that females generally report more symptoms and with a higher severity on baseline testing. Shehata *et al.*, (2009) found that female varsity collision sport athletes scored higher on SSS than males (6.39 *vs* 3.52), however no statistical analysis was carried out. Jinguji *et al.*, (2012) reported similar results in adolescent (13-19 years old) with males reporting a lower number of symptoms than females, however this was not found to be statistically significant. Snyder and Bauer (2014) reported the number of symptoms by subtracting them from a maximum score of 22 (i.e. a lower number representing more symptoms). The study by Snyder and Bauer (2014) found that females reported both a statistically significant higher number of

symptoms than males (18.32 ±4.69 *vs* 20.32 ±2.82, P < 0.001) and a higher SSS (6.35 ±9.22 *vs* 2.98 ±5.79, P < 0.001). Hunt *et al.,* (2016) categorised the symptoms into 4 domains; 'physical' 'emotional', cognitive' and 'fatigue'. Hunt *et al.,* (2016) reported that females within this age group reported significantly more emotional (P < 0.001) and fatigue symptoms P < 0.001) as well as overall symptoms at baseline testing (P < 0.009). These findings are in contrast to that of the current study, which demonstrated that males reported more symptoms than females overall on baseline testing. There are 2 explanations postulated for this finding, the first being that there were a total of 111 males included in this study in comparison to 43 females. The disparity in numbers may have influenced the gender-based averages. The second possible explanation is that with regard to sporting discipline, rugby and soccer participants reported the highest number of symptoms and SSS out of the 3 disciplines included in the current study, with a much higher male representation in both of these disciplines. This may have further influenced the gender comparison with a higher symptom reporting being more attributable to the sporting discipline rather than gender. Therefore, in future studies, equal numbers of male and female participants should be sought from each sporting discipline to provide a more accurate representation. Nonetheless, it is clear that the subjective PCSS elements of the SCAT-3 are influenced by gender, and this must be taken into account by healthcare professionals utilising the tool for either baseline or follow-up testing. It must also be noted that some of the symptoms on the PCSS such as fatigue, trouble falling asleep, irritability and sadness are not unique to concussion and may be present due to a number of other factors in an athletes' life such as the pressures of academic life (El Ansari and Haghgoo 2014) or hydration status (Patel *et al.*, 2007). Robinson and Mc Elhiney (2017) demonstrated that fatigue, low energy and drowsiness are common in non-concussed athletes and suggest that baseline measures should be established over a 7-day period to reduce the possibility of daily variations. Although symptom reporting is a valuable component of concussion assessment, there are clearly various factors outside the realm of concussion that may influence either baseline or follow-up measures. Thus highlighting the importance of

baseline testing, and possibly multiple baselines a year, which correspond to particularly stressful periods in the life of an athlete.

There was no significant difference observed in the current study between males and females for SAC scoring at baseline. Out of a maximum (perfect) score of 30, there was a very similar score demonstrated across gender with males scoring marginally higher (26.5 ±2.1 *vs* 26.1 ±1.7). These findings are consistent with gender scores reported by Snyder and Bauer (2014) who found that males and females scored almost identically on the SAC (25.1 ±2.78 *vs* 25.19 ±3.04) respectively, this was not found to be statistically significant. Jinguji *et al.,* (2012) also reported similar findings across gender with females scoring marginally higher (26.39 ±4.87 *vs* 25.19 ±3.10). Although there was no significance value reported for total SAC score, Jinguji *et al.,* (2012) reported that females scored significantly better than males on the immediate memory sub-component ($P = 0.00$) and the concentration (digits backwards) ($P = 0.01$). Therefore, baseline scoring across previous studies and the current study are consistent, with little difference in total SAC scores between gender.

Similary to SAC results, there were no significant differences observed across gender for mBESS scores in the current study. Male and female scores were almost identical (4.1 ±3.6 *vs* 4.3 ±3.6). Some previous research has reported mBESS scores by subtracting the number of errors from a maximum score of 30 (i.e. a lower score signifying more errors made) (Jinguji *et al*., 2012; Snyder and Bauer 2014). Jinguji *et al.,* (2012) found that females scored significantly better than males (26.85 ±2.67 *vs* 25.43 ±3.63, $P = 0.01$), Snyder and Bauer (2014) reported that females performed better than males but this was not found to be significant (25.57 ±3.45 *vs* 25.07 ±3.53). Therefore the findings from the current study suggest that males and females both make a similar amount of errors on baseline testing (between 3.15 and 4.93), with females performing marginally better than males in some cases.

In conclusion, there is clearly more variation between gender in the more subjective elements of the SCAT-3 such as the self-reported PCSS when compared to the more cognitive and performance-based elements in the form of the SAC and mBESS. It is possible that symptom reporting is goverened by a number of factors such as hormonal, cultural and social factors. Thus further advocating the need for a shift in the paradigm toward a more objective-based assessment criteria for which the potential gender variances are established. This study was potentially limited by the heterogeneity of gender numbers across the different sporting disciplines, it is recommended that this is addressed in future research.

Sport Comparison

Although there are many studies that include participants from various sporting backgrounds, as well as providing baseline/normative data for individual sports, the literature is generally lacking with regard to comparison of SCAT-3 scores across various sporting disciplines. To the best knowledge of the author this was the first study to compare baseline rugby, GAA and soccer SCAT-3 measures.

This study has demonstrated that there are no significant differences observed between sporting-codes (Rugby *vs* GAA *vs* Soccer) included in the current study for any of the SCAT-3 elements. Similarly to the gender comparison, the more subjective elements of the SCAT-3 presented with the most variation across groups. Both rugby and soccer participants reported the highest number of symptoms; 3.1 ±3.5 and 3.1 ±4.5 respectively compared to 1.8 ±2.5 in GAA. The higher number of symptoms reported naturally translates into a higher SSS also, again with rugby and soccer reporting very similar results in the current study.

SAC Scores were very similar across all 3-sporting disciplines, with rugby scoring 26.4 ±2.1, GAA scoring 26.1 ±1.9 and soccer scoring the highest at 26.8 ±2.0. Considering that there were no significant differences identified between either gender or sporting discipline the SAC is arguably the most stable SCAT-3 component with regard to baseline measures.

Scores on the mBESS were also very similar across groups, again with no significant difference observed between sports. Rugby and GAA demonstrated the highest number of errors (4.2 ±3.6 and 4.6 ±4.1 respectively) while the soccer group demonstrated a slightly lower number of errors (3.5 ±2.6). It has been shown that previous ankle injury can have negative performance effects on balance (Wikstrom *et al.,* 2010). This may be a potential confounding factor to mBESS scores and may account for the slight variation in mBESS scores observed in the current study. However, the findings of a systematic review carried out on ankle injury and sprain in sports found that ankle injury is the most common injury type in soccer at 21.2% (weighted percentage) it is also the most common in gaelic football (21.0%) and the 3rd most common in hurling (8.6%) and rugby (11.6%) (Fong *et al.*, 2007). This would suggest that soccer participants would demonstrate higher scores than rugby or hurling players, which was not the case in the current study. Fong *et al* (2007) recruited primarily from sports teams (40.5%), with school and college teams representing a smaller amount (11.0%) of the study population, equating to 51% of the total population. In comparison, the current study was 100% populated from either collegiate athletes and sports teams. Nonetheless individual lifetime incidences of ankle sprain may have influenced the results of the current study. In future research it is recommended that the effects of previous ankle sprain(s) on mBESS performance should be taken into account for analysis. The fact that there were no significant differences observed for mBESS between sports may be due to the fact that the three sports employed in the current study are quite similar in nature. It is recommended that future research take a wider variety of sports into consideration.

History of Concussion Comparison

There were no significant differences observed for any SCAT-3 components when comparing those reporting a history of concussion *versus* no history of concussion, along with small observed effect sizes across the board. There were 73 participants (47%) who reported a previous history of concussion.

The previous concussion (P.C) group reported marginally more symptoms and a higher SSS compared to the no previous concussion (N.C) group. Previously, Shehata *et al.,* (2009) reported that participants with a previous history of concussion reported a higher SSS on baseline testing compared to participants with no previous history of concussion (5.25 *vs* 3.75, SD's not reported) these are comparable to the scores observed in the current study (5.4 ±7.5 *vs* 4.6 ±8.0). Similar findings were reported by Hunt *et al.,* (2016) (6.35 ±8.15 *vs* 4.82 ± 6.33). Valovich McLeod *et al.,* (2012) reported a significant difference in number of symptoms between previous and no previous history of concussion groups with a higher score representing less symptoms (15.5 ±5.7 *vs* 17.6 ±4.8, respectively, P < 0.001). It is clear that there is increased symptom reporting in those with a previous history of concussion. Hunt *et al.,* (2016) commented that it is important to identify if this increase in symptoms is due to residual effects of a previous concussive injury or are they as a result of an increased awareness of concussion and the symptoms associated with the condition.

The SAC scores were almost identical for those with and without a previous history of concussion, displaying a difference of 0.1 ±0.3. This is in agreement with the findings of Zimmer *et al.,* (2015) who reported the exact same SAC scores for student athletes with and without a previous history of concussion (27.18 ±1.85 *vs* 27.18 ±2.06). On the contrary, Shehata *et al.,* (2009) reported that previously concussed athletes performed better than their counterparts with no previous history of concussion on all but one of the SAC elements. 38.9% participants with no previous concussion successfully recalled all 5 words *vs* 33.7% of participants with a previous concussion. A higher % of participants with previous concussion completed the months

backwards compared to their no history of concussion counterparts (93.5% *vs* 90.4%). With regard to digits backward, previously concussed participants also performed better (61% *vs* 46%) and immediate recall also demonstrated those with a previous concussion performed better (98.9 *vs* 94.9% completing the task). However no statistical significance testing was carried out by (Shehata *et al.*, 2009). These conflicting findings may be suggestive that there is a learning effect associated with athletes with a prior history of concussion who may have previously undergone cognitive testing. This possibility has been previously highlighted in the literature (Schneider *et al.* 2010; Yengo-Kahn *et al.*, 2016). The current study did not establish if participants had previously taken part in SCAT-3 assessment or other forms of cognitive testing, however it is recommended that future research take this into account.

Similarly to the PCSS and SAC findings, there was no significant difference observed between those with and without a history of previous concussion (4.2 ±3.7 *vs* 4.1 ±3.4 respectively). Valovich McLeod *et al.,* (2012) reported the same findings, with no significant difference between groups. Zimmer *et al.,* (2015) also reported that those with and without a history of concussion scored the same on the mBESS (25.7 ±3.52 *vs* 25.54 ±4.30 respectively) with a higher score representing a better performance. Therefore it is evident from the literature and the current study that there is no significant difference on mBESS with regard to history of concussion. However it is recommended that the potential influences of previous ankle injury on mBESS as highlighted above in section 5.4.2 be taken into account in future studies.

This study has established baseline and normative values for SCAT-3 measures in male and female rugby, GAA and soccer players. It is evident that differences exist in baseline values for the subjective elements of the SCAT-3 with regard to gender. A higher male symptom reporting was evident, however this is not consistent with the literature and heterogeneous participant numbers across sporting groups with regard to gender may have

skewed results of the current study. As mentioned above, it is important to take into account that athletes may be reporting symptoms such as fatigue, trouble falling asleep etc as a result of the stresses of social, or academic life and may not be soley attribuable to the effects of concussive injury, therefore highlighting the importance of baseline testing, and possibly mutiple baselines at various points in the year. The addition of a wellness monitoring tool could prove a useful component to SCAT-3 interpretation. With regard to SAC and mBESS components of the SCAT-3, there are no significant differences between gender, sporting discipline or previous history of concussion. These findings suggest that the more objective-based elements of the SCAT-3 are more consistent when establishing baselines across a varied population.

OCT

There were no significant differences observed in any sector of the RNFL when comparing gender, sporting discipline or history of concussion. It must be noted that there are many different manufacturers and types of OCT on the market, these devices use varied algorithms and their findings are not directly interchangeable (Huang *et al.*, 2011). Thus, many studies are heterogeneous with regard to device and scan-type and it is difficult to directly compare results of such studies. The current study has established baseline values using SS-OCT.

Findings of the current study demonstrated that females displayed a marginally thicker RNFL than males in all sectors, this difference ranged from 0.1 to 4.7μm. However, none of these differences were found to be significant. This is in agreement with previous research conducted with various other OCT devices. No significant difference or relationship in RNFL thickness between males and females in both older (47.4 ±15.8 years) and younger (9.54 ±3.35 years) populations using a 'Cirrus' and 'Stratus' spectral domain (SD) OCT devices was reported by Bundez *et al.*, (2007); and Queirós *et al.*, (2015). Participants of the current study had a mean age of

20.9 ±4.5 years and similarly demonstrated no significant gender differences with regard to RNFL, these findings bridge the age gap between the studies of Bundez *et al.,* (2007) and Queirós *et al.,* (2015) and in combination with previous studies, demonstrate that there are no significant differences in peripapillary RNFL thickness between males and females in a wide age range, regardless of the type of OCT used to perform the scan.

No significant differences were observed in any RNFL sector when comparing sports. To the best knowledge of the author there has been no previous research conducted with regard to comparison of OCT measures across various sporting disciplines, as such, this is the first study to do so. Therefore it can be concluded that peripapillary RNFL baseline values can be used interchangeably between rugby, GAA and soccer within this cohort. It is recommended that future research include other sporting disciplines to build the normative value database.

With regard to previous history of concussion, there were no significant differences in RNFL thickness observed in any sector for both the left and right eyes. There were marginal differences revealed between groups, these differences ranged from 0.20μm to 2.92μm, however there was no identifiable trend revealed between groups. It has been demonstrated, in an American Football University team, that participants with a previous history of concussion had a significantly thicker RNFL than those without a previous history of concussion (106.8μm *vs* 103.7 μm, P = 0.009) this equates to a difference of 3.1μm (Bixenmann *et al.* 2014), to the best knowledge of the author this is the only previous study to investigate retinal thickness and concussion history. These differences are comparable to the marginal differences observed between groups in the current study, which, in comparison were not found to be statistically significant. It is also important to note that the study by Bixenmann *et al.,* (2014) did not state at what area of the retina the RNFL was measured (i.e. macular or peripapillary), the current study examined peripapillary RNFL thickness. Interestingly, other

neurological dysfunctions such as M.S., Alzheimer's disease and Parkinson's disease have been associated with RNFL thinning rather than thickening (London *et al.*, 2013). Peripapillary RNFL thickenss has been shown to be significantly thinner in M.S. patients when compared to normal, validated and published values (88.5μm *vs* 97.0μm, P < 0.001), a difference of 8.52μm. Therefore the findings of Bixenmann *et al.*, (2014) must be interpreted tentatively and further research is recommended. It must be considered that peripapillary RNFL thickening rather than thinning may be a potential differential structural finding between concussive injury and neurological disease and certainly warrants further investigation. It must be noted that both the current study and that of Bixenmann *et al* (2014) used an athlete self-reported history of concussion. Ideally, in future research, the history and severity of concussion should be confirmed by doctors' records, however this may still pose a challenge due to the fact that concussion can be often under-reported by athletes, as outlined in the review of literature. RNFL thickness has previously been shown to be negatively correlated with age, with a decrease of 2μm for every decade of life (Bundez *et al.,* 2007). Furthermore, eye side and eye dominance has been shown to have a significant effect on RNFL thickness, demonstrating an asymmetry between eyes (Queirós *et al.*, 2015). Therefore, it is recommended that age and eye dominance should be taken into account in future research.

There was a significant difference in macular GCL++ thickness observed between males and females in the superior temporal sector for both the left (P = 0.012) and right (P = 0.007) eyes. There were no significant differences observed in other sectors when comparing gender, sporting discipline or history of previous concussion.

The significant differences in the superior temporal sector in both left and right eyes equated to a difference of 3.0 ±0.8μm and 3.0 ±0.9μm respectively, with males displaying a thicker GCL++ than females. The overall observable trend was that males have a thicker GCL++ than females, this was the case in all sectors with the exception of the inferior sector, where females were marginally thicker than males. The male to female differences ranged from 0.2μm to 3.0μm, with the latter being the statistically

significant superior temporal sector. Previously it has been demonstrated that there is no significant difference in mean (total) GCL++ thickness between males and females using OCT (SS-OCT) which was the apparatus employed in the current study (Wang *et al.*, 2015), this is in agreement with the findings of the current study. In a study by Wang *et al.,* (2015) gender differences between the various sectors of the ETDRS grid were not reported. Nieves-Moreno *et al.,* (2017), reported on gender differences on individual macular layers of the retina broken into the various sectors of the ETDRS grid. It was demonstrated that males had a significantly thicker macular RNFL (every sector except outer temporal), GCL (every sector except central) and IPL (central, inner nasal, outer temporal and inner temporal) than females ($P < 0.05$). Males have also been shown to have significantly thicker overall macular and central macular thickness than females in paediatric studies (Barrio-Barrio *et al.*, 2013; Queirós *et al.*, 2015). Therefore males have a thicker macula GCL++ than females, however this thickness is not always found to be statistically significant and may be dependent on individual sectors, nonetheless, this is a factor which must be taken into account when interpreting baseline/normative values.

There were no significant differences observed in the current study with regard to GCL++ thickness comparison between sports. Similarly to the RNFL findings described above, this is the first study to establish baseline/normative GCL++ data on various field sports and to compare them. There was no identifiable trend in thickness between sports, with minimal differences of approximately 1μm - 2.5μm, these findings suggest that macular GCL++ baselines can be used interchangeably between rugby, GAA and soccer within the age group employed in the current study (Mean: 20.9 ±4.5, Range: 15-39 years).

Examination of previous history of concussion revealed no significant differences in GCL++ between groups in either the left or right eyes. Previously concussed athletes displayed a marginally thicker GCL++ layer than those without a previous history of concussion in all sectors for both

eyes except the superior nasal sector in the right eye. These differences ranged from 0.1µm to 1.7µm. This thickening trend in those with a remote history of concussion has previously been reported (Bixenmann *et al.*, 2014), however similar to the current study, this was not found to be statistically significant. Regardless of the lack of a significant difference identified in these studies, the thickening trend is common to both studies and warrant further investigation.

In conclusion, peripapillary RNFL and macular GCL++ thickness measures of the retina are relatively interchangeable across gender, sporting discipline and history of concussion within the cohort included in the current study. There are some identifiable trends that warrant further investigation. It is recommended that future research allow for the effects of age and eye dominance, furthermore, more definitive concussion patient records, potentially through access to doctors' reports would allow for a more definitive comparison.

Concussion Case Studies

There were 3 suspected concussions reported during the course of the study, 2 of which included a baseline and 14-day follow up, but unfortunately no 48hr or 2-month follow up. Therefore only allowing comparison of the sub-acute response of the SCAT-3 and OCT. The 3rd case study was absent for baseline testing, however 48hr and 14-day measures were gathered, allowing for an observation of the responses of SCAT-3 and OCT measures acutely post injury and the possible resolution/progression of the injury at the 14-day follow up.

SCAT-3

Out of the four SCAT-3 measures included in the current study, subjective symptom reporting (number of symptoms and SSS) displayed an initial increase following injury (cases 1 and 2), demonstrating a strong symptomatic response to the injury. Furthermore, the symptomatic response resolved between the 48hr and 14-day follow-up (case 3). There were unexpected results with regard to the effects of concussion on the SAC component between baseline and 14-day follow up for both case 1 and 2, who both improved in cognitive performance following injury. Whereas, case 3 improved in cognitive performance between the 48hr and 14-day follow up. With regard to mBESS there were mixed findings, case 1 decreased in performance considerably whereas the performance of case 2 did not change at all from baseline to 14-day follow up. Case 3 however improved in performance between 48hrs post injury and 14-days post injury.

PCSS - Subjective symptom reporting elements of the SCAT-3 are clearly affected from baseline to post injury. The number of symptoms reported increased by 19% and 20% in case 1 and 2 respectively pre-post injury. Furthermore the SSS also increased by 47% and 50% for case 1 and 2 respectively. Case 3 demonstrated a resolution of symptoms from 48hr to 14-days post injury. These findings are consistent with that of (Chin *et al.*, 2016) who demonstrated a significant increase in SSS in concussed athletes when compared to non-concussed controls 24hrs post injury ($P < 0.001$) and 8-days post injury ($P < 0.05$), SSS remained elevated but returned close to control levels at 15-days post injury but this was not found to be significant. McCrea *et al.,* (2003) utilised a slightly different 17-item symptom scale but scored symptoms with the same Likert scale that was used in the current study, findings of the study reported concussed athletes demonstrated a higher SSS (difference of 6.68) than controls at 48hrs post injury. This difference resolved to 0.33 at 7 days post injury, statistical significance was not reported.

Therefore, it is clear that both the number of symptoms and SSS increase from baseline levels following injury and begin to return toward baseline levels in the days following injury. The limited follow up data obtained in the current study suggests that these scores remain elevated at 14-days post injury, however previous research has demonstrated that this remaining elevation is not statistically significant at 15-days. It must be noted that a high level of individuality may exist with regard to symptom reporting, which was observed in the 3 case studies in the current study. In light of this, it is recommended that individual baselines be established in order to increase the accuracy of follow-up measures.

SAC - The SAC findings were somewhat mixed, both case 1 and 2 improved from baseline to 14-days post-injury by 7% and 3.8% respectively, this was not expected, considering the athletes were still reporting increased symptoms. The time between baseline testing and follow-up for both case 1 and 2 was approximately 1-month, it is postulated that the improvements in SAC scores observed in case 1 and 2 may be attributable to a learning or exposure effect, which has been previously mentioned in the literature (Schneider *et al.*, 2010; Yengo-Kahn *et al.*, 2016). In contrast to the findings of the current study, Chin *et al.,* (2016) reported a significant difference in SAC between concussed athletes and controls at 24hrs post-injury, but not at 15-days post injury. Nonetheless, the potential learning effects of the SAC must be taken into account in future studies.

mBESS - Findings were mixed with regard to mBESS, there was a large increase in errors made between baseline and 14-days post injury for case 1 (167%) but no change at all for case 2 (0%). Case 3, once again displayed a decrease in errors made between 48hr and 14-days post injury (-14.3%) indicating an improvement of postural control and complimenting the resolution of symptoms and improvement in cognitive function also observed. Chin *et al.,* (2016) reported on mBESS scores for both a firm and foam surface, using 6 trials in total and therefore a maximum number of 60 errors

in comparison to possible 30 mBESS errors in the current study. It was demonstrated that concussed athletes made significantly more errors than healthy controls 24hrs post injury (P < 0.005) and 8 days following injury (P< 0.05), however performance had returned to normal at the 15-day follow up (P > 0.05). Similarly, McCrea *et al.,* (2003) reported a higher number of errors at a 48hr follow up in concussed athletes compared to healthy controls, however concussed athletes actually performed marginally better than controls at a 7-day follow up. Postural control as assessed by the mBESS can be affected by concussive injury, however this may not manifest in all individuals given the myriad and complexity of symptoms associated with concussion.

OCT

To the best knowledge of the author, this is the first study of its kind to examine the acute and sub-acute responses of the RNFL and GCL++ to concussive injury. There were minimal changes (both thickening and thinning) observed in both peripapillary RNFL and Macular GCL++ thickness.

With regard to the RNFL, the highest degree of thinning was observed in the left nasal sector in case 3 between the 48hr and 14-day follow up (-5.5%, 6μm). The highest degree of thickening was observed in the right temporal sector of the case 1 between baseline and 14-day follow-up (+6.1%, 3μm). Total (mean) RNFL thickness changes in the left eye were -1.3%, 0.9% and -2.3% in cases 1-3 respectively and 1.3%, 0.0% and 0.8% in the right eye.

With regard to the GCL++, changes were even more subtle, the highest degree of thinning was observed in the left inferio-temporal sector of case 3 (-1.7%, 2μm), the highest degree of thickening was observed in the right inferio-nasal sector of case 1 (1.7%, 2μm). There was (0.0%) total (mean) thickness changes in all 3 cases for the left eye, whereas the right eye had a 0.8% increase in thickness for case 1 but 0% for both case 2 and 3.

A main limiation of the current study was that secondary to the small amount of follow up data collected in the current study hypothesis testing could not be carried out. Findings reveal that there is minimal change in the RNFL following concussive injury, and no change in the GCL++. Nonetheless, in

light of the findings Bixenmann *et al* (2014), who displayed a significant thickening of the RNFL in those with a remote history of concussion and also demonstrated a thickening trend of the GCL++, further research is warranted. The case study element of this study aimed to examine the acute and sub-acute changes in the retina following injury, however it may be possible that such changes occur over an extended period of time. It is recommended that future longitudinal follow-up research is conducted to examine the possibility that these measures may change over time, taking into account the number of previous concussive insults and potentially the severity of these injuries. Due to the small number of follow-up measures. It is recommended that future research be carried out in conjunction with a hospital, medical centre and/or neurologcial consultant to capture more follow-up data, this would allow for a more controlled follow-up process, the current study recruited participants both locally on site at ITC and remotely, the equipment was somewhat difficult to transport to various locations, this issue was further exacerbated by the logistics of requesting injured participants to report to ITC for follow up testing. Therefore, it is recommended that the equipment would ideally be located in a medical centre or hospital where concussed athletes would report to. In order to further increase follow-up measures, it is recommended that concussed participants are compared to age and gender matched controls, thereby eliminating the dependency of concussive injury occurring from the baseline pool of participants. An ideal sample size was calculated post-hoc using G*power software (Faul *et al.* 2009) with an estimated effect size of F = 0.25, and significance level set to 0.05, it was calculated that for comparison of variables across three groups (i.e. 3 sports) an ideal sample size of 252 particpants would provide a power of 0.95. For comparison of variables across 2 groups (i.e. gender, or history of concussion, an ideal sample size of 210 would provide a power of 0.95. Furthermore, it is recommended that equal representations of participant numbers with regard to sporting discipline and gender is sought after to ensure a more equal analysis.

CHAPTER SIX:
Conclusion

Conclusion:

In conclusion, this research has demonstrated that the iCare Pro Rebound tonometer is a reliable tool when measuring an athletes IOP in a standing position. Limitations have been acknowledged, in particular reliability was only established in a single session, however this served the purpose for the inclusion of the device into study 2 (The Effects of Exercise on Ocular Metrics). The inter-day reliability of the device was not established and therefore the device was ommited from study 3 (The Effects of Concussion on Ocular Metrics). Future research should examine the inter-day reliability of the device prior to its inclusion in a longitudinal study.

The effects of a simulated team sport running protocol on IOP and OCT have been established, demonstrating a dynamic response and a potential causal or associative relationship between IOP and choroidal thickness. Both of which, decreased immediately following exercise in both left and right eyes and returned toward baseline values 10-minutes post exercise in the left eye, with the right choroid still presenting with a decreased thickness at the 10-minute follow up. It has been well establised that aerobic exercise leads to a decrease in IOP, however there are conflicting findings on choroidal responses to exercise in the literature and further research is needed to consolidate these findings with more standardised exercise protocols. There was a minimal thinning response observed in the RNFL, for which there is conflicting evidence in the current literaure. Conversely a minimal thickening response observed in the GCL++. It is recommended that future research explore the potential mechanisms by which these metrics change during and following exercise such as; changes in blood PH, autoregulation mechanisms along with changes in osmotic gradient as a result of intravascular hyponatremia, to name a few. This was the first study to establish the effects of a simulated team sport running protocol on these measures, however these findings as somewhat limited by the relatively small sample size that was utlised in this study (N=11). It is recommended that future research increase the sample size. Although the current study utilised an established protocol, which has previously been proven reliable for various physiological and performance-based measures, it is

recommended that the effects of more sports-specific activities on IOP and OCT measures are established. Such activities may include heading of the ball in soccer or tackling and scrum technique in rugby, considering the established postural effects on IOP.

On baseline testing, it is clear that gender differences exist in SCAT-3 symptom reporting, with this study demonstrating that males report a higher number of symtoms with a higher severity. However, this is conflicting to the majority of previous research. These findings may be be confounded by the unequal distribution of gender within each of the sporting disciplines included. It is recommended that future research ensures that there is equal gender representation in each sporting discipline. Within the cohort included in the study 3, it was observed that male GCL++ was marginally thicker overall, with the only significant difference being observed in the superior temporal sector in both eyes. There were no significant differences observed with regard to sport or history of concussion in the GCL++. Furthermore there were no significant differences observed in RNFL thickness with regard to gender, sport or history of concussion. These findings suggest that baseline OCT data is interchangeable within the sub-groups of this cohort.

The paucity of participant follow up data in study 3, which allowed for just 2 re-evaluation follow-up measures in 3 participants was the main limitation to this study. Evidently, further follow up measures are needed to investigate for any possible aquired structual retinal changes as a result of concussive injury. From the limited follow up data, it was evident that there is a subjective symptomatic resposnse to concussion in the SCAT-3, with symptoms increasing following injury, which resolve in the days following injury, it must be noted that there is high individual variability in the SCAT-3, therefore warranting the need for baseline measures, which are established over a longer time-frame to reduce the effects of potential confounders outside the realm of concussion such as; fatigue, academic and or social stress. With regard to OCT measures, there were minimal changes in thickness in RNFL and GCL++ thickness following concussive injury, with no observable trends in the limited data obtained, as such, this study cannot confirm or refute the effects of concussive injury on the retina. It is

recommended that future research be carried out in conjunction with a hospital and/or neurological consultant to enhance data collection from which practical and clinical inferences can be drawn.

REFERENCES

ABI Ireland. (2014). Implications of Concussion in Sport Joint Committee on Health and Children October 2014. , 2014.

Alla, S., Sullivan, S.J., Hale, L. and McCrory, P. (2009). Self-report scales/checklists for the measurement of concussion symptoms: A systematic review. *British Journal of Sports Medicine*, 43(SUPPL. 1), pp.3–13.

Alwassia, A., Adhi, M., Zhang, J., Regatieri, C., Al-Quthami, A., Salem, D., Fujimoto, J. and Duker, J. (2013). Exercise-induced acute changes in systolic blood pressure do not alter choroidal thickness as measured by a portable spectral-domain optical coherence tomography. *Retina (Philadelphia, Pa.)*, 33(1), pp.160–5.

El Ansari, W. and Haghgoo, G. (2014). Are students' symptoms and health complaints associated with perceived stress at university? Perspectives from the United Kingdom and Egypt. *International Journal of Environmental Research and Public Health*, 11(10), pp.9981–10002.

Anzalone, A.J., Blueitt, D., Case, T., McGuffin, T., Pollard, K., Garrison, J.C., Jones, M.T., Pavur, R., Turner, S. and Oliver, J.M. (2017). A Positive Vestibular/Ocular Motor Screening (VOMS) Is Associated with Increased Recovery Time after Sports-Related Concussion in Youth and Adolescent Athletes. *American Journal of Sports Medicine*, 45(2), pp.474–479.

Appleby, B. and Dawson, B. (2002). Video Analysis of selected game activities in Austrailian Rules Football. *Journal of Science and Medicine in Sport*, 5 (2), pp.129–142.

Archbold, H.A.P., Rankin, A.T., Webb, M., Nicholas, R., Eames, N.W.A., Wilson, R.K., Henderson, L.A., Heyes, G.J. and Bleakley, C.M. (2017). RISUS study: Rugby Injury Surveillance in Ulster Schools. *British Journal of Sports Medicine*, 51(7), pp.600–606.

Aubry, M., Cantu, R., Dvorak, J., Johnston, K., Kelly, J., Lovell, M. and Mccrory, P. (2002). Summary and agreement statement of the first International Conference on Concussion in Sport. *British journal of sports medicine*, 36(1), pp.6–10.

Baechle, T. and Earle, R. (2008). *Essentials of Strength Training and Conditioning*. Third Edit. Leeds, United Kingdom: Human Kinetics.

Balk, L., Mayer, M., Uitdehaag, B.M.J. and Petzold, A. (2013). Physiological variation of segmented OCT retinal layer thicknesses is short-lasting. *Journal of Neurology*, 260(12), pp.3109–3114.

Bangsbo, J., Norregaard, L. and Thorse, F. (1991). Activity Profile of Competition Soccer. *canadian journal of sports sciences*, 16(2), pp.110–116.

Barkhoudarian, G., Hovda, D.A. and Giza, C.C. (2011). The Molecular Pathophysiology of Concussive Brain Injury. *Clinics in Sports Medicine*, 30(1), pp.33–48. Available from: http://dx.doi.org/10.1016/j.csm.2010.09.001.

Barrio-Barrio, J., Noval, S., Galdõs, M., Ruiz-Canela, M., Bonet, E., Capote, M. and Lopez, M. (2013). Multicenter Spanish study of spectral-domain optical coherence tomography in normal children. *Acta Ophthalmologica*, 91(1), pp.56–63.

Batterham, A. and George, K. (2003). Reliability in evidence-based clinical practice: a primer for allied health professionals. *Physical Therapy in Sport*, 4(August 2003), pp.122–128. Available from: http://www.sciencedirect.com/science/article/pii/S1466853X00900105.

Bixenmann, B., Bigsby, K., Hasselfeld, K.A., Khoury, J., Mangine, R.E., Pyne-geithman, G.J. and Clark, J.F. (2014). Retinal and Balance Changes Based on Concussion History : A Study of Division 1 Football Players. *International Journal of Physical Medicine and Rehabilitation*, 2(5).

Blake, C., O'Malley, E., Gissane, C. and Murphy, J.C. (2014). Epidemiology of injuries in hurling: A prospective study 2007-2011. *BMJ Open*, 4(6).

Bowen, A.P. (2003). Second impact syndrome: A rare, catastophic, preventable complication fo concussion in young athletes. *Journal of Emergency Nursing*, 29(3), pp.287–289.

Broglio, S.P., Ferrara, M.S., Macciocchi, S.N., Baumgartner, T.A. and Elliott, R. (2007). Test-retest reliability of computerized concussion assessment programs. *Journal of Athletic Training*, 42(4), pp.509–514.

Brooks, M.A., Peterson, K., Biese, K., Sanfilippo, J., Heiderscheit, B.C. and Bell, D.R. (2016). Concussion Increases Odds of Sustaining a Lower Extremity Musculoskeletal Injury after Return to Play among Collegiate Athletes. *American Journal of Sports Medicine*, 44(3), pp.742–747.

Bruton, A., Conway, J.H. and Holgate, S.T. (2000). Reliability: What is it, and how is it measured?. *Physiotherapy*, 86(2), pp.94–99. Available from: http://www.sciencedirect.com/science/article/pii/S0031940605612114%5Cnh ttp://ac.els-cdn.com/S0031940605612114/1-s2.0-S0031940605612114-main.pdf?_tid=8cd612fa-0719-11e6-a9c7-00000aacb35d&acdnat=1461171881_0ce02e6b3d401aca1e950add8e585b7 f%5Cnhttp://dx.doi.o.

Buckley, C.S. and Blake, C. (2018). The incidence of injury in elite camogie , an in-season prospective study. , 2018, pp.10–15.

Bundez, D.L., Anderson, D.R., Varma, R., Schuman, J., Cantor, L., Savell, J., Greenfield, D.S., Patella, V.M., Quigley, H.A. and Tielsch, J. (2007). Determinants of Normal Retinal Nerve Fiber Layer Thickness Measured by Stratus OCT. *Ophthalmology*, 114(6), pp.1046–1052.

Bussel, I.I., Wollstein, G. and Schuman, J.S. (2014). OCT for glaucoma diagnosis, screeningand detection of glaucoma progression. *British Journal of Ophthalmology*, 98(SUPPL. 2), pp.15–20.

Chen, J.K., Johnston, K.M., Collie, A., McCrory, P. and Ptito, A. (2007). A validation of the post concussion symptom scale in the assessment of complex concussion using cognitive testing and functional MRI. *Journal of Neurology, Neurosurgery and Psychiatry*, 78(11), pp.1231–1238.

Chin, E.Y., Nelson, L.D., Barr, W.B., McCrory, P. and McCrea, M.A. (2016). Reliability and validity of the sport concussion assessment tool-3 (SCAT3) in high school and collegiate athletes. *American Journal of Sports Medicine*, 44(9), pp.2276–2285.

Choe, M.C. (2016). The Pathophysiology of Concussion. *Current Pain and Headache Reports*, 20(6).

Cohen, J. (1988). *Statistical Power Analysis for the Behavioural Sciences*. 2nd Editio. New York: Lawrence Erlbaum Associates.

Collins, M.W., Iverson, G.L., Lovell, M.R., McKeag, D.B., Norwig, J. and Maroon, J. (2003). On-field predictors of neuropsychological and symptom deficit following sports-related concussion. *Clinical Journal of Sport Medicine*, 13(4), pp.222–229.

Collins, M.W., Kontos, A.P., Reynolds, E., Murawski, C.D. and Fu, F.H. (2014). A comprehensive, targeted approach to the clinical care of athletes following sport-related concussion. *Knee Surgery, Sports Traumatology, Arthroscopy*, 22(2), pp.235–246.

Covassin, T. and Elbin, R.J. (2010). The cognitive effects and decrements following concussion. *Open access journal of sports medicine*, 1, pp.55–61. Available from:
http://www.ncbi.nlm.nih.gov/pubmed/24198543%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3781855.

Croke Park. (2017). Gaelic Athletic Association OFFICIAL GUIDE -PART 2. , 2017, pp.42–59. Available from:
http://www.gaa.ie/mm/Document/TheGAA/RulesandRegulations/13/79/82/GAAOfficialGuide2017_Part2_Neutral.pdf.

Curcio, C.A. and Allen, K.A. (1990). Topography of ganglion cells in human retina. *Journal of Comparative Neurology*, 300(1), pp.5–25.

Currier, D. (1990). *Elements of Research in Physical Therapy*. 3rd editio. Baltimore, MD: Williams and Wilkins.

Dahlmann-Noor, A.H., Puertas, R., Tabasa-Lim, S., El-Karmouty, A., Kadhim, M., Wride, N.K., Lewis, A., Grosvenor, D., Rai, P., Papadopoulos, M., Brookes, J., Bunce, C. and Khaw, P.T. (2013). Comparison of handheld rebound tonometry with Goldmann applanation tonometry in children with glaucoma: A cohort study. *BMJ Open*, 3(4), pp.1–6.

Donoghue, D., Murphy, A., Jennings, A., McAuliffe, A., O'Neil, S., Charthaigh, E.N., Griffin, E., Gilhooly, L., Lyons, M., Galvin, R., Gallagher,

S., Ward, S., Mhaille, E.N. and Stokes, E.K. (2009). How much change is true change? The minimum detectable change of the Berg Balance Scale in elderly people. *Journal of Rehabilitation Medicine*, 41(5), pp.343–346.

Duker, J.S., Waheed, N.K. and Goldman, D.R. (2014). *Handbook of Retinal OCT*. 1st editio. Elsevier.

Duthie, G., Pyne, D. and Hooper, S. (2003). Applied Physiology and Game Analysis of Rugby Union. *Sports Medicine*, 33(13), pp.973–971.

Ellis, P.. (2009). *Effect Size Calculations* [online]. Available from: http://www.polyu.edu.hk/mm/effectsizefaqs/effect_size_equations2.html [accessed 27 August 2018].

England Professional Rugby Injury Surveillance Project Steering Group. (2015). England Professional Rugby Injury Surveillance Project. , 2015, pp.1–36.

Faul, F., E., E. and Lang, A.. (2009). G*Power 3: A Flexible Statistical Power Analysis Program for the Social, Behavioural and Biomedical Sciences. *Behaviour Research Methods*, 2009, pp.175–191.

Field, A. (2009). *Discovering Statistics Using SPSS.*

Fong, D.T.-P., Hong, Y., Chan, L.-K., Yung, P.S.-H. and Chan, K.-M. (2007). A Systematic Review on Ankle Injury and Ankle Sprain in Sports. *Sports Medicine*, 37(1), pp.73–94. Available from: http://link.springer.com/10.2165/00007256-200737010-00006.

Fortington, L. V., Twomey, D.M. and Finch, C.F. (2015). Concussion in community Australian football – epidemiological monitoring of the causes and immediate impact on play. *Injury Epidemiology*, 2(1), p.20. Available from: http://www.injepijournal.com/content/2/1/20.

Fraas, M.R., Coughlan, G.F., Hart, E.C. and McCarthy, C. (2014). Concussion history and reporting rates in elite Irish rugby union players. *Physical Therapy in Sport*, 15(3), pp.136–142. Available from: http://dx.doi.org/10.1016/j.ptsp.2013.08.002.

Fuller, C.W., Fuller, G.W., Kemp, S.P.T. and Raftery, M. (2017). Evaluation

of World Rugby's concussion management process: Results from Rugby World Cup 2015. *British Journal of Sports Medicine*, 51(1), pp.64–69.

Fuller, C.W., Taylor, A. and Raftery, M. (2015). Epidemiology of concussion in men's elite Rugby-7s (Sevens World Series) and Rugby-15s (Rugby World Cup, Junior World Championship and Rugby Trophy, Pacific Nations Cup and English Premiership). *British Journal of Sports Medicine*, 49(7), pp.478–483.

Gale, J., Chb, M.B., Wells, A.P. and Wilson, G. (2009). MAJOR REVIEW Effects of Exercise on Ocular Physiology and Disease. *Survey of Ophthalmology*, 54(3), pp.349–355. Available from: http://dx.doi.org/10.1016/j.survophthal.2009.02.005.

Galetta, K.M., Barrett, J., Allen, M., Madda, F., Delicata, D., Tennant, A.T., Branas, C.C., Maguire, M.G., Messner, L. V., Devick, S., Galetta, S.L. and Balcer, L.J. (2011). The King-Devick test as a determinant of head trauma and concussion in boxers and MMA fighters. *Neurology*, 76(17), pp.1456–1462.

Galetta, K.M., Calabresi, P.A., Frohman, E.M. and Balcer, L.J. (2011). Optical Coherence Tomography (OCT): Imaging the Visual Pathway as a Model for Neurodegeneration. *Neurotherapeutics*, 8(1), pp.117–132.

Gardner, A.J., Iverson, G.L., Williams, W.H., Baker, S. and Stanwell, P. (2014). A systematic review and meta-analysis of concussion in Rugby Union. *Sports Medicine*, 44(12), pp.1717–1731.

Gavett, B.E., Stern, R.A., Cantu, R.C., Nowinski, C.J. and McKee, A.C. (2010). Mild traumatic brain injury: a risk factor for neurodegeneration. *Alzheimer's Research & Therapy*, 2(3), p.18. Available from: http://alzres.biomedcentral.com/articles/10.1186/alzrt42.

Giza, C.C. and Hovda, D.A. (2015). The new neurometabloic cascade of concussion. *Neurosurgery*, 75(0 4), pp.S24–S33.

Gómez, J.E. and Hergenroeder, A.C. (2013). New guidelines for management of concussion in sport: Special concern for youth. *Journal of*

Adolescent Health, 53(3), pp.311–313. Available from: http://dx.doi.org/10.1016/j.jadohealth.2013.06.018.

Gupta, V., Gupta, A. and Dogra, M.R. (2005). *ATLAS Optical Coherence Tomography of Macular Diseases*. e-book edi. London and New York: Taylor and Francis.

Guskiewicz, K. (2003). Assessment of postural stability following sport-related concussion. *Current Sports Medicine Reports*, 2, pp.24–30.

Guskiewicz, K., Teel, E. and McCrea, M. (2014). Concussion: Key stakeholders and multidisciplinary participation in making sports safe. *Neurosurgery*, 75(4), pp.S113–S118.

Haley, S.M. and Fragala-Pinkham, M.A. (2006). Interpreting change scores of tests and measures used in physical therapy. *Physical therapy*, 86(5), pp.735–743.

Hammel, N., Belghith, A., Weinreb, R.N., Medeiros, F.A., Mendoza, N. and Zangwill, L.M. (2017). Comparing the Rates of Retinal Nerve Fiber Layer and Ganglion Cell–Inner Plexiform Layer Loss in Healthy Eyes and in Glaucoma Eyes. *American Journal of Ophthalmology*, 178, pp.38–50. Available from: http://dx.doi.org/10.1016/j.ajo.2017.03.008.

Hänninen, T., Tuominen, M., Parkkari, J., Vartiainen, M., Öhman, J., Iverson, G.L. and Luoto, T.M. (2016). Sport concussion assessment tool - 3rd edition - normative reference values for professional ice hockey players. *Journal of Science and Medicine in Sport*, 19(8), pp.636–641. Available from: http://dx.doi.org/10.1016/j.jsams.2015.08.005.

Hong, E.H., Shin, Y.U., Kang, M.H., Cho, H. and Seong, M. (2018). Wide scan imaging with swept-source optical coherent tomography for glaucoma diagnosis. *PLoS ONE*, 13(4), pp.1–15.

Hood, D.C. (2016). Improving our understanding, and detection, of glaucomatous damage: An approach based upon optical coherence tomography (OCT). *Progress in Retinal and Eye Research*, 2016, pp.1–30. Available from:

http://linkinghub.elsevier.com/retrieve/pii/S1350946216300702.

Huang, J., Liu, X., Wu, Z., Guo, X., Xu, H., Dustin, L. and Sadda, S. (2011). Macular and retinal nerve fiber layer thickness measurements in normal eyes with the stratus OCT, the cirrus HD-OCT, and the topcon 3D OCT-1000. *Journal of Glaucoma*, 20(2), pp.118–125.

Huang, R. (2015). The Effect of Dynamic and Isometric Exercise on Refractive State, Accommodation and Intra-Ocular Pressure. *Advances in Ophthalmology & Visual System*, 2(3), pp.1–5. Available from: http://medcraveonline.com/AOVS/AOVS-02-00047.php.

Hunt, A.W., Paniccia, M., Reed, N. and Keightley, M. (2016). Concussion-Like Symptoms in Child and Youth Athletes at Baseline: What Is 'Typical'? *Journal of Athletic Training*, 51(10), pp.749–757. Available from: http://natajournals.org/doi/10.4085/1062-6050-51.11.12.

Hwang, T.S., Jia, Y., Gao, S.S., Bailey, S.T., Lauer, A.K., Flaxel, C.J., Wilson, D.J. and Huang, D. (2015). Optical Coherence Tomography Angiography Features of Diabetic Retinopathy. , 35(November 2014), pp.2371–2376.

iCare. (2017). *iCare Pro Tonometer: Users and Maintenance Manual*. Espoo, Finaland: Icare Finland Oy.

Iester, M., Torre, P.G., Bricola, G., Bagnis, A. and Calabria, G. (2007). Retinal blood flow autoregulation after dynamic exercise in healthy young subjects. *Ophthalmologica*, 221(3), pp.180–185.

IRFU. (2009). A Guide to Concussion in Rugby Union. , 2009, pp.1–51. Available from: http://www.irishrugby.ie/downloads/IRFU-Guide-to-Concussion(1).pdf.

Javaid, F.Z., Brenton, J., Guo, L. and Cordeiro, M.F. (2016). Visual and ocular manifestations of Alzheimer's disease and their use as biomarkers for diagnosis and progression. *Frontiers in Neurology*, 7(APR).

Jeter, C.B., Hergenroeder, G.W., Hylin, M.J., Redell, J.B., Moore, A.N. and Dash, P.K. (2013). Biomarkers for the Diagnosis and Prognosis of Mild

Traumatic Brain Injury/Concussion. *Journal of Neurotrauma*, 30(8), pp.657–670. Available from: http://online.liebertpub.com/doi/abs/10.1089/neu.2012.2439.

Jia, Y. et al. (2015). Quantitative optical coherence tomography angiography of choroidal neovascularization in age-related macular degeneration. *Ophthalmology*, 121(7), pp.1435–1444. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24679442.

Jinguji, T.M., Bompadre, V., Harmon, K.G., Satchell, E.K., Gilbert, K., Wild, J. and Eary, J.F. (2012). Sport concussion assessment tool - 2: Baseline values for high school athletes. *British Journal of Sports Medicine*, 46(5), pp.365–370.

Jorge, J., Ramoa-Marques, R., Lourenço, A., Silva, S., Nascimento, S., Queirós, A. and Gonzalez-Méijome, J.M. (2010). IOP variations in the sitting and supine positions. *Journal of Glaucoma*, 19(9), pp.609–612.

Kim, K.N., Jeoung, J.W., Park, K.H., Yang, M.K. and Kim, D.M. (2013). Comparison of the new rebound tonometer with Goldmann applanation tonometer in a clinical setting. *Acta Ophthalmologica*, 91(5), pp.392–396.

King, D., Gissane, C., Hume, P.A. and Flaws, M. (2015). The King-Devick test was useful in management of concussion in amateur rugby union and rugby league in New Zealand. *Journal of the Neurological Sciences*, 351(1–2), pp.58–64. Available from: http://dx.doi.org/10.1016/j.jns.2015.02.035.

Koh, J.O., Cassidy, J.D. and Watkinson, E.J. (2003). Incidence of concussion in contact sports: A systematic review of the evidence. *Brain Injury*, 17(10), pp.901–917.

Konitola, A. (1997). A New Electromechanical Method for Measureing Intraocular Pressure. *Documenta Ophthalmologica*, 93, pp.265–276.

Koo, T.K., Guo, J.Y. and Brown, C.M. (2013). Test-retest reliability, repeatability, and sensitivity of an automated deformation-controlled indentation on pressure pain threshold measurement. *Journal of Manipulative and Physiological Therapeutics*, 36(2), pp.84–90. Available

from: http://dx.doi.org/10.1016/j.jmpt.2013.01.001.

Kroshus, E., Garnett, B., Hawrilenko, M., Baugh, C.M., Jerel, P., Services, S. and Medicine, Y.A. (2016). HHS Public Access. , 2016, pp.66–75.

Lam, A., Wu, Y.F., Wong, L.Y. and Ho, N.L. (2013). IOP variations from sitting to supine postures determined by rebound tonometer. *Journal of Optometry*, 6(2), pp.95–100.

Lavinsky, F. and Lavinsky, D. (2016). Novel perspectives on swept-source optical coherence tomography. *International Journal of Retina and Vitreous*, 2(1), p.25. Available from: http://journalretinavitreous.biomedcentral.com/articles/10.1186/s40942-016-0050-y.

Leong, D.F., Balcer, L.J., Galetta, S.L., Evans, G., Gimre, M. and Watt, D. (2015). The King-Devick test for sideline concussion screening in collegiate football. *Journal of Optometry*, 8(2), pp.131–139. Available from: http://dx.doi.org/10.1016/j.optom.2014.12.005.

Lincoln, A.E., Caswell, S. V., Almquist, J.L., Dunn, R.E., Norris, J.B. and Hinton, R.Y. (2011). Trends in concussion incidence in high school sports: A prospective 11-year study. *American Journal of Sports Medicine*, 39(5), pp.958–963.

London, A., Benhar, I. and Schwartz, M. (2013a). The retina as a window to the brain - From eye research to CNS disorders. *Nature Reviews Neurology*, 9(1), pp.44–53.

London, A., Benhar, I. and Schwartz, M. (2013b). The retina as a window to the brain - From eye research to CNS disorders. *Nature Reviews Neurology*, 9(1), pp.44–53. Available from: http://dx.doi.org/10.1038/nrneurol.2012.227.

Maddocks, D., Dicker, G. and Saling, M. (1995). The Assessment of Orientation Following Concusion in Athletes. *Clinical Journal of Sport Medicine*, 5(1), pp.32–35.

Maerlender, A., Flashman, L., Kessler, A., Kumbhani, R., Tosteson, T. and McAllister, T. (2010). Examination of the construct validity of ImPACT

computerized test, traditional, and experimental neuropsychology measures. , 24(8), pp.1309–1325.

Makdissi, M., Davis, G. and McCrory, P. (2015). Clinical challenges in the diagnosis and assessment of sports-related concussion. *Neurology Clinical Practice*, 5(1), pp.2–5. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=fulltext&D=ovft&MODE=ovi d&NEWS=N&SEARCH=2163-0402.is+and+5.vo+and+1.ip+and+2.pg&NEWS=n.

Manley, G., Gardner, A.J., Schneider, K.J., Guskiewicz, K.M., Bailes, J., Cantu, R.C., Castellani, R.J., Turner, M., Jordan, B.D., Randolph, C., Dvořák, J., Alix Hayden, K., Tator, C.H., McCrory, P. and Iverson, G.L. (2017). A systematic review of potential long-term effects of sport-related concussion. *British Journal of Sports Medicine*, 51(12), pp.969–977.

Maroon, J.C., Lovell, M.R., Norwig, J., Podell, K., Powell, J.W. and Hartl, R. (2000). Cerebral concussion in athletes: Evaluation and neuropsychological testing. *Neurosurgery*, 47(3), pp.659–672.

Martinez-De-La-Casa, J.M., Garcia-Feijoo, J., Castillo, A. and Garcia-Sanchez, J. (2005). Reproducibility and clinical evaluation of rebound tonometry. *Investigative Ophthalmology and Visual Science*, 46(12), pp.4578–4580.

Maugans, T.A., Farley, C., Altaye, M., Leach, J. and Cecil, K.M. (2012). Pediatric Sports-Related Concussion Produces Cerebral Blood Flow Alterations. *Pediatrics*, 129(1), pp.28–37. Available from: http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2011-2083.

Mc Fie, S., Brown, J., Hendricks, S., Posthumus, M., Readhead, C., Lambert, M., September, A. V. and Viljoen, W. (2016). Incidence and factors associated with concussion injuries at the 2011 to 2014 South African Rugby Union Youth Week Tournaments. *Clinical Journal of Sport Medicine*, 26(5), pp.398–404.

Mccrea, M., Guskiewicz, K.M., Marshall, S.W., Barr, W., Randolph, C., Cantu, R.C., Onate, J.A., Kelly, J.P. and Page, P. (2003). Acute Effects and

Recovery Time Following Concussion in Collegiate Football Players: The NCAA Concussion Study. *Journal of the American Medical Association*, 290(19), pp.2556–2563.

McCrea, M., Kelly, J.P., Kluge, J., Ackley, B. and Randolph, C. (1997). Standardized assessment of concussion in football players. *Neurology*, 48(3), pp.586–588.

McCrea, M., Kelly, J.P., Randolph, C., Kluge, J., Bartolic, E., Finn, G. and Baxter, B. (1998). Standardised assessment of concussion (SAC): On site mental status evaluation of the athlete. *Journal of Head Trauma Rehabilitation*, 13(Journal Article), pp.27–35.

McCrea, M., Kelly, J.P., Randolph, C., Kluge, J., Bartolic, E., Finn, G. and Baxter, B. (1998). Standardized assessment of concussion (SAC): On-site mental status evaluation of the athlete. *Journal of Head Trauma Rehabilitation*, 13(2), pp.27–35.

McCrory, P. et al. (2017a). Consensus statement on concussion in sport—the 5 [th] international conference on concussion in sport held in Berlin, October 2016. *British Journal of Sports Medicine*, 2017, p.bjsports-2017-097699. Available from: http://bjsm.bmj.com/lookup/doi/10.1136/bjsports-2017-097699.

McCrory, P. et al. (2013). Consensus Statement on Concussion in Sport: The 4th International Conference on Concussion in Sport Held in Zurick, November 2012. *British Journal of Sports Medicine*, 47(2), pp.250–258.

McCrory, P. et al. (2017b). Sport concussion assessment tool - 5th edition. *British Journal of Sports Medicine*, 2017, p.bjsports-2017-097506SCAT5. Available from: http://bjsm.bmj.com/lookup/doi/10.1136/bjsports-2017-097506SCAT5.

McCrory, P., Johnston, K., Meeuwisse, W., Aubry, M., Cantu, R., Dvorak, J., Graf-Baumann, T., Kelly, J., Lovell, M. and Schamasch, P. (2005). Summary and agreement statement of the 2nd International Conference on Concussion in Sport, Prague 2004. *British Journal of Sports Medicine*, 39(4), pp.196–204.

Mccrory, P., Meeuwisse, W., Johnston, K., Dvorak, J., Aubry, M., Molloy, M. and Cantu, R. (2009). Consensus Statement on Concussion in Sport : the 3rd International Conference on Concussion in Sport held in Zurich , November 2008 Consensus Statement on Concussion in Sport : the 3rd International Conference on Concussion in Sport held in Zurich , Novem. *Sports Medicine*, 43(Suppl I).

Mcmonnies, C.W. (2016). Intraocular pressure and glaucoma : Is physical exercise beneficial or a risk ?. *Journal of Optometry*, 9(3), pp.139–147. Available from: http://dx.doi.org/10.1016/j.optom.2015.12.001.

Meir, R., Arthur, D. and Forrest, M. (1993). Time and Motion Analysis of Professional Rugby League: a Case Study. *Strength and conditioning coach*, 3(1), pp.24–29.

Mohan, K., Kecova, H., Hernandez-Merino, E., Kardon, R.H. and Harper, M.M. (2013). Retinal Ganglion Cell Damage in an Experimental Rodent Model of Blast-Mediated Traumatic Brain Injury. *Investigative Opthalmology & Visual Science*, 54(5), p.3440. Available from: http://iovs.arvojournals.org/article.aspx?doi=10.1167/iovs.12-11522.

Moore, I.S., Ranson, C. and Mathema, P. (2015). Injury Risk in International Rugby Union: Three-Year Injury Surveillance of the Welsh National Team. *Orthopaedic Journal of Sports Medicine*, 3(7), pp.1–9.

Mucha, A., Collins, M.W., Elbin, R.J., Furman, J.M., Troutman-Enseki, C., Dewolf, R.M., Marchetti, G. and Kontos, A.P. (2014). A brief vestibular/ocular motor screening (VOMS) assessment to evaluate concussions: Preliminary findings. *American Journal of Sports Medicine*, 42(10), pp.2479–2486.

Murgatroyd, H. and Bembridge, J. (2008). Intraocular pressure. *Continuing Education in Anaesthesia, Critical Care and Pain*, 8(3), pp.100–103.

Murphy, J.C., Gissane, C. and Blake, C. (2012). Injury in elite county-level hurling: A prospective study. *British Journal of Sports Medicine*, 46(2), pp.138–142.

Murphy, J.C., O'Malley, E., Gissane, C. and Blake, C. (2012). Incidence of injury in gaelic football: A 4-year prospective study. *American Journal of Sports Medicine*, 40(9), pp.2113–2120.

Najmanova, E., Pluhacek, F. and Botek, M. (2018). Intraocular pressure response to maximal exercise test during recovery. *Optometry and Vision Science*, 95(2), pp.136–142.

Nieves-Moreno, M., Martínez-De-La-Casa, J.M., Cifuentes-Canorea, P., Sastre-Ibáñez, M., Santos-Bueso, E., Sáenz-Francés, F., Morales-Fernández, L. and García-Feijoó, J. (2017). Normative database for separate inner retinal layers thickness using spectral domain optical coherence tomography in Caucasian population. *PLoS ONE*, 12(7), pp.14–21.

Niogi, S.N., Mukherjee, P., Ghajar, J., Johnson, C., Kolster, R.A., Sarkar, R., Lee, H., Meeker, M., Zimmerman, R.D., Manley, G.T. and McCandliss, B.D. (2008). Extent of microstructural white matter injury in postconcussive syndrome correlates with impaired cognitive reaction time: A 3T diffusion tensor imaging study of mild traumatic brain injury. *American Journal of Neuroradiology*, 29(5), pp.967–973.

Omalu, B. (2014). Chronic traumatic encephalopathy. *Progress in Neurological Surgery*, 28, pp.38–49.

Omalu, B.I., DeKosky, S.T., Hamilton, R.L., Minster, R.L., Kamboh, M.I., Shakir, A.M. and Wecht, C.H. (2006). Chronic traumatic encephalopathy in a National Football League player: Part II. *Neurosurgery*, 59(5), pp.1086–1092.

Omalu, B.I., DeKosky, S.T., Minster, R.L., Kamboh, M.I., Hamilton, R.L. and Wecht, C.H. (2005). Chronic traumatic encephalopathy in a National Football League player. *Neurosurgery*, 57(1), pp.128–133.

Patel, A. V, Mihalik, J.P., Notebaert, A.J. and Guskiewicz, K.M. (2007). Neuropsychological Performance , Postural Stability , and Symptoms After Dehydr ... , 42(1), pp.66–75.

PentaVision. (2015). *Layers of the Retina*. Available from: www.ophthalmologymanagement.com/issues/2015/july-2015/learning-to-read-oct.

Pfister, T., Pfister, K., Hagel, B., Ghali, W.A. and Ronksley, P.E. (2016). The incidence of concussion in youth sports: A systematic review and meta-analysis. *British Journal of Sports Medicine*, 50(5), pp.292–297.

Podoleanu, A.G. (2012). Optical coherence tomography. *Journal of Microscopy*, 247(3), pp.209–219.

Prata, T.S., De Moraes, C.G. V, Kanadani, F.N., Ritch, R. and Paranhos, A. (2010). Posture-induced intraocular pressure changes: Considerations regarding body position in glaucoma patients. *Survey of Ophthalmology*, 55(5), pp.445–453.

Putukian, M., Echemendia, R. and Dettwiler-danspeckgruber, A. (2015). Prospective Clinical Assessment Using Sideline Concussion Assessment Tool-2 Testing in the Evaluation of Sport-Related Concussion in College Athletes. , 25(January), pp.36–42.

Queirós, T., Freitas, C. and Guimarães, S. (2015). [Normative Database of Optical Coherence Tomography Parameters in Childhood]. *Acta medica portuguesa*, 28(2), pp.148–157. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26061504.

Qureshi, I. a. (1996). Effects of exercise on intraocular pressure in physically fit subjects. *Clinical and experimental pharmacology & physiology*, 23(8), pp.648–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8886483.

Reynolds, J.D. and Olitsky, S.E. (2011). Pediatric retina. *Pediatric Retina*, 2011, pp.1–462.

Riemann, B.L., Guskiewicz, K.M. and Shields, E.W. (1999). Relationship between Clinical and Forceplate Measures of Postural Stability. *Journal of Sport Rehabilitation*, 8(2), pp.71–82. Available from: http://journals.humankinetics.com/doi/10.1123/jsr.8.2.71.

Roberts, S.P., Trewartha, G., England, M., Goodison, W. and Stokes, K.A. (2017). Concussions and Head Injuries in English Community Rugby Union Match Play. *American Journal of Sports Medicine*, 45(2), pp.480–487.

Robinson, M. and Mc Elhiney, D. (2017). Investigating a seven-day baseline while establishing healthy SCAT3 symptom frequency and severity. *International Journal of Athletic Therapy and Training*, 22(2), pp.7–13.

Roddy, G., Curnier, D. and Ellemberg, D. (2014). Reductions in Intraocular Pressure After Acute Aerobic Exercise. *Clinical Journal of Sport Medicine*, 24(5), pp.364–372. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an =00042752-201409000-00002.

Sahin, A., Basmak, H., Niyaz, L. and Yildirim, N. (2007). Reproducibility and tolerability of the ICare rebound tonometer in school children. *Journal of Glaucoma*, 16(2), pp.185–188.

Salim, Sarwat; Du, Haiming; Wan, J. (2013). Comparison of intraocular pressure measurements and assessment of intraobserver and interobserver reproducibility with the portable ICare Rebound Tonometer in Glaucoma patients. , 2013.

Satue, M. et al. (2017). Retinal and Choroidal Changes in Patients with Parkinson ' s Disease Detected by Swept-Source Optical Coherence Tomography Retinal and Choroidal Changes in Patients with Parkinson ' s Disease Detected by. *Current Eye Research*, 0(0), pp.1–7. Available from: https://doi.org/10.1080/02713683.2017.1370116%0Ahttp://dx.doi.org/10.108 0/02713683.2017.1370116.

Sawada, A. and Yamamoto, T. (2013). Comparison of posture-induced intraocular pressure changes in medically treated and surgically treated eyes with open-angle glaucoma. *Investigative Ophthalmology and Visual Science*, 55(1), pp.446–450.

Sayin, N., Kara, N., Pekel, G. and Altinkaynak, H. (2015). Choroidal thickness changes after dynamic exercise as measured by spectral-domain optical coherence tomography. *Indian Journal of Ophthalmology*, 63(5), p.445. Available from: http://www.ijo.in/text.asp?2015/63/5/445/159884.

Schmidl, D., Schmetterer, L., Witkowska, K.J., Rauch, A., Werkmeister, R.M., Garhöfer, G. and Popa-Cherecheanu, A. (2016). Factors Associated With Choroidal Blood Flow Regulation in Healthy Young Subjects. *Investigative Opthalmology & Visual Science*, 57(13), p.5705. Available from: http://iovs.arvojournals.org/article.aspx?doi=10.1167/iovs.16-20225.

Schneider, K.J., Emery, C.A., Kang, J., Schneider, G.M. and Meeuwisse, W.H. (2010). Examining Sport Concussion Assessment Tool ratings for male and female youth hockey players with and without a history of concussion. *British Journal of Sports Medicine*, 44(15), pp.1112–1117.

Shehata, N., Wiley, J.P., Richea, S., Benson, B.W., Duits, L. and Meeuwisse, W.H. (2009). Sport concussion assessment tool: Baseline values for varsity collision sport athletes. *British Journal of Sports Medicine*, 43(10), pp.730–734.

Signoretti, S., Lazzarino, G., Tavazzi, B. and Vagnozzi, R. (2011). The pathophysiology of concussion. *PM & R : the journal of injury, function, and rehabilitation*, 3(10 Suppl 2), pp.S359–S368. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22035678.

Singleton, C.D., Robertson, D., Byrne, D.W. and Joos, K.M. (2003). Effect of Posture on Blood and Intraocular Pressures in Multiple System Atrophy, Pure Autonomic Failure, and Baroreflex Failure. *Circulation*, 108(19), pp.2349–2354.

Sirotic, A.C. and Coutts, A.J. (2007). Physiological and Performance Test Correlates of Prolonged, High-Intensity, Intermittent Running Performance in Moderately Trained Woman Team Sport Athletes. *Journal of Strength and Conditioning Research*, 21(1), pp.138–144.

Sirotic, A.C. and Coutts, A.J. (2008). The reliability of physiological and performance measures during simulated team-sport running on a non-motorised treadmill. *Journal of Science and Medicine in Sport*, 11(5), pp.500–509.

Snyder, A.R. and Bauer, R.M. (2014). A Normative Study of the Sport Concussion Assessment Tool (SCAT2) in Children and Adolescents. *The Clinical Neuropsychologist*, 28(7), pp.1091–1103. Available from: http://www.tandfonline.com/doi/abs/10.1080/13854046.2014.952667.

Soccer, U.S. (2018). *U.S. Soccer Concussion Guidelines*. Available from: www.ussoccer.com/about/recognize-to-recover/concussion-guidelines.

Spaide, R. (2010). Choroidal imaging with optical coherence tomography. *Medical Retina*, m, pp.132–136. Available from: http://link.springer.com/10.1007/978-3-540-85540-8_15.

Sport Scotland. (2015). FA Concussion Guidelines. , 2015, pp.1–8. Available from: http://www.sportscotland.org.uk/media/1534421/Scottish-Sports-Concussion-Guidance.pdf.

Stamper, R. (2011). A History of Intraocular Pressure and Its Measurement. *American Academy of Optometry*, 88(1), pp.1–14.

Sullivan, L., Thomas, A.A. and Molcho, M. (2017). An evaluation of Gaelic Athletic Association (GAA) athletes' self-reported practice of playing while concussed, knowledge about and attitudes towards sports-related concussion. *International Journal of Adolescent Medicine and Health*, 29(3), pp.1–9.

Tanga, L., Roberti, G., Oddone, F., Quaranta, L., Ferrazza, M., Berardo, F., Manni, G. and Centofanti, M. (2015). Evaluating the effect of pupil dilation on spectral-domain optical coherence tomography measurements and their quality score. *BMC Ophthalmology*, 15(1), pp.1–5. Available from: http://dx.doi.org/10.1186/s12886-015-0168-y.

Teasdale, G. and Jennett, B. (1974). Assessment of Coma and Impaired Conciousness. *The Lancet*, July, pp.81–84.

Thomson, K.L., Yeo, J.M., Waddell, B., Cameron, J.R. and Pal, S. (2015). A systematic review and meta-analysis of retinal nerve fiber layer change in dementia, using optical coherence tomography. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 1(2), pp.136–143. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2352872915000366.

Tjarks, B.J., Dorman, J.C., Valentine, V.D., Munce, T.A., Thompson, P.A., Kindt, S.L. and Bergeron, M.F. (2013). Comparison and utility of King-Devick and ImPACT® composite scores in adolescent concussion patients. *Journal of the Neurological Sciences*, 334(1–2), pp.148–153.

Topcon. (2014). *Topcon IMAGEnet6 Ophthalmic Data System: User Manual*. Topcon.

Tysvaer, A. and Storli, O. (1981). Association football injuries to the brain. A preliminary report. *British journal of sports medicine*, 15(3), pp.163–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7272660%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC1858750.

Union, W.R. Concussion Guidance. , pp.1–12. Available from: http://www.wru.co.uk/downloads/WRUConcussionGuidanceEnglish.pdf.

Valovich McLeod, T.C., Bay, R.C., Lam, K.C. and Chhabra, A. (2012). Representative baseline values on the Sport Concussion Assessment Tool 2 (SCAT2) in adolescent athletes vary by gender, grade, and concussion history. *American Journal of Sports Medicine*, 40(4), pp.927–933.

Vaz, S., Falkmer, T., Passmore, A.E., Parsons, R. and Andreou, P. (2013). The Case for Using the Repeatability Coefficient When Calculating Test-Retest Reliability. *PLoS ONE*, 8(9), pp.1–7.

Ventura, R.E., Jancuska, J.M., Balcer, L.J. and Galetta, S.L. (2015). Diagnostic tests for concussion: Is vision part of the puzzle?. *Journal of Neuro-Ophthalmology*, 35(1), pp.73–81.

Di Virgilio, T.G., Hunter, A., Wilson, L., Stewart, W., Goodall, S., Howatson, G., Donaldson, D.I. and Ietswaart, M. (2016). Evidence for Acute Electrophysiological and Cognitive Changes Following Routine Soccer Heading. *EBioMedicine*, 13, pp.66–71. Available from: http://dx.doi.org/10.1016/j.ebiom.2016.10.029.

Vos, P.E., Alekseenko, Y., Battistin, L., Ehler, E., Gerstenbrand, F., Muresanu, D.F., Potapov, A., Stepan, C.A., Traubner, P., Vecsei, L. and von Wild, K. (2012). Mild traumatic brain injury. *European Journal of Neurology*, 19(2), pp.191–198.

Wang, J., Gao, X., Huang, W., Wang, W., Chen, S., Du, S., Li, X. and Zhang, X. (2015). Swept-source optical coherence tomography imaging of macular retinal and choroidal structures in healthy eyes. *BMC Ophthalmology*, 15(1), pp.1–10. Available from: http://dx.doi.org/10.1186/s12886-015-0110-3.

Wang, Y., West, J.D., Bailey, J.N., Westfall, D.R., Xiao, H., Arnold, T.W., Kersey, P.A., Saykin, A.J. and McDonald, B.C. (2015). Decreased cerebral blood flow in chronic pediatric mild TBI: An MRI perfusion study. *Developmental Neuropsychology*, 40(1), pp.40–44. Available from: http://dx.doi.org/10.1080/87565641.2014.979927.

Whelan, Ruth (GAA Medical, S. and W.C. (2016). Concussion Management Guidelines in the GAA (2013 - 2016). , 2016, p.688.

WHO. (2001). *WHO International Programme on Chemical Safety Biomarkers in Risk Assessment: Validity and Validation*.

Wikstrom, E.A., Naik, S., Lodha, N. and Cauraugh, J.H. (2010). Gait & Posture Bilateral balance impairments after lateral ankle trauma : A systematic review and meta-analysis. *Gait & Posture*, 31(4), pp.407–414. Available from: http://dx.doi.org/10.1016/j.gaitpost.2010.02.004.

Wilde, E.A., McCauley, S.R., Hunter, J. V., Bigler, E.D., Chu, Z., Wang, Z.J., Hanten, G.R., Troyanskaya, M., Yallampalli, R., Li, X., Chia, J. and Levin, H.S. (2008). Diffusion tensor imaging of acute mild traumatic brain injury in adolescents. *Neurology*, 70(12), pp.948–955.

Yang, Z., Tatham, A.J., Zangwill, L.M., Weinreb, R.N., Zhang, C. and Medeiros, F.A. (2015). Diagnostic ability of retinal nerve fiber layer imaging by swept-source optical coherence tomography in glaucoma. *American Journal of Ophthalmology*, 159(1), pp.193–201.

Yengo-Kahn, A.M., Hale, A.T., Zalneraitis, B.H., Zuckerman, S.L., Sills, A.K. and Solomon, G.S. (2016). The Sport Concussion Assessment Tool: a Systematic Review. *Neurosurg Focus*, 40(4), p.E6.

Young, J.S., Hobbs, J.G. and Bailes, J.E. (2016). The Impact of Traumatic Brain Injury on the Aging Brain. *Current Psychiatry Reports*, 18(9). Available from: http://dx.doi.org/10.1007/s11920-016-0719-9.

Zhang, Y., Emeterio Nateras, O.S., Peng, Q., Rosende, C.A. and Duong, T.Q. (2012). Blood flow MRI of the human retina/choroid during rest and isometric exercise. *Investigative Ophthalmology and Visual Science*, 53(7), pp.4299–4305.

Zimmer, A., Marcinak, J., Hibyan, S. and Webbe, F. (2015). Normative values of major SCAT2 and SCAT3 components for a college athlete population. *Applied Neuropsychology:Adult*, 22(2), pp.132–140.

Zimmer, A., Piecora, K., Schuster, D. and Webbe, F. (2013). Sport and team differences on baseline measures of sport-related concussion. *Journal of Athletic Training*, 48(5), pp.659–667.

APPENDICES

Appendix A: Sport Concussion Assessment Tool

SCAT3™

F-MARC FIFA® IIHF Olympic Rings IRB FEI

Sport Concussion Assessment Tool – 3rd Edition
For use by medical professionals only

Name _____ Date/Time of Injury: _____ Examiner: _____
Date of Assessment: _____

What is the SCAT3?[1]

The SCAT3 is a standardized tool for evaluating injured athletes for concussion and can be used in athletes aged from 13 years and older. It supersedes the original SCAT and the SCAT2 published in 2005 and 2009, respectively[2]. For younger persons, ages 12 and under, please use the Child SCAT3. The SCAT3 is designed for use by medical professionals. If you are not qualified, please use the Sport Concussion Recognition Tool[1]. Preseason baseline testing with the SCAT3 can be helpful for interpreting post-injury test scores.

Specific instructions for use of the SCAT3 are provided on page 3. If you are not familiar with the SCAT3, please read through these instructions carefully. This tool may be freely copied in its current form for distribution to individuals, teams, groups and organizations. Any revision or any reproduction in a digital form requires approval by the Concussion in Sport Group.
NOTE: The diagnosis of a concussion is a clinical judgment, ideally made by a medical professional. The SCAT3 should not be used solely to make, or exclude, the diagnosis of concussion in the absence of clinical judgement. An athlete may have a concussion even if their SCAT3 is "normal".

What is a concussion?
A concussion is a disturbance in brain function caused by a direct or indirect force to the head. It results in a variety of non-specific signs and/or symptoms (some examples listed below) and most often does not involve loss of consciousness. Concussion should be suspected in the presence of **any one or more** of the following:

- Symptoms (e.g., headache), or
- Physical signs (e.g., unsteadiness), or
- Impaired brain function (e.g. confusion) or
- Abnormal behaviour (e.g., change in personality).

SIDELINE ASSESSMENT
Indications for Emergency Management
NOTE: A hit to the head can sometimes be associated with a more serious brain injury. Any of the following warrants consideration of activating emergency procedures and urgent transportation to the nearest hospital:

- Glasgow Coma score less than 15
- Deteriorating mental status
- Potential spinal injury
- Progressive, worsening symptoms or new neurologic signs

Potential signs of concussion?
If any of the following signs are observed after a direct or indirect blow to the head, the athlete should stop participation, be evaluated by a medical professional and **should not be permitted to return to sport the same day** if a concussion is suspected.

Any loss of consciousness? ☐ Y ☐ N
"If so, how long?" _____
Balance or motor incoordination (stumbles, slow/laboured movements, etc.)? ☐ Y ☐ N
Disorientation or confusion (inability to respond appropriately to questions)? ☐ Y ☐ N
Loss of memory: ☐ Y ☐ N
"If so, how long?" _____
"Before or after the injury?" _____
Blank or vacant look: ☐ Y ☐ N
Visible facial injury in combination with any of the above: ☐ Y ☐ N

1 Glasgow coma scale (GCS)

Best eye response (E)	
No eye opening	1
Eye opening in response to pain	2
Eye opening to speech	3
Eyes opening spontaneously	4

Best verbal response (V)	
No verbal response	1
Incomprehensible sounds	2
Inappropriate words	3
Confused	4
Oriented	5

Best motor response (M)	
No motor response	1
Extension to pain	2
Abnormal flexion to pain	3
Flexion/Withdrawal to pain	4
Localizes to pain	5
Obeys commands	6

Glasgow Coma score (E + V + M)	of 15

GCS should be recorded for all athletes in case of subsequent deterioration.

2 Maddocks Score[3]
"I am going to ask you a few questions, please listen carefully and give your best effort."
Modified Maddocks questions (1 point for each correct answer)

What venue are we at today?	0	1
Which half is it now?	0	1
Who scored last in this match?	0	1
What team did you play last week/game?	0	1
Did your team win the last game?	0	1
Maddocks score		of 5

Maddocks score is validated for sideline diagnosis of concussion only and is not used for serial testing.

Notes: Mechanism of Injury ("tell me what happened"?):
_____
_____
_____
_____

Any athlete with a suspected concussion should be REMOVED FROM PLAY, medically assessed, monitored for deterioration (i.e., should not be left alone) and should not drive a motor vehicle until cleared to do so by a medical professional. No athlete diagnosed with concussion should be returned to sports participation on the day of injury.

BACKGROUND

Name: _____ Date: _____
Examiner: _____
Sport/team/school: _____ Date/time of injury: _____
Age: _____ Gender: ☐ M ☐ F
Years of education completed: _____
Dominant hand: ☐ right ☐ left ☐ neither
How many concussions do you think you have had in the past? _____
When was the most recent concussion? _____
How long was your recovery from the most recent concussion? _____

Have you ever been hospitalized or had medical imaging done for ☐ Y ☐ N
a head injury?
Have you ever been diagnosed with headaches or migraines? ☐ Y ☐ N
Do you have a learning disability, dyslexia, ADD/ADHD? ☐ Y ☐ N
Have you ever been diagnosed with depression, anxiety ☐ Y ☐ N
or other psychiatric disorder?
Has anyone in your family ever been diagnosed with ☐ Y ☐ N
any of these problems?
Are you on any medications? If yes, please list: ☐ Y ☐ N

SCAT3 to be done in resting state. Best done 10 or more minutes post excercise.

SYMPTOM EVALUATION

3 How do you feel?

"You should score yourself on the following symptoms, based on how you feel now".

	none	mild		moderate		severe	
Headache	0	1	2	3	4	5	6
"Pressure in head"	0	1	2	3	4	5	6
Neck Pain	0	1	2	3	4	5	6
Nausea or vomiting	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Blurred vision	0	1	2	3	4	5	6
Balance problems	0	1	2	3	4	5	6
Sensitivity to light	0	1	2	3	4	5	6
Sensitivity to noise	0	1	2	3	4	5	6
Feeling slowed down	0	1	2	3	4	5	6
Feeling like "in a fog"	0	1	2	3	4	5	6
"Don't feel right"	0	1	2	3	4	5	6
Difficulty concentrating	0	1	2	3	4	5	6
Difficulty remembering	0	1	2	3	4	5	6
Fatigue or low energy	0	1	2	3	4	5	6
Confusion	0	1	2	3	4	5	6
Drowsiness	0	1	2	3	4	5	6
Trouble falling asleep	0	1	2	3	4	5	6
More emotional	0	1	2	3	4	5	6
Irritability	0	1	2	3	4	5	6
Sadness	0	1	2	3	4	5	6
Nervous or Anxious	0	1	2	3	4	5	6

Total number of symptoms (Maximum possible 22) ☐
Symptom severity score (Maximum possible 132) ☐

Do the symptoms get worse with physical activity? ☐ Y ☐ N
Do the symptoms get worse with mental activity? ☐ Y ☐ N

☐ self rated ☐ self rated and clinician monitored
☐ clinician interview ☐ self rated with parent input

Overall rating: If you know the athlete well prior to the injury, how different is
the athlete acting compared to his/her usual self?
Please circle one response:

no different	very different	unsure	N/A

**Scoring on the SCAT3 should not be used as a stand-alone method
to diagnose concussion, measure recovery or make decisions about
an athlete's readiness to return to competition after concussion.
Since signs and symptoms may evolve over time, it is important to
consider repeat evaluation in the acute assessment of concussion.**

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COGNITIVE & PHYSICAL EVALUATION

4 Cognitive assessment
Standardized Assessment of Concussion (SAC)[4]

Orientation (1 point for each correct answer)

	0	1
What month is it?	0	1
What is the date today?	0	1
What is the day of the week?	0	1
What year is it?	0	1
What time is it right now? (within 1 hour)	0	1
Orientation score		of 5

Immediate memory

List	Trial 1		Trial 2		Trial 3		Alternative word list		
elbow	0	1	0	1	0	1	candle	baby	finger
apple	0	1	0	1	0	1	paper	monkey	penny
carpet	0	1	0	1	0	1	sugar	perfume	blanket
saddle	0	1	0	1	0	1	sandwich	sunset	lemon
bubble	0	1	0	1	0	1	wagon	iron	insect
Total									

Immediate memory score total | of 15

Concentration: Digits Backward

List	Trial 1	Alternative digit list		
4-9-3	0 1	6-2-9	5-2-6	4-1-5
3-8-1-4	0 1	3-2-7-9	1-7-9-5	4-9-6-8
6-2-9-7-1	0 1	1-5-2-8-6	3-8-5-2-7	6-1-8-4-3
7-1-8-4-6-2	0 1	5-3-9-1-4-8	8-3-1-9-6-4	7-2-4-8-5-6
Total of 4				

Concentration: Month in Reverse Order (1 pt. for entire sequence correct)

	0	1
Dec-Nov-Oct-Sept-Aug-Jul-Jun-May-Apr-Mar-Feb-Jan	0	1

Concentration score | of 5

5 Neck Examination:

Range of motion   Tenderness   Upper and lower limb sensation & strength
Findings: _____

6 Balance examination

Do one or both of the following tests.
Footwear (shoes, barefoot, braces, tape, etc.) _____

Modified Balance Error Scoring System (BESS) testing[5]
Which foot was tested (i.e. which is the **non-dominant** foot) ☐ Left ☐ Right
Testing surface (hard floor, field, etc.) _____
Condition
Double leg stance: ☐ Errors
Single leg stance (non-dominant foot): ☐ Errors
Tandem stance (non-dominant foot at back): ☐ Errors

And/Or

Tandem gait[6,7]
Time (best of 4 trials): _____ seconds

7 Coordination examination
Upper limb coordination
Which arm was tested: ☐ Left ☐ Right
Coordination score | of 1

8 SAC Delayed Recall[4]
Delayed recall score | of 5

been carried out and no sign of any serious complications has been found. Recovery
time is variable across individuals and the patient will need monitoring for a further
period by a responsible adult. Your treating physician will provide guidance as to
this timeframe.

**If you notice any change in behaviour, vomiting, dizziness, worsening head-
ache, double vision or excessive drowsiness, please contact your doctor or
the nearest hospital emergency department immediately.**

Other important points:

- Rest (physically and mentally), including training or playing sports
  until symptoms resolve and you are medically cleared
- No alcohol
- No prescription or non-prescription drugs without medical supervision.
  Specifically:
   · No sleeping tablets
   · Do not use aspirin, anti-inflammatory medication or sedating pain killers
- Do not drive until medically cleared
- Do not train or play sport until medically cleared

Clinic phone number _____

Date/time of medical review _____

Treating physician _____

Contact details or stamp

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INSTRUCTIONS

Words in *Italics* throughout the SCAT3 are the instructions given to the athlete by the tester.

Symptom Scale

"You should score yourself on the following symptoms, based on how you feel now".

To be completed by the athlete. In situations where the symptom scale is being completed after exercise, it should still be done in a resting state, at least 10 minutes post exercise.
For total number of symptoms, maximum possible is 22.
For Symptom severity score, add all scores in table, maximum possible is 22 x 6 = 132.

SAC[4]
Immediate Memory

"I am going to test your memory. I will read you a list of words and when I am done, repeat back as many words as you can remember, in any order."

Trials 2 & 3:

"I am going to repeat the same list again. Repeat back as many words as you can remember in any order, even if you said the word before."

Complete all 3 trials regardless of score on trial 1 & 2. Read the words at a rate of one per second.
Score 1 pt. for each correct response. Total score equals sum across all 3 trials. Do not inform the athlete that delayed recall will be tested.

Concentration
Digits backward

"I am going to read you a string of numbers and when I am done, you repeat them back to me backwards, in reverse order of how I read them to you. For example, if I say 7-1-9, you would say 9-1-7."

If correct, go to next string length. If incorrect, read trial 2. **One point possible for each string length.** Stop after incorrect on both trials. The digits should be read at the rate of one per second.

Months in reverse order

"Now tell me the months of the year in reverse order. Start with the last month and go backward. So you'll say December, November ... Go ahead"

1 pt. for entire sequence correct

Delayed Recall

The delayed recall should be performed after completion of the Balance and Coordination Examination.

"Do you remember that list of words I read a few times earlier? Tell me as many words from the list as you can remember in any order."

Score 1 pt. for each correct response

Balance Examination
Modified Balance Error Scoring System (BESS) testing[5]

This balance testing is based on a modified version of the Balance Error Scoring System (BESS)[5]. A stopwatch or watch with a second hand is required for this testing.

"I am now going to test your balance. Please take your shoes off, roll up your pant legs above ankle (if applicable), and remove any ankle taping (if applicable). This test will consist of three twenty second tests with different stances."

(a) Double leg stance:

"The first stance is standing with your feet together with your hands on your hips and with your eyes closed. You should try to maintain stability in that position for 20 seconds. I will be counting the number of times you move out of this position. I will start timing when you are set and have closed your eyes."

(b) Single leg stance:

"If you were to kick a ball, which foot would you use? [This will be the dominant foot] Now stand on your non-dominant foot. The dominant leg should be held in approximately 30 degrees of hip flexion and 45 degrees of knee flexion. Again, you should try to maintain stability for 20 seconds with your hands on your hips and your eyes closed. I will be counting the number of times you move out of this position. If you stumble out of this position, open your eyes and return to the start position and continue balancing. I will start timing when you are set and have closed your eyes."

(c) Tandem stance:

"Now stand heel-to-toe with your non-dominant foot in back. Your weight should be evenly distributed across both feet. Again, you should try to maintain stability for 20 seconds with your hands on your hips and your eyes closed. I will be counting the number of times you move out of this position. If you stumble out of this position, open your eyes and return to the start position and continue balancing. I will start timing when you are set and have closed your eyes."

Balance testing – types of errors
1. Hands lifted off iliac crest
2. Opening eyes
3. Step, stumble, or fall
4. Moving hip into > 30 degrees abduction
5. Lifting forefoot or heel
6. Remaining out of test position > 5 sec

Each of the 20-second trials is scored by counting the errors, or deviations from the proper stance, accumulated by the athlete. The examiner will begin counting errors only after the individual has assumed the proper start position. **The modified BESS is calculated by adding one error point for each error during the three 20-second tests. The maximum total number of errors for any single condition is 10.** If a athlete commits multiple errors simultaneously, only one error is recorded but the athlete should quickly return to the testing position, and counting should resume once subject is set. Subjects that are unable to maintain the testing procedure for a minimum of **five seconds** at the start are assigned the highest possible score, ten, for that testing condition.

OPTION: For further assessment, the same 3 stances can be performed on a surface of medium density foam (e.g., approximately 50 cm x 40 cm x 6 cm).

Tandem Gait[6,7]

Participants are instructed to stand with their feet together behind a starting line (the test is best done with footwear removed). Then, they walk in a forward direction as quickly and as accurately as possible along a 38mm wide (sports tape), 3 meter line with an alternate foot heel-to-toe gait ensuring that they approximate their heel and toe on each step. Once they cross the end of the 3m line, they turn 180 degrees and return to the starting point using the same gait. A total of 4 trials are done and the best time is retained. Athletes should complete the test in 14 seconds. Athletes fail the test if they step off the line, have a separation between their heel and toe, or if they touch or grab the examiner or an object. In this case, the time is not recorded and the trial repeated, if appropriate.

Coordination Examination
Upper limb coordination
Finger-to-nose (FTN) task:

"I am going to test your coordination now. Please sit comfortably on the chair with your eyes open and your arm (either right or left) outstretched (shoulder flexed to 90 degrees and elbow and fingers extended), pointing in front of you. When I give a start signal, I would like you to perform five successive finger to nose repetitions using your index finger to touch the tip of the nose, and then return to the starting position, as quickly and as accurately as possible."

Scoring: 5 correct repetitions in < 4 seconds = 1
Note for testers: Athletes fail the test if they do not touch their nose, do not fully extend their elbow or do not perform five repetitions. **Failure should be scored as 0.**

References & Footnotes

1. This tool has been developed by a group of international experts at the 4th International Consensus meeting on Concussion in Sport held in Zurich, Switzerland in November 2012. The full details of the conference outcomes and the authors of the tool are published in The BJSM Injury Prevention and Health Protection, 2013, Volume 47, Issue 5. The outcome paper will also be simultaneously co-published in other leading biomedical journals with the copyright held by the Concussion in Sport Group, to allow unrestricted distribution, providing no alterations are made.

2. McCrory P et al., Consensus Statement on Concussion in Sport – the 3rd International Conference on Concussion in Sport held in Zurich, November 2008. British Journal of Sports Medicine 2009; 43: i76-89.

3. Maddocks, DL; Dicker, GD; Saling, MM. The assessment of orientation following concussion in athletes. Clinical Journal of Sport Medicine. 1995; 5(1): 32 – 3.

4. McCrea M. Standardized mental status testing of acute concussion. Clinical Journal of Sport Medicine. 2001; 11: 176 – 181.

5. Guskiewicz KM. Assessment of postural stability following sport-related concussion. Current Sports Medicine Reports. 2003; 2: 24 – 30.

6. Schneiders, A.G., Sullivan, S.J., Gray, A., Hammond-Tooke, G. & McCrory, P. Normative values for 16-37 year old subjects for three clinical measures of motor performance used in the assessment of sports concussions. Journal of Science and Medicine in Sport. 2010; 13(2): 196 – 201.

7. Schneiders, A.G., Sullivan, S.J., Kvarnstrom. J.K., Olsson, M., Yden. T. & Marshall, S.W. The effect of footwear and sports-surface on dynamic neurological screening in sport-related concussion. Journal of Science and Medicine in Sport. 2010; 13(4): 382 – 386

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Appendix B – Reliability Study – Informed Consent and Health Screening Questionnaire

HUMAN PARTICIPANTS INFORMATION SHEET and

INFORMED CONSENT FORM

Title of study: "Intra-Rater Reliability of the iCARE pro Rebound tonometer

Reason for study: This device meaures intra-ocular pressure (IOP). This is defined as the pressure of the contents inside your eyeball. The purpose of this study is to establish if the tester can attain reproducible meaures with this device in a single setting. If the study is successful then this device will be incorporated into a larger study examining the effects of exercise on IOP.

What is expected of me?:

You will have to attend the physiology laboratory on one occasion. Measurements of the pressure inside both of your eyes will be taken three times with 2-minutes break in between measures. These measurements will be taken in a standing position. The procedure involves a handheld device called a tonometer being held close up to your eye. No numbing drops are required for the pressure measurement. You will feel a slight brush against your eyeball but will experience no pain or discomfort at any point during the testing.

You may feel a slight brush when testing the pressure inside your eyes but you will not feel any pain.

You will not be allowed to partake in the study if;

- You are not aged between 15-40 years old
- You are not actively partaking in Rugby, GAA or Soccer

If you have:

- Current suspected or diagnosed concussion
- History of refractive surgery (LASER eye surgery)
- History of keratoconus (abnormal curvature of the cornea)
- History of glaucoma
- Photosensitive epilepsy
- History of eye trauma
- Diabetes

If you have any questions regarding this study you are welcome to contact; Ben Hunt (Principal Investigator) on 0858102847, email Ben.Hunt@itcarlow.ie; Dr. Clare Lodge (Supervisor) - Claire.Lodge@itcarlow.ie or Dr. David Kent (consultant opthalmologst) – dkent@liverpool.ac.uk.

All personal information gathered in this study will be kept entirely confidential and will comply with data protection guidelines.

Taking part in this study is entirely voluntary. It is your (or your parents) decision and you can withdraw from the study at any time.

By signing this I agree that I fully read and understood this information sheet and consent form and any questions have been answered and I consent that I (or my child) will take part in this study providing that the health questionnaire criteria are met.

Name of participant: _____   Date: _____

Signature of participant: _____

School/College/Team: _____

Name of Parent (if applicable): _____

Signature of Parent (if applicable): _____

Health Screening Questionnaire

Name: _____   School/Club/College_____

Contact number: _____   Male/Female: _____

D.O.B: _____   Age: _____

Please circle your answer to the following questions

1. Do you actively partake in Rugby/GAA/Soccer? – if yes please state which one.	**YES/NO** Sport(s):
2. Do you currently or have you ever suffered from suspected concussion?	**Please tick:** Previous ☐ Current ☐ None ☐
3. Have you ever had LASER eye surgery?	**YES/NO**
4. Do you have any eye conditions? If so please give details.	**YES/NO** Details:
5. Do you have Photosensitive Epilepsy?	**YES/NO**
6. Have you ever had an eye trauma (injury)? If so please give details and which eye. (This doesn't include a black eye)	**YES/NO** Details: **Please tick:** Left ☐ Right ☐
7. Do you have diabetes?	**YES/NO**
8. Do you wear contact lenses?	**YES/NO**
9. Do you have any learning difficulty? If so please give details.	**YES/NO** Details:

Name of participant _____   **Date: _____**

Signature of participant _____

Signature of parent/guardian (if applicable) _____

Appendix C – Exercise Study – Informed Consent and Health Screening Questionnnaire

HUMAN PARTICIPANTS INFORMATION SHEET and

INFORMED CONSENT FORM

Title of study: "The Effects of Exercise on Ocular Metrics."

This study is part of an overall study titled: **"**Ocular Metrics in Concussion: An analytical prospective cohort study to establish normative ocular metrics and their correlation to existing concussion assessment tools in males and females aged 18-31 participating in team sports"

Reason for study: The overall study is aimed at establishing the effects of concussion on ocular metrics. The study is aimed at improving the diagnosis and management of concussion by taking objective measures through the eyes using a technique called optical coherence tomography (OCT). However, if there are significant findings from the main study, it is also necessary to explore the effects of exercise on ocular metrics.

What is Expected of me?: Participation in the trial will take place over the course of 1-week and will involve 3 visits to the physiology laboratory at I.T. Carlow each separated by 48 hrs you will be asked to refrain from other exercise and alcohol for the week. If you wear contact lenses, you will be asked to remove them prior to testing. You must not be suffering from concussion at the time or 6 weeks prior to testing. You must not be suffering from any lower-limb injury that may hamper your ability to complete the treadmill protocol.

Day 1: Familarisation + Anthropometric Data - 20 minutes

Your height and weight will be measured and undergo a final health-screen to ensure it is safe to participate in the trial. You will perform a 5-minute standardised warm-up on the Curve non-motorised treadmill (NMT). You will then perform three 6-second maximal effort sprints with a 2-minute self-paced active recovery in between each sprint. You will then perform a 10-minute self-paced jog on the Curve treadmill to become familiar and comfortable with it.

Day 2: Maximal Sprinting speed (MSS) calculation - 20 minutes

You will perform a standardised warm up on the NMT. You will perform three 6-second maximal sprints with a 2-minute self-paced active recovery in between each sprint. This speed will be used to determine your running speeds for day 3. You will perform another 10-minute self-paced jog on the treadmill to become familiar and comfortable with it.

Day 3: Simulated Team Sport Running Protocol – 50-minutes

Pre exercise measures will be taken of your eyes. The pressure inside your eye will be measured. This involves a handheld device called a tonometer being held close to your eye, you will feel a slight brush against your eyeball but will experience no pain. You will have a picture taken of your eyes. You will place your chin on a rest, the machine will then take an image of you eye using light. You will experience a small flash as the picture is taken. You will not feel any pain or discomfort during this test, which usually takes about to 2-3-minutes to perform. A similar device will be used to measure the prescription (refractive error) of your eyes, this is a standard eye test. You will have to look into a lens and the device automatically measures your eye, this will take about 1-minute. Finally, you will be asked a series of questions about any symptoms (headache, dizziness etc.) you may have. You will be asked to recall and repeat some words, numbers and perform some basic balance and memory testing. These tasks are part of the SCAT3 concussion assessment tool.

You will then perform a 15-minute simulated team sport running protocol which involves running at various changing speeds for the 15-minutes, once the 15-minutes are complete you will have a 2-minute active recovery and a second 15-minutes will be completed. Full instruction will be given before and during the running protocol.

Following this, all pre-exercise measures will be repeated immediately and 10-minutes after exercise.

You will not be allowed to partake in the study if;

-   You are not aged between 18-31 years old
-   You are not actively partaking in Rugby, GAA or Soccer

If you have:

-   Current suspected or diagnosed concussion
-   History of refractive surgery (LASER eye surgery)
-   History of keratoconus (abnormal curvature of the cornea)
-   History of glaucoma
-   Photosensitive epilepsy
-   History of eye trauma
-   Diabetes
-   Current lower limb injury

If you have any questions regarding this study you are welcome to contact; Ben Hunt (Principal Investigator) on 0858102847, email Ben.Hunt@itcarlow.ie

All personal information gathered in this study will be kept entirely confidential and will comply with data protection guidelines.

Taking part in this study is entirely voluntary. It is your (or your parents) decision and you can withdraw from the study at any time.

By signing this I agree that I fully read and understood this information sheet and consent form and any questions have been answered and I consent that I (or my child) will take part in this study providing that the health questionnaire criteria are met.

Name of participant: _____   Date: _____

Signature of participant: _____

School/College/Team: _____

Name of Parent (if applicable): _____

Signature of Parent (if applicable): _____

Health Screening Questionnaire

Name: _____   School/Club/College_____

Contact number: _____   Male/Female: _____

D.O.B: _____   Age: _____

Please circle your answer to the following questions

1. Do you actively partake in Rugby/GAA/Soccer? – if yes please state which one.	**YES/NO** Sport(s):
2. Do you currently or have you ever suffered from suspected concussion?	**Please tick:** Previous ☐ Current ☐ None ☐
3. Have you ever had LASER eye surgery?	**YES/NO**
4. Do you have any eye conditions? If so please give details.	**YES/NO** Details:
5. Do you have Photosensitive Epilepsy?	**YES/NO**
6. Have you ever had an eye trauma (injury)? If so please give details and which eye. (This doesn't include a black eye)	**YES/NO** Details: **Please tick:** Left ☐ Right ☐
7. Do you have diabetes?	**YES/NO**
8. Do you wear contact lenses?	**YES/NO**
9. Do you have any learning difficulty? If so please give details.	**YES/NO** Details:

Name of participant _____   Date: _____

Signature of participant _____

Signature of parent/guardian (if applicable) _____

Appendix D: Exercise Intervention Speed Chart

Speed	Km/hr
Stand	0
Walk	5
Jog	8.5
Run	11
Fast Run	16
Sprint	24.5

HUMAN PARTICIPANTS INFORMATION SHEET and

INFORMED CONSENT FORM

Title of study: "Ocular Metrics in Concussion: An analytical prospective cohort
study to establish normative ocular metrics and their correlation to existing
concussion assessment tools in males and females aged 15-40 participating in
team sports"

Reason for study: Concussion in team sports such as Rugby, GAA and Soccer
has gained a large focus from the media and sports medicine communities in recent
times. In rugby union, concussion is reported to have an incidence of 4.7
concussions per 1000 match hours. Schoolboy rugby players have reported a 26%
lifetime prevalence of concussion.

It is now accepted that suffering a concussive or multiple concussive injuries may
lead to neurological and cognitive consequences in both the short and long term.

There are some pitch-side tools that are used to assess for concussion, but there is
a lack of a direct measurement device, which can quickly reveal if a player is
concussed.

This study is aimed at improving the diagnosis and management of concussion by
taking objective measures through the eyes using a technique called optical
coherence tomography (OCT).

What is expected of me?:

Day 1:

At I.T. Carlow, you will have a picture taken of your eyes, this will be carried out in a
slightly darkened room to allow your eyes to adjust. You will place your chin on a
rest, the device will then take an image of you eye using light. You will experience a
small flash as the picture is taken. You will not feel any pain or discomfort during
this test, which usually takes about to 5-minutes to perform. A similar device will be
used to measure the prescription (refractive error) of your eyes, this is a standard
eye test. You will have to look into a lens and the device automatically takes a
measurement of your eye, this will take about 1-minute. Finally, you will be asked a
series of questions about any symptoms (headache, dizziness etc.) you may have.
You will be asked to recall and repeat some words, numbers and perform some
basic balance and memory testing. These tasks are part of the SCAT3 concussion
assessment tool.

In total, baseline testing will take no more than 10-12 minutes per person.

Only If you receive a suspected concussion

Day 2,3,4: In the unfortunate event that you receive a suspected concussion. You will also be asked to return to I.T. Carlow to have more OCT images taken of your eye and undergo the SCAT3 assessment again. This will be done as soon as possible after the concussion.

If possible this will be repeated 48hrs, 2 weeks, and 2 months after the suspected concussion to investigate for potential changes in the retina.

You will not be allowed to partake in the study if;

- You are not aged between 15-40 years old
- You are not actively partaking in Rugby, GAA or Soccer

If you have:

- Current suspected or diagnosed concussion
- History of refractive surgery (LASER eye surgery)
- History of keratoconus (abnormal curvature of the cornea)
- History of glaucoma
- Photosensitive epilepsy
- History of serious eye trauma (doesn't include black-eyes)
- Diabetes

If you have any questions regarding this study you are welcome to contact; Ben Hunt (Principal Investigator) on 0858102847, email Ben.Hunt@itcarlow.ie; Dr. Clare Lodge (Supervisor) - Claire.Lodge@itcarlow.ie or Dr. David Kent (consultant ophthalmologst) – dkent@liverpool.ac.uk.

All personal information gathered in this study will be kept entirely confidential and will comply with data protection guidelines.

Taking part in this study is entirely voluntary. It is your (or your parents) decision and you can withdraw from the study at any time.

By signing this I agree that I fully read and understood this information sheet and consent form and any questions have been answered and I consent that I (or my child) will take part in this study providing that the health questionnaire criteria are met.

Name of participant: _____ Date: _____

Signature of participant: _____

School/College/Team: _____

Name of Parent (if applicable): _____

Signature of Parent (if applicable): _____

Informed Assesnt Form

Title of study: **"**Ocular Metrics in Concussion: An analytical prospective cohort study to establish normative ocular metrics and their correlation to existing concussion assessment tools in adolescent males and females participating in team sports".

Prinicpal investigator: Ben Hunt

Reason for study: Concussion is an injury that can sometimes happen in team sports when a player hits his/her head. A research study is usually carried out to learn more about a subject. The purpose of this study is to learn more about concussion and to try and improve the way it is tested.

If you decide that you want to be a part of this study, then the principal investigator (Ben Hunt) will come to some of your training sessions and you will be asked to come to I.T Carlow with your parent/guardian.

Day 1: You will travel to I.T Carlow with your parent or guardian. At I.T Carlow, Ben will take a picture of your eyes with a special camera which looks into your eye. Before the picture is taken you will sit in a slightly dark room with your parent or guardian for a few minutes to let your eyes adjust. You will then put your chin on a chin rest and look into the camera. A small amount of light will shine into your eye and the picture will then be taken.

You will not feel anything at all during this test.You will be asked questions about any symptoms (headache, dizziness etc.) you may have. You will be asked to recall and repeat some words, numbers and perform some balance and memory testing. These tests are just to learn about how your balance and memory normally are and are part of the SCAT3 concussion assessment tool. These tests will be performed both before and during training also.

Day 2,3,4: If you get a knock to the head during your sport then you will be asked to come back to IT Carlow with your parent or guardian, you will do the same balance and memory tests from day 1 and Ben will take some more pictures of your eyes.

You do not have to be a part of this study if you do not want to be. If you want to stop after we begin that is fine and your parent/guardian will know all about the study also.

If you understand and want to be a part of this study please write and sign your name below.

Name: _____   Date: _____

Signed: _____

Health Screening Questionnaire

Name: _____   School/Club/College_____

Contact number: _____   Male/Female: _____

D.O.B: _____   Age: _____

Please circle your answer to the following questions

1. Do you actively partake in Rugby/GAA/Soccer? – if yes please state which one.	**YES/NO** Sport(s):
2. Do you currently or have you ever suffered from suspected concussion?	**Please tick:** Previous ☐ Current ☐ None ☐
3. Have you ever had LASER eye surgery?	**YES/NO**
4. Do you have any eye conditions? If so please give details.	**YES/NO** Details:
5. Do you have Photosensitive Epilepsy?	**YES/NO**
6. Have you ever had an eye trauma (injury)? If so please give details and which eye. (This doesn't include a black eye)	**YES/NO** Details: **Please tick:** Left ☐ Right ☐
7. Do you have diabetes?	**YES/NO**
8. Do you wear contact lenses?	**YES/NO**
9. Do you have any learning difficulty? If so please give details.	**YES/NO** Details:

Name of participant _____   **Date: _____**

Signature of participant _____

Signature of parent/guardian (if applicable) _____*