EFFECTS OF SUBCONCUSSIVE HEAD IMPACTS ON CEREBRAL
ACOUSTIC RESPONSE, OCULOMOTOR FUNCTION, AND BALANCE IN
HIGH SCHOOL ATHLETES

by

Alexander A. Salinas

A thesis submitted to the Faculty of the University of Delaware in partial
fulfillment of the requirements for the degree of Master of Science in Exercise Science

Spring 2014

© 2014 Alexander A. Salinas
All Rights Reserved
EFFECTS OF SUBCONCUSSIVE HEAD IMPACTS ON CEREBRAL
ACOUSTIC RESPONSE, OCULOMOTOR FUNCTION, AND BALANCE IN HIGH SCHOOL ATHLETES

by
Alexander A. Salinas

Approved:
__________________________
Thomas W. Kaminski, Ph.D., ATC, FNATA, FACSM
Professor in charge of thesis on behalf of the Advisory Committee

Approved:
__________________________
William B. Farquhar, Ph.D.
Chair of the Department of Kinesiology and Applied Physiology

Approved:
__________________________
Kathleen S. Matt, Ph.D.
Dean of the College of Health Sciences

Approved:
__________________________
James G. Richards, Ph.D.
Vice Provost for Graduate and Professional Education
ACKNOWLEDGMENTS

Several thanks are in order, as an endeavor this great could not be accomplished alone. First, I would like to thank my advisor, Dr. Thomas Kaminski, for his patience and continual support throughout the stages of this project. Additionally, I would like to acknowledge Dr. Buz Swanik and Dr. Joseph Glutting for serving on my thesis committee and aiding in the writing process and statistical analysis, respectively.

Calvin Sibley has provided support throughout the entire course of this project and I could not have asked for a more patient coworker. Joanne Blum, Dan Swasey, Tom McCarten, Malinda Dobbins, Johanna Lukk, Andrew Waer, and Jaclyn Caccese went out of their way to assist in data collection. Jaclyn also aided my understanding of the statistics and instrumentation, as well as provided me with a new research topic when my previous plan collapsed. Finally, I would like to thank my fellow labmates for their varying contributions to this project and my sanity: Andrea DiTrani, Aaron Struminger, Yong Woo An, Sean Stryker, Shawn Hanlon, Molly Johnson, Kelly McGuire, Kelsey Shonk, and Packer Larson.

The past two years would not have been possible without the love and support of my parents, Amalio and Donna, who have endured my triumphs and shortcomings, but always encouraged me to pursue my dreams and push forward. Lastly, I would like to acknowledge Stephanie Gallagher, Elvida Salinas, and countless friends and mentors who have served as a constant reminder that Michigan will always be there for me.
# TABLE OF CONTENTS

LIST OF TABLES ........................................................................................................... vi
LIST OF FIGURES ......................................................................................................... vii
ABSTRACT .................................................................................................................... ix

Chapter

1 INTRODUCTION ............................................................................................................. 1

2 SUBJECTS AND METHODS ......................................................................................... 6
   2.1 Study Participants ................................................................................................. 6
   2.2 Brain Acoustic Monitor ....................................................................................... 6
   2.3 King-Devick Test ................................................................................................. 7
   2.4 Balance Error Scoring System ............................................................................. 7
   2.5 Testing Procedures ............................................................................................... 8
      2.5.1 Baseline Testing ............................................................................................ 8
      2.5.2 Postgame Testing ......................................................................................... 9

2.6 Data Analysis .......................................................................................................... 9

3 RESULTS .................................................................................................................... 10
   3.1 Brain Acoustic Monitor Outputs ......................................................................... 10
      3.1.1 Cerebral Acoustic Response Ratios ............................................................. 10
      3.1.2 Divergence .................................................................................................. 10
   3.2 King-Devick Test ............................................................................................... 11
   3.3 Balance Error Scoring System Output ............................................................... 11

4 DISCUSSION .............................................................................................................. 12

5 FIGURES AND TABLES ............................................................................................. 19

REFERENCES .............................................................................................................. 31
Appendix

A  PARENTAL CONSENT FORM ................................................................. 34
B  ASSENT FORM .................................................................................. 44
C  RECRUITMENT LETTER ...................................................................... 53
D  SPECIFIC AIMS .................................................................................. 55
E  BACKGROUND AND SIGNIFICANCE .................................................... 59
   E.1  Background ................................................................................... 59
   E.2  Subconcussion .............................................................................. 60
   E.3  Pathophysiology ........................................................................... 63
F  PHOTOGRAPHIC RELEASE ................................................................. 65
G  RESEARCH APPROVAL ....................................................................... 68
LIST OF TABLES

Table 1: Participant demographics (Mean ± SD) ........................................ 28

Table 2: Group baseline and posttest data (Mean ± SD) ............................ 29

Table 3: Effect sizes for cerebral acoustic response, oculomotor function, and balance variables... ................................................................. 30
LIST OF FIGURES

Figure 1: The Brain Acoustic Monitor. Two coin-sized sensors were secured to the forehead with an elastic band. A reference sensor was also clamped on the left index finger. Front and side view.................................................. 19

Figure 2: The King-Devick test. The upper left card is the demonstration card that allows participants to become acquainted with testing procedures. The upper right, lower left, and lower right cards are progressively more complex and used for testing................................................................. 20

Figure 3: The Balance Error Scoring System with MobileMat BESS software. Firm surface testing positions include double leg stance (left), single leg stance on non-dominant leg (center), and tandem stance with non-dominant leg in back (right). Participants must maintain posture throughout each trial. These stances are repeated on an unstable surface (2.5” foam pad; not pictured) ............................................................................. 21

Figure 4: Difference in baseline cerebral acoustic ratios between groups, with error bars representing standard deviation. *FB and RUN (p = 0.009) .......................................................... 22

Figure 5: Difference in cerebral acoustic response ratios between groups after physical activity, with error bars representing standard deviation. *FB and SOC (p = 0.023).......................................................... 23

Figure 6: Difference in baseline divergence between groups, with error bars representing standard deviation. †FB and SOC (p = 0.012), FB and RUN (p < 0.001) ‡FB and SOC (p = 0.008), FB and RUN (p < 0.001).............................. 24

Figure 7: Difference in left- and right-brain divergence between groups after physical activity, with error bars representing standard deviation........ 25

Figure 8: King-Devick test time scores (top) and errors committed (bottom) between groups after physical activity, with error bars representing standard deviation......................................................... 26
Figure 9: Differences in balance between groups after physical activity, with error bars representing standard deviation ...........................................................................27

Figure 10: BAM Set-Up........................................................................................................37

Figure 11: King-Devick Test.................................................................................................38

Figure 12: BESS Stances...........................................................................................................39

Figure 13: BESS Scoring Card.................................................................................................39

Figure 14: BAM Set-Up............................................................................................................46

Figure 15: King-Devick Test.................................................................................................47

Figure 16: BESS Stances...........................................................................................................48

Figure 17: BESS Scoring Card.................................................................................................48
ABSTRACT

There is an increasing amount of evidence indicating potentially devastating long-term effects of subconcussive impacts in the absence of clinical symptoms of concussion in high school football players.

**Purpose:** To determine whether subconcussive head impacts produce any immediate cognitive, postural, and physiological changes after athletic participation.

**Methods:** Fifty-nine interscholastic football (FB), soccer (SOC), and track (RUN) athletes provided baseline and post-participation data. Four cerebral acoustic response variables were examined using the Brain Acoustic Monitor (BAM) (Active Signal Technologies, Linthicum Heights, MD). Oculomotor function was assessed via the King-Devick (K-D) test. Balance was evaluated using a computerized version of the Balance Error Scoring System (BESS).

**Results:** Significant changes in left-brain ratio were observed in football players postgame (p = 0.023). Between-group analysis of baseline data for left- and right-brain divergence noted differences as well (FB vs. SOC, p = 0.012, p = 0.008, respectively; FB vs. RUN, p < 0.001, p < 0.001, respectively). There were no significant differences with either oculomotor or balance variables.

**Conclusions:** One game may not provide enough head impact exposure to elicit detectable changes with the utilized instrumentation. Unexpectedly, there were
differences observed in football players’ baseline BAM scores in the absence of significant differences in baseline and post-participation K-D test and BESS scores across all groups, possibly indicating that prior exposures to subconcussive impacts in this cohort of football players may be present.
Chapter 1
INTRODUCTION

Over the past decade, researchers, clinicians, and society have become increasingly interested in sport-related concussions (SRC). This not only involves symptomology, but also the identification and cumulative effects of SRC. Each year, between 1.6 and 3.8 million SRC occur, contributing to the more than $50 billion in annual costs associated with traumatic brain injuries (TBIs) (1-6). Since 2008, all but two states in the USA have passed laws regarding the management of TBIs in youth sports. This has contributed to the education of parents, athletes, and coaches about the manifestation of concussions. Improved symptom recognition allows for appropriate referral to qualified healthcare providers, such as physicians, certified athletic trainers, and other allied healthcare professionals.

Contact and collision sports, such as American football, soccer, ice hockey, and lacrosse have a high incidence of SRC. Concussion incidence rates of 1.55 and 0.59 per 1000 games have been noted in high school American football and soccer players, respectively (7). The incidence rate for football and boys’ soccer has also been reported as 0.64 and 0.19 concussions per 1000 athlete-exposures (8, 9). Lack of reporting on the part of student-athletes wanting to continue playing or not having the capability to recognize SRC signs and symptoms may skew incidence rates. However,
it is hoped continued education and enforcement of rules and regulations may result in incidence rates closer to what is actually occurring (9).

The growing concern regarding long-term effects of concussions has led researchers to examine the onset and duration of physical and cognitive deficits. Concussion research has grown to accommodate an under recognized phenomenon: *subconcussion* (10). Subconcussive blows, or any impact that does not result in a clinically diagnosed concussion, cause an accumulation of damage that does not result in observable symptoms of concussion (1, 10, 11). Additionally, *subconcussion* occurs with rapid acceleration-deceleration of the body or torso, which transmits forces up the spine to the brain producing a “slosh” phenomenon within the cranium (10). These subconcussive head impacts can adversely affect cerebral function (12). Talavage et al. (11) reported neurophysiological deficits (via fMRI) in high school football players without clinically observable symptoms of SRC when compared to preseason baselines. The dorsolateral prefrontal cortex (DLPFC) and cerebellum are associated with working memory and showed significant reductions in fMRI activation levels (11). This group also accrued a significantly greater number of high magnitude impacts (>80g) at the top front of the helmet, directly above the DLPFC (11). As a result, the concussion threshold is likely dynamic and relies on a number of factors, including rotational acceleration, impact location and magnitude, and the accumulation of subconcussive impacts (10, 12-14).

American football and soccer players have a potentially greater risk to develop chronic neurocognitive impairment due to exposure to concussive and subconcussive
forces to the head (9). American football has a high incidence of concussion because of playing style, high rate of impacts, and extent of participation (10). Repetitive heading of the ball in soccer may increase the risk of developing a chronic neurological injury (10). Subconcussive injuries are characterized by damage to the central nervous system in the absence of behavioral deficits (10). Acute cognitive deficits may improve, but subconcussive forces result in irreversible axonal damage and dysfunction (10). Autopsies of ex-professional American football players have shown neurodegeneration beyond that which would be expected based off their lifetime total of clinically diagnosed concussions (1, 11). It is unknown whether a large number of low-magnitude impacts, a small number of high-magnitude impacts, or a combination of both hastens neurodegeneration (15).

It has been previously reported that cerebral blood flow (CBF) is reduced in concussed adolescents compared to control subjects (16). Interestingly, CBF improved toward baseline in only 27% of subjects after 2 weeks and still only 64% after 30 days (16). Reductions in CBF have also been observed in the left posterior, frontal, and subcortical regions of the brain in subjects who suffer from chronic concussive symptoms (17). Acoustic changes, indicated by pulsatile waves impacting the skull, can accompany reduced CBF due to cerebrovascular changes (18). Time variant amplitude and the frequency response of these waveforms can be measured at the forehead. In theory, there is an acoustically detectable change in flow noise when brain injury occurs.
Central to contemporary SRC assessment is consideration for both balance and eye movement testing post-injury (7, 9, 19). There are multiple reports that have indicated oculomotor function is impaired after sustaining a concussion or closed head injury (6, 20, 21). Voluntary eye movement is affected, in addition to reflexive rapid eye movements known as saccades. The King-Devick (K-D) test evaluates brain function through eye movement and requires head-injured subjects to rapidly name lines of numbers off three test cards (6, 21). This quick assessment tool evaluates four cranial nerves (II, III, IV, VI) in less than two minutes. King-Devick test scores are poorer after head trauma and worse after loss of consciousness compared to baseline measures (21). The Balance Error Scoring System (BESS) is often utilized by clinicians as a safe, effective, and affordable balance assessment tool, especially in the absence of sophisticated equipment (7, 19, 22, 23). Finally, there is no information regarding the effects of subconcussive impacts on the above-mentioned assessments.

The effects of repetitive subconcussive head impacts are not fully understood (12, 24). The minimum time span in which concussion-related changes occur has not been determined. Current clinical measures are unable to identify neurological deficits related to an accumulation of subconcussive impacts (11). It remains unknown whether concussion-related deficits will be noticeable after 30-80 minutes of participation in sports with varying degrees of contact and collision. Utilizing measures from the Brain Acoustic Monitor (BAM), K-D test, and BESS, the primary goal of this study was to determine whether subconcussive head impacts cause immediate cognitive, postural, and physiological changes after participation in
athletics. Secondarily, we were interested in differences in baseline data between groups due to past studies associating subconcussive head impacts with various pathological conditions (1, 9-12, 15, 24).
Chapter 2

SUBJECTS AND METHODS

2.1 Study Participants

Cerebral acoustic response, oculomotor function, and balance were assessed in 59 healthy male athletes from a local high school (Table 1). Participants were divided into three groups according to sport, representing varying levels of contact or collision: varsity football (FB), varsity soccer (SOC), or indoor track (RUN). Football players frequently encounter collisions as part of normal gameplay. Soccer players experience occasional contact via impacts with other players and purposeful heading of the ball. Track athletes do not experience contact in their sport and served as the control group.

Participants were excluded from this study if they suffered a lower extremity injury in the 14 days prior to testing. Lack of participation in their respective sport or presenting with symptoms of a sport-related concussion resulted in exclusion from further participation in this study. Prior to testing, all parents and participants signed institutionally approved consent and assent forms, respectively (UD IRB #486706-2).

2.2 Brain Acoustic Monitor

The BAM (Active Signal Technologies, Linthicum Heights MD) was used to evaluate cerebral acoustic responses (Fig. 1). Two coin-sized sensors were fastened to
the subjects’ foreheads as well as a reference sensor on the left index finger. Five to ten 10-second trials were taken from each subject, depending on data/signal quality. The BAM analyzes the incoming signals in both the time and frequency domains. Ratio, in each hemisphere, is measured directly from the time domain signal (raw data). Divergence, in each hemisphere, is measured from the frequency responses given by each brain sensor and a control (digital arterial) sensor. Ratio is an initial crude assessment of signal morphology, which calculates the peak excursion above the mean line divided by the peak excursion below the mean. Divergence is defined as the maximum deviation of the brain signal relative frequency above 0 decibels (dB). In patients with either TBI or mild TBI, the ratio decreases and divergence increases, corresponding to an abnormal variability in cerebral blood flow (18).

2.3 King-Devick Test

The K-D test was used to assess oculomotor function (Fig. 2). Subjects recited the rows of numbers off the demonstration card as quickly as possible without making any errors. The card was held by the reader at a self-selected distance. Glasses and contact lenses were allowed, however using a finger to guide reading was discouraged. Subjects then read each of the three test cards under the same conditions while being timed with a stopwatch.

2.4 Balance Error Scoring System

The BESS was used to assess balance (Fig. 3). Three 20-second trials were conducted under two surface conditions: firm and foam. The three trials were bare feet together, single-leg stance (non-dominant), and tandem stance (non-dominant in
back). Subjects were asked to stand with their eyes closed and hands over their iliac crests for all trials. MobileMat BESS software (Tekscan, Boston MA) was utilized to record errors: hands lifted off iliac crest, opening eyes, stepping, stumbling, or falling, moving the hip into >30 degrees of abduction, lifting forefoot or heel, and remaining out of testing positions >5 seconds.

2.5 Testing Procedures

Two consecutive home football games were chosen for data collection. Eleven subjects were tested in each session. Two consecutive home soccer games were also chosen. Ten subjects were tested in the first session and five in the second session. Control group data was collected from the indoor track team over six weeks of practice; 3-5 subjects were tested each day. Multiple testing sessions were conducted for two reasons: it allowed maximal subject recruitment and reduced attrition post-participation due to shorter waiting times.

2.5.1 Baseline Testing

Three subjects were called to the testing site (high school athletic training room or nurse’s office) during the final period of the school day. One subject was asked to sit down as his forehead was wiped with an alcohol pad and set up on the BAM to allow the sensors to couple to the skin. The BAM trials were conducted by asking the subject to sit comfortably, breathe normally, and close his eyes. The K-D test was also implemented during this time. Meanwhile, another subject was taken through BESS testing procedures. Subjects rotated through the stations to provide
data for the BAM, K-D test, and BESS; this process was repeated for subsequent groups of subjects.

2.5.2 Postgame Testing

Postgame testing data were collected at least 30 minutes after the completion of the game or practice. Subjects were taken through the BAM, K-D test, and BESS on a first come, first serve basis. Participation in the study was complete after this data collection.

2.6 Data Analysis

Statistical analyses were performed using the Statistical Program for the Social Sciences (IBM, Armonk, NY, USA). The independent variables evaluated in this study were the varying levels of contact or collision in three sporting groups. Seven dependent variables were examined. Left/right-brain ratios (LBR/RBR) and left/right-brain divergence (LBD/RBD) functioned as the four measured cerebral acoustic response variables for the BAM. Total time to complete and number of errors committed in the K-D test served as additional variables. Total errors committed across all BESS trials served as the final variable. All data were analyzed with an alpha level set \( a \text{ priori} \) at \( p \leq 0.05 \). Subjects that provided all seven measures before and after participation were included in the data analysis. Separate analyses of covariance (ANCOVA) were used to compare baseline and postgame means within and between groups. Additionally, an analysis of variance (ANOVA) was used to compare baseline means of each factor within groups, and where appropriate, a Bonferroni correction was used for post hoc analysis.
Chapter 3
RESULTS

3.1 Brain Acoustic Monitor Outputs

All BR and BD baseline and posttest data are presented in Table 2. These baseline means served as covariates for their respective groups in the ANCOVA.

3.1.1 Cerebral Acoustic Response Ratios

The ANOVA results comparing baseline cerebral acoustic response ratios indicated no significant differences between the groups for LBR, however there was a significant difference between the groups for RBR ($F = 5.740; p = 0.006$; Fig. 4). On post hoc testing, it was determined that RBR was significantly different between FB and RUN (control group). There was no difference in baseline RBR values between FB and SOC. The baseline to posttest values for RBR remained constant, however LBR was significantly different after exercise between FB and SOC ($F = 4.093; p = 0.023$; Fig. 5). Effect sizes for the above variable are shown in Table 3.

3.1.2 Divergence

The ANOVA comparing baseline divergence values indicated a significant difference in LBD between FB and both SOC and RUN ($F = 11.699; p < 0.001$). Furthermore, there was significant differences in RBD values between FB and both SOC and RUN ($F = 10.588; p < 0.001$; Fig. 6).
In our baseline to posttest comparison for both LBD and RBD, there were no significant differences following the ANCOVA (Fig. 7). Effect sizes for the above variables are presented in Table 3.

3.2 King-Devick Test

King-Devick Test timed scores and errors are displayed in Figure 8. There were no significant differences between groups or from baseline to posttest analysis. The mean K-D test time values ranged from 40.8 – 48.3 seconds. Additionally, very few errors were committed during the K-D test trials. Effect sizes for the above variables are displayed in Table 3.

3.3 Balance Error Scoring System Output

Balance Errors Scoring System scores are displayed in Figure 9. Although the football BESS scores were lower (better) than the other two groups, both baseline and post exercises, these differences were not significant. Effect sizes for the above variable are shown in Table 3.
Chapter 4

DISCUSSION

This study compared the changes across various clinical metrics for assessing SRC after participation in certain high school sports. Our results suggest that the football athletes involved in this study demonstrated changes in LBR immediately after participation, while their counterparts in soccer and running were unaffected (Fig. 5). Although there were significant differences in RBR at baseline comparing football to runners, there were no significant changes in RBR in any group after participation. The nature of tackle football involving the use of helmets inevitably involves repetitive blows to the helmet during the course of a game. The football players involved in this study came from a variety of positions, including lineman, linebackers, and skilled position players, all whom are subject to repetitive impacts based on the nature of their positions. The repetitive impacts can involve a variety of locations surrounding the helmet, and impacts to the top and front likely dominate (11, 13). As a result, the decreased LBR from baseline to postgame may be attributed to these subconcussive impacts. Deficits in cerebral blood flow following concussion in pediatric patients have been observed by Maugans et al. (16); we contend that a similar mechanism is responsible for the changes in cerebral acoustic response. We acknowledge that the significant decrease in LBR in our football participants is very similar to the decrease seen in our control runners, which was not statistically
significant (Fig. 5). One might argue that, due to the low number of subjects across all groups, this decrease in LBR may just be related to measurement error. Although there was a drop in mean ratios in our study (Table 3), they did not fall below the cutoff threshold of 2.0 suggested by Acocello et al. (18), who indicated that values less than 2.0 were a threshold point for brain injury in TBI patients. Correspondingly, our LBR and RBR values for each group were similar to those reported by Acocello et al. (18), and all were above the 2.0 ratio threshold.

Divergence, as outputted from the BAM, is a measure of how far the frequency signal deviates above a relative frequency of 0 dB; each brain sensor is compared to the frequency distribution of the reference sensor to obtain a ratio using a built-in algorithm (18). Differences in baseline divergence values were noted in football players on both sides of the brain. Divergence values less than 10 dB are considered healthy (18). Although there was no significant difference between the groups after participation, the football players did have significantly higher mean left- and right-brain divergence compared to their soccer and track counterparts at baseline (Fig. 6). This finding is especially alarming and may be attributed to prior years of participation in the sport of football and the consequential subconcussive impacts. The exact pathophysiological origin of these differences within the brain is likely complex and cannot be theorized solely by measures of cerebral acoustic response (15).

In addition to the advanced assessment equipment involving the BAM, this study employed a more contemporary and convenient tool commonly used in the evaluation of SRC, namely, the K-D test. This test provided a rapid assessment of
cognitive visual processing and performance (25). We hypothesized there would be oculomotor performance deficits in football players as compared to soccer players and runners after participation. Contrary to our hypothesis, the results did not indicate any significant differences between baseline and post in any of the groups. In fact, and in support of previous research (6, 21), the time to complete the K-D test improved and can most likely be attributed to a learning effect. Our K-D test times fall within the range of those previously reported in non-concussed subjects (6, 21). The literature is void of values involving adolescent subjects to which our study can be compared. Of note, and with regard to the three different high school athlete groups studied, we notice better K-D test performance times in the football players compared to soccer players and runners; likewise, the soccer players had lower times and better performance than the runners (Fig. 8). Perhaps these differences can be attributed to the rapid-decision making nature, especially with regard to both football and soccer, as compared to the runners. For example, soccer and football both require rapid eye movements as play unfolds in their respective sports; unlike runners, who traditionally only look forward as they run.

Since it was reported in 1999, the BESS has been an integral part of concussion assessment and management (26). The usefulness and ease of administering this test allowed us to employ it in our study without much impact on testing time. In particular, the unique and novel computerized BESS test used in this study further enhanced the utility of this test. Similar to the K-D test, we hypothesized that there would be differences in BESS test performance (worse/more errors) in
football players compared to soccer players and runners. Our results determined that there were no significant differences in balance at baseline and after participation (Fig. 9). Interestingly, the graphic representation shown in Figure 9 demonstrates lower values in the football cohort as compared to both soccer and runners. We claim that the majority of errors in the BESS scores across all groups at both baseline and post can be attributed to two of the most difficult BESS conditions, including the tandem and single-leg stances on the foam surface. Although outside the scope of this study, we highly recommend additional study to examine the possibility of removing these two test positions from the BESS; because even in a non-concussed state, they are difficult to perform. The impact of fatigue was a concern in this study due to the proximity of our data collection efforts to the conclusion of the respective sport activity (approximately 30 min). Susco et al. previously reported an interlude of twenty minutes post-exercise as sufficient to reassess balance (22). Considering the lack of differences post-participation in our three groups, we are confident that fatigue did not have an impact in our BESS measures.

Traditional SRC evaluation/treatment has typically involved a multifactorial approach targeting a variety of system measurements. For purposes in our study, we put together a clinically relevant, easy to use, and efficient battery of tests to look at three such systems, including cerebral acoustic response, oculomotor function, and balance. Our results indicate some level of sensitivity with regard to BAM measurements, while oculomotor function and balance assessments were insignificant. Although our results concerning cerebral acoustic response are interesting and
intriguing, further study is warranted. Perhaps the greatest benefit to this new and novel method of assessing SRC is the fact that it can be performed shortly after a suspected injury occurs in a relatively short time period. From a clinical perspective, this is extremely important because return-to-play decisions are often made in very short time periods. Of importance is the fact that the functionally observed impairments (FOI; via BAM) are present in the absence of clinically observed impairments (COI; via K-D test and BESS). This further highlights the premise that time and careful attention to all system impairments post-concussion is warranted. A recent study by Talavage et al. (11) utilizing fMRI in non-concussed football players reinforces that these FOI are present without COI. The absence of COI in the presence of FOI represents stress on neural tissue, which occurs throughout an athletic season, and due to its subclinical nature can avoid detection by a healthcare provider (11). These neurophysiological and neurocognitive performance deficits from subconcussive impacts persist over time and increase the likelihood of long-term neurodegeneration (11, 15). The cause of the onset of FOI is unknown and likely relies on a number of factors, including position, number of years participating in the sport, and concussion history. Speculation regarding these observations is beyond the scope of this study and additional investigation is needed to improve understanding.

There are limitations in the design of this study. Perhaps most importantly, this study sought to observe the proposed effects of subconcussive head impacts, but made no attempt to quantify the impacts accrued between testing sessions. We also point out that our sample size was low and report that we lost seven participants from
baseline to post participation for a variety of technological and logistical reasons. Future studies could involve student-athletes from multiple high schools. However, the convenience of accessing the student-athletes at the high school involved in this study made it easier for us to complete this preliminary work. One unavoidable obstacle in the study of high school athletes is they may participate in several contact or collision sports per year and have constant exposure to subconcussive and concussive impacts. By recruiting numerous high schools, participants will be able to be tested during their “primary” athletic season, further increasing homogeneity within groups. Furthermore, one game may be too short a period to detect subconcussive symptoms. Broadening the scope of this study to one month or one season may produce different outcomes. Subconcussive impacts have cumulative effects (11, 12, 24), therefore recording each participant’s number of years involved with each sport and number of diagnosed concussions may prove beneficial. The BAM has limitations and its measures could have been strengthened by additional testing periods after exercise. This is the first known use of this device on athletes of any level after participation in their respective sports. The device’s injury thresholds were established after studies of severe head trauma and stroke patients and it is unknown if these same thresholds should be adjusted for less severe injuries (18).

In conclusion, the BAM appears to show some usefulness in the assessment of cerebral acoustic response in this cohort of interscholastic athletes. The difference in divergence at baseline between the football players and their soccer and running counterparts is of interest and warrants further study in larger groups of interscholastic
athletes and in a concussed state. This is especially important with recent evidence suggesting neurodegenerative changes in the brain following cumulative head impacts in various retired professional athletes (15). The lack of differences in measures of oculomotor function and balance performance suggest that these two contemporary concussion-related measurements may not be sensitive enough to study changes following subconcussive impacts.
Figure 1: The Brain Acoustic Monitor. Two coin-sized sensors were secured to the forehead with an elastic band. A reference sensor was also clamped on the left index finger. Front and side view.
**Figure 2:** The King-Devick test. The upper left card is the demonstration card that allows participants to become acquainted with testing procedures. The upper right, lower left, and lower right cards are progressively more complex and used for testing.
**Figure 3:** The Balance Error Scoring System with MobileMat BESS software. Firm surface testing positions include double leg stance (left), single leg stance on non-dominant leg (center), and tandem stance with non-dominant leg in back (right). Participants must maintain posture throughout each trial. These stances are repeated on an unstable surface (2.5” foam pad; not pictured).
Figure 4: Difference in baseline cerebral acoustic response ratios between groups, with error bars representing standard deviation. *FB and RUN ($p = 0.009$)
**Figure 5**: Difference in cerebral acoustic response ratios between groups after physical activity, with error bars representing standard deviation.
*FB and SOC ($p = 0.023$)
**Figure 6:** Difference in baseline divergence between groups, with error bars representing standard deviation.

†FB and SOC ($p = 0.012$), FB and RUN ($p < 0.001$)
‡FB and SOC ($p = 0.008$), FB and RUN ($p < 0.001$)
Figure 7: Difference in left- and right-brain divergence between groups after physical activity, with error bars representing standard deviation.
**Figure 8**: King-Devick test time scores (top) and errors committed (bottom) between groups after physical activity, with error bars representing standard deviation.
Figure 9: Differences in balance between groups after physical activity, with error bars representing standard deviation.
Table 1: Participant demographics (Mean ± SD).

<table>
<thead>
<tr>
<th></th>
<th>Football (n = 21)</th>
<th>Soccer (n = 9)</th>
<th>Runners (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>16.5 ± 0.7</td>
<td>16.2 ± 1.4</td>
<td>16.9 ± 1.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>181.5 ± 6.5</td>
<td>178.0 ± 9.2</td>
<td>175.0 ± 6.1</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>87.1 ± 21.3</td>
<td>69.4 ± 10.5</td>
<td>65.5 ± 9.8</td>
</tr>
<tr>
<td></td>
<td>Football</td>
<td>Soccer</td>
<td>Runners</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>LBR&lt;sub&gt;base&lt;/sub&gt;</td>
<td>3.27 ± 0.96</td>
<td>3.11 ± 1.01</td>
<td>3.06 ± 0.80</td>
</tr>
<tr>
<td>LBR&lt;sub&gt;post&lt;/sub&gt;</td>
<td>2.35 ± 0.75</td>
<td>3.05 ± 0.87</td>
<td>2.38 ± 0.62</td>
</tr>
<tr>
<td>RBR&lt;sub&gt;base&lt;/sub&gt;</td>
<td>3.60 ± 1.06</td>
<td>3.60 ± 0.90</td>
<td>2.71 ± 0.83</td>
</tr>
<tr>
<td>RBR&lt;sub&gt;post&lt;/sub&gt;</td>
<td>2.33 ± 0.93</td>
<td>2.83 ± 0.83</td>
<td>2.48 ± 0.81</td>
</tr>
<tr>
<td>LBD&lt;sub&gt;base&lt;/sub&gt;</td>
<td>12.63 ± 7.53</td>
<td>5.01 ± 6.01</td>
<td>3.61 ± 5.11</td>
</tr>
<tr>
<td>LBD&lt;sub&gt;post&lt;/sub&gt;</td>
<td>5.05 ± 4.83</td>
<td>1.31 ± 3.93</td>
<td>5.42 ± 5.61</td>
</tr>
<tr>
<td>RBD&lt;sub&gt;base&lt;/sub&gt;</td>
<td>11.89 ± 9.00</td>
<td>3.85 ± 3.14</td>
<td>3.54 ± 3.65</td>
</tr>
<tr>
<td>RBD&lt;sub&gt;post&lt;/sub&gt;</td>
<td>4.98 ± 5.24</td>
<td>2.07 ± 3.66</td>
<td>6.17 ± 5.19</td>
</tr>
<tr>
<td>K-D&lt;sub&gt;base&lt;/sub&gt; (s)</td>
<td>44.0 ± 7.8</td>
<td>46.9 ± 6.4</td>
<td>48.3 ± 7.3</td>
</tr>
<tr>
<td>K-D&lt;sub&gt;post&lt;/sub&gt; (s)</td>
<td>40.8 ± 7.7</td>
<td>43.9 ± 6.9</td>
<td>44.7 ± 10.1</td>
</tr>
<tr>
<td>Err&lt;sub&gt;base&lt;/sub&gt;</td>
<td>0.2 ± 0.5</td>
<td>0.1 ± 0.3</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Err&lt;sub&gt;post&lt;/sub&gt;</td>
<td>0.2 ± 0.7</td>
<td>0.0 ± 0.0</td>
<td>0.3 ± 0.5</td>
</tr>
<tr>
<td>BESS&lt;sub&gt;base&lt;/sub&gt;</td>
<td>19.0 ± 6.0</td>
<td>20.6 ± 7.7</td>
<td>23.8 ± 7.3</td>
</tr>
<tr>
<td>BESS&lt;sub&gt;post&lt;/sub&gt;</td>
<td>20.7 ± 8.9</td>
<td>23.8 ± 7.5</td>
<td>23.6 ± 7.9</td>
</tr>
</tbody>
</table>

LBR = left-brain ratio; RBR = right-brain ratio; LBD = left-brain divergence; RBD = right-brain divergence; K-D = King-Devick test; s = time in seconds; Err = King-Devick errors; BESS = Balance Error Scoring System (errors)
Table 3: Effect sizes for cerebral acoustic response, oculomotor function, and balance variables.

<table>
<thead>
<tr>
<th></th>
<th>FB-SOC</th>
<th>FB-RUN</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBR_{base}</td>
<td>0.16</td>
<td>0.24</td>
</tr>
<tr>
<td>LBR_{post}</td>
<td>-0.86*</td>
<td>-0.05</td>
</tr>
<tr>
<td>RBR_{base}</td>
<td>-0.01</td>
<td>0.95*</td>
</tr>
<tr>
<td>RBR_{post}</td>
<td>-0.57</td>
<td>-0.18</td>
</tr>
<tr>
<td>LBD_{base}</td>
<td>1.12*</td>
<td>1.43*</td>
</tr>
<tr>
<td>LBD_{post}</td>
<td>0.85</td>
<td>-0.07</td>
</tr>
<tr>
<td>RBD_{base}</td>
<td>1.32*</td>
<td>1.32*</td>
</tr>
<tr>
<td>RBD_{post}</td>
<td>0.65</td>
<td>-0.23</td>
</tr>
<tr>
<td>KD_{base}</td>
<td>-0.41</td>
<td>-0.57</td>
</tr>
<tr>
<td>KD_{post}</td>
<td>-0.43</td>
<td>-0.43</td>
</tr>
<tr>
<td>Err_{base}</td>
<td>0.19</td>
<td>0.74</td>
</tr>
<tr>
<td>Err_{post}</td>
<td>0.56</td>
<td>-0.14</td>
</tr>
<tr>
<td>BESS_{base}</td>
<td>-0.23</td>
<td>-0.72</td>
</tr>
<tr>
<td>BESS_{post}</td>
<td>-0.37</td>
<td>-0.34</td>
</tr>
</tbody>
</table>

*p-value associated with effect size is significant

FB = football; SOC = soccer; RUN = runners
REFERENCES


Appendix A

PARENTAL CONSENT FORM
University of Delaware
Parental Consent Form

Title of Project: Investigation of Cerebral Blood Flow in Healthy and Concussed Athletes

Principal Investigator: Jaclyn B. Caccese

Advisors: Dr. Thomas W. Kaminski, Dr. Andrew Reisman, Dr. Geoffrey Gustavsen

Your child is being asked to participate in a research study. This form tells you about the study including its purpose, what your child will do if he/she decides to participate, and any risks and benefits of being in the study. Please read the information below and ask the research team questions about anything we have not made clear before you decide whether your child may participate. Your child’s participation is voluntary and he/she can refuse to participate or withdraw at anytime without penalty or loss of benefits to which he/she is otherwise entitled. If your child decides to participate, you will be asked to sign this form and a copy will be given to you to keep for your reference.

WHAT IS THE PURPOSE OF THIS STUDY?

The primary purpose of this study is to determine the effects of concussions on cerebral blood flow (blood flow to the brain) across age ranges, and to compare these effects to differences seen in neurocognitive testing. A secondary purpose of this study is to determine the effects of a season of playing a sport, including potentially sub concussive blows, on cerebral blood flow.

To measure cerebral blood flow, quantitatively, we will use the Brain Acoustic Monitor. The Brain Acoustic Monitor (BAM) is an investigational device created by Active Signal Technologies that measures blood flow to the brain non-invasively (no skin will be broken; the two sensors look and feel like a stethoscope). Cerebral blood flow is changed when a person experiences mild traumatic brain injury, such as a concussion. By measuring cerebral blood flow at baseline (before the start of a season) and post-concussion, we can determine the effects that a concussion has on cerebral blood flow. Additionally, by taking measures at the end of a season, and comparing these measures to the baseline measurements, we can determine the effects of a season of playing a sport on cerebral blood flow. Finally, by including high school and collegiate athletes, we can determine the differences in how cerebral blood flow is affected across age ranges.

As an investigational device, one aim of this investigation is to test the BAM in a population of athletes with sports-related concussions. The data collected on both concussed and non-concussed athletes will be shared with Arthur Cooke at Active Signal Technologies to improve sensitivity and specificity of the BAM.
Data obtained in this investigation may be used in the thesis and dissertation of Jaclyn B. Caccese, principal investigator.

Your child is being asked to take part in this study because your child is a student-athlete from a high school near the University of Delaware.

This study will be done over a three-year span, but your child will only be asked to participate for one season. Three hundred student-athletes from the University of Delaware will be invited to participate in this study.

Nine hundred student-athletes from surrounding high schools, including St. Mark’s High School, A.I. DuPont High School, Wilmington Friends School, Tower Hill School, Charter School of Wilmington, and Newark High School will be invited to participate in this study.

Student-athletes will be recruited from the UD intercollegiate D1 teams, including: football, men’s soccer, women’s soccer, and men’s lacrosse, and from UD intercollegiate club teams, including: men’s soccer, women’s soccer, men’s lacrosse, men’s ice hockey, and women’s ice hockey teams. Members of these teams will be recruited because of the head-contact nature of their sport. Additionally thirty UD intercollegiate club men’s cross country or UD intercollegiate D1 women’s cross country runners will be invited to participate.

Interscholastic student-athletes invited to participate will be members of the football, boy’s soccer, girl’s soccer, ice hockey, or boy’s lacrosse teams. Again, members of these teams have been selected because of the head-contact nature of their sport. Additionally, fifty boy’s and girl’s cross country student-athletes will be invited to participate from these schools.

Cross country student-athletes who participate in this investigation may not participate in any head-contact sports during the season. Additionally, cross country athletes included must have no previous history of concussion.

Your child should not participate in this investigation if he/she is currently exhibiting symptoms of a concussion (i.e. headache or a feeling of pressure in the head, temporary loss of consciousness, confusion or feeling as if in a fog, amnesia surrounding the traumatic event, dizziness or "seeing stars", ringing in the ears, nausea or vomiting, or slurred speech) or if a physician as has diagnosed him/her as concussed and he/she is currently unable to participate in his/her sport. If you sustain a concussion during the season that requires an over-night hospital stay, you will be excluded from post-concussion measurements.

WHAT WILL YOU BE ASKED TO DO?

Your child will be asked to report to the athletic training room at your child’s high school for BAM, King-Devick, and BESS tests. ImPACT testing may be done in a computer lab at your child’s high school or in the athletic training room, if necessary.
Your child will be asked to report for two test sessions, if he/she is not diagnosed with a concussion during the season. The first test session will be before the start of your child’s sport season and the second test session will be at the end of your child’s sport season. Each session will take 30-45 minutes of his/her time, this is 60-90 minutes total.

Session 1 – Baseline Measurements (All Student-Athletes)

Before the start of your child’s season, he/she will have BAM readings, ImPACT tests, King-Devick tests, and BESS tests done to serve as baseline measurements. Your child will also fill out a concussion history questionnaire. Please see the description of each test below.

**BAM**

The Brain Acoustic Monitor (BAM), in its most fundamental principle of operation, is a brain stethoscope with a display. Therefore, two non-invasive (does not break the skin or physically enter the body) sensors will be secured to your child’s forehead by an elastic band (see Figure 1) and a reference sensor will be placed on your child’s wrist. Each trial takes 5-10 seconds and your child will have 5 trials of data collected at baseline. Your child will be asked to sit still and refrain from talking throughout testing. No action is required on their part. The BAM does not have FDA approval and is still considered an investigational device.

Figure 10: BAM Set-Up.
**ImPACT Testing**
The Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) test is computerized and takes about 25 minutes to complete. The program measures multiple aspects of cognitive functioning in athletes, including: attention span, working memory, sustained and selective attention time, response variability, non-verbal problem solving, and reaction time. If your child’s school already requires baseline pre-season ImPACT testing, he/she will not be required to do this again. By signing this document you give permission that this information may be shared with the research staff. If your child’s school does not require baseline pre-season ImPACT testing, the research staff will ask him/her to complete this computerized test. ImPACT testing has been proven reliable in post-concussion testing and can be used for return-to-play decisions. If your child sustains a concussion, during the season, you give permission that this information may be shared with his/her athletic trainer and/or physician.

**King-Devick Test**
The King-Devick Test for Concussions is a two-minute test that requires your child to read single digit numbers displayed on cards. The test consists of four cards, a demonstration card and three test cards (see Figure 2). Your child will always be asked to read from left to right and from top to bottom. King-Devick testing has been proven reliable in post-concussion testing and can be used for return-to-play decisions. If your child sustains a concussion, during the season, you give permission that this information may be shared with his/her athletic trainer and/or physician.

Figure 11: King-Devick Test.
**BESS Test**

The Balance Error Scoring System (BESS) evaluates your child's balance by having him/her stand on either the Tekscan mat or a balance mat placed over the Tekscan mat using the stances indicated (see Figure 3). Your child will be instructed to stand as still as possible with his/her hands on his/her hips for each of the conditions listed (total of 6). Each trial will last 20 seconds and the Tekscan mat will automatically score your child's balance. Errors are scored using a standardized scoring system (see Figure 4). Errors for losing balance will be recorded and used in the analysis. If your child's school already requires baseline pre-season BESS testing, he/she will not be required to do this again. By signing this document you give permission that this information may be shared with the research staff. If your child's school does not require baseline pre-season BESS testing, the research staff will ask him/her to complete this balance test. BESS testing has been proven reliable in post-concussion testing and can be used for return-to-play decisions. If your child sustains a concussion, during the season, you give permission that this information may be shared with his/her athletic trainer and/or physician.

Figure 12: BESS Stances. 

Figure 13: BESS Scoring Card.

**Follow-Up Measurements**

Sessions 2-10, 12 – Post-Concussion Testing (Sport-Related Concussed Student-Athletes Only)

If your child is diagnosed with a sport-related concussion by a certified athletic trainer and this diagnosis is confirmed by a physician, your child will be asked to participate in 9 or 10 additional test sessions. By signing this document, you give permission that the diagnosis of a concussion may be shared with the research staff (see “Accessing your medical records” below). Additional test sessions 1-7 will only be 5-10 minutes in length. Test sessions 8 and 9 will be 30-45 minutes in length. Test session 10 is only required in a small subset of the concussed population and will be 30-45 minutes in length. This adds 1 hour and 30 minutes to 3 hours to your child’s total time commitment; therefore, he/she will be asked to volunteer 2 hours and 30 minutes to 4 hours and 30 minutes of his/her time, total.
If your child is diagnosed with a sport-related concussion, your child will repeat BAM, King-Devick, and BESS tests within 24 hours of sustaining a concussion and then again every 24 hours for 7 days (additional sessions 1-8). The ImPACT test will be repeated on day 7 post-concussion only, which is why additional session 8 is 30-45 minutes in length. Your child will then be evaluated again 30 days post-concussion (additional session 9). If BAM measures do not return to baseline by 30 days post-concussion, your child will be asked to test again 6 months post-concussion (additional session 10).

These test sessions may require that your child reports for testing on weekends (Saturdays and/or Sundays).

Session 2 or 11 – End-of-Season (All Student-Athletes)

At the end of your season, regardless of whether or not you have sustained a sports-related concussion, you will have BAM readings, ImPACT tests, King-Devick tests, and BESS tests done to serve as post-season comparisons.

ACCESSING YOUR CHILD’S MEDICAL RECORDS:
If your child sustains a concussion during the time he or she is participating in this study and is seen by a Physician our research team will need access to the diagnosis from your child’s doctor. Federal and state laws, including the Health Insurance Portability and Accountability Act (HIPAA), protect your child’s privacy as it relates to medical records. This part of the informed consent form tells you what information about your child may be collected in this study and who might see or use it.

By agreeing to participate in this research you also authorize the research team to contact the physician your child may see in the case of a concussion. We will ask the doctor to confirm if your child was diagnosed with a concussion or not. This will be the only information requested from your child’s physician.

The use and sharing of your child’s information has no time limit. You can withdraw your permission to use and share your child’s information at any time by writing to Jaclyn B Caccese at the address listed below. If you do withdraw your permission, your child’s part in this study will end and no further information about your child will be collected. Your cancellation would not affect information already collected for the study.

Participation in this research is completely voluntary. If your child agrees to participate, you also authorize us to access his/her medical diagnosis in the case of a concussion. Your decision to participate or not will not affect future medical services and treatment you may need.
WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The Brain Acoustic Monitor (BAM) is a non-invasive device similar to a stethoscope that listens to your heartbeat. **This is not an FDA-approved device.**

There are no known physical risks in completing the computerized ImpACT test or King-Devick test. The tests do require active attention, concentration, and mental effort and have in some cases caused mental frustration (particularly when completed following mild brain trauma or concussion). If severe mental frustration is apparent, testing will be discontinued.

WHAT ARE THE POTENTIAL BENEFITS?

Although there is no guarantee, the use of the three testing procedures (the ImpACT, King-Devick, and BESS tests) may allow team physicians and athletic trainers to make better return-to-play decisions following concussions, if your child sustains a concussion during the season.

The results from the ImpACT, King-Devick, and BESS tests will be shared with athletic trainers and physicians at your child's institution. Because of the investigational nature of the BAM, cerebral blood flow readings will not be shared with any athletic trainers, physicians, coaches, parents, or participants.

Whether or not your child sustains a concussion, the confirmation of the Brain Acoustic Monitor (BAM) as a diagnostic tool for concussions may allow for a more quantitative measurement of brain injury, thus allowing team physicians and athletic trainers to make better return-to-play decisions.

HOW WILL CONFIDENTIALITY BE MAINTAINED?

Although your child will not be anonymous to the researcher, you and your child can be ensured confidentiality outside of that directly associated with the research. Your child’s name will not be utilized in data analysis. His/her paper tests will be identified by randomly assigned subject identifiers, and your child’s name and code will be kept solely by the principal investigator in a locked cabinet.

However, subject information from the ImpACT, King-Devick, and BESS tests may be shared with the athletic training staff and physicians.

All data will be kept for 3 years, as per IRB request. This consent form will be locked in a file cabinet in the Athletic Training Lab at the University of Delaware. This lab is locked when unattended. All other paper data records will be locked in a filing cabinet in the same facility, as well. Electronic Data Records will be stored in password-protected files.

Paper and electronic data records will be stored for three years in password-protected files and then securely destroyed.
BAM data will be shared with Arthur Cooke at Active Signal Technologies (Linthicum Heights, MD). No personal identifiers (i.e. names) will be sent with the data. The files will be sent electronically in an encrypted format. Sharing of this data is required to improve sensitivity and specificity of the BAM. This data will not be used when applying for FDA approval.

Data will be disseminated through group discussions, presentations, and publications with your child’s identifying information removed.

We will make every effort to keep all research records that identify your child confidential to the extent permitted by law. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Your child’s research records may be viewed by the University of Delaware Institutional Review Board, but the confidentiality of your child’s records will be protected to the extent permitted by law.

WILL THERE BE ANY COSTS RELATED TO THE RESEARCH?

There are no costs associated with participating in the study.

WILL THERE BE ANY COMPENSATION FOR PARTICIPATION?

Your child will not be compensated for participation.

WHAT IF YOU ARE INJURED BECAUSE OF THE STUDY?

If your child is injured during research procedures, he/she will be offered first aid at no cost to you if available. Additional medical expenses you may need will be your responsibility or that of your third-party payer. By signing this document you are not waiving any rights that you may have if injury was the result of negligence of the University or its investigators.

DO YOU HAVE TO TAKE PART IN THIS STUDY?

Taking part in this research study is entirely voluntary. Your child does not have to participate in this research. If you and your child chooses for your child to take part, you or your child have the right to stop at any time. If your child decides not to participate or if he/she decides to stop taking part in the research at a later date, there will be no penalty or loss of benefits to which your child is otherwise entitled. Your child’s refusal will not influence current or future relationships with the University of Delaware, the University of Delaware sports medicine staff, including the athletic training staff, your child’s high school, your child’s sports team, or the athletic training staff at your child’s high school.
Your child’s participation may be terminated by investigators if he/she is not cooperating with the instructions that are given.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please contact the Principal Investigator, Jaclyn B. Caccese at 570-417-4780 or the Advisor: Dr. Thomas W. Kaminski at 302-831-6402.

If you have any questions or concerns about your child’s rights as a research participant, you may contact the University of Delaware Institutional Review Board at 302-831-2137.

Your signature below indicates that you are agreeing to allow your child to take part in this research study. You have been informed about the study’s purpose, procedures, possible risks and benefits. You have been given the opportunity to ask questions about the research and those questions have been answered. You will be given a copy of this parental consent form to keep.

By signing this parental consent form, you indicate that you voluntarily agree to allow your child to participate in this study.

_________________________  _______________________
Signature of Parent or Legal Guardian              Date

_________________________
Printed Name of Parent or Legal Guardian

_________________________
Printed Name of Child

_________________________  _______________________
Principal Investigator              Date
Appendix B

ASSENT FORM
University of Delaware
Assent Form

Title of Project: Investigation of Cerebral Blood Flow in Healthy and Concussed Athletes

Principal Investigator: Jaclyn B. Caccese

 Advisors: Dr. Thomas W. Kaminski, Dr. Andrew Reisman, Dr. Geoffrey Gustavsen

Dear High School Student-Athlete:

I am a graduate student (Jaclyn B. Caccese) at the University of Delaware doing research on concussions, specifically blood flow to the brain after a concussion. I am inviting you to participate in a study looking at how blood flow to the brain is affected by concussions and by participating in practices and games for your sport over a season. The results of the study will be used in my thesis and dissertation may allow for a more quantitative measurement of brain injury (blood flow to the brain), thus allowing team physicians and athletic trainers to make better return-to-play decisions.

We will come to your high school for all testing. Your parents will be asked to sign a parental consent form. Then you will be asked to complete a concussion history questionnaire.

You should not participate in this investigation if you are currently exhibiting symptoms of a concussion (i.e. headache or a feeling of pressure in the head, temporary loss of consciousness, confusion or feeling as if in a fog, amnesia surrounding the traumatic event, dizziness or “seeing stars”, ringing in the ears, nausea or vomiting, or slurred speech) or if a physician has diagnosed you as concussed and you are currently unable to participate in your sport. If you sustain a concussion during the season that requires an over-night hospital stay, you will be excluded from post-concussion measurements.

WHAT DO YOU HAVE TO DO?

You will be asked to go to the athletic training room at your high school for BAM, King-Devick, and BESS tests. ImPACT testing may be done in a computer lab at your high school or in the athletic training room, if necessary.

You will be asked to report for two test sessions, if you are not diagnosed with a concussion during the season. The first test session will be before the start of your season and the second test session will be at the end of your season. Each session will take 30-45 minutes of your time, this is 60-90 minutes total.

Participant Initials ________
Session 1 – Baseline Measurements (All Student-Athletes)

Before the start of your seasons, you will have BAM readings, ImPACT tests, King-Devick tests, and BESS tests done to serve as baseline measurements. You will also fill out a concussion history questionnaire. Please see the description of each test below.

**BAM**
The Brain Acoustic Monitor (BAM) is like a brain stethoscope. Therefore, two non-invasive invasive (does not break the skin or physically enter the body) sensors will be secured to your forehead by an elastic band (see Figure 1) and a reference sensor will be placed on your wrist. Each trial takes 5-10 seconds and you will have 5 trials of data collected at baseline. You will be asked to sit still and refrain from talking throughout testing. No action is required on your part. The BAM does not have FDA approval and is still considered an investigational device.

![Figure 14: BAM Set-Up](image)

*ImPACT Testing*
The Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) test is computerized and takes about 25 minutes to complete. The program measures multiple aspects of cognitive functioning in athletes, including: attention span, working memory, sustained and selective attention time, response variability, non-verbal problem solving, and reaction time. If your school already requires baseline pre-season ImPACT testing, you will not be required to do this again. By signing this document you give permission that this information may be shared with the research staff. If your school does not require baseline pre-season ImPACT testing, the research staff will ask you to complete this computerized test. ImPACT testing has been proven reliable in post-concussion testing and can be used for return-to-play decisions. If you sustain a concussion, during the season, you give permission that this information may be shared with your athletic trainer and/or physician.

King-Devick Test
The King-Devick Test for Concussions is a two-minute test that requires you to read single digit numbers displayed on cards. The test consists of four cards, a demonstration card and three test cards (see Figure 2). You will always be asked to read from left to right and from top to bottom. King-Devick testing has been proven reliable in post-concussion testing and can be used for return-to-play decisions. If you sustain a concussion, during the season, you give permission that this information may be shared with your athletic trainer and/or physician.

Figure 15: King-Devick Test.
**BESS Test**

The Balance Error Scoring System (BESS) evaluates your balance by having you stand in bare feet on either the Tekscan mat or a balance mat placed over the Tekscan mat using the stances indicated (see Figure 3). You will be instructed to stand as still as possible with your hands on your hips for each of the conditions listed (total of 6). Each trial will last 20 seconds and the Tekscan mat will automatically score your balance. Errors are scored using a standardized scoring system (see Figure 4). Errors for losing balance will be recorded and used in the analysis. If your school already requires baseline pre-season BESS testing, you will not be required to do this again. By signing this document you give permission that this information may be shared with the research staff. If your school does not require baseline pre-season BESS testing, the research staff will ask you to complete this balance test. BESS testing has been proven reliable in post-concussion testing and can be used for return-to-play decisions. If you sustain a concussion, during the season, you give permission that this information may be shared with your athletic trainer and/or physician.

![Figure 16: BESS Stances.](image1)

![Figure 17: BESS Scoring Card.](image2)

**Follow-Up Measurements**

**Sessions 2-10, 12 – Post-Concussion Testing (Sport-Related Concussed Student-Athletes Only)**

If you are diagnosed with a sport-related concussion by a certified athletic trainer and this diagnosis is confirmed by a physician, you will be asked to participate in 9-10 additional test sessions. By signing this document, you give permission that the diagnosis of a concussion may be shared with the research staff (see “Accessing your medical records” below).

Additional test sessions 1-7 will only be 5-10 minutes in length. Additional test sessions 8 and 9 will be 30-45 minutes in length. Additional test session 10 is only required in a small subset of the concussed population and will be 30-45 minutes in length. This adds 1 hour and 30 minutes to 3 hours to your total time commitment; therefore, you will be asked to volunteer 2 hours and 30 minutes to 4 hours and 30 minutes of your time, total.
If you are diagnosed with a sport-related concussion, you will repeat BAM, King-Devick, and BESS tests within 24 hours of sustaining a concussion and then again every 24 hours for 7 days (additional sessions 1-8). The ImPACT test will be repeated on day 7 post-concussion only, which is why additional session 8 is 30-45 minutes in length. You will then be evaluated again 30 days post-concussion (additional session 9). If BAM measures do not return to baseline by 30 days post-concussion, you will be asked to test again 6 months post-concussion (additional session 10).

These test sessions may require that you report for testing on weekends (Saturdays and/or Sundays).

Session 2 or 11 – End-of-Season (All Student-Athletes)

At the end of your season, regardless of whether or not you have sustained a sports-related concussion, you will have BAM readings, ImPACT tests, King-Devick tests, and BESS tests done to serve as post-season comparisons.

ACCESSING YOUR MEDICAL RECORDS:
If you sustain a concussion during the time you are participating in this study and are seen by a Physician our research team will need access to the diagnosis from your doctor. Federal and state laws, including the Health Insurance Portability and Accountability Act (HIPAA), protect your privacy as it relates to medical records. This part of the informed consent form tells you what information about you may be collected in this study and who might see or use it.

By agreeing to participate in this research you also authorize the research team to contact the physician you may see in the case of a concussion. We will ask your doctor to confirm if you were diagnosed with a concussion or not. This will be the only information requested from your physician.

The use and sharing of your information has no time limit. You can withdraw your permission to use and share your information at any time by writing to Jaclyn B Caccese at the address listed below. If you do withdraw your permission, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected for the study.

Participation in this research is completely voluntary. If you agree to participate, you also authorize us to access your medical diagnosis in the case of a concussion. Your decision to participate or not will not affect future medical services and treatment you may need.

Participant Initials ________
WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The Brain Acoustic Monitor (BAM) is a non-invasive device similar to a stethoscope that listens to your heart beat. This is not an FDA-approved device.

There are no known physical risks in completing the computerized ImPACT test or King-Devick test. The tests do require active attention, concentration, and mental effort and have in some cases caused mental frustration (particularly when completed following mild brain trauma or concussion). If severe mental frustration is apparent, testing will be discontinued.

WHAT ARE THE POTENTIAL BENEFITS?

Although there is no guarantee, the use of the three testing procedures (the ImPACT, King-Devick, and BESS tests) may allow team physicians and athletic trainers to make better return-to-play decisions following concussions, if you sustain a concussion during the season.

The results from the ImPACT, King-Devick, and BESS tests will be shared with athletic trainers and physicians at your school. Because of the investigational nature of the BAM, cerebral blood flow readings will not be shared with any athletic trainers, physicians, coaches, parents, or participants.

Whether or not you sustain a concussion, the confirmation of the Brain Acoustic Monitor (BAM) as a diagnostic tool for concussions may allow for a more quantitative measurement of brain injury, thus allowing team physicians and athletic trainers to make better return-to-play decisions.

HOW WILL CONFIDENTIALITY BE MAINTAINED?

Data will be kept confidential and your information will be assigned a code number. The list connecting your name to this number will be kept in a locked file. When the study is completed and the data have been analyzed, the list will be destroyed. Data will be kept securely in electronic storage formats and saved for three years. Your name will not be used in any report. We will make every effort to keep all research records that identify you confidential to the extent permitted by law. However, subject information from the ImPACT, King-Devick, and BESS tests may be shared with the athletic training staff and physicians. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared. Your research records may be viewed by the University of Delaware Institutional Review Board, but the confidentiality of your records will be protected to the extent permitted by law.

BAM data will be shared with Arthur Cooke at Active Signal Technologies (Linthicum Heights, MD). No personal identifiers (i.e. names) will be sent with the data. The files will be sent electronically in an encrypted format. Sharing of this data is required to improve sensitivity and specificity of the BAM. This data will not be used when applying for FDA approval.
WILL THERE BE ANY COSTS RELATED TO THE RESEARCH?

There are no costs associated with your participation.

WILL THERE BE ANY COMPENSATION FOR PARTICIPATION?

You will not be compensated for participation.

WHAT IF YOU ARE INJURED BECAUSE OF THE STUDY?

In the unlikely event that you suffer an injury as a result of participating in this study, you will be offered first aid at no cost to you if available. Additional medical expenses you may need will be your responsibility or that of your third-party payer. By signing this document you are not waiving any rights that you may have if injury was the result of negligence of the University or its investigators.

DO YOU HAVE TO TAKE PART IN THIS STUDY?

Taking part in this research study is entirely voluntary. You do not have to participate in this research. If you choose to take part, you have the right to stop at any time. If you decide not to participate or if you decide to stop taking part in the research at a later date, there will be no penalty or loss of benefits to which you are otherwise entitled. Your refusal will not influence current or future relationships with the University of Delaware, the University of Delaware sports medicine staff, including the athletic training staff, your high school, your sports team, or the athletic training staff at your high school.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please contact the Principal Investigator: Jaclyn Caccese at 570-417-4780 or the Advisor: Dr. Thomas W. Kaminski at 302-831-6402.

If you have any questions or concerns about your rights as a research participant, you may contact the University of Delaware Institutional Review Board at 302-831-2137.

Participant Initials _______
Your signature below indicates that you are agreeing to take part in this research study. You have been informed about the study’s purpose, procedures, possible risks and benefits. You have been given the opportunity to ask questions about the research and those questions have been answered. You will be given a copy of this consent form to keep.
By signing this consent form, you indicate that you voluntarily agree to participate in this study.

Signature of Participant ____________________________ Date ___________

Printed Name of Participant ____________________________

Principal Investigator ____________________________ Date ___________

Participant Initials ________
Dear Coaches, Parents, and Student-Athletes,

My name is Alex Salinas and I am a master’s student at the University of Delaware; I am also the Assistant Athletic Trainer at St. Mark’s High School. I am doing research on how sub-concussive forces affect blood flow to the brain. I am inviting you to participate in a study looking at how blood flow to the brain is affected by sub-concussive forces over the span of one game. The results of the study may be used in my thesis and may allow for a more quantitative measurement of brain injury (blood flow to the brain), thus allowing team physicians and athletic trainers to make better return-to-play decisions.

I am inviting student-athletes from the University of Delaware, St. Mark’s High School, A.I. DuPont High School, Wilmington Friends School, Tower Hill School, Charter School of Wilmington, and Newark High School. Student-athletes who play football or soccer will be asked to participate because of the head-contact nature of their sport. Additionally, cross-country runners will also be asked to participate to see how cerebral blood flow differs between contact and non-contact sports.

To measure cerebral blood flow, I will be using an instrument called the Brain Acoustic Monitor (BAM). This is a non-invasive (does not break skin or physically enter your body) device that looks and feels like a stethoscope used to measure heartbeat. Readings take 5-10 seconds each and 5 readings will be taken. We will also be comparing BAM results to two existing concussion tests: the King-Devick and BESS. The King-Devick test is a vision test that requires subjects to read single-digit numbers on a card from right to left and top to bottom. The BESS test is a balance test that requires subjects to stand in three stances, each for 20 seconds. They repeat the same three stances with their eyes closed.

These three measurements will be taken twice. The first set of measurements will be taken at the end of school on game day. The second measure will be taken after the game. Approximately 15 athletes will be tested the day of the home game against Dover High School (September 27) and another 15 the day of the home game against Delaware Military Academy (October 4).
More information can be found on the consent form, parental consent form, and child assent form. If you have any questions about this study, please contact the Principal Investigators, Alex Salinas, at 313-506-0277. Additionally, the Advisor, Dr. Thomas W. Kaminski, can be reached at 302-831-6402.

If you have any questions or concerns about your child’s rights as a research participant, you may contact the University of Delaware Institutional Review Board at 302-831-2137.

Thank you,

Alex Salinas, ATC
Appendix D

SPECIFIC AIMS

Traumatic brain injuries (TBIs) have become a highly discussed topic over the past decade, particularly those acquired during athletic participation. Mild traumatic brain injuries (mTBIs) represent a subcategory of TBIs and include sports-related concussions (SRCs). Between 1.6 and 3.8 million mTBIs occur yearly in the United States [1-5]. However, the number of mTBIs that occur annually in the United States may be as higher due to a lack of reporting and therefore a lack of diagnosis [2,4]. Furthermore, approximately 67,000 SRCs occur annually in high school football, a sport with over one million participants nationwide [2]. It is possible, however, that a similar number of SRCs go undiagnosed in this population, as a result of limited access to qualified healthcare, naiveté of the athlete, and lack of supervision [2]. Headaches as well as deficits in balance, vision, and memory are often seen in patients suffering SRCs [2,6-9].

A reduction in cerebral blood flow (CBF) occurs with TBI and concussion [10-15]. There is no research regarding the effects of subconcussive blows on cerebral blood flow after athletic participation. Subconcussive blows have been defined as head impacts that do not result in concussions and are typically associated with contact and collision-type sports [9]. Cerebral blood flow can be monitored by a device known as the Brain Acoustic Monitor (BAM; Active Signal Technologies, Linthicum Heights,
MD). The noninvasive sensors are held against the skull at forehead using an elastic headband. Arterial pulse waves entering the brain create a consistent deformation of the skull that the BAM’s sensors detect. In other words, the BAM acts as a stethoscope for the brain. Distorted waveform readings indicate an abnormality in brain physiology. It is theorized that these distortions are transient and return to normal as the patient’s injury status improves.

The King-Devick (K-D) test measures the speed that one can rapidly identify and name numbers aloud; this is referred to as oculomotor function. Some have recommended using the K-D test as a rapid sideline visual screening tool for concussion; it has been used in football, soccer, and boxing [4,16]. The Balance Error Scoring System (BESS) provides a rapid assessment of the effects of SRC on postural stability [6,17-19]. It has been utilized in numerous studies and proven to be cost-effective, valid, and reliable [6,17-21]. The patient is tested on both stable and unstable surfaces under three conditions: single leg, double leg, and tandem stance.

Healthy male high school-aged subjects will be divided into three groups according to sport: football (varsity), soccer (varsity), and distance runners. The high incidence of collision during the course of a football game makes this group of particular interest in this research project. To a lesser extent, the soccer players, who also receive subconcussive blows to the head due to purposeful heading during competition, are of interest as well. The distance runners, who experience no subconcussive blows to the head as the result of their sport participation, will serve as the control group. Subjects will report prior to competition to provide baseline
measures for the BAM, K-D test, and BESS. Measures will be retaken approximately twenty minutes after the competition ends. Utilizing measures from the BAM, K-D test, and BESS, the primary goal of this study is to determine whether subconcussive impacts can cause immediate cognitive, postural, and physiological changes after an athletic competition.

**Specific Aim 1**: To compare changes in cerebral blood flow in a group of high school athletes affected by varying levels of subconcussive blows in their respective sport.

**Hypothesis 1.1**: Postgame CBF will be significantly decreased in football players compared to both soccer and distance runners.

**Hypothesis 1.2**: Postgame CBF will be decreased in soccer players compared to distance runners.

**Specific Aim 2**: To compare changes in oculomotor function in a group of high school athletes affected by varying levels of subconcussive blows in their respective sport.

**Hypothesis 2.1**: Soccer and football players will have decreased scores on the K-D test postgame as compared to their baseline.

**Hypothesis 2.2**: Distance runners will have no change in oculomotor function after participation than before.

**Specific Aim 3**: To compare changes in balance in a group of high school athletes affected by varying levels of subconcussive blows in their respective sport.

**Hypothesis 3.1**: Postgame balance scores will be decreased more in football players than in soccer players when compared to baseline scores.
**Hypothesis 3.2:** Postgame balance scores will remain unchanged in distance runners compared to baseline.

The expected outcomes of this study will reveal valuable information to sports healthcare professionals (i.e. athletic trainers) regarding the effects of varying degrees of subconcussive forces on CBF, oculomotor function, and balance. If reduced CBF is seen in athletes in the absence of concussion, it may be fair to assume that subconcussive changes occur at the physiologic level in the span of one game. However, symptoms may be so minimal that they are unnoticeable (sub-clinical) to both the healthcare provider and athlete. This may be of importance clinically as a warning signal to limit subconcussive activities until CBF returns to baseline. Past research indicates that poor balance and visual disturbances are often telltale signs of SRCs [1,6-9]. In light of this, poor oculomotor function and balance scores, if they are present, after participation may be an indication of either SRC or what Bailes et al. [9] refers to as “subconcussion” syndrome. Future studies would involve a closer look at changes in these three factors over an entire season, rather than a single competition; this could be expanded to include other collision and contact sports (lacrosse, ice hockey).
Appendix E

BACKGROUND AND SIGNIFICANCE

E.1 Background

Concussions affect the individual physically, cognitively, and emotionally and disrupts daily life [3] Symptoms are transient and vary from person to person [4] Common symptoms include temporarily blurred vision, headache, and dizziness [7,9] Additional symptoms include fatigue, anxiety, irritability, emotional instability, insomnia or hypersomnia, and sensitivity to light and/or noise [1,6-9,13]. Deficits in memory, information processing, problem solving, and attention may also be noted.13 Oculomotor function has been shown to worsen after head trauma [4,16] Current management focuses on the patient being symptom free while under physical and cognitive rest prior to being progressed back to full athletic participation [9]

Sport-related concussions contribute greatly to the more than $50 billion in annual costs associated with TBI [12,22]. In addition to medical expenses and lost productivity, this can limit an adolescent’s ability to drive to or attend school due to the ongoing manifestation of symptoms. Males are approximately 1.5-2 times as likely to experience a SRC as females; however, post-acute cognitive outcomes do not significantly differ between genders [3,23]. Interestingly, high school females are 1.7 times as likely as males to sustain a concussion when participating in comparable sports [8]. A previous study by the Centers for Disease Control and Prevention
indicated that approximately 300,000 SRCs occur each year [3,8]. However, this value is flawed because it only included SRCs that involved a loss of consciousness, which only accounts for 8-19% of cases [3,7,9]. With this in mind, it is safe to assume that the true number of SRCs that occur annually in the United States is somewhere between 1.6 and 3.8 million [3-5,22,23]. Still, this estimate could still be low due to inability to recognize symptoms and thus a lack of reporting.

Over the past several years, sport-related concussions have garnered nationwide attention by the media, researchers, and clinicians. State governments have been passing laws regarding the management of SRCs and are raising awareness [24]. A growing pool of research revealing the long-term effects of multiple concussions has accelerated this process [5]. It has also helped educate parents, athletes, and coaches about the hazards of mismanaging concussions and associated signs and symptoms. Increased awareness allows appropriate referral to healthcare providers, such as doctors and athletic trainers. However, increased education does not necessarily result in improved reporting of concussions [25]. Learning styles vary between persons and generations and concussion education should be modified to target each cohort [25].

E.2 Subconcussion

It has been suggested that there are frequently occurring head impacts in contact or collision sports in which symptoms may not develop [9]. In other words, there may be no outward signs of a concussion at the clinical level [26]. Subconcussive blows are thought to cause an accumulation of damage that does not
result in clinically observable symptoms of concussion; this is now being referred to as subconcussion [2,9]. Bailes et al.[9] describe this under-recognized occurrence as:

…A cranial impact that does not result in known or diagnosed concussion on clinical grounds. It can also occur with rapid acceleration-deceleration of the body or torso, particularly when the brain is free to move within the cranium, creating a “slosh” phenomenon. Subconcussion has its greatest effect through repetitive occurrences whereby cumulative exposure becomes deleterious [9].

A popular method of recording number and magnitude of head impacts is by use of the Head Impact Telemetry (HIT) system. One longitudinal study of a high school football team recorded an average of 652 head impacts per season, per athlete [26]. Linemen accrued the greatest average number of impacts per season (868), while cornerbacks, receivers, and safeties accumulated the least (372) [26]. Of the more than 100,000 head impacts, only 20 were concussive, resulting in 19 athletes being removed from athletic participation. All but one of these athletes sustained a subconcussive head impact that was a greater magnitude than their concussive impact [27]. The number of subconcussive impacts in high school football players does not necessarily influence susceptibility to SRCs, which have an indefinable threshold up to this point [27,28]

A 2007 study [7] showed that subconcussive impacts do not alter performance on the Immediate Post- Concussion Assessment and Cognitive Testing (ImPACT) and Standardized Assessment of Concussion (SAC) in Division III college football players. The ImPACT and SAC were both implemented pre-, mid-, and postseason
and no significant differences were noted in memory, processing speed, concentration, and reaction time of players who did not sustain a concussion [7,9]. These results differ greatly from the observed effects of subconcussion on high school football players [2]. Helmets were implemented with the HIT system to record the number and magnitude of head impacts. Athletes underwent neurocognitive (ImPACT) and neurophysiological (fMRI) preseason, postseason, and at least once during the season.

Four of the 21 athletes had both clinically- and functionally-observable impairment (COI+/FOI+) [2]. The ImPACT and fMRI results for eight subjects without clinically observable impairment were also reviewed. Alarmingly, half of these subjects had functionally observed impairments in the absence of clinically observed impairments (COI-/FOI+) [2]. In addition, this group was shown to have a significantly greater average number of helmet impacts over the season (1090 vs. 656 in the COI-/FOI- and 546 in the COI+/FOI+) [2,9]. This is surprising, as the authors did not expect a third group to arise after reviewing the data.

Subconcussive impacts potentially contribute to the development of subacute and chronic conditions including depression, mild cognitive impairment, chronic traumatic encephalopathy (CTE), and epilepsy [2,9]. Chronic traumatic encephalopathy is a recently defined syndrome characterized by a progressive neurodegeneration caused by repetitive impacts to the head, resulting in the transfer of acceleration-deceleration forces to the brain [9]. Symptoms of CTE have been noted in football and soccer among other sports; however, most of the attention focuses on professional football players who have developed symptoms regardless of whether
they have been clinically diagnosed with a concussion [9,22,29]. Finally, it has been estimated that at least 17% of individuals with multiple concussions will develop CTE in their lifetime [2].

**E.3 Pathophysiology**

Hypotension and hypoxia occur after head injury, significantly increasing mortality and morbidity [12]. Reduced CBF has been observed in the left posterior, frontal, and subcortical regions of the brain in subjects who suffered from chronic concussive symptoms after sustaining a concussion at least two years prior [13]. Hypoperfusion occurs within 24 hours of injury followed by hyperemia from 24-72 hours [12]. Vasospasm and hypoperfusion occur again during days 4-15 [12]. Past research has shown that post-injury CBF was adequate for the reduced metabolic demands after TBI, even though there were a significant number of subjects with significantly reduced cerebral blood flow [12].

There is limited information on the pathophysiology of pediatric concussion. Magnetic resonance imaging (MRI) has shown no evidence of neuronal, axonal, or metabolic disruptions in children with sport-related concussion [10]. These results differ from the aforementioned study [2] that noted differences in fMRI results in subjects with and without a clinically diagnosed concussion. Neuronal and axonal injury has been observed in addition to transient metabolic disruptions in an adult population [10]. When concussed children were compared with healthy controls, significant alterations in CBF were noted; cerebral blood flow was improving toward baseline in only 27% of subjects two weeks post-injury [10]. After 30 days, CBF was
improving toward baseline in 64% of participants [10]. Most of the current evidence on changes in cerebral blood flow is based on TBI or mTBI, with only a recent shift in attention to SRCs; further research on the topic is needed [10,12-14]

The need for additional research on how to monitor and identify symptoms of subconcussion is omnipresent. While research on concussions must continue, gaining knowledge of subconcussion may aid the treatment and overall understanding of the relationship between these two conditions. The proposed study seeks to determine the effects of repetitive blows in select sports with varying levels of contact and collision. While football players are the primary focus of this investigation, soccer players are still capable of developing concussive and subconcussive symptoms during participation.
Appendix F

PHOTOGRAPHIC RELEASE
Photographic Release Form

I hereby grant the Athletic Training Research Laboratory and its research staff the royalty-free rights to publish photographs (digital images) of me in any publications, presentations, media-releases, etc.... in which I appear as a model, subject, and/or patient. I understand that any figure in which I appear may be modified.

Thomas W. Kaminski
Printed Name

Signature

Date: APR 24 2016
Photographic Release Form

I hereby grant the Athletic Training Research Laboratory and its research staff the royalty-free rights to publish photographs (digital images) of me in any publications, presentations, media-releases, etc... in which I appear as a model, subject, and/or patient. I understand that any figure in which I appear may be modified.

Michael Catalano

Printed Name

Signature

Date: 10.23.13
Appendix G

RESEARCH APPROVAL
DATE: February 3, 2014

TO: Jaclyn Caccoese
FROM: University of Delaware IRB

STUDY TITLE: [486706-3] Investigation of Cerebral Blood Flow in Healthy and Concussed Athletes

SUBMISSION TYPE: Amendment/Modification

ACTION: APPROVED

APPROVAL DATE: February 3, 2014

EXPIRATION DATE: August 20, 2014

REVIEW TYPE: Expedited Review

Thank you for your submission of Amendment/Modification materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.