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The Effect of Stochastic Resonance Stimulation on Proprioception and Postural Control in Anterior Cruciate Ligament Reconstructed Patients

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by

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Abstract

The anterior cruciate ligament (ACL) is one of the most commonly injured ligaments in the knee that frequently results in reconstruction surgery. Some degree of chronic proprioception and postural balance deficiency has been reported following ACL reconstruction (ACLR) surgery, which may be associated with a higher risk of ACL re-injury in these patients. *Stochastic resonance* (SR) has been shown to improve proprioception in various clinical populations with comparable postural and proprioceptive deficiencies as the ACLR population.

In this dissertation, the existence of such deficiencies has been investigated in female ACLR participants and healthy controls. The effect of SR on improving the postural balance and knee proprioception in ACLR and healthy populations has also been studied. The ACLR participants were tested at three months (n = 19) and six months post-surgery (n = 15), while healthy participants were tested once (n = 28).

The SR vibration was applied locally to the knee region. Proprioception was evaluated using movement threshold and movement repeatability tests. The effects of the following factors on proprioception were studied: SR (ON vs. OFF), movement direction (flexion vs. extension), and limb condition (ACLR vs. contralateral; ACLR vs. healthy dominant control). Postural balance during single leg standing (duration of 30 sec) was assessed with new measures including entropic half-life (EnHL) and surrogate entropy (ΔE_{surr}). These measures were developed in conjunction with this dissertation. The effects of the following factors on postural balance were studied: SR (ON vs. OFF), limb side (ACLR vs. contralateral; ACLR vs. healthy dominant control), and vision (eyes open vs. eyes closed).

SR vibration successfully improved proprioception in the ACLR and healthy controls. These study results suggest that SR could potentially aid in pre/post-surgery proprioception rehabilitation.

This study showed that a postural balance deficiency was present when the ACLR limb was compared to healthy dominant control limbs. When the ACLR limb was compared to the contralateral, the deficiency was only present when the eyes were closed. These findings may suggest that the postural balance deficiency is subtle. Therefore, more stringent or demanding experimental protocols may be necessary to test postural balance in functional groups with deficiencies such as the ACLR group.

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I could pointlessly exhaust numerous pages about these two sages. However, I resort to a reiteration of what Antiphanes said about Plato: "… *Just as in a far northern city, words froze into ice as they were spoken, and were heard in the summer when they thawed, so the words spoken by Plato to his students in their youth were finally understood by them only in their old age.* " Aristophanes of Attica (c. 446 – c. 386 BC).

Thank you for your everlasting friendship, mentorship, and the insightful talks. I have learned abundantly from you both.

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Thank you, my dear colleagues and friends. You made this uneven voyage smooth (Yeah … but not really you Tomasz!).

Dedication

This dissertation is dedicated to my four pillars of happiness: My darling Mona Badri, my pal Takin Zandiyeh, my beloved mother Manzar Ganjavi, and my constantly missed father Mashallah Zandiyeh (late). If I journeyed this far, you were my wings!

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Likewise, this dissertation is dedicated to my friends, family, and my teachers.

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List of Symbols, Abbreviations, and Nomenclature

Symbol	Definition
ΔE_{surr}	Changes in the sample entropy following surrogate analysis
ACL	Anterior cruciate ligament
ACL-QOL	ACL-QOL questionnaire
ACLR	ACL reconstructed
ANOVA	Analysis of variance
AP	Anterior-posterior direction
ARMA	Autoregressive moving average
BMI	Body-mass index
CHREB	Conjoint health research ethics board
COP	Center of pressure
EnHL	Entropic half life
GEE	Generalized estimating equation
IKDC	International knee documentation committee
JPS	Joint position sense
MANOVA	Multivariate analysis of variance
ML	Medial-lateral direction
QOL	Quality of life
RD	Radial distance
RPP	Reproduction of passive position
RS	Reshape scale
SEn	Sample entropy
SR	Stochastic Resonance
TTDPM	Threshold to detection of a passive movement

Chapter One: **Introduction**

Some degree of proprioceptive deficiency is commonly attributed to the knee following anterior cruciate ligament (ACL) reconstruction surgery, although research outcomes are mixed and findings remain inconclusive (Relph et al. 2014). Since one major source of information for the postural stability control system is somatosensory feedback from the lower limbs, it is theorized that postural control deficiencies might also be demonstrated in ACL reconstructed (ACLR) patients (Kellis et al. 2011). The addition of an optimal non-zero level of random vibration noise through a phenomenon known as *stochastic resonance* (SR) has been shown to improve proprioception in various clinical populations (Moss et al. 2004). However, its effect has never been studied in an ACLR population. The purpose of this dissertation is to investigate the effects of SR noise on proprioception and postural stability in ACLR patients.

1.1 Background

1.1.1 Overview

The ACL is one of four major ligaments of the knee and is the most commonly injured ligament in the human body (Lyman et al. 2009). Serious injury to this ligament normally results in surgical reconstruction, with surgeons in the US conducting over 60,000 to 175,000 ACL reconstructions annually (Lyman et al. 2009).

The ACL is thought to play a role in providing proprioceptive feedback to the central nervous system (Frank & Jackson 1997), although experimental evidence remains inconclusive (Grabiner et al. 1992). Proprioception is known to significantly relate to functional stability in the knee, as well as patient satisfaction and quality of life following ACLR surgery (Dhillon et al. 2011;

Barrett 1991). Poor proprioception is thought to predispose the knee to a higher risk of ACL re-injury (Mandelbaum et al. 2005) or other injuries to the knee (Sinkjær & Arendt-Nielsen 1991).

The role of proprioception is seemingly closely tied to the health of the knee joint and thus is of particular importance. Moreover, proprioception deficiencies are thought to be highest during the first few months following the ACL reconstruction surgery (Angoules et al. 2011). Thus, a potential method leading to improve knee proprioception especially in the first few months following ACLR surgery could be very important, valuable, and highly desirable.

1.1.2 ACLR and proprioception

Improvements in proprioception over time have been reported in the ACLR population (Angoules et al. 2011). Findings in the literature on this topic are varied and inconsistent, with researchers reporting: (1) a lack of significant difference in proprioception between ACLR patients and controls (Angoules et al. 2011), (2) poorer proprioceptive outcomes in the ACLR limb compared to the control limb (Furlanetto et al. 2016; Ma et al. 2014), and (3) improved proprioceptive outcomes in the ACLR limb compared to controls (Co et al. 1993). These varied findings may potentially be attributed to differences in methodologies, age group of the population, time since surgery, the time between injury and surgery, and different surgical interventions (Dhillon et al. 2011).

1.1.3 ACLR and postural sway

Proprioceptive feedback is important for maintaining postural balance. This importance is highlighted by the instantaneous tumble of patients with congenital sensory neuropathy when a room light is suddenly extinguished (Nance & Kirby 1985; Fridén et al. 2001). Postural sway is the outcome of the postural control system's efforts to keep the body's center of mass within the bases of support (feet) (Gantchev & Dimitrova 1996). The pattern of postural sway, as recorded by variations in the center of pressure (COP) on a force platform, is altered by temporary or permanent ailments of the postural stabilizing system (Conforto et al. 2001; Maurer et al. 2001).

Impaired postural stability has been shown in ACL deficient participants (Mizuta et al. 1992; Fridén et al. 1989), but findings in the ACLR population remains inconclusive and sometimes contradictory (Kellis et al. 2011). For example, some researchers reported significant differences between the measures of postural sway in the ACLR limb as compared to the uninjured contralateral limb or healthy controls, while others reported non-significant differences (Clark et al. 2014; Akbari et al. 2015). Nonetheless, postural control impairment in ACL reconstructed patients, especially during challenging tasks, has been suggested (Howells et al. 2011) despite the mixed and inconclusive findings in the available literature.

1.1.4 Stochastic resonance

A phenomenon that is known as stochastic resonance (SR) has been shown to improve proprioception in patients with osteoarthritis, postural stability in the elderly, in those with Parkinson’s disease, and balance control in diabetic and stroke patients (Moss et al. 2004). SR can be defined as: “*Any phenomenon whereby a non-linear system, whether dynamic or non-dynamic, can detect an otherwise undetectable signal by addition of a particular, non-zero level of noise to the system”* (Aihara et al. 2010). It is speculated that SR may provide a modality that enhances proprioception in ACLR patients. The mechanism through which this phenomenon occurs might be through recruitment of proprioceptive structures of the leg (e.g. intact collateral ligaments and capsular receptors, muscle spindles, etc.) to compensate for the deficient ACL receptors. To date, the application of SR to ACLR patients has not been reported in the literature, and thus forms one of the bases of this dissertation.

1.1.5 Proprioception measurement

The most sensitive, repeatable, and precise measure of proprioception in the knee joint is likely the *movement threshold* test (also known as a *threshold to detection of passive motion (TTDPM))* (Lephart & Fu 2000). In this test, the knee is passively moved into either extension or flexion and the participant is asked to perform a specified task (e.g. pressing a button) as soon as the movement is perceived. Another commonly used method is the *joint repeatability test* (also known as a *reproduction of passive positioning (RPP)* test). In this test, the knee is initially passively flexed to a certain desired angle, and the participant is asked to memorize the joint's position. The joint is then moved to other angles, and the participant is asked to reproduce the desired angle (Lephart & Fu 2000). The joint repeatability error is calculated by subtracting the reproduced from the desired angle.

1.1.6 Postural sway measurement

One method to measure postural stability is to study the movements of the *center of pressure* (COP) determined from force platform measurements during single leg stance (e.g. (Baltich, von Tscharner et al. 2014)). The single leg stance task on the force plate is predominantly used in patients with unilateral lower limb injury/pathology (Bonfim et al. 2003; Chmielewski, Rudolph et al. 2002; Harrison et al. 1994; Henriksson et al. 2001). Benefits of studying postural stability using this approach include ease of implementation and minimal participant preparation.

1.1.7 Measures of postural balance

Various measures of postural balance have been developed to study the postural control during quiet standing (Roerdink et al. 2006; Stergiou 2006). These measures usually provide information about the overall movement of the center of pressure (COP) (Deffeyes et al. 2009), but ignore the temporal structure of the signal that may contain information about the postural control strategies (Baltich, von Tscharner et al. 2014; Croft et al. 2008).

The *reshape-scale* method has recently been developed to characterize the postural sway as a part of the current dissertation (Zandiyeh & Von Tscharner 2013). This method systematically changes the order of appearance of the data points in a signal. For example, the reshaped signal for a given scale n is generated by placing the data points n distance apart next to one another (for more details see Appendix A:). The entropy of the signal at each scale is calculated using the sample entropy algorithm (Richman & Moorman 2000). Unlike previous measures of entropy at multiple scales (such as the *coarse graining algorithm* proposed by Costa and colleagues (Costa et al. 2005)), this method doesn't introduce artefacts into calculations as the original standard deviation, length, and probability distribution of the time series data remains intact (Zandiyeh and von Tscharner 2013).

When the reshape scale method is applied to COP data, a transition resembling a sigmoid curve is observed from a strongly ordered structure at short time scales (low sample entropy) to a fully disordered structure at large time scales. The variable *Entropic Half Life* (EnHL) was defined to characterize such a transition (Zandiyeh and von Tscharner 2013). It represents the time scale at which the transition reaches 50% of the maximum entropy, i.e., the entropy of randomly rearranged data points in the original time series (Zandiyeh and von Tscharner 2013). Thus, the

EnHL measure can be viewed as a variable that quantifies the time that elapses before the old positional states are gradually no longer utilized by the postural control system to regulate the present postural activities (Zandiyeh & Von Tscharner 2013). In this sense, EnHL can be speculated to be related to the size of memory of the past used by the postural balance system to regulate the current postural balance position.

The test-retest reliability (repeatability of the results over time) of EnHL values has proven to be similar to the reliability of standard classical measures such as excursion, path length and 95% ellipse area (Baltich et al. 2014). The EnHL method has been used to analyze various biological signals. For example, COP data (Baltich, Emery, et al. 2014; Baltich, Whittaker, et al. 2015; Baltich, von Tscharner, et al. 2015; Baltich, von Tscharner, et al. 2014; Federolf et al. 2015; von Tscharner et al. 2016), electromyography (Enders et al. 2015), and electrocardiogram data (von Tscharner & Zandiyeh 2017) can be named. Overall, the outlined studies indicate that the measure of EnHL is sufficiently sensitive, and repeatable in differentiating between unique COP trajectories in various clinical populations. The considerable sensitivity of EnHL to different experimental conditions observed in the outlined studies makes it a very powerful measure for assessing potential SR-related COP changes in the currently proposed study.

Surrogate analysis has shown very promising capabilities in revealing the complexity within a signal (von Tscharner et al. 2016; von Tscharner & Zandiyeh 2017). Thus, it is expected to be of value in the current research where analysis of signal regularity is an important aspect. The approach is based on the fundamentals of the Fourier transform that expresses a given signal into phase and amplitude components with frequency. Phase in the Fourier space is affected by the order of events in the time domain (Oppenheim & Lim 1981). For example, the phase of a COP signal can be related to the order of postural adjustment events by the postural balance control system. In the surrogate analysis, the phase of a signal is randomized (Theiler et al. 1992); consequently, the order of events in the signal will be randomized. The difference between the entropy of the original and surrogate signals (ΔE_{surr}) reveals the amount of information carried by the phase of the signal prior to the surrogate analysis. In other words, ΔE_{surr} shows how much the order of events (e.g. postural adjustment events) was important in a given signal. For example, if the events were completely randomly ordered ΔE_{surr} will be zero and if the order of events was all that mattered in a signal the $\Delta E_{surr} = 100\%$.

The ΔE_{surr} has been utilized recently in a study of heart rate variability in electrocardiograms to differentiate between healthy and congenital heart failure patients, demonstrating considerable sensitivity and specificity of 87% and 89% respectively (von Tscharner & Zandiyeh 2017). These high sensitivity and specificity values show that the use of this measure has promising potential in successfully differentiating healthy controls from clinical populations under study (von Tscharner & Zandiyeh 2017).

Limited attention has been paid to the importance of information in the phase of a signal especially when the COP signal is studied. With the use of ΔE_{surr}, new insights might follow regarding the importance of timing of events in the postural control system between the ACLR and healthy control groups. If this measure shows high sensitivity and specificity in discriminating the ACLR from the healthy controls, it might lead to a promising tool that could be used to identify ACLR individuals with postural deficiencies. If an association between postural balance and risk of injury can be assumed, such a measure could potentially be employed to suggest whether an individual is fit to return to high impact/twist activities or might benefit from further trainings, physiotherapy, and fitness exercises prior to returning to more challenging activities.

1.1.8 Time and Proprioception/postural sway

Rehabilitation exercises are usually recommended for ACLR patients soon after ACL reconstruction surgery. At approximately three months post-surgery, ACLR patients are recommended to engage in light sporting activities such as jogging (Kvist 2004a). Some authors suggest that the rehabilitation aim is to return the patient to full contact sports activities including cutting and jumping at about six months post-surgery (Zhou et al. 2008; Grindem et al. 2016). Although it is desirable to assist ACLR patients, especially those with the athletic background to return to sports activities as quick as possible, imprudent return to sport following the surgery might expose the patient to higher risks of re-injury (Lephart & Fu 2000; Mandelbaum et al. 2005). The length of time to full recovery and safe return to sports activities remains a continuing topic of debate and research (Reider et al. 2003; Bonfim et al. 2003; Hopper et al. 2003; Roberts et al. 2000). Therefore, it is important to assess the status of the knee joint at these suggested time points (i.e. three months and six months) from the joint proprioception and postural control perspectives. Further, it is valuable to investigate if potential differences in postural balance and knee proprioception become alleviated over time. Interestingly, the majority of the proprioceptive improvement in function were found to occur in the first three months post-surgery compared to later time points (Beard et al. 1996), with little or minimal difference reported after six months post-surgery (Angoules et al. 2011). Therefore, the 3-months post-surgery time point is particularly interesting for the ACLR limb and should be carefully studied and compared to the contralateral/healthy control limb.

1.1.9 Effect of the visual system on postural balance

The central nervous system acquires postural balance information from vestibular, visual, and somatosensory sensations. It allocates the relative importance of each type of information based on the context and comparative significance of the incoming information (Tjernström et al. 2015) and sends corrective commands to the postural muscles so that postural balance can be maintained. When the eyes are closed during bipedal or single leg balance, postural balance deficiencies have been reported in ACL deficient participants (Okuda et al. 2005; O'Connell et al. 1998; Davis 2001; Negahban et al. 2014). Such observations might be due to a sustained sensory impairment in the lower limb proprioception and stability that may manifest via a heavier reliance on vision. Studies on single leg balance in the ACLR population suggested poorer postural balance in the ACLR limb compared to the control limb when eyes were closed (Pahnabi et al. 2014; Henriksson et al. 2001; Harrison et al. 1994; Paterno et al. 2013). However, the differences were not always statistically significance (Howells et al. 2011). Since these findings are inconclusive, it is important to investigate whether the ACLR limb maintains deficient proprioception and postural balance over time compared to an internal control (contralateral limb in the ACLR group) or an external control (healthy dominant limb in the healthy control group) with and without visual information.

1.1.10 Internal/external control

Proprioception experiments on patients with unilateral ACL reconstruction require a control baseline for comparison purposes. Two methodologies have generally been used for unilateral knee injury studies as follows: (1) the contralateral limb serving as the *internal* control, and (2) a limb (usually dominant) from healthy control subjects serving as the *external* control (Fridén et al. 1996; Fridén et al. 1997; Lephart & Fu 1995; Roberts et al. 2000). Potential changes in the contralateral limb following the injury make it difficult to draw relevant clinical comparisons with the contralateral limb (Fridén et al. 2001). This argument emphasizes the importance of using the external control subject approach in the studies on the unilateral ACLR population. Both approaches were utilized in the current study.

1.2 Statement of the Problem

The following knowledge gaps have been identified: (1) Proprioceptive deficiency in the ACLR group is not conclusively established; (2) There is no consensus whether time alleviates the assumed proprioceptive deficiency; (3) Postural stability deficiency in the ACLR group is not conclusively established; (4) It remains unclear if time helps to alleviate the supposed postural balance deficiency; (5) SR has not been used on an ACLR population to date and thus it is unknown whether it can improve proprioception in an ACLR group; (6) similarly it is not clear whether SR can improve the postural stability in an ACLR group.

1.3 Purpose of the Study

The overall objectives of this study were to investigate the potential differences between the postural stability and knee joint proprioception between ACLR and their uninjured contralateral limbs, as well between unilateral ACLR and healthy dominant limbs in control group over time. A further goal was to investigate if SR noise can be utilized to improve the potential proprioceptive and postural balance deficiencies in the ACLR population.

1.4 Significance of the Study

This study provides information about whether postural balance and proprioceptive deficiencies are present in the ACLR limb at three months post-surgery when compared to each contralateral and healthy control limbs, and how these deficiencies change over at six months when compared to the contralateral limb. Further, it provides evidence as to whether SR noise can be utilized in ACLR population to attenuate the potential proprioceptive and postural balance deficiencies.

1.5 Specific aims

SA 1 - To investigate differences in the movement threshold and movement repeatability of the knee joint between ACLR and contralateral limb in ACLR individuals, as well as between ACLR and healthy controls.

SA 2 – To investigate the differences in postural balance measures on ACLR, and contralateral limbs of ACLR individuals, and healthy dominant limbs during single leg balance on the force platform.

SA 3 – To apply SR noise through mechanical vibration transducers to the area around the knee to investigate its effect on proprioception and postural sway in individuals with ACLR and healthy controls.

1.6 Hypotheses

The following hypotheses are tested in this dissertation:

Proprioception:

[H1] Movement repeatability error is higher in the ACLR limb compared to the contralateral limb.

[H2] Movement repeatability error is reduced in presence of the SR noise.

[H3] Movement threshold is larger in the ACLR limb compared to the contralateral limb.

[H4] Movement threshold is reduced following administration of SR noise.

[H5] Movement repeatability error in the ACLR limb at three months post-surgery is larger when compared to the healthy dominant limb.

[H6] The movement repeatability error differences between healthy dominant and ACLR limbs at three months will decrease following administration of SR noise.

[H7] Movement threshold in ACLR limb at three months post-surgery is larger when compared to the healthy dominant limb.

[H8] The difference between the movement threshold in healthy dominant and three months post-surgery ACLR limbs will not be significant following administration of the SR noise.

[H9] Movement threshold at three months is larger than at six months post-surgery.

[H10] Movement repeatability error at three months is larger than six months post-surgery.

Postural sway:

[H11] The EnHL and ΔE_{surr} in the ACLR limb is different from the contralateral limb in ACLR participants.

[H12] The EnHL and ΔE_{surr} at three months is different from the six months post-surgery in the ACLR participants.

[H13] The EnHL and ΔE_{surr} is different between eyes open and closed conditions in the ACLR participants.

[H14] The EnHL and ΔE_{surr} is different between SR ON and SR OFF conditions in the ACLR participants.

[H15] The EnHL and ΔE_{surr} is different the dominant limb of the healthy individuals and the ACLR limb at three months post-surgery.

1.7 Statistical Analyses

Statistical analyses were performed to test the hypotheses outlined about internal and external controls. In comparisons to the internal control, the following study factors were involved:

Postural balance: eyes (open vs. closed), SR (ON vs. OFF), limb side (ACLR vs. contralateral), time (three months vs. six months post-surgery)

Proprioception: direction (flexion vs. extension), SR (ON vs. OFF), limb side (ACLR vs. contralateral), time (three months vs. six months post-surgery)

In comparison to the external control the following study factors were involved:

Postural balance: eyes (open vs. closed), SR (ON vs. OFF), limb side (ACLR vs. healthy control). The statistical analysis was limited to the three month time point only.

Proprioception: SR (ON vs. OFF), limb side (ACLR vs. healthy control). The flexion direction was studied only.

For the postural balance measures over time, the *generalized estimating equation* (GEE) approach was used for the statistical analyses due to missing data at the six-month time point.

The covariance structure with assumption of "independence" was used in the GEE analysis that assumes the correlation between the factors is independent. Repeated measures ANOVA, typically used in biomechanics research, would have removed the data corresponding to a participant in its entirety if any data were missing. This in the current study means removing the postural balance data of 13 out of 19 ACLR participants during the repeated measures ANOVA analysis inevitably reducing the power of the analysis. A Repeated-measures ANOVA was used otherwise.

1.8 Thesis format

Chapter one provides an introduction to the research topic as well as the overall objectives and study hypotheses. Chapter two provides a review of pertinent literature on three main topics: (1) proprioception, (2) postural balance, and (3) SR. The proprioception topic emphasizes proprioception in the knee, sources of joint proprioception, proprioception following ACL deficiency and reconstruction, and the methods of testing proprioception in the knee. The postural balance section contains the definition and sources of postural sway, the effect of ACL deficiency and reconstruction on postural sway, reliance on vision following injury within the reconstruction surgery population, and the effect of time since surgery on postural sway. In the last section, SR is introduced with some background information, the effect of SR on proprioception and postural sway presented, and methods to determine the vibration sensation threshold outlined.

Main articles discussing the details of classical measures of postural balance are cited. Emphasis is placed on the measures that have been developed during this dissertation i.e. EnHL and the ΔE_{surr}. Thus, after a brief paragraph on classical measures, the scientific background regarding the novel measures is provided and recent findings are reported.

The methodology used to test the hypotheses of this dissertation is outlined in Chapter three. This section contains information about the protocols for participant recruitment, determination of vibration sensation threshold, movement repeatability, movement threshold measurement, and the postural balance measurement on the force platform. Lastly, the statistical methods to address the hypotheses are outlined at the end of this section.

The results are presented in two sections: (1) within each population, and (2) between populations. The within-population study is reported in Chapter four. This chapter compares the ACLR limb to the internal control of contralateral limb. For proprioception tests, the conditions included: direction (flexion vs. extension), limb side (ACLR vs. contralateral), and SR (OFF vs. ON). For postural balance tests, the following conditions are studied for ACLR populations: limb side (ACLR vs. contralateral), SR (OFF vs. ON), eyes (open vs. closed) and the time since surgery (three months vs. six months).

The between-population results are presented in Chapter five. In this chapter, the ACLR limbs of the ACLR participants are compared to the dominant limb of healthy controls. Proprioception is tested for the factors of limb side (ACLR vs. healthy control) and SR (OFF vs. ON). The comparison is made only at three months post-surgery, and the direction is restricted to flexion only. For postural balance tests, the following factors are included: limb side (ACLR vs. healthy control), SR (OFF vs. ON), and eyes (open vs. closed).

In Chapter six, the results are discussed. Finally the summary, significance, contribution, limitations, and recommendations for future directions are provided in Chapter seven. The mathematical theory of defining of EnHL as well as numerical simulations to test and validate this measure is shown in Appendix A:. The results of the correlation analysis between body mass, BMI, IKDC 2000 score, and ACL-QOL scores to the postural balance and proprioception outcome measures were presented in Appendix B:. The relevance of the rigorous methodology used in the current work to test SR on the knee has been detailed and discussed in Appendix C:. Finally, in Appendix D:, a copy of questionnaires and ethics approval is attached.

Components of this work on the introduction, validation, and application of the measures of postural balance have been presented and published previously:

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Chapter Two: **Literature Survey**

"I am under obligation to tell what is reported, but I am not obliged to believe it, and let this hold for every narrative in this history."

Herodotus (c. 484- 425 BC)

2.1 Anterior Cruciate Ligament: Brief Overview of Anatomy and Physiology

Ligaments are dense bands of connective tissues that anchor to the joint from both ends and are responsible for connecting and guiding the movement of the joint (Frank et al. 1999; Frank 2004; Haughom et al. 2012). The *Anterior Cruciate Ligament (ACL)* is one of four important ligaments of the knee and is the most commonly operated on (Lyman et al. 2009). Serious injury to this ligament normally results in surgical reconstruction, with surgeons in the US conducting over 60,000 to 175,000 ACL reconstructions annually (Lyman et al. 2009). The roles of the ACL in the knee joint can be classified as (1) biomechanical, and (2) sensory (Frank & Jackson 1997; Frank 2004).

Biomechanically, the ACL primarily controls the anterior translation and secondarily the adduction and internal rotation of the tibia relative to the distal end of the femur (Takeda et al. 1994; Girgis et al. 1975; Haughom et al. 2012; Frank & Jackson 1997).

Nerves associated with the ACL have been speculated to provide proprioceptive (see §2.2) feedback to the central nervous system (Frank & Jackson 1997), although the experimental evidence remains inconclusive (Grabiner et al. 1992). Histological analyses have shown diverse mechanoreceptors in the ACL (Schutte et al. 1987; Zimny 1988; Miyatsu et al. 1993; Duthon et al. 2006; Haus & Halata 1990). A review of the literature provided by Hogervorst and Brand

(Hogervorst & Brand 2005) details the findings regarding the mechanoreceptors of the ACL. Although disagreement exists regarding the types and quantities of receptors, generally the following ACL receptors are reported: (1) Ruffini receptors (stretch sensors) sensitive to movement, accumulated mainly at the femoral attachment of the ACL (Schutte et al. 1987; Zimny 1988); (2) Vater-Pacini receptors (rapid movement sensors) active at extremes of motion and silent otherwise, found in both endings of ACL (Schutte et al. 1987; Zimny 1988); (3) Golgi-like tension receptors activated only with considerable stresses on the ligament, located at the endings and in the body of the ACL (Zimny 1988); and (4) Non-adapting free nerves which are mainly pain receptors, spread almost everywhere throughout the ligament (Duthon et al. 2006; Zimny 1988). About 1% of the total area of the ACL is made up of the first three mechanoreceptors (Relph et al. 2014; Johansson et al. 2000). The combined activity of the first three receptors provides the knee with proprioceptive feedback (see Section 2.2).

2.2 Proprioception/Kinesthesia

2.2.1 Terminology

It is important to establish the semantics around the terms proprioception and kinesthesia that are frequently used in this dissertation (Stillman 2002). Some authors consider that proprioception and kinesthesia refer to different phenomena and should not be used interchangeably (Gilman 2002; Lephart & Fu 2000). For example, it is debated whether proprioception includes the sense of position and movement in the absence of vision (Gilman 2002; Taylor 2009), while kinesthesia is typically used specifically to refer to the sense of movement (Gilman 2002; Lephart & Fu 2000; Jerosch & Prymka 1996b). In contrast, others strongly contend that the difference is not major and the two terms can be used synonymously (Clark & Horch 1986; Schmidt & Lee 2011; Stillman 2002; Proske et al. 1988; Taylor 2009).

Proprioception, as defined by Sherrington (Sherrington 1920), includes senses of joint position and joint movement but also includes senses of force, weight, effort, pressure, vibration, body segment size/shape, and balance (Stillman 2002). It is typical in the proprioception literature to often confine the scope of proprioception limited to the joint position and movement senses (Stillman 2002).

This dissertation, while preserving neutrality in this debate, resorts to synonymy of the terms proprioception and kinesthesia and defines "proprioception" as the awareness of joint position and joint movement in the space sensed by the central nervous system in the absence of vision (Beynnon et al. 1999; Ashton-Miller et al. 2001; Stillman 2002; Stillman et al. 2002). Specifically, joint movement sense is the sensation of movement of different segments of the body relative to one another and includes sensing the direction, velocity, distance, and the timing of the movement (Taylor 2009). Similarly, position sense is responsible for providing feedback about the relative position of different segments of the body with respect to one another (Taylor 2009).

2.2.2 Sources of joint proprioception

Joint proprioception is suggested to be the outcome of the contribution of joint receptors, muscle spindles of the muscles surrounding the joint, and cutaneous receptors in the proximity of the joint (Proske & Gandevia 2009; Lephart & Fu 2000). However, the relative significance of each of these receptors to overall joint proprioception is under debate (Sjölander & Johansson 1997; Schutte et al. 1987; Lephart & Fu 2000; Proske & Gandevia 2009; Taylor 2009). Muscle receptors are commonly thought to be responsible for joint position and joint movement senses (McCloskey 1973; Sittig et al. 1987). Joint receptors are likely responsible for signaling the joint movement sense, acting as joint limit detectors and nociceptors (pain receptors) (Proske et al. 1988; Proske & Gandevia 2009). However, since the signal corresponding to the joint position from the joint receptors is comparably small, it seems unlikely that these receptors can contribute significantly to encode the joint position (Matthews 1982). Finally, the cutaneous sensation is speculated to enhance the effects of the other two proprioceptive inputs (Lephart & Fu 2000).

Despite the lack of consensus regarding the sources of joint proprioception, generally it is agreed that proprioception is adversely affected by joint trauma especially following ACL injury or reconstruction (Adachi et al. 2002; Fridén et al. 1998; Beynnon et al. 1999; Manor et al. 2010; Dyhre-Poulsen & Krogsgaard 2000; Krogsgaard et al. 2002; Corrigan et al. 1992; Beard et al. 1993; Barrack et al. 1989; Mizuta et al. 1992; Lephart et al. 1992; Barrett 1991). Specifically, ACL deficiency (Paterno et al. 2010) is generally associated with neuromuscular changes such as impaired proprioception (Barrack et al. 1989; Barrett 1991; Ciccotti et al. 1994; Lephart et al. 1992), troubled functional activities (Barrett 1991; Seto et al. 1988; Ciccotti et al. 1994; Goldie et al. 1989; Harter et al. 1988; Bynum et al. 1995; Wilk et al. 1994), quadriceps force deficiency, changes in gait (Goldie et al. 1989), changes in electromyographic activity, and changes in muscle control of the knee muscles (Hogervorst & Brand 2005; Kandel et al. 2013; Seto et al. 1988; Goldie et al. 1989; Lephart et al. 1992; Jennings & Seedhom 1994; Jennings & Seedhom 1998).

2.2.3 Proprioception and the ACL deficiency/reconstruction

The effect of ACL reconstruction on joint proprioception has not been widely studied, and the current findings on the topic remain inconclusive (Risberg et al. 1999). Relph and colleagues performed a meta-analysis on proprioception in ACL deficient and ACL reconstructed participants (Relph et al. 2014) and found only 49 relevant articles. However, 43 were excluded due to "poor quality data with a high risk of bias and missing or inadequate outcome data" (Relph et al. 2014). Also, variations in methodologies and analyses between studies make meaningful comparisons difficult if not impractical. Therefore drawing a definitive conclusion on this topic based on the limited body of literature isn't easily attainable.

Findings of impaired knee proprioception have been reported following intera-articular knee injuries (Barrack et al. 1989; Barrett 1991; Beard et al. 1993; Lephart et al. 1997; Robert & Skinner 1988; Jerosch & Prymka 1996b; Corrigan et al. 1992) especially following the ACL deficiency (Beynnon et al. 1999; Borsa et al. 1997; Corrigan et al. 1992; Fridén et al. 1998; Fischer-Rasmussen & Jensen 2000; Barrack et al. 1989; Fridèn et al. 1999; Fridén et al. 1996; Fridén et al. 1997), with only few studies reporting no significant difference in proprioception (Wright et al. 1995).

The literature on joint proprioception following ACL reconstruction have reported mixed and sometimes contradicting findings (Gokeler et al. 2012). Improvements in proprioception over time with the presence of a persistent significant proprioceptive deficiency have been reported (Barrett 1991; Bonfim et al. 2003; Lee et al. 2009; Roberts et al. 2000; Relph et al. 2014). In contrast, others found no significant difference between healthy and ACLR joint proprioception (Lephart et al. 1992; Hopper et al. 2003; Reider et al. 2003; MacDonald et al. 1996; Fremerey et al. 2000; Angoules et al. 2011; Risberg et al. 1999; Furlanetto et al. 2016; Nagai et al. 2013; Fremerey et al. 2001; Chouteau et al. 2012; Ma et al. 2014; Muaidi et al. 2009). Finally, Co and colleagues reported improved proprioception in the ACLR limb compared to the healthy limbs (Co et al. 1993). The source of these outlined discrepancies might be attributed to differences in methodologies, the time between injury and surgery, time since surgery, the age of participants, and surgical techniques (Dhillon et al. 2011).

Proprioception deficiency in the knee is a particularly important topic since proprioceptive function following ACLR surgery (rather than mechanical ligament stability) was found to be 84% correlated to functional[1] stability and 90% correlated to patient satisfaction (Dhillon et al. 2011; Barrett 1991). Further, poor proprioception is speculated to predispose the knee to higher risks of secondary injuries (Sinkjær & Arendt-Nielsen 1991) while improved proprioception and neuromuscular performance have been associated with significant reduction risks of ACL re-injury (Mandelbaum et al. 2005).

Therefore, in conclusion, the understanding regarding proprioceptive deficiency in ACLR patients remains inconclusive based on the available literature. Clearly, understanding the proprioceptive deficiency in ACLR patients may provide insights about some aspects of ACLR joint stability and functional performance, patient quality of life and satisfaction following ACLR surgery, and the risks involved in returning to high impact and fast movement activities.

2.2.4 Proprioception Testing and Methodology

Proprioception experiments using unilateral ACLR participants require a control baseline for comparison purposes. Two choices have generally been utilized in the literature for controls in unilateral knee injury studies: the contralateral limb is used as the *internal* control, and the

[1] Function is repeatedly used in this dissertation. It is important to define function here. Unless otherwise specified, function means neuro-musculoskeletal function, which according to the FARLEX Medical Dictionary is defined as: “the ability of nerves, muscles, and bones to perform or coordinate specific activities”.

healthy dominant or non-dominant limb from healthy controls is used as the *external* control (Fridén et al. 1996; Fridén et al. 1997; Lephart & Fu 1995; Roberts et al. 2000).

Choosing between these choices is more a matter of trade-off. For example, it has been suggested that the potential physiological changes in the contralateral limb following the injury may make the results of statistical comparisons difficult to interpret (Fridén et al. 2001). On the other hand, comparing the injured limb of one individual with the healthy limb of another is also problematic unless attention is closely paid to matching the individuals based on various demographic variables. The matched study design requires a challenging recruitment protocol that could make the study relatively cumbersome.

Having established the comparison baseline either through internal or external controls, the proprioception in the injured/operated limb can be assessed and reasonably compared to the control limb.

There are several methods to test the proprioception in the knee joint. The most sensitive, repeatable, and precise measure of proprioception is likely the *movement threshold* test (also known as *threshold to detection of passive motion (TTDPM))* (Lephart & Fu 2000; Fridén et al. 2001; Barrack, Skinner, Brunet, et al. 1984; Barrack, Skinner, Brunet, et al. 1983; Barrack et al. 1989; Barrack, Skinner, Cook, et al. 1983; Beynnon et al. 1999; Borsa et al. 1997; Clark et al. 1996; Co et al. 1993; Corrigan et al. 1992; Fischer-Rasmussen & Jensen 2000; Fridén et al. 1998; Fridèn et al. 1999; Fridén et al. 1996; Fridén et al. 1997; Hall et al. 1994; Hall et al. 1995; Lephart et al. 1996; Lephart et al. 1992; Liao & Skinner 1994; Pai et al. 1997; Pap et al. 1997; Risberg et al. 1999; Roberts et al. 2000; Rozzi et al. 1999; Safran et al. 1999; Sharma et al. 1997;

Skinner et al. 1984; Skinner et al. 1983; Ashton-Miller et al. 2001). In this test, the knee is passively moved either into extension or flexion. The participant is asked to perform a certain task (e.g. pressing a button) as soon as he/she perceives the movement. The angular speed of the passive movement is usually set to small values (0.5 to 2.5 degrees/sec). Such a slow angular velocity is desired to maximize the stimulation of the joint receptors while minimizing the stimulation of the receptors in muscles surrounding the joint (Fridén et al. 2001; Lephart & Fu 1995).

The *joint repeatability test* (also known as a *reproduction of passive positioning (RPP)* test) is also commonly used to assess proprioception in the knee. In this test, the knee is initially passively flexed to a certain angle, and the participant is asked to memorize the joint's position. The joint is then moved to other angles, and the participant is asked to reproduce the desired angle either actively[1] (Barrack, Skinner, Brunet, et al. 1983; Barrack, Skinner & Cook 1984; Barrack, Skinner, Cook, et al. 1983; Barrack 1983; Birmingham et al. 1998; Corrigan et al. 1992; Dvir et al. 1988; Fischer-Rasmussen & Jensen 2000; Fridén et al. 1996; Fridén et al. 1997; Good et al. 1999; Harter et al. 1988; Kaplan et al. 1985; Roberts et al. 2000; Rozzi et al. 1999; Skinner et al. 1984; Skinner et al. 1983; Skinner et al. 1986; Stillman et al. 1998; Ashton-Miller et al. 2001) or passively[2] (Co et al. 1993; Dvir et al. 1988; Liao & Skinner 1994; Perlau et al. 1995; Safran et al. 1999). Some variations of the above protocol are reported, such as active reproduction of the active motion (Good et al. 1999; Gottlieb et al. 1994; Ishii et al. 1997; Marks 1994; Marks et al. 1993; Newberg 1986), reproduction of the joint position or movement with

[1] The angle is reproduced actively when joint is moved to the desired flexion angle by contraction of muscles across the desired joint (i.e. the knee).
[2] The angle is reproduced passively when the joint is moved to the desired flexion angle by an external mechanism (e.g. dynamometer).

the contralateral limb (Co et al. 1993; Kaplan et al. 1985; McNair et al. 1995; McNair et al. 1996), and reproduction of a passive motion using a goniometer (Barrett 1991; Barrett et al. 1991; Carter et al. 1997; Fridén et al. 1996; Fridén et al. 1997; Jerosch & Prymka 1996a; Jerosch et al. 1996; Roberts et al. 2000; Roberts et al. 1999; Warren et al. 1993; Ashton-Miller et al. 2001).

2.3 Postural Sway

2.3.1 Definition and measures of postural sway

Postural sway is the outcome of the postural control system's efforts to maintain the body's center of mass within the bases of support (feet) (Gantchev & Dimitrova 1996), which is continuously disturbed by movements of body segments relative to one another and the surrounding environment. As stated by Haas, "*Disturbances of postural control are prevalent in several nervous diseases and injuries. Due to strong influences of postural control on movement safety, mobility, independence and essential everyday jobs, patients' quality of life is often sustainably impaired*" (Haas et al. 2006).

Proprioceptive feedback is important for maintaining postural balance. This is highlighted by the instantaneous tumble of patients with congenital sensory neuropathy when a room is suddenly darkened (Nance & Kirby 1985; Fridén et al. 2001). The postural control process includes (1) sensing the position and displacement of body segments, (2) processing the sensory inputs, and (3) generating the appropriate motor response to produce the postural balance (Dettmer et al. 2015; Schmidt 1975; Redfern et al. 2001). Sources of sensory feedback utilized by the postural control system include (1) somatosensory (2) vestibular and (3) visual (Hijmans et al. 2008; Priplata et al. 2006).

The precise neuro-biomechanical mechanism that underlies postural sway remains unclear. It has been associated with the response to bilateral muscle vibrations of the gastrocnemius and tibialis anterior (Massion 1994), internal noise (Gantchev & Dimitrova 1996), a combination of feed-forward (anticipatory control) followed by feedback (modulatory) mechanisms (Res et al. 1995), timing of Cerebellar Vermis (Ouchi et al. 1999), a consequence of blood circulation (Conforto et al. 2001), respiration (Gandevia et al. 2002), and a ballistic like adjustment in muscle length (Loram et al. 2004). Additionally, stochastic as well as determinist variations in settings of the postural controller parameters (analogous to a PID (proportional, integrator, and differentiator) control compensator for an inverted pendulum) have been suggested as a potential mechanism (Gatev et al. 1999; Maurer et al. 2001; Maurer & Peterka 2005).

The information provided by the somatosensory, vestibular, and visual input is utilized by the postural control system to maintain the upright stance. This information is combined and weighted in the central nervous system based on their relative importance and context (Tjernström et al. 2015). The pattern of postural sway, as recorded by variations in the COP on a force platform, is altered by temporary or permanent ailments in the components of the postural stabilizing system including the somatosensory system (Conforto et al. 2001; Maurer et al. 2001). Thus, the performance of the postural control system (e.g. as assessed by measures of postural sway) is frequently studied to investigate the postural deficiency following an ailment, the efficiency of treatments, rehabilitation, or healing process in different populations with the postural balance deficiencies (Tjernström et al. 2015) including ACLR patients.

Various approaches have been employed to assess postural stability (e.g. moving platform (Horak & Nashner 1986), balancing inverted ballistic pendulum (Fitzpatrick et al. 1994), and sudden pull at the waist (Gildenhuys 2003; Gildenhuys et al. 2015)). Postural stability is also quantified as the movement of the *center of pressure* (COP) as measured by the force platform during one-legged or bipedal stance (e.g. (Baltich, von Tscharner et al. 2014)). The single leg stance on the force plate is probably one of the most extensively used approaches to test postural balance in patients with unilateral lower limb injury/pathology (Bonfim et al. 2003; Chmielewski, Rudolph, et al. 2002; Harrison et al. 1994; Henriksson et al. 2001), likely due to its ease of implementation and minimal participant preparation.

2.3.2 Postural sway and ACL reconstruction

The ACL is thought to be an integral part of the peripheral nervous system that provides the somatosensory feedback to the central nervous system about the position and movement of the knee joint (Howells et al. 2011; Johansson et al. 1991). For example, the activation of ACL afferents will change the muscle spindle outputs through a phenomenon known as ACL reflex (Miyatsu et al. 1993). This reflex is mostly associated with the feedback modulatory mechanism (Miyatsu et al. 1993; Krogsgaard et al. 2002; Duthon et al. 2006) that modulates the firing amplitude and timing of the knee muscles. Deficiencies in the somatosensory information provided by the ACL following ACLR is speculated to be related to abnormal joint dynamics, balance, and coordination sometimes observed in the ACL deficient population (Lephart & Fu 2000).

Postural balance following ACLR is primarily tested using the single leg balance setup (Howells et al. 2011; Culvenor et al. 2016). The existence of postural balance deficiency in the ACLR population is inconclusive. For example, significant differences have been reported between the injured and contralateral (or the healthy control) limb (Pahnabi et al. 2014; Mohammadi et al.

2012; Zouita Ben Moussa et al. 2009; Dauty et al. 2010; Bonfim et al. 2003; Shiraishi et al. 1996; Howells et al. 2013; Vathrakokilis et al. 2008; Culvenor et al. 2016; Negahban et al. 2013; Parus et al. 2015; Delahunt et al. 2013), while others have reported that the differences was not significant (Heijne & Werner 2010; Henriksson et al. 2001; Clark et al. 2014; Mattacola et al. 2002; Hoffman et al. 1999). Nonetheless, a general trend towards postural impairment in ACL reconstructed patients, especially during challenging tasks, has been suggested (Howells et al. 2011).

Additional investigations are required to address the question of altered postural control with ACLR. Since some of the reported inconsistencies in results may originate from differences in parameters used to quantify postural sway, experimental setup, and the length of data collection (Kellis et al. 2011), closer attention to specific protocols, analysis techniques, and variables of interest utilized in the methodology is required.

2.3.3 Vision and postural sway

Evaluation of postural stability is typically performed for eyes-open and eyes-closed conditions to understand the extent of reliance upon the visual system in maintaining upright balance (Prieto et al. 1996). The relative importance of vision as an integral source of sensory feedback in the postural control and balance in the ACLR participants is dependent on the context and importance of the task (Tjernström et al. 2015). The somatosensory system in ACL reconstructed patients can be speculated to become impaired following the injury and the subsequent surgery. Therefore it is reasonable to expect heavier reliance on the visual system might follow to circumvent the defective sensory feedback from the joint. Such a change on the reliance upon vision might be indicative of a sustained sensory dysfunction in the affected limb. Era and colleagues studied the postural sway of roughly 8,000 healthy young adults in a randomized study and concluded that postural sway had been shown to increase when eyes were closed (Era et al. 2006; Hansson et al. 2010). Similar findings have been reported by different groups in various clinical populations (Yoon et al. 2012; Nagano et al. 2006; Prado et al. 2007; Blaszczyk & Klonowski 2001; Schmit et al. 2005; Bolbecker et al. 2011; Hughes et al. 1996; Donker et al. 2008; Kouzaki & Masani 2012; Fernie & Holliday 1978; Frenklach et al. 2009; Agostini et al. 2013; Mazaheri et al. 2010; Mancini et al. 2011; Blaszczyk & Orawiec 2011; Kamen et al. 1998; Schieppati et al. 1999; Strang et al. 2011; Oliveira et al. 2009) including ACLD participants (Okuda et al. 2005; O'Connell et al. 1998; Davis 2001; Negahban et al. 2014).

Studies on single leg balance in an ACLR population (Pahnabi et al. 2014; Henriksson et al. 2001; Harrison et al. 1994; Paterno et al. 2013) suggest less postural stability with eyes closed compared to eyes open, although reported differences sometimes didn't reach statistical significance (Howells et al. 2011). It remains unclear whether the effect of vision is more pronounced in the ACLR limb compared to healthy control/contralateral limb. Consequently, it is important to investigate its effect on ACLR and healthy control groups to further our knowledge about the postural deficiencies that might follow after the ACL reconstruction surgery.

2.3.4 Factor of time since surgery

ACLR patients are typically prescribed rigorous rehabilitation exercises following their reconstruction surgery. At about three months post-surgery, ACLR patients are usually suggested to return to light sport activities such as jogging (Kvist 2004a; Scranton et al. 2002; Noyes et al. 2000; Muneta et al. 1998; Eriksson et al. 2001; Peterson et al. 2001; Barrett et al. 2002; Ejerhed et al. 2003; Järvelä et al. 2001; Möller et al. 2001). The aim of rehabilitation is to help the patient to return to a functional level suitable for sport activities entailing cutting and jumping at about six months time (Zhou et al. 2008; Muaidi et al. 2009; Cascio et al. 2004; Kvist 2004a; Muneta et al. 1998; Eriksson et al. 2001; Peterson et al. 2001; Barrett et al. 2002; Ejerhed et al. 2003; Järvelä et al. 2001; Möller et al. 2001; Jorgensen et al. 2001; Kvist 2004b; Bak et al. 1999; Deehan et al. 2000; Aune et al. 2001; Pinczewski et al. 2002). Accurate information is required to assist further developments in rehabilitative programs that might help ACLR patients especially those with athletic backgrounds, to return to sports activities as quickly as possible. However, premature return to sport following ACL reconstruction surgery might expose the patient to higher risks of re-injury (Lephart & Fu 2000). To date, disagreement exists on the required recovery time for proprioceptors, and arguments exist on the adequacy of suggested time points (Reider et al. 2003; Bonfim et al. 2003; Hopper et al. 2003; Roberts et al. 2000). Consequently, it is important to assess the status of the knee joint at these critical time points of three months and six months post-surgery from the joint proprioception perspective as well as the overall performance of postural control system as assessed by postural stability test. Also, most of the proprioceptive improvements in function were reported in the first three months post-surgery (Beard et al. 1996), with little or minimal differences being reported after six months post-surgery (Angoules et al. 2011). Thus, the three month time point is particularly interesting for the ACLR limb and ought to be carefully studied and compared to healthy contralateral as well as healthy control individuals at this time point.

2.4 Stochastic Resonance

SR has been shown to improve proprioception in patients with osteoarthritis (A. T. Collins, Blackburn, Olcott, Yu, et al. 2011; A. T. Collins, Blackburn, Olcott, Miles, et al. 2011), postural stability in the elderly (Costa et al. 2007; Priplata et al. 2002; Rogan et al. 2012; Dhruv et al. 2002; Gravelle et al. 2002), Parkinson patients (Kaut et al. 2011; Turbanski et al. 2005; Ghoseiri et al. 2009; Kaut et al. 2016), and balance control in diabetic and stroke patients (Liu et al. 2002). Initially introduced by Benzi in 1981 (Benzi et al. 1999), SR can be defined as: *"Any phenomenon whereby a non-linear system, whether dynamic or non-dynamic, can detect an otherwise undetectable signal by addition of a particular, non-zero level of noise to the system"* (Aihara et al. 2010). SR has been observed in numerous biological as well as human-made nonlinear systems (Moss et al. 2004). It is important to emphasize the nonlinearity aspect since in a purely linear system addition of noise in the input will lead to increased noise in the output. However, in non-linear systems, an optimal level of noise can be found for which maximum enhancement is achieved, and where further increases in the noise intensity lead to a degraded output (Moss et al. 2004).

The simplest manifestation of SR is referred to as 'Threshold SR' or 'non-dynamical SR' (Figure 1) (Moss et al. 2004) and is constituted of a threshold value, sub-threshold stimulus, and noise (Gingl et al. 1995). This example (Figure 1) shows a sub-threshold stimulus generated using a chaotic Rössler attractor (Rössler 1976). A white Gaussian noise is superimposed on the signal. The amount of information transmitted through the threshold system was used as a measure of enhancement in signal transmission due to the noise (shown in Figure 1 (Bottom)).

As verified visually from Figure 1, for a particular level of noise the optimal amount of information transmitted through this non-linear system is maximized and then gradually decreases as the level of the noise is further increased. It can also be visually verified that for zero level of noise the stimuli can't surpass the threshold and thus no spike will be observed in the output. In contrast, when the level of noise is significantly increased a considerable amount of noise passes through the threshold barrier, and thus the output will be contaminated with noise. Between these two extremes lies an optimal level of noise for which the probability of the threshold crossing increases near the peaks of the stimulus with the pattern and frequency resembling the original stimulus. For this particular and system specific non-zero level of noise, the SR phenomenon will be observed.

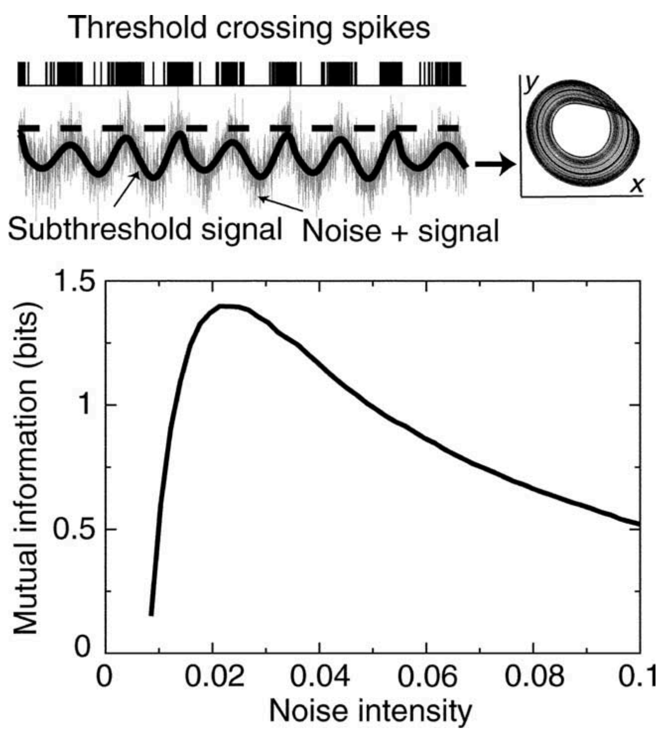

Figure 1 - Stochastic Resonance in a threshold system. (Top-Right) Rössler map in the x and y-direction (see (Rössler 1976) **for more information). (Top-Left) The subthreshold**

signal in the x direction is presented with a superimposed white Gaussian noise. (Bottom) Mutual information i.e. amount of information passed through the threshold with respect to the noise amplitude (image from (Moss et al. 2004) **- Copyright permission courtesy of Elsevier - Clinical Neurophysiology).**

The nonlinearity present in the sensory information processing, cortical dynamics, and neural function makes studying SR an interesting research topic in health sciences (Moss et al. 2004). The role of noise in the response of sensory neurons to weak periodic stimuli was first documented in 1991 (Longtin et al. 1991). Ever since, SR has been studied in various health related studies including its effect on proprioception (A. T. Collins, Blackburn, Olcott, Miles, et al. 2011; Collins & Luca 1994; A. T. Collins, Blackburn, Olcott, Yu, et al. 2011; Lugo et al. 2008; Reeves et al. 2009); sensorimotor performance (Cordo et al. 1996; Liu et al. 2002; Mendez-Balbuena et al. 2012; Iliopoulos et al. 2014; Hur et al. 2014; Dhruv et al. 2002; Martínez et al. 2007), postural stability in elderly (Collins et al. 2003; Costa et al. 2007; Priplata et al. 2003; Priplata et al. 2002; Priplata et al. 2004; Reeves et al. 2009; Pavlik et al. 1999; Gravelle et al. 2002; Rogan et al. 2012; Dettmer et al. 2015), diabetic patients (Hijmans et al. 2008; Priplata et al. 2006), patients with history of stroke (Priplata et al. 2006); healthy participants (Mulavara et al. 2011; Lauper et al. 2009; Kahle & Gribble 2009; Dettmer et al. 2015; Priplata et al. 2002); postural stability of participants with ankle instability (Ross & Guskiewicz 2006; Ross et al. 2007; Ross & Arnold 2012b; Ross & Arnold 2012a; Holmes & Delahunt 2009); participants with lower back pain (Reeves et al. 2009); multiple sclerosis (Schuhfried et al. 2005); and Parkinson's patients (Turbanski et al. 2005; Pal et al. 2009). Further, SR also led to the development of a new generation of cochlear implants that assist patients with auditory impairments to more successfully encode the auditory stimuli (Morse & Evans 1996).

Three main methods and their corresponding mechanisms have been reported in the literature for applying the SR stimuli: mechanical vibrators (Priplata et al. 2003; Costa et al. 2007; Collins et al. 2003; Priplata et al. 2002; Harry et al. 2005), electrical stimulation (A. T. Collins, Blackburn, Olcott, Yu, et al. 2011; A. T. Collins, Blackburn, Olcott, Miles, et al. 2011), and whole body vibration platform (Rogan et al. 2012; Kaut et al. 2011). Electrical SR is likely to change the local field potential in the proximity of mechanoreceptors, encouraging them to fire an action potential for a sub-threshold mechanical movement (Collins et al. 2003).

Various mechanisms have been suggested for the observed effect of mechanically induced SR (either whole body or local stimulation). For example, it has been compared to the effect of tonic muscle vibration stimulation where stimulation of a muscle spindle leads to activation of its alpha motoneurons, and in turn leads to muscle contraction (Hagbarth & Eklund 1966; Burke & Germond 1976). SR has been speculated to bring the membrane potential attributed to the mechanoreceptors close to the firing threshold by changing the ion permeability (Ross & Arnold 2012b; Bezrukov & Vodyanoy 1995) and thus these receptors are more prone to fire in the presence of a sensory signal.

The effect of SR can likely manifest in the following four categories (Lugo et al. 2008):

(1) Unimodal SR: The stimuli and the noise get superimposed at the site of stimulation and are sensed together by local receptors (Collins et al. 1997; Simonotto et al. 1997)

(2) Central SR: The stimuli and the noise enter the same receptor but get superimposed later at the cortical level, and the effect is observed in the signals emanating from the motor cortex (Hidaka et al. 2000). For example, the effect of SR applied to arterial blood pressure receptors optimized the brain stem outputs related to regulating the blood pressure in the circulatory system.

(3) Behavioural SR: The signal and noise enter from separate receptors and get superimposed inside the sensory cortex which might lead to improved perception (Kitajo et al. 2003). Furthermore, improved perception might lead to improved commands from the motor cortex. For example, improved cortical interpretation has been observed when the visual noise was input via one eye and a desired scene from the other (Kitajo et al. 2003).

(4) Cross-modal SR: The SR stimulation is inputted through one site, and the effect is perceived in another site and observed globally (Manjarrez et al. 2007; Lugo et al. 2008). For example, improved postural balance was observed in the presence of an auditory noise (Manjarrez et al. 2007; Lugo et al. 2008).

According to the desired category of SR, the study can be designed such that the stimulation is administered to local receptors directly responsible for the movement under survey or to other receptors that might indirectly promote the desired response. In the current dissertation, both Unimodal and Cross-modal SR are tested. In the proprioception test, the noise is applied to the mechanoreceptors around the knee while the desired stimulus was applied to the knee. Therefore the proprioception test is a Unimodal SR experiment. In the postural balance, however, the

Cross-modal SR is used since the stimulation is applied to the receptors of the knee while the changes in the postural balance are studied.

2.4.1 Vibration sensation threshold

For practical reasons, it is important to report the level of SR vibration stimulation about the vibration sensation threshold. Therefore it is important to measure the vibration sensation threshold in each participant so that the appropriate level of noise can be selected and administrated. Qualitative sensory testing (QST) is a procedure used to quantify the sensory function in participants and is utilized primarily to quantify senses of vibration, temperature, and pain (Shy et al. 2003). The main challenge in QST protocols is to come up with an accurate and reproducible value in a reasonable amount of time. Main protocols to determine the vibration sensation threshold includes the *method of limits* (Sekuler et al. 1973; Dyck et al. 1978), *method of constant stimuli* (Shy et al. 2003), a *method of adjustment*, and the *method of serial exploration* (Yarnitsky 1997).

In the method of limits, the stimulus is introduced by gradually increasing (or decreasing) the stimuli and the participant is asked to indicate the first onset of sensing it (onset of the disappearance of the stimuli). The recorded threshold in this method is dependent on the rate of increase (or decrease) leading to a reaction time artifact. This artifact is mainly problematic in the slow conducting sensations such as thermal and usually is insignificant in the sense of vibration (Yarnitsky 1997).

In the method of constant stimuli, 5 to 9 levels of equispaced intensities of stimuli are selected in advance and randomly applied to the participant. The participant is asked 'post factum' whether she/he feel the stimulus. Although this method is less variable than the method of limits, it requires numerous trials (hundreds of times), which makes it a tedious protocol. To overcome this issue, the *method of levels* is frequently used. In this method, the level of stimuli is adjusted according to the previous response of the participant until the desired level is attained[1].

The method of constant stimuli usually leads to a lower sensation threshold compared to the method of limits (Levy et al. 1989). However it is not reported to be less variable (Muijser et al. 1986) or more sensitive or reproducible (Claus et al. 1990) , and yet it takes a relatively longer time to complete (Yarnitsky 1997; Levy et al. 1989; Muijser et al. 1986; Claus et al. 1990). Although debates regarding the suitability of each methodology continue in the literature, limited comparative research on the methodologies has been reported (Yarnitsky 1997). Further, the sensory threshold value is dependent on many factors including the electrode size, site of stimulation, frequency of stimulation, the rate of change of the stimuli, age, sex, ethnicity, the lab environment, instructions to the participants, the participant's motivation (Shy et al. 2003), and the clinical population under survey. Therefore, there is no clear methodology that is most advantageous to measure a specific sensation in a clinical population.

In this dissertation, the method of limits (for increasing and decreasing stimulus intensity) have been utilized to calculate the vibration sensation threshold since it is a practical and acceptable methodology and can be managed in a reasonable time.

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[1] Other methods such as method of adjustment (The participant is asked to adjust the level of stimulation to the marginally noticeable level) or method of serial exploration (The participant is presented with series of randomly ordered amplitudes of stimulation and the average of the several levels of stimuli is calculated) (Green & Swets 1966).

2.4.2 Effect of SR on proprioception

The ability of the sensory system to detect weak sensory stimuli has been observed to improve with SR (Martínez et al. 2007; Andò 2006; Bahar & Moss 2004; Collins et al. 1996b; Dhruv et al. 2002; Liu et al. 2002; Moss et al. 2004; Richardson et al. 1998; Cordo et al. 1996; Mendez-Balbuena et al. 2012; Iliopoulos et al. 2014; Hur et al. 2014). Specifically, SR enhances the firing activity of the (1) human muscle spindle when the tendon of the parent muscle is stimulated by noise (Cordo et al. 1996), (2) outputs from Golgi tendon organs and primary and secondary endings in a cat model (Fallon et al. 2004), and (3) human tactile sensation (Collins et al. 1996b; Liu et al. 2002; Dhruv et al. 2002; Wells et al. 2005).

Cordo and colleagues have reported improved afferent output from an individual extensor muscle of the wrist while mechanical noise was applied to the corresponding muscle (Cordo et al. 1996). It was observed that, for a specific level of noise, the signal to noise ratio of the muscle spindle output was maximized. In a similar context, (Collins et al. 1996b) demonstrated that the number of correct identifications of an indention on the participant's finger was improved by the application of noise. As the noise stimulus can be speculated to activate cutaneous receptors as well as the corresponding muscle spindles located in the proximity of the stimulation site (Cordo et al. 1996), it remains unclear whether the observed SR occurs in the muscle spindle receptor or may also be attributed to the cutaneous fusimotor reflexes (Matthews & Watson 1981; Johansson & Sojka 1985). Since the substantial sources of proprioception are partially muscle spindle and partially the cutaneous afferents, it is reasonable to theorize that SR might improve the proprioception in a given joint (A. T. Collins, Blackburn, Olcott, Yu, et al. 2011; Collins et al. 2009; A. T. Collins, Blackburn, Olcott, Miles, et al. 2011). It is speculated that SR might improve proprioception (Collins et al. 2009; Ghoseiri et al. 2009) by allowing neurons to optimally transmit the weak sensory signals at a given optimal level of noise (Priplata et al. 2002; Collins et al. 1995; Kawaguchi et al. 2011). Further, the monosynaptic response of a given muscle can be optimized by SR stimulation in the synergic muscle (Martínez et al. 2007), providing evidence for the presence of SR optimizing characteristics in the motor system.

The effect of SR in proprioceptive enhancement has been studied in various clinical populations. Collins and colleagues had reported enhancement in proprioception of the knee when the electrical SR stimulation and a knee sleeve were used simultaneously in healthy individuals (Collins et al. 2009) and participants with osteoarthritis (A. T. Collins, Blackburn, Olcott, Miles, et al. 2011) demonstrated via the knee movement repeatability test. Enhanced proprioception (Mendez-Balbuena et al. 2012; Kimura et al. 2012; Magalhães & Kohn 2011; Lugo et al. 2008) and significantly changed electromyography recordings of the leg muscles during quiet standing with the application of auditory noise (Lugo et al. 2008) was reported, suggesting that the higher CNS might utilize the extra noise to improve sensory information processing (Moss et al. 2004).

Therefore, SR can be hypothesized as a potential modality to enhance proprioception in ACLR patients by recruiting other proprioceptive sensors of the leg (e.g. intact collateral ligaments and capsular receptors (Barrett 1991), muscle spindles (Cordo et al. 1996), and cutaneous receptors (Mendez-Balbuena et al. 2012; Kimura et al. 2012; Magalhães & Kohn 2011; Lugo et al. 2008)) to compensate for the impaired ACL receptors. To date, while the application of SR to ACLR patients has been recommended (A. T. Collins, Blackburn, Olcott, Miles, et al. 2011; A. T. Collins, Blackburn, Olcott, Yu, et al. 2011), the effect of SR on proprioception in ACLR participants, remains unreported.

2.4.3 Effect of SR on postural sway

Reduced postural sway during quiet standing was observed when SR stimulation was applied to the participants via vibrating insoles (Priplata et al. 2002; Collins et al. 2003). The influence of SR on the postural sway in various clinical populations was subsequently investigated. Similar to the findings with proprioception SR was observed to improve postural sway in healthy young adults (Priplata et al. 2002; Priplata et al. 2003), elderly participants (Priplata et al. 2002; Priplata et al. 2003; Dettmer et al. 2015), as well as stroke (Priplata et al. 2006) and diabetic patients (Priplata et al. 2006) where the SR was induced using vibrating insoles. SR was also induced using electrical stimulation, which resulted in improved postural balance (Gravelle et al. 2002) and increased multi-scale complexity of the COP signal in the elderly (Costa et al. 2007)[1], and improved postural balance in patients with ankle instability (Ross et al. 2007; Ross & Arnold 2012b; Ross & Arnold 2012a; Ross & Guskiewicz 2006). Ross and colleagues incorporated SR stimulation into a rehabilitation program in patients with chronic ankle instability and observed more stable postural balance in these patients compared to those with rehabilitation program alone (Ross et al. 2007; Ross & Arnold 2012b; Ross & Arnold 2012a; Ross & Guskiewicz 2006).

Using galvanic vestibular stimulation, the addition of SR noise resulted in improvement of the postural sway in healthy adults (Pavlik et al. 1999; Mulavara et al. 2011), and in patients with Parkinson's disease (Pal et al. 2009). Similarly when SR was applied using the whole body vibration machine, postural sway was improved in the elderly (Rogan et al. 2012), Parkinson's

[1] Refer to (Zandiyeh & Von Tscharner 2013; von Tscharner et al. 2016; von Tscharner & Zandiyeh 2017) for critiques on the approach and interpretations proposed in the outlined article.

patients (Kaut et al. 2011; Kaut et al. 2016; Turbanski et al. 2005), patients with post-partum weak pelvic floor (Lauper et al. 2009), and healthy adults (Lauper et al. 2009).

Based on these findings and similarities between the proprioceptive and postural balance deficiencies in these medical conditions that might have affected the sensory-motor function in the lower limbs, it is speculated that the application of the SR vibration to the area around the knee in the ACLR participants might also lead to improved postural balance in this population. The effect of SR on the postural sway of ACLR patients remains unknown despite previously recommended research in this direction by others (A. T. Collins, Blackburn, Olcott, Miles, et al. 2011; A. T. Collins, Blackburn, Olcott, Yu, et al. 2011).

2.5 Measures of Postural Stability

The center of pressure (COP) trajectory of postural sway is usually used to assess the performance of the postural stabilizing system. Numerous COP measures have been developed to assess the COP data. Most of these measures have been originally presented or reviewed (Maurer & Peterka 2005; Prieto et al. 1996; Costa et al. 2005; Manor et al. 2010; Collins & De Luca 1993; Schubert et al. 2012). Some of these measures include stabilogram diffusion plot (Collins & Luca 1994; Priplata et al. 2004), entropy evaluation, and system determinism (Negahban et al. 2010; Manor et al. 2010) as well as a variety of time and frequency domain analyses (Maurer & Peterka 2005).

The COP signal is traditionally assessed by measures that study the COP in the medial-lateral (ML) and anterior–posterior (AP) directions. Primary attention in these methods usually focuses on the overall amount of displacement of the COP (Deffeyes et al. 2009), while ignoring the information embedded in the temporal structure of the signal emanating from the neuromuscular control strategies (Croft et al. 2008) and thus do not provide insight into the temporal changes in a signal that might reveal the complex sensory-motor mechanism in the postural control (Madeleine et al. 2011; Stergiou & Decker 2011). Analytic tools originating from non-linear dynamics theories can be utilized to address this issue and further investigate the information contained within the temporal structure of a signal (Costa et al. 2002; Richman & Moorman 2000; Pincus 1991).

One such a measure for quantifying a system's temporal structure is *entropy*. Entropy is defined as the rate of information generation within a signal that quantifies its orderliness and regularity (Zandiyeh & Von Tscharner 2013; Richman & Moorman 2000; Cover & Thomas 2006). Entropy has recently been utilized to assess various biological signals (Costa et al. 2002; Costa et al. 2004; Costa et al. 2005; Costa et al. 2007; Richman & Moorman 2000; Valencia et al. 2009; Paraschiv-Ionescu et al. 2008; Lake et al. 2002; Hu & Liang 2012; Kang et al. 2009) including COP trajectory signals (Manor et al. 2010; Kang et al. 2009; Costa et al. 2005; Costa et al. 2007; Glass et al. 2014). Since the works of Kolmogorov-Sinai on the entropy of a theoretical time series with infinite length (Costa et al. 2005), various computing algorithms have been developed, revised, completed, and applied to finite length signals (Grassberger & Procaccia 1983; Eckmann et al. 1986; Pincus 1991; Richman & Moorman 2000; Fogedby 1992; Costa et al. 2002; Costa et al. 2005; Ramdani et al. 2009).

The theory and method to approximate the entropy for a short and noisy time series was first reported in the works of Pincus and colleagues (Pincus 1991; Pincus & Goldberger 1994) and had been further elaborated and modified in the recent algorithm of *sample entropy* (SEn)

(Richman & Moorman 2000). SEn is defined as the negative of the natural logarithm of the conditional probability that the two *m* points sequences that are similar within a threshold value of *r* remain similar after adding the next point (Zandiyeh & Von Tscharner 2013; Richman & Moorman 2000). This method is in close agreement with the theory and will be used in this dissertation to calculate the entropy of the COP time series.

However, it was argued that the SEn calculated for a signal might not be able to satisfactorily extract the complexity of the temporal structure of a signal (Costa et al. 2005; Costa et al. 2003; Costa et al. 2002). Costa and colleagues proposed the multi-scale entropy to provide further insight into the complexity of a given signal. In this method, the original signal is divided into vectors each containing *k* (a natural number) consecutive time points from the original signal. The average value of each vector of length *k* was then calculated. The new signal in the scale *k* was constructed by placing these averages right next to each other while preserving their order in the original signal. The SEn will be calculated afterward for the signal at each scale. Since averaging abates the high frequencies in a signal, this approach shows a change in the sample entropy as the signal is continuously low pass filtered (Costa et al. 2002; Costa et al. 2005; Costa et al. 2003). The drawback of this algorithm is that it changes the length, standard deviation (SD), and probability density function of the signal as the scale increases (Nikulin & Brismar 2004; Zandiyeh & Von Tscharner 2013). SEn is sensitive to the changes in the statistical properties of a signal. Therefore, the pattern of multi-scale entropy acquired by this algorithm might not be representative of the underlying dynamics of the signal alone, but rather may be affected by the outlined changes (Zandiyeh & Von Tscharner 2013).

2.5.1.1 Entropic half-life (EnHL)

The method of *reshape-scale* (RS) was developed as a part of this thesis to serve as a novel multi-scale entropic analysis technique, which does not alter the length, SD, and the probability density distribution of time series data (Zandiyeh & Von Tscharner 2013). The original manuscript is provided in Appendix A:. To build a signal in a reshape scale *k* (a natural number), the data points *k* distance apart in the original signal are selected and placed right next to one another. The SEn is calculated for each *k* value. The conceptual model of an RS algorithm is presented in Figure 2.

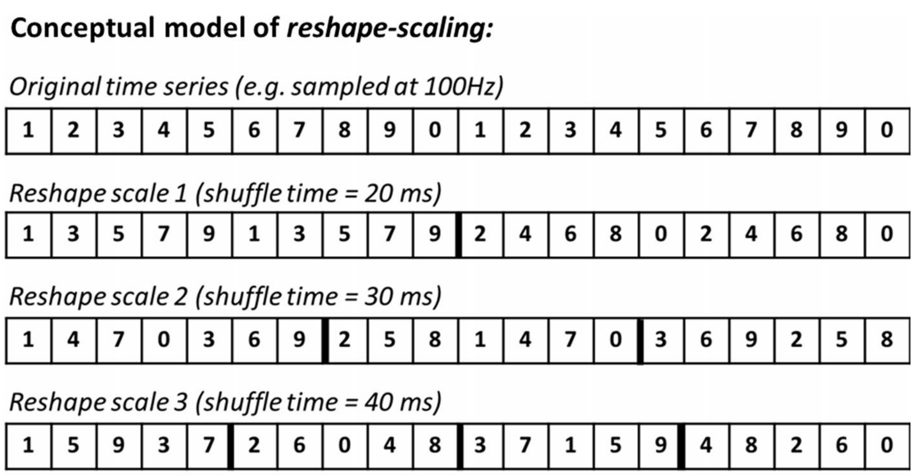

Figure 2 - Conceptual model of the reshape scale method

The RS-method applied to the COP data (Figure 3), generates a monotonic sigmoid shaped transition of SEn versus scale (Baltich, von Tscharner et al. 2014; Zandiyeh & Von Tscharner 2013). This transition starts from a minimal SEn corresponding to the ordered original signal and ends at a maximal value SEn. To calculate the maximum entropy, the signal is randomly permutated so that all data points in the signal appear in a completely random order. The average of the SEn for few realizations of randomly permutated signals is calculated and is reflective of the maximum entropy. To characterize this transition for the COP signal, the scale at which the transition reaches half of the maximum SEn is defined as the *entropic half-life* (EnHL).

The unique characteristic of EnHL is that it provides insight about the length of time information from the past that is utilized by the postural control system to make appropriate postural adjustments (Zandiyeh & Von Tscharner 2013). As a result, larger EnHL values can be interpreted as the postural control system utilizing past information or “memory” from a longer frame compared to smaller EnHL values.

Some other modern measures of complexity such as detrended fluctuation analysis also provide similar insights (See (von Tscharner et al. 2016) for more detailed discussion). However, the EnHL is presented in units of time and therefore is easily interpretable.

The EnHL has been used to analyze various biological signals including the COP (Baltich, Emery, et al. 2014; Baltich, Whittaker, et al. 2015; Baltich, von Tscharner, et al. 2015; Baltich, von Tscharner, et al. 2014; Federolf et al. 2015; von Tscharner et al. 2016), electromyography (Enders et al. 2015), and electrocardiogram (von Tscharner & Zandiyeh 2017).

In a collaborative work in support of this thesis, the test-retest reliability of the EnHL has been evaluated and showed to be comparable to the reliability of classical variables widely used to assess the COP signals (Baltich, von Tscharner et al. 2014). In that study, 27 healthy participants were recruited and tested at the two time-points (one week apart). Each participant performed a single leg balance. The EnHL was calculated for the factors of *time* (week one vs. week two), *Limb* (dominant vs. non-dominant), and *task* (Eyes open on a rigid surface, eyes closed on a rigid surface, eyes open on foam). An excellent relative reliability was found for the EnHL as assessed by the intra-class correlation (0.82-0.91) and was found to be similar to the reliability of classical measures such as excursion, path length, and 95% confidence interval area (See (Baltich, von Tscharner, et al. 2014) for further details).

Combined, the outlined studies intimate that the measure of EnHL is probably sufficiently sensitive, repeatable, and informative in differentiating between different COP trajectories in various clinical populations. The considerably high sensitivity of EnHL to different conditions, make it a strong measure for assessing SR-related COP changes in the currently proposed study. Thus, it has been selected as one of the primary outcome measures for the COP assessments in this dissertation.

2.5.1.2 Phase surrogate analysis (ΔE_{surr})

The measure of ΔE_{surr} is another measure that has been developed in collaborative works by the current author in parallel with the current dissertation. This measure is capable of providing insight about the importance of the timing of events in a given biological signal (von Tscharner et al. 2016; von Tscharner & Zandiyeh 2017). The postural adjustment in the postural balance can serve as an example here. If it is assumed that the postural adjustments appear completely randomly in a recorded COP signal, the ΔE_{surr} will become zero. If the postural adjustments are strictly regulated and executed timely, the ΔE_{surr} will be maximal. The majority of biological signals however, will fall between these two extreme scenarios.

To calculate the ΔE_{surr}, first a Fourier transform of the signal will be calculated. The Fourier transform decomposes a signal into its amplitude and phase components. The phase is the outcome of time of events in the original signal at a given frequency (Oppenheim & Lim 1981). In some time series such as autoregressive-moving average (ARMA) processes, the events in the signal appear in a completely random order and therefore no information is encoded in their phase. Therefore, if the phase is randomized, the information content of the signal will not be altered since no information was originally present in the phase.

Investigating the importance of timing of events in the information content of a COP signal potentially provides information about the role of the postural control system in regulating and controlling postural adjustments. Therefore, it is important to reject the hypothesis that the events in a given signal happen on a completely random basis. The process by which such a test is conducted is referred to as *surrogate analysis* (Theiler et al. 1992).

To create a surrogate realization of a signal, the Fourier transform of the signal is calculated, the phase is replaced by random numbers from $-\pi$ to π, and the inverse Fourier transform is taken to transform the signal back to the time domain. The desired measure of the signal (here SEn) is calculated for the original and the surrogate signal. With a satisfactory number of surrogates it becomes feasible to perform an appropriate statistical test (e.g. student's t-test) to investigate whether a significant difference is observed in the desired measure following the surrogate analysis. If so, the null hypothesis is rejected, and it can be concluded that the timing of events were important and were non-random. Although the method of surrogate analysis dates back to the works by Theiler and colleagues (Theiler et al. 1992) and was used as a "test of non-linearity" in signals, it has never been viewed previously as a potential "measure of regularity" in a signal.

If the SEn is calculated for the surrogate SEn of each RS-scale signal, a monotonic sigmoid shape transition can be observed (see Figure 3), while the transition of the surrogate is usually situated above the transition of the original signal. The amount of information in the phase can be calculated by computing the absolute difference between the SEn of the surrogate and the SEn of the original signal at a given RS-scale (i.e. ΔE in Figure 3). This is because the variable ΔE_{surr} has been defined to quantify the percentage of information in the signal that is present in the phase. When the RS-scale is equal to EnHL, SEn of the original signal is 0.5. Therefore, $\Delta E_{surr}|_{@EnHL} = \frac{\Delta E}{0.5}\%$. Thus, this measure is reflective of the percentage of information contained in the phase of a signal when the RS-scale is equal to EnHL. In the remainder of this dissertation whenever ΔE_{surr} has been used it is a substitute for the more lengthy: $\Delta E_{surr}|_{@EnHL}$.

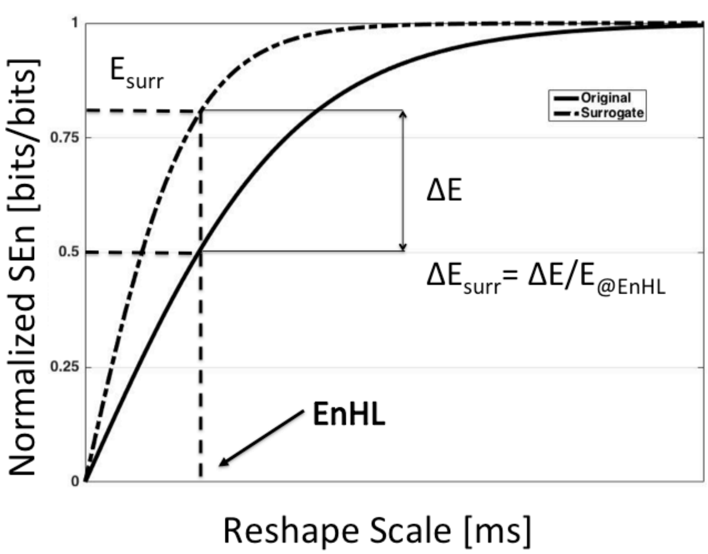

Figure 3 - Transition of the SEn for the time series. The SEn transition shown here is presented by the division to the maximum SEn. EnHL is the reshape scale presented in a unit of time for which the SEn transition will reach 50% of its final value. The $\boldsymbol{E_{surr}}$ is the SEn of the surrogate at EnHL scale. The $\boldsymbol{\Delta E_{surr}}$ is defined as the changes in entropy following the surrogate analysis at EnHL scale divided by $\boldsymbol{E_{surr}}$ i.e. $\boldsymbol{\Delta E_{surr} = \Delta E / E_{surr}}$.

The measure of surrogate entropy is still relatively new with only one study published utilizing it, and the current author is a co-author on this paper. The ΔE_{surr} was used for the first time to differentiate between healthy and congenital heart failure patients with remarkable sensitivity of 87% and specificity of 89% (von Tscharner & Zandiyeh 2017).

Using the ΔE_{surr} might provide insights about the importance of regulation in the timing of the postural adjustments by the postural control system. It will be insightful to see how the timing of postural adjustments will be regulated following ACLR surgery and if more stringent control is placed on the postural adjustments. Therefore, the ΔE_{surr} has been used as one of the outcome measure to assess the COP signal in the current study.

Chapter Three: **Methodology**

> *"... My actions are my only true belongings. I cannot escape the consequences of my actions. My actions are the ground upon which I stand."*
>
> *Thich Nhat Hahn (1926- present)*

This chapter describes methodologies to determine the maximum knee extension angle, vibration sensation threshold, minimum detectable movement of the knee, movement repeatability of the knee, and the postural sway during the single leg stance.

3.1 Experimental Protocols

3.1.1 Participants

This study is the first of its kind in the ACLR group; no data were available from previous studies to provide information for statistical power calculation. Therefore, the current study is based on exploratory study design including 30 healthy and 30 ACLR participants. Furthermore, similar studies in SR on different clinical groups, have used mostly fewer than 30 participants per group (Priplata et al. 2003; Collins et al. 2003; Gravelle et al. 2002; Priplata et al. 2002; Pavlik et al. 1999; Reeves et al. 2009; Rogan et al. 2012; Hijmans et al. 2008; Priplata et al. 2006; Ross et al. 2007; Lugo et al. 2008; Collins et al. 2009).

The Conjoint Health Research Ethics Board (CHREB) at the University of Calgary approved the study, and all participants have provided written consent to participate in the study. The ACL-Quality of life (ACL-QOL) (Mohtadi 1998) and IKDC 2000 subjective knee evaluation forms (Irrgang et al. 2006) were filled out by each participant. The inclusion criteria considered for the ACLR participants were: skeletally mature (16 to 40 years) female adult; less than three months since ACL reconstruction; body mass index (BMI) 18 to 25 kg/m^2; otherwise with no other lower limb injuries within the last six months. The participant was not tested approximately between 3 days before to 3 days after her menstrual cycle (Darlington et al. 2001) and was asked to choose a test day outside of this time. Pregnant participants or participants who had used any medication that might have altered their nervous and muscular performance[1] were excluded (Butler et al. 2006). The participants were excluded if they had any fresh skin injuries (e.g., open wounds) or diagnosed dermal diseases or special skin sensitivities in the areas around the knee. The healthy controls had no history of previous injury to their knees. Excepting that, similar inclusion criteria were used in their recruitment. All ACLR participants were tested at two time points i.e. three months and six months post-surgery while the healthy participants were tested only once.

3.1.2 Maximum knee flexion angle

All angles in this dissertation are reported compared to the maximum knee extension angle (0°). To establish the maximum knee extension angle, the Biodex machine was used (Biodex Multi-joint System Pro 4.0, Biodex Medical Systems Inc., NY, USA). The measurement protocol can be summarized as follows: Each participant was seated on the Biodex, with the back reclined to 90 degrees, with the dynamometer positioned outside the test leg. The knee attachment for the corresponding leg was attached to the dynamometer, and the participant was moved into the desired position with her approximate medial-lateral knee axis of rotation aligned with the dynamometer axis of rotation. The attachment was adjusted so that it was proximal to the medial

[1] Medications such as Adrenergic blocking drugs, anti-convulsion, anti-anxiety, anti-Parkinson, anti-psychotic, anti-depressants, narcotic analgesics, non-narcotic analgesics, narcotic antagonists, and medications causing muscle pain, weakness or drowsiness, and drug addiction.

malleoli of the test leg and secured with Velcro straps. The shoulder, waist, and thigh straps were also utilized to secure the participant on the Biodex chair[1].

The participant was instructed to maximally extend the knee without attempting to lift her thigh from the seat. Three knee extension trials were performed. The Research Tool-Kit 3.0 (the software package provided with the Biodex machine) was used to record the desired angles and to passively flex/extend the knee to the desired angles. The average angle of the three trials was used to estimate the *maximum (average) extension angle*.

3.1.3 Determining the Vibration sensation threshold

The vibration sensation threshold was quantified using an array of five C2 vibrotactile transducers (Engineering Acoustics Inc., Casselberry, FL, USA) placed at roughly one-inch distances from the crest of the patella on the limb of interest (Figure 4). The vibrotactile transducers were controlled using the ATC 3.0 software (Engineering Acoustics Inc., Casselberry, FL, USA) that included a "white-noise" generator to administer a band-limited white noise with a frequency range between 1 to 500 Hz.

The details about the arrangement of vibrators as well as the desired amplitude of vibration has been decided based on pilot tests of 10 ACLR participants. The details of methodology and results are provided in Appendix C:.

The vibration sensation threshold was determined based on increasing the amplitude of SR noise until the participant detected the vibration (increasing amplitude). This was repeated with the amplitude starting above the named detection level and then the gradually decreasing the

[1] The machine was calibrated every month during the period of study according to the suggested calibration protocol provided by the manufacturer.

amplitude (decreasing amplitude) until the participant did not detect the sensation any longer. Five trials in each amplitude direction (increasing/decreasing) were recorded.

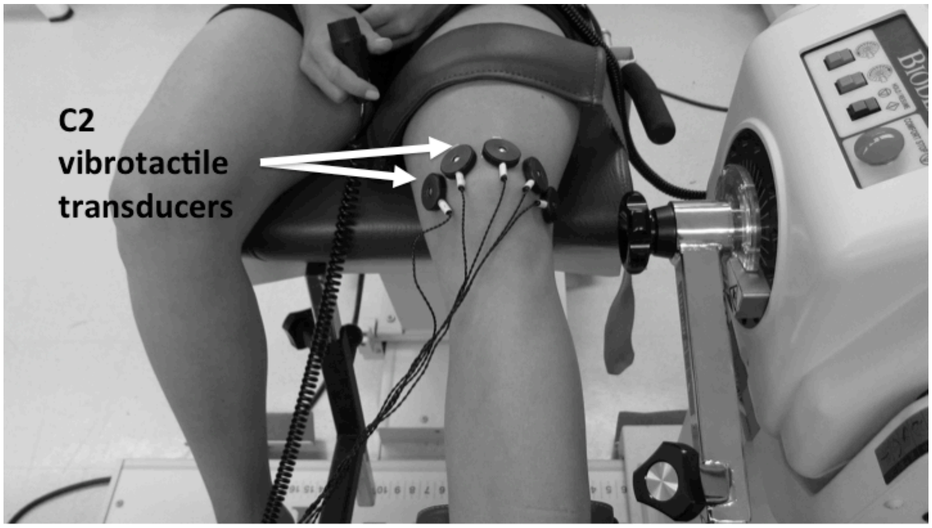

Figure 4 - Experimental setup on the Biodex machine with C2 vibrotactile transducers attached.

Statistical analysis was performed on the vibration sensation threshold to see if the amplitude direction (increasing vs. decreasing) had any effect on the vibration sensation threshold. Using repeated measures ANOVA, it was observed that the vibration amplitude was significantly lower when the increasing amplitude protocol was utilized ($p = 0.008; \eta^2 = 0.40$)[1]. The desired level of SR stimulation for each individual was set at ninety percent of the average of the amplitudes acquired using the increasing gain approach. Furthermore, it was confirmed with participants during the experiment that they were unable to detect the vibration on their skin. The SR

[1] The effect estimates showed that the vibration sensation threshold is 0.0132±0.004 mm smaller when the increasing gain protocol was utilized.

stimulation remained sub-threshold throughout the experiment and thus the participants were blinded to the status of vibration.

The amplitude (gain) is a variable defined in the vibrators' accompanying software and can be converted to displacement in millimeters. However, the absolute value of the amplitude is irrelevant to the objectives of this dissertation and is always reported as the 90% of the individual's vibration sensation threshold.

3.1.4 Determining the minimum detectable movement in the presence and absence of SR noise

To measure the minimum detectable movement and how SR noise influences this, the participant was situated in the Biodex according to the protocols described in the previous section. The joint was passively moved into $15°$ flexion from the initial location. The participant wore earplugs (to block external audio stimuli) and was instructed to close her eyes (to block external visual stimuli) while paying close attention to the movement in her knee. The participant was instructed to press a pushbutton as soon as a movement was felt in her joint. Pressing the pushbutton froze the dynamometer at its position and the angular displacement was recorded with 0.1° precision. In this experiment, the angular velocity of passive flexion/extension was selected to be 0.25 $°/s$. The passive movement of the dynamometer started with a random lag in a randomly selected direction (to minimize the anticipation of the direction by the participants). The participant was requested to determine the direction of movement (flexion or extension). Five trials were tested for each factor of direction (flexion vs. extension), SR (ON vs. OFF), limb side (ACLR vs. contralateral in ACLR participants; dominant vs. non-dominant in the healthy controls) resulting in a total of $5×2×2×2 = 40$ trials total. The average of five replicates for each combination of factors was used for the statistical comparison.

It was observed during the pilot testing, that sometimes a participant might delay before pressing the pushbutton, wanting to be certain of the direction. This cautious approach jeopardized the original objective of the movement threshold measurement since the subjective psychological factor such as uncertainty contaminated the desired outcome. Therefore, participants were instructed not to wait until they were certain about the direction of movement but rather to press the button as soon as they perceived a movement in their knee joint. If the direction wrongly specified by the participant or was unclear to her, the trial was repeated.

3.1.5 Determining the movement repeatability error of the knee in the presence and absence of SR noise

To determine the movement repeatability error in the knee, two sets of experiments were conducted. First, the knee was position at 15° and then flexed passively to 45°. The participant was instructed to memorize the position while the machine remained at that angle for 3 seconds. Following the 3-second pause, the knee was extended back to the original position (15°). The dynamometer passively moved the joint into flexion at the rate of 10˚/sec. The participant was asked to press the push button whenever the knee flexion reached the desired angle memorized. The absolute difference between the desired angle and the angle reproduced was then calculated (movement repeatability in flexion).

In the second protocol, everything remained similar, but the order of the movement was reversed (i.e. the knee was initially flexed to 45 degrees and then passively extended to 15 degrees). The participant was asked to reproduce the 45° flexion position (movement repeatability in extension).

Three practice trails followed by five trials were recorded for the factors of direction (extension vs. flexion), SR (ON vs. OFF), and limb side (ACLR vs. contralateral; healthy dominant vs.

healthy non-dominant) for a total of $5 \times 2 \times 2 \times 2 = 40$ trials. The average of five replicates for each combination of factors was used for the statistical comparison.

3.1.6 Postural sway in the presence and absence of SR noise when the participant is performing single leg balance with eyes open or closed

To measure the postural balance in the current study, participants performed single leg balance with their hands on their hip and standing on one limb with knee slightly bent and foot raised above ground (Figure 5). Duration of each trial was 30 sec.

A) **B)**

Figure 5 - Postural sway setup with participant standing on force plate, A) anterior view with SR transducers visible on right thigh, B) posterior-lateral view

Conditions assessed included eyes (open vs. closed), SR (OFF vs. ON), limb side (ACLR vs. contralateral; dominant vs. non-dominant), time since surgery (three months vs. six months for

ACLR; the only one-time point for healthy controls). For the eyes open condition, participants were asked to stare at a pre-defined location so that their head remained approximately neutral and straight in position. Their COP trajectory was recorded at 2400 Hz using the AMTI force platform (AMTI 0R6-6, MA, USA).

Each participant performed three trials of single leg balance for each condition. Some participants were unable to perform a single leg balance task with their eyes closed. These participants were given a maximum of 10 trials to attempt the task. If three trials were not successfully obtained, the eyes closed data corresponding to those participants were not used in the statistical analysis.

The force plate data was extracted from the ANC files. The center of pressure (COP) was calculated from the AMTI force platform manual. Before data filtering, the fast Fourier transform was utilized to calculate the power spectral density of the COP data in the ML and AP directions, respectively. Observation of the power spectrum revealed that all power was retained in the frequency range of 0.1 to 10 Hz. The recorded COP data at 1200 Hz was first down-sampled to 75 Hz and then bandwidth filtered $[0.1,10]$ Hz using the Wavelet filter outlined in (Tscharner & Schwameder 2001). The SEn was calculated using $m = 2$ and $r = 0.7$ in compliance with (von Tscharner et al. 2016).

3.2 Measures

3.2.1 Movement threshold

The amount of movement (in degrees) was used as the output measure for the minimum detectable movement threshold. The purpose of the experiment was to monitor any differences that arise under the different experimental conditions. It was observed that each individual had a certain movement threshold range. Consequently, before performing the statistical analysis, the data were normalized by subtraction of the minimum and then division by the range of data for each participant uniquely. The summary statistics are provided in the original scale (in degrees) to give insight about the ranges of each variable, while the normalized data was used for further statistical analyses.

3.2.2 Movement repeatability

The absolute difference between the recorded and the desired angle was calculated as the output variable for the movement repeatability test.

3.2.3 Postural sway

The EnHL and ΔE_{surr} were calculated for the COP trajectory in ML and AP directions resulting in a total number of four outcome measures for the postural balance as follows: $EnHL_{ML}$, $EnHL_{AP}$, $\Delta E_{surr_{ML}}$, and ΔE_{surr_AP}.

3.2.3.1 Classical measures of COP

Numerous classical measures that have been traditionally used to assess COP data (Table 1) were also computed for comparison purposes. The details about the associated calculations and their interpretations can be found in (Prieto et al. 1996; Schubert et al. 2012). These measures include time domain distance measures (mean distance, range, root mean square (RMS) of distance, standard deviation (SD) of distance, total excursion, mean velocity), time domain measures of area (confidence circle area, confidence ellipse area, confidence ellipse direction, confidence ellipse large eigenvalue, confidence ellipse small eigenvalue, convex hull area), nonlinear measures (fractal dimension confidence circle, fractal dimension confidence ellipse, fractal dimension radial distance, Hurst coefficient, Lyapunov exponent, detrended fluctuation analysis, mean and standard deviation of Beta), and measures of frequency (central frequency, 50% frequency, 80% frequency, 95% frequency, 99% frequency) mean frequency, total power).

Table 1 - Classic measures of COP analyzed for comparison purposes

Measures 1-36	Measures 37-65
01. Beta mean	37. Lyapunov Exponent AP
02. Beta Std	38. Lyapunov Exponent ML
03. Confidence circle area	39. Lyapunov Exponent RD
04. Confidence ellipse area	40. Mean distance AP
05. Confidence ellipse direction	41. Mean distance ML
06. Confidence ellipse large eigen value	42. Mean distance RD
07. Confidence ellipse small eigen value	43. Mean frequency AP
08. Central frequency in AP	44. Mean frequency ML
09. Central frequency in ML	45. Mean frequency RD
10. Central frequency in RD	46. Mean velocity AP
11. Compact polynomial area	47. Mean velocity ML
12. Convex Hull Area	48. Mean velocity RD
13. DFADimension_AP	49. Total power AP
14. DFADimension_ML	50. Total power ML
15. DFADimension_RD	51. Tottal power RD
16. Fractal Dimension confidence circle	52. Range AP
17. Fractal Dimension confidence ellipse	53. Range ML
18. Fractal dimension radial distance	54. Range RD
19. 50% frequency AP	55. rms distance AP
20. 50% frequency ML	56. rms distance ML
21. 50% frequency RD	57. rms distance RD
22. 80% frequency AP	58. Std AP
23. 80% frequency ML	59. Std ML
24. 80% frequency RD	60. Std RD
25. 95% frequency AP	61. Sway area
26. 95% frequency ML	62. Total excursion AP
27. 95% frequency RD	63. Total excursion ML
28. 99% frequency AP	64. Total excursion RD
29. 99% frequency ML	65. Turn index
30. 99% frequency RD	
31. Frequency dispersion AP	
32. Frequency dispersion ML	
33. Frequency dispersion RD	
34. Hurst coefficient AP	
35. Hurst coefficient ML	
36. Hurst coefficient RD	

3.3 Statistical Analysis for within population exploration

In this section, the statistical analyses that were performed to compare the ACLR limb to the contralateral are described. This type of analysis was used to address all hypotheses excepting: [H5], [H6], [H7], [H8], and [H15]. The outlined hypotheses include comparisons between the ACLR group and healthy controls. The statistical methods to address these hypotheses are presented later in §3.4.

All statistical analyses in this dissertation were performed using SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Macintosh, Version 22.0. Armonk, NY: IBM Corp.).

3.3.1 Anthropometric data of the participants

For the healthy group the means and standard deviations for the following outcome measures were calculated: age [yrs.], height [cm], body-mass [kg], training hours per week [hrs/week], and body mass index (BMI) [kg/m^2]. In the ACLR group, the same outcome measures were recorded at the two time-points of 3 and six months post-surgery.

To assess whether the anthropometric characteristics of the ACLR sample changed significantly over time, a one-way repeated measures ANOVA with the factor of time (three months vs. six months post-surgery) was performed for the measures of height, body mass, training hours, and BMI.

3.3.2 Movement threshold

The movement threshold experiment for the ACLR group consisted of four factors: time (three months or six months post ACLR surgery), limb side (ACLR vs. contralateral), direction (flexion vs. extension), and SR (ON or OFF). A 4-ways repeated measures ANOVA was utilized to study the significance of the main effect and all 2-ways interactions between the outlined factors on the normalized movement threshold. The significance level of $\alpha = 0.05$ was adopted.

3.3.3 Movement repeatability

The absolute value of the difference between the recorded and the desired angle was calculated for the factors of limb side (ACLR vs. contralateral), direction (flexion vs. extension), SR (ON vs. OFF), and time (three months vs. six months). A 4-ways repeated measures ANOVA was used to study the main effects as well as all 2-ways interaction between these factors on the movement repeatability error with $\alpha = 0.05$ deemed significant.

3.3.4 Postural sway

The entropy measures of $EnHL_{ML}$, $EnHL_{AP}$, $\Delta E_{surr_{ML}}$, and $\Delta E_{surr_{AP}}$ were calculated for the COP trajectory of ACLR participants for the factors of limb side (ACLR vs. contralateral), SR (ON vs. OFF), eyes (open vs. closed), and time (three months vs. six months).

There was some participant attrition at the six-month time point. If the repeated measures ANOVA was used it would have removed all of the data from those participants. In addition, data from participants who were not able to perform the single leg standing during the eyes closed condition would have also been discarded. The treatment of data in this way would have resulted in reduced sample size and compromised power in the statistical analyses.

To overcome this limitation, the results were analyzed using the Generalized Estimating Equation (GEE) algorithm, which can take into account missing data without the need for removing the information from the corresponding participant entirely. The data were analyzed using a 4-ways unbalanced repeated measures design with interval outcome variables using a Generalized Estimating Equation (i.e., GEE under the GENLIN procedures in SPSS v.22). The main effects as well as all 2-ways interactions of the outlined factors have been studied.

3.4 Statistical analyses for between population

This section provides the between population comparison (ACLR vs. healthy dominant limbs) to address the hypotheses [H5], [H6], [H7], [H8].

3.4.1 Proprioception

The potential differences in proprioception between healthy and ACLR group at three months post-surgery were assessed using repeated measures ANOVA for the within factor of SR (OFF vs. ON) and the between factor of health condition (healthy vs. ACLR) when the joint moves into flexion. The normalized movement threshold error and movement repeatability error were compared using a two-tailed test. A difference at the significant level of $\alpha = 0.05$ was deemed significant.

3.4.2 Postural sway

Postural sway was assessed using a GEE analysis. In this analysis the postural sway of the ACLR group at three months post-surgery on the ACLR limb was compared to the dominant limb of the healthy control group with the health condition (ACLR vs. healthy dominant) as the between factor and SR (OFF vs. ON) and eyes (open vs. closed) as between factors with $\alpha = 0.05$ deemed significant. The following outcome measures of COP were assessed: $EnHL_{ML}$, $EnHL_{AP}$, $\Delta E_{surr_{ML}}$, and $\Delta E_{surr_{AP}}$.

Shapiro-Wilk normality test was performed to test normality of distributions when ANOVA tests were performed. However, the results of normality tests were not presented in the current dissertation.

Chapter Four: **Results – Exploration within the ACLR population**

In this chapter, the results of comparisons between the ACLR and contralateral limbs on the proprioception and postural balance outcome variables are presented and studied. A summary of anthropometric outcomes and questionnaires for both healthy and ACLR groups are presented and have been compared between the two time points (§4.1 and §4.2 respectively). The proprioception and postural balance outcome variables are compared within ACLR population only (§4.3 and §4.4 respectively). The summary of all key statistical findings in the current chapter is provided in §4.5.

Comparisons between the ACLR and healthy controls on the proprioception and postural balance outcome variables are presented in Chapter Five: Results - Exploration between the ACLR and healthy .

4.1 Anthropometric Data

Initially, 30 healthy participants were recruited and tested for the current experiment. However, the data for 2 participants were found to be corrupted and could not be used in the analysis. Therefore, the results in this section are reported for the remaining 28 participants. Among these healthy participants, 25 were right dominant, and 3 participants were left dominant. On average the anthropometric outcomes for the healthy groups were as follows: *age* 24 (4) (mean (SD)) years*, height* 166 (5) cm*, body mass* 59.2 (5.6) kg*,* self-reported *training hours per week* (TrH) of 6(3), and BMI of 21.6(1.8) kg/m^2.

Attempts were made to recruit 30 ACL reconstructed patients. However, as the recruitment was slow, given the inclusion criteria, a total of 19 participants were recruited over 14 months for the experiment at three months post-surgery. At that point, it was decided that to assure completion of the project in a timely manner, recruitment was halted, and data analyses were begun. Among these recruited participants 4 did not participate in the follow-up appointment at six months post-surgery. Among these initially recruited participants, 18 participants had a dominant right leg, and the remaining participant was left dominant. The left dominant participant was present at the six months follow-up assessment.

On average the anthropometric outcomes for the ACLR population were as follows: (1) At three months post-surgery: age 25(5) years, height 167(8) cm, body mass 68.1(11.8), training hours per week 5(3), and BMI 24.4(3.7) kg/m^2 (minimum 20.3 and maximum 32.8kg/m^2) (2) At six months post-surgery: age 25(5) years, height 168(8) cm, body mass 66.1(12.5), training hours per week 5(3), and BMI 23.4(4.0) kg/m^2 (minimum 17.5 and maximum 32.5kg/m^2).

The effect of time since surgery (3 vs. six months) on the anthropometric outcomes was tested using repeated measures ANOVA for the ACLR group. No significant changes were observed on any of the anthropometric measures between the two-time points. Further investigation indicated that, on average, the body mass and BMI of the participants showed a non-significant decrease from time point 1 to 2 of approximately 2 kg ($p = 0.08$).

4.2 Questionnaires

The IKDC 2000 subjective knee evaluation score for the healthy participants was 97(8)%. The IKDC 2000 score for the ACLR population at three months post-surgery was 56(12)% and at six months reached 71(11)%. For the ACLR population, ACL-QOL questionnaire was also recorded. At three months ACL-QOL in the ACLR group was 49(13)%, and at six months it reached to 62(17)%.

The effect of time (three vs. six months) on the IKDC 2000 subjective knee evaluation score in the ACLR group reached significance ($p < 0.001$) with the average IKDC2000 scores improving by 15(2)% over time. Similarly, the ACL-QOL mean score for the factor of time reached significance ($p < 0.001$) with the scores improving by 13(3)% over time.

4.3 Proprioception

4.3.1 Movement threshold

In this section, the statistical analysis for the movement threshold for the factors of time (three months vs. six months) limb side (ACLR vs. contralateral), direction (Flexion vs. Extension), and SR (ON vs. OFF) are presented. Descriptive statistics of movement threshold are provided in Table 2. The recorded movement threshold has a very small range from 0.4° to 0.8°. The SE of the measurement is relatively small and is about 0.1° on average. Overall, the movement threshold at six months shows a non-significant reduction compared to three months.

Table 2 – Descriptive statistics of the movement threshold [°] under different experimental conditions of time, limb side, direction, and SR

				Movement Threshold [˚]			
						95% CI	
Time	Limb side	Direction	SR	Mean	SE	Low	Up
3 Months (n=19)	ACLR	Flexion	OFF	0.7	0.1	0.4	0.9
			ON	0.7	0.1	0.5	0.9
		Extension	OFF	0.6	0.1	0.3	0.9
			ON	0.5	0.1	0.4	0.7
	Contra.	Flexion	OFF	0.8	0.2	0.5	1.1
			ON	0.7	0.1	0.4	0.9
		Extension	OFF	0.6	0.1	0.4	0.9
			ON	0.6	0.1	0.4	0.8
6 Months (n = 15)	ACLR	Flexion	OFF	0.5	0.1	0.4	0.6
			ON	0.5	0.0	0.4	0.6
		Extension	OFF	0.5	0.1	0.4	0.7
			ON	0.4	0.1	0.3	0.6
	Contra.	Flexion	OFF	0.6	0.1	0.4	0.7
			ON	0.5	0.1	0.4	0.7
		Extension	OFF	0.5	0.1	0.4	0.7
			ON	0.5	0.1	0.4	0.6

The output of the 4-way repeated measures ANOVA for the normalized data in the ACLR group is presented showed that only the effect of SR stimulation reached significance ($p = 0.026; \eta^2 = 0.31$). An effect estimate showed that when SR was ON, the movement threshold decreased by 0.1±0.0˚.

4.3.2 Movement Repeatability

The effect of four factors of time (three months or six months), limb side (right vs. left), direction (flexion or extension), and SR (ON or OFF) on movement repeatability (a measure of proprioception) is reported in this section. Descriptive statistics of movement repeatability are shown in Table 3. Based on this table, it can be seen that the movement repeatability error shows smaller values when SR is ON compared to OFF. The values of SE are fairly comparable at three months and six months post-surgery indicating an overall homogeneity. The values of movement threshold error on average are more than approximately nine times larger than the SE of measurements. This finding suggests a relatively small measurement error.

Table 3 – Descriptive statistics of the movement repeatability error [°] under factors of time (three months vs. six months), limb side (ACLR vs. contralateral), direction (flexion vs. extension), and SR (ON or OFF).

						95% CI	
Time	**Limb Side**	**Direction**	**SR**	Mean	**SE**	**Lower**	**Upper**
3 Months (n = 19)	**ACLR**	**Flexion**	**OFF**	3.5	0.3	2.7	4.0
			ON	2.6	0.3	1.7	2.9
		Extension	**OFF**	2.6	0.2	2.1	3.1
			ON	2.6	0.2	2.1	3.1
	Contra.	**Flexion**	**OFF**	3.6	0.4	2.4	4.3
			ON	2.2	0.2	1.7	2.7
		Extension	**OFF**	3.3	0.4	2.4	3.7
			ON	2.7	0.4	1.9	3.7
6 Months (n = 15)	**ACLR**	**Flexion**	**OFF**	3.8	0.4	2.8	4.7
			ON	2.6	0.3	1.9	3.3
		Extension	**OFF**	3.4	0.6	2.1	4.8
			ON	2.4	0.3	1.7	3.1
	Contra.	**Flexion**	**OFF**	3.0	0.3	2.2	3.8
			ON	2.3	0.3	1.7	3.0
		Extension	**OFF**	3.2	0.3	2.4	4.0
			ON	2.7	0.4	1.8	3.5

The outcome of the 4-way repeated measures ANOVA showed that only the effect of SR reached significance ($p < 0.001; \eta^2 = 0.31$). The study of effect estimates revealed that with SR ON, the movement repeatability decreased by 0.7±0.1˚.

4.4 Center of Pressure Measures

4.4.1 Entropy Measure

In the next four sub-sections, the statistical analyses for each entropic-based outcome measure of COP are reported separately. These measures include $EnHL$ and ΔE_{surr}in ML and AP directions (four measures in total). The effects of the following factors have been studied on the COP measures were included: eyes (open vs. closed), limb side (ACLR vs. contralateral), time since surgery (3 vs. six months), and SR vibration (OFF vs. ON). Each sub-section starts with the descriptive statistics for each outcome measure followed by the results of the statistical analysis of the factors' effects on the outcome.

4.4.1.1 The Statistical Results for $EnHL_{ML}$

The descriptive statistics for $EnHL_{ML}$[ms] are presented in Table 4. It can be observed from this table that, the EnHL is larger in general when eyes are closed compared to eyes open. The SE of measurement seems small and confined to less than 5 ms in majority of conditions. On average, the EnHL in the ML direction is approximately 102 ms.

Table 4 – Summary of descriptive statistics for the $\mathbf{EnHL_{ML}}$[ms] for the factors of limb side, eyes, time, and SR

						95% Wald CI	
Time	**Limb Side**	**SR**	**Eyes**	**Mean**	**SE**	**Lower**	**Upper**
3 Months	**Contra.**	**OFF**	**Closed**	105	5	95	115
			Open	101	4	94	108
		ON	**Closed**	103	3	97	109
			Open	97	3	91	103
	ACLR	**OFF**	**Closed**	112	5	102	121
			Open	100	3	95	106
		ON	**Closed**	113	7	99	128
			Open	96	3	91	101
6 Months	**Contra.**	**OFF**	**Closed**	100	3	95	105
			Open	92	2	87	97
		ON	**Closed**	102	4	94	109
			Open	99	3	93	106
	ACLR	**OFF**	**Closed**	102	3	96	109
			Open	96	2	92	101
		ON	**Closed**	117	12	93	142
			Open	98	5	89	108

The outcome of statistical analysis for $EnHL_{ML}$ showed that the effect of eyes ($p = 0.001$), $Time{\times}SR$ ($p = 0.024$), and $LimbSide{\times}Eyes$ ($p = 0.047$) reached significance. The effect of limb side only marginally missed the significance ($p = 0.05$).

Studying the effect estimate on the interaction of $SR \times Time$ showed that the $EnHL_{ML}$ was increased by 6±3 ms (mean ± SE) when SR was ON only at the six-month time point ($p = 0.043$). Furthermore, the $EnHL_{ML}$ at three months was 7±3 ms larger than at the six-month time point ($p = 0.009$). When SR was ON the difference was not significance.

The posthoc test on the interaction of the $LimbSide \times Eyes$ showed that only when eyes were closed the difference between the $EnHL_{ML}$ of the ACLR and contralateral limbs reached significance ($p = 0.032$). The $EnHL_{ML}$was larger by 9±4 ms on the ACLR limb compared to the contralateral limbs. A study of effect estimate was performed for the factor of eyes on the interaction; it was observed that the effect of eyes on the $EnHL_{ML}$ reached significance for both the contralateral ($p = 0.035$) and ACLR ($p = 0.002$) limbs.

4.4.1.2 The statistical results based on $EnHL_{AP}$

The summary statistics for $EnHL$ [ms] in the AP direction are reported in Table 5. Larger EnHL can be observed in the AP direction compared to the ML direction with small SE values. It can also be observed that the EnHL in AP seems larger at three months compared to six months post-surgery.

Table 5 – Descriptive statistics for outcome measure of the $EnHL_{AP}$[ms] for the factors of time, limb side, SR, and eyes

						95% Wald CI	
Time	Limb Side	SR	Eyes	Mean	SE	Lower	Upper
3 Months	Contra.	OFF	Closed	139	13	114	164
			Open	136	5	126	146
		ON	Closed	125	7	113	138
			Open	123	5	114	132
	ACLR	OFF	Closed	133	6	122	145
			Open	138	5	128	148
		ON	Closed	142	8	126	158
			Open	135	8	120	149
6 Months	Contra.	OFF	Closed	125	7	112	138
			Open	122	4	115	130
		ON	Closed	121	6	110	132
			Open	129	6	118	141
	ACLR	OFF	Closed	129	4	121	137
			Open	135	6	124	147
		ON	Closed	140	13	115	166
			Open	126	5	117	135

The statistical analyses for the $EnHL_{AP}$ showed no significant effect for any of the factors.

4.4.1.3 The statistical results based on $\Delta E_{surr_{ML}}$

The summary descriptive for ΔE_{surr}in the ML direction is presented in Table 6. As it can be observed, the ΔE_{surr} seems smaller when eyes were open compared to eyes closed. The SE of measurements was below 1%.

Table 6 – Summary statistics for the $\Delta E_{surr_{ML}}$[bits] for the factors of time, limb side, SR, eyes

Time	Limb Side	SR	Eyes	Mean	SE	95% Wald CI Lower	95% Wald CI Upper
3 Months	Contra.	OFF	Closed	3.7%	0.5%	2.6%	4.7%
			Open	3.0%	0.5%	2.1%	4.0%
		ON	Closed	3.4%	0.5%	2.5%	4.4%
			Open	2.4%	0.3%	1.7%	3.1%
	ACLR	OFF	Closed	5.0%	0.9%	3.3%	6.8%
			Open	2.5%	0.5%	1.6%	3.4%
		ON	Closed	4.3%	0.7%	3.0%	5.7%
			Open	2.9%	0.4%	2.2%	3.7%
6 Months	Contra.	OFF	Closed	3.8%	0.5%	2.8%	4.8%
			Open	1.6%	0.3%	1.0%	2.3%
		ON	Closed	3.4%	0.7%	2.0%	4.8%
			Open	2.6%	0.6%	1.5%	3.8%
	ACLR	OFF	Closed	3.4%	0.9%	1.7%	5.1%
			Open	2.8%	0.4%	1.9%	3.7%
		ON	Closed	4.2%	0.1%	2.2%	6.1%
			Open	2.6%	0.6%	1.5%	3.7%

The results of the statistical analysis for the $\Delta E_{surr_{ML}}$ showed that main effect of eyes reached significance ($p < 0.001$).

4.4.1.4 The statistical results based on $\Delta E_{surr_{AP}}$

The descriptive statistics for $\Delta E_{surr_{AP}}$ are presented in Table 7. Overall, larger values in ΔE_{surr} can be observed in the AP direction compared to ML direction in the previous section. The SE of measurements seems relatively small. The SE in the AP direction in Table 7 seem larger than the ML direction shown in Table 6. The ΔE_{surr} seems to increase in the AP direction when eyes were closed. Moreover, the ΔE_{surr}seems larger in the ACLR limbs compared to contralateral when eyes were closed.

Table 7 – Summary statistics for $\Delta E_{surr_{AP}}$

Time	Limb Side	SR	Eyes	Mean	SE	95% Wald CI Lower	95% Wald CI Upper
3 Months	Contra.	OFF	Closed	4.8%	1.0%	2.6%	6.8%
			Open	4.3%	0.5%	3.3%	5.3%
		ON	Closed	4.8%	1.1%	2.8%	6.9%
			Open	3.1%	0.7%	1.7%	4.4%
	ACLR	OFF	Closed	8.8%	1.8%	5.3%	12.3%
			Open	3.3%	0.6%	2.2%	4.4%
		ON	Closed	7.8%	1.6%	4.6%	11.1%
			Open	4.3%	0.9%	2.5%	6.0%
6 Months	Contra.	OFF	Closed	6.0%	1.2%	3.6%	8.4%
			Open	2.7%	0.6%	1.5%	3.9%
		ON	Closed	4.6%	1.1%	2.4%	6.7%
			Open	4.4%	0.8%	2.9%	5.9%
	ACLR	OFF	Closed	8.8%	2.1%	4.6%	13.0%
			Open	4.1%	0.7%	2.8%	5.4%
		ON	Closed	6.9%	2.2%	2.6%	11.2%
			Open	4.2%	0.8%	2.7%	5.7%

The statistical analysis of $\Delta E_{surr_{AP}}$ showed that there were main effects of limb side ($p = 0.007$) and eyes ($p = 0.003$). Despite these main effects, there was also an in interaction of $LimbSide \times Eyes$ that reached significance ($p = 0.048$). Study of effect estimate of the $LimbSide \times Eyes$ showed that $\Delta E_{surr_{AP}}$was reduced by 1±1% in the contralateral (p = 0.024) and 4±1% in the ACLR limb (p = 0.006) when the eyes were closed. Thus, the $\Delta E_{surr_{AP}}$ was smaller by 3±1% in ACLR limb compared to contralateral only when the eyes were closed ($p = 0.017$). No difference was observed when the eyes were open.

4.4.2 Classical Measures

The results of the statistical analyses for classical measures of postural sway for the factors of *SR*, *limb side, time,* and *eyes* are shown in Table 8. For each measure, the factor for which the difference reached significance at the level of 0.05 is highlighted, and the corresponding p-value is reported. Multiple comparisons testing and reporting the summary statistics of each of these measures is beyond the scope of this dissertation. However, it is worthy to highlight that the effect of the factor $eyes$ and also $eyes \times SR$ were present in 81% and 44% of measures, respectively. This supports the significance of similar combinations for the newer measures of entropy found in this study.

Table 8 – Result of GEE Analysis for classical measures of postural sway: Only the results that reached significance at 0.05 are displayed in this table.

Measure	Differences Reaching Significance†
Beta	Eyes ($p < 0.001$)
Ellipse Area	-
Central Frequency_AP	Eyes ($p < 0.001$) ; SR x Eyes ($p = 0.001$) ; SR x Eyes x LimbSide x Time ($p = 0.002$)
Central Frequency_ML	Eyes ($p < 0.001$) ; Time x Eyes ($p = 0.051$) ; Eyes ($p = 0.029$) ;
Central Frequency_RD	Eyes ($p < 0.001$) ; Time x Eyes ($p = 0.004$)
DFA Dimension_AP	Time x SR x LimbSide ($p = 0.003$); Time x SR x Eyes ($p = 0.001$)
DFA Dimension_ML	Eyes ($p < 0.001$)
DFA Dimension_RD	Eyes ($p < 0.001$) ; Time x LimbSide ($p = 0.005$)
Fractal Dimension_CE	Eyes ($p < 0.001$) ; SR x Eyes ($p = 0.032$) ; LimbSide x Eyes ($p = 0.023$)
Fractal Dimesnion_RD	Eyes ($p < 0.001$) ; LimbSide x Eyes ($p = 0.038$)
Freq50_AP	Eyes ($p < 0.001$) ; Time x SR x Eyes ($p = 0.007$)
Freq50_ML	Eyes ($p < 0.001$) ; Tme x Eyes ($p = 0.049$); SR x Eyes ($p = 0.011$)
Freq50_RD	-
TurnIdx	SR ($p = 0.005$) ; LimbSide($p = 0.003$)
Freq80_AP	Eyes ($p < 0.001$) ; SR x Eyes ($p = 0.028$)
Freq80_ML	Time x Sr ($p = 0.045$)
Freq80_RD	Eyes ($p < 0.001$) ; SR x Eyes ($p = 0.01$)
Freq95_AP	Eyes ($p = 0.001$); ;SR x Eyes ($p = 0.047$)
Freq95_ML	Eyes ($p = 0.001$) ; SR x Eyes ($p = 0.049$)
Freq95_RD	Eyes ($p = 0.000$) ; SR x Eyes ($p = 0.009$)
Freq99_AP	Eyes ($p < 0.001$) ; SR ($p = 0.022$)
Freq99_ML	-
Freq99_RD	LimbSide ($p = 0.045$) ; Eyes ($p < 0.001$) ; Time x Eyes ($p = 0.029$)
Frequency Dispersion_AP	LimbSide ($p = 0.014$) ; SR ($p < 0.001$); Eyes ($p < 0.001$)
Frequency Dispersion_ML	SR ($p = 0.028$); Eyes ($p < 0.001$) ; Time x SR x LimbSide ($p < 0.008$)
Frequency Dispersion_RD	Eyes ($p < 0.001$) ; Time x Eyes ($p = 0.020$) ; Time x SR x LimbSide ($p = 0.010$)
Hurst Coef_AP	Eyes ($p < 0.001$) ; Time x SR x LimbSide ($p = 0 .003$) ; Time x SR x Eyes ($p = 0.001$)
Hurst Coef_ML	SR ($p = 0.020$) ; Eyes ($p < 0.001$);
Hurst Coef_RD	Eyes ($p < 0.01$) ; Time x LimbSide ($p = 0.005$)
Lyapunov Exp_AP	Eyes ($p < 0.001$) ; SR x Eyes ($p = 0.043$)
Lyapunov Exp_ML	Eyes ($p < 0.001$) ; Time x LimbSide ($p = 0.004$)
Lyapunov Exp_RD	Eyes ($p < 0.001$) ; Time x LimbSide ($p = 0.039$) ; SR x Eyes ($p = 0.018$)

† Significance at 0.05

4.5 Summary

The summary of statistical findings in the current chapter is abridged in Table 9.

Table 9 - Summary of results for comparing within ACLR population

Category	Outcome Measure	Summary of Statistical Findings
Anthropometric†	**Age**	NA**
	Height[cm]	NA
	Body mass [kg]	NA
	TrH [hrs/week]	NA
	BMI [kg/m^2]	NA
Questionnaire‡	**ACL-QOL**	Time ($p<0.001$)
	IKDC 2000	Time ($p<0.001$)
Proprioception§	**Movement Threshold (normalized) [˚/˚]**	SR ($p = 0.026$)
	Movement Repeatability error [˚]	SR ($p < 0.001$)
Postural Balance*	**EnHL in ML [ms]**	Eyes ($p = 0.001$); TimexSR ($p = 0.024$); LimbSidexEyes ($p= 0.047$)
	EnHL in AP [ms]	NA
	ΔE_surr in ML [bit/bit]	Eyes ($p<0.001$)
	ΔE_surr in AP [bit/bit]	LimbSide ($p = 0.007$); Eyes ($p = 0.003$); LimbSidexEyes ($p = 0.048$)

† Factors : Time since surgery (3 months vs. 6 months)

‡ Factors : Time since surgery (3 months vs. 6 months)

§ Factors : Time since surgery (3 months vs. 6 months); LimbSide (ACLR vs. Contralateral); SR (OFF vs. ON); Direction (Flexion vs. Extension)

* Factors : Time since surgery (3 months vs. 6 months); LimbSide (ACLR vs. Contralateral); SR (OFF vs. ON); Eyes (Open vs. Closed)

** NA means no significant difference detected.

Chapter Five: **Results - Exploration between the ACLR and healthy groups**

In this chapter, results of the comparison between the two groups of ACLR participants at three months post-surgery and healthy controls are presented. This chapter reports separately, the results of statistical analyses for the outcome measures of anthropometrics (§5.1), questionnaires (§5.2), proprioception (§5.3), and the postural balance (§5.4). Finally, the summary of all findings in the current chapter is summarized in §5.5.

To overview the results for comparison between ACLR and contralateral limbs, refer to Chapter Four: Results – Exploration within the ACLR .

5.1 Anthropometrics

The outcomes of the univariate ANOVAs analysis between the ACLR group at three months post-surgery and healthy controls on age, height, body mass, training per week, and BMI showed differences between body mass ($p = 0.001$; $\eta^2 = 0.208$) and BMI ($p = 0.001$; $\eta^2 = 0.205$) but not on height or age. The body mass in the ACLR sample was on average 8.9 kg more than the healthy controls. The BMI in the ACLR sample was larger by $2.8 kg/m^2$ compared to healthy controls.

5.2 Questionnaires

The outcome of the ANOVA for IKDC, 2000 subjective knee evaluation score between the ACLR group at three months and healthy controls, showed a significant difference ($p < 0.001, \eta^2 = 0.814$). Scores were on average 41±3% lower (worse) in the ACLR patients at three months post-surgery compared to healthy controls.

The results of the ANOVA on the IKDC 2000 between the ACLR group at six months post-surgery and healthy controls showed that the score for ACLR at six months post-surgery was still significantly different from healthy controls ($p < 0.001$; $\eta^2 = 0.647$). ACLR participant mean score at six months post-surgery was 25±3% lower than that of the healthy control participants.

5.3 Proprioception

The summary statistics corresponding to the measures of proprioception (i.e. movement repeatability error and normalized movement threshold) are provided in Table 10.

Table 10 - Summary statistics for the measures of proprioception in the flexion for the factors of SR (OFF vs. ON) and health condition (ACLR limb vs. control)

Health Cond.	Measure	SR	Mean	SD	Min	Max	95% CI Low	95% CI Up
Control (n = 28)	Movement Rep	OFF	2.9	1.4	0.8	6.5	2.4	3.4
		ON	2.6	1.6	0.7	5.6	2.0	3.2
	Mov Thresh Norm	OFF	0.4	0.2	0.0	0.8	0.3	0.5
		ON	0.4	0.2	0.0	0.8	0.3	0.5
ACLR (n = 19)	Movement Rep	OFF	3.6	1.1	1.1	5.3	3.0	4.1
		ON	2.6	1.2	0.7	5.5	2.0	3.1
	Mov Thresh Norm	OFF	0.6	0.4	0.2	2.3	0.4	0.8
		ON	0.7	0.4	0.3	1.8	0.5	0.9

The results of between-subjects effect tests for the factors of health condition (ACLR limb vs. dominant limb of healthy participants) showed a significant difference in proprioception between the limbs for the normalized movement threshold measure ($p = 0.002$; $\eta^2 = 0.191$). However, the difference was not significant for movement repeatability ($p = 0.356$). In contrast, the effect of SR reached significance for the measure of movement repeatability ($p = 0.006; \eta^2 = 0.155$) but not for normalized movement threshold ($p = 0.681$).

The outcome of the posthoc test on the effect of health condition (ACLR limb vs. dominant limb of healthy participants) showed that the normalized movement threshold error was 0.3±0.1 degrees/degree smaller in the healthy limb compared to the ACLR limb ($p = 0.002$). The outcome of multiple comparison tests for the factor of SR (OFF vs. ON) showed a reduction of 0.7 degrees in the movement repeatability absolute error when the SR stimulation was ON.

5.4 Center of pressure analysis

5.4.1 Entropic half-life analyses

5.4.1.1 Statistical results for $EnHL_{ML}$

The summary statistics of $EnHL_{ML}$ for the between factor of health condition (ACLR vs. healthy controls) and within factors of eyes (open vs. closed) and SR (OFF vs. ON) are presented in Table 11.

Table 11 - Estimated summary statistics for the measure of $EnHL_{ML}$[ms]

EnHL_ML

					95% Wald CI	
HealthCond	**Eyes**	**SR**	**Mean**	**SE**	**Low**	**Up**
CONTROL	CLOSED	OFF	89	6	77	101
		ON	88	5	77	99
	OPEN	OFF	98	7	84	112
		ON	88	4	79	97
ACLR	CLOSED	OFF	112	5	102	121
		ON	113	7	99	127
	OPEN	OFF	100	3	95	106
		ON	96	3	91	101

The outcome of the test for $EnHL_{ML}$ for between and within factors showed that the main effect of health condition ($p = 0.005$) and the interaction effect of $eyes \times health\ condition$ reached significance. Since the interaction was significant, comparisons for the interaction are most relevant.

Pairwise comparisons for $EnHL_{ML}$ for the interaction of $Health\ Condition \times Eyes$ showed that the difference between the $EnHL_{ML}$ for the healthy compared to ACLR limb reached significance only when the eyes were closed ($p = 0.001$). Under this condition the $EnHL_{ML}$was on average 24±7 ms (mean ± SE) shorter in healthy controls. Furthermore, the difference between the eyes condition was only significant for the ACLR limb ($p = 0.007$). When the eyes are closed the $EnHL_{ML}$ is 14±5 ms longer compared to eyes open condition.

5.4.1.2 Statistical results for $EnHL_{AP}$

The summary statistics for the COP measure of $EnHL_{AP}$ for the between factor of health condition (ACLR vs. healthy controls) and within factors of eyes (open vs. closed) and SR (ON vs. OFF) are shown in Table 12.

Table 12 - Summary statistics for the measure of $EnHL_{AP}$ for between factor of health condition (ACLR vs. healthy limb side) and within factors of eyes (open vs. closed) and SR (ON vs. OFF)

EnHL_AP

					95% Wald CI	
HealthCond	**Eyes**	**SR**	**Mean**	**SE**	**Low**	**Up**
CONTROL	**CLOSED**	**OFF**	254	42	172	335
		ON	155	12	132	178
	OPEN	**OFF**	163	18	129	198
		ON	190	19	151	228
ACLR	**CLOSED**	**OFF**	133	6	121	145
		ON	142	8	126	158
	OPEN	**OFF**	138	5	128	148
		ON	135	8	120	150

The result showed that the main effect of health condition ($p = 0.002$) and the interaction of $SR \times Eyes$ ($p = 0.002$) reached significance.

Probing the interaction between SR (OFF vs. ON) and eyes (open vs. closed) revealed that when the SR stimulation was OFF, the difference on the outcome measure when the eyes were open and when they were closed reached significance ($p = 0.029$). When SR was ON however, the difference between the eye conditions was not significant ($p = 0.154$).

The comparison outcome for the effect of the SR factor in $EnHL_{AP}$ for the interaction between SR (OFF vs. ON) and eyes (open vs. closed) showed that SR was significant only when the eyes were closed ($p = 0.017$), reducing the $EnHL_{AP}$ by 45±19 ms. The effect of SR however was not significant when eyes were open ($p = 0.314$).

5.4.2 Surrogate analyses

5.4.2.1 Statistical results for $\boldsymbol{\Delta E_{surr_{ML}}}$

The summary of statistics for $\Delta E_{surr_{ML}}$ for the between factor of health condition (ACLR vs. healthy controls) and within factors of SR (OFF vs. ON) and eyes (closed vs. open) are shown in Table 13.

Table 13 - Summary statistics for $\Delta E_{surr_{ML}}$ for between factor of health (ACLR vs. healthy controls) and within factors of SR (OFF vs. ON) and eyes (open vs. closed)

ΔE_surr_ML						
					95% Wald CI	
HealthCond	**Eyes**	**SR**	**Mean**	**SE**	**Lower**	**Upper**
CONTROL	CLOSED	OFF	0.12	0.02	0.08	0.16
		ON	0.11	0.01	0.09	0.14
	OPEN	OFF	0.12	0.01	0.10	0.14
		ON	0.11	0.01	0.09	0.12
ACLR	CLOSED	OFF	0.05	0.01	0.03	0.07
		ON	0.04	0.01	0.03	0.06
	OPEN	OFF	0.02	0.00	0.02	0.03
		ON	0.03	0.00	0.02	0.04

The test of the model showed that only the effect of health condition reached significance ($p < 0.001$). The pairwise comparisons showed that $\Delta E_{surr_{ML}}$was higher in the healthy control by 8±1% bit/bit (mean ± SE) relative to the ACLR limb.

5.4.2.2 Statistical results for $\boldsymbol{\Delta E_{surr_{AP}}}$

The summary statistics for $\Delta E_{surr_{AP}}$ for the between factor of health condition (ACLR vs. healthy controls) and within factors of eyes (open vs. closed) and SR (OFF vs. ON) are presented in Table 14.

Table 14 - Summary statistics for $\Delta E_{surr_{AP}}$ for the between factor of health condition (ACLR vs. health controls) and within factors of eyes (open vs. closed) and SR (ON vs. OFF)

ΔE_surr_AP

					95% Wald CI	
Health Cond.	**Eyes**	**SR**	**Mean**	**SE**	**Lower**	**Upper**
CONTROL	CLOSED	OFF	0.18	0.03	0.12	0.24
		ON	0.16	0.02	0.13	0.20
	OPEN	OFF	0.16	0.02	0.13	0.19
		ON	0.16	0.01	0.14	0.19
ACLR	CLOSED	OFF	0.09	0.02	0.05	0.12
		ON	0.08	0.02	0.05	0.11
	OPEN	OFF	0.03	0.01	0.02	0.04
		ON	0.04	0.01	0.02	0.06

The results showed that the main effects the main effect of eyes ($p = 0.044$) and health condition ($p < 0.001$) reached significance. Pairwise comparison for the factor of eyes revealed that the $\Delta E_{surr_{AP}}$was larger by 3±1% when eyes were closed. Also, it was revealed that $\Delta E_{surr_{AP}}$was larger in the healthy group by 11±1% bits/bits compared to ACLR group.

5.5 Summary

The summary of statistical findings in the current chapter is abridged in Table 10. The details of these results are presented in subsequent sections of the current chapter.

Table 15 - Summary of results for comparing between ACLR and healthy dominant

Category	Outcome Measure	Summary of Statistical Findings
Anthropometric†	**Age**	NA**
	Height[cm]	NA
	Body mass [kg]	HealthCond (p = 0.001)
	TrH [hrs/week]	NA
	BMI [kg/m^2]	HealthCond (p = 0.001)
Questionnaire‡	**ACL-QOL**	HealthCond (p < 0.001)
	IKDC 2000	HealthCond (p < 0.001)
Proprioception§	**Movement Threshold (normalized) [˚/˚]**	HealthCond (p = 0.002)
	Movement Repeatability error [˚]	SR (p = 0.006)
Postural Balance*	**EnHL in ML [ms]**	Eyes x HealthCond (p = 0.007); HealthCond (p = 0.005)
	EnHL in AP [ms]	HealthCond (p = 0.002); SR x Eyes (p = 0.002)
	ΔE_surr in ML [bit/bit]	HealthCond (p < 0.001)
	ΔE_surr in AP [bit/bit]	HealthCond (p < 0.001); Eyes (p = 0.044)

† Factors : HealthCond (ACLR vs. Healthy dominant)
‡ Factors : HealthCond (ACLR vs. Healthy dominant)
§ Factors : LimbSide (ACLR vs. Healthy dominant); SR (OFF vs. ON);
* Factors : HealthCond (ACLR vs. Healthy dominant); SR (OFF vs. ON); Eyes (Open vs. Closed)
** NA means no significant difference detected.

Chapter Six: **Discussion**

"… True knowledge is to know the extent of one's ignorance."

Confucius (c. 551- c. 479 BC)

This chapter discusses the main findings in the current dissertation. The results from the anthropometrics, questionnaires, proprioception, and postural balance analyses for both the within and between populations are summarized and discussed in subsequent sections. In the sections related to proprioception and postural balance, first, a discussion of the formal hypotheses will be made and followed by a summary of relevant findings for each tested factor.

For the proprioception section, the effects of limb side, SR, and time since surgery are discussed for both within and between populations in §6.4.1, §6.4.2, and §6.4.3 respectively. Finally, the observed proprioceptive findings are discussed within the clinical perspective in §6.4.4.

In the postural sway section, the effects of eyes, limb side, time since surgery, and SR are discussed for both between and within population sample results in §6.5.1, §6.5.2, §6.5.3, and §6.5.4 respectively.

The experimental setup used for testing SR on proprioception in the current dissertation featured some unique considerations. The discussion about these features and comparison of the setup used in this dissertation to those available in the literature are presented in detail in Relevance of methodology used for testing SR on proprioception.

6.1 Anthropometrics

The BMI of the healthy and ACLR groups were roughly similar, based on their descriptive statistics (§4.1). On average the BMI for healthy participants was 21.6-kg/m^2 with minimum and maximum values of 19.5 and 25.1 kg/m^2, respectively. The BMI of the ACLR participants was on average 24.4-kg/m^2 with minimum and maximum values of 20.3 and 32.8-kg/m^2 respectively at three months and 17.5 and 32.5-kg/m^2, respectively at six months post-surgery. While the goal was to recruit participants with BMI value less than 25-kg/m^2, the range was extended upwards for ACLR participants to enable sufficient recruitment within the study timeframe.

The BMI in the ACLR group was on average larger by 2.8-kg/m^2 (§5.1). This increase can be explained primarily by body mass, as the ACLR participants at three months post-surgery were significantly heavier by 8.9 kg compared to healthy participants (§5.1), but there was no significant difference in height between the two groups. .

The body mass (kg) of the ACLR group showed a trend towards decreasing from three months to six months post-surgery, (§4.1). However, the difference was not significant. Decreased body mass observed in some ACLR individuals might be attributed to increased level of physical activity and loss of mean muscle mass. As the joint healing process progresses during this period, generally more rigorous physiotherapeutic exercises are included. While the specific physiotherapy regime wasn't controlled for in this study, some researchers suggested physiotherapy exercises include light jogging at about three months post-surgery (Kvist 2004a) to encourage individuals with ACLR surgery to return to sport activities including "cutting movements" at about six months post-surgery (Zhou et al. 2008; Grindem et al. 2016). The introduction of these cardiovascular, along with other physiotherapeutic exercises, can be speculated as a mechanism by which body mass was reduced. However, this speculation could not be verified based on self-reported training hours for two reasons: (1) the number of training hours at three and six months assessments did not reach statistical significance, and (2) The number of training hours per week do not provide information on the type and intensity of exercise. Alternatively, reduced body mass may be attributed to the loss of lean muscle mass. Although the physical fitness of the participants was not assessed in this study, body composition methods such as those outlined in (Duren et al. 2008) would be useful to evaluate the plausibility of either explanation.

The current study was not designed to test hypotheses regarding changes in body mass/fitness following ACLR surgery. As no significant changes were observed in anthropometric measures, it is unlikely that they acted as covariates in the longitudinal assessment of proprioception and postural stability within this sample.

Body mass has been reported to correlate with measures of postural stability (Hue et al. 2007; Teasdale et al. 2007; Ku et al. 2012; Greve et al. 2007). Thus, the significantly different body-mass between the two groups under study (§5.1) might have potentially affected the postural balance outcomes between the groups.

6.2 Questionnaires

6.2.1 IKDC 2000

The high IKDC 2000 knee evaluation scores (97%) observed in the healthy controls suggest that the knee joints in these participants were healthy and functional[1], and are comparable to scores reported in the literature. For example, (Shelbourne & Gray 2000) have reported a score of 93.6

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[1] The score of 100% means no limitation on daily activities of the knee (N. J. Collins et al. 2011).

(8.3) % for 360 healthy athletes with a mean age of 20.9(1.7) yrs. Anderson and colleagues have reported an average of 90.9(12.8)% calculated across 3,741 healthy participants (Anderson et al. 2006). Comparatively the healthy group in this dissertation reported a potentially better knee function based on this score.

The ACLR participants in the current study scored lower on the IKDC 2000 questionnaire compared to similar studies. As shown in §4.2, the score in the ACLR participants at three months post-surgery scored an average of 56(12)%. This score was significantly improved by 15% at six months post-surgery to 71(11)%. Logerstedt and colleagues reported an IKDC 2000 score of about 85%[1] at six months post ACL reconstruction surgery for a mixed-gender study of 83 participants (Logerstedt et al. 2013). This value seems higher than the reported 71% in the current study.

It may be argued that the higher IKDC 2000 score in the healthy controls compared to the general public and lower scores in the ACLR participants compared to other sample averages at comparable time points may lead to bias in findings in the current work.

Significant improvement was observed over time from three months to six months in the IKDC 2000 score ($p < 0.001$). Such an improvement may imply healing of the knee function over time, as well as the effect of rehabilitative exercises in helping individuals with ACLR to prepare to return to a fully functional life. However, the normal knee functional range of IKDC 2000 scores has been suggested to lay within the 15th percentile of the participant's specific age and

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[1] This value was approximated visually based on the provided bar chart. Quantitative data was not provided in the article.

sex matched population (Logerstedt et al. 2014; Grindem et al. 2011; Logerstedt et al. 2012). Accordingly, the normal cut-off IKDC 2000 score calculated based on the participant's sex and age group is as follows: 18 to 24 years cut-off = 83.9; 25-34 years cut-off = 82.8; and 35-50 years cut-off = 78.5 (Logerstedt et al. 2014). The average of the IKDC 2000 scores in the current study at three months and six months post-surgery fall significantly below the cut-off values for each of these age ranges. This may suggest that although improvements over time were observed in the ACLR participants, on average the participants may not be ready to return to their atheletic activities at six months post-surgery according to the criteria proposed by (Logerstedt et al. 2014).

6.2.2 ACL-QOL

The ACL-QOL was not recorded for the healthy group since this questionnaire is specific to patients with ACL injury/reconstruction. Thus, this discussion is limited to comparing the scores in the ACLR group over time since surgery.

The current findings show that the mean ACL-QOL score at three months was 49(13)% with a 95% confidence interval of (43%, 55%). Little information is available in the literature on ACL-QOL scores at early times post-surgery (e.g. at three or six months post-surgery), as few studies have evaluated this score in their early post-surgery ACLR studies (Filbay et al. 2015). Grant and colleagues have reported a baseline pre-surgery ACL-QOL score of 29.7(14.8)%[1] for ACL deficient patients on average of 20 months post-injury (Grant et al. 2005). Similarly, (Grant & Mohtadi 2010) reported the ACL-QOL score before surgery of 28.9(13.3)%. Comparing the score at three months post-surgery and the outcomes presented in (Grant et al. 2005), it may be

[1] mean±SD

observed that the ACL-QOL at three months post-surgery is relatively higher than those with ACL deficiency.

In this study, the ACL-QOL score at six months increased significantly ($p < 0.001$) by 14% over time and reached to 62(17)% at six months. Despite this highly significant improvement, this value falls 1% shy of a clinically relevant difference of 15 points suggested in (Grant & Mohtadi 2010).

At six months post-surgery, the ACL-QOL score of 62(17)% is comparable to those found at longer follow-ups. For example, Holsgaard-Larsen and colleagues reported a score of 65.1(20.1)% for 23 ACLR patients who were on average six months post-surgery (Holsgaard-Larsen et al. 2014). Similarly, at about 38 months post-surgery a score of 69.9(22)% was reported for 48 ACLR patients (Grant & Mohtadi 2010). Also, (Fältström et al. 2013) reported an ACL-QOL score of 66(20)% for 172 patients with unilateral ACLR at 2 to 10 years post-surgery. Therefore participants at six months post-surgery are on average reporting a comparable ACL-QOL scores compared to those after more than 2 years post-surgery. Based on this result it might be suggested that the ACL-QOL score in the ACLR group reached a steady state level as early as six months post-surgery. This finding is in contrast to the results found for the IKDC 2000 that showed lower score at six months compared to the scores of chronic ACLR group (see §6.2.1).

Alternatively, it has been suggested that the patient-reported ACL-QOL measures sometimes fail to address patient-perceived important and relevant factors related to their quality of life (Carr & Higginson 2001). In other words, although knee deficiencies might be present at six months post-surgery, the measure is not sensitive to them and thus may not capture their effects. The current study has not been designed to address the plausibility of this argument. If such a critique is relevant, it can be speculated that assigning a weighting to the various items in the questionnaire is an approach that could be pursued as suggested by (Mohtadi 1998). Currently, the ACL-QOL is calculated as an average of all questions with equal weights. Future research might provide further insights regarding the relevance of the outlined critique and potentially provide a means to develop a more relevant weighting strategy.

6.3 Vibration sensation threshold

The use of vibration sensation is a novel technique being introduced for potential diagnostic, therapeutic and rehabilitation approaches in joint and neuro-motor control injuries and diseases. Numerous components of this technique remain not well understood or established, including the determination of the appropriate vibration sensation threshold level. One aspect of the current study was to ensure that the SR stimulation remained sub-threshold and unnoticeable by the participants, as suggested previously in similar studies (Priplata et al. 2004; Costa et al. 2007; Ross & Arnold 2012b; Dettmer et al. 2015; Gravelle et al. 2002). The vibration sensation threshold when measured using the increasing amplitude lead to significantly lower values compared to the decreasing amplitude protocol (§3.1.3). In the current study, 90% of the vibration sensation threshold as measured using the increasing amplitude protocol was used to ensure that the stimulation remained sub-threshold throughout the experiment.

6.4 Proprioception

6.4.1 Effect of limb side

To correctly interpret the results for different study factors, it was required to investigate if a proprioceptive deficiency was originally present in the ACLR limbs. With one exception, overall proprioceptive deficiency was not supported in the ACLR limbs compared to either the contralateral or the healthy dominant limbs. It was hypothesized that the movement repeatability error and movement threshold would be larger in the ACLR limb compared to the contralateral limb at three months and six months post-surgery ([H1], [H3]). As shown in §4.3, no significant differences between ACLR and contralateral limb were detected in the movement repeatability error (ACLR vs. contralateral) ($p = 0.577$) and movement threshold ($p = 0.5$). Thus, [H1] and [H3] were not supported (see §4.3.1 and §4.3.2).

Likewise, when the ACLR limb was compared to the healthy controls it was hypothesized that movement repeatability error and movement threshold in the ACLR limb at three months post-surgery would be larger than the healthy dominant limb ([H5] and [H7] respectively). Also, §5.3 showed that the difference between the movement repeatability error in ACLR and healthy dominant limbs was not significant and thus, [H5] was not supported.

The exception to these findings was that the movement threshold in the ACLR limb at three months post-surgery was significantly larger by 0.3 degrees/degree compared to the healthy dominant limb ($p = 0.002$), therefore [H7] was supported.

The current study was designed to investigate the proprioception in the near full extension range (15° of flexion). The absence of significant proprioception difference between the ACLR and control limbs at the extended position (0 to 20°) and flexed position (80 to 100°) as early as three to six months post-surgery has been previously reported (Fremerey et al. 2000; Furlanetto et al. 2016). Nevertheless, deficiency has been previously suggested in the intermediate flexion range (40 to 60°) (Furlanetto et al. 2016; Fremerey et al. 2000; MacDonald et al. 1996; Borsa et al. 1997). In this dissertation, the nearly extended position was studied since it is a typical range exhibited in most daily functional weight bearing tasks. Future studies on other knee positions within this mid-flexion range might provide a broader understanding about chronic proprioceptive deficiency in the ACLR population at this early time point post-surgery.

The current findings are in agreement with studies reported in literature utilizing similar methodologies for recruitment and testing of proprioceptive acuity (Lephart et al. 1992; Hopper et al. 2003; Reider et al. 2003; MacDonald et al. 1996; Fremerey et al. 2000; Angoules et al. 2011; Risberg et al. 1999; Furlanetto et al. 2016; Nagai et al. 2013; Fremerey et al. 2001; Chouteau et al. 2012; Ma et al. 2014; Muaidi et al. 2009; Ozenci et al. 2007). In agreement with the current findings, these studies have reported that proprioceptive differences between the ACLR and controls was not significant. Such non-significant difference in proprioception following ACL reconstruction, especially when the knee is near full extension, may lead to the enhanced feeling of stability in the joint that is usually reported following ACL reconstruction surgery (MacDonald et al. 1996). It must be acknowledged that the current study was not designed to compare the proprioceptive acuity before and after ACL reconstruction surgery, but to assess the proprioceptive acuity of the ACLR limb only post-factum.

Mechanistically, the action of ACL reconstruction can be theorized to improve proprioception in the knee compared to pre-surgery status. Reconstruction has been suggested to correct the impaired and non-physiological axis of rotation of the ACL deficient knee by the physical presence of ACL replacement tissue (Fremerey et al. 2000; Berchuck et al. 1990). Therefore, it can be speculated that the joint is more mechanically constrained and has less likelihood of moving to non-anatomical positions. Consequently, the joint's abnormal movements can be speculated to become more limited following surgery. Therefore, it will be less likely for the postural control system to receive anomalous outputs corresponding to abnormal movements from capsular and other structures of the knee (Reider et al. 2003; Iwasa et al. 2000; MacDonald et al. 1996; Angoules et al. 2011; Ma et al. 2014). By restoring (at least partially) the kinematics of the joint following ACL reconstruction and in the absence of these anomalous sensory outputs, the remaining receptors surrounding the joint have been speculated to recover and the CNS reprogram to cope with the absent receptors of the ACL (Reider et al. 2003; Iwasa et al. 2000; MacDonald et al. 1996; Angoules et al. 2011; Ma et al. 2014). These changes following ACL reconstruction surgery might be speculated as a potential mechanism behind the observed non-significant proprioceptive deficiency observed in the ACLR group following surgery in the current work.

In the current study, the proprioceptive findings differed when the ACLR limb was compared to the healthy controls versus contralateral. Specifically, a movement threshold difference of 0.3 degrees/degrees was reported when ACLR limbs were compared to healthy controls. This difference was not present when the ACLR limb was compared to the contralateral limb. This is a very informative observation since the contralateral limb has frequently been used in knee proprioception literature as the internal control. This study demonstrated that the proprioception results are dependent on the type of control group. It has been suggested in the literature that the contralateral limb undergoes significant neuromuscular changes following ACL reconstruction surgery (Muaidi et al. 2009). Since, the contralateral limb may undergo unpredictable changes following ACL reconstruction, choosing it as a control might not be appropriate for assessment in clinical and rehabilitation studies (Muaidi et al. 2009), particularly in proprioception studies.

In the current study, a similar dependence on the type of control group was observed in the postural balance outcomes. To avoid redundancy, further discussions of the topic will be postponed to §6.5.2.

6.4.2 Effect of SR

The current study showed that SR improved proprioceptive acuity of the knee in the ACLR, contralateral, and healthy dominant limbs. These findings supported hypotheses [H2], [H4] and [H6] but did not support [H8]. Specifically, it was hypothesized that the movement repeatability error will decrease following administration of SR noise at three months and six months post-surgery [H2]. The results showed that the movement repeatability error was reduced significantly by 0.7 degrees in the presence of SR stimulation ($p < 0.001$), supporting [H2].

It was hypothesized that movement threshold will be reduced following administration of SR noise at three months and six months post-surgery [H4]. The absolute movement threshold did decrease following the administration of SR by 0.1 degrees ($p = 0.048$) supporting [H4].

It was hypothesized that the movement repeatability difference between healthy dominant and ACLR limbs at three months would decrease following administration of SR noise [H6]. It was shown in §5.3 that the movement repeatability error was 0.7 degrees smaller when SR was administered and the difference for within factor of SR (ON vs. OFF) reached statistical significance ($p = 0.006$) and [H6] was supported.

It was hypothesized that the difference between the movement threshold in healthy dominant and three months post-surgery ACLR limbs would decrease following administration of the SR noise

[H8]. The results of the statistical comparisons on movement threshold (§5.3) for the effect of SR did not reach statistical significance and ttherefore, [H8] was not supported.

These findings suggest that overall the proprioceptive acuity was improved in the presence of SR stimulation in almost all conditions.

Limited information is available in the literature for cross-validation and comparison about the effect of SR on knee proprioception. The anticipated improvement in proprioception with SR was extrapolated from previous studies that have reported improvement in postural balance in the presence of SR (Priplata et al. 2002; Priplata et al. 2003; Dettmer et al. 2015; Priplata et al. 2006; Gravelle et al. 2002; Costa et al. 2007; Ross et al. 2007; Ross & Arnold 2012b; Ross & Guskiewicz 2006). These researchers theorized that the observed improved postural balance might have been caused by an improvement in proprioception (Gravelle et al. 2002). The only direct study of proprioception in the presence of SR has been performed by Amber Collins in her Ph.D. dissertation and related publications (Collins 2010; Collins et al. 2009; A. T. Collins, Blackburn, Olcott, Miles, et al. 2011).

The amplitude of the proprioceptive changes with SR in the current study is similar to those found in the available literature. For example, the SR stimulation of the knee along with a knee sleeve improved movement repeatability error by 0.1˚ and 0.2˚ compared to baseline (no stimulation and no sleeve) during partial and full load-bearing tasks in healthy young adults (Collins et al. 2009). Similarly, in osteoarthritis patients, an improvement of 0.7 degrees in movement repeatability error was reported under partial weight bearing when SR stimulation and a sleeve were utilized (A. T. Collins, Blackburn, Olcott, Miles, et al. 2011).

Understanding the mechanism of proprioceptive improvement in the knee in the presence of SR stimulation is complicated. The specific proprioceptive components and extent targeted in the presence of SR stimulation remain unclear. SR has also been demonstrated to improve signal detection/transmission in each component of proprioception. For example, SR has been shown to improve the sensory outputs from Golgi tendon organs (Fallon et al. 2004; Dugué et al. 2016), muscle spindles (Cordo et al. 1996; Fallon et al. 2004), and cutaneous receptors located in the proximity of the joint (Collins et al. 1996a; Nozaki et al. 1999; Liu et al. 2002; Ivey et al. 1998; Wells et al. 2005; Wells et al. 2001). Therefore, one can speculate that enhancement in some or all of these components might be responsible for the observed improvement in proprioception in the ACLR group. The current study was not designed to assess the extent to which each element of proprioception has been affected following the SR stimulation.

Nevertheless, the current findings support the primary motivation of the current work that hypothesized proprioceptive enhancement in ACLR patients in the presence of SR. In conclusion, the observed improvements might be related to improved transmission and detection of sensory signals emanating from other proprioceptive structures of the knee including intact collateral ligaments and capsular receptors, muscle spindles, and cutaneous receptors to compensate for the impaired ACL receptors.

6.4.3 Effect of time

Overall, the results of the current study did not show significant improvement in proprioception over a period of three months time. It was hypothesized that the movement threshold and movement repeatability error would be smaller at six months compared to three months post-surgery ([H9] and [H10]). Reduction of 0.1 degrees in absolute movement threshold was observed from 3 to six months post-surgery ($p = 0.049$) when the ACLR limb was compared to the contralateral limb. However, the results were not significant when the movement repeatability error and movement threshold were studied. As can be observed from Table 2 and Table 3 in §4.3, both movement threshold and movement repeatability error showed trends toward reduction over time although the differences were non-significant. Such a trend has previously been suggested following ACLR surgery (Reider et al. 2003), although similar to the current study, the magnitudes of improvement didn't reach statistical significance (Reider et al. 2003).

In the current study, only a trend towards proprioceptive improvement over time has been observed, but the results did not reach statistical significance. Lack of a significant difference in proprioception between these two early time points of three and six months post-surgery might lead to two potential speculations. Firstly, the rate of proprioceptive improvement of the knee might be low. Thus, to observe and quantify any difference over time, participants must be followed for a longer period. Secondly, the proprioception healing may occur rapidly and reach a steady state afterward. Consequently, the three months time point might be too late to observe any significant changes in proprioception. Therefore, it may be important for future research to measure proprioception at earlier time points after the surgery. The current study was not designed to test the plausibility of either of these alternative speculations.

The first speculation (i.e. slow healing rate) doesn't appear highly plausible from the available scientific and clinical literature. The majority of existing literature has that focus on longitudinal follow-up, use three months post- ACLR surgery as the earliest time point and report no significant change in proprioception over time (Angoules et al. 2011; Reider et al. 2003;

Fremerey et al. 2001). Some have continued their longitudinal study to more than 12 months (Ma et al. 2014; Chouteau et al. 2012) and sometimes up to more than 40 months (Fremerey et al. 2001), and similarly were unable to detect significant changes in proprioception after three months post-surgery. Such lengthy longitudinally studies suggest against the plausibility of the slow proprioceptive healing process as suggested by the first speculation.

The speculation that the proprioceptive acuity recovers quickly (e.g. as early as three months post-surgery) and reaches a steady state afterward is supported in the literature (Muaidi et al. 2009; Fremerey et al. 2000; Reider et al. 2003). A potential mechanism behind such a rapid proprioceptive recovery is still under debate. Some researchers have suggested that such a short time might be too brief for the physiological explanations such as healing and re-innervation of the ACL graft (Fridén et al. 1997; Reider et al. 2003; Ochi et al. 1999). Therefore, other mechanisms might be involved in an early correction in the proprioception.

Restoring the mechanical constraints of the ACL following reconstruction may be a plausible explanation for rapid proprioception recovery following surgery (see also §6.4.1). Surgical correction of the mechanical constraint of the joint has been suggested to enhance the interpretation of the sensory cortex about the joint movement (Barrett 1991). Fremerey and colleagues suggested that these physiological changes may start early after ACL reconstruction (Fremerey et al. 2000), so that proprioception recovery may be achieved as early as three weeks (Reider et al. 2003), with the complete recovery between ranging somewhere between three to six months post-surgery (Fremerey et al. 2000).

A plausible mechanism for the observed *trend* towards improvement in proprioception over time might be related to healing, nerve regeneration in the ACL reconstruction graft, and reprogramming in the CNS. Reider and colleagues suggested that over time the joint heals from the surgery and nerves grow into the reconstructed graft (Reider et al. 2003). Histological analyses support this speculation e.g. the presence of morphologically normal mechanoreceptors in ACL tissue has been shown as early as three months post-surgery (Denti et al. 1994). At six months, regeneration of ACL mechanoreceptors and free nerve endings have been reported (Angoules et al. 2011; Ochi et al. 1999; Aune et al. 2001; Shimizu et al. 1999; Aune et al. 1996; Furlanetto et al. 2016). Based on this evidence, it can be speculated that the CNS reconfigures to incorporate these regenerated mechanoreceptors to enhance the proprioception of the knee further. Therefore, re-innervation of the graft and regeneration of nerves inside the joint along with reconfiguration of the cortical program might be speculated as a potential mechanism for the observed trend towards proprioceptive enhancement in the knee.

Reduction in the joint effusion over time has also been suggested as a potential alternative mechanism. Effusion has been known to decrease the sensory output from muscle spindles (Lephart et al. 1992). Muscle spindles are one of the major sources of joint proprioception (Lephart et al. 1992). A gradual reduction in knee effusion overtime might reduce the compromised muscle spindle outputs associated with effusion and therefore, might be speculated as a potential mechanism for the observed trend towards proprioception-improvement over time.

6.4.4 Relevance of the findings

The relevance of the statistical differences in proprioception found between groups needs to be considered within the clinical and scientific realms. The observed changes in proprioception are substantial when the range of measurement is considered. For example, observing 0.1˚ difference due to SR treatment constitutes more than 10% of the measurement range. Furthermore, the observed differences remain comparable to those reported in the literature. For example, similar to the current work, (Borsa et al. 1997; MacDonald et al. 1996; Fischer-Rasmussen & Jensen 2000) reported, respectively 0.1˚, 0.14˚, and the 0.21˚ difference between the movement threshold in the ACL deficient knee compared to the contralateral. Although these differences are statistically significant, it remains unclear if such differences also carry clinical relevance (Reider et al. 2003).

It remains challenging to identify the magnitude of clinically relevant differences in proprioception (Collins et al. 2009), especially in ACLR patients. To define the magnitude of a clinically relevant difference, one possible strategy is to study the changes in proprioception with respect to change in function[1] (Collins et al. 2009). In the current study, the ACL-QOL and IKDC 2000 questionnaires were studied to relate the findings of the current study to a self-reported function and quality of life respectively. Improvements of 13% in ACL-QOL score and 15% IKDC 2000 were observed over time following the surgery. However, overall proprioception did not change significantly over this same time. Thus, it becomes challenging to put the proprioceptive findings into perspective. It might be advisable for the future proprioception studies to include more functional assessment tests in the experimental protocols to provide further insights so that the proprioceptive findings can be related more clearly to function.

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[1] By "*function*" we mean neuro-musculoskeletal function. According to FARLEX Medical Dictionary, function is defined as "The ability of nerves, muscles, and bones to perform or coordinate specific activities".

Another approach to determining the clinical relevance of the proprioceptive changes might be to establish the existence of a deficiency *a priori* in the population under study. In this situation, it becomes possible to put changes in proprioception into perspective by making comparisons to the original clinical deficiency. For example, in their study on osteoarthritis patients, Collins and colleagues quantified the proprioceptive differences between osteoarthritic patients and healthy controls assuming that the difference between the two groups was clinically relevant. Therefore, a reference state was available to put the improvement in proprioception following SR and sleeve condition into perspective (Collins et al. 2009; A. T. Collins, Blackburn, Olcott, Miles, et al. 2011). Using a similar approach for ACLR patients in the current work might be imperative since the presence of proprioception deficiency following ACL reconstruction is to this date unclear and not clinically established. Therefore, it is challenging in the current work to put the observed changes into a clinical context. Further research in this area is required to inform the existence and the potentially the amplitude of clinically meaningful changes in proprioception.

Small values of differences observed in this study may not necessarily be assumed inconsequential. A minor improvement in proprioception acuity has been suggested to potentially lead to significant improvements in function in osteoarthritis populations (Lin et al. 2007; Tsauo et al. 2008). These small differences may potentially be extremely important to keep the joint from injury in perilous situations. As suggested by Mauidi and colleagues: "… while the magnitude of these changes in proprioceptive acuity seems small, the effect on injury might be significant. During normal activity, the control systems operate below the level of conscious awareness and with vulnerable structures, motor control errors of a small magnitude may result in injury" (Muaidi et al. 2009). Similarly, it was suggested in (Collins et al. 2009; Lin et al. 2007;

Tsauo et al. 2008) that minor improvements in proprioception can lead to significant functional improvements. Overall, these studies may suggest the importance of small proprioceptive improvements.

The findings from the current dissertation are in accordance with the outlined literature supporting the importance of small improvements in proprioception. It is speculated here that when an individual is situated in an injury prone situation and the postural control system is stretched and challenged to its extremes, it is likely that slight changes in proprioceptive feedback might determine whether the joint will be injured or not. It must be acknowledged, however, that the current study was not designed to determine the effect of proprioceptive changes on reducing the injury risk or to relate these to functional improvements.

Another plausible explanation about the small amplitude of the differences in the current work is that the proprioception test was not sufficiently challenging for the population of healthy, active, young, athletic females who primarily were injured in sport related activities. When discussing the clinical significance of a finding, it is important to consider the sample under study. Some of the ACLR participants in the current study were determined to return to demanding sports such as soccer, football, or hockey either recreationally or professionally. Returning to sports including pivoting, jumping, and hard cutting is one of the main reasons for some of these patients to undergo ACL reconstruction (Grindem et al. 2016; Grindem et al. 2014; Hefti et al. 1993; Moksnes et al. 2008). Yet, the ACLR patients are at a higher risk of knee injuries including but not limited to the ACL re-injury (Swärd et al. 2010; Shelbourne et al. 2009; Salmon et al. 2005; Myklebust et al. 2003; Grindem et al. 2016). Hence, there must be a deficiency somewhere in the neuro-muscular-skeletal loop that exposes this population to a higher risk of re-injury. Yet, the deficiency was not detected via the available experimental protocols. Based on these arguments, it is rational to speculate that this level of deficiency is potentially so small and subtle that it did not manifest itself under simple tasks such as the movement threshold or movement repeatability tests.

Based on the study findings, the introduction of a new experimental protocol might be necessary for future research to study proprioceptive deficiency in functional ACLR patients. The movement repeatability and threshold protocols are established methods of testing the proprioception acuity in different clinical populations. The proprioceptive deficiencies (if present) in an active and functional population such as the ACLR participants in the current study can be speculated to be more subtle than functionally impaired clinical populations such as those with osteoarthritis, stroke, or Parkinson’s. Although these tests might be sensitive in detecting proprioception deficiency in these functionally challenged clinical populations, they may not be sufficiently challenging for highly functional ACLR participants in revealing a proprioceptive deficiency. In the case of a movement threshold, for example, an ACLR participant detects the movement in most of the cases within a fraction of a degree. This might indicate that the experimental protocol is simply very trivial for this particular group. Under injury-prone situations, however, the response of the neuromuscular system in the ACLR population is probably different than the healthy group. Therefore, it is suggested here that a novel proprioception testing protocol for functioning clinical populations such as ACLR patients should be developed that can assess proprioception in a context that may safely replicate the perilous situations.

Alternatively, it might also be argued that the deficiency might not be present in the proprioception at all and we are looking for the deficiency in the wrong place. Some have supported this perspective and speculated other mechanisms for the higher injury risks in the ACLR population such as cortical changes in the motor cortex (Baumeister et al. 2008) and arthrogenic muscle inhibition of quadriceps (Grant & Dixon 1965; Hopkins & Ingersoll 2010; Ingersoll et al. 2008). It is beyond the scope of the current dissertation to make any speculations about these potential mechanisms.

Differences in proprioception may also have been difficult to detect due to measurement accuracy and precision of the testing device. Proprioceptive outcomes have been reported to up to two decimal places in the literature. Reporting the movement threshold up to that precision with the devices commonly used to measure proprioception is questionable. The Biodex machine, for example, reports angles up to one digit of precision when the Research Toolkit software is utilized (BiodexManualv4x n.d.). The case is very similar when goniometer was used to measure the knee flexion angle. MacDonald and colleagues specifically mention that "Our goniometer scale was not accurate enough; we could only read it to the nearest 0.1 degrees" (MacDonald et al. 1996), and yet they report a difference of 0.14 degrees in their results. Similar issues have been observed in (Collins et al. 2009; A. T. Collins, Blackburn, Olcott, Miles, et al. 2011). It is plausible that the measurements have not been rounded based on the measurement error. This would result in some studies to report finding differences when two digits or more have been used, while those differences may vanish if the data is properly rounded to one digit. The latter was the case in the current dissertation. For example, the minimum and maximum of movement threshold and the associated standard error were (0.4˚, 0.8˚) and (0.0˚, 0.1˚)

respectively (§4.3.1). Such a tight spread of data can potentially limit the ability to detect differences between groups.

6.5 Postural balance

In the current section, the effect of the factors of eyes (open vs. closed), limb side (ACLR vs. healthy control; ACLR vs. contralateral) on measures of postural balance are discussed. The effect of vision on postural balance is discussed in §6.5.1. The results of between and within comparisons for limb side are discussed in §6.5.2. The interaction between the factors of eyes and limb side showed significance, and the interpretation of this interaction is summarized for within and between groups comparisons in a table and discussed in §6.5.2. The effect of time since surgery (three vs. six months) on measures of postural balance is discussed in §6.5.3. The effect of SR (ON vs. OFF) on postural balance is discussed in §6.5.4.

6.5.1 Eyes

In this study, significant differences in postural balance were observed when eyes were closed. It was hypothesized that a significant difference in EnHL and ΔE_{surr} would be observed between the eyes open and closed conditions in the ACLR participants [H13]. A significant difference was observed in the ACLR group between eyes open and closed on $EnHL$ in ML and ΔE_{surr} in both ML and AP directions. Thus, the postural balance in the absence of vision was significantly worse than in the eyes open condition, largely supporting [H13]. The effect of $EnHL$ in the AP direction was not significant between eyes open and closed conditions. Of interest, the $EnHL$ in AP direction was also not sensitive to any other factor in the current study (see §4.4.1.2).

The current results were consistent with previous studies reporting poorer postural balance in the absence of vision in different clinical populations using a similar setup with different outcome measures (Yoon et al. 2012; Nagano et al. 2006; Prado et al. 2007; Blaszczyk & Klonowski 2001; Schmit et al. 2005; Bolbecker et al. 2011; Hughes et al. 1996; Donker et al. 2008; Kouzaki & Masani 2012; Fernie & Holliday 1978; Frenklach et al. 2009; Agostini et al. 2013; Mazaheri et al. 2010; Mancini et al. 2011; Blaszczyk & Orawiec 2011; Kamen et al. 1998; Schieppati et al. 1999; Strang et al. 2011; Oliveira et al. 2009).

Mechanistically, vision plays a key role in providing information to the postural control system. Therefore, the absence of vision was expected to negatively affect the performance of the postural control system, as was shown in the current study. To compensate for the absence of vision, it was conjectured in this dissertation that the postural control system makes the following two adjustments: (1) it increases the memory of the previous postural positions, and (2) the execution of the postural control adjustments are more tightly regulated and regimented.

The first explanation speculates that the postural control system uses the information from previous positions for postural adjustments. If this were not the case, the postural balance would have been a completely random and unpredictable signal. It is known that the structure of COP signal is not random and is comprised of a rich complexity (Baltich, von Tscharner et al. 2014). Therefore, the postural control system must have utilized “memory” of the past.

EnHL provides a means to evaluate the reliance of a given signal on previous data points. When EnHL is used in studying the COP signal, it most likely quantifies the extent to which the postural control system relies on the information from the past (see §2.5.1.1). When vision is absent, one major source of information to the postural control system is removed. Therefore, the postural control system needs to diligently extract as much information as possible from other available data. One way to do this could be to increase the amount of information from previous postural positions (i.e. increase the memory of the past). Therefore, it follows that the EnHL will increase when the eyes are closed. The current findings on EnHL support this speculation (see Table 16 in §6.5.2), the EnHL increased in the absence of vision. In conclusion, one immediate action of the postural control system when visual input is compromised is to increase the size of memory of the past used.

Although it is helpful for the postural control system to maximally increase the memory, the current dissertation speculates that there must be a limit to its extent for two reasons: (1) information from too long ago might be irrelevant and may not be helpful to the postural control system; and (2) as the size of memory increases, the amount of neural calculations required to incorporate the extra information will inevitably increase. Increased calculation load could lead to compromised agility and responsiveness of the postural control system in adjusting the posture.

To limit an unnecessary increase in the size of memory, the postural control system can be expected to ensure that the system is regulated more tightly and each postural adjustment is performed to the fullest extent in a timely manner. Thus logically, it follows that in the absence of vision, the postural control system perceives less room for error, since the individual is at a higher risk of falling and therefore is obligated to adopt a more stringent control of the postural adjustments. Thus, the timing of postural adjustment events must become more regulated and be executed more strictly. The ΔE_{surr} reflects the importance of the timing of events in a given signal. Therefore, in the absence of vision $\Delta E_{surr}$is expected to increase (i.e., there is a heavier reliance on timing of adjustments). The study findings also support this theoretical perspective.

As can be observed, ΔE_{surr} in the ML and AP directions were systematically increased when participants' eyes were closed. The current findings support the notion that when the eyes are closed, a higher control is imposed on the timing of postural adjustment events.

These conjectures could be made only because the appropriate tools of EnHL and ΔE_{surr} were at our disposal. These tools that have been developed alongside this dissertation, are able to examine the fine structures within a signal and provide insights previously unavailable regarding the underlying behaviors of the postural control system. Predominantly used measures of postural control such as 95% confidence ellipse are only able to capture the overall and more global behavior of a signal (Baltich, von Tscharner, et al. 2014). Some nonlinear measures such as Lyapunov exponent, or α in the de-trended fluctuation analysis attempt to provide insights about the temporal structure of the signal (Baltich, von Tscharner, et al. 2014). However, these measures are difficult to interpret and quantify. In contrast, the EnHL for example, is presented in the scale of time and has a direct physical implication (see (von Tscharner et al. 2016) for more detailed discussion on this topic). Similarly, the ΔE_{surr} is related directly to the percentage of information embedded in the timing of events in a signal. Although the mathematical methods needed to calculate these measures are not trivial, the measures themselves are relatively easy to relate to, understand, and interpret for the human body.

6.5.2 Limb side

In summary, the postural balance was not significantly different when the ACLR limb was compared to the contralateral. A significant difference was observed, however, between the ACLR limb and healthy controls. It was hypothesized that significant differences would exist for the EnHL and ΔE_{surr} outcomes based on the ACLR and uninjured contralateral [H11] and

ACLR and healthy dominant limbs [H15]. The outcomes of postural balance when the ACLR limb was compared to contralateral was not significant (see §4.4.1) and thus [H11] was not supported. When the comparison was made between ACLR and healthy dominant limbs, however, significant difference was observed (see §5.4.1), and [H15] was supported.

Furthermore, the difference in measures of postural balance was significant between the ACLR and contralateral limbs only when the participants' eyes were closed. The interpretation on postural balance for this interaction is described in detail in the results section but is also summarized for convenience in Table 16. It can be observed from this table when the eyes are closed, the EnHL in the ML direction and ΔE_{surr} in the AP and ML directions are larger in the ACLR limb compared to contralateral. It is a rather an interesting observation that the postural balance differences between ACLR and controls were non-significant when the participants' eyes were opened.

Table 16 - Comparison between the ACLR and uninjured contralateral limb

Within Subject Comparison

	Eyes Closed		**Eyes Open**	
	ML	**AP**	**ML**	**AP**
EnHL	**p = 0.029** Δ = 8ms‡ 95% CI = (1,16) ms	p = 0.132 Δ = 8ms 95% CI = (-2,17) ms	p = 0.925 Δ = 0 ms‡ 95% CI = (-3,4) ms	p = 0.198 Δ = 5 ms 95% CI = (-2,17) ms
ΔE_surr	**p = 0.048** Δ = 0.6 % 95% CI = (0,1.3)%	**p = 0.017** Δ = 3% 95% CI = (0.5,5)%	p = 0.545 Δ = 0.2 % 95% CI = (-0.4,0.9)%	p = 0.235 Δ = -0.3% 95% CI = (-0.8,0.2)%

† Eyes Closed
‡ Δ = ACLR-Contra.

There is no conclusive evidence for the presence of postural differences between ACLR and controls (see §2.3.2 for details). However, based on the systematic review performed by Howells and colleagues, a trend towards postural deficiency was reported in the ACLR limb (Howells et al. 2011), although the differences sometimes was not significant.

According to the current study, the difference in postural balance depended on whether contralateral or healthy control limbs were used for comparison. This finding might indicate that the contralateral should not be considered equivalent to the healthy control limb in postural balance studies. Similarly, it was observed that the proprioception was different between contralateral and healthy controls (see §6.4.1). These findings support the concern raised by Fridén and colleagues when the contralateral limb is used as the comparison control. They suggested that following an injury; postural balance in the contralateral limb undergoes changes/adaptations. These changes make the comparisons difficult to interpret (Fridén et al. 2001).

Mechanistically, it has been suggested that a bilateral effect might follow a unilateral injury (Muaidi et al. 2009; Roberts et al. 2000; Gauffin et al. 1990; Gauffin et al. 1988). It has been theorized that both lower limbs utilize the same movement control modality. Following the injury, both limbs may resort to a common but less versatile motor program as was suggested following the ankle injury (Muaidi et al. 2009; Gauffin et al. 1988; Waddington & Adams 1999). Such a less versatile program in the ACLR limb may lead to a function deficiency in the contralateral limb. This mechanism that has been suggested for other joints can be speculated in this dissertation also to be applicable to the ACLR population. This might be a potential explanation behind the commonly suggested higher risk of ACL injury in the contralateral limbs (Salmon et al. 2005; Muaidi et al. 2009).

The absence of vision was an important factor in the postural balance between ACLR and contralateral limbs. It was observed that the difference in the ACLR and contralateral limb became significant only in the absence of vision. The current finding agrees with (Henriksson et al. 2001; Paterno et al. 2013) who reported a deficiency in postural balance in ACLR patients when eyes were closed. For example, Henriksson and colleagues reported a trend towards significance difference ($p = 0.051$) between the ACLR and healthy control limbs when eyes were closed. This trend was absent when eyes were open (Henriksson et al. 2001). Bonfim and colleagues have studied single leg balance only when eyes were closed (Bonfim et al. 2003). Similar to the current work, significantly different postural balance outcomes were seen between the ACLR and contralateral limbs when the participants' eyes were closed (Bonfim et al. 2003).

It can be speculated that these results may reflect the subtlety of the deficiency of postural balance in the ACLR population. In the absence of vision, a heavier reliance will be placed on the somatosensory system of the lower limb. Based, on the current findings, the deficiency in the somatosensory system was clearly measureable in the absence of vision. Therefore, at times when the postural system relies more heavily than normal on the somatosensory information, it may fail to respond as effectively as when there is a visual input. This might be problematic, as a higher risk of injury to the ACLR limb can be conjectured during activities relying primarily on somatosensory information (e.g., activities in darkness or when visual information is fast-changing, or limited).

The subtlety of this deficiency raises the question about broader implications beyond sports/daily activities in the darkness. Consider, for example, an injury prone situation when the visual system is distracted by other objectives (e.g. a game situation or navigation in a crowded environment, texting while walking). In these situations, a quick interaction with the sensory receptors and postural control system is essential for the desired postural adjustments. However, vision may not provide the necessary information since it is occupied by some other tasks. Inevitably, heavier reliance will be placed on somatosensory and vestibular systems. When vision information is not available, the combined outcome of these two systems may show signs of deficiency (see Table 16). Therefore, the ACLR limb may be exposed to higher risk of re-injury in these situations.

From the current work, it is not clear whether the deficiency in the ACLR limb is in the motor or sensory system. Therefore, one should be careful about implicating the sensory system alone for the observed deficiencies. Some authors have previously suggested that the deficiency may be present in the motor system alone and not in the sensory system (Furlanetto et al. 2016). Regardless of the mechanism, the outcome is potentially the same: the deficiency is exacerbated in the absence of visual cues. The current study design did not allow an investigation into this supposition. However, an interesting follow-up investigation might be to study if the ACLR limb will show signs of deficiency in postural balance under a visually distracted or reduced condition.

The ΔE_{surr} of the ACLR limbs was significantly larger by 11% and 8% in the AP and ML directions compared to the healthy controls. The relatively high levels of significance ($p < 0.001$) of ΔE_{surr} in the ML (see §5.4.2.1) and AP directions (see §5.4.2.2) are particularly interesting. These values might indicate that the ΔE_{surr} measure is very sensitive in discriminating the postural differences in the ACLR population compared to healthy controls.

A high level of sensitivity and specificity in ΔE_{surr}, has been demonstrated previously in an electrocardiogram study of congenital heart failure disease patients and healthy control participants (von Tscharner & Zandiyeh 2017). In the current study, specificity and sensitivity of this measure has not been quantified. Based on the presented p-value, it can be hypothesized that the sensitivity of the measure in discriminating the postural balance between ACLR and healthy controls might be high. Should for example high specificity and sensitivity of the ΔE_{surr} be confirmed in future studies, the ΔE_{surr} may serve as a diagnostic/clinical measure to quantify differences in the postural control system between healthy and ACLR subjects. Having such a measure might prove to be very informative to clinicians and physiotherapists, since they can investigate the effectiveness of their intervention/treatment to improve the postural balance control with such a tool.

6.5.3 Time

The effect of time was studied in the current work to investigate how postural balance changed in the ACLR limb over time. It was hypothesized that a significant difference in EnHL and ΔE_{surr} would exist between three months and six months post-surgery in the ACLR participants [H12]. The results of the factor of time on the outcome measures of $EnHL$ and ΔE_{surr} in ML and AP directions was not significant (see §4.4 and §5.4). Therefore, the null hypothesis was not rejected and [H12] was not supported.

This finding is in agreement with the majority of longitudinal studies that have reported insignificant changes in postural balance in the ACLR population over time (Chmielewski, Wilk et al. 2002; Ma et al. 2014; Heijne & Werner 2010). Chmielewski and colleagues showed no difference in the postural balance outcomes at 1-week, 6-weeks, and 12-weeks post-surgery

(Chmielewski, Wilk et al. 2002). Ma and colleagues have studied patients at six months and 12 months post-surgery and observed no significant change in the postural balance outcomes (Ma et al. 2014). Heijne and colleagues followed up ACLR patients at 3, 5, 7, 9, 12, and 24 months post-surgery and reported no significant change in postural balance over time (Heijne & Werner 2010).

Four explanations can be suggested for not observing changes in the postural balance over time in this dissertation. Firstly, the status of postural balance following the surgery may not change over time. Secondly, a longer period might be necessary to observe improvements in the postural balance. Thirdly, the physiotherapy and rehabilitation treatments are not effective in improving the postural balance in the ACLR population following the surgery. Lastly, the rehabilitation program might be effective but may not be diligently followed by patients. The current study was not designed to ascertain the veracity of these alternative explanations. To further understand possible mechanisms behind the importance of these changes over time, more detailed longitudinal studies are required that control/investigate the factor of time, the amount of physiotherapy and rehabilitation, and the patients' commitment to the rehabilitation program.

6.5.4 SR

The effect of SR vibration has been studied on the postural balance in the current dissertation. The main effect of SR intervention did not reach statistical significance in postural balance. It was hypothesized that a significant difference in $EnHL$ and ΔE_{surr} would exist between the SR ON and SR OFF conditions in the ACLR participants [H8]. In the within participant evaluation (ACLR vs. contralateral), the difference $EnHL$ in AP and ΔE_{surr} in ML and AP directions between SR OFF and ON was not significant (see §4.4). Similar findings were observed in between participants study (ACLR vs. dominant control) (see §5.4). Therefore, [H8] was not supported.

The results showed that the effect of SR was not significant in either of the postural balance outcomes. These findings are in accordance with most of existing literature on this topic. For example, it was shown by Priplata and colleagues that improvement in the postural balance by applying noise to the sole was large in the elderly population but small in healthy adults (Priplata et al. 2002). Also, it was suggested that postural control in healthy young adults is nearly optimal (Wu et al. 2007). Therefore, SR treatment might not lead to a sensory information enhancement that positively impacts the postural balance in the healthy, young, athletic group studied (Dettmer et al. 2015).

The results of the current study show that a subtle deficiency in the ACLR limb is present that is manifested only in the absence of vision. Previous findings in stroke, diabetes, and osteoarthritis patients (Priplata et al. 2006; Collins et al. 2009) suggest that the benefit of SR stimulation might be closely related to initial performance. More specifically, if the population originally exhibits significant postural deficiency, they may benefit more from SR intervention than those demonstrating near optimal postural balance (Dettmer et al. 2015). Excepting when the eyes were closed, no postural balance deficiency was observed in the ACLR population. Thus, the benefit of using SR might not usually be observed in ACLR patients in improving postural balance.

The current findings do not support the significant differences reported for the SR interventions in previous studies (Priplata et al. 2002; Priplata et al. 2006; Gravelle et al. 2002). A direct comparison between these studies and the current research, however, is difficult since differences in findings might be partially attributed to the difference in methodologies, the population under study, and outcome measures for assessing and quantifying the postural balance as also suggested by (Hijmans et al. 2008; Dettmer et al. 2015).

Targeting the mechanoreceptors of the knee might not produce significant effects on postural balance. It has been suggested that when the level of external perturbation to postural balance is minimal, postural adjustments are performed primarily by the muscles across the ankle joint (Kavounoudias et al. 2001; Gildenhuys 2003; Gildenhuys et al. 2015; Horak et al. 1990; Runge et al. 1999; Runge et al. 1998; Yang et al. 1990). It can be speculated that the information from mechanoreceptors of a joint will be utilized when that particular joint contributes to postural balance. It has been previously suggested that during a one-legged stance, the knee joint is not contributing significantly to postural adjustments (Priplata et al. 2004). Therefore, it can be conjectured that the information from mechanoreceptors of the knee may not be utilized in a task mainly maintained across the ankle. Also, the improvements observed in the proprioception of the knee due to SR in the current study, may not directly impact postural balance. This may explain why proprioception-improvement was observed in the knee but not in postural balance when SR was applied.

Furthermore, it has been suggested that the mechanoreceptors of the foot sole might be very important in providing proprioceptive feedback to the postural control system during quiet standing (Kavounoudias et al. 2001; Diener et al. 1984). This may clarify why studies that applied SR vibration through the foot sole have observed more pronounced postural improvements (Priplata et al. 2002; Priplata et al. 2006; Gravelle et al. 2002).

6.5.5 Classical measures

As it can be observed in §4.4.2, most of these measures provided similar results to what have been found using the EnHL and ΔE_{surr}. For example, effect of the factor $eyes$ and also $eyes \times SR$ were present in 81% and 44% of measures respectively (see Table 8). This might support the previously found significance of similar main and interaction effects for the measures of entropy and thus, might be viewed as a cross-validation step.

Discussing each finding reported in §4.4.2 is beyond the scope of the current work. However, the main objective of showing the results of the classical measures of postural balance was to highlight that, based on these many measures of postural balance, any of the factors in the study reaches significance in one measure or another. As it can be observed in Table 8, the effect of a study factor reaches significance intermittently in one measure or another. The approach of considering all postural balance measures without an *a priori* hypothesis is known as data dredging (also data fishing, data snooping, and p-hacking) (Smith & Ebrahim 2002). This approach is statistically impaired since large numbers of tests are performed on a single data set, and 5% of randomly chosen hypotheses will be significant at the 5% level only by chance alone. In other words, when enough numbers of statistical tests are performed on a data set, it is almost certain that some of them will provide significance by pure chance.

Some examples of potentially biased findings due to selective choices of postural balance measures have been observed. In the literature, a clear rationale, motivation or justification for the choices of measures is frequently lacking. For example, in (Dettmer et al. 2015) the path length in the AP direction has been reported but not in the ML direction. Similarly, in (Gravelle et al. 2002) the standard deviation in ML and maximum excursion in AP has been reported. It is not clear why standard deviation in AP and maximum excursion in ML has not also been reported. Furthermore, (Dettmer et al. 2015) have used approximate entropy as an outcome measure. The approximate entropy proposed by Pincus and colleagues (Pincus 1991) suffer from some limitations that later Richman and colleagues have outlined and corrected in a more recent algorithm of SEn (Richman & Moorman 2000). Although the works in (Dettmer et al. 2015) clearly postdates the introduction of SEn, it is not clear why a measure with known flaws has been used for assessment of their COP.

A solid knowledge about postural balance measures used in the current work (i.e. $EnHL$ and ΔE_{surr}) and their behaviours under different study conditions is available. These measures have been introduced and tested on various clinical populations by the collaborations of the current authors. Behaviour of these measures, particularly EnHL, has been studied in postural balance data. For example EnHL has been tested under different conditions of stance (bipedal, single leg, and tandem standing), mental process (no mental, 2-back test), and footwear (barefoot, control shoe, and unstable shoe) in a collaborative work by the current author, and its behaviours have been monitored under different conditions (Federolf et al. 2015). Furthermore, the test-retest repeatability of this measure has been tested in a collaborative work with the current author (Baltich, von Tscharner, et al. 2014). The relation between the EnHL to the α in de-trended fluctuation analysis has been studied in a collaborative work by the current author in (von Tscharner et al. 2016). The ΔE_{surr}has been for the first time officially introduced in a collaborative work by the current author on electrocardiogram signal and its sensitivity and specificity were quantified in discriminating the patients with congenital heart failure disease compared to healthy controls (von Tscharner & Zandiyeh 2017).

These measures have been tested for the first time in the current dissertation to study the COP signal of the ACLR population under different study factors. Moreover, it is important to note that these measures are informative and are presented in scales that are readily understandable for researchers. For example, EnHL is presented in milliseconds that provide insights about the length of memory potentially used by the postural control system to calculate the new postural adjustment. The ΔE_{surr} is presented in percentage and provides a means to measure how heavily events in postural balance are regulated by the postural control system.

6.6 Summary

The discussion of the current chapter can be summarized into the following 12 main synopses:

I. The anthropometrics measures between the ACLR and healthy control participants were comparable. However, body mass was heavier by 8.9 kg in the ACLR group participants compared to the healthy control group.

II. From the study of the IKDC 2000 knee evaluation questionnaire, it was observed that healthy controls scored significantly higher than the general public.

III. It was observed that the IKDC 2000 scores were higher in the ACLR patients as early as three months post-surgery compared to other ACL deficient patients. At six months post-surgery, the score was still lower than the literature, although the exact statistical comparisons were not possible. The score at six months post-surgery was lower than the suggested 83% cut-off for a return to sports activities suggested in the literature. Based on the IKDC 2000 scores, this might suggest that this group is not prepared to return to sport.

IV. The ACL-QOL increased by an average of 14% from three to six months post-surgery. Significantly higher ACL-QOL was observed as early as three months post-surgery when compared to the data from the literature in other ACL deficient samples. The ACL-QOL at six months post-surgery was not different from the literature on ACLR at 38 months post-surgery. It might be speculated that this score reached a steady state level as early as six months post-surgery.

V. Proprioceptive deficiency in the ACLR limb was not supported in the current study. This lack of deficiency was speculated to be the outcome of ACL reconstruction. It was suggested that the ACL reconstruction increases (at least partially) the kinematic constraints of the knee. Therefore, it will limit the anomalous movements in the joint, which, in turn, will limit the amount of anomalous sensory outputs from the knee joint. Consequently, the central nervous system will be able to rewire and reprogram in the absence of these anomalous outputs to compensate for the absent receptors of the ACL.

VI. Overall it was observed that proprioception improved in the presence of SR. Limited studies were available for cross-validation, and the mechanisms behind the observed improvement are rather involved. However, it has been shown in the literature that SR improves the sensory output from all three major proprioception sources of a joint including muscle spindles, Golgi tendon organs, and cutaneous receptors. Therefore, some or all of these receptors might be responsible for the improved proprioception. The current study was not designed to specify which receptor(s) and to what extent they were responsible for the observed improvement in proprioception.

VII. No improvement in proprioception was observed over time although a non-significant trend towards improvement was observed. In agreement with the literature, it was speculated that healing in proprioception is relatively quick. This quick healing might be attributed to fixing the mechanical constraints of the knee, which can be speculated to improve cortical interpretation of the joint position. This process has been suggested to start early after ACL reconstruction with full proprioceptive recovery as early as 3 to six months post-surgery.

VIII. Significant differences in postural balance were observed between the eyes open and closed conditions. Vision provides important sensory input to postural balance. When eyes were closed, increases in EnHL and ΔE_{surr} were observed. EnHL can be speculated to relate to the size of memory of the past states and used by the postural balance to calculate the necessary postural adjustments. An increase in EnHL was observed in the current dissertation when eyes were closed. The ΔE_{surr} can be related to the timing of postural adjustment events in the postural balance. It was observed that the ΔE_{surr} increased when the eyes were closed. This may be speculated to indicate a more regimented and regulated control by the postural control system on postural balance when vision is absent.

IX. Postural balance was significantly different between the ACLR and contralateral limb only in the absence of visual information. It can be speculated that when the eyes are closed, a heavier reliance will be placed upon sensory information from the somatosensory receptors. This may magnify subtle and otherwise undetectable deficiencies in the postural control system in the ACLR population. This observation might reflect the subtlety of any deficiencies present in the postural control for the ACLR population.

X. The outcome of postural balance and proprioceptive were different when the ACLR limb was compared to contralateral or healthy dominant controls. It can be theorized that the uninjured contralateral undergoes physiological changes following the ACL injury/surgery. This is usually referred to as the bilateral effect of a unilateral injury. Therefore, using the uninjured contralateral might not be as useful in studies of proprioception or postural balance in the ACLR population.

XI. The difference between ΔE_{surr} of the ACLR and uninjured contralateral was noticeably high. Future work should be done for example on the sensitivity and specificity of this measure in discriminating between ACLR and healthy controls. Studies as such might suggest if such measure might serve as a potential diagnostic/clinical measure to quantify the differences in the postural control system between healthy and ACLR individuals. Having such a measure might be very informative and helpful to clinicians and physiotherapists. They may be able to investigate the effectiveness of their intervention/treatments to improve postural balance in the light of this tool.

XII. The effect of SR on postural balance was not significant. SR has been shown previously to improve postural balance in functionally challenged populations while showing minimal effects in functional clinical populations. The ACLR sample that was studied in the current work did not demonstrate significant postural deficiencies with eyes open. Therefore, it is likely that due to non-significance of the deficit, the effect of SR was not significant enough to alter the postural balance in the ACLR population.

Chapter Seven: **Conclusion**

"… then we got into a labyrinth, and, when we thought we were at the end, came out again at the beginning, having still to see as much as ever."

Plato (c. 428- c. 348 BC)

7.1 Summary of findings

The current dissertation investigated the differences in proprioception and postural balance between ACLR limbs at three and six months post-surgery and uninjured contralateral as well as healthy dominant limbs. Postural balance was quantified with two new measures: EnHL and ΔE_{surr}. SR noise vibration, applied to the area around the knee was also investigated for its effects on both proprioception and postural sway in individuals with ACLR.

No proprioceptive deficiency was identified in the ACLR sample relative to their contralateral controls or the healthy group at either three or six month time points post-surgery. However, postural balance deficiency was detected in the ACLR limbs compared to the dominant limbs in the healthy control group. Furthermore, SR improved proprioception in the ACLR, contralateral, and healthy dominant limbs but didn't result in significant improvements in postural balance.

7.2 Significance

Establishing the existence and quantifying the amount of proprioceptive deficiency in the ACLR population are important unanswered research questions in the leading scientific literature. Information about the extent of proprioceptive deficiency in the knee at early times (three and six months) following ACL reconstruction surgery, may assist clinicians in determining appropriate rehabilitative exercises as well as the timing of introducing these exercises. The current dissertation is one of a limited number of longitudinal studies on proprioception in the ACLR population conducted shortly after the reconstruction surgery (i.e. three months and six months post-surgery). Therefore one contribution of this dissertation is that it can inform clinical practice with regards to the presence and the extent of proprioception deficiency in ACLR limb early after the ACL reconstruction surgery.

There was no evidence in the current study of proprioceptive deficiency in the ACLR population when the ACLR limb was compared to the contralateral or healthy controls. However, there is considerable evidence that ACLR patients are at a higher risk of re-injury to the ACL or other structures of the knee. Based on the current findings, two explanations are plausible: (1) there may not be a proprioceptive deficiency in the ACLR population. In this case, the higher risk of re-injury in the ACLR population might be associated with a different mechanism. For example, arthrogenic muscle inhibition or changes in motor cortex following the ACL injury have been suggested in the literature. (2) The proprioceptive deficiency does exist, but the test methods utilized in this study are not sufficiently sensitive to capture it. In this case, it is conclusive whether the proprioceptive deficiency is the cause of higher risk of re-injury in the ACLR population. The latter explanation highlights a need for new experimental protocols to test proprioceptive deficiencies in a functional group such individuals with ACLR.

There is no consensus regarding the presence of postural balance deficiency in the ACLR population in the current scientific and clinical literature. Thus, this also remains an open research question. Postural balance is maintained by a close interaction of integrated sensory and motor system of the lower limb. Observing postural balance deficiency can provide insights about the existence and extent of a deficit within this control and feedback loop. The current study demonstrated a postural balance deficiency in the ACLR limb compared to healthy dominant control limbs. When the ACLR limb was compared to the contralateral, the deficiency was only present when the eyes were closed. These findings might suggest that the deficiency is subtle and therefore, more stringent experimental protocols might be necessary for the future to evaluate the influence of surgical reconstruction on postural balance fully.

SR has been shown in the literature to lead to promising improvements in postural balance and proprioception in various clinical populations. In the current dissertation, SR vibration was directly applied to the area around the knee in an ACLR sample and overall was successful in significantly improving proprioception. It is the first study of its kind on the ACLR group that measures changes in proprioception and postural balance following SR stimulation. The findings are a solid first step in providing critical evidence for suggesting SR as potentially an integral part of proprioceptive rehabilitation following ACL reconstruction surgery. Therefore, this work serves as a foundation for future research on the effects of SR in the ACLR population.

In this dissertation, two measures for quantifying postural balance have been proposed: EnHL and ΔE_{surr}. These measures were able to quantify the fine structures within the postural balance signal that were related to the adjustments in the postural balance control system.

There are other measures of postural balance in the literature that provided comparable information. However, the methods to calculate these measures are typically presented in mathematically complex and sophisticated terms that are not easy to understand or interpret. The new measures overcome these issues. The measure of EnHL, however, quantifies in milliseconds the amount of memory that the postural control system uses from previous states in making subsequent postural adjustments. The larger the value, the more memory of the past is being used. The ΔE_{surr} is presented as a percentage, and carries information regarding the relative importance of the timing of events within a given signal (i.e., the regularity of a signal). If events are purely random in a signal, ΔE_{surr}will be 0%. If the order of events is all that matters in a signal, the measure will be 100%. Therefore, regardless of the involved derivation processes to obtain the ΔE_{surr} value, the measure is readily interpretable and easily understood.

The development of the ΔE_{surr} measure is important from another aspect. In the analysis of a biological signal the information corresponding to the amplitude of the Fourier transform has primarily been investigated. In fact, not many researchers have studied the importance of phase in a signal. However, it has been suggested that the information in the phase (timing of events in a signal) constitutes an important part of the information contained in most biological signals. To date, few researchers have in fact, studied the important of phase in a signal. To address the paucity of approaches to quantify this important information, a new tool, ΔE_{surr}, was developed during this dissertation that studies the information content of the phase of a signal.

7.3 Contributions

The primary contributions of the current dissertation are as follows:

I. There is no consensus regarding the presence of deficiencies in proprioception and postural balance in the ACLR population within the current clinical and scientific literature. The current work represents one of a few studies that have studied postural balance and proprioception longitudinally in an ACLR sample at early time points post-surgery. This work provides evidence related to the outlined research questions and hypotheses (H1 to H15). It may be used to assist in informing clinical understanding of and practice related to proprioception and postural balance in this population.

II. Stochastic resonance has been tested for the first time in an ACLR sample with direct application of mechanical noise on the area around the knee. The current dissertation demonstrated the feasibility of using SR to improve proprioception in ACLR and healthy control populations. No quantifiable benefit was detected with SR for improving postural balance in the ACLR or healthy samples. The results may be used to advise future research on the effects of SR on the ACLR population and other groups with knee injuries or proprioception deficits.

III. The SR test protocols used for quantifying the vibration sensation threshold, selecting the amplitude of vibration, and selecting the stimulation site in this work represent the most conservative and controlled methodology selected from the available literature. This integrated protocol proves a valuable reference for future work for applying SR on ACLR group as well as other clinical populations having comparable lower limb deficiencies.

IV. Two measures of postural balance (EnHL and ΔE_{surr}) were developed in conjunction with the current dissertation. These measures have been successfully applied and interpreted with ACLR patients for the first time and hold promise for a number of other research areas.

7.4 Limitations

The following limitations can be outlined for the current dissertation:

I. The current study was not designed to test participants prior to ACL reconstruction surgery. Therefore, limited information is available about their postural balance and proprioception prior to the surgery. It is not clear whether or not their values would fall within the normal healthy control range.

II. Only participants with ACL reconstruction and minimal injuries to other structures of the knee were recruited in the current work. The rationale for this decision was to control for confounding factors in the study. It can be speculated that a more substantial proprioceptive and postural balance deficiencies might have been observed if the joints of more extensively injured patients were included. Also, it can be speculated that in a group with a more extensively deficient joint, the effect of SR might have been more pronounced.

III. The study was designed to involve only female participants between the ages of 16 to 40 years with BMI between 18-to $25-kg/m^2$. The findings of the current work therefore, are limited to this demographic group. A larger sample size including a greater age range and larger BMI range would need to be conducted to determine whether or not the current study findings are truly representative of the larger population.

IV. The BMI of the ACLR subjects was significantly larger than those of the healthy group. This might have influenced some of the differences observed in the current dissertation.

V. The healthy group in the current study scored higher in the IKDC 2000, and the ACLR group scored lower at three months and six months post-surgery compared to roughly corresponding groups based on values reported in the literature. Therefore, hypothetically some of the differences observed in the current study might have been affected by "better" knee conditions in the healthy group and worse knee condition in the ACLR group.

VI. The amplitude of differences in proprioception findings was relatively small and close to that of expected measurement error. This limits the capability to detect differences that might have been present between the factors that were tested in the experiment.

VII. Proprioception was assessed at near full knee extension. Proprioceptive deficiency in the intermediate flexion range (knee flexion angles between 40 and 60 degrees) has been suggested (Furlanetto et al. 2016; Fremerey et al. 2000; MacDonald et al. 1996; Borsa et al. 1997). The proprioceptive deficiency might have been observed if proprioception was evaluated in the mid-flexion range. However, the near full extension position was of more interest in this dissertation as this position is most commonly used in the majority of weight bearing tasks during daily activities (e.g. heel strike during walking, stair climbing and descending).

VIII. Movement threshold was tested at only one speed of 0.25 degrees/sec. Since movement threshold has shown to be sensitive to the speed of movement as well as the initial position of the knee, it is not clear if different results would be achieved with other test speeds. The speed of 0.25 degrees/sec was selected in the current work to minimize the effect of movement initiation and latency in response that may have contaminated the outcomes.

IX. The vibrator arrangement and the amplitude of stimulation were selected in a pilot study with a sample size of 10 participants. The results of these comparisons between test conditions didn't reach statistical significance. Selection of vibrator arrangement and stimulation amplitude was carried out according to the observed trend. Testing in a larger population might provide stronger evidence and potentially alternate decisions regarding the arrangement and appropriate level of stimulation.

X. Inter-subject repeatability of the outcome measures was not evaluated in the current study. Information about test-retest reliability of measures of proprioception (movement threshold and movement repeatability) and a measure of postural balance (EnHL) are available in the literature for different clinical populations. Especially, for EnHL the current author collaborated in a separate study on the test-retest reliability of this measure. However, the test-retest reliability of the effects observed by SR has not been assessed in the current work or to the best of the author's knowledge, reported in the literature.

XI. The amount of power in the statistical tests was somewhat low in several cases. Although diligent efforts were made to obtain a sample of 30 ACLR participants, administrative constraints, including the timely completion of this dissertation, precluded continued recruitment and testing. However, several results were observed as hypothesized and/or trended in the expected direction. The promising results provide ample stimuli to continue this line of research in the future.

7.5 Future work

Based on the current dissertation, pursuing the following avenues for future research are recommended:

I. To design a new experimental protocol to assess proprioception deficiencies in a functional group such as ACLR.

II. Testing postural balance under more demanding experimental setups such postural balance on a foam board or in response to an external perturbation such as a moving force platform (Nashner et al. 1982; Woollacott & Shumway-Cook 1996) or Dynamic stability testing device (Gildenhuys et al. 2015) to elicit greater differences in the functional ACLR group and the healthy controls.

III. A broader study design, similar to the current work, but with a larger, less restricted sample using a matched pair design to provide insight into the generalizability of the current findings.

IV. Investigate the effect of SR stimulation in conjunction with a post-ACL reconstruction rehabilitation program. The objective of such a study would be to investigate whether the group with SR and rehabilitation show better proprioceptive acuity than the group with rehabilitation program alone.

V. Relatively low-cost SR vibrators could be designed and fabricated for use in sports that are high risk for ACL injury, or re-injury, such as hockey, soccer, football, and skiing. The study would investigate whether the frequency of ACL injury/re-injury is reduced after SR treatment.

VI. Establish the arrangement of vibration stimulators as well as the optimal amplitude of stimulation.

VII. The sensitivity and specificity of ΔE_{surr} and $EnHL$ needs to be evaluated in future studies to investigate whether such a measure may serve as a diagnostic/clinical tool to quantify differences in the postural control system between healthy and ACLR groups of individuals.

VIII. ACL-QOL was used in the current study without weighting the questions. A study with relatively large sample size could be conducted to assign appropriate weights to the questions in the questionnaire, potentially adjusted to each time point since surgery.

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APPENDIX A: RESHAPE SCALE METHOD

In this section, the original manuscript that introduced the entropic half-life (EnHL) is presented (Zandiyeh & Von Tscharner 2013). Introducing this measure is one of the main contributions in this dissertation.

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Reshape scale method: A novel multi scale entropic analysis approach

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HIGHLIGHTS

- A multi scale entropy translation method was introduced/computed for $1/f$ processes.
- Entropic Half Life (EnHL) was defined as a measure for complexity of $1/f$ processes.
- The Multi scale entropy by Costa changes the standard deviation (SD) of the signal.
- The Multi scale entropy changes the probability density function (PDF) of the signal.
- Sample entropy is affected by the changes in SD and PDF of the signal.

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ABSTRACT

The *Reshape Scale* (RS) method was introduced in this article as a novel approach to perform multi scale transition of sample entropy. This method was able to quantify the orderliness in the signal by determining the distance over which the subsequent data points can remain affiliated to one another. *Entropic Half Life (EnHL)* was introduced to characterize such an affiliation. The method was tested for $1/f^{\alpha}$ processes for different α values. Furthermore, the dependency of the multi scale entropy analysis developed by Costa et al. (2002) [6] to the probability density function and the standard deviation of autoregressive signals was studied and discussed.

1. Introduction

1.1. General

In the context of information theory, entropy is defined as the rate of information generation within a signal and quantifies the orderliness and regularity in the signal [1]. Various computing algorithms have been developed, revised, and applied to calculate the entropy of a given signal [2–4,1,5]. One of the most recent algorithms is *Sample Entropy* [1] which is defined as the negative of the natural logarithm of the conditional probability that the two m point sequences similar within a threshold value of r, remain similar after adding the next point [1]. Self matches were excluded in this method [1]. This method however may not be able to fully grasp the complex temporal structures within some signals [6,7]. To get further information about the complexity of a signal, Multi Scale Entropy (MSE) analysis was introduced [6,7]. The original signal was first transformed to a coarse graining scale *CG-scale* by dividing it into non-overlapping blocks containing coarse grained

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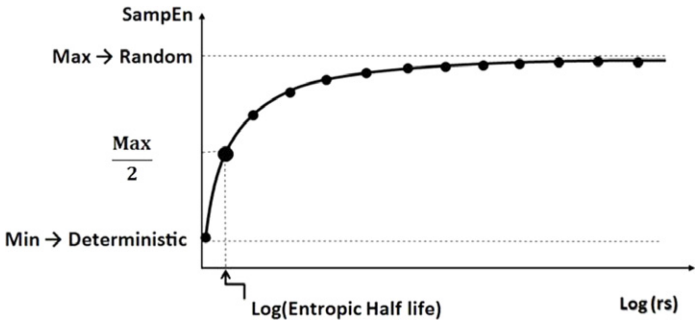

Fig. 1. Entropy vs. different RS scales—the logarithmic scale was used to improve readability.

subsequent data points (DP)s. The average of each block was computed afterwards and the new signal at the CG-scale was constructed by arranging these values while preserving the order [6,7]. Constructing the signal at CG-scale was referred to as *coarse graining* [6]. The Sample Entropy (SEn) was computed for each CG-scale signal. Ultimately, the SEn was plotted as a function of CG-scales. Coarse graining introduces a change in standard deviation (SD) of the data and was therefore previously questioned [8].

The purpose of this study was to introduce a new analysis technique based on reshaping and rearranging the data points (DPs) at a specific reshape scale, τ, in the signal. This technique helps to observe a multi scale transition (MST) of the SEn from originally an ordered signal to a completely randomized one. The transition is characterized by a novel variable, the *Entropic Half Life* (EnHL), which is the scale at which the SEn reaches half of its maximal value. This method will be referred to as the *Reshape Method (RS-method)* and yields an MST from which the EnHL can be computed. The properties of MST will be compared to those of MSE. To be able to make this comparison, the properties of the MSE will be modeled. Specifically, the dependence of MSE to the changes of the (SD) and to the changes of the probability density function (PDF) caused by various CG-scales will be studied.

The RS-method was developed in such a way that the MST shows a transition from low SEn to high SEn with increasing scales. The MST was tested on $1/f^\alpha$ time series which are representative of the majority of real time measurements. $1/f^\alpha$ is a non-stationary random process which is suitable to model evolutionary or developmental systems [9]. The shape of the power spectral density (PSD) function of such signals are proportional to $1/f^\alpha$ for $0 < \alpha < 2$ [9,10]. These processes were observed in various engineering and biological systems e.g. the signals of earthquakes, avalanches, chemical reactions, flux motion in superconductors, and human coordination [11,10] which make them important time series to analyze and study. These time series were used as simulation models for entropy related studies [6,12,13].

In summary, the objectives of this study were: (1) to introduce a multi scale analysis method referred to as the RS method, which will not affect the SD and the PDF of the signal; (2) to introduce a new variable referred to as EnHL; (3) to evaluate this method for $1/f^\alpha$ processes; (4) to study the effect of coarse graining on the changes in the PDF of a given signal; (5) to study how the initial PDF of a signal influences changes in the PDF through coarse graining; (6) to study the effects of the change in PDF of a signal on the SEn values; (7) to study the change in SD of the signal following coarse graining; (8) to study the effect of changes in SD of the signal on the SEn values.

2. Method

2.1. Reshape method

The RS-method was used to rearrange the DPs in a way that the time distance between consecutive DPs increases according to a τ-scale. To generate a signal at scale $\tau \in \mathbb{N}$ using this method, DPs that were τ indexes apart were selected and arranged according to Eq. (1).

$$P_i = [x_{i+0\times\tau}, x_{i+1\times\tau}, x_{i+2\times\tau}, x_{i+3\times\tau}, x_{i+m\times\tau}], \quad \text{where } \{\forall m \in \mathbb{Z}^{\geq 0} \mid m \times \tau + i \leq L\}, i = 1, 2, \ldots, \tau \tag{1}$$

where x_q is the qth DP of the original signal. The last point of each P_i was named as an attachment point.

The signal at scale τ was constructed by appending the P_is to form a new reshaped time series, i.e. $TS_{\text{new}} = [P_1, P_2, \ldots, P_\tau]$. Based on this definition, $\tau = 1$ refers to the original signal.

The SEn for the completely randomized case was computed by taking the average of SEn for thirty realizations of the signal constructed through complete random permutation of all the DPs in the signal. The RS-method uses almost all DPs in the signal so the length, SD, and the PDF of the signal remains unaltered.

The τ was gradually increased and the SEn was computed for each new signal. The transition from small to large scales is illustrated in Fig. 1. The point at which the transition curve crosses half of its maximal value was of particular importance. The τ-scale associated with this point was found through a direct search. This scale was named *Entropic Half Life (EnHL)*. Attention should be paid that the EnHL contains the time dimension for a physical signal.

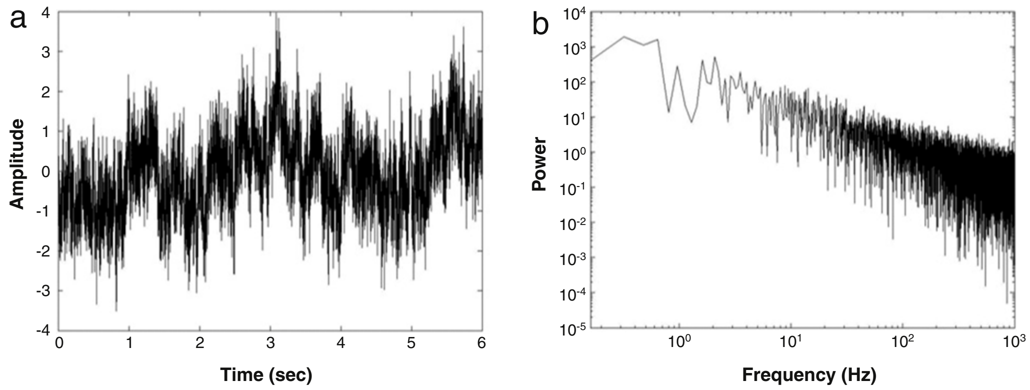

Fig. 2. An example $1/f^{\alpha}$ signal ($\alpha = 1$ in this example) a. The signal relative to time b. Log–log plot of the power spectrum of the signal.

To study the properties of the RS method, $1/f^{\alpha}$ signals with 15,000 DPs were generated according to Ref. [14] for different α and were normalized afterwards. Such a signal in the time and frequency domain (for $\alpha = 1$) is presented in Fig. 2.

2.2. Assessment of the dependencies of MSE on SD and PDF

To study objectives 4 to 8, AR pseudo-random signals with different distributions and AR coefficients, ρ, were generated according to Ref. [15] using the sampling frequency of 2400 Hz generally utilized in our laboratory for biomedical measurements. All AR signals were normalized afterwards by subtracting the mean and dividing by the SD.

To assess the dependency of the SEn to the PDF of the signal, without loss of generality, thirty AR signals with $\rho = 0.5$ and 1000,000 DPs for Rayleigh, Uniform, and Exponential PDFs were generated for the study. The PDF of the signal was computed for each CG-scale and tested against normality with the Jarque–Bera (JB) test [16] using the statistical toolbox of MATLAB® (2012a, The MathWorks, Torrance, California) for type I error of $p \leq 0.05$. The JB statistics quantifies the deviation from the normal with positive real statistics. The JB statistics smaller than 5.99 indicated a significant difference between the distribution of a given scaled signal and the normal distribution.

To demonstrate the sensitivity of the SEn to the PDF of the signal, thirty AR signals with a length of 15,000 DPs were generated and normalized with Uniform, Gaussian, Rayleigh, and Exponential distributions each for $\rho = 0.1, 0.2, \ldots, 0.9$. SEn was computed for all PDFs and ρ values. One way ANOVA with $p \leq 0.05$ was used to compare the results between groups with dissimilar PDFs but identical AR coefficients. Tukey's post-hoc test was utilized to determine the location of difference.

As verified through preliminary numerical assessment, the SD of the signal changed according to $\sigma_{\text{new}} = \sigma_{\text{original}}/\sqrt{S}$ where σ represents the SD of the original random signal and S the CG-scale, displayed independence to the original PDF or AR coefficient of the signal. In this regard, thirty White Gaussian Noise (WGN) signals were randomly generated with 15,000 DPs. The SD of the signal was manipulated in each step according to this equation to imitate the changes in SD of the signal following each CG-scale.

The average of SEn relative to SD of the signal was plotted. The Curve Fitting Toolbox of MATLAB was utilized to fit the $y = ax^b + c$ curve to the data and to investigate the non-linearity of the relation between SEn and SD. Also, SEn was plotted against the CG-scale corresponding to each SD to visualize the changes in SEn of the WGN signal following to the changes in SD representing the coarse graining. An example of Gaussian AR signal with $\rho = 0.5$, its power spectrum, and its PDF is displayed in Fig. 3.

Through this article the SEn was computed based on parameters $m = 2$ and $r = 0.2$ recommended by Richman and Moorman [1].

3. Results

3.1. MST for $1/f^{\alpha}$ processes

The transition from more ordered to disordered reshaped signals for $1/f^{\alpha}$ processes with different α relative to τ-scale and therefore a transition from low to high SEn is shown in Fig. 4. This figure also displays the transition from high scales (one before the last point in Fig. 4) to a fully random situation (last point in Fig. 4).

3.2. Effect of coarse graining on PDF

The changes in JB statistics with respect to the CG-scale are displayed in Fig. 5. The signals with original Exponential, Rayleigh, and Uniform distributions were not significantly different from the Gaussian following the 400, 200, and 25 CG-scales respectively. They all became normally distributed for larger scales.

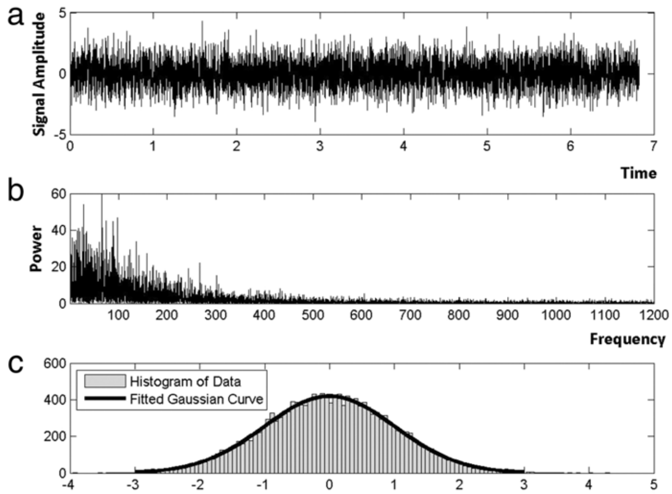

Fig. 3. An example of an Autocorrelated Gaussian Signal ($\rho = 0.5$)—a. Original signal in the time domain; b. Power spectral density; c. Probability density function and its corresponding Gaussian fit.

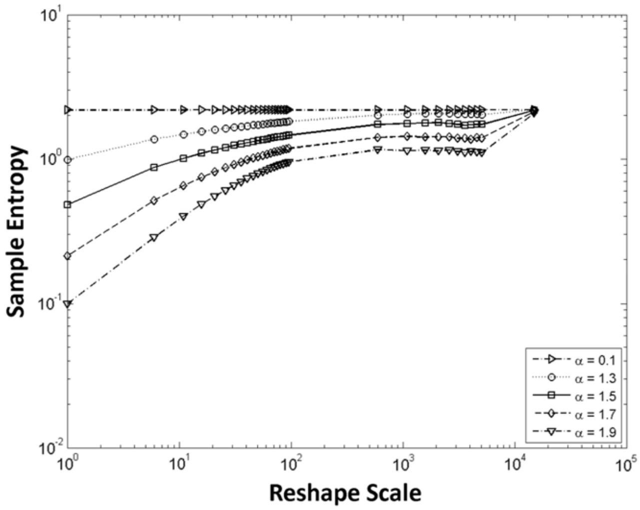

Fig. 4. Multi Scale Transition (MST) applied to $1/f^{\alpha}$ processes with different values of the α (log–log plot). The first set of points were computed for scales below $\sqrt{N}$. The set of points larger than $\sqrt{N}$ show the effect of the attachment points.

3.3. *Effect of PDF on SEn*

The mean (SD) of the SEn for thirty trials per distribution and the AR coefficient were computed (Table 1). The result of one way ANOVA analysis followed by Tukey's post-hoc test are shown in Table 2. For $\rho = 0, 0.1$ a significant difference in SEn was not detected between Uniform and Gaussian distributions. The same happened for $\rho = 0.3$ between Uniform and Rayleigh. For $\rho = 0.2$ and 0.4 to 0.8 a significant difference was observed everywhere. There was a significant difference between the SEn calculation for signals with a similar ρ but dissimilar PDFs.

3.4. *Dependency of MSE on SD*

The dependency of SEn values of a WGN to the changes in SD induced by coarse graining was studied and the results are displayed in Fig. 6(a). The values in the figure were averaged across 30 trials. Error bars were not shown due to relatively negligible values. The decrease in SEn as a function of the changes in the SD of the signal are shown in Fig. 6(b). A non-linear equation of $y = ax^b + c$ was used to interpolate between the discrete points. Coefficients were computed as $a = 10.17,\ b = 0.102,\ c = -7.977$ and the fitting standard error was $RMSE = 0.0030$.

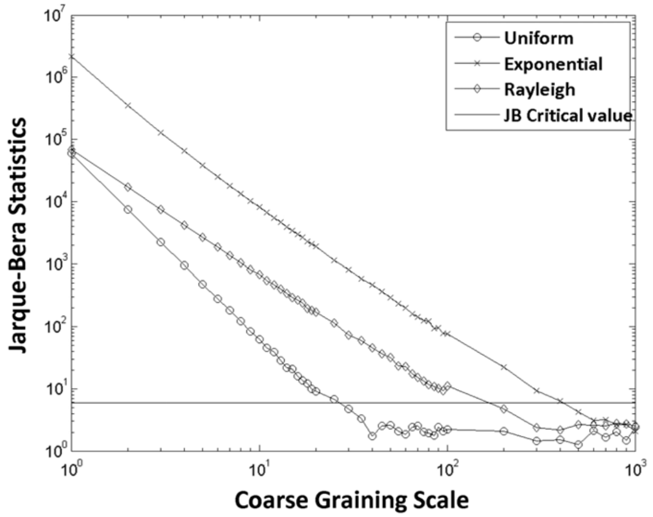

Fig. 5. Jarque–Bera statistics for the CG-scale for Uniform, Exponential, and Rayleigh random signals. The horizontal line indicates the JB_{Critical} value below which the distribution was not significantly different from the normal distribution.

Table 1
Sample entropy of autocorrelated signals of $\rho = 0$ to 0.9 with Uniform, Gaussian, Exponential, and Rayleigh PDF for RS scale $\tau = 1$. Average of 30 trials for each PDF and ρ.

Sample entropy Mean (std.)				
ρ	Uniform	Gaussian	Exponential	Rayleigh
0.0	2.188 (0.003)	2.185 (0.005)	1.706 (0.013)	2.157 (0.005)
0.1	2.179 (0.005)	2.179 (0.006)	1.654 (0.015)	2.147 (0.005)
0.2	2.140 (0.006)	2.155 (0.006)	1.567 (0.014)	2.115 (0.008)
0.3	2.053 (0.011)	2.104 (0.006)	1.421 (0.018)	2.051 (0.009)
0.4	1.881 (0.013)	2.005 (0.006)	1.237 (0.025)	1.935 (0.009)
0.5	1.627 (0.027)	1.847 (0.008)	1.005 (0.024)	1.761 (0.012)
0.6	1.320 (0.034)	1.611 (0.012)	0.791 (0.027)	1.511 (0.020)
0.7	1.005 (0.042)	1.289 (0.019)	0.570 (0.034)	1.196 (0.027)
0.8	0.680 (0.041)	0.868 (0.033)	0.374 (0.034)	0.797 (0.029)
0.9	0.310 (0.049)	0.348 (0.037)	0.172 (0.029)	0.336 (0.055)

Table 2
One-way ANOVA followed by Tukey's HSD post-hoc test applied to SEn computed at RS scale $\tau = 1$ while changing ρ and the probability distribution of the data. Groups that were not significantly different for a given ρ are highlighted.

ρ	F[a]	Not significantly different groups[b]
0.0	30 070.8	U-G
0.1	26 428.2	U-G
0.2	31 164.0	-
0.3	22 376.7	U-R
0.4	16 706.0	-
0.5	11 154.5	-
0.6	6571.0	-
0.7	3069.4	-
0.8	1210.3	-
0.9	104.5	U-R, G-R

[a] F_critical $= 2.6828$.
[b] U : Uniform $-$ G : Gaussian $-$ E : Exponential $-$ R : Rayleigh.

4. Discussion

4.1. The MST and its interpretation

In a measured time series which mimics the $1/f^{\alpha}$ process, the points satisfactorily close to one another were expectedly more correlated compared to the points located at larger time distances. The presented RS-method allowed us to observe

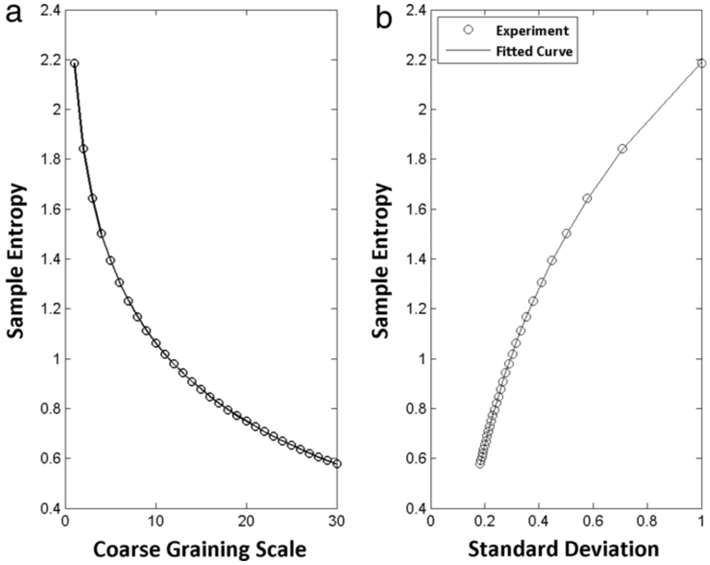

Fig. 6. (a) Changes in sample entropy due to changes induced by the CG-scales. (b) The relation between SEn of the signal to its SD was non-linear. A power law equation with constant $y = ax^b + c$ was utilized for curve fitting where $a = 10.17$, $b = 0.102$ and $c = -7.977$.

MST, a transition of the SEn from low values to large ones as the τ-scale increased. Thus, using the RS-method allowed us to observe how the bonds between the subsequent DPs became loose through the reshaping process. As reshaping reaches satisfactorily large τ-scales, no relationship exists any more between the subsequent DPs.

One can consider such a transition from the perspective of information theory. At low scales the signal may be very regular and hence predictable. Shannon entropy is defined as the average of unpredictability in a random variable, which reflects its information content. So, little information was contained in the signal at low scales. As the time intervals between consecutive points increase, the regularity gradually decays and the signal becomes more complex. A more complex signal can carry more information [17]. At the end of the transition, consecutive points were randomly located relative to one another and therefore the SEn was high while almost no more information was carried by the signal. The RS method allowed us to find the sampling rate corresponding to the EnHL for which the signal was most likely to reveal a high complexity while still carrying relevant information. However, further investigations are required in this regard.

As shown in Fig. 2, for WGN or a very low α, the SEn remained almost constant for different τ-scales. This feature was anticipated as minimal relations existed initially between subsequent DPs of the signal because the DPs were present randomly in the signal. As the RS scale was increased, no further information was gained or lost from the signal as no information originally existed. As the signal deviated further from the WGN (larger α), MST became more pronounced (Fig. 2). Thus when meaningful complexity and a dynamical structure existed within the signal, MST occurred and could be observed. If there was no such information in the signal originally (e.g. WGN), no transition could be observed despite a relatively large entropy value. The MSE however, showed significant decrease as the CG-scale got larger for WGN [6]. Thus, in the MSE method it will be difficult to associate the observed transition of SEn to complexity alone as other parameters such as PDF (Fig. 5) also undergo simultaneous changes. The situation becomes even more complicated as the SEn shows a non-linear relation to the SD (Fig. 6(b)).

There is no general reason why the MST profile should remain relatively consistent for all types of time series. In the case of $1/f^{\alpha}$ processes which cover numerous types of systems, clearly the profile of transition remained consistent and EnHL could be defined. In the present modeled MST there was indeed no fine structure in the transition. Therefore, a single variable, EnHL, together with α already characterized the MST accurately.

The EnHL quantifies the resistance of the signal against becoming random in the process of reshaping. For a digitally measured time series, the EnHL is reported in time units. As the signal gets more structured, the EnHL increases. This can be interpreted from two physiologically interesting perspectives namely feed-forward (the future prediction) and feed-back (memory of the past). According to feed-back interpretation one can view EnHL as an indication of the buffer memory (in milliseconds) for the signal source. If the time series represents some physiologically relevant data, the EnHL indicates the extent for which the past information was utilized by the source to compute the current state of the signal. In the feed-forward view, EnHL quantifies the extent for which a given DP influences the future down-stream state of the signal.

4.2. *Effect of coarse graining and changes in PDF*

In this study, the effects of coarse graining on MSE were investigated. An increase in CG-scale gradually alters the original PDF of the signal to a normal distribution (Fig. 5). The rate of such a change depends on the original distribution of the signal.

Such a change in the PDF and the SD of the signal was expected and can be described according to the *Central Limit Theorem (CLT)* [18]. Due to the dependency of SEn on the PDF of the signal (Tables 1 and 2), such continuous changes in the PDF through coarse graining will affect the SEn. The change in SD due to the coarse graining in AR signals were not dependent on ρ so the results in Section 3.4 can be generalized to the other distributions and AR coefficients. Such a simulation demonstrates that even without a change in the dynamics of the signal, but with isolated manipulation of the SD of the signal, one can observe the changes in SEn.

4.3. Final comments

Preliminary studies showed that the transition is affected by the sampling frequency. In this regard, for some time series due to sub-sampling or over sampling, the transition curve might not be able to reach the EnHL. To overcome such an issue, for the practical signal processing the user is recommended to follow these guidelines: (i) if EnHL is not crossed by the transition curve even for a satisfactory large scale, the length of the signal needs to be increased; (ii) if the transition curve already passed the EnHL prior to performing any reshaping operation, it can be inferred that the signal was sub-sampled or the signal to noise ratio was high. To compensate for this shortcoming, original data collection needs to be conducted with higher sampling frequency while making sure that the signal to noise ratio remains high.

5. Limitation

The RS-method provides appropriate results for $1/f^{\alpha}$ processes. However, this method was also tested for various well known chaotic and limit cycle systems such as those presented in Ref. [19]. The results did not follow monotonic transition and so the EnHL could not be defined for those systems. The application of such a method should be further evaluated and tested for different systems and their performance evaluations are left to future studies.

As stated earlier, the RS-scale is the distance between the indexes of the subsequent DPs of the reshaped signal in the original signal. Obviously the distance of attachment that points to the immediately following DP is larger than the corresponding τ-scale value. As the main purpose of the RS method was to gradually randomize the signal in order to observe the transition, the presence of these points helped to better serve this goal through introducing further randomization. However, to avoid too many attachment points which might affect the interpretability of the results sufficiently long signals are required.

For relatively large scales (approximately for $RS > \sqrt{N}$ where N represents the length of the signal), a premature plateau region was observed especially for large α. This indicates that the RS method was not able to fully randomize the signal (Fig. 2). However, EnHL transition occurs mostly for relatively low scales and far from such saturation regions. Also, to compute the EnHL, the SEn of a fully randomly permuted signal was used to estimate the maximum SEn. With these precautions, the effect of such a plateau region on the EnHL computation should be negligible.

6. Conclusion

A novel method for multi scale entropy analysis was proposed which revealed a distinct transition with increase in scale, τ, from low to high SEn for $1/f^{\alpha}$ signals. This transition was not observable using the MSE analysis. EnHL was introduced as a measure characterizing the midpoint of the MST and thus the MST itself. Although the EnHL displays dependence on α, it reflects a unique additional property of the signal source. In better words, EnHL indirectly quantifies the feed-back memory and/or feed-forward extrapolation capabilities of the signal source. The method can potentially serve as a comparative tool in the context of information theory to find further details about the source which results in the complexity of the recorded signal.

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APPENDIX B: CORRELATION ANALYSIS

B.1. Purpose

This chapter reports on the correlation analyses of BMI, body-mass, IKDC 2000 score, and ACL-QOL scores with the measures of postural balance and proprioception. The correlations have been calculated for the ACLR group at 3 and six months post-surgery. A similar set of analyses was performed on the data from healthy participants including all outlined measures except the ACL-QOL, recalling that the healthy control group did not fill out the ACL-QOL questionnaire.

B.2. Methods

Pearson correlations with two-tailed test of significance at $p < 0.01$ and $p < 0.05$ were calculated for the COP measures of $EnHL_{ML}$, $EnHL_{AP}$, $\Delta E_{surr_{ML}}$, and $\Delta E_{surr_{AP}}$with body mass [kg], BMI [kg/m^2], and IKDC 2000 score under the baseline condition for healthy participants (i.e. SR-OFF, eyes-open, and the dominant limb side). For the ACLR participants, the ACL-QOL score was included in the correlation analysis. The correlations were calculated separately at 3 and six months post-surgery for the ACLR group (i.e. SR-OFF, eyes-open, and the ACLR limb side).

B.3. Results and conclusion

No correlation was significant between the outcome measures of body mass, BMI, ACL-QOL score, and IKDC 2000 with respect to measures of postural balance and proprioception in the ACLR group at either three or six months post-surgery. Similarly, correlations were not significant between the outcome measures of body mass, BMI, and IKDC 2000 and the outcome measures of postural balance and proprioception.

APPENDIX C: RELEVANCE OF METHODOLOGY USED FOR TESTING SR ON PROPRIOCEPTION

C.1. Introduction

In this section, the appropriateness of methodologies utilized to test SR in ACLR patients is presented and discussed. The methodology utilized for determining the vibration sensation threshold has been outlined in §C.2. The method used to determine the level of stimulation with respect to the vibration sensation threshold as well as the arrangement of the vibrations is discussed in §C.3 and §C.4 respectively. Finally, the unique features of the current setup for testing SR on proprioception in the ACLR population have been compared to data available in the extant literature §C.5.

C.2. Determination of vibration sensation threshold

The level of SR stimulation in this study was adjusted based on each participant so that optimal enhancement with SR was potentially achieved. Similar to the current work, some researchers have adjusted the SR stimulation level based on each participant's sensation threshold to the type of stimulation under study (Dettmer et al. 2015; Priplata et al. 2002; Priplata et al. 2006). In contrast, some researchers used a preselected level of SR amplitude across all participants (Rogan et al. 2012; Kaut et al. 2011; Kaut et al. 2016; Gravelle et al. 2002). The theory implies that the maximum effect of SR is achieved when an optimal level of noise is added to the system (see Figure 1). There is no evidence that leads to the assumption that the vibration sensation threshold is identical across participants. Thus, logically if a similar level of SR noise is used across all participants, it may lead to a sub-optimal level of stimulation in some participants. This leads to two problems (1) in some participants, the level of stimulation is sub-optimal, and therefore, SR is not utilized to its maximum capacity; (2) the level of stimulation will be varied with respect to the individual's vibration sensation threshold. As a result, for example, one individual may receive SR noise at 70% and the other at 110%. Due to these discrepancies, each individual may show a different response, and in turn, the measured outcomes might be contaminated by subjective responses. To avoid these issues, the current dissertation used SR amplitude based on the vibration sensation threshold of each individual participant's limb.

The SR vibration amplitude in the current study was kept below the vibration sensation threshold. Thus, the participants were blinded regarding the SR condition. It was verified that the vibration sensation threshold measured using the increasing amplitude method was systematically smaller than that using the decreasing method in both healthy and ACLR groups. Therefore, to keep the vibration unnoticeable throughout the experiment, the vibration sensation threshold was selected using the increasing amplitude protocol.

C.3. SR stimulation amplitude

Another important parameter was the level of SR noise based on the vibration sensation threshold. Following a pilot study, the movement threshold test was performed on 10 participants between 6 and 12 months post-surgery for vibration levels of 30%, 50%, 70%, and 90% of vibration sensation threshold. The stimulation level of 90% showed a maximum improvement in proprioception compared to other vibration levels although the difference between the vibration levels was not statistically significant. Interestingly, this level of stimulation is in accordance with previous SR research that had adopted a 90% of vibration sensation threshold as the desired amplitude of SR noise stimulation (Dettmer et al. 2015; Priplata et al. 2002; Priplata et al. 2006; Hijmans et al. 2008).

C.4. Stimulation site

Another important task was to select the arrangement of SR vibrators on the area around the knee. The arrangement was selected following a pilot experiment on 10 participants who were between 6 and 12 months post-surgery. It was observed that the configuration that including all five vibrators on the quadriceps resulted in the smallest movement threshold, although the results were not statistically significant.

C.5. SR experimental setup

The current study for the first time directly applied SR vibration to the area around the knee to correct for potential proprioceptive and postural deficiencies in the ACLR population. Previously, the SR vibration stimulation sites were applied either locally to the sole (Priplata et al. 2006; Priplata et al. 2003; Priplata et al. 2004; Hijmans et al. 2008; Qiu et al. 2012; Harry et al. 2005), or globally using a whole body vibration (Rogan et al. 2012; Kaut et al. 2011; Kaut et al. 2016). Electrical stimulation was also used in the studies by Collins and colleagues (Collins 2010; Collins et al. 2009; A. T. Collins, Blackburn, Olcott, Yu, et al. 2011; N. J. Collins et al. 2011; A. T. Collins, Blackburn, Olcott, Miles, et al. 2011), where the electrical stimulation was applied through two electrodes placed on lateral sides of the thigh and shank at about two inches from the knee. Direct application of SR vibration to the area around the knee, however, had not been investigated previously.

Unlike previous studies by Collins and colleagues (Collins et al. 2009) where the electrodes for applying SR stimulation were placed inside a knee sleeve, the current study didn't use the knee sleeve. It has been shown that wearing knee sleeves or braces enhances proprioception in the knee (McNair et al. 1996; Herrington et al. n.d.). The current setup tested the effect of SR in the absence of any other accessories that may have interfered with the experimental outcomes.

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TITLE: The Effect of Stochastic Resonance Stimulation on Postural Stability and Proprioception of the Reconstructed Knees 3 and 6 Months Post Surgery.

INVESTIGATORS:

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This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form.

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BACKGROUND

Self awareness is one of the important sensations in our joints. At any instant in time, our joints are aware of their position relative to one another and the surrounding environment. This ability is referred to as *proprioception*. Proprioception plays an important role in controlling the loading and movements in joints. When the anterior cruciate ligament (ACL) is torn, a main ligament in the knee, important portions of proprioceptive feedback are lost. A potential method for improving proprioception is the application of a low amplitude random vibration (you can not feel the vibration) to the skin.

WHAT IS THE PURPOSE OF THE STUDY?

The overall purpose of this study is to investigate the effects of low amplitude random vibration stimulation on standing balance and knee proprioception of ACL reconstructed (ACLR) patients. Subjects will be tested at three and six month post-surgery time points, and compared to a non-injured population. To test the idea, 30 non-injured and 30 ACLR participants will be recruited and tested in our lab in HRIC 3C48A at Foothills Hospital. The ACLR subjects will be tested twice at 3 months and 6 months post-surgery, and the non-injured subjects will be tested only once.

WHAT WOULD I HAVE TO DO?

Interview and Questionnaire (60 min)

If you are recruited as a non-injured individual your knee should be non-injured with no history of serious injury. In an interview prior to the experiment day, we will make sure that you meet our additional inclusion criteria: Skeletally mature (16 to 40 years); < 3 months since ACL reconstruction; Body mass index (BMI) 18 to $25kg/m^2$; otherwise non-injured with no other lower limb injuries within the last 6 months. You will not be tested from 3 days before to 3 days after your menstrual cycle. You will be asked to choose your test day such that it lies outside this period. The experiment will not be conducted if you are pregnant or having major hormonal disorders. You should not be using any medication that may affect your nervous and muscular performance[1]. A Quality of life (QOL) and IKDC2000 forms (a copy of each is attached to this

[1] Medications such as Adrenergic blocking drugs, anti-convulsants, anti-anxiety, anti-Parkinson, anti-psychotic, anti-depressants, narcotic analgesics, non narcotic analgesics, narcotic antagonists, and medications causing muscle pain, weakness or drowsiness, and drug addiction can be named.

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document) will be completed in this session. You should not have any skin injuries (e.g., open wounds) or diagnosed diseases or special skin sensitivities in the areas around the knee.

Test Protocols

You will need to wear shorts that can be rolled up on the sides to allow us to place small measuring and vibration devices on your leg. You can wear a sleeveless shirt which is not too bulky and you will be asked to perform the experiments barefoot.

The experiment is expected to take no more than 4 hours for one set of measurements. A random vibration will be applied to the area surrounding the knee. Up to six small and lightweight vibration actuators will be taped on specific areas surrounding your knee. The locations of concern will be identified by palpation and referring to anatomical landmarks. The amplitude of the vibration will increase from zero until you can marginally feel the vibration. This process will be repeated 5 times and the desired amplitude will be recorded each time. Another 5 trials will be performed changing the amplitude from high to low to confirm the desired threshold. The level of vibration used in the experiment will be below your sensation threshold and therefore you will not be able to perceive the vibrations during the experiment. We may ask to take a photo of you in the test setup, but it will be masked to prevent your identification.

Joint Movement threshold and repeatability Test (120 Min)

Threshold test (60 min)

You will be asked to wear a blindfold and ear plugs during all trials to prevent the influence of visual or auditory input. You will be seated in a reclined position (70 to 85 degrees) on the Biodex machine (http://www.biodex.com). This machine is frequently used by researchers and physiotherapists to test or rehabilitate different joints of human body. It consists of an adjustable chair and a dynamometer. A mechanical link with a supportive pad will be attached to the dynamometer. Your joint will be attached to the link and the dynamometer can move or measure the movement produced by the swinging of your lower leg. Your leg and upper body will be secured with straps and your knee will be slightly flexed (15 degrees). The Biodex will slowly move your limb (0.25 deg/sec) away and toward the initial position. You will be asked to press a button as soon as you are able to sense movement of your limb. Ten trials will be recorded for each direction. The same test will be repeated on your opposite knee.

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Repeatability Test (60 min)

This experiment uses the same setup as in the previous section. Now your knee will be flexed from 10 to 45 degrees. The experimenter will keep your knee at 10 degrees initially and then move it to 45 degrees and keep it there for 10 seconds. You are asked to memorize this position. Your knee will then be extended back to 10 degrees and you will be asked to reproduce the 45 degree angle and push a button when you think the angle is reproduced accurately. You are asked to repeat this process 20 times with and without the vibration. The same test will be repeated but the order of initial and final angles will be reversed. The entire test will be repeated for the opposite knee.

Static Stability Test (60 Min)

Small surface electromyography (EMG) electrodes will be taped on your skin at specific anatomical locations. The wires from the electrodes will go to a small backpack that weights less than 1.5 kilogram that you will wear during the experiment. There is no likelihood of electric shock from this equipment. The skin underlying the electrodes will be shaved with a disposable razor and will be slightly abraded using fine sandpaper. Thereafter, the skin will be cleaned using rubbing alcohol and wiped with water. Reflective marker spheres will be taped to your skin to help us record your joint movements while standing using a number of high speed motion analysis cameras. You will perform one legged standing on a force platform. The force platform is a rigid, rectangular device, located inside the laboratory walkway that measures the forces and moments you apply when standing on it. Ten trials each for 1 min will be recorded in this position for each leg with and without the vibration with one minutes of seated rest after each trial.

WHAT ARE THE RISKS?

It is possible that the gel used in EMG electrodes may cause slight skin irritation. The chance of irritation is very rare and can be diminished by washing the areas with water after the experiment. You may feel discomfort when the adhesive tapes are removed at the end of the experiment. It is also a possibility that the skin may get irritated from these tapes.

WILL I BENEFIT IF I TAKE PART?

If you agree to participate in this study there may or may not be a direct benefit to you. If you are in the study because you have been identified as having ACL reconstruction your condition may be improved during the study but there is no guarantee that this research will help you. The

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information we get from this study may help us to provide better treatments in the future for patients with ACL reconstruction.

DO I HAVE TO PARTICIPATE?

Your participation in this study is absolutely voluntary. You can withdraw from the study at any time without jeopardizing your health care. You need to inform at least one of the investigators listed at the beginning of this form about your withdrawal. Also, researchers can exclude you from the study in case you don't meet the requirement of the study, you are pregnant, you are during the menstrual cycle, or due to unforeseen circumstances.

WHAT ELSE DOES MY PARTICIPATION INVOLVE?

NA

WILL I BE PAID FOR PARTICIPATING, OR DO I HAVE TO PAY FOR ANYTHING?

In case you need to use parking, we can provide you with four hours free parking voucher. Refreshments will be provided during the test.

WILL MY RECORDS BE KEPT PRIVATE?

You will receive an ID number and all your related information will be stored under ID numbers. The relation between ID number and your name is only available to the investigators. The study data will be transferred directly to a digital tape, and a copy will be stored in a specific password protected computer in our lab (HRIC 3C48A). Access to data for assessment purposes will be limited to the investigators only. Data will be collected and stored in a key access controlled laboratory. The computers in the lab are password protected with firewall and virus protection. Data is backed up on a regular basis. For protecting the data from unforeseen circumstances (e.g. flood or fire) an extra copy of the study data will be stored in PI's office at a different location. Only trained study investigators have access to and can work with the study data. In all publications and presentations, subjects will be referred only by numbers (Study ID) or the data will be grouped, with no ability to identify individual study participants.

IF I SUFFER A RESEARCH-RELATED INJURY, WILL I BE COMPENSATED?

In the event that you suffer injury as a result of participating in this research, no compensation will be provided to you by the University of Calgary, Alberta Health Services or the Researchers. You still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

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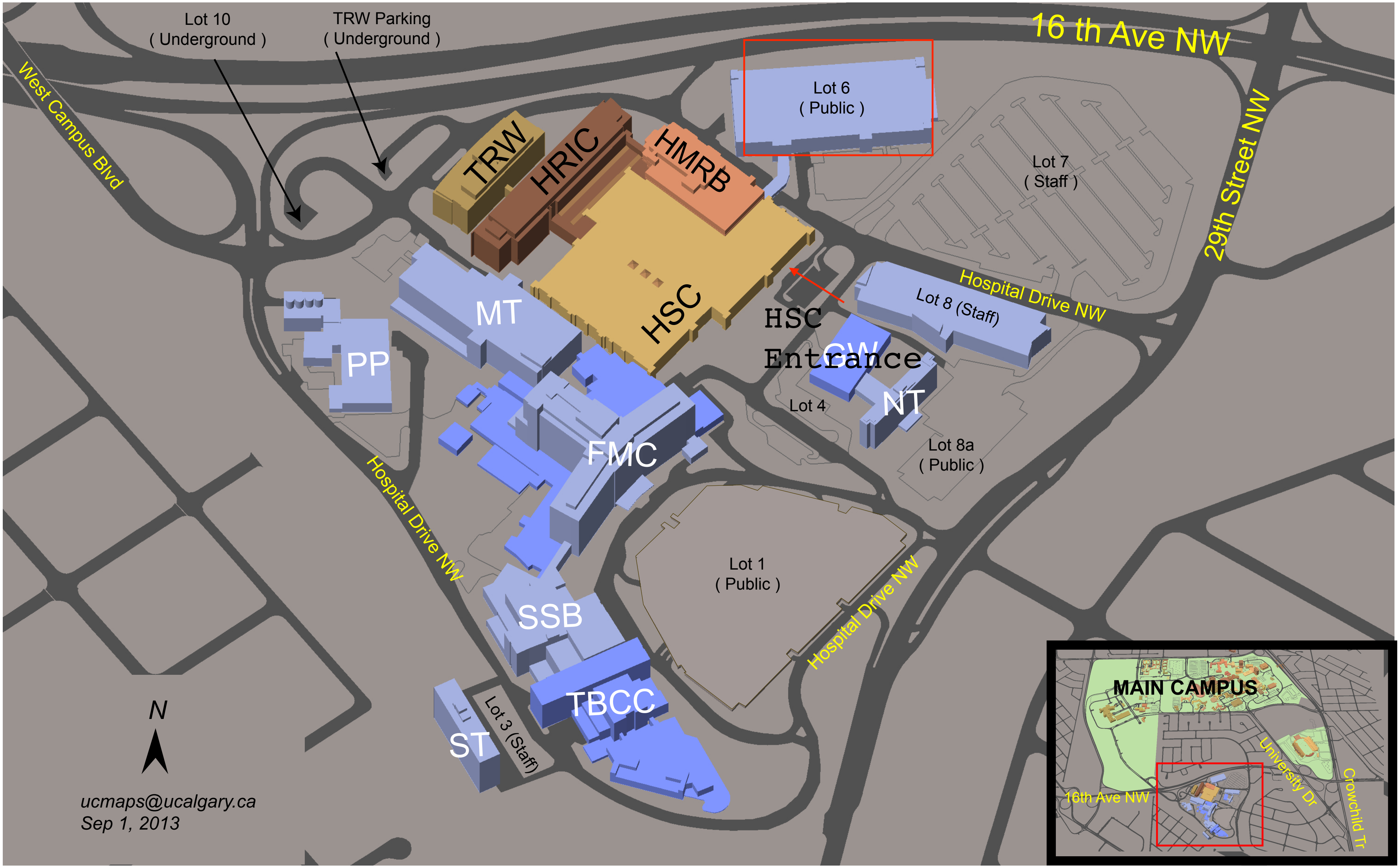
SIGNATURES

Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to participate as a participant. In no way does this waive your legal rights nor release the investigators or involved institutions from their legal and professional responsibilities. You are free to withdraw from the study at any time without jeopardizing your health care. If you have further questions concerning matters related to this research, please contact: Dr. Janet L. Ronsky (403) 220-8134 or Payam Zandiyeh (403) 700-1696. If you have any questions concerning your rights as a possible participant in this research, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

Name of participant	**Signature and Date**
Name of participant's parent/guardian	**Signature and Date**
Investigator/Delegate's Name	**Signature and Date**
Witness' Name	**Signature and Date**

The University of Calgary Conjoint Health Research Ethics Board has approved this research study. A signed copy of this consent form has been given to you to keep for your records and reference.

Foothills Campus



HMRB	*Heritage Medical Research Building*
HRIC	*Health Research Innovation Centre*
HSC	*Health Science Centre*
TRW	*Teaching Research & Wellness*
FMC	*Foothills Medical Centre*
GW	*Grace Womens Health Centre*
MT	*McCaig Tower*
NT	*North Tower*
PP	*Physical Plant*
SSB	*Special Services Building*
ST	*South Tower*
TBCC	*Tom Baker Cancer Centre*

DATE: ______/______/______

NAME/ID # ________________

QUESTIONNAIRE # ________

QUALITY OF LIFE ASSESSMENT

IN

ANTERIOR CRUCIATE LIGAMENT DEFICIENCY

DIRECTIONS: Please answer each question with respect to the current status, function, circumstances and beliefs surrounding your anterior cruciate ligament (ACL) deficient knee. Consider the last three months.

Indicate with a slash (/) on the line, the point ranging from 0 to 100 which most closely represents your situation.

For example, the following question:

Is this a good questionnaire?

0 ____ **100**

Useless **Fantastic**

If the slash is placed in the middle of the line, this indicates that the questionnaire is of average quality, or in other words, between the extremes of 'useless' and 'fantastic'. It is important to put your slash at either end of the line if the extreme descriptions accurately reflect your situation.

Section A:

The first four questions are related to: **SYMPTOMS & PHYSICAL COMPLAINTS.**

1. With respect to your overall knee function. How troubled are you, by "giving way" episodes? (Make a slash at the extreme right if you are experiencing, no giving way episodes in your knee. Please note that this question has two parts. It is concerned with both, the severity (1a) and frequency (1b) of the giving way episodes.)

1a **0** ________________________________ **100**
Major giving way episodes — **Minor giving way episodes**

1b **0** ________________________________ **100**
Constantly giving way — **Never giving way**

2. With any kind of prolonged activity (i.e. greater than half an hour) how much pain or discomfort do you get in your knee?

0 ________________________________ **100**
Severe pain — **No pain at all**

3. With respect to your overall knee function, how much are you troubled by stiffness, or loss of motion in your knee?

0 ________________________________ **100**
Severely troubled — **Not troubled at all**

4. Consider the overall function of your knee and how it relates to the strength of your muscles: How <u>weak</u> is your knee?

0 ________________________________ **100**
Extremely weak — **Not weak at all**

Section B: The following questions are being asked with respect to your job or vocation **(i.e., WORK RELATED CONCERNS).** The questions are concerned with your ability to function at work and how your knee has affected your current work-related concerns. If you are a full-time student/home maker, then consider this and any part-time work together. Consider the last three months.

*** If you are **CURRENTLY NOT EMPLOYED** for reasons **OTHER THAN YOUR KNEE** then place a check on this line. __________

5. **How much trouble do you have, because of your knee with turning or pivoting motions at work?** (Make a slash at the extreme left if you are unable to work because of the knee.)

0 ____ **100**

Severely troubled — **No trouble at all**

6. **How much trouble do you have, because of your knee, with squatting motions at work?** (Make a slash at the extreme left if you are unable to work because of the knee.)

0 ____ **100**

Severely troubled — **No trouble at all**

7. **How much of a concern is it for you to miss days from work, due to problems or re-injury to your knee?** (Make a slash at the extreme left if you are unable to work because of the knee.)

0 ____ **100**

An extremely significant concern — **No concern at all**

8. **How much of a concern is it for you to lose time from "school" or work because of the treatment of your ACL deficient knee?**

0 ____ **100**

An extremely significant concern — **No concern at all**

Section C: The following questions are being asked with respect to your **RECREATIONAL ACTIVITIES, SPORT PARTICIPATION OR COMPETITION.** The questions are concerned with your ability to function and participate in these activities as they relate to your anterior cruciate ligament (ACL) deficient knee. Consider the last three months.

9. How much limitation do you have with sudden twisting and pivoting movements or changes in direction?

0	———————————————————	100
Totally limited		No limits

10. How much of a concern is it for you that your sporting/recreational activities may result in the status of your knee to worsen?

0	———————————————————	100
An extremely significant concern		No concern at all

11. How does your current level of athletic or recreational performance, compare to your pre-injury level?

0	———————————————————	100
Totally limited		No limitations

12. With respect to the activities or sports that you currently desire to be involved with, how much have your expectations changed because of the status of your knee?

0	———————————————————	100
Expectations totally lowered		Expectations not lowered at all

13. Do you have to play your recreation/sport under caution?
(Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0	———————————————————	100
Always play under caution		Never play under caution

14. **How fearful are you of your knee "giving way" when playing recreation/sport?**

(Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 ———————————————————— **100**

Extremely fearful — **No fear at all**

15. **Are you concerned about environmental conditions, such as a wet playing field, a hard court, or the type of gym floor when involved in your recreation/sport?**

(Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 ———————————————————— **100**

Extremely concerned — **Not concerned at all**

16. **Do you find it frustrating to have to consider your knee with respect to your recreation/sport?**

0 ———————————————————— **100**

Extremely frustrated — **Not frustrated at all**

17. **How difficult is it for you to "go full out" at your recreation/sport?**

(Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 ———————————————————— **100**

Extremely difficult — **Not difficult at all**

18. **Are you fearful of playing contact sports?** (Circle the "N/A" at the right of the scale if you do not play contact sport for reasons other than the knee.)

0 ———————————————————— **100** **N/A**

Extremely fearful — **No fear at all**

The following questions are specifically asking about the <u>two most important</u> sports or recreational activities that you do or that you wish to do. Please write them in order of importance.

1.____

2.____

19. How limited are you in playing the number "1" sport/recreational activity? (Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 ______________________________ **100**	
Extremely limited	**Not limited at all**

20. How limited are you in playing the number "2" sport/ recreational activity? (Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 ______________________________ **100**	
Extremely limited	**Not limited at all**

Section D: The following questions are being asked with respect to your **LIFESTYLE.** The questions are concerned with your lifestyle in general and should be considered outside of your work and recreational/sport activities as they relate to your anterior cruciate ligament (ACL) deficient knee.

21. Do you have to concern yourself with general safety issues (e.g. carrying small children, working in the yard, etc.) with respect to your ACL deficient knee?

0 ______________________________ **100**	
Extremely concerned	**No concern at all**

22. How much has your ability to exercise and maintain fitness been limited by your knee problem?

0 ______________________________ **100**	
Totally limited	**Not limited at all**

23. **How much has your enjoyment of life been limited by your knee problem?**

0 ——————————————— **100**

Totally limited — **Not limited at all**

24. **How often are you aware of your knee problem?**

0 ——————————————— **100**

All of the time — **None of the time**

25. **Are you concerned about your knee, with respect to lifestyle activities that you and your family do together?**

0 ——————————————— **100**

Extremely concerned — **No concern at all**

26. **Have you modified your lifestyle to avoid potentially damaging activities to your knee?**

0 ——————————————— **100**

Totally modified — **No modifications**

Section E: The following questions are being asked regarding your **SOCIAL AND EMOTIONAL** concerns with respect to your knee. The questions are about your attitudes and feelings as they relate to your anterior cruciate deficient knee.

27. **Does it concern you that your competitive needs are no longer being met because of your knee problem?** (Make a slash at the extreme right i.e. 100, if your competitive needs are being met. Make a slash at the extreme left i.e. 0 if you do not have any competitive needs.)

0 ——————————————— **100**

Extremely concerned — **Not concerned at all**

28. **Have you had difficulty being able to psychologically "come to grips" with your knee problem?**

0 ———————————————— **100**

Extremely difficult | **Not difficult at all**

29. **How often are you apprehensive about your knee?**

0 ———————————————— **100**

All of the time | **None of the time**

30. **How much are you troubled with lack of confidence in your knee?**

0 ———————————————— **100**

Severely troubled | **No trouble at all**

31. **How fearful are you of re-injuring your knee?**

0 ———————————————— **100**

Extremely fearful | **No fear at all**

Thank you for completing this questionnaire.

IKDC DEMOGRAPHIC FORM

Your Full Name ____

Your Date of Birth __________/____________/____________
Day Month Year

Your Gender: ❑ **Male** ❑ **Female**

Occupation ____

Today's Date _______________/____________/____________
Day Month Year

The following is a list of common health problems. Please indicate "Yes" or "No" in the first column, and then skip to the next item. If you do have the problem, please indicate in the second column if you receive medications or some other type of treatment for the problem. In the last column, indicate if the problem limits any of your activities.

	Do you have the problem?		Do you receive treatment for it?		Does it limit your activities?	
	Yes	No	Yes	No	Yes	No
Heart disease	❑	❑	❑	❑	❑	❑
High blood pressure	❑	❑	❑	❑	❑	❑
Asthma or pulmonary disease	❑	❑	❑	❑	❑	❑
Diabetes	❑	❑	❑	❑	❑	❑
Ulcer or stomach disease	❑	❑	❑	❑	❑	❑
Bowel disease	❑	❑	❑	❑	❑	❑
Kidney disease	❑	❑	❑	❑	❑	❑
Liver disease	❑	❑	❑	❑	❑	❑
Anemia or other blood disease	❑	❑	❑	❑	❑	❑
Overweight	❑	❑	❑	❑	❑	❑
Cancer	❑	❑	❑	❑	❑	❑
Depression	❑	❑	❑	❑	❑	❑
Osteoarthritis, degenerative arthritis	❑	❑	❑	❑	❑	❑
Rheumatoid arthritis	❑	❑	❑	❑	❑	❑
Back pain	❑	❑	❑	❑	❑	❑
Lyme disease	❑	❑	❑	❑	❑	❑
Other medical problem	❑	❑	❑	❑	❑	❑
Alcoholism	❑	❑	❑	❑	❑	❑

Page 2 - IKDC DEMOGRAPHIC FORM

1. Do you smoke cigarettes?

   ❑Yes
   ❑No, I quit in the last six months.
   ❑No, I quit more than six months ago.
   ❑No, I have never smoked.

2. Your height ________ ❑centimeters ❑inches

3. Your weight ________ ❑kilograms ❑pounds

4. Your race (indicate all that apply)

   ❑White ❑Black or African-American ❑Hispanic

   ❑Asian or Pacific Islander ❑Native American Indian ❑Other

5. How much school have you completed?

   ❑Less than high school ❑Graduated from high school ❑Some college

   ❑Graduated from college ❑Postgraduate school or degree

6. Activity level

   ❑Are you a high competitive sports person?

   ❑Are you well-trained and frequently sporting?

   ❑Sporting sometimes

   ❑Non-sporting

IKDC CURRENT HEALTH ASSESSMENT FORM *

Your Full Name ____

Your Date of Birth _________/___________/___________
Day Month Year

Today's Date _____________/___________/___________
Day Month Year

1. In general, would you say your health is: ❑Excellent ❑Very Good ❑Good ❑Fair ❑Poor

2. Compared to one year ago, how would you rate your health in general now?

   ❑Much better now than 1 year ago ❑Somewhat better now than 1 year ago ❑About the same as 1 year ago

   ❑Somewhat worse now than 1 year ago ❑Much worse now than 1 year ago

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

		Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a.	Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	❑	❑	❑
b.	Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	❑	❑	❑
c.	Lifting or carrying groceries	❑	❑	❑
d.	Climbing several flights of stairs	❑	❑	❑
e.	Climbing one flight of stairs	❑	❑	❑
f.	Bending, kneeling or stooping	❑	❑	❑
g.	Walking more than a mile	❑	❑	❑
h.	Walking several blocks	❑	❑	❑
i.	Walking one block	❑	❑	❑
j.	Bathing or dressing yourself	❑	❑	❑

4. During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

		YES	NO
a.	Cut down on the amount of time you spent on work or other activities	❑	❑
b.	Accomplished less than you would like	❑	❑
c.	Were limited in the kind of work or other activities	❑	❑
d.	Had difficulty performing the work or other activities (for example, it took extra effort)	❑	❑

5. During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

		YES	NO
a.	Cut down on the amount of time you spent on work or other activities	❑	❑
b.	Accomplished less than you would like	❑	❑
c.	Didn't do work or other activities as carefully as usual	❑	❑

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

❑Not At All ❑Slightly ❑Moderately ❑Quite a Bit ❑Extremely

7. How much bodily pain have you had during the past 4 weeks?

❑None ❑Very Mild ❑Mild ❑Moderate ❑Severe ❑Very Severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

❑Not at All ❑A Little Bit ❑Moderately ❑Quite a Bit ❑Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of pep?	❑	❑	❑	❑	❑	❑
b. Have you been very nervous?	❑	❑	❑	❑	❑	❑
c. Have you felt calm and peaceful?	❑	❑	❑	❑	❑	❑
d. Did you have a lot of energy?	❑	❑	❑	❑	❑	❑
e. Have you felt down-hearted and blue?	❑	❑	❑	❑	❑	❑
f. Did you feel worn out?	❑	❑	❑	❑	❑	❑
g. Have you been a happy person	❑	❑	❑	❑	❑	❑
h. Did you feel tired?	❑	❑	❑	❑	❑	❑

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

❑All of the time ❑Most of the time ❑Some of the time ❑A little of the time ❑None of the time

11. How TRUE or FALSE is each of the following statements for you?

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
a. I seem to get sick a little easier than other people	❑	❑	❑	❑	❑
b. I am as healthy as anybody I know	❑	❑	❑	❑	❑
c. I expect my health to get worse	❑	❑	❑	❑	❑
d. My health is excellent	❑	❑	❑	❑	❑

2000 IKDC SUBJECTIVE KNEE EVALUATION FORM

Your Full Name____

Today's Date: ______/_______/______
Day Month Year

Date of Injury: ______/________/_____
Day Month Year

SYMPTOMS*:

*Grade symptoms at the highest activity level at which you think you could function without significant symptoms, even if you are not actually performing activities at this level.

1. What is the highest level of activity that you can perform without significant knee pain?

- ❑Very strenuous activities like jumping or pivoting as in basketball or soccer
- ❑Strenuous activities like heavy physical work, skiing or tennis
- ❑Moderate activities like moderate physical work, running or jogging
- ❑Light activities like walking, housework or yard work
- ❑Unable to perform any of the above activities due to knee pain

2. During the <u>past 4 weeks</u>, or since your injury, how often have you had pain?

	0	1	2	3	4	5	6	7	8	9	10	
Never	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	Constant

3. If you have pain, how severe is it?

	0	1	2	3	4	5	6	7	8	9	10	
No pain	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	Worst pain imaginable

4. During the <u>past 4 weeks</u>, or since your injury, how stiff or swollen was your knee?

- ❑Not at all
- ❑Mildly
- ❑Moderately
- ❑Very
- ❑Extremely

5. What is the highest level of activity you can perform without significant swelling in your knee?

- ❑Very strenuous activities like jumping or pivoting as in basketball or soccer
- ❑Strenuous activities like heavy physical work, skiing or tennis
- ❑Moderate activities like moderate physical work, running or jogging
- ❑Light activities like walking, housework, or yard work
- ❑Unable to perform any of the above activities due to knee swelling

6. During the <u>past 4 weeks</u>, or since your injury, did your knee lock or catch?

❑Yes ❑No

7. What is the highest level of activity you can perform without significant giving way in your knee?

- ❑Very strenuous activities like jumping or pivoting as in basketball or soccer
- ❑Strenuous activities like heavy physical work, skiing or tennis
- ❑Moderate activities like moderate physical work, running or jogging
- ❑Light activities like walking, housework or yard work
- ❑Unable to perform any of the above activities due to giving way of the knee

SPORTS ACTIVITIES:

8. What is the highest level of activity you can participate in on a regular basis?

- ❑Very strenuous activities like jumping or pivoting as in basketball or soccer
- ❑Strenuous activities like heavy physical work, skiing or tennis
- ❑Moderate activities like moderate physical work, running or jogging
- ❑Light activities like walking, housework or yard work
- ❑Unable to perform any of the above activities due to knee

9. How does your knee affect your ability to:

		Not difficult at all	Minimally difficult	Moderately Difficult	Extremely difficult	Unable to do
a.	Go up stairs	❑	❑	❑	❑	❑
b.	Go down stairs	❑	❑	❑	❑	❑
c.	Kneel on the front of your knee	❑	❑	❑	❑	❑
d.	Squat	❑	❑	❑	❑	❑
e.	Sit with your knee bent	❑	❑	❑	❑	❑
f.	Rise from a chair	❑	❑	❑	❑	❑
g.	Run straight ahead	❑	❑	❑	❑	❑
h.	Jump and land on your involved leg	❑	❑	❑	❑	❑
i.	Stop and start quickly	❑	❑	❑	❑	❑

FUNCTION:

10. How would you rate the function of your knee on a scale of 0 to 10 with 10 being normal, excellent function and 0 being the inability to perform any of your usual daily activities which may include sports?

FUNCTION PRIOR TO YOUR KNEE INJURY:

Cannot perform daily activities	0	1	2	3	4	5	6	7	8	9	10	No limitation in daily activities
	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	

CURRENT FUNCTION OF YOUR KNEE:

Cannot perform daily activities	0	1	2	3	4	5	6	7	8	9	10	No limitation in daily activities
	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	