Rotator cuff tendinopathy: an investigation of extrinsic and intrinsic mechanisms using ultrasound imaging

by

Karen M McCreesh

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Limerick

Supervised by Prof. Alan Donnelly and Dr. Jeremy Lewis

Submitted to the University of Limerick, August 2014
Declaration

My submission as a whole is not substantially the same as any that I have previously made or currently am making, whether in published or unpublished form for a degree, diploma, or similar qualification at any university or similar institution. I am the author of this thesis and the principle author of the seven articles which form its core.

Signature: ____________________

Karen M McCreesh
Abstract

Rotator cuff (RC) tendinopathy is a common cause of shoulder pain, and can result in significant and prolonged pain and disability in adults. Surgical interventions to treat RC tendinopathy are costly and invasive, with conservative management primarily involving exercise therapy demonstrating at least equivalent effectiveness. However, conflicting opinions and evidence regarding the aetiology of this disorder has led to a lack of specificity of rehabilitation programmes or surgical approaches.

Proposed mechanism of RC tendinopathy are: extrinsic mechanisms, which describes external compression of the RC tendons from the coracoacromial arch; or intrinsic mechanisms, which includes factors directly influencing tendon health such as loading, genetics and ageing. This thesis examined the interaction between two factors i.e. acromiohumeral distance (AHD), and supraspinatus tendon (SsT) thickness, representing extrinsic and intrinsic factors respectively.

Chapter 2 of this thesis describes a series of methodological studies, examining reliability and validity of these measures. These studies demonstrated that ultrasound imaging can be used to undertake reliable and valid measures of AHD and reliable measures of SsT thickness in both RC tendinopathy and painfree populations. As part of a study examining the validity of AHD measurement, a novel shoulder ultrasound phantom was developed which has potential to act as a training tool for shoulder ultrasound examinations and/or injections.

The studies in Chapter 3 examined differences in AHD and SsT thickness in a group of people with RC tendinopathy compared to painfree controls, both cross-sectionally and also in response to a bout of fatigue loading. Acromiohumeral distance is not significantly reduced in those with painful RC tendinopathy (without RC tears) compared to controls. However, the SsT was found to be thicker in those with moderately or severely painful RC tendinopathy, potentially indicating primary intrinsic tendon changes. Additionally, the thickened tendon led to an overall increased subacromial occupation ratio, which may contribute to secondary extrinsic tendon compression. In RC tendinopathy, fatigue loading results in a prolonged (>6hours) reduction in AHD and an increase in SsT thickness, compared to findings of a transient change in AHD (<6 hours) and minimal reduction in tendon thickness in painfree controls.

While undertaking research to provide evidence for practice is critical to building the knowledge base in physiotherapy, a further important consideration is how this knowledge is translated to, and used in, clinical practice. Chapter 5 of this thesis describes the delivery and evaluation of a Community of Practice (CoP) within Primary Care physiotherapists, focused on improving evidence-based knowledge translation in shoulder pain. This qualitative study found that the CoP therapists gained multiple benefits from their involvement including peer support, increased use
of research evidence, and increased confidence in their clinical practice and research utilisation skills. The CoP project also resulted in the production of a website (www.shouldercommunity.com) designed to provide evidence-based information about shoulder pain to therapists and patients.

In conclusion, this thesis provides further evidence supporting intrinsic tendinopathy as a mechanism of RC tendinopathy. Potential interactions with extrinsic mechanisms are explained through changes in the subacromial occupation ratio. The findings of the fatigue loading study provide guidance to clinicians on exercise prescription in RC tendinopathy. The CoP provided a successful means of improving knowledge transfer to clinical practice for Primary Care physiotherapists, which could be transferred to other practice areas and settings.
Acknowledgements

The early stages of this work were inspired by a research visit to Australia - I am grateful to the following people who facilitated my visit, shared their time, and inspired me with their work: Prof Jill Cook and the MONSTERS team, Monash University; Prof Karen Ginn, University of Sydney; Prof Wayne Hing, Bond University; Andrea Mosler, Australian Institute for Sport.

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Paper VI is founded on the work of the Shoulder Community of Practice. Many thanks to Louise Larkin for her work as Research Assistant on this project, and to the CoP physiotherapists for inspiring me throughout the PhD with your motivation, feedback and encouragement.

Many thanks to the people who gave freely of their time to participate in the studies described in this thesis.

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- Physiotherapists of Limerick Primary Care Services
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Appendix 2:

**Supplementary paper:** Adusumilli P, McCreesh K, Evans T. Development of an anthropomorphic shoulder phantom model that simulates bony anatomy for ultrasonic measurement of the acromiohumeral distance. Accepted for publication, J Ultrasound Med

Appendix 3:

Author contributions to papers comprising this thesis

Appendix 4:

Permissions to reproduce published content
List of Publications

Published Papers


Accepted subject to revisions


Submitted and under review

McCreesh K, Anjum S, Crotty J, Lewis J. Ultrasound measures of acromiohumeral distance and supraspinatus thickness are reliable in rotator cuff tendinopathy. Under review, Journal of Clinical Ultrasound


List of conference presentations


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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AGTD</td>
<td>acromion-greater tuberosity distance</td>
</tr>
<tr>
<td>AHD</td>
<td>acromiohumeral distance</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>CI</td>
<td>confidence interval</td>
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<tr>
<td>CoV</td>
<td>coefficient of variation</td>
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<tr>
<td>CS</td>
<td>corticosteroid</td>
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<tr>
<td>CT</td>
<td>Computed Tomography</td>
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<tr>
<td>DICOM</td>
<td>Digital Imaging and Communications in Medicine</td>
</tr>
<tr>
<td>EBP</td>
<td>evidence-based Practice</td>
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<tr>
<td>ECM</td>
<td>extra-cellular matrix</td>
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<tr>
<td>EMG</td>
<td>Electromyography</td>
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<tr>
<td>GRRAS</td>
<td>Guidelines for Reporting Reliability and Agreement Studies</td>
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<tr>
<td>ICC</td>
<td>Intra-class Correlation Coefficient</td>
</tr>
<tr>
<td>MCID</td>
<td>minimal clinically important difference</td>
</tr>
<tr>
<td>MDC</td>
<td>minimal detectable change</td>
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<tr>
<td>MDD</td>
<td>minimal detectable difference</td>
</tr>
<tr>
<td>mm</td>
<td>millimetre</td>
</tr>
<tr>
<td>MMP</td>
<td>matrix metaloproteinases</td>
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<tr>
<td>MRA</td>
<td>Magnetic Resonance Arthrography</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>NPRS/NRS</td>
<td>Numerical Pain Rating Scale/ Numerical Rating Scale</td>
</tr>
<tr>
<td>QAREL</td>
<td>Quality Appraisal for Reliability Studies</td>
</tr>
<tr>
<td>RC</td>
<td>rotator cuff</td>
</tr>
<tr>
<td>SD</td>
<td>standard deviation</td>
</tr>
<tr>
<td>SEM</td>
<td>standard error of measurement</td>
</tr>
<tr>
<td>SPADI</td>
<td>Shoulder Pain and Disability Index</td>
</tr>
<tr>
<td>SsT</td>
<td>supraspinatus tendon</td>
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<tr>
<td>TIMPs</td>
<td>tissue inhibitors of matrix metaloproteinases</td>
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Chapter 1: PhD Literature review and introduction

This review presents a background introduction to the anatomy, physiology and mechanics of the rotator cuff (RC) tendons and the subacromial space. The development of tendon pathology is described, followed by presentation of the predominant current theories underpinning the development of RC tendinopathy. Challenges pertaining to the diagnosis of RC pathology, using both clinical and imaging methods are described. The role of conservative and surgical treatments for RC tendinopathy is outlined.

Central to the chapter is a published paper evaluating the continuum model of tendon pathology (Study I).

This chapter concludes with a statement of thesis aims and an outline of the thesis structure.
1.1 Background and Literature Review

1.1.1 Introduction

Shoulder pain is a highly significant cause of pain and disability in the general population, with an estimated prevalence rate of 7% in the United Kingdom (UK), rising to 26% in the over-60s age group (Luime et al 2004). Approximately 1% of adults consult their general practitioner with shoulder pain each year (Linsell et al 2006), which would be the equivalent of 40,000 Irish adults. More specifically, the most common source of shoulder pain is considered to be RC tendinopathy (van der Windt et al 1995). A myriad treatment approaches exist for RC tendinopathy, including surgery, injections, and rehabilitation, however success rates vary and many of those with shoulder pain continue to report symptoms three years after onset (McFarlane et al 1998). Mechanisms of RC tendinopathy continue to be debated in the literature, resulting in a lack of firm basis on which to plan treatment (Seitz et al 2011).

1.1.2 Shoulder and rotator cuff anatomy

The ‘shoulder’ comprises a complex set of articulations between the upper extremity and the trunk, encompassing the glenohumeral joint, sternoclavicular joint, acromioclavicular joint and the scapulothoracic articulation. The glenohumeral joint involves the articulation between the humeral head and the glenoid fossa of the scapula, and provides the majority of shoulder mobility. The joint has little inherent bony stability, relying on static and dynamic stability from its soft tissues. The rotator cuff (RC), a group of four separate muscles; supraspinatus, subscapularis, infraspinatus and teres minor, are the primary dynamic stabilisers of the glenohumeral joint (Figure 1). They arise from the scapula and insert in a cuff-like manner at the superior, anterior and posterior aspects of the humeral head, fusing with the fibrous joint capsule (Figure 2). Through their combined, inferiorly-directed force vector they counteract the superiorly directed force of the deltoid muscle (in particular middle deltoid), especially in the early stages of shoulder elevation movements (Sharkey et al 1995).
The subscapularis muscle is large and flat, originating from the subscapular fossa, and inserting into the lesser tuberosity of the humerus. It functions to provide anterior stability for the glenohumeral joint, along with the action of internal rotation. The
infraspinatus muscle arises from the infraspinous fossa on the posterior aspect of the scapula, inserting on the greater tuberosity, with innervation from the suprascapular nerve. Closely associated with infraspinatus is the teres minor muscle, arising on the axillary border of the scapula and inserting onto the inferior part of the greater tuberosity, with a nerve supply from the axillary nerve. Both infraspinatus and teres minor provide posterior stability to the glenohumeral joint, and are external rotators. The supraspinatus muscle originates from the supraspinous fossa of the scapula, passing under the coracoacromial arch to insert onto the greater tuberosity, just posterior to the biceps groove, and receives innervation from the suprascapular nerve. The insertional footprint of the supraspinatus tendon is triangular, extending approximately 7mm in the medial-lateral direction and 12mm in the anterior-posterior direction (Mochizuki et al 2008). At their points of insertion is it not possible to distinguish the supraspinatus, infraspinatus and teres minor however, a distinct interval is evident between supraspinatus and subscapularis, known as the rotator interval, which is occupied by the long head of the biceps tendon and the coracohumeral ligament. Anatomy education continues to teach that the supraspinatus muscle initiates abduction of the arm, however, it is evident that all components of the RC muscles contribute to arm elevation (Sharkey et al 1994, Reed et al 2013), and that the stabilizing versus torque producing roles of the RC may vary according to arm position and degree of arm support (Tardo et al 2013). Based on physiological cross-sectional area as a percentage of the total RC, infraspinatus (30%) and subscapularis (42%) have the potential to provide a significantly larger contribution in terms of force production, compared to supraspinatus (20%) (Mathewson et al 2014). Length-tension relationships appear to be critical to RC muscle function, with subscapularis exhibiting high passive tension in positions of lateral rotation and abduction, whereas infraspinatus and supraspinatus had maximum passive tension in the neutral shoulder position, suggesting they have a role in glenohumeral joint stability at rest (Ward et al 2006). The supraspinatus muscle has been shown to consist of architecturally distinct anterior and posterior parts, each with superficial, deep and middle subregions, according to having different muscle fibre pennation angles (Kim et al 2007) and different proportions of muscle fibre types (Kim et al 2013) (See Figure 3).
Figure 3: Supraspinatus muscle architecture, viewed in the suprascapular fossa

(Reproduced with permission from Kim et al 2007)

(Legend: ** indicates tendon, AS=Superficial part of anterior region, PR=Posterior region, AM=Middle part of anterior region)

The supraspinatus tendon (SsT) is comprised of 6-9 independent fascicles, capable of sliding independent of each other, which permits the tendon to continue to transmit tension despite the changing angles of the shoulder joint during movement (Fallon et al 2002). The attachment surface is covered with fibrocartilage, from the tendon proper forward to the greater tuberosity insertion. The ‘rotator cable’ is a thickened bundle of fibres that runs transversely across the supraspinatus and infraspinatus tendons. The crescent shaped area of the infraspinatus and supraspinatus at their distal attachment is termed the ‘rotator crescent’, with the cable area of the tendons being more than double the thickness of the crescent area (Figure 4). The strong rotator cable appears to be critical in retaining function in the presence of RC tears, through a “suspension bridge” effect (Burkhart et al 1993). As the primary load bearing structure in the supraspinatus tendon, the rotator cable may also be responsible for a certain degree of stress-shielding (i.e. removal or redistribution of load) of the crescent area supraspinatus tendon fibres (Mesiha et al 2013).
1.1.3 The subacromial space

The subacromial space is bordered by the coraco-acromial arch (comprised of the acromion and coraco-acromial ligament) superiorly, and by the superior surface of the humeral head inferiorly. It contains the supraspinatus tendon (SsT), subacromial bursa, superior aspect of the shoulder joint capsule and the tendon of the long head of biceps (Figure 5). The subacromial (subdeltoid) bursa is the largest bursa in the body, comprised of two membranes separated by a thin film of lubricating fluid, and extends from under the acromion anteriorly under the coracoacromial ligament. The subacromial bursa is highly innervated with both noioceptors and mechanoreceptors (Soifer et al 1996, Ide et al 1996).
Figure 5: Anterior shoulder showing subacromial space

Anterior view of shoulder. Subacromial space containing rotator cuff tendons, and subacromial bursa, bounded by coraco-acromial arch above and humeral head below. (Adapted with permission from www.shutterstock.com)

1.1.4 Supraspinatus tendon physiology and mechanics

The SsT is the most-studied RC tendon, being that it is most often the source of pathology in this region (van der Windt, 1995). The multi-fascicular structure of the tendon has been described by Fallon et al (2002), however at a microstructural level the tendon also exhibits complex fibre distributions, matching the loading environment in which it functions (Lake et al 2009). Mechanical properties of the tendon are related to the degree of fibre alignment, and are inhomogeneous across the supraspinatus, with the bursal surface exhibiting 15-30 times the mechanical strength as the joint side (Lake et al 2010). Reilly et al (2003) examined strain of the articular and bursal sides of the SsT in cadaver specimens, reporting significantly higher levels of articular side strain, exceeding tendon failure rates, in 100° abduction with 100N of load. Huang et al (2005) used a novel marker displacement method also to examine strain on the bursal and articular sides of the supraspinatus in cadaver shoulders. The authors reported that the articular side exhibited higher strain at 20° and 60° abduction, while strain was greatest on the
bursal side at 90°, and strain was greater at the insertion, compared to the mid-tendon or musculotendinous junction at all angles. While cadaver studies, often of elderly individuals, are somewhat limited in terms of applicability to the general population, they remain one of the most common methods of quantifying human tendon biomechanics. The studies reporting inhomogeneous strain across the SsT suggest that intra-tendinous shearing occurs during arm motion, and this may predispose to intra-tendinous tears. In addition, the higher strain levels on the articular side may provide some explanation for the higher rate of articular sided tendon lesions in the supraspinatus (Fukuda 2000).

1.1.5 Tendon structure and function

Tendons are comprised of extracellular matrix (ECM), containing primarily a dense network of collagen fibrils (Type I and Type III) arranged in parallel fibre bundles, and ground substance, containing water, glycoproteins and proteoglycans, which are important for maintaining the tendon water content. Tendon ECM is produced in the tendon cell, or tenocyte, which is a specialized form of fibroblast found close to the collagen fibrils within the tendon, usually arranged in parallel along the main direction of tension. Tendon structure and function is known to vary at different sites within tendons as well as between tendons in different parts of the body (Benjamin et al 2008). The fundamental role of tendons is the transmission of tensile forces generated by muscle. Tendons can also be subject to non-tensile loading such as compression and shear forces as they pass through and around various anatomical structures, such as bone and retinaculae (Cook and Purdam 2012). Neural elements in tendon are primarily mechanoreceptors (e.g. Golgi tendon organs, Rufini and Pacinian corpuscles; responsible for responding to mechanical stimuli) with very few free nerve endings (responsible for transmitting nociceptive or pain signals).

Tendon cells (tenocytes) are capable of responding to mechanical load through a process of mechanotransduction i.e. the process by which deformation of the tendon ECM and cells provokes a cellular response leading to increased protein synthesis (Sharma & Maffulli 2006). Tenocytes upregulate collagen synthesis when subject to tensile loading, a process confirmed in vitro after both one-off bouts of exercise and
longer term habitual loading (Kjaer et al 2009). In addition, an increase in protein degradation accompanies exercise, with an increased level of matrix metalloproteinases (MMPs, responsible for protein breakdown) and their tissue inhibitors (TIMPs) observed in a microdialysis study of the Achilles tendon response to treadmill running in healthy men (Koskinen et al 2004). A correct balance between tendon matrix production and degradation appears critical to healthy tendon function (del Buono et al 2012).

1.1.6 Definition of terms used in the thesis

This section will clarify and define some important terms used within the remainder of the thesis. There has been ongoing controversy within the literature with regards to the most appropriate diagnostic label for tendon pathology and its clinical manifestations (Khan et al 2002, Mafulli et al 1998). Tendinopathy is the term used to describe the clinical presentation of pain and dysfunction, related to pathology of tendon, while the terms tendinosis and tendinitis are ideally reserved for histologically confirmed tendon degeneration or inflammation respectively. For this thesis the term RC tendinopathy will primarily be used to describe the clinical presentation of shoulder pain and dysfunction, resulting from pathology of the RC tendons. However, since there is no method of determining on ultrasound imaging whether a diffuse hypoechoic appearance of the tendon occurs due to an inflammatory or degenerative process, the term tendinosis is used as a sonographic diagnostic term in the studies in this thesis involving ultrasound imaging, without prejudice as to the histological source of the tendon pathology.

While the RC comprises a group of four muscle and tendons, the most common site of pathology is reported to be the supraspinatus tendon (van der windt et al 1995, Fukuda 2000). However as detailed in Section 1.1.2, these RC tendons have close anatomical relationships and merge together at their insertions (Clark and Harryman 1992), therefore it is difficult to determine, when imaging the RC tendons, where the boundaries of each tendon lie. As the most common site of pathology, the imaging protocols in this thesis focus on the area believed to be primarily occupied by the supraspinatus tendon (Seibold et la 1999). However since there may be contributions from other RC tendons e.g. infraspinatus, in this area of the shoulder, the term RC
tendinopathy, as opposed to supraspinatus tendinopathy, is used as the term to describe the clinical diagnosis for participants with shoulder pain in this thesis.

While diagnostic imaging in RC disorders provides a variety of challenges, including a lack of correlation between structural failure and symptoms (Tempelhof et al 1999), ultrasound has been shown to have equivalent diagnostic accuracy to Magnetic Resonance Imaging (MRI) for RC disorders when findings on arthroscopic surgery are used as a comparator (de Jesus et al 2006). However clear consensus definitions of how to diagnose RC pathology on ultrasound images are not available (Naredo et al 2006), therefore for the studies in this thesis, diagnostic criteria were based on a combination of existing published criteria (Naredo et al 2006, Wakefield et al 2005, Cullen et al 2007). Loss of the normal fibrillar structure of the tendon with a diffuse hypoechoic appearance was labelled tendinosis. A partial-thickness tear was recorded when flattening of the bursal side of the tendon or a distinct/focal hypoechoic defect was seen within, or on either surface of, the tendon (not involving the full thickness of the tendon). A full-thickness RC tear was recorded when the RC tendons could not be visualised because of complete rupture or when there was a focal defect extending from the bursal to the humeral side of the tendon, with or without retraction of the tendon. Bursitis was recorded only when marked fibrotic thickening of the subacromial bursa or bursal fluid > 2mm was present. It is accepted that the distinction between tendinosis, where diffuse loss of ultrasound echo is observed, versus a partial thickness tear, where a focal loss of echo is seen, may be difficult to substantiate in all cases and is dependent on operator skill and avoidance of imaging artefacts. However this sonographic definition of partial thickness tears has been substantiated in studies undertaking comparison with intra-operative findings (Venu et al 2000, Hodler et al 1988).

A range of mechanisms and risk factors have been described as contributing to the development of RC tendon pathology. Seitz et al (2011) conducted a broad review of the mechanisms of RC tendinopathy and defined extrinsic mechanisms as those related to tendon compression or encroachment within the subacromial space, and included acromial shape variants, altered posture or shoulder girdle kinematics, and internal impingement within their definition. Intrinsic mechanisms were defined as those leading to direct degradation of the RC tendons such as age genetics, vascularity and altered tensile loading (increased volume, intensity or frequency). Lewis (2009)
used similar definitions for the terms intrinsic and extrinsic in a review describing the pathoaeiology of RC tendinopathy, where intrinsic tendinopathy was defined as “tendon pathology that originates within the tendon, usually as a consequence of overuse or overload” and extrinsic as primarily related to “mechanical abrasion from the undersurface of the acromion”. In contrast, in describing risk factors for the development of Achilles tendinopathy, Rees et al (2009) use the terms ‘intrinsic’ and ‘extrinsic’ in a different way, suggesting that intrinsic risk factors, such as age and genetics, create a predisposition to tendon injury, while overloading acts as an extrinsic risk factor preceding the development of tendinopathy. The focus of this thesis is on examining the role of altered subacromial space in RC tendinopathy, and in particular to explicate the relative contribution of external tendon compression in the subacromial space versus pathology driven by changes in the tendon itself e.g. altered loading capacity. Therefore, the use of the terms extrinsic and intrinsic mechanisms will be as per the definition of Seitz et al (2011), where extrinsic mechanisms are used to describe any process that leads to external compression originating outside of the RC tendons, while the term intrinsic mechanisms is used to describe mechanisms by which tendon pathology occurs in the absence of external compression.

1.1.7 Tendinopathy

Tendinopathy is the term used to describe pathology of tendon structures of varying degrees, while the related terms tendinosis and tendinitis should be reserved for histologically confirmed tendon degeneration or inflammation respectively. Tendinopathy is believed to present as a failed healing response, with few inflammatory cells, collagen thinning and deterioration, an increase in immature tendon cells, and an increase in vascular ingrowth. Macroscopically, tendinopathy results in a thickening of the tendon, with eventual progression to tearing and rupture (Cook and Purdam 2009). The role of inflammation in the development and progression of tendinopathy has been widely debated, with strong argument against the inflammatory models of tendinopathy in the early 2000’s (Khan et al 2002), but more recent studies suggesting a role for pro-inflammatory mediators in chronic tendinopathy (Rees et al 2013). Evidence for inflammatory involvement in early RC tendinopathy is provided by Millar et al (2010) who identified significantly higher
concentrations of mast cells and macrophages, both key players in the inflammatory process, in the subscapularis tendons of people undergoing surgery for full thickness SsT tears, compared to the torn SsT, and to controls undergoing instability surgery (the subscapularis tendon in those with SsT tears was considered a model for early tendinopathy). Studies of bursal tissue in people with RC tendinopathy have identified higher concentrations of inflammatory substances, such as Substance P and pro-inflammatory cytokines, in those with pain compared to controls or those with other shoulder disorders (Gotoh et al 1998, Voloshin et al 2005) and there appears to be some association between the presence of these substances and pain intensity (Gotoh et al 1998, Santavrita et al 1992).

Numerous models have been proposed to explain the basis for the aetiology and management of tendinopathy, the most recent of which is the continuum model, proposed by Cook and Purdam (2009). In the paper that follows this section (McCreesh et al 2013), the continuum model and related models of tendinopathy are presented and evidence to support or refute the model is discussed (See section 1.2).

1.1.8 Mechanisms of rotator cuff tendinopathy

Proposed mechanisms behind the development of RC tendinopathy are multiple and varied, however they broadly fall into the categories of intrinsic, extrinsic or combined mechanisms. Seitz et al (2011) published a detailed review of these mechanisms, suggesting that subgroups of patients might potentially be identififiable according to mechanisms, and that this might lead to more targeted and effective treatment. Neer (1972) described three main stages of RC tendon pathology. The first involves tendon inflammation and oedema, and reported to occur in those under the age of 25. The second stage is described as tendon fibrosis and tendonitis, occurring in those between 25 and 40 years of age. Stage three involves people over the age of 40 and includes tendon rupture and bony changes in the coracoacromial arch. Lewis (2009) has applied the continuum model of tendinopathy to RC tendinopathy, describing how RC pathology can move between the three stages (reactive, dysrepair and degenerative tendinopathy), with or without the concomitant presence of subacromial bursitis.

1.1.8.1 Extrinsic mechanisms
Extrinsic mechanisms of RC tendinopathy are those pertaining to external compression or impingement of the RC tendons due to anatomical or biomechanical factors within the subacromial space. The main extrinsic factors proposed are subacromial impingement from anatomical alterations of the coracoacromial arch, tendon compression from alterations in scapular biomechanics, and the lesser discussed condition of internal impingement of the RC tendons between the glenoid rim and humeral head.

Historically, Neer (1972) first described the concept of subacromial impingement by the acromion or coraco-acromial ligament, resulting in mechanical abrasion of the tendon and resultant tendon inflammation and breakdown, and concurrently proposed a surgical solution which was acromioplasty and coraco-acromial ligament resection. Aberrant acromial shape is one factor which has been repeatedly proposed as an anatomical contributor to the development of subacromial impingement and RC tendinopathy (Bigliani et al 1986). This concept of subacromial impingement has been the driving theory behind much clinical practice in shoulder pain in the last 40 years, including clinical diagnostic tests that have been developed to reproduce impingement symptoms (Hawkins and Kennedy 1980), radiological examinations assessing the acromial shape (Peh et al 1995), surgical techniques to alter acromial shape (Neer 1972), and rehabilitation interventions designed to ameliorate the impingement through alterations in thoracic or scapular postures (Ellenbecker and Cools 2010).

Inherent to the subacromial impingement model of RC tendinopathy is that the predominant site of tendon damage should be the superior or bursal side of the tendons, as this is the surface that potentially comes into contact with the coraco-acromial arch. However, there is substantial evidence from histological studies that the most common site of RC tendon degeneration and tears is the articular side of the SSST, with intra-substance tears being the second most prevalent (Loehr & Uhtoff 1987, Fukuda 2003). Equally the evidence in relation to the association between acromial shape and RC tendinopathy is conflicting. While studies suggest an association between presence of a hooked (Type III) or sloped acromion and RC tears (Morrison and Bigliani 1987, Hirano et al 2002), others suggest that the prevalence of altered acromial shape is similar among those with and without RC tendon pathology and that the acromial changes seen may be an age-related phenomenon (Ozaki et al
1998, Worland et al 2003). There are a number of studies which provide evidence that altered acromial shape occurs as a result of the development of spurs or enthesophytes on the coraco-acromial arch, as a secondary consequence of RC tendinopathy or stresses on the coracoacromial ligament (Ozaki et al 1988, Panni et al 1996, Chambler et al 2003). Additionally, recurrence of these spurs has been described subsequent to acromioplasty surgery (Anderson & Bowen, 1999). While Neer (1972) emphasised the role of acromioplasty in alleviating impingement and managing RC tears, a number of more recent studies have demonstrated very good post-surgical outcomes for people who underwent RC repair only without acromioplasty (Goldberg et al 2001, McAllister et al 2005), and no differences in outcome for those undergoing subacromial bursectomy alone versus acromioplasty (Henkus et al 2009). A recent large RCT of 180 people with non-traumatic, partial thickness RC tears aged over 55 years randomized to one of three treatments: physiotherapy alone; physiotherapy combined with acromioplasty or combined with RC repair and acromioplasty. No difference in outcome was identified between the groups at one year follow-up (Kukkonen et al 2014). Furthermore, acromioplasty appears not to be protective against further RC degeneration. Kartus et al (2006) followed up patients who had undergone acromioplasty for partial thickness RC tears, and showed that further RC degenerative changes and progression of the tear occurred in many of them. Similarly, a nine-year follow-up study of 96 people post-acromioplasty reported that 19 of them developed a new RC tear during the follow-up period (Hyvonen et al 1998), suggesting that external compression by the acromion was not the source of injury.

While anatomical variants or degenerative bony change of the coraco-acromial arch have been proposed as a static source of subacromial impingement, kinematic abnormalities of scapular and shoulder girdle motion have been suggested as a possible source of dynamic compromise of the subacromial space during shoulder overhead motion (Ludewig and Cook 2000). Some studies have reported decreased scapular posterior tilt and a lack of upward scapular rotation in people with RC tendinopathy; mechanics which may cause inferior positioning of the acromion or a lack of glenoid upward rotation during motion, resulting in a narrower subacromial space and the potential for SsT compression (Ludewig and Cook 2000, Borstad 2006). In contrast, other studies have found few, if any, differences in scapular posture between painful and non-painful shoulders in the same subjects (Hebert et al 2002), or
between those with shoulder pain and controls (Lucasiewicz et al 1999). Additionally some studies demonstrate scapular kinematic alterations that are likely to be favorable for the subacromial space (e.g. increased scapular posterior tilt and upward rotation) (McClure et al 2006), suggesting that changes in scapular orientation may act as compensatory mechanisms to relieve compression on existing painful RC tendons. As confirmed by a recent systematic review by Ratcliffe et al (2013), most studies of the relationship between scapular orientation and subacromial impingement are confounded by very small sample sizes and the use of healthy shoulders in young people as comparators. In addition, there are questions as to whether tests of scapular orientation have adequate reliability to detect clinically important levels of difference, due to relatively large degrees of inter-observer variation (Shadmehr et al 2010). These methodological issues result in a lack of evidence to support any consistent alteration of scapular alignment in those with painful shoulders.

Another potential dynamic mechanism of subacromial space reduction is superior migration of the humeral head, which has been widely described in the presence of RC dysfunction (Keener et al 2009). While the mechanism of this upward humeral head displacement is not clearly understood, lack of inferior stabilisation by the RC, relative to a normal or increased upward pull of the deltoid muscle, is likely to be a plausible explanation. Electromyographic studies of RC activation in people with RC tendinopathy have reported reduced activation levels in supraspinatus and infraspinatus muscles (Reddy et al 2000, Diederichsen et al 2009). Myers et al (2009) found that, compared to pain-free controls, people with RC tendinopathy had reduced RC co-activation ratios and increased middle deltoid activity in the early parts of elevation range, while higher RC co-activation occurred in higher elevation ranges, alterations which would potentially serve to increase the risk of encroachment of subacromial structures during arm elevation. Chopp et al (2010) conducted a radiographic study of the effect of RC fatigue on humeral head position in pain-free shoulders, demonstrating that after a fatiguing protocol, humeral head superior migration increased throughout the range of abduction. A subsequent study using a protocol designed to fatigue the scapular muscles did not lead to any changes in three-dimensional (3D) scapular orientation, suggesting that the changes in humeral head position seen with fatigue are most likely to be related to RC muscle activation changes rather than an altered scapular position (Noguchi et al 2013). Neither of these
studies included symptomatic participants. In contrast, a systematic review of EMG studies examining shoulder and scapular muscle alterations in RC tendinopathy found no evidence for significant differences in the RC muscles in symptomatic groups, with some evidence for small changes in activation of the upper and lower trapezius (Chester et al 2010). It is not clear whether altered muscle activation is a pathogenic factor in the development of RC tendinopathy, through superior humeral migration and resultant tendon impingement, or occurs secondary to tendon degeneration, as a result of a pain inhibition response (Lund et al 1991). Nonetheless, regardless of causation, the interaction of reduced RC muscle activation and a more superior humeral head position is likely to create the conditions where compression of the SsT may be more likely to occur.

Superior migration of the humeral head is commonly quantified by the measurement of acromiohumeral distance (AHD). AHD has been reported to be smaller in patients with RC tendinopathy and to be positively associated with the size of RC tear and degree of fatty degeneration in RC muscles (Saupe et al 2006). Hébert and colleagues (2003) reported that AHD was a predictor of short-term disability in patients with RC dysfunction, while Mayerhoefer et al (2009) demonstrated an association between AHD and functional status. Reliability and validity of AHD measurement in symptomatic populations is unconfirmed (McCreesh et al 2013).

Internal impingement is a less common mechanism of RC tendinopathy, usually described in relation to younger, overhead athletes, with posterior shoulder pain. In end-range positions of shoulder abduction and external rotation, the articular surface of the RC tendons is thought to become impinged between the posterior glenoid rim and the greater tuberosity of the humeral head, leading to tendon degeneration and labral damage (Manske et al 2013).

1.1.8.2 Intrinsic mechanisms

Intrinsic mechanisms of RC tendinopathy relate to factors which directly influence tendon health and quality, causing degeneration that exceeds the tendon’s capacity to heal and repair, and includes factors such as ageing, genetics, vascular changes, adiposity, and overloading.
There is a large body of evidence associating RC tendinopathy with advanced age, with prevalence rates of degenerative RC changes, symptomatic and asymptomatic, steadily increasing from middle age (Tempelhof et al 1999). While age in itself leads to altered tendon properties such as reduced proteoglycan content and poorer quality collagen, it is important to distinguish tendinopathy from normal ageing (Riley et al 1994a, 1994b).

Studies where a high prevalence of RC tears and tendinopathy have been observed amongst siblings suggest that a sub-group of patients with genetic susceptibility to RC tendinopathy may exist (Harvie et al 2004, Tashjian et al 2009), potentially mediated by a wide variety of gene changes (Chaudhury & Carr 2012). Lifestyle factors such as increased adiposity and smoking have also been cited as increasing the risk of tendinopathies. Rechardt et al (2010) identified associations between waist circumference, metabolic syndrome and smoking and the prevalence of RC tendinopathy in a large Finnish population study, with the authors suggesting that altered glucose metabolism and vascular pathology may contribute to tendon damage. A dose-dependent relationship was reported by Baumgarten et al (2010) between smoking and the presence of RC tears in their study of over 500 patients undergoing shoulder ultrasound examinations.

Vascular insufficiency of the RC tendons has long been implicated in the development of RC tendinopathy, driven by Codman’s (1934) “critical zone” theory that the supraspinatus had an area of diminished vascularity 1cm from its insertion, coinciding with the area of most frequent degenerative change. The primary sources of evidence supporting this theory are in vitro or cadaver studies, however more recent in-vivo studies have found no significant area of hypovascularity (Levy et al 2008, Longo et al 2008). In fact, there appears to be a continuum of vascular changes in the RC tendons as tendon pathology progresses i.e. normal at baseline, hypovascularity during the early stage of tendinopathy, hypervascularity with partial tearing, and again, hypovascularity in full thickness tears (Hegedus et al 2010).

Overload (defined as loading beyond the particular physiological capacity of the tendon) is considered to be an important factor in the aetiology of tendinopathy, and is an individual factor related to the capacity of the tendon to tolerate load. Rotator cuff tendinopathy is known to occur more frequently in the dominant limb (Yamamoto et
al 2010), and is highly prevalent in occupations (Melchoir et al 2006) and sports with high rates of upper limb loading (Sein et al 2010). Experimental studies in animals involving overloading of the RC have reported histological and biochemical changes typical of tendinopathy (Solowsky et al 2000). Histological studies have demonstrated that overload leads to greater expression of cartilage genes in rat SsT, suggesting development of a fibrocartilage-like phenotype in response to repetitive loading and compression of the tendon (Archambault et al 2007). Similar overload studies using a rat model of RC tendinopathy have reported increases in cell apoptosis (programmed cell death) (Millar et al 2008) and in concentrations of nitric oxide synthases (Szomor et al 2006). It is clear that as tendon degeneration increases, the tensile strength of the tendon deteriorates (Sano et al 1997), leading to a vicious cycle of poorer capacity of the tendon to cope with load, and a resultant increased rate of degenerative change. Animal studies provide the opportunity to examine models of tendinopathy in a well-controlled experimental environment. While rats, being quadripedal, clearly use an altered model of RC function to humans, they are accepted to be one of the best matched animal models for this purpose (Mathewson et al 2014). However, the clinical relevance of the data from animal studies must be examined carefully in the context of application to human models of tendinopathy.

While overload is commonly part of the history of development of RC tendinopathy, equally underloading can also disrupt normal tendon homeostasis (Cook and Purdam 2009). The anatomy of the rotator cable and crescent, whereby the cable structure carries much of the loading during glenohumeral motion and leads to a certain degree of stress shielding of the crescent area fibres, may predispose the crescent area tendon fibres to poorer load tolerance and greater vulnerability to degenerative changes. Studies identifying the arrangement of multiple tendon bundles and fibre directions within the SsT (Fallon et al 2002, Lake et al 2009), as well as cadaver studies describing inhomogenous strain between the bursal and articular sides of the tendon (Reilly et al 2003, Huang et al 2005) provide some explanation for the propensity to the development of intra-tendinous and articular side tears.

1.1.8.3 Combined mechanisms
While extrinsic and intrinsic mechanisms of RC tendinopathy have been discussed separately (Section 1.1.8.1 and 1.1.8.2), there is clear potential for interaction between both types of mechanism. Primary extrinsic compression, if it occurs, could lead to tendon overload through compression and degenerative changes, which would be worsened in the presence of existing intrinsic risk factors such as advanced age or genetic predisposition. Intrinsic tendon pathology leading to tendon breakdown will result in poorer capacity of the RC tendons to stabilize the humeral head against the upward pull of deltoid, resulting in superior migration of the humeral head, and a reduction in the subacromial space. This reduction in space will lead to greater potential for compression of the tendons under the coraco-acromial arch. Tendon thickening is a common feature of early stages of tendinopathy (Cook and Purdam 2009), with Joensen et al (2009) reporting that a between-shoulder difference in SsT thickness of > 0.8mm provided good predictive diagnostic value for RC tendinopathy. An enlarged SsT takes up more space within the subacromial space, further increasing the likelihood of compression as the space available is reduced. In addition, the larger tendon and superiorly positioned humeral head may push upwards on the coraco-acromial ligament, creating a possible mechanism for the development of a traction spur, which in itself can then provide a source of tendon impingement in the longer term. Soslowsky et al (2000) examined the interaction between these mechanisms in a rat model and showed that while overload alone (intrinsic factor) led to SsT breakdown, this process was accelerated in the presence of interposed soft tissue (in the form of an Achilles tendon allograft) crossing the tendon (extrinsic factor). However there are no studies conducted in humans examining the interaction between intrinsic and extrinsic mechanisms of RC tendinopathy.

1.1.9 Diagnostic challenges in rotator cuff tendinopathy

Multiple clinical tests exist for the proposed diagnosis of RC tendinopathy, however a recent comprehensive systematic review has concluded that a paucity of evidence means that none of these tests can be recommended for use in clinical practice (Hegedus et al 2012). Lewis (2009) has discussed how a variety of factors, such as the close anatomical relationships between the RC tendons, pain inhibition, and the presence of painful bursal tissue, serve to negate the value of specific movement-
based tests for RC pathology. Ultrasound scanning has been shown to have equivalent reliability and validity as Magnetic Resonance Imaging (MRI) for diagnosing RC pathology (De Jesus et al 2006), however the degree of association between structural pathology noted on any form of imaging of the RC and patient symptoms is variable, with many studies noting similar degrees of pathological change in asymptomatic shoulders as symptomatic (Tempelhof et al 1999). Longitudinal imaging studies of lower limb tendon pathology demonstrate a continuum of pathology, with the early phase showing good potential for recovery, compared with relatively little reversibility of pathological changes in the chronic stage (Cook and Purdam 2009). Lewis (2009) has proposed a similar development of pathology in the RC tendons, however radiological evidence to support the changes in the RC tendons is scant.

1.1.10 Treatment of Rotator Cuff tendinopathy

1.1.10.1 Conservative

The most commonly used conservative interventions for RC tendinopathy are physiotherapy (in the form of exercise programmes) and corticosteroid injections (van der Windt et al 1995). Coombes et al (2010) conducted a meta-analysis examining the role of corticosteroid injection in various tendinopathies, concluding that the evidence in RC tendinopathy remains conflicting, which concurs with an earlier review by Koester et al (2007). Zheng et al (2014) reported in a meta-analysis of six high quality trials, that oral non-steroidal drugs are less effective than corticosteroid injections in the short-term for shoulder pain. While some authors report the potential for new targeted drug treatments for RC tendinopathy (Chaudhury & Carr 2012), at present the evidence for any medical treatments remains weak.

A recent systematic review and meta-analysis of exercise interventions for RC tendinopathy concluded that exercise is an effective treatment, but there is still no evidence to determine which types of exercise work best, or which patients benefit most from exercise interventions (Hanratty et al 2012). Exercise programmes are often broad-based including, range of motion and stretching exercises, scapular control exercises, and RC conditioning using various contraction types (isometric, concentric, eccentric), often combined with a plethora of adjunctive treatments such
as manual therapy, taping, massage, dry needling and electrotherapy (Littlewood et al 2012). Some studies of specific exercise approaches, for example eccentric exercise (Maenhout et al 2013), or patient-led exercise (Littlewood et al 2014) have not provided significant benefit beyond a mixed rehabilitation programme, while others have reported greater benefit with a more specific approach (Holmgren et al 2012). In light of the proposed associations discussed already between reduced subacromial space, poor posture and the development of RC tendinopathy, physiotherapy treatment is often aimed at improving scapular posture, and optimising humeral head depression through better RC activation, theoretically increasing the subacromial space or AHD. Acromiohumeral distance has been shown to be affected by shoulder position and muscle forces. Hinterwimmer et al (2003) showed that adducting muscle forces led to a significant increase in AHD compared to abducting forces. The influence of posture on AHD was assessed by Kalra et al (2010), where an upright sitting posture was shown to slightly increase the AHD at 45° of shoulder abduction, compared to slouched posture. A pilot study by Desmeules et al (2004) found that functional improvement following rehabilitation in patients with RC pathology was associated with an increase in AHD measured on ultrasound however no subsequent studies have examined the importance of this factor in patient recovery. These AHD studies have used small sample sizes and clinical, rather than imaging-based, diagnosis of RC pathology. The role of AHD and its relevance to rehabilitation in RC tendinopathy remains unconfirmed.

With the dearth of evidence for the mechanisms initiating and maintaining RC tendinopathy, the eclectic approach in physiotherapy treatment is not surprising. Achilles tendinopathy provides an interesting contrast. Intrinsic (non-compressive) tendinopathy has long been accepted as the primary mechanism underlying mid-portion Achilles tendinopathy. Subsequent to a favourable clinical study advocating a highly specific eccentric exercise programme directly loading the Achilles tendon, this approach dominated clinical practice for a number of years (Alfredson et al 1998). More recent studies have advocated the inclusion of multiple types of muscle contraction for the management of Achilles tendinopathy, but the focus has remained on a tendon loading programme as the first line, largely successful, conservative approach for this problem (Silbernagel et al 2011). It is clear that the evidence base for any specific exercise approach for RC tendinopathy is limited. In fact, despite the
wide body of clinical trials examining conservative interventions for RC tendinopathy, the mechanisms targeted by these interventions or how they have their effect remains poorly studied.

1.1.10 Surgical

The surgical approach to RC tendinopathy has been informed predominantly by extrinsic theories of RC tendinopathy, with subacromial decompression and acromioplasty the main operative approach employed, in addition to the repair of RC tears. A retrospective analysis of trends in the rates of subacromial decompression/acromioplasty surgery in the UK showed that the number of patients undergoing this surgery rose by a huge 746.4% over a 10-year period from 2000 - 2010 (Judge et al 2014). Over a similar time period, Vitale et al (2010) reported a 142% increase in acromioplasty surgery in the New York area of the USA, relative to only a 13% mean rise in other orthopaedic procedures. In a healthcare environment which is increasingly focused on evidence-based practice, it might be assumed that such an increase in a particular treatment option would be reflective of sound evidence for its effectiveness. However this is not borne out by the available research.

A systematic review of 4 studies comparing surgical to non-surgical approaches for RC tendinopathy concluded that long-term results of surgical approaches are not better than those of conservative management (Dorrestijn et al 2009). Similarly a Cochrane review of surgery for RC tendinopathy reported ‘Silver’ level evidence for no difference in outcome between subacromial decompression and conservative management (Coglan et al 2008). A randomized controlled trial involving 140 patients with chronic RC tendinopathy randomised to either arthroscopic acromioplasty followed by supervised exercise, or exercise alone. Follow-up was undertaken at both two and five years, with no difference in outcome between the groups (Ketola et al 2009, and 2013). A concurrent economic analysis of the two treatments showed that the surgical approach incurred more than double the cost of the alternative option. As discussed in Section 1.1.6.1, numerous studies have questioned the role of acromioplasty in the effectiveness of surgery for RC disorders, with equivalent results reported for RC repair or bursectomy alone (Goldberg et al 2001, McAllister et al 2005, Henkus et al 2009).

1.1.11 Summary
This literature review highlighted that potential interactions between extrinsic and intrinsic mechanisms of RC tendinopathy has received little attention in research to date. Surgical interventions for RC tendinopathy continue to be driven by extrinsic theories, with the acromioplasty procedure designed to create more space for the RC tendons under the coracoacromial arch by removing a portion of the underside of the acromion, and in some cases, sectioning of the coraco-acromial ligament (Shi and Edwards 2012). Effectiveness studies report no difference in outcomes between those undergoing acromioplasty procedures compared to conservative care (Ketola et al 2013), or between those undergoing bursectomy alone, without procedures involving the coraco-acromial arch (Henkus et al 2009). The lack of enhanced effectiveness of the acromioplasty approach suggests that by addressing only extrinsic mechanisms, perhaps the surgery is targeting the incorrect mechanism of injury to the tendon. Studies of the effect of exercise-based rehabilitation for RC tendinopathy consistently demonstrate improvements in pain and functional levels, but the effect sizes are often small (Hanratty et al 2012). The lack of understanding of mechanisms of RC tendinopathy may be contributing to a diluted approach for rehabilitation interventions, as clinicians attempt to address multiple factors with ever more complex exercise programmes and adjunctive interventions. There is a need for studies which examine mechanisms of early RC tendinopathy, with the aim of providing guidance for physiotherapy interventions.

1.1.11.1 Key Points

- The mechanisms contributing to the development of RC tendinopathy remain unclear.
- Substantial evidence suggests that acromial changes previously believed to be a primary causative factor in the development of RC tendinopathy may be secondary changes attributable to primary degeneration and insufficiency of the RC tendons.
- Intrinsic changes (e.g. thickening, tears) of the SsT, and reductions in the subacromial space have both been observed in those with RC tendinopathy, but it remains unclear how these factors relate to pain and function.
• Without clarity on the mechanisms involved, current physiotherapy programmes for RC tendinopathy remain non-specific and therefore provide varying levels of effectiveness in the management of painful RC tendinopathy.
• Equally, expensive surgical options, focusing on ameliorating extrinsic factors i.e. acromial shape, fail to provide an enhanced treatment option.
• A better understanding of mechanisms of RC tendinopathy is critical to improve outcomes, reduce unnecessary surgery, reduce healthcare costs, and inform the development of more targeted rehabilitation programmes for RC tendinopathy.
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The next section of the Literature review presents a published review examining models of tendinopathy, in particular evaluating the evidence for the continuum model of tendinopathy presented by Cook and Purdam (2009).

1.2 Study I: Continuum model of tendon pathology- where are we now?

1.2.1 Abstract

Chronic tendon pathology is a common, and often disabling condition, the causes of which remain poorly understood. The continuum model of tendon pathology was proposed in order to provide a model for the staging of tendon pathology, and to assist clinicians in managing this often complex condition (Cook and Purdam 2009). The model presents clinical, histological and imaging evidence for the progression of tendon pathology as a three-stage continuum: reactive tendinopathy, tendon dysrepair, and degenerative tendinopathy. It also provides clinical information to assist in identifying the stage of pathology, in addition to proposed treatment approaches for each stage. The usefulness of such a model is determined by its ability to incorporate and inform new and emerging research. This review examines the degree to which recent research supports or refutes the continuum model, and proposes future directions for clinical and research application of the model.

Keywords: tendon pathology, continuum, imaging
1.2.2 Introduction

Chronic tendon pathology, or tendinopathy, is a highly prevalent musculoskeletal condition affecting both athletes and non-athletes, with the most commonly affected tendons being the Achilles, patella, rotator cuff (RC) and elbow extensor tendons. Clinical management of tendinopathy can be challenging, and clinical trials have failed to provide robust evidence for many of the commonly used interventions (Krogh et al 2012, Coombes et al 2010, Woodley et al 2007). However, since it is broadly agreed that there is much yet to be understood about the causes of tendinopathy (Riley 2008), it is perhaps unsurprising that clinical trials including patients with a range of degrees of tendinopathy report equivocal results (Bennell et al 2010).

This review focuses on the continuum model of tendon pathology, as proposed by Cook and Purdam (2009), which provides a model for the staging of tendon pathology. Historically, research, assessment and treatment of tendon pathology were focused around an inflammatory model of pathology, which progressed to a perspective of the pathology as “failed healing”, followed by the more recent view of a primarily degenerative pathology with minimal inflammatory influence (Mafulli et al 1998). A number of authors have provided theoretical models to explain the basis for development of tendon pathology, or to assist clinicians in managing this condition. Neer (1972) and Blazina (1973) proposed what are essentially classification systems for the RC and patellar tendon respectively. Nirschl (1992) went a step further, and proposed a 5-stage model to describe the progression of tendon pathology using tennis elbow as an example. This model integrated pathological, histological and clinical findings and described a range of tendon states from healthy, through acute and chronic tendonitis, to tendinosis and rupture. Coombes et al (2009) advanced the modelling of lateral epicondylalgia with a framework that incorporated local changes in the muscle and tendon, along with changes in the wider pain system. The EdUReP model was developed by Davenport et al (2005) and is a theoretical framework for the conservative management of tendinopathy, with emphasis on the importance of patient education and controlled loading. However this model did not consider the staging of tendon pathology, or incorporate the growing area of tendon imaging.
In response to the need for a model which would provide an explanation for the diverse presentations of tendinopathy, while also providing a useful tool for clinicians, Cook and Purdam (2009) proposed a generic model of tendon pathology based around a continuum model, incorporating clinical, histological and imaging information. The model describes the early stages of reactive tendon pathology as a non-inflammatory proliferative tissue reaction, usually in response to acute overload or compression. The tendon thickens due to the up-regulation of large proteoglycans, and an increase in bound water, with minimal collagen damage or separation. Tendon dysrepair is characterised by greater tissue matrix breakdown, with collagen separation, proliferation of abnormal tenocytes, and some increase in tendon neovascularity. These two stages are considered to have some degree of reversibility, with the appropriate healing environment. The final stage of degenerative tendinopathy sees a further disruption of collagen, widespread cell death, and extensive ingrowth of neovessels and nerves into the tendon substance, leading to an essentially irreversible stage of pathology. The model is highly clinically applicable, with a framework describing how treatments might be best aligned with the stage of tendinopathy, along with descriptions of the clinical presentation of each stage. This model has the potential to provide a basis for more targeted assessment and treatment approaches in tendinopathy, however it was primarily based on lower limb tendinopathy. Lewis (2010) subsequently applied the model to RC tendinopathy, incorporating bursal pathology, and further emphasising the importance of optimal loading in maintaining normal tendon function and health. Cook and Purdam (2009) stated that the usefulness of this new continuum model will be evidenced in how successfully it can incorporate new and emerging research from pathology, clinical and imaging perspectives. Its applicability to practice will be proven by its uptake by clinicians for the assessment and management of tendinopathy. This review aims to evaluate the degree to explore recent tendon research in the context of the continuum model, and propose future directions for clinical and research application of the model.

1.2.3 Pathology studies

Recent studies of RC tendinopathy have provided further histochemical evidence for the idea of tendinopathy as a continuum. Longo et al (2011) showed that smaller tears
had more cell proliferation, and greater inflammatory cell infiltrate than larger tears, where collagen degeneration was predominant, and few cells were present. Similarly, Murphy et al (2012) examined tissue biopsy specimens from 45 patients with varying degrees of imaging or arthroscopically diagnosed RC pathology. There was significant reduction in vascularity and cell proliferation as pathology progressed towards the most degenerative stage. The results provide evidence of an early inflammatory component in those with tendinopathy but no tendon tears i.e. reactive or early dysrepair stage, while in the later degenerative stages of pathology (patients requiring arthroscopic surgery) there is reduced proliferative and vascular activity within the pathological tendon tissue.

A comprehensive review of the pathophysiology of tendinopathy was provided by Abate et al (2009) describing a “pathogenetic cascade” in which inflammation and degeneration are often concurrent processes. They describe how inflammatory, regenerative and degenerative changes proceed in parallel across early to late stage tendinopathies, resulting in a continuum ranging from healthy tendon to overt painful tendinopathy. Using an “iceberg model”, they propose that asymptomatic tendinopathy converts to symptomatic when higher levels of neural and vascular proliferative change have occurred. Determining the source of pain in tendinopathy remains a significant challenge for researchers. Current theories suggest that the pain arises from biochemical irritants (Fredberg and Stengaard-Pederson 2008), peritendinous tissues (Van Sterkenburg and Niek van Dijk 2011), or neurovascular ingrowth (Lian et al 2006). However, none of these factors have yet been correlated with a subjective measure of pain, and for example, neovascularisation has been widely shown to have little correlation with symptoms or clinical outcome despite the widespread use of injection therapies aimed at reducing it (Wilde et al 2011, Tol et al 2012). Therefore, while the pathological basis for the continuum model remains well supported, the process of transition towards pain in the structurally abnormal tendon is yet to be elucidated.

Healthy tendons are ‘plastic’ structures, capable of adapting to the load environment through alterations of their structural and mechanical properties (Killian et al 2012). The continuum model is strongly based around the effects of loading or unloading on tendon. The response of tendon to loading has been evaluated experimentally in a
variety of animal models (Edelstein et al 2011). While the application of this research has been perhaps primarily targeted towards developing surgical techniques for tendon tears, there is wide potential for such research to inform both the pathological basis for, and clinical application of the continuum model. For example, studies of fatigue loading in rats have demonstrated distinctly different tendon responses to different levels of strain. Sun et al (2008) demonstrated a dose-response effect in rat patellar tendon in vivo when undergoing cyclic loading, where lower strain levels produced a more favourable tissue deformation pattern than moderate or high strain, along with suppression of the activity of pro-inflammatory mediators, versus an increase in these substances in the tendons loaded to higher fatigue levels. Such an in vivo model offers potential to provide further histo-pathological and biochemical evidence to support choosing different exercise interventions for various stages of tendinopathy in humans.

In additional to exposure to loading, there are a multitude of extrinsic and intrinsic factors that may influence the development of tendinopathy (Lewis 2010). Extrinsic factors include local anatomical factors, posture and biomechanical factors, and occupational and sporting activities. Intrinsic and personal factors are also important in the pre-disposition of certain individuals to tendinopathy. Genetic factors have been identified as a predisposing factor in RC (Chaudhry and Carr 2012) and Achilles tendinopathy (Legerlotz et al 2012, Posthumus et al 2010). Metabolic factors also play a role in tendinopathy, with diabetes being a well known risk factor (de Oliveira et al 2011), and associations between adiposity and tendinopathy noted in both Achilles (Gaida et al 2009) and gluteal tendinopathy (Fearon et al 2012). Other than age, none of the tendinopathy models have incorporated intrinsic factors, perhaps due to their limited modifiability. However, such factors may be important in prognosis setting, with poorer capacity for recovery in affected individuals.

Knowledge about pain physiology in relation to musculoskeletal pathologies has advanced greatly in recent years, with a strong emphasis now being placed on the consideration of central sensitisation mechanisms, as well as psychosocial factors, in spinal pain in particular (Moseley et al 2003). There has been limited investigation of the role of these mechanisms in the development of chronic tendon pain. Studies of common elbow extensor tendinopathy have demonstrated the presence of mechanical
hyperalgesia, both locally at the tendon site and contralaterally, which has been proposed to be an indicator of sensitisation of the central nervous system (Coombes et al 2009). Similarly, lowered mechanical pain thresholds have been demonstrated in patellar and shoulder tendinopathy (van Wilgen et al 2011, Hidalgo-Lozano et al 2010). Studies of risk factors for RC dysfunction in occupational populations have generally emphasised the role of mechanical and work-related factors in the development of the disorder (van Rijn et al 2010), however psychosocial factors may be important in prognosis and development of chronicity (Horsley 2011). While this is an area that requires further research, with findings that may differ according to the site of tendinopathy and population, it appears important that the relative contribution of local versus central dysfunction to the individual’s pain presentation is considered in order to provide the most appropriate treatment.

Therefore, the continuum model continues to be supported by pathological research, with the possibility for animal studies to further reinforce the recommendations for load progression in tendinopathy rehabilitation. Ongoing developments in the understanding of how genetic, and metabolic factors, as well as pain physiology, may affect tendinopathy may be important to incorporate as the continuum model evolves.

1.2.4 Clinical studies

It is difficult to apply the continuum model to clinical studies, as no published clinical studies have attempted to subgroup or analyse tendinopathy participants according to stage or degree of pathology. In fact most studies include a heterogenous population of people with pathology of varying duration and severity. However, in an attempt to apply the continuum approach to existing studies, two studies of RC tendinopathy with conflicting results will be discussed. Holmgren et al (2012) carried out a randomised clinical trial involving RC tendinopathy patients who were on a waiting list for subacromial decompression. It is probable that this group of patients were from a relatively homogenous population that may have corresponded with the dysrepair or degenerative sub-categories. The trial compared specific loading exercises, including an eccentric component, to a simple range of motion exercise programme (control). The specific exercise group had significantly better improvement in their functional scores at 12 week follow-up, and only 20% of this
group went on to have surgery, versus 63% of the control group. In a study with contrasting results, Bennell et al (2010) recruited people with shoulder pain from primary care and community settings, and randomised them to receive an exercise and manual therapy intervention or a placebo ultrasound treatment. At the 11 week follow-up, there was no difference between groups in pain and disability scores, and, although the active exercise group showed better improvement in functional scores at 22 weeks, there was no significant between-group difference in pain at this time point. It is likely that the recruitment strategy used by Bennell et al (2010) resulted in quite a heterogenous group of participants, across the spectrum of RC tendon pathology. Since the continuum model suggests that reactive tendinopathy may benefit from reduced loading, it is possible that participants within the reactive subcategory would have done better in the placebo group, as ultrasound is a form of passive unloading, and active exercise may have exacerbated any reactivity present. The only directly comparable outcome measure at baseline between the two studies was the Visual Analogue Scale for pain. Mean resting pain was similar in the two studies (1.7 in the Holmgren study and 2.2 in the Bennell et al study), however activity related pain was higher in the Holmgren et al study (6.4 compared to 4.9 in the Bennell et al study), possibly supporting the greater degree of tendon pathology in the Holmgren study. As these studies were not designed in line with the continuum model, this discussion remains speculative. To further investigate this, future research investigations in tendinopathy could be designed to assess outcome against targeted interventions, according to the sub-categories of the continuum model.

Corticosteroid (CS) injection has been shown to be successful in treating pain in the short-term in both patellar and RC tendinopathy, however this benefit diminishes in the long-term or with more chronic presentations (Smidt et al 2002, Kongsgaard et al 2009). Van Ark et al (2011), in a recent systematic review of injections for patellar tendinopathy, suggest that different injections may be suitable for different stages of disease. For example, for reactive or early stage pathology, corticosteroid may be suitable to address the proliferative mechanisms involved while for dysrepair/degenerative stage other types of injection such as platelet-rich plasma, may be more suitable, in conjunction with loading programme, as they have a more regenerative mechanism of effect. Matthews et al (2006), in a histological study of RC tears, suggest that the use of CS injection for small RC tears may in fact be
detrimental, reducing their ability to heal and directing the tissue into a more degenerative, metabolically inert state. Injections provide another example of a treatment which could be optimised by targeting to the appropriate stage of tendon pathology.

1.2.5 Imaging studies

There have been a number of imaging based studies involving athletic populations that have provided evidence for the continuum model. Malliaris et al (2011) examined the patellar tendons of 58 volleyball players on a monthly basis using ultrasound imaging, and demonstrated that tendons transitioned between different stages of pathology e.g. normal to diffuse thickening, or hypoechoic to diffuse thickening. There was also a significant association between greyscale ultrasound changes and the presence of pain, with pain most likely if the tendon contained a hypoechoic region. Fredberg and Bolvig (2002) studied previously asymptomatic football players found that only players with sonographically abnormal patellar tendons at the beginning of the season went on to develop painful tendons, with no occurrence of pain in players who were sonographically normal in the pre-season. In a recent longitudinal study of asymptomatic ballet dancers, the presence of moderate or severe hypoechoic defects in the patellar and Achilles tendons on ultrasound was a weak predictor of the development of tendon-related pain and disability (Comin et al 2013).

In contrast, imaging has not provided a good basis for determining the outcome of treatment for tendinopathy. Ekeberg et al (2010) described a prognostic study examining factors associated with the success of corticosteroid injections in RC disease, and found that imaging findings (Magnetic Resonance Imaging (MRI) and ultrasound) were not good predictors of patient outcome. Drew et al (2014) systematically reviewed the evidence for the relationship between structural changes in tendon and the outcome of treatment, and made a strong argument against the use of structural changes to explain the effect of therapeutic interventions for tendinopathy. However, they suggest that imaging could perhaps be used to identify diagnostic sub-types within tendinopathy populations in order to better target treatment.
One of the biggest challenges in terms of the use of imaging in tendinopathy is the high degree of prevalence of asymptomatic structural changes - it is not possible as yet to differentiate between symptomatic and asymptomatic tendon pathology on any form of imaging (Moosmayer et al 2009). Similar issues in diagnostic radiology for spinal and knee pain have caused some authors to call for more judicious use of imaging in the clinical setting, and a need for better integration with clinical findings (Chou 2009, Englund et al 2008). Ultrasound has traditionally been the preserve of radiologists, but in recent years has been increasingly adopted as a “point of care” imaging modality by rheumatologists, sports medicine physicians and physiotherapists (Yim and Corrado 2012). This development could be a positive step towards better integration of imaging findings as part of the full clinical examination, which aligns well within the framework presented in the continuum model. Tendinopathy is often associated with ‘latent’ symptoms, developing subsequent to aggravating activity. The development of imaging protocols to assess changes in tendon properties (e.g. vascularity, thickness) in response to loading i.e. immediately after, 24 hours after) may be another method which could help identify tendons in the reactive stage of pathology (Shalabi et al 2004).

Newer protocols have opened up the possibilities for ultrasound imaging to contribute to knowledge regarding the structural properties of tendons. Ultrasound tissue characterisation (UTC) is a method which quantifies echo patterns in the greyscale US image, and provides a 3D reconstruction, which has been shown to be related to tendon histopathology (Van Schie et al 2003). A small study in chronic Achilles tendinopathy found that UTC could reliably distinguish between symptomatic and asymptomatic tendons (van Schie et al 2010). Arya and Kulig (2010) used dynamic ultrasound imaging and dynamometry to assess the stiffness, stress and strain of the Achilles tendon during isometric activity in men with Achilles tendinopathy and matched controls. Tendinopathic tendons exhibited a loss of stiffness and a reduced Young’s modulus (stiffness normalised to tendon geometry), potentially related to the loss of collagen structure in the pathological tendons, and giving some explanation for the loss of functional performance. Similar imaging methods were used by Morrissey et al (2011) to demonstrate a greater increase in Achilles tendon stiffness in response to an eccentric exercise programme in healthy individuals, compared to a similar group undergoing a concentric programme. Notwithstanding the potential limitations
of this 2D method in assessing what is a 3D phenomenon (Magnusson et al 2008), it offers at least some increased capacity to model tendon properties dynamically in-vivo, and in response to therapeutic interventions. Sonoelastography is another ultrasound-based method which provides an estimation of tissue elasticity or ‘hardness’, with pathological areas of tendon exhibiting a softer tissue spectrum. De Zordo et al (2009) showed that sonoelastography is highly sensitive and specific in identifying regions of pathology in the common extensor tendons of patients with clinical signs of lateral epicondylar pain. Further refinement of this technique is likely to provide useful information in staging and treatment planning in tendinopathy (Klauser et al 2010).

Scott and Khan (2010) discuss how a preventive treatment model for tendinopathy using imaging may be a way forward; where susceptible patients could be identified early on using ultrasound imaging, and suitable rehabilitative measures instigated. Fredberg et al (2008) undertook a preventive study aimed at preventing the onset of patellar tendinopathy in soccer players, where players with sonographically abnormal tendons undertook a prophylactic strengthening and stretching programme. This programme failed to prevent development of symptoms, and may in fact have increased the risk in some players. As such, the content of any preventive or early stage programme remains to be determined; however an effective programme could have widespread benefit in reducing the personal and economic cost of chronic tendinopathies.

1.2.6 Summary

It is clear that the continuum model continues to be supported by pathological research; however clinical research has continued to favour a heterogeneous model of tendon pathology, with the result that the optimal intervention for each stage of pathology is still unknown. While imaging has failed to provide a mechanism for this staging process to date, suggestions have been made as to how new developments in imaging technology may be able to further develop this process. The continuum model could be supplemented with prognostic information in terms of patient–based factors, both physical and psychosocial, in order to optimise its use in terms of treatment choice for the individual patient.
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1.3 Thesis Aims

The literature review highlighted continued uncertainty regarding the mechanisms of RC tendinopathy, in particular the importance of the interaction between extrinsic mechanisms, i.e. tendon compression in the subacromial space, and intrinsic changes in the supraspinatus tendon (SsT).

This thesis aims to contribute to the knowledge base to better understand the relationship between intrinsic and extrinsic mechanisms of RC tendinopathy, through the evaluation of ultrasound measures of the subacromial space and the SsT, and how these parameters are altered by the presence of painful tendinopathy and the imposition of load.

Aims:

- To investigate the reliability and validity of ultrasound measures of AHD
- To compare ultrasound measures of AHD and SsT thickness in people with and without RC tendinopathy, and among those with different degrees of shoulder pain
- To examine the short-term effect of fatigue loading on SsT thickness and AHD in people with and without RC tendinopathy

1.3.1 Thesis outline

This thesis is presented in a research publication format. Three papers have been published in peer-reviewed journals, and as of July 30th 2014, one has been accepted subject to revisions, and the remaining three are under review. Some formatting changes have been made to the presentation of the papers in terms of referencing styles, table layout and numbering to provide uniformity across the thesis; however the text appears as it does in the published or submitted articles.

Chapter 1 contains an introductory literature review, together with a published review of the continuum model of tendon pathology. Chapter 2 focuses on methods, and comprises three papers, the first a published systematic review of AHD measurement, the second a published validity study examining construct validity of
AHD measurement, and the third, currently under review, presents a reliability study of ultrasound measures of AHD and SsT thickness. **Chapter 3** presents two clinical studies. The first paper (under review), reports on a cross-sectional study examining AHD and SsT thickness in people with and without RC tendinopathy, while the second paper (accepted for publication) describes an experimental study examining the effect of short term loading on the SsT and AHD. **Chapter 4** comprises a summary and discussion of the preceding papers.

Finally, **Chapter 5** focuses on knowledge translation, and is presented in the format of a paper evaluating a Community of Practice approach to improving knowledge translation in shoulder pain for primary care physiotherapists.
Chapter 2: Methods: Reliability and Validity

This chapter contains three papers, two of which have been published in the peer-reviewed literature, with the third currently under review.

The primary research questions for this chapter were:

- Study II: What is the current evidence for the intra- and inter-rater reliability of radiological methods of measuring AHD in people with RC tendinopathy?
- Study III: What is the construct validity of ultrasound measurements of AHD?
- Study IV: What is the intra- and inter-rater reliability of ultrasound measurements of AHD and SsT thickness in asymptomatic controls and people with RC tendinopathy?
2.1 Study II: Acromiohumeral distance measurement in rotator cuff tendinopathy: is there a reliable, clinically applicable method? A systematic review.
McCreesh KM, Crotty JM, Lewis JS. Br J Sports Med, 2013; Epub ahead of Print

2.1.1 Abstract
Background: Narrowing of the subacromial space has been noted as a common feature of rotator cuff (RC) tendinopathy, and has been implicated in the development of symptoms, and forms the basis for some surgical and rehabilitation approaches. Various radiological methods have been used to measure the subacromial space, which is represented by a two-dimensional measurement of acromio-humeral distance (AHD). A reliable method of measurement could be used to assess the impact of rehabilitation or surgical interventions for RC tendinopathy, however there are no published reviews assessing the reliability of AHD measurement.

Objectives: The aim of this review was to systematically assess the evidence for the intra- and inter-rater reliability of radiological methods of measuring AHD, in order to identify the most reliable method for use in RC tendinopathy.

Study appraisal and synthesis: An electronic literature search was carried out and studies describing the reliability of any radiological method of measuring AHD in either healthy or RC tendinopathy groups were included. Eighteen studies met the inclusion criteria, and were appraised by two reviewers using the Quality Appraisal for reliability Studies (QAREL) checklist.

Results: Eight studies were deemed to be of high methodological quality. Study weaknesses included lack of tester blinding, inadequate description of tester experience, lack of inclusion of symptomatic populations, poor reporting of statistical methods and unclear diagnosis. There was a strong evidence for the reliability of ultrasound for measuring AHD, with moderate evidence for Magnetic Resonance Imaging (MRI) and Computed Tomography(CT) measures, and conflicting evidence for radiographic methods. Overall there was a lack of research in RC tendinopathy populations, with only 6 studies including participants with shoulder pain.

Conclusion: The results support the reliability of ultrasound and CT or MRI for the measurement of AHD, however more studies in symptomatic populations are required. The reliability of AHD measurement using radiographs has not been supported by the studies reviewed.

Keywords: acromiohumeral distance, rotator cuff, reliability
2.1.2 Introduction

Shoulder pain is a common musculoskeletal condition, with point prevalence rates of between 7 and 26% in adults (Luime et al 2004). The most common source of adult shoulder pain is rotator cuff (RC) tendinopathy, which is a multi-factorial condition (Lewis 2010). The supraspinatus tendon (SsT), which runs in the subacromial space, is most commonly affected by pathological change. Narrowing of the subacromial space has been variously ascribed to: loss of RC function leading to superior migration of the humeral head (Deutsch et al 1996), altered acromial morphology (Neer 1972), or postural alterations (Ludewig and Reynolds, 2009). This phenomenon of a reduced subacromial space, and proposed resulting impingement of the RC tendons and subacromial bursa, has been widely implicated in the development of degenerative RC pathology and pain in both athletic and non-athletic populations (Lewis 2010).

The size of the subacromial space is commonly quantified by the measurement of distance between the acromion and the humeral head termed the ‘acromiohumeral distance’ (AHD), using a variety of different radiological methods, including radiographs, CT scans, MRI, and ultrasound. Studies of AHD in asymptomatic shoulders have reported ranges of AHD from 6 to 12 mm in the neutral position (Girometti et al 2001, Schmidt et al 2004, Wang et al 2005). The source of this variation may be due to inter-individual variability, or the variety of measurement protocols used. Generally, AHD is found to be reduced as the arm moves into abduction up to 90°(Giphart et al 2012) and has been shown to be influenced by muscle contraction (Graichen et al 2001), and by muscle fatigue (Chopp at el 2010). In symptomatic populations, radiographic studies have suggested an AHD cut-off point of 6-7mm to indicate the presence of a significant RC tear, with recent work by Goutallier at al (2013) suggesting that a 6mm cut-off is indicative of a large tear, not amenable to surgical repair. Other radiological studies have demonstrated that AHD is smaller in patients with RC tendinopathy (Cholewinski et al 2008), is positively associated with the size of the RC tear and degree of fatty degeneration of the RC muscles (Saupe et al 2006), and is a predictor of both short-term disability (Hebert et al 2003) and functional status (Mayerhoefer et al 2009).
Surgical interventions, such as acromioplasty, as well as many rehabilitation interventions for RC tendinopathy, are based around attempting to correct or ameliorate a reduced AHD, with the expectation that this will improve shoulder symptoms and function (Lewis 2010). It is therefore important that a reliable method of AHD measurement is identified, in order to confirm the veracity of this hypothesis. Reliability of a measurement relates to the degree to which it is consistent, and free from error. There are numerous variables that may influence the reliability of AHD measurement including; type of imaging used, measurement protocol, patient position, presence and degree of tendinopathy, and inter-examiner variables. Although a recent review evaluated AHD measurement by ultrasound in RC tendinopathy (Seitz & Michener 2011), concluding that ultrasound-measured AHD is smaller in individuals with RC tears, no assessment of measurement reliability was carried out. No reviews to date have examined the reliability of any other radiological method. There is a need for a systematic review assessing the reliability of AHD measurement, so that a more robust basis for the assessment of AHD in individuals with RC tendinopathy can be recommended. In turn, the contribution of reduced AHD to shoulder pain and loss of function, and the impact of AHD alteration with physical or surgical interventions could be determined. Therefore, the aim of this review was to systematically assess the evidence for the intra- and inter-rater reliability of radiological methods of measuring AHD in relation to RC tendinopathy.

2.1.3 Methods

2.1.3.1 Inclusion/Exclusion criteria

Studies describing the reliability of a method of measuring AHD by any radiological method (specifically radiographs, MRI/MRA, CT, ultrasound) were the focus of this review. We included studies that reported collection and analysis of any reliability data, whether or not this was a primary aim. Studies involving human adult populations, either healthy subjects or subjects with diagnosed RC tendinopathy of any degree, as well as studies including those with RC tendinopathy as a subset of other shoulder pathologies were included. We excluded studies of patients with non-RC shoulder disorders e.g. instability, and neurological conditions, as the degree and direction of change in AHD is likely to be different in these populations. We did
however conduct a sensitivity analysis to assess how many papers of non-RC disorders were excluded and whether this had any influence on the conclusions of this review. We only included studies published in the English language.

### 2.1.3.2 Search Strategy

The search strategy was developed with the help of a medical librarian, and involved searches of the following databases, from inception until June 2012: PubMed, CINAHL, MEDLINE, AMED, Sport Discus (using a combined search on the EBSCO database); Google Scholar; ProQuest digital dissertations; Cochrane Central Register of Controlled Trials (CENTRAL); and the Physiotherapy Evidence Database (PEDro). Searches were conducted using the search terms and combinations illustrated in Figure 6.

![Boolean logic of search terms](image)

**Figure 6 Boolean logic of search terms**

The names of the radiological methods (e.g CT, MRI) were not used in the final search, as this may have restricted the number of papers identified. We also did not include terms related to reliability, as our aim was to also include papers where
reliability analysis was conducted as a pilot or secondary aspect of the study. The search syntax was modified to match that in use in each of the databases.

The reference list of each relevant full-text article was reviewed to identify any potential additional references, as well as that of the single relevant systematic review identified. Initial screening of articles by title and abstract to remove clearly unrelated titles, was conducted by a single examiner. All identified references were examined by title and abstract in relation to the inclusion and exclusion criteria, independently by two reviewers (KM, JL). Potentially relevant articles were then obtained in full text format. Two reviewers applied the selection criteria to the full text articles, to determine the final ones to be included. A third examiner (JC) was available to resolve disagreement, however was not required. A citation search for all included studies was carried out, but no further relevant studies were identified.

2.1.3.3 Quality Assessment and Data extraction

Quality assessment of the included studies was completed using the Quality Appraisal for Reliability Studies (QAREL) checklist (Lucas et al 2010). As recommended by Lucas et al (2010), piloting of the checklist was carried out as follows: a single study (one of those included in the review) as jointly assessed by the examiners, with discussions and agreement as to how each item was to be defined in relation to this review. Then two studies excluded from this review (as they examined AHD measurement in neurological populations) were independently assessed with the checklist by two examiners (KM, JL). Agreement on the first study was 72%. Further discussions followed, and subsequently agreement on the second study was 100%.

QAREL checklist items are described in Table 1. It was deemed that item 5 of the checklist was not applicable to this review as there is currently no accepted, definitive reference standard for the measurement of AHD. In relation to the final item, regarding statistical measures, we required that studies using an intra-class correlation co-efficient (ICC) reported the model of ICC being used, and also that estimates of precision be presented, in order to achieve a “Yes score” for this item. Two reviewers independently assessed all included studies. Studies were deemed to be high quality if at least 50% of applicable items were rated as “Yes” on the checklist. Data was extracted from the studies using the QAREL extraction form. The appropriateness of the radiological protocols used in the included studies was separately assessed by an
experienced musculoskeletal radiologist (JC). For the purposes of this review, the reliability estimates from ICCs were categorised as suggested by Fleiss (1986) that is, >0.75=excellent reliability, 0.40–0.75=fair to good reliability, and <0.40=poor reliability. Due to the heterogeneous nature of the methods and populations studied, pooling of data was not deemed appropriate in this review. Instead a ‘levels of evidence’ approach was taken, using a modified version of the Cochrane Back Pain Group criteria (van Tulder et al 2003) i.e:

Strong evidence – consistent findings in multiple high quality studies

Moderate evidence – consistent findings in one high quality and one or more lower quality studies

Limited evidence – consistent findings in one or more lower quality studies

No evidence – if there were no studies or conflicting results
2.1.4 Results

The literature search retrieved a total of 2115 citations, from which 2073 non-relevant titles or duplicates were removed in the initial screening by a single examiner (See Figure 7). Two reviewers then assessed the remaining 42 by title and abstract. These were narrowed down to 21 based on the specified inclusion and exclusion criteria. Following the examination of full-text, a further two were obtained from the reference lists. Of these, 18 were included in the review, following exclusion of five papers as

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**Table 1: QAREL checklist items (Lucas et al 2010)**

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<th>QAREL CHECKLIST</th>
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<td>1. Was the test evaluated in a sample of subjects who were representative of those to whom the authors intended the results to be applied?</td>
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<td>3. Were raters blinded to the findings of other raters during the study? <em>(inter-rater studies only)</em></td>
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<tr>
<td>4. Were raters blinded to their own prior findings of the test under evaluation? <em>(Intra-rater studies only)</em></td>
</tr>
<tr>
<td>5. Were raters blinded to the subjects' disease status or the results of the accepted reference standard for the target disorder (or variable) being evaluated? <em>(excluded in this review)</em></td>
</tr>
<tr>
<td>6. Were raters blinded to clinical information that was not intended to form part of the study design or testing procedure?</td>
</tr>
<tr>
<td>7. Were raters blinded to additional cues that are not part of the test?</td>
</tr>
<tr>
<td>8. Was the order of examination varied?</td>
</tr>
<tr>
<td>9. Was the stability (or theoretical stability) of the variable being measured taken into account when determining the suitability of the time interval among repeated measures?</td>
</tr>
<tr>
<td>10. Was the test applied correctly and interpreted appropriately?</td>
</tr>
<tr>
<td>11. Were appropriate statistical measures of agreement used?</td>
</tr>
</tbody>
</table>
three contained reliability co-efficients only, without details of the method of reliability assessment, and 2 did not present the AHD measures separately, but as part of a ratio measure. In the sensitivity analysis, two papers evaluating AHD measurement reliability in non-RC shoulder disorders were identified. Both were carried out in populations with hemiplegic shoulders, and both concluded that ultrasound was a highly reliable method of measurement, aligning closely with the conclusions of the papers included in this review.

Figure 7 PRISMA Flow diagram of search results

2.1.4.1 Quality assessment

Agreement for QAREL items between the two assessors after independent assessment of the 18 studies was 88%, with an average Cohen’s kappa value of 0.95, demonstrating an excellent level of inter-rater agreement (Landis & Koch 1977). Joint discussions resolved remaining areas of disagreement, and the final ratings are displayed in Table 2. Of the 18 studies assessed with the QAREL checklist, eight were deemed to be of high quality. There was limited detail describing the blinding
of examiners, and randomisation of testing procedures, resulting in the majority of studies being rated “Unclear” on items 6, 7 and 8. A high proportion of incorrect statistical analysis, or inadequate information, also led to Item 11 being rated as “No” or “Unclear” for most studies. Six studies gave no information regarding training or experience of the testers, which left the rating for Item 2 “Unclear” for these studies. The decision to include studies which reported reliability data as a secondary aspect only, presented a possible risk of increasing the proportion of lower quality studies. However, there was in fact a similar proportion of high quality studies among both the primary (4/11) and secondary (3/7) reliability studies examined. There was also no difference in the proportion of high quality studies according to radiological modality.
**QAREL ITEMS**

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Study type</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>*High Quality?</th>
</tr>
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<tbody>
<tr>
<td>Duerr 2010</td>
<td>US</td>
<td>1°</td>
<td>Y</td>
<td>?</td>
<td>NA</td>
<td>Y</td>
<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Yes</td>
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<td></td>
</tr>
<tr>
<td>Fehringer et al 2008</td>
<td>XRay</td>
<td>1°</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gruber et al 2010</td>
<td>XRay</td>
<td>1°</td>
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<td>Y</td>
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<td>Y</td>
<td>Y</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Kumar et al 2011</td>
<td>US</td>
<td>1°</td>
<td>N</td>
<td>?</td>
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<td>Y</td>
<td>?</td>
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<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seitz et al 2012</td>
<td>US</td>
<td>2°</td>
<td>Y</td>
<td>Y</td>
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<td>?</td>
<td>?</td>
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<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Quality appraisal of included studies using QAREL checklist

QAREL=Quality Appraisal for Reliability Studies; US= ultrasound MRI= Magnetic resonance Imaging, CT=Computed Tomography, Y=Yes, N=No, NA=Not applicable, ?=Unclear

* For high quality, 50% of applicable items had to achieve a “yes” score

QAREL Item 5 was omitted, considered not applicable due to there being no accepted reference standard for AHD measurement. Study type: 1°= Reliability assessment was a primary aim of the study, 2°= study reported reliability data as a secondary or pilot aspect.
2.1.4.2 Type of study

The details of the studies included in this review in terms of study type, population, testers, methods, reliability data, and mean AHD values reported, divided up according to radiological modality used are summarised in Tables 3-5. Over half of the studies (10/18) employed ultrasound to assess AHD, with four studies using radiographs, two employing MRI only, and two using combined methods (MR and radiographs, or MRI, radiographs and CT). Eight studies assessed intra-rater reliability - these were predominantly studies using US (7/8). Inter-rater reliability or both types of reliability were assessed in five studies each. The majority of studies (12/18) assessed reliability of AHD measurement in healthy or athletic populations, with six investigating people with shoulder pain.

2.1.4.2.1 Ultrasound studies

Of the 10 studies using ultrasound to measure AHD, seven assessed the reliability of a single examiner (intra-rater), while one investigated reliability of two or more examiners (inter-rater), and two studied both types of reliability. Two studies included reliability data on participants with shoulder pain. Kalra et al (2010) studied intra-rater reliability only in 31 participants with MRI-diagnosed RC disease (mean age: 53.5 years), and Pijls et al (2010) studied both inter and intra-rater reliability in 43 people described as having subacromial impingement syndrome (mean age: 51 years) as diagnosed by an orthopaedic surgeon, without giving any details of how diagnosis was determined. The remaining eight studies assessed reliability in pain-free participants (Desmeules at al 2004, Duerr 2010, Kumar et al 2010, Kumar et al 2011, Leong et al 2012, Maenhout et al 2012, Seitz et al 2012, White et al 2012). Mean subject age in the pain-free study groups ranged between 21 and 34 years, with a single study by Kumar et al (2010) involving older participants (mean age 64.2 years). Five studies were deemed to be of high methodological quality (Table 2), and each of these reported a good or excellent level of either inter and/or intra-rater reliability.

The testers undertaking the ultrasound scanning were physiotherapists in seven of the studies (Duerr 2010, Kumar et al 2010 Kumar et al 2011, Leong et al 2012, Maenhout et al 2012, Seitz et al 2012, White et al 2012), variously described as having training ranging from one hour to three months; and radiologists in two of the studies (Desmeules et al 2004, Pijls et al 2010), with one study not providing details of the
raters (Kalra et al 2010). Pijls et al (2010) reported similar degrees of reliability between an experienced radiologist (ICC=0.94) and a novice in ultrasound (ICC=0.92), while in two studies by the same authors, one using a physiotherapist trained in shoulder ultrasound, and the other using student physiotherapists, with limited training or experience, slightly better reliability was reported with the experienced examiner (ICC=0.96-0.99) (Kumar et al 2010) compared to the novices (ICC=0.88-0.91) (Kumar et al 2011).

All studies reported the reliability of measuring separate images of the same subject, while two also studied the intra-rater reliability of repeated measurements of the same image (Pijls et al 2010, White et al 2012). There were varied time intervals used for the repeated scans, ranging from within-session scans, to others taken up to two weeks (Kumar et al 2010), or six weeks later (Maenhout et al 2012). While various factors may influence the normal variation in AHD over time (such as posture, fatigue, activity), no studies described controlling for these factors.

All studies used a high frequency linear transducer (between 5 and 12.5 MHz) to acquire the ultrasound scans. There was variation in transducer placement, with two studies placing it on the anterior part of the acromion (Desmeules et al 2004, Seitz et al 2012), while others used the posterior or mid-acromion (Kalra et al 2010), or did not give adequate details of the testing protocol. There were also differences in how AHD was measured between studies. Six studies described that the measurement of the shortest distance between the acromion and humeral head was assessed, usually along a line parallel to the acoustic shadow cast by the acromion (Desmeules et al 2004, Kalra et al 2010, Maenhout et al 2012, Pijls et al 2010, Seitz et al 2012, White et al 2012). In contrast, three studies measured the distance between edge of the acromion and the tip of the greater tuberosity (Kumar et al 2010, Kumar et al 2011, Leong et al 2012), which anatomically is a longer distance. Duerr (2010) reported equal reliability measuring both of these distances. As the greater tuberosity cannot be visualised when the arm is moved into abduction, the author recommended the alternative measurement as the standard. The neutral shoulder position was used in all studies, while additional scans in various positions of either active or passive abduction (30°, 45°, 60° and 90°) were carried out by seven studies (Table 3).
Overall there was a strong level of evidence for the reliability of ultrasound in the measurement of AHD. Intra-rater reliability was found to be good to excellent with almost all ICC values being above 0.75. However inter-rater reliability was poorer, with the single high quality inter-rater study (Pijls et al 2010) reporting an inter-rater ICC of just 0.70. Since study methods were similar across the ultrasound studies, forest plots were constructed to illustrate the range of ICC values reported (Figures 8 and 9). Standard error of measurement values for AHD were more variable; they were below 1mm in the high quality studies by Duerr (2010) and Seitz et al (2012) and in a number of lower quality studies (Kumar et al 2010, Leong et al 2012, Maenhour et al 2012), however Kalra et al (2010) reported higher SEM values of 0.9-1.6mm in their high quality study. Three studies reported the minimal detectable change (MDC) for AHD measurement, which is an important concept representing the amount of change required to exceed measurement variability. Reported MDC values in neutral shoulder position for AHD were 0.9mm (Duerr 2010) and 1.3mm (Kalra et al 2010), and 2.1mm for acromion to greater tuberosity distance (Leong et al 2012).

Figure 8 Illustrative forest plot of intra-rater reliability of acromiohumeral distance measurement with ultrasound in neutral shoulder position (ICCs +/- 95% confidence intervals, where available)
2.1.4.2.2 Radiograph studies

Among the six studies assessing the reliability of using radiographs to measure AHD, four included people with shoulder pain (Saupe et al 2006, Bernhardt et al 2012, Gruber et al 2010, Werner et al 2008), with Saupe et al (2006), Werner et al (2008) including people with confirmed RC disease, while a further two solely studied pain-free participants (Fehringer et al 2008, Thompson et al 2011). The mean age range of the shoulder pain subjects was from 55-59 years, while the pain-free groups were in the 20-35 year age range (See Table 4). Two studies each assessed either intra-rater (Fehringer et al 2008, Thompson et al 2011) or inter-rater reliability (Saupe et al 2006, Werner et al, 2008), while the remaining two studied both types of reliability (Bernhardt et al 2012, Gruber et al 2010). Three of the radiograph studies were deemed to be of high methodological quality (Saupe et al 2006, Fehringer et al 2008, Gruber et al 2010).

Three studies examined the reliability of radiographs in measuring AHD (Bernhardt et al 2012, Fehringer et al 2008, Gruber et al 2010), one examined digital fluoroscopy (Thompson et al 2011), and two studied radiographs along with other modalities (Saupe et al 2006, Werner et al 2008). Three of the radiograph studies used

![Illustrative forest plot of inter-rater reliability of acromiohumeral distance measurement with ultrasound in neutral shoulder position (ICC +/− 95% confidence intervals, where available)](image-url)
standardised views (Gruber et al 2010, Saupe et al 2006, Werner et al 2008), while Bernhardt et al (2012) examined non-standardised films from various clinics, and Fehringer et al (2008) studied the effect of differing beam angles. The majority of the studies examined the reliability of reading a single set of radiographs, whereas the Thompson et al (2011) and Fehringer et al (2008) studies measured the reliability of reading repeated films of the same participant; with each of the radiographs taken at a different angle or arm position in the Fehringer et al (2008) study. Poor reliability was reported for the measurement of these different views. In the studies by Bernhardt et al (2012) and Gruber et al (2010), it was clear that reliability was enhanced when using standardised radiographs (intra-rater: maximum difference = 3mm), prospectively collected for the study, than when non-standardised radiographs were examined retrospectively (intra-rater: maximum difference = 7mm). In one of the high quality studies, Saupe et al (2006) examined the inter-rater reliability of measuring AHD on standard AP radiographs between an experienced and non-experienced radiologist, and reported excellent reliability (ICC= 0.77), similar to the findings of the poorer quality Werner et al (2008) study, where four observers also achieved excellent inter-tester reliability examining AHD on 40 radiographs. Thompson et al (2011) reported good intra-rater reliability of measuring digital fluoroscopy images taken immediately in succession (ICC=0.75-0.99), with poorer reliability for those taken 9 months apart (ICC=0.3-0.99). It was not possible to undertake any direct comparisons of the reliability data between these studies, as a wide variety of statistical methods of reporting were used. However, overall, due to the use of non-standardised imaging, or poor reporting of statistical analysis, the evidence was conflicting for the reliability of AHD measurement using radiographs, which according to the Cochrane criteria, equates to no evidence.

2.1.4.2.3 CT and MRI studies

Two studies examined the measurement of AHD using open MRI systems (Hinterwinner et al 2003, Moffet et al 1998), while one used conventional MRI (Saupe et al 2006), and another both MRI and CT imaging (Werner et al 2008). A single study, by Saupe et al (2006), was rated as being of high quality.

The method of measurement was similar across all studies using CT or MR imaging, using the shortest distance between the inferior surface of the acromion and the upper
sub-chondral surface of the humeral head (See table 5). Two studies examined inter-rater reliability (Saupe et al 2006, Werner et al 2008). Two also examined intra-rater reliability, with Hinterwimmer et al (2003) achieving this by repeating the scans within a single session, while Moffet et al (1998) did so by re-reading the same scans one month later.

For the open MRI studies, only pain-free subjects were used. Hinterwimmer et al (2003) used a single healthy volunteer for inter-rater reliability assessment and reported low co-efficients of variation, suggesting reasonable accuracy of measurement, while Moffet et al (1998) assessed both inter and intra-rater reliability in 13 pain-free subjects, and reported excellent reliability, with ICCs all >0.75. People with shoulder pain participated in the studies by Werner at al (2008) assessing the reliability of AHD measures with MRI, CT, and radiographs, and Saupe et al (2006) using MRI and radiographs. MRI and CT imaging were shown to be similarly reliable to radiographs in the Werner at al (2008) study, while MRI had better reliability than radiographs in the Saupe et al (2006) study. Since Werner et al (2008) reported their reliability statistics using regression analysis (r=0.8 for CT and MRI), and Saupe et al (2006) reported an ICC value (0.91), it is difficult to make direct comparisons of the degree of reliability. However it appears that good levels of inter-rater reliability were achieved in both studies. Overall, there was a moderate level of evidence for the reliability of AHD measurement using CT and MR imaging (based on results of one high and two lower quality studies).

2.1.5 Discussion

This review evaluated the reliability of AHD measurement using radiological means. The majority of reliability studies assessed ultrasound methods. Study quality, as assessed by the QAREL checklist, was generally poor with less than half of the studies deemed to be of high quality. Major weaknesses of the studies reviewed were in the areas of tester blinding to their own and others measures, as well as to additional cues, such as side of symptoms, while undertaking imaging and/or measurement. While overall levels of reliability were good to excellent across the studies, there was more high quality evidence for the reliability of ultrasound as a method of AHD measurement, than for other modalities.
When assessing the reliability of imaging-based assessments, two distinct aspects of reliability exist. One is the reliability of measuring the image itself, incorporating any variability associated with localising anatomical landmarks, how measurements are made, and measurement error; and which is assessed by carrying out repeated measurements of the same image. The other is the reliability of taking repeated images of the same subject, which encompasses a myriad of variables such as; positioning of the subject, setting imaging parameters, operator-related variability, machine calibration, etc. The first type is likely to yield better reliability co-efficients, with less potential for variation. The second type is more challenging, potentially yielding poorer reliability; however it is important in the context of test-retest studies. All of the ultrasound studies assessing intra-rater reliability assessed the measurement of repeated images, while some also undertook re-measurement of the same images. However the majority of the other imaging studies re-measured the same set of images, which may have led to over-inflation of reliability levels. Thompson et al (2011) and Hinterwimmer et al (2003) carried out repeated imaging (in digital fluoroscopy and open MRI respectively), however this was in a very small number (N=1 and N=5) of pain-free subjects. It is accepted however, that repeated radiation exposure may make this type of study ethically unacceptable for radiograph and CT studies.

Item 9 in the QAREL checklist (Table 1) emphasises the importance of taking into account the stability of the measure when determining the time scale for repeated measures (Lucas et al 2010). The allowance of a significant time lapse between testing sessions, without indicating how possible confounding variables such as fatigue and posture, have been controlled for, threatens the internal validity of the observations being made. In contrast, the studies in this review using time intervals of a few days up to 6 weeks in pain-free subjects reported excellent reproducibility of the AHD measures, despite little description of controlling for confounding variable, suggesting that the measurement is reasonable stable over this time period. However, only within-session reliability of AHD measurement was available in this review for shoulder pain populations, therefore the stability of the measure in RC pathology over time is unknown.
The widespread use of pain-free populations for reliability testing reduces the external validity of the findings, as there may be significant differences in the degree of reliability achieved in pain-free versus shoulder pain populations due to greater challenges of positioning the painful arm and the potential influence of pathology on image quality. One third of the included studies involved people with shoulder pain, and one study (Maenhout et al 2012) included an athletic population. Within the pain-free populations, the age range of subjects tended to be much lower than the typical population age range for RC disorders. The studies by Kumar et al (2010, 2011) demonstrated the importance of including the relevant age groups as controls, due to the lower AHD values in the older age group. In the studies of shoulder pain groups, Kalra et al (2010) and Saupe et al (2006) confirmed the RC pathology using imaging, with Pijls et al (2010) using a clinical diagnosis, and Werner et al (2008) using unspecified diagnostic criteria, and a non-specific shoulder pain group used in the remaining studies (Bernhradt et al 2012, Gruber et al 2010). Unfortunately, the single study to include both shoulder pain subjects and pain-free controls did not separately report the reliability for the two groups (Kalra et al 2010). Further information is also required concerning AHD reliability in athletic versus non-athletic populations.

The issue of tester experience and qualifications is important in any imaging-based study. Ultrasound, in particular, is said to be highly operator-dependant (O’Connor et al 2005). Two of the ultrasound studies stated that radiologists conducted the scans, while the remaining majority stated that operators were physiotherapists with varying, but generally poorly described levels of training and experience in shoulder ultrasound imaging. An experienced and novice ultrasound operator achieved similarly excellent reliability in the Pijls et al (2010) study, while the two studies by Kumar et al (2010, 2011) illustrate better reliability for an operator with moderate levels of training versus physiotherapy students (although both studies achieved ICC >0.75). However, these studies suggest that reliable AHD measures can be achieved with a limited level of ultrasound training, in contrast to the higher level of training and experience needed to accurately undertake full diagnostic assessment of the shoulder. Based on MDC values provided, a single tester can achieve an accuracy level of between 0.9-1.3mm for ultrasound measurement of AHD in neutral, so that any change beyond this can be accepted as true change. No MDC was reported in the inter-tester reliability studies.
In addition to tester variability, the standardisation of imaging protocols for radiographs, CT and MRI are important elements in assessing reliability, clearly evidenced in the Bernhardt et al (2012) and Fehringer et al (2008) studies, where the use of non-standardised radiographs was shown to negatively influence reliability. As previously discussed in the review by Seitz & Michener (2011), different landmarks were used for the measurement of AHD in some of the ultrasound reliability studies. Most authors measured the shortest distance between the inferolateral acromion and the closest part of the humeral head, however others chose to measure AHD from the acromion to the tip of the greater tuberosity (Kumar et al 2010, 2011, Leong et al 2012), while Duerr (2010) carried out both measures. The shortest distance measurement is most closely aligned with the measurement protocols used in radiograph, MR and CT imaging studies, therefore it is suggested that this is the most useful measurement to report. Overall, it is recommended that clearer descriptions of tester experience and standardisation of imaging procedures are provided in imaging reliability studies, to allow better extrapolation of findings across studies.

While reliability of a measurement is critical to inform its use, since it refers to how consistent a measuring device is, it is equally important to evaluate the validity of the measurement, which confirms whether a study measures or examines what it claims to measure. As the subacromial space is a 3-dimensional space, there is an inherent problem in that; conventional radiographic imaging merely measures in two dimensions. There is no evidence or general agreement as to which modality provides a “gold standard” for AHD measurement, which led to the exclusion of Item 5 of the QAREL checklist for this review. With ultrasound, it is not possible to view the under-surface of the acromion due to the acoustic shadow produced by the bone; therefore the area of the smallest AHD may not be viewed or measured accurately. While radiographs provide a clearer view of the bony structures, projection issues and bony overlap may lead to measurement inaccuracies. Both ultrasound and radiographs are conducted in the functional upright position, adding face validity to these measures, however standard MR and CT imaging is carried out with the patient in the supine position, where the lack of the arm weight, gravity and absence of muscle activity may lead to lower AHD values being measured. This was observed in the studies by Werner et al (2008) and Saupe et al (2006), where inter-method
comparisons were carried out between radiographs and CT or MRI. Saupe et al (2006) reported a poor correlation between AHD measured on radiographs and MR images, with AHD values of 2.8mm less on average for the MR images. Similar differences between radiographs and MRI were noted by Werner et al (2008), who used linear regression to provide a conversion formula. While a full discussion of the issues relating to validity of AHD measurement is beyond the scope of this review, it is important that validity is given further consideration before AHD measures are more widely used in diagnosis or treatment.

In summary, ultrasound measurement of AHD demonstrated sufficient intra-rater reliability in healthy populations and in two cohorts of patients with RC tendinopathy to be the recommended method of AHD measurement. However, because low ICC values were reported in the single high quality inter-tester study (Pijls et al 2010), an additional study of people with imaging-confirmed RC pathology is required to ascertain the inter-tester reliability in this population. The evidence for reliability of AHD measured by CT and MRI was moderate, with a number of studies demonstrating good to excellent reliability, generally derived from re-reading of a single set of images. The evidence for radiographs was conflicting, with the use of non-standardised images making comparisons difficult. As the cheapest and most accessible method, with no radiation exposure concerns, and where excellent reliability can be achieved with limited training, ultrasound is the recommended method of AHD measurement.

2.1.5.1 Limitations

This review was comprehensive, including a variety of published sources e.g. peer-reviewed publications, and theses, however we did not search extensively for grey literature, which may have limited the number of studies. We only included English-language papers; however no relevant papers were excluded due to the language restriction. While a lack of information in the published papers caused some studies to be rated as “Unclear” on a number of QAREL items, we did not contact authors for further information, as it was deemed that such a process may be subject to excessive recall bias. The use of the QAREL checklist in this review provided a standardised method of quality assessment (Lucas et al 2010). The piloting process was important in the resulting high level of agreement reached between reviewers in this review.
However, the QAREL checklist is a relatively new quality assessment tool, and as yet no published studies have reported on its reliability, or validity for use in systematic reviews of diagnostic tests. Further testing of its psychometric properties is required before it can be broadly recommended for use. The extent of conclusions that could be reached was limited by the generally low quality of the included studies.

2.1.6 Conclusion

This review found that intra-rater reliability of AHD measurement by ultrasound is well supported in healthy populations, while also highlighting the scarcity of high quality studies in people with RC pathology, and inter-tester reliability studies. There was moderate evidence for the reliability of AHD measurement with CT and MRI, and no evidence for the reliability of radiographic methods. Based on the evidence reviewed, ultrasound is the authors’ recommended method of AHD measurement, however further data on inter-rater reliability in symptomatic populations is required. With regard to MRI and CT; improved standardisation of methods, and assessing the reliability of both repeated imaging and image re-measurement should be considered, to provide a solid basis for the using these methods to measure AHD. At present, radiographs are not recommended for AHD measurement as there is no evidence to support their reliability.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Study Population (Sex; mean age) &amp; tester/s (T)</th>
<th>Methods</th>
<th>Reliability data</th>
<th>Mean AHD (or AGTD) values ± SD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desmeules et al 2004</td>
<td>Inter-rater reliability</td>
<td>N=13 painfree subjects (sex unknown; 34yrs) T=Two radiologists</td>
<td>12.5Mhz linear transducer</td>
<td>Inter-rater AHD:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pos: neutral, 45° and 60° active abduction</td>
<td>0°: ICC=0.86</td>
<td>0°: 9.9(±1.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Most anterior part of acromion, and 1cm posteriorly (mean used)</td>
<td>45° ICC= 0.91</td>
<td>45°: 8.3(±1.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Measure: smallest distance acromion to humeral head</td>
<td>60°: ICC= 0.92</td>
<td>60°: 7.6 (±1.7)</td>
</tr>
<tr>
<td>Duerr 2010</td>
<td>Intra-rater reliability</td>
<td>N= 40 painfree subjects (21F:19M, 28.6yrs) T= Physiotherapist – training unclear</td>
<td>12.5Mhz linear transducer</td>
<td>Intra-rater</td>
<td>0° AHD:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Measures:</td>
<td>Within session (ICC 2,1)</td>
<td>10.7 (±1.8)</td>
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<td>- Anterior edge of acromion to greater tuberosity (AGTD)</td>
<td>0° AHD: ICC=0.87 (0.81-0.92); SEM= 0.3mm; SRD: 0.9mm</td>
<td>0° AGTD:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Anterior edge of acromion to closest point on humerus (AHD)</td>
<td>0° AGTD: ICC:0.92 (0.87-0.95); SEM= 0.3mm; SRD: 0.9mm</td>
<td>1.45 (±2.8)</td>
</tr>
<tr>
<td></td>
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<td>3 Positions:0°, 60°</td>
<td>AHD 60° passive ICC= 0.96 (0.94-0.98); SEM= 0.1mm; SRD: 0.3mm</td>
<td>60° passive abd</td>
</tr>
</tbody>
</table>
passive and 60° active abduction (abd) (scap plane)  

**SRD:** 0.4mm  

**Between-session (4-7 days apart)**  
- 0° AHD: ICC=0.89 (0.83-0.93)  
- 0° AGTD: ICC=0.80 (0.7-0.87)  
- AHD 60° passive ICC= 0.83 (0.75-0.89)  
- AHD 60° active: ICC= 0.82 (0.73-0.88)  

**Kalra et al 2010**  
Intra-rater Reliability  
N= 60  
- 7.5Mhz linear transducer  
- Neutral shoulder  
- 45° active abduction  
- Postures: slouched, normal, and upright  
- M: Post-mid acromion  
- Shortest distance between acromion & humerus  

<table>
<thead>
<tr>
<th>Intra-rater</th>
<th>AHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHD= 8.1(±2.1)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Between-session (4-7 days apart)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60° active abd AHD= 7.8 (±1.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Kalra et al 2010</th>
<th>Intra-rater</th>
<th>N= 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reliability</td>
<td>31 with MRI confirmed RC disease (RCD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(11M:20F; 53.5 yrs)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>29 painfree controls</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(14M:15F; 31.9yrs)</td>
<td></td>
</tr>
<tr>
<td>T=no information</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intra-rater AHD</th>
<th>AHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>(within session) (ICC 2,1)</td>
<td></td>
</tr>
<tr>
<td>0°</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Kumar et al 2010</th>
<th>Intra-rater reliability</th>
<th>N= 32 pain-free subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>(within &amp; between)</td>
<td>(19M:13F, 64.2yrs)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intra-rater AGTD (within session)</th>
<th>AGTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICC: 0.99 &amp; 0.98; SEM: 0.5mm, 0.6mm</td>
<td>Left: 16.8(±4.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Kumar et al 2010</th>
<th>Intra-rater reliability</th>
<th>N= 32 pain-free subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>(within &amp; between)</td>
<td>(19M:13F, 64.2yrs)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intra-rater AGTD (within session)</th>
<th>AGTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICC: 0.99 &amp; 0.98; SEM: 0.5mm, 0.6mm</td>
<td>Left: 16.8(±4.1)</td>
</tr>
<tr>
<td>Study</td>
<td>Intra-rater AGTD (2 weeks later)</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td><strong>Kumar et al 2011</strong></td>
<td>ICC: 0.96 &amp; 0.97; SEM: 0.7mm Right: 17.8(±4.0)</td>
</tr>
<tr>
<td>Inter-rater reliability</td>
<td>N=20 pain-free subjects (9M:11F, 21yrs)</td>
</tr>
<tr>
<td>Intra-rater reliability</td>
<td>T=3 physiotherapy students (1 hour training)</td>
</tr>
</tbody>
</table>

- **T=physiotherapist (“short period of training”)**
- **T1= ICC: 0.88 (0.78-0.94); SEM: 1.5mm**
- **T2: ICC: 0.84 (0.73-0.92); SEM: 1.2mm**
- **T3: ICC: 0.91 (0.85-0.95); SEM: 1.1mm**

**Leong et al 2012**

- **Intra-rater AGTD (ICC 3,1)**
- **Dominant arm (retested 7-10 days apart)**
- **Non-dominant arm (retested 7-10 days apart)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Intra-rater AGTD (retested 7-10 days apart)</th>
<th>Dominant arm (retested 7-10 days apart)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leong et al 2012</strong></td>
<td>ICC: 0.88 (95%CI: 0.78-0.94); SEM: 1.5mm</td>
<td>Dominant arm 22.1(±2.88)</td>
</tr>
<tr>
<td>Intra-rater reliability</td>
<td>N=13 pain-free subjects (5M:8F; 21.8yrs)</td>
<td></td>
</tr>
<tr>
<td>Intra-rater reliability</td>
<td>T=Physiotherapist (3 months US training)</td>
<td>AGTD</td>
</tr>
</tbody>
</table>

- **T=8-12MHz linear transducer**
- **CoV: 13.71%-13.78%**
- **SEM=0.75mm**
- **MDC=2.10mm**

**Leong et al 2012**

- **T1= ICC: 0.88 (0.78-0.94); SEM: 1.5mm**
- **T2: ICC: 0.84 (0.73-0.92); SEM: 1.2mm**
- **T3: ICC: 0.91 (0.85-0.95); SEM: 1.1mm**

**Kumar et al 2011**

- **T=physiotherapist (“short period of training”)**
- **T1= ICC: 0.88 (0.78-0.94); SEM: 1.5mm**
- **T2: ICC: 0.84 (0.73-0.92); SEM: 1.2mm**
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**Kumar et al 2011**

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**Kumar et al 2011**

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- **T2: ICC: 0.84 (0.73-0.92); SEM: 1.2mm**
- **T3: ICC: 0.91 (0.85-0.95); SEM: 1.1mm**
### Intra-rater Reliability

**Maenhout et al 2012**

**N= 33 painfree athletes, (33F; 21.8 yrs)**

T: “specialised in shoulder ultrasonography”

- **5-10Mhz linear transducer**
- **3 positions: neutral, 45° & 60° active abduction**
- **Shortest distance between acromion and humerus**

**Intra-rater AHD (ICC 1,k)** (retested at 6 weeks)

- **0° Abd:**
  - ICC= 0.92, SEM: 0.54mm
  - 11.7mm (±1.6)
- **45° Abd:**
  - ICC= 0.88; SEM=0.87mm
  - 9.7mm (±1.9)
- **60° Abd:**
  - ICC= 0.91; SEM=0.75mm
  - 9.3mm (±1.8)

### Inter-rater Reliability

**Pijls et al 2010**

**N= 43 (50 shoulders)**

Patients with subacromial impingement (diagnosed by orthopaedic surgeon)

**Intra-rater AHD (intra-session)**

- **5-15Mhz linear transducer**
- **Neutral & 60° degrees abduction(abd) (unclear if passive or active)**
- **Shortest distance between acromion and humerus**

**Intra-rater AHD (re-measuring)**

- **@ 0° ABD**
  - Experienced: ICC: 0.94 (95%CI=0.89-0.97)
  - Novice: ICC: 0.92 (95%CI=0.85-0.96)
  - Accuracy : 1.1mm
  - @ 60° ABD
  - Experienced: ICC: 0.9 (95%CI=0.82-0.95)
  - Novice: ICC: 0.87 (95%CI=0.77-0.94)
  - Accuracy: 1.4mm
Novice: Orthopaedic resident images 6 months later

@ 0° ABD
- Experienced: ICC: 0.56 (95%CI=0.22-0.77)
- Novice: ICC: 0.57 (95%CI=0.24-0.78)

@ 60° ABD
- Experienced: ICC: 0.82 (95%CI=0.61-0.91)
- Novice: ICC: 0.85 (95%CI=0.69-0.93)

Inter-rater AHD @ 0°
- ICC: 0.70 (95%CI= 0.43-0.86)

Inter-rater AHD @ 60°:
- ICC: 0.64 (95%CI= 0.33-0.82)

<table>
<thead>
<tr>
<th>Seitz et al 2012</th>
<th>Intra-rater reliability</th>
<th>N= 40 pain-free subjects</th>
<th>4-12Mhz linear probe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20 with scapular dykinesis</td>
<td>3 positions: neutral, or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 without scapular dykinesis</td>
<td>45° and 90° active</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(18M:22F; 26.6 yrs)</td>
<td>abduction in scapular</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>plane</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anterior acromion</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shortest distance</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>between acromion and</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>humerus</td>
<td></td>
</tr>
</tbody>
</table>

Intra-rater AHD (ICC 3,1) (within session)

- ICC: 0.88-0.96
- SEM: 0.5-1.1mm

AHD:
- No dyskinesis:
  0° Abd: 10.9
  45° abd: 8.3
  90° abd: 9.2
T: Physiotherapist (trained)

With dyskinesis
0° Abd: 11.3
45° Abd: 7.9
90° Abd: 8.8

<table>
<thead>
<tr>
<th>White et al 2012</th>
<th>Intra-rater reliability</th>
<th>N=10 painfree subjects (No separate demographic details for this group but overall sample age 24.2 yrs)</th>
<th>Physiotherapist (Training unknown)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• 7.5-12Mhz linear transducer&lt;br&gt;• 3 positions: 0°, 30° &amp; 45° degrees abduction&lt;br&gt;• 3 conditions: rest, isometric IR, isometric ER&lt;br&gt;• Measure: inferior surface of acromion to closest part of humerus Intra-rater AHD (ICC 3,3) retest 3-4 days apart&lt;br&gt;• ICC range: 0.86-0.94&lt;br&gt;• ICC range: 0.98-0.99</td>
<td>AHD: Resting&lt;br&gt;0° Abd: 9.89(±1.6)&lt;br&gt;30° Abd: 10.02(±1.2)&lt;br&gt;45° Abd: 10.02(±1.2)</td>
</tr>
<tr>
<td>Authors</td>
<td>Design</td>
<td>Study Population (Sex; mean age) &amp; tester/s (T)</td>
<td>Methods</td>
</tr>
<tr>
<td>---------------------</td>
<td>--------------------</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Bernhardt et al 2012</td>
<td>Inter-rater reliability</td>
<td>N=30 shoulder pain (indeterminate diagnosis) (17M:13F, 59yrs)</td>
<td>• Radiographs • Routine AP (anterior to posterior) radiographs from various clinics – protocol not standardised for this study</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T= 5 orthopaedic surgeons</td>
<td>• Max difference 7mm (range 0-7mm, SD: 1.4-2.2mm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inter-rater</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Max difference 8mm (Range 0-8mm; SD: 0-3.6mm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inter-method comparison (different beam angles)</td>
<td>• ICC: 0.06, 0.09, 0.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T: 2 orthopaedic surgeons 1 MSK radiologist</td>
<td>Average AHD difference between radiographs 1-4:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 2.41mm (-3.75-8.57)</td>
</tr>
<tr>
<td>Gruber et al 2010</td>
<td>Inter and intra-rater reliability</td>
<td>N=58 non-specific shoulder pain</td>
<td>• Radiographs - standardised AP views</td>
</tr>
</tbody>
</table>
T= 5 orthopaedic surgeons

Max difference: 3mm (0-3mm)  
No statistically significant differences

**Inter-rater:**
Max difference: 4mm (Range:0-4mm)  
No statistically significant differences

**Thompson et al 2011**  
Intra-rater reliability  
N= 5 pain-free subjects  
(5M; 20 yrs)  
T: one rater, no information on experience

- Digital fluoroscopy  
- 5 positions: seated arm in neutral, 30°, 45°, 75° shoulder elevation under both loaded and unloaded conditions

**Intra-rater (ICC 2,1)**

<table>
<thead>
<tr>
<th>Position</th>
<th>Unloaded</th>
<th>Loaded</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICC: 0.75-0.99</td>
<td>0°: 12.8 (±2.1)</td>
</tr>
<tr>
<td></td>
<td>SEMs: 0.01-0.03mm</td>
<td>30°: 6.9 (±2.7)</td>
</tr>
<tr>
<td>45°: 5.2 (±2.1)</td>
<td>45°: 6.1(±3.3)</td>
<td></td>
</tr>
<tr>
<td>75°: 6.1(±3.3)</td>
<td>75°: 4.6(±2.5)</td>
<td></td>
</tr>
</tbody>
</table>

**Short-term (repeated within-session)**

<table>
<thead>
<tr>
<th>Position</th>
<th>Unloaded</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°: 12.8 (±2.1)</td>
<td>0°: 12.5(±2.3)</td>
</tr>
<tr>
<td>30°: 6.9 (±2.7)</td>
<td>30°: 7 (±2.5)</td>
</tr>
<tr>
<td>45°: 5.2 (±2.1)</td>
<td>45°: 4.7 (±1.4)</td>
</tr>
<tr>
<td>75°: 6.1(±3.3)</td>
<td>75°: 4.6(±2.5)</td>
</tr>
</tbody>
</table>

**Long-term: Repeated scans 9 months later**

<table>
<thead>
<tr>
<th>Position</th>
<th>Unloaded</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°: 12.8 (±2.1)</td>
<td>0°: 12.5(±2.3)</td>
</tr>
<tr>
<td>30°: 6.9 (±2.7)</td>
<td>30°: 7 (±2.5)</td>
</tr>
<tr>
<td>45°: 5.2 (±2.1)</td>
<td>45°: 4.7 (±1.4)</td>
</tr>
<tr>
<td>75°: 6.1(±3.3)</td>
<td>75°: 4.6(±2.5)</td>
</tr>
<tr>
<td>Authors</td>
<td>Year</td>
</tr>
<tr>
<td>--------------------</td>
<td>------</td>
</tr>
</tbody>
</table>
| Saupe et al 2006   |      | Inter-rater reliability | N= 63 Shoulder pain patients (36M:27F; 56.1yrs) (RC pathology confirmed on MRI) | T=Two radiologists, one experienced in MSK and one inexperienced | ICC=0.77 | Radiographs  
- Standard AP view, beam angled 20 cranio-caudally  
- Supraspinatus outlet view  
Measure: shortest distance between cortical bone of inferior acromion and subchondral lamina of humeral head |
| Werner et al 2008  |      | Inter-rater reliability | N=40 shoulder pain patients (10 each of RC tears, shoulder instability, osteoarthritis, and frozen shoulder) | T= 4 radiologists | No details | Radiographs  
- True AP views: film focus 1.5m, 20 cranio-caudal tilt  
Measure: shortest distance between humeral head and sclerotic bone of inferior acromion  
Measures divided by a magnification factor of 1.15 |

Table 5 Details of MRI and CT studies
<table>
<thead>
<tr>
<th>Authors</th>
<th>Design</th>
<th>Study Population (Sex; mean age) &amp; tester/s (T)</th>
<th>Methods</th>
<th>Reliability data (AHD)</th>
<th>Mean values (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hinterwimmer et al 2003</td>
<td>Intra- and inter-rater reliability</td>
<td>N=1 pain-free subject (No sex or age information)</td>
<td>• Open MRI: 0.2 T system; T1 weighted echo sequence &lt;br&gt;• Position: Supine, 30° shoulder elevation</td>
<td>Intra-rater (within session, repeated scans): &lt;br&gt;CoV: 1.4%-4.8%</td>
<td>30° elevation: 8.22 (±0.22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T= 3 raters; no information about raters</td>
<td></td>
<td>Inter-rater: &lt;br&gt;CoV: 2.2%-4.8%</td>
<td></td>
</tr>
<tr>
<td>Moffet et al 1998</td>
<td>Intra-and inter-rater reliability</td>
<td>N=13 pain-free subjects (No information on sex; Age:34yrs)</td>
<td>• Open MRI: 0.5T system, through supraspinatus tendon plane &lt;br&gt;• Multiple angular positions in flexion (20-130) and abduction (50-110) &lt;br&gt;• Measure: Participant seated; best image at each position; smallest AHD measured</td>
<td>Intra-rater (re-reading 1 month later) &lt;br&gt;ICC: 0.8-0.98</td>
<td>20° flex: 8.6 &lt;br&gt;50° flex: 5.5 &lt;br&gt;50° abd: 6.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T= Two MSK radiologists</td>
<td></td>
<td>Inter-rater: &lt;br&gt;ICC: 0.77-0.98</td>
<td></td>
</tr>
<tr>
<td>Saupe et al 2006</td>
<td>Inter-rater reliability</td>
<td>N= 63 Shoulder pain patients (36M:27F; 56.1yrs)</td>
<td>• MRI (1.0T &amp; 1.5T systems) &lt;br&gt;- Coronal T1 weighted &lt;br&gt;- Sagittal oblique T1</td>
<td>Inter-rater: &lt;br&gt;ICC:0.91</td>
<td>Coronal oblique: 5.9 (±2.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T= Two radiologists; one experienced in MSK and one</td>
<td></td>
<td>Inter-rater: &lt;br&gt;ICC:0.91</td>
<td>Saggital oblique:</td>
</tr>
</tbody>
</table>


inexperienced - Shoulder neutral

- Measure: shortest distance between cortical bone of inferior acromion and subchondral lamina of humeral head

  - Inter-rater reliability
  - N=40 shoulder pain patients (10 each of RC tears, shoulder instability, osteoarthritis, and frozen shoulder)
  - No age or sex information
  - T=4 radiologists

  

<table>
<thead>
<tr>
<th>Study</th>
<th>Methodology</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Werner et al (2008)</td>
<td>MRI, CT</td>
<td>No information on CT or MR imaging parameters</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measure: Middle image chosen, where largest depiction of glenoid occurred. Shortest distance between inferior acromion and humeral head</td>
</tr>
</tbody>
</table>

Inter-rater: 

- CT: r=0.8
- MRI: r=0.8 (r=0.76 for RC tear group)

Abbreviations for Tables 3-5:

- abd: shoulder abduction; AGTD: acromion greater tuberosity distance; AHD: acromiohumeral distance; SD=standard deviation; CoV: coefficient of variation; F: female; Flex: shoulder flexion; ICC: intra-class correlation; M: male; MDC: minimal detectable change; SEM: standard error of measurement; SRD: smallest real difference; T= tester/testers
References


Chopp JN, O'Neill JM., Hurley K, Dickerson CR. Superior humeral head migration occurs after a protocol designed to fatigue the rotator cuff: A radiographic analysis. J Shoulder Elbow Surg 2010; 19:1137-1144


Fleiss JL. The Design and Analysis of Clinical Experiments. 1986, New York: Wiley


Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics, 1977; 33:159-74


2.2 Study III: Validation of ultrasound measurement of the subacromial space using a novel shoulder phantom model


2.1.1 Abstract

Ultrasound has a high degree of diagnostic accuracy in the assessment of the rotator cuff (RC) tendons. Increasingly, ultrasound is being used to measure other parameters of RC pathology, including the size of the subacromial space, or acromiohumeral distance (AHD). While this measure has been shown to be clinically reliable, no assessment of its validity has been carried out. This technical study reports on the development of a novel ultrasound phantom of the shoulder, and its use in validation of ultrasound measurement of AHD.

There was a close agreement between AHD measures using ultrasound and the true subacromial space of the phantom model, providing support for the construct validity of this measurement. The phantom model has good potential for further development as a training tool for shoulder ultrasound and guided injections.

**Key words:** ultrasound phantom, shoulder, acromiohumeral distance
2.2.2 Introduction

Self-reported prevalence of shoulder pain in adults averages between 15 and 20% in European population studies (Pribicevic 2012), with the most common diagnosis being disorders of the rotator cuff (RC) tendons. Ultrasound has been shown to be comparable in its diagnostic accuracy to magnetic resonance imaging (MRI) for identifying RC tears (De Jesus et al 2009). Ultrasound findings in RC disorders include bursal thickening, tendon hypoechochogenicity, and partial or full thickness tendon tears. Rotator cuff tendinopathy can lead to superior migration of the humeral, due to failure of RC stabilisation, and the resultant narrowing of the subacromial space may cause further tendon impingement (Lewis 2010). A reduction in the subacromial space has been reported in people with painful RC pathology (Saupe et al. 2006), and many interventions for RC pathology e.g. acromioplasty surgery, and exercise programmes, are founded on an attempt to increase the subacromial space, and thus relieve symptoms.

Radiographic examination has been traditionally used to assess for narrowing of the subacromial space in people with RC pathology, by measuring the acromiohumeral distance (AHD). However a recent systematic review found ultrasound to be the best method of AHD measurement, due to good evidence for its reliability, in contrast to the limited evidence for the reliability of radiographic methods (McCreesh et al 2013). Reliability is an important property of a measurement, demonstrating consistency between measures and examiners; however, the validity of a measurement is also important to confirm the accuracy of the method. While studies have been completed comparing different radiological methods of AHD measurement in an attempt to provide some evidence for concurrent validity (Werner et al 2008, Saupe et al 2006, Azzoni et al 2004), there remains no accepted ‘gold standard’ for this measurement, and no studies examining it’s construct validity. In a study aimed at assessing the amount of bone removal during arthroscopic subacromial decompression surgery, Tillander and Norlin (2002) intra-operatively measured AHD in people with and without subacromial pathology. While it was demonstrated that those with subacromial pathology had significantly smaller AHD, there was no comparison made to AHD measurement by any non-invasive method. While the intra-operative method provides a potential in-vivo method of assessing the construct validity of AHD measurement, there are numerous variables associated with the peri-operative condition e.g patient position, arm traction, and introduction of fluid, which prevent it from being an appropriate model for
investigation. Validity of ultrasound imaging methods and measurements is commonly assessed by the use of an appropriate tissue-mimicking phantom (Thijssen et al. 2007, Koski et al. 2010). As no study to date has examined the construct validity of AHD measurement, the aim of this study was to evaluate the construct validity of ultrasound measurement of AHD, using a newly developed shoulder ultrasound phantom.

2.2.3 Materials and Methods

2.2.3.1 Development of the phantom

A novel ultrasound phantom of the shoulder was developed. A DICOM (Digital Imaging and Communications in Medicine) Computerised tomography (CT) dataset of a shoulder was used to create a computerised 3D model of the superior half of the humerus and scapula. A 3D rapid prototyping printer (Vanguard HS HiQ SLS: 3D systems, Rockhill, USA) was used to print a bone phantom for each bone (humerus and scapula) out of DuraForm® PA (3D Systems, Valencia, CA, USA) (see Figure 10). The bones were placed in the correct alignment (with reference to the DICOM images) and rubber washers with epoxy resin were used to create the appropriate spacing. A custom mould was made of an appropriately sized shoulder, into which a compound containing gelatine, psyllium husk powder and chlorhexidine was poured. The bones were then embedded in this compound.

Figure 10 Computerised 3D shoulder model (left), and the printed out bones (right)

Once the compound had set, the model was covered in latex paint to improve durability and resilience (See Figure 11). Our investigation of a sample of the two materials showed that the DuraForm® PA had a speed of sound of 1709 ms\(^{-1}\), while the gelatine compound had a speed
of sound of 1550 ms$^{-1}$, closely matched to the average speed of sound in soft tissue (1540 ms$^{-1}$). Acromiohumeral distance, measured as the shortest distance between the infero-lateral acromion and the adjacent part of the humeral head, was measured directly with Vernier callipers on the completed shoulder “joint” before it was embedded in gelatine. Five measures were taken.

![Completed shoulder phantom model](image)

**Figure 11 Completed shoulder phantom model**

2.2.3.2 Measurement validation

Measurement of AHD on the shoulder phantom was independently undertaken by 2 musculoskeletal sonographers, blind to the true reference value of AHD in the phantom. Ultrasound examination was undertaken with a GE Logiq e ultrasound scanner (GE Medical, Wauwatosa, WI, USA) with a 7-12 MHz linear array transducer. An ultrasound image was taken with the transducer positioned along the line of the humerus, over the anterior part of the acromion, with the subacromial space and humeral head visible. The AHD was then measured as the shortest distance between the inferolateral edge of the anterior acromion and the humeral head, parallel to the acoustic shadow cast by the acromion (see Figure 12 for an image of AHD measurement from a normal shoulder, alongside an image from the shoulder.
phantom). Measurement of AHD was taken using on-screen callipers. Each examiner independently measured AHD on 5 separate images, with the probe removed and repositioned between scans.

Figure 12 Ultrasound image of acromiohumeral distance (AHD) in a normal shoulder (left), and corresponding image of shoulder phantom (right)

2.3.3.3 Data Analysis

Descriptive values were calculated of the mean, standard deviation, and coefficient of variation (CoV) for the calliper measures, and the ultrasound measures (twice by Examiner 1, and a single set from Examiner 2). The values from Examiner 1 were used for the inter-method comparison. A box-plot was constructed to examine the spread of data points. A Bland–Altman plot was constructed for the inter-method comparison between AHD measurement directly using callipers, and by ultrasound. As per the suggestion of Krouwer (2008), the difference between the methods were plotted against the calliper measurements (rather than against the mean of the two measures), as it was deemed the reference method.

2.2.4 Results
Table 6 presents the descriptive values of the AHD measurements by callipers directly on the bony ‘joint’ before embedding, as well as the ultrasound measures by both examiners. All methods also demonstrated excellent reliability, with CoV below 3%. There were no statistically significant differences between AHD measures with the callipers and ultrasound (p=0.27), or between intra-rater (p=0.83) or inter-rater (p=0.09) ultrasound measurements. The boxplot in Figure 13 illustrates good agreement across all measurements, all with medians within 0.5mm of each other and all measures falling within 1mm. The Bland-Altman plot in Figure 14 shows very good agreement with mean difference of only 0.14mm and limits of agreement lying between -0.44 to 0.72mm.

<table>
<thead>
<tr>
<th>Source</th>
<th>Callipers</th>
<th>Ultrasound Tester 1 (time1)</th>
<th>Ultrasound Tester 1 (time2)</th>
<th>Ultrasound Tester 2</th>
</tr>
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<tbody>
<tr>
<td>Mean (mm)</td>
<td>9.9</td>
<td>9.7</td>
<td>9.7</td>
<td>9.4</td>
</tr>
<tr>
<td>SD (mm)</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>CoV (%)</td>
<td>3</td>
<td>1.9</td>
<td>0.9</td>
<td>2</td>
</tr>
</tbody>
</table>

Abbreviations: CoV= coefficient of variation; SD = standard deviation
Values taken from five repeated measurements in each case.

Table 6 Descriptive values for acromiohumeral distance (AHD) measurements of the shoulder phantom directly by callipers, and indirectly using ultrasound by two sonographers.
Figure 14: Bland–Altman plot comparing the acromiohumeral distance (AHD) measurement by callipers and by ultrasound (tester 1 measures).

The mean difference was 0.14mm, and the limits of agreement were between -0.44mm and 0.72mm.

2.2.5 Discussion

This study investigated the construct validity of ultrasound measurement of AHD using a shoulder phantom. The Duraform® PA and gelatine-based phantom proved to be a very suitable model, with a similar look, shape and feel to a real shoulder joint, providing lifelike ultrasound images. Ultrasound-measured AHD values were very close to the true ‘skeletal’ measurement with callipers, confirming construct validity of the ultrasound measures. Reliability of the ultrasound AHD measures was also excellent.

Acromiohumeral distance in normal healthy shoulders ranges between 7 and 12mm (McCreesh et al 2013). A reduction in AHD has been shown to be present in people with RC pathology, with reduction below 6mm thought to be indicative of a significant RC tear (Goutallier et al 2011). Saupe et al (2006) showed that AHD was associated with the degree of fatty degeneration of the RC muscles, which is an important predictor of surgical outcomes for RC repair. In a pilot study of people with shoulder pain undergoing physiotherapy, Desmeules et al (2004) showed that there was a strong positive correlation between an
increase in the AHD and functional improvement following rehabilitation. It is clear that further studies in symptomatic populations are required to ascertain the full clinical value of AHD measurement, but it may prove a useful diagnostic indicator in RC pathology.

Ultrasound has been shown to be a highly reliable method of AHD measurement both in healthy and shoulder pain populations, with CT and MRI demonstrating reasonable evidence for their reliability, but little evidence to support the reliability of radiographic methods (McCreesh et al 2013). Each radiological method of AHD measurement has potential shortcomings. With radiographs, projection issues and bony overlap may lead to difficulty defining the area of measurement. During ultrasound examination, the acromion produces an acoustic shadow that may obscure the area of AHD measurement. The upright positioning for ultrasound and radiographs is consistent with the functional position for the shoulder, however for MRI and CT imaging the patient will assume the supine position, leading to a potentially smaller AHD measurement due to the lack of the effect of arm weight. A comparison of AHD measurement between MRI and radiographs was carried out by Saupe et al (2006) who reported poor correlation between the methods, and consistently lower values for the MRI.

Despite the widespread use of diagnostic ultrasound imaging of the shoulder, there is no published work in the area of ultrasound phantoms of the shoulder. As a pilot phantom, this model had some limitations in terms of AHD measurement, namely the lack of soft tissue-mimicking components, and also the fact that the model was set in the ‘supine’ position, rather than the more usual upright position used for shoulder ultrasound. While we ensured good fixation of the bones, and undertook minimal movement of the phantom, we cannot guarantee that the subacromial space did not alter after embedding in the phantom. We did not undertake an assessment of the attenuation properties of the completed phantom, as we were not intent on creating a phantom with perfect tissue matching properties. Gelatin-water mixtures, with the use of husk material to create a speckle pattern, are well accepted as appropriate for the simulation of soft tissues. A full quantitative assessment of these mixtures has been published by Madsen et al (2005), which shows that the attenuation of our material should lie between 0.3 and 0.5 dB/cm/MHz, and thus be an acceptable soft tissue mimic. The ultrasound image of the phantom shares many characteristics of a true shoulder appearance, with the grainy appearance of the soft tissues and the reflective appearance of the bone model, with the appropriate degree of acoustic shadowing. With further development, the phantom has excellent potential as a model for training in diagnostic shoulder ultrasound, as
it provided images that share similarities with clinical musculoskeletal images of the shoulder. It also has potential as a tool for practicing ultrasound guided shoulder injections. Further development would require addition of realistic tendon phantoms of the RC and biceps tendons, as well as the use of self-healing materials, in order to optimise the usefulness for injection training.

2.2.6 Conclusion

This study provides evidence for the construct validity of AHD measurement using ultrasound, using a novel ultrasound phantom. Further research is required to better understand the relative importance of AHD in shoulder pathology, and how it is affected by rehabilitation and surgery. The shoulder phantom has potential for further development as a training tool for ultrasound shoulder examination and ultrasound-guided shoulder injections.
References


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McCreeesh KM, Crotty JM, Lewis JS. 2013 Acromiohumeral distance measurement in rotator cuff tendinopathy: is there a reliable, clinically applicable method? Br J Sports Med; Online first, doi:10.1136/bjsports-2012-092063


2.3 Study IV: Ultrasound measures of supraspinatus tendon thickness and acromiohumeral distance are reliable in rotator cuff tendinopathy
McCreesh K, Anjum S, Crotty J, Lewis J
(Under review, J Clin Ultrasound)

2.3.1 Abstract

Introduction: Rotator cuff (RC) tendinopathy has been widely ascribed to impingement of the supraspinatus tendon (SsT) in the subacromial space, measured as the acromiohumeral distance (AHD). Ultrasound is suitable for AHD and SsT thickness measurement, but few reliability studies have been carried out in symptomatic populations, and inter-rater reliability is unconfirmed. This study aimed to examine the intra and inter-rater reliability of ultrasound measurements of AHD and SsT thickness in asymptomatic controls and people with RC tendinopathy.

Materials & Methods: Seventy participants were recruited; grouped as controls (n=25), and RC tendinopathy (n=45). Repeated ultrasound measurements of AHD and SsT thickness were obtained, by one rater in both groups, and two raters in the RC tendinopathy group.

Results: Intra and inter-rater reliability co-efficients were excellent for both measures (ICC>0.92), but intra-rater reliability was superior. Minimal detectable change (MDC) values in the symptomatic group were 0.7mm for AHD and 0.6mm for SsT thickness, for a single experienced examiner, rising to 1.2mm and 1.3mm respectively, for a pair of examiners.

Conclusion: The results support the reliability of ultrasound for the measurement of AHD and SsT thickness in symptomatic RC tendinopathy, and provide MDC values for future research studies.

Keywords: acromiohumeral distance, supraspinatus tendon, rotator cuff, reliability
2.3.2 Introduction

Rotator cuff (RC) tendinopathy is a disabling condition of the shoulder, common in older populations and in sports involving overhead movements, such as swimming. The person generally complains of anterolateral shoulder pain, exacerbated by elevated arm positions, as well as weakness and loss of shoulder function. While both intrinsic and extrinsic factors have been proposed to influence the development of the condition (Lewis 2009), compression or impingement of the supraspinatus tendon (SsT) in the subacromial space remains the most widely proposed cause, and it forms the basis for various rehabilitative and surgical treatments.

The size of the subacromial space is quantified using radiological methods to measure the acromio-humeral distance (AHD). Normal AHD, measured using ultrasound in the neutral shoulder position, and measured as the shortest distance between the humeral head and the inferolateral acromion, ranges between 9-12mm in various recent studies (Kalra et al 2006, Pijls et al 2010, White et al 2012). In populations with RC tendinopathy, most authors report reduced AHD in the painful shoulder, with values ranging from 6-12mm being reported in ultrasound studies of people with varying degrees of tendon pathology (Desmeules et al 2004, Pijls et al 2010).

While ultrasound (US) has been shown to be a reliable method of AHD measurement in a number of studies, only two studies could be identified evaluating reliability of US measurement of AHD in people with shoulder pain (Kalra et al 2006, Pijls et al 2010), and only the Pijls et al (2010) study evaluated inter-rater reliability. Kalra et al (2006) assessed the intra-rater reliability of AHD measurement in 60 people (31 of whom had MRI-diagnosed RC tendinopathy), and reported intra-class correlation (ICC) values of 0.92, with a minimal detectable change (MDC) of 1.3mm. However, the reliability data for the symptomatic group was not reported separately to the pain-free subjects. Pijls et al (2010) examined AHD in 43 people clinically diagnosed with subacromial impingement, and reported excellent intra-rater reliability, with ICCs of 0.94 for an experienced examiner and 0.92 for a novice examiner. In contrast, inter-rater reliability of AHD measurement in this study was significantly poorer, with an ICC of 0.70 and wide 95% confidence intervals of 0.43-0.86.

Another feature of RC tendon pathology is thickening of the painful SsT (Joensen et al 2004), ascribed to an increase in tendon water content (Cook & Purdam 2009). The reliability of ultrasound for determining tendon thickness in symptomatic populations has been supported in studies of common extensor (Hee Lee et al 2011), patellar (Gellhorn et al 2013) and
Achilles tendinopathy (Arya & Kulig 2010). Ultrasound has been shown to have good intra-rater reliability for evaluating SsT thickness in pain-free populations (Bjordal et al 2003, O’Connor et al 2004, Leong et al 2012), however there are no published studies examining the reliability of this measure in symptomatic populations. Leong et al (2012) studied the intra-rater reliability of US measures of both SsT thickness and subacromial space in 11 healthy individuals, measuring the longer distance between the acromion and the greater tuberosity (AGTD), as the estimate for subacromial space. Both AGTD and SsT thickness measures were reliable, with ICC values of 0.92 and 0.93, and MDC of 2.1mm and 0.64mm respectively. O’Connor et al (2004) reported intra-rater variability of SsT thickness measurement of just 5% in a healthy population, but a much poorer value of 39% when inter-rater reliability between 2 radiologists was assessed.

It is clear that AHD and SsT thickness are potentially important factors in understanding the pathogenesis of RC tendinopathy. Concurrent thickening of SsT in the presence of a reduced AHD may well contribute further to subacromial impingement, due to increased volume in a smaller space. However, since the majority of reliability assessments have been undertaken in asymptomatic populations, there remain significant gaps in knowledge regarding the reliability of measuring these attributes in symptomatic populations.

Therefore, the aims of this study were
1) to evaluate the intra-rater reliability of ultrasound measures of AHD and SsT thickness in people with RC tendinopathy and in healthy controls
2) to evaluate the inter-rater reliability of ultrasound measures of AHD and SsT thickness in people with RC tendinopathy

2.3.3 Materials & Methods

This study is reported with reference to the recently published Guidelines for Reporting Reliability and Agreement Studies (GRRAS) (Kottner et al 2011).

2.3.3.1 Participants

Two groups of participants were sought for this study, representing healthy controls, or varying degrees of RC tendinopathy, in order to represent a spectrum of normal and pathological tendons. The healthy controls were recruited from the staff of a University, using email and word-of-mouth methods. They were included if they were over the age of 40 (in order to reflect the demographic of those with RC tendinopathy); with no current or recent
(one year) history of shoulder pain, injury or surgery; and no history of neurological, or systemic inflammatory disease. Controls were excluded if they participated regularly (> once a week) in a sport or activity involving upper limb activity. In order to achieve a spectrum of pathology, the RC tendinopathy group were recruited from a combination of community and clinical sources. Community recruitment was carried out from a Masters Swimming Club and from a University staff and student population, via email and word-of-mouth methods. Clinical recruitment was undertaken in a shoulder ultrasound clinic in a Regional Orthopaedic Hospital, where each eligible patient was invited to take part during their scan appointment. The symptomatic group were included if they had a current history of shoulder pain. They were excluded if they had undergone shoulder surgery, or had a history of a neurological, or systemic inflammatory disorder. Potential volunteers were given an information sheet about the study and invited to participate. Intra-rater reliability was evaluated in both healthy controls and those with RC tendinopathy. Inter-rater reliability was evaluated in the clinical population only, as only one of the examiners was available to undertake testing in the community and University setting. Ethical approval was received from the relevant Institutional Review board and all participants gave informed, written consent. The sample size was based on an expected ICC value of 0.90 (with a minimum value of 0.70 in the 95% confidence interval) a α value of 0.05, a β value of 0.20, using two measures, or two raters (Walter et al 1998). Based on these parameters a sample size of 19 was required for both the intra- and inter-rater parts of the study.

2.3.3.2 Diagnosis

The usefulness of clinical tests to provide a diagnosis of shoulder pain has been questioned in a high quality systematic review (Hegedus et al 2012), which suggests that none of these tests can provide an accurate pathological diagnosis. Ultrasound has been shown to have equivalent accuracy to MRI in a large systematic review of RC imaging (de Jesus et al 2009), therefore ultrasound was deemed the most appropriate method of diagnosis for this study. A diagnostic ultrasound assessment was undertaken of all consenting participants, by an experienced musculoskeletal physiotherapist and sonographer.

Many authors have reported that consensus definitions of sonographic RC pathology are lacking, in particular for bursal pathology (Naredo et al 2006). For this study diagnostic criteria were based on a combination of existing published criteria (Naredo et al 2006, Wakefield et al 2005, Cullen et al 2007). Tendinosis was recorded when there was loss of the
normal fibrillar structure of the tendon with an abnormally hypoechoic appearance. A partial-thickness tear was recorded when flattening of the bursal side of the tendon or a distinct/focal hypoechoic defect was seen within, or on either surface of, the tendon. A full-thickness RC tear was recorded when the RC tendons could not be visualized because of complete rupture or when there was a focal defect extending from the bursal to the humeral side of the tendon. Bursitis was recorded only when marked fibrotic thickening of the subacromial bursa or bursal fluid > 2mm was present. Diagnosis was confirmed on the static images by an experienced musculoskeletal radiologist (JC). Healthy controls were excluded from the study at this stage if they were found to have any grey-scale pathology of the RC tendons or subacromial bursa.

For the symptomatic participants, the absence of greyscale pathology of the RC tendons or bursa on ultrasound was an exclusion criterion. Symptomatic participants were included if they had evidence of greyscale RC tendon pathology in the painful side (most painful side was examined if bilateral pain). Symptomatic participants also underwent a standard physiotherapy shoulder examination, and those with frozen shoulder (significant loss of passive and active range of motion) or neck disorders (shoulder pain exacerbated by neck movement) were excluded. No measures of SsT thickness were taken if there was a full thickness tear visualised in the tendon. The second examiner for the inter-rater study (SA) was a specialist registrar in rheumatology with 3 years training and experience in musculoskeletal ultrasound. Both examiners undertook pilot scanning of 5 non-included individuals prior to the study for the purpose of standardising the measurement process.

2.3.3.3 Measures

2.3.3.3.1 Position

Participant was positioned seated on a chair in their normal seated posture, with the arms by the sides, elbow bent to 90° and hands resting on the lap, for AHD measurement. For the supraspinatus measures, the arm was placed into the modified Crass position tendon (Ferri et al 2005) i.e. palm of the hand on the iliac crest, with the elbow directed posteriorly (See Figure 15). This position is more comfortable for RC tendinopathy patients, as it avoids the internal rotation needed in the Crass position, whilst also maintaining the view of the intra-articular portion of the biceps tendon (Middleton 1992).
2.3.3.3.2 Acromio-humeral distance

Ultrasound examination was undertaken with a GE Logiq e ultrasound scanner with a 7-12 MHz linear array transducer (GE Medical, Wauwatosa, WI, USA). The ultrasound transducer was placed longitudinally, along the centre of the acromion (See Figure 15). Kalra et al. (2006) measured AHD over the posterior-mid acromion, while Pijls et al. (2010) state that the US transducer was moved around to find the smallest space, from which point the measurement was taken. Standardisation of the measurement is important in achieving optimum reliability. Since Hyvonen et al. (2003) have shown that compression is most pronounced under the anterolateral part of the acromion, it was decided that this was the most appropriate area to measure. Once both the acromion and humerus were visualised, the transducer was moved forward until the most anterior part of the acromion was in view, with a concurrent clear view of the humeral head underneath, at which point the image was captured. AHD was measured as the shortest distance between the infero-lateral edge of the anterior acromion and the humeral head, along a line parallel to the acoustic shadow cast by the acromion (See Figure 16).
2.3.3.3.3 Supraspinatus thickness

The SsT was scanned in the transverse plane. The transducer was placed on the acromion and moved laterally to visualise the SsT. Once the tendon was in view, the transducer was moved anteriorly until the intra-articular portion of the long head of biceps was visualised, and the image was taken at this point (see Figure 17). A number of studies assessing SsT thickness have measured thickness at one point on the tendon only (Bjordal et al 2003, Wang et al 2005, Malanga et al 2012). However since the tendon is unlikely to be of uniform thickness throughout, we took three measurements within the tendon, and used the average of these to represent the SsT tendon thickness. In addition, other studies have not consistently used a reproducible landmark for measuring the tendon. We identified the long head of biceps in the image. Since the anterior to posterior dimension of the SsT tendon is approximately 2cm (Ruotolo et al 2004), we took measurements between the superior echogenic boundary of the tendon to the humeral head, at points 5mm, 10mm and 15mm posterior to the edge of the biceps tendon (see Figure 17). The mean of these three measures was used for analysis.
2.3.3.3.4 Function and pain

Baseline demographic details were obtained from all participants. All symptomatic participants completed the Shoulder Pain and Disability Index (SPADI), and the Numerical Rating Scale (NRS) for average pain intensity. The SPADI consists of a 5-item subscale measuring pain and an 8-item subscale measuring shoulder-related disability (Williams et al 1995) with a summary score out of 100; higher values indicating greater disability. It has been shown to have good reliability and construct validity in shoulder pain populations (Roy et al 2009). The NRS is a 10 point scale where 0 represents “no pain” and 10 represents “worse possible pain”. Mintken et al (2009) demonstrated that the NRS is reliable and responsive in people with shoulder pain.

2.3.3.3.5 Testing process

All measures were carried out in a single testing session for each participant. The side to be tested first was randomly chosen. During this time the participant did not move from the testing position. Order of testing was, for example, if right side chosen first: right AHD, right SsT thickness, left AHD, left SsT thickness, followed by repeat of the right sided scans, and...
finally the left side again. For the inter-rater study, the order of examiners was randomised. The second examiner left the testing area while the first examiner was undertaking scanning.

Measurement of the scans was undertaken at a separate time from testing, with the examiners blind to the side of symptoms, as appropriate. On-screen callipers were used to take the measurements, with the actual measures obscured on the screen until all measurements had been completed. For the inter-rater study, both examiners measured their own images independently, without access to the other’s images or measurements.

2.3.3.4 Data Analysis

Data was entered in SPSS Version 20 for analysis. Descriptive statistics were used to summarise the demographic characteristics of participants (mean, standard deviation (SD), range). Reliability of AHD and SsT thickness was analysed using the intra-class correlation co-efficient (ICC) with 95% confidence intervals (CI). The ICC model 2,1 (two-way random effects, single or average measures as appropriate), which is suitable when generalisation of the findings to equally trained clinicians is the goal, was chosen. While ICC values above 0.75 are generally classified as demonstrating ‘excellent’ reliability (Portney & Watkins 2000), this may only apply to group level comparisons and values above 0.90 have been recommended for any measure that may be used at the individual level (Kottner et al 2011). In addition, standard error of measurement (SEM), and minimal detectable difference (MDC) were calculated, with the following formulae: 

\[ SEM = SD \sqrt{1 - ICC} \]
\[ MDC = 1.96 \times \sqrt{2 \times SEM} \]

2.3.4 Results

A total of 70 participants were recruited, grouped as healthy controls (n=25), and RC tendinopathy (n=45). See Table 7 for demographic details of each group, and diagnoses and outcome scores for the symptomatic group. Since eight of the RC tendinopathy group had a full-thickness tear of the SsT tendon on the painful side, no tendon thickness measures were available on the painful side for these participants. Twenty-two participants took part in the inter-rater study, of whom three had a full thickness SsT tear, and were thus excluded from the SsT thickness measures.
Table 7 Demographic details

<table>
<thead>
<tr>
<th></th>
<th>Age (Mean +/- SD)</th>
<th>Sex</th>
<th>NRS (Mean +/- SD)</th>
<th>SPADI Total (Mean +/- SD)</th>
<th>Diagnosis</th>
</tr>
</thead>
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<tr>
<td><strong>Controls</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>N=25</td>
<td>50 (7)</td>
<td>17F,8M</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Range: 42-63</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>RC Tendinopathy</strong></td>
<td>57 (14)</td>
<td>25F,20M</td>
<td>5 (1.9)</td>
<td>42 (25)</td>
<td>Supraspinatus tendinosis=21</td>
</tr>
<tr>
<td>N= 45</td>
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<td>Range: 2-8</td>
<td>Range: 16-83</td>
<td>Partial tear supraspinatus=16</td>
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<tr>
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<td></td>
<td></td>
<td>Full thickness tear supraspinatus= 8</td>
</tr>
</tbody>
</table>

NPRS= Numerical rating scale (average pain); SPADI: Shoulder Pain and Disability Index

Intra-rater reliability for AHD and SsT thickness measurement was excellent for both groups, with all ICC values greater than 0.92 (Table 8), and narrow 95% CI. Similar levels of reliability were achieved for both painful and non-painful shoulders. Standard error of measurement values were very small, ranging from 0.1-0.4mm. Values for MDC were also low, showing that, for example, in the RC tendinopathy population, in scans taken by the same examiner, changes of 0.7mm or more in AHD, or 0.6mm or more in SsT thickness in the painful shoulder could be considered true change, beyond that expected from measurement error.

Inter-rater reliability for AHD and SsT thickness measurement was also excellent for the RC tendinopathy group (Table 8), with ICC values greater than 0.9, narrow CIs, and very small values for SEM, ranging from 0.3-0.5mm. Similarly, low MDC values were found, showing that, for an RC tendinopathy group, in scans of the painful shoulder taken by two different examiners, changes of 1.2mm or more in AHD, or 1.3mm or more in SsT thickness, could be considered true change.
Table 8 Intra-rater and inter-rater reliability of acromio-humeral distance (AHD) and supraspinatus tendon (SsT) thickness measurement

<table>
<thead>
<tr>
<th></th>
<th>Side (N)</th>
<th>ICC</th>
<th>95% CI</th>
<th>SEM  (mm)</th>
<th>MDC  (mm)</th>
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<tr>
<td><strong>AHD measurement</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>INTRA-RATER RELIABILITY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>All Shoulders (50)</td>
<td>0.92</td>
<td>0.87-0.95</td>
<td>0.4</td>
<td>1.0</td>
</tr>
<tr>
<td>RC tendinopathy</td>
<td>Painful side (45)</td>
<td>0.98</td>
<td>0.97-0.99</td>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>INTER-RATER RELIABILITY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RC tendinopathy</td>
<td>Painful Side (22)</td>
<td>0.95</td>
<td>0.88-0.98</td>
<td>0.4</td>
<td>1.2</td>
</tr>
<tr>
<td><strong>SsT thickness measurement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>INTRA-RATER RELIABILITY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>All Shoulders (50)</td>
<td>0.93</td>
<td>0.87-0.96</td>
<td>0.2</td>
<td>0.6</td>
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<tr>
<td>RC tendinopathy</td>
<td>Painful side (37)</td>
<td>0.97</td>
<td>0.92-0.99</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>INTER-RATER RELIABILITY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RC tendinopathy</td>
<td>Painful side (19)</td>
<td>0.94</td>
<td>0.80-0.98</td>
<td>0.5</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Table 8 Intra-rater and inter-rater reliability of acromio-humeral distance (AHD) and supraspinatus tendon (SsT) thickness measurement

*ICC* = intra-class correlation; *95% CI* = 95% confidence interval; *SEM* = standard error of measurement; *MDC* = minimal detectable change

### 2.3.5 Discussion

Reduced AHD and thickening of the SsT have been described as features of RC tendinopathy. This study showed that excellent levels of inter- and intra-rater reliability can be achieved using ultrasound to measure both these variables, in painfree and symptomatic shoulders. This is the first study to report excellent levels of inter-rater reliability for AHD measurement in symptomatic shoulders, with ICC of 0.95, and SEM and MDC of 0.4mm and 1.2mm respectively. A comparable study by Pijls et al (2010) reported excellent intra-rater reliability, but a poorer level of inter-rater reliability (ICC 0.7). The MDC values can be used to determine threshold values for real change in a test-retest study. As the intra-rater MDC value for both AHD and SsT thickness measurement were lower than the inter-rater MDC values, it would be advantageous to use a single examiner where possible. Minimal clinically
important difference (MCID) is the degree of difference considered of value to the patient, and requires cross correlation with patient-based measures of change. No studies have reported the MCID values for AHD or SsT thickness measures, and it remains to be determined what degree of change in AHD or SsT thickness is clinically meaningful in the diagnosis and management of RC tendinopathy.

Possible sources of error in AHD and SsT thickness measurement using ultrasound include errors in subject repositioning, location of the correct position from which to capture the image, and localisation of the correct anatomical boundaries from which to undertake the measurement. Since the MDC values for reliability of SsT thickness measures were proportionately higher (as % of the mean value) than those for AHD, this may reflect the more challenging aspects involved in locating the correct measuring position on the tendon. Bone surfaces are generally well-defined on ultrasound making the measurement of AHD potentially easier than SsT thickness, where the less well-defined tendon boundaries must be identified. We attempted to minimise these sources of error in our study by using specified landmarks and measuring protocols, which would be easily achievable in clinical practice.

Ultrasound has traditionally been the preserve of radiology professionals, but in recent years has been increasingly adopted by rheumatologists, sports medicine physicians and physiotherapists in the assessment of musculoskeletal disorders (Yim & Corrado 2012). The examiners in this study were a physiotherapist, with one year of training and experience in musculoskeletal sonography, and a rheumatology registrar, with three years training and experience in musculoskeletal ultrasound, and an excellent level of inter-tester reliability was achieved in the RC tendinopathy group. Pijls et al (2010) compared the reliability of AHD measurement by an experienced radiologist to that of an orthopaedic resident who was a novice in ultrasound, and found that both achieved an excellent level of intra-rater reliability (ICCs= 0.94 and 0.92), although inter-rater reliability was poorer (ICC=0.70). Kumar et al (2011) conducted a study examining the reliability of student physiotherapists in carrying out US-based AHD measurements in painfree shoulders, after just an hour of training. A very good level of reliability was achieved with ICCs of 0.88-0.91 and 0.79, for intra and inter-rater reliability respectively. These studies suggest that despite the operator-dependent nature of ultrasound in diagnosing shoulder pathology (O'Connor et al 2005), the specific technique of measuring AHD in the shoulder can potentially be carried out reliably by clinicians with little ultrasound experience. There are no such studies examining the role of tester experience in measuring SsT thickness.
This study examined AHD with the arm in the participant’s natural resting posture, as it was believed that this would be the easiest method to standardise in the typical clinical setting. Wang et al (2005) found no significant differences when they compared AHD values with the arm in the frontal (in the line of the trunk) versus the scapular plane (in the line of the scapula). Kalra et al (2006) found that reliability diminishes when the AHD was measured in 45° abduction (ICC = 0.76) compared to neutral (ICC= 0.92), while intra-rater ICC values were similar in the Pijls et al (2010) study for neutral and 60° abducted positions. Studies in painfree populations have reported a reduction in AHD as the angle of shoulder elevation increases (Desmeules et al 2004, Maenhout et al 2012), with greater reductions in athletes with poor scapular control (Silva et al 2010). The critical ranges of motion for AHD measurement have not yet been determined in clinical populations. The modified Crass position provided an excellent position for visualisation of the SsT, as well as the intraarticular portion of the biceps tendon, which aided standardisation of measurement, and it was well-tolerated by the symptomatic participants.

There are a number of study limitations. There were a higher proportion of females in the control group (68%) than the symptomatic group (56%). While this may have resulted in lower mean AHD and SsT thickness values for the controls, it would not have affected reliability estimates. We carried out the testing of inter-rater reliability in a clinically recruited RC tendinopathy population only, due to observer availability, however this was the most clinically relevant group for this investigation, and inter-rater reliability has already been established in the pain-free populations for both AHD and SsT thickness measures. Reliability was only assessed using within-session repeated scans – no reliability assessment was carried out using re-measurement of the same images. This type of reliability assessment would elicit a different aspect of reliability i.e. purely the image measurement component, whereas reliability using repeated scans covers the broader issues of retaking the scans, as well as measurement issues. Radiology reliability studies often report only the reliability of image re-measurement, however this approach does not provide a comprehensive view of reliability concerns involved in using imaging in test-retest studies.

2.3.6 Conclusion

AHD and SST thickness can be reliably measured using ultrasound by both a single examiner and a pair of examiners in pain-free shoulders and those with RC tendinopathy. These
meaning of these measures need to be further investigated in the context of rehabilitation and surgical interventions for RC tendinopathy.
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Chapter 3: Clinical Studies

This chapter contains two papers, one of which has been accepted for publication in the peer-reviewed literature, with the other currently under review.

The primary research questions for this chapter are:

a) i) to compare measures of AHD, SsT thickness and subacromial occupation ratio, in people with painful ultrasound-diagnosed rotator cuff (RC) tendinopathy and pain-free controls, and
   ii) to examine whether there is any association between subacromial occupation ratio, and self-reported measures of pain and function in people with RC tendinopathy

b) to examine the short-term effect of fatigue loading on thickness of the SsT and AHD in people with and without RC tendinopathy
3.1 Study V: Thickened supraspinatus tendon but no change in subacromial space in rotator cuff tendinopathy
McCreesh K, Anjum S, Crotty J, Lewis J (Under review, J of Rehabilitation Medicine)

3.1.1 Abstract

**Objective:** To compare subacromial space (i.e. acromiohumeral distance AHD) and supraspinatus tendon (SsT) thickness, and their ratio (subacromial occupation ratio), between controls and people with rotator cuff (RC) tendinopathy

**Study design:** Cross-sectional study

**Subjects:** Thirty healthy controls and 40 people with painful RC tendinopathy (divided into 3 groups of mild, moderate or severe pain).

**Methods:** Ultrasound measurements of AHD and SsT thickness were obtained. Pain intensity (Numerical Rating Scale - NRS) and shoulder function (Shoulder Pain and Disability Index-SPADI) were measured.

**Results:** There was no between-group difference in AHD (p=1.000). There was a significantly thicker SsT in those with moderate (6.1mm, p<0.001) or severe (6.3mm, p<0.001) pain compared to controls (4.8mm). Subacromial occupation ratio was larger in moderate (65%, p<0.001) or severe pain (65.8%, p<0.001) groups compared to controls (50.5%). There were moderate, significant correlations between subacromial occupation ratio and both pain (r = 0.58, p<0.001) and function (r = 0.53, p<0.001).

**Conclusion:** Those with moderate and severe shoulder pain had larger subacromial occupation ratios and thicker SsT compared to controls or those with mild pain. The findings of this study provide possible support for an intrinsic model of RC tendinopathy, with early tendon thickening, followed by increased vulnerability to secondary compression due to a larger subacromial occupation ratio.

**Keywords:** shoulder, rotator cuff, tendinopathy, subacromial space, supraspinatus tendon, ultrasound
3.1.2 Introduction

Shoulder pain is a very prevalent condition, associated with a high rate of chronicity and disability in older adults (Luime et al 2004). Subacromial impingement syndrome (SIS) is a term used to describe a common clinical shoulder condition where the patient complains of anterolateral shoulder pain, particularly in relation to arm elevation, and usually encompasses a diagnosis of rotator cuff (RC) tendinopathy. Historically, this condition has been ascribed to extrinsic compression of the contents of the subacromial space (i.e. supraspinatus tendon (SsT) and sub-acromial bursa) due to altered acromial morphology, which has provided the rationale for surgical approaches involving acromioplasty (Lewis 2011). However in recent years, there has been increasing consideration of the role of intrinsic RC tendinopathy, often seen to occur internally, or on the articular side of the tendon, questioning the role of acromion in the development of pathology. Intrinsic tendon failure leads to degenerative changes in the tendon, and often to pain and loss of function (Lewis 2009). Degenerative changes in the SsT may lead to an increase in tendon thickness, with Joensen et al (2009) reporting a between-side difference in thickness of 0.8mm (i.e. painful side larger) in those with shoulder symptoms. The size of the subacromial space is generally quantified by radiological measurement of the acromio-humeral distance (AHD) (McCreesh et al 2013). Studies of AHD in those with RC tendinopathy, have generally reported lower values in those with RC tears, but varying results in comparisons of less severe tendon pathology (Saupe et al 2006, Goutallier et al 2011). Reasons proposed for the reductions in AHD in RC tears are superior translation of the humeral head occurring due to failure of the RC to provide its usual stabilising role, and postural alterations involving the scapula (Kalra et al 2010).

Both Cholewinski et al (2008), and Leong et al (2012) have examined the subacromial space and SsT thickness in people with RC tendinopathy, with the former study reported thinner SsT and a smaller subacromial space, contrasting with a larger AHD and thicker tendon in the painful shoulders in the second study. Michener et al (2013) recently presented a study examining the ratio between SsT thickness and AHD, termed the ‘occupation ratio’, where AHD and SsT thickness were assessed using ultrasound in 20 people with RC tendinopathy, and 20 matched controls. The RC tendinopathy group had a thicker SsT and larger occupation ratio in the painful shoulder when compared to controls, while AHD was not significantly different between the groups, meaning that while the subacromial space was not reduced in those with pain, the thickened tendon did occupy a greater proportion of the...
available space. The authors suggested that the thickened tendon was evidence of intrinsic tendon pathology, while the larger occupation ratio supported an extrinsic impingement mechanism. There was no assessment made of the relationship between the subacromial measures and either pain or shoulder function.

There is a high prevalence of imaging-diagnosed RC ‘pathology’ in the asymptomatic population, suggesting a lack of association between structural pathology and pain (Tempelhof et al 1999). However it remains to be investigated whether there is any association between other imaging parameters i.e. RC tendon thickness, AHD and occupation ratio, and symptoms. The evaluation of these measures with regard to pain and function in those with RC disorders may add further to the understanding of the mechanisms of this disorder, and could lead to the development of better rehabilitation programmes.

Therefore, the aims of this study were

1) to compare measures of AHD, SsT thickness and subacromial occupation ratio, in people with painful ultrasound-diagnosed RC tendinopathy and pain-free controls,

2) to examine whether there is any association between the subacromial occupation ratio, and self-reported measures of pain and function in people with RC tendinopathy

3.1.3 Methods

3.1.3.1 Participants

Two groups of participants were sought for this study, chosen to represent healthy controls, and people with RC tendinopathy. The healthy controls were recruited from the staff of a University. They were men and women over the age of 18. They were included if they had no history of shoulder pain, or injury in the previous year, no history of shoulder surgery, fracture or dislocation; and participated less than once a week in a sport or occupation involving upper limb loading. They were excluded if they had a history of neurological disorders or systemic inflammatory disease.

The RC tendinopathy group were recruited from both community (sports clubs and University population) and clinical (a shoulder ultrasound clinic) settings, in order to recruit a
broad range of shoulder pain severity. Participants in this group were included if they had a current history of shoulder pain present for greater than 6 weeks, and were over 18 years. They were excluded if they had undergone shoulder surgery, had a history of fracture or dislocation, or had recent (last 6 months) injections or physiotherapy for their shoulder pain. Those with a history of neurological, or systemic inflammatory disorders were also excluded. Potential volunteers were given an information sheet about the study and invited to participate. Ethical approval was granted by the appropriate Ethics Committee, and all participants gave written informed consent.

3.1.3.2 Diagnosis

The usefulness of clinical tests to provide a diagnosis of shoulder pain has been questioned in a number of systematic reviews (Park et al 2005, Hegedus et al 2012), suggesting that none of these tests can provide an accurate diagnosis. Ultrasound has been shown to have equivalent diagnostic accuracy to magnetic resonance imaging (MRI) in a large systematic review of RC imaging (De Jesus et al 2009), therefore ultrasound was deemed the most appropriate method of diagnosis for this study. A diagnostic ultrasound assessment was undertaken of all participants, by a physiotherapist (KM), trained in musculoskeletal sonography and with 18 months experience of shoulder ultrasound imaging.

Definitions of sonographic diagnostic criteria are subject to a degree of subjectivity and often poorly defined. For this study, diagnostic criteria were based on a combination of existing published criteria (Wakefield et al 2005, Naredo et al 2006, Cullen et al 2007). Tendinosis was recorded when there was loss of the normal tendon fibrillar structure, with an abnormally hypoechoic appearance. A partial-thickness tear was recorded when loss of tendon contour or a distinct/focal hypoechoic defect was seen anywhere within the tendon. A full-thickness RC tear was recorded when the RC tendons could not be visualized because of complete rupture or when there was a focal tendon defect extending from the bursal to the humeral side. Bursitis was recorded when marked fibrotic thickening of the subacromial bursa or bursal fluid > 2mm was present. In order to achieve a homogenous sample of controls participants, healthy controls were excluded from the study at this stage if they had ultrasound-diagnosed pathology of the subacromial bursa or RC tendons. For the symptomatic participants, the absence of any RC tendon or bursal pathology on imaging was an exclusion criterion. The ultrasound diagnosis was recorded as tendinopathy, partial or full-thickness tear. Those with
full-thickness tears of the supraspinatus were excluded at this stage of the study, as no SsT thickness measures could be taken.

3.1.3.3. AHD & SsT thickness Measures

All ultrasound measures were taken with participants in a seated position, with the arm in neutral for the AHD measurement and in the modified Crass position (shoulder internally rotated, palm of hand on hip) for the SsT thickness measures. Both shoulders were examined in the control group, and the painful shoulder (or most painful if symptoms were bilateral) in those with RC tendinopathy. A GE Logiq e ultrasound scanner (GE Medical, Wauwatosa, WI, USA) with a 7-12 MHz linear array transducer was used to undertake the scans. Acromio-humeral distance was measured as the shortest distance between the infero-lateral edge of the acromion and the humeral head. Supraspinatus images were taken in the transverse plane, with the intra-articular portion of the long head of biceps (LHB) visible. Thickness measurements were taken 5mm, 10mm and 15mm posterior to the edge of the biceps tendon, as per Figure 18, with the average of these measures used for data analysis.

![Ultrasound images illustrating measurement of the acromiohumeral distance (left) and supraspinatus tendon (right)](image)

3.1.3.4 Subacromial occupation ratio

While Michener et al (2013) described the amount of subacromial space occupied by the SsT as the ‘occupation ratio’, it is important to distinguish this term in relation to the subacromial space, as the term occupation ratio is commonly used to refer to the proportion of the supraspinous fossa occupied by the supraspinatus muscle (Yamaguchi et al 2012). Therefore,
we will use the term subacromial occupation ratio in order to distinguish the terms. Subacromial occupation ratio was calculated by dividing SsT thickness by the AHD, which was then expressed as a percentage.

3.1.3.5 Reliability & Blinding
All scans for this study were undertaken by the same examiner (KM). Measurements from the ultrasound images were undertaken one week after the scans were taken. In order to provide examiner blinding, the on-screen display of the values was obscured using a sticker placed on the screen while measurements were being taken. Values were then later transcribed using a participant code which did not reveal group allocation. A reliability study showed that this examiner achieved excellent intra-rater reliability, with intra-class correlation coefficients of >0.9 for both AHD and SsT thickness measures in people with RC tendinopathy, and minimal detectable difference (MDC) values of 0.6mm for SsT thickness and 0.7mm for AHD (Study IV).

3.1.3.6 Function and pain
Demographic details were obtained from all participants. Shoulder function was assessed using the Shoulder Pain and Disability Index (SPADI), and average shoulder pain intensity was evaluated using the Numerical Rating Scale (NRS). Reliability and responsiveness of the NRS has been confirmed in a shoulder pain population (Mintken et al 2009). Both Turner et al (2004) and Jensen et al (2001) examined scores on the NRS for musculoskeletal pain as they corresponded to mild, moderate and severe pain, and reported appropriate cut-offs of 1-4, 5-6 and 7-10 respectively. Since examining the shoulder ultrasound measures in relation to pain intensity was of interest in this study, the RC tendinopathy group were divided into 3 groups according to these cut-offs. The SPADI comprises sub-scales for both pain and disability (Williams et al 1995), with an overall score out of 100; higher values indicate greater disability, and it has been shown to be suitable for use in those with RC disorders (Engebretsen et al 2010).

3.1.3.7 Data Analysis
Descriptive statistics were used to summarise the demographic characteristics and outcome scores. Data were evaluated for normality using the Shapiro-Wilk test, and no apparent deviations from normality could be detected. As paired t-tests showed no dominance effect
for AHD or SsT thickness in controls, a mean of the measurements from the two shoulders in controls was used. Controls and total RC tendinopathy group were compared for baseline characteristics using t-tests for age, height and weight, and chi-squared test for sex. Subacromial occupation ratio was calculated by dividing SsT thickness by the AHD, expressed as a percentage.

Between-group comparisons were made between controls and the three RC tendinopathy groups (divided according to NRS pain category), for AHD, SsT thickness and occupation ratio using a One-way ANOVA with planned pairwise comparisons (each RCT group compared to controls). The resultant p-values were compared to an appropriately adjusted alpha level to allow for the three comparisons made. Correlation between occupation ratio and both pain and function was evaluated using the Pearson’s correlation coefficient. Effect size was examined by calculating Cohen’s d values, with a small effect being defined as 0.2, medium as 0.5, and large as 0.8 or above (Cohen 1988). Correlation between occupation ratio and both pain and function was evaluated using the Pearson’s correlation coefficient. Significance was set at the p<0.05 level.

### 3.1.4 Results

A total of 78 participants were recruited, grouped as healthy controls (n=30), and RC tendinopathy (n=48). Subsequently eight of the RC tendinopathy group were excluded due to the presence of full thickness supraspinatus tears, leaving 40 in this group. See Table 9 for demographic details of the two groups. There was no statistically significant difference in age, height, weight or sex distribution across the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Controls N=30</th>
<th>RCT N=40</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs) (Mean (SD))</strong></td>
<td>50 (6.0)</td>
<td>53.9 (12.8)</td>
<td>P=0.125</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>14F, 16M</td>
<td>20F, 20M</td>
<td>P=0.445</td>
</tr>
<tr>
<td><strong>Height (cm) (Mean (SD))</strong></td>
<td>165.3 (7.4)</td>
<td>161.4 (6.5)</td>
<td>P=0.335</td>
</tr>
<tr>
<td><strong>Weight (kg) (Mean (SD))</strong></td>
<td>70.0 (8.9)</td>
<td>74.8 (9.7)</td>
<td>P=0.253</td>
</tr>
</tbody>
</table>

**Table 9** Baseline characteristics of the participants.

*Abbreviations: RCT = Rotator cuff tendinopathy, SD = standard deviation, M= male, F= female*
The RC tendinopathy group was then divided according to NRS pain intensity score into three groups: mild pain (n=15), moderate pain (n=15) and severe pain (n=10). See Table 10 for breakdown of characteristics of the three RC tendinopathy groups, including diagnoses and outcome scores.

<table>
<thead>
<tr>
<th>Rotator Cuff Tendinopathy Group</th>
<th>Age (yr) (Mean) (SD)</th>
<th>Sex</th>
<th>Symptom Duration (months) (Mean) (SD)</th>
<th>NRS (Mean) (SD)</th>
<th>SPADI (Mean) (SD)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild pain</strong> N=15</td>
<td>50.2 (12.2)</td>
<td>6F, 9M</td>
<td>9.2 (10.4)</td>
<td>3 (0.8)</td>
<td>22 (12)</td>
<td>Supraspinatus tendinosis=11 Supraspinatus + bicipital tendinosis=1 Partial tear supraspinatus=3</td>
</tr>
<tr>
<td><strong>Moderate Pain</strong> N=15</td>
<td>55.6 (12.8)</td>
<td>9F, 6M</td>
<td>14.8 (14.5)</td>
<td>6 (1.1)</td>
<td>48.4 (11)</td>
<td>Supraspinatus tendinosis=8 Partial tear supraspinatus=7</td>
</tr>
<tr>
<td><strong>Severe Pain</strong> N=10</td>
<td>56.8 (10.5)</td>
<td>5F, 5M</td>
<td>17.4 (16.3)</td>
<td>7.5 (0.7)</td>
<td>65.8 (9.8)</td>
<td>Supraspinatus tendinosis=3 Partial tear supraspinatus=7</td>
</tr>
</tbody>
</table>

**Table 10** Baseline characteristics for rotator cuff tendinopathy groups according to pain intensity category

**Abbreviations:** SD= standard deviation, NRS= Numerical rating Scale; SPADI= Shoulder Pain and Disability Index. F= female, M= male

### 3.1.4.1 Between-Group comparisons

Mean and standard deviations (SD) for AHD, SsT thickness and subacromial occupation ratio values, as well as p values and confidence intervals for comparisons between controls and the RC tendinopathy groups are presented in Table 11.
<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>D (95% CI)</th>
<th>p value</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acromiohumeral distance (mm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>9.74</td>
<td>1.18</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>RCT-Mild pain</td>
<td>9.94</td>
<td>1.04</td>
<td>-0.20 (-0.96, 0.55)</td>
<td>p= 0.590</td>
<td>0.18</td>
</tr>
<tr>
<td>RCT-Moderate pain</td>
<td>9.46</td>
<td>1.41</td>
<td>0.28 (-0.48, 1.04)</td>
<td>p=0.467</td>
<td>-0.16</td>
</tr>
<tr>
<td>RCT severe pain</td>
<td>9.51</td>
<td>0.91</td>
<td>0.23 (-0.66, 1.12)</td>
<td>p= 0.606</td>
<td>-0.09</td>
</tr>
<tr>
<td><strong>Supraspinatus tendon thickness (mm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>4.79</td>
<td>0.73</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>RCT- Mild pain</td>
<td>5.06</td>
<td>0.84</td>
<td>-0.35 (-0.91, 0.21)</td>
<td>P=0.212</td>
<td>0.37</td>
</tr>
<tr>
<td>RCT- Moderate pain</td>
<td>6.05</td>
<td>1.06</td>
<td>-1.33 (-1.89, -0.77)</td>
<td>*p&lt;0.001</td>
<td>1.56</td>
</tr>
<tr>
<td>RCT- Severe pain</td>
<td>6.17</td>
<td>1.01</td>
<td>-1.47 (-2.12, -0.81)</td>
<td>*p&lt;0.001</td>
<td>1.77</td>
</tr>
<tr>
<td><strong>Subacromial occupation ratio (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>49.37</td>
<td>6.20</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>RCT- Mild pain</td>
<td>51.19</td>
<td>8.46</td>
<td>-1.82 (-7.82, 4.18)</td>
<td>P=0.547</td>
<td>0.26</td>
</tr>
<tr>
<td>RCT- Moderate pain</td>
<td>65.02</td>
<td>14.05</td>
<td>-15.65 (-21.60, -9.65)</td>
<td>*P&lt;0.001</td>
<td>1.65</td>
</tr>
<tr>
<td>RCT- Severe pain</td>
<td>65.19</td>
<td>10.05</td>
<td>15.82 (-22.86, -8.77)</td>
<td>*P&lt;0.001</td>
<td>2.17</td>
</tr>
</tbody>
</table>
3.1.4.2 Acromiohumeral distance

There was no statistically significant difference in AHD between the RC tendinopathy groups and the controls, or between any of the RC tendinopathy groups (all \( p \geq 0.017 \)). Effect sizes were very small for these comparisons.

3.1.4.3 Supraspinatus thickness

There was no difference in SsT thickness between those with mildly painful shoulders and controls. There was a significantly thicker SsT in those with moderate pain \( (p<0.001) \) and those with severe pain \( (p<0.001) \), compared to controls, with large effect sizes for these significant comparisons. Those with mild pain also had significantly thinner SsT than the moderate \( (p=0.024) \) and severe pain groups \( (p=0.023) \). There was no difference in SsT thickness between the moderate and severe pain groups \( (p \geq 0.017) \).

3.1.4.4 Subacromial occupation ratio

The boxplot in Figure 19 displays the subacromial occupation ratio data for the controls and the three shoulder pain groups. There was no significant difference in subacromial occupation ratio between controls and those with mild shoulder pain \( (p=0.547) \). However there was a statistically significant difference between the controls and both the moderate \( (p<0.001) \) and severe \( (p<0.001) \) shoulder pain groups, with a large effect size for both comparisons. There was also a statistically significant difference between the mild and moderate \( (p<0.001) \), and mild and severe \( (p<0.005) \) shoulder pain groups, with in each case a larger occupation ratio as pain intensity increased. There was no difference in subacromial occupation ratio between the moderate and severe pain groups.
Figure 19 Boxplot of Subacromial Occupation ratio (%) according to pain intensity on NRS. “No pain” refers to the control group, while the shoulder pain group are divided according to pain intensity (mild, moderate, or severe). NRSCat: Numerical Rating Scale Category, OccRatio: subacromial occupation ratio

3.1.4.5 Correlations

There were significant correlations at a moderate level between subacromial occupation ratio and both pain intensity (defined by NRS pain category, \( r = 0.58, p<0.001 \)) and shoulder function/disability (defined by SPADI score, \( r=0.53, p<0.001 \)).

3.1.5 Discussion

This study identified that while there was no difference in AHD between controls and those with RC tendinopathy, there was an increase both in SsT thickness and the percentage of subacromial space occupied by the tendon (subacromial occupation ratio) in those with moderate or severe shoulder pain, which was not seen in those with mild pain. The subacromial occupation ratio was also significantly associated with both pain intensity and
shoulder function. The results are similar to those reported by Michener et al (2013), although overall values of both AHD and SsT thickness values were smaller. In this study, mean SsT thickness was 4.7mm in the controls and ranged from 5.1-6.2mm in the RC tendinopathy groups compared to 6 and 6.6mm in the Michener et al (2013) study, while our AHD was 9.8mm in controls and from 9.5-9.9mm across the RC tendinopathy groups, in comparison to 11.4mm and 10.8mm. The reason for this difference is not clear; however some explanation might lie in anthropometrics - mean height was lower in this study. The values for SsT thickness and AHD in both studies remain within the ranges reported by a variety of other studies of both healthy and symptomatic populations (McCreesh et al 2013). Interestingly the values for subacromial occupation ratio, which is a relative measure, were more similar between the studies for the control groups (50.5% versus 54.2%), and between the moderate and severe pain group in this study and overall ratio for the pain group in the Michener et al (2013) study (65% and 65.8% versus 61.7%). We suggest that the occupation ratio is a better comparator across studies because as a ratio measure it is less likely to be affected by gender or anthropometrics, as well as the fact that incorporates a measure of the tendon in relation to the subacromial space it occupies.

The aetiology of RC tendinopathy is still poorly understood, and a number of models have been proposed. The continuum model of tendinopathy (Cook and Purdam 2009) describes tendon thickening or swelling as part of both the reactive and dysrepair stages of tendinopathy. This thickening is generally ascribed to a proliferative tendon and an increase in water content. In a review of the role of compressive loading in tendinopathy, Cook and Purdam (2012) discuss how the swollen tendon essentially becomes a “space-occupying lesion” with both internal tendon compression, and extrinsic compression from local anatomical structures, potentially occurring.

In examining the theorised mechanisms behind RC tendinopathy, tendon pain and pathology could be contributed to by intrinsic tendon overload (intrinsic theory), or by tendon compression within the subacromial space (extrinsic theory), or indeed a combination of the two processes (Lewis 2010). Experimental work in rats by Solowsky et al (2002), showed that compression alone (from surgically-created interposition of soft tissue across the SsT) had no adverse effects on tendon structure with normal cage activity, in contrast to rats with normal anatomy undergoing overload with a running programme, where significant tendon structural changes occurred. However in a third group of animals, with both the compression and overload conditions, advanced tendon degenerative changes occurred. The extrinsic, or
acromial, theory is further challenged by the fact that the majority of the structural change in RC tendinopathy is seen on the undersurface of the tendon, where it comes into contact with the humeral head, rather than on the superior bursal side, where acromial compression should have a greater impact (Fukuda et al 1987).

If the extrinsic mechanism of RC tendinopathy was supported, it would be expected that the AHD might be reduced in those with painful tendinopathy, compared to pain-free populations. A reduced AHD in painful shoulders compared to controls was not supported either in this study or in the study by Michener et al (2013). A primarily intrinsic mechanism might be expected to result in thickening of the SsT, as seen in this study in the moderate and severe pain RC tendinopathy groups, and across the shoulder pain group in the Michener et al (2013) study. The subacromial occupation ratio results in this study suggest a basis by which extrinsic compression may occur as a secondary phenomenon. The thickened SsT occupies a greater proportion of the subacromial space and thus potentially could become more vulnerable to compression, even if the space has not changed in size. Further complexity arises from the fact that the presence of painful tendinopathy can have a negative impact on RC muscle function, which may lead to superior migration of the humeral head due to ineffective stabilisation. Notwithstanding the possible effects of secondary compression events, the presence of an increased SsT thickness in the higher pain intensity categories in this study, alongside an absence of difference in AHD, may to lend some support to an intrinsic, rather than extrinsic mechanism of tendinopathy in these participants. This study is of course limited by examining these parameters in a cross-sectional, rather than prospective manner, where we cannot determine whether the thickness changes precede or follow development of pain; however progressive tendon thickening has been extensively reported in studies of lower limb tendinopathies (Cook and Purdam 2009).

Current approaches in RC surgery (i.e. acromioplasty) focus on impingement of the SsT by the acromion and coracoacromial ligament as a cause of RC tendinopathy (Lewis 2011). This study provides some evidence for the possibility that, initially, intrinsic tendon changes might be the primary event, with reduced subacromial space, and tendon’ impingement’ or compression, potentially occurring as a secondary phenomenon. Rehabilitation approaches which involve graduated tendon loading programmes in order to condition the tendon, and encourage return to more normal levels of load tolerance, should be the mainstay of treatment for those without a radiologically confirmed source of tendon impingement e.g. osteophyte. Recent research confirms that exercise approaches achieve equivalent success to surgery for
RC disorders in the short and longer term (Ketola et al 2013). It remains to be seen what the mechanism of effect of exercise in tendinopathy is. While some studies have supported a reduction in tendon diameter as a positive outcome of tendon rehabilitation (Konsgaard et al 2009), a systematic review by Drew et al (2014) suggests that, at present, there is no evidence for a relationship between structural changes in the tendon and pain relief from therapeutic exercise.

Due to the lack of relationship between imaging diagnosis and pathology in RC disorders (Frost et al 1999), we decided against analysing our participants according to imaging findings, and instead, did so on the basis of pain intensity. This study has highlighted a significant, moderately strong association between occupation ratio of the SsT and both pain intensity and shoulder functional score in our group of people with relatively chronic RC tendinopathy disorders. While there are undoubtedly multiple factors beyond structural change involved in the development and progression of shoulder pain (Littlewood et al 2013), this is one of the first studies to find an association between ultrasound findings and pain and function in this population. Studies involving people undergoing fatiguing exercise protocols for the RC have shown that AHD reduces with increasing fatigue, while studies of lower limb tendons have shown that tendon thickness can both increase or decrease as a result of exercise (Tardioli et al 2012), although evidence for SsT response to exercise in humans is lacking. Therefore it would seem that the occupation ratio may change in response to shoulder loading. An examination of whether immediate or longer term changes occur in the SsT and subacromial occupation ratio with loading, as well as any relationship between these changes and pain or shoulder function, may further contribute to understanding the role of these parameters in the development and/or treatment of painful RC tendinopathy.

Limitations

This study used a small convenience sample, with measurements all taken in the neutral arm position. Since studies have shown that AHD decreases with arm elevation (Seitz et al 2012), examining these parameters with the arm in the ranges of motion where symptoms occur may be of interest. While the subcategorisation of the RC tendinopathy group reduced the sample size in each category, effect size calculations showed large effect sizes for the significant comparisons, suggesting that the sample size was appropriate. Ultrasound is a two dimensional method of imaging, which limits its capabilities in imaging three dimensional structures i.e. SsT and AHD, however it offers a quick, inexpensive method which is easily
carried out in clinical practice (McCreesh et al 2013). Although some studies have examined radiological parameters between shoulders in those with RC tendinopathy, it is clear that the unaffected shoulder in those with unilateral pain often displays altered structural and functional properties (Heales et al 2013); therefore we restricted our comparisons to pain-free controls without any evidence of ultrasound-diagnosed pathology. However there is a limitation in the use of a pain and pathology-free population in this study. Since the study examined the SsT thickness in relation to pain, the exclusion of controls with RC tendon pathology (in the absence of pain), may have been a confounding factor increasing the likelihood of finding an association between tendon thickness and pain.

In conclusion, people with moderate or severely painful RC tendinopathy had thicker SsT, and a greater subacromial occupation ratio in the painful shoulder compared to pain-free controls, or those with mildly painful RC tendinopathy. Acromiohumeral distance was not different between the groups. Subacromial occupation ratio was moderately associated with measures of pain intensity and shoulder function. These findings provide some support for a primary intrinsic mechanism of RC tendon pathology, theoretically supporting rehabilitation approaches aimed at improved tendon conditioning, such as graduated loading programmes.
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3.2 Study VI: Altered supraspinatus tendon response to fatigue loading in rotator cuff tendinopathy
McCreesh K, Donnelly A, Lewis J (Accepted subject to revisions, British Journal of Sports Medicine)

3.2.1 Abstract
Background/Aim: Tendon loading leads to multiple changes in tendon properties, which can be different in healthy versus tendinopathic tendons. Most studies into the effect of tendon loading involve lower limb tendons, and suggest that loading causes reduced tendon thickness in the normal tendon, with a reduced response in painful tendons. However, no such studies exist for the rotator cuff (RC) tendons. Therefore, the aim of this research was to examine the short-term effect of loading on thickness of the supraspinatus tendon (SsT) and acromiohumeral distance (AHD) in people with and without RC tendinopathy.

Methods: Participants were 20 healthy controls, and 22 people with RC tendinopathy. Supraspinatus tendon thickness and AHD were measured using ultrasound scans before and at 3 timepoints after a loading protocol (one, six and 24 hours). Loading involved isokinetic eccentric and concentric external rotation and abduction to the point of fatigue.

Results: There was a significant increase in SsT thickness in the RC tendinopathy group at one (7%) and six (11%) hours although only the six hour difference exceeded minimal detectable difference (MDC). There was a small (<MDC), significant reduction (4%) in SsT thickness in controls at 6 hours. The AHD reduced significantly in both groups at one hour, with recovery to normal by 6 hours in controls, and 24 hours in the pain group.

Conclusion: Painful RC tendons showed an altered response to loading and slower return to normal compared to pain-free tendons. In combination with reduced subacromial space, tendon swelling in the RC tendinopathy group may provide evidence for an interaction between intrinsic and extrinsic mechanisms of RC tendinopathy.

Keywords: rotator cuff, tendon, ultrasound, exercise, acromiohumeral distance
3.2.2 Introduction

Mechanical loading of tendon has been shown to induce multiple positive adaptive changes in mechanical, morphological and biomechanical properties in healthy tendon (Heinemeier & Kjaer 2011). However, overloading may influence the degree of this adaptation, and may lead to tendinopathy, in which the early stages may be characterised by; tendon swelling, pain and reduced function, with potential progression to tendon breakdown and tearing in more chronic cases (Cook & Purdam 2009). Tendon loading may therefore have both beneficial and detrimental effects on the tissue. How and why these processes occur remain uncertain and elusive, but greater understanding has the potential to improve the management of painful tendinopathy.

A review of the immediate effects of exercise on tendon structure concluded that while changes in tendon mechanical properties occur with exercise, resembling those reported in pathological tendons, the heterogeneity of existing studies precludes firm conclusions (Tardioli et al 2012). Obst et al (2013) conducted a systematic review examining the immediate effects of exercise on the mechanical and morphological properties of the Achilles tendon, reporting consistent evidence of a reduction in healthy Achilles tendon diameter immediately after exercise, in particular with eccentric contractions. In contrast, an MRI study of the response of symptomatic Achilles tendons to eccentric and concentric loading by Shalabi et al (2004) showed that both types of loading led to increased tendon thickness and MRI signal, indicating possible higher water content or tendon hyperaemia immediately post-exercise. In addition, a number of studies comparing the response of healthy and symptomatic tendons to loading have reported delayed recovery of tendon properties in those with pathology, in terms of slower return to baseline tendon characteristics (Grigg et al 2012, Pingel et al 2013). Therefore it is important to compare both healthy and pathological tendons individually when evaluating the response to load.

Importantly, tendons such as the Achilles and patellar tendons are referred to as energy storage and release tendons, while those controlling the fingers as positional tendons (Thorpe et al 2012), while the rotator cuff (RC) tendons may have components of both functions. The vast majority of studies examining tendon responses to loading include lower limb tendons only, yet RC tendinopathy is a significant source of pain and reduced function in adults, in both occupational and athletic populations. The response of the RC tendons to loading has
not been extensively investigated, with the RC tendons potentially responding differently to the lower limb tendons.

Exercise studies of the RC muscles focus on the effect of fatigue loading on scapular posture and the subacromial space, with reduced subacromial space associated with RC fatigue (Royer et al 2009, Chopp et al 2010) however no studies have examined the effect of load on the RC tendons. In one of the few studies to examine tendon responses in vivo in the upper limb, van Drongelen et al (2007) examined acute changes in biceps tendon diameter in wheelchair athletes (n= 42) after a single basketball or rugby game, a third of whom had shoulder pain. They noted a non-significant increase in tendon thickness related to duration of play, as well as an increase in tendon echogenicity on ultrasound, attributed by the authors to increased fluid content. It is apparent that more research is required that investigates the morphological response of the RC tendons to exercise, both in normal and symptomatic tendons.

Impingement of the supraspinatus tendon (SsT) in a reduced subacromial space is a widely held pathomechanical theory for the development of RC tendinopathy (Neer 1972). However studies examining subacromial space, represented by the linear acromiohumeral distance (AHD), in RC tendinopathy do not consistently report changes compared to pain-free shoulders, except in those with significant RC tendon tears (Azzoni et al 2004, de Witte et al 2014). Increased SsT thickness has also been noted as a feature of RC tendinopathy (Joensen et al 2009). The interaction between a thickened tendon and a potentially reduced subacromial space was examined by Michener et al (2013), calculating the occupation ratio (the ratio between SsT thickness and AHD), in people with shoulder pain and age-matched controls. This study reported a thicker tendon in the group with shoulder pain resulting in a larger occupation ratio, despite no significant between-group difference in subacromial space. These results lend support to a possible intrinsic mechanism of RC tendinopathy (Lewis 2011), where tendon thickening may be an early primary response that may later lead to extrinsic compression as a secondary phenomenon, due to the larger tendon occupying a limited subacromial space. While these cross-sectional studies provided novel information to inform mechanisms of supraspinatus tendinopathy, it is important to examine these processes in a dynamic environment, in response to shoulder loading, as this better replicates the clinical presentation of painful RC pathology. Therefore, the aim of this research was to examine the short-term effect of loading on thickness of the SsT and AHD in people with and without RC tendinopathy.
3.2.3 Materials & Methods

3.2.3.1 Participants

Participants (both controls and shoulder pain group) were recruited from community-based settings (University campus and sports clubs). Controls were males and females over 18 years, and included if they were; free of shoulder pain over the last year, had full pain-free range of motion of their shoulders, did not have any neurological or systemic rheumatological disorders, history of shoulder fracture, dislocation or surgery, or any contraindications to ultrasound imaging. Shoulder pain participants were males and females over 18 years with a current history of unilateral shoulder pain, but still able to undertake physical exercise with their shoulder (defined as 15 minutes of moderate arm exercise, such as tennis or housework). They were excluded if they had bilateral shoulder pain, had ever undergone shoulder surgery, had any neurological or systemic rheumatological disorders, or contraindications to ultrasound imaging. The study received ethical approval from the University of Limerick Research Ethics Committee and all volunteers provided written consent to participate.

3.2.3.2 Measures and diagnosis

Control participants provided details of their age, height, and weight. Those with shoulder pain provided the same data, as well as information about the nature and duration of their shoulder pain. A Numerical Pain Rating Scale (NRS) for average shoulder pain intensity (Mintken et al 2009), and the Shoulder Pain and Disability Index (SPADI) to assess shoulder disability (Williams et al 1995) were also completed. The NRS was completed again at 24 hours post-exercise.

The diagnosis of RC tendinopathy is challenging, with both imaging-based and clinical diagnostic approaches having significant flaws (Lewis 2009). While Hegedus et al (2012) reported that none of the shoulder clinical diagnostic tests provide an accurate diagnosis of pathology, there was marginally better accuracy with a combination of tests. Michener et al (2009) found that, a cut-off of 3 out of five positive tests (painful arc, empty can, external rotation resistance, Neer, and Hawkins and Kennedy) best predicted RC tendinopathy, while less than three positive tests ruled it out. It is well-known that imaging-based RC pathology has been extensively noted in symptom-free shoulders (Tempelohf et al 1999). In order to
best reflect current clinical practice, we decided to combine both clinical and ultrasound diagnoses for the symptomatic participants. All participants underwent a clinical examination using the five tests described by Michener et al (2009). Control participants were required to have a maximum of two positive tests on both shoulders. This was the same requirement for the pain-free side of participants with unilateral shoulder pain, with a minimum of three positive tests on the painful shoulder in this group.

3.2.3.2.1 Ultrasound scans

Ultrasound examinations were undertaken of both shoulders in all participants using a GE Logiq e ultrasound scanner (GE Medical, Wauwatosa, WI, USA), with a 12MHz linear probe, by a musculoskeletal sonographer with two years experience of shoulder ultrasound imaging. Static images were referred for review to a consultant radiologist to confirm diagnoses for the symptomatic group. To produce as homogeneous sample as possible, control participants were excluded at this stage if any grey-scale shoulder pathology, such as tendinosis (loss of the normal fibrillar structure of the tendon with an abnormally hypoechoic appearance), partial tear of the supraspinatus tendon (flattening of the tendon surface or presence of a focal hypoechoic defect within, or on either surface of, the tendon) or full thickness tears (focal defect extending from the bursal to the humeral side of the tendon, or complete non-visualisation of the tendon) was found in either shoulder. Only one control volunteer was excluded using these criteria. For participants with unilateral shoulder symptoms, the pain-free shoulder was also required to be free of grey-scale pathology, while the painful shoulder was required to show some evidence of pathology. Shoulder pain participants with full thickness tears were also excluded from participation. A normal subacromial bursa is either invisible or measures <2mm on ultrasound (van Holsbeeck & Strouse 1993). With such a small size, measurement reliability, with the degree of resolution available on ultrasound, is a significant challenge. In this study no participant had a subacromial bursa thicker than 2mm at baseline or after exercise; therefore no further assessment of bursal thickness was carried out.

For participants fulfilling the clinical and ultrasound inclusion criteria, additional data including SsT in transverse section (for SsT thickness measurement) and AHD were measured. For the AHD measures, the participant was sitting, shoulder neutral, with the hand resting on the lap. An ultrasound image was taken with the transducer was positioned along the line of the humerus, over the anterior part of the acromion, with the subacromial space
and humeral head visible. The AHD was then measured as the shortest distance between the inferolateral edge of the anterior acromion and the humeral head, parallel to the acoustic shadow cast by the acromion.

For the SsT measures, the arm was placed into the modified Crass position i.e. palm of the hand on the iliac crest, with the elbow directed posteriorly. The SsT was scanned in the transverse plane. Once the tendon was in view, the transducer was moved anteriorly until the intra-articular portion of the long head of biceps was visualised, at which point the image was taken. On-screen callipers were used to measure between the echogenic boundaries of the tendon, at points 5mm, 10mm and 15mm posterior to the edge of the biceps tendon, with the mean of these measures used for analysis. Subacromial occupation ratio is a useful variable expressing the relationship between tendon thickness and space occupied; therefore it was calculated by dividing SsT thickness by the AHD, expressed as a percentage.

An intra-rater reliability study for the AHD and SsT thickness measures was previously undertaken in 45 people with RC tendinopathy (Study IV). A set of two ultrasound scans were taken within a single session by one examiner with the probe removed between scans. Measurement was undertaken using onscreen callipers, with the onscreen display of the measure obscured using a sticker. Reliability was excellent (ICCs>0.9), and minimal detectable change (MDC) values of 0.7mm for AHD and 0.6mm for SsT thickness were calculated.

For the main study, AHD and SsT thickness measures were obtained immediately before, and then at three intervals post-exercise; one hour, six hours and 24 hours. To ensure reproducibility all scans were taken by the same examiner, and the participant was placed in the same chair, with the consistent instructions. Measurements were taken on recorded images using the on-screen callipers, at a minimum of one week after testing. All scans were coded to improve blinding to group allocation and time the scan was taken at.

3.2.3.3 Loading protocol

Immediately after the initial ultrasound measurements, each participant performed the loading protocol in a seated position using the Biodex System 3 isokinetic dynamometer (Biodex Medical Systems, Shirley, New York, USA). For the shoulder pain group, the painful shoulder was exercised, while for the control group the side to be exercised was randomly chosen by coin toss. Participants undertook a 5 minute shoulder warm-up,
involving range of motion exercises. Functional difficulties with external rotation and abduction are common in those with RC tendinopathy. Tardo et al (2013) reported that supraspinatus was important in providing a stabilisation role to the shoulder during external rotation, while Reed et al (2013) showed that supraspinatus was activated along with infraspinatus and deltoid in the early ranges of shoulder abduction. Therefore our protocol involved two bouts of exercise; one of concentric and eccentric shoulder abduction, and a second one of concentric and eccentric shoulder external rotation; with order of completion determined randomly by coin toss. The isokinetic protocol was based partly on that described by Roy et al (2011) where 60 reps at 60deg/sec resulted in mean fatigue levels of 38% for external rotation. For this study we increased the speed to 120deg/sec in order to increase the tendon loading, and set the fatigue level at a 35% drop in overall torque for each of the exercise bouts. For external rotation, the participant was seated with the arm in 45º abduction in the neutral plane, and range of motion was set at minimum arc of 45 degrees for external rotation, commencing from a position of 20 degrees internal rotation to at least 25 degrees of external rotation. For abduction, the participant was also seated, with the arm in the neutral plane, and range of motion was from neutral to as close to 90 degrees as was tolerable for the participant (i.e. avoiding moving into the range of the painful arc for the symptomatic group). Three sets of 10 repetitions of each movement direction were completed with 10 seconds rest between sets. Additional sets were undertaken if the requisite fatigue level was not reached after completion of the prescribed sets, or testing was ceased if the required fatigue level was reached before the 3 sets were complete. Testing was also ceased if pain beyond usual resting levels for the participant was experienced, however all participants completed at least 2 sets of each movement direction.

### 3.2.3.4 Data analysis

Data were entered into SPSS version 21 for analysis. Data were assessed using the Shapiro-Wilk test and found to be normally distributed. Significance level was set at p=0.05. Repeated measures ANOVA (with Bonferroni correction) was used to evaluate the changes in SsT thickness and AHD compared to baseline over the subsequent 3 time points (1 hour, 6 hours and 24 hours post-exercise) for each shoulder independently in the two groups. Since occupation ratio is a percentage comprised of the two other variables (AHD and SsT thickness) no further statistical testing was performed on this data.
3.2.4 Results

3.2.4.1 Participants

A total of 20 healthy controls (10 males, mean age 43 years, range 28-59) and 22 people with RC tendinopathy (12 males, mean age 47 years, range 23-67) took part in the study. Demographic characteristics of participants are shown in Table 12, along with ultrasound diagnoses and shoulder pain (NRS) and disability (SPADI) scores for the symptomatic group. Control participants completed slightly more exercise sets (mean 5.8) than the shoulder pain group (mean 4.9).

<table>
<thead>
<tr>
<th></th>
<th>Age (yrs) (Mean) (SD)</th>
<th>Sex</th>
<th>BMI (Mean) (SD)</th>
<th>Symptom Duration (months) (Mean) (SD)</th>
<th>NRS (Mean) (SD)</th>
<th>SPADI total (Mean) (SD)</th>
<th>Ultrasound Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls N=20</td>
<td>43 (9.5)</td>
<td>10F, 10M</td>
<td>27.5 (4.6)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>RC tendinopathy N=22</td>
<td>47 (12.8)</td>
<td>10F, 12M</td>
<td>26 (3.5) 13 (8.4) 4 (1.4) 25 (11.5)</td>
<td></td>
<td></td>
<td></td>
<td>Supraspinatus tendinosis= 16 Partial tear supraspinatus= 6</td>
</tr>
</tbody>
</table>

Table 12 Demographic details

Table 13 details the mean values for SsT and AHD at each time point for the exercised shoulder in each group, and the relevant $p$ values for the ANOVA tests.
Table 13 Mean values of Supraspinatus thickness and acromiohumeral distance for exercised shoulders of both groups and p values for Repeated measures ANOVA

Abbreviations: 0hr= baseline, 1hr= 1 hour post exercise, 6hr = 6 hours post exercise, 24hr= 24 hours post exercise, vs = versus, 95% CI = 95% confidence interval
Symbols: *statistically significant result ** statistically significant result with mean difference greater or equal to the minimal detectable change

3.2.4.2 Supraspinatus tendon thickness

There was a significant reduction in SsT thickness in the control group six hours after exercise, however the mean difference was small (0.2mm, 4%) and did not reach the MDC for this measure. There was no significant difference in SsT thickness relative to baseline at any other time point for either the exercised or the non-exercised shoulder in the control group.

For the shoulder pain group, there was a significant increase in SsT thickness between baseline and both one and six-hour time points, however only the six hour difference (0.6mm,
11%) reached the MDC. Mean SsT thickness 24 hours after exercise was not significantly different to baseline. Examining individual results, it was seen that twelve participants had SsT thickness increases that equalled or exceeded the MDC at one and/or six hours post exercise, and four of these had sustained thickness change at 24 hours. While too small for detailed analysis, these 4 participants were observed to have higher NRS pain scores at 24 hours post exercise, compared to the rest of the group with normalised tendon thickness. There was no significant difference in SsT thickness in the non-exercised shoulder between baseline and at any subsequent time point in this group (p<0.05).

3.2.4.3 Acromiohumeral distance

There was a significant reduction in AHD between baseline and one hour post-exercise in the control group, with a mean difference equal to the MDC. There was no difference in AHD between baseline and either the six or 24 hour measures for controls, or across any time point for the non-exercised side (p<0.05).

In the shoulder pain group there was a significant drop in AHD at both one and six hours after exercise, with the one-hour difference exceeding MDC, while there was no difference at 24 hours. The non-exercised shoulder demonstrated no differences across the study period (p<0.05). Examining individual results showed that all but two of this group had AHD reductions greater than or equal to the MDC at one and/or six hours, but just four had a sustained reduction at 24 hours.

3.2.4.4 Occupation ratio

Figure 20 displays the trends in occupation ratio (SsT as a percentage of AHD) in both groups over time, with a greater increase and slower return to baseline in the RC tendinopathy group.
Figure 20: Subacromial occupation ratio (%) at baseline (0hr) and 3 subsequent time points of 1, 6 & 24 hours post-exercise for A) Controls and B) symptomatic shoulders
3.2.5 Discussion

The main findings of this study are that SsT thickness increased in people with RC tendinopathy one and six hours following isokinetic concentric and eccentric external rotation and abduction exercise. In the control group there was a slight reduction in tendon thickness, with only the increase in SsT thickness at six hours exceeding the MDC for this measure. In addition, AHD was reduced in both groups one hour after exercise, with a significant reduction maintained in the RC tendinopathy group at six hours. The composite measure (subacromial occupation ratio), was consequently also seen to rise at the one hour timepoint, levelling back towards baseline over subsequent time intervals.

Studies of the acute response of normal tendons to exercise have described a multitude of physiological processes including changes in vascularity (Pingel et al 2013), genetic expression (Dideriksen et al 2013), collagen synthesis (Christensen et al 2011), mechanical properties (Wearing et al 2014) and fluid shifts (Langberg et al 1999). Alterations in tendon fluid are the most commonly theorised mechanisms for short-term changes in tendon size or shape in vivo, matching those directly measured in vitro (Han et al 2000). Wearing et al (2014) reported a 6-7 hour recovery timescale from an initial reduction in tendon thickness in the normal Achilles and patellar tendon after loading. Our results reflect those of a number of studies of lower limb tendons which have showed that pathological tendons exhibit an altered loading response compared to healthy tendon. Pingel et al (2013) examined changes in microvascular volume of the Achilles tendons in people with Achilles tendinopathy and healthy controls. While tendon microvascular volume was increased in both groups one hour after running, changes in the patients were more pronounced, with all values returning to baseline 24 hours after exercise. Grigg et al (2012) found that Achilles tendon thickness was reduced in men with and without tendinopathy after eccentric exercise, but that a smaller reduction occurred in the symptomatic group.

Reductions in AHD have been widely noted in response to fatiguing shoulder exercise (Royer et al 2009, Chopp et al 2010), as reflected in the current study. Royer et al (2009) noted an increase in superior humeral migration of up to 4mm, assessed using digital fluoroscopy, in the painful shoulder of 20 males, following a fatiguing RC exercise programme. Chopp et al (2011) examined the mechanisms of subacromial space reduction with fatiguing exercise in 10 healthy volunteers. They reported that since the scapular alterations observed in their
study (i.e. increased posterior tilt) functioned to increase the subacromial space, the reduction in subacromial space was more likely to be due to increased superior humeral head migration, due to reduced RC muscle function. Our study is the first to examine both the AHD and SsT response to exercise simultaneously. The interaction between these parameters is more easily interpreted through the subacromial occupation ratio, which incorporates both aspects, and may help to indicate patients more at risk of extrinsic compression due to a thickened tendon occupying a smaller subacromial space. It appears that a dynamic process operates, where fatigue can lead to superior humeral head migration, along with swelling of a pathological tendon, providing possible evidence for an interaction of intrinsic (tendon swelling) and extrinsic (tendon compression) mechanisms in RC tendinopathy.

Current surgical approaches for RC tendinopathy tend to focus on extrinsic causes of tendon impingement, directed at altering acromial shape, an approach which has come under increasing scrutiny (Shi & Edwards 2012). In rehabilitation, while some exercise approaches emphasise the role of posture and scapular alignment to increase the subacromial space (Ratcliffe et al 2013), most also include some elements directed towards tendon conditioning and pain relief. The findings of this study, as well as the work of Chopp et al (2011), potentially support exercise approaches designed to improve load tolerance of the RC tendons, as well as provide better humeral head control. Examining our control group, it is clear that durations of sporting or occupational loading should be examined in light of the time course of recovery of AHD of at least one to six hours after fatiguing exercise.

3.2.5.1 Limitations

As no information was available as to the effect of exercise type on RC tendon morphology, we decided to include both concentric and eccentric exercise in the study protocol. It is possible that different responses may be elicited to each of these exercise types in isolation, however many sporting and occupational activities are composite movements, using a variety of contraction modes. The RC tendinopathy group performed slightly fewer exercise sets than the control group. As the control group were not purposively matched to the RC tendinopathy group, the statistical analysis undertaken examined the changes in each group independently i.e within group changes, therefore no between group comparisons were carried out. The population studied were recruited from community and sports club settings, rather than from a clinical environment, with the aim of identifying people with less severe RC tendinopathy who could still perform the exercise protocol required by the study. It is possible that those
with more severe shoulder pain might not be able to complete the protocol used in this study, or may have a different response.

3.2.6 Conclusion

Fatiguing concentric and eccentric shoulder exercise led to an immediate increase in SsT thickness in people with RC tendinopathy. There was no change in tendon thickness in a group of pain-free controls. The AHD reduced in both controls and those with RC tendinopathy, but those with shoulder pain demonstrated a delayed return to baseline. This co-occurrence of tendon swelling and subacromial space narrowing in the shoulder pain groups provides a possible evidence of an interaction between intrinsic and extrinsic mechanisms in RC tendinopathy.
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Chapter 4: General Discussion and Conclusions

The purpose of this chapter is to review and discuss the studies presented in the body of the thesis, drawing together the findings in the context of mechanisms of RC tendinopathy. The limitations will be considered and clinical implications of the work will be discussed. This chapter will examine how the work builds on current knowledge and provides a basis for future research.
4.1 Literature review: Chapter 1

Rotator cuff (RC) tendinopathy is a common condition that may result in significant shoulder pain and disability. As an age-related condition, prevalence increases as population ages. Tendinopathy is characterised by deterioration in tendon structure and composition. There is an extensive body of knowledge associating tendinopathies of the lower limbs with exposure to high or unaccustomed levels of loading. Yet for RC tendinopathy, the dominant discourse in terms of mechanism of onset is with regards to extrinsic mechanisms of tendinopathy i.e. tendon impingement or compression in the subacromial space by the coraco-acromial arch, with comparatively little research or clinical consideration of intrinsic tendon pathology or the role of load-induced tendon changes in humans. The extrinsic model also forms the primary driver for surgical approaches involving acromioplasty, as well as some rehabilitation approaches focused on posture and scapular rehabilitation. The literature review for this thesis (Chapter 1) highlights substantial evidence challenging the acromial theories of RC tendinopathy, including the dominance of articular side pathology, lack of association between acromial shape and RC pathology, and the equivocal outcome of acromioplasty surgery relative to approaches not involving the acromion. An alternative extrinsic mechanism also impacting the subacromial space discussed involves superior humeral head migration, with previous studies measuring AHD demonstrating differences between those with and without RC tendinopathy, in particular in those with RC tears. With respect to intrinsic mechanisms, evidence was presented for the potential roles of both over and under-loading in the aetiology of tendon changes in the RC. Tendon thickening, as a consequence of intrinsic tendon changes, was discussed in light of a potential combined mechanism of RC tendinopathy, namely tendon thickening as a result of intrinsic tendon pathology, co-existing with superior humeral head migration as a result of RC insufficiency. It is apparent from the literature review that the role of reduced subacromial space and intrinsic RC tendon changes requires further investigation, in particular in relation to the presence of painful RC tendinopathy, and in response to RC loading.

The continuum model of tendinopathy provides a model describing intrinsic tendon changes and progression of tendinopathy, but it was focused on lower limb tendon pathologies. Lewis (2010) demonstrated how the model might be applicable to RC tendinopathy, with the incorporation of bursal pathology. The narrative review of the continuum model in this thesis
(Section 1.2) discussed how the model is well supported by pathological and imaging research but that its application in clinical research has been more limited to date.

The overall aim of this thesis was to investigate the relationships between intrinsic and extrinsic mechanisms of RC tendinopathy, in particular the size of the subacromial space and thickness of the SsT, in the presence of painful tendinopathy and with the imposition of short-term load.

Chapter 2 focused on methods and comprised three papers, examining reliability and validity aspects of the measurement of AHD and SsT thickness. Chapter 3 presented the clinical studies, which aimed to evaluate the differences in AHD and SsT thickness in people with and without RC tendinopathy, followed by an investigation of the effect of a short-term bout of loading on these same parameters.

4.2 Methods: Chapter 2

The focus in the initial phases of this project was on to determine the most appropriate method for the measurement of the subacromial space. With this aim, a systematic review was undertaken examining all radiographic methods of measuring AHD, namely ultrasound, MRI and CT, in order to identify which method was both reliable and clinically applicable. The review demonstrated that ultrasound was the best researched method in terms of reliability, but overall study quality was relatively poor across the methods. While ultrasound reliability studies reported adequate Intra-class Correlation Co-efficients (ICCs) for healthy populations, the single inter-tester study on symptomatic shoulders reported poorer reliability, suggesting the need for a further investigation of this aspect of the ultrasound method.

Tendon thickening is a common feature of early tendinopathy. Joensen et al (2004) identified a between-shoulder difference of 0.8mm as predictive of supraspinatus tendinopathy, while Arend et al (2014) reported a 93% accuracy of RC tendinopathy diagnosis relative to MRI using an isolated criterion of SsT thickness > 6mm measured using ultrasound. Hence SsT thickness was used in this thesis as a method of quantify intrinsic SsT changes in the RC tendinopathy groups. While not forming part of this thesis, a systematic review was undertaken, in collaboration with another postgraduate student, to examine the reliability of ultrasound measures of tendon thickness. (This study was presented as a conference presentation and published as an abstract– see Appendix 1). While a number of studies were reviewed examining the reliability of ultrasound measurement of SsT thickness (Bjordal et al

**Study IV** was designed to address the deficits in research knowledge in reliability of AHD and SsT thickness measurement by ultrasound, and thus examined inter and intra-rater reliability in those with symptomatic RC tendinopathy and controls. Both measures were found to have excellent intra and inter-rater reliability in both groups. This study also provided MDC values for both measures, with lower intra-rater MDC values, suggesting that use of a single rater is preferable for studies examining change over time in order to achieve minimal error levels. Minimal detectable change values are critical in examining differences in measures between groups or over time, in order that any differences are interpreted with regard to potential measurement error. This reliability study was undertaken using the QAREL checklist (Table 1), in order to guide the quality of the study. The use of reporting checklists is increasingly encouraged or mandatory in medical research; therefore the study was reported using the GRRAS recommendations which are a set of fifteen recommendations regarding how to report studies of reliability or agreement, in order to improve reporting quality (Kottner et al 2011).

It became evident in the AHD systematic review that a no ‘gold standard’ measurement for AHD existed, as each method had inherent weaknesses, for example, related to patient positioning (MRI undertaken in supine lying), projection issues (standardising the projection with radiographs is challenging) and anatomical constraints (the inferior acromion cannot be viewed on ultrasound). In addition, no validity studies of AHD measurement had been undertaken. Determination of a method for evaluation of the validity of AHD measurement presented a variety of options to be explored. Initial preference was for using a direct, in-vivo method i.e. intra-operative measurement, as the gold standard and comparing this to a pre-operative measurement using ultrasound. Warner et al (1994) described the use of an arthroscopic probe with fixed millimetre markings to determine adequate acromial resection during acromioplasty procedures. Tillander and Norlin (2002) reported a pilot study examining a new intra-operative subacromial measuring device, also with the aim of measuring how much bone was removed during an acromioplasty procedure. Pilot explorations of this method were undertaken in collaboration with an orthopaedic surgeon employing a pilot method, using an arthroscopic probe with markings in millimetres (mm), to attempt to take intra-operative subacromial space measurements before undertaking shoulder surgical procedures. It became evident that the constraints of the operative environment i.e.
patient position, traction on the arm, the infiltration of fluid into the shoulder area; all would serve as confounding factors preventing direct comparison of the measures obtained to any clinically useful ultrasound measuring technique.

The second option explored was the use of cadaver shoulders. A number of constraints in this method were identified including the limited availability of, and access to, cadaver shoulders, and the altered properties of cadaver tissues. During the exploration of a suitable validity method, I was concurrently undertaking a postgraduate qualification in Ultrasound Imaging at the University of Leeds, Leeds, UK. I became aware that researchers there had expertise in the development and testing of radiological phantoms. Following discussion with Dr Tony Evans (Senior Lecturer in Medical Physics, University of Leeds), the possibility of developing a shoulder ultrasound phantom with the potential to provide a model for examining the validity of AHD measurement arose. However, based on a review of the literature and the combined expertise and knowledge of the University of Leeds research team, it also became apparent that no-one had previously undertaken the development of a shoulder ultrasound phantom. The potential to undertake such novel phantom development work, along with my research question regarding AHD, provided an excellent opportunity for international research collaboration, which was the catalyst for the shoulder phantom project. While the expertise of the University of Leeds research team was central to the choice of materials and manufacturing method for the phantom, my input in terms of the requirements for the finished phantom and ongoing feedback at each stage regarding the suitability and ultrasound appearance of the materials being tested was an important aspect in ensuring the final phantom provided not only the potential to undertake the AHD validity investigation, but also had the potential to be further developed as an ultrasound training tool. My roles also comprised acquiring a suitable normal human shoulder CT dataset to use as a model for the bony aspect of the phantom, and ensuring that, once manufactured, it was set in the correct anatomical position, and accurately measured with callipers before being embedded in the soft tissue phantom materials. In Appendix 2, an additional paper (accepted for publication in the Journal of Ultrasound in Medicine) is provided which describes the technical processes involved in the development of the shoulder phantom. As described in Study III, the phantom provided a very good model for AHD measurement validation, with some shortcomings in terms of lack of inclusion of phantoms for the peri-articular shoulder soft tissues, leading to differences in the visual ultrasound appearance compared to ultrasound images of a human shoulder. However, in addition to addressing the research question
concerning AHD validity, the final product demonstrated the potential that, with further development, it could be used as an educational aid for the teaching of diagnostic shoulder ultrasound and ultrasound-guided injections. The development process for the phantom is ongoing at the University of Leeds, and may eventually result in the production of a commercially viable shoulder phantom. The process of undertaking this study with the Leeds research team provided valuable experience of working within a multi-disciplinary team, in what was essentially a new discipline. It exposed me to what may be achieved through mutual engagement and knowledge sharing, and has certainly broadened my thinking in terms of seeking collaborators for future research projects.

4.3 Clinical studies: Chapter 3

The literature review highlighted that the interaction between extrinsic and intrinsic mechanisms of RC tendinopathy has received little attention in research to date. Surgical approaches targeting extrinsic mechanisms (acromioplasty) offer similar outcomes to those directed at structural repair (RC repair) or pain relief (bursectomy) (Shi and Edwards 2012). Rehabilitation interventions, while often successful in improving pain and function, are not supported by evidence for specific components or progression of programmes. The lack of clarity on the relative contributions of the subacromial space and intrinsic changes in the SsT to pain and function those with RC tendinopathy challenges physiotherapists to attempt to address multiple mechanisms in these patients, with little direction on how to design or progress exercise programmes. The provision of further evidence to clarify the mechanisms of RC tendinopathy is needed to provide guidance to physiotherapists in their choice of exercise.

The aim of Study V was to compare AHD and SsT thickness between people with and without RC tendinopathy, and to examine any association with pain and function in the RC tendinopathy group. Michener et al (2013) published the first study concurrently examining AHD and SsT thickness, expressing the ratio between them as the occupation ratio. In that study, AHD did not differ between the RC tendinopathy group and controls, while, in contrast, the SsT was significantly thicker (mean difference =0.6mm) in the shoulder pain group, leading to a larger occupation ratio in this group. The 20 people with RC tendinopathy in the Michener et al (2013) study were diagnosed using clinical testing only, without confirmation using imaging. There was no assessment made of any associations between the occupation ratio and shoulder pain or function. Study V built on the research presented by
Michener et al (2013) by including a larger sample with imaging-confirmed RC tendinopathy. This larger sample permitted subgrouping according to the degree of reported pain intensity (mild, moderate or severe). Overall results were similar, in that no difference was found in AHD across any of the groups, however SsT was thicker (by 1.3 and 1.5mm) and occupation ratio larger (by approximately 15%) in the moderate and severe pain groups only. In addition, occupation ratio was moderately associated with both pain and function. It was not possible to compare to the Michener et al (2013) study in terms of pain, as they used the Penn shoulder scale, which is a composite measure of pain and function. The findings from Study V suggest that, in people with early to mid-stage RC tendinopathy, the SsT increases in thickness and is thickest in those with higher pain intensity. The larger tendon occupies more of the available subacromial space, and therefore may be more vulnerable to extrinsic compression from the overlying coracoacromial arch, and/or of creating upward pressure on the coracoacromial ligament. While tendons are capable of responding to compressive load by increasing fibrocartilage content; sustained, or excessive loads may lead to negative tendon matrix changes consistent with tendinopathy (Docking et al 2013). Increasing tendon thickness may be an indicator of these intrinsic tendon changes, reflective of a proliferative tendon response and an increase in tendon water content (Cook and Purdam 2009). Tendinopathy leads to an increased glucosaminoglycan (GAG) content in the RC tendons, which may be responsible for some of the increase in bound water content and tendon thickening (Riley et al 1994).

From this cross-sectional study, a cause-effect relationship between tendon thickness and pain cannot be inferred. For example, it cannot be determined whether having thicker tendons preceded the development of RC tendinopathy in the moderate and severe pain group. In a study of pain-free baseball pitchers, Malanga et al (2012) reported thicker SsT on the dominant side in right but not left handed athletes. While we did not find any dominance effect for SsT thickness in our control group, a proportion of our RC tendinopathy group were regular swimmers which could affect baseline tendon thickness, although most of these were in the mild pain group. An additional confounder may have been symptom duration, since the moderate and severe pain groups reported the presence of symptoms on average for longer than those with mild pain (14.8, 17.4 and 9.2 months respectively). It is possible that the SsT becomes thicker over the duration of time that pain is present, regardless of pain intensity. Tendon thickness may also be subject to diurnal or activity-related variations, with studies of the Achilles tendon demonstrating changes in thickness subsequent to loading
activity (Grigg et al 2009). The findings of Study V suggested the need for further investigation of AHD and SsT thickness parameters in a more dynamic and longitudinal manner, where the effects of time and loading could be evaluated.

Study VI investigated the effect of a short bout of combined concentric and eccentric external rotation and abduction loading on SsT thickness and AHD, examining the ultrasound measures three times post-loading over 24 hours. Based on previous studies demonstrating superior migration of the humeral head in the presence of shoulder fatigue (Chopp et al 2010), one hypothesis that was tested was that AHD would reduce in both controls and those with RC tendinopathy, but that the effect would be more pronounced in those with symptoms. The hypothesis in relation to SsT thickness response was that an increase in tendon thickness may occur in those with RC tendinopathy, with no change in the control group. This was based on one study of biceps tendon response to loading in wheelchair athletes, which showed a non-significant increase in tendon thickness, and studies of the Achilles tendon which reported inconsistent results in terms of tendon thickness response to load (Obst et al 2013). A significant challenge in the design of this study was choosing an appropriate exercise protocol which would provide adequate and measurable levels of fatigue loading, but would still be tolerated by the RC tendinopathy group. While less functional than other forms of loading, the use of System 3 isokinetic dynamometer (Biodex Medical Systems, Shirley, New York, USA) permitted standardisation of the exercises, and monitoring of the degree of fatigue through assessment of overall torque of each exercise set. The shoulder endurance study by Roy et al (2011) suggested that 60 repetitions at 60°/sec of external rotation provided 38% fatigue. In Study VI, the aim was to undertake movement that loaded the SsT. Electromyographic studies by Tardo et al (2013) and Reed et al (2013) suggesting a role for supraspinatus in both external rotation and abduction provided the basis for the choice of movement direction. We also hypothesised that a faster rate of loading would be more suitable for tendon loading and so increased the speed to 120°/sec compared to the Roy et al (2011) study. A total of three sets of 10 reps at 120°/sec (30 each of external rotation and abduction) was determined as the base level for the loading protocol. While the RC tendinopathy group completed slightly fewer mean exercise sets than controls (4.9 vs 5.8) due to earlier onset of fatigue or pain, all participants reached the requisite fatigue level, suggesting that the protocol is appropriate, and could be used in future studies examining RC fatigue.
The study demonstrated that in people with RC tendinopathy, the SsT significantly increased in thickness six hours after fatigue loading. In addition, the AHD was significantly reduced at one and six hours, most likely due to superior humeral head migration following fatigue of the RC muscles. In contrast, in the control group there was small reduction in SsT thickness, which, while statistically significant, did not exceed MDC for this measure. There was also a reduced AHD in this group, but only at the one hour time point. The AHD response in controls demonstrates that RC muscle function, in terms of its humeral head stabilising function, recovered within six hours of fatigue loading. However in those with RC tendinopathy, humeral head position was not restored to baseline until six hours or more after the bout of fatiguing exercise. Assessor blinding was an important aspect of this study. This was achieved by coding scans at the time of testing in a manner which allowed blinding to group allocation or shoulder being tested and time of scan, as well as delaying measurement of the scans until at least a week after testing. The findings of Study VI suggest a period of vulnerability subsequent to fatiguing exercise that may place the shoulder and RC tendons at greater injury risk due to compression, or lack of humeral head control, a risk that is more pronounced in those with existing tendinopathy.

The methods used in Study VI cannot elucidate the cause of the increased tendon thickness observed in the SsT; potential explanations must be extrapolated from other studies. Tendon dimension changes as a result of exercise have been most extensively studied in the Achilles tendon. In-vivo studies of rabbit Achilles tendon water content report water extrusion to the outer edge of the tendon in response to cyclical loading (Han et al 2000, Helmer et al 2004, 2006). Uncrimping of collagen fibres in the exercised tendon may reduce free space within the tendon, creating greater hydrostatic pressure than the surrounding tissue and extrusion of fluid as a result (Wellen et al 2005). This fluid movement across and within tendons may be an important aspect of tendon homeostasis, which may be disrupted in tendinopathy. In the main, studies of healthy Achilles tendons report that both concentric and eccentric loading result in decreased tendon thickness (Grigg et al 2009, Obst et al 2013). People with Achilles tendinopathy have generally been found to have an altered response to loading, either in the form of a smaller initial reduction in tendon thickness (5% reduction versus 21% reduction in thickness in controls) and a slower return to normal tendon dimensions (Grigg et al 2012), or as an increase in tendon thickness (Shalabi et al 2004). These studies, along with Study VI, suggest that fluid movement may be altered in tendinopathy - the tendon no longer extrudes fluid in response to loading and may in fact draw in additional fluid. The lack of fluid
extrusion could be related to the greater GAG content (Riley et al 1994), causing more binding of water and less availability for movement. This altered fluid movement in tendon is likely to be reflective of a much bigger picture of poorer ability of the tendon to respond to mechanical loading in a positive manner.

4.4 Clinical implications

The methods studies presented in Chapter 2 of this thesis provide a reliable and valid method of subacromial space measurement, in conjunction with reliability estimates for SsT measurement. The reporting of the subacromial occupation ratio is encouraged as it provides a more informative and individualised metric of subacromial relationships.

The results of the clinical studies presented in Chapter 3 suggest that the emphasis placed on the subacromial space as a target for surgical or rehabilitative interventions may be misplaced, at least in the earlier stages of RC tendinopathy. While it may play a more important part in the presence of fatigue, as shown by Study VI, early stage interventions may be better directed at improving the capacity of the RC tendons to tolerate load through graduated exercise programmes, rather than on increasing the subacromial space.

Ideal conditions for tendon adaptation to loading are the provision of adequate time, absence of further overloading, in addition to the right metabolic and mechanical environment. Under the appropriate physiological conditions, exercise results in stimulation of collagen turnover, finely balanced between synthesis and degradation, leading to a tendon that is stronger and more resistant to loading (Kjaer et al 2009). If the correct conditions for tendon adaptation are not provided, the tendon may then enter a state of imbalanced healing and repair, resulting in tendinopathic changes. The results from this thesis suggest that fatigue loading of the RC tendons may produce unfavourable conditions for adaptation in people with RC tendinopathy. Swelling as a response to loading suggests altered tendon fluid metabolism, and a reduced subacromial space increases vulnerability to compression. Titrating exercise to the appropriate form and intensity is likely to be a critical part of restoring normal tendon homeostasis. The fatigue loading undertaken for Study V involved both concentric and eccentric contractions, in both external rotation and abduction. Clinicians prescribing exercise for people with RC tendinopathy may be advised to focus on a single type of contraction or a single direction of motion in order to avoid loading to fatigue. In addition, based on the
recovery rate of greater than 6 hours, it may be advisable to limit shoulder strengthening exercise to no more than one bout per day. With further refinement the ultrasound imaging protocol used in Study VI, in addition to examining post-exercise pain levels, and function may help to indicate the person’s current capacity, and provide direction for progression or regression of exercise dose.

In Study I, current models of tendinopathy were examined, in particular the continuum model. The continuum model describes tendon thickening as a feature of early tendinopathy, which concurs with the findings of Study V and VI. It also refers to early tendinopathy as having reactive aspects i.e. latent pain responses and swelling in response to acute overload. As reported in Study VI, the small number of participants for whom SsT thickness had not returned to baseline at 24 hours post-exercise, reported higher levels of pain at that time point. Whether this latent pain response has an inflammatory and/or another basis (neurogenic, mechanical) could not be determined by the methods employed, however it does indicate a potential means to identify those who exhibit a more reactive component to their RC tendinopathy. It reinforces the suggestions from other researchers that the use of a pain-monitoring model approach (i.e. examining pain response 24 hours after loading) may be a helpful way to titrate exercise dosage (Silbernagel et al 2007, Holmgren at al 2012). In terms of mechanical models of RC tendinopathy, this thesis does demonstrate a potential basis for the role of compressive loading, however not as a primary event, but more likely as secondary consequence of intrinsic tendon changes. This may suggest that restoring homeostasis to the tendon is a more relevant initial treatment approach than surgical alteration of the coracoacromial arch.

4.5 Limitations

In order to investigate mechanisms of RC tendinopathy in this thesis, AHD measurement and SsT tendon thickness were chosen to represent the size of the subacromial space (extrinsic mechanisms) and intrinsic tendinopathy of the SsT tendon respectively. These measures are not without their limitations. Acromiohumeral distance measurement using ultrasound does not permit visualisation of any inferiorly placed acromial osteophytes, and measures the subacromial space as a two-dimensional entity, in a single plane only. While a standardised protocol was used, imaging the most anterior aspect of the acromion, the location of the
narrowest aspect of AHD may vary between individuals. In this thesis, AHD measures were undertaken in the neutral arm position only, as the reliability of the measure in higher degrees of elevation is much poorer. As a result of using the neutral position only, people with normal AHD in neutral but reduced AHD in higher degrees of elevation would not have been identified. Supraspinatus thickness measures only take account of one of the RC tendons, albeit the one most commonly affected by tendinopathic change. Tendon cross-sectional area measures were not used as it is not possible to delineate the boundaries of the SsT in cross-section. Again as a 2D measure, and since tendon thickening may not be uniform, the area of most thickness change may not have been the location measured, although three measurement points were taken and averaged.

The population samples used in the studies in this thesis were drawn from a variety of populations, from both community and clinical sources; however it is not known how representative this group were in terms of typical clinical populations. People with full thickness RC tears were excluded from taking part, as they are known to have larger changes in the subacromial space, and the aim was to investigate the early stages of tendinopathy. Diagnosis is challenging in RC tendinopathy, as discussed in Chapter 1, therefore this thesis used a combination of clinical and ultrasound-based measures to include or exclude study participants. The exclusion of people from healthy control groups on the basis of the presence of painfree RC tendon pathology noted on ultrasound imaging could be challenged on the basis that it misrepresents the general population; however this approach was determined based on an attempt to include the most homogeneous sample possible. The specific selection of only those with RC tendon pathology in the shoulder pain groups, and exclusion of those with pathology (i.e. tendon thickening) from control groups, may have acted as a confounder in Study V, whereby it made the finding of an association between pain and SsT thickness more likely.

The work of this thesis focused primarily on impairment-based measures in RC tendinopathy i.e. ultrasound imaging of AHD and SsT thickness, alongside measures of pain and shoulder function. It is accepted that some authors suggest that measuring attributes beyond structural changes, such as measures of depression, stress, and pain sensitivity may be important providing a complete picture of the factors involved in RC tendinopathy (Littlewood et al 2013, Drew et al 2014), however such measures were beyond the scope of this thesis. It is anticipated that such measures could be incorporated into future research to evaluate their relative influence in comparison to impairment-based outcome measures.
4.6 Future Directions for Research

While this thesis indicates that thickening of the SsT occurs in response to fatigue loading, it does not elucidate the mechanisms by which this occurs. More sophisticated methods of analysis would be required to undertake in-vivo analyses of tendon physiological processes, such as micro-dialysis of peri-tendinous fluids, specific MR imaging protocols which might aid visualisation of tissue fluid content, or near infra-red spectroscopy to measure metabolic activity.

Equally while RC muscle fatigue was proposed as the basis for AHD reductions in Study VI, fine wire EMG could be used to provide further evidence of the relationship between RC muscle function and changes in AHD.

The subacromial occupation ratio has been identified as being significantly different in those with RC tendinopathy in Study V, but no cause or effect relationship could be substantiated. It would be useful to examine the ratio before and after physiotherapy treatment for RC tendinopathy, to determine the capacity for change, and investigate any relationship with patient outcomes.

Study VI employed both concentric and eccentric loading to produce RC fatigue. It would be valuable to examine the effects of these types of loading individually and, in addition, to assess the effect of isometric loading. Isometric loading provides muscle and tendon loading without stretch-shortening of the tendon, or through range joint motion, which may provide less potential for compression of the SsT. Recent studies have identified that isometric loading also has a positive influence on mechanical pain thresholds (Hoeger Bement et al 2008, Lemley et al 2014), however evidence to support its use in tendinopathy is lacking at present.

This thesis has provided some guidance for exercise prescription in RC tendinopathy, however there is no evidence to substantiate this advice in terms of achieving better treatment outcomes. There is a need for clinical trials comparing the effect of different exercise dosages and contraction types of RC tendinopathy. I propose that such a trial might examine the effectiveness of a graduated loading programme for RC tendinopathy, but randomise
participants to different exercise dosages, e.g. a daily versus three times a week loading programme. A second trial might compare the use of a mixed concentric and eccentric exercise programme, to a programme based on an initial period of isometric exercise only until tendon reactivity reduces and humeral head control improves, and followed by a progression to other contraction types. Such investigations would help to provide direction as to the relative effectiveness of different exercise types and dosages and potentially improve effectiveness and efficiency of physiotherapy exercise prescription for RC tendinopathy.

4.7 Conclusion

The key findings of this thesis are:

- Ultrasound imaging can be used to undertake reliable and valid measures of AHD and reliable measures of SsT thickness in both RC tendinopathy and painfree populations.
- Acromiohumeral distance is not significantly reduced in those with painful RC tendinopathy (without RC tears) compared to controls.
- However, the SsT was found to be thicker in those with moderately or severely painful RC tendinopathy (but not different in those with mild pain), leading to an overall increased subacromial ratio, which may contribute to tendon compression.
- In RC tendinopathy, fatigue loading of the RC leads to a prolonged (>6 hours) reduction in AHD and an increase in SsT thickness, compared to findings of a transient change in AHD (<6 hours) and no change in tendon thickness in painfree controls.

This thesis provides further evidence to support intrinsic tendon changes as the likely primary event in RC tendinopathy. Suggested guidance for clinicians on the development of exercise programmes for early stages of RC tendinopathy are provided, based on the effects of fatigue loading. Further research should build on this thesis by developing the role of imaging in guiding the progression of rehabilitation programmes, as well as investigating the effectiveness of different components and dosages of exercise.
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Shi LL, Edwards TB. The role of acromioplasty for management of rotator cuff problems: Where is the evidence? Advances in Orthopedics, 2012; Article ID 467571, 5 pages http://dx.doi.org/10.1155/2012/467571


Chapter 5: Knowledge Exchange and Dissemination

This chapter examines the important area of exchange and dissemination of research in order to improve clinical practice. It contains one paper, which is currently under review. It describes the setting up and evaluation of a Community of Practice (CoP) for primary care physiotherapists focused on the area of evidence based practice in managing shoulder pain, a process which ran concurrently with the remaining work of this thesis. While it departs from the nature of work described to date, I believe this section is complementary to the thesis, in examining means of disseminating and exchanging research findings with clinicians, while engaged in the research process.

The literature review for this thesis highlights the challenges facing physiotherapists managing people with shoulder pain, with a plethora of both exercise-based and adjunctive interventions all being advocated. My experience working with primary care clinicians highlighted the difficulties of providing evidence based care, with conflicting information from both clinical and research sources, alongside increasing work pressures and a lack of research utilisation skills and opportunities.

Context has been shown to be an important influence on the way in which knowledge is absorbed and used (Scott et al 2008), therefore CoPs amongst practitioners have emerged as a promising means of sharing knowledge in a meaningful way (Li et al 2009). Academic-clinical partnerships have been shown to provide a useful leadership role in developing evidence based practice initiatives in clinical practice in occupational therapy (Forsyth et al 2005). Also in occupational therapy, Wilding et al (2012) described significant benefits of involvement in a CoP where therapists engaged on a regular basis with academics and each other, through journal clubs and peer sharing of knowledge. However there are no published studies describing or evaluating the role of CoPs in the physiotherapy profession.

The primary research question for this chapter is:

- What are the motivators, barriers and benefits of participation in a shoulder pain Community of Practice (CoP) for primary care physiotherapists?
5.1 Study VII: Shouldering the burden of evidence-based practice: the experiences of physiotherapists partaking in a Community of Practice

McCreesh K, Larkin L, Lewis J

5.1.1 Abstract

**Question:** What are the motivators, barriers and benefits of participation in a Community of Practice (CoP) for primary care physiotherapists?

**Design:** Qualitative study using semi-structured interviews

**Participants:** Twelve physiotherapists partaking in a newly formed Shoulder CoP

**Results:** Activities of the CoP included seven group meetings over nine months (mean attendance 70%), journal clubs, a website and a clinical practice project. A desire for peer support was the strongest motivator for joining the CoP, with improving clinical practice being less apparent. Barriers to participation included time and work pressures and poor research skills. The structure of the CoP, in terms of access to meetings and the provision of preparation work and deadlines for the journal clubs, was reported to be a facilitator to involvement. Multiple benefits ensued from participation. The role of teamwork was emphasised in relation to reducing isolation and achieving goals. The majority of participants reported positive changes to their clinical practice in terms of improved patient education, increased confidence in their own practice, and availability of new resources. All participants reported some element of personal growth and development, in particular in their evidence based practice skills.

**Conclusion:** This study is the first to describe the use of a CoP in physiotherapy. The results provide support for the use of CoPs as a means of continuing professional development for physiotherapists in the workplace, as significant benefits are gained in terms of evidence-based practice (EBP), patient care and therapist development.

**Keywords:** Evidence-based practice; Physiotherapy; Qualitative research
5.1.2 Introduction

All health care professionals are experiencing increased demands to use research evidence in clinical practice. In physiotherapy, demands for evidence-based practice (EBP) have grown since the 1990’s (Turner 2001). A recent systematic review of EBP in physiotherapy highlighted multiple barriers, including time and workload pressures, limited access to research literature, poor skills, and perceived mismatch between research and practice (Scurlock-Evans et al 2014). Interventions to improve EBP were also reviewed, with journal clubs and knowledge broker interventions showing best effectiveness. Bridges et al (2007) surveyed over 900 physiotherapists regarding influences on their propensity to adopt EBP and concluded that multiple strategies would be required to effect change in clinical practice.

The term Communities of Practice (CoP) was developed by Lave and Wenger (1991) to describe learning through practice and participation in groups. Lave and Wenger’s initial interest was in how apprentices learn. However the CoP concept evolved and has come to be used as an intervention tool in a wide range of domains. Communities of practice are “groups of people who share a concern, a set of problems, or a passion about a topic, and who deepen their knowledge and expertise in this area by interacting on an ongoing basis.” (Wenger et al 2001). It is clear that this definition encompasses many entities that are common to everyday clinical practice, such as multi-disciplinary teams or clinical interest groups. For many of these groups learning is incidental to the group’s interaction, while for others learning is the reason they have come together. The characteristics of a CoP are identified as: ‘domain’, the common ground shared by members; ‘community’, the structure that facilitates member’s interactions; and ‘practice’, the specific knowledge, skills and resources shared by members. The CoP is a learning concept which emphasises situational learning within the practice environment, and encourages mutual engagement; joint enterprise, and a shared repertoire of resources. Li et al (2009) examined how CoPs were used in business and healthcare sectors, as well as their effectiveness in promoting best practice. They describe four dominant characteristics of CoPs in these sectors, which are: social interaction among members, knowledge sharing, knowledge creation, and identity building. Ranmuthugala et al (2011) reviewed how and why CoPs are established in healthcare. They noted a shift from focus of CoPs on exchanging information and knowledge, towards more recent research where CoPs were used as a tool to facilitate the implementation of EBP. They also described the
challenges in evaluating the effectiveness of CoPs due to the complex and multifaceted interventions involved.

While many studies have described the use of CoPs in health professions (Rathmuthugala et al 2011), there is no published research describing the use of CoPs in physiotherapy. Wilding et al (2012) described a year-long CoP action research project amongst occupational therapists (OTs) in Australia, and examined the experiences of members. Two major themes emerged- firstly promotion of scholarship, which describes how participants began to think more critically about practice, and secondly, promoting professional confidence, passion and cohesion, where peer support fostered increased confidence in the OTs own practice. It is clear that the CoP model is a potentially valuable framework for the development of practice-based learning in healthcare settings, including physiotherapy. This study describes the formation of a new CoP for physiotherapists working in primary care, focused on the management of shoulder pain. Based on the dearth of relevant research concerning CoPs in physiotherapy, the purpose of this study was to examine the experiences of physiotherapists taking part, in particular in relation to motivators, barriers and benefits of participation.

5.1.3 Methods

5.1.3.1 Participants

The Shoulder Community of Practice Project was developed as a knowledge exchange and dissemination initiative to improve clinical practice in the management of shoulder pain in primary care physiotherapy settings in Ireland. Based on the growing evidence for its usefulness as a practice-based learning tool, the CoP model was determined to be the best framework in which to develop the project. The project involved a number of components, and ran over a 9-month period, led by a physiotherapy academic, who was undertaking research in the area of shoulder pain (KM). See Table 14 for a description of the structure and activities of the CoP. All Shoulder CoP participants were invited to take part in semi-structured interviews to explore their experiences of participating in the CoP. Of the 15 CoP members, 12 consented and were available for interview.
Table 14 The Shoulder CoP project description

<table>
<thead>
<tr>
<th>The Shoulder Community of Practice (CoP) project</th>
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<tbody>
<tr>
<td>• One-day shoulder pain seminar (attended by 120 physiotherapists). Shoulder CoP introduced and physiotherapists invited to join (Aim was for 15-20 members. Inclusion criteria: Physiotherapists, primary care caseload, shoulder pain forms at least 10% of caseload). World Café-style event used to elicit attendees’ priorities and ideas for a Shoulder CoP, which included journal clubs, development of patient and practitioner resources, and discussion groups/peer support.</td>
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<tr>
<td>• Fifteen eligible physiotherapists volunteered to join CoP. Objective-setting exercise with the group, based on World Café data and members own needs, determined the CoP plan which included: monthly journal clubs, a clinical practice project, and website.</td>
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<tr>
<td>• Website developed in parallel with the CoP meetings (<a href="http://www.shouldercommunity.com">www.shouldercommunity.com</a>), and used to disseminate the work of the CoP and facilitate communication between members.</td>
</tr>
<tr>
<td>• Monthly journal clubs themed around areas of interest e.g. exercise in shoulder pain, outcome measures. A range of papers were chosen from member and CoP leader suggestions. Papers reviewed by members in small groups and a joint summary of each paper produced. Support was given for critical appraisal using critical appraisal tools or tutorials provided by a physiotherapy academic (KM) at the early stages with less support later in the process. Meetings, which participants could attend either face-to-face or via teleconference, used to integrate the findings across studies and answer clinical questions. Mean meeting attendance across the 7 meetings was 70%.</td>
</tr>
<tr>
<td>• The CoP leader (KM) acted as meeting chair, facilitated discussions, and acted as content expert as required throughout the process. A research assistant (LL) undertook all CoP administration tasks.</td>
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<tr>
<td>• Clinical project developed after 3 months of the CoP. Based on journal club findings and clinical needs, a protocol was developed for group shoulder exercise classes through discussion and group feedback. These classes were rolled out by some of the physiotherapists over the subsequent months, with CoP meetings used to provide peer support for this initiative.</td>
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5.1.3.2 Design

Semi-structured interviews were conducted by telephone by a research assistant (LL). The question route was devised based on the aims of the research, beginning with an open question and later asking for specific examples (See Table 15). Interviews were audio-recoded and transcribed verbatim. Transcripts were sent to each participant for confirmation. Ethical approval for the study was received from the University Ethics Committee, and all participants gave written informed consent.

Table 15 Interview Question Route

<table>
<thead>
<tr>
<th>Semi-structured Interview Question Route</th>
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<tr>
<td>Tell me about your experience of the Community of Practice (CoP)</td>
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<tr>
<td>Why did you decide to join the Shoulder CoP?</td>
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<tr>
<td>Tell me what challenges you think there are for participating in the CoP.</td>
</tr>
<tr>
<td>Tell me what benefits you think there are for participating in the CoP.</td>
</tr>
<tr>
<td>Can you describe a situation where the use of the CoP has impacted on your clinical practice?</td>
</tr>
<tr>
<td>Can you suggest modifications to the CoP so that it is used to support clinical practice?</td>
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</table>

5.1.3.3 Data Analysis

Thematic analysis was used for data analysis, using the six stage guide as described by Braun and Clark (2006), as it offers the potential to provide a rich and detailed account of the data. Two investigators independently undertook data analysis (KM & LL), both of whom were closely involved in the activities of the CoP, KM as the project leader and LL as a research assistant. A qualitative data analysis package NVivo (V10) was used to assist in performing data coding, and forming initial categories. We took an inductive approach, where the thematic analysis was data-driven and explorative rather than from an existing theoretical
framework. The first stage of analysis consisted of familiarisation with the data through repeated reading. Initial coding was then undertaken, with further refinement into potential themes. At this stage, the two investigators reviewed and discussed the themes generated, and finally, consensus was reached on the naming and definition of themes, and data extracts were chosen to illustrate meaning of each theme. A degree of triangulation was carried out by comparing the themes with the minutes of the final CoP project meeting, where all members attended in person to discuss their experience of the project and to plan for future development of the CoP. Individual interviews had been carried out prior to this meeting.

5.1.4 Results

Twelve physiotherapists (2 males, 10 females) took part in the study. They had an average of 12.7 years of practice experience, with eight working wholly in a primary care setting, and four in both primary and acute care settings. The main themes identified from interviewee responses were ‘Motivation’, ‘Barriers and facilitators’, and ‘Benefits of the CoP’. The findings within the ‘Barriers and Facilitators’, and ‘Benefits’, themes were strongly backed up by comparison with the minutes of the final CoP project meeting.

5.1.4.1 Motivation

As one of the opening questions to the interviews was related to what motivated the therapists to join the CoP, it was unsurprising that motivation emerged as a strong theme in the early part of the interviews. For the majority of participants (9), the motivation to join the CoP was driven out of a sense of being isolated from other physiotherapists in their daily practice, and seeing the CoP as a way of gaining peer support and more interaction with colleagues.

PT06: I decided to join because ..I work in a very small practice and I felt that it was a way of interacting with other physiotherapists and other people with expertise different to my own

PT03: I thought it would be quite a nice thing just to have a community out there that you could access particularly when I work on my own. I’m in a health centre so I mightn’t always have someone I can bounce ideas off.
A desire to improve their clinical practice, or to address perceived gaps in knowledge in the area of managing patients with shoulder pain, was less apparent in the interviews. Only a small number of participants made statements such as;

*PT08: I joined to increase my knowledge and improve my quality of care.*

*PT05: For years I’d never been happy with shoulders ....so that’s why I joined it really to help progress my knowledge, I suppose and help improve the outcome for the patients that I see with shoulder problems*

### 4.1.4.2 Barriers & facilitators

The themes of barriers and facilitators to involvement in the CoP were extensive throughout the data. Since there was overlap between similar factors being considered barriers and facilitators, both are discussed under the same theme heading. ‘Time’ was the main barrier mentioned, while ‘EBP skills’ and the ‘Organisation of the CoP’ emerged as both barriers and facilitators.

#### 5.1.4.2.1 Time

All of the participants cited time pressures, both work and personal, as a barrier to their involvement in the CoP. Most also said that they conducted some CoP activities e.g reading journal articles, outside of their paid working hours.

*PT09: the time aspect, that you do need to invest some of your own time in reviewing the literature and then some work time for the meetings. So that was definitely a bit of a barrier.*

Time was also mentioned as a factor in terms of gaining permission from line managers to participate in the CoP, with three physiotherapists describing how they had to convince their manager of the benefits of their involvement.

*PT02: I suppose I justify it by if I can get better at treating (shoulder patients) they’ll get out the door quicker and it’ll be more effective, so my manager had no problem with it.*
PT11: Within the (health service) when you go to a meeting like that well our boss wants to show what the department is gaining from you going to the meeting.....so there’s that challenge I suppose when you are in ... the public sector with regard to using your time wisely

5.1.4.2.2. Skills

A smaller number of therapists (5) commented that their lack of skills in reading and reviewing journal articles was a barrier to full participation in the journal club at the initial stage. However, comments from others indicated that participants developed skills in reading, understanding, appraising, and summarising as the meetings progressed. The following comments indicate that participation in journal club activities facilitated learning:

PT05: Well when I was reading the journals I have absolutely no background in statistics.... I’ve never done statistics so that would have been a major problem when I was reading these papers

PT04: Maybe a lack of familiarity with some of the research methodologies and that probably was a challenge, but again that’s something that can be embraced and learned out of as well

5.1.4.2.3 Organisation of the CoP

In the main, the organisation of the CoP was seen as a facilitator to participation. While undertaking work for the journal clubs was seen as a challenge for some, physiotherapists appreciated the provision of preparation work before the journal clubs, along with timelines to complete tasks, which provided an impetus to undertake activities that might otherwise not be prioritised as part of a busy clinical workload.

PT06: I suppose a challenge is doing the assignments or whatever project you have on a given month but I think that’s something that you should expect, you shouldn’t get information handed to you because I don’t think you take it in as much anyway.
PT11: because you had deadlines and dates and things it made you do things that you wanted to do but you don’t get around to doing, so that would give you an opportunity or reason for making sure you did those things.

The opportunity to access CoP meetings by teleconference was seen as positive by most participants; however two suggested that face to face meetings provided additional benefits in terms of personal interaction and providing protected time to engage.

PT10 I thought it was very accessible. I loved that we had the teleconferences because I’m coming from (distant site). There was always no issue with me using the teleconference you know rather than being there in person and I thought they worked really, really well.

T05: The first day I did the telephone thing but I just found it easier when I went to the meetings rather than doing the teleconferencing because again I can’t do that at work, I have to do it at home..I think if I go to the meetings I preferred that because then I couldn’t be interrupted and I could keep that time for that.

5.1.4.3 Benefits of the CoP

Each of the participants cited multiple benefits of involvement in the CoP, which were categorised under team-work, clinical practice impact and personal growth.

5.1.4.3.1 Teamwork

The CoP was reported by all participants to provide peer support, which helped reduce the isolation of those working alone or isolated from colleagues. There was also a sense of shared interests in the area of shoulder pain. Therapists also valued the variety of experience and opinions brought by having CoP participants from different practice settings.

PT03 I think you know being part of a group of people who can contact each other and communicate with each other about different shoulder conditions is a really handy thing to do, particularly working as a lone physio in a health centre.

PT07: It linked up people across different settings and allowed a good sharing of information without any judgement

Six out of the 12 participants discussed how more was achieved as part of the group than
could have been accomplished alone, both in terms of amount of information that could be evaluated, but also how others could add different opinions or perspectives.

**PT04:** it certainly was more enjoyable than sitting down reading articles on your own and I think that's kind of an important kind of factor of the Community of Practice, that it is a community as opposed to you sitting at home doing it all yourself and it does break the workload.

**PT09:** I suppose kind of working together with a few people at the one time trying to produce one document was good because you’re taking other people’s views into consideration, so that was useful rather than just critiquing it on your own.

### 5.1.4.3.2 Clinical practice impact

More than half of participants mentioned having increased confidence in their clinical practice that came from enhanced knowledge. Physiotherapists reported improvement particularly in their education of patients and in their choice of evidence based treatment options.

**PT06:** I’m inclined to educate the patients early on in their treatment so that they are aware of all the options and what the current research says about each option. So I definitely have changed my practice with them.

**PT12:** I suppose one of the biggest things really would be that I’d be more focused on using outcome measures because we’ve appraised the articles on the outcome measures and had a look at the evidence base behind those.

For the more expert physiotherapists in the group, clinical practice impact came not so much in terms of practice change, but in reinforcement of existing practice.

**PT10:** Maybe I’ll have a bit more confidence with discussing cases with consultants having had that reinforcement as a group, you know condensing that knowledge.

While the majority of physiotherapists mentioned some positive impact on their clinical practice, one dissented, describing how the CoP was too strongly focused on research, and did not have enough of a clinical focus to meet their needs.
PT08: At the start it was very evidence-based and a lot of it was very theory-driven.....it was very research-based. Clinically I felt it was lacking......I would have thought maybe that there would have been maybe a lot more discussion about ... troublesome patients.

This was in contrast to the views of another participant who found that the CoP was more clinically relevant than traditional CPD activities.

PT01: I found it I suppose very practical, very relevant to what we’re doing here in our day-to-day clinic, which I find some courses and stuff I go to aren’t ....You know I certainly feel I’ve come away with something concrete in my hand and something that I’m using almost day-to-day in my clinical practice

The projects of the CoP were also cited by the participants as having a positive impact on their day-to-day clinical practice. The CoP website was reported to provide an evidence based resource to which patients could be directed.

PT03: I had a patient today with a tear of his rotator cuff so I’ll send him on to (the CoP website) and he’ll be able to get a lot from it because he’s quite big on IT and I know he’s Googled his problem, but I’d rather direct him to something that’s evidence-based than him just to be reading anything that’s on Google.

Three participants highlighted their involvement in the clinical project i.e. running shoulder exercise classes, as having significant impact on their clinical practice

PT04: Probably the development of the classes has been probably the big one in terms of my practice... you know that (the patients) can go to a class and you can discharge them a little bit sooner .... because you know that they’ll be caught, asked if there’s any difficulties. So that’s probably the main change in my practice related to that.

5.1.4.3.3 Personal growth

The physiotherapists described several areas of personal growth and development that resulted from their involvement in the CoP. These included a sense of having been challenged, followed by a feeling of achievement in seeing their skills improve.
PT03: Well the meetings I think they’ve been great particularly for me who hasn’t read a journal in a long time, going back reading journals and evaluating them has been a really nice ... it’s been a nice exercise and I feel like I’ve really improved at doing it over the past few months.

PT10: I really enjoyed it. It really was nice to get back to that critique, that kind of back to your academic head you know and reviewing the literature like that, it was great.

Two-thirds of the physiotherapists described how the fact that they were challenged by the CoP activities was an important part of their development and growth.

PT01: I like being I suppose pushed out of my comfort zone a little bit which is why I did it.

PT 10: I think we’ve done more than I had expected in a short period of time and it was done at the right pace, it challenged people.

PT11: I’ve got a lot more from it than I would have thought personally ...it’s forced me to really sit down and spend time reviewing the literature and coming to my own conclusions. I got the most out of reviewing the journal club so far, it’s been brilliant, and that’s really a personal learning experience really

5.1.5 Discussion

This study is the first to describe the experiences of physiotherapists engaged in a CoP. By the end of the 9 month CoP project period the group had met 7 times, reviewed 25 papers in 6 journal clubs, built and launched a website, and developed and implemented a protocol for shoulder exercise classes. Responses from the interviews indicate outcomes that are typical of a newly established CoP (Li et al 2009), that is, learning together through peer support, knowledge sharing through mutual interaction in the journal clubs and dissemination through the website, and knowledge creation, through development of new resources.

While Dannapfel et al (2014) showed that physiotherapists are highly intrinsically motivated towards EBP, a desire for peer support appeared to be a stronger motive for joining the CoP in this study. This may be a reflection of the fact that most of the participants were based in primary care settings, where they were isolated from regular access to other physiotherapists, but emphasises the potential value of a CoP as a tool for facilitating continuing professional development (CPD) and peer support for primary care clinicians. While the value of peer
learning has been confirmed in undergraduate clinical education (Secomb 2008), there is limited evaluation of its role in the workplace setting. The physiotherapists in this study strongly emphasised the importance of connecting with peers in the CoP, both in terms of motivation to join and in gaining benefit from CoP activities jointly undertaken. How to achieve translation of research knowledge to inform clinical practice is an acknowledged concern raised across all health professions. A systematic review of knowledge translation interventions for rehabilitation professionals concluded that active, multi-component interventions were successful in enhancing both knowledge and practice behaviours in physiotherapists (Menon et al 2009). Gunn and Goding (2009) undertook a qualitative study of CPD among primary care physiotherapists, who reported a wide variety of CPD activities. Similar to our study, there was evidence of change in the therapist’s clinical practice and internal perceptions, in particular confidence, as outcomes of their CPD. Physiotherapists in our study reported practice changes, with particular reference to how they educated patients, and explained the evidence behind their treatment choices, illustrating a knowledge translation process in action (Metzler & Metz, 2010). While the journal clubs were the most valued component of the CoP, participants also appreciated the resources that had been created through the CoP e.g. website, shoulder class protocol, which were transferable and sustainable products of the work that had been undertaken, and further spread the knowledge translation process to physiotherapists beyond the immediate CoP.

The theme of personal development was closely aligned with the sense of being challenged for two-thirds of participants. Some learning theories suggest that learning and growth happens most successfully just outside a person’s ‘comfort zone’, as long as levels of anxiety are managed by providing appropriate supports (Brown 2008). A CoP can provide these supports through the contributions of peers, in addition to careful structuring of CoP activities by the CoP leader. It is noteworthy that, although not a focus of the current study, just two physiotherapists mentioned the usefulness of the academic experience of the CoP leader in guiding the Shoulder CoP, suggesting that participants did not particularly emphasise her role in their CoP experience. Academic-clinical partnerships have been proposed as a way of improving knowledge translation, with Austin et al (2009) describing the positive impact of one such partnership in developing a successful journal club for physiotherapists. However in our study, it appears that role of the academic as the CoP leader was not critical to success and that a similar CoP structure could possibly be developed within a clinical or professional body setting among motivated individuals.
The barriers to involvement in the CoP discussed in this study reflect those commonly cited in the literature as barriers to undertaking evidence-based practice activities, these being time pressures and lack of research skills (Shurlock-Evans et al 2014). However the participants in this study counterbalanced these barriers, mainly through their own motivation to participate, with a 70% attendance rate at CoP meetings. Members used time outside of work to complete reading activities, and improved their EBP skills with guidance from the CoP leader, peer support and practice. During the time of the CoP project, Ireland’s health services were undergoing severe resource challenges, staff shortages and burgeoning waiting lists, with a concomitant difficulty in releasing clinical staff to participate in activities deemed to be non-clinical. Participation in meaningful and appropriate CPD to maintain quality of clinical care remains a priority to support physiotherapy practice. Gibbs (2011) discusses the need to develop innovative means of providing CPD with no direct costs to the health service in such environments. Communities of Practice, which are participant-driven and directly focused on clinical practice, provide such an innovative workplace-based CPD opportunity. We recommend the CoP model to physiotherapy managers, as significant benefits are gained in terms of EBP, patient care and staff development, with excellent motivation from physiotherapists to engage with CoP activities.

The study had a few limitations. The research team was not independent of the CoP process, as it included the CoP leader and research assistant on the CoP project, both of whom undertook data analysis, with interviews conducted by the research assistant. This may have influenced the responses of participants in order to present the project in a positive light to those with whom they have been working. The sample was not complete, as three out of the fifteen CoP participants were unavailable for interview.

5.1.6 Conclusion

This study provides support for the use of a Community of Practice to enhance EBP for primary care physiotherapists. Physiotherapists valued the support and experience of peers in the CoP, and described clear, positive changes in their clinical practice as a result of CoP activities. Barriers to participation were overcome through intrinsic motivation from CoP members, and appropriate organisation of the CoP.
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Appendices

Appendix 1:


Appendix 2:

Supplementary paper: Adusumilli P, McCreesh K, Evans T. Development of an anthropomorphic shoulder phantom model that simulates bony anatomy for Ultrasonic measurement of the acromiohumeral distance. Accepted for publication, J of Ultrasound in Medicine

Appendix 3:

Author contributions to papers comprising this thesis

Appendix 4:

Permissions to reproduce published content
Appendix 1:
A systematic review to investigate the reliability of Ultrasound Imaging in measuring tendon thickness.

McAulliffe S, O’Sullivan K, McCrees K

Presented at the IOC World Conference on Prevention of Injury & Illness in Sport, Monaco 2014

Background Pathological tendons are known to increase in thickness. Ultrasound (US) is an important complementary technique to MRI for assessment of musculoskeletal disorders. Although systematic reviews have confirmed its reliability for the measurement of muscle thickness, no such reviews exist to examine the reliability of US measures of tendon dimensions.

Objective To systematically review the literature on the reliability of Real-time ultrasound to assess tendon dimensions, including thickness and cross sectional area, in human limbs.

Design A comprehensive review of electronic databases was performed by two reviewers using agreed range of keywords. Studies which investigated inter or intra rater reliability of US in measuring tendon thickness were included in this review. The Quality Appraisal of Reliability Studies (QAREL) checklist was used to assess risk of bias.

Setting Included studies performed US analysis in a range of clinical settings.

Participants 698 Symptomatic and asymptomatic participants, mean age range: 17.5–73 years.

Interventions Tendon thickness of a range of upper and lower limb tendons was assessed using US in both transverse and longitudinal planes by physiotherapists, sonographers and other unspecified investigators.

Main outcome measurements Inter and Intra-rater reliability of tendon thickness measures using estimates of both reliability and precision using intraclass correlation coefficients (ICC’s), coefficient of variation (CV%), limits of agreement (LOA), Pearsons correlation coefficient ($r^2$) and 95% confidence intervals (95% CI).

Results Assessment of the risk of bias indicated 15/16 chosen studies was of high quality. ICC values for inter and intra rater reliability ranged from (0.55–0.99), LOA ranged from (0.35–3.50 mm), r2 ranged from (0.43–0.92), 95% CI ranged from (0.43–0.98), CV% ranged from (0–14.44%).
Conclusion The use of real time US methods for assessing upper and lower limb tendon thickness has moderate-to-good reliability; however there is limited assessment of measurement reliability in symptomatic populations. These findings will contribute to the choice of reliable measuring protocols for tendon thickness assessment.
Appendix 2:

Development of an anthropomorphic shoulder phantom model that simulates bony anatomy for ultrasonic measurement of the acromiohumeral distance

Adusumilli P, McCreesh K, Evans T

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Abstract:

The purpose of this study was to create an ultrasound phantom model of the shoulder that was accurate in bone configuration. Its main purposes were for operator training and to measure the acromiohumeral distance of the shoulder. A computerised 3D model of the superior half of the humerus and scapula was rendered and 3D printed. The bone model was embedded in a gelatine compound and set in a shoulder shaped mould. The materials used had speeds of sound that were well matched to soft tissue and epiphyseal bone. The model was specifically effective in simulating the acromiohumeral distance due to its accurate bone geometry.

Key Words

Phantom, Shoulder, Acromiohumeral Distance, Impingement, Ultrasound
**Introduction**

Ultrasound is increasingly becoming a popular tool in the diagnosis and treatment of musculoskeletal disorders (Prins et al 1998, Bianchi & Martolini 2007). The shoulder is an easily accessible joint and therefore one of the most routinely scanned. Shoulder pain is a common joint complaint and is often the result of rotator cuff tendinopathy (RCT). With rotator cuff failure the humeral head may migrate superiorly towards the acromion, leading to a reduction in the subacromial space (SAS). The reduced acromiohumeral distance (AHD) may result in pain due to compression of subacromial tissues (Seitz et al 2011, Bureau et la 2006). A normal AHD can range from 10 to 15 mm when measured on a radiograph (McCreesh et al 2013). The extent of rotator cuff tears and fatty degeneration influences the size of the AHD. An AHD below 7 mm can indicate the presence of RCT (Saupe et al 2006). Ultrasound scanning is an accurate method of evaluating RCT and to monitor the efficacy of treatment. One such use to which it can be put is measuring the AHD in the shoulder, a measurement which is currently taken using radiographic imaging. Ultrasound scanning does not expose the patient to ionising radiation whilst providing good resolution, and therefore could be preferable to radiographic imaging as a first-line imaging modality. In addition, ultrasound is unique because it is a relatively cheap, portable and non-invasive modality, able to examine both dynamic and static states. It has also previously been shown that ultrasound is the most reliable method of measuring AHD (McCreesh et al 2013). Different studies have utilised different methodologies to measure the AHD. The direct measurement between the acromion and the humeral head seems to be the most popular; however some authors measure between the acromion and greater tubercle (McCreesh et al 2013). It is unclear which is the best method; however it is important be consistent with the methods used.

The application of ultrasound imaging to the shoulder joint is frequently undertaken by professionals such as physiotherapists, rheumatologists and sports physicians. Training these persons to recognise the ultrasound anatomy and to develop the necessary skills for image guided injection is important. Ideally this training would be undertaken using a realistic test object or model. Numerous anthropomorphic models are commercially available for a variety of anatomy including the prostate, breast biopsy, thyroid, heart, kidney, scrotum, female pelvis, blood, abdomen, foetus and infant’s head. In addition, individual groups have described recipes for manufacturing ultrasound phantom models and tissue mimicking materials (Clarke et al 1994, Gibson 1995, Pay et al 1998, Osmer 2008, Lo et al 2012). No anthropomorphic phantoms mimicking the shoulder under ultrasound have been described.
Such a model would prove very useful for several reasons. A known AHD measurement in the model can be compared to the measurement made under ultrasound by the operator, in order to provide evidence for validity of the measure. Additionally, the model would be useful for shoulder ultrasound technique and image guided injection training. This report describes the design, implementation and evaluation of a prototype shoulder model.

**Methods**

There were two stages in the creation of the model: material selection and validation, and construction of the model.

(a) Material Selection and validation

Three materials were required: a soft tissue mimic, an outer protective layer and a bone mimic. The details of each one are described in turn below.

(i) Soft Tissue Mimic

Soft tissue mimics manufactured from gelatine have been described in the literature and this was therefore selected for this application (Bude et al 1995, Nicolson & Crofton 1997, Osmer et al 2008, Lo et al 2012). Chlorhexadine solution (0.5% chlorhexadine, 70% denatured ethanol) was added to reduce biodegradation (Chantler et al 2004, Omar et al 2008). To create a more realistic appearance, some scattering medium was required. Psyllium husk powder has been described as suitable for this purpose (Moorhouse et al 2007, Lo et al 2008). No recipes were found using all three ingredients, we began with published recipes that used two of the three ingredients and made modifications in order to get the speed of sound as close to 1540 ms\(^{-1}\) as possible. The soft tissue mimicking compound was made using gelatine (Oxoid), psyllium husk powder (bulkpowders.co.uk) and chlorhexidine (Hydrex Pink).

An ultrasound image was taken of soft tissue samples and the thickness of the sample was measured using the machine’s callipers which were calibrated to 1540 ms\(^{-1}\). The speed of sound in the soft tissue mimic sample \(v_s\) was measured using a conventional B-scanner (Acuson 128XP/10, Siemens Medical). For each sample, the measured thickness as assessed by the machine’s callipers \(s_1\) was compared with actual value obtained using a set of vernier callipers, \(s_2\). Hence \(v_s = s_1/s_2 \times 1540\). Each sample was measured five times. Our final selection was a mixture of 1 litre of water, 150 g gelatine, 25 g psyllium husk powder and 15 ml chlorhexidine which had an estimated speed of sound of 1548(±31) ms\(^{-1}\).
(ii) Outer Protective Layer

To increase the model’s durability, it was decided to apply a layer of liquid latex to the outer surface of the model. The latex layer did not affect the ultrasonic image of the model.

(iii) Bone Mimic Material

Being a complicated non-uniform structure made of several materials, bone is difficult to mimic in phantoms. The two types of osseous tissues are trabecular and compact bone, depending on the function and region of the bone, the composition of the bone varies. In the region of the SAS, the bone is epiphyseal and hence the mimic needed to emulate this.

The speed of sound in epiphyseal bone has been reported as having a wide range of values. No specific information about scapular bone was found and therefore there was no specific target.

A wide variety of bone-mimicking materials have been described, but relatively few have been aimed at mimicking epiphyseal bone. Epoxy resin and HDPE were potential epiphyseal bone mimics described in literature (Clarke et al 1994, Pay et al 1998). It was decided to use a rapid prototyping technique with a 3D printer since that would allow the complex geometry of the shoulder joint to be replicated. DuraForm®PA, a Nylon 12 based material, is commonly used for rapid prototyping a sample of which was evaluated. It is strong with low moisture absorption of 0.07% over 24 hours making it ideal to cope with being embedded in aqueous media.

To measure the speed of sound, a 1cm³ sample of the DuraForm®PA was embedded in a sample of soft tissue mimic and scanned using a conventional B-scanner (Acuson 128XP/10, Siemens Medical). A frozen image was taken and the thickness of the sample was measured using the machine’s callipers which were calibrated to 1540 ms⁻¹. The speed of sound in the sample was calculated using the methods previously described. The speed of sound in the DuraForm®PA was calculated as 1709(±11) ms⁻¹. This speed of sound fell within the range of reported values for epiphyseal bone (Langton et al 1990) and was therefore deemed a suitable material for the bone model.
(b) Construction of the model

(i) Bone Model Manufacture

A DICOM CT dataset of the male shoulder was downloaded (mri.radiology.uiowa.edu/visible_human_datasets.html). The dataset was loaded into OsiriX (www.osirix-viewer.com) software on a Macintosh computer. The 3D surface rendering option was selected. It is possible to choose pre-set values for bone from the surface rendering window, but these were not suitable. As the scapula contains thin regions where the intensity values fall below the threshold, holes which did not exist in reality appeared in the rendered bone. The threshold values were varied until the number of holes was minimised (Figure 1). The model was then exported and saved as an STL file.

![Figure 1: Surface rendering settings and rendered bone model on OsiriX](image)

The STL file was loaded into MeshLab (meshlab.sourceforge.net) (Figure 2). Only the scapula and upper humerus were required, therefore unnecessary bones were removed using the vertices deletion tool. However the rendered model still contained many unnecessary isolated fragments around it (Figure 2). These were removed using the “Remove isolated pieces (wrt diameter)” tool from the cleaning and repairing filters menu, using a setting of 15%. The model contained indentations which needed to be smoothed (Figure 3); therefore the laplacian smoothing filter was applied (Figure 4). The model was smoothed as far as possible without creating holes, but a compromise was required. Higher smoothing settings
result in more averaging, leading to a loss of texture data and creation of holes in the 3D model. This was then saved as an STL file and sent to a rapid prototype manufacturer (Keyworth Rapid Manufacturing Ltd. Leeds, UK).

Figure 2: Rendered model in MeshLab

Figure 3: Unsmoothed scapula and upper humerus in MeshLab
The printed model contained two parts, the scapula and superior humerus. As the subacromial distance is the desired measurement from the phantom model, the humerus and scapula were joined in the glenoid fossa using epoxy resin (Everbuild Stick 2 Rapid Epoxy Syringe). The distance between the humerus and scapula in the dataset was measured using OsiriX; the gap was 1.5 mm superiorly and 1.7 mm inferiorly. The space was achieved by using rubber washers of the appropriate sizes, and the excess part of the washer was cut off using a blade once the epoxy resin had set. Any holes in the model were filled using epoxy resin. Figure 5 shows the bone model.
(ii) Construction of the Mould

A realistic mould in which the soft tissue and bone mimic could be contained was required. A plaster mould of a shoulder was initially created, from which a plastic mould was manufactured; the process is described below.

*Plaster Moulding*

Measurements of the arm diameter and clavicle were taken from the CT dataset. An appropriate volunteer with similar measurements was then identified and a plaster cast of the subject’s shoulder region and upper arm was made. The area to be cast was marked out with a permanent marker on the subject. Pieces of hessian fabric were cut into rectangular strips of approximately 80 mm x 150 mm. A plaster mix was made by adding two parts of fine moulding plaster to one part water; these were mixed slowly in a bucket until it reached a paste-like consistency. The cast was made in two parts: the anterior and posterior portion.

The posterior portion was made first. One strip of the hessian was dipped into the plaster and applied to the body. The same was done with subsequent pieces until the whole posterior area was covered. This was allowed to set for five minutes. The surface was then covered with a further layer of plaster mix to thicken and strengthen the cast. The lateral edge of the cast had liquid wax applied to prevent it sticking to the overlapping edges of the anterior portion, to prevent breakages and to aid removal.

The anterior part of the cast was made in the same way, with the edge slightly overlapping. Both parts were allowed to set on the subject for 15 minutes. The anterior part was removed,
followed by the posterior part. The casts were then left upright on a flat surface to set for a further 24 hours. The internal surfaces of the casts were coated with release agent. All exposed parts other than the superior aspect were then sealed with more plaster dipped hessian. A hole on the superior part of the cast was left open so that plaster could be poured in. This was left for 24 hours.

Once ready, the cast was filled with plaster in order to produce a plaster model of the shoulder. This model was allowed to set for 24 hours before removing it from the cast. The model was left to dry for another five days; it was then cut in the coronal plane along the midline to produce two parts. Figure 6 shows the plaster model of the shoulder (6a is the anterior portion, 6b is the posterior portion).

![Figure 6: Plaster model of the shoulder. A: anterior portion, b: posterior portion](image)

**Creating the vacuum formed plastic mould**

The plaster model was cleaned with a cloth to remove any dust. Petroleum jelly (Vaseline) was then applied to the surface of both parts of the model to allow easy removal from the plastic mould. The plastic mould was created in two parts. Each half of the plaster mould was inserted into a vacuum forming machine (CR Clarke Vacuum Forming Machine 1820). Thermoforming plastic of 1mm thickness (generic) was heated by the machine for 30 seconds at 175°C until it bowed slightly. The mould was then lifted by the machine into the plastic sheet and a vacuum was applied so that a perfect mould was created by the plastic sheet
clinging on to the plaster model. It was important that the edges of the plaster model did not go inwards as this could have resulted in the plaster model being trapped in the plastic mould. A slight outward draft angle (i.e. sloping outwards) was present in the plaster model so it could be easily removed once the plastic had set. The plaster model was easily removed from the mould, by tapping it out. Figure 7 shows the plastic shoulder moulds.

Figure 7: Plastic shoulder moulds a: anterior external surface, b: anterior internal surface, c: posterior external surface; d: posterior internal surface.

Creating the final model

For the final model, just the anterior portion of the mould was used for reasons explained later. The gelatine mixture was made using 4.5 litres of water, 675g of gelatine, 113g of psyllium husk powder and 68ml of chlorhexadine. Boiled water (4.5 litres) was poured into a large container. The gelatine was added slowly to the water whilst mixing gently with a mixing attachment and a drill. Once all the gelatine was added, the mixture was mixed for a further 30 seconds. The froth produced was allowed to settle down. Then, psyllium husk powder was slowly added whilst mixing at a fast pace. Care was taken to avoid adding too much psyllium husk powder at once as this would result in clumping of the powder. Once all the psyllium husk powder was added, it was mixed for a further 30 seconds. The froth
produced was removed using a sieve. The mixture was allowed to cool slightly for 30 minutes at room temperature. The chlorhexidine was then added and the mixture was stirred gently using a spatula.

Whilst the mixture was cooling, the plastic mould was prepared for pouring the gelatine compound: using a vegetable oil soaked paper towel, the inner surface of the mould was coated with vegetable oil. The oil coated mould was placed in the freezer whilst the mixture cooled. After the mixture was stirred, the mould was removed from the freezer and placed in a box deep enough to allow the bottom of the mould to rest at the bottom and provide support to the sides. The box was filled with crumpled newspaper in the areas where the mould was shallower to provide support.

The mould was filled with the mixture and any bubbles on the surface were removed gently with a spoon. The mixture was placed in a fridge. Once a thin skin had formed, the mixture was stirred gently with a spoon to prevent the psyllium husk powder from settling and forming a layer at the bottom. Once the mixture had formed a thicker skin where the surface could be touched without sticking, the bone phantom was pushed into the mixture and positioned in the desired position; the model was suspended in the mixture once left. After a further hour, unevenness in the surface of the gelatine was remedied by mixing 500 ml of water with the appropriate amount of other ingredients and pouring it on to the surface. The model was allowed to fully set for six hours. The model was released by dipping the mould into warm water for 30 seconds making sure that the water does not come into contact with the gelatine mixture. It was then inverted onto a laminated wood sheet and the mould gently shaken.

Three layers of liquid latex (www.mbfg.co.uk) were then applied to the surface of the model using a paint brush. Three hours drying time were allowed between applications. Once a layer of latex was applied, the model was put back into the fridge to prevent any deterioration occurring. Figure 8 shows the appearance of the model.
Measurement of AHD on the shoulder phantom was independently undertaken by two musculoskeletal sonographers, blinded to the reference value of the AHD in the phantom model. The measurements were obtained with a GE Logiq e ultrasound scanner with a 7-12 MHz linear array transducer (GE Medical, Wauwatosa, WI, USA). An ultrasound image was obtained with the transducer positioned along the line of the humerus, over the anterior part of the acromion, with the subacromial space and humeral head visible. The AHD was then measured as the shortest distance between the inferolateral edge of the anterior acromion and the humeral head, parallel to the acoustic shadow cast by the acromion. Measurements were taken with the on-screen callipers. Each sonographer measured the AHD on five separate images, with the probe removed and repositioned between scans. The measurement of the AHD on the bone model was obtained using vernier callipers placed at the equivalent points that the ultrasound measurements, with the on-screen callipers, would have been obtained from. Five separate measurements were taken with the vernier callipers.

**Results**

The appearance of the soft tissue sample under ultrasound can be seen in Figure 9a. The speckled appearance produced by the psyllium husk fibres looks comparable to real soft tissue. The appearance of the DuraForm®PA within the soft tissue mimic can be seen in Figure 9b. The appearance of the DuraForm®PA looks realistic, with a highly reflective surface followed by acoustic shadowing similar to real bone.
Figure 9: a: Ultrasound appearance of the gelatine compound alone. b: Ultrasound appearance of the DuraForm PA embedded within the gelatine compound

In terms of ultrasonic properties, the speed of sound of the gelatine compound was well matched to that of the assumed speed of sound by the ultrasound machine, with a speed of sound of 1550 ms$^{-1}$ compared to assumed value of 1540 ms$^{-1}$. The DuraForm®PA had a speed of sound of 1709 ms$^{-1}$. The reported values for the speed of sound in epiphyseal bone range from 1450 to 2775 ms$^{-1}$. Figure 10 shows the measurement of the AHD in the phantom and from a real patient.

Figure 10: Ultrasound appearance of the subacromial space
The median measurement of the AHD in the bone phantom model made with vernier calipers was 9.8 mm. Table 1 reports the descriptive values of the AHD obtained with the vernier callipers on the bone model as well as the ultrasound measurements made by both sonographers. Figure 11 is a boxplot showing good agreement across all the measurements, with all the medians falling within 0.5 mm of each other. All methods demonstrated excellent reliability, with CoV below 3%.

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<td><strong>CoV (%)</strong></td>
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Table 1: Descriptive values for AHD measurements of the shoulder phantom directly by callipers, and indirectly using ultrasound by two sonographers. Values taken from five repeated measurements in each case.

Abbreviations: CoV= coefficient of variation; IQR = inter-quartile range
Figure 11: Boxplot illustrating the AHD measurement values

Discussion

The phantom was a suitable model, with a similar appearance, shape and feel to a real shoulder joint. Two sonographers were able to accurately measure the AHD using ultrasound, with values close to the true skeletal measurement. The AHD measurements were very reliable as proved by the small CoV for each examiner.

Within the model, the bone mimic had a satisfactory ultrasound appearance (Figure 10); the images look realistic and the shape, as well as the location, of the bone is easily recognisable. There were bright reflections at the bone-soft tissue interface and a shadow formed behind the bone on the ultrasound image, comparable to ultrasound appearance of real bones (Figure 9, 10). The AHD is clearly identifiable in the phantom (Figure 10). Despite this, muscle and tendon texture, i.e. banding around the shoulder joint (Figure 10), was not replicated in the image, as the soft tissue mimic was homogenous. The average AHD measurements taken on
the model fall within the limits of the measurements of the AHD made on the bone model with the vernier callipers.

The production of the model and its constituent materials are relatively inexpensive; making the gelatine compound mixture is also simple. However, the main problematic areas are associated with production. The overall process of rendering the model using OsiriX and MeshLab was lengthy with a steep learning curve, and potentially more so for those less confident with technology. There is some specialist equipment involved which may not be readily available to everyone, such as the vacuum forming machine (for the mould) and the 3D printer. The formulation of the gelatine compound also has good structural integrity and can therefore withstand multiple uses and transportation. However, the gelatine has a limited shelf life and needs to be refrigerated when not in use.

The final model has multiple benefits for training. The soft tissue phantom feels realistic to the touch and behaves like skin in its response to pressure, elasticity, flexibility and friction under the transducer. It also has a close physical resemblance to the bony anatomy of a real shoulder joint: it is accurate in size and shape, and the use of psyllium husk powder simulates the speckled appearance of soft tissue. The model would therefore be useful in training clinicians to measure the AHD. Additionally, the model could prove useful to train clinicians to perform ultrasound-guided injections into the subacromial space; however this was not tested.

Overall, the product achieved the proposed objectives it was designed to meet, although certain limitations were encountered along the production and transportation stages. A compromise was made in the positioning of the bone within the gelatine compound; the two-part model was too heavy to use as well as unstable, and therefore only the anterior mould was used (Figure 8a, 8b). This resulted in the scapula being slightly closer to the surface of the chest. However, the measurement for the AHD could still be made from a realistic positioning of the transducer on the surface of the model. A model with both anterior and posterior portions could possibly be manufactured by using a one part mould set in a block rather than a vacuum-formed plastic sheet.

Further to these structural issues, the subacromial space was positioned deeper in the phantom material than in real life. This was because if the bone was too close to the surface of the soft tissue mimic, the friction between the gelatine and DuraForm®PA bone material whilst manipulating the transducer may cause damage to the surface of the gelatine. However
this is not problematic for the measurement purposes. The model does not articulate, while a patient’s arm needs to be rotated to different positions when performing shoulder ultrasound. The shelf life of the product is not long - the model became unusable in three weeks, this could be further shortened after multiple needle punctures.

The current version of the model is basic. Further development of the model is required to include muscle and tendon mimics to provide the most realistic shoulder soft tissue representation, especially for injection training purposes. Further work needs to be done to be undertaken to develop a more durable, non-biodegradable soft tissue compound that would permit articulation.
References


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Appendix 3:

Author contributions to studies presented in this thesis

Conception and design: KM, JL
Analysis and interpretation: KM, JL
Drafting final manuscript: KM, JL
Administration in relation to submission to journal: KM

Conception and design: KM, JL
Literature searching and selection: KM, JL
Critical appraisal: KM, JL, JC
Analysis and interpretation: KM, JL, JC
Drafting final manuscript: KM, JL, JC
Administration in relation to submission to journal: KM

Conception and design: KM, PA, TE, JL
Development of phantom model: KM, PA, TE, AD
Data collection: KM, PA, SR, TE
Data analysis and interpretation: KM, PA, JL, TE
Drafting final manuscript: KM, PA, TE, JL
Administration in relation to submission to journal: KM

Study IV: McCreesh K, Anjum S, Crotty J, Lewis J Ultrasound measures of supraspinatus tendon thickness and acromiohumeral distance are reliable in rotator cuff tendinopathy. Under review, J Clin Ultrasound
Conception and design: KM,SA, JL
Writing and reviewing ethics application: KM, SA
Subject recruitment: KM, SA, JC
Data collection: KM, SA, JC
Data analysis and interpretation: KM, SA, JL
Drafting final manuscript: KM, SA, JL
Administration in relation to submission to journal: KM
Study V: McCreesh K, Anjum S, Crotty J, Lewis J. Thickened supraspinatus tendon but no change in subacromial space in rotator cuff tendinopathy. Under review, J of Rehabilitation Medicine
Conception and design: KM, SA, JL
Writing and reviewing ethics application: KM, SA
Subject recruitment: KM, SA, JC
Data collection: KM, SA, JC
Data analysis and interpretation: KM, JL
Drafting final manuscript: KM, JL
Administration in relation to submission to journal: KM

Study VI: McCreesh K, Donnelly A, Lewis J. Altered supraspinatus tendon response to fatigue loading in rotator cuff tendinopathy. Accepted subject to revisions, Br J Sports Med
Conception and design: KM, AD, JL
Writing and reviewing ethics application: KM, AD
Subject recruitment: KM
Data collection: KM
Data analysis and interpretation: KM, AD, JL
Drafting final manuscript: KM, AD, JL
Administration in relation to submission to journal: KM

Conception and design: KM, LL, JL
Writing and reviewing ethics application: KM, LL
Subject recruitment: LL, KM
Data collection: LL
Data analysis and interpretation: KM, LL, JL
Drafting final manuscript: KM, LL, JL
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