ABSTRACT

Debilitating shoulder pain is prevalent among wheelchair users, however the causes remain unknown. Shoulder pain is reported to be greater among those who began wheeling after skeletal maturity (adulthood-onset, AO) than among those who began wheeling prior to skeletal maturity (childhood-onset, CO). It is unclear whether functional load-bearing from manual wheelchair use affects glenohumeral bone and cartilage morphology. Bone is known to adapt to loading, however the literature is conflicting regarding cartilage’s capacity to adapt to loading.

We performed a pilot study to quantify bone and cartilage morphology at the glenohumeral joint of manual wheelchair users (nCO=3, nAO=5) and age- and gender-matched able-bodied controls (nC=8). Bone morphology (volumetric bone mineral density (vBMD) and normalized cross-sectional area (nCSA)) was evaluated using quantitative computed tomography. Bone density distribution was assessed across the glenoid and, for the first time, across the humeral head using a novel quantitative CT-Osteoabsorptiometry method. Cartilage morphology (thickness, volume, and surface area) was evaluated using quantitative magnetic resonance imaging, in the first assessment at 3T MRI. This novel combination of methods provides complementary quantitative data of glenohumeral bone and cartilage morphology.

Compared to the AO, the CO in our study had significantly higher (p<0.05) glenoid subchondral nCSA, non-significantly lower glenoid subchondral vBMD, and non-significantly higher humeral head and glenoid trabecular vBMD. A reasonable cross-sectional study (n=22) would likely show higher humeral head and glenoid trabecular vBMD and glenoid subchondral nCSA in CO subjects but would not find differences in nCSA of humeral head total, trabecular, and cortical bone, or glenoid trabecular bone. Surprisingly, vBMD was (non-significantly) lower in the wheelchair users than in the able-bodied controls, however activity levels varied considerably. Significant correlations were found between humeral head and glenoid trabecular vBMD (r=0.94), and between humeral head trabecular vBMD and physical activity scores (r=0.84). Given the small effect sizes and the large variance in humeral head and glenoid cartilage thickness, volume, and surface area, it is not likely that further study of these parameters would provide insight into wheelchair users’ shoulder pain. Gaining a better understanding of how glenohumeral bone and cartilage respond to wheelchair use would allow for rehabilitation programs and wheelchair-design to be tailored to childhood-onset and adulthood-onset wheelchair users.
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<td>Three-dimensional</td>
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<td>aBMD</td>
<td>areal Bone Mineral Density</td>
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<td>Activity of Daily Living</td>
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<td>ANOVA</td>
<td>Analysis of Variance</td>
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<td>Contrast-to-Noise Ratio</td>
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<td>Metabolic Equivalent</td>
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<td>Maximum Intensity Projection</td>
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Chapter 1: Introduction

1 INTRODUCTION

Chronic and debilitating shoulder pain is reported to affect between 30-73% of wheelchair users (1-4). In Canada, approximately 155,000 individuals use a wheelchair for mobility (5). Manual wheelchair users rely heavily on their upper limbs for maintaining their independence, therefore any impairment due to shoulder pain is of great functional and psychological consequence. In addition to performing the usual prehensile and manipulative tasks, the upper limbs of manual wheelchair users are subjected to many additional functional demands, including transfers to and from the wheelchair, and wheelchair propulsion.

With the exception of two studies (6, 7), research into the prevalence and etiology of shoulder pain in wheelchair users has focused exclusively on individuals who began using a wheelchair after skeletal maturity. Central to the present study was a finding by Sawatzky and colleagues (6), that showed that individuals who began using a wheelchair after skeletal maturity (adulthood-onset wheelchair users) reported significantly more shoulder pain than individuals who began using a wheelchair before skeletal maturity (childhood-onset wheelchair users). These authors hypothesized that the difference in shoulder pain between childhood-onset and adulthood-onset groups might arise from differences in pain perception, wheelchair propulsion biomechanics, or functional adaptation of the tissues at the joint. Regarding their hypothesis of tissue adaptation, it is currently unknown whether bone and cartilage at the shoulder joint adapt to the increased loading associated with manual wheelchair use, and if this adaptation occurs, whether it is dependent on the degree of maturation of the tissue.

Understanding the causes of manual wheelchair users’ shoulder pain is the first step towards preventing its occurrence. The present study explored the third hypothesis of Sawatzky et al. regarding the differences in the functional adaptation of bone and cartilage at the glenohumeral joint in childhood-onset and adulthood-onset manual wheelchair users. We believe that increased understanding of how the tissues at the glenohumeral joint respond to loading via wheelchair use will benefit wheelchair users in many ways. First, these data could be used to recommend modifications to the functional tasks performed by current wheelchair users in an attempt to prevent shoulder pain, based on the adaptive capacity of bone and cartilage in childhood-onset and adulthood-onset wheelchair users. If differences are discovered between the way that bone and cartilage adapt to loading pre- and post-maturity, this would suggest modifying spinal cord injury rehabilitation and physiotherapy programs to tailor them to childhood-onset and adulthood-onset wheelchair users. Manual wheelchairs are currently designed based on anthropometric and biomechanical data from
adulthood-onset wheelchair users, however these wheelchairs are used by both adulthood-onset and childhood-onset groups. If differences are found in the way that bone and cartilage adapt to wheelchair use prior to skeletal maturity, this might underscore the need for a wheelchair designed specifically for childhood-onset wheelchair users. Findings of bone and cartilage adaptation, or lack thereof, to wheelchair use could also be presented to insurance boards to justify funding requests for assistive devices that might help prevent shoulder pain, such as lifts to put wheelchairs into vehicles. It is clear that a better understanding of how glenohumeral bone and cartilage respond to wheelchair use would be advantageous to manual wheelchair users, possibly even improving their quality of life.

Under ‘normal’ loading conditions, the development of bone and cartilage are well documented. The cartilaginous fetal endoskeleton undergoes endochondral ossification to become the mature bony human skeleton. The subchondral bone growth front stabilizes before reaching the articulating ends in synovial joints, leaving a layer of cartilage over the articulating ends of the bones (8, 9). The biological or environmental factors that prevent the ossification front from extending to the edge of the joint surface remain unclear (10). The layer of articular cartilage plays a large functional role: it reduces friction between the joint surfaces and distributes large forces across the joint to the underlying subchondral bone (11). Immature bone has been shown to be more responsive to loading stimuli than mature bone. In general, bone is accrued as a result of increased loading and bone is resorbed as a result of decreased loading. These concepts are summarized by Frost’s Mechanostat principle. In trabecular bone, adaptation to loading manifests as a change in bone density whereas in cortical bone it manifests as a change in area. The concept that bone form follows function is widely referred to as Wolff’s law. Bone adaptation is governed by three main factors. First, dynamic rather than static loading drives bone adaptation. Second, only a short duration loading stimulus is necessary to trigger an adaptive response in bone. Third, abnormal loading drives bone adaptation, not routine loading. It appears that cartilage, like bone, is easier lost by disuse than gained by increased use. Decreased loading via immobilization has been shown to decrease cartilage thickness in humans (12, 13), however conflicting results have been seen for the case of increased loading via physical activity. In response to increased loading some studies have seen an increase in cartilage thickness (14-16) or volume (17, 18) whereas others have not found any change (19-21). If cartilage does indeed adapt to loading, it remains unclear whether age affects the degree of adaptation.

Bone and cartilage are believed to be subjected to increased stresses and strains at the shoulder joints of manual wheelchair users because these individuals rely heavily on their upper extremities for mobility and independence. Changes in joint loading can have a profound effect on the development
of a synovial joint, such as the glenohumeral joint, and the resultant bone mineralization patterns (22). Given the highly interactive relationship between bone and cartilage at joint surfaces, bone and cartilage adaptation should ideally be studied in combination. Only a few studies have done so and have reported that articular cartilage and subchondral bone adapt to altered loading conditions in a coordinated way, especially before skeletal maturity (23).

Imaging methods for quantifying bone and cartilage morphology at a joint have only recently become available and have not yet been used to study bone and cartilage in vivo in the shoulders of manual wheelchair users. Since computed tomography (CT) is currently the best modality for imaging bone and magnetic resonance (MR) imaging is currently the best modality for imaging cartilage, multi-modality imaging is needed to quantify bone and cartilage morphology at the shoulder joint. Conventional imaging techniques, such as plain film radiography, are likely insufficient to quantify bone and cartilage morphology. Newer imaging techniques, such as MR and CT, offer substantial promise, especially in combination with the associated quantitative analysis techniques (qMRI and qCT). The advantage of these quantitative analysis techniques is that they allow for precise, objective comparisons of subtle differences in morphological parameters. Quantitative CT (qCT) permits quantification of volumetric bone mineral density (vBMD) and cross-sectional area. CT Osteoabsorptiometry (CT-OAM) allows for visualization of the bone mineralization patterns (and associated bone mineral density) across the joint surfaces. Quantitative MRI (qMRI) allows for quantification of cartilage morphology (e.g. thickness, volume, and surface area). These techniques, or variations of these techniques, have been used previously at the shoulder; however to our knowledge, this is first time they have been used in combination. Moreover, this is the first time that qCT and CT-OAM have been used to study bone morphology at the glenohumeral joint of manual wheelchair users. qCT has been used in two previous studies to assess glenoid mineralization, however a reference phantom was not included in the CT scans and consequently the CT intensity values (in Hounsfield Units) could not be converted to an equivalent vBMD (24, 25). vBMD of the glenohumeral joint has been previously quantified with peripheral qCT (pQCT) but only in cadaveric specimens (26, 27). To our knowledge, qCT has not been used in vivo to quantify vBMD at the glenohumeral joint in human subjects. CT-OAM has been used to assess the patterns of bone mineralization in the glenoid cavity (28-31), but without converting CT intensity to vBMD and therefore quantitative comparisons between subjects were not possible. Moreover, CT-OAM has not been applied to the humeral head and has not been used in the manual wheelchair user population. The qMRI technique has been used to quantify glenohumeral cartilage morphology of healthy individuals (32) and recently, of manual wheelchair users (33). In both of these studies MR imaging
was performed at 1.5T. To our knowledge, the current study is the first to perform 3T MR imaging of glenohumeral cartilage for qMRI analysis, and is the first to use qCT, CT-OAM, and qMRI in combination for an integrated and quantitative assessment of bone and cartilage morphology at the glenohumeral joint of manual wheelchair users.

The fundamental question that motivated this research is whether bone and cartilage at the glenohumeral joint of manual wheelchair users adapt to the increased loading associated with wheelchair use. Answering this question would require many years of research and a full-scale longitudinal study, therefore, for the purpose of this pilot study, this broad question was limited in scope.

This pilot study was performed to assess the feasibility of answering two research questions in a cross-sectional study:

1. Are there differences in bone and cartilage morphology at the glenohumeral joint between childhood-onset and adulthood-onset manual wheelchair users?
2. Are there differences in bone and cartilage morphology at the glenohumeral joint between long-term manual wheelchair users and their able-bodied matched controls?

We hypothesized that:

1. **Humeral head and glenoid cavity trabecular bone mineral density are higher in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.**
   This hypothesis is based on the assumption that the childhood-onset wheelchair users had an adaptational advantage over the adulthood-onset wheelchair users, because the former began loading their shoulders via wheelchair use prior to skeletal maturity. Changes in loading are known to affect the bone mineral density of trabecular bone and increased loading has been shown to result in increased trabecular bone mineral density. Immature bone is known to be more responsive to changes in loading than mature bone.

2. **Glenoid subchondral normalized cross-sectional area is greater in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.**
   This hypothesis is based on the assumption that the childhood-onset wheelchair users had an adaptational advantage over the adulthood-onset wheelchair users because they began wheeling prior to skeletal maturity. We hypothesized that glenoid subchondral cross-sectional area would be greater in these subjects because changes in loading are known to affect the
geometry of cortical bone, and subchondral bone is considered to be a specialized form of cortical bone. Increased loading has been shown to result in increased cortical cross-sectional area and/or thickness.

3. **Glenoid subchondral bone mineral density is lower in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.**
   
   Again, this hypothesis is based on the assumption that the childhood-onset wheelchair users had an adaptational advantage over the adulthood-onset wheelchair users, and therefore we hypothesized that their glenoid subchondral cross-sectional area increased (hypothesis #2) at the expense of vBMD (hypothesis #3). This hypothesis is based on a finding by Ashizawa *et al.* that periosteal bone cross-sectional area was negatively correlated to vBMD in the heavily loaded radius in the playing arm of competitive tennis players (34).

4. **Volumetric bone mineral density is higher in the manual wheelchair users than in the able-bodied matched controls.**
   
   This hypothesis is based on the assumption that manual wheelchair users load their shoulders more than able-bodied individuals as a result of wheelchair propulsion, transfers, and activities of daily living. Increased loading has been shown to result in increased volumetric bone mineral density.

5. **Humeral head and glenoid cartilage volumes are greater in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.**
   
   This hypothesis is based on the assumption that the childhood-onset wheelchair users had an adaptational advantage over the adulthood-onset wheelchair users, because the former began wheeling prior to chondral maturity (~18 yrs). A study by Jones *et al.* showed that immature knee cartilage volume was significantly positively correlated with physical activity (17). To date, mature cartilage has not been shown to undergo morphological changes (e.g. increased or decreased cartilage thickness, volume, or surface area) as a direct result of increased loading.
The objectives of this pilot study were to:

1. Determine the sample sizes required for a full-scale study comparing bone and cartilage morphology between childhood-onset and adulthood-onset wheelchair users.
2. Determine the feasibility of recruiting the wheelchair user populations required for a full-scale study.
3. Implement and apply CT Osteoabsorptiometry (CT-OAM) and quantitative CT (qCT) to quantify 3D bone density distribution and morphology, respectively.
4. Develop a high-resolution 3T MR imaging protocol for glenohumeral cartilage and apply quantitative MR imaging (qMRI) analysis to quantify 3D cartilage morphology.
5. Assess the feasibility of applying qCT, CT-OAM, and qMRI image analysis techniques at the glenohumeral joint in the wheelchair user population.
6. Determine the most relevant parameters of bone and cartilage morphology in the wheelchair user population for a full-scale study, given that many parameters potentially relevant to wheelchair users’ shoulder pain can be measured.
2 LITERATURE REVIEW

2.1 SHOULDER ANATOMY

The shoulder girdle consists of three joints and one articulation (Figure 2-1). These are the sternoclavicular joint, the acromioclavicular joint, the glenohumeral joint, and the scapulothoracic articulation. The sternoclavicular joint provides the only bony connection between the axial skeleton and the upper limb.

The glenohumeral joint is the articulation between the glenoid cavity of the scapula and the head of the humerus (Figure 2-2A). It is the most mobile joint in the human body, and together with the other shoulder girdle joints, enables the placement of the hand in several planes. This extensive mobility is achieved at the expense of bony stability: the glenoid cavity is relatively shallow and flat compared to the much larger, semi-spherical humeral head (36) (Figure 2-2B).
The normal distribution of articular cartilage across the glenohumeral joint surfaces helps to increase joint congruity. Humeral head cartilage is thickest at the centre and thinnest at the periphery, in contrast to the glenoid cavity cartilage, which is thinnest at the centre and thickest at the periphery (32, 36). As the arm is abducted the scapula rotates over the thorax (forming the scapulothoracic articulation, Figure 2-1 inset), placing the glenoid cavity inferior to the humeral head and thus achieving greater bony stability. In addition, the surrounding soft tissues contribute significantly to the stability of the glenohumeral joint. These soft tissues include the glenoid labrum (Figure 2-2), three glenohumeral ligaments (inferior, middle, and superior), the joint capsule, and four rotator cuff muscles (infraspinatus, supraspinatus, subscapularis, and teres minor) (Figure 2-3).
2.2 GLENOHUMERAL JOINT LOADING

The glenohumeral joint is a ball-and-socket joint with three (rotational) degrees of freedom, allowing for three-dimensional (3D) movements of the arm. Abduction of the arm, for example, is achieved not only by rotation at the glenohumeral joint, but also by rotation of the scapula over the thorax. In addition, approximately 17 muscles act on the shoulder girdle. The rotator cuff muscles and the deltoid muscle act in concert to stabilize the semi-spherical humeral head in the shallow glenoid cavity. The force contribution from each muscle varies with the load applied to the arm, the plane of elevation and the degree of elevation of the arm. When the unloaded arm is abducted to 90°, the muscle forces at the glenohumeral joint are approximately 50% of body weight, due to the small muscle moment arm (~3 cm) relative to the moment arm from the centre of mass of the arm (~30 cm when the elbow is extended). Loads at the glenohumeral joint can exceed body weight when the arm is externally loaded. Calculating glenohumeral loads is challenging because this calculation should ideally be performed in 3D and account for muscular contributions. It is important to note that the net glenohumeral joint force is much less than the bone-on-bone contact force (with muscle forces).

For simplicity, the following two-dimensional examples of static equilibrium in the coronal plane are used to illustrate how load is generated at the glenohumeral joint. The first example gives equations for calculating the net glenohumeral joint force (with pure moment). The second example gives equations for calculating the glenohumeral joint bone-on-bone contact force (with muscle forces).
2.2.1 Net glenohumeral joint force and moment

![Free-body diagram of the glenohumeral joint with the arm at 0° of abduction.]

**Figure 2-4 – Free-body diagram of the glenohumeral joint with the arm at 0° of abduction*.**

where  
\[ M = \text{intersegmental resultant moment} \]
\[ R = \text{intersegmental resultant force} \]
\[ W = \text{weight of the arm} \quad (W = mg) \]
\[ r_w = \text{perpendicular distance between the point of joint contact and the point of application of } W \quad (\text{i.e. centre of mass}) \]

*point of joint contact indicated by a star

The intersegmental resultant force R and moment M represent the vector sums of all forces and moments, respectively, generated by the anatomical structures of the joint (e.g. muscles, ligaments, and joint capsule). The resultant force R is assumed to be perpendicular to the joint surface at the point of contact (and \( \theta \) degrees from the horizontal) because the articular cartilage provides nearly frictionless joint surfaces (i.e. frictional forces are negligible). Glenohumeral joint motion is the result of the moments applied by the muscles that cross the joint and is represented in this example by the intersegmental moment M about the point of joint contact (denoted by the star in Figure 2-4). As the arm is abducted the moment arm \( r_w \) increases and in order to maintain static equilibrium the intersegmental moment M must also increase.

\[
\sum F_x = 0 \\
- R_x = 0 \\
- R \cos \theta = 0
\]
\[
\sum F_y = 0 \\
R_y - W = 0 \\
R \sin \theta - mg = 0
\]
\[
\sum M = 0 \\
M - (r_w \times W) = 0
\]
2.2.2 Glenohumeral bone-on-bone contact force

![Free-body diagram of the humerus at 0° of abduction.](image)

where \( J \) = joint (bone-on-bone) contact force  
\( F_{\text{delt}} \) = force exerted by the deltoid muscle  
\( F_{\text{sup}} \) = force exerted by the supraspinatus muscle  
\( W \) = weight of the arm (\( W = mg \))

To calculate the bone-on-bone contact force, the individual muscle forces are included instead of the intersegmental resultant moment. Although several muscles act at the glenohumeral joint, we have only included the contributions of the deltoid and the supraspinatus since these muscles are the primary abductors of the arm. It is assumed that the supraspinatus muscle force \( (F_{\text{sup}}) \) is acting along the horizontal and that the deltoid muscle force \( (F_{\text{delt}}) \) is acting on a line \( \beta \) degrees from the horizontal.

The bone-on-bone contact force is assumed to be perpendicular to the joint surface (and \( \alpha \) degrees from the horizontal) because the articular cartilage provides nearly frictionless joint surfaces. The sum of the moments is calculated about the point of joint contact (denoted by the star in Figure 2-5) with the clockwise direction as positive.

\[
\sum F_x = 0 \\
F_{\text{sup}} + F_{\text{delt}} \cos \beta - J \cos \alpha = 0 \\
\sum F_y = 0 \\
F_{\text{delt}} \sin \beta + J \sin \alpha - mg = 0 \\
\sum M = 0 \\
(r_{\text{delt}} \times F_{\text{delt}}) + (r_{\text{sup}} \times F_{\text{sup}}) - (r_y \times W) = 0
\]

These simplified two-dimensional examples are presented with the arm at 0° of abduction, however it is clear that the loads at the glenohumeral joint increase as the arm is abducted, especially if the hand is supporting an external load. This results from high muscle forces, necessary to maintain equilibrium given the large moment arm of the arm relative to the small moment arms of the muscles. One strategy to reduce glenohumeral loading could be to minimize the moment arm of the arm (e.g. minimize abduction during lifting).
2.3 PREVALENCE OF WHEELCHAIR USE IN CANADA

In 2004, approximately 155,000 Canadians living in private households used a wheelchair for mobility (5). This group represents 0.5% of the total population of Canada. Ninety-six percent (96%) stated that they had a disability and nearly half of these individuals reported disease or illness as the cause (48%). The other common causes were natural aging (25%) and injuries (21%) (5).

2.3.1 Disabilities Resulting in Wheelchair Use

It is estimated that the incidence rate of spinal cord injuries in Canada is approximately 35 per million population per year (39). With the current population estimated at 32 million, this translates into approximately 1,120 new injuries per year. Overall, it is estimated that approximately 36,000 Canadians have a spinal cord injury (SCI) (39). Depending on the severity of the injury (i.e. complete or incomplete), many of these individuals require a wheelchair for mobility. The terms paraplegia and quadriplegia refer to the level of the SCI lesion. Paraplegia refers to full or partial paralysis of the lower limbs only, resulting from a complete or an incomplete spinal cord injury at spinal level T1 or below. Quadriplegia refers to full or partial paralysis of all four limbs and the trunk, resulting from a complete or an incomplete cervical spinal cord injury (C1-C7). By these definitions, it is possible for a quadriplegic with an incomplete lesion to manually propel a wheelchair, or in some cases, walk. Other disabilities that commonly require wheelchair use include myelomeningocele (spina bifida), amputation, post-poliomyelitis paralysis, as well as various neuromuscular and musculoskeletal disorders.

2.4 UPPER EXTREMITY FUNCTION IN WHEELCHAIR USERS

Manual wheelchair users depend greatly on their upper limbs for maintaining their independence (40-47). In able-bodied individuals, the upper extremities are primarily used for prehensile and manipulative tasks. In manual wheelchair users, however, the upper extremities are subjected to many additional functional demands, such as transfers to and from the wheelchair, pressure-relief raises to readjust the seated position (Figure 2-6A), and wheelchair propulsion. On average, manual wheelchair users exert 3,500 propulsive strokes per day (48). For a single year, this equates to more than 1.2 million propulsive strokes applied to the pushrim of the wheel (Figure 2-6B). Given that the life-expectancy of the SCI population is now close to that for the general population (3, 7, 49), and that SCI commonly occurs in early adulthood, it is not uncommon for a wheelchair user to spend several decades of life using a wheelchair (50, 51). Clearly, 40 million or more lifetime wheelchair propulsive strokes can be classified as a repetitive motion, and likely an increase in upper limb use.
compared to before wheelchair use. Since wheelchair users are seated in an environment largely designed for the able-bodied, substantial overhead reaching is required to accomplish everyday tasks (46, 52).

The many additional functional demands result in high compressive, impulsive, and shear forces on the bones, joints, and soft tissues of the upper limbs of wheelchair users (46, 54). A longitudinal study by Boninger et al. (47) found that wheelchair users who imparted a greater weight-normalized radial force (Fr) to the pushrim of the wheel during propulsion (Figure 2-6B) also had worsening shoulder pathology over time, as diagnosed with magnetic resonance imaging (MRI). This is not surprising, given that a force equal and opposite to the radial force applied to the pushrim is directed up the user’s upper limb, thereby driving the humeral head into the rotator cuff muscles and the coracoacromial arch (47). Any impairment of the upper limbs due to shoulder pathology or pain is of great functional and psychological consequence to manual wheelchair users (42, 44, 55).

2.5 PREVALENCE OF SHOULDER PAIN IN WHEELCHAIR USERS

Despite great variation in reported prevalence of shoulder pain, which ranges between 30-73% (6, 40-43, 45-47, 51, 56-62), there is a general consensus that the vast majority of wheelchair users develop debilitating shoulder pain. Shoulder pain in wheelchair users has been widely studied, with some of the earliest work dating back to 1979 (58). The wide range of reported results can be attributed to large variations between studies with regards to study populations, study design, research methods.
and outcomes measures. Moreover, pain is a subjective, self-reported measure, making it inherently difficult to quantify.

2.5.1 Differences between Study Populations

Study populations varied greatly between previous studies with respect to sample size, age, gender, time since injury, neurological lesion level (i.e. paraplegia vs. quadriplegia), completeness of the SCI lesion (i.e. complete vs. incomplete), and type of disability (e.g. SCI, spina bifida, amputee). Subjects also varied greatly with respect to their activity level (sedentary vs. athletic), the activities they performed independently (e.g. wheeling uphill, reaching overhead, transfers, and lifting the wheelchair into a vehicle) and whether they used a manual, power or power-assisted wheelchair or, in some cases, ambulated (i.e. incomplete SCI). Some studies included only long-term wheelchair users (6, 40, 51, 56, 57, 60) but not necessarily spinal cord injured (6, 40, 51, 60), whereas other studies followed subjects immediately after their spinal cord injury, through the rehabilitation process (1, 63). Most studies investigated shoulder pain in the SCI population as a whole (1, 42, 45, 55, 62, 64), however, a few studies included only paraplegic (43, 44, 46, 50, 54, 56, 59) or quadriplegic (65, 66) subjects. Three studies included ambulating SCI subjects who did not depend on wheelchairs for mobility (40, 63, 66). In two of these studies, the ambulating subjects comprised a large percentage of the total subjects: 52% (66) and 33% (40). Few studies made gender distinctions: two studies included only male SCI subjects (46, 62) and another only female wheelchair athletes (40).

2.5.1.1 Childhood-onset versus Adulthood-onset Wheelchair Users

The term childhood-onset wheelchair user refers to an individual who sustained a spinal cord injury as a child and began using a wheelchair prior to skeletal maturity. Conversely, the term adulthood-onset wheelchair user refers to an individual who sustained a spinal cord injury as an adult and therefore began using a wheelchair after skeletal maturity. Research into shoulder pain in wheelchair users has focused almost exclusively on adulthood-onset wheelchair users. Only two studies have documented the prevalence of pain in the childhood-onset wheelchair user population (6, 7). Given the many anatomical differences between a growing and a mature skeleton, research into shoulder pain among childhood-onset wheelchair users is warranted.

2.5.2 Differences in Study Design

Studies of shoulder pain in wheelchair users also varied greatly in terms of study design. Some studies only considered shoulder pain (2, 6, 40, 41, 44, 51, 59, 60, 62, 66, 67), while others
investigated upper extremity pain (1, 42, 46, 61), or even overall body pain (45, 55, 64). Some studies were cross-sectional (6, 40, 42, 44-46, 50, 51, 55, 58, 60-62, 64) while others were longitudinal (1, 55, 62, 63, 66) or even retrospective (57, 68).

2.5.3 Differences in Research Methods and Outcome Measures

Research methods ranged from self-report questionnaires (1, 6, 40-42, 44-46, 50, 51, 55, 56, 60-62, 64, 66), to interviews (6, 7, 46, 59), to physical examinations (1, 43, 44, 46, 50, 56, 59, 61, 62, 65), to exercise interventions (51), to diagnostic imaging including plain film radiography (43, 56, 59, 62, 63, 65, 68, 69), arthrography (59, 65) and magnetic resonance imaging (MRI) (56, 57). Although the physical exams and diagnostic imaging produced the most in-depth investigation of shoulder pain, these methods are both time-consuming and expensive compared to questionnaires and are generally not feasible in large-scale studies (1).

Outcome measures also differed widely between studies. The Wheelchair User’s Shoulder Pain Index (WUSPI) (Appendix B) was used in several studies to assess shoulder pain (6, 40, 41, 44, 50, 51, 60, 66, 67), while other studies used custom-designed questionnaires (42, 46, 61). The main limitation of the custom-designed questionnaires is that the results are difficult to compare between studies. Moreover, the validity of these questionnaires was, for the most part, not assessed. Several studies included physical examinations of the subjects (1, 43, 44, 46, 50, 56, 59, 61, 62, 65). While the results from such examinations were more objective than those from self-report questionnaires, there was no inter-examiner consistency between the studies (3).

Despite the significant variations between study populations, study design, research methods and outcome measures, there was general agreement on which activities of daily living tended to cause shoulder pain among wheelchair users.

2.5.4 Shoulder Pain during Activities of Daily Living

For wheelchair users, shoulder pain is a limiting factor for performing activities of daily living. The activities most commonly associated with shoulder pain include lengthy wheelchair propulsion and/or wheeling uphill (6, 40-42, 44, 58, 60, 61), transfers to and from the wheelchair (41, 42, 46, 58, 61), washing and/or dressing the upper body (41, 42), performing household chores (40), lifting objects from overhead (41, 66), sleeping (40, 41, 46, 60) and loading the wheelchair into a vehicle (44, 46).
2.6 ETIOLOGY OF SHOULDER PAIN

Since wheelchair users depend heavily on their upper limbs for mobility and independence, many researchers believe that overuse of the shoulder joint is the primary cause of shoulder pain. The overuse syndrome is attributed to load-bearing during wheelchair transfers and repetitive strain injuries from wheelchair propulsion (43, 46, 58, 59). Other researchers believe that postural changes due to wheelchair use cause scapular protraction which might in turn cause shoulder pain (3, 44, 49). Although the overuse syndrome is the most commonly assumed cause of shoulder pain, there is very little evidence to support this view (3).

While questionnaires are useful in assessing the prevalence of shoulder pain as a symptom, physical examinations and diagnostic imaging are better able to assess the underlying pathology and the potential cause(s) of pain. Several studies have used diagnostic imaging to investigate the etiology of shoulder pain in wheelchair users. The modalities used range from plain film radiography (43, 62, 65, 70), to arthrography (59, 65), and more recently, magnetic resonance imaging (MRI) (47, 56, 57). The main findings from these studies are grouped into soft tissue pathology, and bone and joint disorders.

Of the pathologies reported at the glenohumeral joint in wheelchair users, the following were related to the soft tissues (the prevalence is given as n/N):

- tendons
  - rotator cuff tendonitis: 7/17 (44)
  - bicipital tendonitis: 1/31 (59), reported by (43) as the most common cause of shoulder pain, however the prevalence rate was not reported
  - impingement syndromes: 15/53 (63), 2/24 (65), 23/94 (59), 9/17 (44)
- muscles
  - chronic and degenerative rotator cuff tears: 1/28 (56), 5/24 (65), 19/26 (57), 15/23 (59), prevalence not reported (47)
  - muscular atrophy causing muscle imbalance: 5/10 (44), review paper (3)
  - subacromial bursitis: 23/31 (59).

The following bone and joint disorders were commonly reported as causes of shoulder pain in wheelchair users (the prevalence is given as n/N):

- glenohumeral joint
  - joint space narrowing: 7/38 (68), 12/86 (62)
  - osteoarthritis with/without osteonecrosis: 2/24 (65)
  - instability: 10/24 (65)
  - capsular contracture and capsulitis: 9/24 (65)
  - calcification: 10/89 (62)
• humeral head
  • avascular necrosis: 5/31 (59)
  • greater tuberosity sclerosis: 3/24 (65)
• decreased range of motion: 20/89 (62)
• osteolysis of the distal clavicle: 5/28 (56)
• acromioclavicular joint
  • joint space narrowing: 38/38 (63), 26/83 (62)
  • arthrosis/arthritis: 2/31 (59), prevalence not reported (47)
  • degenerative disease: 13/24 (65)
• subacromial spur formation: 21/53 (63), prevalence not reported (47)

In addition to being more prone to developing shoulder pathology and pain, manual wheelchair users depend so heavily on their upper limbs that they may not be able to rest a painful shoulder sufficiently to decrease the inflammatory response or for healing to occur (40, 54, 61). When it was possible, resting the shoulder joint was found to be an effective method for alleviating pain (66).

2.6.1 Types of Pain

When investigating the cause of shoulder pain in wheelchair users it is important to first understand the type of pain these individuals are suffering from before being able to devise effective treatment and prevention strategies. Despite the large variability in the type and degree of disability between study subjects (section 2.5.1) only a few researchers (1, 45, 55, 66) highlighted the difference between neurogenic pain and musculoskeletal pain. Neurogenic or neuropathic pain is a direct result of damage to the spinal cord. It usually begins to develop in the months following the SCI and continues to develop over the following years (55). In contrast, musculoskeletal pain is a result of abnormal use and, as such, develops slowly over time (55). One limitation of questionnaire-based studies in assessing the prevalence of shoulder pain among manual wheelchair users is that questionnaires alone cannot differentiate between neurogenic and musculoskeletal pain (1, 66).

2.6.2 Onset of Shoulder Pain

A few studies investigated the onset of shoulder pain. Subbarao and colleagues (61) found that 20% of subjects with shoulder pain began experiencing this pain within the first year following SCI, while 33% did not develop shoulder pain until 15 years or more following SCI. These authors noted the bimodal distribution of pain with respect to the duration of SCI, and proposed that acute trauma causes early pain and cumulative trauma causes late-onset pain. It is possible that the first peak was associated with neurogenic pain and the second peak with musculoskeletal pain, however, these authors did not attempt to classify the type of pain. A prospective cohort study by van Drongelen et al. (1) found that shoulder pain developed soon after injury, during the rehabilitation process. These
investigators followed 169 SCI patients during rehabilitation and found a significant increase in shoulder pain scores over the first three months of rehabilitation, followed by a decrease in pain by the time the subjects were discharged from rehabilitation, which was on average five months later. These investigators observed that, as shoulder muscle mass increased during rehabilitation and as the SCI patients became more accustomed to regular arm exercise for functional tasks that the initial pain decreased and then stabilized over the first year following discharge from the in-patient rehabilitation program. From this, van Drongelen and colleagues posit that shoulder pain is not simply due to overuse injuries.

A study by Salisbury and colleagues (66) also seems to support this non-conventional view. Of 27 quadriplegics surveyed, 70% experienced shoulder pain. Despite having cervical spinal cord injuries, the majority of these subjects were ambulators; only four of the 27 subjects were manual wheelchair users. These authors concluded that there must be factors contributing to shoulder pain post-SCI other than load-bearing due to wheelchair use since the ambulators in their study experienced shoulder pain despite not using a wheelchair. A study by Curtis and Black (40) produced a similar conclusion. These researchers surveyed 46 female wheelchair basketball players regarding shoulder pain and found that only 14% had experienced shoulder pain prior to wheelchair use, whereas 72% experienced shoulder pain since wheelchair use. One third (1/3) of the subjects had disabilities that required wheelchairs for playing sports, but not necessarily for mobility or for performing activities of daily living. That the non-wheelchair dependent subjects also experienced shoulder pain seems to support Salisbury et al.’s (66) opinion that factors other than wheelchair propulsion and transfers contribute to shoulder pain.

2.7 SUMMARY OF SHOULDER PAIN AND PATHOLOGY IN WHEELCHAIR USERS

The initial spinal cord injury greatly limits an individual’s independence but any secondary complications, such as shoulder pain, that cause further functional limitations could cause a marked decrease or even a total loss in remaining functional independence (44, 62). Shoulder pain has detrimental effects on the lives of manual wheelchair users, whether young, old, sedentary or athletic (62).

From this review of the literature on shoulder pain in wheelchair users, it is clear that the majority of wheelchair users experience shoulder pain that negatively impacts their quality of life. Shoulder pain
is, however, merely a symptom. Research on the etiology of shoulder pain has focused on pathology diagnosis and has yet to form a link between wheelchair biomechanics and shoulder pathology. A longitudinal study by Boninger and colleagues (47) that examined clinical magnetic resonance imaging findings in relation to forces applied to the wheelchair pushrim was the first to report an association between shoulder injury and wheelchair propulsion characteristics. Though difficult to prove causation, it is important that research move in this direction if we hope to mitigate or even prevent shoulder injuries and the associated pain in future wheelchair users.

The next sections provide a review of the literature regarding bone adaptation and bone imaging, followed by cartilage adaptation and cartilage imaging.

2.8 BONE ADAPTATION

2.8.1 Types of Bone

On a macroscopic level there are two main types of bone: cortical (compact) bone and trabecular (cancellous) bone. Cortical bone forms a dense outer shell along the shaft of long bones, while trabecular bone is porous and located within the extremities of long bones (Figure 2-7A). Subchondral bone is a specialized form of cortical bone and consists of a dense bone plate underlying the articular cartilage at joint surfaces (Figure 2-7B). The following sections summarize the ways in which these types of bone develop and adapt to loading.

![Figure 2-7 – Characteristics of Bone: A) Long bones [modified from (71)]; B) Subchondral bone [modified from (72)].](image-url)
2.8.2 Bone Development

Long bones of the appendicular skeleton, such as the humerus, develop by endochondral ossification. In this process, the cartilaginous endoskeleton of the fetus is transformed into bone (Figure 2-8). Growth is observable both in length and in diameter. Lengthwise, the growth front stops before reaching the end of the cartilage bud, leaving a layer of cartilage over the articulating end of the bone (Figure 2-9). The dense bone plate underlying the articular cartilage is the subchondral bone. Once the growth plate fuses longitudinal growth ceases, however bone mass and density can still increase in a process known as consolidation.

![Figure 2-8 - Endochondral ossification (modified from (73)).](image)

2.8.2.1 Ossification of the Glenoid Cavity

The glenoid cavity of the scapula consists of subchondral bone. At birth, the main body of the scapula resembles adult morphology and has ossified, however, the glenoid cavity remains cartilaginous (74). The subcoracoid centre, which is responsible for the ossification of the superior third of the glenoid, appears between 8 and 10 years of age. Fusion of its epiphyseal surfaces begins around 14 to 15 years of age and is complete by 16 to 17 years of age in both males and females. The secondary ossification centre for the inferior two thirds of the glenoid appears around 14 or 15 years of age and begins to fuse with the subcoracoid centre. Fusion of the articular surface of the glenoid cavity is generally complete by 17 or 18 years of age (74).
2.8.2.2 Ossification of the Humeral Head

The shaft of the humerus is visible at birth and the secondary ossification centre for the head (proximal epiphysis) appears 2 to 6 months later. Ossification centres also appear for the greater and lesser tuberosities. Between 2 and 6 years of age, the separate ossification centres for the head and the greater and lesser tuberosities fuse to form a compound proximal epiphysis. By puberty, the articular surface of the humeral head is formed. The compound proximal epiphysis eventually fuses with the shaft, once lengthwise growth has ceased. This occurs between the ages of 13 and 17 years in females and between 16 and 20 years in males (74, 75).

2.8.3 Bone Modelling and Remodelling

Throughout skeletal development bone is modelled and remodelled, owing to a delicate balance between bone formation and bone resorption (74). Bone adaptation, via modelling and remodelling, allows structural optimization so that a minimum of bone tissue provides maximal whole-bone strength. Bone modelling refers to original bone formation, whereas bone remodelling refers to changes in existing bone. An important distinction between bone modelling and remodelling is that resorption necessarily precedes bone apposition in remodelling, but not in modelling. Bone modelling not only allows a bone to grow in length and in diameter, but also to adapt its geometry and composition in response to the dynamic stresses and strains it experiences. Bone remodelling serves to repair micro-damage to the bone matrix and maintain skeletal integrity; it generally does not affect the overall shape or size of the bone (74, 76). In the growing skeleton, bone modelling is the dominant mode, whereas bone remodelling dominates in the mature skeleton (74, 77).

Figure 2-9 - Characteristics of a synovial joint; note the layer of hyaline cartilage over the bone ends [reproduced from (38) with permission from Lippincott Williams & Wilkins].
2.8.4 The Effect of Mechanical Loading on Bone

Throughout bone modelling and remodelling the processes of bone resorption (by osteoclasts) and bone apposition (by osteoblasts) are closely coupled. Changes in mechanical loading, such as increased or decreased physical activity, alter the level and distribution of the stresses and strains experienced by the bone cells (78, 79). Although the exact mechanosensing and cell-signalling pathways remain unclear, osteocytes are thought to act as mechanical sensors capable of detecting changes in stress and strain (80). These changes in stress and strain are believed to initiate an osteogenic response, wherein osteocytes recruit osteoclasts and osteoblasts. Under increased loading conditions, bone is accrued faster than it is resorbed, resulting in a net gain of bone mass or density. Conversely, under decreased loading conditions, bone is resorbed faster than it is accrued, resulting in a net loss of bone mass or density. Immature bone is more responsive to changes in mechanical loading than mature bone (74, 81-84) and is most adaptive during the adolescent growth spurt (84). Cortical bone has been shown to be more responsive to changes in cyclic strains prior to skeletal maturity (82, 85).

2.8.4.1 Rules that Govern Bone Adaptation

The basic concepts of bone adaptation proposed by Wilhelm Roux and Julius Wolff more than a century ago are now widely accepted. The translation of Wolff’s general theory of bone adaptation is as follows: “Every change in the […] function of a bone […] is followed by certain definite changes in […] internal structure and external conformation in accordance with mathematical laws.” (83) Although proposed only as a hypothesis, and first by Roux, this theory on bone adaptation has become known as Wolff’s law. This century, Friedrich Pauwels, Dennis Carter (22, 82, 86, 87), Harold Frost (79, 81, 88), Lance Lanyon (78) and Charles Turner (89, 90), among others, have made significant contributions to our knowledge of how bone responds to mechanical loading. Turner (89) summarized what is known about the effect of mechanical load on bone, by proposing three rules that govern bone adaptation: 1) Dynamic loading, not static loading, drives bone adaptation; 2) An adaptive response is triggered by a short duration of mechanical loading. Extending the duration of the loading has diminishing returns on further bone adaptation; 3) Abnormal loading drives bone adaptation. Bone cells become accustomed to and therefore less responsive to routine loading patterns. In contrast to Turner’s third rule, Bertram and Swartz (83) suggested that although bone might respond to a change in loading pattern, the stimulus is related to chronic loading, citing several studies of athletes where bone changes were only detected in long-term players. A possible explanation for this finding is that repetitive loading from physical activity can cause an accumulation
of microscopic damage, which serves as a stimulus for bone adaptation, potentially resulting in hypertrophy (79, 82).

Bertram and Swartz (83) caution of the modern interpretation and over-generalization of Wolff’s “law”; although created based on observations of trabecular bone adaptation, it commonly gets applied to cortical bone. Carter et al. (87) agree that when examining the effect of mechanical loading on bone development, it is important to make the distinction between cortical bone of the diaphysis, formed via direct apposition, and trabecular bone of the epiphysis, formed via endochondral ossification (Figure 2-8). In response to increased or decreased mechanical loading, local trabecular bone density will increase or decrease accordingly and local trabecular orientation may change. In contrast, cortical bone will undergo a change in geometry, observable as a change in thickness or cross-sectional area. Trabecular bone is accrued or resorbed at the level of the individual trabeculae, whereas cortical bone is accrued or resorbed at the endosteal and/or periosteal surfaces of the diaphysis (Figure 2-7A) (87). In addition, cortical bone can also be internally modified by remodelling (i.e. resorption and apposition of intracortical bone). In addition to the differences in location of bone metabolism, cortical and trabecular bone have significantly different rates of bone metabolism (80, 91). In adults, only 2-5% of cortical bone is reported to be renewed each year (76); in contrast, 25% of trabecular bone is renewed each year (80). For trabecular bone of growing joints, the stress distributions created by mechanical loading have been seen to accelerate or retard the ossification process and cartilage growth, and are of fundamental importance in determining the thickness of the articular cartilage covering the joint surface at maturity (87) (Figure 2-9).

Although it is evident that growing bone is governed by mechanical stimuli (86, 87, 92, 93), the cellular mechanisms responsible for bone adaptation remain unclear. It has been suggested that there are potentially different mechanobiological mechanisms responsible for bone resorption due to decreased loading conditions, and bone apposition due to increased loading conditions (79). Bone’s cellular response to mechanical loading appears to be influenced by strain magnitude, rate, type (e.g. compression, tension, or shear), distribution, duration, number of loading cycles, and fluid flow (78, 89, 94), however no single loading parameter has been shown to predict bone adaptation under all conditions.
2.8.4.2 Stress and Strain Magnitude

The magnitude of stress and strain appears to be the most influential loading parameter and has been shown to have a greater effect on bone mass than the number of loading cycles or the strain rate (78, 91, 95). The effect of load magnitude has been observed as changes to trabecular (76) and cortical (78) bone density. Frost proposed an explanation for the effect of load magnitude on bone density in his Mechanostat principle, which suggests that there are mechanical loading thresholds that determine the sensitivity of bone cells to external loading, and that these thresholds are regulated by hormones (81, 88). According to Frost’s Mechanostat principle, bone is accrued when external loads exceed the modelling threshold, and bone is resorbed when external loads are below the remodelling threshold. Intense physical activity can cause external loading to exceed bone’s upper (modelling) threshold, while disuse or immobilization of a limb can cause external loading to fall below bone’s lower (remodelling) threshold. Frost observed precisely this in children wheelchair users with complete paralysis of the lower-limbs: their humeri were “stronger” than their femora; Frost noted that the exact opposite is seen in able-bodied children (79).

2.8.4.3 Load Distribution and Type of Load

Another loading parameter known to influence bone adaptation is the distribution of the load. As stated by Turner (89) in his third rule, bone is more responsive to abnormal strains of non-uniform distribution than to everyday loading patterns. Regarding loading direction, principal tensile and compressive strains are generally regarded as the most important for bone adaptation (89). Finite element models of synovial joints showed that enchondral ossification was accelerated by cyclic shear stresses and decelerated by hydrostatic compression (22), however more recent studies have suggested that hydrostatic stress gradients generated by dynamic strains trigger bone adaptation (89).

2.8.4.4 Fluid Flow

Fluid flow within bone is also believed to influence adaptation. Mechanical loading has been shown to induce fluid flow in the lacuno-canalicular network that exists between the osteocytes. This fluid flow creates shear stress, which is thought to be sensed by the osteocytes. The osteocytes are thought to transform this mechanical stimulus into a cellular signal by producing signalling molecules to regulate the activity of the osteoblasts and osteoclasts (94).
2.8.5 Experimental Studies of Bone Adaptation to Increased Loading

Bone adaptation is a large research field that includes several types of bone (e.g. cortical, trabecular, and subchondral) at various sites (e.g. diaphysis, epiphysis, and synovial joints), across various stages of development (e.g. gestation, development, and maturity) and under different loading conditions (e.g. increased or decreased loading). Of greatest relevance to the current research are the studies that focused on the effect of increased loading on immature and/or mature trabecular and subchondral bone at synovial joints.

In a porcine model, Tanck et al. (96) found that in growing bone, trabecular bone density (as measured by bone volume fraction, calculated as the quotient of bone volume and total volume) adapts to external loading early on, whereas trabecular architecture (orientation) does not adapt to the principal loading direction until later during development. Finite element models have been used by several groups (22, 87, 95, 97-99) to explore the functional adaptation of bone in response to mechanical loading. Carter et al. (87) showed an increase in bone density at the femoral head in response to increased cyclic stresses, however, the overall density distribution pattern remained unchanged. Eckstein and colleagues used finite element models to study subchondral bone adaptation in incongruous joints with deeper sockets (e.g. the hip joint) and found that tensile stresses play a dominant role in subchondral bone remodelling (95, 97, 98).

To what degree mature bone can adapt to mechanical loading remains open for debate. Certain authors (82, 83) have highlighted a methodological issue with many of the studies that claimed to have proved Wolff’s law for mature bone: the experimental protocol itself initiated a state of bone repair. The experimental protocols often involved osteotomy, fracture, mechanical insult or other trauma to the bone. These events alone would trigger an adaptive response, regardless of the change in external loading. Bertram and Swartz (83) purport that there is no concrete evidence of the effect of mechanical loading on healthy, mature bone of the appendicular skeleton.

2.8.5.1 Spinal Cord Injured Subjects

A few studies have investigated the potential for bone accrual in the upper limb bones due to increased loading via wheelchair use, however most of these focused exclusively on the forearm bones (i.e. radius and/or ulna) (69, 100-104, 107). The majority of the studies that investigated bone adaptation in the SCI population focused on lower limb bone loss due to immobilization and the associated increase in risk of fractures and osteoporosis (100-108). The distal tibia, the lumbar spine,
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the femoral neck and Ward’s triangle are the sites most commonly studied. Regarding studies of upper limb bones in the SCI population, one of the first was published by Wing and Tredwell in 1983 (69). Using photon beam densitometry these authors found a higher mean areal bone mineral density (aBMD, mg/cm²) in the distal radius of ten paraplegic swing-through crutch-walkers compared to the able-bodied controls. Similarly, Goktepe et al. (101) found significantly higher aBMD of the distal radius in paraplegic wheelchair basketball players compared to sedentary paraplegic subjects. In a similar study, Tsuzuku et al. (106) compared aBMD at various sites in quadriplegic and paraplegic subjects. These investigators found significantly higher aBMD in the upper extremities of the paraplegic subjects and supported this finding with the notion that paraplegics load their upper extremities to a greater degree than quadriplegics because of having greater upper extremity function. Since these results were obtained using a ‘whole body’ setting on the DXA scanner (section 2.9.1), it was not possible to determine which specific regions of the upper extremities increased in bone density. In the literature there is a paucity of three-dimensional quantitative imaging of the glenohumeral joint in the general population as well as in the wheelchair user population. Three-dimensional imaging of the glenohumeral joint in wheelchair users would likely provide insight into bone adaptation due to wheelchair use and potentially also into the cause(s) of shoulder pain. It is possible that the lack of imaging of the glenohumeral joint and the trend towards research of bone resorption in the lower limbs of wheelchair users result from imaging limitations.

2.8.6 Summary

It is well established that bone responds to loading. Bone is most responsive to uncustomary dynamic loads and only a short-duration stimulus is required to trigger an adaptive response. This adaptive response is observable by a change in cortical thickness or cross-sectional area, or by a change in trabecular bone mineral density or trabeculae orientation. It is also well established that immature bone is more responsive to altered loading conditions than mature bone. At the glenohumeral joint, the glenoid cavity is completely ossified around 17 or 18 years of age, while the humeral head is completely ossified between 13 and 17 years for females and between 16 and 20 years for males. It remains unclear which parameters of loading are the most important for bone adaptation. Stress and strain magnitude appear to trigger an adaptive response, however these parameters alone cannot predict or explain bone adaptation under all conditions. Bone adaptation has been studied in animal models, in human models and in finite element models. To date, studies on wheelchair users have primarily focused on the loss of bone density in the lower limbs due to immobilization, as opposed to potential increases in bone density in the upper limbs due to increased loading from wheelchair use. It
remains unclear how glenohumeral joint bone responds to the loads imposed by manual wheelchair use.

2.9 BONE IMAGING

Bone mineral density (BMD) has most often been assessed using one of three modalities: dual energy x-ray absorptiometry, peripheral quantitative computed tomography, or computed tomography. Bone density distribution has been assessed with computed tomography osteoabsorptiometry. Micro computed tomography and micro magnetic resonance imaging are now being used to assess trabecular bone architecture.

2.9.1 Dual Energy X-ray Absorptiometry

To date, dual energy x-ray absorptiometry (DEXA or DXA) has been the modality most widely used for quantifying bone mineral density (109). While it delivers low radiation exposure, is cost-effective, widely available, and good for predicting fracture risk, DXA can only provide a two-dimensional (2D) measure of bone mineral content (mg), with no information regarding the spatial distribution of the bone mass or discrimination between cortical and trabecular bone (Figure 2-10). DXA results are generally reported as areal bone mineral density (aBMD, mg/cm²), which is not a true density but calculated as the quotient of the measured bone mineral content (mg) and the 2D area scanned (cm²). DXA results are greatly influenced by bone size, such that aBMD values will be higher for a larger individual than a smaller one, even if in reality these two individuals have the same bone mineral density. DXA has been used in several studies to assess the aBMD of the proximal humerus (110-114).

Figure 2-10 – Dual-Energy X-ray Absorptiometry (DXA): A) Scanner (modified from (115)); B) DXA scan of left hip.
2.9.2 Peripheral Quantitative Computed Tomography

Peripheral quantitative computed tomography (pQCT) has been used in more recent studies, since it is three-dimensional (3D) and able to quantify volumetric bone mineral density (vBMD) (mg/cm³). Because pQCT is a tomographic modality, it is possible to distinguish between cortical and trabecular bone on the cross-sectional pQCT images acquired (Figure 2-11B). The major limitation of pQCT is however, as its name suggests, that it can only be used to image the peripheral (appendicular) skeleton (Figure 2-11A). Due to geometrical constraints of the scanner, it is not possible to acquire a pQCT scan of the glenohumeral joint in vivo, however pQCT has been used to assess vBMD of the glenoid cavity (27) and of the humeral head (26, 116) in cadaveric specimens.

![Figure 2-11 – Peripheral quantitative computed tomography (pQCT): A) Scanner. [reproduced from (117)] B) pQCT scan of the lower leg (tibia and fibula).](image)

2.9.3 Quantitative Computed Tomography

Using computed tomography (CT) imaging (Figure 2-12A) and the associated quantitative CT analysis technique (qCT), it is possible to quantitatively measure volumetric bone mineral density (vBMD, mg/cm³) at any skeletal site. In the quantitative CT (qCT) method a bone density reference phantom is scanned with the patient (Figure 2-12B) and allows for conversion from CT intensity to an equivalent bone mineral density. The voxel intensity in a CT scan is measured in Hounsfield units (HU) and quantifies the radiodensity of the tissue. Approximate values for common tissues are -1000 HU for air, 0 HU for water, 40 HU for muscle, 100-300 HU for trabecular bone and 1000+ HU for cortical bone. The main advantages of CT scanning is that it is fast (generally less than a minute) and allows for a 3D assessment of cortical and trabecular bone (Figure 2-12B, C). The disadvantages of CT scanning are the relatively high radiation dose (compared to DXA and pQCT), high cost, and lengthy time required for qCT analysis.
One of the first qCT studies, published in 1976, investigated bone mineralization in the radius and the ulna (118). With a scanning time of five minutes for a single slice, the images acquired were likely to contain significant motion artefacts. Over the past 40 years CT scanning technology has improved substantially and current imaging times are generally less than 10 seconds for the entire region of interest (e.g. multiple slices across a joint). Since Ruegsegger et al.’s original study of the radius and the ulna, the development of qCT for assessing bone mineral density has primarily focussed on trabecular bone of the lumbar spine (119-121) and of the proximal femur (120-122). As a result, most bone density reference phantoms only include materials that span the trabecular bone density range. Designing and manufacturing an accurate and reliable CT bone density reference phantom is quite complex (123) and has, therefore, been the focus of several studies. These studies examined how the choice of reference materials (124-126), overall geometry of the phantom (124), and scanner parameters (124, 125) affected the bone density results. Two studies (127, 128) used CT to assess bone mineralization of the glenoid cavity, but did not include a bone density reference phantom in their scans. Consequently, the results were expressed as CT intensity (in Hounsfield units) and only relative comparisons could be made between subjects. Other studies employed qCT to examine the relationships between bone density and mechanical properties of bone (121, 129-131).

2.9.4 Computed Tomography Osteoabsorptiometry

Computed tomography osteoabsorptiometry (CT-OAM) is a method of depicting subchondral bone mineralization patterns across the joint surface, based on a CT scan (28, 72, 133). CT-OAM allows for a non-invasive, in vivo assessment of the bone density distribution (Figure 2-13). This technique has been applied at numerous joint surfaces, including the glenoid cavity (28-31, 134), the coracoid process of the scapula (135), the inferior acromion (135, 136), the wrist (137), the hip (28) and the
patellofemoral joint (28). It is widely believed that bone mineralization patterns provide insight into the loading history of the joint.

![Figure 2-13 - CT Osteoabsorptiometry of the glenoid cavity [modified from (30)]](image)

2.9.5 Micro Computed Tomography and Micro Magnetic Resonance Imaging

Micro CT (µCT) (Figure 2-14A) and micro MRI (µMRI) have recently been used to study trabecular bone architecture (Figure 2-14B) (103). Both of these modalities can achieve a very high spatial resolution (up to 10µm), allowing for accurate morphological assessments of individual trabeculae (e.g. number, connectivity, and orientation). These modalities were previously limited to small sections of excised bone, however they can now be used with larger bones and even for in vivo imaging of the appendicular skeleton (76).

![Figure 2-14 - Micro CT: A) Scanner [reproduced from (138)]; B) micro CT scan showing trabecular bone architecture [modified from (139)]](image)
2.9.6 Summary

Modern imaging modalities such as DXA, pQCT, CT and µCT are commonly used to image bone. Each modality has its benefits and drawbacks. While DXA has the lowest ionizing radiation dose and cost, it is projection-based and therefore does not allow for separate analyses of cortical and trabecular bone. DXA scans are two-dimensional (2D) and as a result, only areal bone mineral density can be determined. pQCT scans are three-dimensional (3D) making it possible to calculate the volumetric bone mineral density of trabecular and cortical bone separately; however scanning is limited to the peripheral body regions or small cadaveric specimens. CT scans are also three-dimensional and permit the separate evaluation of volumetric bone mineral density of cortical and trabecular bone. The advantage of CT is that scans can be acquired for any region of the body, but the drawback is that a higher dose of ionization radiation is delivered. µCT produces the highest resolution scans of bone, allowing for the evaluation of trabecular bone architecture. The current drawback of µCT is that in vivo imaging is not widely available. Given the advantages and disadvantages listed above, each modality lends itself to a certain type of research study or clinical assessment.

2.10 CARTILAGE ADAPTATION

2.10.1 Articular Cartilage Development

The cartilaginous fetal endoskeleton undergoes endochondral ossification to become the mature bony human skeleton. This process is guided by fetal muscular contractions and movements, and involves several stages (8). The stages include cartilage cell proliferation, maturation, calcification and resorption, followed by bone deposition. The subchondral bone growth front stabilizes before reaching the articulating ends of bones in synovial joints, leaving a layer of cartilage over the articular ends of the bones (8, 9) (Figure 2-9). In humans, cartilage is deemed mature once chondral growth ceases around 18 years of age (140). The biological or environmental factors that prevent the calcification front from ossifying the entire cartilage bud remain unclear (10). The cartilage left on articular bone ends matures into hyaline articular cartilage, which consists of a solid organic (proteoglycan and collagen) matrix and interstitial fluid (predominantly water) (11) (Figure 2-15B). Throughout its depth, cartilage is characterized by three distinct layers: a superficial zone in which the collagen fibrils are oriented tangentially to the surface, a middle zone in which collagen fibrils are transitioning between tangential and radial orientations, and a deep zone in which the collagen fibrils are oriented radially (Figure 2-15A).
In addition to providing nearly frictionless joint surfaces, hyaline articular cartilage also transfers and distributes large forces across the joint to the underlying subchondral bone (11). It is widely believed that load transfer across the joint is accomplished by hydrostatic compression of the interstitial fluid (9, 21, 143, 144). Joint forces are especially large during dynamic activities, however little is known about whether articular cartilage is able to adapt its morphology or composition in response to physiological loading (14, 144). Cartilage, like bone, appears to be more adaptive to increased loading prior to skeletal maturity (145). Frost supports this view and extends it by stating that cartilage modeling cannot occur without growth, therefore cartilage modeling ceases at the same time as chondral growth (~18 years of age) (140).

2.10.2 The Effect of Mechanical Loading on Cartilage

Different types of mechanical loading have been shown to have different effects on cartilage. Intermittent hydrostatic compressive stress is believed to maintain cartilage, while intermittent shear stress is believed to promote ossification and cartilage degeneration (8, 143). In areas of joint contact, the compressive load is primarily transmitted by pressurization of the interstitial fluid, whereas shear and tensile stresses and strains are resisted by the extracellular matrix (collagen network) (9). During development, physiologic joint loading engenders a functional adaptation of the cartilage (8, 9). The biological response of cartilage depends on the magnitude, frequency and duration of the load (14). The loading regimen, which varies over time, generates a range of stresses, strains, fluid flow and pressure throughout the cartilage tissue. This loading regimen forms the loading history of the mature cartilage, which has developed a corresponding location-dependent histomorphology (8). It remains...
unclear, however, how altered loading conditions are sensed by the cartilage cells (chondrocytes) and how functional adaptation ensues.

It appears that cartilage, like other biological tissues, is easier lost by disuse than gained by increased use. Immobilization has been shown to decrease cartilage thickness in humans (12, 13), however conflicting results have been seen for the case of increased physical activity. In response to increased loading some studies have seen an increase in cartilage thickness (14-16) or volume (17, 18) whereas others have not found any change (19-21). To remain within the scope of the current research project, only previous studies of cartilage adaptation to increased loading will be reviewed in the following paragraphs.

2.10.3 Experimental Studies of Cartilage Adaptation to Increased Loading

A group from Finland performed several animal studies (14-16, 146) investigating the effect of running on articular cartilage. In two separate studies of beagle dogs (14, 15), these investigators found that moderate running increased knee cartilage thickness (measured by microspectrophotometry), compared to the control group. These differences were significant in areas of high loading during running, such as the surface of the femur in contact with the patella. Knee cartilage stiffness (14) and glycosaminoglycan (GAG) content (15) (Figure 2-15B) were also greater in the running dogs. In support of the notion that exercise of a healthy joint does not damage cartilage, no macroscopic degenerative changes were observed in either of these studies in the excised joints of the exercised or the controls dogs. The authors concluded that articular cartilage remodels locally in response to physiologic loading, both in terms of quality (increased stiffness and glycosaminoglycan (GAG) content, Figure 2-15) and quantity (increased thickness) (14). In both studies, however, these effects were observed in the immature cartilage of young, growing beagle dogs. It is unclear to what extent these results hold true for mature or aging cartilage.

The effect of lifelong exercise on mature canine articular cartilage was studied by Newton and colleagues (19). In this study, beagle dogs were obtained while skeletally immature but did not begin the exercise protocol until they were skeletally mature according to radiographic and bone density measurements. In addition to using mature dogs, the exercise protocol in this study was 35 times longer (527 weeks or 1.4 years) than in previous studies (15 weeks) (14-16) and included loading to 130% body weight, using weight jackets. In contrast to previous findings for growing canine knee cartilage (14, 15), no differences were found in cartilage thickness or in mechanical properties between the exercising and control dogs (19). In agreement with previous findings, no degenerative
cartilage changes (e.g. fibrillation, erosion, osteophytes) were observed in the excised joints. These authors concluded that regular, lifelong exercise with increased loading does not necessarily cause degenerative joint changes or functional adaptation in mature cartilage.

With technological advances in magnetic resonance (MR) imaging several groups (10, 17, 18, 21) have investigated the adaptive capacity of human articular cartilage. Jones and colleagues performed both cross-sectional (18) and longitudinal (17) studies of the adaptive capacity of knee cartilage in children and found a significant positive association between self-reported physical activity and cartilage volume. Over the course of their longitudinal study (1.6 years) cartilage volume of the medial tibia (but not the patella) increased twice as much in children who were above the median physical activity level (17). These results suggest that developing cartilage adapts to increased loading. Jones et al. did not, however, find significant differences in tibial cartilage thickness, and hypothesized that, as it grows, developing articular cartilage spreads out over the growing subchondral bone area. Their measurements of cartilage thickness were, however, made on sagittal MR scans using callipers and it is possible that this technique was not precise enough to detect small changes over time. It is important that distinctions be made between increased cartilage volume due to increased subchondral bone area (i.e. bone growth) and increased cartilage volume due to increased cartilage thickness (i.e. cartilage development) (10).

Eckstein and colleagues (21, 147) also examined the adaptive capacity of human knee cartilage by comparing quantitative Magnetic Resonance Imaging (qMRI, section 2.11.2) measurements between a group of male and female triathletes and a group of male and female inactive controls. To their surprise, they found no differences in cartilage morphology (i.e. volume and thickness) between the active and inactive groups. The joint surface area was, however, significantly greater in the male athletes, and higher (but not significantly) in the female athletes, compared to the male and female inactive controls. Although these investigators did not explicitly study the effect of loading on developing cartilage, they noted that the subjects recruited for the physically active group had been active throughout their lives, compared to the inactive controls who had never been physically active. These investigators postulated that, during growth, increased mechanical loading of a joint does not increase cartilage thickness, but instead influences the endochondral ossification process, such that a larger epiphyseal (joint) surface is formed (21).

Regarding the lack of change in cartilage thickness, Eckstein et al. (21) suggested that a critical thickness threshold may exist, beyond which cartilage metabolism becomes problematic and load
transmission ineffective. Since cartilage is highly avascular, increasing its thickness beyond a certain threshold might impair the diffusion of nutrients and waste products. It is believed that hydrostatic compression of the interstitial fluid within the proteoglycan-collagen matrix enables the cartilage to transmit large forces across the joint surface (21, 22). As cartilage thickness increases, interstitial fluid displacement increases in the radial direction, which in turns decreases the hydrostatic pressurization and is thought to impair load transmission. Eckstein et al. (21) posit that a functional reduction of the high stresses at the articular surface is better achieved by an increase in joint surface area and compression of cartilage (i.e. compression of the interstitial fluid) than by an increase in cartilage thickness and elastic damping properties.

To our knowledge, a study by Vanwanseele and colleagues is the only study to date to have investigated the functional adaptation of humeral head cartilage in response to increased loading from SCI rehabilitation and wheelchair use (20). These investigators compared humeral head cartilage morphology at 3 and 12 months post-SCI and found no increase in cartilage thickness despite increased mechanical loading of the joint. In fact, maximal humeral head cartilage thickness decreased by 8% over this time period.

Tiderius and colleagues examined the effect of physical activity on cartilage composition at the knee (148). They found greater glycosaminoglycan (GAG) content in the cartilage of elite male runners compared to both moderately active and sedentary adults, and attributed this difference to the adaptive capacity of human cartilage. These authors noted that although the subject groups had similar Body Mass Index (BMI) scores, there were differences with respect to percent body fat, and therefore also with respect to percent body water. The differences in percent body water likely affected the distribution of the MRI contrast agent, resulting in a slight overestimation of the true GAG content in the cartilage of the subjects with a greater percentage of body water (i.e. the elite runners).

Although decreased loading via immobilization has been seen to consistently yield cartilage thinning or atrophy, increased loading conditions have produced a range of results. In a comprehensive review of the effects of exercise on human cartilage, Eckstein and colleagues (10) concluded that the large morphological variability of healthy cartilage between humans is not fully explained by differences in mechanical loading of the joint. These authors highlighted that morphological findings, such as cartilage volume and thickness, represent global measurements and do not, therefore, reflect local adaptive changes that may occur. In contrast to bone and muscle, it appears that mature cartilage
tissue mass does not increase in response to increased mechanical loading. Eckstein and colleagues underscore that although ‘more’ bone or ‘more’ muscle improves the mechanical competence of a joint, ‘more’ cartilage is not known to yield significant improvements (10). These investigators posit that in cartilage, mechanical competence and tissue mass may be uncoupled. Having reviewed studies of genetic influence on cartilage (considered beyond the scope of this literature review) Eckstein and co-workers believe that genetic factors play a more significant role than functional adaptation to external loading in accounting for differences in cartilage between individuals (10).

2.10.4 Summary

The fetal endoskeleton is comprised solely of cartilage and subsequently differentiates into bone via endochondral ossification. A thin layer of cartilage is not ossified and remains on the articular ends of long bones, allowing for nearly frictionless contact between joint surfaces. Articular cartilage transfers large loads to the underlying subchondral bone. It is believed that, in areas of joint contact, compressive loads are primarily transmitted by pressurization of the interstitial fluid, whereas shear and tensile loads are resisted by the extracellular matrix. Cartilage, like other biological tissues, appears to adapt to loading. Several experimental studies have found increased cartilage thickness with increased loading using an immature canine model. Given that these studies were performed on immature beagle dogs, it is unclear to what degree these results hold true for immature, mature, or aging human cartilage. A study of mature beagle dogs failed to find a difference in cartilage thickness between exercise and control dogs, suggesting that mature canine cartilage does not adapt to loading (19). Decreased loading due to immobilization has been shown to result in decreased cartilage thickness in humans, however it is not clear whether cartilage responds to increased loading. The adaptive response of human articular cartilage to loading has recently been studied using magnetic resonance imaging. Study populations varied greatly (i.e. growing children vs. mature adults) and the findings are inconsistent. Some authors have suggested that a critical cartilage thickness exists beyond which cartilage metabolism becomes problematic and load transmission ineffective. These authors have used this concept to explain their findings of a lack of change in cartilage thickness under increased loading conditions. Given that \textit{in vivo} investigations of the functional adaptation of human cartilage are only possible with medical imaging, the most common modalities for cartilage imaging are briefly reviewed in the following sections.
2.11 CARTILAGE IMAGING

2.11.1 Radiography

Historically, in vivo measurements of cartilage thickness have been obtained from plain film radiographs (149). Cartilage thickness can only be indirectly measured from a radiograph by measuring the joint space since cartilage is not radio-opaque and thus does not appear on a radiograph. When joint space is measured from a radiograph it consists of a single point measurement between the subchondral bone on either side of the joint (i.e. measured between bone-cartilage interfaces) and is dependent on the projection angle of the radiograph (150) (Figure 2-16). Cartilage has a complex, 3D structure and therefore cartilage morphology cannot be accurately assessed from a 2D projection, such as a radiograph (144, 151).

![Figure 2-16 - Anterior-posterior radiograph of the tibiofemoral joint, depicting joint space narrowing (JSN) from cartilage thinning [reproduced from (152)]](image)

2.11.2 Quantitative Magnetic Resonance Imaging

Recent advances in MR imaging have made it possible to quantitatively assess cartilage morphology in vivo. One of the greatest benefits of quantitative MR imaging (qMRI) is that it is non-invasive, thereby allowing for a longitudinal study of changes in cartilage morphology (e.g. thickness, volume, surface area) in humans (144). qMRI has primarily been used to quantify cartilage morphology at the knee joint (12, 13, 17, 18, 21, 144, 147, 153-158) (Figure 2-17), however it has been used more recently at other joints including the elbow (151) and the shoulder (20, 32). Determining cartilage morphology with qMRI is superior to measuring the joint space on a radiograph because 3D measurements can be made directly from the cartilage. qMRI analysis is also superior to conventional
histological methods since the MR slices are contiguous (i.e. continuous in the z-direction) with adjacent slices spatially-aligned in the scanning plane (x,y plane). Since spatial relationships between adjacent voxels in MR scans correspond to the true spatial relationships between tissues, MR images allows for accurate measurement of morphological parameters in three-dimensions in vivo (10).

![Figure 2-17 - Quantitative MRI (qMRI) segmentation of cartilage at the patellofemoral joint.](image)

2.11.3 Delayed Gadolinium-Enhanced MRI of Cartilage

Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) is a recent technique that uses MR imaging with a contrast agent to study the composition of the cartilage matrix. Glycosaminoglycan (GAG) molecules are one component of the cartilage matrix that is of interest. GAG molecules are the negatively charged side-chains of the proteoglycans (Figure 2-15B). Although it is not possible to quantify GAG concentrations directly using MR imaging, they can be measured indirectly using a contrast agent. The dGEMRIC method is based on the intravenous injection of a hydrophilic contrast agent (Gadolinium, Gd-DTPA₂) that diffuses into the cartilage and distributes in concentrations inversely proportional to the concentration of GAG molecules. A high GAG concentration in the cartilage will, therefore, result in a low concentration of the contrast agent within the cartilage, yielding a long T1 time in the MR scan. In the resulting dGEMRIC image a colour map is applied to the T1 values to facilitate visualization (Figure 2-18). dGEMRIC has been used to examine the functional adaptation of knee cartilage, by comparing T1 times (as indirect measures of GAG content) between individuals of differing levels of activity (148). Since adaptive or degenerative changes in cartilage likely occur at the biochemical level prior to the morphological level, dGEMRIC may be able to detect such cartilage changes earlier than with qMRI.
2.11.4 Summary

Whereas historically cartilage thickness has been inferred from a radiograph as the joint space between bones, MR imaging allows for direct imaging of cartilage and subsequent assessment of cartilage morphology and composition. qMRI and dGEMRIC are two modern MR-based techniques. qMRI allows for accurate 3D measurement of cartilage morphology (e.g. thickness, volume, and surface area) across the joint surface. The dGEMRIC technique can be used to assess cartilage composition based on the concentration of glycosaminoglycans within the solid cartilage matrix. This technique requires the intravenous injection of a contrast agent, and recent improvements have made 3D dGEMRIC scanning and analysis possible.

2.12 COMBINED ADAPTATION OF BONE AND CARTILAGE

In this review of the literature, very few studies were found that jointly investigated bone and cartilage (16, 23, 159, 160). The majority of these used ex vivo models: the humeroulnar joint (159), the patella (160), and the equine stifle and metacarpophalangeal joints (16). Consequently, these studies could not investigate the combined functional adaptation of bone and cartilage to loading, but instead investigated whether ex vivo subchondral bone properties were correlated to ex vivo cartilage properties. At both the humeroulnar joint and the patella, no correlation was found between the thickness of the subchondral bone plate and the thickness of the overlying cartilage (159, 160). At the highly loaded equine metacarpophalangeal joint, Lewis et al. found that the subchondral bone mineral
density was positively correlated to the tensile stiffness of cartilage (23). These authors support the view that subchondral bone and the overlying articular cartilage respond to mechanical loading in a coordinated manner in order to achieve the overall functional adaptation of the joint. In contrast to these *ex vivo* studies, Oettmeier *et al.* performed an *in vivo* investigation in canine knees and were therefore able to study the combined response of subchondral bone and articular cartilage to long-distance running (16). Similar to their other experimental protocols (14, 15, 146), the protocol in this study also involved young beagle dogs divided into running and control groups. In the running dog group, they found increased thickness of the articular cartilage in all regions of the knee, combined with increased thickness of the subchondral bone plate. These investigators concluded that their “results demonstrate clearly the responsivity and the complexity of the reactions that take place in the two tissues” (16). As emphasized by Oettmeier and colleagues, joint loading and ensuing pathology affect all of the tissues of the joint (e.g. articular cartilage, synovial membrane, and subchondral bone) to some degree, since the joint is an interactively functioning unit (16). To our knowledge, no study has investigated the combined response of subchondral bone and articular cartilage to altered loading conditions *in vivo* in humans.

2.13 SUMMARY

Debilitating shoulder pain is highly prevalent among manual wheelchair users. Central to the present study is the previously reported finding that adulthood-onset wheelchair users reported significantly more shoulder pain than childhood-onset wheelchair users (6). Manual wheelchair users use their upper limbs not only for prehensile and manipulative tasks, but also for mobility and maintaining their independence. As such, shoulder pain among wheelchair users has often been attributed to overuse and repetitive strain injuries. Qualitative imaging of wheelchair users’ shoulders has revealed a wide range of pathologies that affect the bone, cartilage, muscle and other soft tissues of the joint.

The stresses and strains imposed by the activities of daily living have been shown to regulate trabecular and cortical bone mineral density and/or morphology. Given that immature bone adapts to mechanical loading and immature cartilage may also adapt to mechanical loading, we hypothesized that bone and cartilage at the shoulder joint are better able to adapt to mechanical loading in individuals who begin wheeling prior to skeletal maturity compared to those who begin wheeling after skeletal maturity. The potentially time-limited capacity for functional adaptation might possibly explain the differences in reported shoulder pain between childhood-onset and adulthood-onset manual wheelchair users. When investigating the functional adaptation of the glenohumeral joint in wheelchair users, it is ideal to study the combined adaptation of bone and cartilage since both of these
tissues undergo loading at the joint. Moreover, a combined investigation of bone and cartilage adaptation is especially appropriate in joints involving long bones like the humerus, since the bone was formed from an initial cartilage bud via endochondral ossification.
PART A: STUDY DESIGN

3.1 OVERVIEW

This pilot study was designed to quantify bone and cartilage morphology at the glenohumeral joint in long-term manual wheelchair users. More specifically, this study compared bone and cartilage morphology between individuals who began using a manual wheelchair as children (childhood-onset wheelchair users) and individuals who began using a manual wheelchair as adults (adulthood-onset wheelchair users). In order to account for known age-related changes in bone and possible age-related changes in cartilage, an age- and gender-matched able-bodied control was recruited for each wheelchair user subject. In both men and women, bone mineral density is known to increase throughout childhood and adolescence, peak in early-adulthood, plateau, and decrease in late-adulthood (77, 161). Regarding the effect of aging on articular cartilage morphology, there is currently no consensus among researchers (144).

All wheelchair users and able-bodied controls underwent the same study protocol, which involved having a CT scan and a MR scan of their dominant shoulder, and completing three questionnaires. In
addition, all of the wheelchair user subjects underwent a physical examination of their neck and shoulders by a physician. The study population and the study protocol are described in greater detail in the following sections.

3.2 STUDY POPULATION

This study was approved by the Clinical Research Ethics Board at the University of British Columbia, Vancouver, BC (Appendix A). Subject recruitment was conducted by the primary researcher. Adulthood-onset wheelchair users were recruited through the Spinal Cord Injury Research Registry at the GF Strong Rehabilitation Centre (Vancouver, BC). Childhood-onset wheelchair users were recruited through the Orthopaedics department at the BC Children’s Hospital (Vancouver, BC). Able-bodied control subjects were recruited by email and by word-of-mouth. All wheelchair users and able-bodied controls were of legal age (> 18 years) and gave informed, written consent.

All of the wheelchair users and able-bodied controls met the inclusion and exclusion criteria for the study. To be eligible for this study, the wheelchair user subjects had to:

- use a manual wheelchair as their primary means of mobility
- wheel independently
- be at least ten years post-injury
- pass the 3T MR screening (e.g. no orthopaedic hardware)
- pass the CT screening (e.g. not be pregnant)
- be of legal age (>18 years) and able to give informed consent

Potential wheelchair user subjects were excluded if they:

- used a power wheelchair
- had previous shoulder trauma or surgery
- did not pass the 3T MR screening (e.g. had Harrington rods for scoliosis)

Shoulder pain was neither an inclusion nor an exclusion criterion for the wheelchair user subjects.

To be eligible for this study, the control subjects had to:

- be able-bodied
- be the same gender and age (ideally ± 1 year) as the corresponding wheelchair user subject
- pass the 3T MR screening
- pass the CT screening
- be of legal age (> 18 years) and able to give informed consent

Potential control subjects were excluded from this study if they:

- had shoulder pain
- had previous shoulder trauma or surgery
- loaded their shoulders more than ‘normal’ (e.g. physical labourers, weight-lifters, swimmers, and racquet sport players)
All of the wheelchair users and able-bodied controls passed the pre-screening for 3T MR and CT scanning. Due to safety concerns with scanning on a 3T MR magnet, 18 potential wheelchair user subjects were excluded for having Harrington rods for scoliosis, brain shunts, intramedullary pins, implanted pain pumps, or other large implants. One wheelchair user subject was scanned in CT but was excluded from the rest of the study upon discovering during the MR screening that he had a brain shunt. This subject’s CT scan was not analyzed. When the size of an orthopaedic implant was in question, the surgical report was obtained by the researcher and Dr. David Lee, the head radiologist at the UBC hospital, decided whether or not the potential subject could be safely scanned at 3T MRI.

Wheelchair user subjects were placed in the childhood-onset group if they began using a wheelchair at age 16 years or earlier, and in the adulthood-onset group if they began using a wheelchair after 16 years of age. Sixteen years of age was chosen as the upper limit for the childhood-onset group, since it approximates the age by which the glenoid cavity (74) and the humeral head (74, 75) have fully ossified (sections 2.8.2.1 and 2.8.2.2). One subject (CO 2) sustained his spinal cord injury at 16 years of age. This male subject was placed in the childhood-onset group since full fusion of the glenoid cavity and of the humeral head occurs, on average, one or two years later in males than in females. For males, the humeral head is generally fully fused between 16 and 20 years of age, and the glenoid cavity by 17 or 18 years of age.

Five adulthood-onset manual wheelchair users (n = 5) and three childhood-onset manual wheelchair users (n = 3) participated in this study. The five adulthood-onset wheelchair users were of Caucasian decent. Two of the childhood-onset wheelchair users were of Caucasian decent and one (CO 3) was of East-Asian decent. Demographic data are given in Table 3-1. To account for known age-related changes in bone (77, 161) and cartilage (158, 162), an age- and gender-matched able-bodied control subject was recruited for each wheelchair user subject. In seven of eight cases, the control subject was age-matched to within 1.5 years of the age of the corresponding wheelchair user subject. In the eighth case, the control was matched to within 3 years. All able-bodied controls were of Caucasian decent. Demographic data for the able-bodied controls are given in Table 3-2.
## Table 3-1 - Demographic Data for the Manual Wheelchair User Subjects

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Gender (M/F)</th>
<th>Age when scanned (yrs)</th>
<th>Age at Injury (yrs)</th>
<th>Years Wheeling (yrs)</th>
<th>Primary Diagnosis</th>
<th>Level of Lesion</th>
<th>Hand dominance (L/R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO 1</td>
<td>M</td>
<td>26</td>
<td>Birth</td>
<td>21</td>
<td>Meningomyelocele</td>
<td>T10-12</td>
<td>L</td>
</tr>
<tr>
<td>CO 2</td>
<td>M</td>
<td>26</td>
<td>16</td>
<td>10</td>
<td>Traumatic SCI</td>
<td>C5 incomplete</td>
<td>R</td>
</tr>
<tr>
<td>CO 3</td>
<td>F</td>
<td>23</td>
<td>6</td>
<td>17</td>
<td>Traumatic SCI</td>
<td>T9 complete</td>
<td>R</td>
</tr>
<tr>
<td>AO 1</td>
<td>M</td>
<td>49</td>
<td>19</td>
<td>30</td>
<td>Traumatic SCI</td>
<td>C5-6 complete</td>
<td>R</td>
</tr>
<tr>
<td>AO 2</td>
<td>F</td>
<td>42</td>
<td>19</td>
<td>23</td>
<td>Traumatic SCI</td>
<td>T10 complete</td>
<td>R</td>
</tr>
<tr>
<td>AO 3</td>
<td>M</td>
<td>49</td>
<td>23</td>
<td>26</td>
<td>Traumatic SCI</td>
<td>T7-8 complete</td>
<td>R</td>
</tr>
<tr>
<td>AO 4</td>
<td>M</td>
<td>73</td>
<td>43</td>
<td>30</td>
<td>Lower-limb Amputee (T10)</td>
<td>T10 complete</td>
<td>R</td>
</tr>
<tr>
<td>AO 5</td>
<td>F</td>
<td>48</td>
<td>37</td>
<td>11</td>
<td>Traumatic SCI</td>
<td>C7-T1 incomplete</td>
<td>R</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user

## Table 3-2 - Demographic Data for the Able-Bodied Controls

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Gender (M/F)</th>
<th>Age when scanned (yrs)</th>
<th>Age difference from WC user (yrs)</th>
<th>Hand dominance (L/R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO 1 Control</td>
<td>M</td>
<td>26</td>
<td>- 0.33</td>
<td>R</td>
</tr>
<tr>
<td>CO 2 Control</td>
<td>M</td>
<td>27</td>
<td>+ 0.83</td>
<td>R</td>
</tr>
<tr>
<td>CO 3 Control</td>
<td>F</td>
<td>23</td>
<td>+ 0.33</td>
<td>R</td>
</tr>
<tr>
<td>AO 1 Control</td>
<td>M</td>
<td>52</td>
<td>+ 3.00</td>
<td>R</td>
</tr>
<tr>
<td>AO 2 Control</td>
<td>F</td>
<td>42</td>
<td>- 0.92</td>
<td>R</td>
</tr>
<tr>
<td>AO 3 Control</td>
<td>M</td>
<td>50</td>
<td>+ 0.50</td>
<td>R</td>
</tr>
<tr>
<td>AO 4 Control</td>
<td>M</td>
<td>73</td>
<td>- 0.33</td>
<td>R</td>
</tr>
<tr>
<td>AO 5 Control</td>
<td>F</td>
<td>49</td>
<td>+ 1.42</td>
<td>R</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user, WC = wheelchair
3.3 SCANNING SUBJECTS

For every wheelchair user subject CT and MR scans were acquired on a single day. For the able-bodied controls, six had their CT and MR scans on the same day, while two had their scans on different days but within 3 weeks of each other. Experienced radiologists reviewed the CT scans of each wheelchair user and able-bodied control and reported any pathology or anatomical abnormality.

3.4 PHYSICAL EXAMINATION

All wheelchair user subjects underwent a comprehensive shoulder and neck exam by Dr. Jeffrey Pike, a 3rd year Orthopaedic resident with the Vancouver Coastal Health Authority, Vancouver, BC. Dr. Pike gathered information regarding the primary spinal cord injury diagnosis, as well as neck and shoulder pain. In the physical examination the neck, spine, and seated posture were assessed. The glenohumeral, acromioclavicular and sternoclavicular joints were also included in the examination. Distal motor and distal sensory tests were conducted. Shoulder range of motion was assessed using the Apley scratch test (Figure 3-1A) and a total active elevation test (i.e. measurement of the ability to actively raise one’s arms). Muscular strength was assessed for the biceps brachii and the triceps brachii. Strength and function were assessed for the infraspinatus and teres minor muscles (Figure 3-1D), and for the supraspinatus muscle (Figure 3-1E). Impingement of the rotator cuff tendons was assessed with the Neer test (Figure 3-1B), while subacromial impingement and rotator cuff tendonitis were assessed with the Hawkins test (Figure 3-1C). The sulcus test (Figure 3-1F) was performed to check for glenohumeral joint instability in the inferior direction and the anterior-posterior glide test examined glenohumeral joint laxity in the anterior-posterior direction. Other standard shoulder tests performed included the painful arc test and a test for scapular winging.
3.5 QUESTIONNAIRES

All wheelchair users and able-bodied controls completed three questionnaires to quantify shoulder pain, physical activity and dietary calcium intake. The specific questionnaires, their accuracy and reliability, and their scoring are detailed in the following sections.

3.5.1 Pain Questionnaires

Different questionnaires were used to assess shoulder pain and its functional interference in the wheelchair users and the able-bodied controls since these groups perform different activities of daily living. The wheelchair user subjects also completed a questionnaire regarding general body pain and another regarding wheelchair use.

3.5.1.1 Wheelchair User’s Shoulder Pain Index (WUSPI)

Shoulder pain was quantified in the wheelchair users with the Wheelchair User’s Shoulder Pain Index (WUSPI) questionnaire. This 15-item questionnaire (Appendix B) was developed to measure shoulder pain among wheelchair users, as well as the degree to which shoulder pain interfered with function over the previous week (41). Responses for each WUSPI item range from 0 to 10, with higher numbers corresponding to greater pain interference. The WUSPI questionnaire is scored by
adding the value of each item, to a maximum score of 150. The WUSPI has been validated as a tool for assessing the degree to which shoulder pain interferes with function in wheelchair users and has demonstrated high test-retest reliability (ICC = 0.99) (67) and high internal consistency (Cronbach’s $\alpha = 0.97$) (41).

3.5.1.2 Brief Pain Inventory

General body pain was assessed in the wheelchair user subjects with the modified Brief Pain Inventory. Although the Brief Pain Inventory was originally developed and validated by the World Health Organization (WHO) to assess pain levels in cancer patients (163), it has since been modified and validated (for accuracy and repeatability) for use with individuals with a spinal cord injury (64). The Brief Pain Inventory measures not only pain intensity, but also the degree to which pain interfered with activities of daily living over the previous 24 hours. It is a general pain questionnaire, not limited to any particular region of the body. The modified version of the Brief Pain Inventory includes additional questions that assess how pain interferes with function in individuals with physical disabilities. The 15-item short form of the modified Brief Pain Inventory questionnaire was used in this study (Appendix B), and only the seven items that specifically assess the degree to which pain interfered with function were included in the analysis. Responses for each item range from 0 to 10, with higher numbers corresponding to greater pain interference. Scoring is done by computing the mean score of all items. The modified Brief Pain Inventory yielded high internal consistency (Cronbach’s $\alpha > 0.90$) and scores were significantly related to the average pain intensity experienced by subjects over the previous week, making it a valid and reliable measure of pain in physically-disabled individuals (64).

3.5.1.3 General Lifestyle Questionnaire

The wheelchair user subjects also completed the General Lifestyle Questionnaire (Appendix B) to provide information regarding their wheeling habits (e.g. what distance the individual wheels independently each day, if he/she asks for help wheeling uphill). This information was used to supplement the shoulder pain data from the WUSPI questionnaire since the WUSPI measures pain interference during functional tasks but not how often a given task is performed.
3.5.1.4 Disabilities of the Arm, Shoulder and Hand Questionnaire

In order to confirm the pain-free state of their shoulders, the control subjects completed the condensed version of the Disabilities of the Arm, Shoulder and Hand (quick DASH) questionnaire (Appendix B). Shoulder pain was an exclusion criterion for the control subjects therefore all control subjects accepted into this study had reported having pain-free, healthy shoulders. The DASH questionnaire was developed to measure the effect of upper-extremity musculoskeletal conditions on physical function (164). The DASH questionnaire is a valid and reliable outcome measure for patients with upper extremity conditions (165, 166). The condensed version of the DASH, named quick DASH, has 11 items. Responses for each item range from 1 to 5, with higher numbers corresponding to greater pain interference. Scoring is done by adding up the circled value for each question, dividing by the number of questions, subtracting 1 and then multiplying by 25 to get the final DASH score out of a possible 100.

3.5.2 Physical Activity Questionnaires

To assess differences in physical activity levels between subjects, all wheelchair users and able-bodied controls completed a relevant physical activity questionnaire. Increased loading from physical activity is known to trigger an adaptive response in bone (167) and may also trigger an adaptive response in cartilage (17, 18) thus it was desirable to have a general idea of each subject’s level of physical activity. Different physical activity questionnaires were given to the wheelchair users and to the able-bodied controls, since standard physical activities, such as walking and running, are not performed by wheelchair users. Conversely, physical activities common among wheelchair users, such as wheelchair propulsion and arm-cranking, are not applicable to the able-bodied population.

3.5.2.1 Physical Activity Scale for Individuals with Physical Disabilities

Physical activity level was assessed in the wheelchair user subjects with the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD). The PASIPD is a validated 13-item questionnaire designed to determine to what extent (i.e. hours/day) the individual participated in recreational, household, and occupational activities over the previous seven days (168). Moderate internal consistency was reported (Cronbach’s $\alpha$ ranged from 0.37-0.65) (168). For each question (pertaining to a specific activity) there are five options (a-e, pertaining to the duration of the activity). Scoring the PASIPD is somewhat complex since each question (i.e. activity) has a numerical metabolic equivalent (MET) value (e.g. 1.5 MET for light housework compared to 8.0 MET for strenuous sports and recreational activities), and each option (a-e) for that question has a weighting
factor (ranging from 0 if the activity is never performed to 7.71 if the activity is frequently performed). The total score is calculated by multiplying the metabolic equivalent value by the weighting factor, for each question, and then summing the values of all 13 questions. The total score is expressed in MET-minutes per day.

3.5.2.2 International Physical Activity Questionnaire

Physical activity level was assessed in the able-bodied controls using the long-form of the International Physical Activity Questionnaire (IPAQ). The IPAQ was developed as an outcome measure for monitoring physical activity and inactivity internationally (169). The IPAQ is a comprehensive, 7-day recall questionnaire which assesses physical activity in four domains: recreational, domestic, work-related, and transportation-related. A 12-country study (which included Canada) showed that the IPAQ can be used to collect reliable and valid physical activity data across countries in individuals 18-69 years of age (169). The IPAQ score can be reported as a continuous measure by determining the standard metabolic equivalent (MET) and presenting it as median MET-minutes per day (i.e. MET level x minutes of activity x events per week / 7). The specific MET values associated with low intensity, moderate intensity, and vigorous physical activity across the four domains are provided by the developers of the IPAQ (170).

3.5.3 Food Frequency Questionnaire

Dietary calcium intake was assessed in all wheelchair user subjects and able-bodied controls using a general food frequency questionnaire (FFQ). Food frequency questionnaires have been shown to be useful tools in discriminating between subjects with high and low dietary calcium intake (171), as was desired in the present study since there is presently no consensus among researchers as to whether dietary calcium intake affects bone mineral density. The FFQ questionnaire used in this study lists 20 items, ranging from dairy products to green vegetables (Appendix B). For each item, the respondent indicates how often he/she consumes a specified quantity of the food (number of times daily, weekly, or monthly). This particular food frequency questionnaire was originally developed and validated for use with adolescents (172), however similar food frequency questionnaires have been validated for assessment of dietary calcium intake in adults (173). Scoring of the food frequency questionnaire involved converting the daily and weekly responses to a monthly equivalent and summing these with the reported monthly values. The monthly consumption value for each food item was multiplied by its respective calcium equivalent (mg), specified by the creators of the FFQ.
These values were summed to determine the total monthly calcium intake, and the result was divided by 30 to yield the respondent’s mean daily dietary calcium intake (mg/day).

PART B: BONE IMAGING METHODS

Glenohumeral bone was imaged with Computed Tomography (CT). The CT scanning protocol used was developed specifically for this study to produce high-resolution, 3D images suitable for quantitative analysis. The quantitative CT (qCT) analysis method was implemented and customized to the study of glenohumeral bone. The CT Osteoabsorptiometry (CT-OAM) method was implemented and customized for use at the glenohumeral joint and was subsequently applied to assess bone density distribution.

3.6 IMAGING BONE WITH COMPUTED TOMOGRAPHY

In this pilot study, CT scanning was used to acquire images for quantitative analysis of cortical, trabecular and subchondral bone at the glenohumeral joint. Computed Tomography (CT) is superior to other modalities commonly used to image bone, such as dual-energy x-ray absorptiometry (DEXA or DXA) and radiography, since CT is a tomographic method (i.e. generates image “slices” through the body) and does not superimpose anatomical structures as do projection-based modalities like DXA and radiography. In addition, CT scans are three-dimensional, making it possible to differentiate between cortical and trabecular bone. This is important when investigating the functional adaptation of bone, since cortical and trabecular bone are reported to have dissociated bone mineral density (BMD) losses due to immobilization in SCI subjects (100).

In this study, several morphological parameters of bone were assessed from the CT scans, including volumetric bone mineral density (vBMD) and cross-sectional area. For the trabecular bone, the density reported is an apparent vBMD since it includes both mineralized bone as well as bone marrow spaces between the trabeculae. It is important to note that the vBMD values reported are not the physical density of the bone but rather an equivalent density, based on the known materials in the bone density reference phantom (section 3.8.2). The following sections describe the CT scanning of bone, as well as the analysis methods used to quantify bone morphology.
3.7 DEVELOPMENT OF A CT BONE IMAGING PROTOCOL

3.7.1 Pilot Scanning

Two pilot scanning sessions were needed to develop a CT protocol that would produce images of glenohumeral bone suitable for quantitative analysis. Two healthy volunteers participated in the pilot scanning (1 male of 47 years, 1 female of 29 years).

3.7.2 Final Scanning Protocol

All CT scanning (pilot and subject scanning) was performed by a single technician at the Canada Diagnostic Centres (Vancouver, BC) on a Toshiba Aquilion 64 slice helical scanner (Figure 3-2A). The CT technician and I developed the CT scan protocol. The scan parameters of the final protocol are given in Table 3-3. The raw data were not interpolated. All CT datasets were blinded to the researcher at the time of image acquisition by using a unique study identifier (e.g. DOER-MWU-P01) instead of the subject’s name.

Figure 3-2 – CT scanner: A) Toshiba Aquilion 64 CT scanner [reproduced from (132)]; B) CT scan of a right shoulder and a bone density reference phantom.
Table 3-3- CT Scan Parameters – Final Scanning Protocol

<table>
<thead>
<tr>
<th>Imaging Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scanner</td>
<td>Toshiba Aquilion 64</td>
</tr>
<tr>
<td>Scanning Features</td>
<td>Boost3D, Sure Exposure</td>
</tr>
<tr>
<td>Scanning Plane</td>
<td>Axial</td>
</tr>
<tr>
<td>Scanning Energy</td>
<td>135 kVp</td>
</tr>
<tr>
<td>Tube Current</td>
<td>440 mA</td>
</tr>
<tr>
<td>Table Height</td>
<td>80 mm</td>
</tr>
<tr>
<td>In-plane Resolution</td>
<td>0.47 mm x 0.47 mm</td>
</tr>
<tr>
<td>Slice Thickness</td>
<td>0.5 mm</td>
</tr>
<tr>
<td>Matrix Size</td>
<td>512 x 512</td>
</tr>
<tr>
<td>Field of View</td>
<td>240 mm</td>
</tr>
<tr>
<td>Scan Duration</td>
<td>2.8 s</td>
</tr>
<tr>
<td>Number of Slices Acquired</td>
<td>~160 (depending on subject size)</td>
</tr>
</tbody>
</table>

For patient safety, the Aquilion 64 scanner’s Sure Exposure function was enabled during all scans in order to minimize the radiation dose. This function adapts the tube current during scanning based on the anatomy of the patient, as detected in the scout scan (174). For all scanning angles, the thickness and the density of the tissues traversed by the x-ray beam are taken into account when determining the optimal tube current, given the predefined spatial resolution. This function is very useful for shoulder scans, where the attenuation of the x-ray beam is greater in the medial-lateral direction than in the anterior-posterior direction, due to asymmetrical bony geometry (Figure 3-3). This function also benefits individuals with a smaller skeleton since it adjusts the tube current to ensure minimal radiation exposure.
The CT scanner’s Boost3D function was enabled during all scans. The Boost3D function is a three-dimensional adaptive filter that is applied to the raw data in order to reduce image noise and streak artefact (176). Streak artefact appears as high intensity lines across the scan (Figure 3-4). If the streaks are roughly the same intensity and in the same location as the tissue of interest, automated segmentation is not possible since the streaks are mistaken for the tissue of interest. In CT scans of non-cylindrical regions of the body, such as the shoulders, streak artefact is quite common along the direction of greatest attenuation (Figure 3-3).
For every individual scanned, two scout scans (1 coronal, 1 axial) were necessary to ensure that the dominant glenohumeral joint and the bone density reference phantom were both completely within the field of view. The coronal scout scan allowed the technician to set the scanning region for the main scan, which began at the acromion and extended inferiorly to approximately 2 cm distal to the base of the humeral head (Figure 3-5). With a slice thickness of 0.5 mm, this equated to approximately 160 slices, depending on the size of the individual. The radiation dose associated with the two scout scans and the main scan is approximately 2.5 mSv. This amount is equivalent to one year of background radiation exposure, for which estimates range from 2.0 - 3.6 mSv depending on geographical location (177-179).

![Figure 3-5 - CT coronal scout scan for determining the scanning region.](image)

In order to allow for conversion from CT intensity (in Hounsfield units, HU) to a bone density equivalent (mg/cm³ K₂HPO₄), a bone density reference phantom was included in all scans. Details regarding the reference phantom and the conversion from HU to an equivalent bone density are given in section 3.8.2. Since many scanning parameters, such as scanning energy, can affect the resulting CT intensity of the region being scanned, it is essential that the phantom be included in each scan (122).
3.7.2.1 Subject and Phantom Positioning

The phantom was placed on the scanner table and was made level by surrounding it with foam padding (Figure 3-6A). Ultrasound gel packs were placed on top of the phantom, to minimize the gap (air) between the subject and the phantom (Figure 3-4B). Each subject lay supine with his/her dominant shoulder directly above the phantom. The CT technician ensured that the full width of the phantom and the dominant shoulder were both in full view within the scanner’s field of view (Figure 3-2B).

![Figure 3-6 - Bone density reference phantom: A) phantom positioned within foam padding; B) end view showing the five reference rods.](image)

During scanning all individuals lay supine with their dominant arm in external rotation, at 0 degrees of abduction (Figure 3-7A). A Velcro strap was placed around the wrist and waist in order maintain this positioning. The contralateral arm was raised above the head to reduce the amount of unnecessary tissue along the x-ray beam’s path to the shoulder of interest (Figure 3-7B). This served to decrease the minimum necessary radiation exposure.

![Figure 3-7 - Subject positioning for a CT scan of a left shoulder.](image)
3.8 ASSESSING BONE MORPHOLOGY WITH QUANTITATIVE COMPUTED TOMOGRAPHY

In this study, the existing quantitative Computed Tomography (qCT) method was implemented and customized to allow the quantitative measurement of volumetric bone mineral density and cross-sectional area of bone at the glenohumeral joint.

3.8.1 Segmentation Protocols

Segmentation is the process of delineating a structure within an image, which in this case was bone on each slice of the CT scan. To segment a structure it is first necessary to determine the range of slices in which the structure appears. To ensure consistency a protocol was established, which used anatomical landmarks to determine the range of slices to segment. A second protocol was established to define the rules for segmenting the various types of bone (total bone, trabecular bone, and subchondral bone) within the slices of interest. The following sections describe these protocols in detail. I segmented all of the CT scans in Analyze 6.0 (Mayo Foundation, Rochester, MN) using an interactive touch-sensitive screen (Cintiq 21UX, Wacom Technology Corporation, Vancouver, WA) with an electronic pen (Figure 3-8).

3.8.1.1 Protocol for Defining the Segmentation Range for Humeral Head Bone

To segment the humeral head bone, it was necessary to determine which axial slices of the CT scan corresponded to the inferior and superior borders of the humeral head, and to standardize the selection of these slices that were free from partial volume effects. Given its semi-spherical shape, the CT
slices depicting the superior aspect of the humeral head are susceptible to partial volume effects. Partial volume effects occur when multiple tissues are represented by a single voxel in the scan; the resulting voxel intensity is the average of individual tissue intensities. This type of artefact results in the blurring of borders between tissues (e.g. cortical bone and trabecular bone, or cortical bone and muscle), which makes segmentation difficult and vBMD measurements inaccurate. It was therefore desirable to exclude the slices with partial volume effects from the segmentation range and the subsequent quantitative analysis of bone density. The protocol for defining the segmentation range involved identifying anatomical landmarks, which were visible on the scans of all subjects. The humeral head segmentation range was determined by viewing the CT scan in all three anatomical planes simultaneously, since it is difficult to identify the anatomical landmarks from the axial slices alone. The protocol is summarized as follows:

1. The CT scan was viewed simultaneously in the three anatomical planes (sagittal, coronal, and transverse/axial) in Analyze 6.0 (Mayo Foundation, Rochester, MN).
2. The cross-hairs were first centered on the humerus in the axial view (Figure 3-9A, top image). On the sagittal view the vertical cross-hair was placed mid-shaft (Figure 3-9A, bottom image).
3. The corresponding coronal slice was used to determine the inferior border of the humeral head (Figure 3-9A, middle image). The transition between the humeral neck and head served as the anatomical landmark defining the inferior segmentation limit for the humeral head (Figure 3-11). On the coronal slice, the horizontal cross-hair was placed over the most pronounced angle between the humeral neck and head (Figure 3-9A middle image), and the corresponding axial slice number was noted.
4. To determine the superior segmentation border, the cross-hairs were first centered on the humerus in the axial view (Figure 3-9B, top image). In the sagittal view the vertical cross-hair was aligned mid-shaft (Figure 3-9B, bottom image).
5. The greater tuberosity served as the anatomical landmark defining the superior segmentation limit for the humeral head (Figure 3-11). On the coronal view, the horizontal cross-hair was placed at the superior edge of the greater tuberosity (Figure 3-9B, middle image). The slice number of the corresponding axial slice was noted.
Figure 3-9 - Defining the segmentation ranges: A) inferior humeral head, B) superior humeral head, C) inferior glenoid cavity, and D) superior glenoid cavity.

3.8.1.2 Protocol for Segmenting Humeral Head Bone

Total and trabecular bone of the humeral head were segmented on each slice within the segmentation range determined according to the protocol described in section 3.8.1.1. A semi-automated, intensity-based, seed-growing tool was used to segment the total (cortical and trabecular) humeral head bone (Figure 3-10B). Using the electronic pen (Figure 3-8), manual corrections were made on slices where there was not a well-defined cortical bone border. The trabecular bone was manually segmented on each slice using the electronic pen (Figure 3-10C). The thin outer layer of cortical bone was not segmented; it was approximately 1-2 mm in thickness, which is too thin to accurately quantify BMD using qCT given the in-plane resolution of our CT scans (0.47 mm x 0.47 mm) (180, 181).

Two additional regions of interest were defined on the middle slice of the humeral head segmentation range, as per the method previously described by Tingart et al. (26). These regions comprised the trabecular bone nearest to the articular surface of the humeral head (Figure 3-10D). The regions, named articular surface 1 (AS 1) and articular surface 2 (AS 2), were bounded by a line parallel to the glenoid cavity, placed at one third of the diameter of the humeral head. A second line, a perpendicular to the first, divided the articular surface trabecular bone region into anterior (AS 2) and posterior (AS 1) compartments.
For the purposes of reconstructing the humeral head in three-dimensions (3D) to assess the bone density distribution (section 3.8.4) it was necessary to segment the total bone in all slices, including those with partial volume effects which lay outside the segmentation range. It is important to note that this additional segmentation of total bone outside the segmentation range was solely used for the 3D reconstruction and was not included in the quantitative analysis of bone mineral density.

### 3.8.1.3 Bone Parameters Computed for the Humeral Head

The final outcome measures for humeral head bone were equivalent volumetric bone mineral density (equivalent vBMD, mg/cm³ K₂HPO₄) and normalized cross-sectional area (nCSA, mm²/m). Equivalent vBMD was calculated by converting the mean CT intensity values (in Hounsfield units, HU) of the segmented bone regions to an equivalent potassium phosphate density, according to a method described in detail in section 3.8.2. The mean intensity and cross-sectional area for the segmented total and trabecular bone from each slice within the segmentation range were extracted using Analyze 6.0 (Mayo Foundation, Rochester, MN). The cross-sectional area of the cortical bone (and subcortical transitional bone) was calculated in Excel 2003 (Microsoft Corporation, Redmond, WA) by subtracting, for each slice, the trabecular bone cross-sectional area from the total bone cross-sectional area. All cross-sectional area values were normalized to account for size differences between subjects by dividing the cross-sectional area (CSA, mm²) by the height (m) of the individual (Table 4-3).

The total number of slices in the humeral head segmentation range was divided by four to create four equal superior-inferior subdivisions the humeral head (H1, H2, H3, and H4) (Figure 3-11). This was based on the method used by Tingart et al. in a previous study of humeral head vBMD (26). For each
subdivision, mean vBMD and mean normalized cross-sectional area were calculated by computing the mean of these values for all slices within that subdivision.

![Figure 3-11 - Segmentation landmarks and subdivisions of the humeral head.](image)

### 3.8.1.4 Protocol for Defining the Segmentation Range for Glenoid Cavity Bone

Similar to the protocol established for the humeral head (section 3.8.1.1), a protocol was established for determining which axial slices of the CT scan corresponded to the inferior and superior borders of the glenoid cavity, thereby defining the range of slices to segment. This protocol involved viewing the CT scan in the sagittal and coronal planes, since it is difficult to determine the border separating the glenoid cavity from the rest of the scapula from the axial view alone. The following protocol was developed and adhered to:

1. The CT scan was viewed simultaneously in the three anatomical planes (sagittal, coronal, and transverse/axial) in Analyze 6.0 (Mayo Foundation, Rochester, MN).
2. The cross-hairs were centered on the glenoid cavity in the axial view (Figure 3-9C, top image).
3. In the sagittal view, the horizontal cross-hair was placed on the inferior edge of the glenoid cavity (Figure 3-9C, bottom image). The corresponding axial slice number was noted.
4. The cross-hairs were placed on the glenoid cavity in the axial view (Figure 3-9D, top image).
5. In the sagittal view, the horizontal cross-hair was placed on the superior edge of the glenoid cavity (Figure 3-9D, bottom image). The corresponding axial slice number was noted.
3.8.1.5 Protocol for Segmenting Glenoid Bone

Subchondral and trabecular bone of the glenoid cavity were segmented on every slice within the segmentation range determined according to the protocol described in section 3.8.1.4. Subchondral bone of the glenoid cavity was manually segmented, using the electronic pen and tablet (Figure 3-8), on every slice within the segmentation range (Figure 3-12B).

![Figure 3-12 - Segmentation of the glenoid: A) unsegmented bone, B) subchondral bone, and C) trabecular bone.](image)

Trabecular bone medial to the glenoid cavity was manually segmented with the electronic pen and tablet (Figure 3-12C). For simplicity, this region will be referred to as glenoid trabecular bone. Trabecular bone was not segmented on every slice in the glenoid cavity segmentation range since the borders between subchondral, trabecular and cortical bone of the scapula are not clearly defined on the most superior and inferior slices of the segmentation range. Instead, the segmentation range was divided into three sub-regions of equal size (i.e. inferior, middle, and superior) by dividing the total number of glenoid slices by three (Figure 3-13A). Trabecular bone was segmented on the five middle slices of each of the three sub-regions (Figure 3-13B). The medial segmentation limit for the trabecular bone was drawn perpendicularly to the glenoid surface, at a distance equal to half the width of the glenoid cavity (Figure 3-12C). This segmentation protocol was based on the method used by Lehtinen et al. in a previous study which quantified trabecular bone density in the scapula (27).
3.8.1.6 Bone Parameters Calculated for the Glenoid Cavity

The final outcome measures for glenoid bone were equivalent volumetric bone mineral density (equivalent vBMD, mg/cm$^3$ K$_2$HPO$_4$) and normalized cross-sectional area (nCSA, mm$^2$/m). Equivalent vBMD was calculated by converting the mean CT intensity values (Hounsfield units) of the segmented bone regions to a potassium phosphate equivalent density, according to a method described in detail in section 3.8.2. The mean intensity (Hounsfield units) and cross-sectional area for each slice within the segmentation range were extracted for the segmented subchondral and trabecular bone using Analyze 6.0 (Mayo Foundation, Rochester, MN). Normalized cross-sectional area was calculated by dividing the cross-sectional area (CSA, mm$^2$) by the height (m) of the individual (Table 4-3). For each sub-region of the glenoid (i.e. inferior, middle, and superior), mean vBMD and mean normalized cross-sectional area were calculated by computing the mean of these values for all slices within that sub-region.

3.8.2 Converting Intensity to a Bone Density Equivalent

The CT intensity values, extracted from the CT scan in Hounsfield units (HU), were converted to an equivalent volumetric bone mineral density (mg/cm$^3$ K$_2$HPO$_4$) using the quantitative Computed Tomography (qCT) method. In this method a CT conversion equation is derived from the relationship between the known density values of the reference phantom rods and the corresponding intensity values (in HU) in the CT scan (182). qCT software was provided by the phantom manufacturer, however this software was not used in this study. Instead, all conversion equations were derived
manually in Excel 2003 (Microsoft Corporation, Redmond, WA) based on the equations provided in the qCT User’s Manual (equations 4.1 to 4.5 below) (182).

The bone density reference phantom (CT Calibration Phantom Model 3, Mindways Software Inc., Austin, TX) comprised five cylindrical rods, each containing a different known combination of high and low atomic number elements (Figure 3-6B). The relative amounts of the high and low atomic number elements were selected by the manufacturer such that their linear combination produced the same x-ray attenuation curve as a specific density of potassium phosphate (K$_2$HPO$_4$) dissolved in water (183). The details regarding the specific elements used and the ratios in which they were combined are considered proprietary information and remain undisclosed by the manufacturer. Potassium phosphate is a material with similar x-ray attenuation properties to true bone mineral, calcium hydroxyapatite, and is commonly used to express an equivalent bone density (126). The Model 3 reference phantom used in this study contains solid reference materials; solid phantoms have shown improved stability over earlier aqueous models (126). The Model 3 calibration phantom was previously tested by the manufacturer for compatibility with the Toshiba Aquilion 64 scanner used in the present study, however neither the accuracy nor the repeatability were reported (182).

The equivalent bone mineral densities were computed using equation 4.1 (182). The following conversion technique uses Region of Interest (ROI) measurements from the reference materials in the rods of the phantom to estimate the values of $\sigma_{CT}$ and $\beta_{CT}$. Knowing the CT scan intensity values (HU) of the phantom reference materials ($\mu_{ROI}$), it is possible to solve for the K$_2$HPO$_4$-equivalent density of bone in the CT scan ($\rho_{K2HPO4}$):

$$\mu_{ROI} = \sigma_{CT} \cdot \rho_{K2HPO4} + \beta_{CT}$$  \hspace{1cm} (4.1)

where:

- $\mu_{ROI} = \text{voxel intensity (HU) in a ROI of the reference material}$
- $\sigma_{CT} = \text{imaging technique-specific parameter defining the response of the CT scanner to K}_2\text{HPO}_4$
- $\rho_{K2HPO4} = \text{K}_2\text{HPO}_4\text{-equivalent density of the unknown material within the measured ROI}$
- $\beta_{CT} = \text{imaging technique-specific parameter characteristic of the Hounsfield Unit scale}$
Specifically for the Model 3 reference phantom, equation 4.1 is written as:

\[ \mu_{\text{ROI}} = \rho_{\text{H}_2\text{O}} + (\sigma_{\text{ref}})(\rho_{\text{K}_2\text{HPO}_4}) + \beta_{\text{ref}} \]  

(4.2)

where:
- \( \mu_{\text{ROI}} \) = voxel intensity (HU) in a ROI of the reference material
- \( \rho_{\text{H}_2\text{O}} \) = water equivalent density of material within the measured ROI
- \( \sigma_{\text{ref}} \) = imaging technique-specific parameter defining the response of the CT scanner to \( \text{K}_2\text{HPO}_4 \)
- \( \rho_{\text{K}_2\text{HPO}_4} \) = \( \text{K}_2\text{HPO}_4 \) equivalent density of material within the measured ROI
- \( \beta_{\text{ref}} \) = imaging technique-specific parameter characteristic of the Hounsfield Unit scale

The relationship between \( \sigma_{\text{CT}} \) and \( \sigma_{\text{ref}} \) and between \( \beta_{\text{CT}} \) and \( \beta_{\text{ref}} \) are given by the phantom manufacturer (182). They are as follows:

\[ \sigma_{\text{CT}} = \sigma_{\text{ref}} - 0.2174 \]  

(4.3)

\[ \beta_{\text{CT}} = \beta_{\text{ref}} + 999.6 \]  

(4.4)

The water equivalent density (\( \rho_{\text{water}} \)) and the potassium phosphate equivalent density (\( \rho_{\text{K}_2\text{HPO}_4} \)) for each of the five rods in the reference phantom remain constant. These values are supplied by the manufacturer (182) and are listed in Table 3-4. It is important to note that the rods are not physically comprised of water and potassium phosphate, but instead these values represent the linear combination of water and potassium phosphate that would produce the same attenuation curve as the reference material in the corresponding rod. Therefore, the two negative values listed for the potassium phosphate equivalent densities of rods A and B do not imply a negative physical density, but instead describe the required linear combination of water and potassium phosphate.

<table>
<thead>
<tr>
<th>Reference Rod</th>
<th>Water equivalent density (( \rho_{\text{H}_2\text{O}} ), mg/cm(^3))</th>
<th>( \text{K}_2\text{HPO}<em>4 ) equivalent density (( \rho</em>{\text{K}_2\text{HPO}_4} ), mg/cm(^3))</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1012.25 ± 2.27</td>
<td>-51.83 ± 0.12</td>
</tr>
<tr>
<td>B</td>
<td>1056.95 ± 1.94</td>
<td>-53.40 ± 0.10</td>
</tr>
<tr>
<td>C</td>
<td>1103.57 ± 1.69</td>
<td>58.88 ± 0.09</td>
</tr>
<tr>
<td>D</td>
<td>1119.52 ± 1.82</td>
<td>157.05 ± 0.26</td>
</tr>
<tr>
<td>E</td>
<td>923.20 ± 2.12</td>
<td>375.83 ± 0.86</td>
</tr>
</tbody>
</table>

For each subject’s scan, the CT intensity values were extracted from a segmented ROI in each of the five rods in the reference phantom. On every CT slice a circular ROI, measuring approximately 50% of the area of the rod (~140 mm\(^2\)), was segmented in the centre of each rod in order to exclude partial
volume effects. The mean intensity value of each rod was extracted for each slice using Analyze 6.0 (Mayo Foundation, Rochester, MN). The mean intensity ($\mu_{ROI}$) over all slices (~160) was calculated for each rod. Using these intensity values, a linear regression of equation 4.2 was used to determine $\sigma_{ref}$ (slope) and $\beta_{ref}$ (intercept). Equations 4.3 and 4.4 were used to determine $\sigma_{CT}$ and $\beta_{CT}$. A separate conversion equation was determined for each subject (i.e. subject-specific values for $\beta_{CT}$ and $\sigma_{CT}$). For each subject, the CT intensity values (HU) from the segmented ROIs (i.e. $\mu_{ROI}$) were substituted into that individual’s specific conversion equation, to solve for the equivalent bone mineral density ($\rho_{K2HPO4}$):

$$\rho_{K2HPO4} (\text{unknown}) = \left( \mu_{ROI} - \beta_{CT} \right) / \sigma_{CT}$$  (4.5)

The CT intensities of the humeral head total and trabecular regions and of the glenoid subchondral and trabecular regions were converted to an equivalent volumetric bone mineral density accordingly.

### 3.8.3 Repeatability of Assessing Bone Morphology with qCT

The intra-observer precision (repeatability) of the qCT method used in this study was determined by resegmenting the CT scans of two subjects two additional times. The CT scans of one wheelchair user subject (AO 2) and one able-bodied control subject (CO 2 Control) were randomly chosen for re-analysis. I performed the second segmentation approximately four months after the original segmentation, and performed the third segmentation two days after the second segmentation. For the second and third segmentations, the two CT scans chosen for this repeatability study were alternated (i.e. 2nd segmentation of AO 2, then 2nd segmentation of CO 2 Control, then 3rd segmentation of AO 2, then 3rd segmentation of CO 2 Control) to avoid bias associated with myself becoming familiar with the data set. With each analysis, the bone density reference phantom was segmented and these data were used to re-calculate the conversion equation from CT intensity to an equivalent vBMD (section 3.8.2). The humeral head total and trabecular bone and the glenoid subchondral and trabecular bone were resegmented according to the protocols defined in section 3.8.1. For each of these regions of interest vBMD and nCSA were calculated. The normalized cross-sectional area was also calculated for the humeral head cortical bone (described in section 3.8.1.3). The precision of the qCT method was calculated as the percent coefficient of variation (CV %) of the root mean square (RMS) average of the standard deviation (SD) (184). The precision results establish that the qCT method used in the present study is repeatable (Table 3-5).
Table 3-5 - Precision (repeatability) of the qCT method

<table>
<thead>
<tr>
<th>Joint Surface</th>
<th>Parameter</th>
<th>RMS CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humeral Head</td>
<td>Total bone VBMD</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>Trabecular bone VBMD</td>
<td>0.71</td>
</tr>
<tr>
<td></td>
<td>Total bone nCSA</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>Trabecular bone nCSA</td>
<td>1.02</td>
</tr>
<tr>
<td></td>
<td>Cortical bone nCSA</td>
<td>5.57</td>
</tr>
<tr>
<td>Glenoid</td>
<td>Subchondral bone VBMD</td>
<td>1.62</td>
</tr>
<tr>
<td></td>
<td>Trabecular bone VBMD</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>Subchondral bone nCSA</td>
<td>3.16</td>
</tr>
<tr>
<td></td>
<td>Trabecular bone nCSA</td>
<td>2.64</td>
</tr>
</tbody>
</table>

3.8.4 Assessing Bone Density Distribution with Computed Tomography

Osteoabsorptiometry

A modified version of the Computed Tomography Osteoabsorptiometry (CT-OAM) method (28, 72, 133) was developed and used to visualize the distribution of bone mineral density across the articular surfaces of the humeral head and the glenoid cavity. This method entails segmenting the bone of interest, rendering the segmented bone using a projection technique, and applying a colour map to the rendered bone to facilitate visualization of the bone mineralization patterns. In the original CT-OAM method by Muller-Gerbl and colleagues (28, 133) a Maximum Intensity Projection (MIP) algorithm was used to render the segmented subchondral bone of the glenoid cavity. The MIP technique projects 3D voxel data onto a 2D surface. The intensity of each pixel on the projected 2D surface is that of the maximum intensity (HU) of all voxels along the corresponding projection line (normal to the surface). An example of a Maximum Intensity Projection applied to a brain scan is shown in Figure 3-14.
Figure 3-14 – A Maximum Intensity Projection example. The resulting image (far right) consists of the maximum intensity of all pixels encountered along the projection line (thin lines) [modified from (185)].

To facilitate comparisons between our results and existing CT-OAM results for the glenoid obtained using the original method, the segmented subchondral bone of the glenoid cavity was also volume-rendered by means of a Maximum Intensity Projection in this study (Analyze 6.0, Mayo Foundation, Rochester, MN). A lower threshold of 0 HU was used. A lateral glenoid view was used to standardize the alignment of the segmented glenoid bone prior to applying the MIP. This view was chosen because it depicts the full articular surface of the glenoid cavity.

The Maximum Intensity Projection cannot be used to render the bone of the articular surface of the humeral head thus the CT-OAM method was modified in this study and a surface rendering algorithm was used instead. The CT-OAM method has not previously been used to display the bone density distribution across the humeral head, and it is possible that this is due to a methodological limitation of the original CT-OAM method. Anatomically, the cortical bone of the humeral shaft extends further superiorly on the lateral side of the bone (i.e. up to the greater tuberosity, Figure 3-11) than on the medial side (i.e. the articular surface of the humeral head). Viewing the articular surface of the humeral head in the medial-lateral direction, the dense cortical bone of the shaft lies along the same projection lines as the less dense bone of the articular surface of the humeral head. As a result, the Maximum Intensity Projection could not be used to visualize the bone density distribution of the
articular surface of the humeral head since the MIP algorithm projected the lateral shaft densities onto the medial articular surface. Instead, a surface projection algorithm was used to produce a volume-rendered view of the articular surface of the humeral head, by displaying the average CT intensity of first three voxels of the articular surface encountered along each projection line. A medial view of the humeral head was used to standardize the alignment of the segmented bone prior to rendering with the surface projection algorithm. This view was chosen since it best depicts the articular surface of the humeral head.

To better visualize the bone density distribution, a colour map was applied to the CT intensity values of the rendered articular surfaces of the glenoid cavity and the humeral head. To allow for quantitative comparisons between subjects it was necessary that the units of the colour maps be converted from CT intensity (HU) to equivalent vBMD (mg/cm³). Furthermore, it was necessary that the colour map applied to each subject’s bone span the same vBMD range (for our study, 0-1500 mg/cm³). Prior to applying the colour map, the CT intensity values corresponding to 0 and 1500 mg/cm³ of equivalent vBMD were determined for each subject using his/her specific conversion equation. The corresponding intensity values (HU) were used as the upper and lower thresholds when applying the colour map to his/her rendered bones, so that the CT-OAM projections for all subjects shared a common vBMD scale. The colour map upper limit of 1500 mg/cm³ was chosen to include the greatest range of intensities seen across all subjects and controls. The modified CT-OAM method used in this study is an improvement over the existing method because the articular surface of the humeral head can be rendered and because bone density distribution is expressed as vBMD instead of CT intensity. This modified CT-OAM technique produced colour mapped images of the articular surfaces of both sides of the glenohumeral joint, with each colour corresponding to a specific bone density range. These results allowed for visual and quantitative comparisons of bone density distribution between individuals. The relative locations (e.g. anterior glenoid) and values of density maxima were described qualitatively.

3.8.4.1 Validation of CT-OAM

The original CT Osteoabsorptiometry method was validated against x-ray densitometry (133). In x-ray densitometry, the ‘optical density’ is determined by digitizing points from a photograph of a plain-film radiograph of the bone of interest. A colour-map can be applied to the digitized points to depict areas of common density. X-ray densitometry is limited to thin (~2 mm) sections of cadaveric bone, whereas CT Osteoabsorptiometry can be used in vivo. A linear regression analysis was used to
validate the bone mineralization patterns determined using CT Osteoabsorptiometry against those determined using x-ray densitometry. The optical density from x-ray densitometry was highly correlated ($r = 0.92$) with the Hounsfield Units of the CT scan (133).

**PART C: CARTILAGE IMAGING METHODS**

Glenohumeral cartilage was imaged with 3T Magnetic Resonance (MR) imaging. The MR technicians and I developed a 3T MR scanning protocol specifically for this study to produce high-resolution, 3D images suitable for quantitative analysis. Quantitative MR imaging (qMRI) analysis was performed to measure parameters of cartilage morphology.

3.9 IMAGING CARTILAGE WITH MAGNETIC RESONANCE

In this study MR imaging was used to acquire high-resolution scans of the articular cartilage at the glenohumeral joint. MR imaging is currently the modality of choice for *in vivo* imaging of articular cartilage. Scanning glenohumeral cartilage with MR presents a considerable challenge, given its thin and highly curved shape, the relatively small joint space between cartilage surfaces, and the off-centre location of the joint relative to the centre of the scanner’s bore. In contrast to patellofemoral cartilage that is 3-5 mm thick and relatively flat (153), cartilage on the humeral head is approximately 1-2 mm thick and semi-spherical (32, 36). The cartilage in the glenoid cavity is slightly thicker (~1.5-3 mm) and is concave (32, 36, 186).

Since air appears black in a MR scan, joint space between adjacent articular surfaces is helpful for cartilage segmentation. There is generally less joint space at the glenohumeral joint than at the tibiofemoral joint, making it more difficult to segment between the articular surfaces of the glenoid cavity and the humeral head (32). The thin and curved nature of glenohumeral cartilage, compounded with the relatively small joint space, requires a high-resolution MR scan for quantitative analysis (151).

As the magnetic field of the scanner increases, it becomes increasingly important to restrict the size of the scanner bore due to magnetic field inhomogeneities at the edges. Acquiring a high-resolution image of a shoulder on a 3T MR scanner is challenging given the limited size of the scanner bore and the off-centre location of the shoulder.
3.10 DEVELOPMENT OF A 3T MR CARTILAGE IMAGING PROTOCOL

3.10.1 Pilot Scanning

Four 1-hour pilot scanning sessions were needed to develop the final imaging protocol for glenohumeral cartilage. The pilot scans were of four healthy and able-bodied volunteers (2 females, 2 males, age range = 21-29 years). These pilot sessions were used to compare various MR sequences, spatial resolutions, number of slices, and shoulder and coil positions in terms of the quality of the resulting scan. The final scanning protocol was selected because it was the sequence that produced the greatest contrast between cartilage and adjacent tissues and minimal chemical shift artefact, based on visual inspection. Maximal in-plane spatial resolution and minimal scanning time were also deciding factors. The parameters chosen for the final scanning protocol are presented and justified in section 3.10.2.

3.10.2 Final Scanning Protocol

All MR scanning (pilot and subject scanning) was performed at the University of British Columbia (UBC) High Field MR Imaging Centre, in the UBC hospital. Scans were acquired on a 3T Philips Gyroscan Intera MR scanner (Figure 3-15A) by two experienced MR technicians. The MR technicians and I developed a 3T protocol for 3D high-resolution imaging of cartilage at the glenohumeral joint, optimized for quantitative MR imaging (qMRI) analysis. The final scan parameters are listed in Table 3-6.

Figure 3-15 – MR imaging: A) Philips 3T Gyroscan Intera MR scanner, B) MR axial scout scan of a right glenohumeral joint, showing the shim box (dotted box), and position, orientation, and range of the slices (solid box).
Table 3-6 - MR Scan Parameters – Final Scanning Protocol

<table>
<thead>
<tr>
<th>Imaging Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scanner</td>
<td>3T Philips Gyroscan Intera</td>
</tr>
<tr>
<td>Scan Sequence</td>
<td>3D T1 Fast Field Echo (T1 FFE)</td>
</tr>
<tr>
<td>Scan Features</td>
<td>Selective water excitation, High order shim</td>
</tr>
<tr>
<td>Scanning Plane</td>
<td>Oblique coronal</td>
</tr>
<tr>
<td>Repetition Time (TR)</td>
<td>18.9 ms</td>
</tr>
<tr>
<td>Echo Time (TE)</td>
<td>6.4 ms</td>
</tr>
<tr>
<td>Flip Angle</td>
<td>15°</td>
</tr>
<tr>
<td>In-plane Resolution</td>
<td>0.31 mm x 0.31 mm</td>
</tr>
<tr>
<td>Slice Thickness</td>
<td>1.0 mm</td>
</tr>
<tr>
<td>Matrix Size</td>
<td>512 x 512</td>
</tr>
<tr>
<td>Field of View</td>
<td>160 mm</td>
</tr>
<tr>
<td>Number of Excitations (NEX)</td>
<td>2</td>
</tr>
<tr>
<td>Surface Coil</td>
<td>SENSE-flex-M</td>
</tr>
<tr>
<td>Scan Duration</td>
<td>14 min 55 sec</td>
</tr>
<tr>
<td>Number of Slices Acquired</td>
<td>54-60 (depending on subject size)</td>
</tr>
</tbody>
</table>

Imaging was performed on a 3T magnet since it has been shown, for cartilage scans of the knee, that both the signal to noise ratio (SNR) efficiency \( \text{SNR efficiency} = \frac{\text{SNR}}{1/\sqrt{\text{scan time}}} \) and the contrast to noise (CNR) efficiency \( \text{CNR efficiency} = \frac{\text{CNR}}{1/\sqrt{\text{scan time}}} \) increase by a factor of 1.8 using spoiled gradient-echo sequences at 3T, compared to 1.5T (154). The oblique coronal scanning plane (Figure 3-18A and solid box in Figure 3-15B) was chosen since it is perpendicular to the cartilage surfaces of the humeral head and the glenoid cavity, which is ideal as it minimizes partial volume effects. Given the semi-spherical shape of the humeral head, the oblique coronal MR slices will inevitably cut obliquely through the cartilage surface at the periphery of the humeral head, potentially causing partial volume effects.

The 3D T1 Fast Field Echo (T1 FFE) scan sequence is a T1-weighted spoiled gradient echo sequence. This particular sequence is known as T1 FFE by Philips, Spoiled Gradient Recalled Echo (SPGR) by General Electric (GE), and Fast Low-Angle Shot (FLASH) by Siemens. It is the most commonly used sequence for quantification of cartilage morphology (144, 151) since it has been demonstrated to
yield a hyperintense cartilage signal, allowing for excellent depiction of cartilage morphology (154). Moreover, this high-resolution gradient-echo sequence has been shown to be superior to spin-echo sequences for quantitative imaging of shoulder cartilage (187) and free from geometric distortions (144).

The T1 FFE sequence was applied with frequency-selective water excitation in order to achieve fat-suppression, to create sufficient contrast between the cartilage and the surrounding tissues, and to reduce chemical shift artefacts at the bone-cartilage interface (10, 151). Since the positioning of the shoulder within the scanner was offset with respect to the isocentre of the magnet, a high-order shim was used to reduce the inhomogeneities in the external magnetic field (dotted box in Figure 3-15B). The short echo time (TE = 6.4 ms) used in our protocol is in agreement with the recommended value of less than 10 ms (144). The combination of short echo time (TE = 6.4 ms) and repetition time (TR = 18.9 ms) chosen for our protocol allows for a greater T1-weighting, which in turn allows for a more homogeneous signal intensity throughout the cartilage thickness and higher contrast in the resulting scan (151).

In MR imaging there are tradeoffs between spatial resolution, SNR/CNR, and imaging time. In the present imaging protocol, slices were 1.0 mm thick and the in-plane resolution was 0.31 mm x 0.31 mm. These values were chosen since they maximized the spatial resolution, yet minimized the voxel anisotropy (slice thickness / in-plane resolution) and the scan duration. Poor spatial resolution and large voxel anisotropy have been shown to lead to cartilage segmentation errors (188). The combination of scanning at 3T with a 1.0 mm slice thickness, as employed in this protocol, has been shown to yield a higher precision of cartilage volume, thickness and surface area qMRI measurements at the knee joint, than combinations of 3T/1.5 mm thickness, and of 1.5T/1.5 mm thickness (189).

Our choice of in-plane resolution (0.31 mm²) was less than the 0.15 mm² resolution recommended by Graichen et al. (151) for quantifying the morphology of thin cartilage layers, like that of the glenohumeral joint. As determined from our pilot scans, this resolution was sufficient for segmentation since it provided small enough pixels to fully characterize the shape of the cartilage over the entire joint surface. Had we acquired our scans at the recommended spatial resolution (0.15 mm²) (151), our imaging time and voxel anisotropy would have increased dramatically. It is possible to increase the spatial resolution after scanning by interpolating the scanned voxels. This, however, is not equivalent to acquiring the scan at a higher spatial resolution. Post-processing interpolation of image data was not performed in the present study because the borders between adjacent tissues can
become blurred, making segmentation difficult. Moreover, post-processing interpolation can bias towards a uniform segmentation in regions of localized cartilage loss, since regional cartilage defects smaller than the acquired spatial resolution will not be visible (151). Should post-processing interpolation be performed, its effect on the validity and accuracy of the segmentation and analysis would need to be determined (144).

3.10.2.1 Subject Positioning

All subjects lay supine with their dominant arm in external rotation, at 0 degrees of abduction (Figure 3-16C). A SENSE Flex-M shoulder coil (Philips Electronics N.V., Eindhoven, the Netherlands) was positioned on the anterior and posterior aspects of the shoulder (Figure 3-16A). Ultrasound gel packs were wrapped around the shoulder between the two coils to provide homogeneity correction at the tissue-air interface for more accurate fat suppression (Figure 3-16B). A large Velcro strap was wrapped around the subject to maintain the positioning of the ultrasound gel packs and the surface coil (Figure 3-16C). Prior to the main scan of their dominant shoulder, all subjects and controls had two fast localizer scans (1 axial, 1 sagittal) in order to determine the exact position of the glenohumeral joint within the scanner.

Figure 3-16 - Subject positioning for a MR scan of a left shoulder: A) shoulder coil, B) ultrasound gel pack, C) second ultrasound gel pack (blue) and Velcro strap.

3.11 ASSESSING CARTILAGE MORPHOLOGY WITH QUANTITATIVE MAGNETIC RESONANCE IMAGING

Articular cartilage morphology was assessed using quantitative Magnetic Resonance Imaging (qMRI). In this method, quantitative measures are made of the cartilage segmented from a MR scan. The importance of having a well-defined segmentation protocol prior to cartilage segmentation has been emphasized by Koo et al. (153). The following protocols were adhered to in this study.
3.11.1 Segmentation Protocols

Following acquisition, analysis of the MR scan included performing a quality control check, converting the original dicom format to a specific segmentation software format, blinding the data, determining the segmentation range for the humeral head cartilage and glenoid cartilage, segmenting the cartilage, and performing a quality control procedure. All data sets were assessed for image quality by employees of Chondrometrics GmbH (Ainring, Germany), a qMRI analysis company. In addition, MR dicom data were converted to a proprietary format for use with the Chondrometrics segmentation and analysis software (Chondrometrics GmbH, Ainring, Germany). All data sets were blinded prior to my segmentation: at the time of scanning, unique study codes were used to identify the scans instead of subject names (e.g. DOER-MWU-P01), and at the time of data conversion, the data sets were blinded a second time by randomly assigning coded identifiers (e.g. No001).

I performed all segmentation of the MR scans. I was formally trained in the segmentation of cartilage by Dr. Felix Eckstein, one of the primary developers of the quantitative MRI (qMRI) analysis technique, and his colleagues. This training included the segmentation of ten knee data sets, including healthy knees, knees with early osteoarthritis, and knees with severe osteoarthritis. The segmentation of three scans of healthy shoulders was also included in my training.

3.11.1.1 Protocol for Defining the Segmentation Range for Humeral Head Cartilage

To segment the humeral head cartilage, it is first necessary to determine which slices of the MR scan to segment. Given the semi-spherical shape of the humeral head, the first and last MR slices through the head in the oblique coronal plane are susceptible to partial volume effects. A Region of Interest (ROI) was therefore established to ensure consistency in selecting the first and last slices to segment and to exclude all slices with visible partial volume effects. After having examined the oblique coronal shoulder scans from all 16 subjects and controls in this study, I determined that the middle 60% of slices on which the humeral head was visible were consistently free from partial volume effects (Figure 3-17). This 60% ROI was used when segmenting the humeral head cartilage on the MR scan of each subject.
Figure 3-17 – Axial scout scan showing the 60% ROI (dashed box) used to ensure consistency in selecting the segmentation range.

3.11.1.2 Protocol for Defining the Segmentation Range for Glenoid Cartilage

To segment the glenoid cartilage, it is first necessary to determine which slices of the MR scan to segment. The cartilage of the glenoid cavity is concave but not spherical and is roughly perpendicular to the oblique coronal scanning plane in all slices. It is, therefore, less susceptible to partial volume effects than the humeral head cartilage, and thus it was not necessary to establish a segmentation ROI for the glenoid cartilage. Instead, the segmentation range extended from the first to last slices on which the scapula was visibly intact medial to the glenoid cavity. Care was taken to include only the glenoid cartilage in the segmentation and not the surrounding glenoid labrum.

3.11.1.3 Protocol for Segmenting Glenohumeral Cartilage

Segmentation is the process of delineating a structure within an image, which in this case was the articular cartilage of the humeral head and the glenoid cavity in the MR scan. I manually segmented the humeral head and glenoid cartilage plates in the Chondrometrics software (Chondrometrics GmbH, Ainring, Germany) using a standard computer mouse. On each slice within the predetermined segmentation range (sections 3.11.1.1 and 3.11.1.2), a first line was drawn along the bone-cartilage interface (green lines in Figure 3-18B), and a second along the articular surface of the cartilage (pink lines in Figure 3-18B). The separate segmentation of the two sides of the cartilage plate (i.e. the bone-cartilage interface and the articular surface) was necessary to ensure the accurate computation of the morphological parameters using the algorithms described in detail in the following sections. This segmentation was performed for both the humeral head and the glenoid cavity cartilage.
plates. For every slice of each cartilage plate, the voxels between the bone-cartilage interface segmentation line and the articular surface segmentation line were assigned to that cartilage plate. Visually, the cartilage between these segmentation lines was coloured-in (Figure 3-18C). Computationally, these voxels were assigned to the corresponding cartilage plate for the morphological computations (i.e. contributed to the cartilage volume and thickness measurements).

3.11.1.4 Segmentation Quality Control Protocol

The segmentation of anatomical tissues such as cartilage requires a small degree of interpretation by the user in regions where the borders between adjacent tissues are unclear in the scans. Consequently, it is important that all segmentation undergo a quality control procedure in which an independent observer reviews the segmentation for consistency (189). In this study, all data sets were reviewed by Derek Wilson, also trained in cartilage segmentation by Dr. Eckstein and colleagues. I made the corrections suggested by Derek Wilson and performed a ‘Final Test’ in the Chondrometrics software (Chondrometrics GmbH, Ainring, Germany) on each data set. Whereas the quality control reviewer (D.W.) checked for consistency in segmentation and anatomical segmentation errors (e.g. the segmentation line does not follow the cartilage surface), the final test function in the Chondrometrics software checked for procedural segmentation errors (e.g. a broken segmentation line).

![Figure 3-18 - Cartilage segmentation of a right shoulder: A) no segmentation, B) bone-cartilage interface (green) and articular surface (pink) for humeral head and glenoid cartilage, C) filled cartilage plates.](image)

3.11.2 Parameters of Cartilage Morphology

Several parameters of cartilage morphology were calculated for the segmented cartilage plates of the humeral head and the glenoid using the Chondrometrics software (Chondrometrics GmbH, Ainring, Germany). In this software, computation algorithms were applied to the segmented cartilage plates to
compute the mean thickness (mm), the maximum thickness (mm), the surface area (cm²), and the volume (mm³) of the humeral head and the glenoid cavity cartilage. The specific algorithms used for these calculations are described in detail in the following sections.

3.11.2.1 Cartilage Thickness

Mean and maximum cartilage thickness were calculated for the humeral head and the glenoid cavity cartilage. Computations of cartilage thickness must account for out-of-plane deviations that arise from the fact that not all MR slices obtained will be perfectly perpendicular to the cartilage surface (144). This is especially important for spherically-shaped cartilage plates, as on the humeral head. In order to account for out-of-plane deviations, cartilage thickness must be computed in three dimensions, independent of the scanning plane orientation (144). In this study, cartilage thickness was computed using a 3D Euclidean distance transformation (156). The main advantage of this algorithm is that it does not rely on explicit computation of normal vectors, which are difficult to define and compute on discrete surfaces. The algorithm operates as follows:

1. Using a shape-based interpolation, all voxels within the segmented cartilage region are interpolated into an isotropic binary volume.
2. The voxels belonging to the bone-cartilage interface and the articular surface of the cartilage are located and labelled accordingly within the binary volume.
3. Local 3D distance maps are constructed by computing and storing the Euclidean distance between neighbouring voxels within the segmented volume.
4. A global distance map is constructed based on the local distance maps, by computing the minimum Euclidean distance from each voxel within the segmented volume to the bone-cartilage interface.
5. The Euclidean distances are extracted from the 3D distance map from the positions that correspond to the voxels on the cartilage surface. These values correspond to the cartilage thickness.
6. The mean cartilage thickness across the joint surface is determined by computing the arithmetic mean of all the thickness values.
3.11.2.2 Cartilage Surface Area

Cartilage surface area was computed for the humeral head and the glenoid cavity cartilage using a triangulation approach (157). As for cartilage thickness computations, cartilage surface area computations must also account for out-of-plane deviations and must be calculated in 3D, independently of the scanning plane (10). The triangulation approach meets these requirements. On each slice of the segmented datasets, the bone-cartilage interface and the articular surface of the cartilage were extracted. A Euclidean distance measure was used to perform triangulation between contiguous slices (i.e. two neighbouring points along the cartilage surface on the same slice were connected, and then connected to the closest point on the adjacent slice, thereby forming a triangle). The dimensions of the triangles were numerically integrated to calculate the total cartilage surface area. This was done for both the bone-cartilage interface and the articular surface, using the known pixel size (i.e. the in-plane resolution of the MR scan).

3.11.2.3 Cartilage Volume

Cartilage volume was computed by numerical integration of the number of voxels attributed to the cartilage plate during segmentation, knowing the dimensions of the image voxels (i.e. the in-plane resolution and the slice thickness) (155).

3.11.2.4 Accuracy and Precision of qMRI

The development of the qMRI method has focussed on the knee joint (144, 153-157), and as such, the accuracy and precision of the cartilage thickness (156), surface area (157), and volume algorithms (155) have been assessed for the human knee in vivo. The qMRI method has, however, been validated for other joints, including the elbow (151) and the shoulder (32).

Graichen et al. validated qMRI for the humeral head and the glenoid cavity cartilage using cadaveric shoulder specimens (32). Coronal scans were acquired, perpendicular to the glenoid cavity, on a 1.5T scanner using a 3D gradient echo sequence (FLASH) with selective water excitation. Slice thickness was 1 mm and the in-plane resolution was 0.25 x 0.25 mm², with post-processing interpolation to 0.125 x 0.125 mm². The qMRI cartilage volume measurements were compared to the water-displacement of the surgically removed cartilage. The mean systematic difference (average pairwise difference) was +3 % for the humeral head, and +1 % for the glenoid cavity. The mean absolute difference (average absolute pairwise difference) was 4 ± 3 % for the humeral head and 7 ± 6 % for
Chapter 3: Methods

the glenoid cavity. The correlation coefficient was 0.97 for the humeral head and 0.92 for the glenoid cavity. The qMRI cartilage thickness measurements were compared to those obtained using A-mode ultrasound. For both the humeral head and the glenoid cavity, cartilage thickness was underestimated compared to A-mode ultrasound. For the humeral head and the glenoid cavity, the mean systematic differences were -16 % and -17 %, and the absolute systematic differences were 16 ± 8 % and 21 ± 16 %.

The precision (repeatability) of qMRI is related to both the image acquisition and the image analysis (10). Vanwanseele and colleagues assessed the in vivo precision of qMRI measurements at the shoulder (20). More specifically, these authors assessed the immediate test-retest reproducibility for qMRI measurements of humeral head cartilage mean and maximum thickness, surface area, and volume. The precision error (RMS CV %) was smallest for the cartilage surface area (1.5 %) and greatest for maximum thickness (6.5 %). The precision errors for the mean thickness and volume were 4.5 % and 4.3 % respectively. The ratio between intersubject variability and technical precision was 5.2:1 for mean thickness, 3.0:1 for maximum thickness, 4.0:1 for surface area, and 6.1:1 for volume. Given that the precision errors were much lower than the intersubject variability, Vanwanseele and colleagues concluded that the qMRI technique can be used to quantify differences in shoulder cartilage morphology between and within subjects over time. Although the qMRI precision was not explicitly determined in this study, our MR image acquisition was similar to that of Vanwanseele et al. and Graichen et al. (i.e. same MR sequence and scanning plane) and the image analysis was performed using the same qMRI software (i.e. Chondrometrics), having been trained by the same researchers (i.e. Dr. Eckstein and colleagues). Moreover, our subject groups were quite similar to those in Vanwanseele et al.’s study (i.e. wheelchair users and able-bodied individuals).

PART D: STATISTICAL ANALYSIS

Given the numerous bone and cartilage parameters measured in this study, only a subset of these was analyzed statistically to reduce the probability of erroneously detecting a difference. The select parameters (Table 3-7) were chosen in order to best test our hypotheses. The remaining parameters were analyzed descriptively by comparing the mean and the variance between groups and describing any trends observed. Since all subject groups displayed similar trends in vBMD and normalized cross-sectional area between the humeral head subdivisions (H1-H4) and the glenoid cavity subregions (inferior, middle, and superior), global mean values of vBMD and normalized cross-sectional area (nCSA) were computed for the entire segmentation regions of the humeral head and of
the glenoid cavity and were analyzed statistically. Sample data for these parameters were tested for normality by comparing the mean and median values within each subject group. The mode was not included in the comparison because it did not exist, given the small sample size. Skewness was calculated to determine the degree of asymmetry of the sample data, and kurtosis was calculated to determine the peakedness of the sample data. From these normality tests it seemed reasonable to assume that the samples were drawn from normally distributed populations. Based on this assumption, parametric tests were used.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Joint Surface</th>
<th>Primary Morphological Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>Humeral Head</td>
<td>Trabecular vBMD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total nCSA</td>
</tr>
<tr>
<td>Glenoid</td>
<td></td>
<td>Subchondral vBMD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trabecular vBMD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subchondral nCSA</td>
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<tr>
<td>Cartilage</td>
<td>Humeral Head</td>
<td>Volume</td>
</tr>
<tr>
<td></td>
<td>Glenoid</td>
<td>Volume</td>
</tr>
</tbody>
</table>

Statistical analyses were performed in STATISTICA (Release 7.1, StatSoft, Inc., Tulsa, OK, USA) with the significance level set to $p < 0.05$. A two-way analysis of variance (ANOVA) was used to compare the subset of the measured parameters of bone and cartilage morphology (Table 3-7) between the four subject groups (described in section 4.1). The factors were age group (childhood-onset vs. adulthood-onset) and mobility type (wheelchair user vs. able-bodied control).

Based on the effect sizes found in this pilot study, sample size calculations were performed (power 0.80, significance level $p < 0.05$) to determine the sample sizes necessary in a full-scale study to detect significant differences in bone and cartilage morphology between childhood-onset and adulthood-onset wheelchair users.
The Pearson product-moment correlation coefficient was computed in STATISTICA (Release 7.1, StatSoft, Inc., Tulsa, OK, USA) to determine whether an association existed between the following parameters:

1. humeral head trabecular vBMD vs. glenoid trabecular vBMD
2. humeral head trabecular vBMD vs. normalized cross-sectional area
3. glenoid subchondral vBMD vs. normalized cross-sectional area
4. humeral head trabecular vBMD vs. cartilage thickness
5. glenoid subchondral vBMD vs. cartilage thickness
6. humeral head trabecular vBMD vs. shoulder pain
7. humeral head trabecular vBMD vs. physical activity
8. glenoid subchondral normalized cross-sectional area vs. physical activity
9. humeral head trabecular vBMD vs. dietary calcium intake
10. humeral head trabecular vBMD vs. wheelchair user mass
11. glenoid subchondral normalized cross-sectional area vs. wheelchair user mass

Since we were looking for general associations between parameters, not specifically related to any particular subject group, all wheelchair users and able-bodied controls were considered as a single group (n=16). For the correlation analyses involving physical activity, shoulder pain, and subject mass, only the wheelchair users’ data were included (n=8). Significant correlations (p < 0.05) were plotted with the 95% confidence intervals.

Basic descriptive statistics were used to compare the questionnaire data (pain, physical activity, and dietary calcium intake) between subject groups, using Excel 2003 (Microsoft Corporation, Redmond, WA). Data are presented as the mean ± one standard deviation (SD). The questionnaire data were not analyzed for statistical significance to avoid making too many comparisons and erroneously detecting significant differences.
4 RESULTS

The results chapter is divided into four parts: part A presents the results from the clinical assessments, part B the bone imaging and quantitative morphology results, part C the cartilage imaging and quantitative morphology results, and part D the correlations and the sample size calculations.

PART A: CLINICAL ASSESSMENTS

Part A presents the results from the methods of this study unrelated to quantitative imaging. These include the anthropometric data for all subjects, as well as the results from the radiologist’s review of the CT scan, the physical examination, and the questionnaires.

4.1 ANTHROPOMETRIC DATA

Sixteen subjects participated in this study (N = 16). The subjects were specifically recruited for one of four groups (Table 4-1). Due to difficulties in recruiting wheelchair user subjects (section 3.2), only three subjects were recruited for each of the childhood-onset groups (i.e. wheelchair users and able-bodied controls), instead of the targeted five subjects.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Mobility Type</th>
<th>Subject Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood-onset</td>
<td>Childhood-onset wheelchair users (CO)</td>
<td>Childhood-onset controls (CO controls)</td>
</tr>
<tr>
<td>n = 3</td>
<td>n = 3</td>
<td></td>
</tr>
<tr>
<td>Adulthood-onset</td>
<td>Adulthood-onset wheelchair users (AO)</td>
<td>Adulthood-onset controls (AO controls)</td>
</tr>
<tr>
<td>n = 5</td>
<td>n = 5</td>
<td></td>
</tr>
</tbody>
</table>

There was no difference in gender or in mean ± SD age between the wheelchair user subject groups and the corresponding able-bodied control groups (Table 4-2). On average, the subjects in the adulthood-onset wheelchair user group had wheeled for 8 years longer than the subjects in the childhood-onset wheelchair user group.
Table 4-2 - Summary of the Demographic Data for the Subject Groups

<table>
<thead>
<tr>
<th>Subject Groups</th>
<th>Age (years) Mean ± SD</th>
<th>Wheelchair Use (years) Mean ± SD</th>
<th>Gender (M/F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>26 ± 2</td>
<td>16 ± 6</td>
<td>2 M, 1 F</td>
</tr>
<tr>
<td>CO Controls</td>
<td>26 ± 2</td>
<td>N/A</td>
<td>2 M, 1 F</td>
</tr>
<tr>
<td>AO</td>
<td>52 ± 12</td>
<td>24 ± 8</td>
<td>3 M, 2 F</td>
</tr>
<tr>
<td>AO Controls</td>
<td>53 ± 12</td>
<td>N/A</td>
<td>3 M, 2 F</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user

Subject height and weight were self-reported, in order to minimize the invasiveness of the study methods (Table 4-3). Body mass index (BMI) was calculated according to equation 5.1:

\[
BMI = \frac{\text{mass (kg)}}{[\text{height (m)}]^2}
\]  

(5.1)

Table 4-3 - Anthropometric Data for Wheelchair Users and Able-Bodied Controls

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Height (m)</th>
<th>Mass (kg)</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO 1</td>
<td>1.47</td>
<td>64</td>
<td>29.6</td>
</tr>
<tr>
<td>CO 1 Control</td>
<td>1.90</td>
<td>86</td>
<td>23.8</td>
</tr>
<tr>
<td>CO 2</td>
<td>1.75</td>
<td>68</td>
<td>22.2</td>
</tr>
<tr>
<td>CO 2 Control</td>
<td>1.80</td>
<td>86</td>
<td>26.5</td>
</tr>
<tr>
<td>CO 3</td>
<td>1.52</td>
<td>56</td>
<td>24.2</td>
</tr>
<tr>
<td>CO 3 Control</td>
<td>1.75</td>
<td>77</td>
<td>25.1</td>
</tr>
<tr>
<td>AO 1</td>
<td>1.88</td>
<td>61</td>
<td>17.3</td>
</tr>
<tr>
<td>AO 1 Control</td>
<td>1.88</td>
<td>95</td>
<td>26.9</td>
</tr>
<tr>
<td>AO 2</td>
<td>1.63</td>
<td>45</td>
<td>16.9</td>
</tr>
<tr>
<td>AO 2 Control</td>
<td>1.65</td>
<td>66</td>
<td>24.2</td>
</tr>
<tr>
<td>AO 3</td>
<td>1.80</td>
<td>77</td>
<td>23.8</td>
</tr>
<tr>
<td>AO 3 Control</td>
<td>1.85</td>
<td>88</td>
<td>25.7</td>
</tr>
<tr>
<td>AO 4</td>
<td>1.83 (pre-amputation)</td>
<td>59 (post-amputation)</td>
<td>N/A</td>
</tr>
<tr>
<td>AO 4 Control</td>
<td>1.88</td>
<td>83</td>
<td>23.5</td>
</tr>
<tr>
<td>AO 5</td>
<td>1.65</td>
<td>90</td>
<td>33.1</td>
</tr>
<tr>
<td>AO 5 Control</td>
<td>1.65</td>
<td>58</td>
<td>21.3</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user
4.2 RADIOLOGIST’S REPORT ON THE CT SCAN

In general, the radiologists detected more shoulder pathology on the CT scans of the wheelchair user subjects than on those of the able-bodied controls.

4.2.1 Wheelchair User Subjects

All but one of the wheelchair user subjects were found to have a well maintained glenohumeral joint; the exception being a 73 year old male (AO 4). This subject was found to have moderately advanced degenerative changes in the glenohumeral joint including joint space narrowing, however it is important to note that this subject (AO 4) was approximately 20 years older than the other adulthood-onset subjects. With respect to the rest of the shoulder complex, some degree of degenerative change was found in three of the five adulthood-onset wheelchair users. Two of these subjects (AO 1 and AO 2) were found to have mild degenerative changes at the acromioclavicular joint (Figure 2-1). The third subject (AO 3) was reported to have minimal cystic changes in the subcortical posterior glenoid and in the greater tuberosity of the humeral head. No pathology was detected on the CT scans of the three childhood-onset wheelchair users.

4.2.2 Able-Bodied Controls

The glenohumeral joint was reported to be well maintained for all of the able-bodied controls. The majority of these control subjects had no significant abnormality in the rest of the shoulder complex. Calcific tendonopathy of the rotator cuff tendon was reported for two of the control subjects (AO 1 Control and AO 4 Control). Mild osteophyte formation on the anterior glenoid cavity was reported for one control subject (AO 5 Control). Minimal subchondral cyst formation was detected on the antero-medial humeral head of another control subject (AO 3 Control).

4.3 PHYSICAL EXAMINATION

The physical examination revealed that every wheelchair user subject had some degree of shoulder abnormality (Table 4-4 and Table 4-5). Three subjects (CO 2, CO 3, and AO 1) reported low-grade intermittent discomfort in the neck and one subject (AO 3) had bilateral muscular tightness. Mild restriction of neck movement was found in six subjects (CO 1, CO 2, AO 1, AO 3, AO 4, and AO 5). Examination of the spine revealed mild thoracic scoliosis in four subjects (CO 1, CO 2, AO 2, and AO 3). Severe scoliosis was diagnosed in one subject (CO 3). One
subject (AO 1) was diagnosed with mild kyphosis. Good seated posture (i.e. symmetric with level shoulders) was observed in all but two subjects (CO 1 and CO 3).

When asked by Dr. Pike about shoulder pain, five subjects (CO 1, CO 2, CO 3, AO 1, and AO 3) reported shoulder pain, ranging from occasional discomfort (CO 1), occasional and sudden sharp pain (CO 2), non-activity related moderate pain (AO 1 and AO 3), and pain associated with wheelchair sprinting (CO 3). One subject reported tingling in the shoulder joint (AO 3), while clicking was found in the shoulders of three subjects (CO 2, AO 1, and AO 3).

The sternoclavicular joint was normal for all subjects. Crepitus was diagnosed in the acromioclavicular joint of one childhood-onset wheelchair user (CO 2) and four adulthood-onset wheelchair users (AO 1, AO 3, AO 4, and AO 5). Mild bilateral scapular winging was diagnosed in two subjects (CO 2 and AO 1). Muscular strength was normal in all subjects, with the exception of the two quadriplegic subjects (CO 2 and AO 1) who were found to have 80% of normal strength (i.e. were given a grade of 4/5). The global range of motion (ROM) assessed with the total active elevation test (i.e. tests the ability to actively raise one’s arms), revealed a bilateral ROM of 165º or more for all six paraplegic subjects (CO 1, CO 3, AO 2, AO 3, AO 4, and AO 5). The two quadriplegic subjects had somewhat less ROM: 150º left/160º right (CO 2), and 80º left/110º right (AO 1).

The Neer test for impingement of the rotator cuff tendons was negative for all subjects, with the exception of one adulthood-onset wheelchair user (AO 1). The Hawkins test, which tests for subacromial impingement and rotator cuff tendinitis, was negative for all subjects except two adulthood-onset wheelchair users (AO 1 and AO 3). The painful arc test was positive for one subject only (AO 1), indicating tissue impingement beneath the coracoacromial arch. The sulcus test revealed a normal amount of inferior glenohumeral joint laxity in all subjects. The anterior-posterior glide test revealed a normal amount of glenohumeral joint laxity in the anterior-posterior plane in one subject (AO 2) and slightly greater laxity in all other subjects.
### Table 4-4 - Physical Examination Findings (1 of 2)*

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Neck Pain</th>
<th>Neck Exam</th>
<th>Spine Exam</th>
<th>Posture</th>
<th>Shoulder Pain</th>
<th>Sterno-clavicular Joint</th>
<th>Acromio-clavicular Joint</th>
<th>Scapular Winging</th>
<th>Strength (out of 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO 1</td>
<td>None</td>
<td>Mild restriction</td>
<td>Mild thoracic scoliosis</td>
<td>Upper trunk shifted left</td>
<td>Occasional discomfort</td>
<td>Normal</td>
<td>Normal</td>
<td>None</td>
<td>5/5 all</td>
</tr>
<tr>
<td>CO 2</td>
<td>Low-grade discomfort</td>
<td>Mild restriction</td>
<td>Mild thoracic scoliosis</td>
<td>Symmetric, shoulders level</td>
<td>Occasional sharp pain, clicking</td>
<td>Normal</td>
<td>Crepitus</td>
<td>Mild bilateral</td>
<td>ER, IR, abduction 4/5 left arm</td>
</tr>
<tr>
<td>CO 3</td>
<td>Low-grade discomfort</td>
<td>Normal</td>
<td>Major scoliosis</td>
<td>Shoulders level in chair because scoliosis curves offset</td>
<td>Occasional pain with wheelchair sprinting</td>
<td>Normal</td>
<td>Normal</td>
<td>None</td>
<td>5/5 all</td>
</tr>
<tr>
<td>AO 1</td>
<td>Low-grade discomfort</td>
<td>Mild restriction</td>
<td>Mild kyphosis</td>
<td>Symmetric, shoulders level</td>
<td>Moderate pain, clicking</td>
<td>Normal</td>
<td>Crepitus</td>
<td>Mild bilateral</td>
<td>ER 4/5 bilateral</td>
</tr>
<tr>
<td>AO 2</td>
<td>None</td>
<td>Normal</td>
<td>Mild thoracic scoliosis</td>
<td>Symmetric, shoulders level</td>
<td>None</td>
<td>Normal</td>
<td>Normal</td>
<td>None</td>
<td>5/5 all</td>
</tr>
<tr>
<td>AO 3</td>
<td>Bilateral muscular tightness</td>
<td>Mild restriction</td>
<td>Mild thoracic scoliosis</td>
<td>Symmetric, shoulders level</td>
<td>Moderate pain, tingling, clicking</td>
<td>Normal</td>
<td>Crepitus</td>
<td>None</td>
<td>5/5 all</td>
</tr>
<tr>
<td>AO 4</td>
<td>None</td>
<td>Mild restriction</td>
<td>Normal</td>
<td>Symmetric, shoulders level</td>
<td>None</td>
<td>Normal</td>
<td>Crepitus</td>
<td>None</td>
<td>5/5 all</td>
</tr>
<tr>
<td>AO 5</td>
<td>None</td>
<td>Mild restriction</td>
<td>Normal</td>
<td>Symmetric, shoulders level</td>
<td>None</td>
<td>Normal</td>
<td>Crepitus</td>
<td>None</td>
<td>5/5 all</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user, ER = external rotation, IR = internal rotation,

*pathological findings shaded grey
<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Total Active Elevation (max 180°)</th>
<th>Neer Test</th>
<th>Hawkins Test</th>
<th>Sulcus Test (&lt;0.5 cm = normal)</th>
<th>Anterior-Posterior Glide</th>
<th>Distal Motor (out of 5)</th>
<th>Distal Sensory</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO 1</td>
<td>165° bilateral</td>
<td>Negative</td>
<td>Negative</td>
<td>&lt;0.5 cm</td>
<td>Slight laxity</td>
<td>5/5 all</td>
<td>Normal</td>
</tr>
<tr>
<td>CO 2</td>
<td>150° left, 160° right</td>
<td>Negative</td>
<td>Negative</td>
<td>&lt;0.5 cm</td>
<td>Slight laxity</td>
<td>3/5 left, 5/5 right</td>
<td>Normal</td>
</tr>
<tr>
<td>CO 3</td>
<td>165° bilateral</td>
<td>Negative</td>
<td>Negative</td>
<td>&lt;0.5 cm</td>
<td>Slight laxity</td>
<td>5/5 all</td>
<td>Normal</td>
</tr>
<tr>
<td>AO 1</td>
<td>80° left, 110° right</td>
<td>Positive</td>
<td>Positive</td>
<td>&lt;0.5 cm</td>
<td>Slight laxity</td>
<td>3/5 left, 5/5 right</td>
<td>Normal</td>
</tr>
<tr>
<td>AO 2</td>
<td>170° bilateral</td>
<td>Negative</td>
<td>Negative</td>
<td>&lt;0.5 cm</td>
<td>No laxity</td>
<td>5/5 all</td>
<td>Normal</td>
</tr>
<tr>
<td>AO 3</td>
<td>170° bilateral</td>
<td>Negative</td>
<td>Positive</td>
<td>&lt;0.5 cm</td>
<td>Slight laxity</td>
<td>5/5 all</td>
<td>Normal</td>
</tr>
<tr>
<td>AO 4</td>
<td>170° bilateral</td>
<td>Negative</td>
<td>Negative</td>
<td>&lt;0.5 cm</td>
<td>Slight laxity</td>
<td>5/5 all</td>
<td>Normal</td>
</tr>
<tr>
<td>AO 5</td>
<td>170° bilateral</td>
<td>Negative</td>
<td>Negative</td>
<td>&lt;0.5 cm</td>
<td>Slight laxity</td>
<td>4/5 C7-T1</td>
<td>Slight decreased light touch sensation from C7-T1 dermatomes</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user

*pathological findings shaded grey
4.4 QUESTIONNAIRES

Shoulder pain, physical activity, and dietary calcium intake questionnaire responses from the wheelchair user subjects and the able-bodied controls are summarized in Table 4-6 and described in detail in the following sections. The questionnaire data were analyzed descriptively, but not for statistical significance.

Table 4-6 - Summary of Questionnaire Data (mean ± SD)

<table>
<thead>
<tr>
<th>Subject Groups</th>
<th>Pain</th>
<th>Physical Activity</th>
<th>Calcium Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WUSPI Shoulder Pain (max. 150)</td>
<td>BPI General Pain (max. 70)</td>
<td>quick DASH Arm Pain (max. 100)</td>
</tr>
<tr>
<td>CO</td>
<td>11 ± 7</td>
<td>4 ± 4</td>
<td>N/A</td>
</tr>
<tr>
<td>AO</td>
<td>31 ± 32</td>
<td>11 ± 11</td>
<td>N/A</td>
</tr>
<tr>
<td>CO Controls</td>
<td>N/A</td>
<td>N/A</td>
<td>2 ± 3</td>
</tr>
<tr>
<td>AO Controls</td>
<td>N/A</td>
<td>N/A</td>
<td>1 ± 1</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user

4.4.1 Pain Questionnaires

Shoulder pain, general body pain and wheeling habits were measured for the wheelchair user subjects, while shoulder pain alone was measured for the able-bodied controls.

4.4.1.1 Wheelchair User’s Shoulder Pain Index

On average, the childhood-onset wheelchair user subjects reported less shoulder pain interference during functional tasks than the adulthood-onset subjects. The mean ± SD Wheelchair User’s Shoulder Pain Index (WUSPI) score was 11 ± 7 for the childhood-onset wheelchair users and 31 ± 32 for the adulthood-onset wheelchair users (Table 4-6). The variance is large for the adulthood-onset group because two of the five adulthood-onset wheelchair users reported no shoulder pain (Table 4-7).
Table 4-7 -Wheelchair User Subjects' Questionnaire Data

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>WUSPI Shoulder Pain Score (maximum 150)</th>
<th>BPI General Pain Score (maximum 70)</th>
<th>PASIPD Physical Activity Score (MET-hrs/day)</th>
<th>FFQ Dietary Calcium Intake Score (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO 1</td>
<td>18</td>
<td>3</td>
<td>23</td>
<td>589</td>
</tr>
<tr>
<td>CO 2</td>
<td>5</td>
<td>0</td>
<td>23</td>
<td>962</td>
</tr>
<tr>
<td>CO 3</td>
<td>11</td>
<td>8</td>
<td>52</td>
<td>1040</td>
</tr>
<tr>
<td>AO 1</td>
<td>39</td>
<td>9</td>
<td>8</td>
<td>379</td>
</tr>
<tr>
<td>AO 2</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>277</td>
</tr>
<tr>
<td>AO 3</td>
<td>76</td>
<td>27</td>
<td>35</td>
<td>1477</td>
</tr>
<tr>
<td>AO 4</td>
<td>41</td>
<td>17</td>
<td>16</td>
<td>877</td>
</tr>
<tr>
<td>AO 5</td>
<td>0</td>
<td>4</td>
<td>10</td>
<td>1006</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user

4.4.1.2 Brief Pain Inventory

On average, the childhood-onset wheelchair user subjects reported less general body pain than the adulthood-onset subjects. The mean ± SD general body pain score, measured with the Brief Pain Inventory (BPI) questionnaire for SCI populations, was 4 ± 4 for the childhood-onset and 11 ± 11 for the adulthood-onset wheelchair users (Table 4-6). Individual BPI scores are listed in Table 4-7.

4.4.1.3 General Lifestyles Questionnaire

In general, the childhood-onset wheelchair users and the adulthood-onset wheelchair users reported similar wheelchair use. The responses to the General Lifestyles Questionnaire, used to assess the wheeling habits of the wheelchair user subjects, are summarized in Table 4-8 with infrequent responses shaded grey.
<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Time spent in WC (hrs/day)</th>
<th>Distance wheeled daily (km)</th>
<th>Get help wheeling uphill? (Y/N)</th>
<th>Lift WC into car? (Y/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO 1</td>
<td>14</td>
<td>&lt; 0.5</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>CO 2</td>
<td>2-4**</td>
<td>&lt; 0.5</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>CO 3</td>
<td>8-10</td>
<td>1</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>AO 1</td>
<td>17</td>
<td>&lt; 0.5</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>AO 2</td>
<td>9-10</td>
<td>&lt; 0.5</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>AO 3</td>
<td>16-18</td>
<td>2 - 5</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>AO 4</td>
<td>10</td>
<td>&lt; 0.5</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>AO 5</td>
<td>16</td>
<td>0</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair user, AO = adulthood-onset wheelchair user, WC = wheelchair; *infrequent responses shaded grey, **household ambulator

4.4.1.4 Disabilities of the Arm, Shoulder and Hand Questionnaire

Both able-bodied control groups experienced very minimal arm, shoulder or hand pain. Of a maximum possible score of 100, the mean ± SD quick DASH score was 2 ± 3 for the childhood-onset controls and 1 ± 1 for the adulthood-onset controls (Table 4-6). The two questions that did elicit a positive response were whether the individual had difficulties 1) opening a tight jar, or 2) with recreational sports like golf and tennis. The three female subjects (CO 3 control, AO 2 control, and AO 5 control) indicated that they had ‘mild difficulty’ with these activities, however this is more likely due to a lack of muscular strength or skill than due to pain. A 73 year old male subject (AO 4 control) indicated that he experienced mild shoulder pain while working at the computer. All other control subjects reported no difficulty or pain in performing tasks with their arms, hands or shoulders (Table 4-9).
Table 4-9 - Able-Bodied Control Subjects' Questionnaire Data

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>quick DASH Pain Score (maximum 100)</th>
<th>IPAQ Physical Activity Score (MET-hrs/day)</th>
<th>FFQ Dietary Calcium Intake Score (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO 1 Control</td>
<td>0</td>
<td>8</td>
<td>1174</td>
</tr>
<tr>
<td>CO 2 Control</td>
<td>0</td>
<td>10</td>
<td>1105</td>
</tr>
<tr>
<td>CO 3 Control</td>
<td>5</td>
<td>8</td>
<td>533</td>
</tr>
<tr>
<td>AO 1 Control</td>
<td>0</td>
<td>6</td>
<td>370</td>
</tr>
<tr>
<td>AO 2 Control</td>
<td>2</td>
<td>9</td>
<td>1099</td>
</tr>
<tr>
<td>AO 3 Control</td>
<td>0</td>
<td>7</td>
<td>316</td>
</tr>
<tr>
<td>AO 4 Control</td>
<td>2</td>
<td>2</td>
<td>557</td>
</tr>
<tr>
<td>AO 5 Control</td>
<td>2</td>
<td>14</td>
<td>1259</td>
</tr>
</tbody>
</table>

CO Control = control for childhood-onset wheelchair user, AO Control = control for adulthood-onset wheelchair user

4.4.2 Physical Activity Questionnaires

4.4.2.1 Physical Activity Scale for Individuals with Physical Disabilities

The results from the self-reported Physical Activity Scale for Individuals with Physical Disabilities (PASIPD) questionnaire showed that the childhood-onset wheelchair users were more physically active than the adulthood-onset wheelchair users. Of a maximum possible score of 200 MET-hrs/day, the mean ± SD physical activity score was 33 ± 16 for the childhood-onset group and 15 ± 12 for the adulthood-onset group (Table 4-6). Individual PASIPD scores are given in Table 4-7.

4.4.2.2 International Physical Activity Questionnaire

Physical activity levels were similar between the childhood-onset control subjects and the adulthood-onset control subjects. The mean ± SD physical activity scores (MET-hrs/day), measured with the International Physical Activity Questionnaire (IPAQ), were 9 ± 1 for the childhood-onset control subjects and 8 ± 4 for the adulthood-onset control subjects (Table 4-6). Individual IPAQ scores are presented in Table 4-9.
4.4.3 Food Frequency Questionnaire

Dietary calcium intake varied considerably between subjects however group means were similar between the four subject groups. The mean ± SD dietary calcium intake scores (mg/day), assessed using the self-report food frequency questionnaire (FFQ) were 864 ± 241 for the childhood-onset wheelchair users, 803 ± 489 for the adulthood-onset wheelchair users, 937 ± 352 for the able-bodied controls for the childhood-onset group, and 720 ± 432 for the able-bodied controls for the adulthood-onset group (Table 4-6). Individual scores for daily dietary calcium intake are given in Table 4-7 for the wheelchair user subjects and in Table 4-9 for the able-bodied controls.

PART B: BONE MORPHOLOGY RESULTS

Part B presents the bone morphology results measured with quantitative Computed Tomography and the bone density distribution results assessed with a modified Computed Tomography Osteoabsorptiometry method.

4.5 QUANTITATIVE COMPUTED TOMOGRAPHY

4.5.1 Conversion Equations

The relationship between CT scan intensity and equivalent volumetric bone mineral density, defined by the conversion equation, was very similar for all subjects (Figure 4-1). The conversion equation is defined by the CT scanner properties, the scanning protocol, and by the body composition of the individual being scanned, and as a result, the conversion equation is subject-specific. The conversion equations for two subjects (CO 1 and CO 3 Control) yielded a slightly lower equivalent vBMD than the other subjects for a given CT intensity (HU) (Figure 4-1).
4.5.2 Statistical Analysis of Bone Mineral Density

Volumetric bone mineral density was measured at five sites (Table 4-10), three of which were included in the two-way analysis of variance with main effects of age group (i.e. childhood-onset vs. adulthood-onset) and mobility type (i.e. wheelchair users vs. able-bodied controls) (Table 4-1). These sites were the humeral head trabecular bone, the glenoid subchondral bone, and the glenoid trabecular bone.
### Table 4-10 - Summary of vBMD Results (mg/cm³ K₂HPO₄)

| Subject Group | Humeral Head | | | Glenoid | | |
|---------------|--------------|--------------|--------------|--------------|--------------|
|               | Mean ± SD vBMD of total bone | Mean ± SD vBMD of trabecular bone | Mean ± SD vBMD of AS ROIs | Mean ± SD vBMD of subchondral bone | Mean ± SD vBMD of trabecular bone |
| CO            | 176 ± 83     | 112 ± 56     | 181 ± 81     | 642 ± 129    | 229 ± 93     |
| AO            | 144 ± 35     | 79 ± 29      | 156 ± 43     | 701 ± 124    | 173 ± 56     |
| CO controls   | 192 ± 40     | 132 ± 32     | 194 ± 39     | 684 ± 102    | 267 ± 41     |
| AO controls   | 166 ± 39     | 101 ± 33     | 161 ± 35     | 823 ± 108    | 187 ± 52     |

CO = childhood-onset wheelchair users, AO = adulthood-onset wheelchair users, AS ROIs = Articular Surface Regions of Interest

### 4.5.2.1 Humeral Head Trabecular vBMD

For the number of subjects tested, the mean value of the humeral head trabecular vBMD was not significantly different between the childhood-onset groups (122.21 ± 42.27) and the adulthood-onset groups (90.07 ± 31.46) \( F(1, 12)=2.91, p = 0.11 \). The mean value of humeral head trabecular vBMD was not significantly different between the wheelchair users (91.40 ± 40.88) and the able-bodied controls (112.85 ± 34.18) \( F(1, 12)=1.27, p = 0.28 \). The interaction effect between age group and mobility type was also non-significant \( F(1, 12)=0.0016, p = 0.97 \).

### 4.5.2.2 Glenoid Cavity Subchondral vBMD

For the number of subjects tested, the mean value of the glenoid cavity subchondral vBMD was not significantly different between the childhood-onset groups (662.69 ± 106.55) and the adulthood-onset groups (761.76 ± 126.98) \( F(1, 12)=2.73, p = 0.12 \). The mean value of the glenoid cavity subchondral vBMD was not significantly different between the wheelchair users (678.49 ± 120.35) and the able-bodied controls (770.72 ± 121.46) \( F(1, 12)=1.88, p = 0.20 \). The interaction effect between age group and mobility type was also non-significant \( F(1, 12)=0.44, p = 0.52 \).
4.5.2.3 Glenoid Cavity Trabecular vBMD

For the number of subjects tested, the mean value of the glenoid cavity trabecular vBMD was not significantly different between the childhood-onset groups (247.89 ± 67.79) and the adulthood-onset groups (179.75 ± 51.39) \([F(1, 12)=4.74, p = 0.0502]\), however the difference bordered on statistical significance based on our definition of \(p < 0.05\). The mean value of the glenoid cavity trabecular vBMD was not significantly different between the wheelchair users (193.87 ± 71.50) and the able-bodied controls (216.74 ± 61.28) \([F(1, 12)=0.68, p = 0.43]\). The interaction effect between age group and mobility type was also non-significant \([F(1, 12)=0.14, p = 0.71]\).

4.5.3 Statistical Analysis of Bone Cross-Sectional Area

Normalized cross-sectional area was measured at five sites (Table 4-11), two of which were included in the statistical analysis. These sites were the humeral head total bone and glenoid subchondral bone.

| Table 4-11- Summary of Bone Normalized Cross-Sectional Area Results (mm\(^2\)/m) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Subject Group   | CO              | CO controls     | AO              | AO controls     |
| Humeral Head    | Mean ± SD       | Mean ± SD       | Mean ± SD       | Mean ± SD       |
|                 | cortical nCSA   | trabecular nCSA | total nCSA      | subchondral nCSA|
|                 | 167 ± 36        | 826 ± 135       | 1000 ± 149      | 34 ± 4           |
|                 | 159 ± 29        | 768 ± 124       | 928 ± 140       | 24 ± 2           |
| Glenoid         |                 |                 |                 |                 |
|                 | 171 ± 20        | 819 ± 118       | 990 ± 137       | 28 ± 7           |
|                 | 166 ± 17        | 794 ± 91        | 961 ± 103       | 22 ± 5           |
|                 |                 |                 |                 | 114 ± 22         |

CO = childhood-onset wheelchair users, AO = adulthood-onset wheelchair users, nCSA = normalized cross-sectional area

4.5.3.1 Humeral Head Total Bone Normalized Cross-Sectional Area

For the number of subjects tested, the mean value of the humeral head total bone normalized cross-sectional area was not significantly different between the childhood-onset groups (994.74 ± 127.98) and the adulthood-onset groups (944.16 ± 117.20) \([F(1, 12)=0.57, p = 0.47]\). The mean value of the humeral head total bone normalized cross-sectional area was not significantly different between the wheelchair users (954.66 ± 137.70) and the able-bodied controls (971.59 ± 107.72) \([F(1, 12)=0.03, p = 0.87]\). The interaction effect between age group and mobility type was also non-significant \([F(1, 12)=0.10, p = 0.76]\).
4.5.3.2 Glenoid Subchondral Bone Normalized Cross-Sectional Area

The mean value of the glenoid subchondral normalized cross-sectional area was significantly greater in the childhood-onset groups (30.70 ± 6.37) than in the adulthood-onset groups (23.08 ± 3.65) \[F(1, 12)=10.16, \ p = 0.008\] (Figure 4-2). For the number of subjects tested, the mean value of the glenoid subchondral normalized cross-sectional area was not significantly different between the wheelchair users (27.57 ± 5.88) and the able-bodied controls (24.30 ± 6.05) \[F(1, 12)=2.63, \ p = 0.13\]. The interaction effect between age group and mobility type was also non-significant \[F(1, 12)=1.05, \ p = 0.33\].

![Glenoid Subchondral Bone CSA](image)

* Figure 4-2 – Two-way ANOVA main effect of age group on glenoid subchondral cross-sectional area.

4.5.4 Descriptive Analysis of Bone Mineral Density

The control groups displayed a trend towards higher equivalent vBMD than the manual wheelchair user groups to which they were matched (Table 4-10). At four of the five sites where vBMD was measured, the controls for the childhood-onset wheelchair users had the highest vBMD of all four subject groups. These four sites were the total, trabecular and articular surface ROIs of the humeral head, and the trabecular bone of the glenoid cavity. For the subchondral bone of the glenoid cavity, however, the controls for the adulthood-onset wheelchair users had the greatest vBMD. These trends are merely descriptive as no statistical analysis was performed on the results presented in this section.
Chapter 4: Results

Ranking the subject groups in descending order of vBMD produced the following trend for four of the five measurement sites:

1. controls for the childhood-onset wheelchair users (CO controls)
2. childhood-onset wheelchair users (CO)
3. controls for the adulthood-onset wheelchair users (AO controls)
4. adulthood-onset wheelchair users (AO)

For the fifth measurement site, the subchondral bone of the glenoid cavity, the descending-vBMD ranking order was:

1. controls for the adulthood-onset wheelchair users (AO controls)
2. adulthood-onset wheelchair users (AO)
3. controls for the childhood-onset wheelchair users (CO controls)
4. childhood-onset wheelchair users (CO)

Detailed descriptive vBMD results for the subregions of the humeral head and the glenoid cavity are presented in the following sections.

4.5.4.1 Humeral Head

The mean number of CT slices in the humeral head segmentation range (section 3.8.1.1) of all subjects and controls was 47, thus there were on average 12 slices in each subdivision (H1-H4). For each individual, the average vBMD value was determined for each subdivision by computing the mean vBMD of the 12 slices.

The mean vBMD calculated for the total bone (cortical and trabecular bone) (Figure 4-3) was approximately twice that of the trabecular bone alone (Figure 4-4). Comparing vBMD across the four subdivisions of the humeral head, both total bone (Figure 4-3) and trabecular bone (Figure 4-4) had the highest vBMD in the superior quarter of the humeral head (H4).
Figure 4-3 – Equivalent vBMD of total bone of the humeral head.

Figure 4-4 – Equivalent vBMD of trabecular bone of the humeral head.
For the articular surface regions of interest (AS ROIs), both wheelchair user groups (i.e. childhood-onset and adulthood-onset) displayed a trend towards having higher volumetric bone mineral density in region 1 (AS 1) than in region 2 (AS 2) (Figure 4-5). These articular surface regions include only trabecular bone, with region 1 corresponding to the antero-medial aspect of the humeral head, and region 2 corresponding to the postero-medial aspect of the humeral head.

![Humeral Head Articular Surface ROI vBMD](image)

*Figure 4-5 – Equivalent vBMD of trabecular bone of the articular surface ROIs of the humeral head.*

As described in section 3.8.1.2, the articular surface ROIs consisted of trabecular bone segmented near the articular surface of the humeral head on the middle slice of the humeral head segmentation region (H1-H4). For all subject groups, the articular surface ROIs displayed higher vBMD than the full trabecular bone segmentation for either H2 or H3 (i.e. the middle subdivisions) (Figure 4-4), indicating a trend towards higher trabecular bone vBMD nearest to the articular surface of the humeral head.
4.5.4.2 Glenoid Cavity

The mean number of CT slices in the glenoid segmentation range (section 3.8.1.4) of all subjects and controls was 65, thus there were on average 22 slices in each subregion (i.e. inferior, middle, and superior) (Figure 3-13A). For each individual, the average vBMD value was determined for each subregion by computing the mean vBMD of the 22 slices.

The glenoid cavity subchondral bone showed a trend towards higher vBMD in the older subjects (i.e. adulthood-onset wheelchair users and controls) than in the younger subjects (i.e. childhood-onset wheelchair users and controls) (Table 4-10). The vBMD of the subchondral bone plate of the glenoid cavity (Figure 4-6) was on the order of 3-4 times higher than the vBMD of the total and trabecular bone of the humeral head (Figure 4-3 and Figure 4-4). For all four subject groups, glenoid subchondral vBMD was highest in the middle subregion (Figure 4-6).

![Figure 4-6 – Equivalent vBMD of subchondral bone of the glenoid cavity.](image)
The vBMD of the glenoid subchondral bone plate was, on average, 2-3 times higher than the vBMD of the glenoid trabecular bone (Figure 4-7). As was observed for the vBMD of the subchondral bone, the vBMD of the trabecular bone was also highest in the middle subregion of the glenoid cavity (Figure 4-7).

![Glenoid Trabecular vBMD](image)

Figure 4-7 – Equivalent vBMD of trabecular bone of the glenoid cavity.

4.5.5 Descriptive Analysis of Cross-sectional Area

The younger subjects (i.e. childhood-onset wheelchair users and controls) displayed a trend towards having greater normalized cross-sectional area than the older subjects (i.e. adulthood-onset wheelchair users and controls) at four of the five measurement sites (Table 4-11). These four sites were the humeral head cortical, trabecular, and total bone, and the glenoid trabecular bone. At the fifth site, the glenoid subchondral bone, the adulthood-onset wheelchair users and controls had greater normalized cross-sectional area than the childhood-onset wheelchair users and controls.
4.5.5.1 Humeral Head

The normalized cross-sectional area of the total bone was very similar for all subject groups for all of the humeral head subdivisions. The normalized cross-sectional area of the total bone was highest in the middle subdivisions of the humeral head (H2 and H3) (Figure 4-8). With the exception of the lowest quarter of the humeral head (H1), normalized cross-sectional area of the total bone showed a trend towards being slightly greater in the younger subjects (i.e. childhood-onset wheelchair users and controls) than in the older subjects (i.e. adulthood-onset wheelchair users and controls).

![Humeral Head Total Bone CSA](image)

**Figure 4-8 – Normalized cross-sectional area of the humeral head total bone.**

The normalized cross-sectional area of the cortical bone was also very similar between the subject groups and remained somewhat constant across all humeral head subdivisions (H1-H4) (Figure 4-9). With the exception of the most superior quarter of the humeral head (H4), normalized cross-sectional area of the cortical bone was slightly greater in the younger subjects (i.e. childhood-onset wheelchair users and controls) than in the older subjects (i.e. adulthood-onset wheelchair users and controls).
The normalized cross-sectional area of the humeral head trabecular bone displayed the same trend as that of the total bone: it was highest in the two middle subdivisions of the humeral head (H2 and H3) (Figure 4-10). With the exception of the inferior quarter of the humeral head (H1), the normalized cross-sectional area of the trabecular bone was slightly greater in the younger subjects (i.e. childhood-onset wheelchair users and controls) than in the older subjects (i.e. adulthood-onset wheelchair users and controls).
4.5.5.2 Glenoid Cavity

For all subject groups, the normalized cross-sectional area of the glenoid subchondral bone plate was greatest in the middle region (Figure 4-11).
For the glenoid trabecular bone, the normalized cross-sectional area was similar between the inferior and middle regions and was lower in the superior region (Figure 4-12).
4.6 COMPUTED TOMOGRAPHY OSTEOABSORPTIOMETRY

No clear bone density distribution patterns were found for the articular surfaces of the glenohumeral joint using a modified Computed Tomography Osteoabsorptiometry (CT-OAM) method, however all subjects displayed higher vBMD on the glenoid than on the humeral head.

4.6.1 Glenoid Cavity

No clear trend of glenoid mineralization emerged from the CT-OAM results for the childhood-onset wheelchair users and their controls (Figure 4-13) or for the adulthood-onset wheelchair users and their controls (Figure 4-14). The right glenoid is shown for all subjects except one (CO 1) who was left-handed and therefore had his left shoulder scanned. In Figure 4-13, however, his left glenoid is viewed as a right glenoid to facilitate comparisons with the other right glenoid cavities.

All three childhood-onset wheelchair users demonstrated an anterior density maximum in the glenoid cavity. Subject CO 3 demonstrated high vBMD across the majority of the glenoid surface, whereas CO 1 did not. The former subject (CO 3) was a very active wheelchair athlete.
with approximately double the self-reported physical activity score of the other childhood-onset wheelchair subjects (Table 4-7). Two childhood-onset controls (CO 2 Control and CO 3 Control) also displayed an anterior glenoid density maximum, whereas one childhood-onset control (CO 1 Control) displayed a superior-central density maximum.

No single pattern of mineralization was common among the adulthood-onset wheelchair users (Figure 4-14). Three subjects (AO 1, AO 3, and AO 4) displayed an anterior density maximum, whereas two subjects (AO 2 and AO 5) appeared to have a more centrally located density maximum. Four of the five adulthood-onset control subjects (AO 1 Control, AO 2 Control, AO 3 Control, and AO 5 Control) displayed a centrally located high density region. Of these, two subjects (AO 2 Control and AO 5 Control) had central-superior regions of maximum density, one subject (AO 1 Control) had a central-inferior region of maximum density, and one subject (AO 3 Control) displayed maximum density across the majority of the glenoid surface. The fifth control subject (AO 4 Control) displayed a bicentric distribution of density with maxima located anteriorly and posteriorly.

4.6.2 Humeral Head

For all subjects, the bone of the articular surface of the humeral head was less densely mineralized than the subchondral bone of the glenoid cavity. The childhood-onset wheelchair users all displayed anterior density maxima on the humeral head (Figure 4-15, N.B. that a left humerus is displayed for CO 1). In contrast, the childhood-onset control subjects all displayed a central density maximum (Figure 4-15).

The location of the humeral head maximum density did not appear to follow a trend among the adulthood-onset wheelchair user subjects (Figure 4-16). Density maxima were located on the anterior aspect of the articular surface for two subjects (AO 4 and AO 5), centrally for two other subjects (AO 2 and AO 3), and inferiorly for one subject (AO 1). The bone density distribution of the humeral head in the adulthood-onset controls displayed two trends (Figure 4-16). Anterior density maxima were seen for two subjects (AO 2 Control and AO 5 Control), while central density maxima were seen for three subjects (AO 1 Control, AO 3 Control, and AO 4 Control).
Figure 4-13 – CT-OAM of the glenoid cavity for the childhood-onset (CO) wheelchair users and controls.

Figure 4-14 – CT-OAM of the glenoid cavity for the adulthood-onset (AO) wheelchair users and controls.
Figure 4-15 – CT-OAM of the humeral head for the childhood-onset wheelchair users and controls (N.B. A left humerus is shown for CO 1).

Figure 4-16 – CT-OAM of the humeral head for the adulthood-onset wheelchair users and controls.
PART C: CARTILAGE MORPHOLOGY RESULTS

Part C presents the cartilage morphology results measured with quantitative Magnetic Resonance Imaging.

4.7 QUANTITATIVE MAGNETIC RESONANCE IMAGING

Of the three parameters of cartilage morphology measured for the humeral head and the glenoid cavity (Table 4-12), only cartilage volume was analyzed statistically using a two-way analysis of variance with the main effects of age group and mobility type.

<table>
<thead>
<tr>
<th>Subject Groups</th>
<th>Humeral Head</th>
<th>Glenoid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td>Volume (mm³)</td>
<td>Surface Area (cm²)</td>
</tr>
<tr>
<td>CO Controls</td>
<td>2252.33 ± 333.01</td>
<td>18.66 ± 2.80</td>
</tr>
<tr>
<td>AO Controls</td>
<td>2100.60 ± 333.62</td>
<td>19.51 ± 4.91</td>
</tr>
<tr>
<td>CO Controls</td>
<td>2590.00 ± 130.22</td>
<td>21.13 ± 2.38</td>
</tr>
<tr>
<td>AO Controls</td>
<td>2260.40 ± 393.09</td>
<td>19.54 ± 2.65</td>
</tr>
</tbody>
</table>

CO = childhood-onset wheelchair users, AO = adulthood-onset wheelchair users

4.7.1 Statistical Analysis of Cartilage Morphology

4.7.1.1 Humeral Head Cartilage Volume

For the number of subjects tested, the mean value of the humeral head cartilage volume was not significantly different between the childhood-onset groups (2421.17 ± 292.14) and the adulthood-onset groups (2180.50 ± 353.89) \([F(1, 12)=1.98, p = 0.19]\) (Figure 4-17A). The mean value of the humeral head cartilage volume was not significantly different between the wheelchair users (2157.50 ± 318.52) and the able-bodied controls (2384.00 ± 349.63) \([F(1, 12)=2.11, p = 0.17]\).
The interaction effect between age group and mobility type was also non-significant [$F(1, 12)=0.27$, $p = 0.61$].

### 4.7.1.2 Glenoid Cavity Cartilage Volume

The mean value of the glenoid cavity cartilage volume was not significantly different between the childhood-onset groups (675.83 ± 118.24) and the adulthood-onset groups (700.40 ± 195.10) [$F(1, 12)=0.07$, $p = 0.79$] (Figure 4-17B). The mean value of the glenoid cavity cartilage volume was not significantly different between the wheelchair users (642.75 ± 115.15) and the able-bodied controls (739.63 ± 201.56) [$F(1, 12)=1.14$, $p = 0.31$]. The interaction effect between age group and mobility type was also non-significant [$F(1, 12)=0.001$, $p = 0.98$].

### 4.7.2 Descriptive Analysis of Cartilage Morphology

Cartilage surface area and thickness were not analyzed statistically however descriptive analyses of these results are presented in the following sections. The cartilage volume results, which were analyzed statistically, are also analyzed descriptively in the following sections.

### 4.7.2.1 Cartilage Volume

The differences in cartilage volume between the subject groups were not significant for either the humeral head or the glenoid cavity (Figure 4-17). The control subjects displayed a trend towards having slightly greater cartilage volume than the corresponding group of wheelchair users. In most cases, the standard deviation of the samples within each group exceeded the difference between group means.
4.7.2.2 Cartilage Surface Area

For the number of subjects studied, the surface areas of the humeral head and the glenoid cartilage plates were not different between the subject groups (Figure 4-18). In general, the control subjects displayed a trend towards having greater cartilage surface area than the corresponding group of wheelchair users. In most cases, the standard deviation of the samples within each group exceeded the difference between group means.
4.7.2.3 Cartilage Thickness

**Mean Cartilage Thickness**

For both the humeral head and the glenoid cavity, mean cartilage thickness was nearly identical between the subject groups (Figure 4-19).

![Figure 4-19](image)

*Figure 4-19 – Mean cartilage thickness of A) the humeral head (HH), B) the glenoid cavity.*
Maximum Cartilage Thickness

Very little difference was seen in the maximum cartilage thickness between the subject groups (Figure 4-20). The maximum cartilage thickness (Figure 4-20) was approximately twice the mean cartilage thickness (Figure 4-19).

**Figure 4-20 – Maximum cartilage thickness of A) the humeral head (HH), B) the glenoid cavity.**

**PART D: CORRELATIONS AND POWER ANALYSIS**

4.8  CORRELATIONS

4.8.1  Humeral Head and Glenoid Cavity vBMD Correlation

Volumetric bone mineral density was strongly correlated ($r = 0.94$, $p < 0.01$) between trabecular bone of the humeral head and of the glenoid cavity (Figure 4-21).
4.8.2 Bone Morphology and Questionnaire Data Correlations

Volumetric bone mineral density of trabecular bone of the humeral head was not associated with the wheelchair users’ WUSPI shoulder pain scores ($r = -0.09$, $p = 0.83$). Neither humeral head trabecular vBMD nor glenoid subchondral vBMD were correlated with the FFQ dietary calcium intake scores ($r = 0.46$, $p = 0.08$ and $r = 0.17$, $p = 0.52$, respectively). No association was found between the glenoid subchondral bone normalized cross-sectional area and the wheelchair users’ PASIPD physical activity scores ($r = 0.49$, $p = 0.22$), however an association was found between humeral head trabecular vBMD and the wheelchair users’ PASIPD physical activity scores ($r = 0.84$, $p < 0.01$) (Figure 4-22).
4.8.3 Bone Morphology and Wheelchair User Mass Correlations

Neither humeral head trabecular vBMD nor glenoid subchondral normalized cross-sectional area were associated with wheelchair users’ mass (kg) ($r = -0.02$, $p = 0.97$ and $r = -0.07$, $p = 0.86$, respectively).

4.8.4 vBMD and Cross-Sectional Area Correlations

For the humeral head, trabecular vBMD was not correlated with trabecular normalized cross-sectional area ($r = -0.37$, $p = 0.15$). For the glenoid cavity, no association was found between the subchondral vBMD and the subchondral normalized cross-sectional area ($r = -0.07$, $p = 0.79$).

4.8.5 Bone and Cartilage Morphology Correlations

No correlations were found between humeral head mean cartilage thickness and humeral head trabecular vBMD ($r = 0.39$, $p = 0.13$) or between glenoid mean cartilage thickness and glenoid
subchondral vBMD ($r = -0.12$, $p = 0.65$). No correlations were found between humeral head cartilage volume and humeral head trabecular vBMD ($r = 0.09$, $p = 0.73$) or between glenoid cartilage volume and glenoid subchondral vBMD ($r = -0.03$, $p = 0.92$). No correlations were found between humeral head cartilage surface area and humeral head trabecular vBMD ($r = -0.29$, $p = 0.28$) or between glenoid cartilage surface area and glenoid subchondral vBMD ($r = 0.06$, $p = 0.82$).

4.9 POWER ANALYSIS

This pilot study was not sufficiently powered to detect significant differences in bone and cartilage morphology between the subject groups. Based on the effect sizes and variances measured in this pilot study, sample size computations revealed that 22 subjects would be required in each wheelchair user group (i.e. childhood-onset and adulthood-onset) in order to detect differences (power = 0.80, $p < 0.05$) in bone morphology, specifically humeral head and glenoid cavity trabecular vBMD and glenoid cavity subchondral cross-sectional area (Table 4-13). To detect statistically significant differences (power = 0.80, $p < 0.05$) in cartilage morphology, 22 subjects would be required in each wheelchair user group to detect a difference in the humeral head cartilage thickness between childhood-onset and adulthood-onset wheelchair users (Table 4-13).
### Table 4-13 - Sample Size Estimates*

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Parameter</th>
<th>Sample size required</th>
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<tbody>
<tr>
<td>Bone</td>
<td>HH total vBMD</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>HH trabecular vBMD</td>
<td>22</td>
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<tr>
<td></td>
<td>Glenoid subchondral vBMD</td>
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<td>Glenoid trabecular vBMD</td>
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<td>HH trabecular bone nCSA</td>
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<td>HH mean cartilage thickness</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Glenoid mean cartilage thickness</td>
<td>250</td>
</tr>
</tbody>
</table>

HH = humeral head; vBMD = volumetric bone mineral density,  
nCSA = normalized cross-sectional area  
*suitable parameters for future studies are shaded grey

Although a full-scale cross-sectional study with 22 childhood-onset and 22 adulthood-onset wheelchair users would likely find statistically significant differences between these groups with respect to certain parameters of bone and cartilage morphology (Table 4-13), it is unknown whether these differences would be clinically significant. Given that wheelchair users’ shoulder pain motivated this research, clinical significance could be defined as morphological differences that equate to differences in shoulder pain. Pain is a subjective measure and inherently difficult to quantify and compare between individuals; therefore instead of discussing the clinical relevance of a parameter we will instead discuss its suitability for a full-scale study. We assume that parameters with a large effect size and a small variance are more likely to be relevant to shoulder pain within these groups of wheelchair users and therefore suggest that these parameters are suitable to include in future studies.
5 DISCUSSION

5.1 SUMMARY OF RESEARCH QUESTIONS AND HYPOTHESES

The primary goal of this pilot study was to implement and apply quantitative imaging techniques to assess bone and cartilage morphology at the glenohumeral joint of manual wheelchair users and able-bodied controls. Although shoulder pain is very prevalent in manual wheelchair users, its causes remain unknown.

This pilot study was performed to assess the feasibility of answering two research questions in a cross-sectional study:

1. Are there differences in bone and cartilage morphology at the glenohumeral joint between childhood-onset and adulthood-onset manual wheelchair users?
2. Are there differences in bone and cartilage morphology at the glenohumeral joint between long-term manual wheelchair users and their matched able-bodied controls?

We hypothesized that:

1. Humeral head and glenoid cavity trabecular bone mineral density are higher in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.
2. Glenoid subchondral normalized cross-sectional area is greater in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.
3. Glenoid subchondral bone mineral density is lower in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.
4. Volumetric bone mineral density is higher in the manual wheelchair users than in the able-bodied matched controls.
5. Humeral head and glenoid cartilage volumes are greater in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.

Despite modern imaging capabilities and the associated potential for gaining insight into the cause(s) of wheelchair users’ shoulder pain, very little research has focused on quantifying glenohumeral bone and cartilage morphology in wheelchair users. In this study, three image analysis techniques were implemented and applied: quantitative CT (qCT), CT Osteoabsorptiometry (CT-OAM), and quantitative MRI (qMRI). These techniques have been used independently to various degrees and in various populations; however we believe that this is the
first study to combine these techniques for an integrated assessment of glenohumeral bone and cartilage morphology.

5.2 HYPOTHESIS 1

*Humeral head and glenoid cavity trabecular bone mineral densities are higher in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.*

This hypothesis is based on the assumption that the childhood-onset wheelchair users had an adaptational advantage over the adulthood-onset wheelchair users, because the former began loading their shoulders via wheelchair use prior to skeletal maturity. Changes in loading are known to affect the vBMD of trabecular bone, and increased loading has been shown to result in increased trabecular bone mineral density. Immature bone is known to be more responsive to changes in loading than mature bone.

For both the humeral head and the glenoid cavity, trabecular vBMD was (non-significantly) higher in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users. Although vBMD of trabecular bone has not previously been quantified at the glenohumeral joint in childhood-onset and adulthood-onset manual wheelchair users, our findings are supported by the widely accepted theory that bone density increases throughout childhood and adolescence, peaks in early adulthood, plateaus, and decreases in late adulthood. In response to increased loading, bone’s adaptive capacity is much greater during the adolescent growth spurt than after maturity (84), which might also explain our non-significant finding of higher trabecular vBMD in the childhood-onset wheelchair users than the adulthood-onset wheelchair users. The magnitude of the difference in mean vBMD between the childhood-onset wheelchair users and the adulthood-onset wheelchair users was very similar to the magnitude of the difference in mean vBMD between the childhood-onset controls and the adulthood-onset controls (Figure 4-4 and Figure 4-7). This suggests that our non-significant finding is more likely due to known age-related changes in bone density than to differences in the functional adaptation of bone to wheelchair use.
5.2.1 Trabecular vBMD of the Humeral Head

In general, humeral head trabecular vBMD was higher in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users. Our sample size calculations estimate that a study with 22 childhood-onset wheelchair users and 22 adulthood-onset wheelchair users would detect a statistically significant difference in humeral head trabecular vBMD between these groups. Based on the effect sizes and variances of our pilot data, humeral head trabecular vBMD is likely a suitable parameter to include in a full-scale study of bone morphology in wheelchair users.

Our vBMD values for trabecular bone of the humeral head are in close agreement with the only previously published vBMD results for the humeral head. Using pQCT, Tingart et al. measured humeral head vBMD in 17 cadaveric specimens (mean age 71 years, range 59-98 years) (26). We compared their results to those of the adulthood-onset able-bodied controls in our study (mean age 53 years, range 42-73 years) since these two groups were believed to be the most similar in terms of age and mobility. Total and trabecular mean vBMD values from the present study were in the same range and had comparable variance (Figure 5-1 and Figure 5-2).

![Comparison to previously reported humeral head total vBMD](image)

*Figure 5-1 - Comparison of humeral head total vBMD values.*
Our vBMD values for trabecular bone generally lie within the widely accepted, and somewhat arbitrarily defined, density range of 90-1260 mg/cm$^3$ quoted in the literature (76). The vBMD values of trabecular bone found for the older subject groups in this study (i.e. the adulthood-onset wheelchair users and controls) were sometimes below 90 mg/cm$^3$, especially in the inferior portion of the humeral head (Figure 4-4). In our study, this low-density trabecular bone of the humeral head was included in our measurement of vBMD since manual segmentation was performed. It is important to note that a threshold-based automated segmentation of trabecular bone would have excluded voxels below the lower threshold (e.g. 90 mg/cm$^3$). Consequently, the reported mean vBMD for humeral head trabecular bone would have been overestimated with an automated segmentation technique. That both our total and trabecular vBMD values are lower than those reported by Tingart et al. may be in part attributable to methodological differences between studies. Tingart et al. acquired pQCT scans of older cadaveric humeral head specimens and used the scanner’s software to determine vBMD of the segmented total and trabecular bone regions. In contrast, we acquired CT scans from younger human subjects and then manually calculated the conversion from CT intensity to vBMD based on the CT intensity values of a bone density reference phantom. In addition, Tingart et al. scanned cadaveric humeral head specimens dissected free of soft tissue, whereas in our study, scans were acquired in vivo, therefore synovial...
joint fluid, muscle, and adipose tissue surrounded the humeral head bone. Although the in-plane resolution was similar between studies (0.46 x 0.46 mm\(^2\) in our study vs. 0.59 x 0.59 mm\(^2\) in Tingart et al.), slices were five times thinner in our study (0.5 mm vs. 2.5 mm in Tingart et al.)

The general trend observed for vBMD between the four subdivisions of the humeral head in our pilot data are in agreement with the recurring finding that bone mineral density is highest in the upper region of the humeral head (H4, Figure 4-3 and Figure 4-4). Saitoh et al. reported that trabecular bone in the superior portion of the humeral head has the greatest amount of bone mineral, based on results from dual-photon absorptiometry and bone mineral analyses (190). Similarly, we found that trabecular vBMD was highest, for all four subject groups, in the superior region of the humeral head (H4) (Figure 4-4). For trabecular and cortical bone, Tingart et al. reported that vBMD was highest in the superior quarter of the humeral head, and decreased in each inferior region (i.e. vBMD H4 > H3 > H2 > H1) (Figure 5-1 and Figure 5-2). In our study, trabecular vBMD followed this trend in the adulthood-onset control group (Figure 5-2), which is our subject group most comparable to that of Tingart et al., in terms of age and mobility type. This trend of decreasing vBMD with decreasing humeral head level was also observed for trabecular bone in the other subject groups (Figure 4-4). Similarly to Tingart et al., we generally saw an increase in total bone vBMD (i.e. trabecular and cortical bone) in the most inferior region (H1) (Figure 4-3). The H1 region is bordered inferiorly by the humeral shaft thus the increase in total bone vBMD seen in this region is consistent with the transition from less dense humeral head bone into highly dense cortical bone of the shaft. It is important to note that these findings are merely descriptive because differences in vBMD between humeral head subdivisions were not tested for statistical significance in the present study.

5.2.2 Trabecular vBMD of the Glenoid Cavity

Our non-significant finding that trabecular vBMD of the glenoid cavity was higher in younger subjects (i.e. childhood-onset wheelchair users and controls) than in older subjects (i.e. adulthood-onset wheelchair users and controls) is supported by the findings of Couteau et al. that CT intensity of the glenoid was higher in younger subjects than older subjects (24). These investigators did not convert CT intensity to an equivalent vBMD value, therefore no direct comparisons were made with the results from this study. Based on our sample size calculations, a study with 20 childhood-onset wheelchair users and 20 adulthood-onset wheelchair users would be powered to detect a statistically significant difference in glenoid trabecular vBMD between
these groups. The effect sizes and variances in our pilot data suggest that glenoid trabecular vBMD is likely a suitable parameter to include in a full-scale study of bone morphology in wheelchair users.

Our vBMD values for trabecular bone of the glenoid cavity lie within the widely accepted, and somewhat arbitrarily defined, density range of 90-1260 mg/cm$^3$ (76). For the adulthood-onset control group in this study, the trabecular vBMD values for the glenoid are similar to previously reported vBMD values for a similar subject group (i.e. able-bodied adults) in a study by Lehtinen et al. (27) (Figure 5-3). For the inferior and middle glenoid regions, our vBMD values are in close agreement with those of Lehtinen et al. For the superior glenoid region, the trabecular vBMD values for the adulthood-onset controls in this study are approximately 40% less than those reported by Lehtinen and colleagues. In general, there is less variance among our trabecular vBMD results than those of Lehtinen et al. Methodological differences between studies may, in part, explain these differences in reported trabecular vBMD. Lehtinen et al. acquired a single pQCT slice at the middle of each glenoid region (i.e. inferior, middle, and superior). In contrast, we scanned the entire glenoid cavity, divided the total number of slices by three, thereby assigning each slice to a glenoid region (i.e. inferior, middle, and superior), and subsequently segmented the five middle slices of each region. As a result, our trabecular vBMD results are an average of five 0.5 mm slices, whereas those reported by Lehtinen et al. are based on a single 2.5 mm slice. Consequently their reported vBMD values depend considerably on the location at which the pQCT slice was acquired.
The glenoid trabecular vBMD values for the adulthood-onset controls in this study are also supported by the findings of Mansat et al. (25) who measured the apparent density of glenoid trabecular bone samples (n = 74 from 6 healthy glenoids, ages not reported) by dividing the mass of the bone plug by its volume. These investigators reported a mean apparent density of 282 ± 60 mg/cm³, which is similar to our value of 267 ± 41 mg/cm³ for the childhood-onset controls (n = 3) (Table 4-10), but higher than our value of 187 ± 52 mg/cm³ for adulthood-onset controls (n = 5). The within group variances are less in our study. The difference in reported mean density is likely attributable to age differences between their specimens and our subjects, or to methodological differences: we measured vBMD using qCT, whereas Mansat et al. measured vBMD from mass and volume.

Our finding, for all subject groups, that the trabecular vBMD was highest in the middle region of the glenoid (Figure 4-7) is supported by the results from two other studies of trabecular bone density in healthy cadaveric glenoid specimens (24, 25) who reported that CT intensity was highest in the middle glenoid region.
5.3 HYPOTHESIS 2

Glenoid subchondral normalized cross-sectional area is greater in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.

This hypothesis is based on the assumption that the childhood-onset wheelchair users had an adaptational advantage over the adulthood-onset wheelchair users because they began wheeling prior to skeletal maturity. We hypothesized that glenoid subchondral cross-sectional area would be greater in these subjects because changes in loading are known to affect the geometry of cortical bone, and subchondral bone is considered to be a specialized form of cortical bone. Increased loading has been shown to result in increased cortical cross-sectional area and/or thickness.

In our pilot data, the normalized cross-sectional area of glenoid subchondral bone was significantly greater in the younger subjects (i.e. childhood-onset wheelchair users and controls) than in the older subjects (i.e. adulthood-onset wheelchair users and controls). No previously reported results of glenoid subchondral cross-sectional area were found with which to compare these results. For all glenoid regions (i.e. inferior, middle, and superior), the normalized cross-sectional area of the glenoid subchondral bone was highest in the childhood-onset wheelchair users. In our pilot data, the childhood-onset wheelchair users had higher glenoid subchondral normalized cross-sectional area relative to their controls, than did the adulthood-onset wheelchair users relative to their controls. The childhood-onset wheelchair users had the highest normalized cross-sectional area of all groups and the values for the three other groups were lower and relatively close to each other. This suggests that the higher normalized cross-sectional area of glenoid subchondral bone in the childhood-onset wheelchair users is related to adaptation and not to age.

For all subject groups, the normalized cross-sectional area of subchondral bone was greatest in the middle glenoid region (Figure 4-11), which is consistent with the known geometry of the glenoid cavity: the glenoid width is maximal in the middle region. Although glenoid anthropometry has been measured previously, no studies have reported the cross-sectional area of the subchondral bone plate. The most commonly reported measures are subchondral bone thickness, glenoid height, depth, radius of curvature, and shape (191-195).
5.4 HYPOTHESIS 3

Glenoid subchondral bone mineral density is lower in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.

Again, this hypothesis is based on the assumption that the childhood-onset wheelchair users had an adaptational advantage over the adulthood-onset wheelchair users, and therefore we hypothesized that their glenoid subchondral cross-sectional area increased (hypothesis #2) at the expense of vBMD (hypothesis #3). This hypothesis is based on a finding by Ashizawa et al. that periosteal bone cross-sectional area was negatively correlated to vBMD in the heavily loaded radius in the playing arm of competitive tennis players (34).

The non-significant trend observed in this study that glenoid subchondral volumetric bone mineral density was slightly lower in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users (Figure 4-6) and that normalized cross-sectional area was significantly higher in childhood-onset wheelchair users than in the adulthood-onset wheelchair users (hypothesis #2) is consistent with a finding reported by Ashizawa et al. These authors reported that periosteal cross-sectional area was negatively correlated to vBMD in the heavily loaded radii of competitive tennis players and hypothesized that the mid-radius bone size increased at the expense of bone density (34). In the current study, however, a negative correlation was not found between glenoid subchondral normalized cross-sectional area and vBMD (section 4.8.4). For all glenoid regions, subchondral vBMD was highest in the adulthood-onset control group and was lower, and relatively similar, for the other three subject groups. It is important to note that the within-group variances were larger than the differences between group means. Our sample size calculations show that 45 childhood-onset and 45 adulthood-onset subjects would be required to detect significantly higher vBMD in the latter group. Given the small effect sizes and the large variances between the adulthood-onset wheelchair users and the childhood-onset wheelchair users in this study (Figure 4-6), glenoid subchondral vBMD is not likely a suitable parameter to include in a full-scale study of bone morphology in manual wheelchair users.

The subchondral vBMD values for the adulthood-onset controls in this study were approximately 40% higher than those reported by Lehtinen and colleagues, however the variances were comparable (Figure 5-4). Comparisons between studies were limited to our adulthood-onset control group (n = 5) since these subjects were presumed to be the most similar, with respect to
age and physical activity history, to the cadaveric specimens (n = 20) used by Lehtinen et al. Part of the difference in reported subchondral vBMD is likely explained by the difference in age between the specimens in Lehtinen et al.’s study (mean 72 yrs, range 59-102 yrs) and our adulthood-onset controls (mean 53 yrs, range 42-73 yrs), given the widely accepted concept that bone density begins to decrease in late adulthood (~50 yrs). Discrepancies between subchondral vBMD values are also likely attributable to significant methodological differences between the studies. In the pQCT-based study by Lehtinen et al., the conversion to vBMD was done using the pQCT scanner’s software whereas in our study the qCT method was used to manually compute the conversion between CT intensity and vBMD based on a bone density reference phantom. In our study, scanning was performed in vivo, therefore the glenoid bone was surrounded by synovial joint fluid, muscle, and adipose tissue. In contrast, Lehtinen et al. scanned cadaveric glenoid specimens from which all soft tissue had been removed. It is possible that the presence of air in their specimen could have decreased the resulting CT intensity (HU) since air is less dense than the bone marrow (fat) that is adjacent to the subchondral bone plate in vivo. During segmentation, Lehtinen et al. included the cortical bone on the anterior and posterior borders of the glenoid cavity in addition to the subchondral bone plate, whereas we included only the subchondral bone plate. Given their scanning resolution (in-plane = 0.59 mm x 0.59 mm and slice thickness = 2.5 mm) it is possible that the thin cortical bone on the anterior and posterior borders of the glenoid was subject to partial volume effects, resulting in a lower vBMD value due to averaging with neighbouring trabecular bone. Moreover, Lehtinen et al. did not segment the subchondral/cortical bone and calculate its vBMD directly, but instead calculated subchondral/cortical vBMD (mg/cm³) by dividing the difference of total and trabecular bone mineral content (mg) by the difference of total and trabecular bone volumes (cm³). In contrast, we manually segmented the subchondral bone plate and measured vBMD directly from the segmented region using the qCT method.
Our results for the adulthood-onset controls are similar to those of Lehtinen et al. in that both displayed comparable vBMD values between the middle and superior glenoid regions, and lower vBMD in the inferior region (significantly lower in Lehtinen et al.). In our pilot data, glenoid subchondral vBMD was quite consistent across the three glenoid levels (i.e. inferior, middle, and superior) but was slightly higher in the middle region. In contrast, Lehtinen et al. reported that subchondral vBMD was highest in the superior glenoid region (27). Based on the observations from these studies, it appears that vBMD differences are greatest between the superior and inferior glenoid regions.

5.5 HYPOTHESIS 4

*Volumetric bone mineral density is higher in the manual wheelchair users than in the able-bodied matched controls.*

This hypothesis is based on the assumption that manual wheelchair users load their shoulders more than able-bodied individuals as a result of wheelchair propulsion, transfers, and activities of daily living.
To our surprise, mean volumetric bone mineral density (vBMD) was lower in the wheelchair users than in the able-bodied controls. Though not statistically significant, this trend was observed at all five measurement sites (Table 4-10) for both childhood-onset and adulthood-onset age groupings (i.e. vBMD childhood-onset wheelchair users < vBMD childhood-onset controls, and vBMD adulthood-onset wheelchair users < vBMD adulthood-onset controls). It is important to note that this trend was less pronounced than the trend of higher vBMD in the childhood-onset subjects than in the adulthood-onset subjects (section 5.2). Based on the vBMD results for the wheelchair users and the able-bodied controls, our sample size calculations suggest that very large studies would be required (n = 30 for humeral head trabecular bone, n = 90 for glenoid trabecular bone, and n = 60 for glenoid subchondral bone) in order to detect statistically significant differences in these parameters between these groups. Establishing that wheelchair users have significantly less vBMD than do able-bodied controls would not provide insight into why childhood-onset wheelchair users experience less shoulder pain than adulthood-onset wheelchair users, therefore it is not recommended that such a study be pursued.

This non-significant trend observed in our pilot data of lower vBMD in the wheelchair users than the able-bodied controls is supported by an unexpected finding by Ashizawa et al. that vBMD was slightly but significantly less in the radius of the loaded playing arm than in the contralateral arm in competitive tennis players (34). Direct comparisons between contralateral limbs are ideal but not possible with manual wheelchair users since both arms are loaded approximately equally during wheelchair use. With the manual wheelchair user population, measurements would ideally be repeated over time in a longitudinal study beginning at the onset of wheelchair use, allowing for comparisons between a subject’s morphological data before and after wheelchair use and consequently allowing for drawing a more direct conclusion regarding changes in bone morphology due to changes in loading. Although we cannot draw conclusions regarding changes in vBMD due to changes in loading from our cross-sectional data, we did assess associations between vBMD and loading.

We found a significant positive correlation between humeral head trabecular vBMD and physical activity score (Figure 4-22), which is consistent with Wolff’s law of bone adaptation. This positive correlation and the finding of lower vBMD in the wheelchair user subjects suggest that the manual wheelchair users in our study were in fact loading their shoulders less than the able-bodied controls. Prior to analyzing our results, we had assumed that all manual wheelchair users necessarily loaded their shoulders more than able-bodied individuals, by propelling the
wheelchair, transferring to and from the wheelchair, and performing daily tasks (e.g. overhead reaching). Both the quantitative imaging results and the questionnaire responses suggest that this assumption is incorrect. The physical activity and the general lifestyles questionnaire data (Table 4-7 and Table 4-8) indicate that several of the manual wheelchair users in this study were quite sedentary (i.e. AO 1 does not lift his wheelchair into his car and AO 5 does not wheel outside her home). It is difficult to directly compare shoulder loading via physical activity between wheelchair users and able-bodied controls: not only were different questionnaires administered to these groups, but the IPAQ questionnaire given to the able-bodied controls was not specific to the shoulder. This highlights a need for an upper extremity use score for the able-bodied population that would be more comparable to the PASIPD questionnaire for individuals with physical disabilities.

Examining the individual data of each wheelchair user and his/her able-bodied control, there is one pairing (CO 3 and CO 3 Control) where the control subject is clearly not loading her shoulders more than the wheelchair user. This is reflected by this wheelchair user’s higher vBMD values and the greater degree of mineralization seen in her CT-OAM results, compared to her able-bodied control (Figure 4-13, Figure 4-15). This wheelchair user (CO 3) is a wheelchair track athlete who trains intensively and competes at a competitive level (e.g. competitor at the 2005 Canada Summer Games and 2008 Paralympics hopeful). In light of the fact that some of the wheelchair users in our study barely loaded their shoulders while others heavily loaded their shoulders, it should not be assumed that manual wheelchair users necessarily load their shoulders more than able-bodied individuals. Given our small sample sizes (n = 3 for the childhood-onset groups, n = 5 for the adulthood-onset groups) it is not likely that the mean vBMD values for the wheelchair user groups in this study are representative of the larger wheelchair user population.

In addition to differences in shoulder loading via physical activity between wheelchair users and able-bodied controls, it would appear that peak glenohumeral contact forces are greater during able-bodied activities of daily living than during everyday wheelchair propulsion, and that the former make a greater contribution to bone mineral density. Contrary to our original assumption that wheelchair propulsion generated higher glenohumeral loads than general upper limb use in able-bodied individuals, there is some evidence that the opposite is true: glenohumeral contact forces are considerably greater during higher-load activities of daily living (ADLs) of able-bodied individuals than during low-intensity manual wheelchair propulsion. Peak contact forces at the glenohumeral joint of able-bodied individuals while performing ADLs were reported by Anglin et
al. to exceed 1500 N (196). These results are greater than the peak contact forces of 800-1400 N found at the glenohumeral joint of wheelchair users during low-intensity wheelchair propulsion (197), suggesting that the activities of daily living performed by able-bodied individuals, such as lifting a 10 kg suitcase, are more likely to trigger an adaptive response in bone at the glenohumeral joint than manual wheelchair propulsion at an everyday level of intensity. Since the glenohumeral joints of wheelchair users are not exclusively loaded by low-intensity wheelchair propulsion it is important to consider the loading contributions from other functional demands, such as pressure-relief raises.

Although peak glenohumeral loads are less during low-intensity wheelchair propulsion than during able-bodied ADLs, pressure-relief raises (Figure 2-6) and uphill wheeling generate high glenohumeral moments and may therefore make a greater contribution to glenohumeral joint loading and resulting vBMD in manual wheelchair users than everyday wheelchair propulsion on level ground. Peak glenohumeral moments associated with pressure-relief raises in wheelchair users have consistently been reported around 45 Nm (198, 199). In contrast, peak glenohumeral moments much lower (~8 Nm) during low-intensity wheelchair propulsion on level ground (199). Negotiating a curb and wheeling up an incline have also been reported to generate much higher peak glenohumeral moments than low-intensity wheelchair propulsion (~75 Nm and 47 ± 19 Nm respectively) (199, 200). Furthermore, the peak glenohumeral moments increased significantly as the ramp incline was increased: the peak glenohumeral flexion moment increased by 225% from level wheeling to the highest ramp (1:8 rise:run ratio) (200). The high glenohumeral moments associated with pressure-relief raises and wheeling uphill and the low glenohumeral moment associated with everyday wheelchair propulsion suggest that the former wheelchair-related activities contribute more to glenohumeral joint loading (and resulting vBMD) in manual wheelchair users.

Both our vBMD findings and the general lifestyles questionnaire data support this notion: the subjects who asked for assistance wheeling uphill had generally lower vBMD than the other wheelchair users, even though all subjects wheeled independently on level ground. It appears as though the quadriplegic subjects (CO 2, AO 1) and a high level paraplegic subject (AO 5) in our study did not load their shoulders to the same degree as the other wheelchair users or the able-bodied controls in this study. In general, quadriplegics have less functional capabilities than paraplegics and may, therefore, seek more assistance in performing certain tasks (e.g. wheeling uphill and transfers). This was true of the quadriplegics (CO 2, AO 1) and a high-level paraplegic
(AO 5 with SCI at C7/T1) in our study who reported needing help wheeling uphill. In contrast, none of the lower-level paraplegics in our study required assistance wheeling uphill and in general, had vBMD values closer to those of their able-bodied controls. In the case of the wheelchair athlete (CO 3), her vBMD values were much higher than those of her able-bodied control. Given that wheeling uphill is the activity associated with the highest peak loads on the glenohumeral joint, the lack of independent uphill wheeling among quadriplegic subjects in our study may partially explain why these subjects generally had lower vBMD than paraplegic wheelchair users and able-bodied controls. Although peak glenohumeral contact forces and moments provide insight into glenohumeral joint loading, they do not directly relate to vBMD. Lim et al. showed that shoulder loading, via the same activities of daily living as studied by Anglin et al. (196), affected the trabecular architecture of the glenoid cavity (201). Lim and colleagues did not, however, include vBMD in their analysis so further research is needed to determine the direct effect of loading via ADLs on trabecular vBMD of the glenoid cavity.

The significant correlation we found between humeral head trabecular vBMD and physical activity score supports the concept that bone density is positively related to physical activity. One of the least active individuals in this study (AO 1, quadriplegic) was found to have the lowest vBMD for the humeral head total bone and the glenoid subchondral bone. He was tied with a 73 year old wheelchair user subject (AO 4) for the lowest vBMD for humeral head trabecular bone and tied with two 73 year old subjects (AO 4 and AO 4 control) for glenoid trabecular bone, which supports the widely accepted views that bone density is positively associated with loading and negatively associated with aging. In support of the view that bone density increases with increased loading, the most active subject in this study (CO 3, wheelchair athlete) was found to have the highest vBMD for humeral head total and trabecular bone, as well as glenoid trabecular bone.

Despite the general trend towards lower glenohumeral vBMD in manual wheelchair users than able-bodied controls, it remains possible that the wheelchair users increased their vBMD subsequent to wheelchair use, relative to their vBMD prior to wheelchair use. Due to the cross-sectional design of this study, we do not know each subject’s mean humeral head and glenoid vBMD prior to wheelchair use. Consequently, it is not possible to determine whether vBMD increased in the wheelchair user subjects in response to increased loading, decreased in response to decreased loading, or remained unchanged. A longitudinal study would be required to
determine how altered loading conditions due to wheelchair use affect glenohumeral bone morphology.

5.6 HYPOTHESIS 5

*Humeral head and glenoid cartilage volumes are greater in the childhood-onset wheelchair users than in the adulthood-onset wheelchair users.*

This hypothesis is based on the assumption that the childhood-onset wheelchair users had an adaptational advantage over the adulthood-onset wheelchair users, because the former began wheeling prior to chondral maturity (~18 yrs). A study by Jones *et al.* showed that immature knee cartilage volume was significantly positively correlated with physical activity (17). To date, mature cartilage has not been shown to undergo morphological changes (e.g. increased or decreased cartilage thickness, volume, or surface area) as a direct result of increased loading.

5.6.1 Humeral Head Cartilage Volume

The mean volume of humeral head cartilage measured for the wheelchair users in this study \((n = 8)\) is in close agreement with Vanwanseele *et al.*’s finding for wheelchair users \((n = 7)\) at both 3 and 12 months post-SCI (Figure 5-5). In contrast, the mean volume of humeral head cartilage for the able-bodied controls in this study \((n = 8)\) is less than that reported by Vanwanseele *et al.* and Graichen *et al.* for able-bodied individuals \((n = 7\) and \(n = 8\), respectively). The difference in results between studies may be explained by the following problem related to measuring cartilage volume with qMRI. qMRI cartilage volume measurements depend on cartilage thickness and surface area measurements. As such, cartilage volume is affected not only by the thickness segmented on each slice but also by the number of slices segmented. In this study, partial volume effects were noticeable on the peripheral slices of the humeral head and consequently a 60% region of interest was established for segmentation (section 3.11.1.1). It is therefore likely that fewer slices were segmented for the humeral head cartilage in our study than in the studies by Vanwanseele *et al.* and Graichen *et al.*, resulting in a smaller cartilage volume measurement in our study.
5.6.2 Glenoid Cartilage Volume

Our results for the mean volume of glenoid cartilage were considerably less than those reported by Graichen et al. in the only other known investigation of glenoid cartilage volume. Using qMRI, Graichen et al. measured glenoid cartilage volume in specimens from healthy individuals (n = 8) and reported a mean value of $1.65 \pm 0.40$ cm$^3$ (32). In comparison, the values measured in this study (Table 4-12) are less than half those of Graichen et al. (Figure 5-6).
In this study we had hypothesized that the childhood-onset wheelchair users would have greater humeral head and glenoid cartilage volumes than the adulthood-onset wheelchair users. This hypothesis was based on the previous findings by Jones et al. that immature medial tibia cartilage volume increased twice as much over time (1.6 yrs) in the most physically active children (17).

In the present study, cartilage volume was not different between childhood-onset and adulthood-onset wheelchair user subjects, nor was it different between wheelchair user subjects and able-bodied controls. Tiderius et al. emphasized that an increase in cartilage volume would require an expansion of the collagen network in the extracellular matrix, and contended that this is unlikely in mature cartilage since type II collagen has a very slow turnover rate (148).

5.7 BONE MORPHOLOGY FINDINGS UNRELATED TO A HYPOTHESIS

5.7.1 vBMD of the Articular Surface Regions

Our non-significant finding that trabecular vBMD was higher in regions closest to the articular surface of the humeral head than over the full cross-section of humeral head agrees with the findings of Tingart and colleagues who also found higher vBMD near the articular surface of the humeral head (26). For all subject groups in our study, trabecular vBMD near the articular surface of the humeral head (i.e. in the articular surface ROIs) was approximately double that of the full
cross-section of the humeral head (Figure 4-4 vs. Figure 4-5). It is important to note that the articular surface ROIs were measured on the two middle slice of the humeral head segmentation region, therefore vBMD comparisons were made to the middle subdivisions of the humeral head (H2 and H3). Assuming that the humeral head trabecular bone nearest to the articular surface (i.e. on the medial side) is more heavily loaded than the bone on the lateral side of the proximal humerus, these findings of increased vBMD in the articular surface ROIs are supported by Wolff’s law of bone adaptation. In contrast to Tingart et al., who found that trabecular vBMD was significantly higher in the posterior ROI than in the anterior ROI, we found that trabecular vBMD was generally higher (but not significantly) on the anterior portion of the articular surface (i.e. AS 1) than on the posterior portion (i.e. AS 2) (Figure 4-5).

5.7.2 Humeral Head Normalized Cross-Sectional Area

Within each of our subject groups our findings for the normalized cross-sectional area of total and trabecular bone follow logically from the known semi-spherical shape of the humeral head. The normalized cross-sectional area of total and trabecular bone was smallest at the base of the humeral head (H1), increased through the middle of the humeral head (H2 and H3), and decreased at the top of the humeral head (H4) (Figure 4-8 and Figure 4-10). As expected, the cross-sectional area of humeral head cortical bone remained more or less constant across all humeral head subdivisions (Figure 4-9). In general, the normalized cross-sectional area of total, trabecular and cortical bone was very similar between the four subject groups (Figure 4-8, Figure 4-9, and Figure 4-10). Given the effect sizes and variances in our pilot data, at least 50 wheelchair user subjects would be required in each group (i.e. childhood-onset and adulthood-onset) to detect a statistical significance in humeral head normalized cross-sectional area. In light of these sample size predictions, it is not likely that the normalized cross-sectional area of the humeral head is a suitable parameter to include in a full-scale study of bone morphology in wheelchair users, as it does not appear that it would provide insight into differences in shoulder pain between childhood-onset and adulthood-onset wheelchair users.

Our results for the humeral head normalized cross-sectional area are consistent with extrapolated results from a previous study by Iannotti et al. (191). The cross-sectional areas of perosteal and endocortical bone are commonly reported for the humeral shaft, however no cross-sectional area data were found for the humeral head with which to compare our results directly. Previous studies have quantified glenohumeral bony anatomy using cadaveric specimens (191), roentgenograms of
cadaveric specimens (194), radiographs (202) and MR imaging (191), however none of these studies measured cross-sectional area. The only study in which cross-sectional area could have been measured was that of Iannotti et al. in which measurements were obtained directly from cadaveric specimens and indirectly from MR scans of human subjects; all other studies were limited by projection-based imaging methods. Since their objective was quantifying normal glenohumeral anatomy and not functional adaptation to load-bearing, Iannotti et al. did not measure cross-sectional area but instead measured parameters such as the radius of curvature and the thickness of the humeral head. In an attempt to compare our data with those of Iannotti et al., we assumed a circular cross-section of humeral head bone and computed the area of a circle using the mean humeral head radius (from the axial view) reported by Iannotti et al. for human subjects (23 ± 2.5 mm) (191). This equated to a circular area of 1662 mm², and dividing by the mean height of our subjects (1.74 m) (since subject height was not reported by Iannotti et al.) yielded a mean normalized cross-sectional area of 955 mm² for the humeral head total bone. This value is in close agreement with our findings for normalized cross-sectional area of total bone at the middle humeral head levels (H2 and H3) where Iannotti et al. made their measurements (Figure 4-8).

5.7.3 Glenoid Trabecular Normalized Cross-Sectional Area

For the trabecular glenoid bone, the cross-sectional area was smallest in the superior glenoid region (Figure 4-12) which is consistent with the known geometry of the glenoid cavity: the width of the glenoid cavity is smallest in the superior region. In our segmentation protocol for trabecular glenoid bone, the depth was made equal to half of the glenoid width on that CT slice (section 3.8.1.5), therefore our finding of smaller trabecular bone cross-sectional area in the superior glenoid region follows logically from the smaller glenoid width in this region. Our pilot data suggest that 70 childhood-onset and 70 adulthood-onset wheelchair users would be required to detect a statistically significant difference in glenoid trabecular normalized cross-sectional area between these groups. Based on the effect sizes and variances in our pilot data, it does not appear that this parameter is suitable to include in a full-scale study of bone morphology in relation to shoulder pain in wheelchair users.

5.7.4 Bone Density Distribution

No clear trends emerged for glenoid cavity bone density distribution between the childhood-onset and the adulthood-onset wheelchair users, or between the wheelchair users and the able-bodied
controls (Figure 4-13 to Figure 4-16). There are no existing findings to which to compare our results since CT Osteoabsorptiometry (CT-OAM) has not been used previously to examine bone density distribution at the glenohumeral joint in manual wheelchair users. CT-OAM has, however, been used to examine the mineralization patterns of glenoid bone in both normal and pathologic shoulders. Pathological shoulder conditions examined using CT-OAM included tears of supraspinatus tendon, anterior glenohumeral instability and recurrent dislocation, and presence of sublabral foramen.

Our CT-OAM findings for the highly active wheelchair athlete (CO 3) in our study are consistent with those of Muller-Gerbl et al. from one of the original CT-OAM studies, in which they reported markedly higher CT intensity values (HU) as well as a more expansive regions of maximum density in the glenoid cavities of highly active gymnasts (n = 11), compared to less active (but healthy) individuals (n = 20) (28). The CT-OAM results of the wheelchair athlete in this study (CO 3) clearly demonstrate a more expansive region of high bone density across the glenoid cavity than those from the more sedentary wheelchair users and controls (e.g. AO 1 and AO 5). In the same study, Muller-Gerbl et al. also reported anterior and posterior locations of density maxima in younger individuals (age range not given but data presented for a 36 year old), in contrast to a single central density maximum in older individuals (age range not given but data presented for a 78 year old). In contrast, our CT-OAM bone density distribution results were not as readily classified based on location for any subject groupings, and no clear trends emerged for younger and older subject groups.

In contrast to our varied results for the able-bodied subjects, Schulz et al. found two characteristic locations of density maxima in the healthy glenoid (n = 44): anterior-superior and posterior (30). These authors related these findings to function, highlighting that internal rotation of the arm results in stresses on the anterior glenoid surface. In the present study, density maxima were noted more frequently on the anterior-superior aspect of the glenoid than on the posterior aspect (Figure 4-13 and Figure 4-14). Schulz and colleagues also examined glenoid mineralization patterns in abnormal shoulders with sublabral foramina, which they defined as an “isolated complete detachment of the capsulolabral complex from the anterior-superior glenoid rim” (134). Compared to healthy shoulders (n = 10), the presence of a sublabral foramen (n = 10) did not affect the location of the anterior-superior density maxima. In contrast, shoulders with a torn supraspinatus tendon (29) or with an anterior instability (31) yielded different mineralization patterns, which these authors attributed to altered loading conditions. In our study anterior
glenoid density maxima were more commonly noted among the wheelchair users than the able-bodied controls. The pronounced anterior density maxima in the glenoid cavity of certain wheelchair users in this study (e.g. CO 3 and AO 4) may reflect their wheelchair propulsion style and the associated internal rotation of the arms. It is important to note that the anterior density maxima were not exclusive to the wheelchair users nor were they observed for all of the wheelchair users. Based on a finite element analysis, Eckstein et al. noted that the distribution of subchondral bone density assessed with the CT-OAM method can provide insight into the functional adaptation and the loading history of subchondral bone, but that CT-OAM alone cannot be used to directly to infer the long-term distribution of pressure at the articular surface (97).

Although it has been applied to the glenoid cavity in several studies, CT-OAM has never been used to assess the bone density distribution of the humeral head. This is likely due to the shortcomings of volume rendering a full-depth bone with a maximum intensity projection (MIP) algorithm. By using a surface projection algorithm to render the humeral head instead of the MIP, we were able to map the density distribution across the articular surface of the humeral head. It is important to note that because both the Maximum Intensity Projection and the surface projection algorithms are projection-based rendering techniques, the results are position-dependent. As a consequence, the resulting bone density mapping will be different if the alignment of the reconstructed bone model is changed prior to rendering. In this study, anatomical landmarks and standardized views were used in an attempt to standardize the alignment across subjects. We believe that we achieved a reasonably similar alignment of the humeral head and the glenoid cavity for all subjects, allowing us to qualitatively compare the resulting CT-OAM mineralization patterns.

Our finding that the glenoid is more mineralized than the articular surface of the humeral head is in agreement with the literature. In our study, all subjects displayed a greater degree of bone mineralization on the glenoid cavity than on the articular surface of the humeral head (Figure 4-13 vs. Figure 4-15, and Figure 4-14 vs. Figure 4-16). This finding supports Frost’s theoretical results, which showed that the concave joint surface undergoes greater loading (averaged over time) than the convex surface, resulting in higher bone mineral density on the concave surface (140). Frost’s model predictions of higher subchondral bone density in the glenoid cavity than on the humeral head were confirmed experimentally in this study.
5.8 CARTILAGE MORPHOLOGY FINDINGS UNRELATED TO A HYPOTHESIS

5.8.1 Humeral Head Cartilage Thickness

Mean humeral head cartilage thickness values for the four groups in this study lie in the middle of the wide range of previously reported values from qMRI human studies, MR cadaver studies, anatomical cadaver studies, and stereophotogrammetry (Figure 5-7).

![Reported Values of Humeral Head Cartilage Thickness](image)

Figure 5-7 - Comparison of reported humeral head cartilage thickness, mean ± SD.

A recent study by Vanwanseele et al. is the only published work to have used qMRI to measure cartilage thickness in manual wheelchair users (20). Vanwanseele et al. reported a mean humeral head cartilage thickness of 1.29 ± 0.30 mm for able-bodied subjects (n = 7) and 1.00 ± 0.12 mm and 0.99 ± 0.13 mm for spinal cord injured subjects (n = 7) at 3 months and 12 months post-injury. The mean humeral head cartilage thickness reported for the adulthood-onset wheelchair users in our study is approximately 20% greater than that reported by Vanwanseele et al. for either of their wheelchair user groups (i.e. 3-months and 12-months post-SCI). It does not appear that these differences are due to methodological differences, since Vanwanseele et al.’s results for the able-bodied individuals are very comparable to our results for able-bodied individuals. Moreover, both studies performed qMRI analysis in collaboration with Dr. Felix Eckstein, one of
the leading researchers in the qMRI field. We performed our qMRI analysis with the Chondrometrics software (Chondrometrics GmbH, Ainring, Germany), developed by Dr. Felix Eckstein and colleagues, and it is likely that Vanwanseele et al. used the same software for their qMRI analyses. Although both studies included spinal cord injured subjects, the subjects in Vanwanseele et al.’s study were recently injured (< 1 year post-SCI) whereas the subjects in our study were long-term wheelchair users, having wheeled for 10 years or more. It is possible that at 3 months post-SCI the individuals in Vanwanseele et al.’s study were only beginning to use a wheelchair and were not yet heavily loading their shoulders. In a longitudinal study of knee cartilage in wheelchair users, Vanwanseele and colleagues noted that cartilage thickness decreased over time due to immobilization (12). Although thinning of humeral head cartilage due to disuse has not been reported, this might be a possible explanation for the lower cartilage thickness in individuals at 3-months and 12-months post-SCI. A study by Graichen et al. was the only one other study to measure glenohumeral cartilage thickness using qMRI; their results for the humeral head were comparable to those for all four groups in the present study (Figure 5-7). Graichen et al. reported a mean cartilage thickness of 1.2 ± 0.09 mm for the humeral head (n = 8) (32) which is in close agreement with our values of 1.28 ± 0.05 mm for the childhood-onset wheelchair users, 1.19 ± 0.23 mm for the adulthood-onset wheelchair users, 1.31 ± 0.10 mm for the childhood-onset controls, and 1.24 ± 0.20 mm for the adulthood-onset controls (Table 4-12).

The range of mean humeral head cartilage thickness measurements from cadaver studies (1.23 – 1.45 mm) also supports the values found in this study (1.19 – 1.31 mm). A study by Meachim found a mean cartilage thickness of 1.45 mm (range 0.8-1.9 mm) on the humeral head (n=32) (203) and no significant differences in cartilage thickness when specimens were grouped by age or by gender. Hodler et al. also measured cartilage thickness on cadaveric humeri (n = 10), both from anatomical sections and MR scans (187). These investigators found a mean cartilage thickness of 1.23 ± 0.52 mm from the anatomical sections and 1.49 ± 0.45 mm from MR, using a similar imaging sequence to the one used in this study, and concluded that MR-based measurements of thin cartilage tend to overestimate this thickness. Yeh et al. also reported that MR-based measurements of humeral head cartilage tend to overestimate thin regions and underestimate thick regions (186). These authors reported anatomical section and MR-based cartilage thickness measurements of 1.24 ± 0.50 mm and 1.07 ± 0.47 mm for the humeral head (n = 14). Using stereophotogrammetry, Soslowsky et al. reported a mean cartilage thickness of 1.44 ± 0.30 mm for the humeral head (n=28) (36). Our results for humeral head cartilage thickness, which range from 1.19 mm to 1.31 mm, are comparable to these previously reported results.
5.8.2 Glenoid Cartilage Thickness

The mean glenoid cartilage thickness values for the groups in this study were found to be lower than previously reported (Figure 5-8). Far fewer studies measured glenoid cartilage thickness than humeral head cartilage thickness. Glenoid cartilage measurement techniques included qMRI of human subjects, anatomical sections of cadaveric specimens, and stereophotogrammetry. The glenoid cartilage thickness values found in this study are nearest to the value reported by Graichen et al. in the only other study that measured glenoid cartilage thickness with qMRI (Figure 5-7). Graichen et al. reported a mean cartilage thickness of 1.7 ± 0.13 mm for the glenoid cavity (n = 8) (32), while in our study, mean glenoid cartilage thickness ranged from 1.17 ± 0.17 mm to 1.25 ± 0.23 mm across the four subject groups (Table 4-12). Contrary to their observations for the humeral head, Yeh et al. found that MR-based measurements of glenoid cartilage neither overestimated nor underestimated the actual thickness (186). These authors reported anatomical section and MR-based cartilage thickness measurements of 1.88 ± 0.63 mm and 2.02 ± 0.71 mm for the glenoid cavity (n = 17). Soslowsky et al. used stereophotogrammetry to measure glenoid articular cartilage thickness and reported a mean cartilage thickness of 2.16 ± 0.55 mm (n = 13) (36). The values reported by Yeh et al. and by Soslowsky et al. were higher than our results (Figure 5-8).

![Reported Values of Glenoid Cartilage Thickness](image-url)

*Figure 5-8 - Comparison of reported glenoid cartilage thickness.*
5.8.3 Humeral Head Cartilage Surface Area

The humeral head cartilage surface area results for the wheelchair users and the able-bodied controls in this study are consistent with previously reported values for wheelchair users and able-bodied individuals, respectively (Figure 5-9). The humeral head cartilage surface area values measured for the wheelchair users in this study (n = 8) are very similar to those reported for the wheelchair users in a study by Vanwanseele et al. (n = 7) (20) (Figure 5-9). We found a mean cartilage surface area of 18.66 ± 2.80 cm$^2$ and 19.51 ± 4.91 cm$^2$ for the childhood-onset and adulthood-onset wheelchair users respectively, compared to 19.23 ± 2.44 cm$^2$ and 18.84 ± 2.44 cm$^2$ at 3 and 12 months post-SCI in Vanwanseele et al.’s study. Soslowsky et al. measured the surface area of humeral head cartilage using stereophotogrammetry (36). Distinguishing between genders, these authors reported 17.34 ± 2.04 cm$^2$ for male specimens (n = 15) and 13.36 ± 2.20 cm$^2$ for female specimens (n = 16), both of which are somewhat lower than our results.

![Figure 5-9 - Comparison of reported humeral head cartilage surface area.](image)
5.8.4 Glenoid Cartilage Surface Area

Glenoid cartilage surface area, measured using qMRI, has not been previously reported. The only values with which to make comparisons were obtained using stereophotogrammetry (36). Soslowsky et al. reported mean glenoid cartilage areas of $5.79 \pm 1.69 \text{ cm}^2$ for male specimens ($n = 11$) and $4.68 \pm 0.93 \text{ cm}^2$ for female specimens ($n = 13$). Our findings for glenoid cartilage area (Table 4-12) are in close agreement with these values (Figure 5-10).

![Reported Values of Glenoid Cartilage Surface Area](image)

Figure 5-10 - Comparison of reported glenoid cartilage surface area.

5.9 WHEELCHAIR USERS’ SHOULDER PAIN

The descriptive finding in this study that shoulder pain interfered more with functional tasks in adulthood-onset wheelchair users than in childhood-onset wheelchair users supports the finding reported by Sawatzky et al. in the only previous study to quantify shoulder pain in childhood-onset and adulthood-onset wheelchair users with the WUSPI (6). These investigators reported percentage WUSPI pain scores of $7.6 \pm 10.5\%$ for the childhood-onset group ($n = 31$) and $18.8 \pm 20.1\%$ for the adulthood-onset group ($n = 22$), which are in close agreement with our findings of $7.3 \pm 4.6\%$ (original WUSPI score = $11 \pm 7$) for the childhood-onset group ($n = 3$) and $20.7 \pm 21.3\%$ (original WUSPI score = $31 \pm 32$) for the adulthood-onset group ($n = 5$). Given the small sample sizes and the large variances, we did not test the difference in mean WUSPI scores for
It is difficult to directly compare the WUSPI values between studies, since each research group has derived its own way to account for WUSPI questions left blank by subjects. Sawatzky et al. reported WUSPI scores as a percentage of the total possible score, while Samuelsson et al. reported the average WUSPI score of the questions answered (4.1 ± 2.6 in paraplegics, n= 56) (44), and Curtis et al. calculated a performance-corrected WUSPI score by multiplying the average WUSPI score by the number of questions on the WUSPI questionnaire (15.6 ± 20.5 in female basketball players, n = 46) (40). In contrast, we did not need to adjust our original WUSPI scores (sum of scores for each question) since every subject in our study answered all 15 questions. More important than the actual WUSPI score is the trend towards greater shoulder pain interference in the adulthood-onset wheelchair users than the childhood-onset wheelchair users first noted by Sawatzky et al. (6) and reconfirmed in the present study.

5.10 STUDY LIMITATIONS

5.10.1 Cross-sectional Design

The main limitation associated with the cross-sectional design of this pilot study was that it was not possible to evaluate the functional adaptation of bone and cartilage to wheelchair use (if it occurs). This would require making repeated measurements over time so that comparisons could be made between each subject’s bone and cartilage parameters before and after wheelchair use. Given the limited time-frame for this study, it was not feasible to perform a longitudinal investigation. The cross-sectional design of this pilot study was, however, useful for implementing the various quantitative image analysis methods to determine the effect sizes in our pilot data and calculate the sample sizes required for a full-scale cross-sectional study (section 5.12).

5.10.2 Differences between Subjects

There were several differences between the wheelchair user subjects recruited for this pilot study that could have affected the bone and cartilage morphology results. First, both paraplegics and quadriplegics were included provided they were manual wheelchair users who wheeled independently. Although there are potentially differences between paraplegics and quadriplegics with respect to shoulder pain and wheeling techniques, manual wheelchair users were recruited regardless of SCI lesion level in an attempt to represent the manual wheelchair population as a whole and avoid biasing the acquired bone and cartilage pilot data. In addition, recruitment was
simplified by making the study open to all manual wheelchair users, regardless of their lesion level.

One childhood-onset wheelchair user (CO 2) was spinal cord injured at 16 years of age. He was placed in the childhood-onset group since the humeral head is not fully ossified in males until 16 to 20 years of age. Ossification of the glenoid cavity, however, is generally complete by 17 or 18 years of age, so it is possible that his bones and cartilage did not have adequate time to adapt to loading from wheelchair use prior to skeletal maturity.

Not all of the wheelchair users in this study had the same primary diagnosis. Seven of the eight wheelchair users were traumatically spinal cord injured whereas one childhood-onset wheelchair user (CO 1) was congenitally spinal cord injured. This subject was diagnosed with meningomyelocoele (i.e. spina bifida) at birth and as a result, was never ambulatory and received substantial assistance performing daily tasks, especially as a young child. This suggests that he may not have loaded his shoulders to the same degree as other childhood-onset wheelchair users who were more independent. Although spina bifida is not known to affect bone or cartilage morphology, it remains possible that this condition may have influenced his bone and cartilage development and resulting morphology. This subject is now quite independent, and not only drives himself but also lifts his wheelchair into his car, indicating that he does load his shoulders substantially on a regular basis.

It was observed that the wheelchair users loaded their shoulders to various degrees during wheelchair propulsion; some subjects wheeled quite briskly (e.g. CO 3 and AO 3) while others wheeled rather slowly (e.g. AO 1 and AO 5). Their physical activity levels were also quite varied: one subject was a highly active wheelchair athlete (CO 3), one was a scuba-diver (AO 4) and others were quite sedentary (AO 2 and AO 5). The range of levels of physical activity among our subjects is, however, likely representative of the general wheelchair user population. In a study of the functional adaptation of bone and cartilage to increased loading, loading (via physically activity and typical wheelchair use) would ideally be controlled. This was not possible in the present study because it would have further increased recruitment difficulties if we had excluded eligible subjects because they were sedentary.

The body mass index (BMI) scores varied substantially between subjects, but the distribution of scores was probably representative of the general wheelchair user population. Using this measure,
two subjects were classified as underweight (i.e. BMI < 20), with BMI scores of 16.9 (AO 2) and 17.3 (AO 1) while two others were classified as overweight or obese (i.e. BMI > 26), with scores of 33.1 (AO 5) and 29.6 (CO 1). It is important to note that BMI is, however, a crude measure of healthy body weight since it does not account for mass due to larger bones or muscle. In the case of subject CO 1, he did not appear overweight, but was short (1.47 m or 4'10") with a stocky build. It is unknown whether his short stature, uncharacteristic of mature adult males, resulted from having spina bifida. The BMI scores (and the range of subject mass) suggest that shoulder loads during wheelchair transfers and pressure-relief raises are considerably different between subjects. Based on our pilot data, no correlation was found between humeral head trabecular vBMD and subject mass, or between glenoid subchondral cross-sectional area and subject mass.

It was not possible to compare long-term childhood-onset wheelchair users to long-term adulthood-onset wheelchair users who had wheeled for the same length of time, and length of time wheeled may have affected the bone and cartilage morphology results. The adulthood-onset wheelchair users had, on average, wheeled for 8 years longer than the childhood-onset wheelchair users. The intent was to recruit wheelchair users such that the childhood-onset and adulthood-onset groups had wheeled for the same mean number of years (i.e. had loaded their shoulders via wheelchair use for the same length of time), however, this was not possible given our recruitment difficulties. It is possible that the discrepancy in the number of years of wheelchair use between childhood-onset and adulthood-onset wheelchair users affected the bone and cartilage morphology results (i.e. on average, the glenohumeral joints of the adulthood-onset wheelchair users had undergone wheelchair-related loading for 8 years more than the glenohumeral joints of the childhood-onset wheelchair users, and consequently had a longer period over which adaptation could have occurred). We were, however, able to recruit wheelchair users who had wheeled for at least 10 years. Ensuring that all of our subjects were indeed long-term wheelchair users was deemed more important for our pilot study of glenohumeral loading than having an equal number of years wheeled by childhood-onset and adulthood-onset wheelchair user groups.

The inherent difficulty in comparing bone and cartilage between childhood-onset and adulthood-onset wheelchair users is the difference in the mean age between groups: those who began wheeling as children are now young adults, and those who began wheeling as adults are now 40+ years of age. Given the known age-related changes in bone density, it would be inappropriate to directly compare vBMD values between these groups. For this reason, able-bodied controls were recruited and matched for gender and age (matched to ± 1.5 years for 7 controls and to ± 3 years...
for 1 control) however no attempt was made to match for height, weight, BMI, ethnicity, physical activity level, dietary calcium intake, or other factors that might have influenced bone and cartilage morphology. Matching subjects and controls for all of these variables would have been very difficult as it was already difficult to find age- and gender-matched controls that were eligible for scanning and able to spend four hours on a weekday participating in our study. The only perfect match would be comparing a loaded limb to a contralateral unloaded limb, as did previous studies on bone density in the forearms of tennis players. This is obviously not possible with wheelchair users, since both shoulders are loaded during wheelchair use. We feel that the benefits of having included able-bodied controls in our study outweigh the drawbacks of not having perfectly matched pairs.

A limitation is that height, which was used to normalize the cross-sectional area measurements, was self-reported. This was done to minimize the invasiveness of the study methods, since wheelchair users cannot readily stand against a wall to have their height measured. Height could have been measured while the subject was lying on the scanner bed; however this would not have been appropriate for the double-leg amputee in our study (AO 4). An alternative that is recommended for future studies is to measure the arm span and use this value to normalize the cross-sectional area measurements.

5.10.3 Study Methods

5.10.3.1 Limitations associated with the questionnaires

The primary limitation of using questionnaires to assess shoulder pain, physical activity level and dietary calcium intake is that results are self-reported and it is widely known that respondents embellish what they report (e.g. healthier diet or higher level of physical activity). In addition, the shoulder pain and physical activity questionnaires were recall measures, and there is the possibility that subjects forgot to include relevant data or that the recall period was not representative. For the wheelchair user subjects, shoulder pain was assessed with the WUSPI, a 7-day recall questionnaire. One subject (CO 2) noted that although he had experienced very little shoulder pain over the previous week, he did occasionally suffer from very intense shoulder pain. This occasional shoulder pain was only noted anecdotally and not in his WUSPI score. One alternative to recall questionnaires would have been asking subjects to keep a log of their shoulder pain, physical activity, and dietary calcium intake over a set time period (e.g. one month). Recording in logs is much more onerous for the subject than completing a short
questionnaire. Logs are also prone to errors, for example, if a subject forgets to record data on a particular day. Since the shoulder pain, physical activity, and dietary calcium intake data obtained from the questionnaires were only used for descriptive purposes, we believe that the benefit of having these data far outweighs their imperfect nature.

Another limitation is that different questionnaires were used for the wheelchair users and the able-bodied subjects in order to assess shoulder pain and physical activity, however this was necessary given the differences in functional and recreational activities performed by these groups. Although it is not possible to directly compare the scores from different questionnaires, these data provided useful background information regarding the habits of each wheelchair user and able-bodied control. A limitation of the physical activity and pain questionnaires given to the able-bodied controls is that neither the IPAQ nor the quick DASH was specific to the shoulder. There is no physical activity questionnaire specific to the shoulder for able-bodied individuals, likely because physical activity in this population generally involves the lower limbs (e.g. running, walking, or cycling). The food frequency questionnaire (FFQ) used in this study was originally designed for use with adolescents and may therefore not have included the appropriate sources of dietary calcium intake in adults. Despite this limitation, the FFQ scores did provide a general idea of dietary calcium intake between subjects, which was the purpose of using the questionnaire.

5.10.3.2 Limitations of assessing bone morphology with CT

Calculating apparent volumetric bone mineral density with qCT, as we did in this study, is not equivalent to calculating true volumetric bone mineral density by dividing the ash-weight of a bone specimen by its volume. The former method was chosen for this study because it is non-destructive and can be used in vivo, whereas the latter clearly cannot. The accuracy with which vBMD can be quantified from a CT scan is, in large part, determined by the bone density reference phantom. Most qCT studies to date have assessed vertebral trabecular bone and, as a result, most of the phantoms developed for qCT contain materials in the trabecular bone density range. In our study, we quantified vBMD in both trabecular and subchondral bone at the glenohumeral joint. The phantom we used (detailed in section 3.8.2) was specifically designed as a spine phantom, and consequently the density of subchondral and cortical bone in our scans was above the phantom’s range. In the trabecular bone density range, the relationship between CT intensity (HU) and vBMD is linear (Figure 4-1) and was therefore extrapolated to the cortical and
subchondral bone density range. This extrapolation is commonly done, although it remains a limitation of the cortical and subchondral vBMD measurements reported (121).

Subchondral (i.e. cortical) bone phantoms are not readily available since reference materials in this density range would be highly susceptible to beam hardening effects (183). The energy spectrum of the x-ray beam used in CT scanning is polychromatic (i.e. contains x-rays at various energies). As the x-ray beam traverses tissues the lower energy x-rays are preferentially absorbed thus the energy spectrum of the remaining x-ray beam increases, a phenomenon known as beam hardening. In consequence, the resulting CT intensity (HU) of a tissue traversed by the ‘hardened’ beam will be different than that from the original beam. If highly dense materials were used in the bone phantom reference rods to approximate subchondral/cortical bone density, these materials would likely produce beam hardening effects. The beam hardening effects could be decreased by decreasing the diameter of the rods, however that would, in turn, likely create partial volume effects (i.e. when a single voxel contains multiple tissues thus the resulting intensity is an average of the respective intensities). In our search for a cortical bone phantom, none were found to be commercially available and only one study reported having used one (130). The reference material in that particular phantom was tricalcium phosphate, which has attenuation properties similar to hydroxyapatite, and a density range of 1.24 to 2.05 g/cm³ was reported.

5.10.3.3 Limitations of assessing cartilage morphology with MR

One limitation of our assessment of cartilage using MR imaging was that the scans were not reviewed for pathology (e.g. fibrillation or tears) by a trained radiologist. Although a few local defects were noted during segmentation, the qMRI method does not explicitly account for these. Because qMRI analysis provides global measures of cartilage morphology (i.e. thickness, volume, or surface area of the entire cartilage plate), it is insensitive to localized defects in cartilage, which might be a source of pain among wheelchair users. Moreover, early morphological differences might not be observable at the global level by qMRI analysis, especially at the glenohumeral joint where cartilage is very thin (< 3 mm) and highly curved. Another challenge of the qMRI method is determining the number of slices to segment (i.e. the number of slices free of partial volume effects), which was accomplished in the present study by determining a 60% ROI. This ensured segmentation consistency between subjects in this study, however it does not facilitate comparisons between our results and those from other studies, since a different size of ROI may have been used. It is important to realize the effect that the size of
ROI has on the reported cartilage volume and surface area values. Although our choice of a 60% ROI underestimated the cartilage volume and surface area of the entire humeral head, it is believed that a conservative ROI is better than trying to segment cartilage on slices with visible partial volume effects.

A further limitation of our study is that a few of our MR scans showed signs of truncation artefact in the humeral head cartilage, which may have affected our segmentation and the resulting qMRI values. Truncation artefacts have been reported to occur in MR imaging of cartilage, most commonly when using a 3D fat-suppressed spoiled gradient-recalled sequence (SPGR) (204). Truncation artefact in cartilage presents as rippled bands of hypointensity and hyperintensity, creating a false laminar appearance (205). This type of artefact occurs at high contrast interfaces (e.g. bone-cartilage interface), where sharp edges are represented by high spatial frequency data. If these high frequency data are undersampled it is no longer possible to accurately estimate the sharp edge (i.e. a step function) and truncation artefacts are created. Given that hyperintense cartilage is bounded by hypointense subchondral bone (or suppressed fatty marrow) on one side and hypointense synovial joint fluid on the other, high contrast interfaces are present with potential for truncation artefact to occur. The truncation artefact observed in our scans was partly due to our choice of scan sequence, matrix size, and number of phase and frequency encoding steps (Table 3-6). Given that the truncation artefact was located within the humeral head cartilage itself and that it obscured the borders of this cartilage plate, it is not surprising that the truncation artefact increased the difficulty of segmenting the humeral head cartilage in our scans. Segmentation of humeral head cartilage was, however, possible in the few scans with truncation artefact because the artefact only affected small regions of the cartilage and the segmentation line could be drawn based on the known anatomical shape of humeral head cartilage.

5.11 STUDY CONTRIBUTIONS

Through the implementation and application of quantitative image analysis techniques we have developed an integrated multi-modality approach for assessing bone and cartilage morphology in vivo at the glenohumeral joint. To our knowledge, this has not been done before in humans. In vivo assessments are beneficial since they are related to clinical symptoms, they eliminate the effects of tissue degradation in embalmed or frozen specimens, and that parameters of bone morphology can be measured longitudinally to provide insight into functional adaptation to load-bearing. Of the few studies that have jointly investigated bone and cartilage morphology, two
examined knee cartilage in canine models (23, 206) and one examined humeroulnar cartilage in cadaveric specimens (207).

To our knowledge, this is the first quantitative assessment of volumetric bone mineral density and cross-sectional area of the humeral head and the of glenoid cavity in manual wheelchair users. Previous bone density assessments in wheelchair users have been limited to the lower limb or the distal aspect of the upper limb and measured areal BMD using DXA. Not only does our method measure volumetric BMD, but it also does so right at the glenohumeral joint, which is likely more clinically relevant to shoulder pain in wheelchair users.

5.11.1 Technical Contributions

- Since this was the first 3T qMRI study of glenohumeral cartilage, a 3T MR imaging protocol was developed for this purpose. The few studies reported in the literature that have applied qMRI analysis to glenohumeral cartilage performed scanning at 1.5T, making our 3T MR imaging protocol novel. The advantage of scanning at 3T compared to 1.5T is that, in theory, there is double the signal to noise ratio (SNR) at 3T than at 1.5T. The contrast to noise ratio (CNR) between cartilage and the surrounding tissues is also greater at 3T than at 1.5T, facilitating the segmentation of cartilage and potentially leading to more accurate quantification of cartilage morphology (154).

- The segmentation protocols developed in this study for trabecular and subchondral bone of the humeral head and of the glenoid cavity are very detailed, allowing for a comprehensive and repeatable analysis. These protocols were based on previously reported methods for the humeral head (26) and the glenoid cavity (27). The existing protocols had been specifically designed for assessing bone quality to guide component design and implant fixation. Given that the research question motivating this study related to bone’s capacity to respond to loading, we tailored the existing protocols to produce relevant measures of vBMD (i.e. vBMD of humeral head total and trabecular bone, and glenoid subchondral and trabecular bone). In addition, we added the novel measurement of normalized cross-sectional area of humeral head and glenoid bone, since it may be relevant to the functional adaptation of glenohumeral bone.

- The combined qCT and CT-OAM assessment performed in this study provides complementary bone morphology data: overall mean vBMD and localized density
distribution. To our knowledge, these techniques have not been used together in any previous study. Pairing the quantitative aspect of qCT and the spatially descriptive aspect of CT-OAM provides a more comprehensive assessment of bone mineralization across the joint surface than either of these methods alone. qCT analysis yields one mean value of vBMD for the entire humeral head. This value is the mean value of all pixels segmented on each slice and then averaged over the entire humeral head or glenoid cavity. Clearly this vBMD value is a global mean value and does not account for regional variations in vBMD. Conversely, CT-OAM in its original form is qualitative because bone density distribution is expressed in Hounsfield units.

- Our modified CT-OAM method allows for the bone density distribution to be expressed in vBMD. Not only is this novel, it is also a significant improvement over the existing qualitative method because quantitative comparisons can be made between individuals.

- In this study we assessed the bone density distribution across the articular surface of the humeral head using a modified CT-OAM method. This is a significant contribution since bone mineralization patterns can now be assessed for both articular surfaces of the glenohumeral joint, whereas assessments were previously limited to the glenoid cavity. The advantage of assessing bone density distribution on both sides of the joint is being able to compare the locations of high density between the two sides of the joint, thereby expanding our ability to assess bone’s adaptive response to loading. The statistically significant correlation we found between humeral head and glenoid trabecular vBMD (Figure 4-21), emphasizes the importance of assessing both articular surfaces of a joint.

5.11.2 General Study Design Contributions

- In this pilot study we identified several logistical challenges associated with scanning at two imaging centres and coordinating a time and location for the physical examination with the physician. It was decided that it was preferable to book daytime CT and MR appointments on scanners located at different sites, since these scanners were not used for clinical scans in hospitals. The alternative was to tentatively book after-hours appointments on hospital scanners at the same location, but run the risk of the scanner being needed for a trauma case. We recommend our approach for a full-scale study, since it is less inconvenient for the subjects than having scanning appointments cancelled on short notice.
In this pilot study we identified the obstacle of scanning wheelchair users with orthopaedic hardware, among other implants, in a 3T MR scanner. We identified recruitment difficulties and a potential bias in the wheelchair subjects eligible for this study: it is possible that the presence of Harrington rods for scoliosis reduces the range of motion of the spine, thereby altering kinematics at the glenohumeral joint during manual wheelchair propulsion, and possibly increasing or decreasing the risk of developing shoulder pain. It is unknown whether glenohumeral bone and cartilage morphology differ significantly between wheelchair users with and without Harrington rods. Given that we required wheelchair users to have wheeled for ten years or more and that incidence of scoliosis, and subsequent correction with Harrington rods, increases with the number of years of wheelchair use, it was quite difficult to recruit subjects who did not have implanted hardware that posed a safety concern at 3T.

Recruitment of the childhood-onset wheelchair users (n = 3) was especially difficult, given that traumatic spinal cord injuries are less common in children (< 16 years) than in young and middle-aged adults. Given the limited subject pool, even in major Canadian cities such as Vancouver, it is unlikely that 22 eligible wheelchair users could be recruited for the childhood-onset group. For the present study (N = 16), recruitment and scanning took 6 months. From this, it is estimated that it would take between 1-1.5 years to recruit and scan the 44 (total) wheelchair user subjects required to detect differences in bone morphology. Furthermore, this estimate neglects the fact that the wheelchair user subject pool is limited and (thankfully) not growing quickly. Recruitment of the age- and gender-matched able-bodied controls was easier than the wheelchair users, however it was somewhat difficult to find individuals able to participate during the day on a weekday.

This pilot study allowed us to determine the analysis time required for the quantitative image analysis techniques (i.e. qCT, CT-OAM, and qMRI). Approximately 10 hours are required, per subject, to assess bone morphology using the combination of qCT and CT-OAM. Given the sample size estimate of 22 subjects in each of the childhood-onset and adulthood-onset wheelchair user groups (i.e. 44 subjects in total), approximately 440 hours of analysis time (and $24,200 in scanning costs) would be required. Approximately 5 hours of analysis time are required, per subject, to assess cartilage morphology using qMRI. Given the sample size estimate of 22 subjects in each of the childhood-onset and adulthood-onset wheelchair user groups (i.e. 44 subjects in total) approximately 220 hours
of analysis time (and $17,600 in scanning costs) would be required. For a combined assessment of bone and cartilage morphology in these groups it would take one researcher, working 40 hours per week, a total of 4 months to analyze the scans.

5.12 RECOMMENDATIONS FOR A FULL-SCALE STUDY

A full-scale cross-sectional study is recommended to further investigate glenohumeral bone morphology in childhood-onset and adulthood-onset wheelchair users. The recommended parameters to measure and the required sample sizes are outlined in the following sections.

5.12.1 Sample Sizes

- As determined from our sample size calculation, 22 childhood-onset and 22 adulthood-onset wheelchair users would be required to detect any significant differences (power = 0.8, p < 0.05) in humeral head and glenoid trabecular bone mineral density, and in glenoid subchondral bone cross-sectional area. It is recommended that these bone morphology measures be determined by qCT analysis.

- Given the small effect sizes and the large variances in the measures of cartilage morphology, it is not likely that cartilage thickness, volume, or surface area are clinically relevant to wheelchair users’ shoulder pain. It is not recommended that future studies investigating cartilage adaptation at the glenohumeral joint of wheelchair users measure cartilage morphology with qMRI.

5.12.2 Parameters to Measure

Based on the effect sizes found in this pilot study, we recommend measuring the following parameters since we believe they are the most suitable to include in a study of glenohumeral bone morphology and associated shoulder pain in the wheelchair user population:

- Humeral head trabecular vBMD
- Glenoid trabecular vBMD
- Glenoid subchondral normalized cross-sectional area
Given the small sample sizes required to detect statistical differences in these parameters (n = 22), these parameters may be the most clinically relevant to shoulder pain in wheelchair users, and may potentially provide insight as to why shoulder pain is more prevalent in adulthood-onset wheelchair users.

In addition, we recommend assessing cartilage composition with the MR-based dGEMRIC method (section 2.11.3). In this study, few differences were found in cartilage morphology with qMRI and it is believed that the dGEMRIC method might be better able to detect subtle changes in glenohumeral cartilage composition, if they exist, between childhood-onset and adulthood-onset wheelchair users.

5.12.3 Longitudinal Study

Following the full-scale cross-sectional study, a longitudinal study is recommended in order to assess the functional adaptation of bone and cartilage at the glenohumeral joint in manual wheelchair users, in response to increased loading. In contrast to a cross-sectional study, a longitudinal study would allow comparisons of a wheelchair user’s glenohumeral morphology to be made over time to determine what changes, if any, result from wheelchair use. When comparing longitudinal measures of childhood-onset wheelchair users, it would be necessary to distinguish between changes in bone and cartilage resulting from functional adaptation and changes resulting from maturation.

- It is recommended that baseline measurements be obtained as soon as possible after the onset of wheelchair use, in an effort to provide an accurate representation of the subject’s glenohumeral health prior to wheelchair use. It is suggested that follow-up measurements be acquired 1 year, 3 years and 5 years after baseline. It is acknowledged that this would further increase the difficulty of recruiting subjects, since only new SCI subjects would be eligible.

- At all time-points (i.e. baseline and follow-ups) it is recommended that the following measurements be acquired: a CT scan of the dominant shoulder, a MR scan of the dominant shoulder, a physical examination by a physician, as well as questionnaire data regarding shoulder pain, physical activity, and dietary calcium intake.
• In addition, height (estimated by the arm span) should be measured and weight (i.e. mass) self-reported. Arm span should be used to normalize the cross-sectional area measurements. The questionnaire data should be used to monitor changes over time with respect to shoulder pain, level of physical activity, and diet.

• Substantial increases or decreases in subject mass and physical activity between time-points would give an indication of changes in glenohumeral loading. It is recommended that these data be used to determine whether the individual increased or decreased glenohumeral loading as a result of wheelchair use, thereby assigning the individual to the appropriate subject group.

5.12.4 Combined Assessment of Bone and Cartilage

• When investigating functional adaptation to load-bearing at a joint such as the glenohumeral joint in manual wheelchair users, it is ideal to study both bone and cartilage. Frost emphasizes the interdependency of these tissues, stating that “chondral growth and modeling solely determine the orientations, shapes, and sizes of joint surfaces […]. The bone that replaces cartilage by endochondral ossification merely copies the chondral shape while it adjusts its amount and stiffness according to [the Mechanostat theory]” (140). Multi-modal imaging is required for the combined study of bone and cartilage since no current modality can simultaneously acquire the high-resolution, high-contrast scans of bone and cartilage that are necessary for quantitative analysis of tissue morphology.

• For a truly integrated assessment of bone and cartilage morphology at the glenohumeral joint, it is suggested that the bone and cartilage results be combined using image registration techniques. Using geometrical transformation algorithms, the reconstructed three-dimensional bone and cartilage models (from segmentation of the CT and MR scans respectively) could be spatially aligned. In the registered bone and cartilage model, these tissues would have the same spatial relationships as they do within the glenohumeral joint in vivo. Using this registered model, it would be possible to compare, for instance, bone density and cartilage thickness at a given location on the joint.
5.13 CLINICAL RELEVANCE

This study was motivated by a clinical concern: shoulder pain in manual wheelchair users. On the topic of shoulder pain in wheelchair users, van Drongelen et al. stated that “further research would benefit from surveys combined with physical and technical exams” (1). We believe that the pilot data acquired in this study are relevant to the wheelchair user population since we studied wheelchair user subjects in vivo, and we acquired a broad range of data as suggested by van Drongelen et al., including shoulder pain questionnaire responses from the subjects, shoulder examination findings from a physician, and quantitative imaging measurements of bone and cartilage morphology from CT and MR scans respectively. To our knowledge this is the first study to perform a combined investigation of bone and cartilage at the glenohumeral joint in manual wheelchair users.

We believe that increased understanding of how the bone and cartilage at the glenohumeral joint respond to loading via wheelchair use will benefit wheelchair users in many ways. First, these data could be used to recommend modifications to the functional tasks performed by current wheelchair users in an attempt to prevent shoulder pain, based on the adaptive capacity of glenohumeral bone and cartilage in childhood-onset and adulthood-onset wheelchair users. If differences are discovered between the way that bone and cartilage adapt to loading pre- and post-maturity, this would suggest modifying spinal cord injury rehabilitation and physiotherapy programs to tailor them to childhood-onset and adulthood-onset wheelchair users. Manual wheelchairs are currently designed based on anthropometric and biomechanical data from adulthood-onset wheelchair users, however these wheelchairs are used by both adulthood-onset and childhood-onset groups. If differences are found in the way that bone and cartilage adapt to wheelchair use prior to skeletal maturity, this might underscore the need for a wheelchair designed specifically for childhood-onset wheelchair users. Findings of bone and cartilage adaptation, or lack thereof, to wheelchair use could also be presented to insurance boards to justify funding requests for assistive devices that might help prevent shoulder pain, such as lifts to put wheelchairs into vehicles. It is clear that a better understanding of how glenohumeral bone and cartilage respond to wheelchair use would be advantageous to manual wheelchair users, possibly even improving their quality of life.
6 CONCLUSIONS

In this study we assessed bone and cartilage morphology at the glenohumeral joint in manual wheelchair users and able-bodied controls using quantitative imaging techniques. This pilot study was performed to assess the feasibility of answering the following two research questions in a cross-sectional study.

*Research Question 1: Are there differences in bone and cartilage morphology at the glenohumeral joint between childhood-onset and adulthood-onset manual wheelchair users?*

- A cross-sectional study (n = 22) would likely detect higher humeral head and glenoid trabecular vBMD in childhood-onset wheelchair users than in adulthood-onset wheelchair users. This would support the view that bone adapts to increased loading prior to skeletal maturity, and that this adaptation could be relevant to the development of shoulder pain.

- Glenoid subchondral bone normalized cross-sectional area was significantly greater in the younger subjects (i.e. childhood-onset wheelchair users and controls) than in the older subjects (i.e. adulthood-onset wheelchair users and controls) (p < 0.05). The childhood-onset wheelchair users had the highest normalized cross-sectional area and the values for the three other groups were lower and relatively close to each other. This suggests that the higher cross-sectional area of glenoid subchondral bone in the childhood-onset wheelchair users is related to adaptation and not to age.

- Despite the childhood-onset wheelchair users having non-significantly lower glenoid subchondral vBMD and higher normalized cross-sectional area than the adulthood-onset wheelchair users, our pilot data suggest that no negative correlation exists between glenoid subchondral vBMD and normalized cross-sectional area. This suggests that glenoid subchondral cross-sectional area does not increase at the expense of vBMD under increased loading conditions.

- Our pilot data suggest that a full-scale study would not find significant differences in the normalized cross-sectional area of humeral head total, trabecular, and cortical bone, or glenoid trabecular bone, between childhood-onset and adulthood-onset wheelchair users, or
between wheelchair users and able-bodied controls. It is therefore unlikely that a full-scale study of these parameters would provide insight into wheelchair users’ shoulder pain.

- No clear trend emerged for bone density distribution across either of the glenohumeral joint surfaces, although for all subjects in our study, mineralization was greater on the glenoid cavity than on the humeral head. It is unlikely that a full-scale study of bone density distribution would yield insight into the causes of shoulder pain in manual wheelchair users.

- Very large studies (i.e. n = 55 and n = 250) would be required to detect differences in humeral head and glenoid cartilage volume between childhood-onset and adulthood-onset wheelchair users. It is not likely that further studies of cartilage volume, even with these large sample sizes, would provide insight into the cause of shoulder pain in wheelchair users.

- A cross-sectional study (n = 22) would likely detect higher cartilage thickness in childhood-onset wheelchair users than in adulthood-onset wheelchair users. This would support the view that cartilage adapts to load during skeletal development.

Research Question 2: Are there differences in bone and cartilage morphology at the glenohumeral joint between long-term manual wheelchair users and their able-bodied matched controls?

- To our surprise, the manual wheelchair users in our study had (non-significantly) lower bone mineral density than their able-bodied controls. We believe that this is because some of the wheelchair users in this study loaded their shoulders to a lesser degree than their matched able-bodied controls. This is supported by our finding that there was a significant positive correlation between humeral head trabecular vBMD and physical activity score. It is important to note that the non-significant trend in our pilot data of lower vBMD in wheelchair users than in able-bodied controls was less pronounced than the trend towards lower bone mineral density in the older subjects (i.e. adulthood-onset wheelchair users and controls) compared to the younger subjects (i.e. childhood-onset wheelchair users and controls). Although both age and loading conditions are known to affect vBMD, our data suggest that the influence of age is more predominant than that of loading.
A reasonable cross-sectional study (n = 22) would likely find differences between childhood-onset and adulthood-onset manual wheelchair users in:

- humeral head trabecular vBMD
- glenoid trabecular vBMD
- glenoid subchondral normalized cross-sectional area

It is unlikely that a full-scale study would detect differences in:

- humeral head total vBMD
- glenoid subchondral vBMD
- humeral head total bone nCSA
- humeral head trabecular bone nCSA
- humeral head cortical bone nCSA
- glenoid trabecular nCSA
- bone density distribution

This suggests that including the latter parameters of bone morphology in a full-scale study would not provide insight into the functional adaptation of glenohumeral bone in response to wheelchair use. These parameters are, therefore, not likely to provide insight into shoulder pain in manual wheelchair users.

No differences were found in the parameters of cartilage morphology measured in this pilot study. A cross-sectional study (n = 22) would find differences in:

- humeral head mean cartilage thickness

It is unlikely that a full-scale study would detect differences in:

- glenoid mean cartilage thickness
- humeral head cartilage volume
- glenoid cartilage volume
- humeral head cartilage surface area
- glenoid cartilage surface area

This suggests that either glenohumeral cartilage does not adapt to loading from wheelchair use, or that morphological changes are too small to detect with the qMRI method. In future studies, it is recommended that cartilage composition be assessed with the dGEMRIC method in lieu of assessing cartilage morphology with qMRI.

If bone and cartilage are found to adapt differently to wheelchair use based on the age that wheelchair use began, it is hoped that this knowledge will lead to modifications of the activities performed by childhood-onset and adulthood-onset wheelchair users. This knowledge could be used to customize rehabilitation programs for new wheelchair users based on the individual’s age.
at the time of spinal cord injury, as well as to reduce shoulder loading in adulthood-onset manual wheelchair users (for example, recommending that they ask for assistance wheeling uphill and use a power-lift to put their wheelchair into their vehicle). Although gaining a better understanding of how glenohumeral bone and cartilage respond to wheelchair use will not cure shoulder pain, determining whether bone and cartilage adaptation are clinically relevant to shoulder pain is one step towards the ultimate goal of preventing shoulder pain in manual wheelchair users.
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APPENDIX A

ETHICS CERTIFICATE OF APPROVAL
Certificate of Expedited Approval: Renewal
Clinical Research Ethics Board Official Notification

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INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT
Other, Vancouver Coastal Health Authority

CO-INVESTIGATORS:
Hawkins, Robert, Orthopaedics; LaFrance, Amy, Mechanical Engineering

SPONSORING AGENCIES:
Rick Hansen Man In Motion Foundation

TITLE:
Quantitative Assessment of the Functional Adaptation of Bone and Cartilage at the Glenohumeral Joint in Manual Wheelchair Users

APPROVAL RENEWAL DATE: 8 September 2005
TERM (YEARS): 1
AMENDMENT: 
AMENDMENT APPROVED: 

CERTIFICATION:
In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The Chair of the UBC Clinical Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved for renewal by the UBC Clinical Research Ethics Board.

The CREB approval for renewal of this study expires one year from the date of renewal.

[Signature]

Approval of the Clinical Research Ethics Board by one of:
Dr. Gail Bellward, Chair
Dr. James McCormack, Associate Chair
APPENDIX B

QUESTIONNAIRES
Wheelchair Users Shoulder Pain Index

Date ____/__/____
Name _______________________________________
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### Self-care

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<tbody>
<tr>
<td>Lift objects from overhead</td>
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<tbody>
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184
# GENERAL LIFESTYLE QUESTIONNAIRE

**Name:**

**Date:**

**D.O.B.:**

**Address:**

**Phone:**

**Email:**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Traumatic SCI</th>
<th>Meningomyelocele</th>
<th>Lipomyelomeningocele</th>
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<tbody>
<tr>
<td></td>
<td>Meningocele</td>
<td>Other</td>
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**Date of Injury (SCI only):**

**Lesion level:**

| Shunt? | Yes | No |

**MSK or Neuro Surgeries:**

<table>
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<th>Age at surgery:</th>
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**Treatment for shoulder problems:**

| Yes | No |

**Explain if yes:**

| Category of ambulatory: | non-ambulator | household ambulator |

**Do you walk with crutches or walker when/if you walk at home?**

| Yes | No |

**Age first used wheelchair:**

<table>
<thead>
<tr>
<th># Yrs of wheelchair use:</th>
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**Hours per day in wheelchair:**

**Mode of transportation:**

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<th>(circle the one most used)</th>
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<tr>
<td>drive car/van</td>
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<tr>
<td>passenger in car / taxi</td>
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<tr>
<td>bus</td>
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<tr>
<td>Handidart</td>
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**If you drive, do you lift your WC into the car on your own?**

| Yes | No |

**On average, how far would you wheel in a day outside of home or office?**

| None | 1-3 blocks | 1km | 2-5 km | >5km |

**Do you get assistance in wheeling long distances or up hills?**

| Yes | No |
Do you need help with the following activities of daily living?

<table>
<thead>
<tr>
<th></th>
<th>No help</th>
<th>Some help</th>
<th>Complete help</th>
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</thead>
<tbody>
<tr>
<td>Dressing</td>
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<tr>
<td>Bathing</td>
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<tr>
<td>Preparing meals</td>
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<tr>
<td>Grocery shopping</td>
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<td>Housekeeping</td>
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<td>Banking/Finances</td>
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</table>

Type of Wheelchair:          Brand:                       Model:

Everyday use: (circle)
- Quickie: ____________
- Action: ____________
- Ti sport: ____________

Sports (circle)
- Basketball: Tennis: Rugby: Road Racer: Track & Field: Handcycling: Recreational wheelchair: Other: ____________

Do you play or participate in any organized or non-organized sports? Yes  No

If yes, which ones? (circle any)

How often do you participate in sports or physical activity?
- Daily: Weekly: Monthly: ____________

On average how many hours does an activity last?
- <30 min: 30min-1hr: <1hr: ____________

Are you limited in participation of sports due to shoulder pain? Yes  No

If so, how? ____________

QUESTIONS FOR RADIOGRAPHIC SECTION OF STUDY
Are you willing to have x-rays done of your shoulder? Yes  No

Are you willing to have an MRI of your shoulder? Yes  No

Name of family doctor: ____________________________

Name of orthopaedic surgeon: _____________________
Brief Pain Inventory (Short form)

Date ______ / ______ / ______ Time: ______

Name________________________________________

Last

First

1) Throughout our lives most of us have had pain from time to time (such as headaches, sprains and toothaches). Have you had pain other than these everyday kinds of pain today?

1. yes
2. no

2) Where do you feel pain? (shade in) Which spot hurts the most? (mark x).

3) Please rate your pain by the one number that best describes your pain at its worst in the last 24hrs.

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<tbody>
<tr>
<td>No Pain</td>
<td>Pain as bad as you can imagine</td>
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4) Please rate your pain by the one number that best describes your pain at its least in the last 24hrs.

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5) Please rate your pain by the one number that best describes your pain on average.

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6) Please rate your pain by the one number that tells how much pain you have right now.

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7) What treatments or medications are you receiving for pain?

8) In the last 24 hrs, how much relief have pain treatments or medications provided? Please indicate the percentage that most shows how much relief you have received?

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
No Pain

9) Indicate the one number that describes how, during the past 24 hrs, pain has interfered with your....

A. General activities

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B. Mood

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C. Wheeling ability

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D. Normal work/school (includes both work/school inside and outside the home)

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E. Relations with other people

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<td>Completely Interferes</td>
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F. Sleep

<table>
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<tr>
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<td>Completely Interferes</td>
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G. Enjoyment of life

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<td>Completely Interferes</td>
</tr>
</tbody>
</table>
THE QuickDASH
OUTCOME MEASURE

INSTRUCTIONS

This questionnaire asks about your symptoms as well as your ability to perform certain activities.

Please answer every question, based on your condition in the last week, by circling the appropriate number.

If you did not have the opportunity to perform an activity in the past week, please make your best estimate of which response would be the most accurate.

It doesn’t matter which hand or arm you use to perform the activity; please answer based on your ability regardless of how you perform the task.
Name: ___________________________        Date: ______________________

<table>
<thead>
<tr>
<th>Activity</th>
<th>NO DIFFICULTY</th>
<th>MILD DIFFICULTY</th>
<th>MODERATE DIFFICULTY</th>
<th>SEVERE DIFFICULTY</th>
<th>UNABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Open a tight or new jar.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Do heavy household chores (e.g., wash walls, floors).</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Carry a shopping bag or briefcase.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Wash your back.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Use a knife to cut food.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rating</th>
<th>NOT AT ALL</th>
<th>SLIGHTLY</th>
<th>MODERATELY</th>
<th>QUITE A BIT</th>
<th>EXTREMELY</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. During the past week, to what extent has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rating</th>
<th>NOT LIMITED AT ALL</th>
<th>SLIGHTLY LIMITED</th>
<th>MODERATELY LIMITED</th>
<th>VERY LIMITED</th>
<th>UNABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptom</th>
<th>NONE</th>
<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE</th>
<th>EXTREME</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Arm, shoulder or hand pain.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>10. Tingling (pins and needles) in your arm, shoulder or hand.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rating</th>
<th>NO DIFFICULTY</th>
<th>MILD DIFFICULTY</th>
<th>MODERATE DIFFICULTY</th>
<th>SEVERE DIFFICULTY</th>
<th>SO MUCH DIFFICULTY THAT I CAN'T SLEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? (circle number)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

QuickDASH DISABILITY/SYMPTOM SCORE = \(\left(\frac{\text{sum of n responses}}{n}\right) - 1\) x 25, where n is equal to the number of completed responses.

A QuickDASH score may not be calculated if there is greater than 1 missing item.
**WORK MODULE (OPTIONAL)**

The following questions ask about the impact of your arm, shoulder or hand problem on your ability to work (including homemaking if that is your main work role).

Please indicate what your job/work is: ______________________________________________________

☐ I do not work. (You may skip this section.)

Please circle the number that best describes your physical ability in the past week.

<table>
<thead>
<tr>
<th>Did you have any difficulty:</th>
<th>NO DIFFICULTY</th>
<th>MILD DIFFICULTY</th>
<th>MODERATE DIFFICULTY</th>
<th>SEVERE DIFFICULTY</th>
<th>UNABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. using your usual technique for your work?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. doing your usual work because of arm, shoulder or hand pain?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. doing your work as well as you would like?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. spending your usual amount of time doing your work?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

**SPORTS/PUBLISHING ARTS MODULE (OPTIONAL)**

The following questions relate to the impact of your arm, shoulder or hand problem on playing your musical instrument or sport or both. If you play more than one sport or instrument (or play both), please answer with respect to that activity which is most important to you.

Please indicate the sport or instrument which is most important to you: ______________________________________________________

☐ I do not play a sport or an instrument. (You may skip this section.)

Please circle the number that best describes your physical ability in the past week.

<table>
<thead>
<tr>
<th>Did you have any difficulty:</th>
<th>NO DIFFICULTY</th>
<th>MILD DIFFICULTY</th>
<th>MODERATE DIFFICULTY</th>
<th>SEVERE DIFFICULTY</th>
<th>UNABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. using your usual technique for playing your instrument or sport?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. playing your musical instrument or sport because of arm, shoulder or hand pain?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. playing your musical instrument or sport as well as you would like?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. spending your usual amount of time practising or playing your instrument or sport?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

**SCORING THE OPTIONAL MODULES:** Add up assigned values for each response; divide by 4 (number of items); subtract 1; multiply by 25.

An optional module score may **not** be calculated if there are any missing items.
PHYSICAL ACTIVITY SCALE FOR PERSONS WITH PHYSICAL DISABILITIES

Instructions: This questionnaire is about your current level of physical activity and exercise. Please remember there are no right or wrong answers. We simply need to assess your current level of activity.

Leisure Time Activity
1. During the past 7 days how often did you engage in stationary activities such as reading, watching TV, computer games, or doing handcrafts?
   1. Never (Go to question #2)
   2. Seldom (1–2d)
   3. Sometimes (3–4d)
   4. Often (5–7d)
   What were these activities?

On average, how many hours per day did you spend in these stationary activities?
   1. Less than 1hr
   2. 1 but less than 2hr
   3. 2–4hr
   4. More than 4hr

2. During the past 7 days, how often did you walk, wheel, push outside your home other than specifically for exercise. For example, getting to work or class, walking the dog shopping, or other errands?
   1. Never (Go to question #3)
   2. Seldom (1–2d)
   3. Sometimes (3–4d)
   4. Often (5–7d)

On average, how many hours per day did you spend wheeling or pushing outside your home?
   1. Less than 1hr
   2. 1 but less than 2hr
   3. 2–4hr
   4. More than 4hr

3. During the past 7 days, how often did you engage in light sport or recreational activities such as bowling, golf with a cart, hunting or fishing, darts, billiards or pool, therapeutic exercise (physical or occupational therapy, stretching, use of a standing frame) or other similar activities?
   1. Never (Go to question #4)
   2. Seldom (1–2d)
   3. Sometimes (3–4d)
   4. Often (5–7d)
   What were these activities?
On average, how many hour per day did you spend in these light sport or recreational activities?
1. Less than 1hr
2. 1 but less than 2hr
3. 2–4hr
4. More than 4hr

4. During the past 7 days, how often did you engage in moderate sport and recreational activities such as doubles tennis, softball, golf without a cart, ballroom dancing, wheeling or pushing for pleasure or other similar activities?
   1. Never (Go to question #5)
   2. Seldom (1–2d)
   3. Sometimes (3–4d)
   4. Often (5–7d)
   What were these activities?

On average, how many hours per day did you spend in these moderate sport and recreational activities?
1. Less than 1hr
2. 1 but less than 2hr
3. 2–4hr
4. More than 4hr

5. During the past 7 days, how often did you engage in strenuous sport and recreational activities such as jogging, wheelchair racing (training), off-road pushing, swimming, aerobic dance, arm cranking, cycling (hand or leg), singles tennis, rugby, basketball, walking with crutches and braces, or other similar activities?
   1. Never (Go to question #6)
   2. Seldom (1–2d)
   3. Sometimes (3–4d)
   4. Often (5–7d)
   What were these activities?

On average, how many hours per day did you spend in these strenuous sport or recreational activities?
1. Less than 1hr
2. 1 but less than 2hr
3. 2–4hr
4. More than 4hr
6. During the past 7 days, how often did you do any exercise specifically to increase muscle strength and endurance such as lifting weights, push-ups, pull-ups, dips, or wheelchair push-ups, etc?
1. Never (Go to question #7)
2. Seldom (1–2d)
3. Sometimes (3–4d)
4. Often (5–7d)
What were these activities?

On average, how many hours per day did you spend in these exercises to increase muscle strength and endurance?
1. Less than 1hr
2. 1 but less than 2hr
3. 2–4hr
4. More than 4hr

**Household Activity**
7. During the past 7 days, how often have you done any light housework, such as dusting, sweeping floors or washing dishes?
1. Never (Go to question #8)
2. Seldom (1–2d)
3. Sometimes (3–4d)
4. Often (5–7d)

On average, how many hours per day did you spend doing light housework?
1. Less than 1hr
2. 1 but less than 2hr
3. 2–4hr
4. More than 4hr

8. During the past 7 days, how often have you done any heavy housework or chores such as vacuuming, scrubbing floors, washing windows, or walls, etc?
1. Never (Go to question #9)
2. Seldom (1–2d)
3. Sometimes (3–4d)
4. Often (5–7d)

On average, how many hours per day did you spend doing heavy housework or chores?
1. Less than 1hr
2. 1 but less than 2hr
3. 2–4hr
4. More than 4hr
9. During the past 7 days, how often you done *home repairs* like carpentry, painting, furniture refinishing, electrical work, etc?
   1. Never (Go to question #10)
   2. Seldom (1–2d)
   3. Sometimes (3–4d)
   4. Often (5–7d)

   On average, how many hours per day did you spend doing *home repairs*?
   1. Less than 1hr
   2. 1 but less than 2hr
   3. 2–4hr
   4. More than 4hr

10. During the past 7 days how often you done *lawn work or yard care* including mowing, leaf or snow removal, tree or bush trimming, or wood chopping, etc?
    1. Never (Go to question #11)
    2. Seldom (1–2d)
    3. Sometimes (3–4d)
    4. Often (5–7d)

    On average, how many hours per day did you spend doing *lawn work*?
    1. Less than 1hr
    2. 1 but less than 2hr
    3. 2–4hr
    4. More than 4hr

11. During the past 7 days, how often have you done *outdoor gardening*?
    1. Never (Go to question #12)
    2. Seldom (1–2d)
    3. Sometimes (3–4d)
    4. Often (5–7d)

    On average, how many hours per day did you spend doing *outdoor gardening*?
    1. Less than 1hr
    2. 1 but less than 2 hr
    3. 2–4hr
    4. More than 4hr

12. During the past 7 days, how often did you *care for another person*, such as children, a dependent spouse, or another adult?
    1. Never (Go to question #13)
    2. Seldom (1–2d)
    3. Sometimes (3–4d)
    4. Often (5–7d)
On average, how many hours per day did you spend caring for another person?
1. Less than 1 hr
2. 1 but less than 2 hr
3. 2–4 hr
4. More than 4 hr

**Work-Related Activity**
13. During the past 7 days, how often did you work for pay or as a volunteer? (Exclude work that mainly involved sitting with slight arm movement such as light office work, computer work, light assembly line work, driving bus or van, etc.)
1. Never (Go to END)
2. Seldom (1–2 d)
3. Sometimes (3–4 d)
4. Often (5–7 d)

On average, how many hours per day did you spend working for pay or as a volunteer?
1. Less than 1 hr
2. 1 but less than 4 hr
3. 5 but less than 8 hr
4. 8 hr or more
INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the vigorous and moderate activities that you did in the last 7 days. Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

☐ Yes

☐ No → Skip to PART 2: TRANSPORTATION

The next questions are about all the physical activity you did in the last 7 days as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, heavy construction, or climbing up stairs as part of your work? Think about only those physical activities that you did for at least 10 minutes at a time.

_____ days per week

☐ No vigorous job-related physical activity → Skip to question 4

3. How much time did you usually spend on one of those days doing vigorous physical activities as part of your work?

_____ hours per day

_____ minutes per day

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like carrying light loads as part of your work? Please do not include walking.

_____ days per week

☐ No moderate job-related physical activity → Skip to question 6
5. How much time did you usually spend on one of those days doing moderate physical activities as part of your work?

_____ hours per day

_____ minutes per day

6. During the last 7 days, on how many days did you walk for at least 10 minutes at a time as part of your work? Please do not count any walking you did to travel to or from work.

_____ days per week

☐ No job-related walking ➔ Skip to PART 2: TRANSPORTATION

7. How much time did you usually spend on one of those days walking as part of your work?

_____ hours per day

_____ minutes per day

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the last 7 days, on how many days did you travel in a motor vehicle like a train, bus, car, or tram?

_____ days per week

☐ No traveling in a motor vehicle ➔ Skip to question 10

9. How much time did you usually spend on one of those days traveling in a train, bus, car, tram, or other kind of motor vehicle?

_____ hours per day

_____ minutes per day

Now think only about the bicycling and walking you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the last 7 days, on how many days did you bicycle for at least 10 minutes at a time to go from place to place?

_____ days per week

☐ No bicycling from place to place ➔ Skip to question 12
11. How much time did you usually spend on one of those days to bicycle from place to place?
   _____ hours per day
   _____ minutes per day

12. During the last 7 days, on how many days did you walk for at least 10 minutes at a time to go from place to place?
   _____ days per week
   ☐ No walking from place to place

   Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

13. How much time did you usually spend on one of those days walking from place to place?
   _____ hours per day
   _____ minutes per day

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the last 7 days in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, chopping wood, shoveling snow, or digging in the garden or yard?
   _____ days per week
   ☐ No vigorous activity in garden or yard

   Skip to question 16

15. How much time did you usually spend on one of those days doing vigorous physical activities in the garden or yard?
   _____ hours per day
   _____ minutes per day

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate activities like carrying light loads, sweeping, washing windows, and raking in the garden or yard?
   _____ days per week
   ☐ No moderate activity in garden or yard

   Skip to question 18
17. How much time did you usually spend on one of those days doing moderate physical activities in the garden or yard?

____ hours per day

____ minutes per day

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate activities like carrying light loads, washing windows, scrubbing floors and sweeping inside your home?

____ days per week

☐ No moderate activity inside home

Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY

19. How much time did you usually spend on one of those days doing moderate physical activities inside your home?

____ hours per day

____ minutes per day

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the last 7 days solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the last 7 days, on how many days did you walk for at least 10 minutes at a time in your leisure time?

____ days per week

☐ No walking in leisure time

Skip to question 22

21. How much time did you usually spend on one of those days walking in your leisure time?

____ hours per day

____ minutes per day

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do vigorous physical activities like aerobics, running, fast bicycling, or fast swimming in your leisure time?

____ days per week

☐ No vigorous activity in leisure time

Skip to question 24
23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?
   
   ____ hours per day
   ____ minutes per day

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

   ____ days per week

   □ No moderate activity in leisure time

   *Skip to PART 5: TIME SPENT SITTING*

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?

   ____ hours per day
   ____ minutes per day

**PART 5: TIME SPENT SITTING**

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend sitting on a **weekday**?

   ____ hours per day
   ____ minutes per day

27. During the **last 7 days**, how much time did you usually spend sitting on a **weekend day**?

   ____ hours per day
   ____ minutes per day

*This is the end of the questionnaire, thank you for participating.*
Food Frequency Questionnaire

Name:____________________________ Date:__________________________

We would like to know about some of the foods you eat. For each food listed please fill in how often you usually eat a portion of the size stated. If you eat the food:

• every day or more than once a day, fill in how many times you have it per day
• less than once a day but more than once a week, fill in the times per week
• less than once a week, but more than once a month, fill in the times per month
• less often than once a month, or never eat it, put an ‘X’ under ‘do not eat’.

Example: Janice has a glass of orange juice every morning, along with two slices of toast. She usually has two sandwiches at lunch, and eats french fries about 3 times per week. She almost never eats cauliflower.

<table>
<thead>
<tr>
<th>Food</th>
<th>Per day</th>
<th>Per week</th>
<th>Per month</th>
<th>Don’t eat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orange Juice, 1 cup</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>French fries, regular serving</td>
<td></td>
<td>3</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Cauliflower, ½ cup (125 ml)</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Bread or toast, 1 slice</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### NUMBER OF TIMES I EAT THE FOOD

<table>
<thead>
<tr>
<th>Food</th>
<th>Per day</th>
<th>Per week</th>
<th>Per month</th>
<th>Don’t eat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bread or toast, 1 slice or 1 roll</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muffin, 1 large</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pizza, 1 medium slice</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheeseburger or veggie burger with cheese</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheese: 1 slice processed OR 1 piece</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hard cheese (plain or in sandwich)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broccoli, ½ cup (125 ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gai-lan (Chinese broccoli), ½ cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bok-choi (Chinese cabbage), ½ cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ice cream (large scoop)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frozen yogurt (large scoop)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast food milkshake</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cottage cheese, ½ cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food</td>
<td>Per day</td>
<td>Per week</td>
<td>Per month</td>
<td>Don’t eat</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>---------</td>
<td>----------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>Yogurt, small (174 ml) carton or equivalent</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
</tr>
<tr>
<td>Canned salmon or sardines with bones, ½ small can</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
</tr>
<tr>
<td>Soft drink, 1 can or large glass</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
</tr>
<tr>
<td>Tofu, 2 oz (60 gm)</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
</tr>
<tr>
<td>Milk on cereal</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
</tr>
<tr>
<td>Orange juice, 1 cup</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
</tr>
<tr>
<td>Milk (any type including chocolate), 1 cup</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
</tr>
<tr>
<td>Macaroni &amp; cheese, 1 cup (250 ml)</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
<td>_______</td>
</tr>
</tbody>
</table>

I usually drink (choose one only)
- milk OR
- chocolate milk OR
- soy milk OR
- rice milk

Are you allergic to any foods?
- NO
- YES: (what foods?________________________________________________________)

Do you use any vitamin and/or mineral supplements? (This question is not about medications)

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Daily</th>
<th>&gt;3x/week</th>
<th>1-3x/week</th>
<th>&lt;1/week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Multivitamin/mineral</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Iron</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Calcium</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Other</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
</tbody>
</table>

What is the brand/name of the supplement?________________________________________________________

THANK YOU!