

**Validating Internal Density Calibration in The Proximal Humerus to Estimate Bone
Stiffness Using Finite Element Analysis for Stemless Shoulder Arthroplasty**

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Stemless humeral head components are a popular choice for patients undergoing shoulder arthroplasty for end-stage osteoarthritis (OA). OA is known to alter bone density in the humeral head, which can compromise implant stability and increase the need for surgical revisions. Current pre-operative clinical assessments are limited in evaluating bone mineral density (BMD) and fail to consider the mechanical properties of bone in the region directly supporting the stemless component, leaving a critical gap in understanding the structural integrity of the bone supporting the stemless component. Traditionally, in-scan phantom calibration determines volumetric bone mineral density (vBMD) from greyscale intensity in computed tomography (CT) images, but this method is rarely used in clinical practice due to limited time and resources. As a result, alternative density measures for determining accurate vBMD from clinical CT images are needed. Internal density calibration using internal tissues as references has been validated in the spine and hip, however, it has yet to be validated in the proximal humerus. Additionally, vBMD derived from internal density calibrated images has yet to be linked to finite element model (FEM) apparent stiffness in the context of stemless shoulder arthroplasty. Establishing stiffness as a measure of bone mechanical properties is a first step in accurately predicting bone strength in clinical CT images.

The purpose of this thesis was to 1) determine the correlation between phantom and internal density calibration in the proximal humerus using three different tissue combinations, 2) compare vBMD in an end-stage OA patient group to a non-pathologic group, and 3) determine the correlation between vBMD and apparent stiffness. Non-pathologic cadaveric single-energy CT images containing a dipotassium phosphate (K_2HPO_4) phantom were used to analyze a 10 mm thick volume of interest (VOI) directly below the anatomic neck. Phantom and internal density calibration was performed on each phantom-containing cadaveric specimen. vBMD was extracted and FEMs were generated from the VOI. The internal calibration with the lowest bias was used to calibrate images for all end-stage OA patient specimens. VOIs were created for cortical, trabecular, and combined (integral) bone compartments across specimens and vBMD was extracted for each compartment. FEMs were generated using the integral VOI to estimate apparent stiffness.

Statistical analysis revealed a strong correlation between internal and phantom density calibration, establishing internal calibration as a valid metric for determining vBMD (AAAdC $R^2 = 0.80$; AAAdCM $R^2 = 0.88$; ACM $R^2 = 0.90$). The ACM (Air, Cortical Bone, Skeletal Muscle) tissue combination had

the lowest error (Mean: 13.08 mgK₂HPO₄/cm³). The end-stage OA patient group had significantly lower integral (Patient: 119 mg K₂HPO₄/cm³; Cadaver: 159 mg K₂HPO₄/cm³), cortical (Patient: 518 mg K₂HPO₄/cm³; Cadaver: 643 mg K₂HPO₄/cm³), and trabecular (Patient: 79.8 mg K₂HPO₄/cm³; Cadaver: 110 mg K₂HPO₄/cm³) vBMD than the non-pathologic cadaveric group (p<0.001), highlighting the biological relevance of vBMD. Mean apparent stiffness was found to be significantly lower in the end-stage OA group (672 MPa) relative to the non-pathologic cadaveric group (1261 MPa) (p < 0.001), however stiffness was not correlated with cortical vBMD in either group (Patient: R² = -0.018, p = 0.73; Cadaver: R² = -0.018, p = 0.71), suggesting the need for a multi-factorial approach when quantifying mechanical properties using FEMs.

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Finally, I would like to recognize the constant outpouring of love and encouragement from my family. My incredible mama and papa, who taught me the value of education and who have always believed in me, and my loving husband Dallen, who emboldened me to pursue this degree even though it meant we would be newlyweds living apart. Words cannot express my gratitude and love for them, and I am so grateful we will be together forever.

Dedication

I dedicate this work to my younger self – a girl who remained endlessly curious and was always determined to make a difference in the world. She moved forward with courage even when the path ahead was unclear. May she always be proud of what she has accomplished.

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List of Abbreviations

AAdM – Air, adipose, skeletal muscle internal tissue combination

AAdCM – Air, adipose, cortical bone, and skeletal muscle internal tissue combination

ACM – Air, cortical bone, skeletal muscle

BMD – Bone mineral density

CT – Computed tomography

FE – Finite element

FEM – Finite element model

FOV – Field of view

HU – Hounsfield units

OA – Osteoarthritis

oCT – Opportunistic computed tomography

QCT – Quantitative computed tomography

ROD – Phantom calibration

ROI – Region of interest

vBMD – Volumetric bone mineral density

VOI – Volume of interest

Chapter 1

Introduction

Stemless humeral head components are a popular choice for patients undergoing shoulder arthroplasty for end-stage osteoarthritis (OA) (Athwal, 2016; Favre et al., 2016). However, OA is known to alter bone density in the humeral head, which can compromise implant stability and increase the need for surgical revision (Botha et al., 2010; Li et al., 2013). Current pre-operative clinical assessments are limited in evaluating bone mineral density (BMD) and fail to consider the mechanical properties of bone in the region directly supporting the stemless component (Knowles, Kusins, et al., 2020; Kusins, Knowles, Targosinski, et al., 2022). Traditionally, in-scan phantom calibration determines volumetric bone mineral density (vBMD) from greyscale intensity in CT images but is rarely used in clinical practice (Brunnquell et al., 2021; Cann & Genant, 1980; Knowles et al., 2016; Matheson et al., 2024; Michalski et al., 2020). Alternative density measures for determining accurate vBMD from clinical computed tomography (CT) are needed. While internal density calibration using internal tissues as references has been validated in the spine and hip, it has yet to be validated in the proximal humerus (Michalski et al., 2020). Additionally, vBMD has yet to be linked to finite element (FE) analysis estimating apparent stiffness in the context of stemless shoulder arthroplasty. While several studies have compared diseased bone relative to non-diseased bone in the humeral head, no studies have evaluated the bone directly below the resected humeral head that provides support to stemless humeral head components used in shoulder arthroplasty (Blakeney et al., 2021; Knowles et al., 2016; Reeves, Athwal, et al., 2018; Reeves et al., 2021; Ritter et al., 2024a). Establishing the relationship between vBMD and apparent stiffness, a measure of bone mechanical properties, through finite element models (FEMs) is a first step in accurately predicting bone strength from clinical CT images.

1.1 Purpose

The purpose of this thesis was to validate an internal density calibration method in the proximal humerus for determining vBMD in the context of shoulder arthroplasty. This research also links quantitative computed tomography (QCT) data to mechanical properties through FE analysis estimating bone stiffness.

1.2 Research Objectives

1.2.1 Objective 1

To determine the correlation and bias between vBMD and apparent stiffness from internal density calibration using three different referent tissue combinations 1) Air, Adipose, Cortical Bone (AAdC), 2) Air, Adipose, Cortical Bone, Skeletal Muscle (AAdCM), and 3) Air, Cortical Bone, Skeletal Muscle (ACM), compared to phantom calibration (ROD) in the proximal humerus.

1.2.2 Objective 2

To compare integral, cortical, and trabecular vBMD between an end-stage OA patient group and a non-pathologic cadaveric group using internal density calibration.

1.2.3 Objective 3

To determine the correlation between integral, cortical, and trabecular vBMD and apparent stiffness in an end-stage OA patient group and non-pathologic cadaver group using internal density calibration.

1.3 Hypothesis

It was hypothesized that there will be a strong correlation ($R^2 > 0.8$) between phantom calibration and the ACM internal calibration method thereby validating this method for use across samples (Matheson et al., 2024). Using the ACM internal calibration, it was hypothesized that vBMD and apparent stiffness would be higher in the non-pathologic cadaveric group relative to the end-stage OA group, and apparent stiffness would be strongly correlated ($R^2 > 0.8$) with integral, cortical, and trabecular vBMD in both groups.

1.4 Clinical Value

Validating internal density calibration in the proximal humerus for use on patient CT images has potentially significant clinical implications by providing surgeons with an objective measure of vBMD. This work serves as a first step in applying internal calibration as an accurate method to assess vBMD based on opportunistic CT (oCT), regardless of scanner settings or patient variability.

This is valuable for patients undergoing shoulder arthroplasty for end-stage OA as it allows surgeons to make a pre-operative plan based on patient specific morphology and density.

Clinical CT scans of the shoulder with internal based density calibration have yet to be used as inputs into FEMs. The use of FEMs considers patient specific morphology and the mechanical properties of bone to estimate stiffness. Establishing this relationship between vBMD and apparent stiffness is a first step in predicting patient-specific bone strength in the proximal humerus, allowing surgeons to simulate how a patient's bone might respond to an implant. Stiffness measurements could provide practical knowledge of the mechanical properties of patient-specific tissue for pre-operative planning, improving on methods currently used.

Chapter 2

Literature Review

2.1 Shoulder Osteoarthritis

In the shoulder, osteoarthritis (OA) is characterized by morphological degeneration of articular cartilage, changes in subchondral bone architecture, and osteophyte formation in the humeral head (Goldring & Goldring, 2010; G. Li et al., 2013; Thomas et al., 2016). With pathologic progression, these changes alter bone mineral density (BMD) within the humeral head which can impact implant fixation (Botha et al., 2010; G. Li et al., 2013). BMD is strongly correlated with bone stiffness and strength in OA populations, and reductions in BMD compromise mechanical integrity (Knowles et al., 2022; Kusins, Knowles, Targosinski, et al., 2022). Any loss in bone strength poses a risk for implant stability, increasing the likelihood of post-operative complications and the need for surgical revisions (Kusins et al., 2022A; Kusins et al., 2022B; Ritter et al., 2024). Despite its recognized importance, there are no standardized metrics for determining bone stiffness or strength in patients with end-stage OA (Knowles et al., 2020A; Tabarestani et al., 2023).

2.2 Shoulder Arthroplasty

Shoulder replacement surgery, also known as shoulder arthroplasty is a surgical procedure in which there is a prosthetic substitution of the humeral head and/or the glenoid within the glenohumeral joint (Caniggia et al., 1999). This procedure has become widely regarded as an effective surgical treatment for glenohumeral joint degeneration due to bone diseases such as OA (Harris et al., 2023; Reeves, Athwal, et al., 2018).

2.2.1 Relevant Anatomy

The glenohumeral joint is located between the humeral head of the humerus bone and the glenoid of the scapula and is held together by a complex collection of muscles, tendons, and ligaments ([Figure 2.2.1](#)) (Botha et al., 2010). Depending on the patient and their prognosis, both the humeral head and the glenoid may be replaced with prosthetic components during shoulder arthroplasty (Botha et al., 2010).

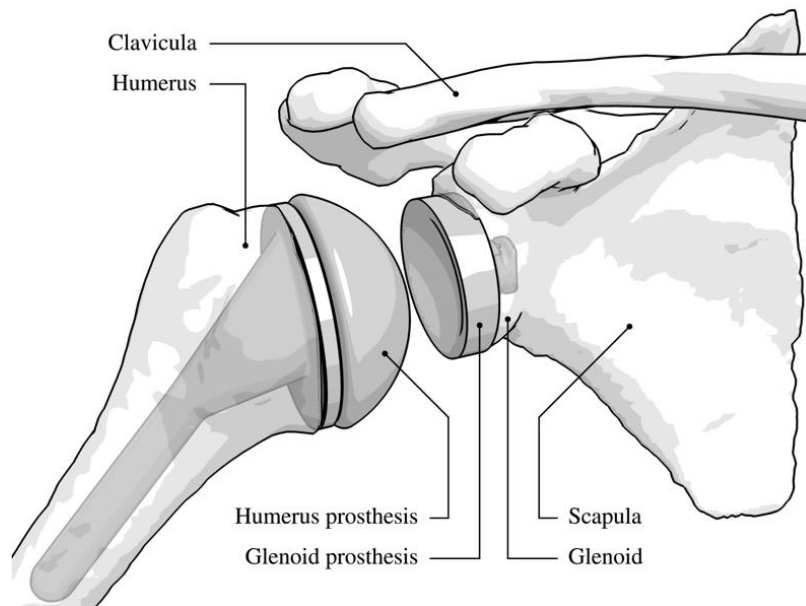


Figure 2.2.1 Bones of the glenohumeral joint after shoulder arthroplasty where both the humeral head and the glenoid have been replaced (Botha et al., 2010)

The humeral head is the articulating surface of the humerus within the glenohumeral joint. It is the most proximal section of the bone, proximal to the anatomical neck ([Figure 2.2.2](#)). During shoulder arthroplasty, the humerus is cut at the anatomical neck and the humeral head is resected (Nash et al., 2021; Reeves, Athwal, et al., 2018). The metaphysis is the section of the humerus that lies between the anatomical neck and the surgical neck. This section of bone is what supports the component when a stemless shoulder arthroplasty is performed. Below the surgical neck is the diaphysis, or shaft, of the humerus which contains the medullary cavity ([Figure 2.2.2](#)).

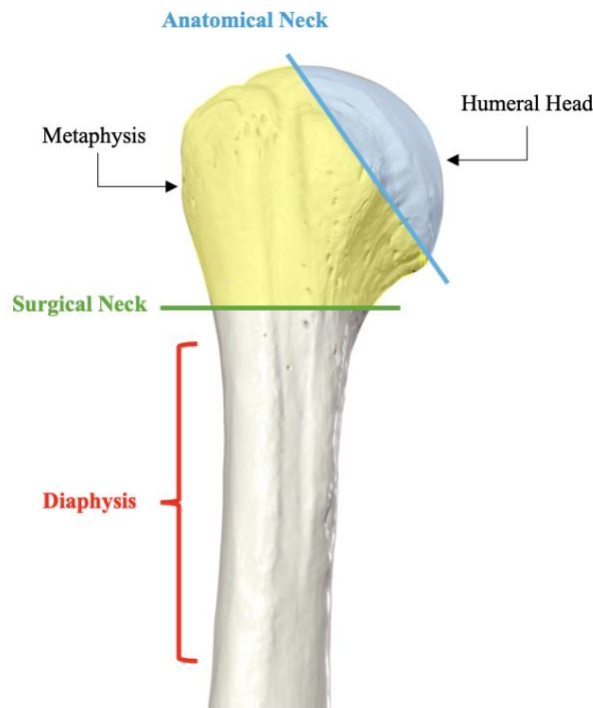


Figure 2.2.2 Relevant anatomy of the humerus in the context of shoulder arthroplasty.

2.2.2 Cortical and Trabecular Bone

Cortical bone forms the dense outer shell of bone and is primarily responsible for providing structural strength and transmitting mechanical loads. It is transversely isotropic, specifically bone strength is greatest under compression in the longitudinal direction and weakest under tensile loading in the transverse direction (Morgan et al., 2018). In long bones, cortical bone is arranged cylindrically with concentric parallel units known as lamellae arranged in the direction of mechanical stress (Hart et al., 2017; Osterhoff et al., 2016). In the diaphysis, the periosteum, a dense fibrous membrane, forms the outermost layer while the endosteum, a thin membrane, lines the inner surface (Buckwalter & Cooper, 1987; Hart et al., 2017). This structure creates an incredibly stiff material with a high elastic modulus.

Trabecular bone, by contrast, forms the porous inner framework of bone and consists of a lattice-like network of beams known as trabeculae, organized in the direction from which the greatest stresses are experienced (Buckwalter & Cooper, 1987; Hart et al., 2017). This compartment is characterized by a high surface area to volume ratio and is mechanically adapted to resist compressive

loads by distributing stress throughout the bone (Hart et al., 2017). Although less dense than cortical bone, trabecular bone contributes significantly to the overall mechanical behavior of the proximal humerus, particularly in the metaphyseal region, where it supports compressive forces and facilitates implant fixation in procedures like stemless shoulder arthroplasty.

Notably, the degree of mineralization in bone tissue is similar between cortical and trabecular bone, with mechanical differences between the two primarily the result of their distinct structural organization (van der Klift et al., 2005). In the humerus, the relative distribution of cortical and trabecular bone varies along its length from proximal to distal ends ([Figure 2.2.3](#)). Cortical thickness is greatest in the diaphysis and gradually decreases towards the proximal humerus, becoming thinner in the humeral head. Since the metaphyseal region, particularly the surgical neck, provides critical support in load bearing and implant support in the context of stemless shoulder arthroplasty, cortical thickness in the surgical neck provides essential structural support and contributes to the mechanical stability required for successful implant fixation (Willems et al., 2021). Meanwhile, the trabecular bone compartment becomes increasingly prominent proximally, forming a porous, energy-absorbing scaffold that supports compressive loading. The quality and architecture of the trabecular bone in the metaphysis, in combination with adequate cortical thickness, are critical for ensuring initial implant stability and long-term success of stemless designs.

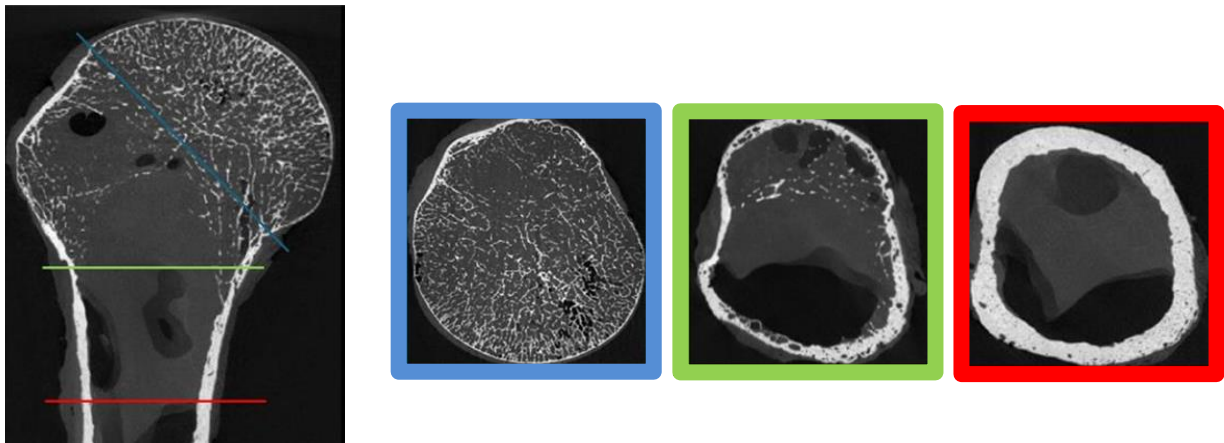


Figure 2.2.3 MicroCT images of proximal humerus showing distribution of trabecular and cortical bone. Slices have been taken from the anatomical neck (blue), surgical neck (green), and diaphysis (red).

2.2.3 Stemless Shoulder Arthroplasty

In recent years there has been a rapid increase in the number of commercially available shoulder arthroplasty implants. As such, surgeons may now select the most suitable design and method of fixation to best suit the patient's morphology and density. The conventional stemmed humeral component design replaces the humeral head with a metal hemisphere mounted on a stem that inserts into the medullary cavity of the humeral diaphysis ([Figure 2.2.4a](#)) (Mariotti et al., 2014). Conversely, newer stemless humeral components consist of a metal hemisphere, with no stem, anchored to the metaphyseal trabecular bone, directly below the resected plane at the anatomic neck ([Figure 2.2.4b](#)) (Alidousti et al., 2017; Mariotti et al., 2014; Shin et al., 2021). Therefore, for stemless components, only the diseased bone of the humeral head is removed for fixation (Mariotti et al., 2014).

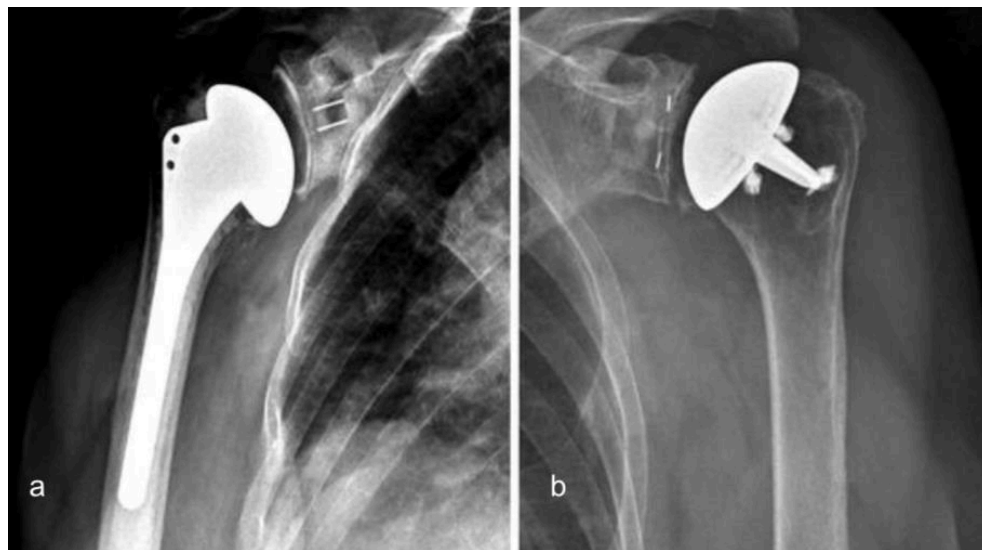


Figure 2.2.4 Radiographic image of stemmed (a) vs stemless (b) components for shoulder arthroplasty (Mariotti et al., 2014).

In general shoulder arthroplasties are designed to last 10-15 years meaning patients are likely to undergo at least one revision surgery in their lifetime (Evans et al., 2020; Knowles, et al., 2020). Given how the demand for shoulder arthroplasty is increasing at a rate of 8.2% per year for individuals < 55 years, and a rate of 12.1% per year for individuals > 55 years (Padegimas et al., 2015), stemless shoulder arthroplasty offers a considerable advantage for surgical OA treatment by preserving non-diseased bone for future revisions (Looney et al., 2022; Mariotti et al., 2014).

Several studies have reported equivalent short-term and mid-term functional outcomes and revision rates between stemmed and stemless humeral components (Gill et al., 2024; Looney et al., 2022; Märtens et al., 2021A, 2021B; Wiater et al., 2020; Zbeda et al., 2023). Stemless implant survival rate was found to be 93.5% eight years after initial surgery (Beck et al., 2018), and a systematic review of stemless shoulder arthroplasty reported the revision rate three years post operatively was 5.1%, with glenoid component loosening being the most frequent etiology (Willems et al., 2021).

Long term clinical outcomes for stemless shoulder arthroplasty have yet to be reported given the novelty of the stemless design. However, no contraindications have been identified for individuals over 70 receiving stemless arthroplasty (Baumgarten, 2023) and patient sex is not predictive of postoperative outcomes (Chang et al., 2022). In many studies, stemless shoulder components were reported as a superior option given the shorter operative time, lower levels of blood loss, better alignment when restoring patient-specific anatomy, better outcomes in reducing rotational malalignment, and better postoperative pain and ROM outcomes (Brabston et al., 2020; Cox et al., 2021; Koch et al., 2021; Liu et al., 2020; Nash et al., 2021; Shin et al., 2021; Werner et al., 2023). The lack of stem also made for easier component removal during revision (Liu et al., 2020). Given these results, sparing the humeral diaphysis for future revisions through stemless arthroplasty provides a strong argument for use over a stemmed arthroplasty design (Issa et al., 2022).

However, while stemless arthroplasty preserves bone, the component relies heavily on the properties of bone in the proximal humerus section beyond the plane of resection. This can be a potential downside if the section of bone does not offer sufficient support for the implant due to bone disease (Athwal, 2016; Brabston et al., 2020). Defining bone stiffness measures for the surgical success of stemless humeral components relies on accurate measures of bone mechanics in this region of interest. Unfortunately, objective preoperative measures of proximal metaphyseal bone quality are currently lacking (Athwal, 2016; Hayden et al., 2023).

For stemless shoulder arthroplasty, the 0 - 20 mm region below the anatomic neck is essential for supporting the implant's fixation features (Reeves, Athwal, et al., 2018). When considering the fixation of the central peg of the stemless component, Reeves et al. found that optimal apparent density was within the 15 - 20 mm region below the anatomic neck and that there was a relatively lower apparent density was within the 0 - 10 mm region. This 0 - 10 mm region directly supports the backside of the component. Therefore, accurate measurements of bone quality in this 0 - 10 mm

region are essential for successful stemless shoulder arthroplasty since low bone density can result in unstable humeral implant fixation, increasing risk of post-operative complications and the need for surgical revisions (Kusins et al., 2022A; Kusins et al., 2022B; Ritter et al., 2024). Ensuring bone quality can be accurately evaluated in this region of bone has clinical relevance for surgical planning of stemless shoulder arthroplasty.

2.3 Current Measures of Bone Density

2.3.1 Thumb Test

The thumb test is an inter-operative measure commonly used by surgeons performing shoulder arthroplasty to assess metaphyseal bone quality at the resection plane of the proximal humerus ([Figure 2.3.1](#)) (Hatta et al., 2023). The surgeon will place their thumb on the resected surface of the proximal metaphyseal bone and apply a minimal force. If the bone is impacted, the bone density is considered not strong enough to support the fixation of an implant (Hayden et al., 2023). However, this test is a subjective measure of bone stiffness in response to an applied stress and has low reproducibility between examiners, relying on the magnitude and location of force applied by the surgeon (Hatta et al., 2023; Hayden et al., 2023). When compared to bone density measurements (HU) taken from preoperative CT scans of the proximal humerus, the thumb test was found to be a poor predictor with surgeons only successfully identifying poor bone quality in 42% of patients with low bone density (Hayden et al., 2023). This test is also extremely limiting in that this assessment can only be performed during surgery, after the humeral head has been resected, thereby limiting preoperative understanding for implant selection and surgical preparation. A more standardized, reproducible, and accessible, assessment of bone stiffness is perhaps a more suitable way to assess bone quality for arthroplasty.

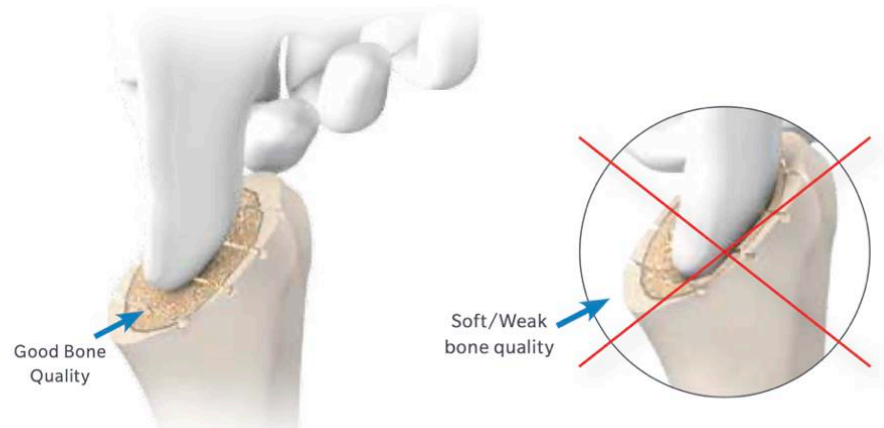


Figure 2.3.1 Thumb test used by surgeons to assess metaphyseal bone quality intraoperatively (Zimmer Biomet, 2011)

2.3.2 Opportunistic CT

Studies have highlighted the importance of considering patient morphology when selecting implant design as such it is common practice for surgeons to order a CT scan during surgical planning to determine to select a suitable implant design based on morphology (Reeves et al., 2018; Robertson et al., 2000). Since single energy CT is the most widely used 3D diagnostic imaging modality, these images can be used opportunistically to assess BMD without the need for additional scans (Engelke et al., 2015). This is known as opportunistic CT (oCT) and has been increasingly recognized as a valuable tool for assessing bone quality in orthopedic applications, including shoulder arthroplasty, by extracting quantitative BMD measurements from standard clinical scans originally acquired for anatomic evaluation (Anderson et al., 2018; Bartenschlager et al., 2023).

2.3.3 Hounsfield Units

CT images provide voxel information on the densities of tissues within the image frame provided in a scale of Hounsfield Units (HU). The HU is the relative quantitative measurement of the physical density of a tissue, it is proportional to the attenuation of an X-ray beam from the CT scanner through the tissue (DenOtter & Schubert, 2024). The level of attenuation, or the coefficient of radiation, through a tissue is used to construct a grayscale CT image. Tissues of higher densities have greater X-ray beam absorption and appear bright in the CT image; tissues of lower densities have lower X-ray

beam absorption and appear dark (DenOtter & Schubert, 2024). For bone tissue, HU is proportional to mineral density based on x-ray attenuation (McNabb-Baltar et al., 2022).

Currently, HU thresholds are used as a tool for screening and diagnosis. Pervaiz et al. (2013) found a significant difference in HU values in the proximal humerus of normal and osteoarthritic bone. Studies have also shown reliable estimations of BMD in the spine, wrist, femur, and femoral neck from HU values measured in the proximal humerus (Anderson et al., 2018; Earp et al., 2021). However, the HU outputs from these studies are highly variable, with large standard deviations in reported results (Hayden et al., 2023). While positive correlations between HU and BMD are important for validating the HU measurement as a first step in determining bone strength from CT images, reliable, quantifiable, and location specific measures of BMD are essential for surgical planning. This is especially true for individuals with OA undergoing shoulder arthroplasty.

A limitation of HU as a standardized measure of bone mineral density is that resulting HU values vary based on several factors such as x-ray beam energies (kilovoltage settings), the body segment of interest, patient size, position of patient in the scanner, scan to scan differences, scanner drift, as well as phantom orientation (Bott et al., 2023; Cann & Genant, 1980; Levi et al., 1982). HU values are therefore incredibly specific to the scanner setting and protocols (Bott et al., 2023). The selected x-ray beam energy, also known as tube voltage (kVp), will result in a specific level of tissue attenuation, which alters the HU value (Anderson et al., 2018; DenOtter & Schubert, 2024; Troy & Edwards, 2018). The selected reconstruction kernel will also affect the contrast levels of the CT image, changing the HU values in the proximal humerus (Knowles et al., 2024). The calibration of the scanner is also subject to change; while all CT scanners should recognize air as -1000 HU and water as 0 HU, based on the initial calibration (Pretorius, 2011), different scanners have been found to report varying HU values for water (Levi et al., 1982). Even when the settings are the same, different scanners will produce different HU values for the same patient, inducing quantitative differences in HU up to 7% (Eggermont et al., 2018; Troy & Edwards, 2018). The use of HU also relies on the selected field of view (FOV). Best practice is to select as small a FOV as possible that still encompasses all relevant anatomy thereby decreasing pixel size and increasing image resolution (Al-Naser & Tafti, 2025). Acquisition FOV has been found to greatly impact HU distributions, and no post-processing can recover accuracy lost through suboptimal FOV selection (Davis et al., 2018). Therefore, since HUs depend on the selected CT parameters, which are not consistent across clinical settings, HU as a measure of bone density lacks reliability and repeatability.

2.3.4 Volumetric Bone Mineral Density

HU units can be scaled to estimated vBMD using linear relationships between known density parameters and HU (Troy & Edwards, 2018). This is traditionally performed using a calibration phantom which is of value in research and in clinical trials to accurately measure and track changes in bone density. A linear relationship is established between voxel-specific intensity, measured in HU, and vBMD using either phantom or internal density calibration ([Section 2.4](#)). This method for quantifying BMD from CT images through calibration is known as quantitative CT (QCT).

To yield vBMD, values within the bone segment of interest are averaged across the volume, providing a standardized measure of bone density measured in units of voxel specific dipotassium phosphate (K_2HPO_4) density [mgK_2HPO_4/cm^3] (Matheson et al., 2024). Integral vBMD, which includes both the cortical and trabecular compartments, is most often used, however, cortical and trabecular vBMD can be assessed on their own through cortical bone segmentation, allowing for the mechanical contributions of each compartment to be considered separately. This is valuable since the densitometric relationships of bone can vary by anatomical location, as highlighted in [Figure 2.2.3](#), and bone compartment (Knowles et al., 2016). In the context of shoulder arthroplasty, isolating a specific volume of interest to assess BMD allows for a detailed consideration of bone quality which can help when selecting implant designs.

Unfortunately current clinical measures of vBMD for surgical planning of stemless shoulder arthroplasty only refer to the resected humeral head or the humeral shaft which fails to consider variations in bone quality where the implant is supported (Reeves et al., 2021). This is problematic since apparent bone density, defined as density divided by the total volume occupied by the bone plus pore and marrow space, has been reported as gradually decreasing in the proximal humerus from the proximal to distal end, below the resection plane, with the highest apparent bone density located proximal to the anatomic neck, the section of bone resected during implant fixation, and the lowest apparent bone density located just below the anatomic neck (Alidousti et al., 2017; Johanson et al., 1993; Reeves, et al., 2018; Saitoh et al., 1994) ([Figure 2.3.2](#)). However, these values for apparent density may be misleading since they take an average of all voxel-specific pixel intensities within the slice volume, including pore and marrow space and the method used to define these values was not subject-specific (Reeves, et al., 2018).

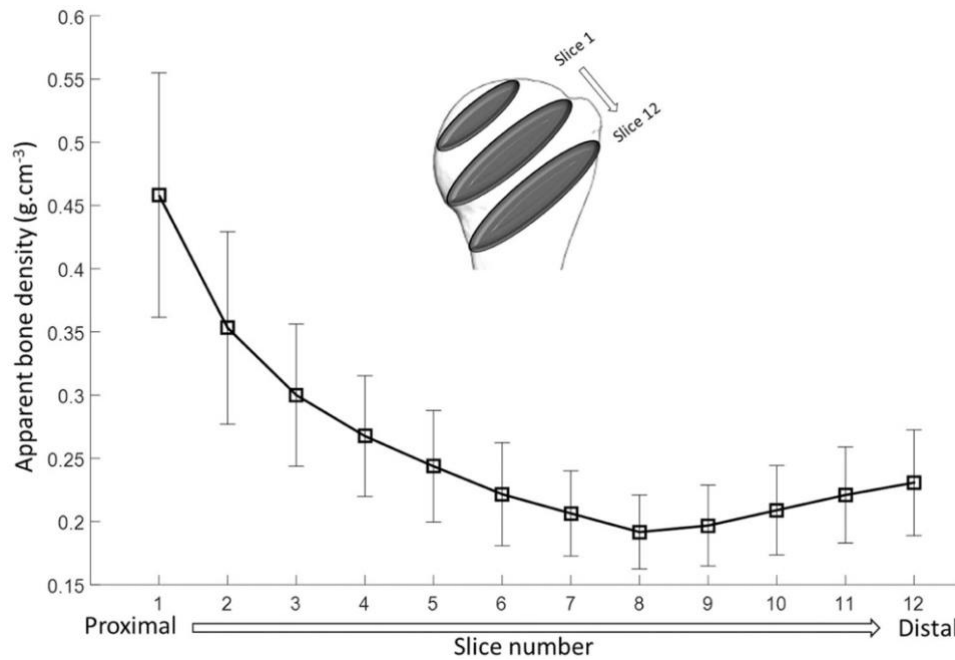


Figure 2.3.2 Variation in apparent bone density within slices of the proximal humerus. Slices move distally from the most proximal point (Alidousti et al., 2017).

Even when trabecular and cortical bone are separated within the CT scan to yield trabecular or cortical specific vBMD, the space within the canals of cortical bone and between trabeculae is still included within the average, thereby failing to account for the true density of the bone itself. Volume, cortical and trabecular bone composition, and pore space all vary from the proximal to distal end of the humerus, the actual bone density may be higher or lower than reported in each slice. Integral vBMD is not able to capture local variations. Since integral vBMD is used as a surrogate for the mechanical strength of the bone supporting the stemless component, inaccuracies within these measures may lead to inaccurate selection of patients that are candidates for stemless components.

Some limitations in using vBMD are that kilovoltage settings from the CT scanner and the bone reconstruction kernel that can alter HU values and therefore estimated vBMD values, similar to how acquisition settings can change HU values (Giambini et al., 2015; Troy & Edwards, 2018). Phantom calibration can account for kilovolt changes but cannot account for differences in reconstruction kernels (Troy & Edwards, 2018). So, while vBMD may be a more standardized measurement of bone density compared to HU, since density calibration can correct scanner variations, our objective understanding of density, and therefore apparent bone strength, in the proximal humerus is still

limited (Troy & Edwards, 2018). Given the ambiguity in current vBMD measurements, a more reliable and functionally meaningful estimate of bone strength in the proximal humerus needs to be established. Finite element modelling (FEM) offers a way to simulate mechanical loading and estimate bone strength based on the material properties derived from vBMD. In the context of stemless shoulder arthroplasty, the 10 mm section below the humeral resection at the anatomic neck, the area directly supporting the stemless humeral component, serves as a location to quantify vBMD and relate vBMD measures to mechanical strength (Reeves et al., 2021).

2.4 Density Calibration Methods for Quantitative Analysis

2.4.1 Phantom Calibration

Determining vBMD from clinical CT scans relies on a linear standardized relationship between HUs to units of radiological density [$\text{mgK}_2\text{HPO}_4/\text{cm}^3$] to produce QCT images. In research, this density calibration is performed using a dipotassium phosphate (K_2HPO_4), or hydroxyapatite (HA) phantom containing rods calibrated to materials with known mass attenuation values, and therefore known densities ([Figure 2.4.1](#)) (Cann & Genant, 1980). The calibration phantom is placed within the CT scanner's field of view (FOV), often underneath specimen, to serve as a calibration metric for determining tissue densities within the image (Engelke et al., 2015; Matheson et al., 2024). The known densities of the rods, provided by the manufacturer, can be segmented (isolated) within the image to generate a linear standardized relationship for converting HU to vBMD ([Figure 2.4.2](#) and [2.4.3](#)) (Eberle et al., 2013). However, in most clinical settings, CT images are taken without a calibration phantom since phantom based calibration requires additional resources and has the potential to introduce imaging artifacts through beam hardening, scatter, and/or air pocket formation between the specimen and phantom (Michalski et al., 2020)

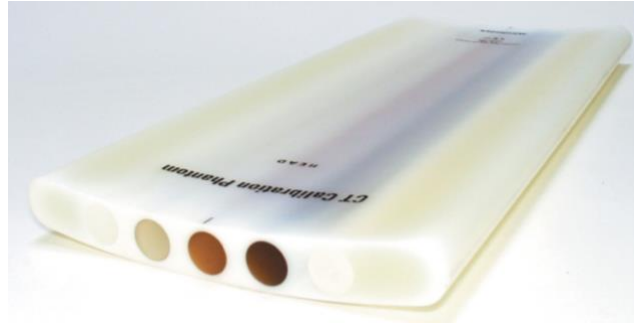


Figure 2.4.1 Liquid dipotassium phosphate (K_2HPO_4) phantom with known rod densities.

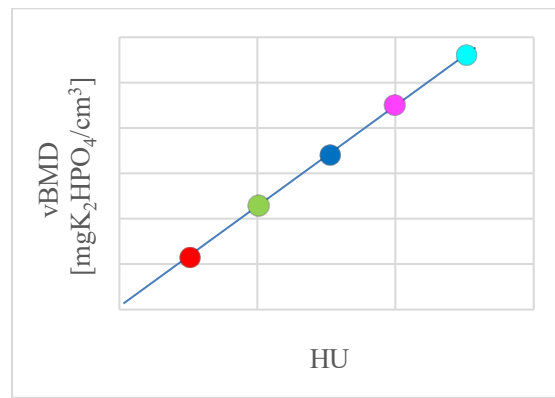


Figure 2.4.2 Visualization of the linear standardized relationship between HU and vBMD (mgK_2HPO_4/cm^3).

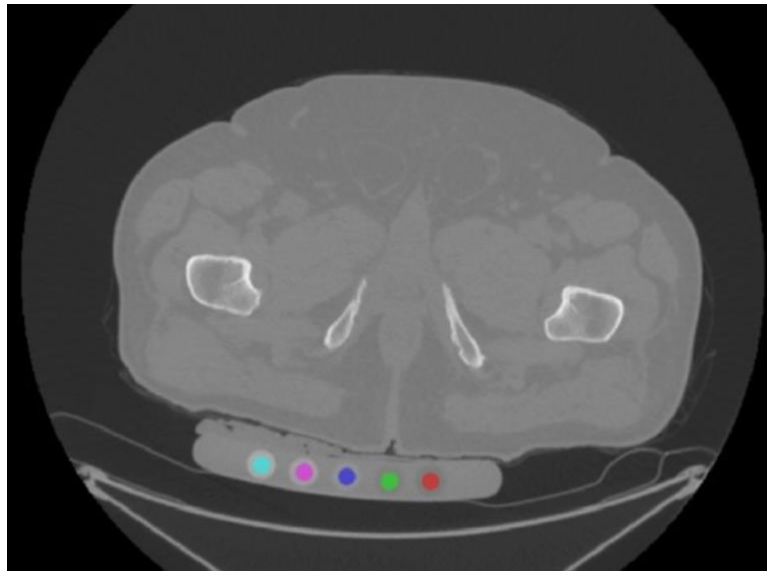


Figure 2.4.3 Phantom calibration in the abdominal cavity, axial view (Matheson et al., 2024). Phantom rod segmentation visible at the base of the image. Highest density ROI (cyan) and lowest density ROI (red).

2.4.2 Internal Density Calibration

Recently, an internal density calibration method has been developed that uses tissues with known densities as references to convert CT images into bone equivalent QCT (Michalski et al., 2020). This method uses internal tissues as reference to establish the linear standardized relationship between voxel-specific intensity (HU) and vBMD (Figure 2.4.4). Tissue ROIs are selected within each image and their corresponding mass attenuation values are assigned so equivalent K_2HPO_4 density can be determined based on correlating HU values (Michalski et al., 2020). Best practice is to select as large a ROI as possible to obtain representative tissue density values, averaging out small variations (Anderson et al., 2018; Chityala et al., 2004). Ideally ROIs avoid bone defects and focal lesions, but this is not always possible when measuring HU values in patients with bone disease (Anderson et al., 2018). This method has been established in the spine and hip using air, adipose, blood, skeletal muscle, and cortical bone as ROIs (Figure 2.4.5) (Matheson et al., 2024; Michalski et al., 2020). Each tissue will have subject- and scan- specific attenuation values that establish a unique linear standardized relationship for converting HU to vBMD within a CT image (Matheson et al., 2024).

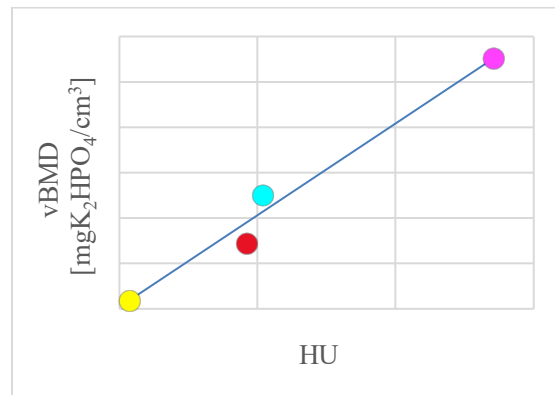


Figure 2.4.4 Visualization of the linear standardized relationship between pixel intensities (HU) and air (yellow), adipose (red), skeletal muscle (cyan), and cortical bone (purple) vBMD

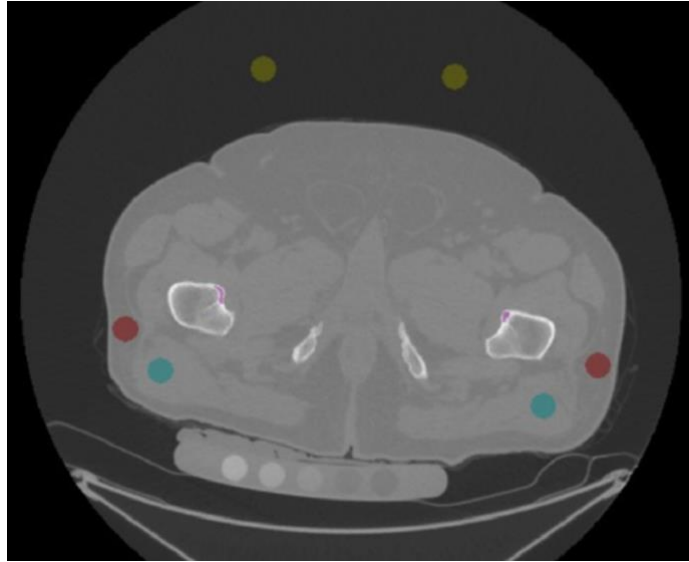


Figure 2.4.5 Internal density calibration in the abdominal cavity (Matheson et al., 2024). ROIs include adipose (red), air (yellow), cortical bone (purple), and skeletal muscle (blue). The potassium phosphate phantom with known rod densities is visible at the base of the image though, not used in this calibration method.

While a valuable tool, internal density calibration is prone to error since the attenuation values of tissue do not cover as wide of range as the known attenuations within a phantom, and tissue attenuation values may vary by scanner settings and by patient. The linear standardized relationship, established based on tissue attenuation values, relies heavily on the attenuation value of cortical bone, which has a much higher density than other internal reference tissues (Bott et al., 2023). A small shift in bone HU will have a large impact on the linear standardized relationship, and therefore the conversion from HU to vBMD (Bott et al., 2023); and any small differences in calculated vBMD can have a large impact on the estimated mechanical properties of the sample, specifically estimations of bone stiffness (Michalski et al., 2020). However, the combination of air, skeletal muscle, and cortical bone has been found to yield the most accurate vBMD estimates, with the mean error between phantom vBMD and internal vBMD being 0.06% in the femur (Matheson et al., 2024; Michalski et al., 2020). This indicates that with the correct method, internal density calibration can yield equivalent vBMD results to phantom based calibration.

While internal density calibration has been validated in the spine and hip, no validated internal density calibration method has been created for the proximal humerus, limiting the use of this method in upper-extremity imaging. This is important since attenuation values, and related bone stiffness, are

skeletally site-specific and are affected by bone quality and pathology (Knowles et al., 2016; Morgan et al., 2003; Schileo et al., 2007). Differences in shoulder anatomy and increased attenuation when scanning through the torso, relative to hip and spine anatomy, may lead to challenges in selecting referent tissues for the internal calibration method. As such there is a risk that the internal calibration method created by Michalski et al. 2020, which also uses a standard reconstruction kernel, does not produce reliable density values when compared to phantom based calibration, which can skew results. Given how attenuation values are site-specific and are altered by ROI and reconstruction kernel, understanding which internal calibration tissue combinations yield the lowest bias in the proximal humerus using a bone reconstruction kernel, are required to align with current scanning protocols at our centre. Thereby establishing a validated method for determining vBMD in the proximal humerus in the context of shoulder arthroplasty. Once the relationship has been determined between vBMD outputs from the internal density calibration and phantom calibration in the proximal humerus, internal density calibration may be sufficient to quantify vBMD in clinical settings and in CT images not containing a phantom.

2.5 Mechanical Properties

2.5.1 Bone Stiffness and Strength

Stiffness, also known as elastic or Young's modulus, can be defined as the resistance of a material to elastic deformation under load. It can be graphically represented as the slope of the stress strain curve in the linear, elastic region. Stiffness is an intrinsic mechanical property of a tissue determined by the stress a tissue experiences in response to an applied strain, measured in units of [MPa] ([Figure 2.5.1](#)) (Schileo et al., 2020). The structural organization of cortical and trabecular bone contributes significantly to overall bone stiffness (Helgason et al., 2008; Hildebrand et al., 1999; Schileo et al., 2020). Cortical bone, due to its dense and highly mineralized structure, exhibits a higher Young's modulus compared to trabecular bone, which has a more porous architecture (Hart et al., 2017). As a result, the relative proportion of cortical to trabecular bone within a given region will influence the site-specific mechanical behavior of bone.

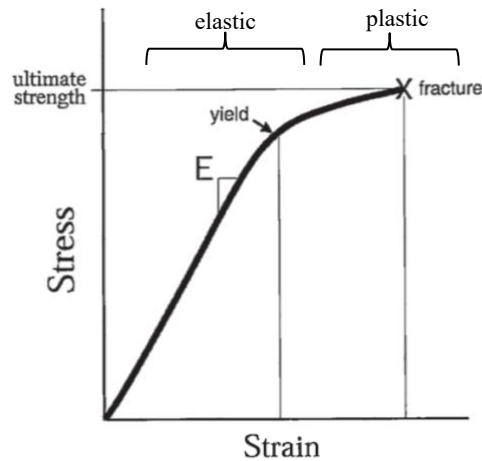


Figure 2.5.1 The stress strain curve for bone. Stiffness (E) is defined as the slope within the linear elastic region. The yield point is when elastic deformation becomes plastic deformation. Strength is calculated as yield or ultimate strength within the non-linear plastic region (Turner, 2006).

Bone strength, defined as either yield strength or ultimate strength can only be determined within the non-linear, plastic region, which can be difficult to model. However, it has been reported that there is a significant correlation between stiffness and bone strength, meaning bone stiffness can provide a linear estimate of bone strength (Helgason et al., 2008; Keller et al., 1990). Stiffness can therefore be used as a predictive measure of bone strength by creating subject-specific FEMs, using vBMD values from CT scans as input to provide information for understanding the mechanical properties of the bone segment of interest (Eberle et al., 2013).

2.5.2 Density-Modulus Relationship

BMD strongly correlates with the stiffness and yield strength of bone, accounting for 70% of variance in estimated values (Helgason et al., 2008; Keller et al., 1990). The relationship between bone density and stiffness is known as the density-modulus relationship; defined mathematically as the relationship between the densitometric measure of bone (BMD) and stiffness (E). It is this relationship that can be assigned to FEMs so that as voxel density increases, the stiffness of each element in the FEM will increase, resulting in an overall increase in specimen stiffness and load to failure (Michalski et al., 2020). The density-modulus relationship can be calculated using Equation 2 where variables α and β have been validated through in vitro mechanical testing of cadaveric sections, with stiffness (E) in [MPa] and bone density in [$\text{mgK}_2\text{HPO}_4/\text{cc}$] (ρ) based on calibration by a K_2HPO_4 phantom (Eberle et al., 2013).

$$E = \alpha \rho^\beta \quad (\text{Equation 1})$$

Density-modulus relationships are site-specific, relying heavily on the morphology and density of bone in the region of interest (Helgason et al., 2008; Morgan et al., 2003; Schileo et al., 2007). As has been seen in the femur, and other anatomic locations, subject specific FEM results will vary significantly based on the assigned density–modulus relationship (Knowles et al., 2016; Schileo et al., 2007). Using the density-modulus relationship established through individual CT images has been shown to improve the accuracy of subject specific FEM results (Eberle et al., 2013). Since at the whole bone level, these relationships neglect to include estimations of trabecular orientation and architecture, differences in trabecular architecture, cortical thickness, and tissue modulus will all impact how apparent stiffness values will vary based on anatomical site (Helgason et al., 2008; Hildebrand et al., 1999; Schileo et al., 2020). As such, there is no significant correlation in stiffness measurements between bone sites, highlighting the importance of establishing measurements to determine site-specific apparent stiffness (Patton et al., 2019).

2.5.3 FEM Estimated Apparent Stiffness

Apparent stiffness refers to the overall resistance of a bone segment to elastic deformation under load, accounting for both the material properties and structural geometry of the segment of interest through FEMs (Knowles, Kusins, et al., 2020; Yeni & Fyhrie, 2001). The benefit of using apparent stiffness as a predictive measure of bone strength is that it allows for both the morphology and the mechanical properties of the bone segment to be considered, reducing the ambiguity of using averaged regional vBMD alone. Masks are used to isolate the tissue segment of interest from patient specific CT images as inputs to FEMs to estimate apparent stiffness (Knowles et al., 2024). Cortical bone mapping may be used to generate a threshold between the cortical and trabecular bone to determine the relative contributions of cortical and trabecular bone compartments to bone stiffness in the proximal humerus through CT based FEM (Schileo et al., 2020; G. Treece & Gee, 2018).

In the context of shoulder arthroplasty, considering the mechanical behavior of the proximal humerus allows for a practical application of bone stiffness. For example, assessing cortical bone stiffness pre-operatively may provide valuable information about the strength of the bone segment supporting the stemless component since it has been reported that the cortical bone bears a larger percentage of the total applied load compared to trabecular bone in the femur (Schileo et al., 2020).

Additionally, considering only the 10 mm region directly below the plane of resection could provide biologically relevant insight into how the region supporting the component will respond under strain.

Chapter 3

Methods

3.1 Methods Overview

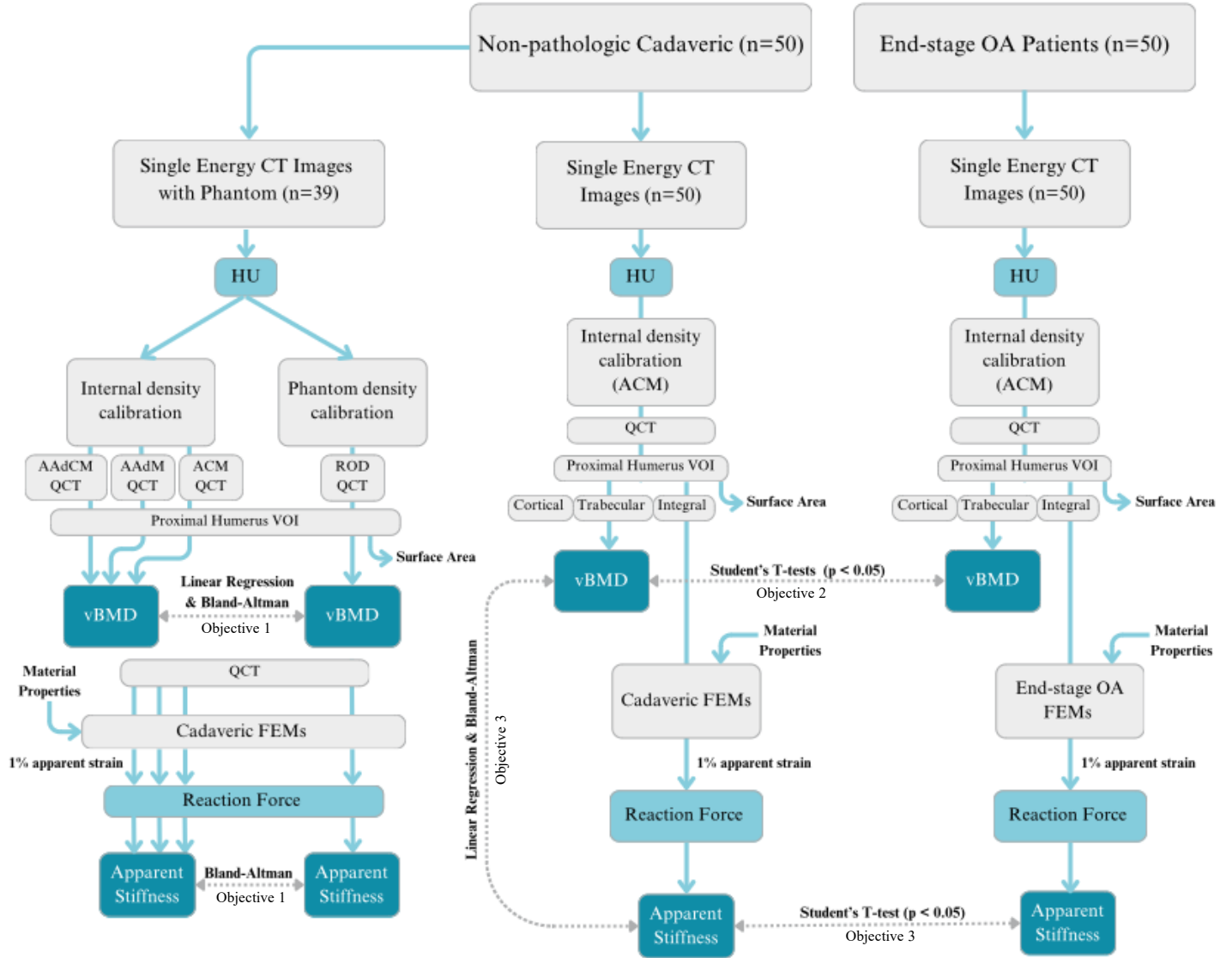


Figure 3.1.1 Flow chart depicting methods overview for entire thesis. Acronyms are defined as follows: Hounsfield units (HU), quantitative computed tomography (QCT), internal calibration method according to tissue combination (AAdCM, AAdM, ACM), phantom calibration (ROD), volume of interest (VOI), volumetric bone mineral density (vBMD), finite element models (FEM).

3.2 Specimen Information

3.2.1 Cadaveric Images

Single-energy CT images from fifty non-pathologic cadaveric shoulder specimens were selected from our pre-existing lab database. Thirty-nine contained a dipotassium phosphate (K_2HPO_4) calibration phantom (Model 3 CT Calibration Phantom, Mindways Software Inc., Austin, TX, USA) in the scan field of view (FOV). The rest were selected at random. Of the fifty specimens, 12 were female, 38 were male, ranging in age from 50 to 93 years ($M = 69.56$, $SD = 9.72$).

3.2.2 Patient Images

Clinical single-energy CT images from fifty patients undergoing shoulder arthroplasty to treat end-stage OA at the Roth McFarlane Hand & Upper Limb Centre (London, Ontario) were used as the pathologic group. Of the fifty patients, 17 were female, 33 were male, ranging in age from 38 to 84 years ($M = 63.36$, $SD = 9.97$).

3.2.3 Scan Parameters

Each scan was performed on a GE Discovery CT750 HD scanner located at the Roth McFarlane Hand & Upper Limb Centre (London, Ontario) at 120 kVp, 200 mA, 0.625 mm slice thickness, 512 x 512 image resolution and pixel spacing ranging from 0.547 mm to 0.902 mm. All images were reconstructed using the Boneplus reconstruction kernel which provides high spatial resolution and contrast within the image (Yan et al., 2021). This image protocol is consistent with pre-operative CT imaging used at the Roth McFarlane Hand & Upper Limb Centre.

3.3 Isolating the Volumes of Interest

3.3.1 Integral VOI

The humerus was segmented in each image using a global threshold and standard HU window ($HU > 225$) (Mimics v.20.0, Materialise, Leuven, BE). A closed morphology operation, combining dilation and erosion, was used to fill cavities in the mask (Materialise, 2025). Region growing and semi-automated morphological tools were used to isolate and fill the proximal end of the humerus for vBMD measurements and FEM generation ([Figure 3.3.1](#)). A 10 mm region directly below the

anatomic neck was isolated by aligning a 10 mm cuboid below the ideal plane of resection, simulating the bone directly supporting a stemless humeral component (3-matic v.18.0, Materialise, Leuven, BE) (Reeves, Athwal, et al., 2018). Placement was informed by an orthopedic surgeon specializing in shoulder arthroplasty. A Boolean intersection was applied to isolate the common VOI for analysis across calibration methods (MeshLab v2023.12) ([Figure 3.3.2](#)).

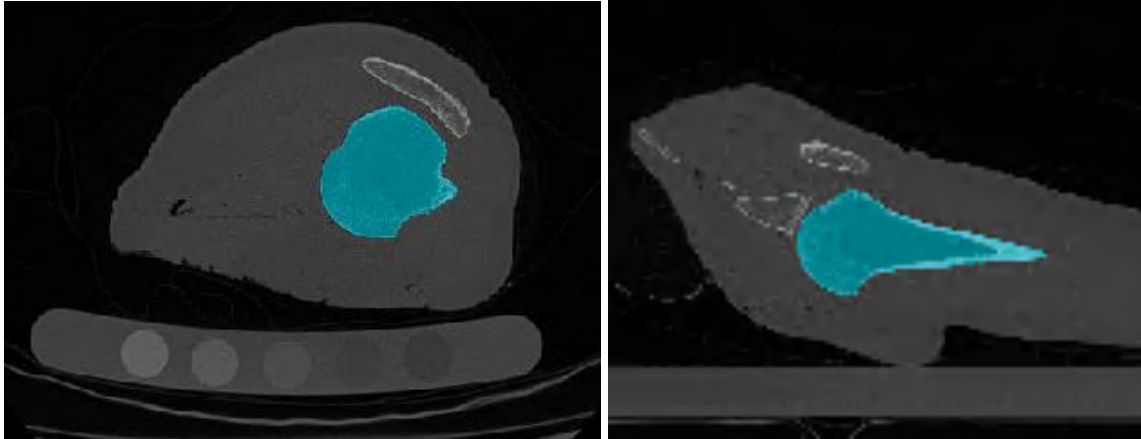


Figure 3.3.1 Filled mask of the proximal humerus segment created in Mimics. Seen in the (a) coronal and (b) sagittal plane.

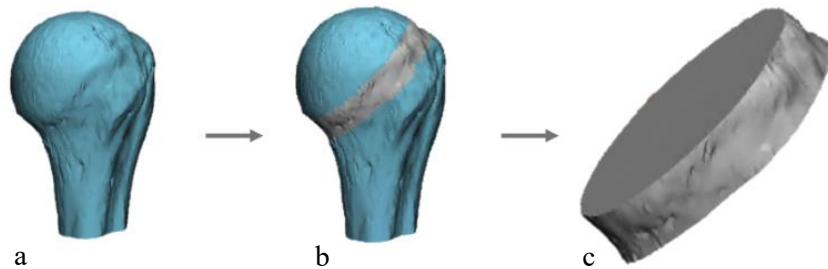


Figure 3.3.2 Method for isolating the 10 mm integral VOI. a) A part was created of the proximal end of the humerus from the raw DICOMs (Mimics). b) A 10 mm cuboid was aligned distal to the resection plane (3-Matic). c) A Boolean intersection (Meshlab) was then applied to isolate the VOI for analysis.

3.3.2 Cortical and Trabecular VOI

For all specimens, cortical bone was segmented again in Mimics by generating a new mask with a threshold of 475 HU, based on the cortical peak seen on the thresholding graph (Majed et al., 2019; Materialise, 2025). A closed morphology operation was used again (Materialise, 2025). A part was

generated from the cortical shell mask and a Boolean Intersection operation was used with the previously aligned integral VOI to isolate the cortical VOI ([Figure 3.3.3a](#)). A Boolean Minus operation was used to subtract the cortex from the integral VOI to isolate the trabecular VOI ([Figure 3.3.3b](#)). The three VOIs can be seen in [Figure 3.3.4](#).

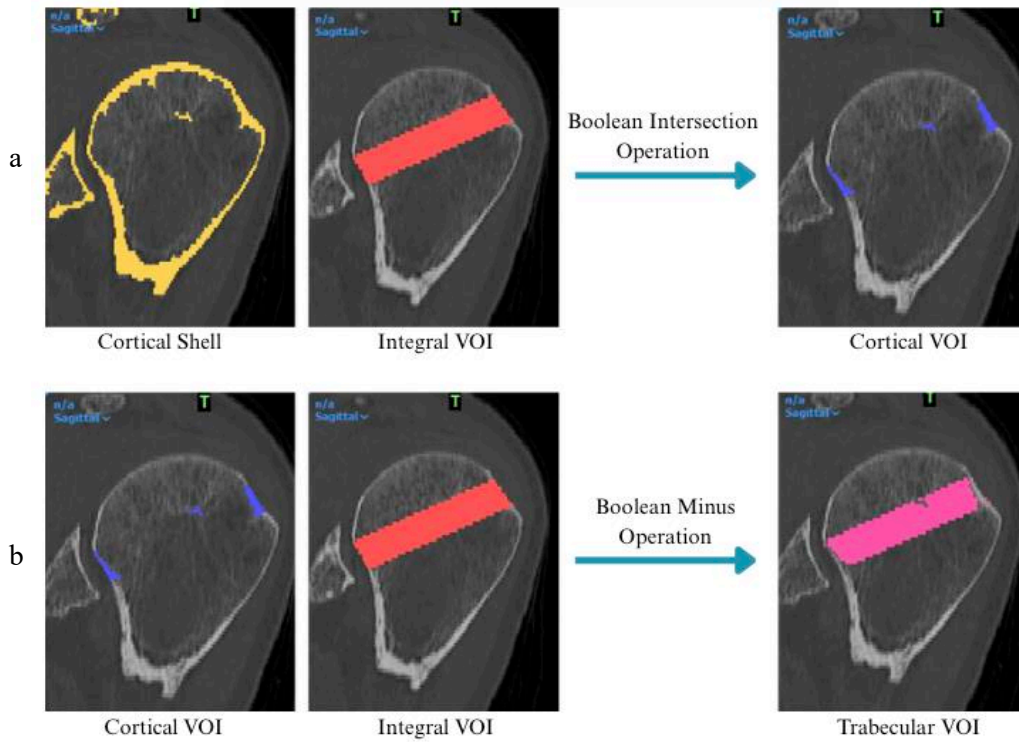


Figure 3.3.3 Creation of cortical and trabecular VOIs (Mimics). a) A Boolean intersection was applied to isolate the cortical VOI by overlaying the integral VOI with the cortical shell. b) A Boolean minus was applied to isolate the trabecular VOI by overlaying the cortical VOI with the integral VOI.



Figure 3.3.4 Integral, cortical, and trabecular VOIs.

3.4 Density Calibration Methods for Quantitative Analysis

3.4.1 Phantom Calibration

Phantom calibration was performed by manually segmenting the phantom rods in each image (ITK-SNAP v4.2.0), and after correcting for water as described by the Model 3 CT phantom user manual, a linear relationship was established between the in-scan phantom HUs and the known K_2HPO_4 density ([Figure 3.4.1a](#)) (Boden et al., 1989). Custom code (<https://github.com/Bonelab/Ogo/>) was used to produce calibrated QCT images in $[mgK_2HPO_4/cm^3]$.

3.4.2 Internal Calibration

For the internal calibration method, ROIs were manually selected for air (A), adipose (Ad), and skeletal muscle (M) as follows: air was taken outside the body, adipose was taken subcutaneous, and skeletal muscle was taken from the subscapularis, infraspinatus, or deltoid depending on the need to avoid muscle fat infiltration ([Figure 3.4.1b](#)). Blood was excluded as cadaveric tissues do not contain a defined blood-filled artery for measurement and for patients scans there is not a large enough ROI within the field of view of the shoulder. ROI placement was at the same level as the proximal humerus VOI to reduce the potential for HU variations due to beam hardening (Boden et al., 1989; Matheson et al., 2024; Michalski et al., 2021). The proximal humerus was segmented within each image using a semi-automated method of applying a Hessian-based bone enhancement filter combined with a graph cut technique (Besler et al., 2021; Boykov & Funka-Lea, 2006). The bone was then thresholded to determine the highest HU value between 1000 – 1500 HU for cortical bone (C) (Pretorius, 2011). Internal calibration was performed using three different referent tissue combinations 1) Air, Adipose, Cortical Bone (AAdC), 2) Air, Adipose, Cortical Bone, Skeletal Muscle (AAdCM), and 3) Air, Cortical Bone, Skeletal Muscle (ACM), to determine the combination with the lowest mean difference compared to phantom calibration (ROD) (Matheson et al., 2024). The same source code used for the phantom calibration was used to produce internally calibrated QCT images in $[mgK_2HPO_4/cm^3]$.

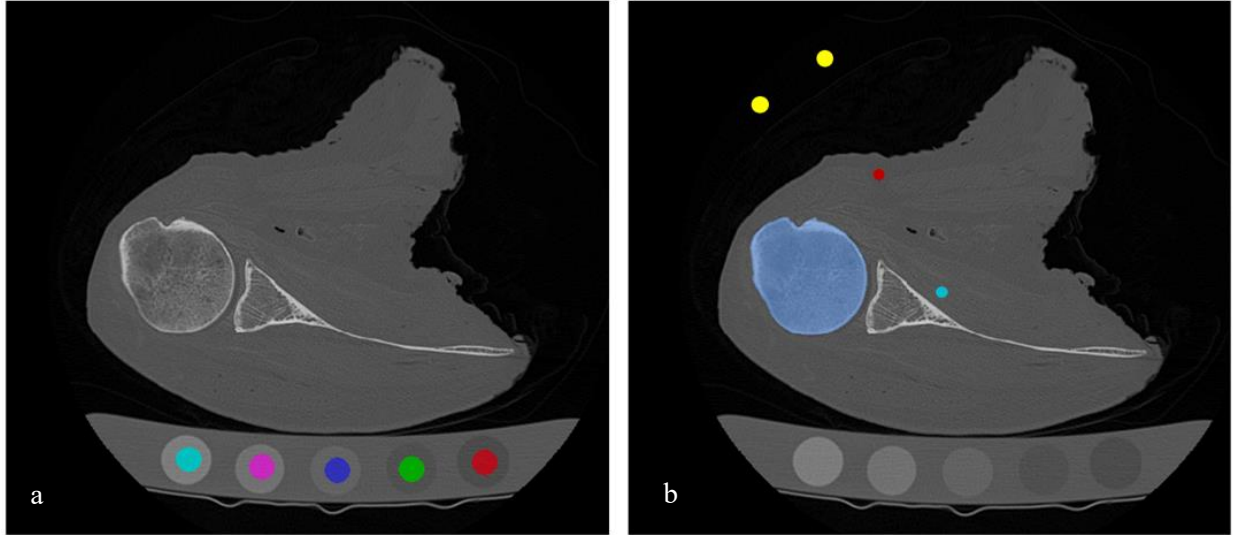


Figure 3.4.1 Density calibration methods for QCT image analysis. a) Phantom calibration. K_2HPO_4 can be seen at the base of the image. Each rod is manually segmented 10 slices from each end and then interpolated (ITK-SNAP) to establish the linear conversion between HU and K_2HPO_4 density using the highest (teal) and lowest (red) densities. b) Internal calibration. Referent tissues of air (yellow), adipose (red), and skeletal muscle (teal), were segmented manually at the level of the proximal humerus. Cortical bone (blue) was thresholded to determine the highest HU value which is essential for establishing the HU-density conversion.

3.5 vBMD Extraction

The subject specific VOIs were overlaid with both phantom and internal density calibrated QCT images to extract vBMD (3D-Slicer v.5.6.2) (Kikinis et al., 2014).

3.6 Finite Element Model Creation

The isolated integral VOIs were converted to a triangular surface mesh with an absolute maximum 1.5 mm edge length and 0.15 mm geometrical error using embedded tools (3-matic). The surface area of the proximal and distal ends was taken using the mark plane tool ([Figure 3.6.1](#)).

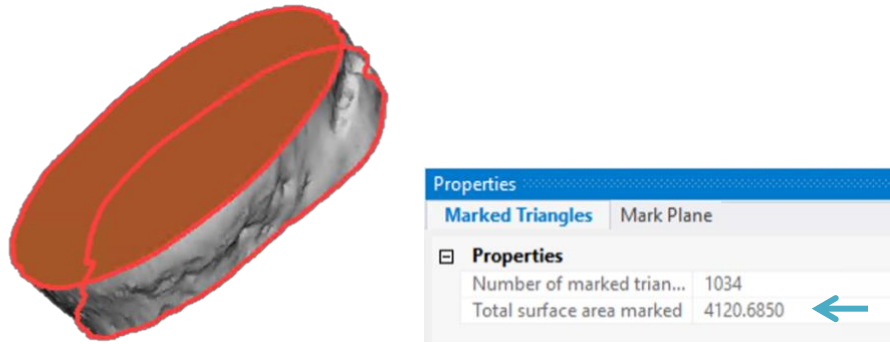


Figure 3.6.1 Apparent surface area extraction (A) of the proximal and distal ends of the 10 mm proximal humerus segment (orange) (3-Matic).

Integral VOIs were volume meshed with 4-node linear tetrahedral elements (C3D4) using finite element software (Abaqus v.2022, Simulia, Providence RI, USA) (Figure 3.6.2a). Material properties were assigned to the volume mesh by overlaying the subject-specific, and calibration method-specific, density calibrated QCT image (Bonemat v.3.2) (Taddei et al., 2007). The density modulus relationship ($E_{bone} = 12,486\rho_{qct}^{1.16}$) (Eberle et al., 2013; Knowles et al., 2024) was then applied through the entire density range of the model (Figure 3.6.2b).

FEMs were generated with the proximal and distal surfaces of the VOI acting as rigid bodies, with guiding nodes fixed to all nodes on the proximal and distal surfaces (Abaqus). The local coordinate system was aligned with the x-y plane along the proximal surface and the z-axis pointing distally. A 1% apparent strain (0.1 mm displacement) (Courtney et al., 1996) was applied along the z-axis from the proximal surface with the distal surface fully fixed. The reaction force on the distal surface at the maximum applied displacement was collected (Figure 3.6.2c).

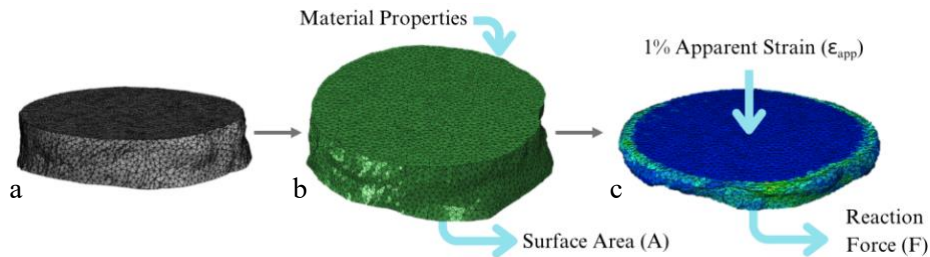


Figure 3.6.2 Finite element model generation. a) Triangular surface mesh of VOI (3-Matic). b) Tetrahedral volume mesh with assigned material properties (Bonemat). c) FEM with a 1% applied compression strain (Abaqus)

Apparent stress was calculated by taking the reaction force of the FEM simulation (F), divided by apparent area averaged across the proximal and distal VOI surfaces (A) (Equation 2). Apparent stiffness (E) was calculated as the apparent stress divided by the applied apparent strain (Equation 3).

$$\sigma_{app} = \frac{F}{A}$$

(Equation 2)

$$E_{app} = \frac{\sigma_{app}}{\varepsilon_{app}}$$

(Equation 3)

All statistics were performed using custom code written in R studio (v2024.04.1+748).

Chapter 4

Validate the use of Internal Density Calibration

4.1 Purpose

To determine the correlation and bias between vBMD and apparent stiffness from phantom density calibration and internal density calibration, using three different referent tissue combinations, in the proximal humerus.

4.1.1 Research Questions

Can internal density calibration be used for conversion of HU to vBMD in the proximal humerus when a phantom is not present in the image? Which tissue combination is best for yielding equivalent vBMD and apparent stiffness results to that of phantom calibration?

4.1.2 Hypothesis

Internal calibration will be equivalent to phantom calibration when determining vBMD and apparent stiffness. The ACM method will have the greatest correlation (Matheson et al., 2024).

4.1.3 Rationale

If an internal density calibration method is equivalent to phantom calibration, then phantoms are not required for determining vBMD from the greyscale image (HU). This is valuable because vBMD is a more meaningful metric than HU and is consistent across scanner settings and models. It also means that internal calibration can be used in the end-stage OA patient group for determining apparent stiffness since phantoms are not present in the images. If the correlation between phantom calibration and an internal calibration method is greater for apparent stiffness values than vBMD values, then mechanical properties might be a better metric for assessing bone quality.

4.2 Methods

4.2.1 Cadaveric Images Containing a Phantom

The thirty-nine non-pathologic cadaveric shoulder specimens containing a dipotassium phosphate (K_2HPO_4) calibration phantom in the scan FOV were used for this study. Integral VOIs were generated for each specimen using the methods outlined in [Section 3.3.1](#).

4.2.2 Density Calibration for Quantitative Analysis

Phantom calibration (ROD) and internal calibration, using each tissue combination (AAAdC, AAAdCM, and ACM), was performed according to the method outlined in [Section 3.4](#). vBMD was extracted for phantom and internal QCT images using each specimen's integral VOI ([Section 3.5](#)).

4.2.3 HU Value Extraction

HU values from each tissue ROI were extracted from the QCT txt file to compare to expected HU values for each tissue ([Table 4.2.1](#)) (Pretorius, 2011).

	Air (A)	Adipose (Ad)	Cortical Bone (C)	Skeletal Muscle (M)
Mean (HU)	-997.75	-55.29	1256.98	10.98
SD (HU)	1.61	22.33	14.40	29.98
Expected (HU)	-1000	-60	1200	40

Table 4.2.1 Mean and standard deviation of HU values across specimens for each tissue ROI. Values extracted from the QCT txt file. Expected HU values are based on values outlined in Chapter 2 of Radiology Secrets Plus, Third Edition (Pretorius, 2011).

4.2.4 FEM Creation

Four different FEMs were created of each of the thirty-nine-phantom containing cadaveric images for each calibration method (ROD, AAAdC, AAAdCM, ACM) for a total of 156 FEMs ([Section 3.6](#)).

4.2.5 Statistics

To evaluate the agreement between phantom and internal calibration methods, linear regression and Bland-Altman analyses were performed comparing vBMD values derived from each internal calibration tissue combination (AAAdC, AAAdCM, ACM) against the phantom calibration reference. The internal calibration tissue combination with the lowest mean difference, lowest percent error, and

narrowest limits of agreement in the Bland-Altman plots, was considered the best combination. To examine the relationship between bone density and apparent stiffness, linear regression was used to assess the correlation between vBMD and apparent stiffness across all subjects, separately for each calibration method. The agreement between stiffness estimates derived from phantom versus internal calibration was further assessed using Bland-Altman analysis. Percent error was calculated using Equation 4 where the predicted value was based on the internal calibration method the and the actual value was based on the phantom calibration.

$$\% \text{ Error} = \frac{\text{Predicted} - \text{Actual}}{\text{Actual}} \times 100$$

(Equation 4)

4.3 Results

4.3.1 Internal Calibration Tissue Combinations

Linear regression showed a strong correlation between vBMD values from phantom and internal density calibration (AAAdC $R^2 = 0.80$; AAAdCM $R^2 = 0.88$; ACM $R^2 = 0.90$) and a slope not significantly different from 1 ($p < 0.001$) ([Figure 4.3.1a](#)). Bland-Altman analysis revealed the ACM tissue combination had the lowest error, with a mean bias of 13.08 mgK₂HPO₄/cm³ (9.98%) with 95% limits of agreement ranging from -11.44 to 37.60 mgK₂HPO₄/cm³ ([Figure 4.3.1b](#)) ([Table 4.3.1](#)). On average internal density calibration overestimated phantom-based vBMD for all tissue combinations.

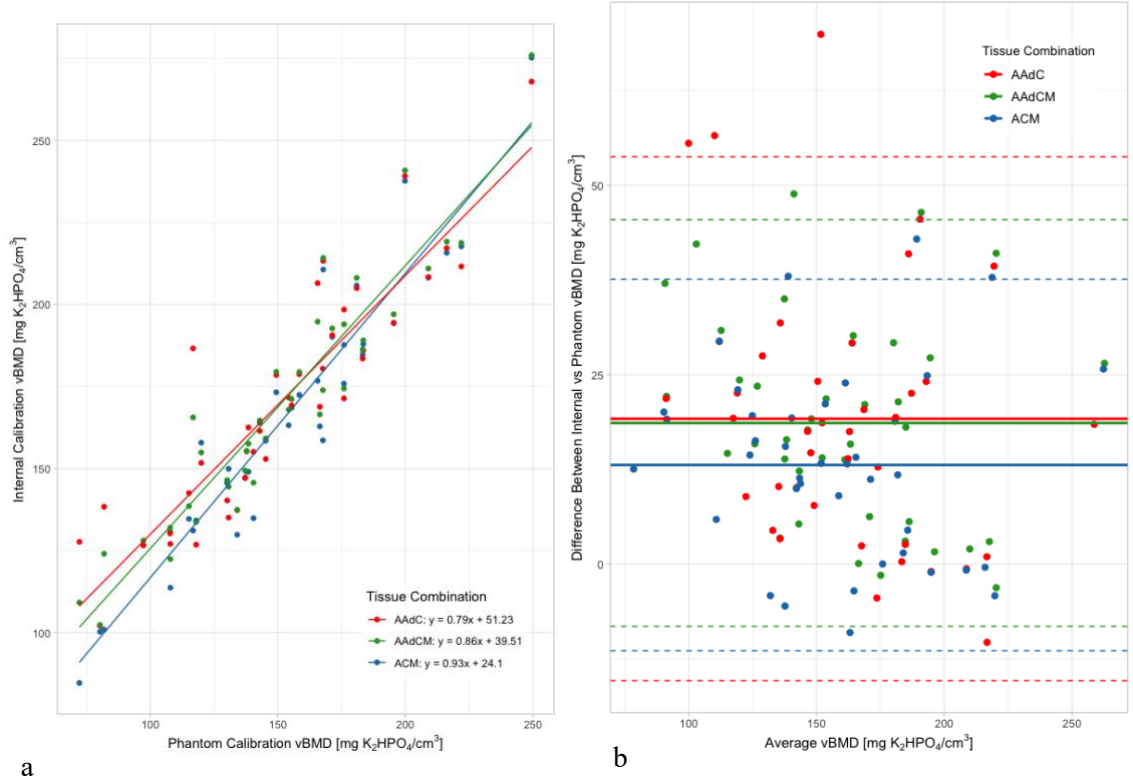


Figure 4.3.1 Comparing calibration methods. a) Linear regression showing correlation between vBMD [mgK₂HPO₄/ cm³] from internal calibration according to tissue combination relative to phantom calibration. b) Bland-Altman plot for vBMD [mgK₂HPO₄/ cm³] for internal calibration according to tissue combination relative to phantom calibration.

	AAdC	AAdCM	ACM
Mean Difference [mgK ₂ HPO ₄ / cm ³]	19.18	18.61	13.08
Upper Limit [mgK ₂ HPO ₄ / cm ³]	53.74	45.46	37.60
Lower Limit [mgK ₂ HPO ₄ / cm ³]	-15.40	-8.23	-11.44
Percent Error [%]	15.71	14.61	9.98

Table 4.3.1 Bland Altman results showing mean differences, upper and lower limits of agreement, and percent error for vBMD values from each internal calibration tissue combination, relative to phantom calibration.

4.3.2 Stiffness derived from internal versus density calibration

Linear regression showed moderate correlations between apparent stiffness and vBMD values for each calibration method (AAdC $R^2 = 0.61$; AAdCM $R^2 = 0.63$; ACM $R^2 = 0.66$; ROD $R^2 = 0.66$) and slopes not significantly different from 1 ($p < 0.001$) (Figure 4.3.2). Bland-Altman analysis revealed

the ACM tissue combination had the lowest error in estimated apparent modulus, compared to phantom-vBMD derived FEMs, with a mean bias of 65.90 MPa (5.46%) and 95% limits of agreement ranging from -165.01 to 296.81 MPa (Figure 4.3.3) (Table 4.3.2).

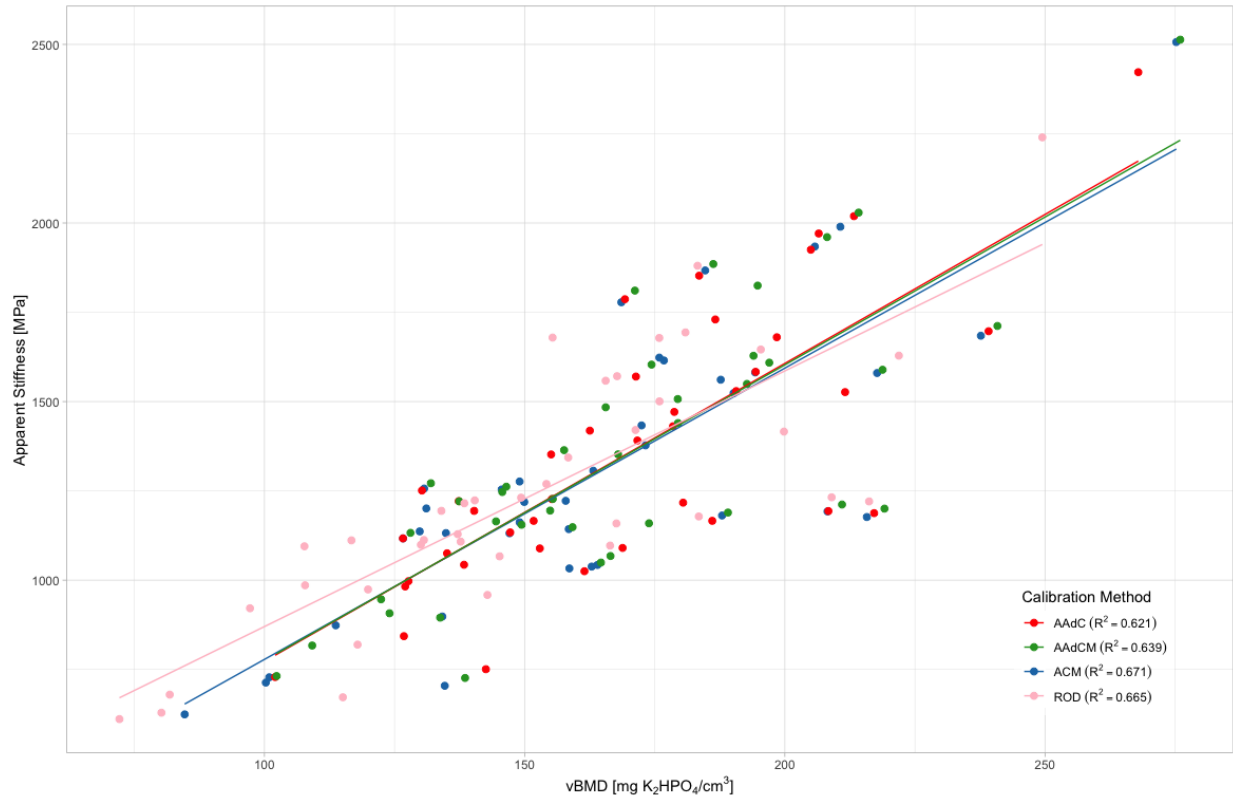


Figure 4.3.2 Linear Regression showing the correlation between vBMD [mgK₂HPO₄/cm³] and apparent stiffness [MPa] for each calibration method.

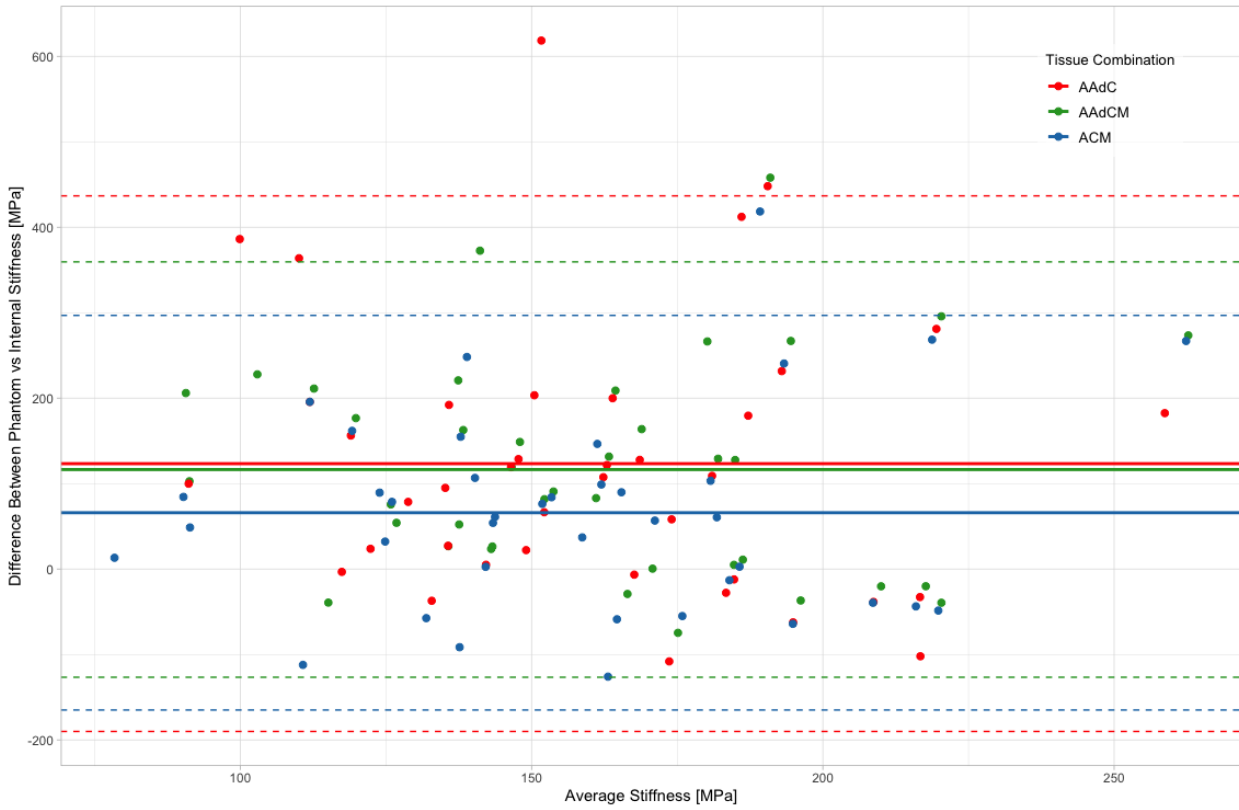


Figure 4.3.3 Comparing stiffness derived from internal calibration method relative to phantom calibration in the group of thirty-nine non-pathologic cadaveric images containing a phantom. Bland-Altman plot for apparent stiffness [MPa] values for internal calibration according to tissue combination vs. phantom calibration. Dashed lines indicate ± 1.96 standard deviations (SD) of the mean (solid line).

	AAdC	AAdCM	ACM
Mean Difference [MPa]	123.30	116.39	65.90
Upper Limit [MPa]	436.70	359.44	296.81
Lower Limit [MPa]	-190.11	-126.66	-165.01
Percent Error [%]	11.55	10.27	5.46

Table 4.3.2 Bland Altman results showing mean differences, upper and lower limits of agreement, and percent error for apparent stiffness values from each internal calibration tissue combination, relative to phantom calibration.

4.4 Discussion

This study aimed to evaluate whether internal density calibration methods could serve as a reliable alternative to phantom calibration for quantifying proximal humerus vBMD and estimating bone stiffness from single energy CT scans. Specifically, vBMD values and FEM-derived stiffness were compared across three internal tissue combinations (AAAdC, AAAdCM, ACM) relative to phantom-based calibration (ROD). The findings demonstrate that internal calibration methods are strongly correlated with phantom-derived vBMD, with the ACM combination (air, cortical bone, skeletal muscle) showing the highest agreement. ACM produced the lowest mean bias and narrowest limits of agreement in both vBMD and stiffness estimates, providing the highest agreement with the gold standard phantom calibration. Furthermore, all calibration methods preserved a relationship between vBMD and apparent stiffness, reinforcing the biomechanical relevance of internally calibrated images. These results support the use of internal calibration, particularly the ACM tissue combination, as a practical alternative in settings where phantom-based calibration is unavailable.

Following the recommendation by Matheson et al., 2024, each tissue combination used in this study included cortical bone and air. Research at the hip demonstrated that any combination using cortical bone and air as referent tissues yields comparable results to phantom calibration. The inclusion of air provides a stable and well-established mass attenuation value that should be consistent between individual scans, while the use of cortical bone as a referent establishes an appropriate upper boundary for the linear regression framework underlying the internal calibration method (Pretorius, 2011). Our results in the proximal humerus support findings in the hip that the ideal tissue combination is air, skeletal muscle, and cortical bone (Matheson et al., 2024). Notably, the inclusion of skeletal muscle improved the agreement to phantom calibration, as demonstrated by the AAAdC combination (air, adipose, cortical bone) having the lowest agreement. This is interesting given that the mean HU value for skeletal muscle in this dataset is lower than expected (10.98 HU), with a large standard deviation (± 29.98 HU). This discrepancy may explain the larger mean differences observed in our proximal humerus results compared to results in the hip (Matheson et al., 2024). One factor that could be contributing to the lower reported HU value in skeletal muscle may be the decreased hydration levels of the cadaveric specimens. Dehydration reduces water content, decreasing tissue density (Hackney et al., 2012). Since the musculature of the shoulder is generally smaller than that found in the hip, another contributing factor may be fat infiltration in the skeletal muscle ROIs, which would further reduce the HU value (Engelke et al., 2018). Future studies should

prioritize the selection of skeletal muscle ROIs that yield HU values within the expected range and exhibit minimal HU variation.

It is important to note that this internal calibration method was originally developed using patient images of living tissue, which may explain the higher mean difference in vBMD in the proximal humerus (ACM: 13.08 mgK₂HPO₄/ cm³) relative to the hip (ACM: 1.13 mgK₂HPO₄/ cm³) (Matheson et al., 2024). Future work should evaluate the performance of internal density calibration relative to phantom calibration in the proximal humerus of live patients undergoing shoulder arthroplasty for end-stage OA. If such studies yield results consistent with those observed at the hip, the internal density calibration method could provide a solution for estimating vBMD in patients undergoing shoulder arthroplasty for end-stage OA where phantoms are not present in the CT image.

Results from the FEMs further validate the use of the ACM internal calibration method, over the other calibration methods, in the proximal humerus when phantoms are not present in the image. However, vBMD only explained 67% of the variance in apparent stiffness for both phantom calibration and the ACM internal calibration method, highlighting the FEM's current limitations in fully capturing the complex mechanical properties of bone, when compared directly to integral vBMD, without experimental validation (Yang et al., 2023). This raises the possibility that FEM derived stiffness may not accurately reflect the true mechanical response of the proximal humerus to the stemless humeral component. While the density-modulus relationship was derived from the literature (Eberle et al., 2013), it has not yet been experimentally validated in the proximal humerus. Importantly, this relationship was defined using K₂HPO₄ density, minimizing potential confounding bias introduced through density conversion, required by many other published density-modulus relationships (Eberle et al., 2013; Knowles et al., 2019). While the CT image itself considers the density and composition across the specimen, the density-modulus relationship is essential for establishing how the tissue will respond under stress. Further validation of the density-modulus relationship might reveal the need to differentiate cortical and trabecular bone within the FEM. If cortical and trabecular bone exhibit different modulus values at a given density, a non-uniform, region-specific density modulus relationship may be needed to accurately represent their mechanical behaviors.

Another limitation is that the FEM loading conditions may not perfectly replicate the loading of the stemless component on the resected plane. This study does not account for shear forces to simplify

computational time, which may contribute to off-axis loading due to the anisotropic nature of bone (Bayraktar & Keaveny, 2004). Additionally, in the context of stemless shoulder arthroplasty, it may be important to consider the material properties of the stemless component itself and how it interacts with the bone. There are several studies which examine the different techniques for securing the implant with different backing designs to optimize load transfer, highlighting the importance of considering patient-specific vBMD and morphology when selecting a suitable stemless implant (Gregory et al., 2023; Reeves, Langohr, et al., 2018; Ritter et al., 2024b).

Overall, results of this study support the use of internal density calibration as a valid method for using internal density calibrated images as input to FEMs for estimating stiffness in the proximal humerus. This study also provides initial site-specific apparent stiffness values, which have yet to be established in the proximal humerus region. The novelty of this research lies in applying the internal calibration method in the proximal humerus and utilizing these internally calibrated QCT images as FEM inputs. By linking bone density measures with estimated stiffness values, this approach accounts for the mechanical properties of bone in the region supporting the humeral component, offering potential improvements to preoperative planning for stemless shoulder arthroplasty.

Chapter 5

Determine vBMD in Trabecular and Cortical bone

5.1 Purpose

To compare cortical, trabecular, and integral vBMD and apparent stiffness in the end-stage OA group (n=50) to that of the non-pathologic cadaveric group (n=50).

5.1.1 Research Question

What are the vBMD values in end-stage OA patients undergoing shoulder arthroplasty compared to vBMD in a non-pathologic group?

5.1.2 Hypothesis

It was hypothesized that the vBMD values will be lower in the end-stage OA group compared to the non-pathologic cadaveric group, rejecting the null hypothesis that there will be no significant difference between the mean of the cadaveric group and the patient group for integral, cortical, and trabecular vBMD.

5.1.3 Rationale

Separation of the cortical and trabecular bone allows for consideration of volume and tissue contribution to vBMD. This may provide important information for surgical planning since some stemless components are primarily fixed/supported by the trabecular bone while some are fixed/supported by the cortical shell. Since force transduction is supported primarily by cortical bone, assessing cortical vBMD may be critical in selecting and optimizing stemless implant designs.

5.2 Methods

5.2.1 Isolating the Integral Bone VOI

All fifty non-pathologic cadaveric shoulder specimens and fifty end-stage OA patients' specimens were used in this study. The proximal humerus was segmented for each specimen using the method described in [Section 3.3.1](#) to yield integral VOI. Cortical VOIs and trabecular VOIs were generated according to the method described in [Section 3.3.2](#).

5.2.2 Internal Density Calibration for Remaining Specimens

The ACM internal density calibration method outlined in [Section 3.4.2](#) was applied to the remaining cadaver images (n=11) and all patient images (n=50) to produce a total of 100 QCT images.

5.2.3 vBMD Extraction

For each specimen, vBMD was extracted (3D-Slicer) by overlaying the integral VOI, cortical VOI, and trabecular VOI, respectively, with the ACM calibrated QCT ([Section 3.5](#)). Each VOI was converted to a segmentation node and the calculate statistics operation was used to output mean vBMD.

5.2.4 Statistics

To compare vBMD from the end-stage OA group to the non-pathologic cadaveric group, independent samples two-tailed student's t-tests were used for each bone VOI (integral, cortical, trabecular). Normality was assessed. Homogeneity of variance was assessed with Levene's test. If the assumption of equal variances was violated, the Welch's t-test, was used.

5.3 Results

vBMD was compared between the end-stage OA group and the non-pathologic cadaveric group for integral, cortical, and trabecular bone ([Figure 5.3.1](#)). Normality tests confirmed normal distributions for each bone VOI across both groups. Cortical vBMD did not meet the assumption of equal variances as such Welch's t-test was used. Integral vBMD was significantly lower in the end stage OA group (119 mg $\text{K}_2\text{HPO}_4/\text{cm}^3$) relative to the non-pathologic cadaveric group (159 mg $\text{K}_2\text{HPO}_4/\text{cm}^3$) ($p < 0.001$). Cortical vBMD was significantly lower in the end-stage OA group (518 mg $\text{K}_2\text{HPO}_4/\text{cm}^3$) compared to the non-pathologic cadaveric group (643 mg $\text{K}_2\text{HPO}_4/\text{cm}^3$) ($p < 0.001$). A similar trend was observed in trabecular bone, with the OA group having a significantly lower vBMD (79.8 mg $\text{K}_2\text{HPO}_4/\text{cm}^3$) compared to the cadaveric group (110 mg $\text{K}_2\text{HPO}_4/\text{cm}^3$) ($p < 0.001$). These results are consistent with our hypothesis that vBMD values would be significantly different in the end-stage OA group for integral, cortical, and trabecular bone compared to non-pathologic cadaveric group.

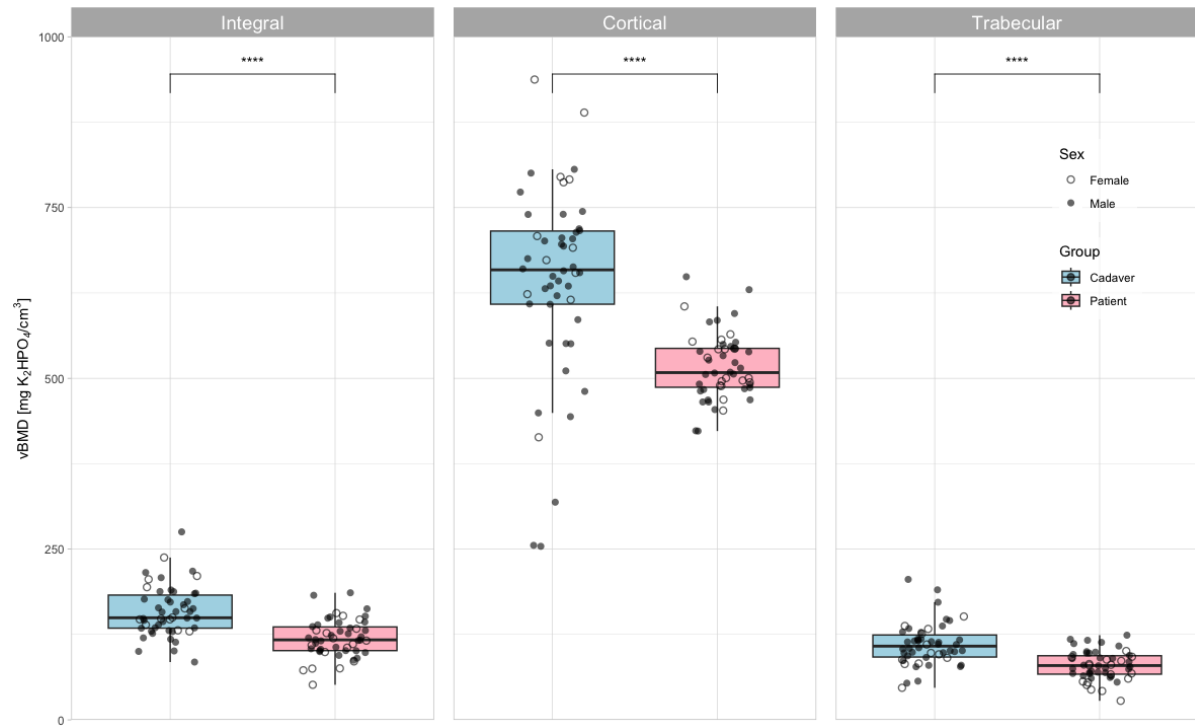


Figure 5.3.1 Boxplot showing vBMD values for the end-stage OA patient group (pink) and the non-pathologic cadaveric control group (blue) across the three bone VOIs indicated by each panel (integral, cortical, trabecular). Box edges represent the interquartile range (25th to 75th percentiles) with the median indicated by the solid line. Individuals are represented as filled (male) and empty (female) data points. Significance indicated ($p < 0.001$ ‘***’).

5.4 Discussion

Across all bone VOIs the end-stage OA patient group demonstrated lower vBMD values relative to the cadaveric control group, with the most pronounced difference seen in the cortical VOI. While integral vBMD reflects a combination of cortical and trabecular vBMD, it is strongly influenced by the large volume of the trabecular compartment. Trabecular bone has a lower mineral density because of its lattice-like architecture, meaning trabecular vBMD measurements are substantially lower than those of cortical bone because it occupies a larger proportion of bone volume. In contrast, cortical bone has a higher vBMD because of its dense, compact structure and smaller bone volume. Importantly, the mineralization of bone tissue itself remains relatively constant (van der Klift et al., 2005). Therefore, decreases in vBMD are largely attributed to increased porosity and structural

deterioration rather than changes in the intrinsic mineral content of the bone matrix (Seeman & Delmas, 2006; Zebaze et al., 2010).

Trabecular bone is subject to localized bone loss with OA progression resulting in increased prevalence of void spaces in the trabecular microarchitecture (Whittier et al., 2021). Since vBMD is an average of the volume, it captures void spaces that may be present in the trabecular bone, thereby lowering the vBMD output value and not presenting an accurate vBMD value. A way to account for this in future would be to use void space segmentation which has been developed using HR-pQCT data to address any missing trabeculae in the vBMD analysis (Bugbird et al., 2025).

Analyzing cortical and trabecular bone separately is rarely performed clinically; however, given the marked variability in vBMD between cortical and trabecular bone VOIs, targeted measurements may be useful when there is a risk of void spaces in the trabecular bone, as is the case in patients with end-stage OA. This is relevant in the context of stemless shoulder arthroplasty as implant fixation depends on adequate trabecular bone quality in the metaphyseal region (Gregory et al., 2023; Hatta et al., 2024; Ritter et al., 2024a). Studies have shown that low trabecular BMD increases the risk of poor implant fixation and intraoperative conversion to a stemmed implant (Anderson et al., 2020; Gregory et al., 2023; Hatta et al., 2024). It is also highlighted that no objective tests are yet available to determine the bone quality for a stemless prosthesis (Athwal, 2016; Hatta et al., 2023, 2024). While a threshold has been developed for determining the need for a stemmed component based on trabecular bone density, this threshold relies on HU values from preoperative CT scans, a subjective measure (Gregory et al., 2023). These results suggest that a method that determines bone compartment specific vBMD may be useful for guiding implant choice, especially when one considers how cortical and trabecular bone densities correlate with initial implant loading and fixation behaviour (Ritter et al., 2024a). Separating cortical from trabecular vBMD, rather than relying solely on an integral vBMD value, would enhance surgical decision-making, allowing surgeons to select the component design and fixation strategy based on patient-specific bone composition. In instances where an individual has low trabecular vBMD, a cortical rim-supported stemless implant might be better suited (Ritter et al., 2024a).

The lower vBMD values observed in the end-stage OA group relative to the non-pathologic cadaveric group, for each bone VOI, are consistent with our expected results. OA alters the material properties of bone, resulting in hypo-mineralisation and different organic and water fractions

suggesting a defect in the bone matrix with disease progression, decreasing vBMD (Li & Aspden, 1997). The cortical bone VOI showed the greatest difference, indicating that a reduction in cortical thickness and/or a reduction in the density of the cortical bone is consistent during OA progression, within this VOI. While trabecular bone is still reduced, it does not have as large of an effect on vBMD output. Reductions in vBMD may allow for this measure to be used as an imaging biomarker of OA disease progression and to screen candidates for stemless shoulder arthroplasty.

While most cortical bone segmentation is performed using thresholding, this method is limited in its ability to separate cortical and trabecular bone using single-energy CT images and requires further validation in the proximal humerus against micro-CT, which offers higher spatial resolution for cortical bone mapping (G. M. Treece et al., 2010). This study used a common threshold to separate cortical bone, however, a subject specific approach might better account for inter-individual variation in cortical morphology and density, potentially improving vBMD estimates and reducing bias. This is especially relevant in older specimens and diseased populations where cortical thinning and increased porosity, specifically in the proximal humerus, can make it difficult to identify cortical bone relative to trabecular (Helfen et al., 2017). Additionally, while the cadaveric non-pathologic group was determined to be “non-pathologic” because disease status was not reported, there is a potential that the cadaveric group was affected by confounding factors such as unaccounted for degenerative bone diseases and tissue hydration levels which may affect vBMD output. Ideally, future research should explore vBMD in integral, cortical, and trabecular bone in end-stage OA patients relative to a healthy patient population.

Chapter 6

Correlation Between vBMD and Apparent Stiffness

6.1 Purpose

To compare apparent stiffness values in the end-stage OA group relative to the non-pathologic cadaveric group. To determine the correlation between integral, cortical, and trabecular vBMD and apparent stiffness in the patient and cadaver group using the internal density calibration method with the greatest correlation.

6.1.1 Research Question

What are the correlations between integral, cortical, and trabecular vBMD and apparent stiffness in the proximal humerus?

6.1.2 Hypothesis

It was hypothesized that apparent stiffness would be higher in the non-pathologic cadaveric group than in the end-stage OA group. It is anticipated that integral, cortical, and trabecular vBMD will be strongly correlated with apparent stiffness in both groups, but the slope and y-intercept values are expected to differ.

6.1.3 Rationale

If vBMD and apparent stiffness are strongly correlated, FEMs may not be needed for estimating stiffness in the proximal humerus. By linking bone density with apparent stiffness values, the mechanical properties of bone in the region supporting the humeral component are considered.

6.2 Methods

6.2.1 Finite Element Model Creation for Remaining Specimens

For the remaining eleven non-pathologic cadaveric samples without a phantom, and the fifty end-stage OA patient samples, only one FEM per sample was created using the ACM internally calibrated QCT images produced in [Section 5.2.2](#). Integral VOIs ([Section 3.3.1](#)) were used to generate FEMs following the same methods outlined in [Section 3.6](#).

6.2.2 Statistics

Independent student's t-tests were used to compare apparent stiffness values in the end-stage OA patient (n=50) and non-pathologic cadaveric (n=50) groups. Linear regression was used to determine the correlation between vBMD and apparent stiffness in the end-stage OA patient group to that of the non-pathologic cadaver group. An analysis of covariance (ANCOVA) was used to compare the slope and intercepts between the OA and non-pathologic groups. Statistical significance was indicated by $\alpha = 0.05$.

6.3 Results

Normality tests confirmed normal distribution of apparent stiffness values in both groups and variance was determined to be equal. Mean apparent stiffness was found to be significantly higher in the non-pathologic cadaveric group (1261 MPa) than the patient group (672 MPa) ($p < 0.001$) ([Figure 6.3.1](#)).

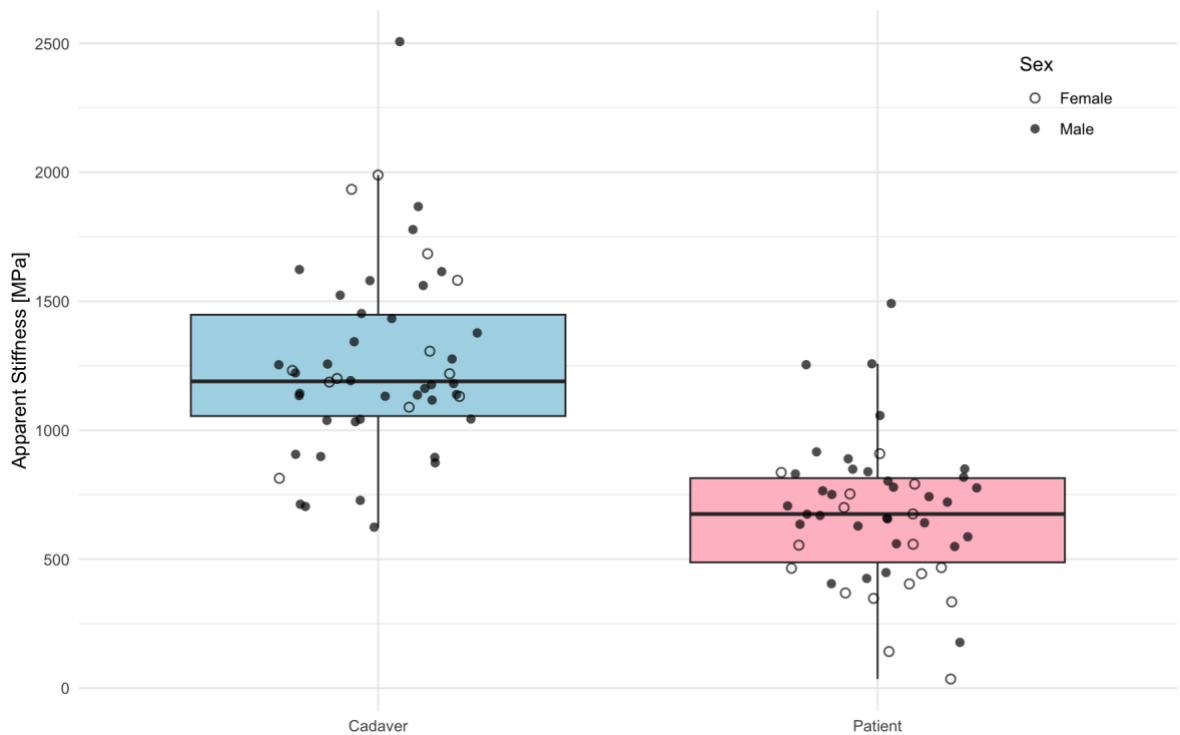


Figure 6.3.1 Boxplot showing distribution of apparent stiffness values in the end-stage OA patient group (pink) relative to the non-pathologic cadaveric control group (blue). Box edges represent the interquartile range (25th to 75th percentiles) with the median indicated by the solid line. Individuals are represented as filled (male) and empty (female) data points.

In the fifty non-pathologic cadaveric images and the fifty end-stage OA patient images, linear regression was used to determine a significant relationship between integral vBMD and stiffness in both groups (Cadaver: $R^2 = 0.69$, $p < 0.001$; Patient: $R^2 = 0.27$, $p < 0.001$), with higher integral vBMD associated with increased apparent stiffness ([Figure 6.3.2](#)). There was no significant relationship between cortical vBMD and stiffness for either group (Cadaver: $R^2 = -0.018$, $p = 0.71$; Patient: $R^2 = -0.018$, $p = 0.73$), indicating minimal predictive value of cortical vBMD for stiffness. Trabecular bone showed significant positive associations in both groups (Cadaver: $R^2 = 0.40$, $p < 0.001$; Patient: $R^2 = 0.21$, $p < 0.001$). Overall, there was a weak correlation between vBMD and apparent stiffness across groups and bone VOIs.

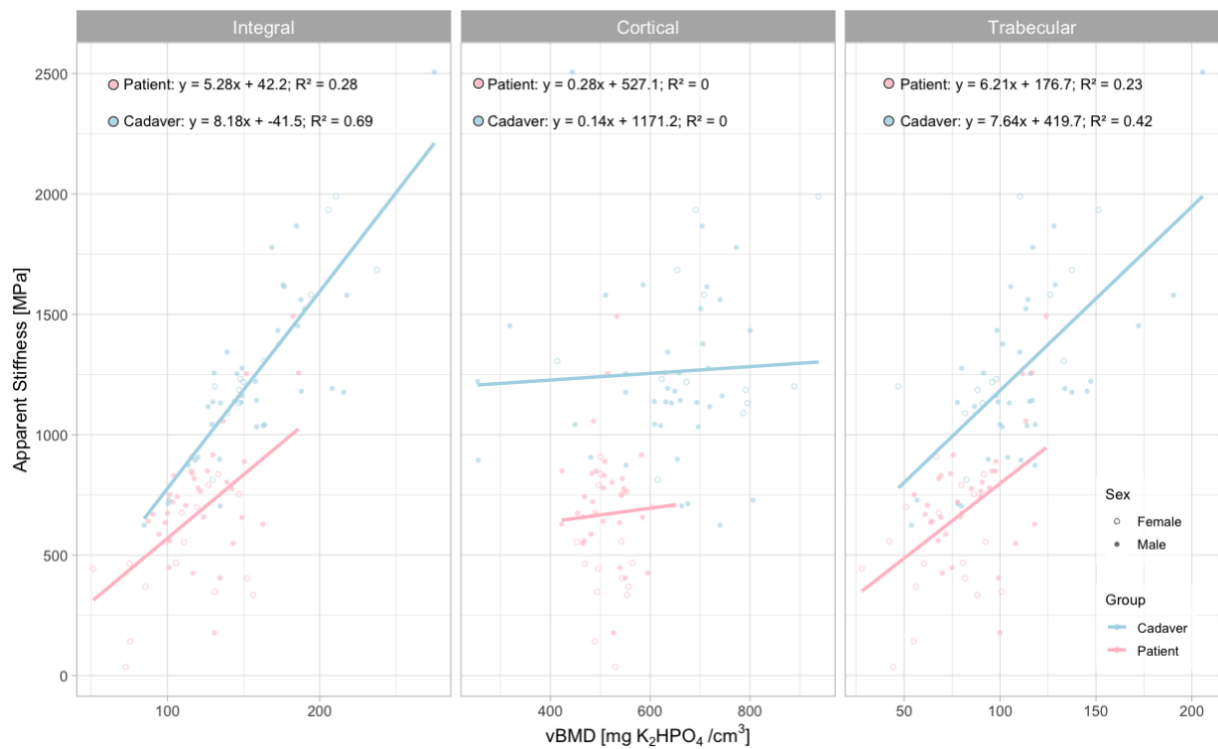


Figure 6.3.2 Linear Regressions showing the correlation between vBMD for each bone VOI and apparent stiffness in both the non-pathologic cadaveric group (blue) and the end-stage OA group (pink). Linear regression equations and R^2 values included on the graph. Individuals are represented as filled (male) and empty (female) data points.

An ANCOVA was performed separately for integral, cortical, and trabecular bone to examine the relationship between vBMD and apparent stiffness, and to test for differences between cadaveric and patient samples ([Table 6.3.1](#)). For each bone compartment vBMD was a significant predictor of stiffness ($p < 0.001$), with higher vBMD associated with increased stiffness. A significant main effect of group was present in each compartment ($p < 0.001$). For integral bone, there was a significant interaction effect for vBMD and group ($p < 0.05$), but no significant interaction effects for cortical and trabecular bone suggesting similar slopes between cadaver and patient groups.

Bone	Term	Df	Sum Sq	Mean Sq	F Value	p-value	Significance
Integral	vBMD	1	12,290,120	12,290,120	256.00	7.73e-29	***
	Group	1	1,669,669	1,669,669	34.80	5.49e-08	***
	vBMD x Group	1	199,983	199,983	4.17	0.044	*
	Residuals	96	4,607,619	47,996			
Cortical	vBMD	1	2,730,422	2,730,422	26.0	1.69e-06	***
	Group	1	5,968,580	5,968,580	56.90	2.58e-11	***
	vBMD x Group	1	1,995	1,995	0.02	0.891	
	Residuals	96	10,066,395	10,066,395			
Trabecular	vBMD	1	9,599,185	9,599,185	104.17	1.79e-20	***
	Group	1	2,564,187	2,564,187	37.44	2.04e-08	***
	vBMD x Group	1	29,897	29,897	0.44	0.51	
	Residuals	96	6,574,123	68,480			

Table 6.3.1 ANCOVA results for apparent stiffness predicted by vBMD and group (cadavers and patient) with interaction effects by bone compartment (integral, cortical, and trabecular bone). Significance indicated ($p < 0.05$ ‘’, $p < 0.001$ ‘***’).*

6.4 Discussion

The non-pathologic cadaveric group consistently exhibited higher stiffness values across bone types relative to the end-stage OA patient group. These results are in line with our expected hypothesis and support the notion that OA changes the mechanical properties of bone in the proximal humerus.

These changes are most likely due to cortical thinning and trabecular deterioration which contribute to reduced stiffness (Hayden et al., 2023; Kusins, Knowles, Martensson, et al., 2022). Additionally, there is greater variability between vBMD and apparent stiffness in the end-stage OA group relative to the non-pathologic cadaveric group across bone VOIs. This can partially be attributed to differences in vBMD. Lower vBMD is known to contribute to both lower and more variable apparent stiffness values, both of which were observed in the end-stage OA group (Carballido-Gamio et al., 2013). The bone mineralized matrix determines load-bearing ability therefore reductions in mineral content per volume directly weaken the ability of bone to resist deformation (Carballido-Gamio et al., 2013; Unal et al., 2018). Low vBMD is also linked to spatially non-uniform stress distributions throughout the bone structure, amplifying local strain concentrations and mechanical variability (Carballido-Gamio et al., 2013; Keyak et al., 2005). As discussed previously, in the context of OA, these effects are compounded by disease-related changes to bone composition such as hypo-mineralization and altered organic and water fractions, further reducing the mechanical integrity of bone (B. Li & Aspden, 1997). It is therefore fair to assume individuals with OA in the glenohumeral joint will show a decrease in stiffness in the humerus and weaker correlations between vBMD and stiffness. However, even with comparable vBMD values, the non-pathologic cadaveric samples demonstrated higher stiffness across bone VOIs. This demonstrates that the FEMs may be able to capture subtle changes within the bone structure that relate to the force distribution throughout the bone and contribute to the measured apparent stiffness. These subtle differences are lost when comparing vBMD, which averages the density of a voxels within a VOI.

Integral and trabecular vBMD had a significant relationship with apparent stiffness in both groups with a moderate correlation, indicating some predictive utility. On the other hand, cortical vBMD did not significantly predict stiffness in either group, suggesting limitations in using cortical vBMD alone as a predictor of mechanical properties. This is surprising since visual observation of the FEM after simulation ([Figure 6.4.1](#)) suggests that compressive forces on the proximal humerus are primarily supported by the cortex, with the trabecular bone contributing little to no load bearing under simulated conditions, which is in line with previous work in the femur (Schileo et al., 2020). A strong correlation between apparent stiffness and cortical vBMD would mean a stemless component design could be selected based on cortical bone mechanical properties alone, although this warrants further investigation.

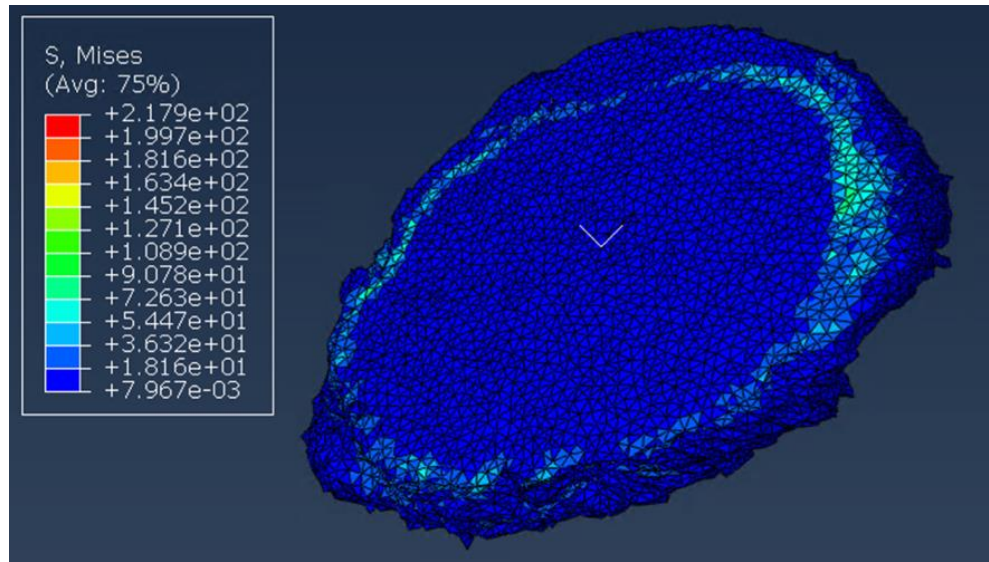


Figure 6.4.1 Example of an end-stage OA proximal humerus FEM after a 1% strain, 0.01 mm displacement, has been applied. Greater reaction forces are indicated by the teal and green tetrahedrons. Displacements magnified.

Since the relationship between apparent stiffness and vBMD does not have a strong correlation, this study highlights the need for FEMs to capture the complex mechanical behavior of bone, especially in patient-specific models. If stiffness were directly proportional to vBMD, simple regression models could replace computational simulations. Since the FEMs used in this study only consider the distribution of a single quantitative measure (vBMD), future studies might consider a multifactorial approach where additional tissue properties such as water content, cortical thickness, microarchitecture, and organic matrix parameters might be used to more accurately capture apparent bone stiffness (Querido et al., 2025).

FEMs are known to overestimate stiffness, particularly when linear tetrahedrons are used over hexahedrons, as was the case in this study. While computationally efficient, and useful for complex geometries, linear tetrahedrons are less accurate in capturing bending and shear behavior and may artificially stiffen the model (Benzley et al., 1995; Cifuentes & Kalbag, 1992; Tadepalli et al., 2011). However, since this FEM analysis involves a simplified uniaxial loading scenario, the use of linear tetrahedrons is unlikely to significantly compromise the general mechanical trend within the proximal humerus. Future work should be performed to determine the different apparent stiffness outputs using hexahedral elements, relative to linear tetrahedrons, specifically in the proximal humerus in the context of shoulder arthroplasty to better approximate true tissue-level mechanics.

Another limitation of this study is that the density-modulus relationship was derived from non-pathologic cadaveric bone containing both cortical and trabecular compartments (Eberle et al., 2013). Since this relationship was created using integral bone, when this density-modulus is applied separately to cortical and trabecular bone, the correlation between vBMD and apparent stiffness are expectedly weaker. This is consistent with the results above that indicate that integral vBMD is the strongest predictor of apparent stiffness across both cadaveric and patient groups. Additionally, the density-modulus relationship was developed using cadaveric femurs which means it is not anatomically specific to the proximal humerus. As such, the assigned material properties may not capture the true material behaviour of the proximal humerus, especially in patient samples. Experiential validation is needed to develop a density-modulus relationship specific to the proximal humerus for application in shoulder biomechanics.

Chapter 7

Conclusion

7.1 Implications

In agreement with previous literature, the results of this thesis demonstrate that opportunistic screening of bone quality in the proximal humerus using internal calibration can be performed using routine CT scans obtained for shoulder arthroplasty (Ritter et al., 2024). Implementation of patient-specific internal density calibration in a preoperative planning tool, rather than relying on subjective measures such as the thumb test and HU values, could significantly improve surgical planning and implant selection. This research demonstrates that internal density calibration in the proximal humerus can produce equivalent vBMD results as phantom calibration, meaning phantoms would not be needed in a clinical setting. Internal calibration has been validated in the proximal humerus. Additionally, the correlations between vBMD and apparent stiffness indicate there is value in considering the mechanical properties of bone, beyond bone mineral density, in the proximal humerus since there may be additional factors contributing to bone strength. Overall, the results highlight how internal density calibrated images may be used for estimating stiffness in the proximal humerus through patient specific FEMs. Eventually, FEMs may be a valuable tool for advancing pre-operative planning software in the context of shoulder arthroplasty.

7.2 Limitations

The most impactful limitation to this research is that the assigned material properties have not yet been validated in the proximal humerus VOI used in this research. This has an impact on the resultant apparent stiffness values since it may not accurately represent the true tissue response to strain. Cadaveric specimens should be tested mechanically, considering cortical and trabecular bone contributions, to select a valid apparent modulus. Another limitation is the method in which the cortical shell was isolated. Ideally, cortical bone mapping should have been performed using a patient specific vBMD threshold instead of a HU threshold. Future work should aim to establish the ideal vBMD threshold for cortical bone separation using MicroCT images as validation. Finally, while this research uses an adequate sample size to determine correlations, a larger sample size would be invaluable for increasing the generalizability of the research, strengthening correlations, creating a machine learning model, and assessing implant outcomes.

7.3 Future Research

This study estimated bone stiffness based on the stress-strain relationship, future research should aim to calculate bone strength, by identifying the yield point to capture tissue failure more accurately. Additionally, future work should aim to reduce bias in the internal density calibration method specifically for the shoulder by quantifying variability introduced by anatomical differences, imaging parameters, and tissue ROI selection. Developing machine learning models to automate vBMD extraction and stiffness estimation could enhance the efficiency and reproducibility of this workflow, allowing this research to be used more practically. Another goal should be to use void space analysis to generate more accurate vBMD measures, especially in trabecular bone. Finally, an essential step will be to correlate vBMD and apparent stiffness with clinical outcomes in a large group of patients who have undergone stemless shoulder arthroplasty. Linking vBMD and bone mechanical properties from patient specific CT images to implant stability and revision rates, will help validate these quantitative imaging methods and provide biological relevance. This validation could help guide preoperative planning and support the development of personalized implant selection criteria.

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