Association between patellofemoral joint alignment and morphology to superlateral Hoffa's fat pad edema

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Boston University
BOSTON UNIVERSITY
SCHOOL OF MEDICINE

Thesis

ASSOCIATION BETWEEN PATELLOFEMORAL JOINT ALIGNMENT AND MORPHOLOGY TO SUPEROLATERAL HOFFA’S FAT PAD EDEMA

by

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B.S., Suffolk University, 2011

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Master of Science
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ACKNOWLEDGMENTS

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ASSOCIATION BETWEEN PATELLOFEMORAL JOINT ALIGNMENT AND MORPHOLOGY TO SUPEROLATERAL HOFFA’S FAT PAD EDEMA

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ABSTRACT

Background: Osteoarthritis is a leading cause of disability in people of 65 and older. Researches have shown several possible factors leading to knee osteoarthritis development. Patellofemoral joint maltracking has been thought to be associated with or caused edema in the knee; which is thought to be the early signs of osteoarthritis. Hoffa's fat pad is an intra-articular component of knee located under the kneecap. It has also been suggested as one marker for osteoarthritis, when MRI shows a presence of edema in it. Recently, edema in the superolateral region of Hoffa's fat pad has been hypothesized as a distinct signal than the edema on other regions. There is an interest in finding the relation of this superolateral edema with other factors of osteoarthritis development.

Objective: This thesis research project is aimed to assess the relation of kneecap-thighbone (patellofemoral) joint alignment, femoral trochlea morphology, and patellar height to edema in the superolateral region of Hoffa’s fat pad especially in the population with average age above 65 years old. The hypothesis is that the flatter trochlear morphology and abnormal patella alignment will have higher risk of superolateral edema.
**Methods:** This is a cross-sectional study using a subset data from Multicenter Osteoarthritis (MOST) study, specifically at 60-month visit. This study measured the patellofemoral measurements (sulcus angle, lateral and medial trochlear inclination angle, trochlear angle, Insall-Salvati ratio, patellar tilt angle, and bisect offset) as the predictor variables, and semiquantitative scoring of MRI edema in superolateral Hoffa’s fat pad as the outcome variable. Logistic regression analyses were performed to find the strongly associated patellofemoral measurements to superolateral Hoffa’s fat pad edema.

**Results:** From the logistic regression analysis, trochlear angle, Insall-Salvati ratio, and bisect offset were highly associated with the superolateral edema. A further analysis, by categorizing the measurements to quartiles, was found that only the highest quartiles of both bisect offset and trochlear angle are associated with superolateral Hoffa’s fat pad edema when compared to the reference quartile. All quartiles of Insall-Salvati ratio are strongly associated with superolateral edema when compared to the reference quartile.

**Conclusion:** Current study presents that people above 65 years old with high trochlear angle, extreme lateral patellar translation or bisect offset, and high patella riding have high risk of having superolateral Hoffa’s fat pad edema.

**Keywords:** patellar maltracking; patellar tendon-lateral femoral condyle friction syndrome; patellofemoral measurements; superolateral Hoffa fat pad edema; femoral trochlear morphology; patella alignment; MOST;
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Axial view of patellofemoral joint along with parts being focused in this study, such as posterior condyle, sulcus or trochlear groove, and trochlear peak.

Illustration of the process in deciding the posterior condyle line (PCL) and maximum patellar width (MPW). MRI slice presented here is only example. PCL is decided by the MRI slice with most posterior condyle and MPW is by the widest patella slice.

Illustration of trochlear morphology assessments. Line (a) is posterior condyle line (PCL) with medial and lateral legend. Line (b) is sulcus angle (SA), angle (c) is medial inclination angle (MTI), angle (d) is lateral inclination angle (LTI), angle (e) is trochlear angle (TA). The bottom image is an example of depiction of trochlear morphology assessment done on a slice of MRI.
Illustration of patellofemoral joint alignment assessment. Line (f) is maximum patellar width (MPW), line (g) is the lateral-midline length of MPW, and angle (h) is patellar tilt angle (PTA). The right image is an example of depiction of patellofemoral joint alignment assessment done on a slice of MRI where the patella width is the widest.

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<tr>
<td>BMC</td>
<td>Boston Medical Center</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<td>BO</td>
<td>Bisect Offset</td>
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<tr>
<td>BU</td>
<td>Boston University</td>
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<tr>
<td>BUMC</td>
<td>Boston University Medical Campus</td>
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<tr>
<td>BUSM</td>
<td>Boston University School of Medicine</td>
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<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
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<td>ISR</td>
<td>Insall-Salvati Ratio</td>
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<td>LTI</td>
<td>Lateral Trochlear Inclination</td>
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<td>MOST</td>
<td>Multicenter Osteoarthritis</td>
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<tr>
<td>MPW</td>
<td>Maximum Patellar Width</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>MTI</td>
<td>Medial Trochlear Inclination</td>
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<tr>
<td>NSAID</td>
<td>Non Steroidal Anti-Inflammatory Drug</td>
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<tr>
<td>OA</td>
<td>OsteoArthritis</td>
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<td>OR</td>
<td>Odd Ratio</td>
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<tr>
<td>PCL</td>
<td>Posterior Condyle Line</td>
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<td>PFJ</td>
<td>Patello-Femoral Joint</td>
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<td>PTA</td>
<td>Patellar Tilt Angle</td>
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QOL ................................................................. Quality of Life
SA ................................................................. Sulcus Angle
SHFP ............................................................. Superolateral Hoffa's Fat Pad
TA ................................................................. Trochlear Angle
UAB ............................................................. University of Alabama, Birmingham
UCSF ........................................................... University of California, San Fransisco
UI ................................................................. University of Iowa
WORMS ....................................................... Whole Organ MRI Scoring System
INTRODUCTION

AGING AND KNEE OSTEOARTHRITIS

The population of the United States is aging due to the Baby Boomer generation. The 2014 census projected that by 2030, the number of individuals above age 65 will almost double and comprise one fifth of the population (Figure 1).\textsuperscript{1,2} As people age, complications arise and have potential to decrease quality of life (QoL). A common cause of decreasing QoL is from frequent knee pain and the primary cause of knee pain in people above 50 years is osteoarthritis.

Figure 1: Trends of aging population in United States based on prediction on the most recent census. Data based on US CENSUS 2015.
Osteoarthritis (OA) is a disease commonly associated with older age and a leading cause of lower limb disability.\textsuperscript{3–5} Research has associated knee OA with aging, genetics and knee injuries, all which leads to pain (Figure 2).\textsuperscript{6,7} The pain associated with knee OA limits the physical abilities of those afflicted, oftentimes resulting in physical disability, and eventually affecting the QoL in older population.\textsuperscript{8} The knee pain incidence rises as the elderly group grows in proportion and this has been documented on results from the Framingham study, where the prevalence of knee pain over 20 years had almost doubled.\textsuperscript{9} With this growing issue, research for treatment and prevention of knee OA and pain are becoming a priority.

![Diagram](image)

Figure 2: A diagram of proposed theory of osteoarthritis relation with pain, quality of life, as well as the focus of this project on synovitis and bone morphology and alignment.

There is a need to prioritize prevention for knee OA because of the limited treatments for OA. Generally, those treatments are not reversing the effect of OA but only treating the symptoms. For example, drugs such as NSAIDS, prescribed for OA patients target pain, and have to be taken regularly. Another common treatment is to inject a hyaline liquid to act as a surrogate cartilage. This too only provides temporary relief to the patients. More invasive procedures, such as osteotomy and knee joint
replacement, have been suggested as a last resort when other treatments fail.\textsuperscript{10,11} Unfortunately, the best prevention method is not yet established due to the complexity of knee OA disease/biology.

Knee OA is primarily diagnosed using radiographs to estimate cartilage loss by joint space narrowing (i.e. cartilage loss is not directly assessed with radiographs). X-ray has been the standard to diagnose OA for decades. However, those with pain (symptomatic OA) are not necessarily diagnosed with radiographic knee OA.\textsuperscript{12,13} Williams et al. reported only 43\% of people who had pain were diagnosed with radiographic knee OA from x-ray assessments.\textsuperscript{13,14} This structure-symptom discordance highlights that radiographs may not the best diagnostic tool for OA. Additionally, OA is a more complex disease process than a simple relationship between joint space narrowing, an estimate of cartilage loss, and pain. Furthermore, cartilage is aneural and not a source of pain.

Other surrounding tissues in and around knee joint are innervated and a potential cause of pain. Attention has shifted from estimates of cartilage loss to a complex framework involving tissues such as subchondral bone, synovium, menisci, ligaments, periarticular muscles, the joint capsules, and infrapatellar fat pad. Inflammation in the soft tissues of knee joint may be a cause of pain. Inflammatory features such as tissue swelling are commonly found during the clinical exam of frequent knee pain. Interleukin and tumor necrosis factors, which are inflammatory mediators, are also found in the joint with OA.\textsuperscript{15} One particular site prone to inflammation is the synovial membrane, referred to as synovitis.
Under normal conditions, the synovium is two to three cells thick. In an inflamed state, the synovium is thickened and found to have an increased number of inflammatory cells. Synovitis has been associated with knee pain, and to bone marrow lesions, joint effusion, as well as osteophytosis, all of which are considered signs of OA. Synovitis can be assessed by changes of signal intensity visualized on MRI. Studies of synovitis hope to provide insight into the potential treatment of OA by targeting inflammation and preventing disease progression. However, direct visualization of synovitis may require invasive surgery. Therefore, by using a marker detected through imaging such as MRI, clinicians anticipate having the ability to more easily diagnose OA or identify the early signs of OA. Currently, a hyperintensity signal or edema sign be seen on fat-suppressed MRI around the synovial membrane. This signal is accepted as a surrogate marker for synovitis. This surrogate signal is commonly detected in the Hoffa’s fat pad region.

HOFFA’S FAT PAD AND THE PATELLOFEMORAL JOINT

Infrapatellar or Hoffa’s fat pad (HFP) is an intracapsular but extrasynovial tissue in the knee joint located inferior to the patella and posterior to the patellar tendon (Figure 3). It fills the area between patellar tendon, anterior femoral condyle, and the anterior tibia and also is closely located to the cartilage surface. HFP is highly innervated, thus a potential cause of pain, and contains synovial fluid and active immune cells. Synovitis in HFP can be detected by signal hyperintensity changes on T2-weighted MRI.
Figure 3: Illustration of sagittal view of knee. Organs illustrated here are the focus of this project. Important bone parts include femur and patella. Blue line is cartilage which usually the focus of osteoarthritis diagnosis. Red line is synovial membrane, which the inflammation is thought to be the source of pain. Superolateral Hoffa’s fat pad, located exactly under the patella, is the main outcome of this project.

**BONE ANATOMY**

There are three main bones of the knee joint that may be affected by OA; the femur (thighbone), tibia (shinbone), and patella (kneecap). At the inferior part of femur where the knee joint is located, the anterior is shaped as a concave groove called the
trochlea (Figure 4). This groove is shaped similarly to the posterior/back of the patella and acts as the articulating surface for patella. The superior patella is connected to the quadriceps femoris muscle on the superior part and patellar tendon on the inferior part. Therefore, the patella is an important component of the knee joint. This articulation between femoral trochlea and patella is called patellofemoral joint (PFJ).

Knee pain, especially in the anterior (front) knee, is commonly accepted to be caused by PFJ maltracking and impingement. PFJ maltracking involves abnormal medial-lateral translation of the patella with respect to the trochlear groove. This abnormal feature has been studied as an important association to knee OA. Several morphological assessments of the trochlear groove, such as trochlear inclination angle, are risk factors for signs of knee OA (i.e., bone marrow lesions, cartilage loss). Additionally, this maltracking may lead to impingement of the nearby tissues, particularly Hoffa’s fat pad.

Figure 4: Axial view of patellofemoral joint along with parts being focused in this study, such as posterior condyle, sulcus or trochlear groove, and trochlear peak.
Of late, clinicians and researchers have described an edema signal specifically located at the superolateral region of the Hoffa’s fat pad (SHFP). Chung et al. hypothesized SHFP edema may be related to PFJ maltracking. They found in patients with lateral anterior femoral condyle ‘fat impingement syndrome’, more than half of the patients were diagnosed with high patella riding. It was a qualitative study within a small group of patients. Although there was no statistical result to compare between the groups, they suggested friction syndrome and fat pad impingement relationship to SHFP edema.

Chhabra et al. supported this impingement syndrome as SHFP edema and suggested a systematic approach in knee assessment. They suggested to assess the patellar height, sulcus condition, and patellar tilt as a way to detect maltracking. However, their result did not explain which features were associated with SHFP edema or the cause of impingement. In theory, SHFP edema occurs when the fat pad gets impinged between the patellar tendon and the lateral anterior femur (tibia) during knee extension (flexion). Impingement of the SHFP may be more likely in knees with abnormal alignment or abnormal morphology of the femoral trochlea.

**STUDY RATIONALE**

There is still little knowledge on the relationship between SHFP edema and knee OA and knee pain. As knee OA can cause knee pain, SHFP edema is thought to be related to knee pain as well. Features of knee OA (e.g., cartilage loss) are associated with PFJ maltracking. Thus, it is hypothesized that SHFP edema is related or has similar
relationship with PFJ maltracking. Creating assessment to detect maltracking early on is hoped to give time for treatment or to quickly treat the problem and prevent it from worsening.

Recent studies have investigated the relationship between PFJ alignment and trochlear morphology with respect to SHFP edema.\textsuperscript{34–38} However, these studies have observational, retrospective study designs (i.e. retrospective cohort studies, and case-control studies), all which were designed to compare characteristics of people with SHFP edema to subjects without SHFP edema. These studies included a younger age population and limited a number of subjects above 60 years. Therefore, it is imperative to study risk factors for early signs of knee OA (such as SHFP edema) in a large sample of those with or at risk for knee OA. Furthermore, a meta-analysis study suggested that females, older individuals, and those who have high BMI, are at an increased risk for knee OA which in turn may lead to SHFP inflammation.\textsuperscript{5} Thus, a study is needed to also adjust for these covariates.
METHODS

STUDY OBJECTIVES AND DESIGN

This study objective was to find features of PFJ alignment and femoral trochlea morphology most associated with SHFP edema assessed through MRI. The primary hypothesis was that at least one feature would play a role in the SHFP edema, but this study would only be able to offer insight to this relationship. The ultimate goal of this study was to add knowledge to risk factors for the Hoffa’s fat pad edema and provided evidence for potential development of treatment/prevention method for knee OA. This study could also offer insight of prevalence of SHFP edema.

The design of this study was cross-sectional. The predictor variables were features of PFJ alignment and femoral trochlea morphology. The outcome variable was the SHFP edema. Both predictors and outcome were assessed in one time point.

MOST STUDY

The Multicenter Osteoarthritis (MOST) Study is a longitudinal cohort study, with a total of 6 study visits beginning in 2003. The baseline visit was performed from 2003 until 2005. The follow-up visits occurred at 15 months after baseline, 30-month, 60-month, 72-month, and 84-month time points. The overall objective of MOST study is to identify any risk factors in symptomatic and radiographic knee OA, as well as comparing the risk factors of people with the pre-existing knee OA versus people with high risk of knee OA. Participants were recruited and had baseline exams either at The University of Alabama at Birmingham (UAB) or The University of Iowa (UI). The data was managed
and coordinated by The University of California, San Francisco (UCSF). The data
analysis and radiograph readings were performed by Boston University (BU).

Inclusion criteria at the baseline included:

1. Participants were community-dwelling men and women aged 50-79 years at the time of recruitment.
2. Sex and age distributions were kept in proportion to the U. S. population.
3. Participants included either had preexisting knee OA or were at high risk of developing knee OA.

Exclusion criteria included:

1. Knee replacement surgery on both knees (bilateral knee replacement).
2. Unable to complete informed consent.
3. Plans to move out of the area during the follow-up time.
4. Illness with short survival time, or
5. Diagnosed with other rheumatoid or other inflammatory arthritis.

Participants were contacted through phone for the follow-up visits. The surviving participants were interviewed on all visits and had clinical exams on all visits except at the 72-month follow up. Knee radiographs were obtained during the clinical exams on all visits. Knee MRIs were obtained for participants who did not have contraindications. These MRI results were graded for various MRI features of knee OA using Whole Organ MRI Scoring system (WORMS).\textsuperscript{39,40}
CURRENT STUDY SAMPLE POPULATION

This thesis project was an ancillary study of the parent study. In this study, the data used was from MOST 60-month visit. Predictor and outcome variables were read from MRI and x-ray results of the 60-month clinical exams. One knee per participant was assessed due to financial restrictions in the MOST parent study. MRI outcomes were assessed in one knee per subject. Covariates data were obtained in a SAS dataset. Covariate data included sex, age, BMI, and study site. Data were de-identified and prepared by the UCSF data-coordinating center. SHFP edema was assessed by a team of radiologists at Boston University working on another project using similar data from MOST.

RISK FACTORS AND OUTCOME

Assessments of trochlear morphology, PFJ alignment, as well as the SHFP edema were new measurements specific to this MOST ancillary study and were not assessed in the parent study. The trochlear morphology assessment consisted of the sulcus angle (SA), lateral and medial trochlear inclination angle (LTI and MTI), and trochlear angle (TA). Patellar height was measured as the Insall-Salvati Ratio (ISR). Patellofemoral joint alignment was assessed using the patellar tilt angle (PTA) and bisect offset (BO). These seven variables served as the predictor variables for this study.

MRI edema on superolateral section of Hoffa's fat pad (SHFP) was the outcome variable for this study. Previous assessment of overall HFP edema for the MOST study was based on the WORMS. The original WORMS system does not differentiate SHFP.
edema from other edema in HFP. Therefore, in this current study, a modified WORMS system was used, specifically differentiating the edema on SHFP and edema and other sites in Hoffa’s fat pad.

**ASSESSMENT OF TROCHLEAR MORPHOLOGY**

All measures of trochlear morphology were assessed on the axial MRI slice where the medial and lateral posterior femoral condyles were the most posterior (Figure 5). Knees from individuals where the lateral and medial posterior condyles were more than 2 slices apart were excluded. First, the sulcus angle (SA) was assessed as the angle between the medial and lateral trochlear facets (Figure 6). For all measurements, when osteophytes were present, attempts were made to measure the bone as if there was no osteophyte by following the curvature of the bones.

Next, the posterior condylar line (PCL) was drawn by connecting the medial and lateral posterior femoral condyles (Figure 5). The lateral trochlear inclination angle (LTI) was defined as the angle made by a line along the lateral trochlear facet, used for the SA measurement, with the PCL. Medial trochlear inclination angle (MTI) was defined as the angle made by the line along the medial trochlear facet, used for the SA measurement, with the PCL.

Finally, trochlear angle (TA) was measured as the angle between a line along the most anterior points of medial and lateral trochlear facets with the PCL. The vertex of the angle was placed at medial condyle. If the lateral condyle was angled at a higher point
with respect to PCL, then the angle was deemed positive. If it not, the angle was deemed negative.

**ASSESSMENT OF PATELLOFEMORAL JOINT ALIGNMENT**

First, the axial MRI slice that contained the maximum patellar width (MPW) was determined by finding the slice where the patella had the widest transverse axis (Figure 7). A perpendicular line to PCL that passed through the center of trochlear groove was drawn on the same slice as PCL. Then, this line and PCL were copied to the MPW slice. The lateral intersection between PCL and the maximum width line creates a vertex that is the patellar tilt angle (PTA). PTA was positive if PCL was below the MPW, and vice-versa. Bisect offset (BO) was defined as the percent of the patella lateral to the midline (Equation 1).

**ASSESSMENT OF PATELLA HEIGHT**

The vertical position of patella was measured on the lateral semi-flexed x-ray. This study used Insall-Salvati ratio (ISR) (Equation 2), a ratio of vertical length of patella (LP) and the length of patellar tendon (LT) (Figure 8). LP was measured from the most superior/posterior point of patella to the most inferior point. LT was measured from the tibial tuberosity to the inferior point of patella.

All PFJ alignment and trochlear morphology readings were performed using OsiriX version 7.0.
Figure 5 Illustration of the process in deciding the posterior condyle line (PCL) and maximum patellar width (MPW). MRI slice presented here is only example. PCL is decided by the MRI slice with most posterior condyle and MPW is by the widest patella slice.
Figure 6 Illustration of trochlear morphology assessments. Line (a) is posterior condyle line (PCL) with medial and lateral legend. Line (b) is sulcus angle (SA), angle (c) is medial inclination angle (MTI), angle (d) is lateral inclination angle (LTI), angle (e) is trochlear angle (TA). The bottom image is an example of depiction of trochlear morphology assessment done on a slice of MRI.
Figure 7 Illustration of patellofemoral joint alignment assessment. Line (f) is maximum patellar width (MPW), line (g) is the lateral-midline length of MPW, and angle (h) is patellar tilt angle (PTA). The right image is an example of depiction of patellofemoral joint alignment assessment done on a slice of MRI where the patella width is the widest.

\[ BO = \frac{\text{lateral} - \text{midline MPW}}{\text{MPW}} \times 100\% \]

Equation 1 Equation used to calculate bisect offset in this study. It is a ratio of patella offset from the middle trochlear groove.
Figure 8 Method of measuring the length of patella (LP) (i) and length of patellar tendon (LT) (j), through sagittal x-ray.

\[
\text{ISR} = \frac{LP}{LT}
\]

Equation 2 Equation used to calculate Insall-Salvati Ratio in this study. It is a ratio of length of patella and length of patellar tendon.

**HOFFA’S FAT PAD SIGNAL HYPERINTENSITY (SYNOVITIS)**

**SCORING**

The presence of SHFP edema was assessed on the sagittal T2-weighted MRI by a team of radiologists (Guermazi et al.) based on previous study criteria. Signal changes seen on MRI were a surrogate marker for synovitis. The grading was ranked as 0 (no edema or synovitis), 1 (small edema or mild chronic synovitis), 2 (moderate edema),
or 3 (severe edema)(Figure 9).

Figure 9 Example of sagittal MRI slices of SHPF edema. Normal condition is shown as picture (a) while the edema on each severity is (b), (c), and (d).

DATA COLLECTION AND STATISTICAL ANALYSIS

All data were first recorded in Microsoft Excel. Data for PFJ alignment, trochlear morphology, and SHFP edema were combined using SAS version 9.4. The same software was used for the statistical analyses. Charts were made using R version 3.2.3.
Descriptive statistics were used for all variables (exposure, outcome and covariates) used in the study. Mean, standard deviations and ranges for continuous variables and frequency counts were used for categorical variables. SHFP edema was dichotomized into presence (>0) and absence (=0).

To determine the best exposure variables that were most associated with the presence of SHFP edema, first each exposure variable was analyzed with the presence of SHFP edema in logistic regression model. Then, all variables were included in one model and analyzed using logistic regression. Age, BMI and sex were included in the model. Next, SAS backward selection function was performed to predict the best associated variables. As an additional confirmation, the published variable selection using logistic regression by Bursac et al. was included when comparing the best variables to predict SHFP edema. The results of all variable selection methods were compared by its p-value and Wald-chi square score.

After the best variables were selected, each predictor variable was divided into quartiles and analyzed in logistic regression analysis with the presence of SHFP edema as the outcome and age, BMI and sex as covariates. The reference quartile of each variable was determined based on a priori hypothesis as the quartile with the lowest edema prevalence. As PFJ alignment has been shown to be an intermediate between trochlear morphology and OA, bisect offset and patellar tilt angle analyses were adjusted for the morphology variables that had been selected on previous method. The p-value for trend of the quartiles was calculated from the continuous value of the variables.
RESULTS

BASELINE CHARACTERISTICS

1132 subjects had their knee MRI (one knee per subject) assessed at the 60-month study. Several subjects had poor quality MRI or x-ray and as such the trochlear morphology, PFJ alignment or SHFP edema could not be determined. The posterior condyle line was difficult to determine in some instances. This happened when the most posterior slice of the lateral and medial posterior condyle was more than 2 slices apart. There were some subjects with bipartite patella where the patella was composed of 2 bones instead of one fused bone. The baseline characteristics of the excluded subjects were found to be indifferently than the analyzed subjects. This study included subjects whose data was complete or per-protocol and did not perform statistical imputation for intention-to-treat analysis. Thus, the total analysis included 1082 subjects.

AGE, SEX, AND BMI

The age of subjects at the 60-month visit ranged between 55 to 84 years, with a mean age of 66.8 years (Table 1). The BMI of subjects ranged between 16.9-50.6 kg/m² at the 60-month visit with a mean BMI of 29.7 kg/m². Comparing between sexes, there were nearly twice as many female subjects compared to males in the sample, and the females were slightly older, but had smaller BMI scores than male subjects (Table 2). With respect to study sites, there was no observable difference between the populations recruited from Alabama or Iowa (Table 3). The sex differences between the sites were also similar.
Table 1. A descriptive statistics of age and BMI of the sample population analyzed in this study (MOST 60-month study visit).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1082</td>
<td>66.8</td>
<td>7.5</td>
<td>55.3-84.8</td>
</tr>
<tr>
<td>BMI</td>
<td>1082</td>
<td>29.7</td>
<td>4.8</td>
<td>16.9-50.64</td>
</tr>
</tbody>
</table>

Table 2. A descriptive statistics of the proportion of sex in the study, including the age and BMI differences.

**SEX DIFFERENCES**

<table>
<thead>
<tr>
<th></th>
<th>FEMALES (N=683, 63.1%)</th>
<th>MALES (N=399, 36.9%)</th>
<th>p-diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Range</td>
<td>Mean</td>
</tr>
<tr>
<td>Age</td>
<td>67.0</td>
<td>7.5</td>
<td>55.3-84.8</td>
</tr>
<tr>
<td>BMI</td>
<td>29.4</td>
<td>4.9</td>
<td>18.3-44.4</td>
</tr>
</tbody>
</table>

*t-test

Table 3. An exploratory descriptive statistics of age and BMI differences between sites.

**SITE DIFFERENCES**

<table>
<thead>
<tr>
<th></th>
<th>ALABAMA (N=408)</th>
<th>IOWA (N=674)</th>
<th>p-diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Range</td>
<td>Mean</td>
</tr>
<tr>
<td>Age</td>
<td>66.6</td>
<td>7.4</td>
<td>55.5-84.7</td>
</tr>
<tr>
<td>BMI</td>
<td>29.4</td>
<td>4.8</td>
<td>16.9-42.9</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>258</td>
<td>Male</td>
</tr>
</tbody>
</table>

*t-test
**chi-square test
**MORPHOLOGY AND ALIGNMENT**

Table 4 shows the descriptive statistics for the trochlear morphology, Insall-Salvati Ratio and PFJ alignment. Some measurements have negative values to show their orientations are not in the normal direction. For TA, the negative value happens when the lateral trochlear peak is more posterior or shorter than the medial peak. For PTA, it happens when the patella tilt more toward medial with respect to PCL. Some subjects did have a very negative value of TA or PTA, such as negative eleven and negative nine respectively. However, out of eleven subjects with either extreme negative TA or PTA (less than negative five), none was found with SHFP edema. Therefore, those subjects were not excluded from the analysis.

One unusual subject had negative MTI value, as the medial trochlear groove was declined rather than inclined in respect to the PCL. The subject was a 64 years old female with no SHFP edema, a normal BO and ISR, a wide SA, and a slight negative PTA. Since it was only one subject and the other measurements were not that unusual, the subject was not excluded from the analysis.

The overall position of patella in this study population tended towards the lateral side as shown by the mean of BO of more than 50%. Four subjects, all females, had their patella way off laterally from the middle, resulting in BO greater than supposedly maximum value of 100%. Only one of those subjects had moderate SHFP edema even though her BO was not the most extreme. Those subjects were also kept for the analysis.
Table 4. A descriptive statistics of trochlear morphology, ISR, and PFJ alignment results (n=1082).

<table>
<thead>
<tr>
<th>Exposure variables</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trochlear Morphology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulcus angle degree</td>
<td>135.7</td>
<td>9.1</td>
<td>103.5</td>
<td>164.0</td>
</tr>
<tr>
<td>Lateral trochlear inclination angle degree</td>
<td>23.3</td>
<td>5.0</td>
<td>6.6</td>
<td>40.7</td>
</tr>
<tr>
<td>Medial trochlear inclination angle  degree</td>
<td>21.3</td>
<td>6.5</td>
<td>-0.6</td>
<td>42.3</td>
</tr>
<tr>
<td>Trochlear angle degree</td>
<td>4.1</td>
<td>3.4</td>
<td>-11.3</td>
<td>17.6</td>
</tr>
<tr>
<td><strong>Alignment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patellar tilt angle degree</td>
<td>10.3</td>
<td>5.6</td>
<td>-9.8</td>
<td>34.1</td>
</tr>
<tr>
<td>Bisect offset %</td>
<td>59.6</td>
<td>9.7</td>
<td>33.9</td>
<td>111.4</td>
</tr>
<tr>
<td>Insall-Salvati Ratio ratio</td>
<td>1.1</td>
<td>0.2</td>
<td>0.6</td>
<td>1.6</td>
</tr>
</tbody>
</table>

**SHFP EDEMA**

The majority of the subjects did not exhibit SHFP edema (Table 5). While 10% experienced low-level edema, less than 3% of subjects experienced either moderate or severe edema combined. Despite combining all the grades of edema into one category the percentage of edema experienced was 12.8%.

Table 5. Descriptive statistics of edema score and dichotomous edema presence.

<table>
<thead>
<tr>
<th>SHFP Edema score</th>
<th>absent</th>
<th>mild</th>
<th>moderate</th>
<th>severe</th>
<th>present*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>586</td>
<td>80</td>
<td>15</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>357</td>
<td>31</td>
<td>11</td>
<td>0</td>
<td>97</td>
</tr>
<tr>
<td>Total</td>
<td>943 (87.2%)</td>
<td>111 (10.3%)</td>
<td>26 (2.4%)</td>
<td>2 (0.2%)</td>
<td>139 (12.8%)</td>
</tr>
</tbody>
</table>

*Sum of low, moderate, and severe SHFP edema
STATISTICAL TEST RESULTS

Several methods were performed to find the measurements that were associated with having SHFP edema (Table 6). Each variable (SA, LTI, MTI, TA, ISR, PTA, BO) was first analyzed individually. For the rest of the analyses, all variables were concurrently included as well as age, BMI and sex. All methods showed TA, ISR, and BO as the variables most strongly associated with SHFP edema. Thus, the next analysis focused only on TA, ISR, and BO. Age, BMI, and sex were not statistically significant but kept as covariates for analysis.

Odd ratios of each quartile for each variable are shown in Table 7. In agreement to the variable selection result, only TA and ISR showed significant trends between each quartile. Each quartile of ISR showed significant differences between each other. On the other hand, TA showed significant increase in the odds of having SHFP edema only on the highest quartile. PFJ alignment results were analyzed with adjustment of ISR and TA. The reference quartiles for ISR, TA and BO were the first quartile as there is an increasing SHPF edema prevalence.

PFJ alignment logistic regression analyses (PTA and BO) were adjusted by ISR and TA (Table 8). Only BO was shown to have a significant association with the SHFP edema. Both TA and BO odd ratios were significant only when the highest quartile was compared to lowest quartile. On the other hand, ISR odd ratios were significant in all quartiles.
Table 6. Results of four model selection methods to find the most associated variables to SHFP edema.

<table>
<thead>
<tr>
<th>Variables*</th>
<th>Univariate</th>
<th>Multivariate</th>
<th>Backward selection**</th>
<th>Bursac-Hosmer Purposeful Selection**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulcus angle</td>
<td>1.7701</td>
<td>0.1834</td>
<td>0.3857</td>
<td>0.5345</td>
</tr>
<tr>
<td>Lateral trochlear inclination angle</td>
<td>0.3991</td>
<td>0.5275</td>
<td>0.411</td>
<td>0.5214</td>
</tr>
<tr>
<td>Medial trochlear inclination angle</td>
<td>1.9785</td>
<td>0.1596</td>
<td>0.0095</td>
<td>0.9224</td>
</tr>
<tr>
<td>Trochlear angle</td>
<td>11.719</td>
<td>0.0006</td>
<td>10.5433</td>
<td>0.0012</td>
</tr>
<tr>
<td>Patellar tilt angle</td>
<td>1.5493</td>
<td>0.2132</td>
<td>0.0099</td>
<td>0.9206</td>
</tr>
<tr>
<td>Bisect offset</td>
<td>29.976</td>
<td>&lt;.0001</td>
<td>5.4432</td>
<td>0.0196</td>
</tr>
<tr>
<td>Insall-Salvati Ratio</td>
<td>89.9137</td>
<td>&lt;.0001</td>
<td>64.4798</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Sex</td>
<td>3.0166</td>
<td>0.0824</td>
<td>0.2107</td>
<td>0.6462</td>
</tr>
<tr>
<td>Age</td>
<td>3.3526</td>
<td>0.0671</td>
<td>1.0234</td>
<td>0.3117</td>
</tr>
<tr>
<td>BMI</td>
<td>3.0318</td>
<td>0.0816</td>
<td>3.2889</td>
<td>0.0698</td>
</tr>
</tbody>
</table>

* Wald-Chi square and P-value
**empty cell means the covariate does not included in the best model predicted
### Table 7. Result of logistic regression analysis between quartiles of trochlear morphology variables with SHFP edema

<table>
<thead>
<tr>
<th></th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sulcus angle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n(range)</td>
<td>271 (103.49-129.74)</td>
<td>270 (129.77-135.70)</td>
<td>271 (135.71-141.74)</td>
<td>270 (141.75-164.04)</td>
<td></td>
</tr>
<tr>
<td>with SHFP edema (%)</td>
<td>29 10.7%</td>
<td>28 10.4%</td>
<td>46 17.0%</td>
<td>36 13.3%</td>
<td></td>
</tr>
<tr>
<td>OR(95%CI)</td>
<td>1 (REF)</td>
<td>0.975 (0.56-1.69)</td>
<td>1.682 (1.02-2.78)</td>
<td>1.197 (0.71-2.02)</td>
<td>0.278</td>
</tr>
<tr>
<td><strong>Lateral trochlear inclination</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n(range)</td>
<td>270 (6.58-20.01)</td>
<td>271 (20.02-23.14)</td>
<td>271 (23.17-26.34)</td>
<td>270 (26.35-40.66)</td>
<td></td>
</tr>
<tr>
<td>with SHFP edema (%)</td>
<td>37 13.7%</td>
<td>33 12.2%</td>
<td>36 13.3%</td>
<td>33 12.2%</td>
<td></td>
</tr>
<tr>
<td>OR(95%CI)</td>
<td>1.151 (0.69-1.91)</td>
<td>1.00 (0.60-1.68)</td>
<td>1.106 (0.66-1.84)</td>
<td>1 (REF)</td>
<td>0.536</td>
</tr>
<tr>
<td><strong>Medial trochlear inclination</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n(range)</td>
<td>270 (-0.58-17.13)</td>
<td>270 (17.19-21.48)</td>
<td>272 (21.51-25.62)</td>
<td>270 (25.63-42.32)</td>
<td></td>
</tr>
<tr>
<td>with SHFP edema (%)</td>
<td>39 14.4%</td>
<td>39 14.4%</td>
<td>35 12.9%</td>
<td>26 9.6%</td>
<td></td>
</tr>
<tr>
<td>OR(95%CI)</td>
<td>1.474 (0.86-2.52)</td>
<td>1.488 (0.87-2.53)</td>
<td>1.374 (0.80-2.36)</td>
<td>1 (REF)</td>
<td>0.284</td>
</tr>
<tr>
<td><strong>Trochlear angle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n(range)</td>
<td>271 (-11.25-1.82)</td>
<td>270 (1.83-4.11)</td>
<td>272 (4.12-6.24)</td>
<td>269 (6.26-17.62)</td>
<td></td>
</tr>
<tr>
<td>with SHFP edema (%)</td>
<td>26 9.6%</td>
<td>27 10.0%</td>
<td>37 13.6%</td>
<td>49 18.2%</td>
<td></td>
</tr>
<tr>
<td>OR(95%CI)</td>
<td>1 (REF)</td>
<td>0.973 (0.55-1.72)</td>
<td>1.405 (0.82-2.41)</td>
<td>1.933 (1.15-3.25)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Statistically significant numbers are bolded

Adjusted for age, BMI, and sex
Table 8. Logistic regressions results between quartiles of alignment variables with SHFP edema

<table>
<thead>
<tr>
<th></th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bisect offset</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n(range)</td>
<td>270 (33.91-53.08)</td>
<td>271 (53.09-58.33)</td>
<td>271 (58.35-64.80)</td>
<td>270 (64.84-111.43)</td>
<td></td>
</tr>
<tr>
<td>with SHFP edema (%)</td>
<td>22  8.1%</td>
<td>26  9.6%</td>
<td>31  11.4%</td>
<td>60  22.2%</td>
<td></td>
</tr>
<tr>
<td>OR(95%CI)</td>
<td>1 (REF)</td>
<td>1.02 (0.55-1.90)</td>
<td>1.20 (0.66-2.20)</td>
<td>2.24 (1.27-3.96)</td>
<td>0.0005</td>
</tr>
<tr>
<td><strong>Patellar tilt angle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n(range)</td>
<td>270 (-9.84-6.66)</td>
<td>271 (6.7-9.97)</td>
<td>271 (9.98-13.8)</td>
<td>270 (13.83-34.11)</td>
<td></td>
</tr>
<tr>
<td>with SHFP edema (%)</td>
<td>37  13.7%</td>
<td>28  10.3%</td>
<td>39  14.4%</td>
<td>35  13.0%</td>
<td></td>
</tr>
<tr>
<td>OR(95%CI)</td>
<td>1 (REF)</td>
<td>0.713 (0.41-1.24)</td>
<td>1.07 (0.63-1.83)</td>
<td>0.83 (0.48-1.45)</td>
<td>0.367</td>
</tr>
<tr>
<td><strong>Insall-Salvati Ratio</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n(range)</td>
<td>270 (0.63-0.96)</td>
<td>273 (0.96-1.07)</td>
<td>268 (1.07-1.18)</td>
<td>271 (1.18-1.59)</td>
<td></td>
</tr>
<tr>
<td>with SHFP edema (%)</td>
<td>11  4.1%</td>
<td>15  5.5%</td>
<td>38  14.2%</td>
<td>75  27.7%</td>
<td></td>
</tr>
<tr>
<td>OR(95%CI)</td>
<td>1 (REF)</td>
<td>1.378 (0.62-3.06)</td>
<td>3.854 (1.92-7.73)</td>
<td>8.658 (4.45-16.85)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Statistically significant numbers are bolded
Adjusted for age, BMI, and sex
*Additionally adjusted for ISR and TA
DISCUSSION

CURRENT FINDINGS

Edema on MRI is a sign of inflammation of the tissues related to OA and is visualized by a change in signal intensity. Edema in the synovial region is a sign of synovitis, which is a state of inflammation in the synovial membrane. Hoffa’s fat pad, a highly innervated part of the knee, is thought to be impinged by abnormal bone morphology or malalignment. This impingement may result in increased edema in the fat pad on MRI. A shallow trochlea and malaligned patella have been associated with impingement and signs of OA especially in PFJ region. Yet, it is less understood what the relationship is in the superolateral region of Hoffa’s fat pad. Thus, the relation of trochlear morphology and patellar alignment to edema on the superolateral part of the Hoffa’s fat pad was investigated.

This study used data from the MOST study. The population in MOST consisted of individuals with a high risk of developing, or who were diagnosed with osteoarthritis. As prevalence of joint pain as well as OA is reported to be 15-20% of the United States population, a random sample of the general population may not produce quality data with adequate OA patients or outcomes of interest. Thus, by selecting a niche from the overall population, this study hoped to obtain an adequate sample size of OA patients for analysis and observation of the disease.

The sulcus angle, lateral and medial trochlear inclination, trochlear angle, patellar tilt angle, bisect offset, and Insall-Salvati ratio were assessed in relation to SHFP edema.
SHFP edema was present in 13% of the sample. Results showed TA, BO, and ISR were associated with the SHFP edema.

![Graph showing the prevalence of edema in each quartile](image)

**Figure 10. Prevalence of edema in each quartile. Comparison between TA, BO, and ISR showed linear trends of increasing edema.**

As the TA increased (i.e., the lateral trochlear facets projected more anterior), the number of subjects with edema increased as well. Although statistical analysis showed that the significant difference in subjects with edema was only between those in the highest TA group vs. the lowest TA group, there was a strong linear trend of increasing edema with increasing TA quartiles (p=0.002). This can be seen in Figure 10 where the percentage of edema in each quartile increased across TA quartiles. Similarly, both BO and ISR showed increasing trends across quartiles (p=0.0005, p<0.0001 respectively).
Additionally, ISR quartiles 2-4 showed a significant increase of edema compared to quartile 1.

One hypothesis of this study was that the flatter trochlear morphology, such as high sulcus angle and low trochlear inclination angle, would be associated with edema as it is to patellofemoral OA. This was thought to be due to increased instability of the PFJ with a flattened trochlea. Other hypotheses were derived from the idea that patellar malalignment, such as the laterally displaced patella and higher patella positions, were associated with OA. Current results do not confirm the first hypothesis. However, based on the relation between TA and edema, if the lateral trochlear facet was more anterior than medial, the chance of having edema was higher. Current results confirms the second hypothesis that malalignment of patella was related to edema. Although PTA did not show a significant relation to edema, the other two alignment measures were related. Thus, a patella that was positioned very laterally or very superior with respect to trochlear groove has a higher chance of edema in the SHFP.

**IMPLICATIONS OF THIS STUDY**

Results from this study may help clinicians to assess these measures of morphology and alignment in their patients. As this study was cross-sectional, reverse causation is unlikely (i.e., edema unlikely to cause morphology changes), however, these measures may predict a patient’s chance of developing edema. Moreover, patients without edema have exhibit a high trochlear angle (i.e., lateral trochlea projects further anterior) or a laterally malaligned patella have a greater chance of developing edema.
Additionally, a small increase in the superior position of the patella can greatly increase the prevalence of edema. Thus, assessment of patella alta, defined as ISR >1.2, should be included during assessment of the knee.

Clinicians have suggested a variety of OA treatments from invasive surgeries to physical therapies. With respect to this study, pharmacological interventions have been particularly prescribed to treat the inflammation of OA. In this case, similar interventions can be used to treat the SHFP edema. The non-pharmacological interventions include education, weight-loss, and biomechanical treatment (i.e., bracing and taping). A study investigating the use of bracing for PFJ OA, found that bracing could change patellar alignment. The result of that study presented a possibility of treating high ISR or BO by realigning the patella to a better position or location. This study demonstrates that early detection combined with early intervention using braces has the potential to prevent SHFP edema.

**COMPARISON WITH OTHER STUDIES**

Chung et al. first coined SHFP edema as the result of PFJ maltracking and impingement, and then Subhawong et al. supported this idea by using quantitative measurements. More studies followed soon there after, using different measurement methods. Not all of the previous studies conclusions align with the current study’s results. One possible factor is the difference in population age (Table 9). Other studies did not have a specified age range to examine SHFP edema and might not have adjusted for covariates. This study purposefully chose people 65 years and older as they
are a more vulnerable to OA. Therefore, the result of this study may be applicable to only individuals 65 years of age and older, while results from previous studies might be more relevant for younger populations. However, this study fills the gap of knowledge for older individuals.

Table 9. Comparison between studies assessing SHFP edema

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>SAMPLE SIZE</th>
<th>AGE</th>
<th>DESIGN</th>
<th>OBJECTIVE</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chung et al. (2001)³³</td>
<td>42 random</td>
<td>33 years</td>
<td>retrospective cohort</td>
<td>To find any MRI observation from knee with lateral pain</td>
<td>A descriptive analysis of SHFP edema, first to report SHFP edema</td>
</tr>
<tr>
<td>Subhawong et al. (2010)³⁴</td>
<td>50 random</td>
<td>36 years</td>
<td>case control</td>
<td>To find associated anatomical parameter with SHFP edema</td>
<td>t-test result showed SA was associated while BO was not. BO method was different</td>
</tr>
<tr>
<td>Chhabra et al. (2011)³⁷</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>To create a systematic knee assessment to find malalignment and edema</td>
<td>SA, LTI, TA, PTA, ISR were parameters to focus on knee assessments</td>
</tr>
<tr>
<td>Jibri et al. (2011)³¹</td>
<td>100 control vs. 100 edema</td>
<td>33 years</td>
<td>case control</td>
<td>To find any difference in parameter on SHFP edema group with normal group</td>
<td>ISR and BO had high prevalence on edema group from t-test analysis</td>
</tr>
<tr>
<td>Campagna et al. (2012)³⁵</td>
<td>30 edema vs. 60 control</td>
<td>33 years</td>
<td>case control</td>
<td>To find associated anatomical parameter with SHFP edema</td>
<td>Regression analysis showed TA and PTA were not associated while ISR was highly associated</td>
</tr>
<tr>
<td>De Smet et al. (2012)³⁶</td>
<td>80 random</td>
<td>group 1 = 30 group 2=50</td>
<td>case control</td>
<td>To assess clinical assessment of impingement and SHFP edema</td>
<td>Clinical diagnoses of impingement were associated with SHFP edema</td>
</tr>
</tbody>
</table>

In general, previous studies had compared quantitative measurements using t-test analysis. With that analysis, they were only able to show the difference between normal and edema groups for average morphological measurements. By using logistic regression analysis, this study was able to depict the chances of developing edema or the prevalence
of edema based on the knee morphology or alignment. Further, the effect of age, BMI, and sex as possible covariates were also assessed and standardized in order to be able to make apple-to-apple comparisons. Accordingly, this study was able to provide more detailed analyses than previous studies through its use of the logistic regression model.

**STRENGTHS OF THIS STUDY**

The primary strength of this study was the large sample size and older age population, which no other studies have addressed as the risk factors for OA and SHFP edema. Additionally, data for this study came from the MOST cohort, which was designed to study risk factors for OA. This study gives a broader population sample compared to other studies that used one hospital or clinic. MOST inclusion criteria were designed to be a representative sample of overall US population as well. Thus, this study data is believed to be representative of current US population.

**LIMITATIONS OF THIS STUDY**

This study was cross sectional. Therefore, only a measure of association can be assessed and no causality can be inferred. Most of the published studies had similar issues as no long-term prospective study or clinical trial has been done. However, from a biological perspective, bone morphology should be considered first before edema or OA. That idea is more plausible than OA causing abnormal bone morphology. Also, bone morphology and alignment may take years to develop while OA may be apparent or
symptomatic sooner. Therefore, although no causality can be inferred, the pathway that abnormal bone morphology and alignment lead to edema is justifiable.

While MRI is a common procedure used to diagnose edema and OA, it may not be the most ideal method of analysis for bone morphology as compared to CT scans as most of the unmeasured data was due to the quality of the bone image. Thus, the accuracy of the MRI measurements may not be as accurate as compared to measurement done in CT scan images.

**METHODOLOGICAL CONSIDERATIONS**

This study had to exclude 4.4% of subjects because no reference slice or PCL could be determined. Therefore, no further readings were performed. It is imperative to have a reference or standard procedure to decide whether a slice will be used as readings from subject to subject. Unfortunately, PCL may not be a flawless method as this study shows. Irregular subjects whose posterior condyle between lateral and medial were far apart more than 2 MRI slices had their MRI deemed unreadable as this study was not designed to specifically assess these subjects. However, they might be a very niche group that has to be analyzed separately than the current study objective. Additionally, the number of subjects excluded in this study was less than 5%. Based on observations, those subjects’ PFJ morphology and alignment were generally similar to other included subjects and even if the readings were done, the result of analysis may not change significantly.
Furthermore, with the plethora of bone measurement methods, the current study only assessed a small proportion of available methods in bone assessments. Other studies used some of the methods found here as well as a whole different set of methods. This limitation causes difficulties in comparing between studies as well as reproducibility. Nevertheless, the methods used in this study were chosen based on some of the previous studies and assumptions.

**POSSIBLE FUTURE STUDIES**

The MOST study involved a total of 6 visits. New studies can be executed using data from the remaining visits. By comparing data on different time points, there is the possibility of drawing conclusions on the progress of OA and/or edema.

This study does not include the pain or QoL assessments in the analysis due to its focus on MRI edema as the outcome. Thus, another cross-sectional study looking at these risk factors on bone morphology and alignment in relationship to pain or QoL is also possible.

On the other hand, if a new prospective cohort study is planned, it may be better suited to address all the limitations in the data gathering as mentioned previously. To address the imaging issue, a similar cross-sectional study looking at the association between bone morphology, alignment and SHFP edema can be repeated but with a better imaging method for assessing the bones, such as CT scan. Other than using CT scans, this study can also be repeated by assessing the bone morphology and alignment using 3D imaging and advanced software.
In designing a future prospective study, the assessment methods should also be planned carefully. As seen in all published studies, every study used different assessments even though their study populations were similar. This led to difficulty to compare their results, especially for meta-analysis. A large study such as this study but using all the published bone assessment will take a long time to finish and may not be viable for researchers or clinicians. Therefore, a comparative study assessing the best method for SHFP edema may be needed first.
CONCLUSION

This study found that a flatter trochlea was not associated with SHFP edema, but trochlear angle was associated. Specifically, a large difference between lateral and medial trochlear peak increased the chance of a patient developing edema of the knee. Patellar height, measured in Insall-Salvati ratio, was also associated with a higher chance of edema. As the patella gets higher in location the prevalence of SHFP edema increased. Also, the more laterally displaced patella measured by bisect offset was associated with higher prevalence of edema. This study result may enable to clinicians to predict early onset of OA from abnormal morphology or malalignment, which in turn may help to prevent further OA progression or pain development.
APPENDIX

DIAGRAM OF ANATOMICAL TERM OF LOCATION
**DATA;**

DATA two;

SET merged;

BO = latpat/mpw*100;

ISR = lt/lp;

****SLE BINARY;

IF sle_v3 eq 0   THEN v3_sle=0;

ELSE IF sle_v3 gt 0  THEN v3_sle=1;

ELSE v3_sle=.;

****REDUCING ANALYSIS TO NON-MISS;

IF NMISS (OF  sa lti mti ta pta v3_sle
isr v3_age v3bmi) = 0;

RUN;

PROC RANK DATA=two GROUPS=4

OUT=three;

VAR sa lti mti ta pta isr bo;

RANKS qsa qlti qmti qta qpta qbo qisr;

RUN;

PROC FORMAT;

VALUE S_SEXF

0='FEMALE'

1='MALE';

VALUE SITEAAA

1='UAB'

2='UIOWA';

VALUE SCOREF

8='POOR QUALITY'

-9='EXCLUDED';

VALUE EDEMAF

0='NORMAL'

1='EDEMA';
RUN;

DATA thesis1 ;
SET three;

LABEL
sa='Sulcus angle'
l ti='Lateral inclination angle'
m ti='Medial inclination angle'
t a='Trochlear angle'
pta='Patellar tilt angle'
l atpat='Patellar lateral-mid length'
bo='Bisect offset'
isr='Insall-Salvati Ratio'
pclslice='Slice number of PCL'
mpw='Maximum patellar width'
mpwslice='Slice number of MPW'

v3_sle='presence of SHFP edema'

FORMAT v3_sle EDEMAF. ;
RUN;

**BASELINE;

PROC MEANS MAXDEC=2;
VAR v3_age v3bmi ;
RUN;

PROC UNIVARIATE freq plots normaltest ;
VAR sex;
RUN;

PROC MEANS MAXDEC=3;
VAR SA LTI MTI TA ISR PTA BO ;
RUN;
***EXPLORATORY;

PROC SORT;
VAR SEX;
RUN;

PROC MEANS;
VAR v3_age;
CLASS sex;
RUN;

PROC MEANS;
VAR v3bmi;
CLASS sex;
RUN;

PROC TTEST;
CLASS sex;
VAR v3_age v3bmi;
RUN;

PROC SORT;
VAR site;
RUN;

PROC FREQ;
TABLES sex*site/nocol nopercent norow chisq;
RUN;

PROC MEANS;
VAR v3_age;
BY site;
RUN;

PROC TTEST;
CLASS site;
VAR v3_age;
RUN;

PROC MEANS;
VAR v3bmi;
BY site;
RUN;

PROC TTEST;
CLASS site;
VAR v3bmi;
RUN;

**OUTCOME BASELINE;

PROC FREQ;
TABLES sex*sle_v3/nocol nopercent norow;
TABLES sex*v3_sle/nocol nopercent norow;

**MODEL SELECTION;

PROC LOGISTIC;
MODEL V3_SLE= sa;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= lti;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= mti;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= ta;
RUN;
PROC LOGISTIC;
MODEL V3_SLE= isr;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= pta;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= bo;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= v3_age;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= sex;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= v3bmi;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= sa lti mt i ta is r pta bo
v3_age v3bmi sex;
RUN;

PROC LOGISTIC;
MODEL V3_SLE= sa lti mt i ta is r pta bo
v3_age v3bmi
sex/SELECTION=B A C K W A R D ;
RUN;

%PurposefulSelection
(thesis1,
v3_sle,
sa lti mt i ta pta bo is r sex v3_age
v3bmi,
0.25, 0.1, 15, 0.15)
**ODD RATIO WITH MODEL OF**

ISR+TA->BO->SLE

as well as p for trend;

PROC LOGISTIC;
CLASS qsa (REF='0');
MODEL v3_sle = qsa v3_age v3bmi sex;
RUN;

PROC LOGISTIC;
CLASS qlti (REF='3');
MODEL v3_sle = qlti v3_age v3bmi sex;
RUN;

PROC LOGISTIC;
CLASS qmti (REF='3');
MODEL v3_sle = qmti v3_age v3bmi sex;
RUN;

PROC LOGISTIC;
CLASS qta (REF='0');
MODEL v3_sle = qta v3_age v3bmi sex;
RUN;
PROC LOGISTIC;
CLASS qisr (REF='0');
MODEL v3_sle = qisr v3_age v3bmi sex;
RUN;
PROC LOGISTIC;
MODEL V3_SLE= qta qisr v3_age v3bmi sex;
RUN;
PROC LOGISTIC;
CLASS qpta (REF='1') qisr (REF='0') qta (REF='0');
MODEL v3_sle = qpta qisr qta v3_age v3bmi sex;
RUN;
PROC LOGISTIC;
CLASS qisr (REF='0') qta (REF='0');
MODEL v3_sle = qta qisr qta v3_age v3bmi sex;
RUN;
PROC LOGISTIC;
CLASS qisr (REF='0') qta (REF='0');
MODEL v3_sle = qta qisr qta v3_age v3bmi sex;
RUN;
PROC LOGISTIC;
CLASS qbo (REF='0') qisr (REF='0')
qta (REF='0');
MODEL v3_sle = qbo qisr qta v3_age v3bmi sex;
RUN;
PROC LOGISTIC;
CLASS qisr (REF='0') qta (REF='0');
MODEL v3_sle = bo qisr qta v3_age v3bmi sex;
RUN;
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CURRICULUM VITAE

RAFAEL WIDJAJAHAKIM
Email: rafaelwh@bu.edu
Year of birth: 1989

EDUCATION

Boston University, Boston, MA
Master of Science in Clinical Investigation, 2016 (Anticipated)

Suffolk University, Boston, MA
Bachelor of Science in Biology, Chemistry minor, 2011

HEALTH-RELATED EXPERIENCE

Boston Children Hospital, Boston, MA
Division of Infection Disease, HealthMap
Research intern, 2015

Performed data mining, cleaning, and quality check of vaccination data from counties in the US. Curated public health prevention and surveillance system (HealthMap) in detecting disease outbreak, specifically on Indonesia and Malaysia languages news feed, and ABRAID project to capture tropical infectious diseases. Gathered the data of disease outbreak on the HealthMap program made by bioinformatics team.

Brigham and Women’s Hospital, Boston, MA
Division of Endocrinology, Diabetes & Metabolism, Men’s Health Unit
Research assistant, 2013-2014

Assisting at clinical research group, rotated between different types of clinical research study; focusing on androgen and muscle strength in elderly. Participated in accelerating a trial recruitment method in one study site, boosting recruitment from 4 participants a month into 20 participants and reached the top site recruitment ranking in 5 months period.

BASIC SCIENCE RESEARCH

Silicon-oxygen polymers (siloxanes) research
Title: Preparation of 1,1,3,3-tetramethyldisiloxane-1,3-diol via hydrolysis
Suffolk University, Boston, MA
2010-2011
Advisor: Dr. Denyce Wicht

Performed study of silicon-oxygen polymers (siloxanes) found in most of personal care products. Conducted isolation and purification of silanol molecules, and analysis of the compound via AAS, NMR, and GC-MS. Derivatization of molecules from aqueous solution into organic solution.

**ConE in Bacillus subtilis research**

Title: Double Mutagenesis Test of reactive ConE protein in *Bacillus Subtilis*
Suffolk University, Boston, MA
2011
Advisor: Dr. Melanie Berkmen

Research on horizontal gene transfer protein, ConE, in *Bacillus subtilis* using ELISA, PCR, EMSA, and double-mutagenesis tests.

**Green sea urchin research**

Title: Influence of Odors of The Purple Sun Star, *Solaster endeca*, and of Adult Urchins on Movement of The Juvenile Green Sea Urchin, *Strongylocentrotus droebachiensis*
Suffolk University, Boston, MA
2009-2010
Advisor: Dr. Carl L. Merrill

Conducted an observational test of green sea urchin responses toward the presence of a predator chemical cue in flowing seawater with purpose to study the survival behavior.

**CONFERENCES**

**Accepted Abstract**

Osteoarthritis Research Society International, Amsterdam, Netherlands
31 March 2016 – 3 April 2016


**Poster Presentation**

Suffolk University Science Banquet, Boston, MA
14 April 2011
Environmental Symposium, Bridgewater, MA
20 November 2010

Suffolk University Science Banquet, Boston, MA
24 April 2010

New England Biology Conference, Bridgewater, MA
10 April 2010

VOLUNTEER & ORGANIZATION
Boston University CTSI Study Design and Statistical Analysis Consultation
Boston University Office of Postdoctoral and Development Professional Affair
PERMIAS - Indonesian College Students Community in the US
Boston City Blessing Church Care and Usher team
Dana Farber Cancer Institute Patient Ambassador

Boston University Medical Campus Toastmaster
Suffolk University Health Career Club; Executive Board
Suffolk University Beta Beta Beta Biological Honor club; Executive Board
Suffolk University International Student Association; Executive Board
Suffolk University The Journey Programs for leadership development

AWARDS AND HONOR
Magna Cum Laude
Dean's High Honor
Outstanding Inorganic Chemistry Award
Outstanding Organic Chemistry Award
Junior Level Biology Award

SOFTWARE SKILL
Microsoft Office (Word, Excel, PowerPoint, Outlook, OneNote)
Adobe (Photoshop, Lightroom, InDesign, Illustrator)
Windows OS
Mac OS
Statistical analysis software (SAS and R)
Data visualization software (Tableau)

LANGUAGE

English – proficient
Indonesian – native
Japanese – beginner