Biomaterials and Biomechanics in Bioengineering, *Vol. 3, No. 1 (2016) 27-35*
DOI: http://dx.doi.org/10.12989/bme.2016.3.1.027

Methods to determine the volume of infrapatellar fat pad as an indicator of anterior cruciate ligament tear

B. Cheruvu[*1], J. Tsatalis[2a], R. Laughlin[3b] and T. Goswami[1,3c]

[1]*Department of Biomedical Engineering, Wright State University, 3640 Colonel Glenn Highway, Dayton, OH 45435, USA*
[2]*Department of Radiology, Wright State University, Boonshoft School of Medicine, 3640 Colonel Glenn Highway, Dayton, OH 45435, USA*
[3]*Department of Orthopedic Surgery, Sports Medicine, and Rehabilitation, Wright State University, Boonshoft School of Medicine, 3640 Colonel Glenn Highway, Dayton, OH 4543, USA*

(Received March 3, 2015, Revised December 9, 2015, Accepted December 18, 2015)

Abstract. Anterior knee pain is a major problem among adolescents and young adults especially those who participates in sports. The most common pathogenesis of anterior knee pain can arise from compression and shear forces in the patellofemoral joint. It is also caused by impingement of infrapatellar fat pad. Fat pad impingement can occur when the fat pad becomes swollen and inflamed due to a direct blow or chronic irritation. As a result, the bottom tip (or inferior pole) of the patella can pinch the fat pad. One of the many causes of swollen fat pad can be secondary to anterior cruciate ligament (ACL) injury. The aim of this study was to compare the infrapatellar fat pad volume in patients with acute ACL injury and a group of age-, gender-, and activity- matched controls with intact ligament. Axial magnetic resonance (MR) images have been performed on 32 patients with torn ACL and 40 control patients. The volume of the fat pad was measured digitally from MR image by using a 3d Reconstruction software, ellipsoidal approximation, and a MATLAB code. The results were compared between patients with torn ACL and control group. Patients with a torn ACL had a significantly larger fat pad than the controls (P=0.01). There was no significant difference between the methods used to measure the infrapatellar fat pad volume (P=0.83-0.87). Thus, lesions of the infrapatellar fat pad is often associated with ACL injury.

Keywords: patellofemoral; ACL injury; infrapatellar fat pad; Knee

1. Introduction

Anterior knee pain is a common problem which primarily affects adolescents and young adults. The most common mechanism for anterior knee pain arises from combination of compression and shear forces across the patellofemoral joint. Static experiments show that at 60° of knee flexion, one can experience twice the body weight at the patellofemoral joint Smallman *et al*. (2012). There

*Corresponding author, Ph.D., MD, E-mail: cheruvu.3@wright.edu
[a]MD
[b]MD
[c]DSc.

http://www.techno-press.org/?journal=bme&subpage=7 ISSN: 2465-9835 (Print), 2465-9959 (Online)

are multiple anatomical structures which can produce anterior knee pain. These structures include medial and lateral retinaculum, the patellar subchondral bone, the anterior synovium, joint capsule, and patellar tendon and infrapatellar fat pad. There is little research in which the pattern of pain referral produced by irritation of these structures. To provide an accurate diagnosis and treatment of anterior knee pain, it is important to identify the sources of pain.

Infrapatellar fat pad is bounded by the patella anteriorly as well as synovial lined knee joint posteriorly (Fig. 1) Dragoo *et al*. (2012). It is made up subcutaneous tissue which contains a network of fibrous cords. It consists of columns of fat which are confined in small chambers of fibrous connective tissue Skiadas *et al*. (2013). These columns are often reinforced with network of elastic transverse and diagonal fibers which connect the outside walls of the sepate Han *et al*. (2014). This fat tissue is not influenced by nutrition, therefore the size and volume of the fat pad varies widely among individuals. The fat pad is often metabolized only in severe malnutrition Ballegaard *et al*. (2014).

Anterior knee pain is often caused by an impingement between patellofemoral or femorotibial joints due to edematous changes in the infrapatellar fat pad Collins *et al*. (2012). Because of its anatomical location, patients with an Anterior Cruciate Ligament (ACL) injury can have subsequent injury to the infrapatellar fat pad Alentorn-Geli *et al*. (2009). This phenomenon occurs in torn ACL which develops instability in the knee which would then cause posterior femoral translation in relation to tibia Agel *et al*. (2005). The instability of the joint due to an ACL injury can generate patterns of lesions in infrapatellar fat pad. The lesions commonly found on infrapatellar fat pad include edema, tears, scars and synovial proliferation Dragoo *et al*. (2012). Edema can be defined as an increased signal intensity within the fat pad found on MRI (Agel *et al*. 2005, Dragoo *et al*. 2012). In a retrospective study of 100 patients with ACL injury, edema was found in 48% of patients with torn ACL compared to 24% in intact ACL (Agel *et al*. 2005).

This is the first study to measure the volume of the infrapatellar fat pad in patients with acute ACL injury. The aim of this study was to explore potential methods for quantifying infrapatellar fat pad using magnetic resonance images (MRI) in individuals with acute ACL injury to matched controls. Clinical data which included a retrospective database of 32 patients with ACL injury and matched controls was used to determine the accuracy of these methods. Using the clinical data, the volume of infrapatellar fat between both groups compared.

2. Materials and methods

2.1 Study design and participants

Our institutional review board approved this retrospective study, which involved a search of patient medical records and waived the requirement for informed consent because there was no change in patient diagnosis or treatment. After receiving approval from the institutional review board, the surgery records for knee procedures taking place at our institution of two full-time orthopedists were reviewed from 2006-2013. Patients having knee procedures were tagged and further investigated to find if they had received an MRI during their diagnostic workup. The study group consisted of patients whose ACL was torn or partially torn based on the radiologists' impression from the MRI. The control group was made of patients whose ACL was described as intact, however patients were still included in the study if pathology other than an ACL tear or partial tear was discovered. Therefore the study group consisted of 32 patients and 40 patients in the control group.

The average age of the patients who had ACL injury was 32 years, range of 12 to 59 years. However, the control group (group 2) consisted of 40 patients, 28 males and 12 females, respectively. In patients with an intact ACL, the average age was 35 years, range of 12 to 76 years. There was no significant difference between the age, gender, side of injury, mechanism, and BMI between study and control groups. The average BMI in both groups were 29 and 28 for the study and control groups respectively. Clinically, malnutrition has been defined as a BMI less than 14. Therefore, in our case, the fat tissue is not influenced by nutrition. Group matching was performed according to following factors; gender, age, mechanism, and BMI. Characteristics of the different groups are given in Table 1.

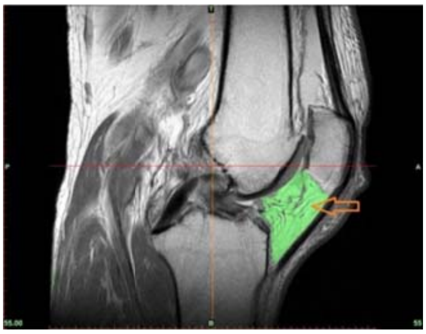


Fig. 1 The arrow points the location of the infrapatellar fat pad on sagittal view of a T2 MRI

Table 1 Patient characteristics of group

Demographic		Study	Control	Test Variable	P Value
Total number of cases		32	40		
Gender	Male	21	28	Chi = 0.157	0.801
	Female	11	12		
Side	Right	15	22	Chi = 0.640	0.479
	Left	17	17		
Age	Average (years)	32	35	T = -2.082	0.43
	Range (years)	12-59	12-76		
	Unknown	2	1		
Mechanism	Contact (trauma)	12	9	Chi = 2.761	0.100
	Noncontact	14	26		
	Unknown	6	5		
BMI	< 25	8	11	Chi = 0.164	0.692
	≥ 25	14	19		
	Unknown	10	10		
	Average	29	28		0.65
	Range	21-45	23-45		

BMI - Body Mass Index (wt in kg/ ht in m^2)
*statistically significant

2.2 MR Imaging

All MRI scans were performed on a 1.5 Tesla General Electric (Milwaukee, Wis.) Signa MRI scanner. T1-weighted images in 4 mm-thick cuts were evaluated based on the integrity of the image, with no gap between slices. Patients were positioned in a supine position with the knee held in full extension. Fig. 1 depicts the location of the infrapatellar fat pad on a patient with an intact ACL.

2.3 Volumetric analysis of the fat pad

Infrapatellar fat pad volume was measured from the axial plane images using 3D reconstruction software (Mimics, Materialise Inc., Belgium). The MRI images were imported into software, by using the threshold segmentation algorithm to select the region of interest. By using the 'Edit mask in 3D' in Mimics to construct the infrapatellar fat pad based on prior knowledge of human anatomic data. Fig. 2 shows the 3D reconstruction of the infrapatellar fat pad with which analysis performed. The cross sectional area of each slice was measured by the software using a region growing strategy which was based on the pixilation threshold. Volume of the 3D reconstructed image can be determined by software as well as using an ellipsoidal approximation using the following equation Chuckpaiwong *et al*. (2010)

$$Ellipsoidal\ volume = \left(\left(\frac{Height}{2}\right) * \left(\frac{width}{2}\right) * \left(\frac{depth}{2}\right) * \left(\frac{4}{3}\right) * \pi\right) \quad (1)$$

The height, width, and length was determined based on measurements taken from 3D image (Fig. 3).

Volume was also determined using a MATLAB (Mathworks Inc) code. All of the axial slices from the tibial tuberosity to the slice before the inferior patellar pole were used. A manual trace on each slice was performed to define the region of interest (ROI) (Fig. 4(a)). The ROI is a portion of the image which allows the image to have a filter. The ROI would create a binary mask in which

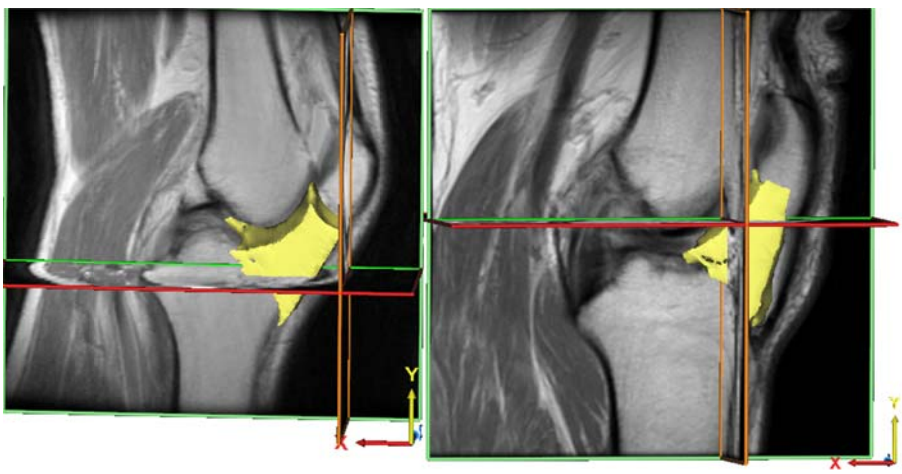


Fig. 2 3D reconstruction of the fat pad used for analysis. The left panel is for infrapatellar fat pad found in a patient with intact ACL.The right panel shows an infrapatellar fat from a patient with torn ACL. In both panels, *X* axis denotes anterior to posterior view. Similarly the *Y* axis points to superior/inferior directions

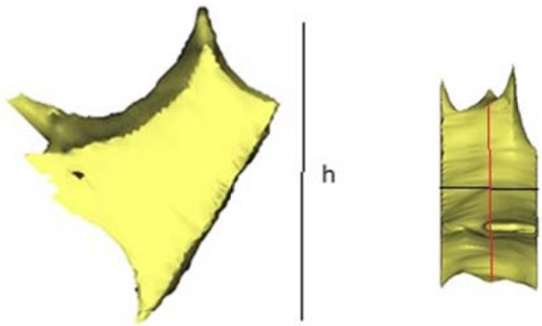
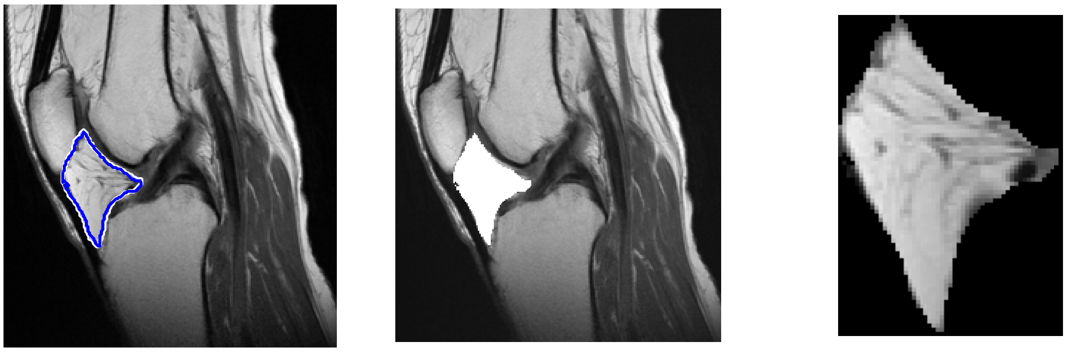


Fig. 3 The annotations for determining measurement of the fat pad for ellipsoidal calculation. The red line demarcates the width and black line demarcates the depth as seen in the right panel



(a) (b) (c)

Fig. 4 The gray scale image which would be used in the MATLAB program. The blue line represents the trace which the user to input. The b panel shows ROI removed from 2D MRI slice. The C panel shows infrapatellar fat pad which was removed from the slice to measure its area

pixels that define the ROI set to 1 and the others as zero. This binary mask was modified in which the pixels that define the ROI set to 1, and placed within the image (Fig. 4(b)).Then using a semi-automated process it determines the area of the region (Fig. 4(c)). Once the tracing was inputted by the user the area determined based on MATLAB function which would determine total number of pixels found within that region. Volume was calculated based on planar summation multiplied by the slice thickness.

2.4 Statistical analysis

Analysis was performed using JMP 7.0 (SAS institute, 2007) and significance was set at $P<0.05$. Differences between groups were determined using independent sample t-tests. The mean volumes and surface area of the fat pad evaluated by two tailed t-test between control and patients with acute ACL injury. BMI was treated as a continuous variable.

It has been assumed that each method is independent in their methodology for determining volume of infrapatellar fat pad. Bland-Altman plot would be used to determine the methods to measure the fat pad with high accuracy.

Table 2 Comparison of volumes from various methods

Group	Mimics	Ellipsoidal	MATLAB
Study:	36.16	36.32	37.85
Control	23.79	23.76	24.99
Standard Deviation	13.75	13.37	13.24

Table 3 Comparison of infrapatellar fat pad between two groups

Characteristic	Study	Control	P value
Volume (mL)			
Mean	36.160	23.788	0.010
Range	12-85	11.6-52.8	
Standard Deviation	21.7	13.7	
Surface Area (mm^2)	9868.07	7685.88	0.041
Range Surface area (mm^2)	4287-17693	4403-19750	
Standard Deviation	4560		

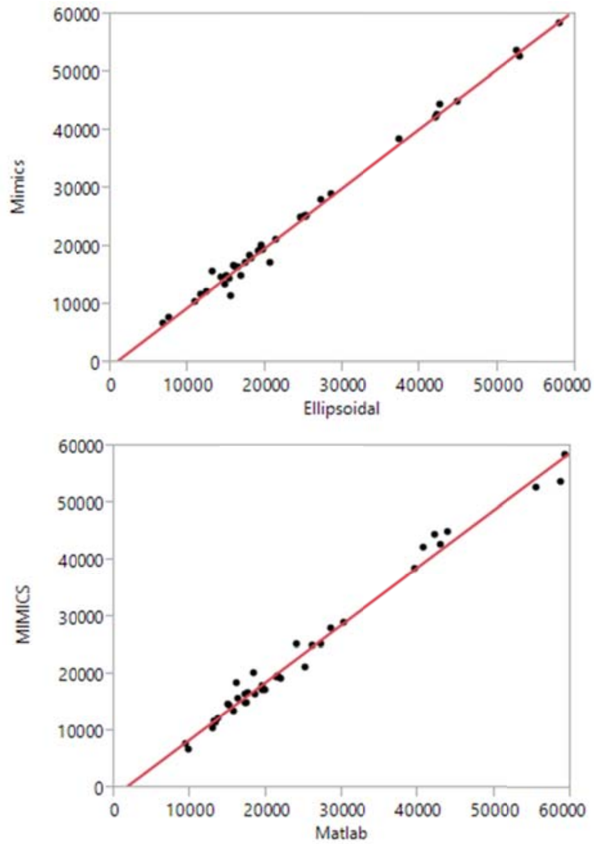


Fig. 5 Bland-Altman plots which compares Volume determination using Mimics and ellipsoidal equation, and MATLAB. The right panel (a) was a comparison between Mimics and ellipsoidal equation. The left panel (b) was a comparison between Mimics and MATLAB

3. Results

As seen in table 1, there are 24 patients who had an unknown BMI. Since our study investigated the relationship between BMI and volume of infrapatellar fat pad, those patients were removed from population for analysis.

The summary of the results are shown in Table 2. There is a strong correlation between the volumes determined by ellipsoidal model and MRI. It was determined that the coefficient of determination to be 0.99. The volume estimated by MATLAB was found to be within a band of $\pm x2$ MRI values (24.99 mm^3; R^2=0.98) and may be considered with high statistical confidence. No significant difference was observed between the two groups (p of 0.87 and 0.83) for ellipsoidal and MATLAB respectively (Figs. 5(a) and 5(b)).

Significant differences were observed in the mean volume of the fat pad of the knee between patients with an intact ACL and those with acute ACL injury (Table 3). Significant differences were also seen in the mean surface area of the fat pad of the knee between the two groups.

4. Discussion

Anterior knee pain is a common problem among athletes. Anterior knee pain is often caused by an impingement of the patellofemoral joint caused by edematous changes in the infrapatellar fat pad. Non-invasive methods to determine the size of the infrapatellar fat pad can play role in the preventing this disorder. Using a cohort of patients with acute ACL injury, this study had found that these patients had a greater volume of the infrapatellar fat pad. Due to its location, the changes in morphology of the fat pad is often related to patients with ACL injury.

Measurement of fat pad volume from the MR images had appeared to be a useful indicator of fat pad morphology. Recently, a study had validated the fat pad volume from MR against direct measurement of fat pad volumes in porcine knees Chuckpaiwong *et al*. (2010). In a study of four cadavers aged from 80 to 95 with no medical history of knee surgery, the infrapatellar fat pad was removed from its surrounding structures, and measurements were made with calipers Abreu *et al*. (2008). Volume of the fat pad was determined by Archimedes principle. The average volume of the fat pad was 24 ml with a range of 12-36 ml. Here volume was determined with 3D reconstruction of the fat pad, which had average 23.78 ml. Therefore, imaging data reconstruction is able to predict accurately the fat pad generation during ACL injury. We had a larger range of 11 to 44 ml may due mainly to prevalence of bodily fluids in the joint and live subjects. The volume of infrapatellar fat pad in another study of 15 osteoarthritic patients and another 15 aged matched with no history of arthritis or knee pain, population was 20.70 with a standard deviation of 3.3 cm^3 Chuckpaiwong *et al*. (2010). In a recent study of using MR images, the mean volume of infrapatellar fat pad obtained from asymptomatic knees had determined to be 19.53 with a standard deviation of 3.64 cm^3 Cluvenor *et al*. (2011).

Our findings show that there is no relationship between the size of the infrapatellar fat pad of the knee and the BMI (p=0.7060). It suggests that the infrapatellar fat pad is not regulated by overall fat adiposity. Present study compared the volume of fat pad among patients with acute ACL injury. The patients with ACL injury have significantly larger infrapatellar fat pad in terms of volume and surface area when compared to age matched control group, p of 0.01 and 0.04 respectively. A possible reason for this finding is that the trauma from the injury may cause hemorrhage in the neighboring structures, which thus increases its volume.

This study was limited by the quality of the MR images, especially to measure the volume of the fat pad. The fat pad is bounded by inferior pole of the patella. The images had shown poor differentiation of fat pad margins proximal to this point. A slice thickness of less than 3.5 mm would have resulted in more accurate volume. The average volume of the infrapatellar fat pad has been shown to be varied based on knee flexion. It is unclear about the time frame between the onsets of ACL injury and MRI imaging of the knee. The MRI scans were performed based on physical examination findings and pain level experienced by patients. There were also other factors such as personal preferences for imaging time which would pose a problem to standardizing the time between ACL injury and MRI imaging. The other limitation can be that the various risk factors between the two populations not considered in treatment.

5. Conclusions

In conclusion, patients with a torn ACL ligament had a larger infrapatellar fat pad measured from MR compared with their asymptomatic counterparts. The size of the fat pad is not related to BMI. The ellipsoidal model and MATLAB approximation of volume had shown to have no difference when compared to that determined by Mimics, with p-values of 0.87 and 0.83 respectively. There is no statistical significance between BMI and volume of infrapatellar fat pad. Volume determinations using ellipsoidal approximation model had been shown to be comparable to that determined by MRI and MATLAB code within a statistical band of $\pm x2$.

References

Abreu, M.R., Chung, C.B., Trudell, D. and Resnick, D. (2008), „Hoffa's fat pad injuries and their relationship with anterior cruciate ligament tears: New observations based on MR imaging in patients and MR imaging and anatomic correlation in cadavers", *Skeletal Radiol.*, **37**(4), 301-306.

Agel, J., Arendt, E.A. and Bershadsky, B. (2005), "Anterior cruciate ligament injury in National Collegiate Athletic Association basketball and soccer a 13-year review", *Am. J. Sport. Med.*, **33**(4), 524-531.

Alentorn-Geli, E., Myer, G.D., Silvers, H.J., Samitier, G., Romero, D., Lázaro-Haro, C. and Cugat, R. (2009), "Prevention of non-contact anterior cruciate ligament injuries in soccer players. Part 1: Mechanisms of injury and underlying risk factors", *Knee Surg., Sports Traumatol., Arthroscopy*, **17**(7), 705-729.

Ballegaard, C., Riis, R.G., Bliddal, H., Christensen, R., Henriksen, M., Bartels, E.M. and Boesen, M. (2014), "Knee pain and inflammation in the infrapatellar fat pad estimated by conventional and dynamic contrast-enhanced magnetic resonance imaging in obese patients with osteoarthritis: A cross-sectional study", *Osteoarthritis Cartilage*, **22**(7), 933-940.

Chuckpaiwong, B., Charles, H.C., Kraus, V.B., Guilak, F. and Nunley, J.A. (2010), "Age-associated increases in the size of the infrapatellar fat pad in knee osteoarthritis as measured by 3T MRI", *J. Orthopaed. Res.*, **28**(9), 1149-1154.

Collins, N.J., Bisset, L.M., Crossley, K.M. and Vicenzino, B. (2012), "Efficacy of nonsurgical interventions for anterior knee pain", *Sport. Med.*, **42**(1), 31-49.

Culvenor, A.G., Cook, J.L., Warden, S.J. and Crossley, K.M. (2011), "Infrapatellar fat pad size, but not patellar alignment, is associated with patellar tendinopathy", *Scand J. Med. Sci. Sport.*, **21**, 405-411.

Dragoo, J.L., Johnson, C. and McConnell, J. (2012), "Evaluation and treatment of disorders of the infrapatellar fat pad", *Sport. Med.*, **42**(1), 51-67.

Han, W., Cai, S., Liu, Z., Jin, X., Wang, X., Antony, B. and Ding, C. (2014), "Infrapatellar fat pad in the knee: is local fat good or bad for knee osteoarthritis?", *Arthritis Res. Ther.*, **16**(4), R145.

Skiadas, V., Perdikakis, E., Plotas, A. and Lahanis, S. (2013), "MR imaging of anterior knee pain: a pictorial essay", *Knee Surg., Sport. Traumatol., Arthroscopy*, **21**(2), 294-304.

Smallman, T.V., Race, A. and Ekroth, S. (2012), "The Mechanical Link between the Infrapatellar plica and the Fat pad-Role in the etiology of anterior knee pain", *J. Bone Joint Surg., British*, **94**(SUPP XXXVIII), 100-100.

MC