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A procedure to estimate the origins and the insertions of the knee ligaments from computed tomography images

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ABSTRACT

The estimation of the origin and insertion of the four knee ligaments is crucial for individualised dynamic modelling of the knee. Commonly this information is obtained *ex vivo* or from high resolution MRI, which are not always available. Aim of this work is to devise a method to estimate the origins and insertions from CT images. A reference registration atlas was created using a set of 16 bone landmarks visible in CT and 8 origins and insertions estimated from MRI and in vitro data available in the literature for three knees. This atlas can be registered to the set of bone landmarks palpated on any given CT using an affine transformation. The resulting orientation and translation matrices and scaling factors can be used to find also the ligament origin and insertions. This procedure was validated on seven pathological knees for which both CT and MRI of the knee region were available, using a proprietary software tool (NMSBuilder, SCS srl, Italy). To assess the procedure reproducibility and repeatability, four different operators performed the landmarks palpation on all seven patients. The average difference between the values predicted by registration on the CT scan and those estimated on the MRI was 2.1±1.2 mm for the femur and 2.7±1.0 mm for the tibia, respectively. The procedure is highly repeatable, with no significant differences observed within or between the operators ($p>0.1$) and allows to estimate origins and insertions of the knee ligaments from a CT scan with the same level of accuracy obtainable with MRI.

INTRODUCTION

The main role of the ligaments, which connect bone with bone, is to provide mechanical stability to the joints, guiding their movements and preventing excessive motion. The knee is the largest and complex joint of the human body and has four major ligaments: Medial Collateral (MCL), Lateral Collateral (LCL), Anterior Cruciate (ACL) and Posterior Cruciate (PCL). In clinical applications and biomedical research individualised musculoskeletal models are currently used for many purposes such customized prosthetic implants (Bert, 1996; Reggiani et al., 2007), computer-aided surgery (Zanetti et al., 2005), gait analysis (Kepple et al., 1997) or automated image segmentation (Ellingsen et al., 2010). In orthopaedic surgery a geometric model of the patient's bone can reproduces the basics morphometry in order to perform a correct computer based surgery (Radermacher et al., 1998).In gait analysis an accurate geometrical model is fundamental to create a realistic musculoskeletal model (Kepple et al., 1997).

Many computational dynamic models of the knee have been developed (Arnold et al., 2010; Blankevoort and Huiskes, 1996; Guess et al., 2011; Kia et al., 2014; Shelburne and Pandy, 2002) to understand the forces and the strains on the knee structures, such as the ligaments, during static and locomotion activities. Improving the accuracy of these models could help to discover the causes of ligaments' injury and guide the surgical treatment in order to improve the functional outcome (Woo et al., 2006). A subject specific model of the knee is also essential for total knee arthroplasty in the preoperative phase in order to assure the durability and the reliability of the joint implant especially for younger patient with a greater physical activity (Zanetti et al., 2005). The accurate estimation of the origin and insertion of these ligaments is a crucial step in all the above applications.

Subject specific models of the knee can be generated using information obtained either *ex vivo,* probing fresh cadavers, or from high resolution Magnetic Resonance Imaging (MRI).

Brand et al. (1982) used measurement on three cadavers to obtain a set of lower extremity origin and insertion coordinates. These procedures are complex and cumbersome, therefore many studies utilized a few number of specimens, limiting the impact of the findings. In addition, the data obtained from cadavers have proven to be valid for modelling the knees they have been acquired for, but may likely not translate to other subjects (H. Bloemker, 2012). Many studies proposed methods to create subject specific model by scaling a generic template in order to measure inaccessible point such as the origin and insertions of the knee ligaments (Brand et al., 1982; Lewis et al., 1980). This procedure that involves the scaling of a generic template provides to build one cloud of palpable points on a cadaver specimen and corresponding points on the in vivo subject. Calculating the transformation between these two landmark clouds allows measuring inaccessible points.

The parameters needed to determine a rigid body transformation are a rotation matrix, a translation vector and a scaling factor. Lew and Lewis (1977) demonstrated that the application of data obtained from cadavers directly to *in vivo* subject is not suitable, some kind of scaling is proper because of the dimension differences between the in vivo subject and the cadaveric specimens. Morrison (Morrison, 1970), in order to study the mechanics of knee joint in relation to normal walking, developed a technique to scale uniformly along the axes bony landmarks from dry bone data and an experimental subject. Lew and Lewis (1977) formulated a scaling technique that includes the Morrison method to scale inaccessible points from a dried bone specimen to an in vivo subject. This technique provides anisotropic scaling along three mutually orthogonal axes defined in both rigid bodies and is based on the use of four landmarks palpable on the subject and four on the corresponding specimen. The landmarks used to determine the rigid body transformation will contain some errors that come from the palpation of those points on the reference specimen and the experimental subject. Challis (1995) suggested a procedure using a linear least-square method which attempted to take into account those errors. Unfortunately this method allows the calculation of the rigid body transformation parameters assuming that the scaling is uniform along the three axes. Anisotropic scaling technique has been presented by Lewis et al. (1980), using eight landmarks on both the specimen and the experimental subject, the results revealed that the anisotropic scaling was more accurate than the isotropic scaling.

In view of all that has been mentioned so far, it can be said that previous studies validated procedures that allow calculating inaccessible points on *in vivo* subjects using different osteometric scaling techniques. In these studies the analysis of human subject *in vivo* has been performed without using CT or MRI scan images. Since only a minimal set of skeletal landmarks can be palpated through external palpation, the number of the landmarks used in the previous methods was very low. Lewis et al. (1980) demonstrated that anisotropic scaling improves the identification of anatomical landmarks locations, particularly when a large number of points were used in the scaling. Also, a detailed description of the landmarks selected were not present in the previous studies, the lack of standard and well defined guidelines for the palpation of the these landmarks affects the accuracy of the rigid body registration (Van Sint Jan and Della Croce, 2005).

The purpose of this study was to create a procedure to estimate the origins and the insertions of the knee ligaments by: providing a reproducible and repeatable anatomical landmark cloud for virtual palpation, creating a registration atlas and using an affine transformation (rotation, translation, anisotropic scaling). The accuracy of this procedure will be assessed through comparison with results obtained from MRI.

MATERIALS AND METHODS

The dataset used in this study (D1) has been provided by Medacta International SA (Castel S. Pietro, Switzerland). It consists of seven set of images obtained from seven different patients (64 ± 5 years) who have undergone a Total Knee Replacement. Each patient's dataset includes Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) of pathological knee that underwent surgery and the bone geometries obtained by segmenting the CT data. In addition to D1, a second dataset (D2) has been obtained from the multibody models of the human knee project (Guess et al., 2011, 2010; H. Bloemker, 2012). These models are based on three cadaver knees (Table 1) that have been mechanically tested in a dynamic knee simulator. Knee geometries (bone, cartilage, and menisci) were derived from MRI and ligament insertions were obtained from both MRI and probing the cadaver knees. D2 also contains information on ligament modelling, including the origin and insertion locations.

(Figure 1)

The first part of this study aims at creating a reproducible and repeatable bone landmarks cloud to be palpated on CT scan images. A detailed standard description of body landmarks through manual or virtual palpation is available in literature (van Sint Jan, 2007). Among these, a subset of landmarks (see Figure 2) belonging to the knee, tibia and fibula has been chosen. This landmark cloud has then been identified on each subject dataset through virtual palpation. NMSBuilder (SCS srl, Italy) has been used to visualize the 3D geometry and to perform the virtual palpation (location of anatomical points over a 3D visualisation) and the registration between the landmark clouds. The virtual palpation has been performed by four expert operators on both D1 and D2. Each operator performed the virtual palpation on ten knees (cases), repeating the operation three times for each knee (trials). Three operators performed the procedure using NMSBuilder, whereas the fourth one used an in-house tool developed by Medacta International SA. Reproducibility and repeatability were assessed using repeated measures analysis of variance (ANOVA). In particular, a repeated measure ANOVA was performed for each operator considering the “case” as between group factor and the “trial” (3 levels) as within factor. Three separate ANOVA, one for each test, were then performed considering the operator as between group factor and the cases as within group factor (10 levels).

Once reproducibility and repeatability of the bone landmarks had been assessed, they were palpated on D2 in order to create a reference landmark cloud (C_R), and on D1 in order to create a subject-specific landmark cloud (C_S). Once palpated, the two clouds had to be registered. An affine transformation was used to this purpose. The method that allows the calculation of the parameters that describe an affine transformation between two paired landmark clouds is called, in statistical shape analysis, *Procrustes Analysis* (Grimpampi et al., 2014). In particular, the affine transformation that maps C_R to C_S is composed by a 3x3 transformation matrix, which includes Translation (T= $\langle T_x, T_y, T_z \rangle$), Rotation (R= $\langle R_x, R_y, R_z \rangle$), and scaling (S= $\langle S_x, S_y, S_z \rangle$) parameters. This operation is implemented in Lhp Builder following the method proposed by Berthold and Horn (1987). Once T, R and S are calculated, it is possible to register on C_S also those landmarks belonging only to C_R, which, in our case, are the origins and insertions of the four knee ligaments. The ensemble of C_R and of the eight origins and insertions of the knee ligaments composes the so-called Registration Atlas (*RA*). The error associated to the registration procedure is called Procrustes Distances (*PD*) and represents the geometric distance between C_S and C_R. These values estimate the accuracy of the procedure.

The scaling operation, necessary to take into account anthropometric differences due to age or gender (Fehring et al., 2009), might have as a consequence the fact that landmarks in C_R are not always located on the bone surface. For this reason, a visual inspection needs to be performed after the registration and adjustments need to be taken. These adjustments were performed using an ad-hoc Lhp Builder function, names “snap to surface”, which allows to move the landmark along the axes characterized by the minimal distance from the closest surface. The repeatability of this operation has been assessed by having one operator repeating it for three times on each case in D1 (after having performed the calculation of the origins and insertions of the knee ligaments using the RA, as described in the following paragraph).

Using the three models from the D2 dataset, four atlases were created: one for each model and one as the average of the previous three (Atlas 1, Atlas 2, Atlas 3, and Atlas M). Not having a proper gold standard available, the four atlases have been compared in terms of Procrustes Distance between the landmarks of C_R registered on the subjects and the landmarks of C_S palpated on the seven subjects.

Once the best RA had been selected, it was used to estimate the origin and the insertions of the knee ligaments of all the cases in D1. Initially, the origin and insertions were calculated through the affine transformation using the CT scan, successively the verification of the positions of those landmarks has been performed using MRI scan where it was possible to estimate the ligaments attachments. In NMSBuilder, the landmarks that represented the origins and insertions of the ligaments were moved whenever the position was considered wrong in according with those images. Then, we compared the distances between the data obtained from the CT scan with those corrected with MRI.

RESULTS

The results of the ANOVA performed on the data obtained from the various operators showed that the procedure is highly repeatable, with no significant differences observed within (*p=0.748* for trial 1, *p=0.966* for trail 2, and *p=0.992*, for trial 3, respectively) or between operators (*p=0.430* for operator 1, *p=0.572* for operator 2, *p=0.187* for operator 3, and *p=0.685* for operator 4, respectively). These findings suggest that changing the operator does not affect the repeatability and the reproducibility of the virtual palpation of the selected anatomical landmarks cloud. In contrast, the ANOVA revealed that the case factor influences the repeatability of the virtual palpation ($p<0.001$): the specific morphology of a knee or the low resolution of the CT images can be a cause for lower precision in the identification of the landmarks.

Since there was no between-operators effect, the precision of the virtual palpation was evaluated in terms of standard deviation of the landmarks positions, palpated by the four operators over the three trials. The standard deviation ranged from 0.02 mm to 7.71 mm (Table 2).

The registration of the four Atlases (Atlas 1, Atlas 2, Atlas 3, Atlas M) on D2 revealed that the Atlas M gives the best result in terms of PD. The mean PD between the landmarks of C_R registered on the seven subjects, and the landmarks of C_S palpated on the seven subjects (see Tables 3 and 4) was 2.34 ± 0.59 mm for the femur and 1.53 ± 0.50 mm for the tibia, respectively (averaged on the seven subjects).

The mean PD between the origin and insertions of ligaments calculated with the Registration Atlas M and those ones estimated from the MRI were 2,3 ± 0,3 mm (0,4 mm < *PD* < 3,9 mm) on the femur and 2,7 ± 1,0 mm (1,4 mm< *PD*< 4,4 mm) on the tibia (averaged over the seven subjects) (see Tables 5 and 6).

The "snap to surface" operation was highly repeatable, with the standard deviation of the position of the ligament attachments after the "snap to surface" ranging from 0 to 0.3 mm.

DISCUSSION

This study presented a procedure to estimate, with high accuracy, origins and insertions of the knee ligaments starting from a reproducible and repeatable landmark cloud virtually palpated on a CT scan. The proposed procedure has been evaluated through a comparison with the same estimations as obtained from MRI, which, as shown by Taylor et al. (2013) can be considered as a reliable reference.

Despite many studies have noted the importance of scaling anatomical landmarks from cadaveric specimen to calculate inaccessible points (Brand et al., 1982; Lew and Lewis, 1977; Lewis et al., 1980), we are not aware of other studies providing a methodology to estimate the knee ligaments attachments from a CT scan. Other methods proposed to create subject-specific musculoskeletal models, focused on the mathematical development of the scaling technique needed to estimate the coordinates of bone points not accessible through manual palpation. The results reported show that our methodology allows calculating the knee ligaments attachments with an average RMS error of 2,4 mm on the femur and 2,9 mm on the tibia. The relevance of these errors certainly depends on the practical use of the estimated quantities. A sensitivity analysis of their effects on the estimation of additional parameters, such as ligaments strain during dynamic tasks, could be the objective of further studies.

True accuracy of our estimates should be assessed with *ex vivo* studies. The only study that we are aware of proposing a methodology to estimate inaccessible points that have been validated in-vitro is the one by Kepple et al. (1998), who reported RMS errors of 6.6 mm on the femur and 5,8 mm on the tibia. In a very recent study Pellikaan et al. (2014) reported a mesh morphing based method which allows to estimate the muscle attachment sites of the lower extremity with a mean error smaller than 15 mm, as assessed through ex-vivo testing. This method is based on the assumptions that the bone geometry is strongly correlated with the muscle attachment sites. This assumption, as highlighted by the authors, was based on clinical experience and it may be not applied to pathological patients (D1) with bone deformities. It has to be pointed out, in addition, that these authors only analysed muscle insertions and data concerning the origins and insertions of the ligaments have not been reported.

The reproducibility analysis showed an absence of significant interactions both between and within factors, confirming that the virtual palpation procedure that provides the input of the method is not operator-dependent. In addition, one of the operators performed the virtual palpation within a different software environment and obtained results that were overlapping to those form the other operators in terms of repeatability. This suggests that the changeover of the virtual palpation software can occur without losing precision.

Repeatability findings suggest that an inevitable source of error for our method lies in the morphological differences between different subjects: some landmarks can be determined more precisely than others (see Table 1) since some anatomical regions of knee change substantially from subject to subject (Fehring et al., 2009). The variability we found, in addition, was likely also due to the fact that pathological knees, presenting irregular or deformed surfaces, were part of our dataset. Hence, it is conceivably to hypothesise that the expertise of the operators and the use of standard and well-defined guidelines for the definition of the anatomical landmarks for the virtual palpation can both contribute to improve the accuracy of the proposed procedure.

The RA created for the purpose of this study is calculated from three knee specimens obtained from donors of 70 years of age, and has been used to predict the ligament attachments for a population that was only slightly different in terms of age (65 years on average). Future research should be conducted to verify whether the accuracy of the method could be compromised when used in subjects of a different age range.

In conclusion, keeping in mind the generalizability limitations imposed by the number of investigated knees, the proposed procedure can be deemed adequately robust. It allows estimating the origins and the insertions of the knee ligaments from a CT scan with an accuracy level that is equivalent to that reachable using MRI images. As such, this procedure can be used to improve the accuracy of dynamic patient specific knee models in order to have a better understanding of the forces and the strains on the knee structures, such as the ligaments, during static and locomotion activities.

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TABLES

Landmark	SD Min (mm)	SD Max(mm)
FLE	0.02	5.97
FBE	0.56	2.37
FUE	0.06	2.31
FME	0.38	5.30
FAM	0.16	3.02
FMC	0.08	3.04
FLC	0.04	1.74
FLG	0.16	2.67
FMG	0.06	3.18
FPS	0.23	7.71
FMS	0.31	6.46
TTC	0.1	7.67
TLR	0.03	4.72
TMR	0.11	3.99
TGT	0.22	3.91
LCL	0.03	1.38

Table 1 – *The table shows the precision of the landmark positions in terms of Standard Deviation.*

	Mean Distance (mm)	Min (mm)	Max (mm)
SUBJECT 1	2,6 ± 0,8	1,8	4,2
SUBJECT 2	2,2 ± 0,9	1,1	4,5
SUBJECT 3	2,5 ± 1,8	0,3	5,8
SUBJECT 4	2,5 ± 1,6	0,2	5,1
SUBJECT 5	2,6 ± 2,3	0,7	7,3
SUBJECT 6	2,1 ± 0,8	0,7	3,3
SUBJECT 7	1,9 ± 1,1	0,6	4,2

Table 2 – *Registration Atlas registered on the seven subjects (femur)*

	Mean Distance (mm)	Min (mm)	Max (mm)
SUBJECT 1	2,1 ± 1,1	0,6	2,9
SUBJECT 2	1,9 ± 1,9	0	3,7
SUBJECT 3	1,1 ± 0,4	0,7	1,6
SUBJECT 4	2,1 ± 1,2	0,5	3,1
SUBJECT 5	1,0 ± 0,6	0,3	1,7
SUBJECT 6	1,3 ± 0,8	0,4	2,2
SUBJECT 7	1,2 ± 0,7	0,4	2,2

Table 3 – *Registration Atlas registered on the seven subjects (tibia)*

	Mean Distance (mm)	Min (mm)	Max (mm)
SUBJECT 1	2,5 ± 2,9	0,0	5,5
SUBJECT 2	1,3 ± 2,3	0,1	4,7
SUBJECT 3	3,9 ± 2,8	0,0	6,3
SUBJECT 4	3,1 ± 3,9	0,0	8,0
SUBJECT 5	2,1 ± 1,9	0,0	4,7
SUBJECT 6	0,4 ± 0,7	0,0	1,4
SUBJECT 7	1,3 ± 2,6	0,0	5,3

Table 4 – *Mean Distance between the insertion and the origin of the ligaments predicted and the ones estimated on the MRI images (femur)*

	Mean Distance (mm)	Min (mm)	Max (mm)
SUBJECT 1	4,4 ± 4,2	0,0	10,2
SUBJECT 2	2,6 ± 1,8	0,0	4,1
SUBJECT 3	2,5 ± 5,1	0,0	10,2
SUBJECT 4	/	/	/
SUBJECT 5	1,4 ± 1,7	0,0	3,2
SUBJECT 6	2,8 ± 5,6	0,0	11,3
SUBJECT 7	2,7 ± 3,1	0,0	6,1

Table 5 – *Mean Distance between the insertion and the origin of the ligaments predicted and the ones estimated on the MRI images (tibia). The subject 4 in not included in this comparison because the MRI data was incomplete*

	Age at death	*Gender*	*Right or Left*	*Height(in)*	*Weight(lbs)*
Knee #1	*77*	*Male*	*Right*	*70*	*220*
Knee #2	*55*	*Female*	*Left*	*67*	*160*
Knee #3	*78*	*Female*	*Right*	*65*	*130*

Table 6 *– Information regarding each cadaver knee used in this study to create the Registration Atlas*

FIGURES

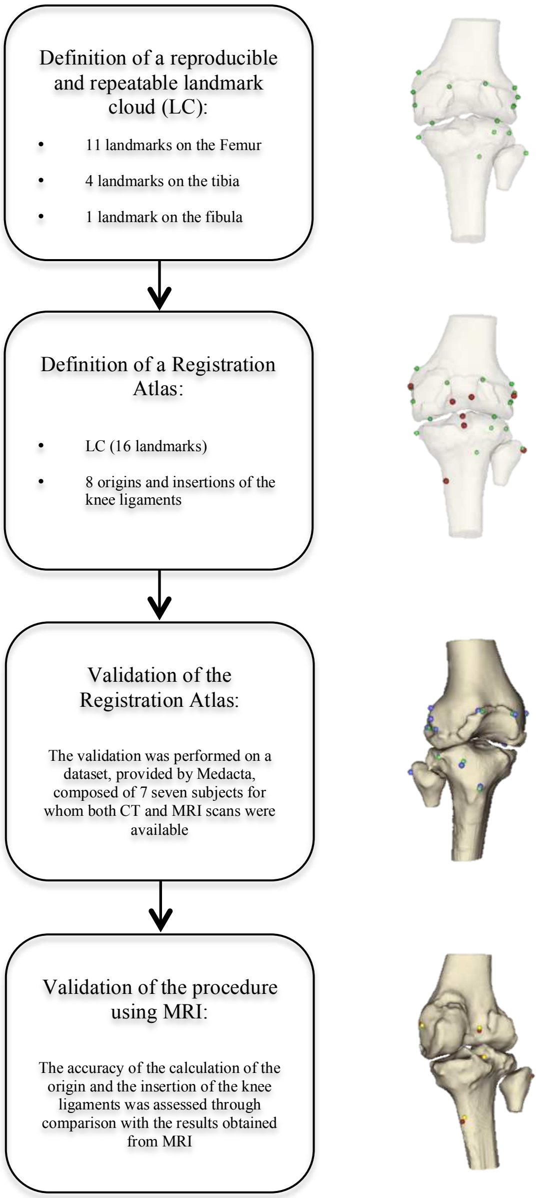

Figure 1 - *Schematic representation of the procedure: 1) Creation of a repeatable bone landmarks cloud palpable on CT scan images. 2) Definition of a reference landmarks cloud called Registration Atlas composed by reproducible and repeatable landmarks and the origin and insertion of the knee ligaments. 3) Validation of the RA 4) Calculation of the origin and insertion of the knee ligaments using CT scan and validation using MRI images*

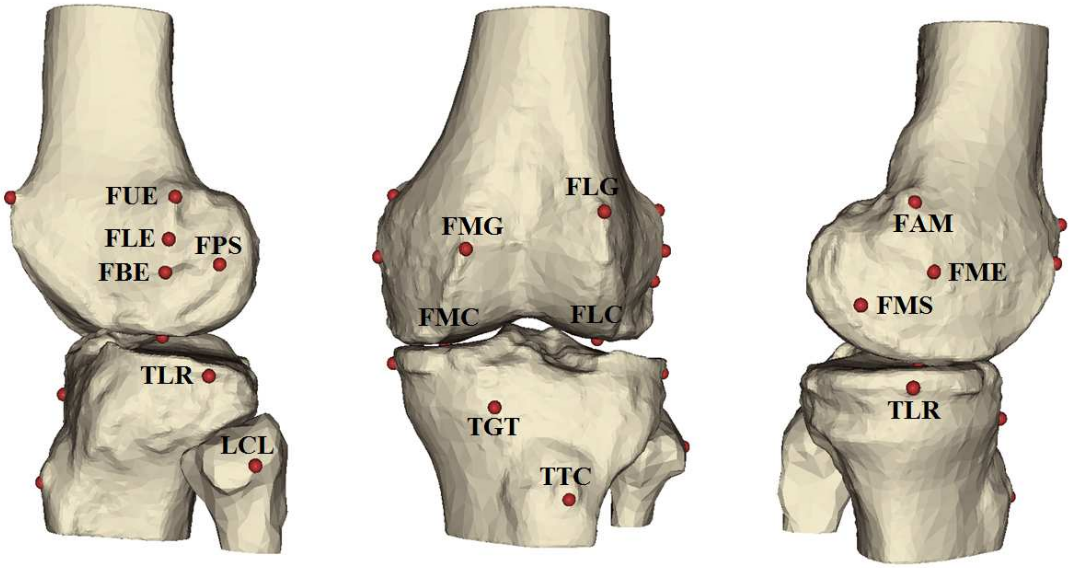

Figure 2 – *Set of landmarks selected using the "Colour Atlas of Skeletal Landmark Definitions" (Serge Van Sint Jan 2007). FME- Medial Epicondyle, FAM-Tubercle of the Adductor Magnus muscle, FMS-Medial Sulcus***,** *FLE- Lateral Epicondyle, center of tubercle, FUE-Lateral Epicondyle, FBE Lateral Epicondyle***,** *FPS-Popliteal Sulcus, FLG-Antero-Lateral ridge of the patellar surface Groove, FMG-Antero-Medial ridge of the patellar surface Groove, FLC-Most distal point of the Lateral Condyle***,** *FMC-Most distal point of the Medial Condyle***,** *TLR-Lateral Ridge of tibial plateau, TMR-Medial Ridge of tibial plateau***,** *TGT -Gerdy Tubercle, TTM-Tibia, Tuberosity medial edge, LCL-Attachment of the collateral Lateral Ligament*