PREDICTING SURGICAL OUTCOMES IN PATIENTS WITH RECURRENT PATELLAR DISLOCATION

by

Dario De Caro

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Dario De Caro

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The following individuals read and discussed the thesis submitted by student Dario De Caro, and they evaluated the student's presentation and response to questions during the final oral examination. They found that the student passed the final oral examination.

Clare Fitzpatrick, Ph.D.	Chair, Supervisory Committee
Mahmood Mamivand, Ph.D.	Member, Supervisory Committee
Trevor Lujan, Ph.D.	Member, Supervisory Committee
Nathan L. Grimm, M.D.	Member, Supervisory Committee

The final reading approval of the thesis was granted by Clare Fitzpatrick, Ph.D., Chair of the Supervisory Committee. The thesis was approved by the Graduate College.

DEDICATION

Dedicated to my family and all those who supported me during these two years.

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Thank you to Dr. Clare K. Fitzpatrick for giving me the opportunity of working in her lab and on this project, for having always been available and helpful with any doubt I had, mostly at the beginning when everything was new for me, and for the flexibility she gave me during these two years for my extra-curricular activities as a student-athlete. I would also like to thank Dr. Mahmood Mamivand, Dr. Trevor Lujan and Dr. Nathan Grimm for accepting being part of this supervisory committee and for the guidance and feedback they gave for this project. In addition, thanks to my colleagues in the Computational Bioscience Laboratory for being able to create the best work environment I could have asked for. Last but not least, thanks to my coaches for believing in me as an athlete and giving me the chance to pursue also my athletic goals.

ABSTRACT

Introduction

Lateral dislocation of the patella is a common injury in active adolescents and young adults. Patients who are ultimately managed surgically have a significantly lower risk of recurrent dislocation. However, determining the optimal surgical treatment remains a challenge, with patients sometimes undergoing multiple surgeries prior to successful stabilization. The aim of this study is to computationally evaluate patients that have undergone multiple surgeries to correct for recurrent lateral patellar dislocation and predict their clinical outcome.

Methods

Our patient cohort consisted of 16 patients with patella dislocation. Patient-specific imaging were used to create three-dimensional (3D) finite element (FE) models of the knee joint and evaluate patellofemoral (PF) stability at multiple time points pre- and post-surgery for each patient. We applied these models to predict the clinical success or failure of each surgery. Specifically, the FE model simulated a knee extension activity while a tibia external torsion, a recognized cause of patellofemoral pain and instability, was applied to assess PF stability. A healthy control group of 12 participants was also included to assess the ability of the model to identify successful outcomes. In addition, five anatomic factors of risk were measured, and statistical analysis was performed to establish if significant differences exist among pre-surgery, post-surgery and healthy control groups. Lastly, a logistic regression model was implemented, trained with anatomic values, and used to classify subjects into likelihood of dislocation categories in order to differentiate between successful and unsuccessful surgical outcomes. Feature scaling and feature combination (namely, principal component analysis (PCA)) was applied to improve the predictive performance of the regression model.

Results

Of 12 control participants, 12 pre-surgery subjects (8 patients after an initial unsuccessful MRPLR and 4 without any), and 9 post-surgery subjects (5 after a successful trochleoplasty and 4 patients after MPFLR), the FE model correctly predicted 29 out of 33 surgery outcomes (87.9% accuracy). Post-surgery simulations predicted patellofemoral stability metrics similar to the healthy control group. Particularly, post-trochleoplasty subjects were associated with an increased ability to provide constraint force on the patella lateral facet, and a lower involvement of the medial patellofemoral ligament, particularly close to full extension. A one-way ANOVA showed that four out of five anatomic factors were significantly different between the pre-surgery and the control group, and three of them also between the pre- and post- surgery group, suggesting that the surgery was able to restore a physiological condition. Lastly, logistic regression classification performance demonstrated 72.2% and 78.9% accuracy before and after PCA, respectively.

Conclusion

The overall aim of this study is to provide surgeons with a useful and validated computational tool that can predict the likelihood of patellar dislocation and differentiate, prior to clinical intervention, between a successful versus unsuccessful surgery, to determine the optimal treatment pathways for individual patients. Preliminary results are promising, but an improvement of the model and a larger clinical dataset are necessary to improve accuracy and comprehensively validate model performance.

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LIST OF ABBREVIATIONS

A-A	Adduction-Abduction
A-P	Anterior-Posterior
CT	computerized tomography
CR	conventional radiography
DKCT	Dynamic kinematic computed tomography
DOF	Degree of Freedom
F-E	Flexion-Extension
FE	Finite element
ICP	Iterative Closest Point
I-E	Internal-external
IS	Insall-Salvati
M-L	Medial-lateral
MPFL	Medial patellofemoral ligament
MPFLR	Medial patellofemoral ligament reconstruction
MR	Magnetic resonance
MRI	Magnetic resonance imaging
PCA	Principal component analysis
PF	Patellofemoral
RF	Rectus femoris
S-I	Superior-Inferior

TF	Tibiofemoral
TP	Trochleoplasty
TT	Tibial tubercle
TTO	Tibial tubercle osteotomy
TT-TG	Tibial tubercle-trochlear groove
VI	Vastus intermedius
VL	Vastus lateralis
VM	Vastus medialis
2D	Two-dimensional
3D	Three-dimensional

CHAPTER ONE: INTRODUCTION

1.1 Overview on patella dislocation

Definition, incidence and management

Dislocation of the patella is a common injury in active adolescents and young adults accounting for 2% - 3% of the knee joint injuries [4]. Patellar dislocation occurs when the patella disengages completely from the trochlear groove. The patella is usually dislocated laterally, and subsequently causes rupture of the medial patellofemoral ligament (MPFL) in about 90% of patients [22]. Acute patellar dislocations typically occur as a result of trauma, usually a non-contact twisting injury to the knee, or from a direct blow to the medial aspect of the knee. A common mechanism is external tibial rotation with the foot fixed on the ground [17]. When dislocations are isolated and the existing patellar mechanics and anatomy can accommodate the rehabilitation processes, non-surgical management is preferred [2]. Most common non-surgical rehabilitation process consist of initial immobilization in a cast, splint or locked orthosis to allow the soft tissues to heal, followed by active mobilization with physiotherapy. Particularly, physiotherapy should be started with an emphasis on quadriceps and vastus medialis oblique strengthening, core strengthening and proprioception. The patient can be allowed to weight bear as tolerated. Icing and NSAIDs are usually also suggested to reduce pain and swelling [17]. However, patients who are ultimately managed surgically have a significantly lower risk of recurrent dislocation at 2 to 5 years follow-up [25], suggesting that pathoanatomy plays a dominant role in patellar instability. In addition, other complications associated with non-surgical management include osteochondral fracture and degenerative arthritis. There exist also some potential risks of surgical-management including infection, saphenous nerve neuritis and rupture (specifically for medial patellofemoral reconstruction (MPFLR)), a loss of ability to kneel comfortably and proximal tibial fracture (specifically for osteotomies). Postoperative rehabilitation depends on the surgery completed. Recovery from surgery can last from 6 months to a year, and physiotherapy is vital after a period of immobilization [17].

<u>Anatomic risk factors</u>

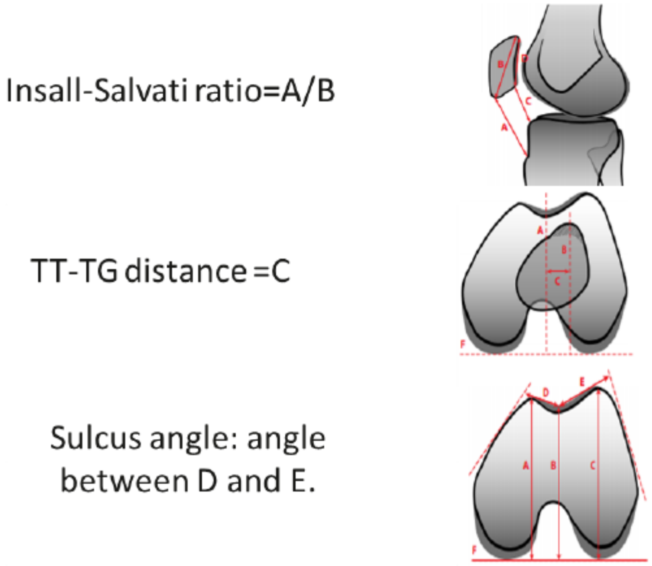

Figure 1 Anatomical factors associated with patellar dislocation[5] (Arendt et al., 2016).

Anatomic abnormalities that have been shown to correlate with a higher rate of patellar dislocation reoccurrence include an increased Insall-Salvati (IS) ratio, tibial tubercle-trochlear groove (TT-TG) distance and femoral sulcus angle [15, 28, 6, 3] [Fig. 1].

IS ratio is a measure of patella height and it is defined as the ratio of the length of the patellar tendon (measured from the distal pole of the patella to the tibial tuberosity) to the maximum length of the patella (measured from the distal pole to the proximal pole of the patella). To measure patellar height, several measurement methods and imaging modalities are in use. IS ratio is the only measurement that showed good intra- and inter-observer reliability on conventional radiography (CR), computerized tomography (CT) and magnetic resonance imaging (MRI) [30]. IS ratios defined for patella alta and baja are 1.52 and 0.79 respectively in females and 1.32 and 0.74 respectively in males. Values inside those ranges are considered normal [26].

TT-TG distance is a measure of lateralization of the tibial tuberosity in relation to femoral trochlea. Normal values for TT-TG have been found to be 12.7 ± 3.4 mm and > 20 mm in pathological cases [8].

Femoral sulcus angle is the angle that is formed by the trochlear opening of the knee, measured between the medial and lateral facets. Its normal value is 135±10º. When the angle of the groove is >145-150º, trochlear dysplasia can be diagnosed.

Near full extension, the primary anatomic variant that contributed to patellar instability is related mostly to trochlear dysplasia. In contrast, at greater flexion angles, patellar instability is more related to the location of the tibial tuberosity [11, 16].

Surgical options

Determining the optimal surgical treatment remains a challenge, with patients sometimes undergoing multiple surgeries prior to successful stabilization. Common surgical options are trochleoplasty, tibial tubercle osteotomy (TTO) and MPFLR[31] [Fig. 2].

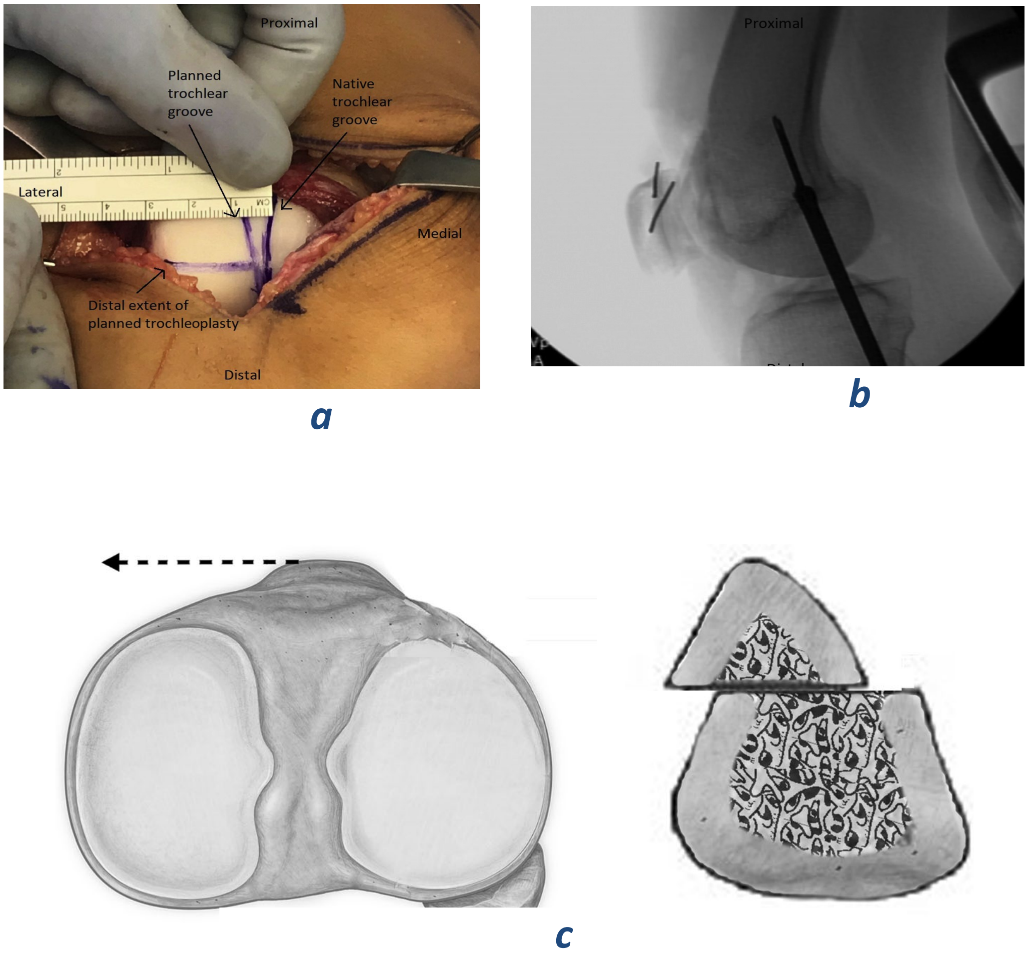

Figure 2 Trochleoplasty (a) Medial patellofemoral ligament reconstruction (b), and tibial tubercle osteotomy (c) [16, 31] (Vogel and Pace, 2019; Grimm et al, 2018).

Trochleoplasty is a surgical option for addressing patellar instability in patients with severe trochlear dysplasia. Trochlear dysplasia may be classified into four types[9] [Fig. 3]:

- Type A: The trochlea is shallower than normal, but still symmetrical and concave.
- Type B: The trochlea is flat or convex in axial images.
- Type C: There is no spur, and in axial views the lateral facet is convex and the medial hypoplastic.
- Type D: In the axial view, there is clear asymmetry of the height of the facets, also referred to as a cliff pattern.

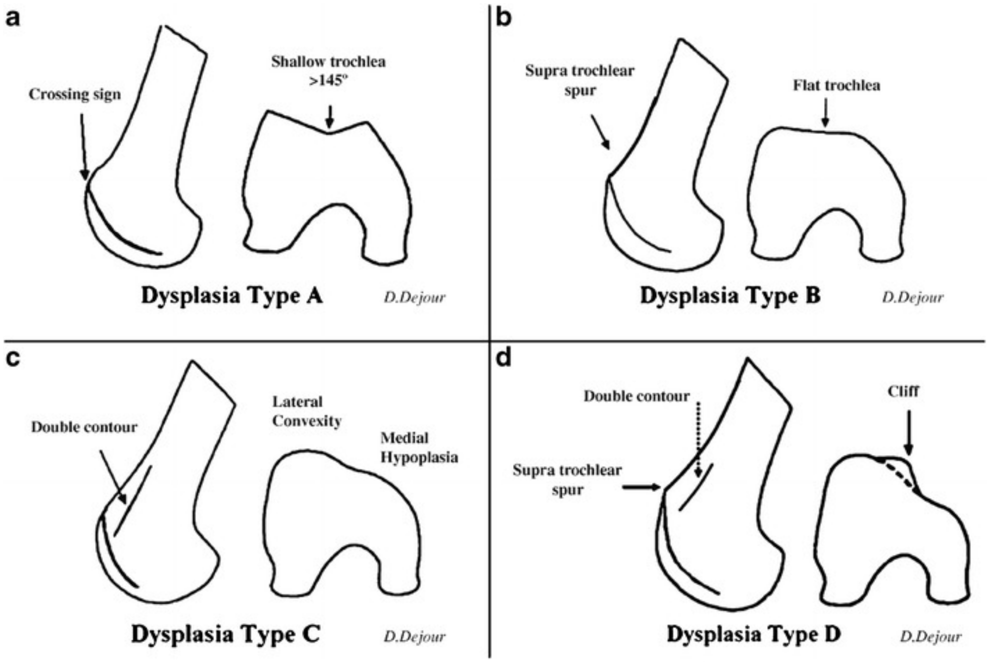

Figure 3 Different types of trochlear dysplasia[9] (Dejour et al., 2010)

The main types of trochleoplasties are lateral facet elevation and trochlear deepening [Fig. 4]. Types B and D are the most suitable to deepening trochleoplasty.

Lateral facet elevating trochleoplasty is indicated for type C dysplasia, although no consensus of indication criteria exists. Type A dysplasia does not merit any procedure.

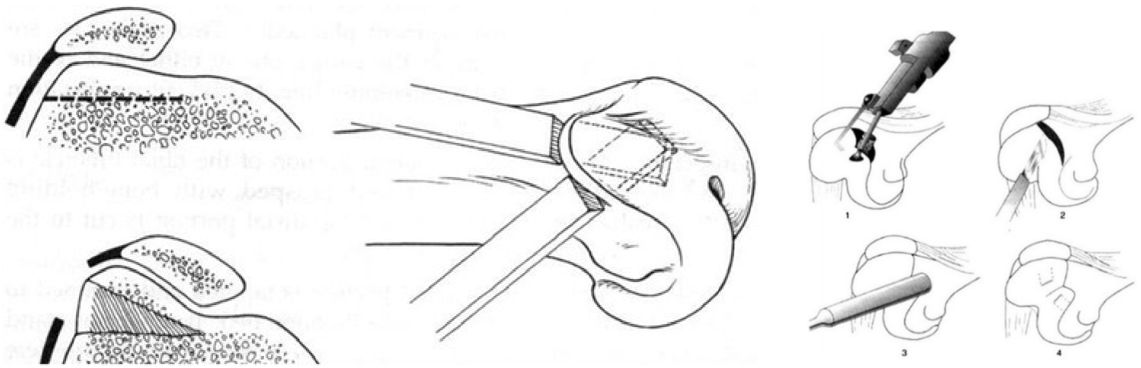

Figure 4 Lateral facet elevation (left) and trochlear deepening (right)[21] (Nolan et al., 2018).

TTO indications include patellofemoral maltracking or malalignment, patellar instability, patellofemoral arthritis, and focal patellofemoral chondral defects. With TTO, the goal is to move the tibial tubercle in a direction that will either improve patellar tracking or offload the medial or lateral patellar facet to improve pain and function. This action typically involves anterior, medial, lateral, or distal translation of the tibial tubercle [24]. Particularly, medialization has been recommended in the literature for TT-TG distance values over 20 mm [Fig. 5].

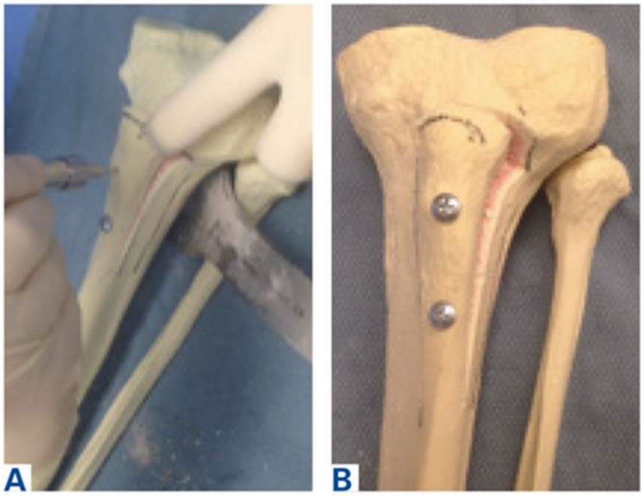

Figure 5 **Tibial tubercle medial transfer [24] (Saltzman et al., 2017).**

Lastly, reconstruction of the MPFL is suggested to reduce the high incidence of recurrent dislocation. MPFL is considered to be the most important soft tissue structure to restrain lateral patella dislocation, and it is often damaged during patellar subluxation or dislocation. Surgical treatment is generally recommended after a second dislocation [18]. The MPFL is typically reconstructed using a semitendinosus or gracilis tendon autograft [12].

However, although there is some evidence to support surgical over non-surgical management of primary patellar dislocation in the short term, the quality of this evidence is very low [25]. In addition, there is not a clear course of action on what the best surgery is for a particular patient. For this reason, objective quantitative data is needed to establish the best surgical approach on a patient-specific basis. Both experimental and computational approaches have been tested in previous studies to investigate how patella dislocate.

1.2 Previous studies

Experimental studies

A recent systematic review of biomechanical and kinematic studies [10] provide some evidence that a dislocation is likely to occur during early knee flexion with external rotation of the tibia and contraction of the quadriceps. The force required for the dislocation to occur would also have to be sufficient to overcome the soft tissue restraints of the patella, in particular the MPFL. However, the usage of cadaveric methods (which was predominant in the studies included in the review), despite allowing to perform direct injury studies and passively assess the biomechanics of a joint, is associated with some limitations. Indeed, often it is difficult to obtain specimens of the correct age to represent the demographic most affected by that injury, and it is not possible to truly replicate the involvement of the muscles surrounding the joint. Furthermore, it is difficult to recreate the types of loads that a joint may undergo during an injury as well the influence of any external factors.

Other experimental studies were performed *in vivo* and focused on correlation of patellar maltracking and instability. Specifically, dynamic kinematic computed tomography (DKCT) was used to visualize and quantify patellar maltracking patterns, and severity of maltracking was correlated with the presence or absence of patellar instability symptoms. Results showed several patellar maltracking patterns in patients with patellar instability [29]. However, morphological factors that may influence maltracking patterns such as TT-TG distance, patella alta, and trochlear dysplasia were not accounted for in this study. In general, experimental studies, although useful to assess for patella instability, are not able to indicate if either a conservative method or a surgical approach is better for that particular patient and eventually predict the outcome of a specific surgical procedure. These limitations can be negated to a certain degree using computer simulation models

Computational studies

Computational models have been used to correlate anatomic parameters with patellar tracking for subjects with recurrent patellar instability. Knee models are usually created from CT or MRI scans and dynamic simulations are performed. Results showed that, during an extension activity, parameters related to trochlear dysplasia and tibial tuberosity position were both related to patellar tracking, but the relationship changed with the flexion angle [11].

The use of patient-specific computational models also allows us to quantitatively evaluate the effect of different surgical options on patellofemoral (PF) joint stability metrics relative to the underlying anatomy. Particularly, previous computational studies which have simulated procedures to correct for patellar dislocation show that patient-specific intervention that corrects underlying anatomic abnormalities is the only surgical option to have non-significantly different results compared with the healthy equivalent control group across all joint stability metrics [1][Fig. 6].

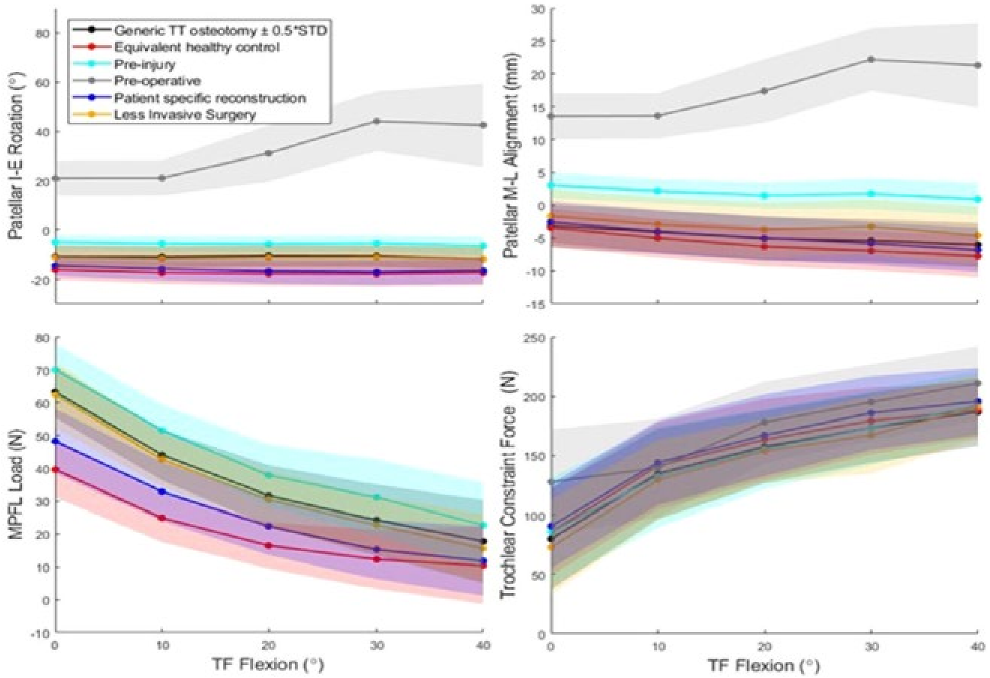

Figure 6 **Patellofemoral stability metrics for different groups at each flexion angle[1] (Alvarez et al. 2020).**

While these simulations result in stability metrics and allow us to develop a relative ranking across a variety of procedures, it is not obvious if the differences identified between simulations are clinically relevant to patient outcomes and surgical success. Notably, in previous simulations PF stability has been assessed in the absence of clinical data to determine whether the ‘virtual’ surgery would have a real-world impact on that patient’s clinical outcome. Additionally, these studies typically apply a generic or stylized loading condition rather than reproduce more complex loading conditions of daily living that put a patient at risk of patellar dislocation during in vivo activity.

1.3 Research goal

The aim of this study is to computationally evaluate patients that have undergone multiple surgeries to correct for recurrent lateral patellar dislocation and evaluate how well these models can predict their clinical outcome. We will use patient-specific imaging to create three-dimensional (3D) finite element (FE) models of the knee joint and evaluate PF stability at multiple time points pre- and post-surgery and determine whether our computational approach can accurately predict the success or failure of each surgery. Specifically, the FE model will simulate a knee extension activity, namely a chair rise. A tibia external torsion, a recognized cause of patellofemoral pain and instability[27], will be applied during the extension to test PF stability. A healthy control group will also be included to assess the ability of the model to identify successful outcomes. In addition, anatomic factors will be measured, and statistical analysis will be performed to establish if significant differences exist among different groups. Lastly, a logistic regression model will be implemented, trained with the values of each factor and used to classify patients according to success or failure of surgical outcomes and predict risk of dislocation. Finally, computational and regression models will be compared in terms of computational cost and classification performance.

CHAPTER TWO: MANUSCRIPT “PREDICTING SURGICAL OUTCOMES IN PATIENTS WITH RECURRENT PATELLAR DISLOCATION”

2.1 Introduction

Lateral dislocation of the patella is a common injury in active adolescents and young adults. Patellar dislocation occurs when the patella disengages completely from the trochlear groove. When dislocations are isolated and the existing patellar mechanics and anatomy can accommodate the rehabilitation process, non-surgical management is preferred [2]. However, patients who are ultimately managed surgically have a significantly lower risk of recurrent dislocation at 2 to 5 years follow-up [25], suggesting that pathoanatomy plays a dominant role in patellar instability. Anatomic abnormalities that have been shown to correlate with a higher rate of patellar dislocation reoccurrence include an increased I-S ratio (a measure of patella height), TT-TG distance and trochlear and femoral sulcus angle (a measure of trochlear dysplasia)[15, 28, 6, 3]. Near full extension, the primary anatomic variant that contributed to patellar instability is related mostly to trochlear dysplasia. In contrast, at greater flexion angles, patellar instability is more related to the location of the tibial tuberosity [16].

Determining the optimal surgical treatment remains a challenge, with patients sometimes undergoing multiple surgeries prior to successful stabilization. Common surgical options are trochleoplasty, TTO and MPFLR [31].

The use of patient-specific computational models allows us to quantitatively evaluate the effect of different surgical options on PF joint stability metrics relative to the underlying anatomy. Particularly, previous computational studies which have simulated procedures to correct for patellar dislocation show that patient-specific intervention that corrects underlying anatomic abnormalities is the only surgical option to have results that are statistically equivalent to a healthy control group across all joint stability metrics [1]. While these simulations result in stability metrics and allow us to develop a relative ranking across a variety of procedures, it is not obvious if the differences identified between simulations are clinically relevant to patient outcomes and surgical success. Notably, in previous simulations PF stability has been assessed in the absence of clinical data to determine whether the 'virtual' surgery would have a real-world impact on that patient's clinical outcome. Additionally, these studies typically apply a generic or stylized loading condition rather than reproduce more complex loading conditions of daily living that put a patient at risk of patellar dislocation during in vivo activity.

The aim of this study is to computationally evaluate patients that have undergone multiple surgeries to correct for recurrent lateral patellar dislocation and evaluate how well these models can predict their clinical outcome. We will use patient-specific imaging to create 3D FE models of the knee joint and evaluate PF stability at multiple time points pre- and post-surgery and determine whether our computational approach can accurately predict the success or failure of each surgery. Specifically, the FE model will simulate a knee extension activity, namely a chair rise. Tibia external torsion, a recognized cause of patellofemoral pain and instability [27], will be applied during the extension to test PF stability. A healthy control group will also be included to assess the ability of the model to identify successful outcomes. In addition, the anatomic risk factors described above will be measured and statistical analysis will be performed to establish if significant differences exist between different groups. Lastly, a logistic regression model will be implemented, trained with the values of each factor and used to classify patients and predict risk of dislocation. Finally, computational and regression models will be compared in terms of computational cost and classification performance.

2.2 Methods

Data collection

MR scans of the knee joint from 16 patients (10 females and 6 males) with recurrent lateral patellar dislocation were obtained at multiple time points for a total of 21 models (not all of the subjects had scans both pre- and post-surgery). Specifically, 12 pre-surgery subjects (8 patients after an initial unsuccessful MRPLR and 4 without any) and 9 post-surgery subjects (5 after a successful trochleoplasty and 4 patients after MPFLR). Twelve additional subjects (6 males and 6 females, mean age ± standard deviation: 21.5 ± 2.1) with no patella injury history and MR scans obtained as part of a separate biomechanics study, were included in the dataset as a healthy control group, for a final total of 33 models.

Model development

MR scans were imported and segmented using commercially available reconstruction software (Amira, ThermoFisher) to create a subject-specific 3D model of each knee joint. [Fig. 7]. Each model includes femur, tibia and patella bone and cartilage geometries. Generic quadriceps muscles and tendons, patella ligaments (PL) and MPFL structures were scaled and aligned to match the subject-specific bone and cartilage geometry [Fig.8].

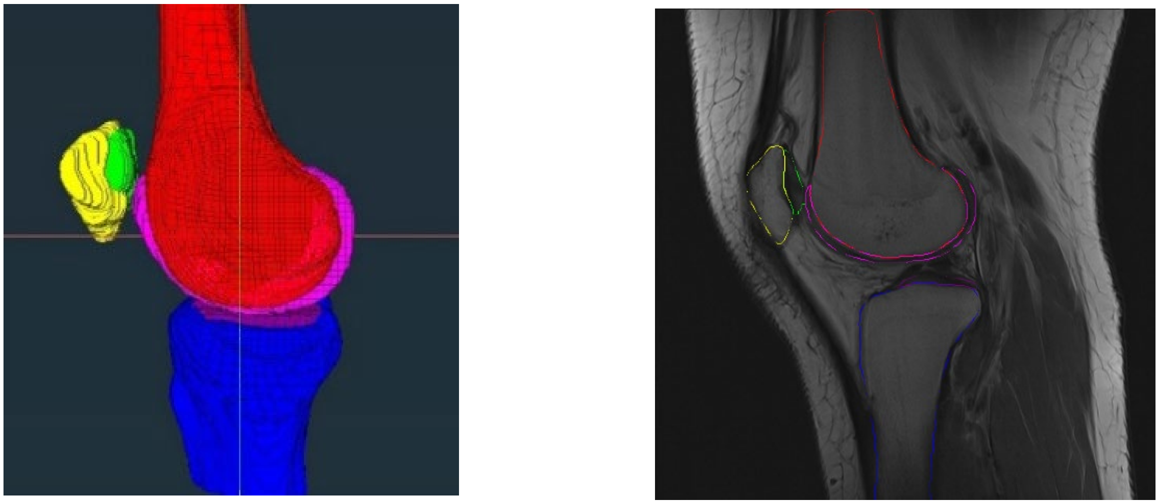

Figure 7 Bones and cartilage geometries segmentation in Amira from MRI subject-specific scans.

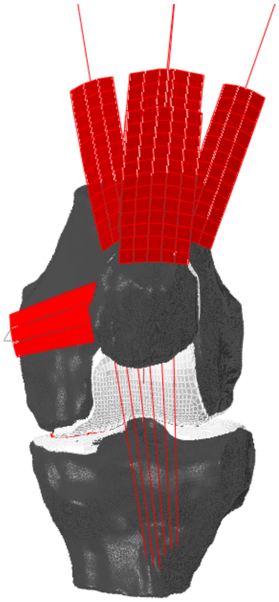

Figure 8 3D Finite element model of a patient-specific knee joint reconstructed from MR scans.

Models from difference time points were aligned with one another using an iterative closest point (ICP) algorithm. Local tibiofemoral and patellofemoral joint coordinate systems were created to define the 6 degrees of freedom (DOF) translational and rotational axis. Particularly, for the tibiofemoral joint, the flexion-extension axis was fixed to the femoral local coordinate frame, while the internal-external axis was fixed to the tibial local coordinate frame. Abduction-adduction motion occurs about the floating axis.

Anatomical landmarks were located for each patient. Specifically:

- the highest, lowest, most medial and most lateral point on the patella;
- the most anterior point on the medial and lateral facets and the deepest point in the trochlear groove;
- the most anterior point on the tibial tuberosity.

Five geometric factors were calculated at the original pose (full extension) from the reconstructed 3D model: IS ratio (a measure of patella height), TT-TG distance, femoral sulcus angle, lateral trochlear inclination and patella bisect offset index.

- IS ratio is the ratio of the patellar tendon length to the superior-inferior length of the patella.
- Sulcus angle is calculated between the most anterior point on the medial and lateral facets and the deepest point in the trochlear groove.
- Lateral trochlear inclination is the inclination angle is measured between the bony contours of the lateral trochlear facet and a posterior condylar tangential line.
- TT-TG distance is measured as the medial–lateral (M–L) distance (measured parallel to the posterior condylar line) from the anterior point of the tibial tuberosity and the deepest point of the trochlear groove.

- The patella bisect offset index is defined as the proportion of the patella lying lateral to the midline as a percentage of the whole patellar width [19] [Fig. 9].

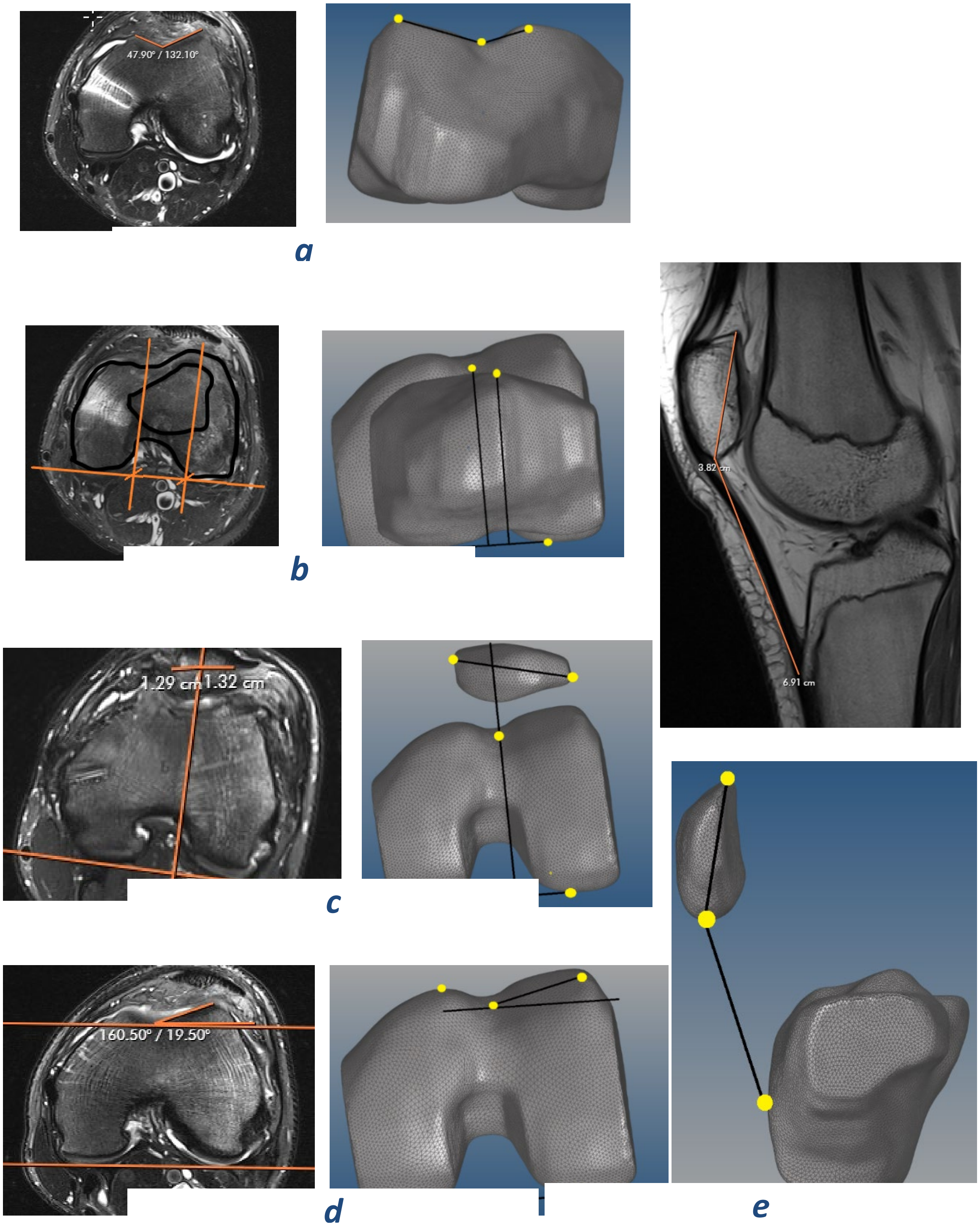

Figure 9 Anatomical factors associated with patellar dislocation measured from the 3D model and from the scans: sulcus angle (a), TT-TG distance (b), patella bisect offset index (c), lateral trochlear inclination (d) and IS-ratio (e).

Finite element model

Bone geometries were imported into Hypermesh (Altair Engineering), and the surfaces were meshed as two-dimensional (2D) rigid triangular elements of 1mm size. Cartilage was represented as eight-noded hexahedral elements using an automated hexahedral meshing software implemented in MATLAB [23]. The patellar tendon was modeled as six non-linear springs. Quadriceps tendons were modeled as 2D membranes (quadrilateral elements) with embedded fiber-reinforced springs.

The finite element model was created in Abaqus/Explicit (Simulia), and a dynamic simulation was performed. An initial force of 100 was applied to the quadriceps, distributed with a ratio of 20:20:35:25 respectively across the rectus femoris (RF), vastus intermedius (VI), vastus lateralis (VL) and vastus medialis (VM) [13]. An 8N force was applied to the MPFL to create a pre-tensioned state at full extension and allow for a slack MPFL later in flexion [13, 1]. Sensitivity analysis on the MPFL pre-tensioning force was performed, increasing and decreasing the initial value of 8N by 50% and evaluating differences in the classification performance. A compression force of 50N was applied between the tibia and the femur to ensure articular TF contact throughout the simulation. While loaded, the knee was flexed to the starting pose of the knee extension activity close to 90° TF flexion. Starting from this flexion pose, a chair rise activity was simulated. Specifically, experimental data were used to define tibiofemoral flexion-extension (F-E) and internal-external (I-E) rotations and M-L and anterior-posterior (A-P) displacement through the whole activity. Adduction-abduction (A-A) rotation and superior-inferior (S-I) displacement DOF were kinematically unconstrained, with their motions determined by articular contact between femur and tibia. A pressure-overclosure relationship of 3.2

MPa/mm between femur and tibia cartilage was defined [14]. The force on the quadriceps was defined through the activity using experimental data with quadriceps force ranging from 100N to 750 N. A 30° external rotation was applied to the tibia to evaluate patellofemoral joint stability. External tibia torsion has been recognized as one of the potential risk factors for patella dislocation [7].

Post-processing

For each simulation, a series of patellofemoral joint stability metrics were evaluated. This analysis focused on the last 40° of extension, where the anatomic resistance to dislocation is reduced and soft-tissue constraint necessary to maintain a stable joint is increased [13]. Specifically, total ligament force in the MPFL and contact force on the patella articular surface were collected throughout the activity. The patella was defined as dislocated if the total force on the patella cartilage switched from a medial to a lateral direction, indicating that it disengaged completely from the trochlear groove. A virtual trochleoplasty was subsequently simulated on the post-surgery group to increase the depth of the femoral sulcus angle to 140° to evaluate sensitivity to the magnitude to the trochleoplasty change.

Five one-way ANOVA tests (one for each anatomical factor) were performed between the healthy control group, the pre-surgery group, and the post-surgery group to test the null hypothesis that no significant differences exist in the mean value of each factor among groups. Statistical significance was set to 0.05. Test of normality and equality of variance were also performed. Post-hoc Tukey tests were performed to establish which groups showed significant difference. Power analysis was performed to establish the statistical power of the test with the current dataset size.

Classification model

Lastly, anatomic factors were used to train a logistic regression model to predict the likelihood of dislocation, with a threshold of 0.5 set to define a binary classification (0 = No dislocation, 1 = Dislocation)[20]. Specifically, 0 was assigned to the post-op and healthy control groups and 1 to the pre-op group. Stratified K-fold cross validation was used as a partitioning strategy for the dataset in order to effectively build a more generalized model. The whole dataset was randomly split into independent K-folds without replacement. K-1 folds were used for the model training and one fold was used for performance evaluation. This procedure was repeated K times (iterations) so that we obtained K number of performance estimates for each iteration. K was set to 4, so we obtained a train-test set size ratio of 75:25. Classification performance was evaluated using confusion matrices. Feature scaling and feature combination (principal component analysis (PCA)) was applied. Specifically, a Min-Max scaler was used to standardize the values of the anatomical factors in a range between 0 and 1 for each patient, and PCA was performed to extract the principal components (PC) of maximum variance, with the goal of reducing the dimension of the model, avoiding overfitting and improving the classification performance. Specifically, the number of PC to be extracted was selected as to generate a cumulative sum of explained variance above the threshold of 80%. Overfitting was evaluated including accuracy of classification on the training set and comparing it with the one on the test set.

2.3 Results

The finite element model was able to predict 29 out of 33 surgery outcomes (87.9% accuracy). The misclassifications came from three pre-surgery simulations, where the model was not able to predict the dislocation (3 false negative) and one post-surgery simulation, where the model predicted a false dislocation (1 false positive). By decreasing the MPFL initial force to 4N, the classification performance was not affected in any of the groups. Lastly increasing the force value up to 12N, four pre-surgery and one post-surgery studies were misclassified (4 false negative and 1 false positive) [Table 1].

Table 1 Sensitivity analysis on effect of MPFL pre-tensioning force on classification performance.

ACCURACY	8N	4N	12N
PRE-SURGERY	9/12	9/12	8/12
POST-SURGERY	8/9	8/9	8/9
CONTROL GROUP	12/12	12/12	12/12
OVERALL	29/33	29/33	28/33

Five one-way ANOVA tests (one for each anatomical factor) were performed between pre-surgery (PRE), post-surgery (POST) and healthy control group (CTRL). Post-hoc Tukey tests were performed to establish which groups showed significant difference. Significance was set to 0.05 [Fig. 10 and Table 2 and 3]. IS ratio was the only factor to show no significant difference among groups. For all the other factors, the healthy control group was significantly different from the pre-surgery group, but not from the post-op group. Lastly, pre- and post-surgery groups differ significantly for bisect offset index, sulcus angle and lateral trochlear inclination, indicating that the surgery was able to restore a physiological condition.

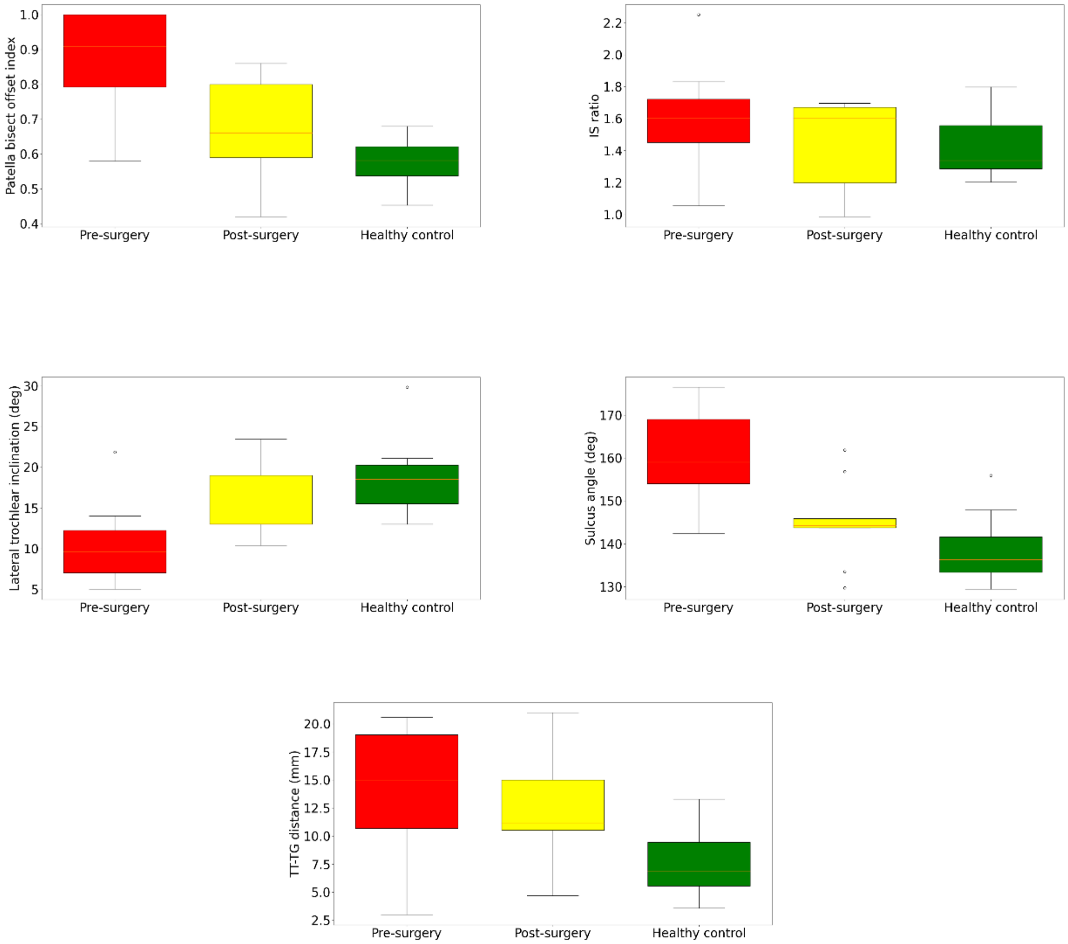

Figure 10 Distribution of data for each group and anatomical factor.

Table 2 Average value of each anatomical factor for each group.

AVERAGE VALUE			
ANATOMICAL FACTOR/GROUPS	PRE-SURGERY	POST-SURGERY	HEALTHY CONTROL
IS Ratio	1.6	1.4	1.4
Sulcus angle (deg)	160	145	138
TT-TG distance (mm)	14.3	12.3	7.7
Bisect offset index	0.87	0.67	0.58
Lateral trochlear inclination (deg)	10	16	18

Table 3 Post-hoc Tukey test results for each anatomical factor among pre-surgery (PRE), post-surgery (POST) and healthy control group (CTRL). Highlighted values below the significance threshold.

POST-HOC TUKEY TEST P-VALUE RESULTS			
ANATOMICAL FACTOR/GROUPS	PRE VS POST	PRE VS CTRL	POST VS CTRL
IS Ratio	0.3322	0.2085	0.9
Sulcus angle	0.003	0.001	0.2782
TT-TG distance	0.5849	0.0032	0.066
Bisect offset index	0.0027	0.001	0.2244
Lateral trochlear inclination	0.0312	0.001	0.3702

However, the statistical power of the analysis is limited by the current dataset size, as the results of the power analysis performed (assuming a large effect size) show [Fig. 11].

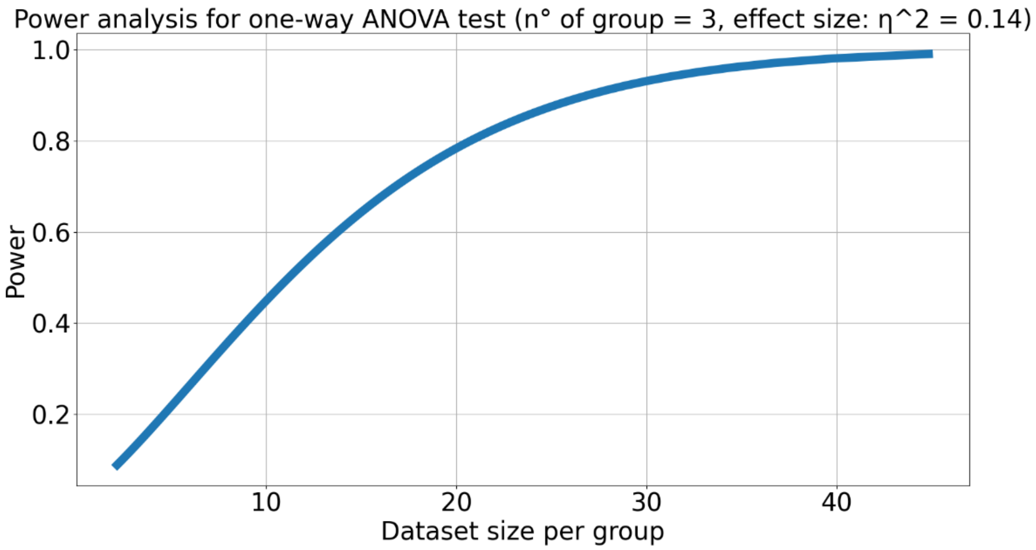

Figure 11 One-way ANOVA test power analysis

Information about the total ligament force in the MPFL and contact force on the patella cartilage were collected throughout the activity, focusing on the last 40° of extension. [Fig. 12]. Post-surgery studies showed results similar to the healthy control group. Particularly, a deeper sulcus angle is associated with an increased ability to provide constraint force on the patella lateral facet, and a lower involvement of the MPFL, mostly in the last degrees of extension. The same analysis was carried out with the 'virtual trochleoplasty' group [Fig. 13]. The virtual surgery group showed better results in terms of trochlear constraint force at each flexion angle. The healthy control group still perform best, most likely due to the better average value for the others anatomical factors. No significant differences have been showed for the MPFL total force.

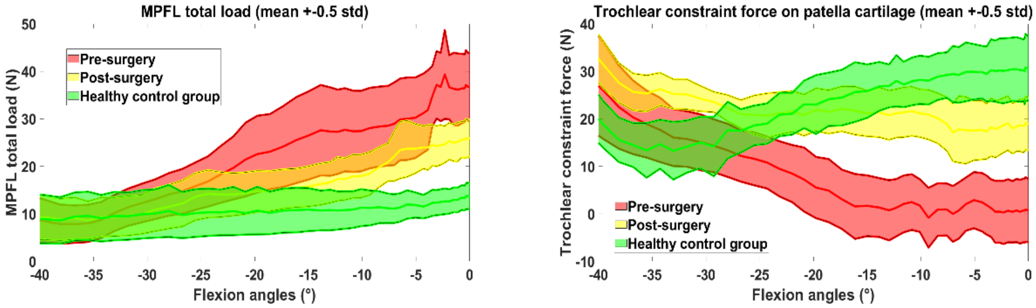

Figure 12 Average total MPFL constraint force (left) and contact trochlear constraint force on patella cartilage (right) at different flexion angles for different groups.

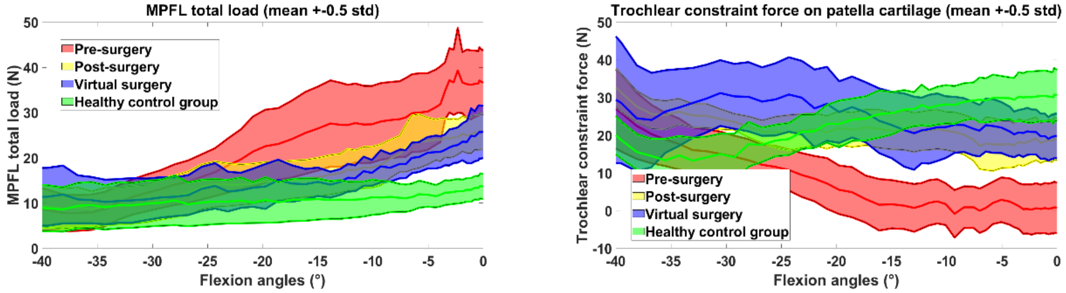

Figure 13 Effect of virtual trochleoplasty on patellofemoral joint stability metrics.

Logistic regression model performance was also evaluated. IS ratio was excluded from the training features, as it was not significantly different among groups. Results obtained from the four different dataset splits were averaged, normalized (in a range between 0 and 1) and shown as a confusion matrix. Specifically, values on the main diagonal represents percentage of true negative (correctly predicted no-event values), and true positive (correctly predicted event values). On the opposite diagonal, percentage of false positive (incorrectly predicted event values) and false negative (incorrectly predicted no-event values) are shown, where event = dislocation. Comparison between classification performance on the training and test set was analyzed to check for overfitting. An overall score of 72.2% and 87.8% was recorded respectively on test and training set. In general, the model performed worse than the FE simulations [Fig. 14].

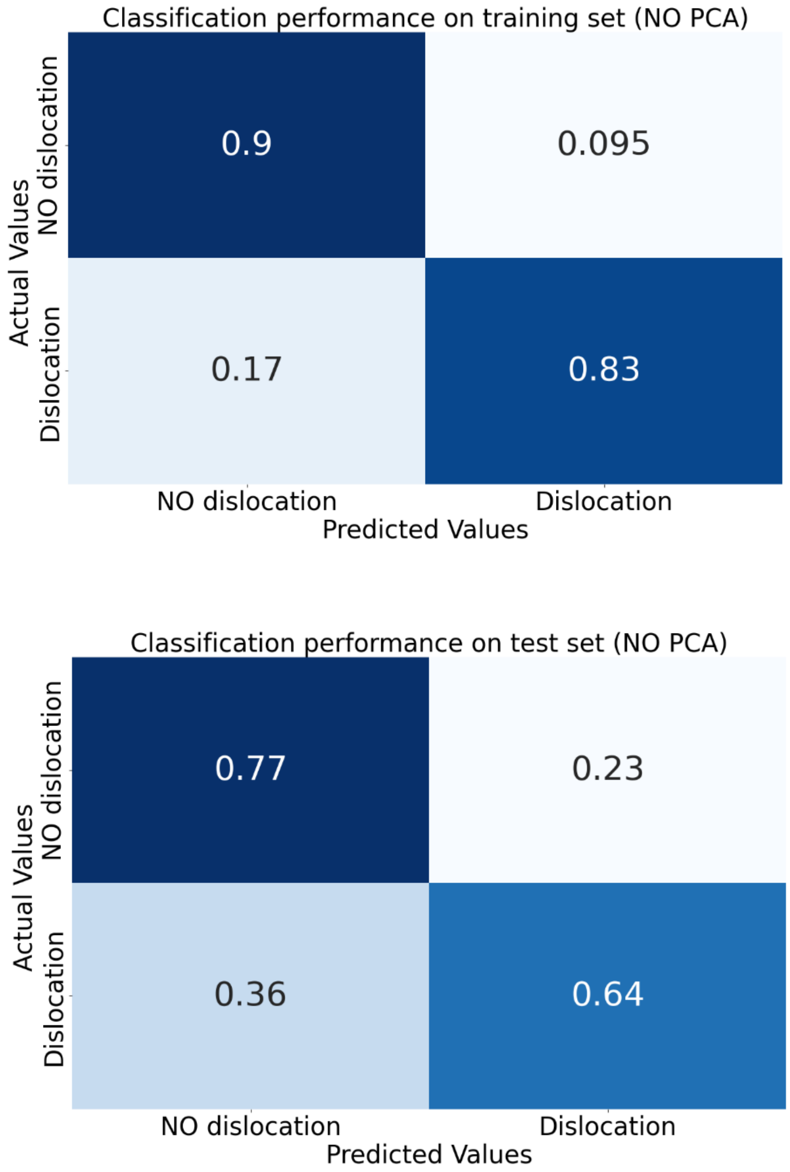

Figure 14 Logistic regression classification performance.

Feature scaling and feature combination (PCA) were applied to try to improve model performance. Two principal components were extracted, accounting for a cumulative explained variance of 85.9% (respectively 67.1% the first component and 18.8% the second) [Fig. 15].

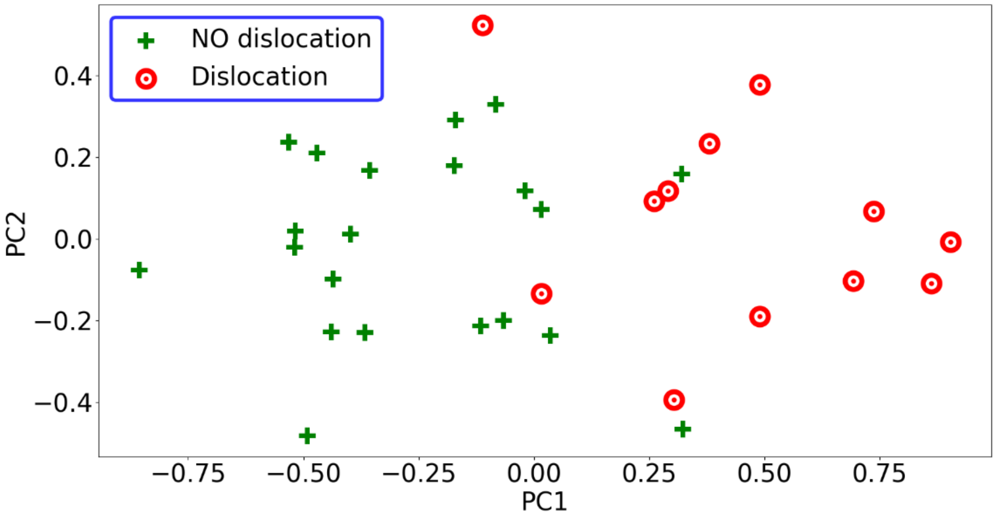

Figure 15 Data distribution after applying PCA.

The overall performance of the classifier improved to 78.9% on the test set, but decreased down to 83.9% on the training set, reducing the overfitting [Fig. 16].

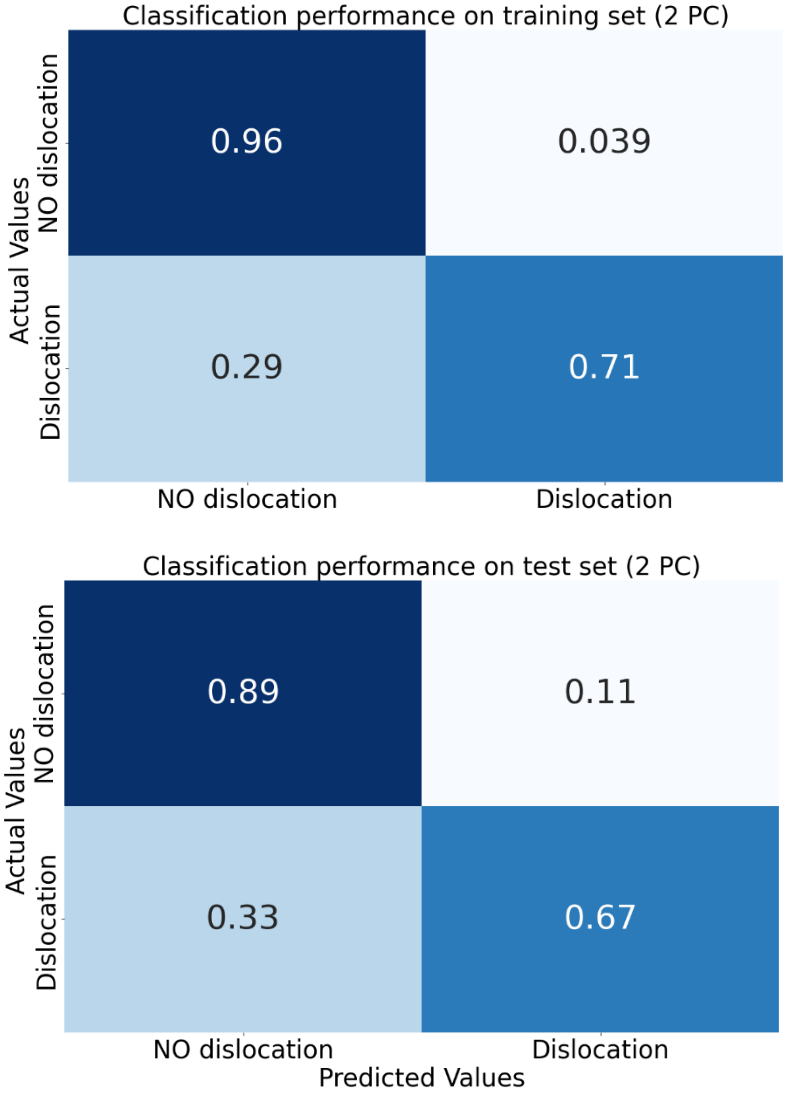

Figure 16 Logistic regression classification performance after applying PCA.

2.4 Discussion

The overall aim of this study was to provide surgeons with a useful and validated computational tool that can predict the likelihood of patellar dislocation and differentiate, prior to clinical intervention, between a successful versus unsuccessful prospective surgery, to determine the optimal treatment pathways for individual patients. Two different approaches – finite element simulations and logistical regression - were used.

The finite element model is able to provide additional information beside the prediction of dislocation. Specifically, total constraint force on the MPFL and total contact force on the patella cartilage are useful metrics to establish the mechanism of dislocation and potential risk of MPFL rupture. This may also be used in future work to evaluate risk of patellofemoral osteoarthritis due to changes in conformity between patellar and femoral articular surfaces after trochleoplasty. In addition, the overall accuracy was higher. However, this method is more time consuming because it requires additional pre-processing steps as soft tissue scaling and alignment and the simulation has a higher computational cost. The logistic regression model only requires the anatomical factors values for each patient to be trained, and it is much faster to run. All the geometrical factors used in the statistical analysis and the regression model were collected and measured from the 3D model. A comparison with the measurement made from the scans could be helpful to establish the accuracy and repeatability of the method and possibly define correction factors between the two different approaches. Overall, both models are able to predict patella dislocation given specific anatomical factors.

The first section of this study is part of the computational approach framework used to investigate patella dislocation. It goes one step forward from previous studies, as the model is fit on patients with recorded clinical data, and it simulates a real daily activity. The regression model represents a new and useful alternative, particularly efficient in terms of computational cost. To date and as far as known, it is the first study that applies a logistic regression model to predict risk of patella dislocation.

Preliminary results are promising, but an improvement of the models and an extension of the dataset is necessary to improve the accuracy. Particularly, only MPFLR and trochleoplasty were considered as surgical options, as they were the only surgical procedures performed on the subjects available through our current dataset. In order to expand the scope of this analysis to a more comprehensive assessment of potential surgical options, patients with TTO performed (which would significantly change the IS ratio and TT-TG distance values) should also be included.

There are also some simplifications and limitations associated with the FE model. PL is the only soft tissue geometry for which an automatic alignment process has been implemented. Particularly, the post prominent point on the tibia (tibial tubercle) and lowest point on the patella are localized and used as the attachment site of the PL for each bone. MPFL and quadriceps are manually aligned based on bony landmarks. For this reason, the attachment site could slightly change subject-by-subject, affecting the kinematic of the simulation and increasing the total time of the pre-processing (already affected by the manual segmentation of the scans). To overcome this problem, the best solution (particularly to improve patient-specific quadriceps alignment) would be to obtain full lower limb scans of the subjects, that would allow identification of attachment sites at hip. Alternatively, in absence of subject-specific data, a reproducible method (similar to that used for PL) could be implemented to ensure consistency among subjects. In addition, only one loading condition has been tested. Although this represents an improvement of previous model (where analysis did not simulate real activities), external tibial torsion is not the only way that can lead to patella dislocation.

Lastly, as regards the classification model, only logistic regression has been used as a predictor model. In addition, although those five anatomical parameter are considered the main risk factors for patella dislocation, others can be added to train the model and evaluate eventual changes in the performance.

CHAPTER THREE: CONCLUSION

3.1 Summary

- The overall goal of this study was to create both a validated and reliable computational and classification model to predict risk of patellar dislocation. Subject-specific 3D models of the knee joint were created from MRI scans and dynamic simulations were performed. An automatic process for measuring anatomical factors was implemented and used to collect patients' data to train a logistic regression classification model. Key findings of the study were:
- Statistical analysis showed significant differences among groups for four out of five anatomical factors considered, indicating that the pathoanatomy is relevant for risk of dislocation.
- The computational model had an overall prediction accuracy of 88%, working particularly well when predicting no dislocation. In addition, the simulation is also able to provide additional information, including total force in the MPFL and contact force on patella cartilage which are good indicators of dislocation patterns.
- The logistic regression model had an overall prediction accuracy of 72% if trained with all the four significant parameter, performing worse than the FE model. However, after applying feature scaling and PCA, the performance improved up to 78%. Moreover, the computational cost is dramatically reduced when compared with the FE model.

- The automatic process of measuring of geometrical factors provided a repeatable way of collecting anatomical data, reducing the pre-processing time consumption and enabling to be consistent through subjects.

3.2 Limitations

There were some limitations are associated with the study. The dataset size was limited by the surgical information provided on the patients. Some of the subjects did not have either post-surgery scans or details about the surgery performed, so a complete pre- and post-operative dataset was not included for each patient. In addition, only MPFLR and trochleoplasty were considered as surgical options, as they were the only surgical procedures performed on the subjects available through our current dataset.

There are also some simplifications and limitations associated with the FE model. PL is the only soft tissue geometry for which an automatic alignment process has been implemented. Particularly, the post prominent point on the tibia (tibial tubercle) and lowest point on the patella are localized and used as the attachment site of the PL for each bone. MPFL and quadriceps are manually aligned based on bony landmarks. For this reason, the attachment site may vary from subject to subject, affecting the kinematic of the simulation and increasing the total time of the pre-processing (already affected by the manual segmentation of the scans). In addition, only one loading condition has been tested. Although this represents already an improvement of previous model (where analysis did not simulate real activities), external tibial torsion is not the only way that can lead to patella dislocation. Moreover, the joint kinematic profile was not collected on a subject-specific basis, but a general profile was created averaging data collected in previous experimental studies.

Lastly, as regards the classification model, only logistic regression has been used as a predictor model. In addition, although those five anatomical parameters are considered the main risk factors for patella dislocation, others can be added to train the model and evaluate eventual changes in the performance.

3.3 Future work

In order to expand the scope of this analysis to a more comprehensive assessment of potential surgical options, patients with TTO performed (which would significantly change the IS ratio and TT-TG distance values) should also be included.

As regards the FE model, the best solution for quadriceps alignment would be to obtain full lower limb scans of the subjects that would allow for identification of subject-specific muscle attachment sites at hip. Alternatively, in absence of subject-specific data, a reproducible method (similar to the one used for PL) could be implemented to be at least consistent among subjects. In addition, other activity potentially risky for patella dislocation could be simulated beside external tibia torsion or sensitivity analysis on other parameters beside the MPFL connector pre-tensioning force can be performed and classification performance compared with the original model.

Lastly, as regards the classification model, different approaches can be tested. Particularly, other classification models beside the logistic regression one can be tried or other anatomical parameters can be collected and used as training features.

3.4 Scientific contributions of this work

The computational model developed will allow surgeons to simulate virtual surgical planning with desired values for each of the anatomical factor, test the outcome, and establish the best surgical option on a subject specific base. The regression model represents a new and useful alternative, particularly efficient in terms of computational cost. To date and as far as known, it is the first study that applies a logistic regression model to predict risk of patella dislocation. The scientific contributions of this work is represented by:

- Poster presentation at the Orthopaedic Research Society (ORS) annual meeting in Tampa, FL (4th-8th of February 2022).
- In preparation: planned publication in *The American Journal of Sports Medicine*.

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