Unraveling Patellofemoral Pain: Subgroup Identification Through Biomechanical Analysis Leveraging Machine Learning and Wearable Sensors

University of Massachusetts Amherst

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Dissertation Proposal
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Dissertation Committee:
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- Wouter Hoogkamer, PhD
- Doug Martini, PhD
- Madalina Fiterau, PhD

Motivation

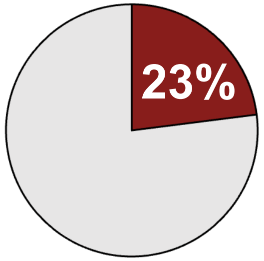
50 million
people in the US are runners

~50%
are injured each year

Patellofemoral pain
is one of the most common running related injury

Statista (2023), van Gent et al. (2007), Willy et al. (2019)

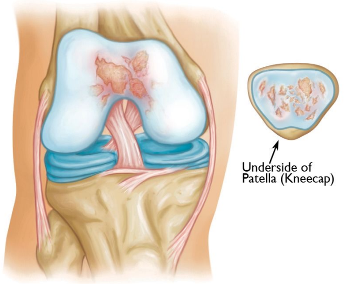
Patellofemoral Pain (PFP)



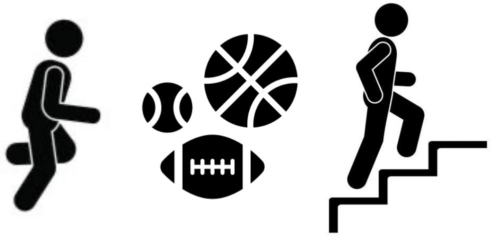
Estimated prevalence of ~23% in adult population

$ $

Substantial healthcare related costs



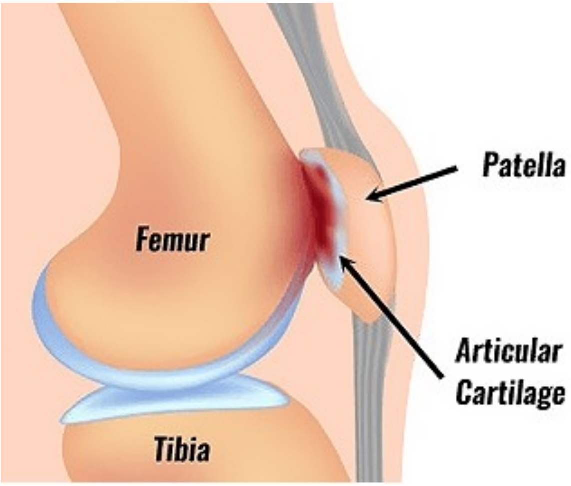
Potential precursor to patellofemoral arthritis



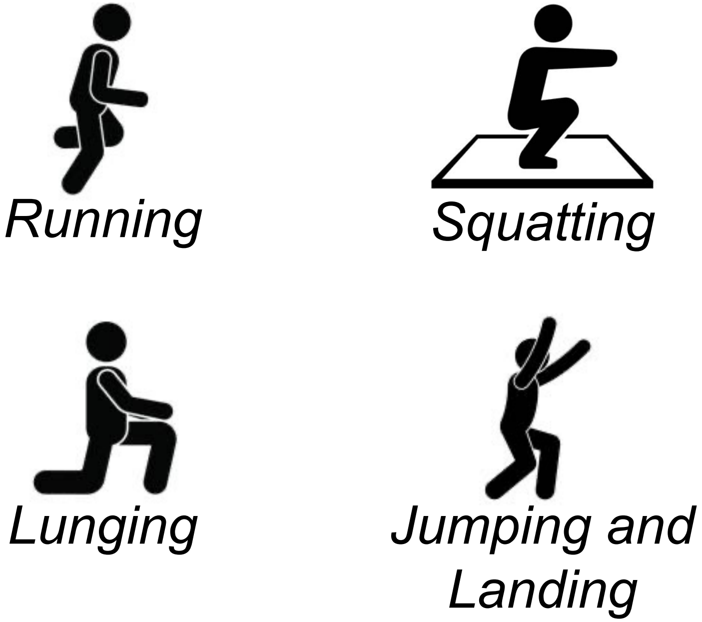
Prevents participation in sports and activities of daily living

Smith et al. (2018), Young et al. (2021), Utting et al. (2005), Willy et al. (2019)

Characterizing PFP



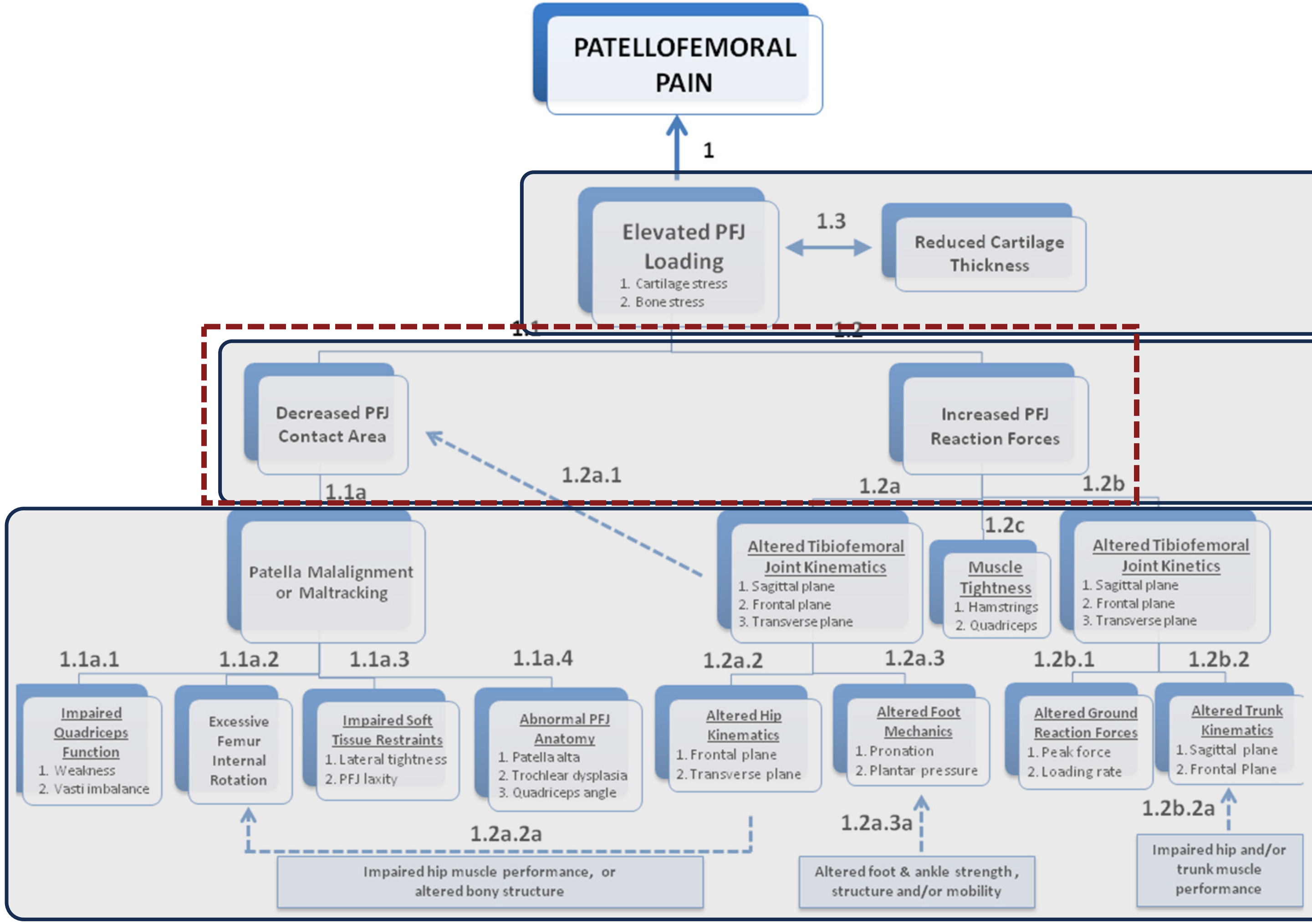
Characterized by achy or sharp pain around the patellofemoral joint



Pain is exacerbated by activities involving high levels of knee flexion

Willy et al. (2019), Taunton et al. (2002)

Pathomechanical Model



PFP is associated with elevated patellofemoral joint (PFJ) loading

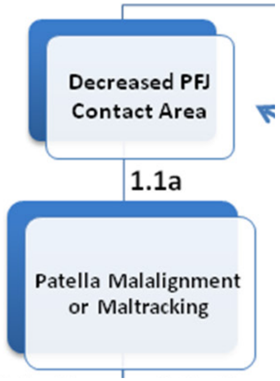
Two mechanisms:

1. Decreased PFJ contact area
2. Increased PFJ reaction forces

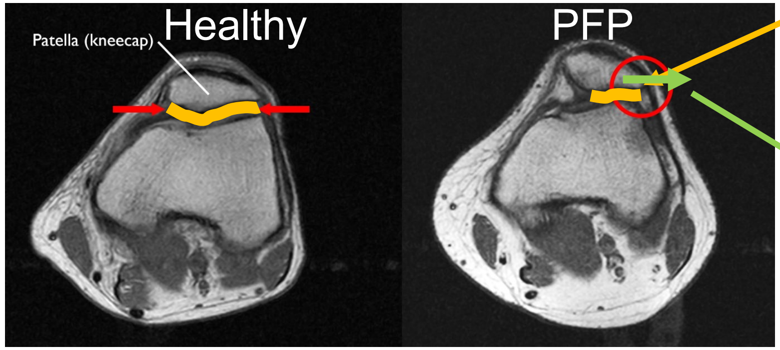
Several factors associated with mechanisms of PFP

Powers et al. (2017)

Mechanisms of PFP



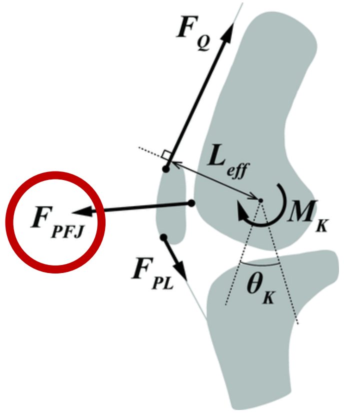
- **Contact area** describes the area of articulation between the patella and femur
- **Malalignment** is deviation of the patella from the trochlea of the femur



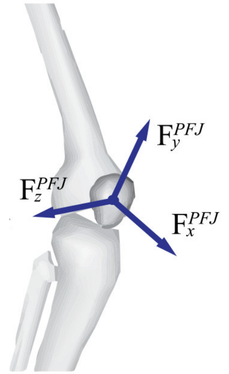
Decreased contact area

Lateral subluxation (malalignment)

Individuals with PFP exhibit decreased contact area and malalignment



Resultant reaction force



Reaction force components

Lower **resultant** contact force, but greater **lateral** component of contact force in individuals with PFP

Biedert & Gruhl (1997), Salsich & Perman (2013)

Chen & Powers (2014), Powers et al. (2017), Hart et al. (2022)

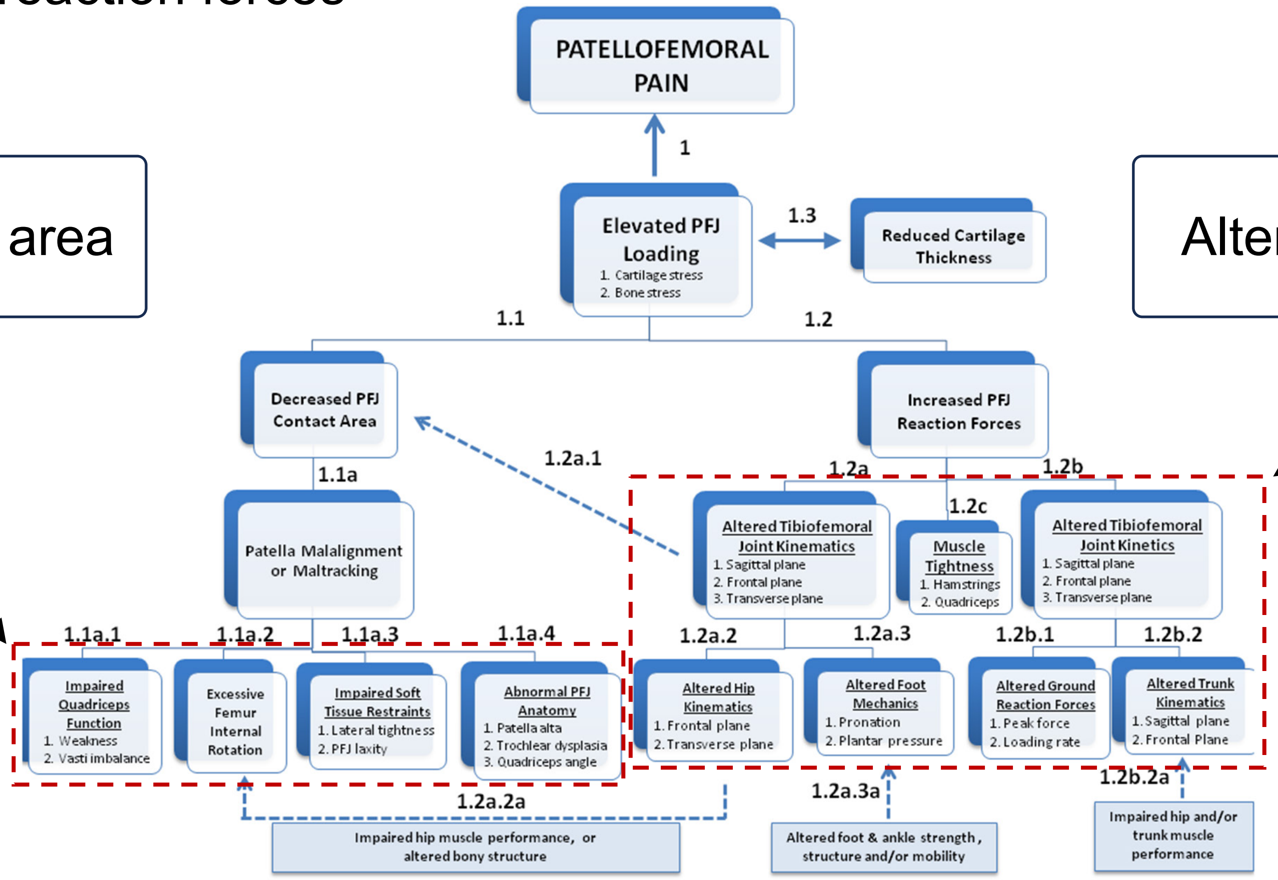
Biomechanical factors

Two mechanisms:

1. Decreased PFJ contact area (associated with malalignment)
2. Altered PFJ reaction forces

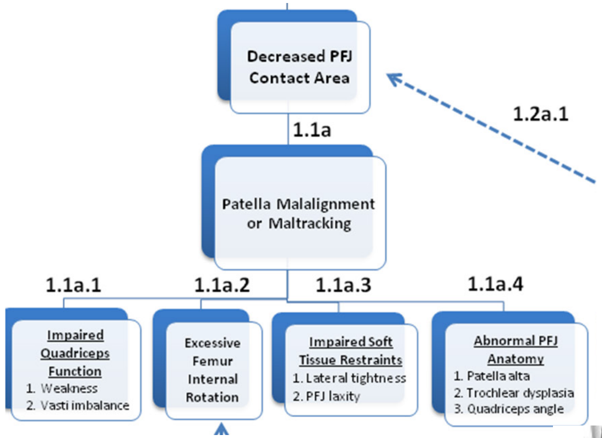
Decreased PFJ contact area

Altered PFJ reaction forces



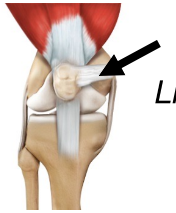
Powers et al. (2017)

Biomechanical factors



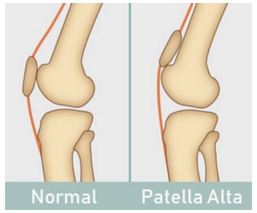
Impaired quadriceps function

Excessive femur internal rotation

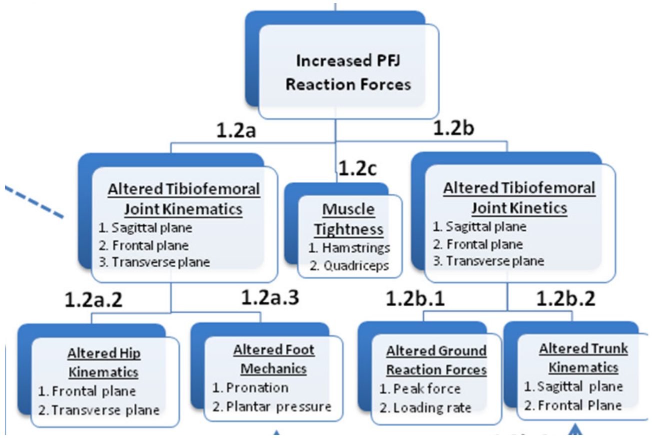


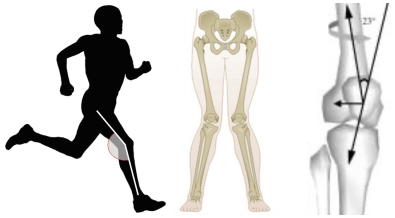
Medial Patellofemoral Ligament (MPFL)

Impaired soft tissue restraints

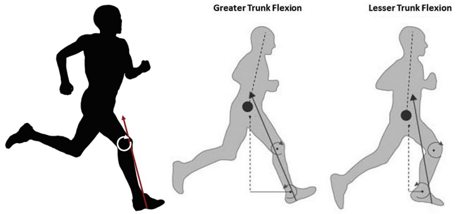


Abnormal PFJ anatomy

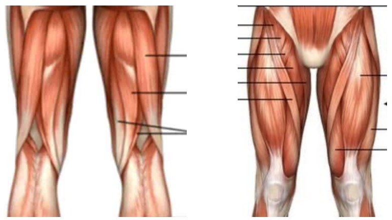




Altered tibiofemoral kinematics



Altered tibiofemoral kinetics



Hamstrings *Quadriceps*

Muscle tightness

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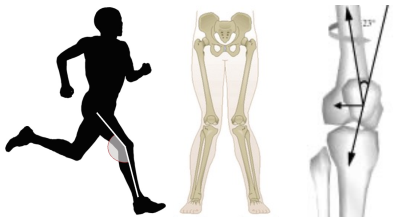
Hudson & Darthuy (2009), Lankhorst et al. (2012), Powers et al. (2017), Varadarajan et al. (2010), Barton et al. (2009), Bazzett-Jones et al. (2013), Powers (2010), White et al. (2009)

Biomechanical factors

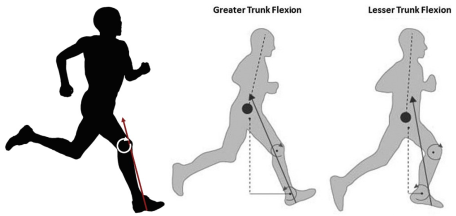
Individuals with patellofemoral pain may be experiencing **one or several** of these factors

Impaired quadriceps function

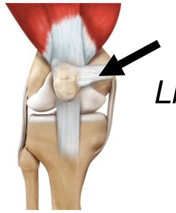
Excessive femur internal rotation



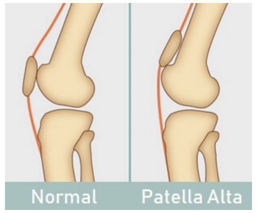
Altered tibiofemoral kinematics



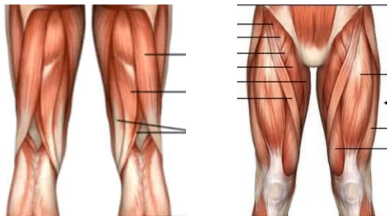
Altered tibiofemoral kinetics



Impaired soft tissue restraints



Abnormal PFJ anatomy



Muscle tightness

Hudson & Darthuy (2009), Lankhorst et al. (2012), Powers et al. (2017), Varadarajan et al. (2010), Barton et al. (2009), Bazzett-Jones et al. 2013, Powers (2010), White et al. (2009)

Inconsistent findings are common

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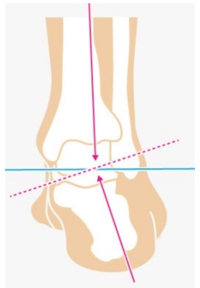
Excessive femur internal rotation

- PFP > Healthy (Souza & Powers 2009)
- PFP = Healthy (Wilson & Davis 2008)

Rearfoot eversion (pronation)



Right Foot

- PFP > Healthy (Barton et al. 2009)
- Not a risk factor for PFP (Noehren et al. 2013)

Knee extension moment

- PFP < Healthy (Chen & Powers 2014)
- PFP = Healthy (Besier et al. 2009)

Recent systematic review and meta-analysis

- Only found evidence of reduced knee flexion angles and knee extension moments (Bazett-Jones et al. 2022)

Inconsistent findings suggest patient or subgroup specific pain mechanisms

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Subgrouping

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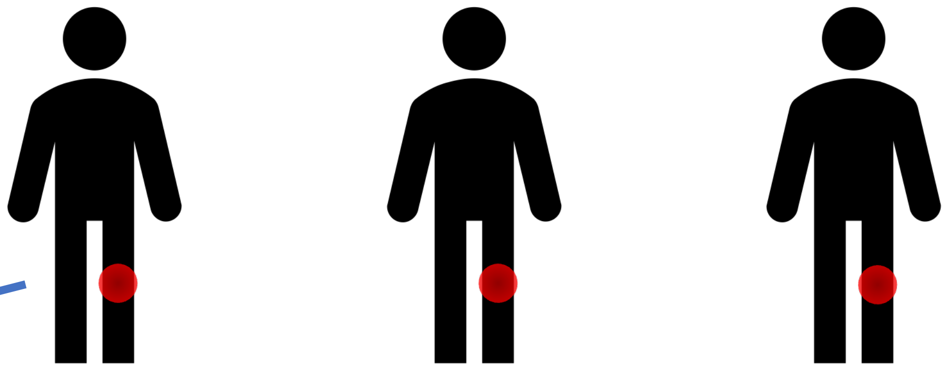
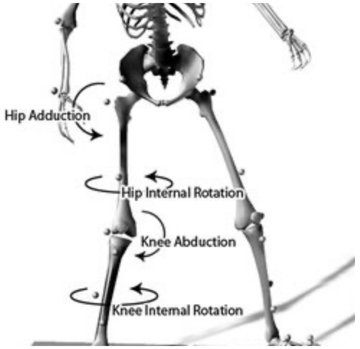


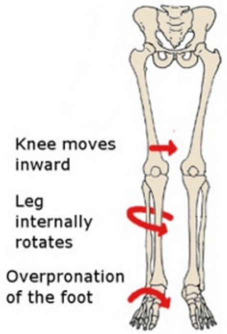
Three individuals with a general diagnosis of patellofemoral pain

Patient 1:
- Excessive femur internal rotation and hip adduction



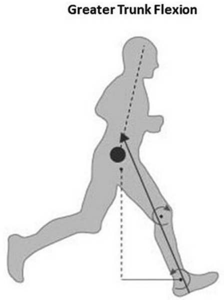
Altered tibiofemoral kinematics

Patient 2:
- Foot pronation and shank internal rotation



Altered tibiofemoral kinematics

Patient 3:
- Increased ground reaction forces and forward trunk lean



Altered tibiofemoral kinetics

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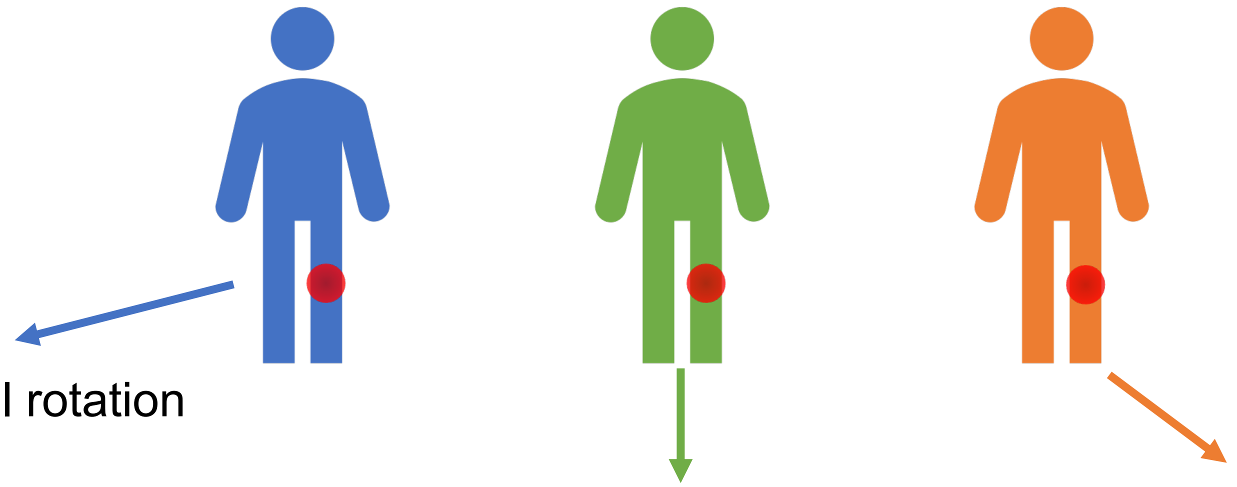
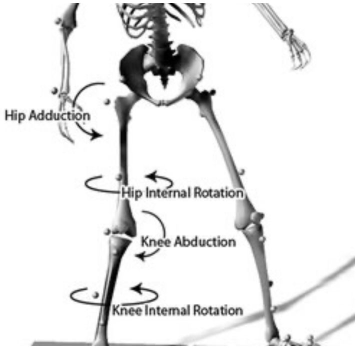
Neal et al. (2016), Souza et al. (2009), Barton et al. (2009), Powers (2003), Powers et al. (1999), Bazett-Jones et al. (2013)

Subgrouping



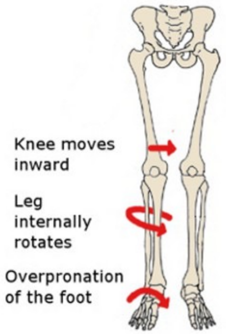
Subgroup specific diagnosis potentially leading to **targeted treatment**

Patient 1:
- Excessive femur internal rotation and hip adduction



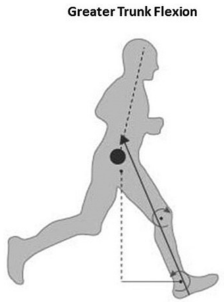
Altered tibiofemoral kinematics

Patient 2:
- Foot pronation and shank internal rotation



Altered tibiofemoral kinematics

Patient 3:
- Increased ground reaction forces and forward trunk lean



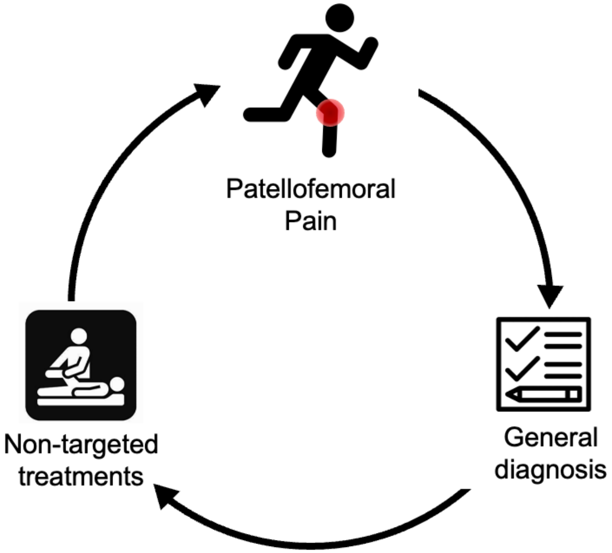
Altered tibiofemoral kinetics

Neal et al. (2016), Souza et al. (2009), Barton et al. (2009), Powers (2003), Powers et al. (1999), Bazett-Jones et al. (2013)

Current PFP treatment

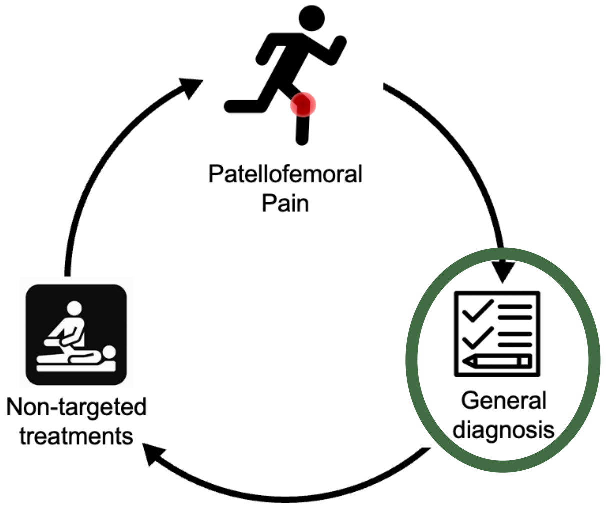
- **Current treatment options:**
  - Patellar taping
  - Physical therapy
  - Ice
  - Rest
  - Lowering training volume

- In many patients, treatments are not effective
  - High rate of recurrence → up to 94%
  - Poor patient reported outcomes



Willy et al. (2019), Sandow & Goodfellow (1994)

Targeted PFP treatment



Improve diagnoses by identifying factors leading to PFP

- ✓ Targeted treatment approaches
- ✓ More effective at mitigating PFP
- ✓ Improved patient outcomes
- ✓ Lower recurrence rates

A key first step for targeted treatment is **identifying subgroup specific factors leading to development of PFP**

Witvrouw et al. (2013), Selfe et al. (2018)

PFP Subgrouping

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Original article

OPEN ACCESS

Are there three main subgroups within the patellofemoral pain population? A detailed characterisation study of 127 patients to help develop targeted intervention (TIPPs)

James Selfe,[1] Jessie Janssen,[1] Michael Callaghan,[2] Erik Witvrouw,[3] Chris Sutton,[1] Jim Richards,[1] Maria Stokes,[4] Denis Martin,[5] John Dixon,[5] Russell Hogarth,[1] Vasilios Baltzopoulos,[6] Elizabeth Ritchie,[7] Nigel Arden,[8] Paola Dey[1]

Cli

Confident that subgroups exist

3. Weak and overpronated

Lower Extremity Kinematics in Runners with Patellofemoral Pain during a Prolonged Run

TRACY A. DIERKS[1], KURT T. MANAL[2], JOSEPH HAMILL[3], and IRENE DAVIS[2,4]

3. Other

[RESEARCH REPORT]

RESEARCH ARTICLE Open Access

No studies have identified subgroups during dynamic, pain exacerbating activities such as running using data driven approaches

Modifiable Clinical, Biomechanical, and Imaging Features

Ricky Watari[1,2], Sean T. Osis[1,3], Angkoon Phinyomark[4] and Reed Ferber[1,2,3,5*]

Clinical tests, imaging, biomechanics

1. Strong
2. Pronated and malaligned
3. Weak
4. Flexible

Pelvis acceleration

- Two female subgroups, but only one male subgroup

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Selfe et al. (2016), Drew et al. (2019), Dierks et al. (2011), Watari et al. (2018), Selfe et al. (2018)

Aim 1

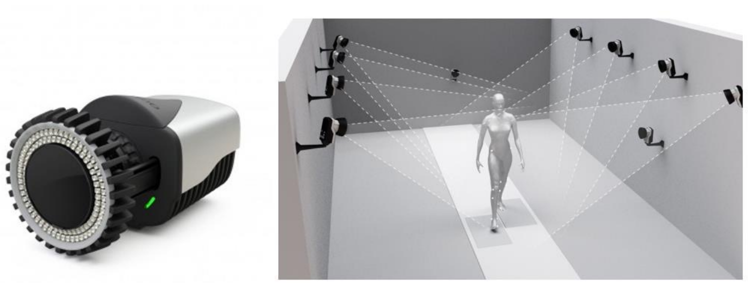
Abnormal running kinematics and kinetics are known to contribute to development of PFP, but the exact subgroup specific alterations are not well understood

Aim 1: Identify biomechanical clusters (i.e., subgroups) of individuals with PFP in a rested state with laboratory-based motion capture data.

Hypothesis 1.1: Distinct subgroups will exist based on three-dimensional kinematic and kinetic features of the injured limb during running.

Hypothesis 1.2: Clustering performance will improve with the inclusion of deep knee flexion activities such as squatting, lunging, and jumping.

Aim 2



Motion capture systems are not typically available in clinical settings

Inertial measurement units:

- Portable
- Cost-effective
- User-friendly

Aim 2: Determine if IMU-based features can be used to classify subgroups.

Hypothesis 2.1: IMU data from treadmill running will lead to a high classification accuracy (> 80%).

Hypothesis 2.2: Inclusion of IMU features from deep knee flexion tasks (squatting, lunging, and jumping) will improve classification accuracy.

Prolonged running

- Pain and fatigue inducing prolonged runs have been shown to impact biomechanics:
    - ↓ hip abductor and external rotator strength
    - ↑ foot eversion
    - ↑ shank internal rotation
    - ↑ knee external rotation
    - ↑ anterior pelvic tilt

Only evaluated running mechanics in a constrained environment (i.e., on a treadmill)

Dierks et al. (2008), Dierks et al. (2011), Noehren et al. (2012), Bazett-Jones et al. (2013)

Aim 3

The impact of prolonged running on overground running biomechanics is not known.

Aim 3.1: Quantify the impact of a prolonged run on unconstrained (overground) kinematics and kinetics in all individuals with PFP.

Hypothesis 3.1.1: Several key kinematic and kinetic variables will change during overground running following a prolonged running bout.

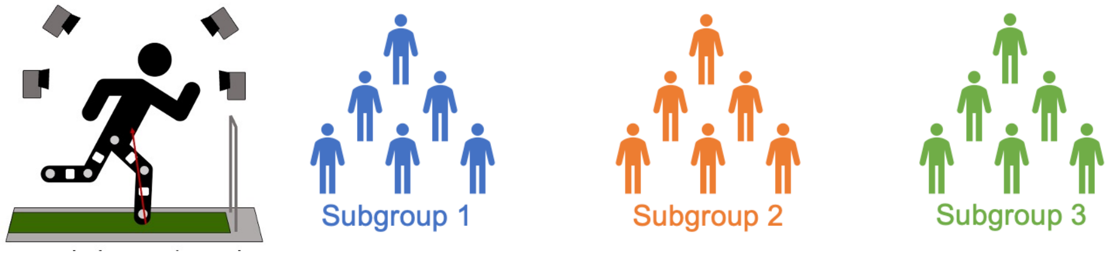
Hypothesis 3.1.2: Knee extension moments, a variable quantifying loading of the knee joint, will be associated with subjective pain scores.

Important to understand if identified subgroups change following a prolonged run.

Aim 3.2: Quantify the impact of a prolonged run on unconstrained (overground) kinematics and kinetics in identified subgroups.

Hypothesis 3.2.1: Subgroup specific kinematic and kinetic adaptations will be observed, but the exact subgroup specific adaptations cannot be hypothesized without knowledge of the subgroups.

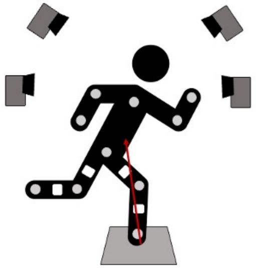
Aim 1: Identify subgroups of individuals with kinematic and kinetic running features



Aim 2: Evaluate if IMUs can accurately classify the identified subgroups with supervised models

Clinically translatable

Aim 3: Quantify the impact of a prolonged run on unconstrained (i.e., overground) running



Changes in all PFP?

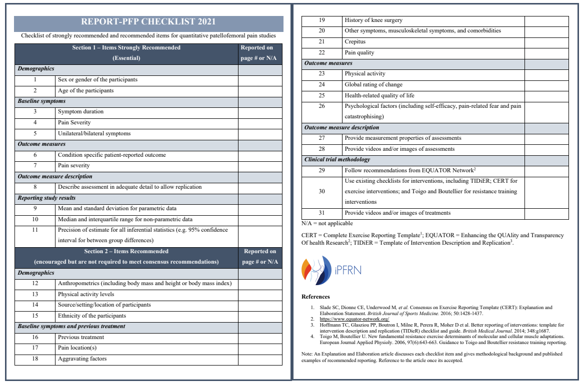
Changes in subgroups?

Participants

- 40 individuals with a diagnosis of patellofemoral pain
  - Equal split between males and females
  - No other musculoskeletal injuries
- Age range: 18 – 40
  - Upper range limits potential joint damage or arthritis
- Physically active
  - Must be able to run on a treadmill and complete deep knee flexion activities

Forms and Instrumentation

- Forms:
  - Informed consent
  - Physical activity and readiness questionnaire
  - iPFRN questionnaire



REPORT-PFP CHECKLIST 2021

Checklist of strongly recommended and recommended items for quantitative patellofemoral pain studies

Section 1 – Items Strongly Recommended (Essential)		Reported on page # or N/A
Demographics		
1	Sex or gender of the participants	
2	Age of the participants	
Baseline symptoms		
3	Symptom duration	
4	Pain Severity	
5	Unilateral/bilateral symptoms	
Outcome measures		
6	Condition specific patient-reported outcome	
7	Pain severity	
Outcome measure description		
8	Describe assessment in adequate detail to allow replication	
Reporting study results		
9	Mean and standard deviation for parametric data	
10	Median and interquartile range for non-parametric data	
11	Precision of estimate for all inferential statistics (e.g. 95% confidence interval for between group differences)	
Section 2 – Items Recommended (encouraged but are not required to meet consensus recommendations)		**Reported on page # or N/A**
Demographics		
12	Anthropometrics (including body mass and height or body mass index)	
13	Physical activity levels	
14	Source/setting/location of participants	
15	Ethnicity of the participants	
Baseline symptoms and previous treatment		
16	Previous treatment	
17	Pain location(s)	
18	Aggravating factors	
19	History of knee surgery	
20	Other symptoms, musculoskeletal symptoms, and comorbidities	
21	Crepitus	
22	Pain quality	
Outcome measures		
23	Physical activity	
24	Global rating of change	
25	Health-related quality of life	
26	Psychological factors (including self-efficacy, pain-related fear and pain catastrophising)	
Outcome measure description		
27	Provide measurement properties of assessments	
28	Provide videos and/or images of assessments	
Clinical trial methodology		
29	Follow recommendations from EQUATOR Network[2]	
30	Use existing checklists for interventions, including TIDiER; CERT for exercise interventions; and Toigo and Boutellier for resistance training interventions	
31	Provide videos and/or images of treatments	

N/A = not applicable

CERT = Complete Exercise Reporting Template[1]; EQUATOR = Enhancing the QUAlity and Transparency Of health Research[2]; TIDiER = Template of Intervention Description and Replication[3].

iPFRN

References

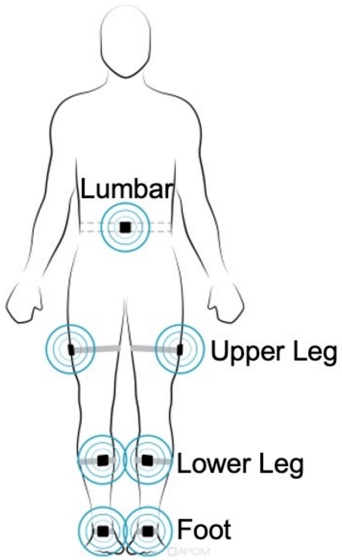
1. Slade SC, Dionne CE, Underwood M, *et al.* Consensus on Exercise Reporting Template (CERT): Explanation and Elaboration Statement. *British Journal of Sports Medicine.* 2016; 50:1428-1437.
2. https://www.equator-network.org/
3. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *British Medical Journal.* 2014; 348:g1687.
4. Toigo M, Boutellier U. New fundamental resistance exercise determinants of molecular and cellular muscle adaptations. European Journal Applied Physioly. 2006, 97(6):643-663. Guidance to Toigo and Boutellier resistance training reporting.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of recommended reporting. Reference to the article once its accepted.

International Patellofemoral Pain Research Network Questionnaire

- Participant instrumentation:
  - 42 retroreflective markers
  - 7 IMUs (Opal – APDM)

Markers



IMUs

Jewell (2018)

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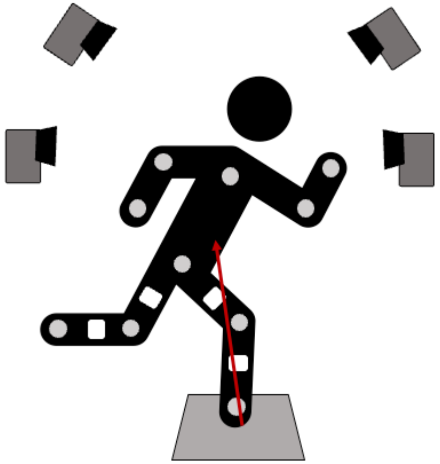
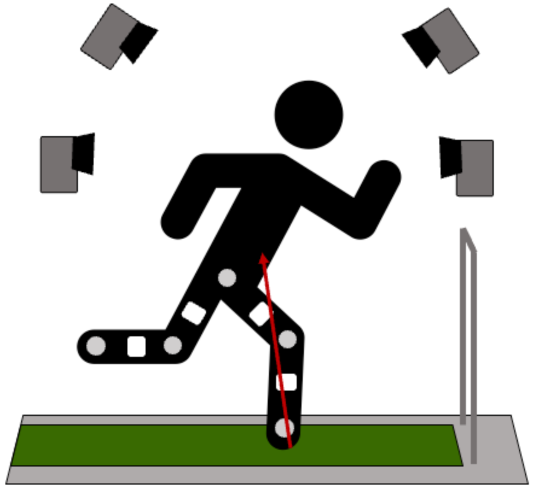
Protocol

Overground



- Running
  - Preferred and set speeds
- Squatting
- Lunging
- Counter movement jump

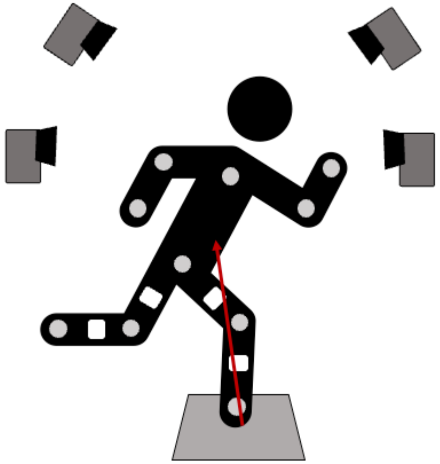
21 Minute Treadmill Run



Data recorded every two minutes:

- Marker trajectories
- Ground reaction forces
- IMU signals
- Self-reported pain (0-10)
- RPE

Overground



- Repeat all activities from before the prolonged treadmill run

Hardware

- Qualysis Track Manager (QTM)
  - Marker trajectories (128 Hz)
  - Force data (1920 Hz)
- Moveo Explorer
  - Angular velocity
  - Linear acceleration
- QTM and Moveo Explorer will be synced with a 5-volt TTL pulse

Data Processing

Track all marker data in QTM

Calculate kinematics and kinetics with Visual 3D

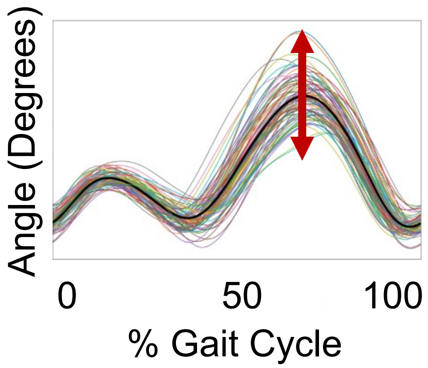
Export angular velocity and linear acceleration data with Moveo Explorer

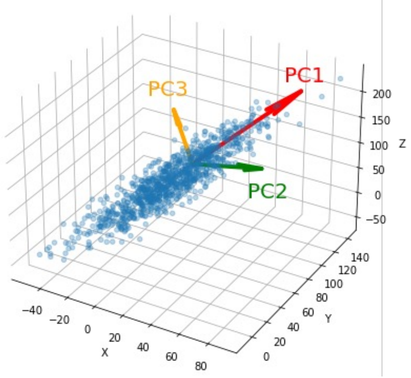
All further analysis in Python

Data Reduction

Kinematic and kinetic variables:

- Foot eversion
- Shank rotation
- Knee angles (3 planes)
- Hip adduction and rotation
- Femur rotation
- Pelvis orientation (3 planes)
- Knee flexion moment
- Hip flexion moment





Principal Component Analysis

- *Reduce kinematic and kinetic waveforms*

101 data points → 3-4 data points explaining majority of variance

Aim 1: Subgroup identification through clustering

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- PC scores from selected variables will be concatenated into one matrix:
  - Each row represented a single stride
  - Each column represents a single PC

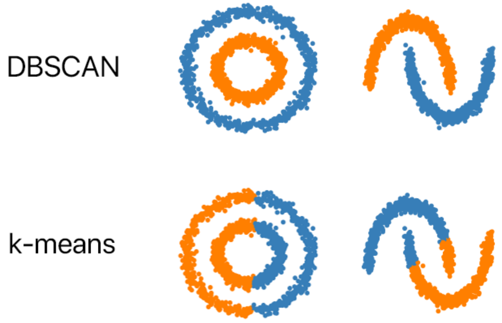
Participant ID	Stride #	KFA PC_1	KFA PC_2	KFA PC_3	KAA PC_1	KAA PC_2	KAA PC_3	…	AIA PC_3
P001	1	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P001	2	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P001	3	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
…	…	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P002	1	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P002	2	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P002	3	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
…	…	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P040	3199	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P040	3200	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score

~3200 strides

~50 features

- PC scores will be fed into a clustering model (DBSCAN)

- Why DBSCAN?
  - Can find clusters of arbitrary shapes
  - Robust to noise and outliers
  - Doesn't require input of number of clusters



- Subgroups will be characterized by comparing PC scores of kinematic and kinetic variables:
  - 2 subgroups: t-tests
  - >2 subgroups: ANOVA with post-hoc testing where appropriate
  - Significance level: $p = 0.05$

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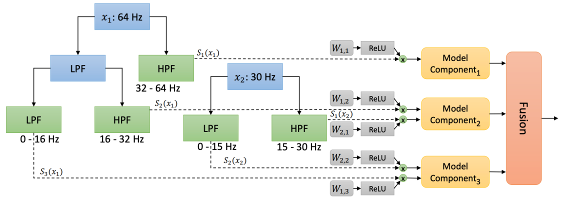
Ester et al. (1996)

Aim 2: Subgroup classification with IMUs

- Now that there are labels assigned to data points, supervised methods can be used to classify subgroups

- IMU signals will act as input data

Population with labels from mocap



Train and test supervised model with IMU data

Classify into subgroups

- Evaluate model performance with accuracy, precision, recall, etc.
- Optimize input features by maximizing classification accuracy

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Deznabi & Fiterau (2023)

Aim 3: Quantifying the impact of a prolonged run

Kinematic and kinetic variables:

- Foot eversion
- Shank rotation
- Knee angles (3 planes)
- Hip adduction and rotation
- Femur rotation
- Pelvis orientation (3 planes)
- Knee flexion moment
- Hip flexion moment

Aim 3.1

All participants

- Compare variables from before to after treadmill run with paired sample t-tests
- Significance level: $p = 0.05$

Aim 3.2

- Compare change scores ($\Delta_{PC\ Score}$) between subgroups

$$\Delta_{PC\ Score} = PC\ Score_{Post} - PC\ Score_{Pre}$$

- 2 subgroups: t-tests
- >2 subgroups: ANOVA with post-hoc testing where appropriate
- Significance level: $p = 0.05$

Review and Summary

- Patellofemoral pain is a common musculoskeletal condition with multiple mechanisms
- Determining subgroups of people with PFP and the associated biomechanical factors leading to pain remains a paramount goal
- We are confident that subgroups exist based on results of previous studies
- Identifying subgroups with data driven approaches using running biomechanical data has not yet been explored (*aim 1*)
- Clinically translatable subgroup identification systems could improve the diagnostic process and inform targeted treatments (*aim 2*)
- The impact of prolonged running on unconstrained running mechanics is not well understood (*aim 3*)

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  - Doug Martini, PhD
  - Madalina Fiterau, PhD




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- Kinesiology Faculty and Grad Students
- Front office staff
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Questions?

University *of* Massachusetts Amherst

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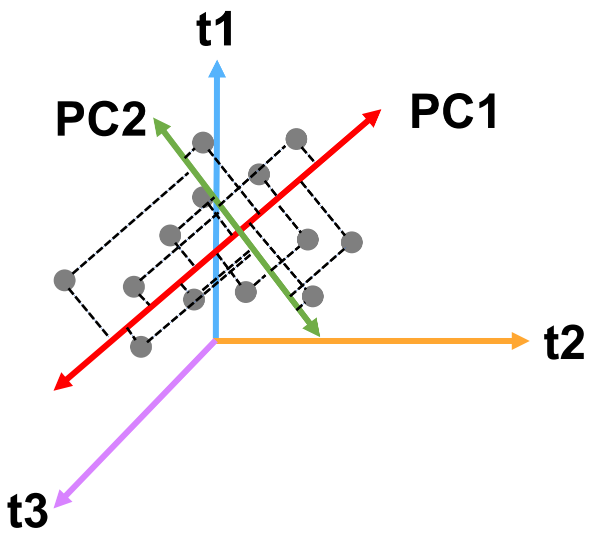
Principal Component Analysis

~3200 observations

Observation #	t1	t2	t3	…	t101
1	Datapoint	Datapoint	Datapoint	…	Datapoint
2	Datapoint	Datapoint	Datapoint	…	Datapoint
3	Datapoint	Datapoint	Datapoint	…	Datapoint
…	Datapoint	Datapoint	Datapoint	…	Datapoint
3200	Datapoint	Datapoint	Datapoint	…	Datapoint

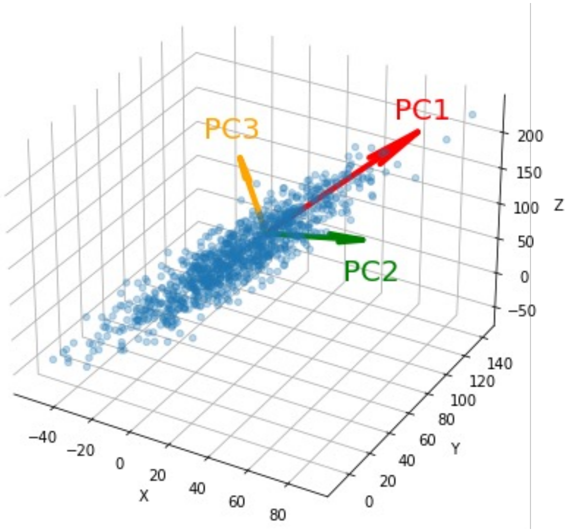
101 timepoints



Observation #	PC1	PC2	PCN
1	PC Score	PC Score	PC Score
2	PC Score	PC Score	PC Score
3	PC Score	PC Score	PC Score
…	PC Score	PC Score	PC Score
3200	PC Score	PC Score	PC Score

PCs collectively explain 90% of variance

Original Waveform = $A PC_1 + B PC_2 + \ldots + X PC_N$



Sample size estimation

- Power analysis showed that sample size of n=10 should be sufficient to see statistical differences and large effect sizes
- We expect to find 2-3 subgroups:
  - 13 – 20 individuals per subgroup

Variable	Sample Size Estimation
Hip internal rotation angle	16 per group
Contralateral pelvic drop	11 per group
Knee adduction angle	11 per group

Sample size estimations based on kinematic variables

*G*Power*

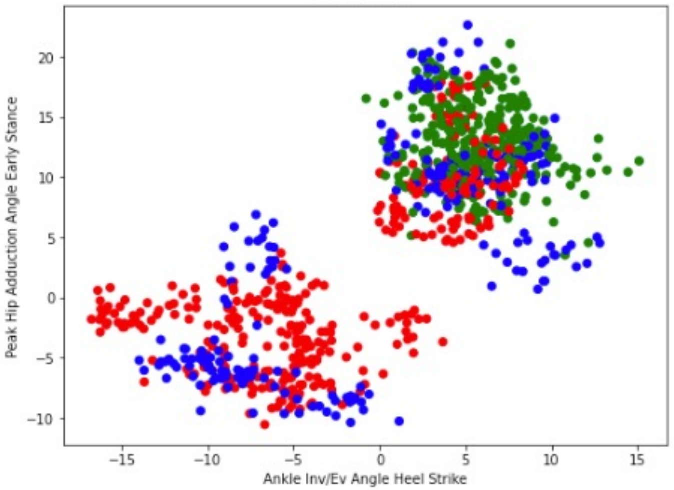
Pilot analysis

- Treadmill running kinematics for 3 groups:
  - Healthy
  - Currently experiencing PFP
  - Recovered from PFP

Healthy

Injured

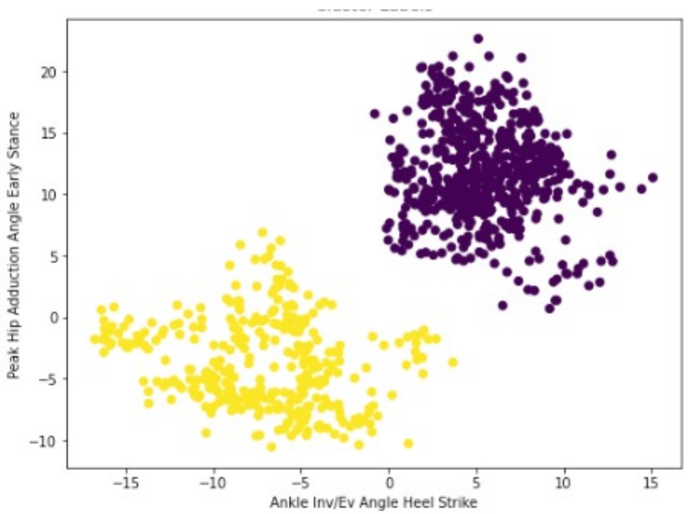
Recovered



Clustered groups

Subgroup 1

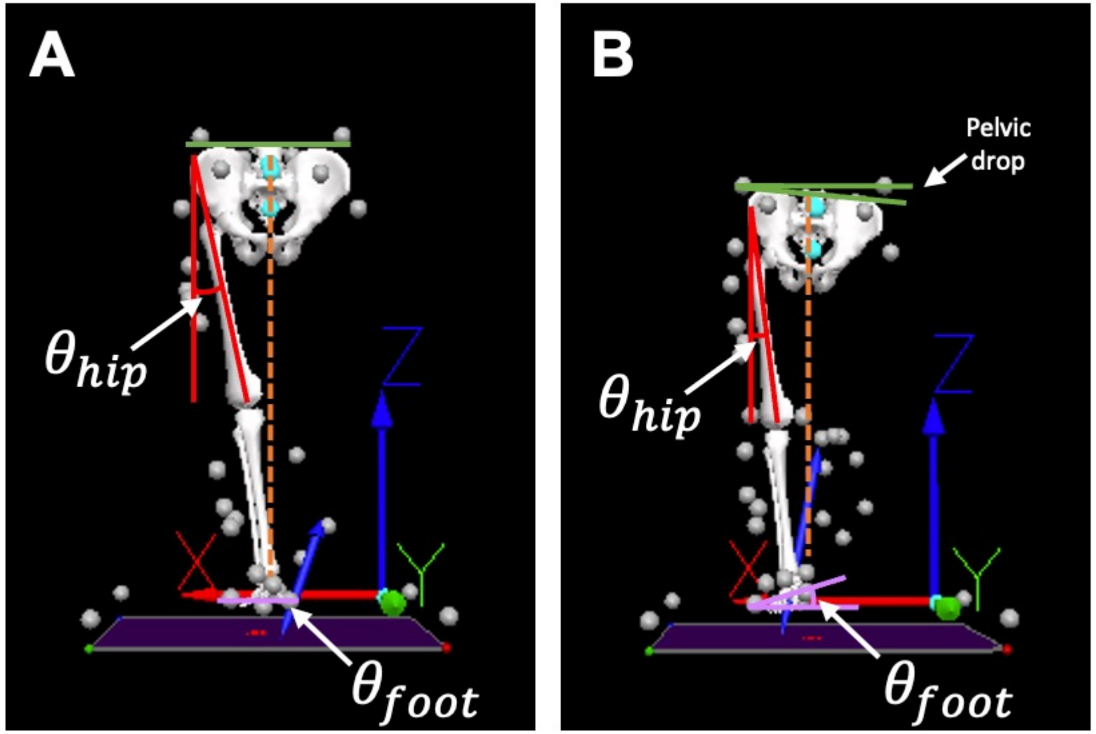
Subgroup 2



Identified two distinct subgroups with kinematic features

1. Extracted only the injured runners from two subgroups
2. Classified two subgroups with ~95% accuracy using IMU data

Subgroup visualization



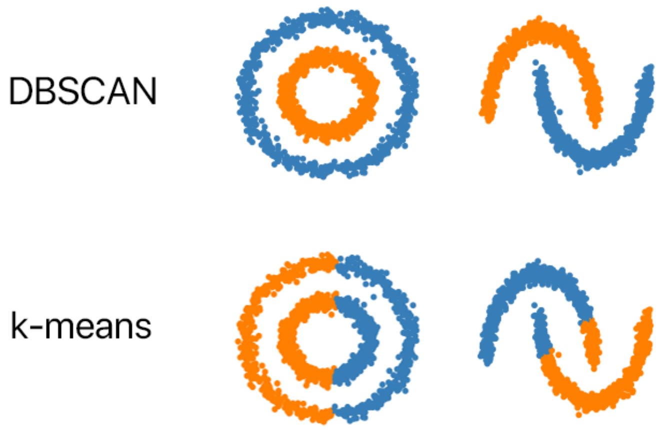
Models of two separate individuals with patellofemoral pain at foot strike

Altered tibiofemoral kinematics through two distinct pathways:

- Subject A:
  - Larger hip adduction angle (θ_{hip})
  - Increased foot pronation (θ_{foot})
  - Less contralateral pelvic drop
  - Distal pathway?
- Subject B
  - Smaller hip adduction angle (θ_{hip})
  - Less foot pronation (θ_{foot})
  - Greater contralateral pelvic drop (pelvic drop)
  - Proximal pathway?

Clustering algorithms

- **DBSCAN**
  - Clusters are identified by dense regions separated by areas of lower density
  - Can find clusters of arbitrary shapes
  - Robust to noise and outliers
  - Doesn't require input of number of clusters
- **K-Means**
  - Centroid based clustering algorithm
  - Assumes clusters are spherical
  - Required input of number of clusters



Feature selection for subgrouping (aim 1)

- 50 features may not be necessary to identify clusters or subgroups
- Test several feature combinations to maximize silhouette score
    - Silhouette score is a measure of cohesion or similarity between groups

Participant ID	Stride #	KFA PC_1	KFA PC_2	KFA PC_3	KAA PC_1	KAA PC_2	KAA PC_3	…	AIA PC_3
P001	1	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P001	2	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P001	3	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
…	…	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P002	1	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P002	2	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P002	3	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
…	…	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P040	3199	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score
P040	3200	PC Score	PC Score	PC Score	PC Score	PC Score	PC Score	…	PC Score

May not need all features to effectively identify subgroups

Dimensionality reduction for visualization

- Dimensionality reduction projects data into lower dimensional space while retaining the same patterns within the data
- **t-sne:**
  - t-distributed stochastic neighborhood embedding
  - Helpful for visualizing clusters of highly dimensional data

Image credit

https://orthoinfo.aaos.org/en/diseases--conditions/patellofemoral-arthritis/

https://orthoinfo.aaos.org/en/diseases--conditions/patellofemoral-pain-syndrome/

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