# Identification of Osteoarthritis Kinematic Phenotypes Using Cluster Analysis on Knee Kinesiography Data

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***Abstract*—Previous studies highlight that identifying phenotypes is crucial for developing effective treatments for knee osteoarthritis (OA). This study aims to identify kinematic phenotypes in a knee OA population and characterize them by patient biomechanical markers which are functional parameters used in clinical settings. Knee kinematics are measured using the KneeKG® (Knee Kinesiography) system, a technology that objectively assesses 3D knee kinematics. Kinematic data were categorized into homogeneous groups using a clustering process with a discriminant model called Balanced Iterative Reducing and Clustering using Hierarchies (BIRCH). We identified five distinct phenotypes, exhibiting significant statistical differences ($p < 0.05$) in 3D kinematics, and linked these phenotypes to biomechanical markers measurable in clinical settings.**

***Keywords—knee oesteoarthritis, gait analysis, phenotype, cluster analysis, kinematic data***

## I. INTRODUCTION

Knee osteoarthritis (OA) is a complex disease with multifactorial causes, making treatment approaches to reduce pain and improve quality of life challenging. One of the reasons regularly brought up is the very high inter-individual variability in this population [1]. As a result, an increasing number of studies are seeking to define phenotypes. For instance, phenotype definition has been based on anatomical/structural information obtained by imaging [2], on biological information [3] and/or musculoskeletal information [4]. To our knowledge, there is currently no phenotype based on kinematic information within the OA population.

Biomechanical markers derived from kinematic curves such as flexion/extension, abduction/adduction, and external/internal rotation, are increasingly recognized to be risk factors for disease progression in knee OA [5]. These markers are not only associated with pain [6], but they are also sensitive to clinical improvement following targeted exercise [7]. Therefore, they could have a high potential to guide physical therapy for patients who will not undergo total knee replacement. Furthermore, they could be a helpful tool to individualize the approach to total knee replacement for surgical planning. To measure biomechanical markers, we can use the KneeKG® system that was designed to objectively measure parameters in a three-dimensional (3D) dynamic, weight-bearing context and in a clinical setting [8]. A number of medium to large cohort studies or randomized controlled trial (RCT) [9] have been conducted in the past years using the KneeKG®, providing us with data suited for clustering approaches.

Early diagnosis of knee OA and the implementation of an effective procedure to monitor its progression are still challenging. While previous research [10]–[13] have reported phenotypes identification as a critical and important step in the development of treatment for the knee OA, no study has yet fully investigated such identification among knee OA population using kinematic parameters. To propose clinical meaningful OA phenotype, van Spil et al. [14] have investigated a consensus-based framework designed with a panel of 25 members selected encompassing an array of expertise in OA related topics, career stages, and geographical origins. Among their recommendations, they claim that OA classification systems should include measures from more than one domain. Thus, the phenotypes should be different in terms of clinically relevant variables. They also highlighted the importance of data-driven approaches (over expert opinion approaches), as long as these data are of high quality, have a clinical meaning and are reproducible. Our study is in line with the idea of including measures from more than one domain and represents a first step towards a general characterization of the phenotypes. Its main contribution is to develop a new methodology (1) To identify kinematic phenotypes within a knee OA population and (2) To link these phenotypes to biomechanical markers measured in clinical settings. The proposed approach uses the kinematics curves (flexion/extension, abduction/adduction, and tibial

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internal/external rotation) measured via the KneeKG® system during a gait task, providing practical clinical insights into OA classification. These kinematic data represent the knee movement in three dimensions. Clusters are characterized in terms of demographic and biomechanical markers.

## II. Methods

The methodology used to identify kinematic phenotypes is summarized in Fig. 1. It involves (1) data collection and (2) data standardization, (3) clustering for phenotypes identification, (4) phenotype validation and (5) phenotype characterization (interpretation and description). The following subsections describe these steps including the measurement device.

### A. Knee Kinesiography System

The measurement device is a tool labelled KneeKG® (Emovi Inc., Canada). It stands for Knee Kinesiography and utilizes a knee marker attachment system designed to reduce skin-motion artifacts [15]. The KneeKG® aims at assessing knee kinematics in order to identify biomechanical risk factors related to OA progression (Fig. 2). It comprises a set of trackers fixed on the KneeKG®, an infrared camera (Polaris Spectra, Northern Digital Inc., Quebec, Canada) providing 3D positions of the trackers at a rate of 60 Hz, and a computer equipped with the KneeKG® software suite (Emovi, Inc.) storing data points for each gait cycle in three dimensions [8]. The reliability and accuracy of the KneeKG® system have been investigated [15].

### B. Datasets

This study is a secondary analysis of a large randomized controlled trial (RCT; ISRCTN16152290) conducted between the years 2015 and 2019 on OA patients who were not on a waiting list for a total knee replacement. Patients were enrolled if they reported pain $\geq 4/10$ on a numerical scale and had a confirmed knee OA graded 2 or more according to the Kellgren-Lawrence (KL) radiographic severity scale [16]. Details related to this RCT, including the sample size and the inclusion and exclusion criteria, can be found in [9]. The protocol of this previous study was approved by the research ethics boards of the École de Technologie Supérieure (No: H20150505) and the Centre Hospitalier de l'Université de Montréal (No: CE.14.339). For this present study, a second approbation was granted by these ethical committees in order to access the database (subsequent use of secondary data).

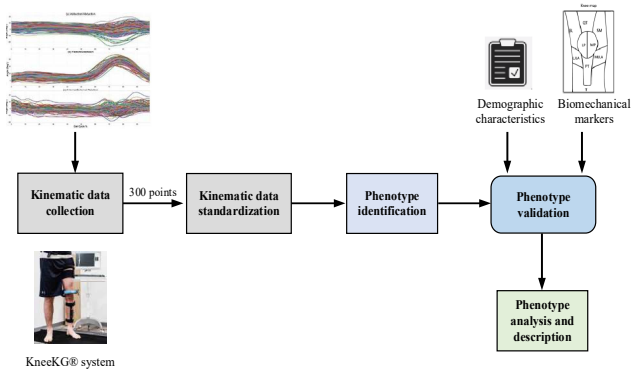


Fig. 1. Block diagram of the adopted methodology.

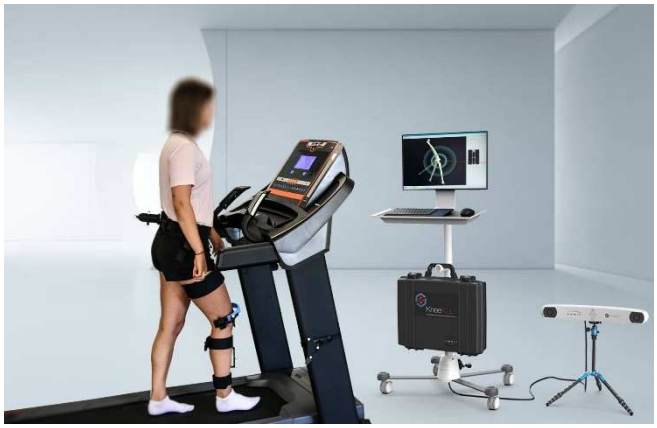

Fig. 2. Knee Kinesiography (KneeKG®) system.

### C. Data Standardization

The delineation of each gait cycle's beginning and end is determined based on the flexion/extension signal plan, with equivalent points identified in the adduction/abduction and internal/external rotation signals. Each gait cycle is normalized to range from 1% to 100% of the gait cycle for each kinematic dimension. For each patient, approximately 15 representative cycles are extracted from the flexion/extension signal to establish a median pattern for this specific movement. Subsequently, matching cycles are identified within the adduction/abduction and internal/external rotation signals, aligning with the cycles chosen for the flexion/extension analysis. This approach guarantees that the median patterns derived for the adduction/abduction and internal/external rotation movements are based on the identical representative cycles as those selected for the flexion/extension. Consequently, this methodology yields a total of 300 measurement points, distributed evenly across the three kinematic dimensions—flexion/extension, adduction/abduction, and internal/external rotation—with each dimension contributing 100 points. We standardize the data using a scaling technique where the values are centered around the mean with a unit standard deviation. Indeed, the recorded data are heterogeneous (i.e., range at different scales) since the knee' movement amplitude in 3D is different according to the movement plane (sagittal, frontal, and transverse).

TABLE I. Biomechanical Markers (B1 to B12) Used in Clincal Settings

| | | | |
|---|---|---|---|
| **Calibrate parameter** | | B1 | Varus functional lower limb alignment |
| **Gait Phases** | **at initial contact** | B2 | Varus alignment |
| | | B3 | Knee flexum |
| | | B4 | External tibia rotation |
| | **during loading** | B5 | Varus thrust |
| | | B6 | Valgus thrust |
| | | B7 | Limited flexion excursion |
| | | B8 | Internal tibia rotation |
| | **during stance** | B9 | Varus alignment |
| | | B10 | Fixed flexion |
| | **during swing** | B11 | Decreased maximum flexion |
| | **during all gait phases** | B12 | Decreased sagittal plane range of motion |

### D. Biomechanical Markers

The biomechanical markers are parameters routinely extracted and assessed in clinical biomechanical studies involving knee OA population, as summarized in Table I.

### E. Cluster Analysis for Phenotype Identification

Based on the measurement points of all patients, we perform a clustering in order to identify homogeneous groups that have similar features. Once the groups formed, the mean patterns (average of the kinematic curves within each homogeneous group) are computed to obtain the knee kinematic phenotypes. In this paper, groups also refer to clusters or phenotypes.

*1) Clustering model:* We apply a hierarchical clustering algorithm named Balanced Iterative Reducing and Clustering using Hierarchies (BIRCH) [17]. The main advantage of BIRCH is its ability to incrementally and dynamically cluster incoming multi-dimensional data in an attempt to produce the best quality clustering. This is suitable for kinematic data and offers the opportunity to perform clustering in case of high dimensional data. Moreover, BIRCH can find high-quality clustering with only a single scan of a dataset and can efficiently handle noise caused by the kinematic data variability [18].

*2) Optimum number of clusters:* The optimum number of clusters or groups is determined using Elbow method which is one of the most common and technically robust approaches. In this method, the sum of distances of observations from their cluster centroids, called Within-Cluster-Sum-of-Squares (WCSS), is computed. Plotting WCSS against increasing k (number of clusters) can show an 'elbow' which demarks significant drop-in rate of increase. The optimal number of groups corresponds to an elbow point which achieves reasonable performance without having too many groups.

*3) Cluster evaluation:* The clustering model is evaluated using the intra-class correlation coefficient (ICC), which informs how similar elements in the same cluster are. It provides a measure of homogeneity within the clusters. The values of ICC range from 0 to 1. A very small value for ICC implies that the within-cluster variance is much greater than the between-cluster variance, and an ICC of 0 shows that there is no correlation within a cluster.

### F. Phenotype Validation and Characterization

We validate the identified phenotypes by utilizing the 1D statistical parametric mapping (SPM). SPM is increasingly employed for continuum data (e.g., kinematic data) by the biomechanics research community to assess the overall difference on each plane through a complete gait cycle [19].

TABLE II. INTRA-CLUSTER CORRELATION COEFFICIENT (ICC) WITHIN EACH GROUP (G1 TO G5)

| | G1 | G2 | G3 | G4 | G5 |
|---|---|---|---|---|---|
| **Flexion/Extension** | 0.43 | 0.44 | 0.35 | 0.3 | 0.37 |
| **Abduction/Adduction** | 0.66 | 0.62 | 0.62 | 0.62 | 0.66 |
| **Rotation** | 0.48 | 0.53 | 0.61 | 0.54 | 0.29 |

This statistical analysis aims to compare the identified phenotypes in order to confirm that they are indeed different. To characterize the different phenotypes, we perform a Chi-square and analysis of variance (ANOVA) tests to assess between-groups differences in terms of: (i) demographic characteristics (age, sex, BMI) and (ii) biomechanical markers, described in Table I, which are a set of 12 kinematic parameters used in clinical settings by the KneeKG® system.

## III. RESULTS

Numerical simulations were conducted with Python 3.7 (standard scientific and visualization packages: sklearn 0.24.2, matplotlib 0.99). The optimum number of groups is fixed to five via the Elbow method, which utilizes Within-Cluster-Sum-of-Squares. The resulting clusters (G1 to G5) are verified using the intra-cluster correlation coefficient (ICC), with Table II detailing ICC values ranging from 0.29 to 0.66. This indicates a significant correlation among knee kinematic curves within each group.

### A. Identified Phenotypes

The identified phenotypes are described in Fig. 3. Five phenotypes are obtained by averaging the 3D kinematic curves within each homogeneous group identified by the BIRCH clustering. The number *n* of observations per group (cluster) is indicated on the upper corner of Fig. 3 (Figs. 3a, 3b, 3c). The results presented in Figs. 3d, 3e, 3f (second line of Fig. 3) are related to the 1D-SPM statistical analysis in which the gray area indicates the percentage of the gait cycle where the five phenotypes are different. Our results showed a statistical difference of the identified phenotypes in the three planes and throughout the whole gait cycle.

### B. Interpretation and Description of the Phenotypes

ANOVA test allows to assess between-groups differences in terms of the demographic characteristics of the participants (Table III), and the biomechanical markers which are biomechanical parameters used in clinical settings (Table IV). Based on an ANOVA, Table III shows that there is no statistical difference in terms of age and BMI in the different groups. The statistical analysis in terms of biomechanical markers states several significant differences as shown in table (Table IV).

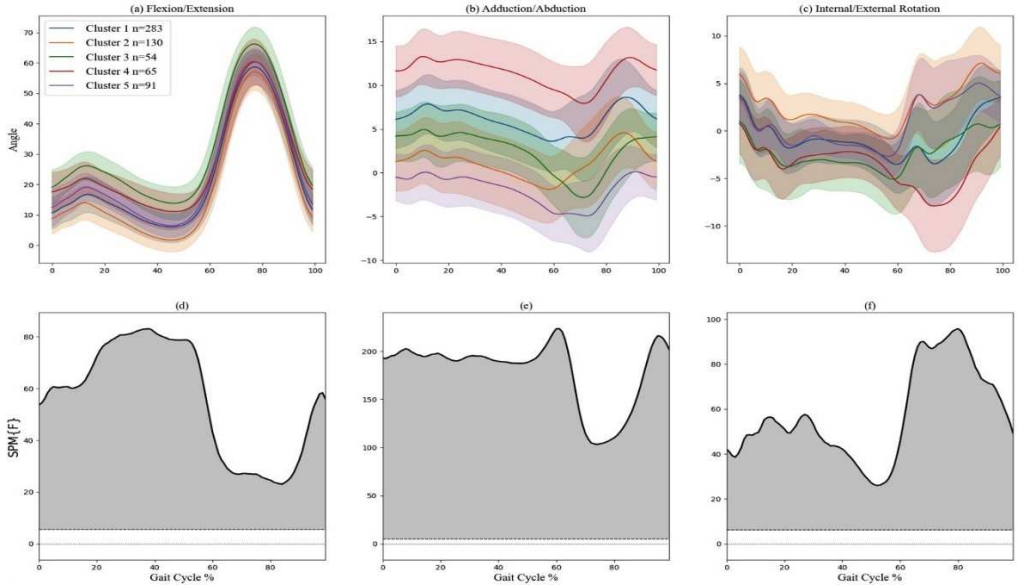


Fig. 3. Five phenotypes are identified based on 623 knee kinematic observations (Line 1) and the corresponding SPM{t} with a significance threshold α = 0.05 (Line 2). The gray area indicates the percentage of the gait cycle for which the five phenotypes are different.

TABLE III. DEMOGRAPHIC CHARACTERISTICS OF 616 KNEE KINEMATICS OBSERVATIONS FROM 409 PATIENTS

| | G1 | G2 | G3 | G4 | G5 |
|---|---|---|---|---|---|
| **N** | 279 | 130 | 52 | 65 | 90 |
| **Age $\bar{X}$ ($\sigma$)** | 64.02(9.00) | 63.72(10.05) | 62.02(9.37) | 64.08(13.45) | 60.58(8.83) |
| **BMI $\bar{X}$ ($\sigma$)** | 30.54(5.32) | 31.21(5.87) | 30.10(4.59) | 31.28(5.13) | 28.14(5.71) |

## IV. DISCUSSION

In this research, we introduced a clustering methodology utilizing the BIRCH (Balanced Iterative Reducing and Clustering using Hierarchies) approach to discern and define kinematic phenotypes in the osteoarthritis (OA) population. To our understanding, this study represents the pioneering effort of its kind, with no comparable studies found in the literature for OA phenotype classification. Indeed, we identified five distinct phenotypes by averaging 3D kinematic curves within each homogeneous group, as illustrated in Figs. 3a, 3b, and 3c. These phenotypes exhibit statistically significant differences across the three planes, depicted in Figs. 3d, 3e, and 3f. Our findings indicate the feasibility of efficiently deriving phenotypes based on knee kinematics, measured using a knee kinesiography system. Consequently, these phenotypes provide an objective assessment of knee movement patterns in the OA population.

The number of observations per group, and therefore making up a phenotype, differs from one group to another. For example, Group G1 includes 283 observations while Group G5 comprises 91 (Fig. 3). This demonstrates that the G1 phenotype is the most prevalent within the considered OA population. The analysis of demographic characteristics (Table III) shows that there are no statistical differences between the different groups. This demonstrates that the various phenotypes are not a consequence of these characteristics.

TABLE IV. STATISTICAL RESULTS: CLINICAL INTERPRETATION OF THE PHENOTYPES

| | **Clusters comparison** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Biomechanical markers** | **G1G2** | **G1G3** | **G1G4** | **G1G5** | **G2G3** | **G2G4** | **G2G5** | **G3G4** | **G3G5** | **G4G5** |
| Varus thrust during loading | 0.001 | * | 0.534 | * | 0.171 | 0.003 | 0.015 | * | 0.493 | * |
| Varus functional lower limb | * | 0.506 | * | * | * | * | 0.147 | * | * | * |
| Varus alignment at initial contact | * | * | * | * | * | * | * | * | * | * |
| Valgus thrust during loading | 0.001 | * | 0.193 | * | 0.001 | 0.299 | * | * | 0.938 | * |
| Knee flexum at initial contact | * | * | * | 0.007 | * | * | * | 0.183 | * | * |
| External tibial rotation | * | * | * | 0.470 | * | * | * | 0.742 | * | * |
| Varus alignment during stance | * | * | * | * | * | * | * | * | * | * |
| Internal tibial rotation | * | * | * | 0.728 | * | * | * | 0.704 | * | * |
| Limited flexion excursion | 0.076 | 0.149 | 0.121 | 0.187 | 0.013 | 0.858 | 0.011 | 0.021 | 0.747 | 0.021 |
| Fixed flexion during stance | 0.009 | 0.062 | 0.183 | 0.003 | 0.952 | 0.653 | 0.532 | 0.718 | 0.695 | 0.407 |
| Maximum flexion during swing | 0.002 | * | 0.083 | 0.041 | * | 0.001 | * | * | * | 0.914 |
| Sagittal plane range | 0.007 | 0.53 | 0.002 | 0.347 | 0.021 | * | 0.147 | 0.127 | 0.216 | 0.002 |

Note: *p<0.001

The biomechanical markers, described in Table I, Table IV, highlighted interesting characteristics of each phenotype especially for Group 4. The latter is characterized by a significantly higher abduction angle, indicating a unique biomechanical profile (red curve in Fig. 3). Notably, the varus biomarker (varus functional alignment and varus thrust) is markedly elevated in this group and statistically higher than Groups 2, 3 and 5. Interestingly, Group 4 shares a notable similarity in biomarker tendencies with Group 3, where knee flexum tends to be higher than in other groups, and internal and external tibial rotation tends to be lower. This observation highlights commonalities in the biomechanical characteristics of both Group 3 and Group 4, further underlining the nuanced nature of arthrosis subgroups and offering valuable insights for targeted therapeutic interventions.

Group 2 has a different biomechanical profile, marked by significantly low knee flexum, and low internal and external tibial rotation, whereas Group 5 presents with the lowest varus scores, wherein varus alignments (i.e., valgus), which are significantly different from other groups. Furthermore, the varus functional alignment in Group 5 is lower but similar to the one in Group 2, while the varus thrust also being lower is comparable to Group 3. This distinctive combination of biomechanical markers in Group 5 further underscores the diverse nature of arthrosis subgroups, suggesting potential variations in disease mechanisms and highlighting the need for tailored therapeutic approaches based on specific kinetic patterns within this patient population.

## V. Conclusion

This study identified five distinct phenotypes in the knee osteoarthritis (OA) population using 3D kinematic data captured with a Knee Kinesiography exam (KneeKG® system). The findings reveal that each phenotype has a distinct combination of biomechanical markers, which are objective functional parameters used in clinical settings and associated with OA progression and patient-reported outcomes. These results indicate the potential of this approach to tailor treatment plans based on the identified phenotypes, offering a more personalized care strategy for knee OA patients. Future research will expand on these findings by improving the robustness of the identified phenotypes, incorporating additional clinical parameters, such as quality of life measures, patient-reported outcomes using the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire and knee OA radiographic grades.

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