Quantifying Individual Deviations in Gait: A Normative Modeling Framework for Personalized Assessments

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Summary

As larger datasets of human motion become more available, normative modeling frameworks that account for population and site variation can enhance the clinical impact of these data. This study demonstrates the power of quantifying individual-level deviations from predicted normative distributions, providing valuable insights for both personalized patient assessments and more sensitive group-level comparisons across diverse clinical populations.

Introduction

Historically, research and clinical assessment in biomechanics have relied on group averages and case-control designs that categorize individuals into distinct groups (e.g., those with and without knee osteoarthritis). This approach overlooks the inherent variability within the human population, making it difficult to quantify whether an individual's movement pattern is truly atypical or simply within the natural range of variation. Normative modeling [1,2] offers a powerful alternative by mapping functional outcomes (e.g., kinematics) from relevant health-related covariates across a broad population, enabling the quantification of meaningful deviations at the individual level. This study demonstrates the application of normative modeling to biomechanical data to enhance personalized clinical assessment and provide a more refined approach to understand movement variation across diverse populations.

Methods

A normative modeling framework [1,2] using hierarchical Bayesian regression was trained on a large gait biomechanics dataset (N = 607; age range: 17–88 years) of individuals without mobility impairments across 12 sites, collected using markerless motion capture (Theia3D, Theia). Knee flexion angles (KFA) were predicted at each percentage of the gait cycle, using age and sex as fixed effects and collection site as a random effect. The resulting models describe the expected distribution of knee flexion angles in a healthy population while accounting for variations due to age, sex, and site. To demonstrate clinical utility, z-scores were calculated from model predictions of a single total knee arthroplasty (TKA) participant at four time points: pre-surgery, 6 weeks, 6 months, and 1-year post-surgery. Z-scores quantify deviations from the expected normative distribution, adjusted for the participant's age and sex. Additionally, 55 participants with moderate and 137 with severe knee osteoarthritis were scored to illustrate utility for group-level comparisons. The mean absolute z-score and the mean absolute raw knee flexion angle for each participant were computed and pairwise comparisons between groups were performed using Welch's t-test. Hedges' g effect sizes were calculated to assess the magnitude of differences. Model fit was characterized by root mean squared error (RMSE) and Pearson correlation between true and predicted values.

Results and Discussion

The average model RMSE was 3.8°, with a Pearson r of 0.25 ($p = 0.004$). Figure 1 illustrates the patient-specific scoring of a TKA participant through the course of improvement post-surgery, where their mean absolute z-score quantified the largest improvement between the 6 weeks (z-score = 2.1 SD) and 1-year post-surgery (z-score = 0.66 SD). The moderate vs. severe group comparisons revealed statistically significant differences with larger effect sizes using z-scores, but not with raw angles, highlighting the improved sensitivity of this approach in detecting differences that could have clinical relevance (Table 1).

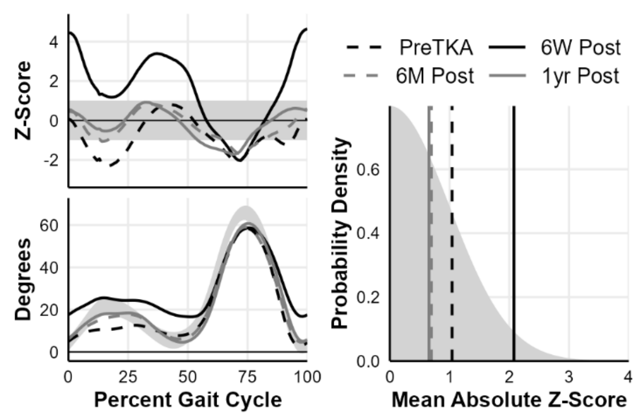

Figure 1: Top: Patient z-scores showing deviation from the predicted normal distribution across the gait cycle. Bottom: Corresponding knee flexion angles. Right: Mean abs z-score at each timepoint vs. normal distribution. Shaded region: ±1 SD of normal.

Table 1. Mean (SD) of Z-scores vs. Raw KFA

	Moderate	**Severe**	$\mathbf{p_{adj}}$	**ES**
Mean |Z-score| (SD)	1.24 (0.80)	1.56 (0.81)	0.016	-0.39
Mean |Raw KFA| (Deg.)	25.9 (4.5)	25.9 (5.0)	0.931	0.014

Conclusions

Normative modeling improves personalized biomechanical assessments by accounting for inter-subject and measurement variability, allowing for precise quantification of deviations from normative distributions. This approach can enhance the accuracy of clinical evaluations and provide valuable insights for personalized treatment in diverse clinical populations.

References

[1] Rutherford S et al. (2022). *Nat Protoc*, **17**: 1711-1734.
[2] Bayer JM et al. (2022). *NeuroImage*, **264**: 119699.