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Machine Learning Groups Patients by Early Functional Improvement Likelihood Based on Wearable Sensor Instrumented Preoperative Timed-Up-and-Go Tests



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ABSTRACT

Background: Wearable sensors permit efficient data collection and unobtrusive systems can be used for instrumenting knee patients for objective assessment. Machine learning can be leveraged to parse the abundant information these systems provide and segment patients into relevant groups without specifying group membership criteria. The objective of this study is to examine functional parameters influencing favorable recovery outcomes by separating patients into functional groups and tracking them through clinical follow-ups.

Methods: Patients undergoing primary unilateral total knee arthroplasty ($n = 68$) completed instrumented timed-up-and-go tests preoperatively and at their 2-, 6-, and 12-week follow-up appointments. A custom wearable system extracted 55 metrics for analysis and a K-means algorithm separated patients into functionally distinguished groups based on the derived features. These groups were analyzed to determine which metrics differentiated most and how each cluster improved during early recovery.

Results: Patients separated into 2 clusters ($n = 46$ and $n = 22$) with significantly different test completion times (12.6 s vs 21.6 s, $P < .001$). Tracking the recovery of both groups to their 12-week follow-ups revealed 64% of one group improved their function while 63% of the other maintained preoperative function. The higher improvement group shortened their test times by 4.94 s, ($P = .005$) showing faster recovery while the other group did not improve above a minimally important clinical difference (0.87 s, $P = .07$). Features with the largest effect size between groups were distinguished as important functional parameters.

Conclusion: This work supports using wearable sensors to instrument functional tests during clinical visits and using machine learning to parse complex patterns to reveal clinically relevant parameters.

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While total knee arthroplasty (TKA) is a successful end-stage treatment for osteoarthritis that commonly improves joint function and reduces pain, further investigation for treatment refinement is needed to decrease the recovery time and economic burden of this procedure. Preoperative function can be a predictor of postoperative functional improvement [1,2]. Rapid functional recovery in the first 3 months following TKA can additionally affect hospital funding, predict long-term recovery, and be used to adjust patient expectations realistically [3]. Objective measurement is

important for functional evaluation, but subjective patient-reported outcome measures (PROMs) remain a more commonly used tool. These self-reported surveys are convenient to deploy but completion of multiple measures by patients requires significant time and effort. Patients often do not complete the provided questionnaires entirely, rendering the collected data incomplete or inconsistent, and these measures have been shown to differ from objectively assessed functional performance [4–6].

The emergence of wearable sensor systems has permitted more efficient data collection providing objective measures that can be compared across patient populations or multiple clinical time-points of the same patient for recovery analysis. Functional tests such as the timed-up-and-go (TUG) or 3-minute-walk test can be completed by patients quickly in clinic and benefit from portable instrumentation for objective measurement [7]. The TUG test is of interest because it combines knee-relevant activities of standing from a chair, walking to a 3-m goal, turning about the goal, and returning to the seated start position, encompassing a variety of weight-bearing joint stressors. This test has been previously used in assessing TKA patients by timing the completion of the test, and differences of more than 2.27 s represent a clinically meaningful change in function [8]. Further analysis and joint measurement can be leveraged with the use of wearable sensors. As patient functional data are abundantly available with numerous measured parameters, patterns throughout individual patient recovery or across patient populations become difficult to identify by an observer. Unsupervised machine learning offers the ability to identify complex multivariate patterns in data and can group similar patient populations together without predefining group labels or membership criteria. Similarities and differences between patient groups throughout their recovery can reveal functional parameters prevalent in positive or negative outcomes.

The purpose of this study is to measure functional performance of TKA patients before and during their short-term recovery period and apply unsupervised machine learning to separate patients into different functional groups based on derived performance to highlight parameters influencing short-term functional improvement.

Methods

IRB approval was obtained for studies investigating patients scheduled to undergo primary unilateral TKA as a treatment for osteoarthritis. Patients were prescreened to ensure they did not have inflammatory arthritis or alcoholism before being recruited at their preadmission appointment and each patient provided informed written consent before participation. Individuals who had language and/or cognitive barriers, neuromuscular disorders, and operative or nonoperative leg amputations or who required a wheelchair for mobility were excluded. Demographic information was obtained from an orthopedic database, and Short Form 12, Western Ontario and McMaster Universities Osteoarthritis Index, Knee Society Score (KSS), and University of California Los Angeles (UCLA) Activity Score questionnaires were obtained at the preoperative, 6, and 12-week clinical appointments. Surgeons also completed the Office Knee Evaluation at each of these timepoints.

At preoperative, 2, 6, and 12-week appointments, patients were instrumented with a validated wearable sensor system consisting of an iPod Touch and 4 lightweight inertial sensors (one mounted above and below each knee) while completing 3 trials of the TUG test [9]. A custom software application was used to extract the recorded functional tests from the wearable sensor system and segment the test into 5 phases: sit to stand, walking to the goal, turning about the goal, walking back to the start, and sitting in the starting chair. Observer bias was minimized using autonomous test

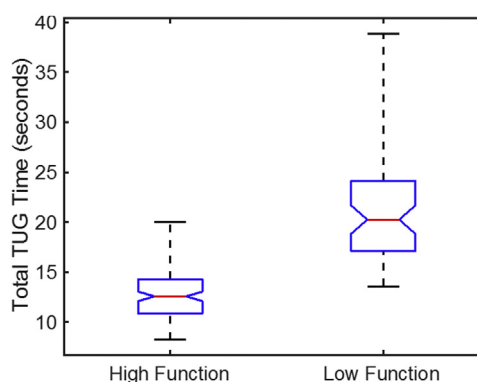


Fig. 1. Box and whisker plot of total TUG completion time of both groups preoperatively showing a large overlap in times between groups. TUG, timed-up-and-go.

start, finish, and segment separation and a step detection algorithm was used to extract steps for operative and nonoperative legs. A total of 55 spatiotemporal and functional metrics were extracted from raw test data including lower leg motions, upper leg motions, joint movement in 3 dimensions, flexion/extension velocities and accelerations, step range of motion (ROM), number of steps, turn directions, and segment completion times.

Extracted functional and spatiotemporal metrics from preoperative tests were combined into feature rows and stacked. Each feature column was standardized to have zero mean and unit standard deviation, so all features varied on a similar scale. All preoperative samples were fed into an unsupervised K-means clustering algorithm which separated patients into 2 groups. This algorithm is effective for finding groupings in unlabeled data that may be otherwise difficult to identify. It iteratively separates data points into k number of groups by comparing the similarity of data samples across all features and rearranges the group membership for maximum separation. Binary groups were not decided initially but this ideal number of groups was validated by observing a minimal Calinski-Harabasz index with $k = 2$, tested on a range of 2–6 [10].

A 1-way multivariate analysis of variance (ANOVA) was used to find PROM differences between the 2 separated clusters and Anderson-Darlington tests were used to confirm the normality of all preoperative PROM distributions ($P < .05$). One-way ANOVA was also used to find significant differences in the derived spatiotemporal and functional metrics between groups. Additionally, Cohen's D was computed for each feature to determine which of the derived metrics had the largest effect size and contributed the most to differentiating the 2 clusters.

The preoperative functional clusters were tracked forward to their 12-week appointments and a mixed-effects ANOVA with repeated measures test was performed on TUG total completion times of both groups at the preoperative, 2-, 6-, and 12-week timepoints. Derived metrics that remained significantly different between groups at both preoperative and 12-week timepoints with the largest effect sizes were observed as the most important persistent functional differences and were also analyzed using a mixed-effects ANOVA with repeated measures to compare improvement between preoperative and 12-week trials.

Results

A total of 94 patients were eligible to participate in this study but 18 were excluded because they missed/rescheduled their preoperative or 12-week appointments. An additional 8 patients were excluded because they underwent alternate interventions from the

Table 1
Mean ± SD Values of Patient Characteristics and Questionnaire Outcomes of High and Low Function Preoperative Clusters.

Mean ± SD	High Function	Low Function	P Value
Age (y)	65.6 ± 9.1	71.5 ± 10.3	.018
BMI (kg/m ²)	32.8 ± 5.8	34.9 ± 6.3	.180
UCLA Activity Score ^b	4.9 ± 2.1	3.8 ± 1.6	.001
SF-12 Mental	53.3 ± 11.0	51.7 ± 9.8	.493
SF-12 Physical	33.1 ± 8.3	29.7 ± 8.9	.079
WOMAC Pain	46.6 ± 17.3	45.5 ± 17.9	.682
WOMAC Stiffness	41.2 ± 19.0	46.2 ± 24.3	.123
WOMAC Function	49.3 ± 18.7	49.8 ± 11.0	.838
WOMAC Total	46.1 ± 15.8	47.2 ± 13.8	.620
KSS Symptoms	16.0 ± 4.1	15.3 ± 3.8	.246
KSS Satisfaction	13.7 ± 7.6	14.5 ± 7.1	.506
KSS Expectations	14.0 ± 1.3	13.0 ± 2.0	<.001
KSS Functional Activities	37.9 ± 16.7	32.3 ± 12.5	.029
KSS Knee Objective Indicators ^a	34.4 ± 18.5	33.8 ± 17.8	.813
Knee Evaluation Function ^a	50.7 ± 13.6	41.8 ± 23.1	.007
Knee Evaluation Total Knee ^a	43.0 ± 15.3	39.3 ± 16.1	.201
Knee Evaluation Total ^a	93.7 ± 25.4	78.1 ± 33.0	.003

Bolded items indicates the significant differences between groups ($P < .05$). "a" Indicates surgeon-reported measures and "b" indicates distinctions above minimal clinically important differences. BMI, body mass index; KSS, Knee Society Score; SD, standard deviation; SF-12, Short Form 12; UCLA, University of California Los Angeles; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

study protocol. The remaining 68 patients (male:female [M:F] = 34:34) were included in the study aged 67.5 ± 9.8 years with a body mass index of 33.5 ± 6.0 kg/m². Clustering feature rows for all preoperative TUG trials (3 per patient) partitioned patients into 2 groups with sizes 46 and 22 (M:F = 20:26 and M:F = 14:8). Seven patients had at least 1 TUG trial sorted into each group but were separated into the group with majority membership. Comparison of spatiotemporal metrics revealed the mean total TUG completion time (the only traditionally recorded TUG metric) of the larger group's trials was significantly faster than the smaller group (12.6 s vs 21.6 s, $P < .001$) but there was a large overlap in trial times between groups (Fig. 1). Despite the large group containing slow trials and the small group containing fast trials, these 2 groups were labeled "high function" and "low function," respectively, due to their mean total TUG time. The high function group was younger, scored higher in UCLA, KSS Functional Activities, Office Knee Evaluation Function (surgeon reported), and Office Knee Evaluation Total (surgeon reported) questionnaires and had slightly higher (KSS) expectations (Table 1). Most of the novel derived measures (48/55) were also significantly different between groups ($P < .05$) including all spatiotemporal metrics (Table 2) which is expected because the K-means algorithm separates clusters to achieve a maximum separation across all features equally. The 10 derived metrics with the largest effect size can be seen in Table 3.

The mean total TUG time for sorted patients was not only different between groups preoperatively, but also at the 6-week (5.4 s, $P = .01$) and 12-week (4.2 s, $P = .02$) follow-ups. Total time was not significantly different at 2 weeks ($P = .55$) where the mean patient time increased for both high and low function groups (by

Table 2
Mean ± SD of Spatiotemporal Metric Differences Between Preoperative Patient Clusters.

Mean ± SD	High Function	Low Function	P Value
Total time	12.7 ± 2.4	21.6 ± 5.7	<.0001
Sit to stand	1.1 ± 0.5	2.2 ± 1.3	<.0001
Walking to goal	3.8 ± 0.8	6.6 ± 2.0	<.0001
Turning at goal	0.6 ± 0.3	1.1 ± 0.5	<.0001
Walking to chair	4.8 ± 1.0	8.1 ± 2.0	<.0001
Stand to sit	1.8 ± 0.5	2.8 ± 1.5	<.0001

SD, standard deviation.

Table 3
Mean ± Standard Deviation of Top Distinguishable Functional and Spatiotemporal Metrics Between Groups at Preoperation and Their Effect Size (D).

Metric Description	High Function	Low Function	D
Time taken walking back to test start after turning (s)	4.8 ± 1.0	8.1 ± 2.0	1.604
Mean additive operative lower leg motion during steps (°)	124.5 ± 14.4	92.1 ± 12.0	1.601
Total test time (s)	12.6 ± 2.4	21.6 ± 5.7	1.591
Mean additive nonoperative lower leg motion during steps (°)	128.7 ± 15.4	96.0 ± 11.2	1.571
Time taken walking from initial stand to begin of turn (s)	3.8 ± 0.8	6.6 ± 2.0	1.510
Mean additive operative upper leg motion during steps (°)	90.0 ± 14.7	63.4 ± 9.8	1.470
Mean additive nonoperative upper leg motion during steps (°)	91.1 ± 14.9	65.1 ± 7.6	1.468
Mean nonoperative step peak flexion velocity (°/s)	289.9 ± 57.2	196.2 ± 22.0	1.428
Mean nonoperative step peak extension velocity (°/s)	282.3 ± 59.5	197.8 ± 37.6	1.271
Mean nonoperative step peak flexion acceleration (°/s ²)	5412.1 ± 1692.7	3129.9 ± 895.6	1.247

All features are significantly different between groups ($P < .001$).

9.2 s and 7.6 s, respectively). Mean total time of the high function group improved 0.87 s ($P = .07$) from preoperative to 12 weeks (Table 4) while the low function group improved 4.94 s ($P = .005$). Of the patients in the high function group, 26% (12) had meaningfully improved function (completion time decreased by >2.27 s from preoperation to 12 weeks postoperation), 63% (29) maintained function, and 11% (5) had worsened function (completion time increased by >2.27 s). Of the patients in the low function group, 64% (14) had improved function, 27% (6) maintained function, and 9% (2) had worsened function. A comparison of individual TUG segment times for all trials of both groups at each timepoint can be seen in Figure 2. The most distinguishable features between the 2 groups at 12 weeks and their effect sizes can be seen in Table 5. The top 3 most distinguishable features at the 12-week timepoint (top of Table 5) have been plotted alongside the same dimensions of the 2 cluster centroids found using all 55 metrics to visualize their strong influence on the preoperative group separation (Fig. 3). Six test samples from the low function group with exceptionally low operative step motion are shown in Figure 3 due to their operative leg function being too impaired to correctly detect any distinct steps. A failure to detect these steps has resulted in zero motion during steps but it is expected that this remains a meaningful result. Early improvement of key metrics for both groups can be seen in Table 6.

Discussion

The unsupervised clustering performed in this study successfully separated wearable sensor instrumented performance tests

Table 4
Mean Functional Group TUG Total Completion Time Changes and CI Between Preoperative Performance and Each Recovery Point (Negative Values Indicate a Total Time Improvement).

Timepoint Comparison	High Function	95% CI	P Value	Low Function	95% CI	P Value
Preoperative to 2 wk	+9.2 s	+13.3 to +5.1	<.001	+7.6 s	+21.4 to +6.1	.400
Preoperative to 6 wk	+0.4 s	+1.8 to -1.0	.472	-2.9 s	+2.1 to -7.9	.373
Preoperative to 12 wk	-0.9 s	+0.1 to -1.8	.076	-4.9 s	-1.3 to -8.5	.005

Bolded items indicates the significant differences between groups ($P < .05$). CI, confidence interval; TUG, timed-up-and-go.

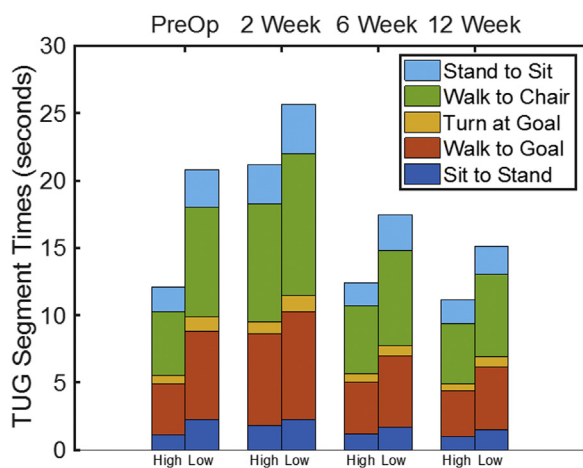


Fig. 2. Mean TUG segment times for each functional group over their early recovery period.

based on derived functional metrics into clinically relevant groups. Literature has previously linked preoperative functional performance to postoperative functional improvement; however, this study has highlighted functional parameters that differentiate between patients who are likely to gain function [1,2]. Other work predicting gait recovery following TKA has employed a different method to first label samples as responders or nonresponders of parameter improvement and train a classifier to make this prediction. The authors suggest the unsupervised grouping and cluster analysis performed in the present work is more effective for distinguishing important functional parameters and real-world generalization because group membership is not defined, but organically created based on the unbiased structure of the data [11].

The objective measures extracted from the short and easy-to-implement TUG test have been able to distinguish function preoperatively with many significant differences between groups whereas there are few differences in PROMs and overlapping TUG completion times. It can be seen in Table 1 that despite several PROMs being significantly different between groups, only the UCLA Activity Score varied more than its minimal clinically important difference of 0.92 [12,13]. This presents evidence that there are

Table 5
Mean \pm Standard Deviation of Top Distinguishable Functional and Spatiotemporal Metrics Between Groups at 12 wk Postoperation and Their Effect Size (D).

Metric Description	High Function	Low Function	D
Mean additive operative upper leg motion during steps ($^{\circ}$)	96.1 \pm 15.0	76.8 \pm 18.9	1.043
Mean additive nonoperative lower leg motion during steps ($^{\circ}$)	135.0 \pm 15.4	114.8 \pm 22.2	1.004
Mean additive operative lower leg motion during steps ($^{\circ}$)	131.2 \pm 16.3	109.5 \pm 27.1	0.961
Time taken walking from initial stand to begin of turn (s)	3.4 \pm 0.7	4.7 \pm 2.0	0.933
Mean additive nonoperative upper leg motion during steps ($^{\circ}$)	97.5 \pm 15.1	81.6 \pm 16.8	0.919
Total test time (s)	11.8 \pm 2.7	16.0 \pm 6.5	0.893
Time taken walking back to test start after turning (s)	4.5 \pm 1.2	6.1 \pm 2.5	0.868
Time taken to stand from the seated start position (s)	1.7 \pm 0.7	2.1 \pm 0.9	0.800
Mean additive operative flexion during steps ($^{\circ}$)	87.0 \pm 16.1	73.9 \pm 15.2	0.774
Mean operative flexion range during steps ($^{\circ}$)	42.4 \pm 7.9	36.5 \pm 7.5	0.714

All features were significantly different between groups ($P < .001$). Bold indicates features that were also distinguished in the preoperative timepoint analysis.

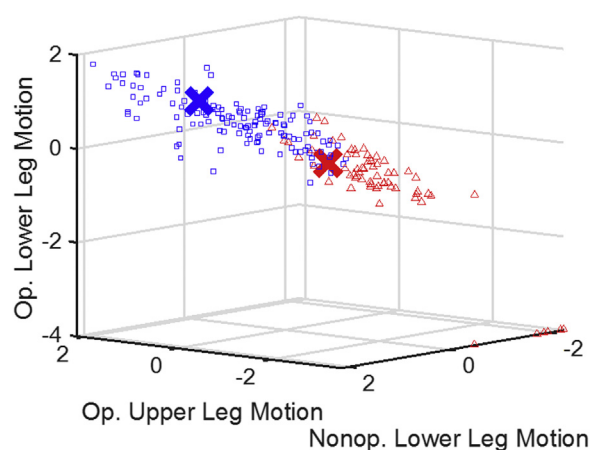


Fig. 3. Z-scores of the top 3 most distinguished metrics persisting to the 12-wk follow-up appointments for each trial and their influence on initial preoperative clustering. Solid crosses (x) represent group centroids found using all 55 derived metrics. Blue squares and red triangles indicate high and low function group trials, respectively. Nonop., nonoperative; Op., operative.

functional performance differences that cannot be distinguished using subjective self-reported measures when comparing patients with different expectations.

Tracking the 2 functionally separated groups through to 3 months revealed that one group was much more likely to improve relative to the other. Test results for new patients can be compared to the 2 groups clustered in this study to determine the most similar expected recovery path, and this information can be used to provide realistic recovery expectations for patients. The analysis performed has relied on total TUG time as a reliable overall performance metric and tool for labeling groups but it should be highlighted that other derived metrics had larger effect sizes between groups and were determined to be more relevant parameters influencing the resulting group memberships (Table 3 and 5). Identified features distinguishing the functional groups at 12 weeks included both operative and nonoperative leg metrics which suggests test completion and movement compensation strategies were captured. The low function group had larger improvements in all relevant additive motion metrics (Table 6) but these values never exceeded those of the high function group. Increased ROM has been previously linked to better outcomes but the results of this study indicate that the total additive amount of motion expended during activities by both operative and nonoperative legs is also functionally important [14,15]. Both groups improved these metrics significantly during recovery which supports that the metrics are influencing shorter TUG times, which did decrease for both groups but not by a meaningful difference for the high function group.

Although it may be thought that higher functioning preoperative patients have less possible function to regain and will likely show less functional improvement, there is still a benefit of including the instrumented TUG test at preoperative visits because this functional differentiation was possible with the derived metrics and the current work has shown that PROMs alone cannot reliably report function to this granularity. Additionally, it is important to note in the preoperative groups that 7 patients in the “low” function group had mean total TUG times faster than the worst “high” function time. Similarly, there were 7 patients in the “high” function group with times slower than the best “low” function group time, indicating that total TUG time alone would not be enough to sort the groups in this way. Of the 7 patients in the “low” function group with favorable times that have been labeled likely to improve, 5 of them have improved their total time above the TUG minimal clinically important difference of 2.27 s [8]. Of the

Table 6

Operative and Nonoperative Improvement of Top Persisting Motion Metrics Between Preoperative and 12-wk Follow-Ups for Each Group.

Metric Description	High Function	95% CI	P Values	Low Function	95% CI	P Values
Mean additive operative upper leg motion during steps	6.1	10.2–2.0	.002	13.3	19.5–7.1	<.0001
Mean additive nonoperative lower leg motion during steps	6.3	10.7–1.9	.003	18.8	25.3–12.4	<.0001
Mean additive operative lower leg motion during steps	6.6	11.4–1.8	.004	17.4	24.6–10.2	<.0001
Mean additive nonoperative upper leg motion during steps	6.4	10.3–2.4	.001	16.5	22.3–10.7	<.0001

CI, confidence interval.

7 patients in the “high” function group with less favorable times labeled not likely to improve, only 3 of them have improved above the same threshold. These patients who were sorted into the low function group who had more favorable times have still shown improvement despite a smaller possible improvement range while patients sorted into the high function group who had less favorable times have not improved despite a larger possible improvement range. These special cases suggest the cluster separation better indicates likelihood of improvement than overall functional level.

Some limitations were noted with the study performed. During data collection, 7 patients repeated one of their trials sufficiently different from the others that the samples were split between both groups. Although a single patient cannot belong to multiple functional groups, the separation of tests may be a valid result because repetitions of the same test can be slightly different due to fatigue, test familiarity, confusion, or perhaps a stumble or stiffness. During clustering, it was decided to keep each trial as a separate sample to best separate functional groups but when future data are compared to find the most relatable path, it may be more practical to take an average across multiple trials for more generalized predictability.

The follow-up time analyzed was limited to the early recovery period of 12 weeks. Despite recovery following TKA usually lasting 1 to 2 years, the authors believe valuable information can be obtained during the early recovery phase, and this time period can be important for health economics [16]. As alternative joint replacement payment models such as Medicare’s Bundled Payments for Care Improvement Program are introduced, early outcome prediction becomes valuable for allocating care costs. Under model 2 of the Bundled Payments for Care Improvement Program, hospitals will be reimbursed for costs saved in the first 90 days following surgery and patients with early improvement will likely require less frequent early care [17]. Fast functional improvement and early ambulation reduces hospital length of stay which also reduces the likelihood of costly readmissions due to infection [18–20]. A longer follow-up will be necessary to determine how function changes in each group until patients are fully healed.

The current work has shown that preoperative functional assessment can benefit from the use of wearable sensor instrumentation and machine learning techniques can identify multivariate patterns that would be otherwise difficult to see by an observer. Groups of patients following similar short-term recovery paths have been identified and future test data can be compared to similar path prediction to better influence patient expectations. There was little evidence that the PROMs collected in this study related to the results found using the derived functional and spatiotemporal metrics. Obtaining PROMs proved much more time-consuming for patients and the process was more cumbersome when it became time to store and digitize the measures, further motivating the use of an automated sensor system that can record performance tests in only a few minutes and provide instantaneous analysis.

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