June 10, 2022

Rune Labs, Inc.
℅ Courtney Lane
CEO/Principal Consultant
Anacapa Clinical Research Inc.
2421 Sunset Dr.
Ventura, CA 93001

Re: K213519
Trade/Device Name: Rune Labs Kinematics System
Regulation Number: 21 CFR 882.1950
Regulation Name: Tremor Transducer
Regulatory Class: Class II
Product Code: GYD
Dated: May 11, 2022
Received: May 13, 2022

Dear Courtney Lane:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for
Jay Gupta
Assistant Director
DHT5A: Division of Neurosurgical,
Neurointerventional
and Neurodiagnostic Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K213519

Device Name
Rune Labs Kinematic System

Indications for Use *(Describe)*
The Rune Labs Kinematic System is intended to quantify kinematics of movement disorder symptoms including tremor and dyskinesia, in adults (45 years of age or older) with mild to moderate Parkinson's disease.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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rune labs

510(k) Summary

Contact Details

Applicant Name: Rune Labs Inc.
Applicant Address: 649 Irving Street, San Francisco, CA 94122, United States
Applicant Contact Telephone: 360-606-2929
Applicant Contact: Mr. Brian Pepin
Applicant Contact Email: brian@runelabs.io

Correspondent Name: Anacapa Clinical Research Inc.
Correspondent Address: 2421 Sunset Dr., Ventura, CA, 93001, United States
Correspondent Contact Telephone: 805-856-8141
Correspondent Contact: Dr. Courtney Lane
Correspondent Contact Email: courtney@runelabs.io

Device Name

Device Trade Name: Rune Labs Kinematics System
Common Name: Tremor transducer
Classification Name: Transducer, Tremor
Regulation Number: 882.1950
Product Code: GYD

Legally Marketed Predicate Devices

Predicate # K140086
Predicate Trade Name: Personal Kinetigraph (PKG) System
Product Code: GYD

Device Description Summary

The Rune Labs Kinematic System collects derived tremor and dyskinesia probability scores using processes running on the Apple Watch, and then processes and uploads this data to Rune's cloud platform where it is available for display for clinicians.

The Rune Labs Kinematic System uses software that runs on the Apple Watch to measure patient wrist movements. These movements are used to determine how likely dyskinesias or tremors are to have occurred. The times with symptoms are then sent to the Rune Labs Cloud Platform using the Apple Watch's internet connection, which is then displayed for clinician use.

The Apple Watch contains accelerometers and gyroscopes which provide measurements of wrist movement. The Motor Fluctuations Monitor for Parkinson's Disease (MM4PD) is a toolkit developed by Apple for the Apple Watch that assesses the likely presence of tremor and

dyskinesia as a function of time. Specifically, every minute, the Apple Watch calculates what percentage of the time that tremor and dyskinesia were likely to occur. The movement disorder data that is output from the Apple's MM4PD toolkit have been validated in a clinical study (Powers et al., 2021[1]).

The Rune Labs Kinematic System is software that receives, stores, and transfers the Apple Watch MM4PD classification data to the Rune Labs Cloud Platform where it is available for visualization by clinicians. The device consists of custom software that runs on the users' smart watch and web browsers.

Intended Use/Indications for Use

The Rune Labs Kinematic System is intended to quantify kinematics of movement disorder symptoms including tremor and dyskinesia, in adults (45 years of age or older) with mild to moderate Parkinson's disease.

Indications for Use Comparison

The predicate indication for use statement is as follows:

> "The Personal Kinetigraph (PKG) System is intended to quantify kinematics of movement disorder symptoms in conditions such as Parkinson's disease, including tremor, bradykinesia and dyskinesia. It includes a medication reminder, an event marker and is intended to monitor activity associated with movement during sleep. The device is indicated for use in individuals 46 to 83 years of age."

Rune Labs does not currently detect bradykinesia so this symptom measurement is removed. However, bradykinesia can still be assessed clinically by the clinicians and/or reported by the patient so this change does not constitute a change in the type or level of risk compared to the predicate device.

Medication reminders, event markers, sleep movement, and activity measurements are not included with the Rune Labs Kinematic System. However, this functionality is readily provided by commercially available off-the-shelf software. Therefore, this change does not constitute a significant change in type or level of risk compared to the predicate device.

The algorithm used in the Rune Labs Kinematic System was validated in a clinical study[1] on adults with Parkinson's disease with an age range of 71.4 yrs [±8.9 standard deviation]. The lower cutoff therefore represents three standard deviations from the mean for patients in the validation study, and the upper cutoff is likely limited by the life expectancy of the user. Parkinson's disease typically affects only adults aged 60 or older, and their life expectancy is

[1] Powers R, Etezadi-Amoli M, Arnold EM, Kianian S, Mance I, Gibiansky M, Trietsch D, Alvarado AS, Kretlow JD, Herrington TM, Brillman S, Huang N, Lin PT, Pham HA, Ullal AV. Smartwatch inertial sensors continuously monitor real-world motor fluctuations in Parkinson's disease. Sci Transl Med. 2021 Feb 3;13(579):eabd7865. doi: 10.1126/scitranslmed.abd7865. PMID: 33536284.

estimated to be 83.3 years[2]. Therefore, this change does not constitute a significant change in type or level of risk compared to the predicate device.

The environment of use for the PKG System and Rune Labs System are similar, but the Rune Labs device can be used continuously whereas the PKG Watch must be mailed back to the company for data analysis after several days' use. Continuous monitoring is likely to improve the ability for physician's to monitor their patients over time so this change does not constitute a significant change in type or level of risk compared to the predicate device.

Technological Comparison

The key operating principle of the system and the predicate is the recording and analysis of the patient's wrist movement to provide a report to the clinician regarding the presence or absence of movement disorders systems.

Comparison of Outputs and Features

The Rune Lab device outputs are the percentage of the time that tremor and dyskinesia were likely to occur while the PKG device outputs are an estimate of when tremor is present, a percent time that tremor is present (PTT), and an estimate of dyskinesia scores every two minutes over 10 days. The PKG device also provides information about bradykinesia (see above).

While the technological details of the tremor and dyskinesia detection algorithms are not the same as the predicates, this difference does not raise new types of safety or effectiveness questions because the algorithms used were both correlated with accepted scientific methods, such as the UPDRS III.

Comparison of Data Transmission

There is a difference between the Rune Kinematic System and the predicate device with respect to the mechanism of data transmission. Rune Labs uploads data from the Apple Watch to the Rune Labs Cloud Platform using either a cellular or wireless network. The predicate device requires the device to be mailed back to the manufacturer for processing, and then a report is emailed to the clinician.

We have noted that a newer device by the same manufacturer has been cleared by the FDA and is deemed substantially equivalent to the predicate device (K161717[3]), which uses wireless communication to upload the patient data via the internet. This device can be considered a reference device for the Rune Kinematics and serves to demonstrate that the type of communication protocols used do not impact the safety and effectiveness of the device, provided that controls are in place that the data is preserved across the the various communication methods, which we have shown in our verification testing.

[2] https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/symptoms-causes/syc-20376055

[3] https://www.accessdata.fda.gov/cdrh_docs/pdf16/K161717.pdf

Comparison of System Design

The Rune Labs device is a software-only device that interfaces with a toolkit provided by a consumer electronics device manufacturer (Apple) whereas the predicate device is a hardware and software system. However, the Apple Watch is used as the hardware component for other medical devices, such as the Apple electrocardiograph device (DEN180044) and photoplethysmograph device (DEN180042), which can be considered reference devices. Rune Labs will monitor and evaluate toolkit and Apple Watch releases to ensure that software or hardware changes released by the manufacturer do not affect the device performance. Therefore this difference will not impact the safety or effectiveness of the device.

Summary of Technical Comparison

Overall, the differences in the usability and design of the Rune Labs Kinematics System, which allows for longer use and direct upload of data, do not affect the safety and effectiveness of the device as compared to the predicate device.

Non-Clinical and/or Clinical Tests Summary

Software testing established that the system meets the software requirements and user needs for the intended uses.

Apple's MM4PD has been clinically validated as described in Powers et al. (2021)[1], and the validation is summarized below. Table 1 shows baseline demographics for patients used in the validation studies.

	Pilot study PD patients in-clinic + 1 week live-on	Longitudinal patient study PD patients long-term live-on	Longitudinal control study Elderly controls
Age [± Standard Dev]	68.1 yrs [±9.0]	71.4 yrs [±8.9]	74.7 yrs [±5.4]
Years with PD [± Standard Dev]	6.5 yrs [±5.6]	10.3 yrs [±6.5]	n/a
Gender	36 Female, 82 Male	69 Female, 156 Male	85 Female, 85 Male, 1 unknown
Most Affected Side	62 Right / 39 Left / 17 unspecified	105 Right / 120 Left	n/a
History of Tremor	-	166/225 Participants	n/a
History of Dyskinesia (History of Chorea)	-	94/225 Participants (66/94 with dyskinesia)	n/a
History of Freezing Gait	-	85/225 Participants	n/a
History of Slow Gait	-	172/225 Participants	n/a
		*self-reported history	

Table 1: Subject demographics for the Powers et al. (2021) study[1]

1.1. Measured Watch displacements compared to motion measurements

The measured watch movement was correlated with the measurements taken from a commercially available motion tracking system (Vicon; see Figure 1). A healthy control subject simulated tremor movements with varying amplitudes while wearing the Apple Watch in seated and standing positions. The Pearson correlation coefficient between displacement measured by the motion capture system and the watch estimate was 0.98 in a control subject with a mean signed error of -0.04 ± 0.17 cm.

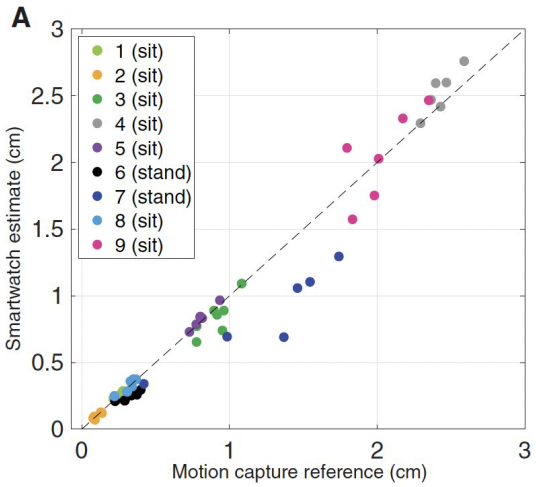

Figure 1: Apple Watch estimate of motion as a function of measurements from a commercially available motion capture system (Vicon). From Powers et al., 2021, Figure 3A.

1.2. Tremor Validation

The tremor detection algorithm was developed using data collected from the following data sets:

1. **Pilot study:** N=69 subjects in the pilot study, with tremor reported during a stationary task (mainly sitting tasks such as cognitive distraction or hands-in-lap but also during standing periods)

2. **Longitudinal patient study:** subjects in the longitudinal patient study design set (first 143 subjects enrolled) with tremor reported during a stationary task

3. **Longitudinal control study:** All day living data from additional subjects without Parkinson's (N=236 subjects, >59,000 hours of data)

The mean daily tremor detection rate for all subjects from the longitudinal patient study was compared to the clinician's overall tremor rating, which takes both constancy of tremor and severity into account. Design set patients were used to determine the tremor detection algorithm, and a hold-out set was used to ensure that these cutoffs were well correlated in additional subjects. The daily tremor percentage was calculated as the total detected tremor time divided by the total time period the watch was worn. Watch wear time excluded periods where the subject was likely asleep or where the watch was not being worn as indicated by a lack of device movement. This percentage was then averaged across all the days the subject was in the study. Six subjects were excluded because they had insufficient data for analysis. The Spearman's rank correlation coefficient between the daily tremor percentage and the clinicians' tremor constancy score was calculated.

All-day tremor estimates from the longitudinal patient study, as quantified by an individual's mean percentage of time with tremor detected per day, correlated with their MDS-UPDRS

tremor constancy score assessed during a brief, in-clinic visit at the start of the study, with a Spearman's rank correlation coefficient of 0.72 in the design set (n = 95) and in the hold-out set (n = 43) (Figure 2).

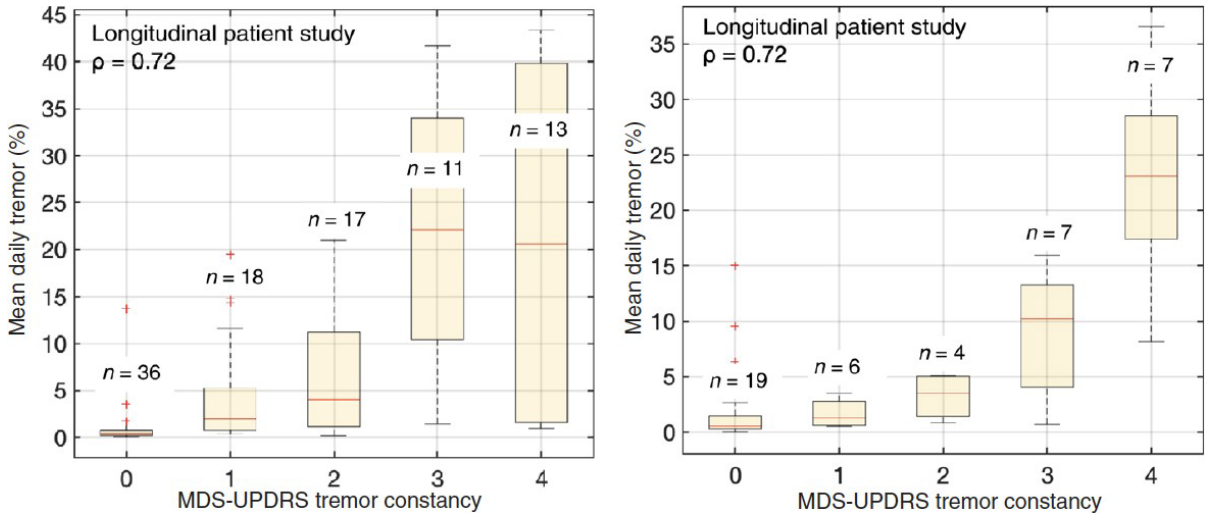

Figure 2: Mean daily tremor percentage compared to MDS-UPDRS tremor constancy score from the longitudinal study for the design set (left; n = 95) and hold-out set (right; n = 43). Rank correlation coefficient for the design set is 0.72; for the hold-out set rank correlation coefficient is also 0.72. From Powers et al., 2021, Figure 3D and E.

False positives occurred 0.25% of the time when evaluated in 171 elderly, non-PD longitudinal control subjects using over 43,300 hours of all-day data. False positives were also rare during targeted activities in young, healthy controls, such as manual teeth brushing (8%) and playing a musical instrument (2%; see Table S2 in Powers et al., 2021).

1.3. Dyskinesia Validation

The dyskinesia detection algorithm was designed using data collected from the following data sets:

1. **Pilot study:** N=10 subjects from the pilot study, divided evenly between subjects observed to have choreiform dyskinesia regularly affecting the wrist on which the watch was worn and subjects with no history of any dyskinetic symptoms (one week of all-day data for each subject)

2. **Longitudinal patient study:** N=97 subjects from the longitudinal patient study design set (first 143 subjects enrolled), consisting of 22 subjects with choreiform dyskinesia and 75 with no history of choreiform dyskinesia (>25,000 hours of all-day data)

3. **Longitudinal control study:** N=171 subjects without Parkinson's from the Longitudinal Control study (>59,000 hours of all-day data)

The dyskinesia algorithm was designed and validated across 343 participants with PD (61 with dyskinesia) and 171 elderly, non-PD controls. The choreiform movement score (CMS) was calculated from sensor data in the pilot study and compared to dyskinesia ratings from three MDS-certified experts during multiple MDS-UPDRS assessments. The CMS was used to classify data into 1 minute segments where dyskinesia was likely or not.

CMS showed significant differences ($P < 0.001$) for all pairwise comparisons using a Wilcoxon rank sum test across three groups: (i) 65 subjects with confirmed absence of in-session dyskinesia by all three raters (89 tasks), (ii) 69 subjects with discordant dyskinesia ratings (109 tasks), and (iii) 19 subjects with confirmed dyskinesia across all three raters (22 tasks, Figure 3).

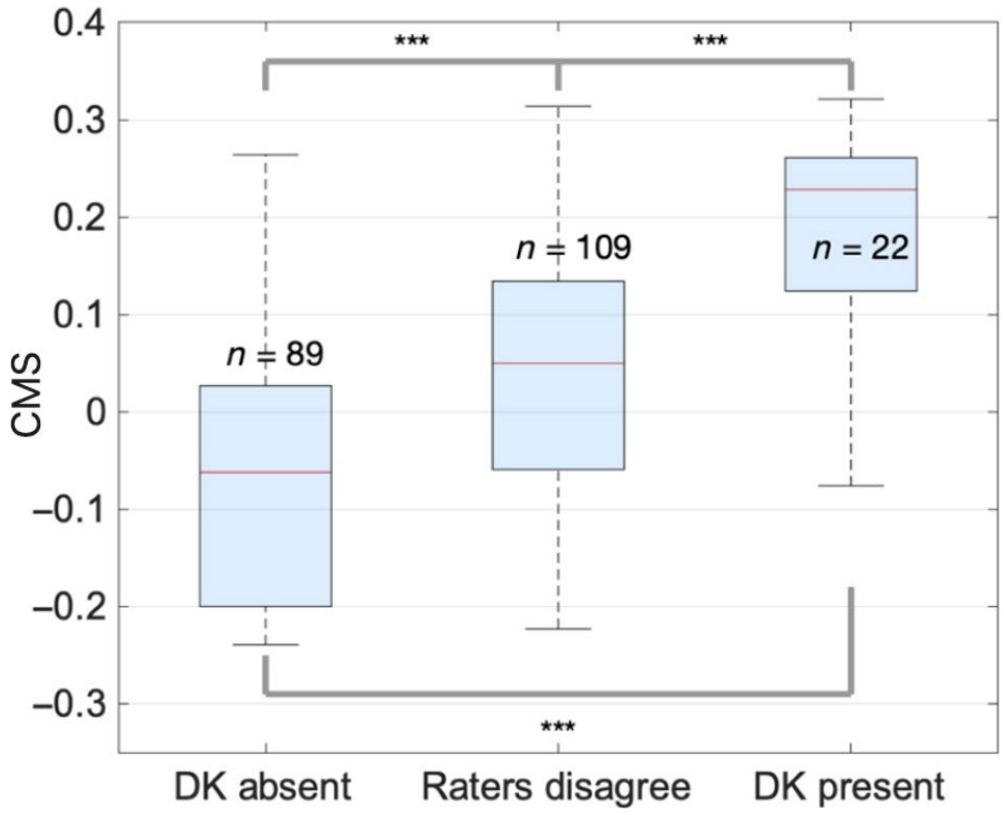

Figure 3: Chorea movement scores computed during in-clinic cognitive distraction tasks for the pilot study differentiated between the presence or absence of dyskinesia (DK) as based on expert ratings ($p < 0.001$ for all pairwise comparisons, using Wilcoxon rank sum test).

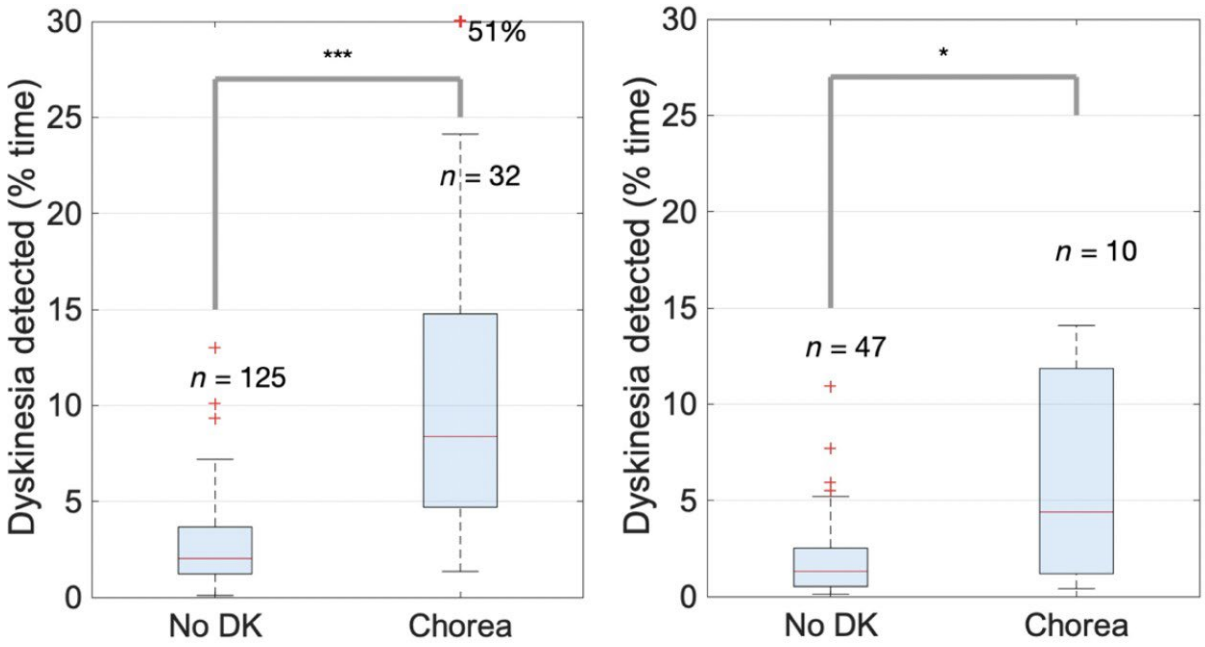

Figure 4: Mean daily dyskinesia percentage compared to dyskinesia ratings from the longitudinal study for the design set (left) and hold-out set (right). The amount of dyskinesia detected in patients significantly differed between subjects with and without chorea in both the design set (p<0.001 using Wilcoxon rank sum test) and hold-out set (p=0.027 using a Wilcoxon rank sum test). From Powers et al., 2021, Figure 4D and E.

The amount of dyskinesia detected by MM4PD significantly differed between subjects with PD with known chorea and those without, in both cross-validation and hold-out datasets. In the cross-validation design set (Figure 4, left), dyskinesia was detected for an average of 10.7 ± 9.9% (mean ± standard deviation) of the day in 32 subjects with chorea. In contrast, dyskinesia was detected for 2.7 ± 2.2% of the day in 125 patients with PD with no known dyskinesia ($p < 0.001$, Wilcoxon rank sum test). In a hold-out dataset from the longitudinal patient study, the percentage of time dyskinesias were detected for the chorea group (5.9 ± 5.3%) significantly differed from subjects with no reported dyskinesias (2.0 ± 2.2%) ($P = 0.027$, Wilcoxon rank sum test; Figure 4, right).

Dyskinesia false-positive rates were low across common activities like walking (1%). In all-day data from elderly, non-PD controls in the longitudinal control study, the median false-positive rate was 2.0% (Powers et al, 2022, Table S2). However, specific activities that mimic choreiform movements, such as playing the piano, had high false-positive rates (Powers et al, 2022, Table S2).

1.4. Clinical Validation Summary

Overall, the outputs of the MM4PD algorithm provide detection of tremor and dyskinesia

symptoms in Parkinson's disease patients that are well correlated with clinical ratings of tremor constancy and dyskinesia presence.

Conclusions

While the Rune Labs Kinematics System Indications for Use are not identical to the Indications for Use of the predicate device, the minor differences do not alter the intended effects or impact safety or effectiveness, as they are achieved using the same mechanisms of action and the same types of data. Moreover, the minor differences in the Indications for Use of the Rune Labs Kinematic System does not change the type of risk or increase the level of risk as compared to the predicate device. The Rune Labs Kinematic System therefore is considered substantially equivalent to its predicate device.