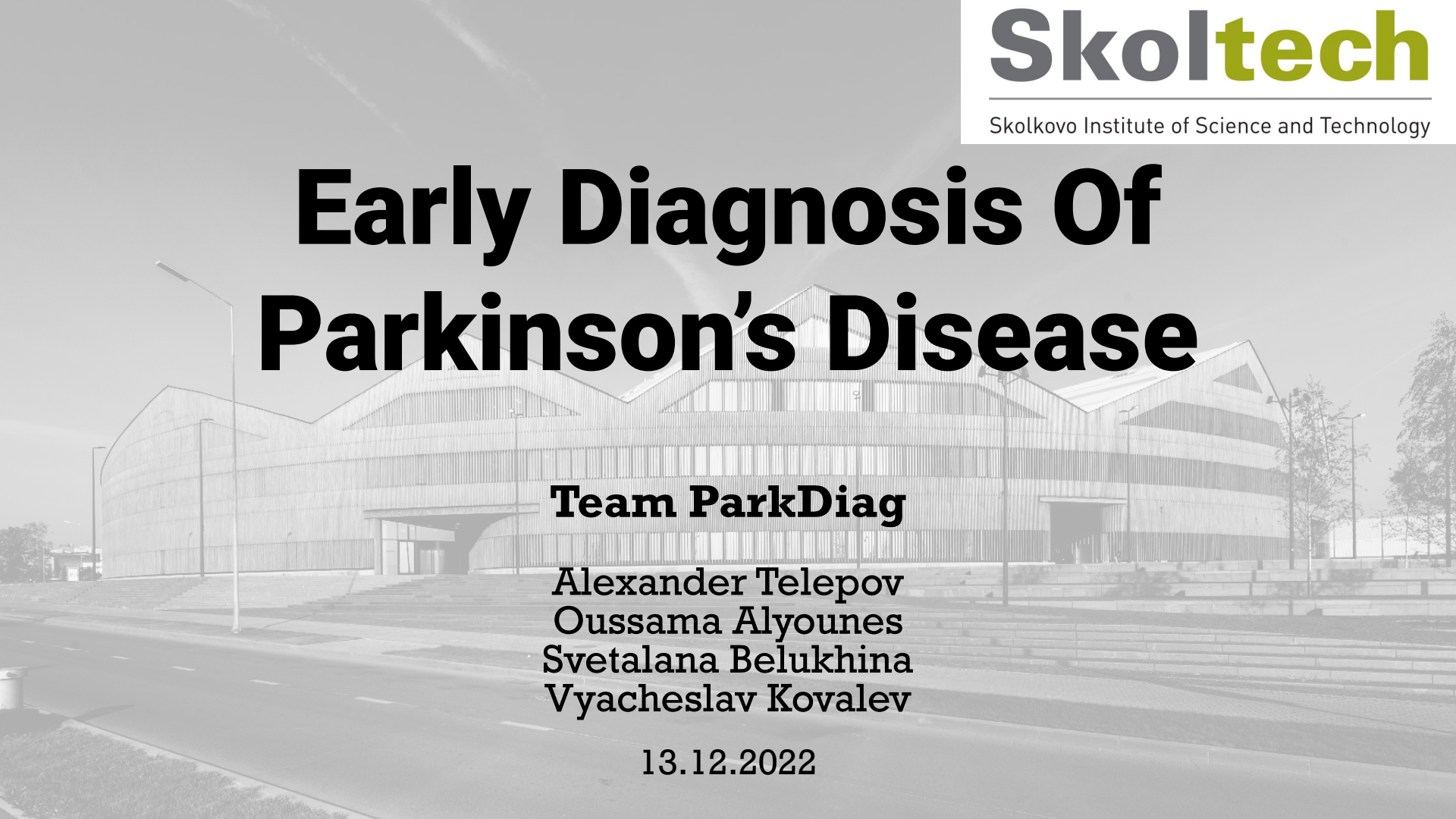

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Early Diagnosis Of Parkinson's Disease

Team ParkDiag

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13.12.2022

Indication + Service + Benefit

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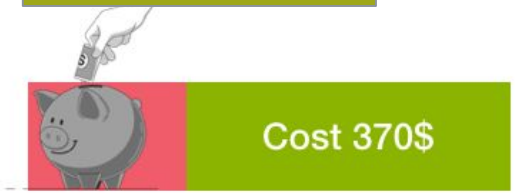
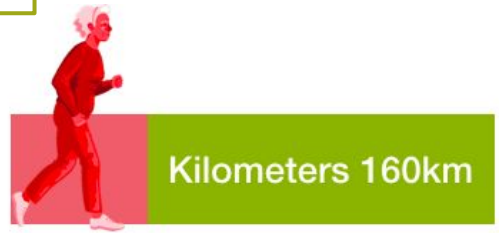
Parkinson Disease ICD-10 Version:2019: G20

*Current therapy is more effective on the **early stages of Parkinson***

ParkDiag Early diagnostics of Parkinson with your smartphone





- Our software **“ParkDiag”** is capable of **early diagnosing** of **Parkinson’s disease** through **voice** recordings.
- **“ParkDiag”** guarantee at least **94.84% accuracy** **for early diagnosis of PD** while **usual methods** guarantee **less than 75%**.
- **Easily installed on your smartphone.** With high technology depends on **5 voice features** (Harsh, falsetto, tense, crikey, breath).

Team ParkDiag

MOA & POC Experiments

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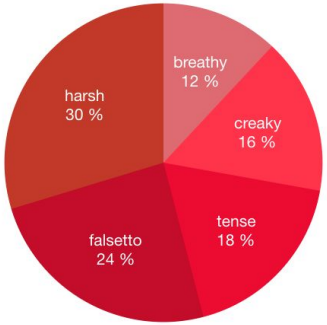


- 78% of early untreated PD subjects indicate vocal impairment.
- We are depending on 5 features in the voice to diagnose PD in early stages.

Fig.1 Composition voice quality in Parkinson's speech

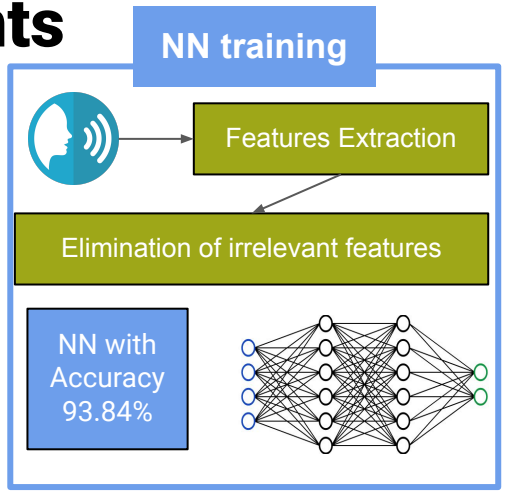


Table.1 Relative characteristics of symptomatic biomarkers

	Sensitivity	Specificity
Rapid eye movement sleep behavior disorder	Low (~50% of PD patients occur RBD in 2 years)	High (76% risk of PD at 10 years)
Olfactory dysfunction	High (>80% of early PD)	Low
Voice	High (65-98.35% according to ~30 papers)	High (67-91.06% according to ~30 papers)

Measure the 5 voice features in voice through our application for people diagnosed with PD

113 PD patient

Female 46% | Male 54%

<60yo 32% | >60yo 68%

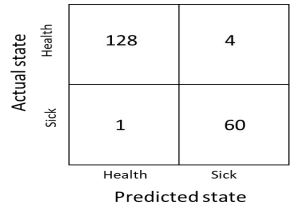
Early 16% | Mid 24% | Late 60%

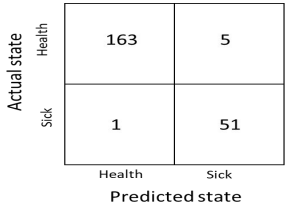
200 Healthy patient

Female 46% | Male 54%

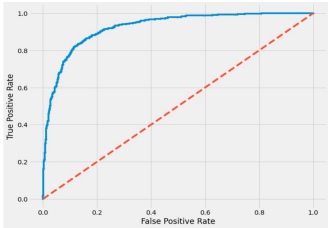
<60yo 57% | >60yo 43%

Usual treatment of PD (Levodopa)





New method works correctly



- Detecting PD in voice works on both genders accuracy above 93%.

[1] J. Rusz, R. Cmejla, H. Ruzickova, E. Ruzicka, Quantitative acoustic measurements for characterization of speech and voice disorders in early untreated Parkinson's disease, J. Acoust. Soc. Am. 129 (1) (2011) 350–367.
[2] Cernak, Milos, et al. "Characterisation of voice quality of Parkinson's disease using differential phonological posterior features." Computer Speech & Language 46 (2017): 196-208.

Our Claims

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1	A software capable of extracting the five voice features “Harsh, falsetto, tense, crikey, breath” from the voice sample differentiating the modal and non-modal phonations using phonological posteriors adapted by a deep learning method.
2	The software according to claim 1 capable of using said features to determine an early diagnosis of Parkinson's disease using Euclidean distance method calculating similarity of non-modal and disordered statistics, and the inverse of the distances to obtain the composition of non-modal phonation in Parkinson's disease.
3	The software according to claim 1 for diagnosing Parkinson's disease for female older than 60 years old with more than 99% accuracy.

Regulatory Guidelines

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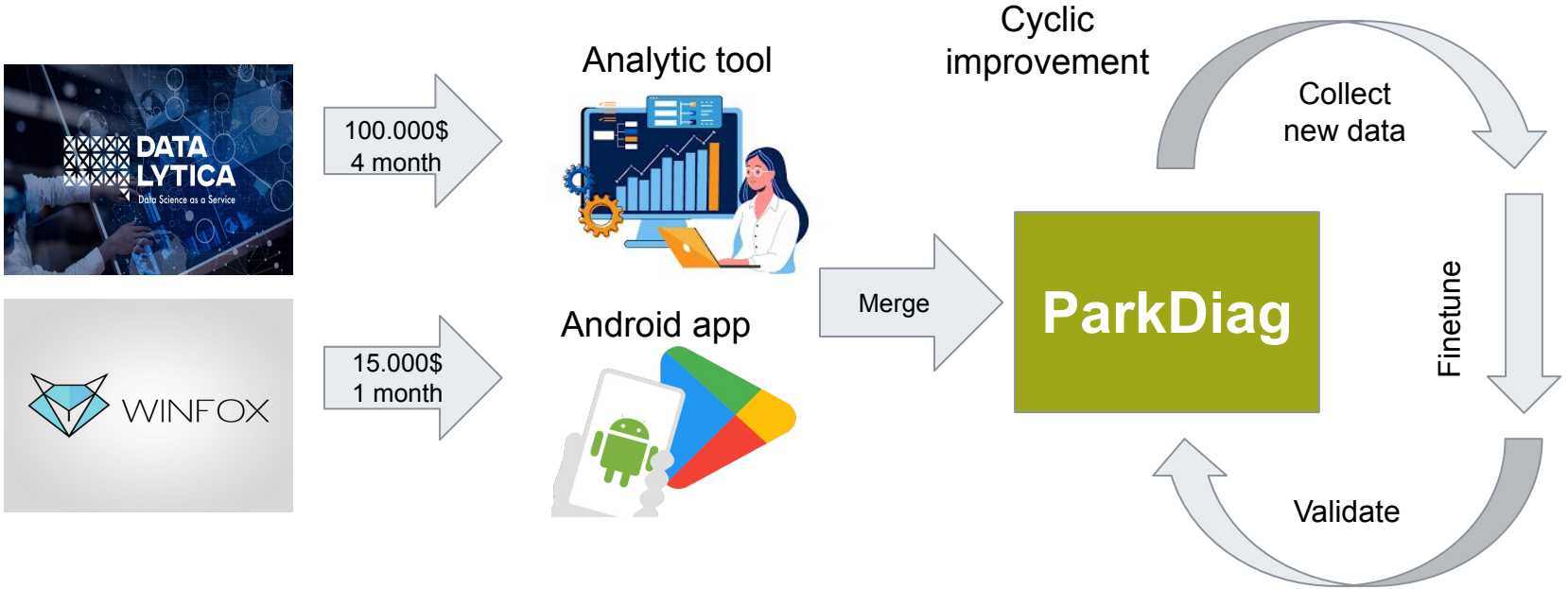
	Policy for Device Software Functions and Mobile Medical Applications, FDA	Council Directive 93/42/EEC, Medical Device Class IIa, EUR-Lex	Personalized Medical Devices, IMDRF
Existing Devices	pkg	STAT-ON	
MANUF	Reporting a Medical Device Reporting (MDR) to FDA: • **30 day reports of deaths**, serious injuries and malfunctions. • **5 day reports** for an event designated by FDA or an **event that requires remedial action to prevent an unreasonable risk** of substantial harm to the public health.	**The manufacturer must authorize the notified body** to carry out all the necessary inspections and supply it **with all relevant information**, in particular: • the documentation on the quality system, • the data stipulated in the part of the quality system relating to design, such as the **results of analyses, calculation tests,** etc.**,** • inspection reports and **test data, calibration data, qualification reports of the personnel concerned**, etc.	• **The manufacturer** of a custom-made medical device **should first ensure that all elements of the custom-made medical device definition are met**, obtaining the documented request and specific design characteristics **from an authorized healthcare professional.** • These authorized healthcare professional should be **knowledgeable** about the **available safety and performance information in respect of the requested device.**
QC	Quality System Requirements, Sec. 820.5: In general 8 main requirements. **Each manufacturer shall establish quality system procedures and instructions.**	• **Every product is examined individually** and the appropriate tests defined in the relevant standard. • a limit quality corresponding to a probability of acceptance of 5%, with a **non-conformity percentage of between 3 and 7%.**	It is **recommended** that the **Quality management system (QMS)** be **subject to third-party oversight** (e.g., an auditing organization or regulatory agency).
Source	**FDA** [1]https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-device-software-functions-and-mobile-medical-applications	**European Union** [2]https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31993L0042	**IMDFF** [3]https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-200318-pmd-rp-n58.pdf

Manufacturing & Delivery



Delivery:

- ParkDiag will be delivered via **android app**

Manufacture:

- App and model can be developed **independently**
- After **~4 month** we will have **working product** at cost **~115k $**
- Predictive model will be **continuously improved** using new data

Device Validation Protocol

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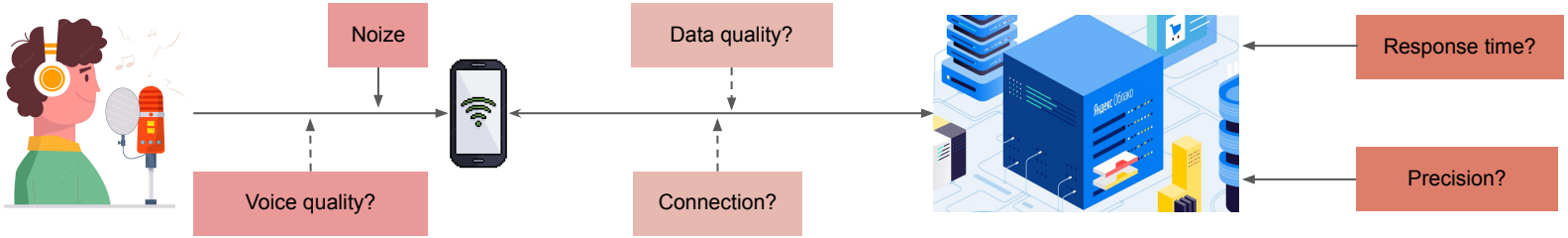

Performance validation	Tech-side validation	User validation
Input control. Voice/Signal validation	Server control	

1) Noize recognition - SNR might be more that 25dB
2) Voice quality - voice text have to give more than 75% word matches with text on screen. SpeechAPI - API for this purpose

1) Accuracy tests based on DS [1][2][3]
2) Response time. Queues problem solution is Yandex cloud
3) Server connection test
4) Data Validation method

1) Up to date version control check
2) Log user activity
3) Cross-platform app development framework

[1] Parkinson Speech Dataset with Multiple Types of Sound Recordings Data Set https://archive.ics.uci.edu/ml/datasets/Parkinson+Speech+Dataset+with++Multiple+Types+of+Sound+Recordings

[2] Parkinsons Data Set https://archive.ics.uci.edu/ml/datasets/parkinsons

[3] Animal Sound Archive https://www.gbif.org/dataset/b7ec1bf8-819b-11e2-bad2-00145eb45e9a

Pre-Clinical Design

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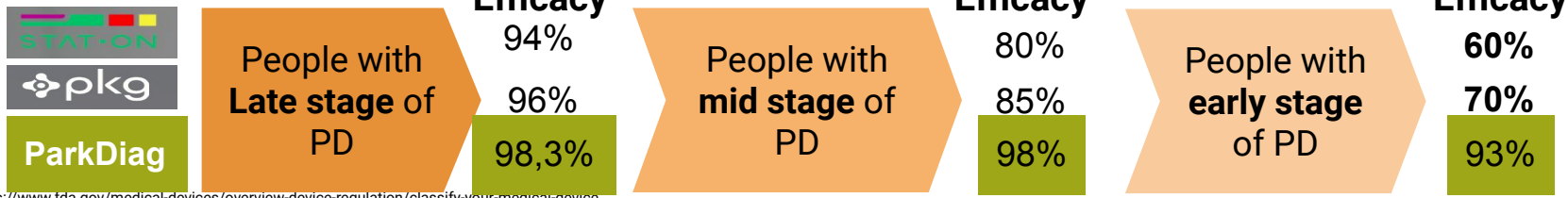
- According to 510k our MDSW is in low risk class.
- We are conducting two type of pre-clinical trial in parallel:

1. Development of our product (**ParkDiag** software).

	Phase I	Phase II	Phase III
Indication	Device should be safe to use: model should miss sick patients rarely.	• Phase I indication • Device should be efficient: on average if should be cheaper then doctor visit	Phase II indication at bigger scale
Design	Experiment would check statistical hypotheses about relations of doctor and model prediction outcomes probabilities, mentioned in indication fields. Patients would be selected randomly from females under 60 y.o who applied to neurologist under any neurological disease until there will be at least 10 sick persons. Rest candidates will be filtered to get 100 candidates in total. Groundtrooth diagnosis would be estimated with consilium of professional neurologists in fied.		
Endpoints	Method probability of false negative less than average docktor false negative probability	• Phase I endpoints • Method weighted (on cost) probability of false positive less than average docktor false positive probability	Phase II endpoints with bigger significance
# of patients	100	115	322

2. Comparison with existing devices in the market (they depend on the movement of the body).



[1] https://www.fda.gov/medical-devices/overview-device-regulation/classify-your-medical-device
[2] Accuracy of clinical diagnosis of Parkinson disease A systematic review and meta-analysis Giovanni Rizzo, Massimiliano Copetti, Simona Arcuti, Davide Martino, Andrea Fontana, Giancarlo Logroscino Neurology Feb 2016

Team Role

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Skolkovo Institute of Science and Technology

Belukhina Svetlana

Life Science, MOA+POC

Oussama Alyounes

SES, QC and patent

Kovalev Vyacheslav

Manuf + QC

Telepov Alexander

DS, Preclin+Reg+Clin