

What can Artificial Intelligence tell us about Brain Health?

Hyeokhyen Kwon, Ph.D., M.Sc.
Assistant Professor

J. Lucas McKay, Ph.D., M.S.C.R.
Associate Professor



EMORY
UNIVERSITY
SCHOOL OF
MEDICINE

Department of
Biomedical Informatics



Wallace H. Coulter Department of
Biomedical Engineering



EMORY
UNIVERSITY

No relevant conflicts

Hyeokhyen Kwon: No conflict of interest



Lucas McKay: Consulting for Biocircuit technologies



Outline

- Clinical evaluation of Parkinson's disease (McKay)
- AI solution for Parkinson's disease in clinic (Kwon)
- Future direction for AI at home (Kwon)
- Long-term view (McKay)

What is Parkinson's Disease (PD)

2nd most common neurodegenerative disorder.

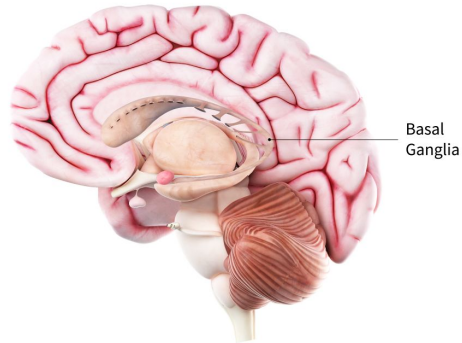
MORTALITY
>3x GREATER
for PEOPLE WITH PARKINSON'S than
for those without the disease (Hamilton & Yang et al. 2019)

TOTAL ANNUAL COST OF PARKINSON'S
DISEASE IN THE U.S.
= \$51.9 BILLION

What is Parkinson's Disease (PD)

Parkinson's Disease (PD) occurs when dopamine-producing cells in the basal ganglia die, often due to environmental exposures.

The basal ganglia are involved in movement planning and execution, but also in various nonmotor functions.



PARKINSON'S



ALL THE SAME BUT ALL DIFFERENT

Parkinson's disease symptoms are assessed clinically with a standardized motor exam ("MDS-UPDRS-III")



3.6b. Pronation-supination movements-LUE (2/4, SAF)

3.17b. Rest tremor amplitude-LUE (2/4, SAF)

3.17b. Rest tremor amplitude-LUE (2/4, SAF)

Other domains - gait, balance, speech, masked face



Our center uses motion capture technology during behavioral testing to make measurements more fine-grained

Use of 3D Motion Capture for Kinematic Analysis in Movement Disorders

The emerging technology, 3D motion capture, can improve diagnosis, clinical decision-making, and clinical trial precision in movement disorders.

Richa Tripathi, MD, MS,* J. Lucas McKay, PhD, MSCR,* and Christine D. Esper, MD, FAAN



Three-dimensional (3D) motion capture, a digital method of tracking and measuring body movements in space, has applications in various fields, including sports, entertainment, industrial engineering, and clinical practice. The fundamental principle of this technology involves using a precise arrangement of numerous cameras to track and record body motions in 3 dimensions.

State-of-the-art motion capture systems achieve the highest level of accuracy by using reflective markers placed on predetermined anatomic landmarks. Although there is no universally agreed-upon set of kinematic markers, the commonly used ones, such as the Helen Hayes and Cleveland Clinic marker sets, have many similarities and are often referenced. The markers are illuminated by multiple fixed cameras projecting light at specific frequencies, which is then reflected and captured by the cameras. The precise positioning of the cameras enables specialized software to use images from multiple cameras to calculate the exact 3D position of each marker through triangulation. By incorporating kinematic models based on participant-specific measurements and anthropometric reference data, these 3D marker coordinates can be transformed into clinically relevant variables, such as patterns of flexion and extension of individual joints over time. Because of the logistical challenges associated with applying markers and calibrating motion capture systems for individual patients, emerging markerless motion capture technologies use recent advances in computer vision technologies to achieve similar results using synchronized recordings from consumer-grade video cameras. Validation of

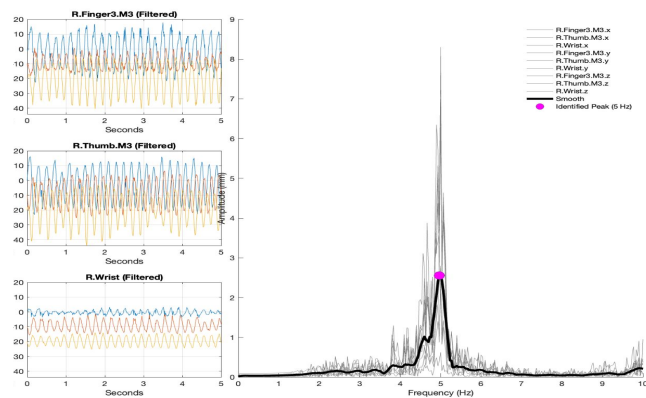
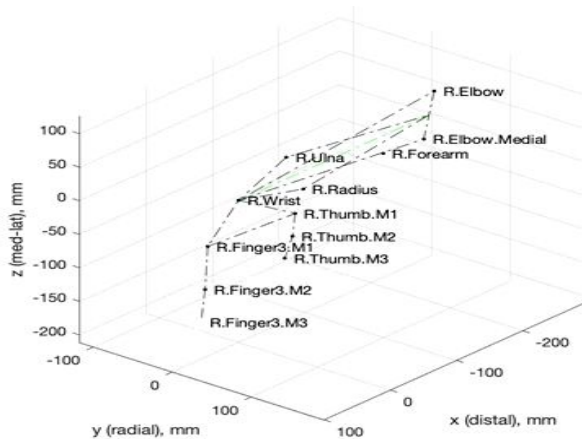
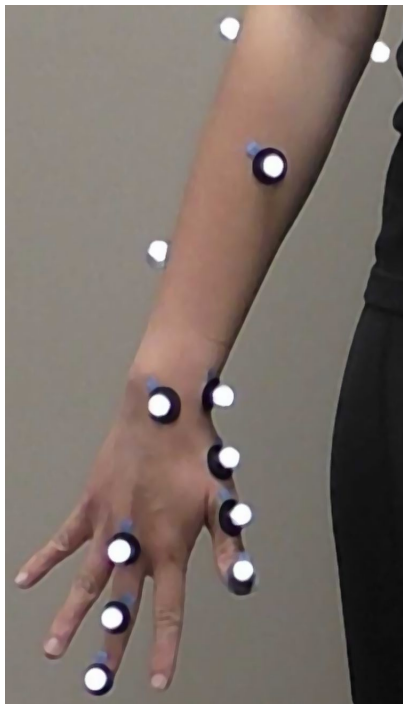
these markerless approaches against the standard marked systems is ongoing.¹ Data from 3D motion capture can be used in clinical practice to measure movements including joint angles, gait characteristics, and tremor amplitudes and frequency.

It is the authors' belief that 3D motion capture holds promise as a valuable tool for neurologists, offering potential benefits by augmenting data captured in validated clinical rating scales, minimizing subjectivity associated with human raters, and enhancing reliability. It allows for continuous measurements of symptom severity, potentially surpassing the precision of ordinal clinical rating scales. This heightened precision may enhance sensitivity in identifying preclinical disease, disease progression, and postintervention changes, and may assist in the diagnostic process (eg, tremor categorization).

Motion Capture

The authors' center (Emory University School of Medicine, Atlanta, GA) uses a Vicon (Hauppauge, NY) 3D optical motion capture system instrumented with 14 Vicon Vero cameras and 3 FLIR (Wilsonville, OR) Blackfly S BFS-U3-2353C cameras for color video, a raised floor and 2 AMTI (Arlington, VA) HPS400600HF-2K-SYS force plates, Nexus (Austin, TX) v2.15 software, and a Vicon Lock box to integrate analog signals with the system. The motion capture system is capable of triangulating and recording the instantaneous 3D coordinates of each infrared reflective spatial marker attached to the individual's skin or clothing before motor testing in real-time. Sixty spatial markers are applied to a standardized set of bony landmarks (augmented Helen Hayes full body marker set; Figure 1, A and B). Each marker is an infrared-reflective sphere with

Tremor quantification in EMR



Gait outcomes in EMR

GAIT ANALYSIS					
<i>Spatiotemporal Indices:</i>	RIGHT	NORMALS	LEFT	RT/NOR M	LT/NORM
Step Length Avg (cm)	45.06	64.88	49.18	69.45	75.81
Standard Deviation	1.81	7.6	1.68		
Number of Steps	15	10	13		
Stride Length Avg (cm)	93.94	129.82	94.57	72.36	72.85
Standard Deviation	2.65	15.05	2.57		
Number of Strides	12	10	11		
Forward Velocity Avg (cm/s)	75.25	118.34	75.37	63.59	63.69
Standard Deviation	2.57	17.83	2.6		
Number of Strides	12	10	11		
Cadence Avg (steps/min)	95.52	109.46	95.4	87.27	87.16
Standard Deviation	2.25	8.52	3.02		
Number of Steps	12	10	11		
Total Support Time (%)	65.82	60.56	64.11	108.68	105.86
Standard Deviation	0.85	0.87	1.64		
Number of Strides	12	10	11		
Swing Phase (%)	34.19	39.44	35.89	86.68	91
Standard Deviation	0.85	0.87	1.64		
Number of Strides	12	10	11		
Initial Double Support Time (%)	15.06	10.53	15.22	143.03	144.49
Standard Deviation	1.38	0.83	0.73		
Number of Strides	12	10	11		
Single Support Time (%)	35.89	39.44	34.19	91	86.68
Standard Deviation	1.64	0.87	0.85		
Number of Strides	11	10	12		
Step Width (cm)	15.49	11.97	15.49	129.41	129.41
Standard Deviation	1.08	3.31	1.08		
Number of Trials	5	10	5		

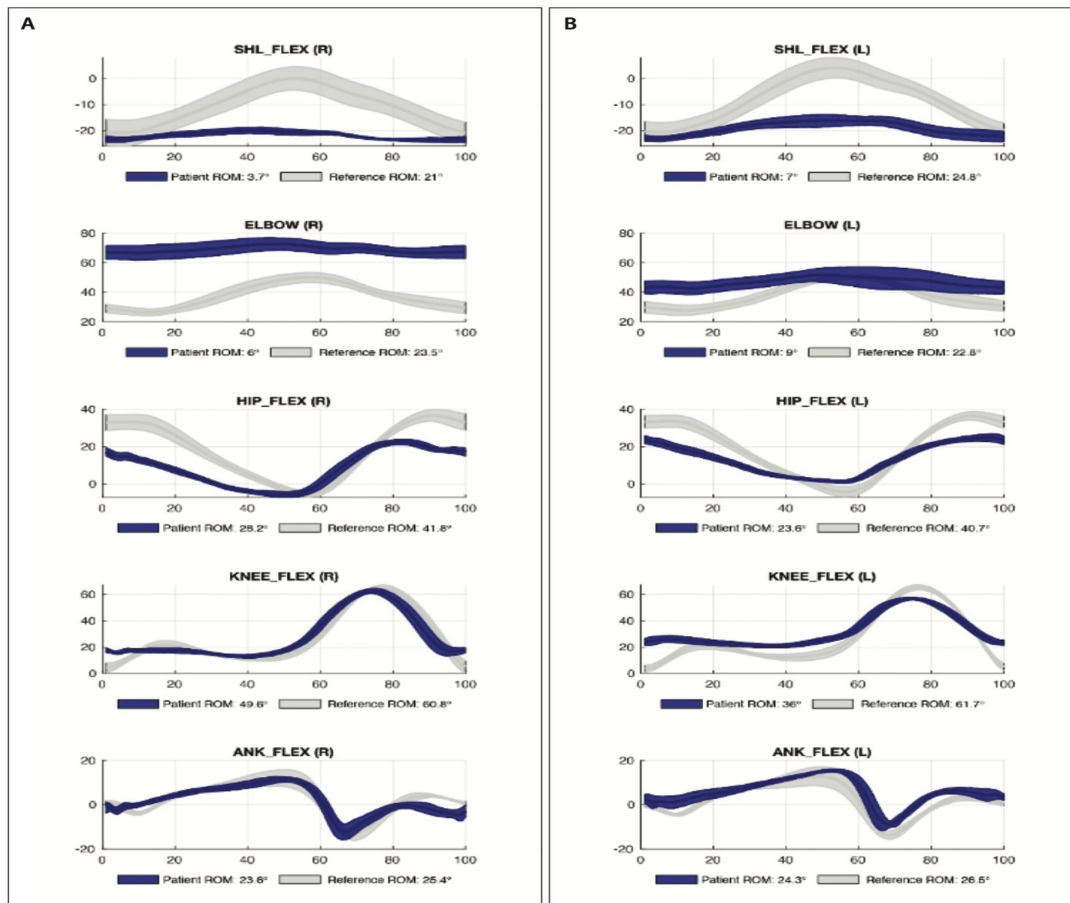


Figure 3. Kinematic analysis of gait in Parkinson disease. Images corresponding to the right (A) and left (B) sides of the body are shown. Each subplot shows an individual sagittal plane joint angle versus time, expressed as 0 to 100% of the gait cycle. Comparison of the shoulder and elbow (top 2 rows; blue) versus reference data (gray) reveals frank reduced arm swing (eg, on the right side [A], 3.7 degrees of shoulder motion for the individual versus 21 degrees of motion for the reference data). Note also the increased fixed flexion of the elbow on the right side—an asymmetry common in Parkinson disease. This individual's lower-limb gait patterns were not remarkably different from those of healthy individuals (HIP_FLEX, KNEE_FLEX, ANK_FLEX).

Freezing-of-Gait (FOG)



FoG is “mysterious”

1. FoG can be resistant to pharmacological medications
2. FOG phenotypes are varying across patients :
mixture of tremor (violent shakes) and rigid (akinetic)

The New Freezing of Gait Questionnaire: Unsuitable as an Outcome in Clinical Trials?

Femke Hulzinga, MSc,¹ Alica Nieuwboer, PhD,¹ Bauke W. Dijkstra, MSc,¹ Martina Mancini, PhD,² Carolien Strouwen, PhD,³ Bastiaan R. Bloem, MD, PhD,⁴ and Pieter Gais, PhD^{5*}

Clinical standard measurements for FOG are insufficient

ABSTRACT: Background: Freezing of gait (FOG) is a common gait deficit in Parkinson's disease. The New Freezing of Gait Questionnaire (NFOG-Q) is a widely used and valid tool to quantify freezing of gait severity. However, its test-retest reliability and minimal detectable change remain unknown.

Objective: To determine the test-retest reliability and responsiveness of the NFOG-Q.

Methods: Two groups of freezers, involved in 2 previous rehabilitation trials, completed the NFOG-Q at 2 time points (T1 and T2), separated by a 6-week control period without active intervention. Sample 1 (N = 57) was measured in ON and sample 2 (N = 14) in OFF. We calculated various reliability statistics for the NFOG-Q scores between T1 and T2 as well as correlation coefficients with clinical descriptors to explain the variability between time points.

Results: In sample 1 the NFOG-Q showed modest reliability (intraclass correlation coefficient = 0.68 [0.52–0.80]) without differences between T1 and T2. However, a minimal detectable change of 9.95 (7.90–12.27) points emerged for the total score (range 28 points, relative minimal detectable change of 35.5%). Sample 2 showed largely similar results. We found no associations between cognitive-related or disease severity-related outcomes and variability in NFOG-Q scores.

Conclusions: We conclude that the NFOG-Q is insufficiently reliable or responsive to detect small effect sizes, as changes need to go beyond 35% to surpass measurement error. Therefore, we warrant caution in using the NFOG-Q as a primary outcome in clinical trials. These results emphasize the need for robust and objective freezing of gait outcome measures.

Freezing of gait (FOG) is a prominent and debilitating symptom of Parkinson's disease (PD). It affects up to 80% of PD patients during the course of the disease.^{1–3} FOG is defined as the inability to progress forward stepping despite the intention to walk and reach a destination.⁴ Furthermore, FOG is one of the most frequent causes of falls in PD, thus contributing to high fall rates ranging from 35% up to 90%.^{1,5,6} FOG seriously impedes daily life functioning and overall quality of life.^{7,8} So far, the treatment of FOG, including pharmacological, surgical, and rehabilitation interventions, is only partially effective.^{4,9} Therefore, new and more personalized rehabilitation approaches are now being developed. To evaluate their effectiveness, valid and reliable

assessment is necessary to document FOG severity and its progression.

A recent review of Mancini and colleagues¹⁰ highlighted that FOG assessment is hampered by several factors in clinical and laboratory settings. First, the episodic and unpredictable nature of FOG increases the likelihood of missing the event during formal or "online" performance tests of gait. Second, various "testing effects" may be at play that enhance or reduce the occurrence of FOG, such as consciously attending to walking, stepping in broad and well-lit corridors, and experiencing medication effects and stress.^{3,10,11} To overcome these issues, Giladi and colleagues¹¹ developed the original Freezing of Gait Questionnaire (FOG-Q), which was later revised

¹KU Leuven, Department of Rehabilitation Sciences, Neurorehabilitation Research Group, Leuven, Belgium; ²Department of Neurology, Oregon Health & Science University, Portland, Oregon, USA; ³UHasselt, Faculty of Rehabilitation Sciences, Rehabilitation Research Center, Hasselt, Belgium; ⁴Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Department of Neurology, Centre of Expertise for Parkinson & Movement Disorders, Nijmegen, the Netherlands

*Correspondence to: Dr. Pieter Gais, Department of Rehabilitation Sciences, Teruurssevest 101, 3001 Leuven, Belgium; E-mail: pieter.gais@kuleuven.be

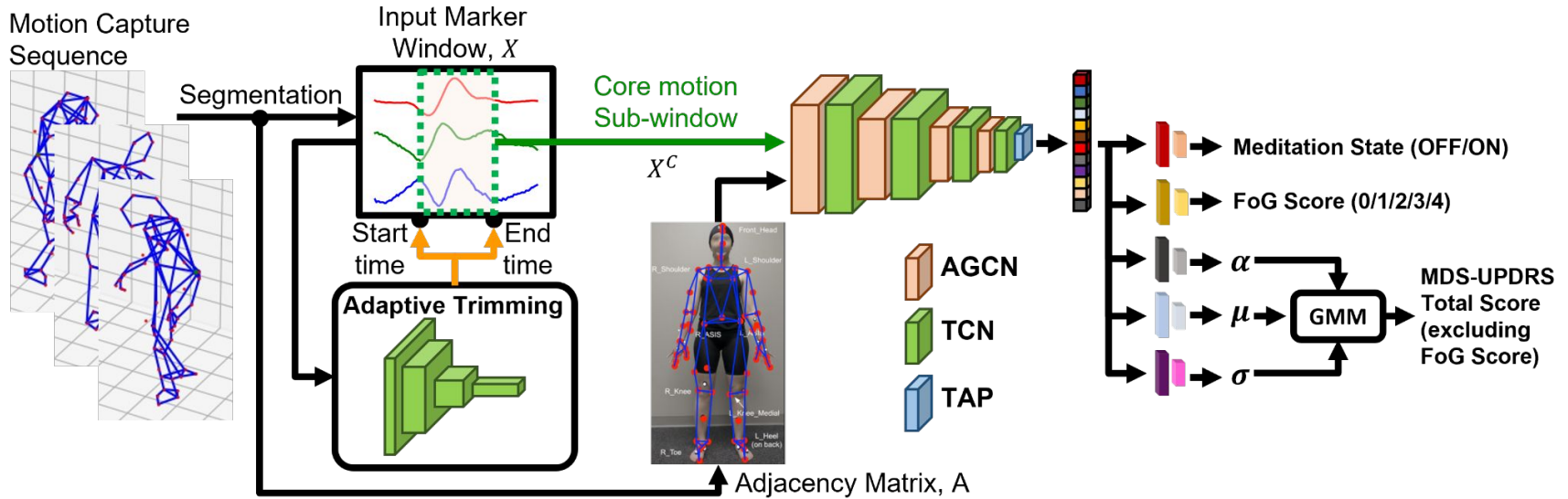
Keywords: new freezing of gait questionnaire, freezing of gait, minimal detectable change, reliability.

Relevant disclosures and conflicts of interest are listed at the end of this article.

Received 21 November 2019; revised 13 December 2019; accepted 30 December 2019.

Published online 14 January 2020 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mdc3.12893

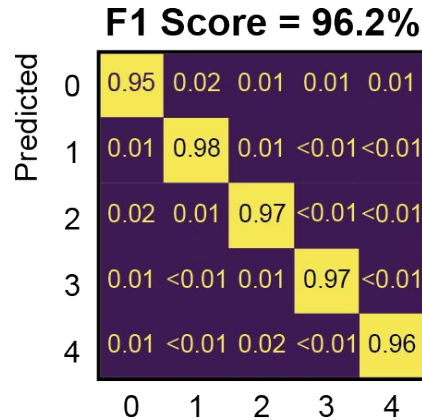
Explainable AI (XAI) for FOG



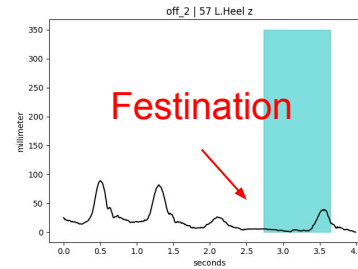
Explainable AI (XAI) for Freezing-of-Gait

Automatically Detected FOG Score
from 3D kinematics

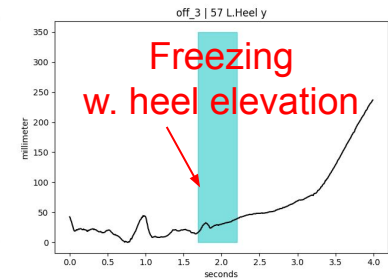
**MDS-UPDRS-III FOG item
Classification**



Validated Sub-movements with
Clinical Experts (“Explainable”)



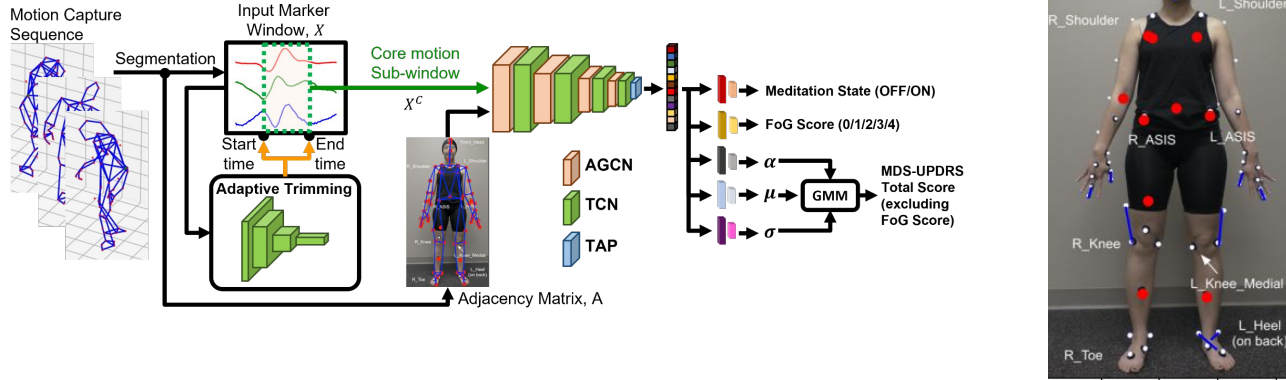
Moderate FOG



Severe FOG

Explainable AI (XAI) for Freezing-of-Gait

Automatically Detected FOG phenotypes across Whole Body



- Top 10 most influential joints
- Top 10 most Influential limbs

Toward Accessible, Affordable, Scalable AI for Brain Health

Hyeokhyen Kwon, Ph.D., M.Sc.
Assistant Professor



EMORY
UNIVERSITY
SCHOOL OF
MEDICINE

Department of
Biomedical Informatics



EMORY | COLLEGE OF ARTS AND SCIENCES

Computer Science



Georgia
Tech.

Wallace H. Coulter Department of
Biomedical Engineering



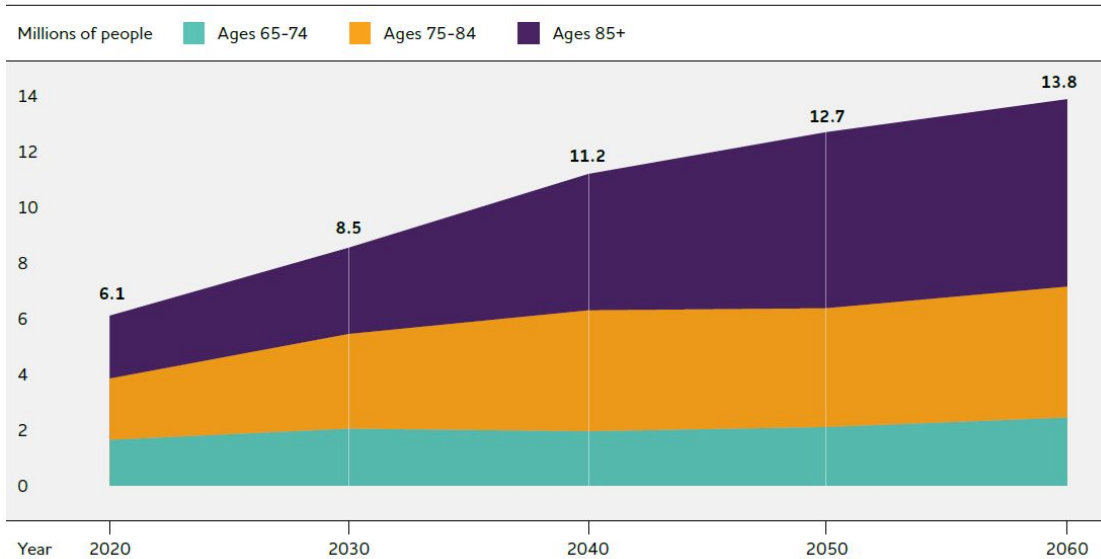
EMORY
UNIVERSITY

Georgia Tech  **Machine Learning**

Challenges in Managing Brain Health

Projected number of older people with Alzheimer's Dementia

Projected Number of People Age 65 and Older (Total and by Age) in the U.S. Population with Alzheimer's Dementia, 2020 to 2060



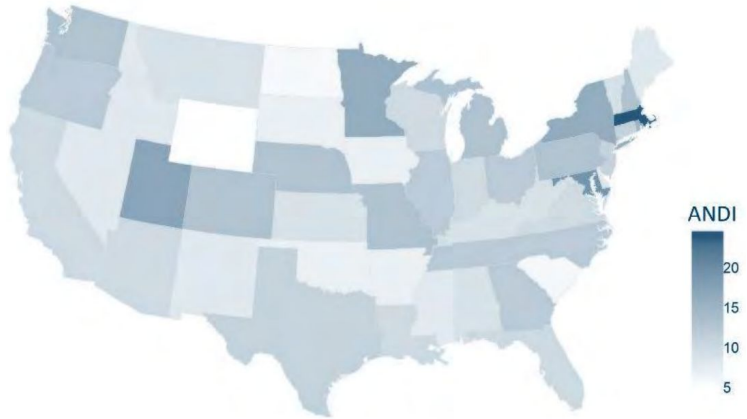
1 in 3 seniors
die with Alzheimer's or another dementia

Challenges in Managing Brain Health

Unmet needs with limited number health workers



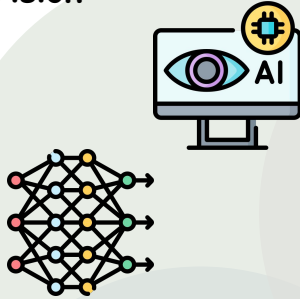
20% decrease in mental health workers in the next decade



20 states are *Dementia neurology deserts*

Machine Learning and Computing for Behavior Sensing

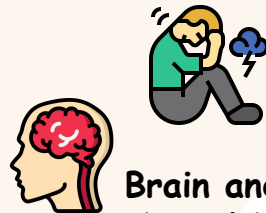
Machine Learning
Computer Vision



Ubiquitous Computing
(or Mobile Devices)



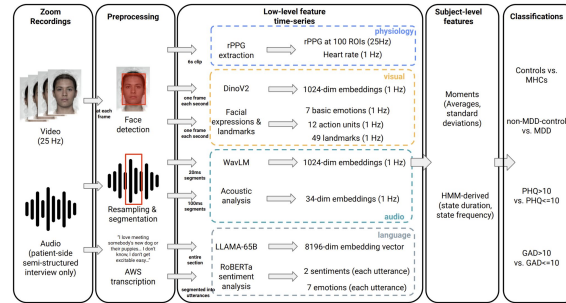
Human
Behaviors



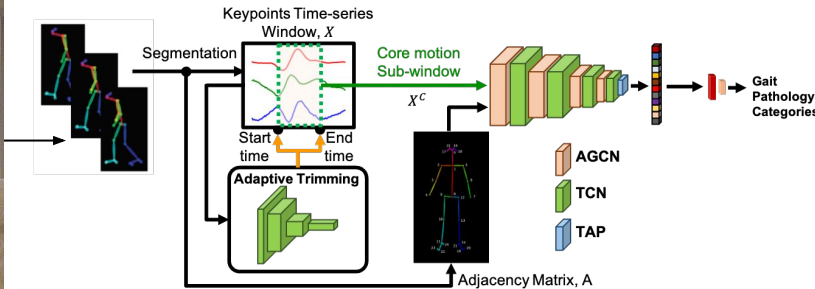
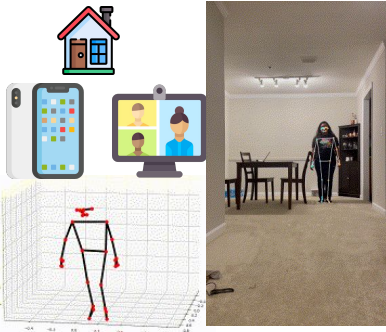
Brain and
Mental Health

- Smart Telehealth

Smart Telehealth with Multi-modal & On-device AI



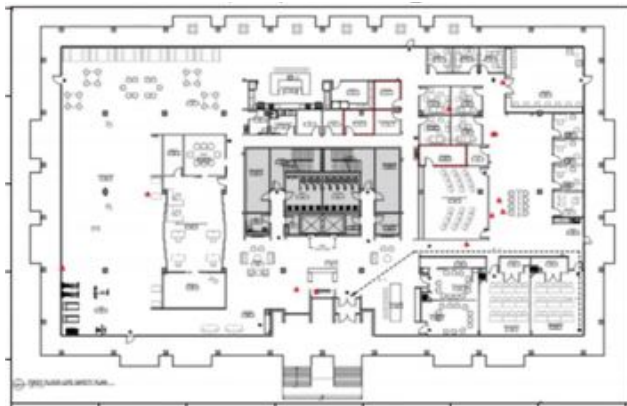
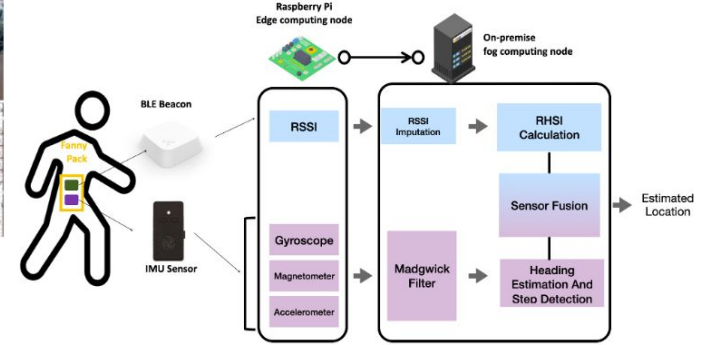
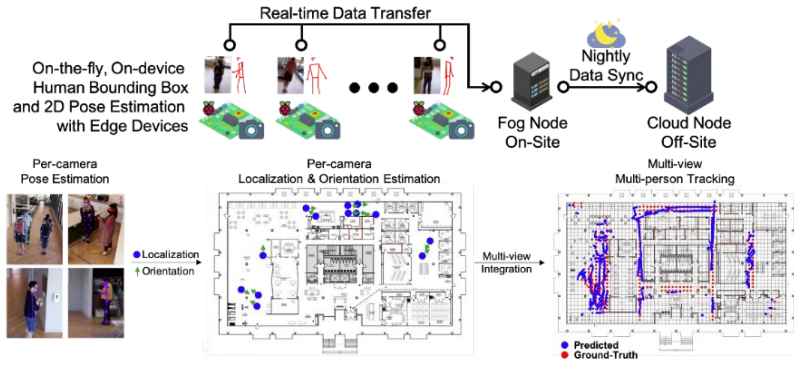
Facial, audio, language foundation models



Shriners Hospitals for Children

Realtime, On-device Mobile Computer Vision

Smart Hospital with Privacy-preserving AI



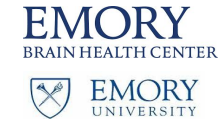
40 cameras + 30 microphones + Wearables

Continuous, Passive, Privacy-preserving

Patient Monitoring in **1700m²**

- Multi-person Tracking

- Social Interaction Detection

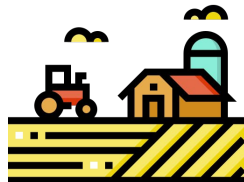


Emory Autism Center

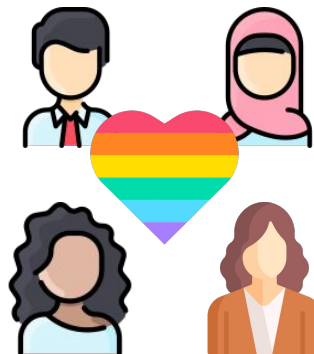


Toward Accessible, Affordable, and Fair AI for Health

Across urban and rural communities



Including various people from different gender/ethnic/socioeconomic

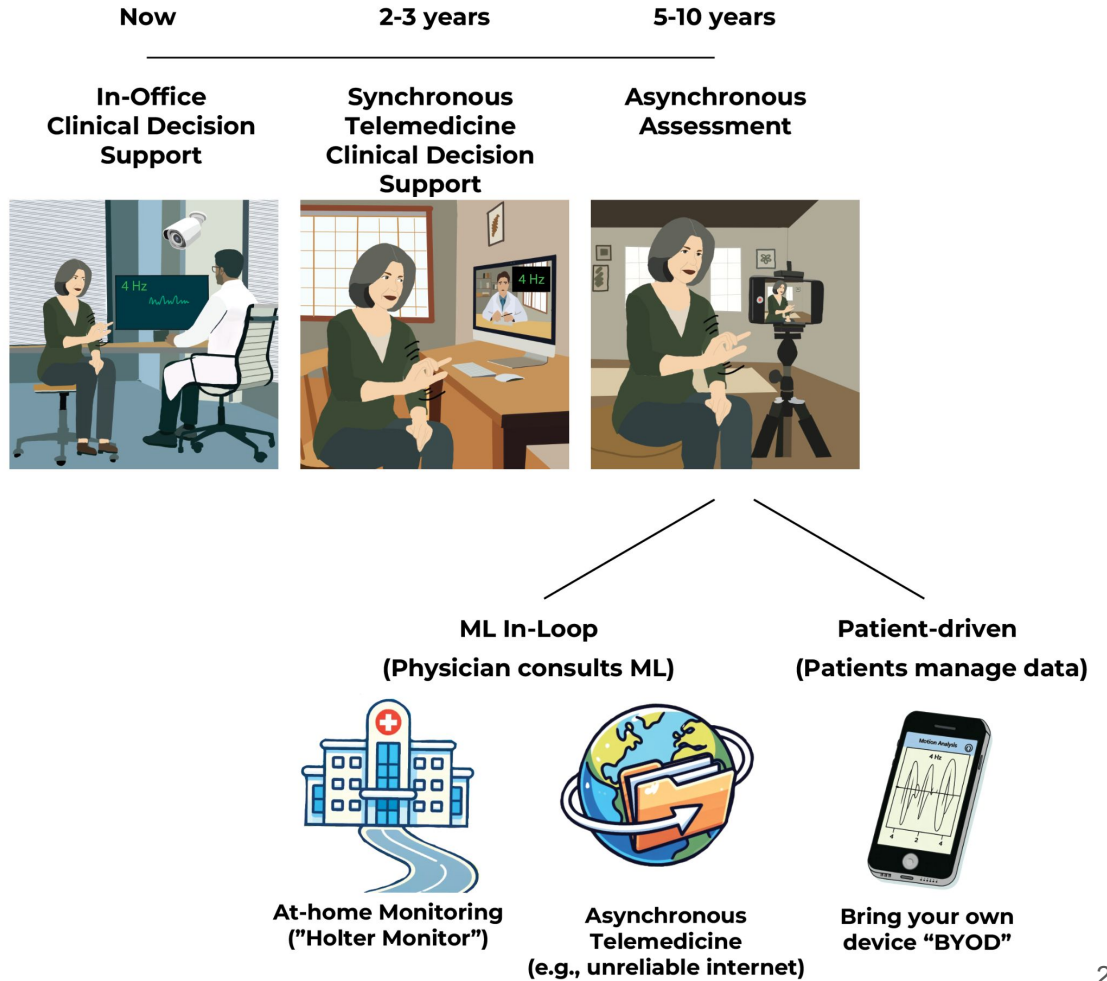


Toward Accessible, Affordable, Fair Health AI

- ✓ Affordable, accessible health monitoring in daily living
- ✓ Help patients/clinicians to make informed decision



A longer-term view



Acknowledgements



**Minoru
Shinohara,
Ph.D., FACSM**



**Trisha Kesar,
PT, Ph.D.**



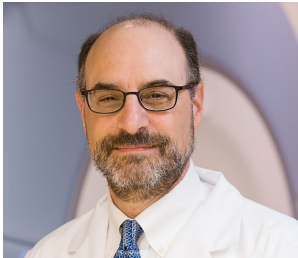
**Gari D. Clifford,
DPhil**



**Ross Chafetz,
PT, DPT,
Ph.D., MPH**



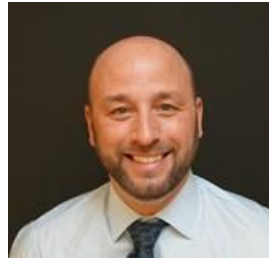
**Christine Esper,
MD**



**Stewart Factor,
DO**



**Jeremy P.
Bauer, MD**



**Joe Krzak,
PT, Ph.D.,
PCS**



Shriners Hospitals
for Children

THE JAMES M.
COX
FOUNDATION



and more ...

ORACLE

Curtis Family Fund
Sartain Lanier Family Foundation (SAF)
NIH K25HD086276 (JLM)

Contact Information

Hyeokhyen Kwon, Ph.D., M.Sc.
Assistant Professor



hyeokhyen.kwon@emory.edu

J. Lucas McKay, Ph.D., M.S.C.R
Associate Professor



lucas@dbmi.emory.edu

