

Development of Novel Digital Clinical Endpoints and a Global Standard of Measures for Application in Sensor Based Assessment of Mobility and Balance

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Clinical Research and Development

Investing in Digital Innovation and Transformation

“Software is changing how clinicians practice medicine, how consumers manage their own health and how patients and providers interact.”

Deloitte.

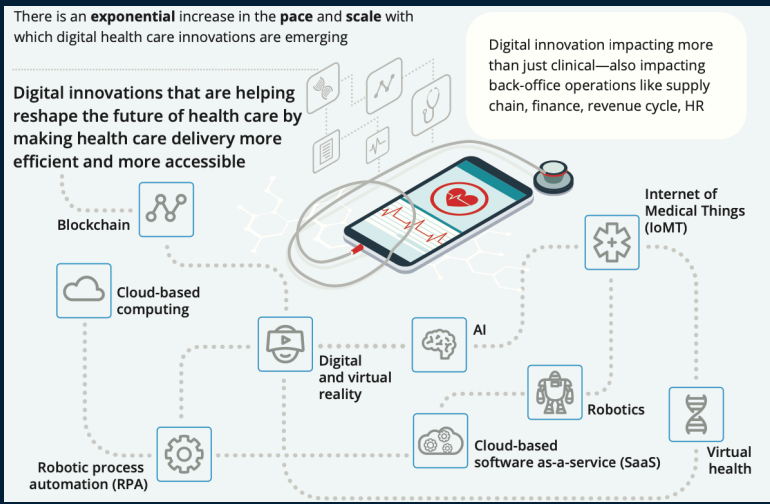
One revolutionary development in digital health technology is software that can perform complex medical functions—
Software as a Medical Device.

Software that can diagnose conditions,
suggest treatments,
and inform clinical management



Global Health Outlook

Digital Innovation and Transformation



How is digital helping?

- diagnosis & treatment
- quality
- speed & accuracy
- accelerating the development of new drugs and devices
- personalization
- self-service
- patient experience
- training

Digital innovation is **supporting** and **augmenting** workers and not replacing them. It is allowing highly trained resources to focus on more **valuable, patient-facing** activities.

Digital technologies are supporting health systems' efforts to transition to new models of patient-centered care and "smart health" approaches to drive innovation, increase access and affordability, improve quality, and lower costs.

Virtual health

64% of consumers point to convenience and access as important benefits of virtual health

Physicians' top benefits:

- improved patient access to care
- improved patient satisfaction
- staying connected with patients and their caregivers

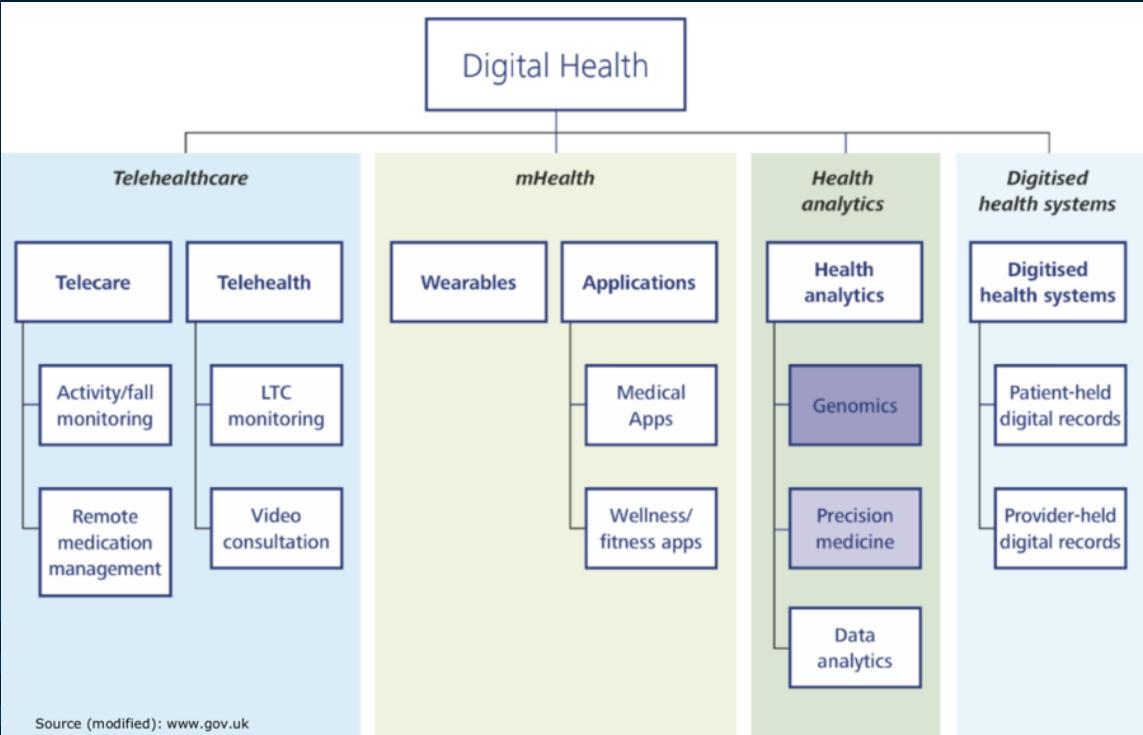
Barriers of virtual health

- lack of reimbursement
- complex licensing requirements
- high cost of the technologies
- reliability/errors
- privacy & security



European Medicines Agency

Digital Health



EMA Experience with review of Digital Technology proposals in Medicine Development Programs

U.S. Food and Drug Administration

Digital Health

- Many medical devices now have the ability to connect to and communicate with other devices or systems.
- Devices that are already FDA approved or cleared are being updated to add digital Features.
- New types of devices that already have these capabilities are being explored.

Many stakeholders are involved in digital health activities, including patients, health care practitioners, researchers, traditional medical device industry firms, and firms new to FDA regulatory requirements, such as mobile application developers



- Wireless Medical Devices
- Mobile medical apps
- Health IT
- Telemedicine
- Medical Device Data Systems
- Medical device Interoperability
- **Software as a Medical Device (SaMD)**
- General Wellness
- Cybersecurity

Mobilize-D

Connecting Digital Mobility Assessment to Clinical Outcomes for Regulatory and Clinical Endorsement

Mobilise-D will build an all-encompassing, clinically-valid digital mobility assessment system capable of use across all conditions where mobility loss is relevant and bring with it a personalized approach to healthcare for the benefit of citizens in the EU and globally

Our ultimate goal is to provide a validated, robust set of algorithms to measure digital mobility outcomes and in turn, inform therapeutic development, clinical practice, precision medicine, industrial development and stakeholder approval.”

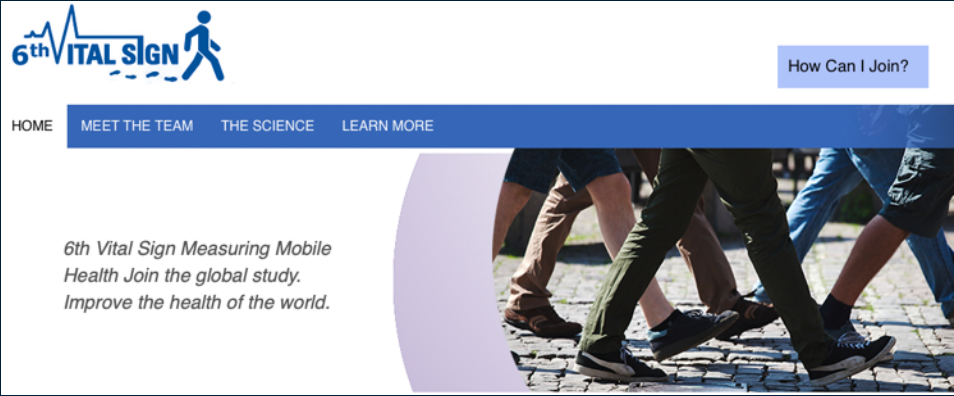
Professor Lynn Rochester





6th Vital Sign

Duke Clinical Research Institute



Research Trends

“Sensors for Gait, Human Movement Analysis and Health Monitoring”



sensors

an Open Access Journal by MDPI

Sensors for Gait, Human Movement Analysis, and Health Monitoring

Guest Editor:

Dr. Marco Iosa

IRCCS Foundation Santa Lucia,
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Deadline for manuscript
submissions:

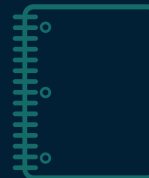
31 December 2020

Message from the Guest Editor

This Special Issue aims to highlight the most recent research regarding sensors and their applications in gait analysis and, more generally, human movement analysis, including in health monitoring.

Contributions are invited from groups active in this field of research.

- gait analysis
- locomotion
- movement assessment
- motion capture
- stereophotogrammetry
- inertial measurement unit
- health monitoring



Motion Sensors

In Silico Digital Twins



Estimating wearable motion sensor performance from personal biomechanical models and sensor data synthesis



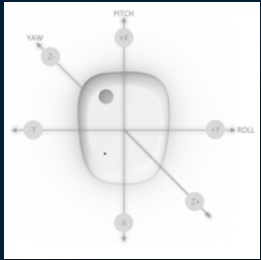
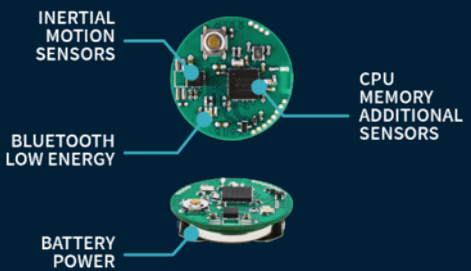
Oliver Amft and Adrian Derungs

Digital Health, Friedrich-Alexander-Universität
Erlangen-Nürnberg (FAU), Erlangen, 91052, Germany



Materials

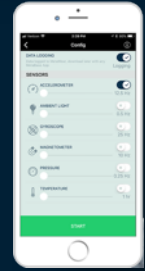
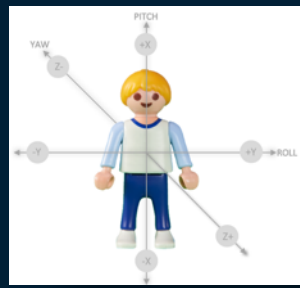
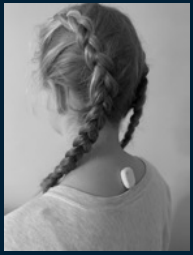
Inertial Measurement Unit



mbientlab

mbientlab MMR 9-axis IMU Fusion Sensor

The MetaMotionR (MMR) is a wearable device that offers real-time and continuous monitoring of motion and environmental sensor data.



Materials

Software



- SAS Viya Analytic Platform

https://www.sas.com/en_us/software/viya.html

- SAS Event Stream Processing

https://www.sas.com/en_us/software/event-stream-processing.html

- SAS Analytics for IoT

https://www.sas.com/en_us/software/analytics-iot.html



Test Subjects

Fun Science Project for the Whole Family

Morbidity = Enthesitis¹

- Subjects: females in their mid-teens
- Symptoms much worse in one twin
- Assessment was made without therapeutic intervention



Morbidity = Psoriatic Arthritis²

- Subject: Male in his mid 50's
- Assessment was made without therapeutic intervention



¹*Enthesitis*: Tenderness at the site of attachment of bone to a tendon, ligament, or joint capsule

²*Psoriatic Arthritis*: Arthritis associated with psoriasis. The exacerbations and remissions of arthritic symptoms do not always parallel those of psoriasis

(Taber's Cyclopedic Medical Dictionary)

Assessment Protocol

Berg Balance Scale

Berg Balance Scale (BBS)

Item Description: SCORE (0–4)

- | | |
|-------|---|
| _____ | 1. Sitting to standing |
| _____ | 2. Standing unsupported |
| _____ | 3. Sitting unsupported |
| _____ | 4. Standing to sitting |
| _____ | 5. Transfers |
| _____ | 6. Standing with eyes closed |
| _____ | 7. Standing with feet together |
| _____ | 8. Reaching forward with outstretched arm |
| _____ | 9. Retrieving object from floor |
| _____ | 10. Turning to look behind |
| _____ | 11. Turning 360 degrees |
| _____ | 12. Placing alternate foot on stool |
| _____ | 13. Standing with one foot in front |
| _____ | 14. Standing on one foot |
| _____ | Total |

Equipment needed:	Ruler, 2 standard chairs (one with arm rests, one without), footstool or step, stopwatch or wristwatch, 15 ft walkway
Time needed:	15–20 minutes
Scoring:	A five-point ordinal scale, ranging from 0–4. “0” indicates the lowest level of function and “4” the highest level of function. Total score = 28
Interpretation:	41–56 = low fall risk 21–40 = medium fall risk 0–20 = high fall risk <36 fall risk close to 100%

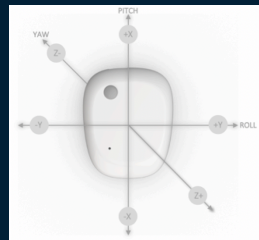
Subject Assessment

Recording Protocol

- IMU was placed at the base of the C7 vertebra
- Acceleration and Gyroscopic recordings were made
- Data were collected at a sample rate of 50 Hz
- Each recording lasted 30 seconds
- Recordings allowed an initial 5 second period for subject to stabilize

elapsed (s)	x-axis (g)	y-axis (g)	z-axis (g)	x-axis (deg/s)	y-axis (deg/s)	z-axis (deg/s)
0.00	-0.0086	-0.0002	-0.0099	-0.1070	0.6970	0.4150
0.02	-0.0096	0.0028	-0.0119	0.1710	0.5140	0.4650
0.04	-0.0096	0.0068	-0.0109	0.3770	0.3960	0.3770
0.06	-0.0136	-0.0022	-0.0099	0.3120	-0.1870	0.1370
0.08	-0.0076	-0.0022	-0.0049	0.3510	-0.4840	0.0380
0.10	-0.0016	-0.0002	-0.0029	0.5720	-0.7930	0.3050
0.12	-0.0006	0.0018	-0.0059	-0.1070	-1.8250	-0.3010
0.14	0.0014	0.0008	-0.0039	-0.1750	-1.7190	-0.2740
0.16	0.0014	0.0008	-0.0049	0.4540	-1.1890	0.2400
0.18	-0.0026	0.0028	-0.0039	0.4610	-0.9870	0.6900
0.20	-0.0006	0.0038	-0.0009	-0.1790	-0.4650	1.1200
0.22	0.0004	0.0008	0.0001	-0.2100	-0.3660	1.0180
0.24	0.0024	0.0008	-0.0009	-0.0910	-0.6210	0.8840
0.26	0.0024	0.0028	0.0011	-0.0230	-0.5180	1.0140
0.28	0.0004	-0.0002	-0.0029	0.2020	-0.1450	0.8120
0.30	0.0004	-0.0002	-0.0049	0.2520	0.3320	0.7280
0.32	-0.0006	0.0008	-0.0049	0.5180	0.4000	0.6360
0.34	-0.0046	0.0008	-0.0059	0.5600	0.0110	0.2710
0.36	-0.0036	0.0018	-0.0059	0.4190	0.4460	0.1600
0.38	-0.0036	0.0038	-0.0049	0.4650	0.7810	0.2520

- Acceleration was measured in units of gravitational force (g).
- Gyroscopic measurements of rotation were made in Degrees per Second (deg/s)



Test Subjects

Recording Protocol



- Four assessments were made for each subject in triplicate
 - Standing with eyes open
 - Standing with eyes closed
 - Standing with eyes open supported
 - Standing with eyes closed supported

Data Preparation

Accelerometer Data

- 1st 5 seconds discarded to allow subject to settle into position
- Discarded initial 5 seconds of time series
- Retained following 20 seconds for analysis
- Aggregated accelerometer data
 - Z-normalized
 - By axial plane
 - Eyes open vs. closed
 - Standing supported vs. unsupported

Eyes Open: X axis (deg/s)

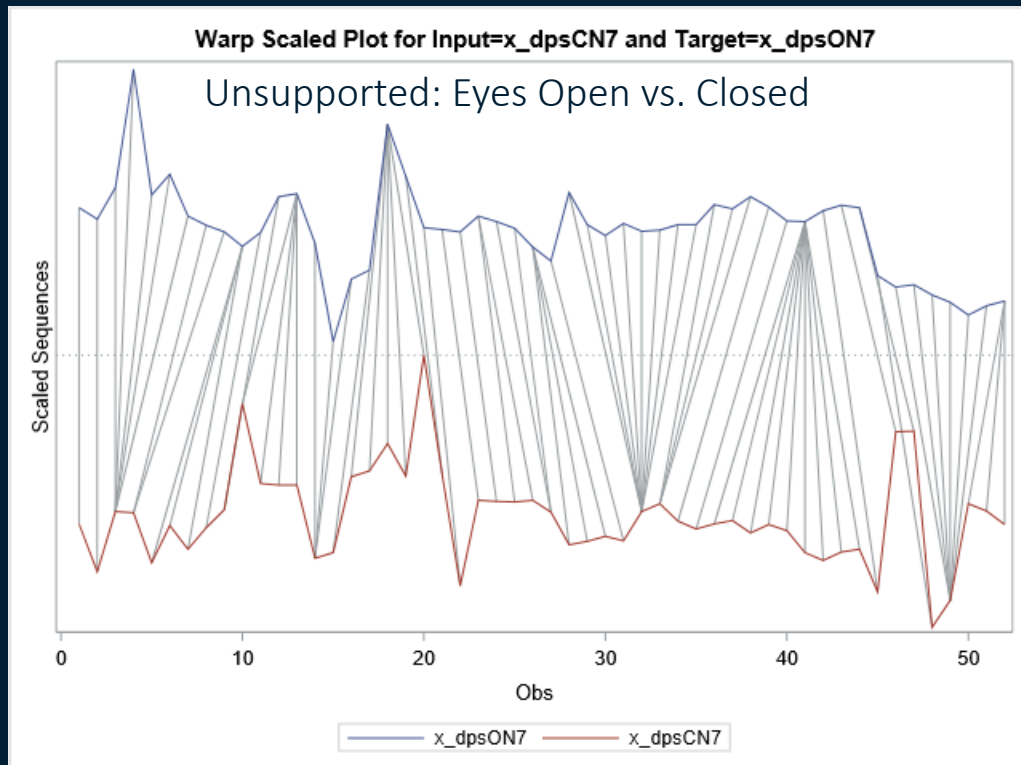
Seconds	Supported	Unsupported
5.02	0.305	0
5.04	0.152	-0.091
5.06	0.091	-0.122
5.08	0.213	-0.061
5.1	0.305	0
5.12	0.213	0.061
5.14	0.03	0.061
...	...	...

Data Analysis

Compared subject data using Dynamic Time Warping (DTW)

DTW is a method for assessing the similarity of 2 time series that may vary in timing

- PROC SIMILARITY
- Warp constraint = 10%
- Time Series Comparisons
 - Unsupported: Eyes Open/Closed
 - Supported: Eyes Open/Closed
 - Eyes Open: Unsupported/Supported
 - Eyes Closed: Unsupported/Supported



DATA Analysis

Subject Segmentation - Classification

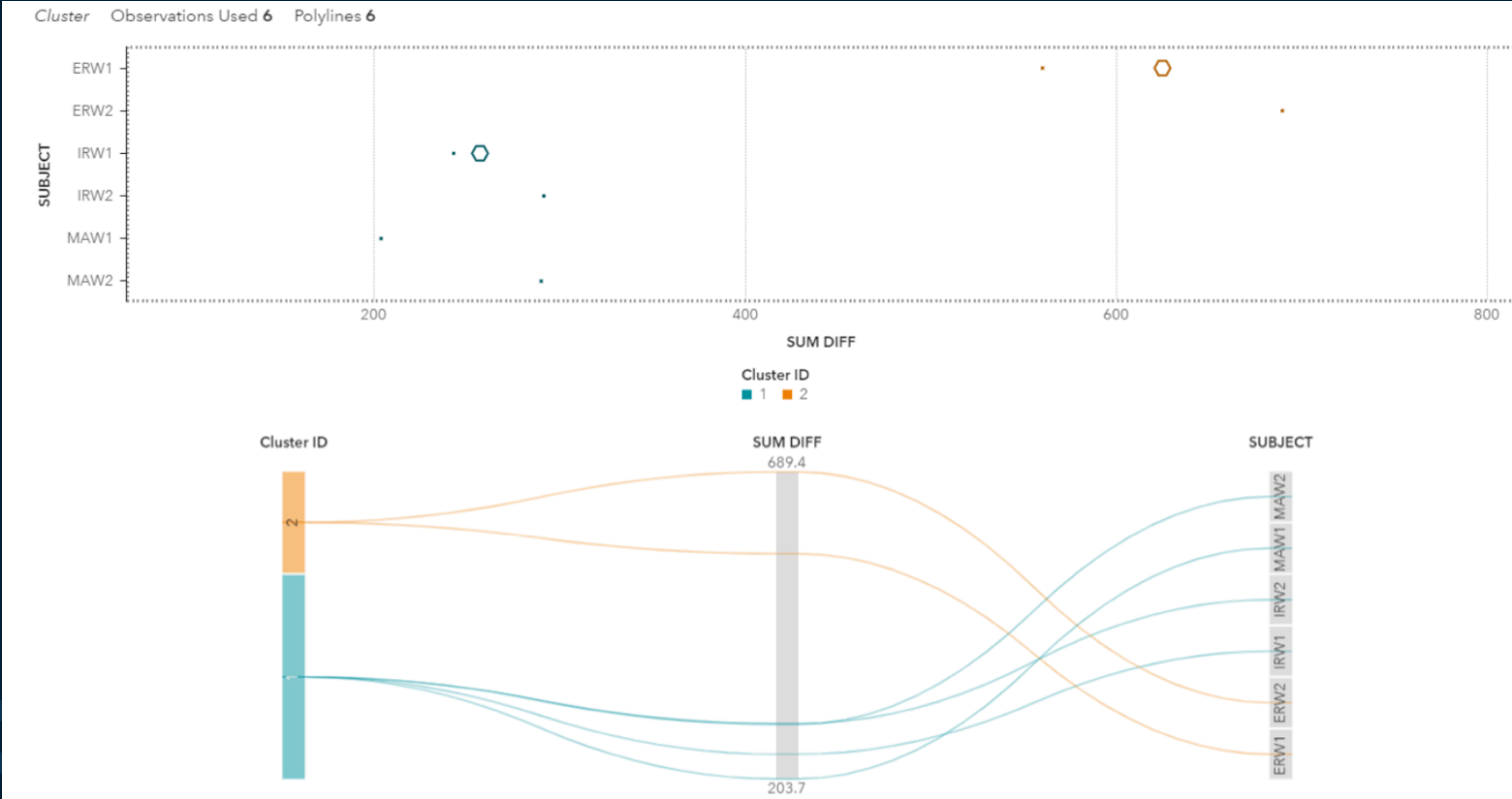
- Summed minimum (x, y, z) and maximum (x, y, z) relative path means from similarity analysis for each subject
- Difference between summed means used to compare subjects/replicates

Unsupported: Eyes Open vs. Closed		
REP	SUBJECT	SUM DIFF
1	ERW	599.0
2	ERW	862.9
1	IRW	198.1
2	IRW	122.8
1	MAW	372.6
2	MAW	321.4

Eyes Open: Supported vs. Unsupported		
REP	SUBJECT	SUM DIFF
1	ERW	560.1
2	ERW	689.4
1	IRW	242.8
2	IRW	291.4
1	MAW	203.7
2	MAW	290.0

Clustering Analysis

Unsupported – Eyes Open vs. Eyes Closed



DATA Analysis

Similarity Matrix: X Axis - Unsupported, Eyes Open

<i>SUBJ/REP</i>	ERW 2	ERW 1	IRW 2	IRW 1	MAW 2	MAW 1
ERW 2 →	0.0	124.5	1168.0	368.5	352.9	150.8
ERW 1 →	124.5	0.0	1137.5	349.2	256.9	121.0
IRW 2 →	1168.0	1137.5	0.0	864.6	1001.1	1157.3
IRW 1 →	368.5	349.2	864.6	0.0	271.8	256.3
MAW 2	352.9	256.9	1001.1	271.8	0.0	281.9
MAW 1	150.8	121.0	1157.3	256.3	281.9	0.0

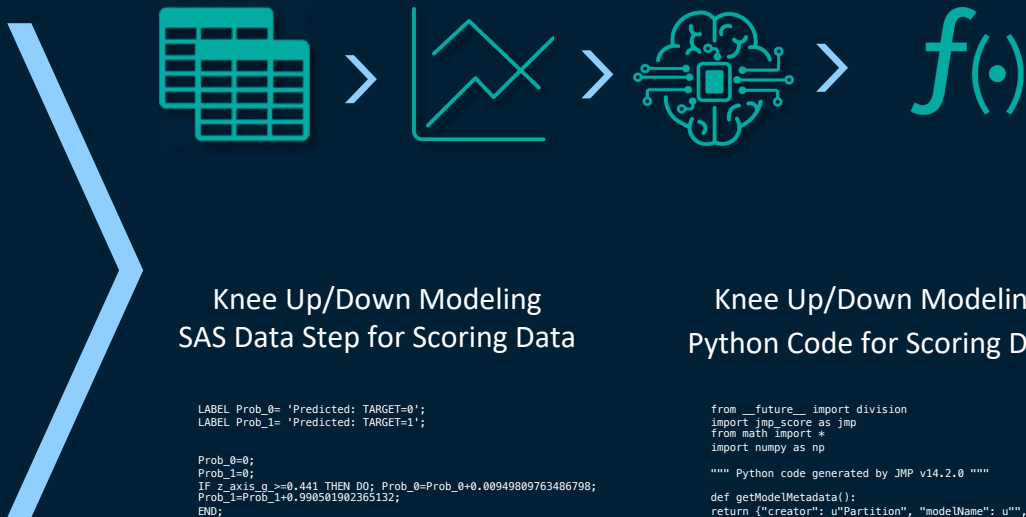
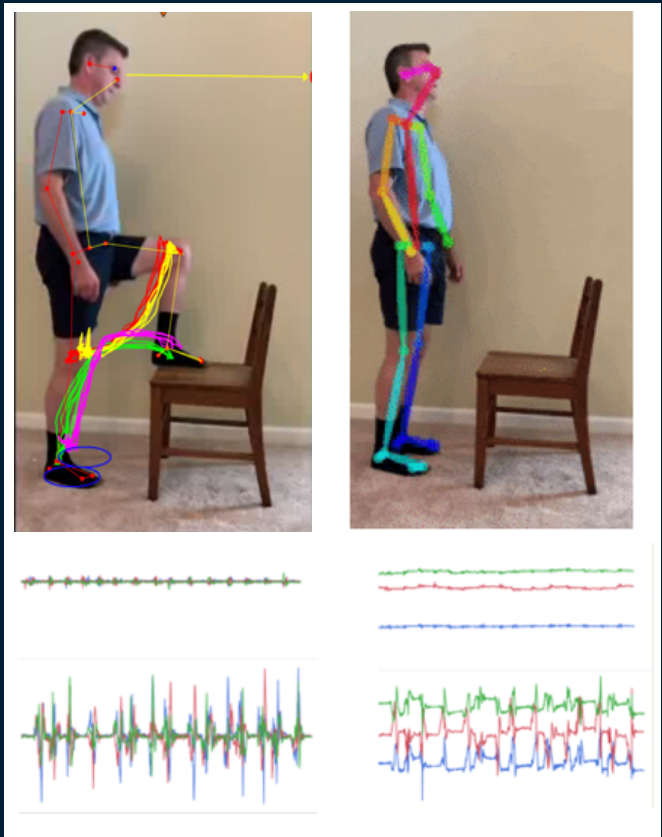
Discussion

Observations & Considerations for Future Study

- Supported baseline provides a nominal starting point for comparison
- Unsupported eyes open vs closed compares non-vestibular and vestibular balance
- Replicates demonstrate the results are reproducible
- Variance in pathophysiology and severity of medical conditions can be detected
- Adjusting support height (elbow bend) or developing a different method of support may result in a better nominal measure, thereby decreasing variability of within subject measurements

Digital Twin

Video Training and Sensor Data



Knee Up/Down Modeling
SAS Data Step for Scoring Data

```

LABEL Prob_0= 'Predicted: TARGET=0';
LABEL Prob_1= 'Predicted: TARGET=1';

Prob_0=0;
Prob_1=0;
IF z_axis_g_>=0.441 THEN DO; Prob_0=Prob_0+0.00949809763486798;
Prob_1=Prob_1+0.990501902365132;
END;
ELSE DO;
IF y_axis_g_>=0.08 THEN DO; Prob_0=Prob_0+0.0625819090296167;
Prob_1=Prob_1+0.937418090970383;
END;
ELSE DO; Prob_0=Prob_0+0.984192837130963;
Prob_1=Prob_1+0.0158071628690365;
END;
END;

```

Knee Up/Down Modeling
Python Code for Scoring Data

```

from __future__ import division
import jmp_score as jmp
from math import *
import numpy as np

""" Python code generated by JMP v14.2.0 """

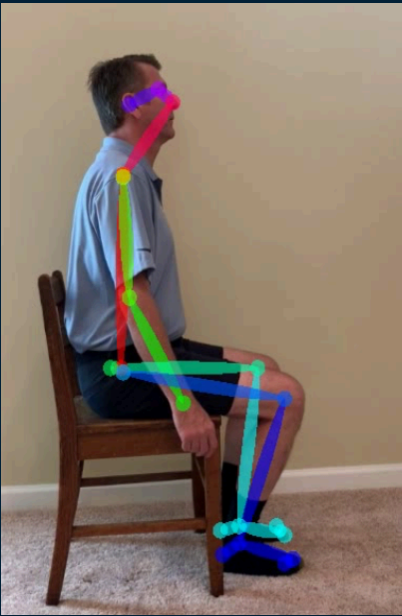
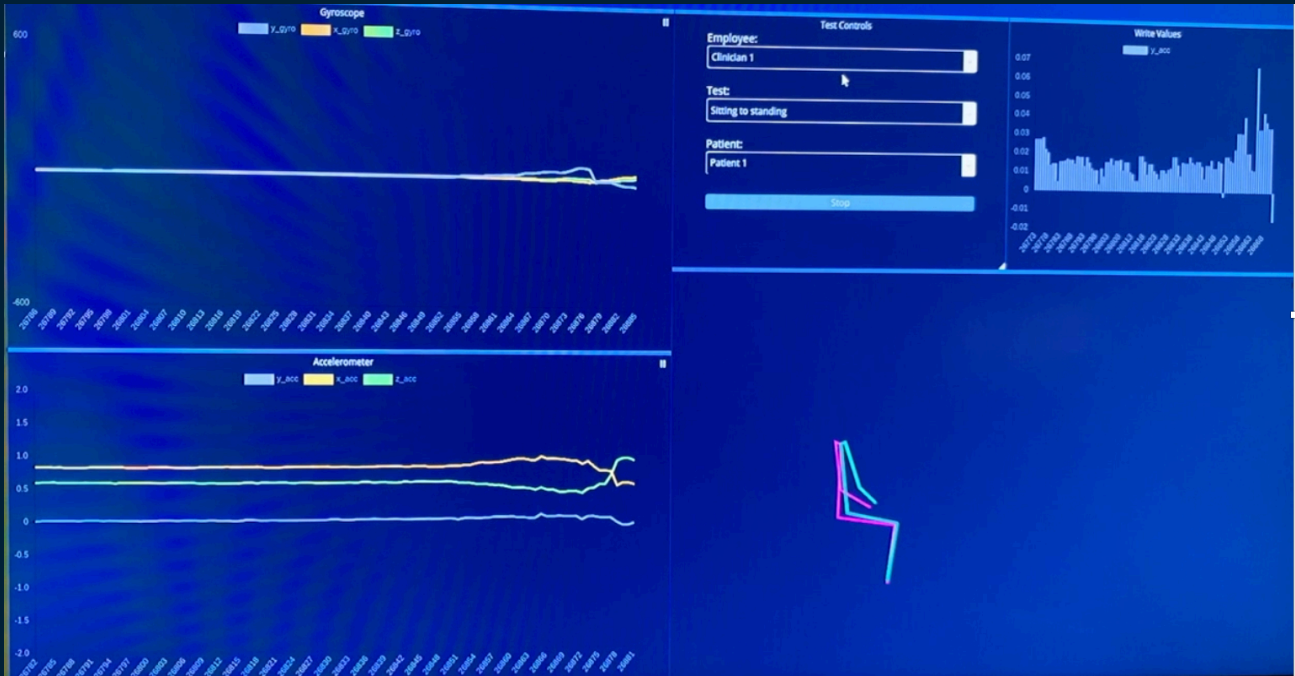
def getModelMetadata():
    return {"creator": "u"Partition", "modelName": "u",
            "predicted": "u"TARGET", "table": "u"MAW_KNEE_TRAINING",
            "version": "u"14.2.0", "timestamp": "u"2019-09-05T02:20:29Z"}

def getInputMetadata():
    return {
        u"y-axis (g)": "float",
        u"z-axis (g)": "float"
    }

```

Multimodal Assessment

Digital Twin



Patient Information

Patient name: Simpson, Homer J.

Patient ID: CD43240232

Gender: Male

Age: 58 years

Height: 74 inches

Weight: 176 pounds

📅 March 10, 2020



Assessment Information

Standing - eyes open 

Standing - eyes closed

Stand to sit 

Sit to stand

Right knee up/down Left knee up/down

Completion

30%

🕒 March 10, 2020 09:45

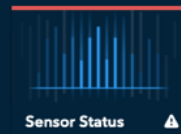


Assessment Description

Standing - eyes closed

Subject stands on a flat hard surface barefoot for 20 seconds with feet together at the heels and arms at the side looking directly ahead. The patient tries to maintain his or her balance.

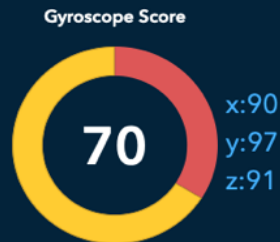
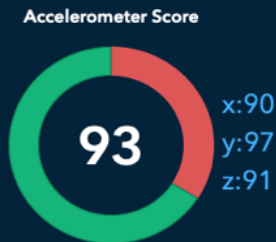
For safety, it is essential that the observer stand close to the patient to prevent potential injury if the patient were to fall.



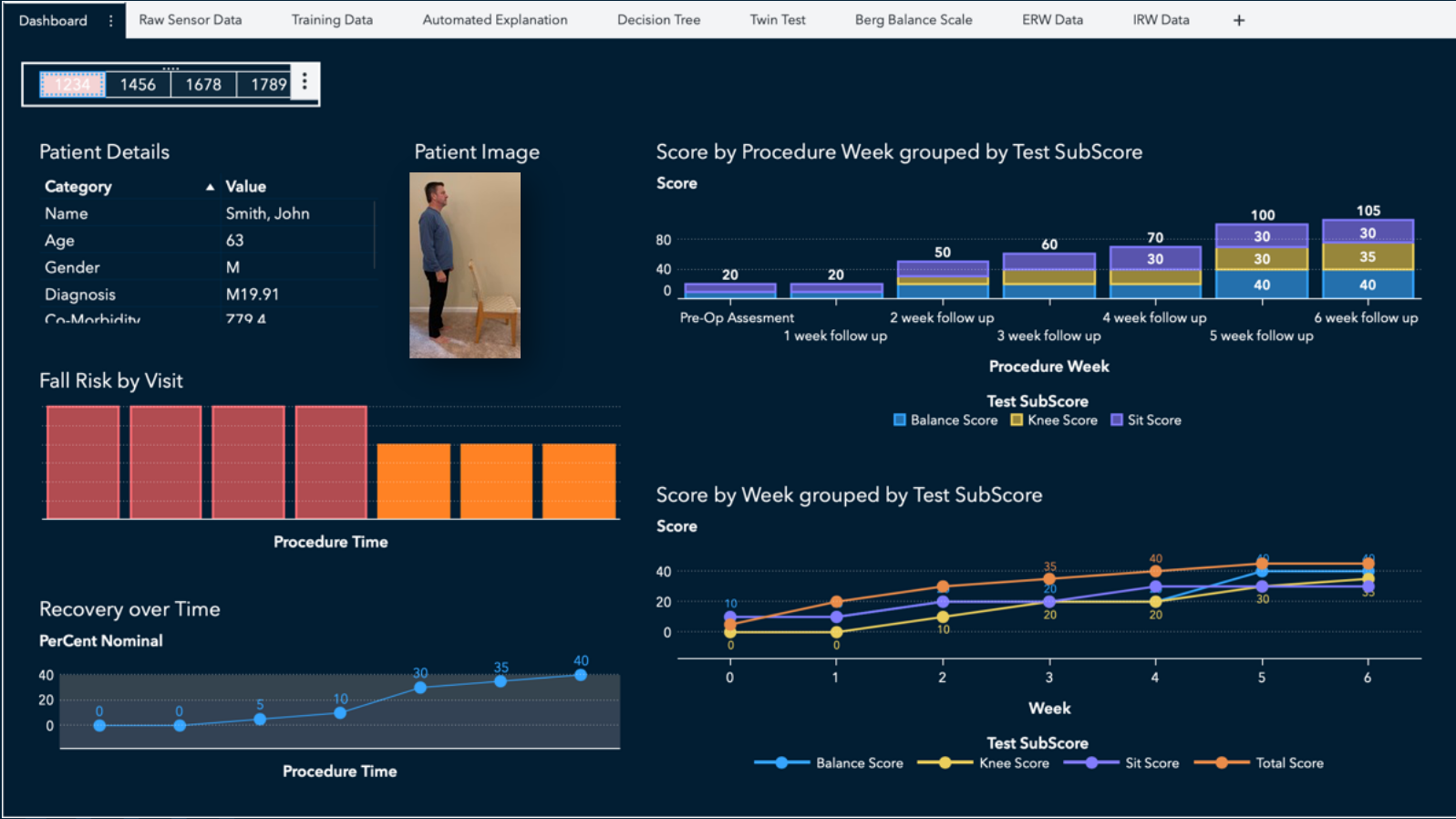
Sensor Status

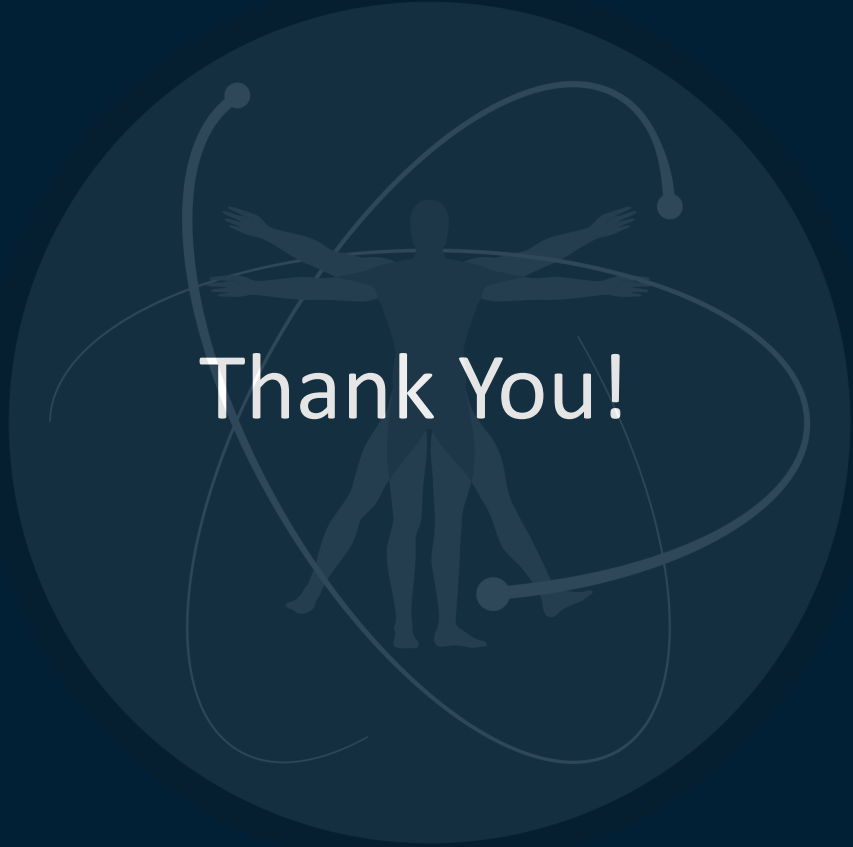


Camera Status



Enabling Hybrid/Virtual Clinical Trials



A large, faint, circular graphic in the center of the slide. Inside the circle is a silhouette of a Vitruvian Man figure. Overlaid on the figure are several thin, light-blue lines that form elliptical orbits, similar to the Copernican heliocentric model, with small dots at the foci. The text "Thank You!" is centered over this graphic in a white, sans-serif font.

Thank You!