THE POTENTIAL OF THE DIGITAL TWIN AS A DISRUPTOR OF HEALTHCARE: PERSPECTIVE FROM MEDICAL DEVICES

MARK PALMER, MD, PHD
DISTINGUISHED SCIENTIST
STRATEGIC SCIENTIFIC OPERATIONS
DIGITAL TWINS
DEFINITION

DIGITAL TRANSFORMATION
- Discovery & Ideation
- Invention & Prototyping
- Product Launch
- Regulatory Submission
- Post-Market Monitoring

PRODUCT LIFECYCLE
- Pre-Clinical & Clinical
- Pre-Clinical & Clinical

AS-MANUFACTURED MODEL(S) + REAL-WORLD DATA

ACTIONABLE INFORMATION
- Physics-based Models
- Reduced Order Models
- Statistics
- AI/ML

MANUFACTURED ASSETS
- Performance optimization
- Preventative Maintenance
- Planned replacement of parts
- Enhancements
- Planned obsolescence/retirement
DIGITAL TWINS
DEFINITION

- Discovery & Ideation
- Invention & Prototyping
- Pre-Clinical & Clinical
- Regulatory Submission
- Product Launch
- Post-Market Monitoring

DIGITAL

AS-MANUFACTURED

REAL-WORLD DATA

HEALTHCARE

- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life

MANUFACTURED ASSETS

- Performance optimization
- Preventative maintenance
- Planned replacement of parts
- Enhancements
- Extend service life

- Physics-based Models
- Reduced Order Models
- Statistics
- AI/ML

AS-MANUFACTURED MODEL(S)

REAL-WORLD DATA

PHYSICS-BASED MODELS

REDUCED ORDER MODELS

STATISTICS

AI/ML

PRODUCT LIFECYCLE

Pre-Clinical & Clinical

Regulatory Submission

Product Launch

Post-Market Monitoring
DIGITAL TWINS IN HEALTHCARE
“HOLY GRAIL”

CLINICAL OBJECTIVES
- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life

MODIFIABLE FACTORS
- Diet
- Exercise
- Sleep
- Environment

MEDICATION
- Therapy
- Surgery
- Implantables

PREDICT IMPACT ON PHYSIOME
Digital twins exist at the nexus of physical engineering, data science, and machine learning, and their value translates directly to measurable business outcomes.*
DIGITAL TWINS IN HEALTHCARE
CURRENT PERSPECTIVES

PHYSICAL SCIENCE
- Anatomy & Physiology
- Use Conditions
- Physics of Device

DIGITAL THREAD
- Electronic Health Record
- Sensors
- Internet of Things

HEALTHCARE
- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life

IF THIS IS OUR FOUNDATION, HAVE WE ALREADY FAILED?

Largest sources of data is coming from individuals when they are at most challenging state of health.
### Digital Twin in Healthcare: Challenges

#### 1. Defining the Reference State

<table>
<thead>
<tr>
<th>Physiome</th>
<th>Evidence Based Medicine*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genome</td>
<td>Roots in clinical education</td>
</tr>
<tr>
<td>Transcriptome</td>
<td>Goal: reduce variability in resources and outcomes</td>
</tr>
<tr>
<td>Proteome</td>
<td>Ideally generated from Randomized Control Trials</td>
</tr>
<tr>
<td>Metabolome</td>
<td>Analysis assumes “statistical homogeneity”</td>
</tr>
<tr>
<td>Morphome</td>
<td>Trials do not map well to real world (bias, tails)</td>
</tr>
</tbody>
</table>

- *Individuals differ at every level of their physiome*
- *Differences impact how they respond to modifiable factors*
- *Changes over lifetime*

![Image](image.png)

#### Modifiable Factors

- Diet
- Exercise
- Sleep
- Environment

- Medications
- Therapy
- Surgery
- Implantables

#### Personalized Medicine*

- Roots in pharmacology
- Goal: Pharmacogenetics for tailoring of drugs
- Function of ~ 33% of genome still unknown
- Role of gene-gene interactions uncertain
- Assumes “statistical heterogeneity”
- Designing and funding RCT is challenging

---

*2012 De Leon, “Evidence-Based Medicine versus Personalized Medicine: Are They Enemies?”*
### Digital Twin in Healthcare: Challenges

#### 2. The Data (Minimize Interaction with Health System)

#### Clinical Analog
- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life

#### Modifiable Factors
- Diet
- Exercise
- Sleep
- Environment

#### Data Streams
- Diet
- Location/GPS
- Activity monitors
- Some vitals
- Sleep monitors
- Biomarkers

- Medications
- EHR
- Vitals
- Labs
- Imaging
- Biomarkers
- Genetic analysis

- Are the existing clinical measurements optimal for predicting health?
- How do we generate accessible and affordable streams of data?
- How to ensure data quality? (e.g., bad sensor placement)
- Majority of variables that define physiome are inaccessible
- Reliance on longitudinal “health record”
**DIGITAL TWIN IN HEALTHCARE: CHALLENGES**

3. DEFINING THE DISEASE OR ABNORMAL STATE

### PHYSIOME

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Genome</td>
<td>Individuals differ at every level of their physiome</td>
</tr>
<tr>
<td>Transcriptome</td>
<td>Differences impact how they respond to modifiable factors</td>
</tr>
<tr>
<td>Proteome</td>
<td></td>
</tr>
<tr>
<td>Metabolome</td>
<td>Changes over lifetime</td>
</tr>
<tr>
<td>Morphome</td>
<td></td>
</tr>
</tbody>
</table>

### MODIFIABLE FACTORS

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>Medications</td>
</tr>
<tr>
<td>Sleep</td>
<td>Therapy</td>
</tr>
<tr>
<td>Environment</td>
<td>Surgery</td>
</tr>
<tr>
<td></td>
<td>Implantables</td>
</tr>
</tbody>
</table>

- How to manage genotypic expression of disease risk?
- How to manage genotypic expression of disease in absence of phenotype?
- Normal range for one individual may be pathological for another
- Time scale of onset of disease
- Time course of the disease
CHRONIC DISEASE
Digital twins exist at the nexus of physical engineering, data science, and machine learning, and their value translates directly to measurable business outcomes.*

* The Digital Twin: Compressing time-to-value for digital industrial companies, GE
DIGITAL TWINS IN CHRONIC DISEASE
DEVICES & HUMANS

PHYSIOLOGY

The Peripheral Nervous System
Cranial Nerves

HEALTHY
- complex milieu of overlapping control systems
- Multiple pathways influencing parameter of interest
- Coupled PDE’s

CHRONIC DISEASE
- Control systems are saturated
- Deviation from reference is clear
- Measurements well defined
- Axes of intervention well defined
- Coupled ODE’s
Digital Twins in Chronic Disease
Sensor Enabled Devices & Humans

Physical Products in the Real World
- Injection Ports
- Mobile Monitoring Tools
- Insulin Pumps with built-in Continuous Glucose Monitoring

Virtual Products and Light Weight Models
- Machine Learning

Actionable Predictions
- Emergency Protocol
- Warning Protocol
- Systems Normal
DIGITAL TWINS IN CHRONIC DISEASE
CLOSED LOOP GLUCOSE MANAGEMENT SYSTEM

- Algorithm adapts to individual patient’s glucose metabolism
- Automatically adjusts basal (background) insulin every five minutes based on CGM readings
- Patient administers bolus for meals
- Algorithm is resistant to over or underestimation of carb consumption
- Stops insulin up to 30 minutes before reaching preset low limits

HELPS IMPROVE TIME IN RANGE.

JOHN’S A1C. BEFORE 8.1 AFTER 6.1

**Representative of actual patient Carelink™ data. Individual results may vary.

With SmartGuard™ technology, John’s glucose levels are automatically adjusted, so he is free to live life more in the moment.

- IN RANGE: 70-180 mg/dL
- HIGH: 180-400 mg/dL
- LOW: <70 mg/dL
HEALTHCARE

- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life

“Clinical medicine seems to consist of a few things we know, a few things we think we know (but probably don’t), and lots of things we don’t know at all.”

THANK YOU