Clinical Therapeutics/Volume ▮, Number ▮, 2018

Commentary

How Sensors, Devices, and Biomarkers Can Transform Precision Medicine: Perspectives From a Clinical and Translational Science Institute

Jill L. Maron, MD, MPH[1]; and Graham B. Jones, PhD[2]

[1]Mother Infant Research Institute at Tufts Medical Center, Boston, Massachusetts; and [2]Tufts Clinical and Translational Science Institute, Boston, Massachusetts

ABSTRACT

Purpose: The ability of sophisticated sensors and medical devices to monitor critical biomarkers has the potential to greatly advance precision medicine initiatives. A stakeholder event was organized to develop working models for the evolution of the field.

Methods: A workshop devoted to the subject matter was held at the Tufts Clinical and Translational Science Institute involving clinicians, device developers, regulators, engineers, and scientists.

Findings: Several areas for collaborative development were identified and interested teams offered resources for development of research programs.

Implications: The diversity of relevant stakeholders presents a major opportunity and challenge in translational research. It is evident that the CTSI national network can take a leadership role in the rapidly advancing and potentially transformative field of digital biomarkers. (*Clin Ther*. 2018;▮:▮▮▮–▮▮▮)

Key words: CTSI, devices, digital biomarkers, precision medicine, sensors.

INTRODUCTION

The drive toward precision medicine promises to transform managed health care and is already starting to bear dividends.[1] Advances in molecular biology have led to the emergence of a growing number of therapeutics based on companion diagnostics, which allow us to stratify clinical trials. At the commodity end of the spectrum, the availability of affordable genomic profiling services (eg, 23andMe) is educating consumers on the realities of pharmacogenomics. Emergent disruptive technology is also being witnessed in the rapid development of digital tools that track health-related information based on smartphones and other consumer products. Recent estimates suggest that >300,000 unique apps are now on the market fueling close to 350 different types of consumer-worn devices.[2] The impact of this new field, which has been dubbed "digital medicine," will take time to establish, but a regulatory framework has now been introduced to help guide development.[3] Enthusiasm is high, and the ability to track physical activity and basic health information is being augmented by a number of exciting applications, including cell phone accessories that conduct ECG analyses[4] and wrist-worn monitors to track individuals as they progress from healthy into diseased states.[5]

Other developments of new sensor technologies that can track biomarkers and communicate with a control device are opening up new possibilities in medicine. A watershed moment was the recent introduction of the first autonomous closed-loop insulin management system, which has been dubbed the "artificial pancreas."[6] The implanted glucose sensor communicates with the insulin injector through wireless technology, and the same principles are even being investigated in an integrated glucose-sensing contact lens.[7]

Development of the field will require seamless interactions between technology innovators, regulatory agencies, and clinical centers, in what constitutes

Accepted for publication January 2, 2018.
https://doi.org/10.1016/j.clinthera.2018.01.004
0149-2918/$ - see front matter

a near perfect embodiment of translational research. As such, it is logical that the national network of Clinical and Translational Science Institutes (CTSIs) will play a pivotal role in the process, and efforts to stimulate these interactions will be increasingly important. In an attempt to catalyze activity at the regional level, the Tufts CTSI recently devoted its annual Translational Research Day to the topic "Sensors, Devices and Biomarkers in Medicine." Headquartered in Boston, Massachusetts, the Tufts CTSI network has some 40 contributing partners, including academia, industry, and research hospitals.[8] Combined, it is affiliated with >1250 clinical trials involving >300 investigators. Augmenting these clinical capabilities, medical device engineering is well represented (Tufts University, Massachusetts Institute of Technology [MIT], and Northeastern University), preclinical research centers have been established (Tufts Medical Center and MIT), and its corporate partners (Pfizer, Eli Lilly) are engaged in research on digital medicine technologies.

TRANSLATIONAL RESEARCH DAY

The Tufts CTSI annual Translational Research Day was held November 14, 2017. The 1-day event was structured to combine formal presentations, panel discussions, and case studies with an overview of translational resources and funding opportunities.[9] A poster and networking session helped develop personal interactions among the >140 delegates in attendance from the New England area.

The first session, on Innovations in the Industry, featured work from corporate partners. Eli Lilly, a groundbreaking leader in the managed care of diabetes mellitus, presented on its advances in closed loop sensing technology. These integrated feedback and delivery loops not only hold significant promise for improving the daily management of diabetes but may also be applied to numerous other medical indications in which drug delivery best occurs within a real-time feedback system. Pharmaceutical companies are equally engaged in neurologic disorders, specifically those that affect a patient's ability to continue to perform daily functions. Pfizer announced a partnership with the technology company Akili and outlined the potential for use of hand-held devices to track prodromal stages in Alzheimer's disease. Such devices would significantly improve quality of life for both patients and their caregivers. These presentations underscored the need for clinical grade information, noting that interdevice measurement variability has hampered the use of several ubiquitous consumer devices.[10]

Addressing this theme, a session on Sensors and Devices focused on engineering challenges for digitally enabled medical devices. Researchers from Tufts described the need for contextualized information in cardiac monitoring devices and on the biocompatibility of designed materials. A team from Northeastern University reported on the use of dermal-based sensors that can track biomarkers by using commercial cell phone technology for monitoring. These miniaturized biosensors can easily be placed into the extracellular space beneath the dermal layer to provide accurate readouts of drug concentrations or analytes. Furthermore, their nanoscale design broadens their applicability across the age spectrum, for use in patients spanning toddlerhood to the elderly. Another presentation outlined the caveats surrounding interpretation of behavioral measurements captured from mobile devices or wearable smart technology. Worn or carried daily, these devices "learn" the behavioral and social patterns of their owners. By posing questions directly to the user throughout the day, these next-generation devices quickly determine not only day-to-day activities but can also assess the emotional and health status of its user. Such information can provide meaningful prompts to the wearer ranging from timely medication reminders to stress reduction techniques.

A session on Biomarker Development and Application featured an overview from the US Food and Drug Administration on their biomarker classification program, which has outlined a total of 7 discrete categories.[3] These categories are designed to eliminate confusion about ambiguous definitions and key terminology that may significantly impede translation of novel biomarkers to patient care. The BEST (Biomarkers, Endpoints, and Other Tools) Resource provides a glossary of terminology for use across patient populations and among various stakeholders to improve clarity and consistency of terminology and to advance public health. This presentation was followed by a clinical study from