

DIGITAL MEDICINE

Transforming Medicine via Digital Innovation

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The lack of plasticity of the medical profession and health care system in the face of new technology and information is about to be challenged on two major fronts in digital medicine: wireless technologies and genomics. These two areas have been characterized by unprecedented innovation and discovery at a breakneck pace. Whereas the 2000s saw the introduction of digital life-style devices, the 2010s will probably be known as the era of digital medical devices. These devices have exceptional promise for changing the future of medicine because of their ability to produce exquisitely detailed individual biological and physiological data.

THE ERA OF WIRELESS DIGITAL DEVICES

Perhaps the most remarkable life-changer in the past decade has been the introduction and rapid mass adoption of wireless mobile digital devices. The ways in which we listen to and acquire music, e-mail and communicate via phone and texting, access the Internet, and read books and periodicals electronically have all been radically transformed. In stark contrast, the ways in which diseases are monitored and treated have remained relatively static. The practice of medicine is well known to be extremely difficult to change, even when there is compelling evidence from rigorous randomized clinical trials that new practices should be adopted (1). The lack of plasticity of the medical profession and health care system in the face of new technology and information is about to be challenged in two major areas in digital medicine: wireless technologies and genomics. These areas have been characterized by unprecedented innovation and discovery at a rapid pace and are the subject of this Commentary. Personalized electronic health records are the third major component of digital medicine, but it is unclear whether these will have substantial effects in coming years (2).

NON-INVASIVE SENSORS FOR MEDICAL METRICS

Non-invasive disposable sensors are being developed that can continuously track a wide variety of physiological metrics, including heart rhythm, blood pressure, respiratory rate, the oxygen saturation of hemo-

globin, blood glucose concentrations, brain waves, and many more (Fig. 1). In fact, a perfect storm has created unparalleled opportunities for innovation in wireless medical technology. Simultaneous progress along five fronts includes (i) the ever-growing use of cell phones by over 4 billion users around the world, (ii) enhanced bandwidth with third- and fourth-generation international mobile telecommunication standards, (iii) pervasive connectivity, (iv) the development of smart phones with computing power equal to that of a personal laptop computer, and (v) ingenious sensors. Wireless medical technology generally involves the following features: A body area network is created by a sensor worn on the body that emits a signal about some physiological parameter that is transmitted, typically via Bluetooth (a wireless communications protocol for data exchange), to a gateway receiver, which either physically resembles or is a smart phone. The signal is then transmitted by this receiver to the Internet and processed and can be sent on virtually anywhere, including back to the patient, to a medical provider or caregiver, or to a dedicated monitoring facility.

Consumers are quickly driving the use of wireless sensors for health and fitness. In just over a year, 1.2 million consumers have purchased a body area network in the form of a shoe (3). This Nike shoe, which has a sensor in its sole, communicates exercise-related data such as distance traveled and velocity to an iPhone or iPod. With appropriate software applications, sophisticated exercise metrics such as oxygen consumption and metabolic work can also be monitored. Another popular device among consumers measures electrical activity in the brain, with the aim of improving sleep. Known as the Zeo sleep coach, three sensors in a head-



Fig. 1. Airstrip Technologies remote continuous vital sign monitoring via the iPhone. This software delivers real-time data about the vital signs (including blood pressure, heart rhythm and rate, blood oxygen level, and body temperature) of any patient who is in a hospital intensive care unit to a doctor's or nurse's smart phone.

band capture brain waves and transmit the data to what looks like an alarm clock but also includes a real-time minute-by-minute display of the various stages of sleep. The device gives the user precise data on time spent in deep, rapid eye movement sleep or light sleep, as well as time awake, mapping any disruptions and the quality of sleep. Other consumer items in common use include activity sensors that are essentially wireless pedometers, wireless scales, and over 10,000 health-related software applications for the iPhone, such as those that set up graphic displays for manually entered blood glucose levels, blood pressure, and weight.

MEDICAL APPLICATIONS

Such health and fitness products are the forerunners of non-invasive wireless sensors for medical applications. Recently, for example, a smart bandage for monitoring congestive heart failure was approved by the Food and Drug Administration. The adhesive patch, placed on the chest, has multiple sensors that continuously moni-

Table 1. Top 10 targets for wireless medicine. BP, blood pressure; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 s; RR, respiratory rate.

Disease	Number affected (millions) in United States	Metrics potentially measured by wireless devices
Alzheimer's disease	5	Vital signs, patient's location, activity, balance
Asthma	23	RR, FEV1, blood oxygen level, air quality, pollen count
Breast cancer	3	Presence of a suspicious mass, as detected by ultrasound self-exam
COPD	10	RR, FEV1, blood oxygen level, air quality
Depression	21	Medication compliance, activity, communication
Diabetes	24	Blood glucose levels, calories ingested and expended
Heart failure	5	Cardiac pressures, body weight, BP, fluid status
Hypertension	74	Continuous BP, medication compliance
Obesity	80	Weight, blood glucose levels, calorie intake and output, activity
Sleep disorders	40	Sleep phases, sleep quality, RR, apnea, vital signs, blood oxygen level, heart rhythm

tor heart rhythm and rate, fluid status (because excessive fluid accumulation in the chest is a symptom of congestive heart failure), respiratory rate, body position, activity, heart rate variability, and body temperature. A randomized trial is being planned to assess this technology for reducing rehospitalizations for heart failure, which is one of the most pressing clinical problems in cardiovascular medicine (4). As summarized in Table 1, a variety of other common chronic medical conditions can either be monitored via wireless sensors or have the potential to be addressed in such a manner in the future.

Beyond remote monitoring with physiological sensors, body area networks can be used to track or even administer medications. Pills with digestible sensors, activated by gastric juice to emit an identifier signal, are already in clinical trials to test treatment compliance in patients with conditions such as hypertension or tuberculosis. Another pill-related technology allows for wireless activation of the pill at a specific part of the intestinal tract. Furthermore, a skin-adhesive polymeric patch has been developed that can be activated with a wireless device to administer a particular dose of a medication transdermally at a specific time.

The breakthroughs in wireless medical technology also extend to imaging. High-resolution real-time ultrasound imaging can be acquired by handheld devices that resemble cell phones and then transmitted over the Internet. This newfound capability sets up the potential for mobile imaging for a variety of uses, such as fetal monitoring or echocardiography for monitoring heart disease.

PROGRESS IN GENOMICS

In parallel with these remarkable advances in wireless technology, there has been exceptional progress in the identification of major genes and pathways linked to more than 80 common polygenic diseases. Since April 2007, via genome-wide association studies (5, 6), more has been learned about the genetic underpinnings of common diseases than during the rest of human history. As with wireless sensors, there has been a newly initiated consumer movement that has developed as genome-wide scans became available. In such a scan, hundreds of thousands of commonly occurring single-nucleotide polymorphisms (minor allele frequency >5%) are genotyped. The research-grade genomic data currently provide information about allelic markers of susceptibility to (or protection from) more than 50 diseases as well as several key pharmacogenetic interactions. Interestingly, demonstrating what is rapidly achievable in the current era of digital medicine, the results of such a scan can be loaded onto an iPhone. This ability allows the patient to carry his or her genome scan data to review with a physician, for consideration of an anticipated prescription, or guidance for prevention of a condition for which high risk was indicated. Although this scenario is new, it epitomizes the notion of consumer empowerment and highlights the mobile phone as the anchoring repository of data.

However, genome-wide scanning clearly explains less about the heritability of polygenic diseases than was hoped or expected from the common-disease, common-variant hypothesis, which predicts that common genetic variations are associated with, and in

some cases cause, most of these diseases. This gap in knowledge about what accounts for the heritability of common polygenic diseases, or the so-called “dark matter of the genome,” remains, which means that targeted or whole-genome sequencing must be used to determine whether low-frequency and rare variants with high penetrance will fill in the holes (7). The extraordinary technological advancement in next-generation sequence platforms has positioned rapid, affordable, whole-human genome sequencing to be in use years before it was anticipated (8). What can readily be anticipated as a limitation, however, is that for both wireless and genomic digital technology, there will be a virtual data flood. This challenge will need to be addressed with sophisticated methods of processing data, the development of algorithms, and advanced bioinformatics. Another related and shared concern is the potential downside of having such rich data in digital form: the need for protecting privacy and security.

Acknowledging these challenges, there is an exciting convergence of biology and physiology unlike anything seen before. The ability to have information regarding specific individuals on variations at the genomic, as well as the epigenomic, proteomic, or metabolomic, level, along with the physiological phenotyping derived from continuous monitoring, was unforeseen. This capability represents a powerful means of disease prevention. Imagine a genomic panel that indicated a high risk of diabetes mellitus in an individual who therefore now uses a sensor that adheres to the skin that continuously tracks blood glucose levels, promoting lifestyle changes or facilitating tailored phar-

macologic approaches. Or imagine a woman with an increased risk of breast cancer who can monitor herself for breast cancer using a smart phone with the capability of acquiring and transmitting ultrasound images. Even today, remote wireless monitoring can be used to detect previously undiagnosed yet important heart rhythm disorders in individuals who carry DNA markers associated with increased risk for atrial fibrillation or ventricular tachyarrhythmias.

Before disease prevention becomes achievable, there should be ample opportunity for improved management of existing conditions. For example, hypertension is notoriously underdiagnosed and poorly controlled. Continuous monitoring of individuals at risk or already diagnosed may lead to more optimal control and avert end-organ damage. Similarly, monitoring for sleep disorders will be greatly simplified, preempting the need for hospital-based sleep laboratories. Reducing the toll of secondary complications associated with these

conditions, among many others, exemplifies both the overall public health benefit and the opportunity to lower health care costs.

Whereas the 2000s were characterized by the introduction of digital life-style devices, the 2010s will probably be known as the era of digital medical devices. Knowledge of exquisitely detailed individual biological and physiological data has exceptional promise for changing the future of medicine.

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