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# DISRUPTIVE DOZEN

2018 | WORLD MEDICAL INNOVATION FORUM



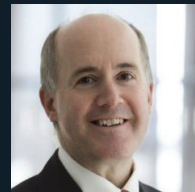
## THE DISRUPTIVE DOZEN artificial intelligence

The culture of innovation throughout Partners HealthCare naturally fosters robust discussions about new “disruptive” technologies and which ones will have the biggest impact on health care. The Disruptive Dozen was created to identify and rank the technologies that Partners faculty feel will break through over the next decade to significantly improve health care. This year, the Disruptive Dozen focuses on relevant advances and opportunities in artificial intelligence (AI).

## 2018 World Medical Innovation Forum co-chairs



**Anne Klibanski, MD**  
Chief Academic Officer, Partners  
HealthCare; Laurie Carrol Guthart  
Professor of Medicine, Academic Dean for  
Partners, Harvard Medical School  
World Forum Co-Chair



**Gregg Meyer, MD**  
Chief Clinical Officer, Partners  
HealthCare; Professor of Medicine,  
Massachusetts General Hospital  
and Harvard Medical School  
World Forum Co-Chair

## Disruptive Dozen | 2018

### The Nomination Process

From late October through December 2017, more than 40 half-hour interviews, both in-person and by telephone, were conducted with leading faculty from Brigham and Women's Hospital, Massachusetts General Hospital and Partners HealthCare to elicit their nominations of the AI-based technologies they believe will have the greatest impact on health care at any point in the next decade. The interviews resulted in 50 nominated technologies that varied from the broad in scope to highly specific.

### Selection Process

Twenty leading Partners faculty gathered in December to form a committee of "selectors" to jointly choose and rank the final 12 technologies. Anne Klibanski, MD, Chief Academic Officer, Partners HealthCare and Gregg Meyer, MD, Chief Clinical Officer, Partners HealthCare served as selection committee moderators and were supported by Partners Innovation staff. To receive consideration for the final Disruptive Dozen, nominated technologies met the following criteria:

#### CRITERIA 1

The innovation has strong potential for significant clinical impact at some point in the next decade and offers significant patient benefit in comparison to current practices. The innovation may also have a significant benefit to the delivery/efficiency of health care.

#### CRITERIA 2

Nominated AI-related innovations have a high probability of successful commercial deployment—e.g., payers will be expected to support it.

#### CRITERIA 3

The innovation must be on the market sometime before April 2028. Ideally, the final selections will include a blend of both near-term and long-term disruptive technologies — that is, those coming to market in the next three to four years as well as ones that will come to market later in the decade.

## Final Scores and Announcement at the World Medical Innovation Forum

Selection committee members jointly ranked the innovations from 1 to 12 using the initial scoring and further discussion. The selection committee ranking is final and will be announced April 25, 2018 in a one-hour panel at the World Medical Innovation Forum. The session will be moderated by Katherine Andriole, PhD and Keith Dreyer, DO, PhD, and feature 12 faculty members selected to briefly comment on each technology.

## Melding Mind and Machine

With some high-tech gadgetry, scientists are melding the human mind with machines — computers and algorithms that can eavesdrop on the brain's signals and then translate the information into actions, like typing words on a digital keyboard or moving a robotic arm. Such brain-computer interfaces (BCIs) have been the stuff of sci-fi flicks for decades, but now they are rapidly evolving into real-world devices, propelled by artificial intelligence that can rapidly decode and anticipate the brain's complex, dynamic activity.

The technology, while still in its infancy, holds remarkable promise for patients suffering from a range of devastating neurological diseases or injuries. That means people with paralysis could regain the power of movement, and people with conditions such as amyotrophic lateral sclerosis (ALS) or locked-in syndrome could communicate meaningfully with loved ones.

Researchers are already taking some tangible steps toward these goals. For example, in a study published in 2016, a research team in Pittsburgh helped a man with paralysis partially regain the sense of touch — a critical sensation that underpins many types of movement. Using microelectrodes implanted in a region of the man's brain that processes the sensation of touch, together with a robotic arm equipped with sensors on the fingertips, the researchers were able to make him feel as if his own hand was being touched. This notable advance — providing the sense of touch through a prosthetic device — builds upon this group's and other teams' earlier work on BCIs that enabled people with paralysis to control the movement and dexterity of a robotic arm using signals from their own brains.

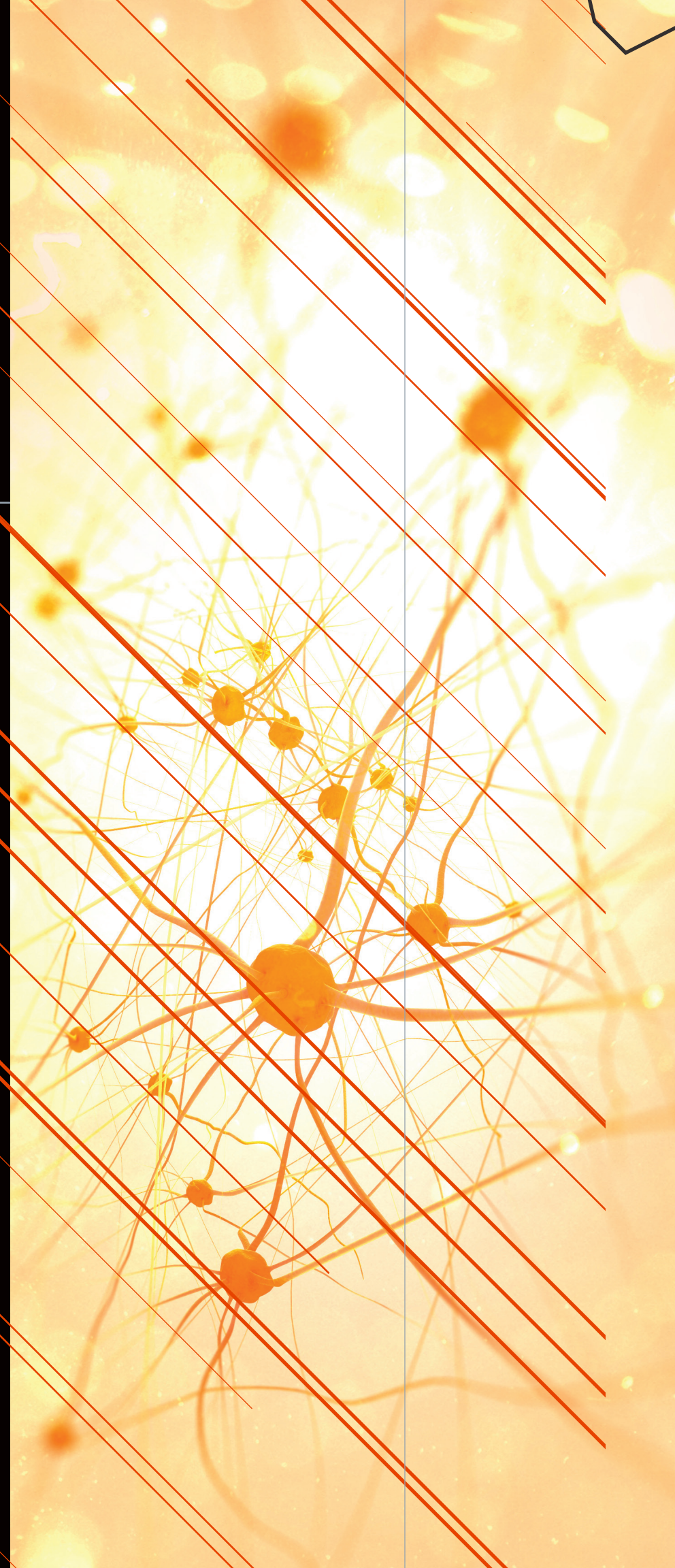
In another impressive development, an international team of researchers, including investigators in the U.S., Switzerland, and Germany, recently restored locomotion in two monkeys, each with partial spinal cord injuries that paralyzed only one leg. A core element of this work involves an innovative brain-spinal interface, which allows the brain to bypass the injured portion of the spinal cord and wirelessly communicate with downstream nerves to enable walking. While more research is needed to further test the brain-spinal interface in animal models before clinical studies can be undertaken, the findings lay the foundation for a potential therapeutic intervention to restore the normal flow of information within a damaged spinal cord.

Such an advance could have a significant clinical impact. According to the World Health Organization, as many as half a million people worldwide suffer from spinal cord injuries each year. So far, efforts to heal or replace damaged spinal nerves, either with drugs or regenerative methods, have proved disappointing.

In a similar vein, a consortium of investigators at several leading research organizations in the U.S., is harnessing BCIs to help people with a variety of neurological conditions, including spinal cord injury, brainstem strokes, and ALS. In recent studies, they have shown that their investigational system can enable people with tetraplegia to perform a variety of tasks using just their own thoughts — like controlling a robotic arm, manipulating a computer screen to point-and-click and type up to 40 words per minute, and even move their own upper limbs.

This device is now being further evaluated in a multi-site clinical trial of up to 15 people with tetraplegia to assess the device's safety and demonstrate its feasibility. If successful, this pilot study will provide the groundwork for a broader effort to test the device and measure its efficacy.

While still experimental, these and other BCIs are ushering in a new era of AI-based neurotechnologies that promise to restore the power of mobility and communication to hundreds of thousands of people with debilitating neurological conditions. ||



## Next-Gen Radiology

The digital acquisition of radiological images has had wide-reaching effects in medicine. Now, with the rise of computer vision and other artificial intelligence-based approaches, it is possible for computers to scrutinize these images for subtle variations and textures that human eyes cannot discern. That means automated methods for reading and interpreting CT scans, MRIs, and X-rays are within reach, giving radiologists new tools to systematically quantify image features and use them to help understand disease biology and predict outcomes.

Cancer researchers are actively evaluating the application of AI in quantitative imaging to predict a tumor's pathogenicity, genetic makeup, or treatment response. As an example, prostate cancer is among the most common cancers and a leading cause of cancer-related death in men in the United States. However, accurately diagnosing the disease remains a significant challenge — one brought into stark relief by the risks patients face from both under- and over-treatment.

To help gauge the aggressiveness of a patient's tumor, doctors often turn to the Gleason score — a measurement applied to tumor biopsies that reflects cancer cells' appearance under a microscope. While Gleason scores can be important indicators of prostate cancer severity and prognosis, tumor biopsies represent just a tiny piece of a larger tumor, often heterogeneous tumor, so these scores are not always an accurate reflection of tumor pathology.

But what if it were possible to predict the aggressiveness of a prostate tumor directly from a radiological image rather than a biopsy? That could mean faster, more accurate prognoses for patients as well as a better quality of life, as biopsies of the prostate gland are not only painful but also increase infection risk.

Researchers across the world are now leveraging AI-based methods in pursuit of this goal. For example, groups in the US and China are using machine learning and deep learning respectively to create automated tools that can improve the diagnosis of prostate cancer. By analyzing patients' MRIs, these tools seek to help doctors better distinguish malignant and benign forms of the disease, and pinpoint highly aggressive subtypes (such as those with high Gleason scores). These efforts, when combined with other modalities for disease diagnosis and prediction, promise to improve the precision of prostate cancer treatment.

In other types of cancer, gaining access to tumor tissue, particularly in remote body sites, is extremely difficult — making biopsies highly invasive and a generally less favorable option. This is often the case in lung cancer. Yet such inaccessibility can complicate efforts to accurately diagnose the disease and identify the most effective treatments.

Again, AI is paving a new path. By mining radiological images of lung tumors, researchers are pioneering methods to help predict tumor pathology, enabling a kind of “virtual biopsy” that can speed diagnosis and improve treatment. For example, a team in Boston recently used machine learning to analyze high-resolution CT images of patients with non-small-cell lung cancer (NSCLC), captured before and after three weeks of treatment with the targeted therapy, gefitinib. Through this pilot study, the researchers uncovered radiological signatures that helped predict tumors' epidermal growth factor receptor (EGFR) mutation status and response to gefitinib.

These findings help underscore the potential of an emerging field, called radiomics, which harnesses image-based algorithms to visually — and non-invasively — characterize tumor phenotypes and genetic makeup. Such an approach could enable more rapid diagnoses and improve treatment, for example, by distinguishing patients who are sensitive and/or resistant to a given drug. Moreover, because of the widespread use of clinical imaging, the added cost of these benefits would be low. \\\



## Disseminating Medical Expertise to Areas that Need it Most

Replacing physicians has been cited as an aim of artificial-intelligence-based approaches to health care. Yet beyond the hype and hyperbole, there is a much more likely — and worthy — application of AI to medicine: infusing clinical expertise into regions where doctors are in short supply.

A key case in point: the global shortage of radiologists. The problem is particularly pronounced in low-resource settings, where both the diagnostic equipment and clinical experts to interpret imaging results are lacking. Consider that more radiologists work in the hospitals lining Longwood Avenue in Boston than all of West Africa. Yet wealthier nations are not immune to these challenges. For example, two analyses released in 2016 predict that European countries, including the U.K., will soon feel the squeeze of a shortage of radiologists and a growing tide of patients seeking CT and MRI scans.

Artificial intelligence (AI) can help fill this gap, and researchers are working on multiple fronts to develop AI-based applications for a range of important health conditions. Consider tuberculosis (TB), which is among the top ten causes of death worldwide. According to the World Health Organization, over 10 million people were sickened by TB in 2016 and nearly 2 million died. The vast majority of these deaths were in low- and middle-income countries.

Chest X-rays form a key linchpin of TB diagnosis. Although they are not sufficient to definitively diagnose the disease, they provide a cheap, rapid, and effective way of screening the lungs for TB-related abnormalities — particularly in areas where the disease is prevalent. Some progress has been made in improving global access to and affordability of X-ray machines, but many regions are still plagued by a lack of physicians with expertise in diagnostic radiology. That means patients often fail to get even the most basic screening tests, delaying TB diagnosis and treatment.

Now, various research teams, including ones in Texas and Pennsylvania, are harnessing deep-learning methods to create automated tools for TB detection on chest X-rays. The accuracy of these models is quite high, approaching, and in some cases, even matching the performance of clinical experts. These efforts suggest that, by harnessing AI, it will soon become feasible to extend the reach of radiologists to places that currently lack care providers.

In a similar vein, investigators across the world are pursuing ways to transform the performance and interpretation of ultrasound technology. Many of these initiatives focus on the development of portable ultrasound devices that work in conjunction with smartphones or other handheld devices. This work is helping to improve portability and drive down the cost of ultrasound technology, which in turn, will help improve patient access, particularly in low-resource settings.

But price is not the only disruptor. Researchers in New York and Connecticut are developing a portable ultrasound device that harnesses semiconductor chips rather than piezoelectric crystals, which are the basis of conventional ultrasound machines. Moreover, the new device does not require multiple probes for imaging at different depths in the body — its single probe can carry out diverse functions, including fetal and obstetric exams, cardiac and peripheral blood vessel imaging, abdominal imaging, and musculoskeletal exams. This technology also incorporates a machine-learning-based system to improve image acquisition as well as analysis. Together, these innovations could not only broaden the use of ultrasound — even expanding it to consumers — but also make it as routine and indispensable as stethoscopes and blood pressure cuffs are currently. **\\**

## Getting Back to Face Time: AI Tools that Help Reduce Physicians' Computer Use

Just as computers have propelled major advances in modern medicine, their presence has also become a significant burden. That's because the amount of time physicians now spend on the computer — reviewing clinical data and completing required documentation in electronic health records (EHRs) — has soared. It is estimated that physicians spend roughly half of their day on documentation and less than a third with their patients. Put another way, for each hour of face-to-face interaction with patients, physicians log almost two hours on administrative computer tasks. Moreover, many physicians spend time at home, typically one to two hours each night, to stay abreast of their computer work.

The upshot? Physicians often report feeling dissatisfied with their work lives. A 2016 survey of more than 6,000 U.S. doctors revealed that the vast majority used EHRs, and that this group was frustrated with how much time they spend on the computer. The survey also reported that these physicians were more prone to professional burnout.

Despite the gravity of the problem, straightforward solutions are elusive, particularly as missing, inaccurate, or difficult-to-interpret documentation represents a major source of revenue loss for hospitals and other health care organizations. Moreover, EHRs, even with their flaws, hold remarkable promise for improving clinical care.

Nevertheless, several research teams and organizations are now working on effective ways to reduce physicians' screen time. Multiple efforts are focused on improving the infrastructure of EHRs: for example, more user-friendly interfaces, better alignment with clinicians' actual workflows, and enhanced interoperability between systems. In addition, researchers are also turning to artificial intelligence (AI) and machine learning to help lighten physicians' computer workload by automating tasks they now perform by hand. If Netflix can choose the next television series you'll want to binge-watch, why can't AI anticipate the information doctors need to submit digitally?

For example, a team based in Santa Monica, California is now working on creating AI-based tools that will help physicians reclaim valuable time with their patients and improve professional satisfaction. Their approach involves scanning patient records for relevant medical information, proposing a likely diagnosis, and creating the necessary documentation for downstream services, including billing. The team likens their AI system to a digital "co-pilot" that mimics how physicians make decisions and takes on the most mundane, administrative tasks. The ultimate goal of these and other AI-based efforts focused on clinical documentation is to relieve doctors of repetitive and time-consuming computer work — which is ideally suited for machines anyway — and allow them more time for doing what they do best: caring for patients. \\\



## Minimizing the Threats of Antimicrobial Resistance and Infections Associated with Antibiotic Use

The introduction of effective antibiotics in the 1940s ushered in an era of optimism with rapid declines in deaths due to infections. Since that time, however, antibiotic resistance has emerged rapidly, and too few antibiotics are making it through the development pipeline. That means once curable infections could soon become more virulent and even untreatable.

Indeed, the decline in the usefulness of antibiotics is troubling on multiple fronts, but perhaps one of the most serious is the accompanying rise in infections with multi-drug resistant organisms, particularly in hospitals and other health care settings. The danger lies not just in the “super bugs” themselves, but also in another infection linked to antibiotic use, *Clostridium difficile* colitis.

*C. difficile* causes life-threatening diarrhea, primarily in those recently treated with antibiotics. While there are good treatments for *C. difficile*, as many as 25% of patients will relapse. The bacteria can survive in the environment for months, increasing the risk of transmission. Strikingly, in the period from 2000 to 2007, deaths from *C. difficile* rose 400%. In 2011, nearly half a million Americans became infected with *C. difficile* and roughly 30,000 patients died within a month of diagnosis. Moreover, *C. difficile* represents the leading cause of healthcare-associated nosocomial infection in the U.S., costing acute care facilities approximately \$5 billion each year.



Researchers are now working on multiple fronts to combat this formidable health threat. That includes efforts to leverage machine learning and other artificial intelligence (AI) approaches. For example, researchers in Massachusetts and Michigan are developing a tool that uses clinical data from patients’ electronic health records (EHRs) to create an AI-based risk score that reflects a patient’s likelihood of developing a *C. difficile* infection. The score incorporates diverse types of data, including medications, procedures, health care settings, health care staff, lab results, vital signs, patient demographics, patient history, and admission details. Not only does this approach integrate thousands of variables, it also models changes in risk during the course of an inpatient hospital stay, making it possible to create daily estimates of *C. difficile* infection risk for each patient. These risk predictions can then be used to develop targeted interventions, such as infection control strategies and antimicrobial stewardship, to help minimize the dangers posed by this formidable bacterium.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is another pathogen that poses significant health care challenges. In hospitals, MRSA is associated with serious and invasive conditions, including pneumonia, surgical site infections, and sepsis. More than 80,000 invasive MRSA infections occur annually in the U.S. These infections are more lethal, costly, and difficult to treat than those involving non-resistant forms of *S. aureus*: it is estimated that MRSA costs the U.S. health care system approximately \$10 billion each year.

Investigators are turning to AI to help tackle these challenges, too. For example, a research team in Massachusetts is using machine learning to identify the earliest signs of MRSA infection by mining data in patients’ EHRs, including both clinical and non-clinical information. Their method seeks to identify MRSA cases before they are diagnosed, giving physicians advance warning and helping them more effectively target preventive and therapeutic measures. On a similar front, researchers in the U.K. recently developed a machine-learning method to predict MRSA virulence based solely on the microbe’s genome sequence. By analyzing different genomic features, including single nucleotide polymorphisms and small structural changes, the team’s method could pinpoint clinical isolates that are likely to produce severe complications in patients. Such an automated tool, when combined with EHR-based approaches like those described above, could provide an additional layer of information to help clinicians better tailor treatment according to the needs of individual patients. That kind of precision is essential to preserving the long-term success of our current — and future — antibiotic arsenal. \\\



## Harnessing the Power of Digital Pathology

Through its decades-long practice of digitizing clinical images, radiology is providing an early proving ground for machine learning-based approaches for disease detection, diagnosis, and prognosis. With a vast, rich pool of radiological images, researchers have access to the raw material needed to develop and hone new disease-detection algorithms, which are helping to drive the AI revolution in health care. Now, other sub-specialties are beginning to follow suit.

For example, in the U.S., the ability to digitize pathology slides in a clinical setting recently became possible, with the first whole-slide imaging system for digital pathology approved by the FDA in April 2017. The size of digital pathology images far exceeds that of radiological images. Even though a slide contains just a small slice of human tissue, it is often viewed under a microscope at multiple magnifications, generating numerous fields of view — all of which must be digitally captured. In addition, radiological images are typically viewed in grayscale, whereas pathology often deals with full color images.

Despite these challenges, researchers in academia and biopharma are already beginning to harness new capabilities in digital pathology. For example, teams in the U.S., Ireland, and the Netherlands are creating automated, machine-learning-based methods to detect cancer cells on a digital pathology slide. Although the tools are still under development and not yet available for routine clinical use, the goal is to give pathologists smarter, less time-consuming, and more precise methods to determine which patients have cancer and which patients don't — and to help pinpoint the most effective treatments. Initial work is aimed at detecting a handful of cancer types, including breast, prostate, lung, and colorectal cancers. Eventually, these AI-based diagnostics will achieve sufficient training to identify any solid tumors.

Investigators are also working to extend the power of digital pathology to disease prognosis. A research team based in California recently developed an automated method that detects nearly 10,000 different features within whole-slide pathology images to distinguish different lung cancer subtypes and predict patient survival. The group set out to explore ways of improving the treatment of two types of non-small cell lung cancer, adenocarcinoma and squamous cell carcinoma, which can vary dramatically in terms of the recommended paths for treatment and overall prognosis, and are often difficult to differentiate based on microscopic inspection alone.



To tackle this problem, the California researchers leveraged existing image repositories, including over 2,000 histopathology images from The Cancer Genome Atlas (TCGA). With machine learning, they designed a tool that can scrutinize tumor cells for a wide array of cancer-specific traits, including those that cannot be discerned by the human eye. Those features include straightforward elements such as cell size and shape, as well as more subtle characteristics, like the size and shape of cell nuclei, cell texture, and the relative positions of neighboring cells.

The researchers' method accurately predicted survival (long-term versus short-term) in patients diagnosed with stage 1 adenocarcinoma or squamous cell carcinoma. While lung and other tumors are currently classified according to grade (how irregular the tumor cells appear under the microscope) and stage (if and how far it has spread beyond its original anatomic location), this system is known to be imperfect. There can be wide variability within a single stage or grade of tumor. For example, in the TCGA cohort, over half of stage 1 adenocarcinoma patients died within 5 years of diagnosis, while about 15% lived for over a decade. This work provides a glimpse of a new generation of AI-based, data-driven methods in pathology, that can help clinicians tame complexity and make more precise diagnoses and outcome predictions for their patients. \\\

## Bringing “Smart” Machines to Medicine

Self-driving cars are poised to disrupt the transportation industry, and there is a similar revolution underway in health care. This effort seeks to engineer a new generation of “smart” medical equipment that melds scanning with interpretation, monitoring with treatment, and merges data from disparate devices into a common, readily interpretable stream. The goal: to help clinicians better monitor patients’ health in real-time and evaluate an ever-increasing stack of clinical information, thereby enabling the most informed decisions possible.

A key frontier for designing and deploying such intelligent systems is the intensive care unit (ICU), where clinicians treat patients with complicated, life-threatening conditions. Each year, some six million patients are cared for in ICUs across the U.S. The departments are filled with an array of life-saving equipment, including monitors, pumps, ventilators, and drug infusers. Typically these devices do not talk to each other. In addition, they churn out data at an impressive rate, producing thousands of data points a day for just one patient.

Moreover, these machines contain their own suite of alarms, generating a cacophony of beeps and blares that alert doctors and nurses to a crisis — sometimes. False alarms are commonplace in ICUs and elsewhere in hospitals, and alarm fatigue, where clinicians become desensitized to the incessant sounds, is a widespread problem that jeopardizes patient safety. In 2014, The Joint Commission established a new patient safety goal centered on improving alarm systems and reducing alarm fatigue, making innovation in this area a priority for hospitals nationwide.

Now, teams across the country are harnessing artificial intelligence to create new tools that enhance patient monitoring in ICUs and reduce information overload for clinicians. For example, researchers in states like California, Massachusetts, and Minnesota are developing systems that harmonize, integrate, and display patient data from diverse types of clinical sensors, forming a kind of digital dashboard that can be viewed at the bedside of ICU patients. Other groups, including one in New Jersey, are using machine learning to make individual devices smarter — like ventilators that can sense when their pacing is off or when complications such as pneumonia are brewing, and pumps that can monitor how much fluid has been infused into a patient and whether the flow rate needs to be changed. With the rise of such smart systems comes the capacity for enhanced prediction — such as signaling a life-threatening event, like an abnormal heart rhythm, before it happens. For critically ill patients, that advance warning could be vital.

In a similar vein, efforts are also underway to make other clinical tools and technologies smarter. For instance, MRI scans can be lengthy procedures that require patients to spend as long as an hour lying motionless in a narrow enclosure. Although the end result — exquisitely detailed images of the body’s inner structures — is often instrumental in planning downstream clinical care, the patient experience can be unpleasant. But what if these machines could be made more intelligent — able to acquire images more quickly, for example, or ending MRI scans once lesions or other items of interest have been visualized? These questions are now being explored using machine learning techniques by groups across the U.S. and the world. The end results could help reduce scan time by as much two-thirds.

CT leaves room for improvement, too. With CT scans, a major concern is the level of radiation that patients receive, with higher quality images typically requiring higher doses of radiation. But with artificial intelligence, researchers in places like California, Massachusetts, Pennsylvania, and the U.K. are devising ways to enhance CT image quality algorithmically rather than with radiation. Although the radiation dose from a single CT scan poses minimal risks, for patients who require multiple scans over time, the cumulative effects may warrant concern, not to mention the exposures of young children. The results of recent AI-based studies suggest that one day it will be possible to generate diagnostic-quality CT scans with radiation doses that are orders of magnitude lower than the levels currently used — similar to the radiation exposure on a flight from Boston to London. \ \



## Reading the Tea Leaves of Cancer Immunotherapy

The immune system protects the body from a host of foreign invaders. Over the last few years, therapies that leverage these defenses to fight cancer — so-called cancer immunotherapies — have yielded impressive outcomes in combating some forms of the disease. Yet as promising as these therapies are, they currently help only a small subset of patients; the majority of patients do not respond. This picture is further muddled by the treatments' risk of severe side effects and their high cost. And yet, there are currently no reliable biomarkers that can help physicians identify patients for whom immunotherapies will be most effective.

To lend greater clarity to the clinical use of cancer immunotherapies, researchers across the world are working on multiple fronts to uncover cellular and molecular signals that can help differentiate the responders from the non-responders. For example, a team in Boston is searching for molecular patterns in tumor samples to uncover predictive biomarkers. Their work makes use of multi-dimensional methods that scan for scores of different proteins found within tumor cells as well as neighboring cells. Given the high complexity of these data, the researchers are harnessing sophisticated, machine-learning algorithms to help propel their image analyses and pinpoint molecular patterns in patients' tumor tissue that may signal whether a specific type of immunotherapy is likely to be effective.

The ultimate goal is to develop a kind of scoring system that can help stratify patients according to their likelihood of responding to this powerful new class of cancer drugs. These treatments encompass a range of immune-based therapies, from checkpoint inhibitors, which rev up the immune system to help destroy tumor cells to cancer vaccines to so-called CAR-T cells, which use a genetically rewired version of patients' own immune cells to unleash a more potent attack on tumors.

Researchers are working on nearer-term solutions, too. This is because some types of cancer immunotherapies have recently had their labels expanded, creating an even more urgent need for clinical tools that can help molecularly stratify patients.



A case in point: immune checkpoint inhibitors. As of May 2017, some of these drugs are now approved for the treatment of any unresectable or metastatic solid tumor associated with the genetic abnormality known as microsatellite instability. This abnormality is currently detected clinically using either tissue or gene-based analysis. However, performing these tests on all qualifying patients presents major technical and financial hurdles.

So, a research team in Cambridge, MA applied machine learning techniques to design a method for readily identifying patients whose tumors have high microsatellite instability based on genomic characteristics (such as copy number, point mutations, and insertion-deletion events). This information is already routinely collected from cancer patients at some hospitals and therefore may not always require further testing. In those cases, this new approach offers a rapid, low-cost method for screening patients' tumors for microsatellite instability and determining whether patients are candidates for this new treatment. \ \

## Risky Business: Using EHRs to Predict Disease Risk

A holy grail of modern medicine is to make health care more precise — that is, better at detecting declines in patients' health as early as possible and delivering more powerful, molecularly-honed, and personalized (or patient-specific) treatments that can halt, or even reverse, the course of disease. With the rise of electronic health record (EHR) systems over the last decade, the vast majority of U.S. hospitals capture individuals' medical information in a digital format to help streamline and improve the business aspects of health care, including decreasing cost, increasing efficiency, and improving the quality and safety of care. Digital EHRs are now enabling a new wave of biomedical and clinical research, generating new knowledge to improve clinical decision-making — and helping to realize the goals of so-called precision medicine.

Given the wealth of data contained in EHRs, researchers are turning to artificial intelligence, and specifically machine and deep learning, to more effectively harness these "big data." Such efforts come with significant challenges, though. First, EHRs contain a diverse array of data types and formats, ranging from simple numbers (age, height, and weight, for example) and categories (such as gender and marital status) to clinical information (like vital signs and laboratory tests), medical billing codes, doctors' and nurses' notes, medical imaging, and more. In addition, EHRs are often incomplete and inaccurate. These features can further complicate AI-based approaches to EHR analyses.

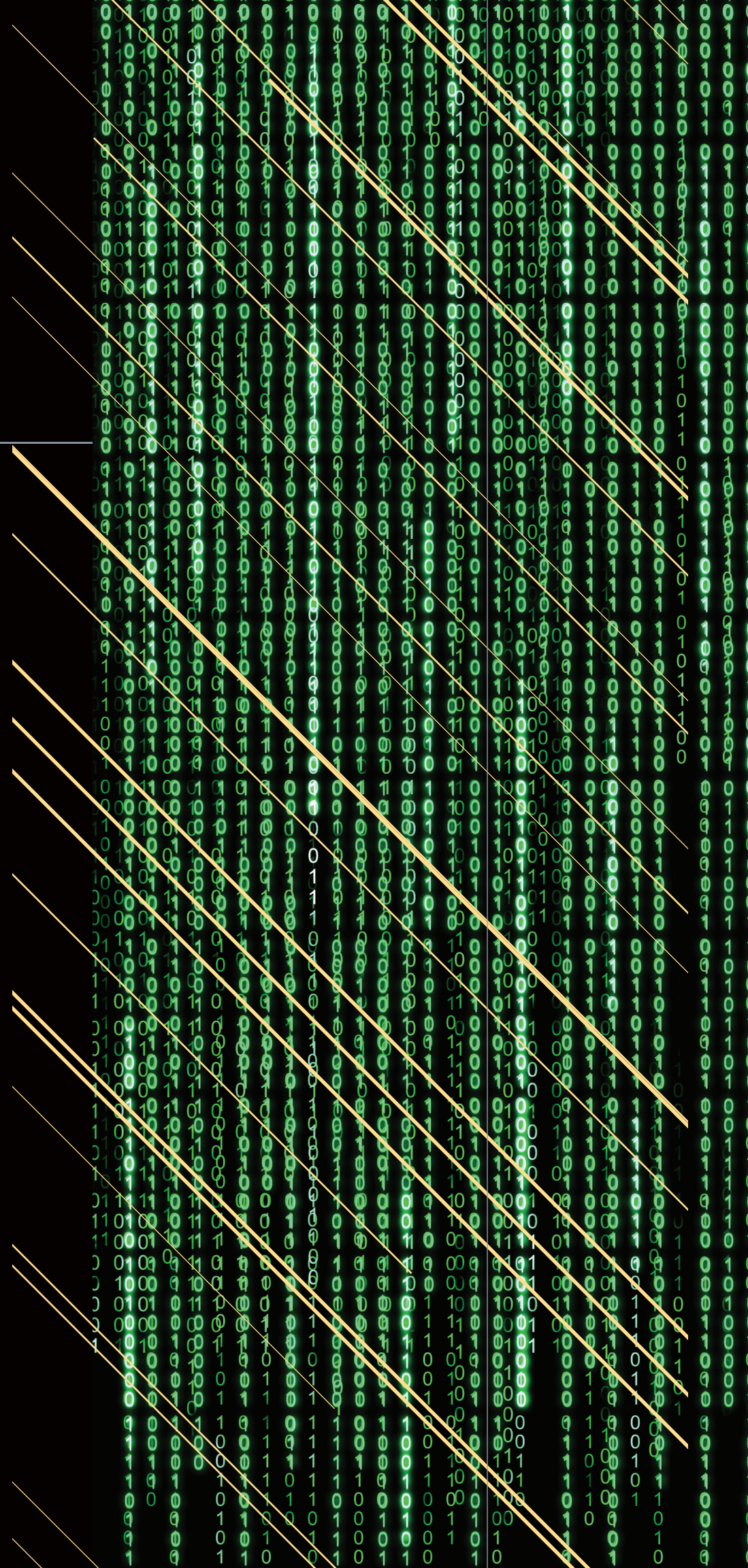
Nevertheless, there are some tantalizing signs of progress. For example, researchers in Boston developed a machine-learning method to provide real-time tracking of influenza infections based on EHR data. Each year in the U.S., some 50,000 people die as a result of the flu and its complications. Indeed, the U.S. Centers for Disease Control and Prevention (CDC) monitors influenza and influenza-like infections based on reports from health care providers, yet its estimates of viral activity come with a time lag of one to two weeks. Efforts to design tools that provide real-time estimates — such as Google Flu Trends (GFT), which used Internet search results — have so far proved disappointing. (GFT was discontinued in 2015 after it misread the severity of the 2013 flu season.)

By integrating EHR data with historical flu trends and machine-learning techniques, the Boston team created a new tool that can predict flu activity at both regional and national levels in real-time. Remarkably, its predictions are as accurate as those provided by the CDC and are available at least a week earlier. This kind of real-time disease surveillance can enable public health organizations to better utilize resources for treatment and prevention.

Another recent advance in EHR analysis makes use of a promising branch of machine learning known as deep learning. The power of this approach lies in part in its ability to unearth novel connections among data without the guidance of a human expert, who would otherwise specify patterns to search for. Using such deep learning methods, a team of New York researchers recently developed a method for predicting patients' future health. The team trained it using roughly 700,000 individual patient records. Notably, they engineered their tool to forecast not just one type of illness, but nearly 80 different conditions, including cancers, heart disease, diabetes, and psychiatric disease.

In initial tests, its performance proved quite remarkable, particularly for forecasting severe forms of diabetes, certain types of cancer (liver and rectal), and schizophrenia — a condition that is often vexing for clinicians to predict. The New York team tested their method on some 75,000 patient records to determine its accuracy of predicting different conditions within a one-year interval.

Despite the groundswell of enthusiasm around these and other deep learning techniques, there is also a healthy dose of concern. That's because deep learning algorithms typically operate much like a "black box" — that is, they yield answers, but it is difficult to ascertain exactly how these answers were generated. Such opacity could prove challenging to their acceptance and adoption for use as decision-support tools, particularly in fields like medicine, where clinicians have not only a desire to understand but also are ultimately responsible and accountable for the clinical decisions they make. Indeed, researchers worldwide are working on ways to address this problem by developing methods that enable more transparent AI-based systems. \l



## Can Personal Devices Improve Your Health?

Digital devices permeate our lives. For most of our waking hours, we sport mini-computers strapped to our wrists or tucked into a pocket. We rely on these gadgets for an ever-expanding array of tasks, and without them (or their sufficiently juiced batteries), modern life can come to a screeching halt. It seems almost natural, then, that we ask: How can these digital companions make us healthier — can they warn us of an impending heart attack, say, or predict the early stages of Alzheimer's disease?

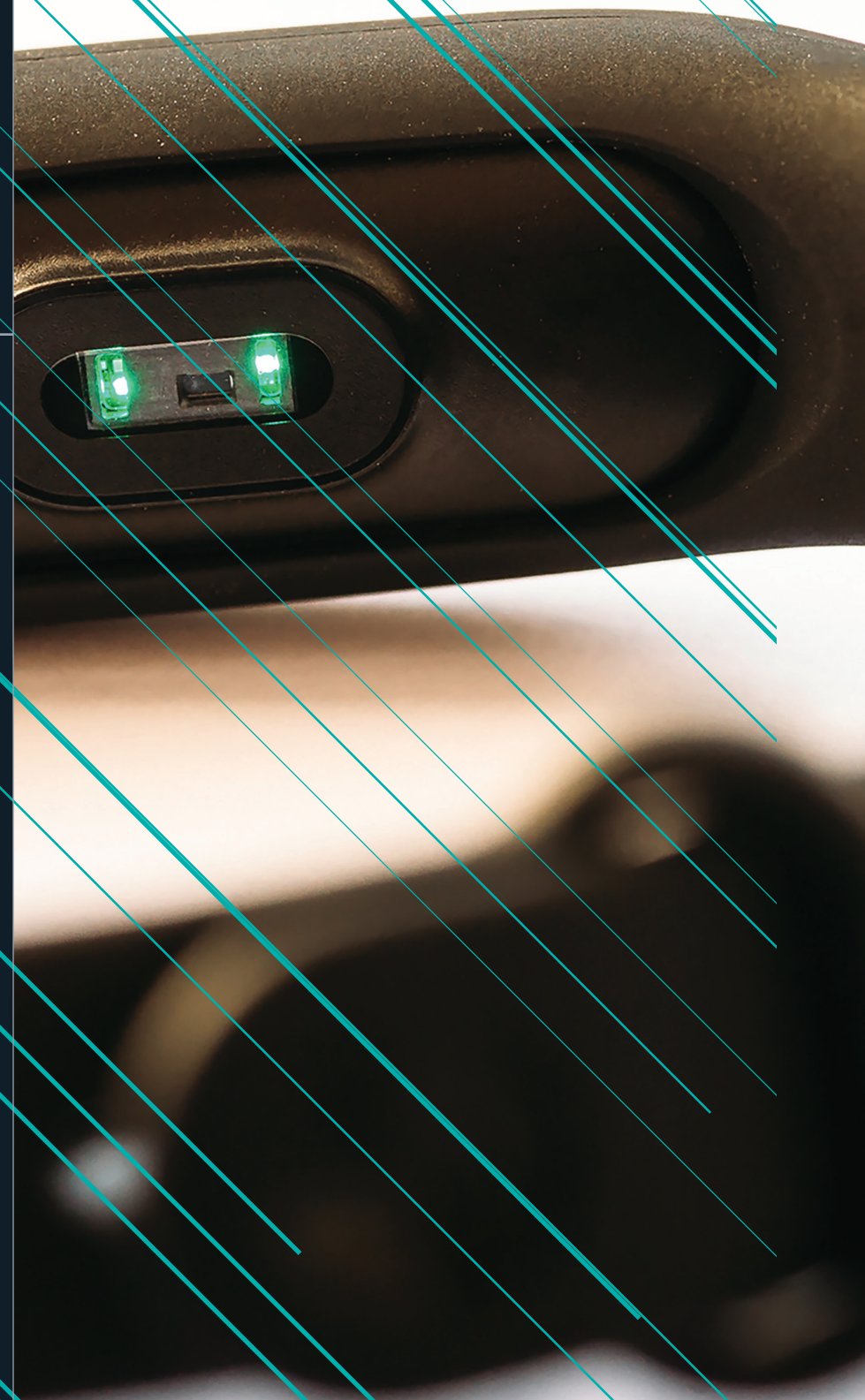
That's precisely the goal of a new wave of research that seeks to harness the vast amounts of data that are collected passively by personal devices, such as Fitbits, Apple Watches, and smartphones, throughout the day. For example, how often does an individual stand up and move around? How far does she typically walk and for how long? What is her gait like? How often does she leave the house or make phone calls? How frequently does she send text messages? How fast does she type?

To sort through the "big data" that flow from these devices, researchers are turning to different forms of artificial intelligence, or AI, to create a kind of "digital phenotype" that could help monitor patients' health over time. For example, a team in Boston is leveraging this approach to study patients who have recently undergone treatment for brain cancer. In many forms of the disease, the standard-of-care post-treatment is fairly straightforward: patients receive an MRI scan every few months to check for complications or recurrence. The Boston researchers are now looking for ways to stratify these patients, using digital phenotyping, for example, to help pinpoint those who require more aggressive interventions. They and others believe that smartphones will become another tool in clinicians' toolbox to help identify acute changes in patient behavior that indicate a decline in health.

A sweeping, NIH-funded consortium spanning 13 universities and non-profit organizations is pursuing similar goals. But first, it is addressing some of the shortcomings of the current generation of commercial wearable devices. These devices gather only a few types of user health data and do not display raw sensor data. Because of these and other limitations, they are not well suited to the kinds of research required to determine how wearables can be leveraged to predict disease and improve health.

Thus, the research team has designed a series of wearable devices that can collect diverse types of sensor data and operate for a full day on a single battery charge. These include a watch-style gadget that decodes hand and arm movements and measures not just heart rate — as most of today's wearables do — but also heart rate variability; a micro-radar sensor to enable the detection of heart and lung activity without the need for skin contact (via electrodes); and a set of "computational eyeglasses" that provide real-time eye and gaze tracking. The team has also created smartphone apps that can connect wirelessly to their devices to collect sensor data and generate a digital profile of the user's health.

With these tools, the investigators are tackling a range of health problems, including addiction, cigarette smoking, heart failure, and obesity. However, the approach is broadly applicable and could also help unearth insights into a range of other conditions. Importantly, the team's work is open-source, so wearable device developers could leverage this work to build new sensors and apps for their own products. //



## A Picture is Worth a Thousand Words

In medicine, an image on a computer screen is more than just a picture; it is millions, even billions of data points that can be systematically scrutinized and mined for connections to health and disease. Understanding how these data points vary within and between images — and patients — stretches the limits of human cognition. Indeed, medical images are acquired by clinicians in fields across the medical spectrum, including radiology, pathology, dermatology, ophthalmology, as well as some surgical specialties.

Now, artificial intelligence, or AI, is transforming how these digital images are analyzed and interpreted in various spheres of health care. With advances in computer vision and machine learning technology, a new era of automated disease detection is dawning, providing clinicians with tools to more rapidly — and in some cases, more accurately — diagnose, characterize, and predict the course of disease.

This revolution is expanding to encompass an increasingly important source of clinical images: smartphones. Although smartphone photos are generally less standardized and more variable in quality than conventional clinical images, there is a growing array of AI-based tools that seek to harness these photos for a variety of medical purposes including preventative care, monitoring of chronic disease, and providing expert care to underserved areas. Indeed, this area is likely to grow substantially: by 2021, there will be some six billion smartphone subscribers worldwide.

One promising area of research that seeks to harness this near-ubiquitous source of images involves the diagnosis of rare genetic disorders in young children. Since a significant fraction of these conditions include craniofacial abnormalities, a team of researchers in the U.K. recently developed facial-recognition software that can analyze ordinary photos for signs of developmental disease. The tool analyzes discrete features of the jaw, mouth, nose, eyes, and brow and then compares them to a database of over 90 disorders. These data are then used to construct a list of possible diagnoses.

The power of this approach lies not only in its ability to aid in diagnosis — indeed, the majority of children with a genetic disorder never receive a definitive diagnosis — but also in revealing clusters of unrelated patients who suffer from the same condition, especially if the cause of their illness is unknown. These individuals could be candidates for genome sequencing, thereby helping to unearth the genetic underpinnings of their disorder.

Another exciting application of AI to smartphone images emerged last year from researchers in Palo Alto, California. The team developed an algorithm that was trained using more than 1 million images to detect skin cancer. Each year, there are more than 5 million new cases of skin cancer in the U.S. For melanoma, the deadliest form of the disease, early diagnosis is crucial. If caught early, the 5-year survival rate is over 99 percent, yet that figure plunges to around 14 percent if the disease goes undiagnosed until its most advanced stages.

By analyzing photographs of moles and other skin lesions — including photos taken with everyday devices, such as smartphones — the Palo Alto team's software was able to distinguish benign from malignant skin cancers, including melanomas. Notably, the method's diagnostic accuracy was comparable to that of 21 board-certified dermatologists. If deployed widely on mobile devices, this skin cancer detection method could help dramatically expand access to diagnostic expertise in dermatology.

Additional efforts are underway to put low-cost health care tools into the hands of those who need them. For example, scientists in Israel and the U.S. are using computer vision and machine learning to develop an inexpensive, rapid test for cervical cancer. In rural health care clinics in Africa and other nations, women typically lack access to first-line cervical cancer screening methods, such as Pap and HPV tests. And yet, of the nearly 300,000 women who die each year of cervical cancer, the majority live in low-resource countries.

The researchers' approach harnesses a decades-old discovery that acetic acid — essentially, vinegar — turns precancerous lesions white when applied to the cervix. Although clinicians can visualize these lesions directly, accurate diagnoses require significant expertise and training. Armed with a small device that clips on to a smartphone to capture photos of the cervix — and AI tools that are then applied to those photos — the team is now working to overcome this challenge and broaden the reach of early detection efforts in cervical cancer. \\\

## AI at the Bedside

As medicine has grown in complexity, the amount of data a single patient can generate — even during a brief hospital stay — has skyrocketed. This big data challenge is reflected in the array of clinical measurements that clinicians can gather at patients' bedsides, such as blood pressure readings, electrocardiograms (ECGs), and electroencephalograms (EEGs). For critically ill patients or those whose conditions require constant monitoring, these routine readings can quickly swell into vast oceans of data, complicating physicians' efforts to make timely, sound decisions.

Consider the case of EEGs. ICU patients with neurological conditions, such as a ruptured brain aneurysm, typically receive constant EEG monitoring for about two weeks. Neurologists now examine this data by eye, searching for changes in the size, shape, and frequency of the waveforms. Yet due to the massive volume of information that comes with EEG, it is feasible for doctors to review these patients' recordings only twice a day, searching for specific signatures that can forecast a seizure — or other signs of neurological illness. But what if EEG data could be mined continuously in an automated fashion to preempt adverse events?

Researchers, including a team in Boston, are working toward this goal by harnessing artificial intelligence (AI). Using machine-learning (ML) approaches, the team has developed an algorithm initially designed to address another important and vexing problem: Deciding whether or not to withdraw care from comatose patients. Indeed, these patients represent a deeply challenging group. Doctors currently base their recommendation to continue (or discontinue) supportive care on multiple variables, both clinical signs and electrophysiological signals. Yet the tools for assessing these variables generally lack precision.

To help bridge this gap, the Boston team developed a method to automatically quantify patients' brain activity in response to external stimuli — a measurement known as EEG reactivity, which can often help predict comatose patients' outcomes. Typically, clinicians visually inspect the EEG outputs and compare them pre- and post-stimulation — an approach that may miss subtle variations. With ML-based, data-driven methods, it is possible to detect these and other EEG changes automatically. In a proof-of-principle study, the group's method showed significant promise, performing at least as well as the consensus opinion of three expert EEG readers. Now, researchers are working to hone and improve this tool so that at any point in time it can assign a probability score that accurately reflects a patient's likelihood of recovery in six months, helping to bring greater precision to the care of comatose patients.

Using similar techniques, researchers are leveraging AI to help analyze and interpret ECGs, another form of physiological monitoring that strains humans' capacity to discern slight variations, particularly in high volume data. In contrast, automated computer algorithms can swiftly process these readings, resolving and evaluating each individual heartbeat. Researchers have begun to leverage these algorithms to help predict patients who are at high risk of acute cardiac events.

For example, in a 2011 study, researchers in Michigan and Massachusetts identified a set of so-called "computational biomarkers" — signals derived from AI-based analyses of continuous ECG data — that are strongly associated with cardiovascular death following acute coronary syndrome (ACS), an umbrella term describing conditions under which blood flow to heart muscle is blocked. Collectively, the identified biomarkers reflect distinct aspects of cardiac function, such as the amplitude differences between successive heartbeats, and can be used to evaluate differences in one patient's ECG readings from those with a similar condition. When combined with existing models for prediction, these ECG-based biomarkers significantly improved risk stratification of patients with ACS.

Now, another Massachusetts-based team is harnessing this approach to scrutinize ECGs from hundreds of thousands of patients to uncover biomarkers linked to sudden cardiac death (SCD). This condition arises when the heart abruptly stops beating, typically stemming from electrical disturbances that interrupt the organ's normal rhythm. SCD is the leading cause of natural death in the U.S., responsible for more than 300,000 deaths each year — often adults in their 30s and 40s with undiagnosed genetic predisposition for heart disease. The researchers' goal is to develop an ECG-based tool that can serve as an early warning system, helping doctors identify patients who are at high risk of SCD. \\\



## 2018 Disruptive Dozen artificial intelligence

Below is our Disruptive Dozen for 2018, which was guided through the nomination and selection-ranking process by our committee, each earning scores along the way.

We present these disruptors to you in order of their rank after the final committee voting was completed.

The medical professionals listed below, experts in artificial intelligence, were each paired with a specific disruptive innovation.

At the Forum presentation, each expert explained its potential impact on artificial intelligence in the decade ahead.

### 12 | Melding Mind and Machine

Leigh Hochberg, MD, PhD  
Director, Center for Neurotechnology and Neurorecovery, Neurology, MGH; Senior Lecturer, Neurology, HMS

### 11 | Next-Gen Radiology

Alexandra Golby, MD  
Neurosurgeon, Director of Image-guided Neurosurgery, BWH; Professor, Neurosurgery, Radiology, HMS

### 10 | Disseminating Medical Expertise to Areas that Need it Most

Jayashree Kalpathy-Cramer, PhD  
Assistant in Neuroscience, MGH; Associate Professor, Radiology, HMS

### 9 | Getting Back to Face Time: AI Tools that Help Reduce Physicians' Computer Use

Adam Landman, MD  
VP and CIO, Brigham Health

### 8 | Minimizing the Threats of Antimicrobial Resistance and Infections Associated with Antibiotic Use

Erica Shenoy, MD, PhD  
Associate Chief, Infection Control Unit, MGH; Assistant Professor, HMS

### 7 | Harnessing the Power of Digital Pathology

Jeffrey Golden, MD  
Chair, Department of Pathology, BWH; Ramzi S. Cotran Professor of Pathology, HMS

### 6 | Bringing "Smart" Machines to Medicine

Mark Michalski, MD  
Executive Director, MGH & BWH CCDS

### 5 | Reading the Tea Leaves of Cancer Immunotherapy

Long Le, MD, PhD  
Director, Computational Pathology and Director, Technology Development, Center for Integrated Diagnostics, MGH; Assistant Professor, Pathology, HMS

### 4 | Risky Business: Using EHRs to Predict Disease Risk

Ziad Obermeyer, MD  
Assistant Professor, Emergency Medicine, BWH; Assistant Professor, HMS

### 3 | Can Personal Devices Improve Your Health?

Omar Arnaout, MD  
Co-Director, Computation Neuroscience Outcomes Center, Attending Neurosurgeon, Department of Neurosurgery, BWH; Member of the Faculty, HMS

### 2 | A Picture is Worth a Thousand Words

Hadi Shafiee, PhD  
Director, Laboratory of Micro/Nanomedicine and Digital Health, BWH; Assistant Professor, HMS

### 1 | AI at the Bedside

Brandon Westover, MD, PhD  
Director, MGH Clinical Data Animation Center, MGH; Assistant Professor, HMS

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