

Emerging and disruptive technologies

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ABSTRACT

Several emerging or disruptive technologies can be identified that might, at some point in the future, displace established laboratory medicine technologies and practices. These include increased automation in the form of robots, 3-D printing, technology convergence (e.g., plug-in glucose meters for smart phones), new point-of-care technologies (e.g., contact lenses with sensors, digital and wireless enabled pregnancy tests) and testing locations (e.g., Retail Health Clinics, new at-home testing formats), new types of specimens (e.g., cell free DNA), big biology/data (e.g., million genome projects), and new regulations (e.g., for laboratory developed tests).

In addition, there are many emerging technologies (e.g., planar arrays, mass spectrometry) that might find even broader application in the future and therefore also disrupt current practice. One interesting source of disruptive technology may prove to be the Qualcomm Tricorder XPrize, currently in its final stages.

INTRODUCTION

We live in an age where many technologies have disrupted or transformed both our everyday lives and commerce (e.g., the worldwide web, tablets, cell phones, wifi, the Cloud, Skype, Amazon, Expedia, Google) (1). Likewise, in laboratory medicine, automation, computers, immunoassay, monoclonal antibodies, and PCR are examples of technologies that were considered disruptive and now are routine in everyday practice. Currently, there are several emerging and potentially disruptive technologies that could unexpectedly displace an established technology and modify the practice of our profession. This article briefly explores a number of technologies that have made a major impact on the practice of laboratory medicine in recent years or are poised to have an impact in the future.

CANDIDATE TECHNOLOGIES

In this article, I have chosen to discuss the following disruptors: robots, 3-D printing, technology and technology convergence, point-of-care technologies, new types of specimens, big biology/data, and the regulations.

Robots

The manual and labor intensive laboratories of the early 1900s have evolved to the highly automated laboratories of today in which robotics plays a major role (e.g., automated analyzers, total automation systems). Mobile general-purpose dual arm robots represent a new phase of automation (<http://www.motoman.com>). This type of robot is employed in some laboratories to perform repetitive tasks, such as ELISAs (enzyme-linked immunosorbent assay), assays that were previously performed by technologists. This trend inevitably will lead to a depopulation of the laboratory (humans outsourced to machine labor). Based on these advances, it is

not difficult to envisage deployment of autonomous artificial intelligence-enabled humanoid robots in the future, which would lead to a further depopulation of the laboratory (2).

3-D printing

Replicators, based on 3-D printing technology, are finding use in research and manufacturing, especially for prototyping (<http://3dprinting.com/what-is-3d-printing/>). In the routine clinical laboratory, a possible future role for this technology could include on-demand manufacture of spare parts, including key parts and components for laboratory equipment. The use of replicators therefore would result in a greater degree of autonomy for the laboratory (3).

Technology and technology convergence

There are many technologies and facets of technology that may influence the future development of laboratory medicine. Massively-parallel planar microarray-based analytical methods already dominate nucleic acid sequencing. In one version of this type method, an array of micro-sized spots (a microarray) of oligonucleotides on the surface of a small chip are used to simultaneously test a sample for the presence of sequences complementary to the immobilized oligonucleotides. The simultaneous nature of the testing dramatically improves throughput compared to previous methods. It is expected that this type of testing may become more widespread and heavily utilized in the future for both genomic (<https://www.genome.gov/10000533>) and proteomic applications (4).

At the same time, the test menu for mass spectrometry, a technology that competes with microarrays for some applications, is expanding. The current applications for mass spectrometry span proteomics, genomics, neonatal testing, steroid profiles, drug testing, vitamin D testing, and microbial identification. Mass spectrometry-based microbial identification is an example

of an application that has been disruptive in microbiology. The broad scope of potential applications for mass spectrometry, from metals to macromolecules, positions this technology for even greater disruptive impact in the future.

Finally, the Qualcomm Tricorder XPrize provides a view of several emerging technologies that may ultimately turn out to be disruptive (<http://tricorder.xprize.org/>). The vision of this \$10 million prize is to “Imagine a portable, wireless device in the palm of your hand that monitors and diagnoses your health conditions. That’s the technology envisioned by this competition, and it will allow unprecedented access to personal health metrics.” The competition currently is in its final stage. DNA Med Institute (DMI), a company that has developed a hand-held analyzer for testing whole blood (<http://www.dnainstitute.com/>), is among the finalists. The DMI technology is based on “nano dipsticks”; small pads on the dipsticks react with blood components, and the resulting fluorescent signals from the pads are scanned in a flow cell. NASA has already utilized this analyzer in zero gravity conditions (5).

Technology convergence is the integration of two or more different technologies within a single device or system. This has been a trend for smart phones that now commonly integrate a telephone with other capabilities and features, including a camera, GPS, PDA, MP3 player, and wireless access (e.g., internet and email). Medical testing now can be added to this list of features. Initially, this was via medical apps, e.g., for heart rate (6), but now there are glucose testing devices that plug into a smart phone port (e.g., iHealth Align) (<https://ihealthlabs.com/glucometer/ihealth-align/>) or a computer (e.g., CONTOUR® NEXT USB) (<https://www.contournext.com/our-products/contour-next-products/contour-next-usb-meter/>). Clearly, this technological advance ultimately may disrupt conventional glucose meters.

Point-of-care technologies

The use of disposable electronics is one interesting example of a disruptive trend in point-of-care testing. These devices simplify operator use of lateral flow tests and provide more detailed diagnostic information and an improved user-interface (so-called digital pregnancy tests). The Clearblue Advanced Pregnancy Test with Weeks Estimator is the most sophisticated of these devices. It contains two tests strips: one detects hCG and the other measures the level of hCG to estimate time since ovulation (1-2 weeks, 2-3 weeks, 3+ weeks) (<http://www.clearblueeasy.com/pregnancy-test.php>).

The device controls the timing of the assay, and the disposable electronics and optical reader within the test cartridge measure the strip results to provide a simple, digital readout in words and numbers on the LCD display.

One of the latest developments in digital pregnancy tests is the First Response™ Pregnancy Pro, a wireless technology-enabled pregnancy test stick that connects via Bluetooth® to a smart phone. An app on the smart phone provides test instructions, indicates the time remaining to the result (and provides distractions to reduce stress while waiting for the test result), displays the result of the test, and suggests next steps (<http://www.firstresponse.com/en/Products/Pregnancy/Pregnancy-PRO>).

Smart contact lenses are another example of a novel point-of-care technology. One such product, under joint development by Google and Novartis, includes a glucose-sensing electrode and telemetry, so that glucose levels in the fluid bathing the eye can be monitored and the data transmitted to a remote device (7). In addition, the recently FDA-cleared Triggerfish® smart contact lens detects changes in ocular dimension for monitoring the patterns of intraocular pressure fluctuations in order to improve the management of glaucoma (8).

There are also on-going and major changes in access to tests and testing. The consumer now can choose from numerous locations that provide direct testing (e.g., pharmacies, Retail Health Clinics) (9) and also has many available routes to obtain diagnostic medical tests. These include Direct to Consumer Testing via the internet, collection kits for drugs of abuse and infectious diseases (e.g., Home Access® Express HIV-1 Test System) (http://www.homeaccess.com/ExpressHIV_Test.asp), and pharmacogenomic tests available from the pharmacy (e.g., Harmonyx test for attention deficit hyperactivity disorder)(10). One new company's focus is on at-home heart health testing, using a small analyzer and disposable cartridges. Test information is sent to the cloud, and the test results are sent back to the user in ~ 5 minutes, together with tips on how to improve their results (<http://techcrunch.com/2016/03/23/former-apple-exec-launches-at-home-blood-test-startup/>). Direct to consumer testing is controversial and arguments center around the ethical, legal, medical aspects and the societal impact of such testing (<http://www.ascp.org/content/docs/default-source/pdf/2a03e13e-a766-4c4f-aa82-c82f953d2988.pdf>).

New types of specimens

Traditionally, laboratory medicine has focused on the analysis of nucleic acid isolated from cellular specimens (e.g., white blood cells, buccal cells, FFPE (formalin-fixed, paraffin-embedded) tissues). The discovery that blood also contains cell-free DNA has led to intense interest in the analytical possibilities of this specimen type. Cell-free DNA refers to relatively small pieces of circulating DNA that originate from a person, a fetus, or a cancer (so-called liquid biopsy) (11). Already, there are several cell-free DNA-based methods for trisomy testing (12), and plans have been announced for large scale tumor-free DNA testing to enable the early detection of cancer in

asymptomatic individuals (<http://www.grailbio.com/>). The emerging success of cell-free DNA as a specimen is not without controversy, especially in its performance as a screening test for fetal aneuploidy compared to standard methods (13), but in the future, it has the potential to displace other sources of nucleic acid for a range of testing purposes.

Big biology/data

Large-scale mega-sequencing projects involving thousands to millions of subjects are a recent phenomenon (<http://blog.oup.com/2015/02/millions-genomes-project/>). At the current time, there are several studies (either in planning stages or in progress) involving one million subjects, including studies organized by the Beijing Genomics Institute (BGI) (14), National Institutes of Health (NIH) (<https://www.nih.gov/precision-medicine-initiative-cohort-program/scale-scope>), Veterans Affairs (VA) (<http://www.research.va.gov/mvp/>), and others planned for 100,000 (UK, <https://www.genomicsengland.co.uk/the-100000-genomes-project>) and 200,000 subjects (<http://www.grailbio.com/>).

The general goal of these studies is to determine how best to use genomics in healthcare. Some studies, such as the UK 100,000 Genomes Project, have focused on specific types of patients, e.g., patients with rare diseases and their families, and patients with cancer. The hope is that these studies will provide new insights into genetics and health that will lead to the development of more effective, and potentially disruptive, testing. In fact, the first patients diagnosed through the UK 100,000 Genomes Project were reported in 2015 (<http://www.genomicsengland.co.uk/first-patients-diagnosed-through-the-100000-genomes-project/>).

Regulations

The regulation of clinical laboratories (e.g., CLIA'88) and in vitro diagnostic devices (e.g.,

Table 1 Classification of primary problem of problematic LDTs (16)

A	Tests that yield many positive results when the disease or condition is not actually present (false-positives)
B	Tests that yield many negative results when the disease or condition is actually present (false-negatives)
C	Tests with the potential to yield both many false-positive and false-negative results
D	The factor detected has no clear relevance to the disease
E	Tests linked to treatments based on disproven scientific concepts
F	Tests that undermined drug approval or drug treatment selection
G	Other unvalidated tests

FDA clearance, CE Marking) has been beneficial for the quality of clinical laboratories and clinical testing. In the United States, the FDA has announced its plans for regulating laboratory developed tests (LDTs) (15), and a recent publication has outlined the public health evidence for FDA oversight of LDTs (16). This publication provides 20 case studies of problematic LDTs that are classified into seven different primary problems (Table 1) (16). The issues identified relate to test performance (false positive, false negative), lack of clinical validation or validity, and adverse impact on therapy.

The impending regulation of LDTs would be a major disruption for clinical laboratories in terms of the cost and resources that potentially are required to comply with new LDT regulations. At this early stage in the process, it is difficult to predict the effect of such new regulations, but it is possible that the number of laboratories offering LDTs would decrease. Most likely, the tests would be consolidated and sent to laboratories that are willing to make the necessary investment required to comply with the final regulations (e.g., reference laboratories).

CONCLUSIONS

Plotting the future course of laboratory medicine is difficult, and history has shown that attempts to predict future developments are often unsuccessful (17). This article presents selected developments that have the potential to change the way in which laboratory medicine is practiced in central laboratories or at the point of care. Many of these are based on emerging technologies that are still in the early stages of development and thus their potential for disruption has yet to be determined.

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