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Review

Digitalization and artificial intelligence in laboratory medicine

Ali Riza Sisman[1], Banu Isbilen Basok[2]

[1]Department of Medical Biochemistry, Dokuz Eylul University, Faculty of Medicine, Izmir, Turkey
[2]Department of Medical Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, Izmir, Turkey

Abstract

In parallel with the increasing number and variety of medical tests and the widespread use of electronic health records combined with the growing capabilities and capacity of computers have attention to "big data." Processing and extracting meaningful interpretations from such vast and complex data require artificial intelligence (AI) that refers to complex software systems that enable computers to augment and even imitate human intelligence and decision-making. Machine learning (ML) is a subfield of AI that uses algorithms to parse and learn data and then apply this new learning to make predictions and informed recommendations.

In recent years, the effects that the digitalization of healthcare services will have on medicine, especially laboratory medicine as seen in the industry, the economy, and social life. The abundance of health data will lead to a shift from analytical competence in diagnostic tests to the ability to integrate data and simultaneously interpret them within the clinical context. Therefore, "computational laboratory medicine" units should be established and integrated into resident and undergraduate education curricula. Using the computational approach, the promise of improved medical interpretation will further increase the effectiveness of laboratory diagnostics in the process of intensive dialogue/consultation and clinical decision-making. Medical laboratories may play an active role in the future as a "nerve center of diagnostics" and joining the patient and physician to form a "Diagnostics 4.0" triangle.

As the big data continue to grow in healthcare, the need for implementing AI and ML techniques into laboratory medicine is inevitable. In this new AI-supported era, clinical laboratories will move towards a more specialized role in translational medicine, advanced technology, management of clinical information, and quality control of results generated outside the laboratory. The field of laboratory medicine should consider such a development sooner rather than later.

Keywords: Artificial intelligence, big data, black box, diagnostic 4.0, computational laboratory medicine, explainable artificial intelligence, machine learning

A new trend in healthcare

The current trend in health care is a shift from a disease-centered model to a patient-centered model, from a paternalistic physician-patient relationship to an egalitarian partnership, and from empirical to data-based evidence [1, 2]. In parallel with the increasing number and variety of medical tests, it is estimated that the number of data generated in the evaluation of a patient will reach 10.000 in 2020. The output obtained from molecular biology studies and the widespread use of electronic health records (EHR) combined with the growing capabilities and capacity of computers has attention to "big data." It is once again clear how important it is to process big data in the fight against the disease and in the development of vaccines or drugs during these days when we fight the Covid-19 outbreak as humanity [3]. Processing and extracting meaningful interpretations from such vast and complex data, as seen in the Covid-19 outbreak, require the use of various computational tools and methods.

Address for correspondence: Banu Isbilen Basok, MD. Department of Medical Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, Izmir, Turkey
Phone: +90 532 565 17 67 **E-mail:** drisbilen@yahoo.com **ORCID:** 0000-0002-1483-997X

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The big data strategy can bring about significant savings from doctor visits and laboratory tests. While data may be worth its virtual weight in gold, access to data is key [4]. High-quality data will also result in higher quality output. Apart from the protecting well-being of people, it is believed that the use of big data could save over 300 billion dollars in global health costs annually [5]. Discussions of big data often refer to "harnessing the power of data." Big data in healthcare refers to the varied and complex data that are too difficult to analyze and manage using conventional software or hardware [6, 7]. These include large data sets obtained from demographic, clinical, diagnostic, and public health records that are used to guide decisions about diagnosis, patient care, resource allocation, and epidemiological trends.

What is artificial intelligence?

Processing big data, which is high-volume and multidimensional, requires artificial intelligence (AI) or machine learning (ML). AI refers to complex software systems that enable computers to augment and even imitate human intelligence and decision-making. AI systems are dynamic and constantly evolving, able to analyze data, learn from information, and make predictions and decisions. ML is a subfield of AI that uses algorithms to parse and learn data by constructing statistical prediction models from datasets and estimates a new data instance and then applies this new learning to make predictions and informed recommendations. By analyzing large amounts of training data, the algorithm perceives the experts' decisions and learns patterns, applying what it learns to new samples. Errors in detection or diagnosis made by the algorithm can be corrected by an expert. However, more importantly, the algorithm can also learn what is correct from these errors. The main distinction between AI and other software or computer-based technologies is that AI has the capacity to learn and improve with data and experience. Other technologies can execute complex tasks but are not able to perform actions or draw conclusions to improve clinicians' and patients' care decisions if they are not specifically programmed.

Causality and the black box perception

ML models are typically neither mechanistic nor causal. They largely capture non-linear correlations between variables and clinical outcomes and are therefore perceived as "black boxes." The main advantage of modern ML approaches is that they do not require a detailed understanding of causal relationships or mechanisms. However, the main limitation is the difficulty of interpretation. Therefore, a major question is how much ML methods can turn into causal models in the future.

Assessing the accuracy of AI, measuring how well the system is performing as assistance to experts, and saving AI from being a "black box" is important. To prove the utility of an AI application, it must be evaluated in comparison not only with other AI solutions but with experts as well. However, this is rarely done due to the lack of publicly available knowledge bases for providing real-life data. Clinical data generated from a growing number of genomic testing platforms enable AI solutions to identify subgroups [8].

Since the time of Galileo Galilei in the 16th century, the scientific method has consisted of forming and experimentally testing hypotheses. While ML techniques can make sense of big data and provide accurate predictions, they are generally unable to provide deeper theoretical, mechanistic, or causal insight into an observed phenomenon. Data science and AI cannot replace conventional, hypothesis-oriented research. One reason for this is that ML models typically capture statistical connections, such as correlations from data. However, correlation does not mean causality. Even if acceptable predictive performance can be achieved, the lack of a clear causal or mechanistic interpretation in ML models may impede physicians' acceptance of data science-based solutions.

Recently, the explainable AI (XAI) concept is introduced into healthcare due to the aforementioned limitations of current AI models [9]. The explainable AI models allow users to understand the way a specific model operates and the underlying reasons for the produced decisions with a more focused decision and higher accuracy [10]. It is possible to predict that explainable AI/ML can show a promising future to increase the practical use of AI in healthcare.

Transparency and reproducibility

AI is a popular field that is seeing increasing demand for the services it provides. That said, detailed information about AI techniques and models are not clearly presented, and there are also significant methodological differences from company to company. The reproducibility of experimental results is an essential feature of science. Therefore, the reproducibility of ML outcomes and experiments is very important. As ML algorithms usually have numerous adjustable components, their performance can be influenced by the scale and quality of training data, empirical hyperparameter settings, and optimization processes. Many publications fail to explain simplifying assumptions or implementation details, making it difficult to reproduce the results. This, combined with the fact that researchers often do not share their source code, makes reproducibility a major challenge. Even if all these details are shared, testing reproducibility is not easy because it requires the reproducing party to meticulously examine the code and scripts necessary to produce the results, or the algorithm and parameters have to be included in the article to enable the creation of a new script. These discussions encourage the publication of well-defined research methods and protocols and thus help improve AI technologies. Even after overcoming such obstacles, AI solutions can only be widely adopted in healthcare with formally tested and closely monitored assessments that yield real-world benefits. A trait specific to the field of computer science and

especially AI is that researchers in public and private sectors tend to orally present their findings in scientific meetings and publish discussions instead of turning their studies into articles in refereed journals [11].

To facilitate patient participation in the AI-powered digital health transformation, physicians should educate patients about personalized medicine, the benefits/risks of AI, and data sharing and protection. Healthcare providers must be sensitive to varying degrees of patient preferences for privacy and obtain consent for the collection and use of patient data as appropriate. Awareness of health literacy should be raised to help patients benefit from modern technology-intensive healthcare systems and become accustomed to shared decision-making processes. Ethical principles should be established for the development and use of AI applications, especially to ensure their appropriate, rational, and beneficial use in healthcare.

Diagnostic 4.0 and the digital era

The U.S. Food and Drug Administration (FDA) defines digital health as a field encompassing wearable devices, mobile health (mHealth), telemedicine, personalized medicine, EHRs, and healthcare information technology (IT) [12].

In recent years, the digital revolution has been rapidly transforming the industry, the economy, and social life. Based on these changes, we can predict the effects that the digitalization of healthcare services will have on medicine, especially laboratory medicine. Disruptive technologies will fundamentally change the demand for and performance and interpretation of laboratory tests in the future and will enable the collection of test results from various sources for the added benefit of the patient. Smart textiles and implantable sensors will measure myriad laboratory parameters, and this data will be stored in cloud services. These will likely enable laboratory medicine to evolve toward a higher level of visibility that redefines the patient–doctor–laboratory relationship and places it at the center of diagnostic information rather than being the hidden champion of big data. For example, accessing digital health data will enable laboratory medicine to contribute as it currently does to medical communication more effectively. In this respect, a substantial study will be required regarding the way we conduct our profession and the need will emerge for new educational concepts and continuous professional development.

"Creative destruction" is a technical term described in the early 1940s by the Austrian economist Joseph Schumpeter regarding macroeconomics [13]. The concept states that existing systems are destroyed by new systems that emerge and supplant them. The triggers are typically technological leaps that act as destructive elements [14]. Between destructive events, an increasing complexity improves existing technology until the next cycle of creative destruction. The series of industrial revolutions that started in the 19th century with the steam engine is the most noteworthy example of Schumpeter's hypothesis [15].

What place will medical laboratories have in the digital era?

The classical role of the medical laboratories is to provide information to and assist the clinician with diagnosis and follow-up. Thus, the main role here is that of the clinician. Diagnostic results are generally only evaluated by a physician and although the laboratory is a hidden champion in the overall process, it is rarely seen by the patient. However, modern medicine is shifting from a focus on disease to a focus on the patient. Medical laboratories may play a more active role in the future as a "nerve center of diagnostics" and joining the patient and physician to form a "Diagnostics 4.0" triangle (patient–physician–laboratory) [15, 16]. The field of laboratory medicine should consider such a development sooner rather than later.

Today, digitalization, automation, and laboratory information software have been commonplace in the clinical laboratories. Still, many laboratory processes are performed manually or partially digitized. However, there are efforts to improve the preanalytic, analytic, and post-analytic processes of the clinical laboratories with the AI-support. Examples of such studies are an AI-supported system that predicts patient waiting time in the phlebotomy unit and organizes the entire blood collection process or the autoverification of test results using an ML approach [17, 18]. ML approach can also implement for further processes, such as predicting out-of-control events in internal quality control studies, detecting instrument failures before even they occur, or determining compatibility between analyzers in central laboratories where several instruments running the same parameters are tested. It is possible to increase the examples of how to correct a problem or to improve a process with the assistance of AI, and those who will determine any requirement are laboratory professionals.

Will history repeat itself? At the turn of the 20th century, laboratory tests started in doctor rooms and were later moved to private laboratories and hospital laboratories. Automation technologies were developed for cheap production and laboratories began to be automated and consolidated in the second half of the 20th century. However, developments in measurement technologies, point-of-care testing (POCT), and more importantly, wearable sensor technologies that can be placed on patients raise the question of whether a reversal of this process in laboratory medicine will bring about decentralized laboratories. According to Mario Plebani's comment on applying Giambattista Vico's recurring cycle theory to clinical laboratories, there are periods of centralization and decentralization [19]. If the patient performs his/her own test and gets results with ML algorithms from mobile devices and portals, will the clinician and laboratory specialist be eliminated? These questions are starting to arise frequently these days. For the time being, however, medical laboratories and the medical laboratory specialist will continue to exist until the breaking point is reached or disruptive technology is introduced. The reasons for this and future fields of laboratory medicine

and specialist are given in Table 1. The abundance of health data will lead to a shift from analytical competence in diagnostic tests to the ability to integrate data and simultaneously interpret them within the clinical context. The promise of improved medical interpretation will further increase the effectiveness of laboratory diagnostics in the process of intensive dialogue/consultation and clinical decision-making between physicians and patients [15].

As the trend toward laboratory consolidation gradually declines, advances in disruptive POCT technology will continue. Automation, robotics, and IT will increase the effectiveness and efficiency of laboratory procedures. The demand for automation and robotics is expected to continue to rise. It is not unreasonable to believe that machines may play an important role in clinical laboratories in the future [20].

How will medical laboratory expertise evolve with diagnostics 4.0?

The power of laboratory expertise arises from the combination of analytical and clinical knowledge. Unfortunately, this is not possible in present routine practice because test orders are accompanied by limited clinical information. Today, easy access to real-time information offers laboratory personnel opportunities for the prevention and early treatment of diseases. Similarly, continuous monitoring devices and applications will lead to more effective healthcare services.

The inclusion of laboratory test data in EHRs from various sources will bring on new challenges for laboratory medicine concerning controlling the quality of pre-analytical and analytical steps, interpreting the results, and timing the collection of samples. Data from different sources will only be useful if they are consistent. In the era of Diagnostics 4.0, medical laboratories should develop new approaches to quality assessments to make help solve such harmonization problems in electronic health (eHealth) and mHealth structures.

Medicine has lagged slightly behind in digitalization for several reasons; one reason is that that the physician–patient privilege requires the absolute protection of all data from analysis and communication outside the physician's office. In the digital era, such concerns are being increasingly questioned, and patients are more open to this issue. It is also a subject of debate whether generations who share their identities online will be opposed to sharing their personal big data, including their medical records, if there is an associated benefit. Essentially, patients and physicians must follow new rules. The physician–patient privilege, namely the protection of the patient's rights and safety within the boundaries of medicine, is controlled by strict legal regulations in most countries. However, in an actual situation where individual health data are collected, stored, and managed outside the medical field, strict enforcement of patient rights is

Table 1. The future of laboratory medicine in the digital era

Where will laboratory medicine focus in the digital era?
Implementing a total quality management
Focusing on test value instead of the test volume
Ensuring effective diagnostic management
Clinical effectiveness
Output
Patient safety and risk management
Operational efficiency
Consolidating conventional tests
Quality control
Focusing on "accuracy medicine" as well as personalized medicine
Reducing laboratory errors
Reducing inappropriate test orders
Ensuring global standardization of tests
Consolidating routine tests
Developing new tests
Managing point-of-care testing or "near-patient testing"
Technology acceptance
Quality assurance
Training
Consultancy
Verifying test interpretation algorithms
From the "silo model" where information is stuck in one place, to the clinic and patient integration
Clinical communication: Consultation and counseling

practically impossible. Therefore, a lower level of legal rules, such as consumer protection rights, will likely emerge in the future.

In summary, predictions about the future of laboratory medicine continue to be a source of interest for healthcare professionals. We can imagine that the clinical laboratory will largely retain its classical role in laboratory medicine, even in the digital health era. Genome projects are expected to improve our perspective on the link between DNA sequences and disease. Clinical laboratories will move towards a more specialized role in translational medicine, advanced technology, management of clinical information, and quality control of results generated outside the laboratory (Table 1). It seems that two simultaneous processes will transpire in parallel. The first is the consolidation of conventional laboratory tests, and the second is an expanding new market for POCT. The rapid development of ITs will further increase the consultancy role of clinical laboratories by facilitating the remote control of POCT analyzers and direct contact with patients [19].

Conclusion

- Big data require a strong computational infrastructure,
- New tools and technologies like AI and ML should be used for the rapid and efficient use of vast and continuously growing data,
- Openness to interdisciplinary studies within and between institutions is needed,
- Legal regulations should not lag behind technological innovations,
- "Computational laboratory medicine" units should be established and integrated into resident and undergraduate education curricula,
- All this information clearly shows that learning health systems and learning laboratories will gain importance in the future!

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