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Artificial intelligence in medicine☆

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ABSTRACT

Artificial Intelligence (AI) is a general term that implies the use of a computer to model intelligent behavior with minimal human intervention. AI is generally accepted as having started with the invention of robots. The term derives from the Czech word *robota*, meaning biosynthetic machines used as forced labor. In this field, Leonardo Da Vinci's lasting heritage is today's burgeoning use of robotic-assisted surgery, named after him, for complex urologic and gynecologic procedures. Da Vinci's sketchbooks of robots helped set the stage for this innovation. AI, described as the science and engineering of making intelligent machines, was officially born in 1956. The term is applicable to a broad range of items in medicine such as robotics, medical diagnosis, medical statistics, and human biology—up to and including today's "omics". AI in medicine, which is the focus of this review, has two main branches: virtual and physical. The virtual branch includes informatics approaches from deep learning information management to control of health management systems, including electronic health records, and active guidance of physicians in their treatment decisions. The physical branch is best represented by robots used to assist the elderly patient or the attending surgeon. Also embodied in this branch are targeted *nanorobots*, a unique new drug delivery system. The societal and ethical complexities of these applications require further reflection, proof of their medical utility, economic value, and development of interdisciplinary strategies for their wider application.

1. Introduction

Artificial intelligence (AI) is generally accepted as having started with the invention of robots. The word robot, spelled *robota* in Czech, was introduced into the literature by the writer Karel Capek in his 1921 play, "R.U. R" (*Rossum's Universal Robots*). It signified a factory where biosynthetic machines are used as forced labor. In the middle of the last century, Isaac Asimov immortalized the word "robot" in a collection of short stories of modern science-fiction. The first mention of a humanoid automaton, however, can be traced back to the third century in China when a mechanical engineer, Yan Shi, presented to the Emperor Mu of Zhou, a human shaped figure of mechanical handiwork built with leather, wood and artificial organs [1].0 In the 12th century, a Muslim golden age scholar, polymath, inventor, and mechanical engineer named al-Jazari created a humanoid robot able to strike cymbals. During the Renaissance period, Leonardo da Vinci made a detailed study of human anatomy to design his humanoid robot. His sketches drawn in 1495, were only rediscovered in the 1950s. Leonardo's robot was a *knight robot* that was able to stand-up, sit-down, wave arms and move head and jaw. It was operated by pulleys and cables. More important than his accomplishments in this area, da

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Vinci's sketchbooks were a source of inspiration for a generation of robotic researchers, some of whom worked at NASA.

In medicine, a surgical system made by the American company, *Intuitive Surgical*, was named *Da Vinci* in recognition of his inspirational impact. It was approved by the Food and Drug Administration (FDA) in 2000, and the number of units in operation around the world is now over 5000. *Da Vinci* surgical systems facilitate complex surgery using a minimally invasive approach, and can be controlled by a surgeon from a console. The system is commonly used for prostatectomies and gynecologic surgical procedures. It is starting to be used for cardiac valve repair.

The evolution of robots made a change in direction with the first robot to be recognized as revolutionary in its mechanical realistic conception being the "Flute Player", conceived in the 18th century by the French inventor, Jacques de Vaucanson, as an innovative "automaton" playing the pipe. It had a repertoire of 12 songs. Two centuries later, William Gray Water became famous in 1948 for the fabrication of the first electronic autonomous robot, which he named Machina Speculatrix. His goal was to demonstrate how the brain functions. It revealed that connections between a small number of "brain cells" could lead to very complex behaviors. John McCarthy coined the term "artificial intelligence" (AI) in 1955, defining it as "the science and engineering of making intelligent machines". He was very influential in the early development of AI. With his colleagues he founded the field of AI in 1956 at a Dartmouth College conference on artificial intelligence. The conference gave birth to what developed into a new interdisciplinary research area. It provided an intellectual framework for all subsequent computer research and development efforts.

During the following years, computers started to solve many complex mathematical problems that soon became of interest to the Department of Defense of the USA. Then, after a period of slowdowns in the 80's, a new golden era restarted with the use of logistic data mining and medical diagnosis. Instruments with increasing computational power were developed. This new capability allowed *Big Blue* to finally beat the world Chess champion, Gary Kasparov on May 11, 1997.

Today, AI is considered a branch of engineering that implements novel concepts and novel solutions to resolve complex challenges. With continued progress in electronic speed, capacity, and software programming, computers might someday be as intelligent as humans. One cannot neglect the important contribution of contemporary cybernetics to the development of AI.

Defined as a trans-disciplinary approach, cybernetics aims for control of any system using technology that explores system regulation, structure and constraints, most notably mechanical, physical, biological, and social. The origin of cybernetics is attributed to Norbert Wiener [2], who formalized the notion of feedback, with implications for engineering, systems control, computer science, biology, neuroscience, philosophy, and the organization of society. Fields that were most influenced by cybernetics are (if we exclude game theory) systems theory, sociology, psychology (especially neuropsychology and cognitive psychology), and theory of organizations.

Today literature on AI is abundant and unbridled. AI was portrayed as a possible threat to the world economy during the 2015 economic forum held at Davos, where Stephen Hawking even expressed his fear that AI may one day eliminate humanity [3]. We will not discuss here the use of this rapidly developing field in military, security, transport or manufacturing; instead, the focus of our chapter is on medicine and health systems.

2. Artificial Intelligence in Medicine: The Virtual Branch

The application of AI in medicine has two main branches: virtual and physical. The virtual component is represented by *Machine Learning*, (also called *Deep Learning*) that is represented by mathematical algorithms that improve learning through experience. There are three types of machine learning algorithms: (i) unsupervised (ability to find patterns), (ii) supervised (classification and prediction algorithms based on previous examples), and (iii) reinforcement learning (use of sequences of rewards and punishments to form a strategy for operation in a specific problem space). First, AI has boosted and is still boosting discoveries in genetics and molecular medicine by providing machine learning algorithms and knowledge management. An example of successes in medicine is the unsupervised protein–protein interaction algorithms that led to novel therapeutic target discoveries [4]. The methodology used a combination of adaptive evolutionary algorithms and state-of-the-art clustering methods, named "evolutionary enhanced Markov clustering". It permitted prediction of over 5000 protein complexes, of which over 70% were enriched by at least one gene ontology function term [4]. Novel computational methodology is also being developed to identify DNA variants such as single nucleotide polymorphisms (SNPs) as predictors of diseases or traits, using novel evolutionary embedded algorithms that are more robust and less prone to over-fitting issues that occur when a model has too many parameters relative to the number of observations [5].

Today's "systems thinking" about health care not only focuses on the classical interactions between patients and providers but takes into account larger-scale organizations and cycles. Furthermore, the health care system must not be stationary but must learn from its own experiences and strive to implement continuous process improvements. This is a multi-agent system (*MAS*), where a set of agents situated in a common environment interact with each other. This process involves building or participating in an organization, which uses AI to achieve significant progress.

An example of such a process in medicine is the development of problematically complex ecosystems for treating chronic mental diseases [6]. Instead of focusing on health expenditures (in public health systems) or cost recovery (in health management organization), the *MAS* approach proposes to capture the dynamics of individual patients, including their responses to received medications as well as their behavioral interactions within a larger societal ecosystem. This global care coordination technology allows process mapping, facilitates control, and better supports changes to the system with a demonstrated increase in response to medication, decrease of costs and more efficacious interventions. Its implementation has allowed health systems managers to analyze the dynamics of system performance across changes in social, medical and criminal justice components [7].

Included in the virtual applications of AI are electronic medical records where specific algorithms are used to identify subjects with a family history of a hereditary disease or an augmented risk of a chronic disease. AI is used to improve organizational performance by enabling individuals to capture, share and apply their collective knowledge to make “optimal decisions in real time”. As a consequence, electronic medical records and health care process management are crucial to achieve the desired quality. From current patients' record keeping of variable quality, information needs to be captured in a digital format accessible as individual data as well as in aggregated forms for epidemiological research and planning. Major efforts are required from academia and the information technology industry to achieve desired efficacy and minimize cost.

The current status of medical records is mostly in the form of incommunicable silos of wasted information for the health system and for knowledge acquisition. Laboratories and clinics need to collaborate to accelerate the implementation of electronic health records [8]. Data need to be captured in real-time, and institutions should promote their transformation into intelligible processes. New scientific and clinical findings should be shared through open-source, and aggregated data must be displayed for open-access by physicians and scientists and made automatically available as point-of-care information. Integration and interoperability including ethical, legal and logistical concerns are enormous, particularly with the forthcoming addition of “omics-based” data. The simplification, readability and clinical utility of data sets should be made evident, and each result must be questioned for its clinical applicability. Our group has developed such a design as illustrated in Fig. 1. Electronic medical or health records are essential tools for personalized medicine and for early detection and targeted prevention, again with the aim of increasing their clinical value and decreasing health costs [9].

Further virtual application of AI in medicine is the use of *softbots*, as psychotherapeutic avatars [10]. Avatars stem from the famous 2009 James Cameron movie which features a hybrid human–alien created to facilitate communication with people from the planet known as Pandora. The use of emotionally sensitive teachable avatars is receiving recognition in medicine [11]. It has been applied to pain control in children with cancer (called “*pain body*”) and it is able to detect early emotional disturbances in youngsters in native American reservations, including suicidal tendency. This approach seems to work better than human interventions [11]. One of

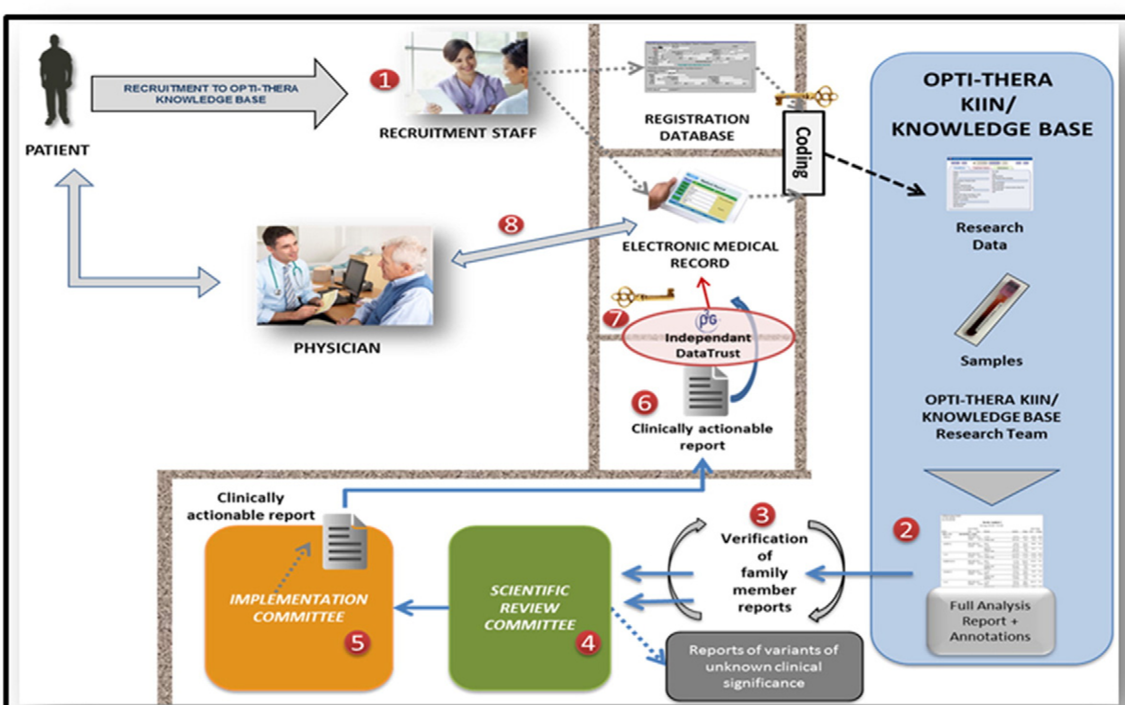

Fig. 1 – DataTrust Pipeline Flow Integration. Figure from Kirby, E., Tassé, A.M., Knoppers, B.M., Joly, Y., Ngueng Feze, I., Dalpé, G., Phillips, M.S., Tremblay, J., Hamet, P. (2016). *P3G DataTrust—Developing a DataTrust (P3G-DT) Service for Personalized Medicine Research and Therapeutic Optimization*. Manuscript in preparation.

the clearest examples is the control of paranoid hallucinations when the subject designs his own avatar representing the persecutor in his mind. The system encourages the subject to engage in discussions with his persecutor who progressively learns to moderate such destructive behavior. Initial successes with this technology have been demonstrated by achievement of a lower level of hallucinations and vocal threats. Perhaps the most useful function will be in care of the elderly, where the frequency, reassuring nature, and kindness of what is said are all important elements of improved communication. Avatars have been also applied to home care, and for biological and physical monitoring with 3D vision [12].

3. Artificial Intelligence in Medicine: The Physical Branch

The second form of application of AI in medicine includes physical objects, medical devices and increasingly sophisticated robots taking part in the delivery of care (*carebots*) [13]. Perhaps the most promising approach is the use of robots as helpers; for example, a robot companion for the aging population with cognitive decline or limited mobility. Japanese carebots are the most advanced forms of this technology. Robots are used in surgery as assistant-surgeons or even as solo performers [14]. One of the most impressive examples of the utility of robots is their ability to communicate with and teach autistic children. Here, and in many other situations that might benefit from robotic intervention, important ethical considerations will have to be resolved before it will become possible to use AI-robots routinely in today's medical environment. Apart from ethical issues, a major challenge in this new dimension of medical care is the clear need for standardized, comparative evaluation of the effect of robotic systems on health indicators, and measures of changes in psychological and physical status, side effects, and outcomes [15].

4. Use of Robots to Monitor Effectiveness of Treatment

Robots can also be useful in the evaluation of changes in human performance in such situations as rehabilitation [16]. Another area where AI might be helpfully employed is for monitoring the guided delivery of drugs to target organs, tissues or tumors. For example, it is encouraging to learn of the recent development of nanorobots designed to overcome delivery problems that arise when difficulty of diffusion of the therapeutic agent into a site of interest is encountered. This problem occurs when the therapist is attempting to target the core of a tumor which tends to be less vascularized, anoxic, but most proliferatively active. To overcome limitations of mechanical or radioactive robotics, researchers have attempted to harness a natural agent with desired properties as a replacement of "intelligent" nanoparticles alone. For this purpose, they are studying a special type of marine coli, called *Magnetococcus marinus* which travels spontaneously to low oxygenated zones. Initial guidance is provided by an external magnetic source and then inherent properties of nanorobots are put into play. These nanorobots can be covalently bound with nanoliposomes bearing therapeutic properties. Early data have disclosed a significant increase in the gradient of desired drug into the hypoxic zones [17].

Most of these novel applications of AI in medicine need further research, particularly in areas of human–computer interactions. Moshimo Mori [18] introduced in 1970 the notion of *uncanny valley* in which an important theme is the human–robot interaction (HRI) field. In these studies humanoid robots were evaluated for their apparent humanity, eeriness and attractiveness as factors making perception of robots either acceptable, feared or rejected [19].

5. Conclusion

AI for personal use is going to stay with us much as genetics will continue to provide personal services. It is therefore important to consider how AI will also serve the development of our health care systems. Takashi Kido [20] proposed *MyFinder* as a personalized community computing to resolve challenges of personalized genome services, acting jointly with AI and shaping the personalized and participative health care of the future. The goal of this platform is to provide personal genome environment interaction in both directions: impact of genes on diseases, health and drug responses, and impact of our environment, behavioral and wellness on our gene activities. The World Economic 2016 Forum named *open AI ecosystem* as one of the 10 most important emerging technologies. With the unprecedented amount of data available, combined with advances in natural language processing and social awareness algorithms, applications of AI will become increasingly more useful to consumers. This is particularly true in medicine and healthcare where there are many data to be utilized from patient medical records and lately also from information obtained by wearable health sensors. This huge volume of data should be analyzed in detail, not only to provide patients who want suggestions about lifestyle, but also to generate information aimed at improving healthcare design, based on the needs and habits of patients. It is important to tear down the prejudices and fears regarding AI and understand how it could be beneficial and how we can cope with its perceived or real drawbacks. The biggest apprehension we have is that AI will become so sophisticated that it will surpass human brain capabilities and eventually will take control over our lives. However, if we succeed in creating ethical standards, developing measures of success and effectiveness, making it available to the mainstream, and not only to the Ivy League medical institutions, by making AI tools open-source and user-friendly and of proven clinical utility, then societal benefits will accrue from the use of AI.

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Conflict of Interests

None.

REFERENCES

[1] Needham J, Kuhn D, Tsien T-H. Science and civilisation in China. Physics and physical technology; pt. 2, mechanical engineering. Cambridge University Press; 1965.
[2] Wiener N. Cybernetics: or control and communication in the animal and the machine. Paris: JSTOR; 1948.
[3] World Economic Forum. Global risks 201510th ed. ; 2015.
[4] Theofilatos K, Pavlopoulou N, Papasavvas C, Likothanassis S, Dimitrakopoulos C, Georgopoulos E, et al. Predicting protein complexes from weighted protein–protein interaction graphs with a novel unsupervised methodology: evolutionary enhanced Markov clustering. Artif Intell Med 2015;63(3):181–9.
[5] Rapakoulia T, Theofilatos K, Kleftogiannis D, Likothanasis S, Tsakalidis A, Mavroudi S. EnsembleGASVR: a novel ensemble method for classifying missense single nucleotide polymorphisms. Bioinformatics 2014;30(16):2324–33.
[6] Silverman BG, Hanrahan N, Bharathy G, Gordon K, Johnson D. A systems approach to healthcare: agent-based modeling, community mental health, and population well-being. Artif Intell Med 2015;63(2):61–71.
[7] Kalton A, Falconer E, Docherty J, Alevras D, Brann D, Johnson K. Multi-agent-based simulation of a complex ecosystem of mental health care. J Med Syst 2016;40(2):1–8.
[8] Castaneda C, Nalley K, Mannion C, Bhattacharyya P, Blake P, Pecora A, et al. Clinical decision support systems for improving diagnostic accuracy and achieving precision medicine. J Clin Bioinform 2015;5(1):1.
[9] Hellwege JN, Palmer ND, Raffield LM, Ng MC, Hawkins GA, Long J, et al. Genome-wide family-based linkage analysis of exome chip variants and cardiometabolic risk. Genet Epidemiol 2014;38(4):345–52.
[10] Luxton DD. Recommendations for the ethical use and design of artificial intelligent care providers. Artif Intell Med 2014;62(1):1–10.
[11] Bartgis J, Albright G. Online role-play simulations with emotionally responsive avatars for the early detection of native youth psychological distress, including depression and suicidal ideation. Am Indian Alsk Native Ment Health Res 2016;23(2):1–27.
[12] Pouke M, Häkkilä J. Elderly healthcare monitoring using an avatar-based 3D virtual environment. Int J Environ Res Public Health 2013;10(12):7283–98.
[13] Cornet G. Robot companions and ethics a pragmatic approach of ethical design. J Int Bioethique 2013;24(4):49–58 [179-80].
[14] Larson JA, Johnson MH, Bhayani SB. Application of surgical safety standards to robotic surgery: five principles of ethics for nonmaleficence. J Am Coll Surg 2014; 218(2):290–3.
[15] Knight BA, Potretzke AM, Larson JA, Bhayani SB. Comparing expert reported outcomes to National Surgical Quality Improvement Program risk calculator–predicted outcomes: do reporting standards differ? J Endourol 2015; 29(9):1091–9.
[16] Simonov M, Delconte G. Humanoid assessing rehabilitative exercises. Methods Inf Med 2015;54(2):114–21.
[17] Felfoul O, Mohammadi M, Taherkhani S, de Lanauze D, Xu YZ, Loghin D, et al. Magneto-aerotactic bacteria deliver drug-containing nanoliposomes to tumour hypoxic regions. Nat Nanotechnol 2016;11(11):941–7.
[18] Mori M. Bukimi no tani [the un-canny valley]. Energy 1970;7:33–5.
[19] Destephe MBM, Kishi T, Zecca M, Hashimoto K, Takanishi A. Walking in the uncanny valley: importance of the attractiveness on the acceptance of a robot as a working partner. Front Psychol 2015;6:1–11.
[20] Kido T. Genetics and artificial intelligence for personal genome service MyFinder. Intimate community computing for scientific discovery papers from the AAAI 2011 spring symposium; 2011. p. 8–11.