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Editorial Comment

EDITORIAL COMMENT

Artificial intelligence in medicine and nephrology: hope, hype, and reality

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In 1665, Robert Hooke, a contemporary and rival to Isaac Newton, proclaimed the arrival of the telescope and the microscope as the "adding of artificial organs, to the natural". These new tools allowed for new discoveries to be made "with prodigious benefits to all sorts of useful knowledge" [1]. So too, has the arrival of the semi-conductor chips, and computer hard- and software have allowed for the extension of natural knowledge into artificial realms, now known generically as artificial intelligence (AI). AI has now diversified into many forms, such as machine learning (supervised or unsupervised), deep learning, and artificial neural networks [2]. Whereas AI has recently exploded into an ever-present and very commonly discussed notion, the concept is not new. The general topic of AI was recurring theme in antiquity and attracted the interest of Rene Descartes, Thomas Hobbes, and Gottfried Leibniz, all three of whom believed that human thought and reason could be reduced to mathematical calculation [3]. The science fiction genre of the mid-1930s often featured speculative AI themes. In 1950, Alan Turing published a seminal and highly influential paper entitled "Computing Machinery and Intelligence" that introduced the now famous "Turing Test" for machine-based thinking and the recognition of simulated intelligence. The term AI was first coined in 1956 at a Workshop Conference in Dartmouth, NH, USA by John MCarthy. The Deep Blue project of IBM that lead to the defeat of the Chess Champion Gary Kasparov in 1997 was a signal event [3]. But the advent of large learning models (LLMs) in 1992, the development of generative machine learning in 2014, and the introduction of generative transformers by Google and OpenAI in 2017 ignited a feverous interest in the potential of AI to make knowledge more useful to mankind and medicine. Indeed, artificial neural network models have simulated *in silico* the layered working of the cerebral cortex of humans. Artificial general intelligence, in which consciousness, self-awareness, and emotions can be acquired by mechanical/electronic devices, seems intrinsically possible or even probable. But for now, AI remains without compassion, love (or hate), malice (or altruism), or revengeful or wishful thoughts.

Thus, AI is neither sentient nor sapient, at least in its present formulation [4]. It is what it is designed to do: learn from data that it is fed and generate outputs according to programs and pathways intrinsic to the machine learning process. Herein lies the strengths and weaknesses of AI and its potential for both good and harm. This short essay will examine these aspects of AI applied to the medical profession, with emphasis on the field of nephrology. These aspects include medical research, drug discovery and design, clinical trial execution, medical practice (detection diagnosis, prognosis, and treatment decision-making), image analysis and interpretation, patient self-care, and writing and dissemination of reports among its many applications. As such, it is not intended to be comprehensives as the enormous and literature devoted to this general topic has long since made this an impossible task. Several well-written and easily approachable books have recently appeared that give a detailed examination of the inner workings of AI, its pitfalls and potential, both in medicine and other fields [5–7].

THE HOPE

The prospects for AI to improve the understanding, detection, diagnosis, prognosis prediction, and therapy of disease states in man have fueled the enormous expansion of scholarly peer-reviewed publications related to AI from virtually none in 1985 to about 4% of all publications in the areas of Life and Health Sciences in 2023 [1]. The lay press has feature articles on AI on an almost daily basis and in February 2024, a company (NVIDIA), strongly devoted to AI enabling architecture, achieved

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a US$2 trillion capital value. Huge amounts of funding are being channeled to not-for-profit and for-profit entities fostering rapid development of both proprietary and open access programs of AI. Will this prodigious investment of time, effort, and money lead to incremental gains in the health of society at large? This seems to be certainly true for the residents of high-income counties, but the diffusion of these benefits to those marginalized by geography or social status may be very slow. The marriage of advances in precision medicine and systems biology with the analytical power of AI, in its many forms, might unleash a new era of medical care and research driven by physicians and scientists and their ubiquitous AI companions. Such high hopes must be balanced by the recognition of the quirks, biases, and uncertainties intrinsic to the AI algorithms and processes [8–10]. These issues give rise to tensions between the good and harm of AI [8]. Tensions also seem likely to arise between proprietary and open access AI, but gains in efficiency/productivity for new therapeutic/diagnostic product development and the business of medical practice in the broadest sense seem inevitable. Evolution of the electronic medical record and the incorporation of AI into its structure will give rise to anticipated improvements in the usability and health promoting effects of these very large databases. But much uncertainty still exists concerning the actual value-added dimensions of this proposition [11–13]. The application of machine learning to image analysis and interpretation carries the prospect of substantial, and largely beneficial, alterations in the practices of radiology, dermatology, and pathology (including renal pathology). The personal smartphone is a logical vehicle for leveraging the communication skills of AI for improvements in physician–patient interaction. Report generation can be simplified and automated as the hoped-for benefits of generative machine learning becomes more widespread. More accurate predictive algorithms for short- and long-term outcomes, including acute kidney injury and kidney failure, are anticipated as AI permeates more deeply into large and demographically diverse data [14, 15], including the electronic medical record [16]. But exactly how these new paradigms will be used to improve health care systems remain a matter of debate [11–13]. These are but a few of the issues, risks, and anticipated benefits to be realized in the AI-dominated era of medicine and science (see also the very influential expanded ideas of Deep Medicine promulgated by Eric Topol in his magnificent book [6]).

THE HYPE

For every new development in medicine and science a cycle (often called the Gartner Hype Cycle™) consisting of initial inflated enthusiasm, followed by increasing mitigating concerns and disillusionment and ending when some new equilibrium/plateau that expresses true reality is reached [17]. It is hard to say exactly where AI is in this cycle, due to the pace and enormity of change. But it does seem clear, that AI has some intrinsic, difficult to overcome defects that might eventually affect its Gartner cycle plateau. These pitfalls have been particularly explored in medicine [9, 11]. Large language models are subject to accuracy issues and data biases, weak and fickle inputs, privacy, and ethical concerns [9]. The models are also prone to hallucinations and glitches [9–11]. If the inputs are imprecise, faulty, non-representative of the universe of facts or biased the outputs can be quite unreliable, such as the "black box" phenomenon commonly present in data science: "garbage in garbage out" (Fig. 1). Many data sets in medicine and nephrology suffer from these defects, and are thus very unsuitable for development of AI generated algorithms. Computer-assisted data analysis involving unsupervised hierarchical clustering [18] may also be hampered by "overfitting" of the data in ways that might encourage specific outcomes.

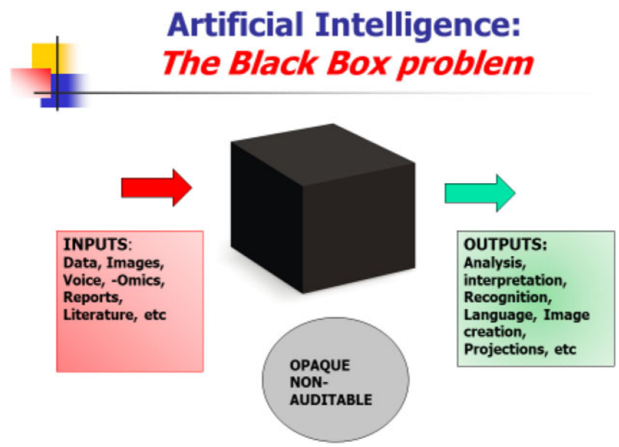

Figure 1: A diagrammatic representation of the "Black Box" problem for Machine Learning and Artificial Intelligence.

Thus, the expected benefits of AI created algorithms using large datasets as the learning substrate must always be balanced by a careful assessment of the risks of error, and inadvertent manipulation of data, in the broadest sense. An international conference called RAISE (Responsible Artificial Intelligence for Social and Ethical Health Care), held in October 2023 in Cape Neddick, Maine, USA, examined AI from a perspective of "do no harm—and the most good" [8, 13]. Rising from the sense that AI "is the future" the conference participants endorsed practical next steps to mitigate the hazards of each identified issue facing wide application of AI in the field of health care and research in the form of "calls to action." The details are worth reading. The conference report addresses thorny issues of: (i) who benefits from AI and how should the achievement of outcome expectations be assessed? (ii) Should AI be a separate voice or a friendly helper? (iii) How best can patient data be collected in a fair and responsible fashion that avoids bias and error? (iv) How can AI be made accessible to both patients and regulators? (v) How can AI best be paid for? The over-arching theme of this seminal report was that if AI is to achieve its true potential in health care and research then leadership needs to provide enthusiastic support and to make sure that the focus is on the public (rather than the private) good.

Other broadly based agencies, such as The National Academy of Medicine, are taking the AI revolution very seriously [19]. Many intangible risks of the "hype" of AI have been exposed. One in particular is worthy of a more nuanced description [20]. Drs Fogo, Knobichler, and Bajema, all well-known and respected nephrologists/pathologists, took aim on the application of AI generated analysis and interpretation of kidney biopsies. Such a process is actually occurring with many pathologists annotating kidney biopsy specimens digitally transformed to "feed" the AI algorithms facilitating conversion to a machine learning process culminating in a LLM generated report of the main distinguishing features of the biopsy tissue. This will bypass the careful review of the pathology by a human eye (and brain). The essential benefits of a human review will be lost in translation, and an interpretation bereft of pathogenic consideration will be the result according to these authors. Kidney pathology will default to a "pattern of injury" recognition system. The intellectual ferment hidden behind the stains and the images will be subdued. Can this be called "progress"? The use of AI to create algorithms from inputs, such as pixels from images, can be difficult to interpret (because of the "black box" phenomenon mentioned previously). Some of the items evaluated in a kidney biopsy are subjective in nature and show high inter-observer variation when human eyes (and brains) are the data gathering device. How much better will an AI program be in detecting and deciphering subtle differences in pixel configuration and intensity in a digitized version of a slide? The use of "saliency mapping" as a technique to highlight features that were particularly significant in the output generation can greatly improve the use of AI in high stakes decision-making such as in health care [21].

THE REALITY

The key notion embedded in the reality of AI, is that it is here to stay. It would be unimaginable that a Luddite-like movement would spontaneously arise and derail the emerging status of AI as an era-defining development. This is not to say that AI will be able to avoid becoming subject to growing calls for its systemic regulation by government or by voluntary organizations. The Biden administration began this process in 2023 and other governments have followed this lead [22]. The majority view is that AI must be developed as a public good, benefiting humankind in its most all-encompassing sense [8, 13]. But, at present, the fundamental architecture enabling AI, the silicon chip, is in the hands of private enterprise. However, many of the programs utilizing this technology are in the public domain as open access. Four of the most widely used LLM in bio-medicine are open access (Google's Flan-PaLM and Med-PaLM, and OpenAI's ChatGTP and BioGTP) [2]. It also seems likely that subscription models (with firewalls) for access to AI will increase over time. It also seems very logical that the nascent fields of precision medicine and AI will gradually coalesce, and this process has already begun. The very large data generated by spatial single cell transcription technology, metabolomics, proteomics, and genomics in kidney disease research lend themselves readily to AI algorithms facilitating unsupervised hierarchical cluster analyses [18]. If the gold-mine of data emerging from reductive biology kidney research is ever to be integrated into a meaningful whole organism schema, then AI is a welcome partner in the exercise.

The "low hanging fruit" for AI in medicine is in report/document generation, imaging processing analysis and interpretation, and in creating efficiencies within the complex system of appointments, scheduling, manpower use, and communication that characterizes the practice of medicine. Drug design and development and the conduct of clinical trials will benefit greatly from joining AI with structural biology in the former [23] and the use of AI generated patient "avatars" to simulate the clinical trials process in the latter [24]. AI, particularly in its deep learning and artificial neural network modes can be very useful for creation of prognosis prediction models and for diagnosis of complex disease states, such as acute and chronic kidney injury [14–16, 25, 26]. Already numerous examples of the successful application of these AI processes in diagnosis and prognostication and in "real-life" situations [25, 26], with modest results. It seems that therapeutic decision-making, via creation of individually specific algorithms of care, will also very likely be improved by application of AI technology.

Although the potential of harm from errors or biases still exists in AI applied to direct patient care, the continued improvement in the AI models and systems augurs for a favorable outcome in the longer term. The disciplines of medicine and nephrology that rely heavily on image creation, recognition, analysis, and interpretation (such as radiology, dermatology, and pathology) are likely to be profoundly affected by AI (see The Hype section). Exactly what will be the extent and nature of this transformation remains uncertain, largely evolving about whether AI will be a "separate voice or a friendly helper."

THE FUTURE

The rapid and accelerating pace of developments in the broad field of AI in commerce, communications, education, research, and clinical medicine make predictions of the likely future very uncertain and risky. It seems probable that AI will continue to "invade" nearly every walk of life. In medicine and nephrology the most "vulnerable" domains seem to be in image processing and interpretation, prediction tools, analysis of large data sets (e.g. spatial single cell transcriptomics, proteomics, whole genomics, electronic health records) for clustering of biological pathways and clinical reasoning, rational drug design, and improved efficiencies of clinical trials, preparation of reports, and documents, and enhancing the patient–physician interaction. It seems inevitable that the processes of AI and precision medicine will coalesce into a unified paradigm of medical care. General purpose algorithms of medical management will gradually become obsolete and will likely be replaced with a multitude of individually specific management pathways created by machine learning and artificial neural networks and easily accessible on computer platforms.

Very clearly, the acquisition of sentience and sapience by AI would be an epoch-making development, forcing mankind to recognize and come to grips with a new conscious entity. This prospect, more than any other, demands very careful thought, deliberation, and very likely government and non-governmental regulation similar to that which occurred with the advent of human cloning and germ-line genomic modification. How the benefits of AI will be distributed equitably among the world's population, rich and poor, also demands the most careful attention as the future unfolds.

To conclude this brief essay and to illustrate the potential changes that might occur in medicine/nephrology I have imagined a fantasy of patient care in 2050, only about 25 years from now. Miguel, a civil engineer was diagnosed with IgA nephropathy in 2035 by a combination or proteomics, immune-serology and genomics using an AI generated algorithm. A kidney biopsy was not deemed necessary. His 10 variable International Risk Prediction Tool (v.5.3; Chat-GTP-5) indicated a 10-year risk of developing ESKD of 4.3% (low- intermediate risk). Based on these determinations, he was managed by a once daily "polypill" of generic RAS/EA receptor inhibitor, a flozin and a third-generation non-steroidal aldosterone receptor antagonist designed (by AI) to optimize reno-protective effects and minimize side effects. At the time of diagnosis, a Bluetooth-enabled microchip was implanted in the right forearm subcutaneous tissue and connected to a smartphone. The chip was capable of monitoring on a continuous basis three interstitial fluid biomarkers, including cystatin C, and the smartphone was enabled with an AI medical assistant program (IAN, integrated AI network) intended to communicate with Miguel on a regular basis concerning his medical status verbally by voice simulation and by generated text messages. In the summer of 2050, while on a business assignment in Croatia, Miguel receives this message on his smartphone: "Miguel, I have detected a worrisome trend in your eGFR values over the past 6 months. I strongly recommend that you have your urinary proteome and your urinary red blood cell excretion re-measured upon your return to the USA.

You may need additional therapy to slow progression of your IgAN. A kidney biopsy and image interpretation under pathologic consultation may be required. Thank you, my friend." Far fetched? Perhaps, but I think this imaginary scenario illustrates how precision medicine, individually specific algorithms and AI may evolve in the not-too-distant future. As Sir William Osler said in 1901, "He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all." Substitute AI for books in this well-worn aphorism and I think you will understand what this essay is trying to say.

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CONFLICT OF INTEREST STATEMENT

None declared.

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