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ARTIFICIAL INTELLIGENCE IN MEDICAL CARE SECTOR: SYSTEMIC REVIEW

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Abstract

The term "artificial intelligence" (Al) refers to the idea of machines being capable of performing human tasks. A subdomain of Al is machine learning (ML), which "learns " intrinsic statistical patterns in data to eventually cast predictions on unseen data. Deep learning isa ML technique using multi-layer mathematical operations for learning and inferring on complex data like imagery. This succinct narrative review describes the application, limitations and poissible future of Al-based dental diagnostics, treatment planning, and conduct, for example, image analysis, prediction making, record keeping, as well as dental research and discovery. Al-based applications will streamline care, relieving the dental workforce from laborious routine tasks, increasing health at lower costs for a broader population, and eventually facilitate personalized, predictive, preventive, and participatory dentistry. However, Al solutions have not by large entered routine dental practice, mainly due to 1) limited data availability, accessibility, structure, and comprehensiveness, 2) lacking methodological rigor and standards in their development, 3) and practical questions around the value and usefulness of these solutions, but also ethics and responsibility. Any Al application in dentistry should demonstrate tangible value by, for example, improving access to and quality of care, increasing efficiency and safety ofservices, empowering and enabling patients, supporting medical research, or increasing sustainability. Individual privacy, rights, and autonomy need to be put front and center; a shift from centralized to distributed/federated learning mayaddress this while improving scalability and robustness. Lastly, trustworthiness into, and generalizability of; dental Al solutions needto be guaranteed; the implementation of continuous human oversight and standards grounded in evidence-based dentistry should be expected. Methods to visualize, interpret, and explain the logic behind Al solutions will contribute ("explainable Al"). Dental education will need to accompany the introduction of clinical Al solutions by fostering digital literacy in the future dental workforce.

Keywords: decision-making, diagnostic systems, informatics, dental, deep learning, machine learning.

Introduction

The term "artificial intelligence" (Al) was coined in the 1950sand refers to the idea of building machines that are capable Of performing tasks that are normally performed by humans.Machine learning (ML) is a subfield of Al, in which algorithmsare applied to learn the intrinsic statistical patterns and struc- tures in data, which allows for predictions of unseen data (Fig. 1). A popular type of ML model are neural networks (NNs), which outperform more classical ML algorithms in particular on complex data structures such as imagery or language.

The main constituent of any NN is the artificial neuron, which is a mathematical non-linear model that was inspired by the human neuron. By stacking and concatenating artificial neurons and connecting those layers using mathematical oper-ations, a network is engineered that aims to solve a specific task like image classification (e.g., radiographic image showing a decayed tooth: yes or no).

The term "deep learning" is a reference to deep (multi- layered) NN architectures. These are particularly useful for complex data structures, such as imagery, as they are capable of representing an image and its hierarchical features such as edges, corners, shapes, and macroscopic patterns. Deep NNs are considered universal approximation machines (Hornik1991). Given a set of mathematical constraints, NNs are able to approximate any function and map any input (such as a radio-graphic image of a decayed tooth) to a given output (such as "decayed tooth"). If a sufficiently large amount of data and computational resources are available, such NNs can be trainedto represent the intrinsic statistical patterns of the provided data. During the training process, data points and correspond- ing labels (classification task) or numerical results (regressiontask) are repetitively passed through the NN. Thereby, the con- nections between the neurons, also referred to as model weights, are iteratively optimized with respect to minimizing the prediction error (the difference between true and predictedoutcome). A trained NN can predict the outcome of unseen data by passing the new data int throu the network.

Software 1.0

the new data point through the network.

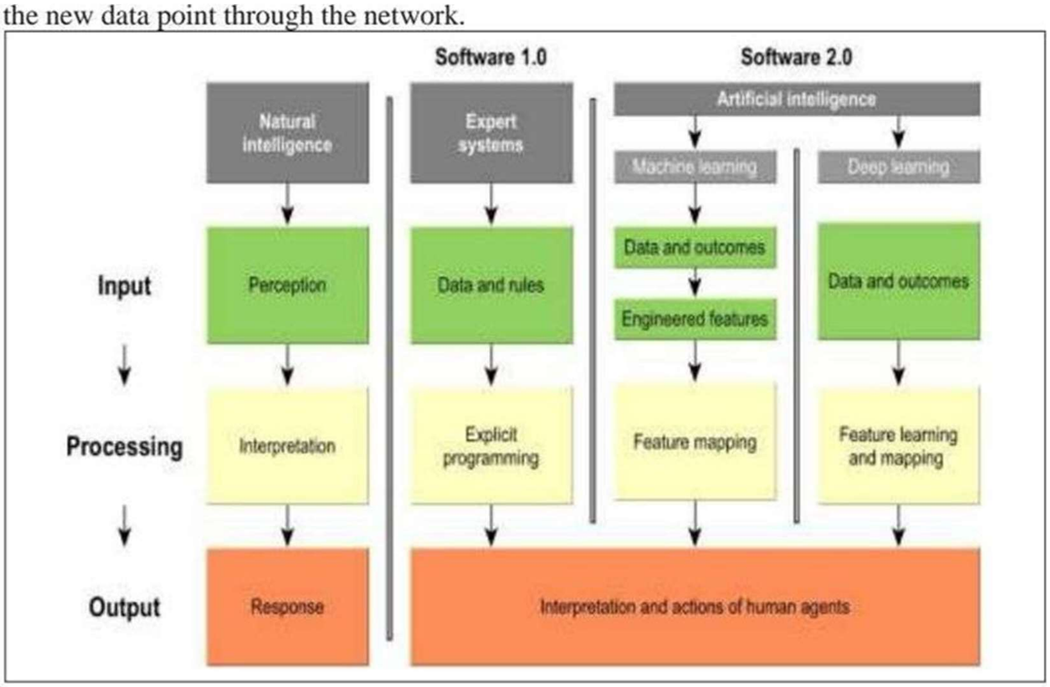

Figure 1. Natural and computer intelligence. Natural intelligence is characterized by perception, interpretation and biological response. In contrast, computer intelligence does so far not replace human responses, but largely supports human interpretation and action. Traditional software (1.0) as onepillar of computer intelligence is supported by rules-based expert systems; they take data and explicitly programmed logical rules to generate narrow, specialized outcomes, thereby outperforming humans in these tasks. Software 2.0 instead uses data and outcomes to infer the rules: In classical machine learning, the features are first engineered by human experts and then learned (e.g., regression modeling). In deep learning, relevant features are learned and mapped in one step, without human feature engineering; this allows to leverage even complex data structures like imagery or language.Modified after Kolossvåry et al. (2019).

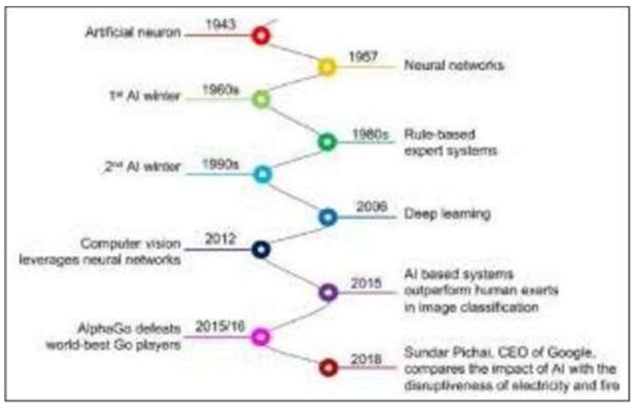

Figure 2. Milestones in the development of artificial intelligence (Al). Al refers to machines that are capable of performing tasks that are normally performed by humans. Machine learning (ML) involves the representation (learning) of intrinsic statistical patterns and structures indata, which allows for predictions for unseen data. "Deep Learning" is aform of machine learning in which multi-layered (deep) neural networks(NNs) are trained to learn features of complex data structures (e.g., image data or language). The history of Al is characterized by ups and downs; after numerous setbacks, optimism is greater today than ever before.

In the last 70 y, Al applications were perceived as both chance and menace (Fig. 2). During that period, numerous set-backs occurred, often referred to as "Al-winters," where the expectations in this technology where not met by the actual outcomes. Today, the optimism is greater than ever before; thelast decade was marked by extraordinary achievements in the field of ML and in a broader sense, Al. For instance, the textual output of state-of-the-art natural language models became so convincing that readers cannot distinguish between humanwritten or artificially generated texts. Face recognition becameso proficient that the technology's potential to affect civil liber- ties caused activists, watchdog groups, and lawmakers to act upon it. It appears that finally Al technologies shifted from fan-tasy to reality; conversation about its impact on society, eco- nomics, healthcare, and politics are taking place in manydifferent fields and disciplines. Dentistry should be among them.

The Chances of Al in Medicineand Dentistry

There has been a significant uptake of these technologies in medicine, too, so far mainly in the field of computer vision. Anumber of drivers for this uptake have been identified (Naylor 2018):

1) Diagnostic imaging is central in many healthcare fields, with Al being especially suitable to overcome the vari- ability in subjective individual examination and to increase the effectiveness of care while lowering costs by eliminating rou- tine tasks.

2)Digital health data are ubiquitously collected

3) Al allows to integrate different and heterogenous data domains, for example, medical/dental history, socio- demographic and clinical data, imagery data, biomolecular data, social network data, etc., thereby making the best use of these multi-level data and allowing to grasp their interaction.

4) Al facilitates research and discovery, by adding in silico experimentation options to conventional research hierarchies, complementing other research levels and existing modeling strategies. 5) As discussed, Al may streamline routine work and increase the faceto-face time doctors/dentists and their patients have ("humanizing care"). This may not only come via diagnostic assistance systems, but voice, speech, and text rec- ognition and translation, enabling doctors/dentists to reduce time for record keeping (Israni and Verghese 2019). 6) Al alsopromises to make healthcare more participatory, especially if patients provide their data actively, for example using wear- ables, etc. Patients will be empowered by self-monitoring andself-management. 7) Using these continuously collected data may also overcome the disadvantages of "on-off-medicine" (Topol 2019), where patients are seen only for a few minutes, while most health conditions are usually acquired over years, and come and go in (oftentimes escalating) intervals (e.g., peri- odontal disease). Continuous noninvasive monitoring of health and behavior will enable a much deeper, individual understanding of the drivers and processes underlying health and disease. 8) Diagnostic and treatment costs may be decreased, thereby relieving healthcare systems burdened by an ageing society with an increasingly high numbers of com- plex, chronically ill cases. Al may also help to address short- ages in workforce, as observed and expected to continue in many parts of the globe, thereby supporting to reach the World Health Organization (WHO)'s Sustainable Development Goals(https://www.who.int/sdg/en/).

The Challenges and Ways Forward

Despite all the potential, Al solutions have not by large enteredroutine medical practice. In dentistry, for example, convolu- tional NNs have only been adopted in research settings from 2015 onwards, mainly on dental radiographs, and the first applications involving these technologies are now entering theclinical arena (Schwendicke et al. 2019). This is all the more surprising when acknowledging that dentistry is especiallysuited to apply Al tasks: l) In dentistry, imagery plays an important role and is at the cornerstone of most patients ' dental voyage, from screening to treatment planning and conduct. 2) Dentistry regularly uses different imagery materials from the same anatomical region of the same individual, regularly accompanied by non-imagery data like clinical records and general and dental history data, including systemic conditions, and medications. Moreover, data are often collected over multiple time points. Al is suited to integrate and cross-link these data effectively and improve diagnostics, prediction, and decision-making. 3) Many dental conditions (caries, apical lesions, periodontal bone loss) are relatively prevalent. Building up datasets with a high number of "affected" cases can be managed with limited efforts.

We see three main reasons why dentistry has not yet fully adopted Al technologies. Tackling these reasons will help to make dental Al technologies better and facilitate their uptake in clinical care.

First, medical and dental data are not as available and acces-sible as other data, due to data protection concerns and organi-zational hurdles. Data are often locked within segregated, individualized, and limitedly interoperable systems. Datasets lack structure and are often relatively small, at least when com-pared with other datasets in the Al realm. Data on each patientare complex, multi-dimensional, and sensitive, with limited options for triangulating or validating them. Medical and den-tal data, for example from electronic medical records, show low variable completeness, with data often missing systemati-cally and not at random. Sampling often leads to selection bias, with either overly sick (e.g., hospital data), overly healthy (e.g., data collected by wearable devices), or overly affluent (e.g., data from those who afford dental care in countries lack-ing uni versal healthcare coverage) individuals being over- represented. Al applications developed on such data will be inherently biased (Gianfrancesco et al. 2018).

Second, processing data, and measuring and validating results is oftentimes insufficiently replicable and robust in den-tal Al research (Schwendicke et al. 2019). It remains unclear how datasets were selected, curated, and preprocessed. Data is oftentimes used for both training and testing, leading to "data snooping bias" (Gianfrancesco et al. 2018; England and Cheng2019). It is usually not possible to define a "hard" gold stan- dard and there is no agreement on how many experts are required to label a data point and how to merge different labelsofsuch "fuzzy" gold standards (Walsh 2018).

Third, the outcomes of Al in dentistry are often not readily applicable: The single information provided by most of today'sdental Al applications will only partially inform the required and complex decision-making in clinical care (Maddox et al. 2019). Moreover, questions toward responsibilities and trans- parency remain.

The Table summarizes the limitations in existing Al approaches in dentistry and provides our assumptions how thefield will tackle these in the future. Overall, and more gener- ally, Al in medicine and dentistry needs to (Academy of Medical Sciences 2018; European Commission 2019):

1. demonstrate value by; improving access to and quality of care; increasing efficiency and safety of pro-vided services; empowering and enabling patients to participate and steer their healthcare; supporting medi-cal research and innovation; increasing healthcare sus-tainability and ecologic responsibility. The latter iscoming into focus: Despite their excellent performance,one drawback of large deep learning Al models is theirextreme training complexity. It was estimated thattraining highly complex models produces 1,438 C02

Table. Al in Dentistry Now and in a Possible Future Scenario.

Aspect	Now	Future
Sample size	Largely under 2,000 instances/images	Millions of multi-level connected instances
Data sources	Single hospitals, insurance claims data	Federated learning; data from multiple institutions
Focus	Detection of structures on imagery, modelling	Multi-class detection of pathologies, predictive association modelling, decision support
Training mode	Supervised learning	Unsupervised or semi-supervised learning
Testing mode	Cross-validation	Hold-out test set, independent datasets
Metrics	Measures of accuracy (accuracy, area-under-the-curve,Fl-score, segment overlap, etc.)	Measures of value (impact on treatment decision, clinical and patient-repolted outcomes, cost-effectiveness) andtrustwolthiness (explainable Al)
Study types	Diagnostic accuracy studies on retrospectively collected data	Randomized controlled trials or large cohort studies collecting data prospectively

(lbs) emissions, which is almost as much as a roundtripflight between New York City and San Francisco (1,984C02 (lbs) per passenger), and can increase up to 625,155 (lbs), which is more than the average lifetimeemissions of a US car including fuel (126,000 C02 (lbs)) (Strubell et al. 2019). The usage of more efficienthardware, application of smaller models and integra- tion of prior knowledge ("hybrid models") will assist inmaking Al more sustainable (Bubba et al. 2019).

2.respect and protect individual privacy, rights and autonomy by; respecting data confidentiality and gov-ernance; meeting ethical, regulatory and legal require-ments; being transparent about data usage and allowingtraceability and accessibility of data. We assume a major shift from centralized to distributed/federated Al training schemes. Data will no longer be centrally gathered and processed, but Al models will go to wherethe data reside; training will be performed locally , andonly updates will be shared between the distributed Almodels. The advantages of this distributed/federated learning are scalability and privacy. Various robust and communication-efficient training schemes for feder- ated learning have been developed (Sattler et al. 2019).

3.maintain trustworthiness and ensure robustness and generalizability by; implementing continuous human agency, oversight and validation; providing a mecha- nism for evaluation and regulation comparable to those accepted and established in evidence-based medicine and dentistry; reporting the development and validation of any Al solution along the TRIPOD criteria (Moons et al. 2015); guarantying equitability and non-discrimination;retaining the responsibility with the healthcare professional, who in return needs to be educated accordingly;building a workforce with the required skillsets and capacities (digital literacy or "matureness") (The TopolReview 2019). Two aspects need to be highlighted here: To foster trust in Al, it is of utmost importance to understand and to be able to explain what the model is doing. Due to their complexity, Al systems have been often regarded as black boxes, which do not provide any feedback why and how they arrive at their predictions. In the last few years, there have been enormous developments in the field of explainable Al (XAI). Various methods have been developed to visualize, interpret and explain what Al systems are doing (Sameket al. 2019) (see Fig. 3). Further, medical Al research needs standards (National Institute of Standards and Technology 2019). Dental researchers are called to action to participate in the development of such stan- dards, for example, relating to l) concepts and termi- nology, 2) data principles (Wilkinson et al. 2016), 3) sample size estimation (El Naqaet al. 2018); 4) metrics;

5) performance testing and methodology, 6) risk man- agement; and 7) value and trustworthiness. The International Telecommunications Unit and the WHOhave recently launched a focus group informing stan- dardization of Al applications in medicine. A topic group on "Dental diagnostics and dentistry" has just been founded (https://www.itu.int/en/ITU-T/focus-groups/ai4h/Pages/default.aspx).

Notably, two further developments can be expected: Al sys- tems will bring together different types of information (e.g., visual and textual) which are able to reason. For instance, recent Visual Question Answering systems (Osman and Samek2()19) are able to answer free text questions about a given image. The reasoning abilities of current Al models even go sofar that they pass a medical licensing examination (Wu et al. 2018). Second, significant advances will be achieved in the field of embodied Al. These systems not only master the aspects of perception and reasoning but have some planning abilities to actively interact with the environment. In contrast to current narrow Al system which only solve specific tasks (playing Go, classifying images, detecting cancer, etc.), embodied Al aims to solve complex tasks similar to humans. There is progress in some components required to build embodied Al (e.g., continuous learning, multi-task learning, few-shot learning), however, a comprehensive general Al sys-tem is not in reach yet.

Conclusion

The next decade will prove if this time the expectations for tangible Al applications are met by actual outcomes or if once

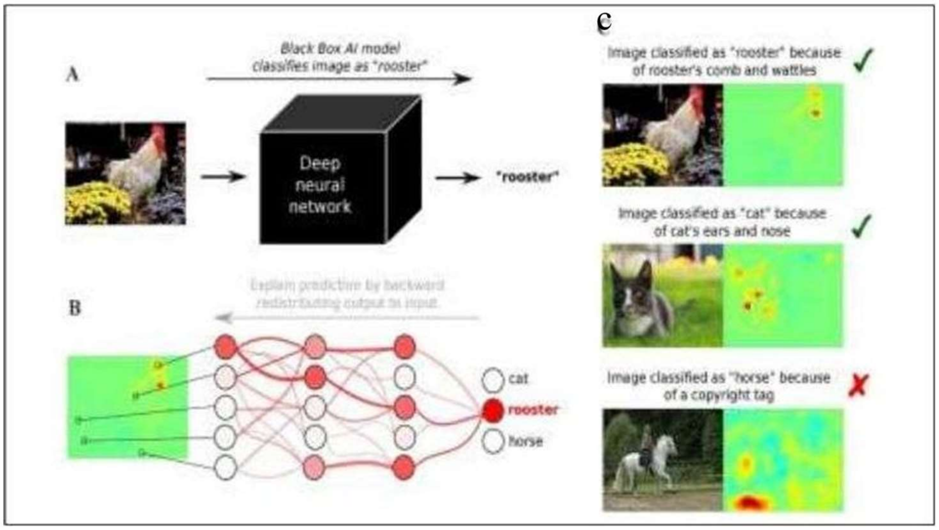

Figure 3. More transparency through explainable Al (XAI). (A) Today's Al models are often considered black boxes, because they take an input (e.g., an image) and provide a prediction (e.g., "rooster") without saying how and why they arrived at it. (B) Recent XAI methods (Samek et al. 2019) redistribute the output back to input space and explain the prediction in terms of a "heatmap," visualizing which input variables (e.g., pixels) were decisive for the prediction. (C) This allows to distinguish between meaningful and safe prediction strategies, for example, classifying rooster images by detecting the roster's comb and wattles or classifying cat images by focusing on the cat's ears and nose, and so-called Clever Hans predictors (Lapuschkin et al. 2019), for example, classifying horse images based on the presence of a copyright tag.

again an Al-winter buries hopes and excitement. In particular in healthcare, the stakes are high. There is reasonable concernabout data protection and data security and about handing overcritical medical decisions to computers. However, Al has the potential to revolutionize healthcare and, with it, dentistry; Almay assist in addressing the weaknesses harshly criticized in conventional dental care (Watt et al. 2019). Dentistry and, spe-cifically, dental research, has a role to ensure that Al will makedental care better, at lower costs, to the benefit of patients, pro-viders, and the wider society.

Author Contributions

F. Schwendicke, J. Krois, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; W. Samek, contributed to design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript. All authors gave final approval and agreeto be accountable for all aspects of the work.

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