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REVIEW ARTICLE

A SYNOPSIS OF MACHINE AND DEEP LEARNING IN MEDICAL PHYSICS AND RADIOLOGY

Zohal Alnour Ahmed Emam[1], Emel Ada[2]

[1] Dokuz Eylul University, Institute of Health Sciences, Department of Medical Physics, Izmir, Turkey
[2] Dokuz Eylül University, Faculty of Medicine, Department of Radiology, Izmir, Turkey

ORCID: Z.A.A.E. 0000-0003-1601-7424; E.A. 0000-0002-0463-0945

Corresponding author: Zohal Alnour Ahmed Emam, **E-mail:** zohal.alnour@gmail.com
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ABSTRACT

Machine learning (ML) and deep learning (DL) techniques introduced within the fields of medical physics, radiology, and radiation oncology (RO) have come a long way in the past few years. A great many applications have proven to be an efficacious automated diagnosis and radiotherapy system. This paper outlines DL's general concepts and principles, key computational methods, and resources, as well as the implementation of automated models in radiology and RO research. In addition, the potential challenges and solutions of DL technology are also discussed.

Keywords: deep learning, machine learning, radiology, radiation oncology, medical physics

INTRODUCTION

Artificial Intelligence (AI) and its breakthrough technologies have changed the entire world around us in the past few decades. In view of its powerful automation functions in many disciplines, AI is the greatest advancement in modern life and the fourth industrial revolution in the world (1). The community has great interest in the use of ML and DL algorithms intended for the medical arena, considering that radical technologies of patients' detection and computing capabilities progressively increase (2).

The advanced technology of AI represents unique professional solutions to medical physics problems, as a means to use ML and DL effectively and legally in radiology and RO applications. A key theme of the recent research demonstrates the impact of the successful advanced data analysis methods on medical physics, while discussing the drawbacks of the automation (3-5). This work is a review of scientific and medical literature for publicly accessible official publishers based on recent online resources. The outcomes expected to influence the medical literature, by providing an overview perspective to ML and DL modeling.

Key Points

1. Learning the basic concepts of ML and DL.
2. Platforms and datasets as tools for modeling data science work related to medical physics.
3. Application areas of radiology and RO (lesion's segmentation, detection, imaging characteristics, image processing and reconstruction, treatment planning, quality assessment and assurance).
5. Challenges and strategies.

Fundamental Concepts and Principles

AI is a computer system theory and production capable of simulating human's thought and behavior (6). ML is a sub-part of AI designed to interpret data and acquire decision-making skills. It includes computer training, which requires how to use sample

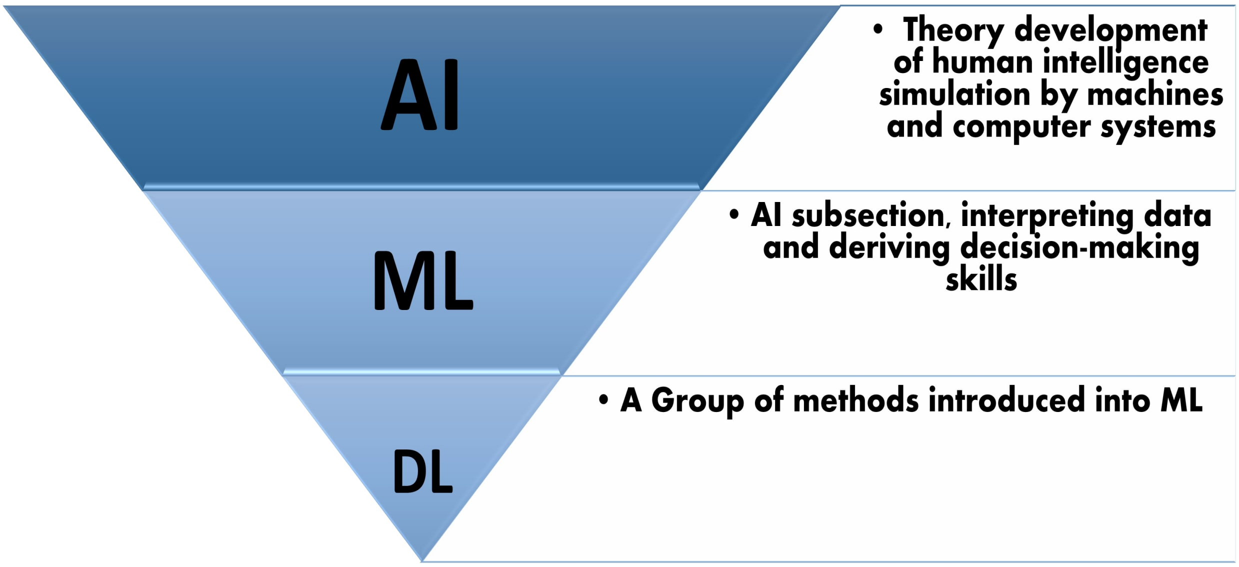

Figure 1. Demonstrates the interrelationship of ML and DL technology as a subcategory of a broad field of artificial intelligence innovation

data or experience to optimize performance results (7). DL is a set of methods introduced in ML, which attempts to analyze the potential patterns embedded in the data under practical constraints. The subject has performed remarkably in a wide variety of fields (8). The association of ML and DL as AI subcategories is shown in Figure 1.

ML and DL Models

ML and DL most powerful algorithms have been addressed through several types of training strategies. Supervised learning (SL) is a method that enforces the model's enforcement, to align marked data with a goal relation to the input outputs. The key examples of SL learning are the Decision Tree, Random Forest, KNN, Linear Regression, and logistic models. Unsupervised learning is a set of approaches that eliminate the need to capture target information. K-means an exemplar of USL that can divide the dataset into groups for specified features. Semi-supervised learning (semi-SL) avails using part of the datasets without labeling targets. Semi-SL models incorporate labeled and unlabeled data, which are further subdivided into semi-SL classification and semi-SL Clustering. Reinforcement Learning (RL) enables an agent to learn by interacting through a present system or environment to produce states based on the agent's actions (9). Markov Decision Process models are applied in ML for discrete, stochastic, and sequential environments decision making. RL incorporates the superior perception in DL to deal with a more complex task.

Supervisory Neural Networks

Algorithm-based supervised DL can decipher complex tasks in the real world and specific disciplinary problems. Supervised neural network is an artificially modeled neural network with a dense multi-layer structure that produces results like training network labels. The layers are connected by activating neurons, which are simulated in a way of structure and function of actual biological human brain neurons. An example of natural and artificial neural work on an object or disease detection process is shown in Figure 2. Supposing the system in which convolutional neural network attempts to interpret the brain image by training neurons to discover the core disease class in an analogous way as in a human brain (10).

The Models designed by classical neural networks (ClassNet), convolutional neural networks (ConvNet), or recurrent neural networks (RNNs) are usually used as label-based networks in DL. These models mainly combine particular modules to perform tasks defined in the supervision process. First, linear function means that the input is multiplied by a constant weight. The second is a non-linear activation function, including a sigmoid, an S-shaped curve, which is 0 to 1. The hyperbolic tangent function (tanh) is an S-shaped curve with a range of -1 to 1. The most used activation function is the rectified linear unit (ReLU) (11), which returns zero when the input is negative, and returns the linear value of the input if it is positive. The third function is required in a probability-weighted prediction of the output as SoftMax.

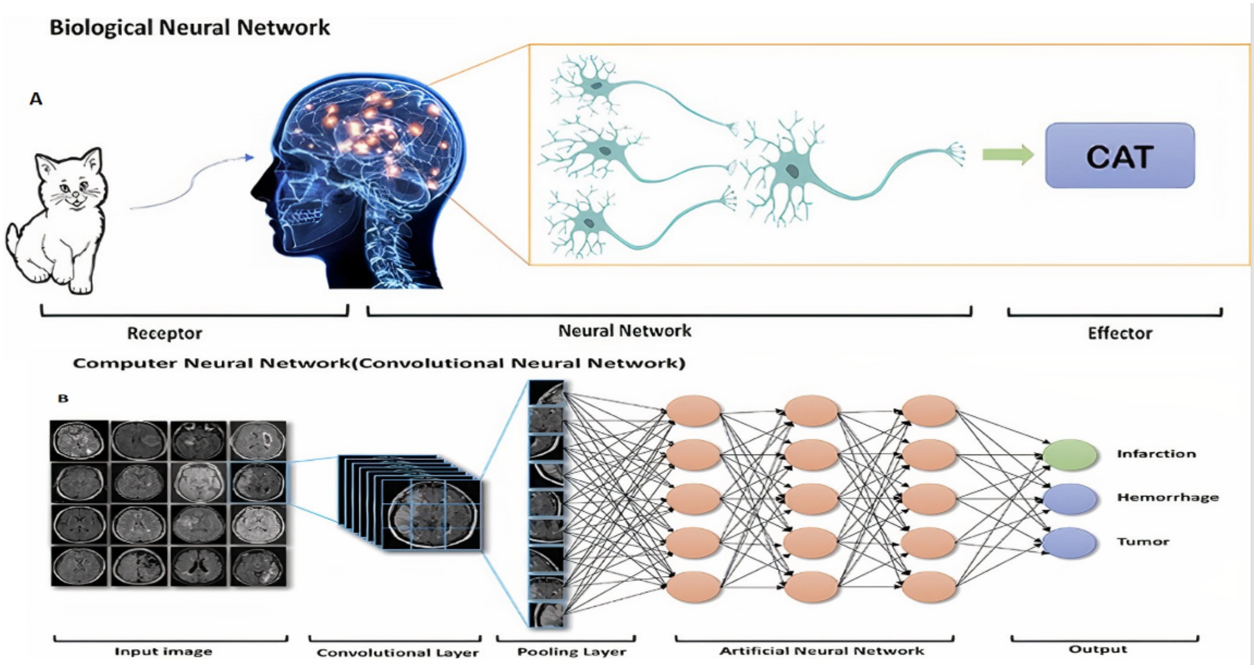

Figure 2. Explains the heuristic relationship between biological and artificial neural networks when performing recognition and classification functions (a). Object recognition through biological neural networks (b). The artificial structure of the deep neural network to identify brain diseases. Source (Zaharchuk et al, 2020).

The Classical Neural Network or Fully Connected Neural Network (FCN) are modeled in the basis of the statistical artificial neural network (ANN). Convolutional Neural Networks (ConvNet) are advanced version of the classic artificial neural network. It is possible to gain access to ConvNet as the most robust network that efficiently manages structured and unstructured complex data types. They involve coevolutionary calculations that combine with the layer of data to generate new characteristic images and feed them into the next layer (12). ConvNet can perform image recognition, segmentation, video analysis and natural language processing tasks effectively. The U-net (13), with its 3D version V-net (14), is a common segmentation architecture. Recurrent neural networks are used for the prediction of sequence data such as writing, speech, time series. Long and short-term memory networks (LSTM) and gated recurrent units (GRU) are the most used forms of RNN (15,16).

Unsupervised DL Models

Unsupervised DL models commonly include automatic encoders and Boltzmann's machines. Autoencoder is a method that uses neural networks for feature learning purposes. There are several types of autoencoders, including convolutional autoencoders, punctured autoencoders, denoising autoencoders, sparse autoencoders, stacked autoencoders, and so forth (17). A Boltzmann machine network (BMN) is made up of symmetrically linked neurons that make stochastic predictions. It contains a basic learning method that enables to discover the characteristics of training data that reflect complex rules (18). Restricted Boltzmann Machine (RBM) and Stack, Deep Belief Network (DBN) are prominent examples of BMN (19).

Semi-Supervised DL Models

Semi-supervised learning models are proposed to create predictions similar to provided knowledge of data structures. One of the recent architectures is the Generative Adversarial Network (GAN). GAN is a combination of basic neural network generator and discriminator. The Networks application can extend from an image and text generation to new drug discovery processes, for example (20). Holistic approach, an area of research in a semi-supervised learning that attempts to unify the existing dominant techniques into a coherent system to achieve good quality results.

Reinforcement DL Models

Deep reinforcement learning (DRL) is a method by which intelligent agents act in the environment through scientific explorers. DRL algorithms can be

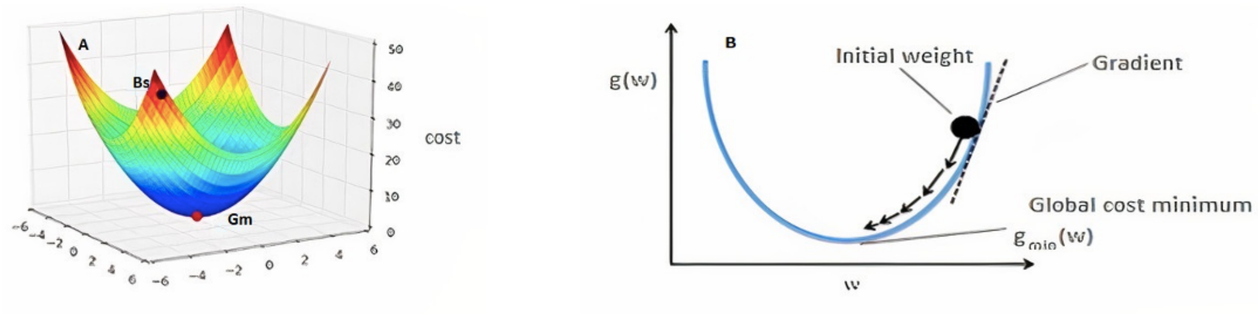

Figure 3. Illustrates the gradient descent optimization graph (a) from the bias (Bs) to the global minimum (Gm) (b) realizing the optimization to find the weight vector (w) of the steepest decline in the cost gmin (w)

divided into model-based and model-free methods such as value-based and policy-based strategies. The fundamental value-based algorithm is known as the Q-learning algorithm. Model-based methods use predictive models to plan and update to study the world, and then build strategies based on that model. The policy-based model will unambiguously learn the function of the stochastic strategy, which maps behavior through sampling (21).

Model Training and Optimization Algorithm

Model training is a process in which optimization of model parameters takes place. In supervised or semi-supervised learning algorithms, the goal of training is to minimize the cost function or naming (loss function) and update the parameters that affect the network in a good way. Several types of cost functions can be creatively described, such as cross entropy and dice coefficients or new methods that combine both methods (22). Optimizer's methods such as stochastic gradient descent (SGD) or Adaptive Moment Estimation (ADAM) can help alleviate potential high memory usage issues (23).

Tools for Research

Modeling Platforms

ML and DL frameworks have played a key role in linking theory with program practice. There are many platforms that can be used for this type of modeling work, such as TensorFlow™, Caffe, Pytorch, MATLAB®, Theano, etc. TensorFlow, a platform of Google Brain team, which designed using Python, can become a one-stop framework for ML and DL modeling goals. It's the core open-source library for developing and training models (24). TensorFlow 2 integrates with Keras to provide an advanced DL application programming interface (API), which can be simple, flexible, and powerful modeling functions (25).

PyTorch is the fastest growing community and support environment in automatic differentiation module for dynamic calculations in a Pythonic space (26). Caffe (27), developed by Berkeley AI Research (BAIR). Caffe is a framework, written in C++ with a Python interface. MATLAB® statistics and ML, deep learning, and RL toolboxes allow models to be built from their existing packages, including all outstanding architectural modeling (28). MATLAB® researchers often benefit from large community-based support models built into other frameworks (such as TensorFlow, Keras, PyTorch, Caffe, etc.). Through direct imports into their environment.

Datasets

Datasets obtained in radiology and RO have promoted the development of medical research in the era of artificial intelligence. Patient data acquisition is primarily carried out through advanced techniques, which can represent an effective source for acquiring the datasets for modeling. Imaging modalities for these techniques can go beyond computed tomography (CT), single photon emission computed tomography (SPECT), and positron emission tomography (PET) and magnetic resonance imaging (MRI). In addition to radiotherapy-planning techniques of sophisticated forward-planned intensity-modulated (fIMRT), inverse-planned intensity modulated (iIMRT), 3D conformal radiation therapy (3D-CRT) and Volumetric modulated arc therapy (VMAT).

Some established medical institutions have made great efforts to release a considerable number of datasets. The National Cancer Institute (NCI) provides a comprehensive resource guide for scientists and an extensive list of databases. The dataset covers research areas, including cancer diagnosis, treatment, and other medical physics-related issues. The Cancer Imaging Archive (TCIA) is

Table 1. Explains the recently reviewed applications of DL in diagnosis, treatment, and image processing research

Proposed method. by	Anomaly/case under study	Year	Imaging Modality	Planned Task	Training/Testing Dataset	Validation Dataset	Network Dimension	DL Model	Evaluation Metrics
Jojoa Acosta et al (42)	Melanoma	2021	Digital Dermatoscope	Classification	1995/598 İmages of the ISBI[1] challenge 2017	149 image	2D	MR_CNN[1] Resnet152	Best of six modals' overall accuracy: 0.904 Sensitivity: 0.820 Specificity: 0.925
Moreau et al (59)	Tumor growth	2021	Simulation technique	Dose fractionation Simulation	Lattice-gas, cellular automaton for tumor growth and effect of radiotherapy simulation.	-	2D	Tabular Q-learning DQN[1] DDPG[1] RL	Best algorithm TCP: 100% D^{1}_{mean} (32.1 ± 0.2) Gy[1] N_{fract} (8.2 ± 0.1) T^{1}_{mean} (195.8 ± 1.4) h[1]
Zhen et al (61)	Liver tumor	2020	MRI[1]	Classification	1,210 patients (31,608 image) for training	201 patients (6,816 images) External cohort	2D	CNN	AUC[1]: 0.946 vs. 0.951, 95 % CI[1], p = 0.664 Malignant vs. benign discriminative model
Van Dijk et al (56)	Head and Neck cancer	2020	CT[1]-scan	OAR Segmentation	589/104 Patient	-	2D	DLC[1] Neural network	Quantative performance measurement DSC[1]: 0.74 D_{mean}: 1.1 D_{max}: 0.8 Gy
Shen et al (58)	Prostate cancer	2020	IMRT[1]	Radiation treatment planning	10/64 Patient	-	3D	Virtual treatment planner DRL[1]-based neural network	Quality score of 8.44 (± 0.48) from 9
Siar et al (40)	Brain tumor	2019	MRI	Detection	1666/226 Image	-	2D	CNN	Accuracy 99.12%
Fu et al (48)	Prostate cancer	2019	MRI CT-scan	Cross-modality synthesis	20 Patient	K-fold cross validation (k=5)	2D and 3D	CNN	DSC: (0.82 ±0.04) Recall: (0.84 ± 0.04) Precision: (0.80 ± 0.08) Average values for the 3D CNN bone region

[a]International Symposium on Biomedical Imaging, [b]Mask and Region-based Convolutional Neural Network, [c]Deep Q network, [d]Deep deterministic policy gradient, [e]Dose, [f]Gray, [g]Time, [h]hour, [i]Magnetic Resonance Imaging, [j]Area under the receiver operating characteristic curve, [k]Confidence Interval, [l]Computed Tomography,[m]DL contouring, [n]Dice similarity coefficient, [o]Intensity-modulated radiation therapy, [p]Deep Reinforcement Learning

Adopted from: (Affane et al., 2020) (76).

an ever-growing dataset that mainly includes DICOM's CT, MRI, and PET images of organ structures, radiation treatment plans, and dose data (29). Another impressive archive is the Cancer Genome Atlas (TCGA), which contains a series of important cancer-inducing gene mutations to improve the standard of diagnosis and treatment (30). As well, the dataset released by challenges is a valuable resource for the medical research community to solve various problems, such as the Grand and Brain Tumor Segmentation (BraTS) challenge (31).

Applications of AI in Radiology and RO

Medical Diagnosis-Established Research Models

Organ, Lesion Segmentation

Segmentation is the process of dividing an image into non-overlapping regions. It is usually used to highlight a specific area of interest through the generated map.

These maps provide the possibility that the target area segmented by the machine is related to the specified area or ground truth. DL is applied to segment several organs or lesions, using an entire image or image patches. The segmentation of fibroglandular tissue and breasts, as well as cranio-maxillofacial bone components, is accomplished by a derivative of the popular network architecture U-net (32,33). Holistic Nested Network is another DL architecture that has been successfully applied to segment prostate and brain tumors (34).

Radiomics, Radiogenomics Analysis and Characterization

In-depth reviews of ML and DL methods used in radiomics or quantitative image analysis, showing diverse clinical applications, research prospects and computing platforms (35). Applications of ML based radiomics in gliomas and prostate is utilized to predict the expression of multiple pathological biomarkers, with acceptable accuracy and stability (36,37). DL methods can also be used as feature extractors for tumor characterization. This concept is widely employed to study the relationship between genetic and radiological characteristics, and to extract patient-specific characteristics of glioma and non-small cell lung cancer (38,39).

Lesion Detection

Anomaly detection is a crucial process, it involves some difficulties, and in many clinical situations can lead to human error. Over the years, many studies have focused on automated detection algorithms as they can to reduce errors and time costs, while simplifying clinical workflow and providing a high-quality diagnosis (40,41,42). Thorough work has been done through deep convolutional neural networks and its pre-trained architectures to use X-rays, chest CT scans, and MRI imaging data to detect, multiple lung lesions, common lesions (pulmonary nodules), and microbleeds in the brain (43-45).

Image Processing

Image processing through DL models is applied extensively to enhance the quality of medical images in the past few years. Effective solutions for convolutional neural networks have been proposed to improve bone suppression and reconstruct high-quality PET images (46,47). Multiple studies have confirmed the integration between modalities and the development of artificial CT, MRI, and PET images based on DL (48-52).

Quality Assessment

Quality assessment is a critical issue that can be managed by DL. The pre-trained VGG19 fine-tuned convolutional architectures can predict whether a CT scan meets the minimum diagnostic image quality requirements that a thoracic radiologist will accept (53). As an indicator of technical analysis and review, the Deep-ConvNet model with T2-weighted MRI liver dataset is used for a task-driven automatic image quality assessment (54). Radiologists, pathologists, or other histopathological or genomic examinations should be performed during the evaluation process to better identify cancer signs (55).

RO Successful Trends

The AI system has triggered the research of routine and common RO tasks with its powerful efficiency. These cover the basic processes of the workflow from patient assessment to quality assurance and patient follow-up. The process may go beyond simulation, target and risk organ contours, treatment planning, and beam delivery (56-59).

Radiotherapy Treatment Planning

The automated treatment planning is subdivided in stages of beam direction selection, dose and fluence map estimation, and delivery parameter generation (57). DRL is used in treatment planning to model various aspects of the human body planner, automate dose fraction routines, and develop radiation plan adaptation strategies (58,59). Certain AI methods of adaptive radiotherapy can facilitate dose modification through the technology by providing clinical decision support (60).

In the route of developing methods for planning and predicting doses and toxicity to normal tissues, for certain tumor locations such as cervix and prostate, the ConvNet transfer-learning VGG-16 and AlexNet were established (61,62).

Quality Assurance and Response to Treatment

Quality assurance (QA) is an essential concept, serves in properly apply radiation or to cancer treatment. Applications of ML in QA tools are introduced to improve the optimization of radiotherapy by automating patient's plan verification and dosimetry (63). ML highlights the interesting

aspects of tumor response modeling, the likelihood that tissue becomes normal, and the normal tissue complication probability. Moreover, it also includes the trade-off between complexity and interpretability between structured and unstructured data for radiation effect modeling and prediction (64).
DL as well can be used to evaluate treatment response over time. ConvNet, for example, with a dynamic contrast-enhanced MRI breast examination protocol is used to check the response to neoadjuvant chemotherapy (65). The feasibility of applying ConvNet in patients CT bladder datasets was studied to help determine cancer's treatment response (66).

Commercial Software Developed

Apropos of commercial software and application developers targeting AI in radiology and radiation oncology, they have introduced an interactive software device based on the ML and DL models connected to the network. These devices help to automatically collect data and perform routine clinical tasks in an efficient manner.

ML and DL, Radiology Established Models

Given the current application of AI in radiology imaging, it has been clinically used by major technology companies, namely Butterfly Networks, Arterial, AI4MedImaging, Avicenna.AI, and IBM Watson. Butterfly Network, Inc., a healthcare technology company that provides portable entire-body ultrasound, has released the Butterfly Blueprint, a system-wide framework designed to facilitate the measurement and deployment of ultrasound across all healthcare systems to provide bedside information for clinical decision-making (67). Visualizing and quantifying blood flow autonomously in the body using MRI datasets is now possible through Arterys products. In addition, the company has developed an AI technology to detect breast cancer, calcification, and density assessment. Likewise, it aids in the diagnosis of chest and lung abnormalities. It can also provide the advantage of identifying neurological disorders (68). One of the currently useful Conformitè Europëenne (CE) certified products is AI4Cardiac Magnetic Resonance Software, produced by AI4MedImaging for functional and anatomical diagnosis of heart disease at the ideal time (69). A high-performance AI tool developer Avicenna.AI, handing over AI expedients for neurovascular and thoracic-abdominal pathology (70). IBM product's intended for a fast medical images processing and interpreting the data from a variety of the databases. These AI solutions control radiology workflows and simplify information deployment with cloud-based access. Besides, availing disease diagnosis by means of materializing patients' relevant information (71).

ML and DL, Medical Device Brands in RO

Several large, leading medical equipment manufacturers in the field of radiation therapy, such as Varian and Elekta, have used AI as an efficacious solution in their advanced technologies. Ethos™ Therapy is a radiation therapy system developed by Varian Medical Systems that uses artificial intelligence (AI) and machine learning to perform adaptive radiation therapy with an actual on-couch daily replanning. The automated system works by acquiring kV-cone beam computed tomography (CBCT) images, detecting selected normal organ structures, and propagating target structures from reference images to kV-CBCT images. Therefore, a session patient model is used to generate a scheduled, and an optimized adaptation plan. As for the acceptability and confirmation of the system's work in each process, it is governed by the users' decisions (72,73).
IntelliMax® is the software part of Elekta Care™. The platform is capable of providing predictive monitoring, diagnosing, and correcting problems. Through this system, maintenance issues can be identified and resolved before they occur, and problem resolution is accelerated. It is offered by a securely controlled remote access function that is concerned with proactive support and planned maintenance of linac equipment. Most recently, unplanned clinical downtime has been eliminated with the IntelliMax pro Linac Electron gun replacement (74).

Research Challenges and Viable Remedies

Medical physicists are in a unique position to face the challenges of ML and DL research and implementation. The main challenge of ML and DL, namely, to achieve meaningful research with scientific and practical value is the data size. The severity of the data size problem depends on how the data sample is combined with the dimension of the problem (4,5). This obstacle is described as the curse of dimensionality, which indicates that as the dimensionality of the problem increases, the size of the training data needs to be increased. Another challenge known as overfitting arises when the model parameters are more to be covered by the available data. When it is assumed that the training set is sufficient to complete the distribution of the data, hyperparameters help adjust the performance of DL by using large models with more parameters than the data (75). The interpretability of the model represents a powerful challenge. It describes the directness of knowledge and the information that ML and DL obtains from the input data. As well, it helps to understand and verify the accuracy of the model, which is why it is essential for many applications in the real world. Often, a DL model is denoted as a "black box," because researchers know nothing about what the extremely nonlinear model includes (4). This has been a substantial barrier to further use of DL models in a variety of world-wide applications.

Robustness signifies the responsiveness of the model output to the disturbance of the input variable. A high degree of sensitivity means weak strength. The robustness of the DL model in the field of healthcare is closely related to patient safety and the quality of healthcare. The enhancement of the training dataset is an effective way to increase the robustness of the model. If the model is unstable, it is recommended to use vulnerable samples for further model refinement in the training data (5).

The key areas of current focus are RO, diagnostic radiology, nuclear medicine, dosimetry, and health physics. From the detailed discussion of ML and DL, the guide for successful research in the application of the comprehensive field of medical physics is excerpted. Before conducting new research, the data should be carefully reviewed to prevent problems such as errors, deviations, distortions, and confusing factors. Because it is difficult to obtain enough data in many applications of medical physics. Transfer learning is one of the efficient ways of reducing the data size requirement. As the name suggests, transfer learning refers to the way in which a model built for one task is used as a starting point for the second similar or modified work in another model. GPU programming is particularly useful for solving the challenges of large models and substantial amounts of computational data. Most DL programming frameworks such as TensorFlow and PyTorch support the GPU environment, so this solution is highly recommended. Various of methods have been developed to solve the problem of overfitting. Changing the number and values of network parameters and reducing model complexity is one way to reduce overfitting. Another way is to expand the dataset. GAN has demonstrated its ability to synthesize more realistic samples, thus by using GAN we can participate in solving the problem of dataset scarcity and overfitting.

DISCUSSION

Recent medical physics research in radiology and RO tends to explore numerous of innovative local methods of DL, starting from algorithm development, combining multidisciplinary functions, or simulating existent technical working environment conditions to achieve process goals. Table 1 lists the retrospective case methods used in contemporary instances and their evaluation performance. The modeling technique of Jojoa Acosta et al. (42) is a comprehensive training, tested on six models, and successfully classified melanoma from dermoscopic images based on the deep residual learning framework. Modeling a classifier’s first stage, convolutional neural network automatic masking region of interest and using a validation set can rate a significant elevation in their models’ performance. Using relatively more epochs in the training step and reducing the learning rate can provide the best processing results. Moreau et al. (59) use tumor growth models to develop radiation dose treatment plans. Their DRL agents are effectively skilled to optimize dose fractionation, reacting with the tumor's tissue effects in the simulated irradiation environment while sparing the healthy cells. Thereby, can autonomously obtain dose adaptation action guided by rewards, in each tumor situation. The results specified in the evaluation index section of Table 1 represent Gray's average dose and its associated fractions and average time estimates (in hours) as the lower value obtained from the deep Q network algorithm. The virtual treatment planner proposed by Shen et al. (58) based on a network of reinforcement learning. It is trained to simulate the intensity-modulated radiotherapy environment to optimize prostate cancer and can be generalized to other issues using different planning techniques. Zhen et al (61), make use of massive hepatocellular lesions’ datasets, driving the diagnosis by means of a multi-classifier based convolutional neural network. The research has achieved remarkable results. Compared to earlier efforts, it emphasizes linking clinical data with imaging sets in the framework to improve classification operations. Another key point of using an independent external validation set, meanwhile it is valuable for adjusting model parameters or verifying its performance.

CONCLUSION

The review taken a snapshot through AI to study the latest diagnostic and treatment automation technologies in the scope of medical physics. It can be inferred that DL is a rapidly developing research field with broad prospects in medical physics applications. As well, DL has proven to be one of the most proficient ML innovations in unstructured data modeling. ML and DL can effectively solve most medical imaging, radiology, and RO tasks. AI developments along with medical physicists' work should be across the board to develop entirely automated practices.

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