v. 3, n. 21, 2023

Journal of
Engineering
Research

APPLICATION OF ARTIFICIAL INTELLIGENCE IN IMAGE DIAGNOSIS

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Journal of Engineering Research ISSN 2764-1317 DOI 10.22533/at.ed.3173212313061

Abstract: Artificial intelligence (AI) is human-like intelligence triggered by *software*. It is a set of complex mathematical models based on the structure and functioning of biological neurons. The present work aims to present, based on the scientific literature, the fundamentals as well as the applications of AI in diagnostic imaging. Among the different AI tools with potential to aid diagnostic imaging, computer-aided diagnosis (CAD) and the convolutional neural network (CNN) stand out. CAD is a computational system that uses results from automated quantitative analysis of radiographic images recorded in a database. The use of CAD aims to verify the radiologist's interpretation and improve the accuracy of the imaging diagnosis, using the computer response as a reference. As contributions of this tool, one can cite the aid to image processing through a computational system containing a database with patterns considered normal and abnormal. CNNs, on the other hand, are capable of identifying molecules with potential in the treatment of cancer and interpreting computed tomography images using a worldwide database of images associated with typical diagnostic terms. The use of AI as a diagnostic aid aims to propose a system that can be implemented in traditional imaging exams. Although still incipient, the expectation is that we will experience advances in the area of diagnostic imaging as new AI algorithms are developed for this purpose.
Keywords: Artificial intelligence; Imaging diagnosis; Algorithms; Deep learning.

INTRODUCTION

Artificial intelligence (AI) is human-like intelligence triggered by software. It is a set of complex mathematical models based on the structure and functioning of biological neurons and constitute tools capable of generating models based on biological systems with statistical confirmation, and not on unsupported predictions (ABBOD et al. 2007).

To do so, AI uses not only knowledge from computing, but also from biology, engineering, statistics, philosophy, physics, linguistics, mathematics, medicine and psychology. It is a recent field of science, starting in 1956, when technology was very limited due to the lack of computers capable of processing a similar amount of data allowed from the evolution of artificial neural networks. In turn, artificial neural networks (ANN) are systems that process information through interconnections between simple processing units, called artificial neurons. These, in turn, originate from a mathematical model of a biological neuron (ALVAREZ et al. 2003). Currently, with technological advances, it is possible that computers are able to store, process and consequently be applied in various areas such as health and cybersecurity. Thus, scientists invest in the creation of devices capable of simulating the human capacity to reason, make decisions and solve problems (TUNES, 2019).

One of the applications of AI is to improve diagnostic imaging services. Techniques such as X-ray, computed tomography (CT), mammography, ultrasonography, bone densitometry and magnetic resonance imaging (MRI) are used according to the physician's clinical suspicion and are important tools for diagnosing and determining the prognosis of various pathologies. -MARQUES, 2001).

In addition to the imaging exams presenting differences related to the clinical aspect, they also differ in terms of the physical principle. In this context, both conventional radiography and CT use ionizing radiation for image formation. However, the X-ray is ideal for detecting bone fractures while the CT provides greater detail of the images, being useful in identifying areas of encephalic hemorrhage, tumors, cysts, fractures, effusions, among other things. Mammography shares the principle of ionizing radiation, but is used only for the diagnosis of breast neoplasms. Ultrasonography, on the other hand, is a non-invasive test that provides information about the internal architecture of organs, without the use of radiation, but through high-frequency sound waves. These waves are transmitted by the transducer to the interior of the body, being absorbed and reflected in different degrees and captured again by the transducer and displayed in the device (AUGUSTO et al. 2000). In addition, bone densitometry is a diagnostic imaging method that determines the bone mineral density of the patient's anatomical regions, allowing the diagnosis of metabolic and endocrine bone diseases that involve changes in the metabolism of inorganic salts calcium and phosphorus in the human body (DENADAI et al. al. 1998).

While conventional radiography projects all the structures crossed by the X-rays in a single plane, CT allows the reproduction of the human body in slices or axial sections and in several planes, making it possible to reconstruct images in the sagittal and coronal planes, in addition to 2D or 3D reconstructions through software. Thus, CT shows the structural relationships in depth, showing images of the human body in slices, allowing the visualization of all structures in layers and in high definition. However, because it is composed of many images, the time required to complete the exam is much greater, which generates work overload, a condition that significantly increases the occurrence of human failures in the process (NÓBREGA, 2016). Thus, the reduction of human failures can be implemented by computer-aided diagnosis (CAD). This comprises an AI technique that uses pattern recognition and thus highlights suspected abnormalities, allowing the professional radiologist to review the exam and interpret it correctly (KATZEN et al. 2018). Another AI application includes telediagnosis, which enables the physician to diagnose based on images captured by radiologists or remotely, which, in addition to optimizing time, enables medical care for patients who live in areas where diagnostic services are not available. per image are precarious. Thus, the computer-aided telediagnosis system TCAD (Computer-Supported Telediagnosis), or Tele-CAD, allows people to access adequate medical care for regions lacking infrastructure and enables the sharing of medical resources between user units, making the restrictive factors that distance patients from quality medical care overcome geographic, temporal and socioeconomic barriers. In addition, TCAD is able to reduce the cost of equipment and software, as well as simplify its operation, maintenance and support (NÓBREGA, 2016).

In line with the evolution in the field of diagnostic imaging, as well as the need to train professionals in the area, including radiologists and biomedical specialists in diagnostic imaging, understanding the contributions of AI in this area is extremely important. Thus, the present work aims to present the fundamentals as well as the different applications of AI in diagnostic imaging.

MATERIALS AND METHODS

A theoretical study of a bibliographic review carried out between July 2018 and November 2019 was carried out. For this purpose, the search words *artificial intelligence, computer-aided diagnosis, application of AI in diagnostic imaging, machine learning and deep learning.* The databases explored were SCIELO, PubMed, academic Google and academic journals. No exclusion criteria were applied.

RESULTS AND DISCUSSION

AI can be applied to medicine in many ways, whether through binary classification, medical image segmentation, estimation of continuous measurements, and workflow automation (PARK et al. 2018). In this review, AI-based methodologies will be explored with application to different clinical medicine scenarios with a focus on image-based diagnosis.

ANNs have been a field of great motivation in research involving neuroscience, more specifically in the part of the brain called the visual cortex. When a biological neuron receives a visual stimulus, it carries this information to the retina, where a signal or action potential is sent that travels through a sequence of brain regions through neuronal interconnections. This signal transmission is a complex chemical process, which involves the release of neurotransmitters to communicate between neurons. Each of these neurons identifies specific features of the image corresponding to the visual stimulus. Thus, the neurons in the initial regions detect simple geometric shapes in the image, such as corners and edges, and the neurons in the final regions have the function of detecting more complex graphic shapes composed of numerous simple graphic shapes detected in previous regions (BEZERRA, 2016). An ANN contains a system of artificial neurons, with each unit performing a computation based on the other units to which they are connected. The artificial neurons are organized in consecutive layers and the connections between them are controlled by real values called weights. The simplest ANN contains a single layer, composed of a single neuron, but networks of this nature are quite limited. However, it is possible to build more complex networks through a procedure of composing computing blocks organized in layers (BEZERRA, 2016)

Figures 1 and 2 schematically illustrate the elements of the most common RN architecture called the Feed Forward Network (*Feedforward Neural Network*). In this architecture, the network forms a directed graph, in which the vertices represent the neurons, and the edges represent the weights of the connections. The layer that receives the data is called the input layer, and the one that produces the final result of the computation is called the output layer. Between the input and output layers, there may be a sequence of L layers, where the internal processing of the network takes place. Each element in this sequence is called a hidden layer. After its training, the network is able to perform a mapping of vectors in the D-dimensional space to vectors in the C-dimensional space (BEZERRA, 2016).

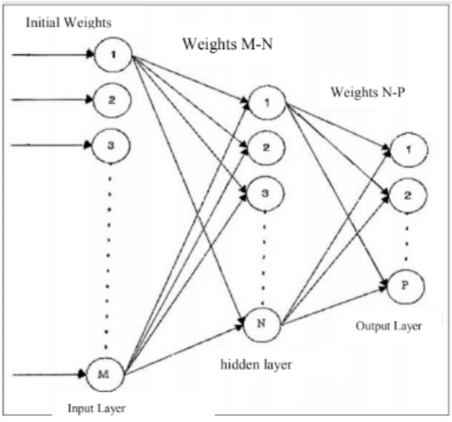

Figure 1: Schematic representation of the Fed Ahead Network

Source: AZEVEDO-MARQUES, 2001.

The use of AI is a tool that can help in image processing, through a computational system containing a database with patterns considered normal and abnormal. Thus, at the time of the examination, the professional may have the easiest indication of the pattern that is out of the ordinary, which will lead him to prioritize his attention for the examination. In addition, the computational system allows a total 3D manipulation of the image, allowing the addition of colors in the biological structures according to their densities, and improving the detailing of the image (AZEVEDO-MARQUES, 2001).

Among the different AI tools with potential to aid diagnostic imaging, computer-aided diagnosis (*"computer-aied-dianosis"* - CAD) and the *convolutional neural network* (CNN) stand out. Computer-aided diagnosis can be defined as a diagnosis that uses the result of automated quantitative analysis of radiographic images recorded in a database. The use of CAD aims to verify the radiologist's interpretation and improve the accuracy of the imaging diagnosis, by using the computer's response as a reference (AZEVEDO-MARQUES, 2001). It is important to point out that the computer is only used as an additional information tool, and the final diagnosis will be made by the professional radiologist. CAD has been extensively studied for the detection of breast and chest lesions and its use allows for a clearer image, making visible lesions and microcalcifications that cannot be seen through conventional mammography (AZEVEDO-MARQUES, 2001). Such a tool becomes very useful since 30% to 50% of cases of breast cancer detected by means of mammography present associated clusters of microcalcifications, and 26% of cases of non-palpable breast cancer present associated nodules on mammography and 18% present nodules and microcalcifications (AZEVEDO-MARQUES, 2001).

In Figure 3, the image shows a segmentation method *stretching* widely used in image processing and aims to increase contrast. The image-difference technique is used to enhance microcalcifications and nodules by suppressing the structures in the background of the image, caused by the normal anatomy of the breast. It is a threshold method or *thresholding*, based on statistics of pixel values, with the purpose of binary representation of the image (AZEVEDO-MARQUES, 2001).

In the study by AZEVEDO-MARQUES (2001), the analysis of the images represented in Figure 3 demonstrated a sensitivity of 98.3% for the detection of clusters of microcalcifications and 72% for the detection of nodules, with an average false-positive rate of 1 cluster or nodule per image. In another study aiming to compare the reading of a sequence of images using ImageChecker for the detection of clusters of microcalcifications and nodules between two radiographies and between a radiologist and the CAD system, no significant differences were observed, demonstrating the efficiency of the CAD system (AZEVEDO -MARQUES, 2001).

Image processing is performed for enhancement and segmentation of the lesions, allowing the subdivision of the image according to specific characteristics. After enhancement and segmentation, it is possible to add attributes to the images for quantification, such as size, contrast and shape of their constituent objects, making it possible to observe lesions that are not compatible with human vision and enabling a more accurate and reliable diagnosis (AZEVEDO-MARQUES, 2001).

AI involves the use of a computer for data processing, aiming at distinguishing between normal and abnormal patterns, based on attributes extracted from images. Techniques related to this area of knowledge include methods for feature selection, such as those based on the separation between the probability distributions of classes and genetic algorithms, and classifiers, such as those based on discriminant analysis techniques, expert systems based on specific rules and ANN statistical methods.

CAD systems use techniques from two areas of knowledge: computer vision, which involves image processing for enhancement, segmentation and feature extraction, and AI, which includes methods for feature selection

Figure 2: Mathematical representation of the Fed Ahead Network

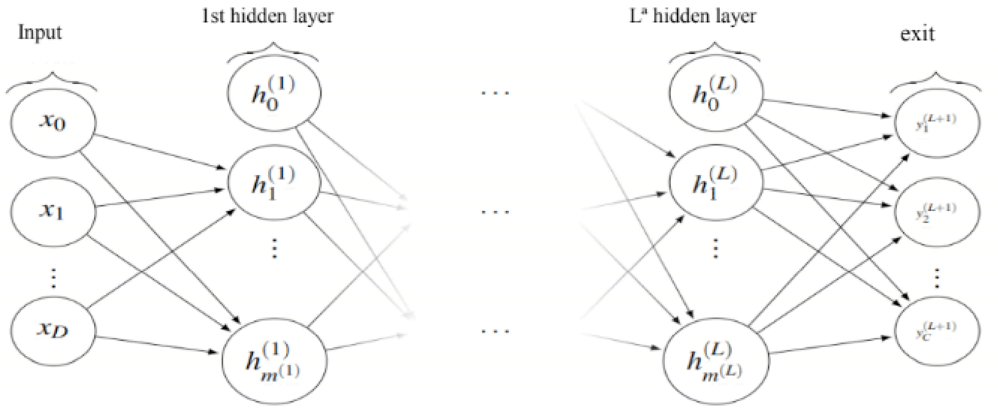

Figure 2: Mathematical representation of the Fed Ahead Network

Subtitle: ANN with (L + 1) layers, with D units in the input layer and C units in the output layer. The lth hidden layer contains m ([1]) units. Source: BEZERRA, 2016.

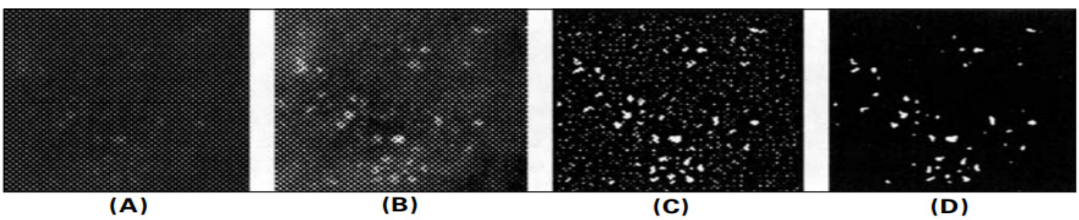

Figura 2. Exemplo de segmentação de imagem. **A:** Região de interesse contendo um agrupamento suspeito de microcalcificações. **B:** Imagem após "stretch". **C:** Imagem-diferença. **D:** Imagem segmentada.

Figure 3: Image segmentation example

Subtitle: Digitized mammogram containing cluster of suspicious microcalcifications. A: region of interest containing a suspicious cluster of microcalcifications. B: Image after "stretch". C: Image-difference. D: segmented image. Source: (AZEVEDO-MARQUES, 2001).

Figure 4: Representation of data processing in CNNs

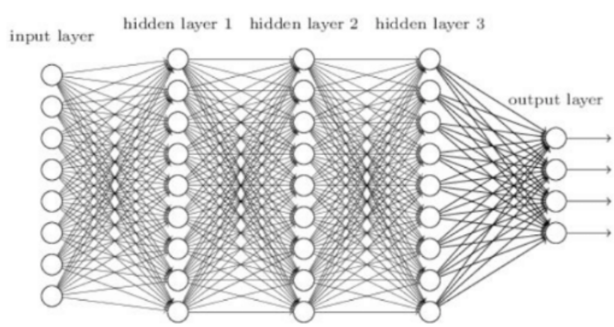

Figure 4: Representation of data processing in CNNs

Subtitle: input layer: input layer; hidden layer 1, 2 and 3: hidden layer; output layer: output layer. Lines represent the internal connections. Source: *Deep Learning Book* - Introduction to convolutional neural networks. Available in:http://deeplearningbook.com.br/introducao-as-redes-neurais-convolucionais/

and pattern recognition. CAD can be applied to all imaging modalities, including conventional radiography, computed tomography, magnetic resonance imaging, ultrasonography, and nuclear medicine. It is also possible to develop CAD schemes for all types of examination of all parts of the body, such as skull, thorax, abdomen, bone and vascular system, among others (AZEVEDO-MARQUES, 2001).

AI has been an active field of research since the 1950s, and currently, algorithms have achieved sub-human performance being applied in several areas of health as a diagnostic aid, such as the identification of metastatic tumors of unknown origin called test of origin (TOT), in the diagnosis of indeterminate thyroid nodules, which can reduce unnecessary surgeries by up to 81% (TUNES, 2019).

Image segmentation is time-consuming and extensive work, being a source of possible human error. However, the application of AI through the Convolutional Neural Network (CNN) makes this process faster and more automatic, whose representation of the data process is shown in Figure 4. CNN is an application that removes the barriers that prevent the optimization of exams, with the reduction of time and effort during CT image segmentation for example (MINNEMA et al. 2018).

Studies indicate that CNNs are capable of identifying molecules with potential in the treatment of cancer, as well as helping to quickly and accurately diagnose patients who have symptoms of cardiovascular disease evaluated by magnetic resonance imaging. In addition, it is capable of interpreting CT images, for example, using a worldwide database of images associated with typical diagnostic terms. CNN also allows early detection of diabetic retinopathy, which is one of the main causes of blindness, tumors such as melanoma (available from IBM, *International Business Machines Corporation*), and to non-invasively monitor the evolution of tumors (FLORINDO, 2019). CNN applied in image construction is done with precision and is considered the gold standard in patients previously submitted to craniotomy and cranioplasty (MINNEMA et al. 2018).

Medicine is one of the fields most benefiting from AI, which optimizes complex and imperfect processes such as differential diagnosis. This is a domain area of *Machine Learning (ML),* which comprises an area of computer science that means machine learning (LUGO-REYES et al. 2014). It is a tool that is rapidly gaining importance in radiology, as it allows the exploration of patterns in image data and patient records for more accurate quantification, diagnosis and prognosis (LANG, 2018). Along with ML, AI methods are excellent for automatically recognizing complex radiographic patterns in image data and providing quantitative rather than merely qualitative assessments (HOSNY et al. 2018). This aid can be useful, since the radiologist's diagnosis is based on a subjective assessment, being subject to intra- and interpersonal variation, as well as loss of information due to the subtle nature of the radiological finding, poor image quality, overlapping structures, visual fatigue or even distraction (AZEVEDO-MARQUES, 2001).

LM applications have been studied for application in pulmonary function tests. ML uses CNN models that allow the recognition of obstructive patterns on CT, responsible for the differential diagnosis of pulmonary obstructive diseases. In addition, the use of LMA offers accurate results in various lung CT exams, such as obstructive lung function, in forced oscillation tests, breath analysis, lung sound analysis and telemedicine (DAS, 2017).

AI and ML have influenced medicine in many ways. In this context, recent advances

Journal of Engineering Research ISSN 2764-1317 DOI 10.22533/at.ed.3173212313061

in the fields of AI and ML have caused a great impact on image analysis in the fields of microscopy and radiology. Improvements in computational hardware are allowing researchers to revisit old artificial intelligence algorithms and experiment with new mathematical ideas. The application of these methods is very wide, and can be implemented from microscopy, for tomographic image reconstruction, as well as for diagnostic planning (MANDAL et al. 2018). Multicolor flow cytometry analyzes are used to identify minimal residual disease of acute myeloid leukemia and myelodysplastic syndrome after treatment. However, manual interpretation has drawbacks such as time demand and interpretation variations. AI, with its expertise in assisting repetitive or complex analyses, represents a potential solution to these disadvantages. AI algorithms can produce efficient and clinically relevant multicolor flow cytometry analysis. This approach also has a major advantage in the ability to integrate with other clinical trials (KO et al. 2018).

AI based on deep learning (DE) has been of great interest globally in recent years. AP has been widely adopted in image recognition, speech recognition and natural language processing, but it is just starting to make an impact in healthcare as it is not yet used in clinical routine (TING et al. 2018). AP allows complex computational models to process multiple layers of processing emphasizing different levels of abstraction. Thus, it has revolutionized speech knowledge, visual recognition and object detection and many other domains like drug discovery and genomics. In addition, the AP through the use of backpropagation algorithms indicates how the machine must change its internal parameters used to calculate the representations in each layer representation of the inner layer. The CNN applied in AP brought advances in the processing of images, video, speech and audio (BEZERRA, 2016).

AP constitutes a sub-area of ML, and both aim to simulate the behavior of the human brain, such as visual and speech recognition and natural language processing. AP algorithms produce representations according to priorities registered in the input data, through layers of sequential processing in an ANN (BEZERRA, 2016). In the area of ophthalmology, AP has been applied in fundus photography, optical coherence tomography and visual fields, achieving robust performance in the detection of diabetic retinopathy and retinopathy of prematurity, glaucoma-like optic disc, macular edema and age-related macular degeneration. The identification of these pathologies with the use of AI and AP is done in the simplest and fastest way. AP in eye imaging can be used in conjunction with telemedicine as a potential solution to screen, diagnose and monitor major eye diseases in patients in primary care and community settings. However, there are also potential challenges with the application of PA in ophthalmology, including clinical and technical challenges, explainability of algorithm results, medico-legal issues, and physician and patient acceptance of algorithms that may carry risks of distortions (TING et al. 2018). Recent studies of AI algorithms are under development for use in photographic screening of diabetic retinopathy. To be clinically acceptable, these systems must also be able to classify other fundus abnormalities and clinical features at the point of care, not requiring sophisticated devices. The performance proved to be promising, but not yet at the level necessary for its clinical application (STEVENON et al. 2018).

AI enables machines to provide unparalleled information value across a multitude of industries and applications. Researchers have used AI to analyze unstructured, large-volume medical data and to perform clinical tasks such as identifying diabetic retinopathy or diagnosing skin malignancies. Applications of AI techniques, specifically machine learning and, more recently, deep learning, are beginning to emerge in gastrointestinal endoscopy. The most promising of these efforts has been computer-assisted detection of colorectal polyps and computer-aided diagnosis. These systems demonstrate high sensitivity and accuracy when compared to expert human endoscopists. AI has also been used to identify gastrointestinal bleeding, detect areas of inflammation, and even diagnose certain gastrointestinal infections (ALAGAPPAN et al. 2018).

Medical imaging assesses the tumor and its environment in its entirety, which makes it suitable for monitoring the temporal and spatial characteristics of the tumor. Progress in computational methods for processing and analyzing medical images, especially those based on AI, has converted these images into quantitative and detailed data associated with clinical events in oncological management. Based on a large amount of radiographic images and application of AI and ML, researchers have developed and validated radiomic models that can improve the accuracy of diagnoses and assessments of therapeutic responses (LIU et al. 2019). CT has several tools that allow you to perform analysis, take measurements, check density, measure lesions, hemorrhages, cysts and tumors. In more specific situations such as cerebrovascular accident (CVA) or encephalic hemorrhage, the ''map/diffusion" function allows the doctor to have a clear and detailed view of the area affected by the extravasation of blood. In the 1970s, the first CT scanners already used iterative reconstruction algorithms, but this resource was not applied in the clinical routine due to the deficiency of computational tools. It was only in 2009 that the first iterative reconstruction algorithms were commercially available to replace the conventional projection. This technique has since caused a veritable evolution in the field of radiology, and within a few years all major CT vendors have introduced iterative reconstruction algorithms into clinical routine, which have rapidly evolved into increasingly advanced reconstruction algorithms. The complexity of these algorithms varies from hybrid algorithms based on models to fully iterative algorithms. AI will further enhance the performance of reconstruction methods (WILLEMINK et al. 2018).

Several studies have been carried out with the objective of validating the statistical methods for verifying the performance of tools in diagnosis and prediction. In this regard, research was conducted to verify algorithm based on deep learning developed to differentiate lung cancer (disease) from benign tumor (non-disease) in pulmonary nodules on plain chest X-ray (PARK et al. 2018). When the results of a test or diagnostic algorithm are binary, discrimination performance is usually measured in terms of sensitivity (proportion of positive test in subjects with disease) and specificity (proportion of negative subjects in subjects who do not have disease). Even though the deep learning algorithm presents the final results in a dichotomous way (e.g. malignant vs benign), the algorithm internally calculates a percentage (continuous output) (Table 1), and then applies the threshold configuring the final result (Table 2). Therefore, depending on the threshold levels that are applied to the initial percentage, various pairs of sensitivity and specificity values are obtained (Table 2). Thus, when the threshold for diagnosing lung cancer is lowered, sensitivity increases while specificity decreases, and vice versa (Table 2).

Continuous output	Cancer	Benign disease
0	0	5
0,1	2	103
0,2	6	90
0,3	5	21
0,4	5	8
0,5	8	5
0,6	15	8
0,7	20	5
0,8	25	4
0,9	11	1
1,0	3	0
Total	100 patients	250 patients

Table 1. Results obtained from a hypothetical study to evaluate the performance of the algorithm based on deep learning.

Subtitle: Data represent number of patients and continuous output for differentiating disease (cancer) and non-disease (benign nodules) from chest X-ray images. Source: Adapted from Park et al. 2018.

Criteria for diagnosing lung cancer	Sensitivity (%)	Specificity (%)	1 - Specificity (%)
≥ 0,1	100	2	98
≥ 0,2	98	43,2	56,8
≥ 0,3	92	79,2	20,8
≥ 0,4	87	87,6	12,4
≥ 0,5	82	90,8	9,2
≥ 0,6	74	92,8	7,2
≥ 0,7	59	96	4
≥ 0,8	39	98	2
≥ 0,9	14	99,6	0,4
≥ 1,0	3	100	0

Table 2. Sensitivity and specificity of the algorithm based on deep learning for the diagnosis of lung cancer after application of the threshold

Subtitle: data represent percentages calculated from applying various thresholds to the results in Table 1. Source: Adapted from Park et al. 2018.

One of the main challenges of AI in the field of diagnosis is the validation and evaluation of their performance, so that AI results are clinically reliable. The terms validation refers to the fine-tuning stage of model development and testing refers to the process of verifying model performance. Since the performance of a diagnostic model is affected by the spectrum of disease manifestation, clinical confirmation of the performance of an AI-based diagnosis is required. Clinical verification of the performance of an AI tool in aiding diagnosis requires external clinical validation in a target patient population. This procedure is crucial to avoid overestimation of performance and possible spectrum biases. Thus, the best clinical verification of a diagnosis obtained from AI requires a demonstration of its value through its effect on patient outcomes, in addition to performance metrics, which can be achieved through clinical trials or observational research..

CONCLUSION

Computer-aided diagnosis based on AI, AP and ML methods aims to propose a system that can be implemented in imaging exams, allowing them to help professionals in the more accurate determination of pathological characteristics. And so, to promote the efficiency of imaging exams, in terms of temporal optimization and the analysis process. The development of AI algorithms is still incipient, but technological and computational advances promise a revolution in diagnostic imaging and medicine, in addition to other areas. The challenges in exploring the potential of AI in medicine can be considered circumstantial, which are related to societal and intrinsic social behaviors as well as those related to the capabilities of underlying science and technology. Both must be resolved for both society and the professional class to benefit greatly from AI.

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