OPEN ACCESS

TiLS Journal

NARRATIVE REVIEW

ARTIFICIAL INTELLIGENCE AND COMPUTED TOMOGRAPHY AS AN EARLY DIAGNOSTIC TOOL IN COVID-19 PATIENTS: A RELIABLE ALTERNATIVE DURING THE PANDEMIC?

Andrada-Raluca Artamonov[1,2*], Ileana Ramona Barac[1,2], Octavian Andronic[1,3]

[1] Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[2]Clinical Ophthalmology Emergency Hospital, Bucharest, Romania
[3]University Emergency Hospital of Bucharest, Romania

Corresponding author
Andrada-Raluca Artamonov
andrada.artamonov@yahoo.com

Received: 01 November 2021
Accepted: 15 November 2021
Published: 15 January 2022

This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.

ABSTRACT
COVID-19 pandemic is a global healthcare crisis with unprecedented responses and unpredictable outcomes. An important cause of hospital burden and physician burnout around the world, it acted as a catalyst for accelerated digitalization, including Artificial Intelligence. As far as diagnosis is concerned, RT-PCR represents the gold standard, but has multiple flaws, the most important of them consisting of the current validity of the investigation. A controversial alternative might be chest Computed Tomography, especially in highly affected areas, and a high number of software algorithms have been designed in order to assist this process. The purpose of this review is to present the actual stage of Artificial Intelligence development in medical imaging, by highlighting the reliability of using computers for COVID-19 pneumonia detection on chest CT. At the same time, we aim to provide insights and deduct conclusions on how the current challenges in the field can be overcome and how expectations could be calibrated in order to advance diagnostic strategies with the purpose of fighting a healthcare crisis.

Keywords: COVID-19, diagnosis, Computed Tomography, Artificial Intelligence, Machine Learning, Deep Learning

INTRODUCTION

Coronavirus disease 2019 (COVID-19) has become a major global health issue, as the outbreak was labeled a pandemic on 11 March 2020 by the World Health Organization[1]. It emerged in Wuhan City, Hubei Province, China, in December 2019, in the form of a pneumonia of unknown aetiology, later confirmed to be caused by a novel strain of coronavirus (2019-nCoV), genetically different from both MERS-CoV and SARS-CoV[2]. The species was classified as *Severe acute respiratory syndrome-related coronavirus 2* (SARS-CoV-2)[3], and rapidly spread throughout the world, burdening national healthcare systems. Many countries chose to enforce stern measures, such as quarantines for suspected cases, lockdowns for entire cities or regions, limitations of travel and leisure activities, with a yet undetermined, but possibly profound long-term impact on both quality of life and macroeconomy[4].

The diagnostic gold standard for the SARS-CoV-2 infection is represented by quantitative Reverse Transcription Polymerase Chain Reaction (RT-qPCR), using viral RNA extracted from respiratory tract samples[5], and multiple protocols have been developed for targeting various sequences in the genome[6]. The specimens are obtained using either nasopharyngeal or oropharyngeal swabs, tracheal aspirate, bronchoalveolar lavage[7] or induced sputum[8]. However, it has been shown that the current use of RT-qPCR might pose some challenges. The biggest concern is related to the validity of the investigation, which still comprises a subject of debate in the medical community[9]. Specificity is satisfactory, with potential false positive results in asymptomatic patients, due to sample contamination.

On the other hand, sensitivity rate remains unclear, ranging from 66% to 80%, with an ever blurrier cut-off in asymptomatic patients[7]. This means that a singular negative result is insufficient in excluding COVID-19, and the test has to be repeated multiple times[7],[10].

Physicians can potentially diagnose COVID-19 pneumonia using Computed Tomography (CT), with suggestive pulmonary lesions having been identified and classified. It is recommended by the World Health Organization in some particular situations, only for symptomatic patients: when RT-PCR is not readily available, when RT-PCR result is negative, but clinical suspicion is high, and in order to decide between hospitalization and discharge, or between ward admission and ICU[11]. The most prominent CT finding is represented by ground-glass opacities (GGO) of circular shape, either peripheral, bilateral, or multifocal. Other typical presentations include crazy-paving pattern (GGO with visible inter- and intralobular septal thickening), patchy consolidations, and reverse halo sign (GGO surrounded by a ring of consolidation)[12]–[14]. Multiple Artificial Intelligence (AI) algorithms have been created so as to interpret CT images[15], with the purpose of assisting COVID-19 diagnosis.

As there are still many unanswered questions about the pathophysiology of the disease, major implications exist for both the treatment guidelines and the approval of a vaccine in the following months. As a consequence, the pandemic remains an important healthcare problem worldwide. In this context, the use of Artificial Intelligence in making an early COVID-19 diagnosis based on CT abnormalities might become a good alternative so as to optimize the medical process and to alleviate some of the pressure off healthcare workers. The purpose of this review is to present the actual stage of Artificial Intelligence development in medical imaging, by highlighting the reliability of using computers for COVID-19 pneumonia detection on chest CT. At the same time, we aim to provide insights and deduct conclusions on how the current challenges in the field can be overcome and how expectations could be calibrated in order to advance diagnostic strategies with the purpose of fighting a healthcare crisis.

MATERIALS AND METHODS

We conducted a thorough search on PubMed, Scopus and Google Scholar, using the keyword *(Coronavirus disease OR COVID-19) AND diagnos* AND (CT OR Computed Tomography) AND (Artificial Intelligence OR Machine Learning OR Deep Learning OR Neural Networks)*. We included all the available peer-reviewed, open access, English language articles, with relevance to the subject (e.g. centered on early diagnosis, as opposed to further classification or prognosis of the disease) and precise methodology, as considered by the author of this paper.

RESULTS AND DISCUSSIONS

Artificial Intelligence – the why and the how

In order to have a better understanding of what AI encompasses in today's world, we believe it is essential to look back at the history of the field, and follow the steps which led to an impressive technological expansion. To be able to fully embrace the revolutionary discoveries, a profound comprehension of the fundamental concepts is mandatory.

Last century, AI branched off computer science to exclusively focus on developing systems which mimic human intelligence. The main goal was to program computers to perform complex tasks, previously considered to require human expertise. It ultimately became an umbrella term which now comprises multiple well established subdivisions[16]. A relatively recent scientific area, it was first described in 1956 by MIT researcher John McCarthy, during a conference at Dartmouth College. After several centres of excellence emerged throughout the Anglosphere, the interest shifted from a general perspective towards perfecting specific issues[17]. Only three years later, Arthur Samuel wrote the first game-playing algorithm, which enabled a computer to win at checkers against people[18]. Starting with inflexible protocols, highly dependent on the limitations of the code, researchers focused on solving problems which were time consuming for humans, but very well defined[19].

Even though the academic and business interest towards the emerging discipline was huge, it took almost two decades for the concept to start being applied to medicine. One such example is represented by MYCIN, an AI system developed at Stanford University, which could recommend appropriate antibiotics by following a large set of binary rules, based on 'if-then' statements. Even though it was reported to perform better than infectious disease physicians, it was never approved for clinical practice. This early form of AI was called an 'expert system' and, by mimicking the decision-making process of a human, was the first successful AI software[20]. Given the complexity and especially the unpredictability of clinical practice, it was ultimately impossible to implement a code which comprised all the possible real-life variations[21]. When the realm of AI capabilities reached its borders at the time, and did not match the expectations, a profound decrease in public attention followed, and this 1980s phenomenon was known as 'AI winter'[17].

In the following years, technological development accelerated within scientific fields, marked by the world-changing breakthroughs, such as personal computers, World Wide Web and mobile phones. Computer science experienced unprecedented growth and prominent results, striking both excitement and fear of the unknown[22]. The surge of digitalization and social media content shaped the concept of 'Big Data' and revived interest in developing AI[19]. In recent years, this remarkable progress culminated in the 2011 televised Jeopardy competition, when IBM's Watson won against the global champions[17],[23]. Based on lines of algorithm which have been designed more than 50 years earlier, but equipped with third millennium technology[23], Watson opened a new era of scientific advancement and public recognition regarding AI. It is important to highlight that software prototypes can be fairly easy to write, hardware components have been significantly improved[23],[24], and concerted efforts towards open-sourcing are made[25]. Consequently, the world witnessed an explosion of developing projects in the industry, countless research directions and promising outcomes, in one of the most challenging quests of the contemporary world.

Today, AI and Machine Learning (ML) became almost interchangeable terms[21]. However, ML is actually a subset of AI, concerned with statistical analysis algorithms which continuously improve themselves by being exposed to more data, and thus make more accurate predictions over time. Ultimately, ML is a mathematic model perfectly applied to the specific data set it was created for, and, in turn, it becomes able to predict labels for new data[24]. In other words, computers can 'learn' patterns by experience, not needing to be programmed with explicit rules. However, they are not independent – humans have to manually identify distinctive features in the data set beforehand[16], and essentially tell the machines what they should be looking for. These features consist of singular, measurable, specific characteristics, such as lumen diameters, size of various lesions and types of nodules[19]. Even though, taken on its own, ML is a groundbreaking technology, it has its limitations: apart from the fact that it still requires human expertise and the software has to be very task-specific, defining the optimal features can be problematic. For example, teaching a computer to recognize certain tissues based on pixel brightness, which humans recognize intuitively, might be more difficult than expected[16].

As the process of learning is considered an inherent attribute of the human brain, it was the human brain itself which served as source of inspiration in developing ML[21]. Computer science researchers took the concept even further by developing a subset of ML called Artificial Neural Network (ANN), which is structured similarly to the nervous tissue, with a network of 'nodes' as the equivalent of neurons. The elements are organized in multiple layers – the input layer, the 'hidden' layer (whose nodes have connections with all the nodes from the previous layer), and the output layer. These multiple associations among nodes allow multiple statistical and mathematical calculations. Furthermore, the strength of these connections is evaluated by their weight, on which the output (i.e. the expected result) is highly dependent. The weight can be estimated by iterative processes of training[25].

A neural network with more than one 'hidden' layer is called a Convolutional Neural Network (CNN) and encapsulates a new type of learning, called Deep Learning (DL). One of the 'hidden' layers is a convolution layer, whose elements are called 'kernels' and act like signal filters[25]. They identify data features, combines them, and ultimately creates an ordered estimation of patterns[23]. DL can be either supervised, when data is previously labeled by a human and the machine tries to identify features within designated classes, or unsupervised, when it is only provided with raw data[26]. Thus, by using (and actually needing) greater amounts of data and computing capacity[19], DL solves the ML issues and brings a new dimension into the AI perspective. The ultimate goal is to create an intelligent computer which is capable of producing meaningful content when faced with large amounts of data, which no human could revise on its own.

DL is a powerful method for a computer to teach itself without crossing three main borders: the hardware infrastructure, the availability of data sets, and the appropriateness of it[19]. In terms of technical equipment, computational power can nowadays be supported by graphics processing units, widely known as GPUs, which are specialized electronic circuits designed for image data manipulation[23]. Moreover, data storage is easier than before, due to cloud development, and the breakthrough of 'Big Data' meant almost endless data resources. Perhaps the most important of these is ImageNet, a massive visual database specifically designed to support AI-software research on image recognition[27]. ImageNet launched a challenge for developers to create DL algorithms, and in 2012 a CNN-based software won by reaching 85% accuracy[23], which has since then continuously improved.

Appropriate data preparation is another limitation of DL, as it poses several issues. Firstly, even though some DL algorithms can work unsupervised, correct data labeling is still paramount when considering current medical field regulations, but it is labor-intensive, time consuming, and sometimes subjective. Secondly, image quality has to be as good as possible, in order to produce the expected results. However, in specialties such as radiology or pathology, textbook cases are not always the norm, and the line between an appropriate image and an inoperative image might be blurry. Thirdly, the variance of data is extremely important in avoiding bias in favour of the most frequently occurring feature and underrepresentation of another. Ideally, data should be evenly distributed. For instance, if a specific CT lesion is very rare, suitable CTs to be used in AI training sets are even rarer. When later investigating unlabeled images, it becomes more likely for the computer to miss that certain lesion. A large amount of data is important in providing appropriate training, test and validation sets, ensuring the reliability of the algorithms[19]. However, a technical solution to some of these issues might be represented by *transfer learning*, which is a different approach to training a CNN and works by effectively transferring the knowledge previously accumulated from a data set and directly apply it to another data set, with a fundamentally different type of data. In medicine, this means training the software with non-medical images, and it has been shown that these CNNs performed equally well when compared to 'traditionally' trained CNNs[26]. Two other factors which have been shown to increase accuracy are a higher number of layers, as well as the number of 'epochs', meaning the number of times the algorithm runs through the entire data set[26]. Equally important, performance of a DL system is measured so as to identify possible underfitting (the computer missed an important pattern) or overfitting (the computer connects random noise)[25]. On the other hand, initial-phase testing showed that, despite promising results, computers can still make flagrant mistakes, which humans do not[26], by relying solely on mathematical logic and missing critical judgement of a situation.

The medical assessment of Artificial Intelligence

At present, AI has started playing a part in multiple medical fields and the scientific interest keeps growing every year. So far, noticeable breakthroughs have been made in pathology[28], dermatology[29], ophthalmology[20], cardiology[30], gastroenterology[31], microbiology[32], genetics[33], pharmacology[34], surgery[35], and imaging[15].

Taking into account that radiology was one of the pioneers of medical digitalization and that it had already been transformed by the implementation of Computer-Aided Detection (CAD)[36],[37] and Picture Archiving and Communication System (PACS)[38] in recent past, computer databases were more easily accessible to researchers compared to other types of medical information. As a consequence, various research directions followed rapidly. A great range of ML algorithms have been designed in order to interpret both traditional investigation modalities, including radiography[39], Computed Tomography[15], Magnetic Resonance Imaging[40], sonography[41], mammography[42], and more sophisticated techniques, like ^{18}FDG-PET/CT[43] or SPECT[44]. Marked outcomes focus on nodule identification and classification[45], organ segmentation[46] and lesion diagnosis[15], as well as more complex analyses, leading to the development of *radiomics*, an emergent field concerned with the extraction of massive amounts of quantitative data[25].

However, the quick progress of medical AI software led to a series of concerns and controversies, regarding tightly connected technical, scientific, ethical, legal and financial issues. Initial challenges include overcoming the great need for computing power, extremely reliable and efficient algorithms, as well as highly skilled human resource, capable of sustaining such an increasing demand[22]. In turn, this pressure leads to the necessity of massive investments in research infrastructure[23], essentially funded by private companies, thus raising questions about ways to balance profit and scientific integrity. In this stage, one stringent issue is concerned with software training by using medical databases which contain any kind of patient identification labels, which should be manually de-identified beforehand[19].

After being designed and tested, each algorithm has to go through a long and elaborated process of validation from an evidence-based perspective, so as to obtain clinical approval. This might be translated to years before actually reaching practice, and so far, most AI medical breakthroughs find themselves in this stage. However, understanding the nature of the processes happening behind the 'hidden' layers of DL is sometimes difficult[25], which contradicts the fundamental concept of scientific proof and poses one of the biggest challenges of AI in medicine. In the scientific community, many AI-themed articles face a high level of criticism regarding insufficient information on methodology, which consequently alters reproducibility and leads to rejection from publishing[47], or alternatively choosing non-peered reviewed journals[48]. This might represent an alarming signal for finding ways to bridge the gap between physicians and computer scientists. Another intricately linked issue is represented by the technical jargon, i.e. 'validation' designates a step in algorithm training, or a step in algorithm testing after having been trained, or the clinical connotation of the word[48], which might lead to confusion and misinterpretation of study results.

Furthermore, legal regulations are as important as scientific consensus. With tasks performed by AI increasing in complexity, so do the rules. For instance, an software with an exclusively assisting purpose follows a different legal path compared to an unsupervised algorithm[19]. One of the most debated issues is that of liability, on who is to be held responsible for possible malpractice caused by software failure: the scientist who designed it, the tech company, the hospital or the radiologist? So far during the digital history, the answer concerning CAD was that the physician was at fault[26], but DL is fundamentally different in nature, so the legal outcome might be different as well. Another problem is that of privacy: would the vendor have access to patient information[19] and how vulnerable to cybernetic attacks would the system be?

After meeting the technical, medical and legal requirements, implementation of AI technology faces another noticeable problem: the financial costs of purchasing the software and ensuring the necessary hardware infrastructure in hospitals. Depending on local government health policies, this could initially lead to important disparities between countries, between regions of the same country or between public and private hospitals.

This would also impact everyday practice of radiology in multiple ways, in which case AI should have a more prominent role during training, from both a theoretical and practical ground, which is in line with radiologists' perspective on the issue[49]. However, some ethical considerations are raised regarding the role of radiologists during the DL revolution in the medical field, as they have one of the most important voices in this matter. There might be a risk of bias associated with prestige, autonomy and job security, but the best interest of the patient should prevail[50].

Equally essential to a smooth transition towards an AI-dominated medicine, public expectations should be addressed with patience and understanding, by both physicians and authorities. Concerns might include dissatisfaction with the lack of human interaction itself, i.e. the empathic side of the physician, as opposed to the algorithmic approach of a computer, as well as worries about privacy and personal safety, and demands for thorough explanations about the new technology in layman's terms, so as to ensure transparency, to build trust and compliance.

COVID-19, Artificial Intelligence and the unknown

In the light of unprecedented governmental measures in recent history, COVID-19 pandemic resulted in accelerated digitalization throughout the world[51], in order to ensure acceptable continuity in economy, education, healthcare, as well as social interaction. This represents a concerted attempt to adapt to the new reality, by covering the basic societal needs in an online environment. However, the unfortunate event of 2020 might transform into a catalyst for technological revolution in computer science, including or even targeting AI, which can be seen as a solution to a multitude of newly arisen or deepened issues. For instance, only 8 months after the emergence of the virus and 6 months after declaring the pandemic, conducting a quick PubMed search using the keyword *Artificial Intelligence AND COVID-19* leads to over 200 peer-reviewed articles, a unique surge in the scientific world, compared to the usual timeframe of evidence-based research. So far, a large number of articles explored the use of AI in the context of the pandemic, in a collection of different facets: anticipating the epidemic curve[52], outbreak surveillance and tracking systems[53], radiography[54] or CT features[15], predicting the risk for severe disease[55] and identification of potential therapeutic agents[56],[57]. Many more experimental studies are still under peer review, reflecting the great promises of AI, especially in regards to diagnosis or vaccine and drug development.

As previously stated in the beginning of this paper, even though RT-qPCR represents the diagnostic gold standard at the moment, it has multiple flaws and poses a sum of challenges, especially considering the urgency of the pandemic and the impact of a delayed diagnosis on both individual and epidemiological grounds. Firstly, public availability of viral sequences reflecting the genetic diversity of SARS-CoV-2[58], coupled with insufficient information on genome stability[59], and the possibility of mutations and emerging strains, especially *in vivo* [60]. All these issues would become a source of underdiagnosing. Secondly, the lack of consensus regarding whether upper or lower respiratory tract specimens provide more accurate results[8],[10]. Thirdly, the time-consuming nature of the procedure, with results taking several hours or even days, as well as the expensive equipment and the need for highly trained personnel[61]. However, the greatest concern is related to the current validity of the diagnostic test, currently under debate[9], considering reported false negative cases[62]–[64] and the risk they pose both to the patient and the community. Specificity of RT-qPCR is satisfactory, with potential false positive results in asymptomatic patients, due to sample contamination. However, sensitivity rate is unclear, ranging from 66% to 80%, with an ever blurrier cut-off in asymptomatic patients[7]. This means that a singular negative result is insufficient in excluding COVID-19, and the investigation has to be repeated multiple times[7],[10].

Another potential diagnostic method is chest CT, which might identify typical COVID-19 pneumonia lesions and become an important asset in quick patient evaluation. It is recommended by the World Health Organization in some particular situations, only for symptomatic patients: when RT-PCR is not readily available, when RT-PCR result is negative, but clinical suspicion is high, and in order to decide between hospitalization and discharge, or between ward admission and ICU[11]. The most prominent finding is represented by GGO of circular shape, either peripheral, bilateral, or multifocal. Other typical abnormalities include crazy-paving pattern (GGO with visible inter- and intralobular septal thickening), patchy consolidations and reverse halo sign (GGO surrounded by a ring of consolidation)[12]–[14]. Frequently, both lungs are affected, and sometimes all five lobes simultaneously. The findings are situated mostly in the peripheral parts of the lower zones, in multifocal areas, and posteriorly[12]. On the other hand, lung cavitation, pleural effusion, lymphadenopathy and calcification are commonly absent[12],[14]. So as to ensure standardization, various classifications have been developed. The Dutch Radiological Society proposed CO-RADS (COVID-19 Reporting and Data System), a categorical assessment scheme for chest CT. On a scale from 1 (very low) to 5 (very high), it quantifies the suspicion of pulmonary involvement, with high discriminatory power[65].

At the moment, it remains unclear whether CT should take a more prominent role in COVID-19 diagnosis, especially in highly affected epidemic areas. Scientific literature describes several cases of repeatedly negative RT-PCR results with positive CT findings, which argue in favour of using lung CT, but only as an assisting tool in suspected patients[62]–[64].

Several retrospective studies were conducted so as to compare RT-PCR and chest CT findings, and all of them concluded that CT has a higher sensitivity, ranging from 93-98%, in identifying distinctive lesions in patients with initial negative RT-PCR results[66]–[69]. However, the 53% specificity was considerably lower[68]. This is linked to another pressing problem, represented by the fact that radiologists showed a broad range of variance in differentiating COVID-19 on chest CT, with sometimes moderate, unsatisfactory accuracy[70]. One explanation might be the resemblance of COVID-19 pulmonary abnormalities with other viral pneumoniae, such as MERS, SARS and Influenza[14]. This raises the ethical question of choosing between underdiagnosing, but conserving hospital beds for confirmed cases versus overdiagnosing, but ensuring a greater chance at medical care for atypical cases, which is especially controversial in a pandemic context. Even though the aforementioned studies agreed that CT is a valuable tool, which could be successfully integrated in diagnostic protocols, consensus was not reached whether it is reliable enough to be used as a screening or even as a primary diagnostic tool in epidemic areas, or if it should remain as an addition to potentially flawed RT-PCR results. The contradictory conclusions might be due to small cohort sizes, in conjunction with public distress and pressure for early answers caused by the pandemic. The answer to these issues are paradoxical in nature, because clinical validation takes time, but hospitals need solutions as soon as possible.

An important finding is that as far as 54% of asymptomatic patients were shown to have CT lesions, particularly GGO[71]. This underlines the difference chest Computer Tomography can make in early monitoring of patients at risk, or in isolating infected individuals from the community as soon as possible. Alternatively, there are RT-PCR confirmed cases with either atypical CT images, or no findings at all in the initial stage of the disease[69], rendering lung CT an unreliable method to be used solely. Even though RT-PCR results usually come in at least several hours[61], it sometimes takes up to 3 days for pulmonary lesions to appear on CT[69].

Artificial Intelligence might bring answers to some of these issues.

One domain where algorithms are undeniably better is data quantification. As previously stated, AI excels at interpreting massive amounts of mathematical operations, which could translate to extended and precise analyses of multiple parameters, such as lesion volume and density, distance from pleura[72], airway wall thickness and percent of consolidation versus normal parenchyma[73]. On the one hand, this is very useful in correctly assessing the real extension of the disease and in making an accurate diagnosis. On the other hand, it significantly eases the job of the physician, by cancelling a mundane, time-consuming task, in exchange for time to focus on more complex work. Another key quality of this AI feature is quick processing, as algorithms are notably faster than humans. One study showed that AI spends approximately 15-25 seconds per case, while radiologists spend approximately 50-150 seconds per case[72]. Another estimated that the computer spends on average 10 seconds per scan, while the physician spends 10 minutes[74]. In the context of a healthcare crisis, this might become an essential asset for burdened hospitals and burned out physicians, by reducing wait time and allowing doctors to examine a higher number of patients, by improving workflow and by ensuring a more efficient response to emergencies.

As far as making a diagnosis, current DL software programs were shown to have an accuracy ranging from 62-99,51% [75],[15] in correctly detecting SARS-CoV-2 abnormalities on chest CT. One study compared the results of 10 well-known CNNs, with impressive findings – the best algorithm was able to score 99,51% in accuracy, 100% in sensitivity and 99,02% in specificity[15]. These noticeable differences probably reside in technical characteristics, regarding both algorithm design and further algorithm training, with possible data sets issues due to limited availability of reliable COVID-19 slices. However, the wide range of outcomes underlines the future challenges of legal regulators in order to filter and further classify available software, as well as hospitals' need for qualified advice in purchasing the best technologies.

In assessing the real benefit of using AI, one direction of interest is represented by comparing the achievements of computers against those of humans. In this regard, multiple studies stated that AI is better than junior-level physicians[72],[76]. However, in regards to senior-level specialists, results vary depending on the AI method of choice. Computers' accuracy scores can be worse[77], approximately equal[76], and in some cases significantly better[15]. This suggests that refining the software in the future could elevate computer accomplishments to the level where they would become consistently better than humans. Another interesting finding was that one AI algorithm provided 100% sensitivity, but only 25% specificity, while radiologists scored 89% and 94% in sensitivity, but 100% in specificity[72]. This underlines the statement that, at the moment, the best option might be represented by a close cooperation between man and machine, by contributing with unique strengths and complementing each other's weaknesses. This idea is supported by the fact that reports of AI and physicians working in conjunction were proven better than either AI or radiologists working alone[76]–[78].

An equally important matter is evaluating whether AI is capable of reliably distinguishing COVID-19 from other ailments on chest CT, especially pneumonia of other aetiologies. One experimental study investigated the outcome of CT slice classification as either *infected* or *non-infected*, and compared the results with those of other competitive software programs, with promising conclusions[79]. This underlines the current efforts of tech industry to provide quality answers to this global issue, by continuously improving in a race against the clock. Other studies explored whether AI can differentiate between COVID-19 pneumonia and common pneumonia, and reported 87% to 97,7% accuracy values[74],[78]. Multiple studies expanded the scope, by including non-pneumonia chest images, ranging from 84,78% to 99,87% accuracy[76],[80],[81]. Firstly, independent studies obtained lower values then those reported initially in the original studies, which points at the absolute necessity of reproducibility and peer confirmation for all these promising results. Secondly, it is important to underline that the inclusion of non-pneumonia slices led to broader training sets and more variance, which also bore a greater resemblance to reality, and might represent one of the reasons why these algorithms scored higher. In the same note, a study which also included non-pneumonia images, but only considered Influenza A viral pneumonia, resulted in only 86,7% accuracy[82], likely from the same culprit of narrow data. On the other hand, another experimental study rendered fundamentally different results from those already presented, and concluded that DL cannot be trusted in distinguishing COVID-19 from community-acquired pneumonia[83]. In the light of these findings, it is imperative that more comprehensive experimental studies are conducted before reaching medical practice, in order to assess the real validity of the investigations.

A step forward has been made by designing software based on CO-RADS classification[84],[85], which might be an important bridge between experimental and clinical use of AI, by standardizing CT results and encouraging study reproducibility and research dissemination.

An important addition to the algorithms might be associating CT findings with clinical and laboratory data, such as fever, cough, sputum and white blood cell counts. This was shown to outperform a CT-only DL analysis[77]. Moreover, correlation has been shown to exist among typical SARS-CoV-2 CT lesions and multiple clinical and biological parameters[76], such as age, body temperature, respiratory rate, oxygen saturation, liver markers, coagulation markers, inflammatory markers, as well as electrolyte and acid-base balance[76]. The positive outcomes can be explained in the same way as previously shown: providing the computer with a wider range of data leads to more variance, thus to stronger connections in the 'hidden' layers of the software and consequently to better predictions. This is more similar to real-life situations and to the clinical judgement of a physician.

Another advantage of using DL for chest CT interpretation is the computer's ability to simultaneously diagnose and predict disease severity based on specific features of the scan[86]. Fast targeting of high-risk patients on hospital admission is a valuable asset. Moreover, this has been achieved by an unsupervised algorithm, which was able to provide significant results without human assistance[86]. While this might represent another milestone in AI autonomy, it will firstly have to face one of the longest journey towards clinical approval and regulation. If reached, this kind of software has the potential to fundamentally change medical practice, in a scenario where physicians and computers work side by side instead of in a hierarchical manner, or even where doctors are gradually replaced. This might be the answer to many issues, such as healthcare workers shortage, patient population growth (either over time or during a crisis), human bias and physical limitations. At the same time, it might create fundamentally different problems, such as technical vulnerabilities, lack of critical judgement in highly atypical cases, and public acceptability. In a fully integrated digital scenario of the future, DL could incorporate not only singular investigations, but electronic health records and even lifestyle factors from verified social media profiles.

At the moment, it is impossible to accurately predict the path which AI will follow. However, it is safe to assume that it will play an extremely important role in the future of healthcare. It is paramount to raise awareness and to educate non-specialized population over the matter. It is even more important to teach radiology residents and medical students the basic concepts behind the technology and its applicability. One way or another, DL will change medical practice forever, and we seem to find ourselves at the down of another scientific revolution.

Limitations of our review include journal accessibility, as well as exclusion of all the pre-print articles, very large in number, which could have provided a different perspective upon the subject. As the COVID-19 pandemic is still unfolding, comprehensive reviews are necessary at every step of research progress, which is rapidly changing. Suggested future directions include both AI software design, its continuous improvements and new achievements, and COVID-19 diagnostic methods refinement. We predict that the currently available information will change over the course of the following months, and literature reviewing will be once again mandatory.

CONCLUSIONS

The accelerating digitalization process generated by the COVID-19 healthcare crisis led to an increased interest towards Artificial Intelligence. This technology shows promising potential in becoming a valuable aid in patient diagnosis. Even though aetiology confirmation is mandatory and RT-PCR represents the present gold standard, it remains a flawed method. Furthermore, an emergency situation might require a different approach. While CT has not yet been proven enough for a completely reliable detection, neither has RT-PCR, especially in an early context. However, lung imaging does provide encouraging results, if further upgraded with medical and engineering advancements. In this situation, AI might be a valuable solution to alleviate the pressure off the healthcare system and to improve patient management, with favourable perspectives. At the moment, it is not ready to be implemented in clinical settings, as it has to overcome many technical, scientific, ethical, legal and financial challenges. Even though this process will take much time and many resources, it promises to leave us more prepared in fighting future crises.

REFERENCES

[1] "World Health Organization. (2020, March 11). WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Retrieved from: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-c." https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020 (accessed Aug. 17, 2020).

[2] N. Zhu *et al.*, "A novel coronavirus from patients with pneumonia in China, 2019," *N. Engl. J. Med.*, vol. 382, no. 8, pp. 727–733, Feb. 2020, doi: 10.1056/NEJMoa2001017.

[3] A. E. Gorbalenya *et al.*, "The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2," *Nature Microbiology*, vol. 5, no. 4. Nature Research, pp. 536–544, Apr. 01, 2020, doi: 10.1038/s41564-020-0695-z.

[4] A. Haleem, M. Javaid, and R. Vaishya, "Effects of COVID-19 pandemic in daily life," *Curr. Med. Res. Pract.*, vol. 10, no. 2, pp. 78–79, Mar. 2020, doi: 10.1016/j.cmrp.2020.03.011.

[5] V. M. Corman *et al.*, "Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR," *Eurosurveillance*, vol. 25, no. 3, Jan. 2020, doi: 10.2807/1560-7917.ES.2020.25.3.2000045.

[6] E. Ortiz-Prado *et al.*, "Clinical, molecular, and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19), a comprehensive literature review," *Diagnostic Microbiology and Infectious Disease*, vol. 98, no. 1. Elsevier Inc., p. 115094, Sep. 01, 2020, doi: 10.1016/j.diagmicrobio.2020.115094.

[7] G. Pascarella *et al.*, "COVID-19 diagnosis and management: a comprehensive review," *Journal of Internal Medicine*, vol. 288, no. 2. Blackwell Publishing Ltd, pp. 192–206, Aug. 01, 2020, doi: 10.1111/joim.13091.

[8] H. Han, Q. Luo, F. Mo, L. Long, and W. Zheng, "SARS-CoV-2 RNA more readily detected in induced sputum than in throat swabs of convalescent COVID-19 patients," *The Lancet Infectious Diseases*, vol. 20, no. 6. Lancet Publishing Group, pp. 655–656, Jun. 01, 2020, doi: 10.1016/S1473-3099(20)30174-2.

[9] Y. Li *et al.*, "Stability issues of RT-PCR testing of SARS-CoV-2 for hospitalized patients clinically diagnosed with COVID-19," *J. Med. Virol.*, vol. 92, no. 7, pp. 903–908, Jul. 2020, doi: 10.1002/jmv.25786.

[10] M. Cevik, C. G. G. Bamford, and A. Ho, "COVID-19 pandemic—a focused review for clinicians," *Clinical Microbiology and Infection*, vol. 26, no. 7. Elsevier B.V., p. 842, Jul. 01, 2020, doi: 10.1016/j.cmi.2020.04.023.

[11] "Use of chest imaging in COVID-19." https://www.who.int/publications/i/item/use-of-chest-imaging-in-covid-19 (accessed Aug. 28, 2020).

[12] S. Güneyli, Z. Atçeken, H. Doğan, E. Altınmakas, and K. Ç. Atasoy, "Radiological approach to COVID-19

pneumonia with an emphasis on chest CT," *Diagn. Interv. Radiol.*, vol. 26, no. 4, pp. 323–332, Jul. 2020, doi: 10.5152/dir.2020.20260.

[13] F. Pan *et al.*, "Time course of lung changes at chest CT during recovery from Coronavirus disease 2019 (COVID-19)," *Radiology*, vol. 295, no. 3, pp. 715–721, Jun. 2020, doi: 10.1148/radiol.2020200370.

[14] Z. Y. Zu *et al.*, "Coronavirus Disease 2019 (COVID-19): A Perspective from China," *Radiology*, vol. 296, no. 2, pp. E15–E25, Aug. 2020, doi: 10.1148/radiol.2020200490.

[15] A. A. Ardakani, A. R. Kanafi, U. R. Acharya, N. Khadem, and A. Mohammadi, "Application of deep learning technique to manage COVID-19 in routine clinical practice using CT images: Results of 10 convolutional neural networks," *Comput. Biol. Med.*, vol. 121, p. 103795, Jun. 2020, doi: 10.1016/j.compbiomed.2020.103795.

[16] G. Chartrand *et al.*, "Deep Learning: A Primer for Radiologists," *RadioGraphics*, vol. 37, no. 7, pp. 2113–2131, Nov. 2017, doi: 10.1148/rg.2017170077.

[17] E. H. Shortliffe, "Artificial Intelligence in Medicine: Weighing the Accomplishments, Hype, and Promise," *Yearb. Med. Inform.*, vol. 28, no. 1, pp. 257–262, Aug. 2019, doi: 10.1055/s-0039-1677891.

[18] A. L. Samuel, "Some Studies in Machine Learning Using the Game of Checkers," *IBM J.*, vol. 3, no. 3, pp. 210–229, 1959, doi: 10.1147/rd.33.0210.

[19] M. Van Assen, S. J. Lee, and C. N. De Cecco, "Artificial intelligence from A to Z: From neural network to legal framework," 2020, doi: 10.1016/j.ejrad.2020.109083.

[20] U. Schmidt-Erfurth, A. Sadeghipour, B. S. Gerendas, S. M. Waldstein, and H. Bogunović, "Artificial intelligence in retina," *Progress in Retinal and Eye Research*, vol. 67. Elsevier Ltd, pp. 1–29, Nov. 01, 2018, doi: 10.1016/j.preteyeres.2018.07.004.

[21] A. S. Ahuja, "The impact of artificial intelligence in medicine on the future role of the physician," *PeerJ*, vol. 2019, no. 10, 2019, doi: 10.7717/peerj.7702.

[22] F. Pesapane, M. Codari, and F. Sardanelli, "Artificial intelligence in medical imaging: threat or opportunity? Radiologists again at the forefront of innovation in medicine," *European Radiology Experimental*, vol. 2, no. 1. Springer, p. 35, Dec. 01, 2018, doi: 10.1186/s41747-018-0061-6.

[23] K. J. Dreyer and J. R. Geis, "When Machines Think: Radiology's Next Frontier Dreyer and Geis," *Rev. Comment. n Annu. OrAtiOn Radiol.*, vol. 285, no. 3, 2017, doi: 10.1148/radiol.2017171183.

[24] M. Kohli, L. M. Prevedello, R. W. Filice, and J. R. Geis, "Implementing Machine Learning in Radiology Practice and Research," *Am. J. Roentgenol.*, vol. 208, no. 4, pp. 754–760, Apr. 2017, doi: 10.2214/AJR.16.17224.

[25] G. Choy *et al.*, "Current Applications and Future Impact of Machine Learning in Radiology," *Radiology*, vol. 288, no. 2, pp. 318–328, Aug. 2018, doi: 10.1148/radiol.2018171820.

[26] M. P. McBee *et al.*, "Deep Learning in Radiology," *Acad. Radiol.*, vol. 25, pp. 1472–1480, 2018, doi: 10.1016/j.acra.2018.02.018.

[27] E. Klang, "Deep learning and medical imaging," *Journal of Thoracic Disease*, vol. 10, no. 3. AME Publishing Company, pp. 1325–1328, Mar. 01, 2018, doi: 10.21037/jtd.2018.02.76.

[28] U. Djuric, G. Zadeh, K. Aldape, and P. Diamandis, "Precision histology: how deep learning is poised to revitalize histomorphology for personalized cancer care," *npj Precis. Oncol.*, vol. 1, no. 1, p. 22, Dec. 2017, doi: 10.1038/s41698-017-0022-1.

[29] S. S. Han, M. S. Kim, W. Lim, G. H. Park, I. Park, and S. E. Chang, "Classification of the Clinical Images for Benign and Malignant Cutaneous Tumors Using a Deep Learning Algorithm," *J. Invest. Dermatol.*, vol. 138, no. 7, pp. 1529–1538, Jul. 2018, doi: 10.1016/j.jid.2018.01.028.

[30] S. F. Weng, J. Reps, J. Kai, J. M. Garibaldi, and N. Qureshi, "Can Machine-learning improve cardiovascular risk prediction using routine clinical data?," *PLoS One*, vol. 12, no. 4, Apr. 2017, doi: 10.1371/journal.pone.0174944.

[31] O. F. Ahmad, D. Stoyanov, and L. B. Lovat, "Human-machine collaboration: Bringing artificial intelligence into colonoscopy," *Frontline Gastroenterology*, vol. 10, no. 2. BMJ Publishing Group, pp. 198–199, 2019, doi: 10.1136/flgastro-2018-101047.

[32] K. P. Smith, A. D. Kang, and J. E. Kirby, "Automated interpretation of blood culture gram stains by use of a deep convolutional neural network," *J. Clin. Microbiol.*, vol. 56, no. 3, Mar. 2018, doi: 10.1128/JCM.01521-17.

[33] Y. Yuan *et al.*, "Deepgene: An advanced cancer type classifier based on deep learning and somatic point mutations," *BMC Bioinformatics*, vol. 17, no. Suppl 17, Dec. 2016, doi: 10.1186/s12859-016-1334-9.

[34] A. Zhavoronkov, Q. Vanhaelen, and T. I. Oprea, "Will Artificial Intelligence for Drug Discovery Impact Clinical Pharmacology?," *Clin. Pharmacol. Ther.*, vol. 107, no. 4, pp. 780–785, Apr. 2020, doi: 10.1002/cpt.1795.

[35] N. Mirchi, V. Bissonnette, R. Yilmaz, N. Ledwos, A. Winkler-Schwartz, and R. F. Del Maestro, "The virtual operative assistant: An explainable artificial intelligence tool for simulation-based training in surgery and medicine," *PLoS One*, vol. 15, no. 2, 2020, doi: 10.1371/journal.pone.0229596.

[36] M. L. Giger, H. P. Chan, and J. Boone, "Anniversary paper: History and status of CAD and quantitative image analysis: The role of Medical Physics and AAPM," *Medical Physics*, vol. 35, no. 12. John Wiley

and Sons Ltd, pp. 5799–5820, 2008, doi: 10.1118/1.3013555.

[37] R. A. Castellino, “Computer aided detection (CAD): An overview,” *Cancer Imaging*, vol. 5, no. 1. BioMed Central, pp. 17–19, 2005, doi: 10.1102/1470-7330.2005.0018.

[38] M. Alhajeri and S. G. S. Shah, “Limitations in and Solutions for Improving the Functionality of Picture Archiving and Communication System: an Exploratory Study of PACS Professionals’ Perspectives,” *J. Digit. Imaging*, vol. 32, no. 1, pp. 54–67, Feb. 2019, doi: 10.1007/s10278-018-0127-2.

[39] M. Harris *et al.*, “A systematic review of the diagnostic accuracy of artificial intelligence-based computer programs to analyze chest x-rays for pulmonary tuberculosis,” *PLoS One*, vol. 14, no. 9, 2019, doi: 10.1371/journal.pone.0221339.

[40] V. Roblot *et al.*, “Artificial intelligence to diagnose meniscus tears on MRI,” *Diagn. Interv. Imaging*, vol. 100, no. 4, pp. 243–249, Apr. 2019, doi: 10.1016/j.diii.2019.02.007.

[41] X. W. Liang, Y. Y. Cai, J. S. Yu, J. Y. Liao, Z. Y. Chen, and N. N. Wang, “Update on thyroid ultrasound: A narrative review from diagnostic criteria to artificial intelligence techniques,” *Chinese Medical Journal*, vol. 132, no. 16. Lippincott Williams and Wilkins, pp. 1974–1982, Aug. 20, 2019, doi: 10.1097/CM9.0000000000000346.

[42] A. Rodriguez-Ruiz *et al.*, “Can we reduce the workload of mammographic screening by automatic identification of normal exams with artificial intelligence? A feasibility study,” *Eur. Radiol.*, vol. 29, no. 9, pp. 4825–4832, Sep. 2019, doi: 10.1007/s00330-019-06186-9.

[43] L. Q. Zhou *et al.*, “Artificial intelligence in medical imaging of the liver,” *World J. Gastroenterol.*, vol. 25, no. 6, pp. 672–682, 2019, doi: 10.3748/wjg.v25.i6.672.

[44] D. Świetlik and J. Białowąs, “Application of artificial neural networks to identify Alzheimer’s disease using cerebral perfusion SPECT data,” *Int. J. Environ. Res. Public Health*, vol. 16, no. 7, Apr. 2019, doi: 10.3390/ijerph16071303.

[45] N. Nasrullah, J. Sang, M. S. Alam, M. Mateen, B. Cai, and H. Hu, “Automated lung nodule detection and classification using deep learning combined with multiple strategies,” *Sensors (Switzerland)*, vol. 19, no. 17, Sep. 2019, doi: 10.3390/s19173722.

[46] Z. Akkus, A. Galimzianova, A. Hoogi, D. L. Rubin, and B. J. Erickson, “Deep Learning for Brain MRI Segmentation: State of the Art and Future Directions,” *Journal of Digital Imaging*, vol. 30, no. 4. Springer New York LLC, pp. 449–459, Aug. 01, 2017, doi: 10.1007/s10278-017-9983-4.

[47] J. Gregory, S. Welliver, and J. Chong, “Top 10 Reviewer Critiques of Radiology Artificial Intelligence (AI) Articles: Qualitative Thematic Analysis of Reviewer Critiques of Machine Learning/Deep Learning Manuscripts Submitted to JMRI,” *J. Magn. Reson. Imaging*, vol. 52, no. 1, pp. 248–254, Jul. 2020, doi: 10.1002/jmri.27035.

[48] S. H. Park and H. Y. Kressel, “Connecting Technological Innovation in Artificial Intelligence to Real-world Medical Practice through Rigorous Clinical Validation: What Peer-reviewed Medical Journals Could Do,” *J. Korean Med. Sci.*, vol. 33, no. 22, May 2018, doi: 10.3346/jkms.2018.33.e152.

[49] Q. Waymel, S. Badr, X. Demondion, A. Cotten, and T. Jacques, “Impact of the rise of artificial intelligence in radiology: What do radiologists think?,” *Diagn. Interv. Imaging*, vol. 100, no. 6, pp. 327–336, Jun. 2019, doi: 10.1016/j.diii.2019.03.015.

[50] M. A. Mazurowski, “Artificial Intelligence in Radiology: Some Ethical Considerations for Radiologists and Algorithm Developers,” *Academic Radiology*, vol. 27, no. 1. Elsevier USA, pp. 127–129, Jan. 01, 2020, doi: 10.1016/j.acra.2019.04.024.

[51] R. De’, N. Pandey, and A. Pal, “Impact of digital surge during Covid-19 pandemic: A viewpoint on research and practice,” *Int. J. Inf. Manage.*, 2020, doi: 10.1016/j.ijinfomgt.2020.102171.

[52] Z. Yang *et al.*, “Modified SEIR and AI prediction of the epidemics trend of COVID-19 in China under public health interventions,” *J. Thorac. Dis.*, vol. 12, no. 3, pp. 165–174, Mar. 2020, doi: 10.21037/jtd.2020.02.64.

[53] T. P. Mashamba-Thompson and E. D. Crayton, “Blockchain and artificial intelligence technology for novel coronavirus disease-19 self-testing,” *Diagnostics*, vol. 10, no. 4. MDPI AG, 2020, doi: 10.3390/diagnostics10040198.

[54] K. Murphy *et al.*, “COVID-19 on the Chest Radiograph: A Multi-Reader Evaluation of an AI System,” *Radiology*, vol. 296, no. 3, p. 201874, May 2020, doi: 10.1148/radiol.2020201874.

[55] X. Jiang *et al.*, “Towards an artificial intelligence framework for data-driven prediction of coronavirus clinical severity,” *Comput. Mater. Contin.*, vol. 63, no. 1, pp. 537–551, Mar. 2020, doi: 10.32604/cmc.2020.010691.

[56] J. Stebbing *et al.*, “COVID-19: combining antiviral and anti-inflammatory treatments,” *The Lancet Infectious Diseases*, vol. 20, no. 4. Lancet Publishing Group, pp. 400–402, Apr. 01, 2020, doi: 10.1016/S1473-3099(20)30132-8.

[57] Y. Y. Ke *et al.*, “Artificial intelligence approach fighting COVID-19 with repurposing drugs,” *Biomed. J.*, May 2020, doi: 10.1016/j.bj.2020.05.001.

[58] D. K. W. Chu *et al.*, “Molecular Diagnosis of a Novel Coronavirus (2019-nCoV) Causing an Outbreak of

Pneumonia," *Clin. Chem.*, Jan. 2020, doi: 10.1093/clinchem/hvaa029.

[59] T. Phan, "Genetic diversity and evolution of SARS-CoV-2," *Infect. Genet. Evol.*, vol. 81, p. 104260, Jul. 2020, doi: 10.1016/j.meegid.2020.104260.

[60] Z. Shen *et al.*, "Genomic diversity of SARS-CoV-2 in Coronavirus Disease 2019 patients," *Clin. Infect. Dis.*, Jul. 2020, doi: 10.1093/cid/ciaa203.

[61] L. J. Carter *et al.*, "Assay Techniques and Test Development for COVID-19 Diagnosis," *ACS Cent. Sci.*, vol. 6, no. 5, pp. 591–605, May 2020, doi: 10.1021/acscentsci.0c00501.

[62] H. Feng, Y. Liu, M. Lv, and J. Zhong, "A case report of COVID-19 with false negative RT-PCR test: necessity of chest CT," *Jpn. J. Radiol.*, vol. 38, no. 5, pp. 409–410, May 2020, doi: 10.1007/s11604-020-00967-9.

[63] D. Li *et al.*, "False-negative results of real-time reverse-transcriptase polymerase chain reaction for severe acute respiratory syndrome coronavirus 2: Role of deep-learning-based ct diagnosis and insights from two cases," *Korean J. Radiol.*, vol. 21, no. 4, pp. 505–508, Apr. 2020, doi: 10.3348/kjr.2020.0146.

[64] L. Da Chen *et al.*, "A COVID-19 patient with multiple negative results for PCR assays outside Wuhan, China: a case report," *BMC Infect. Dis.*, vol. 20, no. 1, p. 517, Jul. 2020, doi: 10.1186/s12879-020-05245-7.

[65] M. Prokop *et al.*, "CO-RADS: A Categorical CT Assessment Scheme for Patients Suspected of Having COVID-19-Definition and Evaluation," *Radiology*, vol. 296, no. 2, pp. E97–E104, Aug. 2020, doi: 10.1148/radiol.2020201473.

[66] T. Ai *et al.*, "Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases," *Radiology*, vol. 296, no. 2, pp. E32–E40, Aug. 2020, doi: 10.1148/radiol.2020200642.

[67] C. Long *et al.*, "Diagnosis of the Coronavirus disease (COVID-19): rRT-PCR or CT?," *Eur. J. Radiol.*, vol. 126, p. 108961, May 2020, doi: 10.1016/j.ejrad.2020.108961.

[68] Z. Wen *et al.*, "Coronavirus Disease 2019: Initial Detection on Chest CT in a Retrospective Multicenter Study of 103 Chinese Subjects," *Radiol. Cardiothorac. Imaging*, vol. 2, no. 2, p. e200092, Apr. 2020, doi: 10.1148/ryct.2020200092.

[69] Y. Fang *et al.*, "Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR," *Radiology*, vol. 296, no. 2, pp. E115–E117, Aug. 2020, doi: 10.1148/radiol.2020200432.

[70] H. X. Bai *et al.*, "Performance of Radiologists in Differentiating COVID-19 from Non-COVID-19 Viral Pneumonia at Chest CT," *Radiology*, vol. 296, no. 2, pp. E46–E54, Aug. 2020, doi: 10.1148/radiol.2020200823.

[71] S. Inui *et al.*, "Chest CT Findings in Cases from the Cruise Ship 'Diamond Princess' with Coronavirus Disease 2019 (COVID-19)," *Radiol. Cardiothorac. Imaging*, vol. 2, no. 2, p. e200110, Apr. 2020, doi: 10.1148/ryct.2020200110.

[72] Q. Ni *et al.*, "A deep learning approach to characterize 2019 coronavirus disease (COVID-19) pneumonia in chest CT images," *Eur. Radiol.*, pp. 1–11, Jul. 2020, doi: 10.1007/s00330-020-07044-9.

[73] M. P. Belfiore *et al.*, "Artificial intelligence to codify lung CT in Covid-19 patients," *Radiol. Medica*, vol. 125, no. 5, pp. 500–504, May 2020, doi: 10.1007/s11547-020-01195-x.

[74] T. Yan, P. K. Wong, H. Ren, H. Wang, J. Wang, and Y. Li, "Automatic distinction between COVID-19 and common pneumonia using multi-scale convolutional neural network on chest CT scans," *Chaos, Solitons and Fractals*, vol. 140, p. 110153, Nov. 2020, doi: 10.1016/j.chaos.2020.110153.

[75] X. Wu *et al.*, "Deep learning-based multi-view fusion model for screening 2019 novel coronavirus pneumonia: A multicentre study," *Eur. J. Radiol.*, vol. 128, p. 109041, Jul. 2020, doi: 10.1016/j.ejrad.2020.109041.

[76] K. Zhang *et al.*, "Clinically Applicable AI System for Accurate Diagnosis, Quantitative Measurements, and Prognosis of COVID-19 Pneumonia Using Computed Tomography," *Cell*, vol. 181, no. 6, pp. 1423-1433.e11, Jun. 2020, doi: 10.1016/j.cell.2020.04.045.

[77] B. P. Little *et al.*, "Artificial intelligence-enabled rapid diagnosis of patients with COVID-19," doi: 10.1038/s41591-020-0931-3.

[78] H. X. Bai *et al.*, "AI Augmentation of Radiologist Performance in Distinguishing COVID-19 from Pneumonia of Other Etiology on Chest CT," *Radiology*, p. 201491, Apr. 2020, doi: 10.1148/radiol.2020201491.

[79] D. Singh, V. Kumar, Vaishali, and M. Kaur, "Classification of COVID-19 patients from chest CT images using multi-objective differential evolution–based convolutional neural networks," *Eur. J. Clin. Microbiol. Infect. Dis.*, vol. 39, no. 7, pp. 1379–1389, Jul. 2020, doi: 10.1007/s10096-020-03901-z.

[80] S. Yang *et al.*, "Deep learning for detecting corona virus disease 2019 (COVID-19) on high-resolution computed tomography: a pilot study," *Ann. Transl. Med.*, vol. 8, no. 7, pp. 450–450, Apr. 2020, doi: 10.21037/atm.2020.03.132.

[81] H. Ko *et al.*, "COVID-19 pneumonia diagnosis using a simple 2d deep learning framework with a single chest CT image: Model development and validation," *J. Med. Internet Res.*, vol. 22, no. 6, Jun. 2020, doi: 10.2196/19569.

[82] X. Xu *et al.*, "A Deep Learning System to Screen Novel Coronavirus Disease 2019 Pneumonia," *Engineering*, Jun. 2020, doi: 10.1016/j.eng.2020.04.010.

[83] J. Pu *et al.*, “Any unique image biomarkers associated with COVID-19?,” *Eur. Radiol.*, p. 1, 2020, doi: 10.1007/s00330-020-06956-w.

[84] J. J. R. Hermans *et al.*, “Chest CT for triage during COVID-19 on the emergency department: myth or truth?,” *Emerg. Radiol.*, p. 1, Jul. 2020, doi: 10.1007/s10140-020-01821-1.

[85] N. Lessmann *et al.*, “Automated Assessment of CO-RADS and Chest CT Severity Scores in Patients with Suspected COVID-19 Using Artificial Intelligence,” *Radiology*, p. 202439, Jul. 2020, doi: 10.1148/radiol.2020202439.

[86] S. Wang *et al.*, “A fully automatic deep learning system for COVID-19 diagnostic and prognostic analysis,” *Eur. Respir. J.*, vol. 56, no. 2, p. 2000775, Aug. 2020, doi: 10.1183/13993003.00775-2020.