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Comparison of artificial intelligence to the veterinary clinician's diagnosis of thoracic nodules

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Abstract

Medical imaging procedures are difficult to analyze even for experienced specialists, partly due to the structures that are difficult to detect with the naked eye, and partly due to a large number of not very specific, very similar details.

In human medicine, artificial intelligence (AI) has been used in thorax radiographs in multiple conditions, although AI used in veterinary radiology sprang up a little later than in human medicine, it still has fast development in different aspects, pulmonary detection is one of the common cases.

Early detection of lung nodules is important for early intervention and increasing the survival rate. Although computed tomography (CT) has better accuracy in pulmonary detection, accuracy variation can still occur due to different clinicians' experiences.

In human medicine, AI has shown variable success and variable sensitivity in pulmonary detection and classification by radiographs and CT scanning. However, studies testing for AI used in veterinary radiology pulmonary nodule detection are limited.

The aim of this study is to test and compare the accuracy, sensitivity, and specificity between an AI software and a clinician for detecting canine pulmonary nodules from thoracic CT images, using a university teaching hospital radiologist's interpretation as the reference standard.

The AI software only reaches 50.0% sensitivity, 75.0% specificity, and 62.5% accuracy, which didn't overperform the result of the clinician. Findings suggest that, although AI tools can possibly assist veterinarians in daily radiography reading and improve the quality of care, they should be validated before their application to daily clinical work.

Contents

1. Introduction

In human and veterinary medicine, lung nodules could serve as a potential indicator of lung cancer and metastasis,[1,27] and the size of pulmonary nodules is also related to the prevalence of malignancy from 0-82%.[2] This emphasizes the importance of pulmonary nodule detection in staging cancer and evaluating the success of therapy both in human and veterinary medicine. Most pulmonary metastatic lesions rarely produce clinical signs even with advanced metastasis, and dogs having thyroid carcinomas, urinary bladder transitional cell carcinomas, and osteosarcoma are prone to have metastasis, thus, thoracic radiography should be considered on all dogs with confirmed or suspected primary neoplasms.[4,18] A few studies may hint at a potential correlation between pulmonary metastasis and tumor malignancy, staging, and prognosis in veterinary medicine. In one study about appendicular osteosarcoma in dogs, the presence of nodules in thoracic computed tomography (CT) scan did not influence the overall survival, but after surgery, those dogs with more nodules had a shorter survival time.[3] In another study about feline oral squamous cell carcinoma, the possibility of thoracic metastasis was about 10%.[6]

Diagnostic imaging plays an essential role in the diagnosis and staging of cancer in small animal patients. Conventional radiography is still the first choice for imaging the thorax in most clinics, to detect masses, nodules, and abnormalities in the thorax. However, it may have limitations in differentiating lesions or nodules from the mediastinum, lung lobes, and thoracic wall. One study shows that the mean sensitivity of pulmonary nodule detection of both digital radiographs and screen-film radiographs is only approximately 65%.[20] CT has better contrast resolution and less overlying anatomic noise, which makes it more sensitive and accurate in pulmonary nodule detection, recommended in every patient with neoplasm and risk in metastasis, for example on female dogs with malignant mammary tumors.[9]

Due to the expansion of telemedicine, the fast growth of radiography cases, and the increasing workloads of radiologists, the interest in artificial intelligence (AI) in veterinary diagnostic imaging nowadays is growing. It can be a screening tool, driving to assist veterinarians in interpreting radiographs, in emergencies, and in multiple patient caring, which can decrease diagnosis errors and enhance working efficiency.[14] AI already has considerable potential in radiographs in human medicine. To date, in companion animals, the focus is primarily on thorax image interpretation, however, studies testing the use of AI applications in veterinary diagnostic imaging especially in pulmonary nodule detection are limited and have yet to be assessed.

2. Literature review

2.1. AI used in human medicine

In human medicine, AI has been used in thorax radiographs in multiple conditions, such as pneumothorax detection in emergency scans, with high specificity, to reduce the time to treatment.[28] Moreover, different algorithms have been developed, for the detection of traumatic vertebrae fractures, pneumonia, tuberculosis, and bone age assessment.[29,30,32,35] Some of the AI programs on the market have also been tested, with a high accuracy when distinguishing normal and abnormal chest radiographs.[33] Not just in thorax radiographs, AI has also been used in hip fracture detections from pelvic radiographs in humans, with equivalent performance to radiologists.[34]

2.2. AI used in veterinary medicine

One study shows an AI algorithm was able to detect canine pleural effusion with almost 90% accuracy.[36] Another study testing AI in the diagnosis of canine pulmonary edema shows high accuracy, sensitivity, and specificity.[44] Cardiopathy is also a new field of vision in which AI can be used in thoracic radiographs, such as left atrial enlargement, right ventricular enlargement, and VHS calculation.[14,38,39,40,41,42] Moreover, some of the AI programs are able to identify and classify different findings in thoracic radiographs, with acceptable accuracy and low overall error rate, including alveolar pattern, interstitial pattern, bronchial pattern, pneumothorax, pleural effusion, tracheal collapse, pulmonary mass, megaoesophagus, and no findings.[37.38,39,43] However, one study showed, that in the identification of 15 labels in canine thoracic radiographs, the error rate of 13 board-certified radiologists is lower than four pre-trained AI programs.[40] Except for the use in thorax radiographs, one study also shows AI can be used for measuring femoral angles from three-dimensional CT reconstructions, reducing the time of evaluation.[45] There are also two studies show AI used in oncology, one delineating, and segmenting the retropharyngeal lymph nodes from surrounding tissues in dogs CT studies, contribute to radiation therapy planning,[46] another one as a non-invasive method to predict hepatic malignancy by analyzing CT heterogeneity in canine liver masses.[47]

2.3. Variation of the accuracy of radiographs and CT in pulmonary nodules detection

In dogs, compared to CT, the lower cost and higher availability make a 3-view thoracic radiography a conventional evaluation for pulmonary metastatic disease. However, there is a quite high missing rate of pulmonary nodule detection in radiography, and sensitivity could also be affected by the position and increased lung opacity caused by concurrent problems.[7,25] One study indicates 90% of pulmonary nodules detected on CT were failed to reveal on thoracic radiography, while all pulmonary nodules detected on thoracic radiography were seen on CT.[4] Common misdiagnosis of pulmonary nodules in radiographs including end-on vessels, bone, skin nodules, and nipples. Besides, radiography has a limit in pinpointing whether the lesion is from the lung, the pleural cavity, or the mediastinum, which underscores the need for a more accurate approach. Surprisingly, there are studies showing lung ultrasonography may have a similar sensitivity to radiography, and MRI has acceptable sensitivity for pulmonary nodules detection only if the lesions are larger than 4 mm, but caution should be raised due to the low specificity, CT confirmation is suggested before conclusion.[13,21]

Pulmonary nodules have several varieties, including but not limited to, the size, shape and opacity, and overlapping with other tissue. Nodules should reach a certain size to be recognized on a radiograph, the lowest size of pulmonary nodules to be detected on CT in dogs is approximately 1 mm compared to 5-9 mm on radiographs.[4,5] The principles of image formation of a CT scanner are similar to a conventional X-ray machine, but with cross-sectional images of the body. There have been plenty of studies have agreed that CT has superior contrast resolution, fast image acquisition, and lack of overlying noise, thus has a higher accuracy and sensitivity, and greater diagnostic confidence in small pulmonary nodule detection,[3,4,8,9] and by combined with survey thoracic radiographs, it can provide additional information that could impact management, therapy plans, and prognosis.[10] Poor aeration of the lung as a result of anesthesia during the CT scanning may decrease nodules' legibility, but standardized breath-hold techniques can increase lung inflation and the difference between nodules and lung, thereby improving the detection possibility.[4] However, with the higher cost and need for sedation even anesthesia, CT is unlikely to completely replace thoracic radiography.

2.4. Variation of the accuracy of manual pulmonary nodules detection

The accuracy of pulmonary nodule detection and interpretation may vary based on the training level and experience of practitioners.[11,12,16] In one study about student radiographic interpretation quizzes, the median score was only 49%.[15] Another study shows pitch and reconstruction interval, also nodule size did not significantly influence nodule detection, interobserver and intraobserver variations may have more influences.[19] In both human medicine and veterinary medicine, overdiagnosis is also a major concern in lung scanning, which may result in unnecessary treatment.[1,16] Thus, the interpretation of radiographs can be challenging for clinicians not trained well and even for experienced clinicians. However, organized and standard training and certification examinations are lacking in most countries except in the United States and Europe.

3. Objectives

The first aim of this study is to test and compare the accuracy, sensitivity, and specificity between an AI software and a clinician for detecting canine pulmonary nodules from thoracic CT images, using a university teaching hospital radiologist's interpretation as the reference standards, the second aim is to reveal publications related to artificial intelligence in veterinary radiology.

4. Materials and Methods

The AI software is created and trained by a mechatronic engineering student using machine learning, as part of the collaboration between the University of Veterinary Medicine Budapest and the Technical University (Master's degree in health engineering, as a diploma project, aiming to correctly estimate whether a nodular lesion is found on a given patient's CT scan. The cases used for training were from human CT scans available online. The training set is a total of more than 120 GB of CT recordings, and in order to increase the amount of samples, the images were mirrored and rotated. Then the training set is split into teaching, validation, and test sets, in a ratio of 70/15/15.

Totally 40 canine cases were collected from a teaching hospital of a veterinary university, and all had a CT contrast examination of the entire thorax. All images were selected and evaluated by a radiologist in the teaching hospital with 25 years of experience as a standard reference. All cases were placed randomly for AI and clinician interpretation. The AI and clinician were not aware of the cases' clinical information and the results of examinations.

All images were received by the AI software and clinician in standard DICOM format, and the clinician viewed images on a dedicated station (RadiAnt DICOM viewer).

All results were collected and arranged in an Excel file (Figure 1), separated into two possible categories: pulmonary nodules positive (PN+) or pulmonary negative (PN-).

	Radiologist		AI		Clinician	
	Positive	Negative	Positive	Negative	Positive	Negative
Case 1	●		●		●	
Case 2		○		○	●	
Case 3	●			○	●	
Case 4		○		○		○
Case 5	●		●		●	
Case 6	●		●			○
Case 7		○		○		○
Case 8	●			○	●	
Case 9		○	●			○
Case 10		○		○		○
Case 11	●		●		●	
Case 12		○		○		
Case 13	●			○	●	
Case 14		○		○		○
Case 15		○	●		●	
Case 16		○	●			○
Case 17		○		○		○
Case 18		○		○		○
Case 19		○		○		○
Case 20		○	●		●	
Case 21	●		●		●	
Case 22		○		○		○
Case 23		○		○		○
Case 24	●			○	●	
Case 25	●		●		●	
Case 26	●			○	●	
Case 27		○		○		○
Case 28	●		●		●	
Case 29	●			○		○
Case 30		○		○		○
Case 31	●		●		●	
Case 32	●		●		●	
Case 33	●			○	●	
Case 34		○		○		○
Case 35		○	●		●	
Case 36	●			○	●	
Case 37	●		●		●	
Case 38		○		○		○
Case 39		○	●			○
Case 40	●			○	●	

Figure 1.
Interpretation results of the radiologist, AI and clinician.

For cases diagnosed by a radiologist as PN+, positive AI and clinician diagnoses were classified as True Positives (TP), while negative AI and clinician diagnoses were classified as False Negatives (FN). For cases diagnosed by a radiologist as PN-, negative AI and clinician diagnoses were classified as True Negative (TN), while positive AI and clinician diagnoses were classified as False Positive (FP) (Table 1). The sensitivity was calculated as TP/(TP+FN). The specificity was calculated as TN/(TN+FP). Overall accuracy was calculated as (TP+TN)/(TP+TN+FP+FN). The positive predictive value (PPV) was calculated as TP/(TP+FP), and the negative predictive value was calculated as TN/(TN+FN). The Youden's index was calculated as sensitivity+Specificity-1.

Table 1.
The basis for sensitivity and specificity calculations displaying which studies were considered true positives, true negatives, false positives, and false negatives

	Radiologist PN+	Radiologist PN-
AI/Clinician PN+	True Positive (TP)	False Positive (FP)
AI/Clinician PN-	False Negative (FN)	True Negative (TN)

5. Results

A total of 40 cases were included in the study, images evaluated by the radiologist reported 19/40 PN+ and 21/40 PN-. The AI software reported 15/40 PN+ and 25/40 PN-, while the clinician reported 22/40 PN+ and 18/40 PN- (Table 2).

Of the 19 PN+ diagnosed by the radiologist, the AI software agreed on 10 (52.6%) of the cases, while the clinician agreed on 17 (89.5%) of the cases. Of the 21 PN- diagnosed by the radiologist, the AI software agreed on 15 (71.4%) of the cases, while the clinician agreed on 16 (76.2%) of the cases. The AI software reported a true diagnosis in all 25/40 cases and, a false diagnosis in 15/40 cases, while the clinician reported a true diagnosis in all 33/40 cases, a false diagnosis in 7/40 cases (Table 3). The sensitivity, specificity, overall accuracy, positive predictive, negative predictive, and Youden's index are calculated and compared between the AI software and the clinician (Table 4).

Examples of pulmonary nodules correctly and incorrectly identified by the AI software are reported in Figures 2 and 3, respectively.

Examples of pulmonary nodules missing by the AI software and clinician are shown in Figures 4 and 5, respectively.

Table 2.
Comparison of PN diagnosis of the radiologist, the AI software, and the clinician

	Radiologist	AI	Clinician
PN+	19	15	22
PN-	21	25	18
Total	40	40	40

Table 3.
Comparison of PN diagnosis agreement of the radiologist, the AI software, and the clinician

	True Positive	False Positive	True Negative	False Negative
AI	10	5	15	10
Clinician	17	5	16	2

Table 4.
Comparison of sensitivity, specificity overall accuracy, positive predictive, negative predictive, and Youden's index between the AI software and the clinician

	Sensitivity	Specificity	Overall accuracy	Positive predictive	Negative predictive	Youden's index
AI	50.0%	75.0%	62.5%	66.7%	60%	0.25
Clinician	89.5%	76.2%	82.5%	77.2%	88.9%	0.66

Figure 2.
Example of a pulmonary nodule correctly identified by the AI software, the arrow shows a significantly identifiable radiopaque nodule.

Figure 3.
Example of image falsely identified by the AI software as having pulmonary nodule. The arrow shows a small round radiopaque tissue which is the cross section of a vessel.

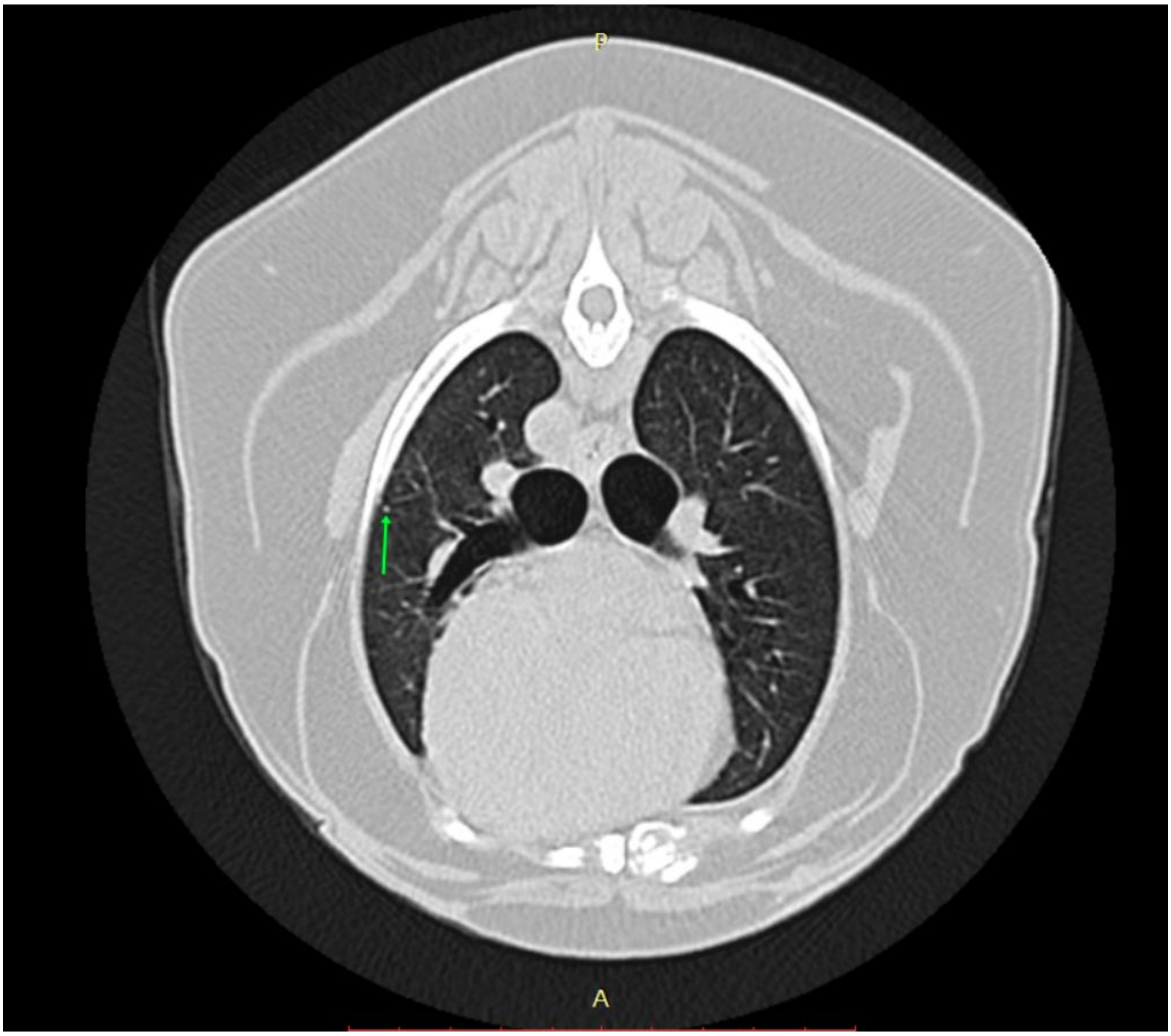

Figure 4.
Example of pulmonary nodule missing by the AI software, the arrow shows a small radiopaque nodule.

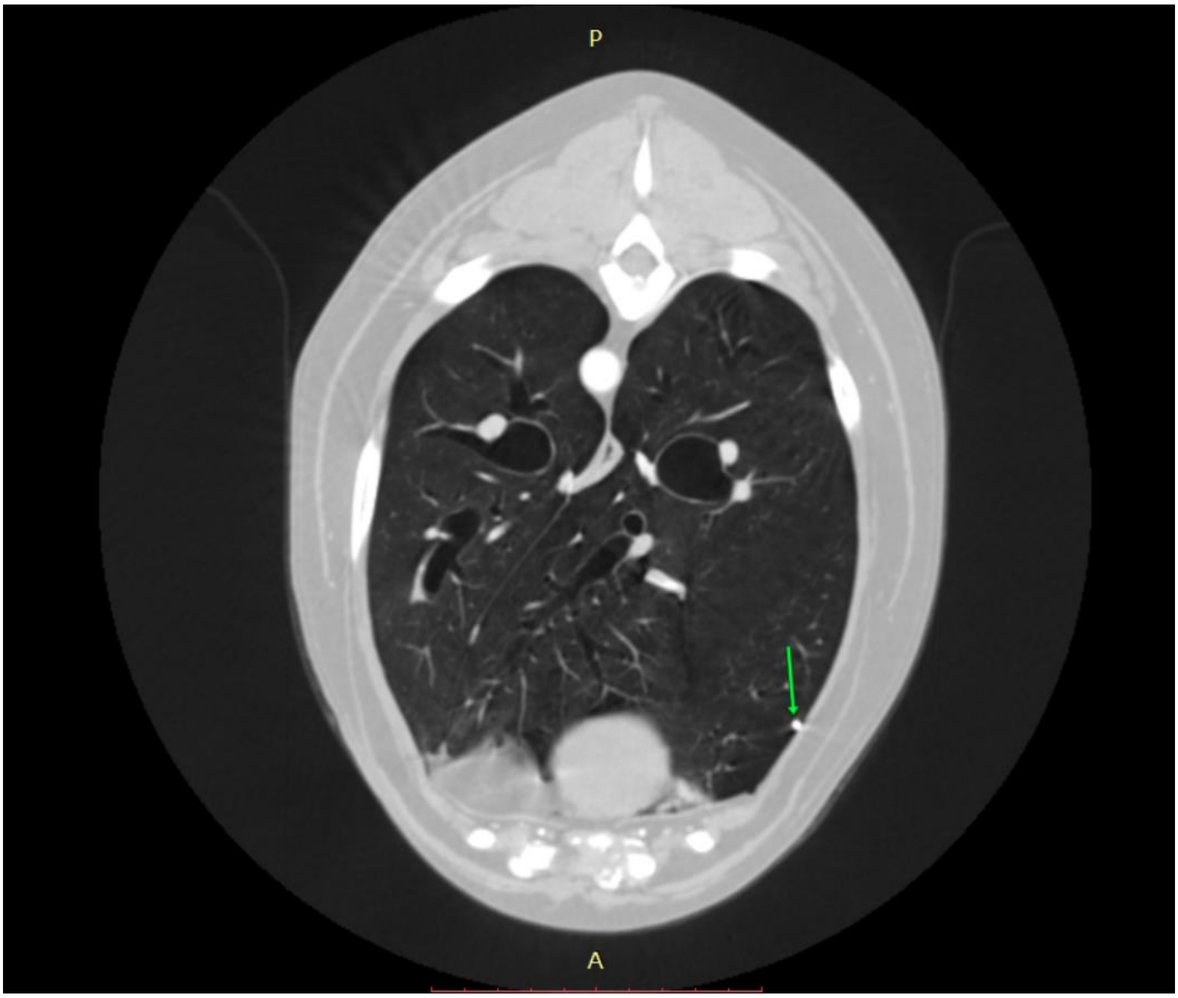

Figure 5.
Example of pulmonary nodule missing by the AI software, the arrow shows a small radiopaque nodule.

6. Discussion

To date, diagnostic imaging is still a basis of clinical evaluation, a quick and reliable interpretation is essential in daily practice, especially in a busy clinic. Imaging procedures are difficult to analyze even for experienced specialists, partly due to the structures that are difficult to detect with the naked eye, and partly due to a large number of not very specific, very similar details. Hence, the need for a tool to assist the daily routine diagnosis is increasing, and artificial intelligence is a branch of computer science designed to perform tasks that simulate human intelligence.

There are two types of AI methods that are widely used today. The first one is machine learning algorithms based on predefined engineered features, with clear parameters based on expert knowledge. The other one is a deep learning algorithm that does not require explicit feature definition and can automatically learn feature representations from data.

A suitable optimized AI or other program should be:

- easy to install and use
- able to scan CT images taken of the patient in seconds automatically
- after processing, could select the details it finds suspicious, drawing the doctor's attention
- able to help standardize image interpretation for different radiologists' experience, providing a second opinion for clinicians

Of course, even with high accuracy, a competent doctor is still needed to check and double-read the results of the program, it can significantly speed up the entire diagnosis process and reduce the false results.

Although AI used in veterinary radiology sprang up a little later than human medicine, it still has fast development in different aspects, particularly in thorax radiographs, and pulmonary detection is one of the common conditions.

Pulmonary nodules are often linked to lung cancers or metastasis.[1,27] Early detection of lung nodules is important for early intervention and increasing the survival rate.

Although CT shows better nodule detection performance, most of the small nodules are uncertain and need further evaluation. When searching for a tumor, a doctor often has to look through hundreds of CT (computed tomography) images, which is burdensome for the doctor and can take a long time, in addition, there are often not one, but several smaller tumors. This results in an increased workload, which could severely disturb the communication between physicians and radiologists' interpretation and be time-consuming. In places or rural areas where radiology examinations or radiologists can not be provided, direct care providers highly rely on teleradiology, and increasing workload could bring in sub-standard reports and misdiagnosis, this could severely impact patients' care and consequences. Thus, with the help of AI, radiologists can pay more attention to those cases with higher risk, can help correct potential misdiagnoses, and can provide immediate information to primary care providers in order to process more diagnostic tests and treatment without delay. Multiple studies in human medicine have shown variable success and variable sensitivity of AI in pulmonary detection and classification, by radiographs and CT scanning, to enhance physicians' performance.[48,49,50,51,52] However, studies testing for AI used in veterinary radiology pulmonary nodule detection are limited. One human medicine study uses a deep learning system to classify the malignant and benign nature of lung nodules.[31] One study from the USA assessed a commercially available AI product for detecting pulmonary nodules in canine thoracic radiography, result supports that AI would have a high positive predictive value but a lower negative predictive value.[53] Another study from Germany showed although the sensitivity of computer-assisted detection (CAD) of pulmonary nodules detections is lower than examiners, the sensitivity of examiners can be increased with the help of CAD.[54]

In order to develop accurate AI software, a training set must have adequate and appropriate dataset size, high-quality images, case varieties, accurate findings, and diagnosis on each training case. Overfitting is a common problem when the training set size is small. If the network receives the given patterns too many times during network learning, after a while it will not learn the patterns, but practically memorize the images. Moreover, providing at least more even number of cases of both nodules (<3 cm) and masses (>3 cm) will be better for the training of AI software. If there is not enough data available, a half-solution can be performed, for example, mirrored and 90° rotated images.

All the radiographs used for testing in this study came from the same institution, this could potentially lead to interpretation errors when using lower-quality radiographs. For example, the density of the slices has a lot of influence, the nodule appears elongated on a high-resolution image (it can look like a blood vessel), while on a low-resolution image, the blood vessel is compressed along its length (it can look like a nodule). If the background (the lung and surrounding tissues) changes significantly, it can make the work of the neural network not be able to estimate accurately. This suggests when validating a new AI software, it would be better to use datasets from different equipment of different operators.

One of the limitations of this study is there is no gold standard for example histopathology results were available to determine the true nature of the nodules, and further investigation will be necessary. Although catching sight of pulmonary nodule in a dog with malignant neoplasm may suggest metastasis, due to unspecific CT features, it is possible that some of the lesions resulted from benign or others, such as hematoma, hemangiosarcoma, osteosarcoma, lipoma, granulomas, fungi, abscess, septic embolus, parasites, immune-mediated diseases, congenital abnormalities, among others.[22,23,24,26] When developing an AI in the veterinary radiology field, providing a golden standard to optimally train an AI is questionable, to date the radiologist's reports have been mostly used as a golden standard. Although a histopathology report can be an alternative, not all cases have a final histopathologic diagnosis.

In human medicine, in North America, there are strict guidelines that AI algorithms must follow to gain approval, but there are no equivalent regulations in veterinary medicine. This could leave the veterinary profession vulnerable to misleading and potentially harmful diagnostic claims. Although most AI software is trained by a large and independent data set, it is still believed that the new technology should undergo an extensive validation process before its application to daily clinical work. In the meantime, practitioners need to understand both the value and pitfalls, as well as the potential errors that an AI product may cause. They are powerful but may give inappropriate answers. One study shows that non-radiologist clinicians have more trust in AI-issued reports confirmed by radiologists, but do not feel comfortable with reports produced by AI independently.[17] This raised the attention that radiologists should take over the responsibility before introducing AI into the practice and be actively involved in the interpretation, if any abnormality is detected, a veterinarian or radiologist should further double-check the images.

Ethical consideration of AI is one of the issues in human medicine, for example, a misuse of data has the potential to cause harm. This could possibly apply to veterinary medicine since we have the ability to perform euthanasia and the lack of regulatory validation for the new technologies to market. Thus, veterinarians and radiologists shall get involved when developing and using an AI, the products shall be transparent and provide information relating to data use, training, and validation. Besides, veterinarians shall be influenced only by the welfare and needs of the animals, safeguard medical information and records also the privacy of clients, and keep studying, applying, and advancing scientific knowledge. When errors occur, an analysis should be carried out to find out what is faulty.

In the future, AI may not only assist image interpretation, but it could also identify and filter those off-grade radiographs caused by, for example, improper positioning, the technicians would repeat the exam, increasing the efficiency of the clinical workflow.

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Thesis progress report for veterinary students

Name of student: ....Guo Jiaen...

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Thesis title: The use of artificial intelligence in CT diagnostics of pulmonary nodules in canine patients

Consultation – 1st semester

Timing				Topic / Remarks of the supervisor	Signature of the supervisor
	year	month	day		
1.	2023.	09.	18.	Topic selection	
2.	2023.	10.	01.	Source of literature, keywords for searching, research plan	
3.	2023.	10.	22.	Evaluation of the available literature data	
4.	2023.	11.	02.	Getting familiar with the AI software	
5.	2023.	11.	16.	First experience with data collection	

Grade achieved at the end of the first semester: ......5...............................

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Consultation – 2nd semester

Timing				Topic / Remarks of the supervisor	Signature of the supervisor
	year	month	day		
1.	2024.	02.	02.	First impressions about data analysis	
2.	2024.	03.	05.	Conclusion of data analysis	
3.	2024.	03.	20.	Preliminary evaluation of the written thesis I.	

4.	2024.			Preliminary evaluation of the written thesis II.	
5.	2024.				

Grade achieved at the end of the second semester: ....5....

The thesis meets the requirements of the Study and Examination Rules of the University and the Guide to Thesis Writing.

I accept the thesis and found suitable to defense,

....
signature of the supervisor

Signature of the student: ....

Signature of the secretary of the department: ....

Date of handing the thesis in....2024/11/20....