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Article

The use of computer vision to differentiate valley fever from lung cancer via CT scans of nodules

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SUMMARY

Pulmonary diseases, notably lung cancer and valley fever, pose significant health risks. Therefore, a swift and accurate diagnostic tool is imperative. This study sought to harness advanced technologies, integrating computer vision techniques with computed tomography (CT) scans, to differentiate between lung cancer and valley fever, thereby enhancing diagnostic precision. We hypothesized that the MATLAB-based software tool developed would discern minute and distinct features of lung nodules specific to either lung cancer or valley fever with more precision than traditional diagnostics. Upon use of Otsu's thresholding and object size filtering, distinct morphological features were extracted from binary versions of the images. The MATLAB-based software consistently detected and differentiated lung cancer and valley fever based on the nodules' features, such as solidity, extent, and roundedness, among others. While size wasn't a consistent indicator as per previous studies, features like solidity showed great contrast between the distinct images. Overall, the software demonstrated promising potential in providing features to differentiate between two critical pulmonary diseases. However, a future study is needed with a larger number of images to further validate and refine the prediction algorithm prototype developed in this work, ensuring its accuracy for potential implementation in clinical settings. Once the technique is fully developed, it could reduce the chances of human error and expedite early detection and intervention. Future enhancements may incorporate other imaging modalities, promoting diagnostic capabilities. The study underlines the transformative role of machine learning-based analysis of CT scans in revolutionizing healthcare diagnostics.

INTRODUCTION

Pulmonary diseases contribute to a substantial number of deaths in the United States, with 1,273 lung cancer deaths and 772 chronic obstructive pulmonary disease deaths occurring by 1998 according to the National Longitudinal Mortality Study (NLMS) spanning the years 1985 to 1996 (1). The spectrum of pulmonary diseases encompasses a diverse range of conditions that affect the respiratory system, with causes ranging from environmental exposures to genetic predispositions (2). These disorders can significantly impact respiratory function, leading to symptoms such as difficulty breathing, coughing, and chest tightness (3). Among these diseases, lung cancer and valley fever stand out as notable threats to respiratory health and overall well-being (4,5). Lung cancer, one of the leading causes of cancer-related deaths globally, poses a severe challenge to healthcare systems and individuals alike (6). Valley fever, also known as coccidioidomycosis, is a fungal infection caused by the inhalation of spores from soil-dwelling fungi (5,7). This disease is endemic to certain regions of the United States, particularly the southwestern states such as Arizona, California, and New Mexico (7). Traditional diagnosis can be a lengthy and time-consuming process, resulting in delayed diagnosis and treatment (8).

The diagnosis of lung cancer is a multifaceted process that combines clinical evaluation, imaging studies, and invasive procedures. Physicians initiate the diagnostic journey by evaluating a patient's medical history, identifying risk factors such as smoking, and assessing symptoms like persistent cough, chest pain, or unexplained weight loss (4,9). Imaging plays a pivotal role, with chest X-rays, computed tomography (CT) scans, positron emission tomography, and magnetic resonance imaging providing detailed views of the lungs and helping determine the extent of the disease (10). Definitive diagnosis often involves a biopsy, where a tissue sample is obtained through procedures like bronchoscopy, needle biopsy, or surgical intervention (9,11). Diagnosing valley fever involves a combination of clinical assessment, serological tests, imaging studies, and laboratory analyses (12). Physicians consider symptoms such as fever, cough, and fatigue, particularly in individuals residing in or traveling to regions endemic for Coccidioides, the causative agent of valley fever (12). Serological tests, including enzyme immunoassays, detect antibodies specific to the fungus and provide valuable diagnostic information (12). Imaging studies, such as chest X-rays or CT scans, contribute to the identification of lung infiltrates or nodules, typically benign masses in the lungs found during imaging tests, offering additional insights into the severity of the infection (12). In both lung cancer and valley fever, imaging plays a pivotal role in the diagnosis process.

As technology continues to advance, it becomes crucial to harness the power of machine learning and artificial intelligence in the medical field to enhance diagnostic and treatment capabilities (13). These transformative technologies have the potential to revolutionize diagnostics and treatment, paving the way for more accurate and effective healthcare practices (14). One area where this progress is particularly evident is in the field of medical imaging. Traditionally, X-rays have been a fundamental tool in medical imaging, providing valuable insights into the presence of abnormalities or injuries

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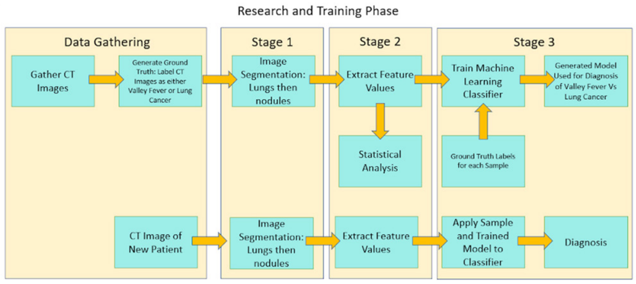

Figure 1: Overview of research and training phases. The top row shows the data gathering and training and bottom shows the clinical phase steps. The training software was put through these steps to output the extracted features of each CT scan image. During the clinical phase, physicians will obtain CT scans of new patients and can use the trained machine learning model from the training phase to identify lung features and diagnose the patient (future goal).

within the body (15). In medical imaging, multiple different images are often taken to obtain different perspectives of the lung and surrounding structures, including the sagittal and coronal views, for a comprehensive evaluation of pulmonary diseases. In the sagittal view, a vertical plane passes through the body longitudinally, dividing it into left and right sections (16). A specific type of sagittal plane, the median sagittal plane, runs down the midline of the body, separating it into equal halves. This allows for the examination of internal structures within the lungs, such as blood vessels and airways. Meanwhile, the coronal plane is a vertical plane perpendicular to the median plane. It divides the body into anterior (front) and posterior (back) parts, enabling evaluation of lung structure and surrounding tissues, aiding in the assessment of conditions like lung nodules, tumors, and pneumonia (17).

These imaging techniques are invaluable for diagnosing and monitoring pulmonary conditions, such as lung cancer and infections, by providing a detailed visualization of the anatomy and pathology within the chest cavity (18). However, when it comes to diagnosing complex conditions or obtaining detailed information about specific organs or tissues, more advanced imaging techniques are often required. This is where CT scans come into play (19,20). CT scans utilize a series of X-ray images taken from different angles to create cross-sectional images of the body (20). Through a CT scan, radiologists can see four defining features crucial to a proper diagnosis: nodule diameter in greatest dimension, nodule density, border characteristics, and the presence of cavitation, an area of the lung filled with gas (21). The presence of cavitation will be shown through an empty or hollow space shown on the CT scan (22).

In 2022, research conducted by Zaharudin et al. provided insights into the management of lung nodules, aiding in the evaluation of benign and malignant tumors in the diagnosis of tuberculosis (21). This research employed statistical methods such as the Chi-square test, Mann-Whitney U test, and simple logistic regression (21, 23). Their results indicated that border characteristics, such as the appearance and definition of nodule edges, were of utmost importance when evaluating the nodule features. So, using this knowledge and additional factors, the machine learning approach will be able to diagnose patients accurately and quickly with lung cancer or valley fever. While there have been previous studies done

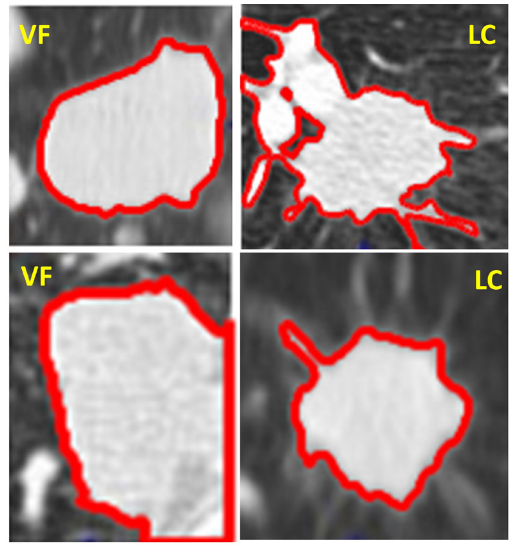

Figure 2: Lung nodule image segmentations. The segmentations of valley fever (VF) and lung cancer (LC) nodules are shown. The MATLAB-based software was fed these images to produce accurate results indicating morphological features specific to each disease. The segmented outline and original cropped images were overlaid for the purpose of visualization.

manually (24), mainly using X-rays to recognize pneumonia using apparent features such as pleural effusion, to the best of our knowledge, this research was the first to propose a program that distinguishes two detrimental diseases using specificity and accuracy of image segmentation and classification.

In our study, we aimed to utilize computer vision, or techniques such as segmentation and classification allowing a software to analyze and interpret visual data, to differentiate between lung cancer and valley fever using the four defining features listed above. With our training software, or program designed for experimentation, relying on segmentation and classification we were able to measure major indicators of lung cancer and valley fever nodules such as size, density, solidity, and diameter. This proactive approach holds the potential to prolong patient lives and optimize their chances of recovery. In this paper, we segmented nodules from CT scans and then extracted a set of features, using the MATLAB-based software, that can be used to identify characteristic indicators of lung cancer and valley fever. These features can be used in our proposed computer vision and machine learning pipeline. This proposed application will address two specific aims: the early detection and diagnosis of lung cancer and distinguishing between valley fever and lung cancer using nodule imaging.

RESULTS

Our MATLAB-based software showed contrasting visual aspects of the lung cancer nodules compared to the valley fever infected nodules. Steps of a typical machine learning and training algorithm include data gathering, training, and the clinical phase (**Figure 1**). Stage 2: Feature Extraction was the main focus of our research. The training software was put through these steps to output the results of each CT scan image including circularity, density, equivalent diameter, and nodule segmented outlining. Four nodule extractions,

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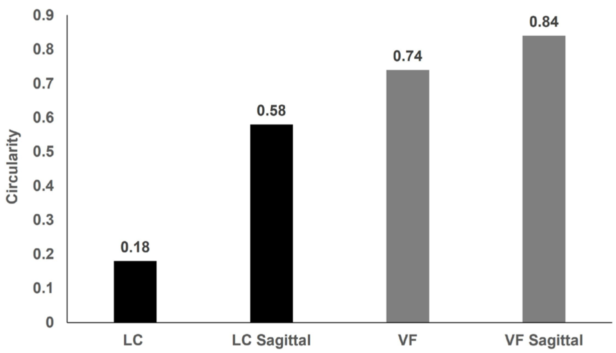

Figure 3: Circularity patterns of nodules. Nodule circularity of valley fever (VF) and lung cancer (LC) nodules measured in pixels for both coronal and sagittal view. Images of nodules respective to each disease were fed to the software for it to output exact measures of circularity. The bars represent the average of the two images used for analysis, and the number at the top of each bar indicates the average, with the number of samples (n = 2).

two of which are valley fever nodules and the other two of which are lung cancer nodules are shown (**Figure 2**). The apparent and non-apparent features were then translated to exact measurements by the MATLAB-based software, to provide detailed examination. Two of the most crucial extraction features, solidity (how solid objects appear) and extent (the spread of objects within the images), increased in the valley fever nodules (**Table 1**). This indicates that valley fever nodules have a higher level of opacity, perhaps due to the dust particles and fungus growth inside the lungs, but also may point to the severity of valley fever since higher levels of opacity indicate more dense features inside the lungs (25). Another important feature is measuring the roundedness, or circularity, of the nodule (**Figure 3**). The lung cancer nodules proved to be much less rounded than the valley fever nodules and therefore more spiculated, or spiked at the surface, as shown by the sharp edges of the lung cancer nodule extractions (**Figure 1**). As for lung size, the diameter measurement indicated that the valley fever nodules to have a smaller size than lung cancer. We compared diameters across the different angles taken of the nodules (**Figure 4**). The software identified the primary lung nodule features, which could then be associated with each disease for a more accurate diagnoses. The source code used to generate our results can be found at https://github.com/VincentOn/ExtractNodules.

DISCUSSION

As pulmonary diseases, including lung cancer and valley fever, continue causing numerous deaths each year, it is important to implement rising technologies into current healthcare practice. This is especially important considering that valley fever is easily confused with other diseases in the healthcare practice (26). Considering frequent misdiagnosis, in this study we provided useful information about the features that can be used to differentiate between valley fever and lung cancer nodules. This information might be useful in developing software that utilizes computer vision techniques to automatically detect and differentiate between lung cancer and valley fever in CT images of patients. CT scans will allow for greater advantages than X-rays, such as improved sensitivity to nodules and enhanced visualization.

Sample	LC	LC Sagittal	VF	VF Sagittal
Area (pixels)	5373	2343	2573	3253
MajorAxisLength (pixels)	116.91	59.05	72.49	75.81
MinorAxisLength (pixels)	73.90	53.61	46.38	56.08
Eccentricity	0.78	0.419	0.769	0.67
Orientation (degrees)	-37.01	-36.45	-72.25	34.00
ConvexArea (pixels)	8844	2775	2704	3453
FilledArea (pixels)	5589	2343	2573	3253
Solidity	0.61	0.84	0.95	0.94
Extent	0.45	0.62	0.81	0.73
Perimeter (pixels)	603.79	222.25	206.26	217.76
MaxFeretDiameter (pixels)	149.33	73.50	76.61	78.57
MaxFeretAngle (degrees)	-137.44	-123.91	-125.97	132.42
MinFeretDiameter (pixels)	89.57	56.62	47	60.46
MinFeretAngle (degrees)	126.49	100.30	0	59.74

Table 1: Characteristics of valley fever (VF) and lung cancer (LC) nodule. Exact measurements of the lung nodules found from CT scans by the novel software's segmentation using the "regionprops" function from MATLAB's Image Processing Toolbox. The numbers represent the average of the two images used for analysis (n = 2).

Following training, the software can be implemented in the clinical setting, contributing to early and accurate diagnosis.

Peterson et al. found that the lung nodules for lung cancer and valley fever differed by size, smoothness, and density (27). This analysis was done by visual inspection with two chest radiologists. While this method is appropriate, it is also inherently subjective. This affects many of their metrics such as their evaluation of smoothness and density. Their manual measurements would also limit their results to less descriptive features, such as diameter and region thickness. By applying computer vision, additional metrics, such as texture, extent, and density, can be extracted for more perspectives and more precise analysis of lung cancer and valley fever. These features will also reduce the visual bias of the radiologists and allow them to make a more informed diagnosis.

While many kinds of features can be extracted, they vary in their ability to discriminate between the two conditions. Of the observed samples, nodule size was not consistent with Peterson et al.'s findings since larger nodules indicated valley fever. Working with only a few 2D segmentations at specific locations, our study simply states that it is possible to

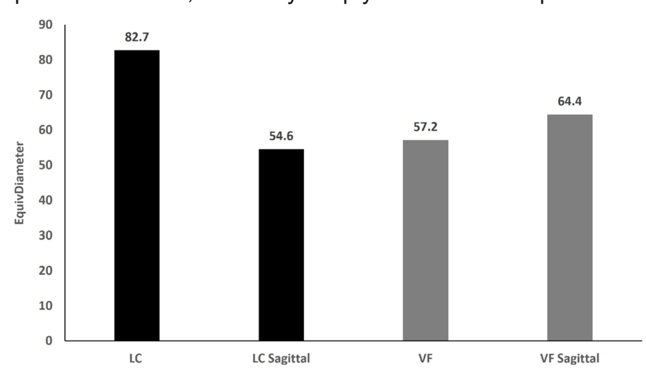

Figure 4: Diameter patterns of nodules. Diameter of valley fever (VF) and lung cancer (LC) nodules measured in millimeters for both coronal and sagittal view. Images of nodules respective to each disease were fed to the software for it to output exact measures of diameter. The bars represent the average of the two images used for analysis, and the number at the top of each bar indicates the average, with the number of samples (n = 2).

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Nodule Features	Biological Relevance	Potential Extracted Feature
Size	Measured in millimeters; larger nodules are more likely to be malignant than smaller nodules (27)	Diameter, Area, Perimeter, Major Axis, Minor Axis, Radius
Intensity	Higher intensity can indicate the presence of calcifications and fat, while low intensity indicate fluid-filled regions (18, 26)	Density, Variance, Texture Patterns
Morphological	Spiculated borders of a nodule can indicate malignancy; smooth and well-defined modules are less likely to be cancerous (27)	Solidity, Extent, Eccentricity, Protrusions
Location	A nodule close to major structures, such as blood vessels, airways, or the pleura, might raise concerns about potential complications or treatment options (18)	Centroid

Table 2: Extractable computer vision features of lung nodules. List of features that could be extracted via the novel software and their potential biological relevance.

Features Over Time	Biological Relevance	Potential Extracted Feature
Growth	Indication of detrimental diseases including Lung Cancer, fungal infections, or inflammatory infections such as Sarcoidosis (27)	Change in Area, Direction of Growth
Intensity change	Dense nodules may suggest the presence of calcifications or mineralization, while less dense nodules indicate fluid-filled, or less solid masses (18, 27)	Change in Intensity, Density change, Pattern Changes

Table 3: Extractable computer vision features of lung nodules over time. List of features that occur over time in the lung nodules as well as their potential biological relevance.

extract features while not making any biological conclusions. This indicates that viewpoint is extremely important and volume analysis is beneficial. This is likely due to the size of lung nodules in a CT scan being dependent on the imaged location. While CT scans typically cover the entire lung, they capture different viewpoints, such as the sagittal views. The variation in location within the lung can affect the apparent size of nodules due to the differences in perspective and lung anatomy (28). A possible improvement would be to acquire 3D scans or analyze a 3D reconstruction of the lung nodules. One of the most interesting features extracted is solidity. Solidity is the proportion of pixels in the convex hull (the smallest convex shape that can contain a specific shape) of the nodule that are also in the nodule itself. In the context of lung nodules, solidity indicates how filled or compact the nodule appears in its space, with a higher value suggesting a more dense structure and a lower value suggesting an irregular or fragmented appearance. The closer this value is to 1, the more convex the nodule is. This also implies that the nodule is smoother. Our results for solidity are consistent with the observations in Peterson et al. (27). Similar findings are shown with circularity (a measure of roundness given as a function of the object's area and perimeter) and extent (a ratio related to an object's bounding box, or surrounding geometric shape).

While we provide comparison of several of the features individually, it should be noted that combinations of features might provide a more accurate diagnosis. In future versions, the software will be enhanced to support other imaging modalities, including X-rays, in order to provide complementary perspectives (29). Studying multiple features at the same time can be difficult for a human being, but by using machine learning more conclusions can be made about the differences between valley fever and lung cancer nodules. Despite the obtained results, we have to note that we only used a small number of chest images due to restrictions on the availability of images for non-medical researchers. This limitation affected our ability to carry out a statistical analysis. While only single-value features were extracted for simplicity, multi-valued features may offer additional insights for future studies. Although we have provided useful information on determining the metrics that can be used by the software to distinguish between valley fever and lung cancer, our findings open the door for more sophisticated methods involving a large number of images and statistical analysis. This paper proposes a software solution that utilizes computer vision techniques to automatically detect and differentiate between lung cancer vs valley fever in CT images. By leveraging the advantages of CT scans over x-rays, such as improved sensitivity to nodules and enhanced visualization capabilities (30,31), the software aims to contribute to the early and accurate identification of these diseases.

MATERIALS AND METHODS

This program extracts and saves morphological features from segmented lung CT images. This includes a range of potential computer vision features that can be extracted, along with their corresponding biological relevance (**Tables 2 and 3**). Lung CT scans were acquired from Peterson et al. by cropping the regions indicated as nodules (27). Four images were tested: two representing valley fever and two indicating lung cancer. The images were converted to grayscale, and Otsu's thresholding was applied. Otsu's method binarizes the grayscale image by automatically calculating an optimal threshold to separate objects of interest from the background (32). Following this, object size filtering was applied to the binary output to eliminate smaller connected components such as other structures, noise, or artifacts. After the images were cropped, the largest objects remaining were the nodules of interest. Once a silhouette of the nodule was obtained, morphological features were extracted from the binary image. The segmented outline and the original cropped images were overlayed (**Figure 2**).

All features were extracted using the "regionprops" function from MATLAB's Image Processing Toolbox (33) (**Table 1**). Nodule diameter refers to the size of the nodule, measured as the longest distance across it and measured in millimeters. Nodule density includes evaluation of texture categorized as a solid (dense) or mixed (a combination of solid and less dense areas) appearance. Border characteristics involve the description of the edges of the nodule. It can be smooth (even and regular), lobulated (having lumps or bumps), or spiculated (having irregular or spiky edges).

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