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Report Proof of Concept
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DEEPLUNG-CT
A SYSTEM FOR AUTOMATIC TEMPORAL ANALYSIS OF PULMONARY NODULES FOR CANCER ASSESSMENT THROUGH CT SCANS

Report developed by:
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1. Abstract

Few works provide automatic support on the temporal evolution of pulmonary nodules. In this document, we present an end-to-end solution able to run asynchronous automatic pipeline analysis, to detect, quantify and predict nodules and their malignancy. Our system shows the results of the temporal analysis of pulmonary nodules in an intuitive and informative front-end interface, designed to support clinicians in their daily decision-making routine.

2. Introduction

Radiologists through the visual inspection of computed tomography (CT) scan images can detect and measure the evolution of abnormal tissue in the lungs of the patient's chest [1,2]. Unfortunately, in the light of the aggressiveness of this disease, its important incidence in the adult population, and the constant need of specialized professionals, it is required to provide accurate and efficient tools to reduce the workload of clinicians as well as helping them to make critical decisions.

Providing automatic support for the detection and diagnosis of lung cancer is not new and, intense efforts have been made deploying machine learning and artificial intelligence techniques [3-5]. Specifically, for lung cancer, outstanding performances have been achieved in a brief period of time, outperforming conventional approaches for nodule detection [6], pixel segmentation [7], or lung cancer classification [8]. Despite all these efforts, most of the research focuses primarily on a single CT scan so that valuable information on patient trajectories is missed or overlooked.

In this paper we describe a system that aims to take a step forward in supporting radiologists for lung cancer assessment. To this end, the system takes into consideration the evolution of the pulmonary nodules in the predictive modelling task. Therefore, we have developed a pipeline that automatically detects lung nodules and re-identifies them from different CT scans. Additionally, it quantifies nodule growth and provides the associated malignancy. The system is also composed by a web front end that permits, in an informative and intuitive way, visualizing the results of the temporal lung nodule analysis.

3. Description about the problem to solve

Lung cancer assessment is a challenging, time-consuming and tedious work in which radiologists must determine the most appropriated interventions for patients. This process mainly involves the detection of pulmonary nodules, the quantification of growth and the prediction of malignancy. To support physicians in this complex process, the area of computer vision and artificial intelligence has contributed with an extensive and rich literature on the matter.

During nodule detection radiologists have to screen the entire lung CT volume, searching for small suspicious regions or nodules (normally between 3 mm to 30 mm) [24]. To this end, several deep learning works [15-17] have been provided through two step processes. Typically, these solutions consist on a 2D region proposal network (RPN), to detect the nodule candidates, and a 3D convolutional neural network (CNN), to filter nodule candidates from the normal tissues. More recent approaches address this task in a single-stage process [18-20] integrating both components (the RPN and the CNN classification) in a same 3D architecture, to directly predict the 3D bounding boxes that surround the nodules.

Another important task for lung cancer assessment is quantifying the size of the nodule. Usually, this process is manually performed by the experts, but it entails a significant inter-observer variability (e.g. 3 mm of nodule diameter difference [21]). To support clinicians in this task, several deep learning solutions have been proposed. In [18, 19], authors propose to automatically learn the diameter of the nodule by adding a new output to the nodule detection network. Other solutions [13,23] propose building pulmonary nodule segmentation networks, relying on the U-Net [22] framework, to automatically determine the pixels of the nodules, and subsequently quantifying the size of the nodules. Alternatively, other solutions have addressed this problem using generative networks. For instance in [25], a hierarchical probabilistic U-Net (HPU) is detailed to model inter-observer segmentation variability by combining the generative ability of the variational auto-encoders [14], with the accuracy of segmenting images of the U-Net. To do this, during training, a posterior U-Net like network, conditioned on the radiologist ground truth nodule, is added to transfer the latent features to a prior U-Net like network by injection, at distinct levels of the decoder part of this network.

Another crucial task for radiologists is lung cancer diagnosis. In [26], an end-to-end deep learning-based pipeline was presented for lung cancer prediction using two CT studies per patient (current and previous year). This approach applied three 3D CNN networks, one for analysing the image at lung CT level, other at nodule patches level, and a final one, to provide cancer risk prediction using outcomes from the previous two components. In [27], a deep learning approach was proposed for assessing lung cancer risk with a 3-year span as well as assessing lung cancer-specific mortality.

In the following sections, we present an integrative solution capable of managing the temporal evolution of lung tumours and supporting physicians in the aforementioned tasks.

4. Implementation of Solution

4.1 Temporal Lung Nodule Assessment

In [12], we presented and evaluated an automatic and flexible pipeline to support radiologists in the nodule follow-up analysis. This pipeline takes as an input two images from the same patient at different time-points (T1 and T2), identifies lung nodules, and estimates their malignancy and growth. The pipeline consists of 4 main components (see Figure 1): 1) nodule detection, which is done independently on each image; 2) nodule re-identification, which finds the correspondence between nodules across time points; 3) nodule malignancy classification; and 4) nodule growth quantification.

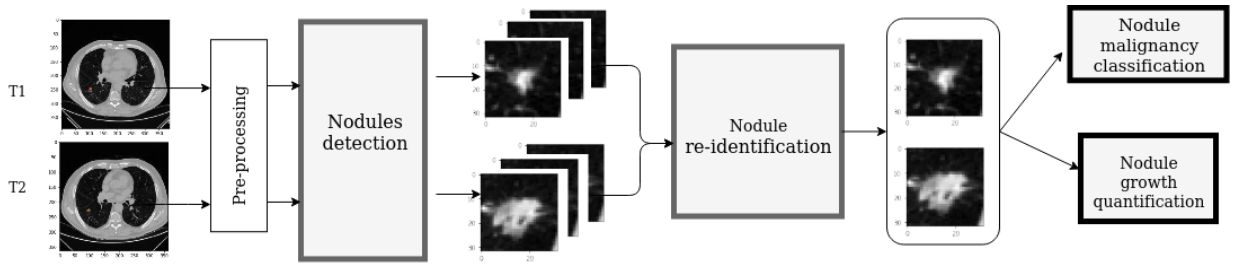

Figure 1. Pipeline architecture for the temporal analysis of lung nodules

The entire pipeline analysis is summarized as follows (For further details regarding each of the components and its evaluation, we address the reader to the original paper [12]):

- Before to automatically analyse both studies, the pipeline performs an initial pre-processing with the aim of standardizing the input images. Then, the pipeline performs the detection of the pulmonary nodules on each of the CT scan images individually. To do this, the pipeline uses a deep neural network which follows a Faster-RCNN schema [21] adapted for 3D images of [128x128x128]. The output of this network is the location of the nodules (x, y, z coordinates), the diameter, and a probability of being a nodule.

- Once the nodules from the two different CT scans of the same patient are detected, the pipeline performs a re-identifying process to find matching nodules from both CTs. To this end, the pipeline implements a 3D Siamese neural network (3D-SNN) composed of a feature extraction component and a tailored classification head component [10]. The feature extraction component expects as input two nodule patch images of [32x32x32] from two different studies. These images are analysed by a two-stream 3D ResNet-34 network with pre-trained weights obtained from [9]. The classification head component receives the previously extracted temporal and spatial features and predicts whether both nodule images match. To do this, the classification component is configured with a L1-pairwise distance, a flattening layer, and a fully connected (FC) block with a final FC layer (with one unit).

- Given the re-identified nodules, the pipeline is aimed at quantifying the nodule growth. To this purpose, the pipeline uses a hierarchical probabilistic network [25]. This network can generate multiple consistent segmentation outputs for a given nodule patch image. Thanks to this property of the network, a Monte Carlo sampling (N=1000) is performed to estimate a random vector of N diameters for the nodule. Repeating this process for the re-identified nodule images, the network provides the expected diameter growth (as the mean difference of both random diameter vectors) and its associated uncertainty (as the squared root of the sum of the variances of the difference of both random diameter vectors).

- In parallel, the pipeline also performs a nodule malignancy classification for each of the re-identified nodule pairs. To do this, a network (TS-3DCNN-MAL) was trained using clinically confirmed pulmonary nodules (either benign or cancerous). The network relied on a two-stream 3D CNN, defined in [11], attached with a classification head component that eventually provides the cancer probability risk for the nodule. One of the particularities of this network is that the classification head component concatenates 6 additional probability features, coming from a nodule malignancy network for each of the re-identified nodules. This network, defined in [9], was trained using nodule malignancy annotations provided by the radiologists (without clinical confirmation). Therefore, this network outputs 3 features (one per each of the 3 nodule malignancy categories used: benign, suspicious, and malignant) per each of the nodules to classify.

4.2 Front End Interface

We have developed a web front end interface to demonstrate the viability of the current solution. Thanks to this interface, an end user is able to upload several image studies of a patient, to perform the temporal nodule analysis (described in section 3), and examine the corresponding results in a visual and practical way.

Figure-2 shows the findings detected for a single image study. In the main panel of the screen, we find, on the left side, a slice navigator with the axial slice of the lung in which a nodule was found. On the right side, we find a clickable table with the nodules detected by the pipeline. The table also shows information regarding the location, diameter, “subjective” malignancy, and other related features computed from the pipeline results (e.g. nodule area in the slice, volume, and density). Below the slice navigator, we observe a zoom component which shows an augmented view of the area of interest in which the nodule was found. This zoom component is updated every time the user moves the cursor above the main slice navigator. The nodules are automatically surrounded by a red circle. Other extra functionalities are available for the radiologists such as showing the pixel segmentation of the nodule, adding comments directly on the slice image or a full-screen view.

Figure 2. Findings section screen of the front end interface with the results of a CT study

Figure-3 shows a screen with the results of the temporal evolution of a selected nodule. The re-identified nodules can be examined directly using the two slice navigators located on the centre of the screen. However, a table with the detected and re-identified nodules from both studies is shown on the bottom part of the screen. Furthermore, the screen also shows the exploration capabilities of the tool by showing a zoom component, updated when the user moves the cursor over the slice navigator.

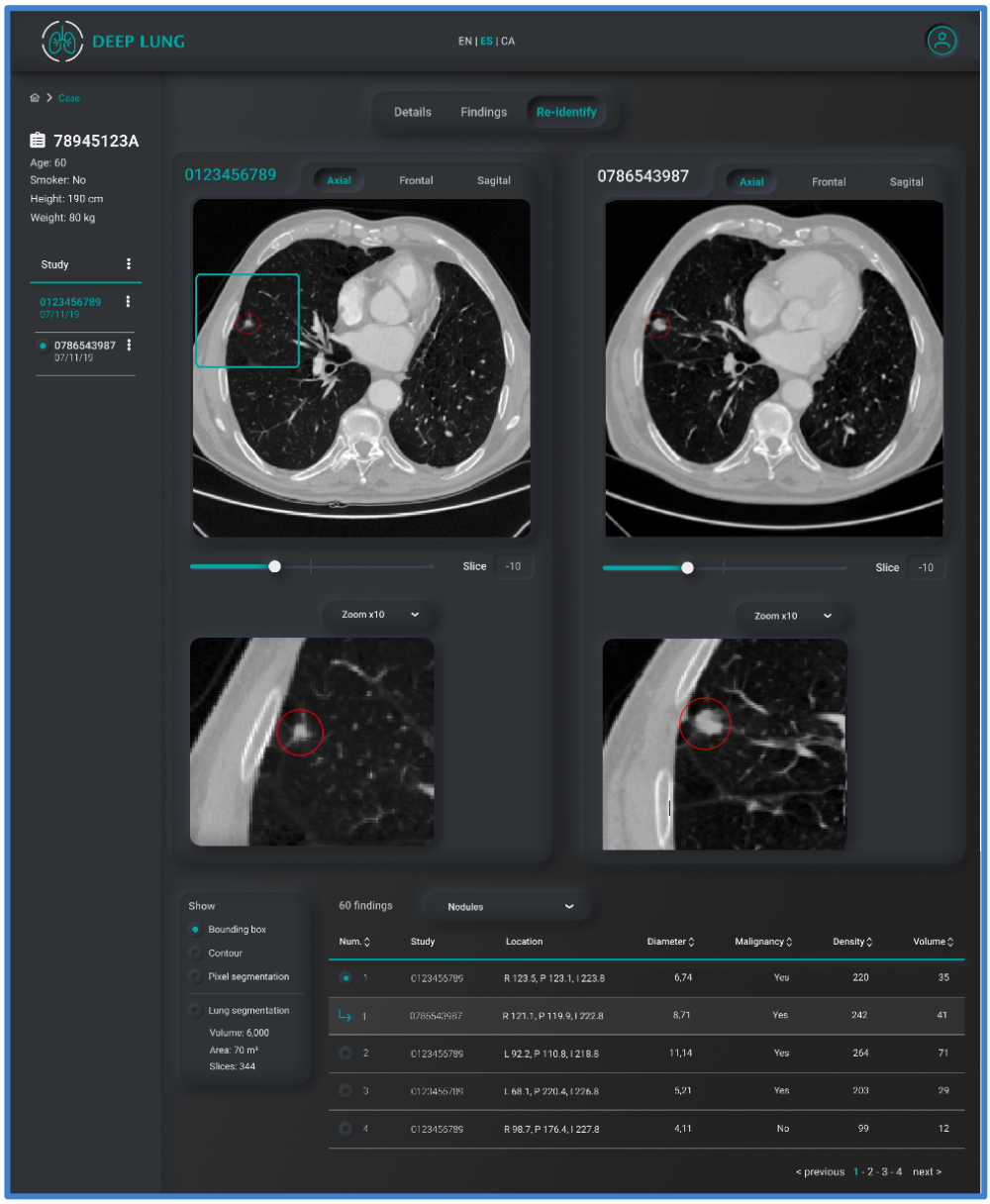

Figure 3. Screen with the results of the re-identification analysis. In this particular example, we observe the same nodule found in both CT studies, its growth (from 6.74 to 8.71 mm) as well as its malignancy (i.e. cancer risk).

5. Potential Impact of Solution

Our system offers several aspects that could potentially impact and benefit the current radiological practice:

- Nowadays, most lung cancer decision support systems ignore the time course of the nodules, which can lead to misleading or incorrect conclusions. Our system incorporates this temporal information in the modelling stage of the predictive methods allowing to predict more reliable and accurate outcomes.

- Our system allows to run end-to-end automatic pipeline analysis which partially automatize the whole radiological workflow involved in lung cancer assessment. This should permit saving time to the specialists and cost to the clinical institutions.

- Our system counts with an intuitive and informative front end that should allow clinicians to be more effective and efficient in their day-to-day routines. Precisely, the front end was organized to summarize in few screens all crucial information and main functionalities resulting from the automatic temporal lung nodule analysis.

In this paper we addressed the problem of supporting radiologists in the lung nodule follow-up. To this end, we presented a system able to run deep learning pipeline analysis, capable of detecting nodules, re-identifying them on different studies, providing nodule growth and the probability of being cancerous. Finally, a front-end interface was proposed to run the temporal lung nodule analysis and visually examine the corresponding results, in an intuitive and informative way, to support clinicians save time and provide more accurate diagnoses.

6. Acknowledgements

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