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## Pattern Recognition



journal homepage: www.elsevier.com/locate/pr

# Multi-crop Convolutional Neural Networks for lung nodule malignancy suspiciousness classification

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#### ARTICLE INFO

Article history: Received 28 January 2016 Received in revised form 29 April 2016 Accepted 24 May 2016

Keywords: Lung nodule Malignancy suspiciousness Convolutional neural network Multi-crop pooling

#### ABSTRACT

We investigate the problem of lung nodule malignancy suspiciousness (the likelihood of nodule malignancy) classification using thoracic Computed Tomography (CT) images. Unlike traditional studies primarily relying on cautious nodule segmentation and time-consuming feature extraction, we tackle a more challenging task on directly modeling raw nodule patches and building an end-to-end machinelearning architecture for classifying lung nodule malignancy suspiciousness. We present a Multi-crop Convolutional Neural Network (MC-CNN) to automatically extract nodule salient information by employing a novel multi-crop pooling strategy which crops different regions from convolutional feature maps and then applies max-pooling different times. Extensive experimental results show that the proposed method not only achieves state-of-the-art nodule suspiciousness classification performance, but also effectively characterizes nodule semantic attributes (subtlety and margin) and nodule diameter which are potentially helpful in modeling nodule malignancy.

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#### 1. Introduction

Lung cancer is an aggressive disease carrying a dismal prognosis with a 5-year survival rate at 18% [1]. Despite the development of multi-modality treatments over the past decade, lung cancer remains the leading death of cancer and accounts for approximately 27% of all cancer deaths [2]. Technological advances in Computed Tomography (CT) have been routinely used in lung cancer detection, risk assessment, and clinical management. In particular, the increasing quantity of CT image assays has created a unique avenue for data-driven analysis to capture underlying cancer characteristics at a macroscopic level, allowing identification of prognostic imaging biomarkers [3].

In this study, we investigate the problem of automatic lung nodule malignancy suspiciousness classification using CT imaging data. The annotation of nodule malignancy suspiciousness has permitted a chance to evaluate consensus assessments from

URL: http://www.3dmed.net (J. Tian).

http://dx.doi.org/10.1016/j.patcog.2016.05.029 0031-3203/© 2016 Elsevier Ltd. All rights reserved. different experienced radiologists. Specifically, the automatic classification of malignancy suspiciousness on CT studies is a worthy task, because it would facilitate radiologists to assess early risk factors which is essential in lung cancer research [4,5]. A typical implication of such analysis is to provide useful cues for subsequent therapeutic plannings and holds promise for improving individualized patient management. For example, distinct malignancy likelihood derived from imaging can be used to recommend follow-up treatments including CT surveillance (e.g. low likelihood score) or biopsy test and surgical resection (e.g. high likelihood score) [6]. Despite different approaches were proposed for lung nodule diagnosis, novel data-driven techniques are required to advance the predictive power with CT imaging, especially for the prediction on malignancy suspiciousness.

Image-based techniques for analyzing lesions are normally performed with detection [7,8], segmentation [9–12], hand-crafted feature engineering [13,14], and category labelling [15–18]. Zinovev et al. [19] adopted a belief decision tree approach to predict nodule semantic attributes. Chen et al. [20] proposed to use a neural network ensemble scheme to distinguish probably benign, uncertain and probably malignant lung nodules. Han et al. [16] used a 3-D image-based texture feature analysis for nodule diagnosis. More recently, Balagurunathan et al. [14] and Aerts et al. [13] extracted a number of nodule image features to investigate their prognostic

Please cite this article as: W. Shen, et al., Multi-crop Convolutional Neural Networks for lung nodule malignancy suspiciousness classification, Pattern Recognition (2016), http://dx.doi.org/10.1016/j.patcog.2016.05.029

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#### Table 1

Some classification results on LIDC-IDRI dataset from literatures. "NA" denotes "nodule attributes" and "MS" denotes "malignancy suspiciousness".

Related work	Label	Accuracy	AUC	Sample size
Zinovev et al. [19]	NA	54.32%	-	914
Chen et al. [20]	MS	78.70%	-	47
Han et al. [16]	MS	-	0.927	1356

power. Related studies on the Lung Image Database Consortium and Image Database Resource Initiative (LIDC-IDRI) dataset [21] are shown in Table 1. However, all these methods rely on nodule segmentation as a prerequisite. Notably, automatic nodule segmentation may affect classification results since methods such as region growing and level set typically depend on initialization. Working on these segmented regions may yield inaccurate features that lead to erroneous outputs. To derive a suspiciousness-sensitive descriptor in CT imaging, we need to overcome at least two major obstacles: the difficulty of nodule delineation caused by a large range of nodule morphology variation, and the challenge posed by the nodule radiological heterogeneity for computational models to capture quantitative characteristics.

Image patch-based approaches provide an alternative way for the region of interest (ROI) definition [22,23]. Researchers are seeking visual feature descriptors, such as Local Binary Patterns (LBP) [24] and Histogram of Oriented Gradients (HOG) [25], to refine measurement on lung cancer imaging. Nevertheless, the yielded textural features are largely determined by the parameter setting. Thus, using them to accurately describe the variability of lung nodules is difficult.

In response to these challenges, we utilize the Convolutional Neural Network (CNN) [26–28] to build an end-to-end computational architecture which is robust in lung nodule image feature extraction and malignancy suspiciousness classification. We propose a computational architecture—the Multi-crop Convolutional Neural Network (MC-CNN)—to learn high-level suspiciousnessspecific features for lung nodule classification. As outlined in Fig. 1, our approach automatically classifies nodule malignancy suspiciousness by extracting a set of highly compact features. It is an end-to-end architecture which embeds nodule feature extraction into a hierarchical network. The proposed method simplifies conventional lung nodule malignancy suspiciousness classification by removing nodule segmentation and hand-crafted feature (e.g., texture and shape compactness) engineering work. Our main contributions can be summarized as follows:

- 1. We demonstrate that even without nodule segmentation and hand-crafted feature engineering which are time-consuming and subjective, the high-level features extracted by our MC-CNN from detected nodule patches are able to present high interclass variations related to nodule malignancy suspiciousness (Fig. 2), bridging the gap between the raw nodule image and the malignancy suspiciousness.
- 2. We propose a multi-crop pooling operation which is a specialized pooling strategy for producing multi-scale features to surrogate the conventional max-pooling operation. Without using multiple networks to produce multi-scale features, the proposed approach applying on a single network is effective in computational complexity (Section 4.2).
- 3. Beyond nodule malignancy suspiciousness classification, we extend the proposed approach to quantify nodule semantic labels as well as to estimate nodule diameter that may potentially assist researchers in evaluating malignancy uncertainty (Section 4.5). Our results showed the possible applications of the proposed method in other lung nodule-relevant analysis that may potentially assist researchers in evaluating malignancy uncertainty.

Applying a supervised learning scheme in deep feature extraction, our approach is in contrast with an auto-encoder approach [30] that applied an unsupervised learning method without prior labeling information. The proposed method also differs from our previous work based on the multi-scale CNN model [31] which utilized multiple CNNs in parallel with different scales of nodule images. In [31], a resampling strategy was used to uniformly represent nodule patches. However, multiple networks become the main burden for training CNNs efficiently since they involve more computational costs, especially when dealing with high-resolution images. As opposed to the design of multiple CNNs [31], the proposed model simplified the training process by replacing multiple CNNs with the multi-crop pooling architecture that is specially tailored to lung nodule malignancy suspiciousness classification. Furthermore, our model underscored the knowledge extraction from feature space rather than image space. In other words, the computation is specified on the intermediate convolutional features (i.e., feature space), rather than different scales of raw input signals (i.e., image space).

The rest of the paper is organized as follows. Section 2 introduces the proposed multi-crop CNN architecture. Section 3 presents the detail of the dataset and data augmentation. Section 4 describes the experimental setup and results. Section 5 is the discussion and Section 6 concludes the paper.



**Fig. 1.** The proposed MC-CNN architecture for lung nodule malignancy suspiciousness classification. The numbers along each side of the cuboid indicate the dimensions of the feature maps. The inside cuboid represents the 3-D convolution kernel and the inside square stands for the associated 2-D pooling region. The dimension of the final hidden feature layer is marked at the bottom. The output layer is a softmax layer that predicts the probability of the class of nodule malignancy suspiciousness, i.e., low malignancy suspiciousness and high malignancy suspiciousness. The pink arrow indicates a multi-crop pooling layer that serves as a surrogate of a max-pooling layer for improving classification performance. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.)

Please cite this article as: W. Shen, et al., Multi-crop Convolutional Neural Networks for lung nodule malignancy suspiciousness classification, Pattern Recognition (2016), http://dx.doi.org/10.1016/j.patcog.2016.05.029

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