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Automatic detection of subsolid pulmonary nodules in thoracic computed tomography images

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ABSTRACT

Subsolid pulmonary nodules occur less often than solid pulmonary nodules, but show a much higher malignancy rate. Therefore, accurate detection of this type of pulmonary nodules is crucial. In this work, a computer-aided detection (CAD) system for subsolid nodules in computed tomography images is presented and evaluated on a large data set from a multi-center lung cancer screening trial. The paper describes the different components of the CAD system and presents experiments to optimize the performance of the proposed CAD system. A rich set of 128 features is defined for subsolid nodule candidates. In addition to previously used intensity, shape and texture features, a novel set of context features is introduced. Experiments show that these features significantly improve the classification performance. Optimization and training of the CAD system is performed on a large training set from one site of a lung cancer screening trial. Performance analysis on an independent test from another site of the trial shows that the proposed system reaches a sensitivity of 80% at an average of only 1.0 false positive detections per scan. A retrospective analysis of the output of the CAD system by an experienced thoracic radiologist shows that the CAD system is able to find subsolid nodules which were not contained in the screening database.

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1. Introduction

Lung cancer is the most deadly cancer in both men and women. The American Cancer Society estimates that lung cancer will account for 28% of all cancer-related deaths in the United States in 2012 (American Cancer Society, 2012). This can be largely attributed to the fact that at present, the 5-year survival rate for all stages combined is only 16% (American Cancer Society, 2012). The 5-year survival rate is 52% for cases detected when the disease is still localized, but only 15% of lung cancers are diagnosed at this early stage (American Cancer Society, 2012). Therefore, early detection of lung cancer, in which it is still treatable, is of major importance to reduce lung cancer mortality.

In the last decade, many screening trials have been initiated to investigate the potential of early detection of lung cancer with low-dose chest computed tomography (CT). Lung cancer in an early stage manifests itself as a pulmonary nodule. Thin-slice helical chest CT scans have a sub-millimeter resolution at which very pulmonary nodules can be detected and therefore, this exam is able to show early stage lung cancer (Henschke et al., 1999). In November 2010, the National Lung Screening Trial (NLST) published a 20% lung cancer mortality reduction in their study group which received 3 annual rounds of low-dose CT screening in comparison to their control group, which received 3 annual rounds of chest X-ray screening (Aberle et al., 2011). This was the first study which showed clear scientific evidence that screening for lung cancer reduces lung cancer mortality.

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Pulmonary nodules are described as round opacities, well or poorly defined, measuring up to 3 cm in diameter (Hansell et al., 2008). Pulmonary nodules can be differentiated into subsolid and solid nodules (Hansell et al., 2008). Solid nodules have homogeneous soft-tissue attenuation on CT scans. Subsolid nodules can be further differentiated into non-solid nodules (synonym: ground glass nodules) and part-solid nodules (synonym: semi-solid nodules). Non-solid nodules manifest as focal areas of hazy increased attenuation that do not obliterate the bronchial or vascular margins. Areas of hazy increased attenuation are called ground glass opacity and therefore, these nodules are also referred to as ground glass nodules. Part-solid or semi-solid nodules contain both ground glass and solid components. In the Early Lung Cancer Action Project (ELCAP), 81% of all positive findings at baseline were solid nodules and 19% were subsolid nodules, which indicates that subsolid nodules are less common in screening (Henschke et al., 2002). However, this study published a significantly larger malignancy rate of 34% for subsolid nodules, compared to 11% for solid nodules (Henschke et al., 2002). Consequently, about half of the lung cancers found in this study originated from subsolid nodules. Therefore, early detection of subsolid nodules is of major importance.

Computer-aided detection (CAD) of lung nodules in chest CT scans is an extensively researched area in medical research. Although many systems have been proposed for detection of solid nodules (e.g.Tan et al., 2011; Messay et al., 2010; Murphy et al., 2009; Sousa et al., 2009; Ye et al., 2009; Li et al., 2008; Retico et al., 2008; Bellotti et al., 2007; Dehmeshki et al., 2007; Enquobahrie et al., 2007; Marten and Engelke, 2007), only few studies have focused on detection of subsolid nodules (Jacobs et al., 2011; Tao et al., 2009; Ye et al., 2007; Zhou et al., 2006; Kim et al., 2005). In a study by Beigelman-Aubry et al. (2009), it was shown that both a CAD system designed for solid nodules, and radiologists have difficulties in detecting subsolid nodules. Therefore, dedicated CAD algorithms for subsolid nodules are needed.

A few papers have been published on computerized detection of subsolid nodules. Kim et al. (2005) described a slice-based CAD system using texture and intensity features. The system classified regions of interest (ROI) on manually chosen slices from CT examinations of 14 patients into ground glass opacity (GGO) or non-GGO. Performance was measured using receiver operating characteristic (ROC) analysis on all ROIs and showed an area under the ROC curve of 0.92. Zhou et al. (2006) developed an automatic scheme for both detection and segmentation of subsolid nodules based on vessel suppression, intensity and texture analysis. They reported good performance but the test data set contained only 10 subsolid nodules. Ye et al. (2007) presented a voxel-based method with rule-based filtering that was tested on 50 CT examinations with 52 subsolid nodules. They reported a high sensitivity of 92.3% but also a high false positive (FP) rate of 12.7 per scan. Tao et al. (2009) developed a multi-level detection scheme with classification at voxel-level and object-level. They focused on small volumes of interest (VOIs) generated by a candidate detector algorithm which was not otherwise specified. The method was tested on a set of 1100 VOIs including 100 positive ones, from 153 healthy and 51 diseased patients. Results were provided for VOIs only, and neither the FP rate per scan nor the total number of VOIs per scan were reported. Finally, we published a preliminary version of our subsolid nodule CAD system which we trained and evaluated on a data set of 140 scans from one site of a large lung cancer screening trial. In this study, we reported promising results as we reached 73% sensitivity on the independent test set at an average of 1.0 FP/scan (Jacobs et al., 2011).

In this work, a novel automatic computer-aided detection system for subsolid nodules is presented and evaluated on a large database of a multi-center lung cancer screening trial.

The first algorithms for subsolid nodule detection have been evaluated on rather small amounts of data ranging from 10 to 50 thoracic CT scans containing between 10 and 52 subsolid nodules in total (Kim et al., 2005; Zhou et al., 2006; Ye et al., 2007). The most recent study used 1100 subvolumes from CT scans from around 200 subjects of which 100 subvolumes contained subsolid nodules (Tao et al., 2009). In this study, we collected cases from two sites of a large lung cancer screening trial and included all CT examinations in which subsolid nodules were annotated, leading to a larger database than presented by prior studies. Data collection is described in detail in Section 2.

The different components of the proposed CAD system, including candidate detection, feature calculation and classification, are described in Section 3. In comparison to the publication by Tao et al. (2009), which is the most recent publication on subsolid nodule detection, we describe a full CAD system including the candidate detection step, which was not specified in the publication by Tao et al. (2009). Different classes of features have been utilized in previous publications. The first work by Kim et al. (2005) and Zhou et al., 2006 only used texture and intensity features. In the publications by Ye et al. (2007) and Tao et al. (2009), shape features are added to the feature set. In this work, we add another class of features by including context features which are calculated at the image-level, describing the relation of an area of ground glass opacity to its surroundings such as the lung, airways, vessels and other nodule candidates. We performed an experiment to show that these type of features benefit the classification performance. Experiments to optimize the configuration of the CAD system are also explained in Section 3. We experiment with many different classifiers to find the optimal classifier for this classification task. This is an important optimization of the CAD system which has also been mentioned as future work by prior publications (Tao et al., 2009).

Section 4 outlines the results of the CAD system on the independent test set. This section also reports the performance of a solid nodule CAD system on our database with many subsolid nodules and how the combination with a subsolid nodule CAD would benefit the detection performance for detection of subsolid nodules. At the best of our knowledge, we believe this has not yet been done in any publication to date.

In order to get a good insight into the performance of the CAD system and its potential to be applied in a clinical setting, an experienced thoracic radiologist reviewed the CAD marks of the CAD system on the independent test set and the results of this investigation are presented in Section 5. Finally, we discuss the performance and limitations of the proposed CAD system and opportunities for future work in Section 6 and conclude in Section 7.

2. Materials

Data for this study was collected from the NELSON trial, a large multi-center lung cancer screening trial, organized in the Netherlands and Belgium (van Klaveren et al., 2009). NELSON is an ongoing randomized control trial established to test if screening for lung cancer by low-dose CT in high-risk (ex-)smokers will lead to a 25% mortality reduction in lung cancer mortality.

In total, the trial includes 7557 participants who receive multiple rounds of screening with low-dose CT. All pulmonary nodules which were found during visual reviewing of the CT scans were recorded in the trial database. Among other characteristics, the screening radiologists indicated the location, diameter and nodule type of all detected pulmonary nodules; calcified, solid, part-solid or non-solid (van Klaveren et al., 2009). This database served as reference standard for our CAD analysis. We collected all thin-slice,

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