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CT-texture analysis of subsolid nodules for differentiating invasive from in-situ and minimally invasive lung adenocarcinoma subtypes

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Lung neoplasm;
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Texture analysis

Abstract
Purpose: The purpose of this study was to evaluate the usefulness of computed tomography-texture analysis (CTTA) in differentiating between in-situ and minimally-invasive from invasive adenocarcinomas in subsolid lung nodules (SSLNs).
Material and methods: Two radiologists retrospectively reviewed 49 SSLNs in 44 patients. There were 27 men and 17 women with a mean age of 63 ± 7 (SD) years (range: 47—78 years). For each SSLN, type (pure ground-glass or part-solid) was assessed by consensus and CTTA was conducted independently by each observer using a filtration-histogram technique. Different filters were used before histogram quantification: no filtration, fine, medium and coarse, followed by histogram quantification using mean intensity, standard deviation (SD), entropy, mean positive pixels (MPP), skewness and kurtosis.

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Results: We analyzed 13 pure ground-glass and 36 part-solid nodules corresponding to 16 adenocarcinomas in-situ (AIS), 5 minimally invasive adenocarcinomas (MIA) and 28 invasive adenocarcinomas (IVA). At uni- and multivariate analysis CTTA allowed discriminating between IVAs and AIS/MIA ($P < 0.05$ and $P = 0.025$, respectively) with the following histogram parameters: skewness using fine textures and kurtosis using coarse filtration for pure ground-glass nodules, and SD without filtration for part-solid nodules.

Conclusion: CTTA has the potential to differentiate AIS and MIA from IVA among SSLNs. However, our results require further validation on a larger cohort.

Subsolid lung nodules (SSLNs) are defined by hazy increased opacities in lung parenchyma preserving broncho-vascular structures [1]. When they persist more than 3 months on repeated computed tomography (CT), the prevalence of malignant lesions is higher than for solid nodules, reaching 18% for pure ground-glass nodules and 63% for part-solid nodules, being mostly adenocarcinomas [2—4].

The 2011 IASLC/ATS/ERS classification and the 2015 WHO classification of lung tumors define 3 grades of lung adenocarcinoma including adenocarcinoma in-situ (AIS), minimally invasive adenocarcinoma (MIA) and invasive adenocarcinoma (IVA) [5,6]. These grades are closely linked to lesion prognosis and are therefore key factors for patient management.

Patients with AIS and MIA have a 100% 5-year survival after surgery and they can be operated with limited resection, which has a lower morbidity compared to conventional lobectomy [7]. However, according to the IASLC/ATS/ERS classification, pathological analysis of subsolid nodules should be done on a full resection piece as the diagnosis of AIS and MIA cannot be made based on small specimens such as trans-thoracic core-needle or aspiration biopsies [6]. Preoperative CT assessment is therefore essential prior to proposing limited resections for non-invasive lesions and optimal surgical resections for IVA. Several morphologic CT-criteria were originally proposed for differentiating between those grades [4], and the latest recommendations from the Fleischner Society in 2013 [8] advise using the maximal axial diameter of the nodule as well as the size of its solid component for decision-making. However, those criteria are still perfectible and the Fleischner society actually recognizes in its recommendations the need for more data concerning a quantitative approach to SSLNs [8].

Quantitative CT texture analysis (CTTA) has shown promising results in lung cancer for solid nodules and lung masses, with correlations established between heterogeneity and biomarkers as well as intra-tumoral hypoxia [9—12]. However, little data is available concerning the application of CTTA to subsolid nodules [13,14], although kurtosis [13] and entropy [14] parameters may have some potential in differentiating IVAs among SSLNs. However, to our knowledge, several existing texture parameters remain untested in SSLNs, such as the value of kurtosis, skewness and MPP in pure ground-glass nodules [14] and MPP in part-solid nodules [13]. Moreover, none of the previous approaches included an initial image filtration step, which in addition to providing crucial information concerning biological heterogeneity by highlighting anatomical features of different sizes and intensity-variation, also reduces the variability due to acquisition parameters and the impact of photon noise [15,16].

The purpose of this study was to evaluate the usefulness of CTTA in differentiating in-situ or minimally invasive from invasive adenocarcinomas in SSLNs.

Material and methods

Patients

Study ethical approval was obtained on 29/9/2014 (CECIC IRB 5891). Given the retrospective nature of the analysis, the institutional review board waived patients' written consent. Anonymity was ensured for all patient data.

We reviewed the thoracic surgery database of 2 European university hospitals for surgically resected SSLNs between 2004 and 2015. Of 66 eligible patients with 71 nodules, we excluded 22 patients with 22 nodules for the following reasons:

- the patient had contrast-enhanced CT (18 patients and 18 nodules);
- CT was performed with a slice thickness > 3 mm (1 nodule in 1 patient);
- the patient did not have lung adenocarcinoma at histopathological analysis of the full resection piece (atypical adenomatous hyperplasia: 1 nodule in 1 patient; focal interstitial fibrosis: 2 nodules in 2 patients).

The study population consisted of a total of 44 patients. There were 25 men and 19 women with a mean age of 62 ± 7 (SD) years (range: 47—78 years).

CT acquisition

Chest CT examinations were performed using the following scanners: Philips Brilliance® 64 (Philips Medical Systems, Eindhoven, The Netherlands), Siemens Somatom Sensation® 16 (Siemens Healthineers, Erlangen, Germany) and Somatom Definition® 64 (Siemens Healthineers). Due to the retrospective nature of the study, different CT-protocols were used.

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