European Journal of Radiology 100 (2018) 58–65

Contents lists available at ScienceDirect

European Journal of Radiology

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

Research article

Improving the prediction of lung adenocarcinoma invasive component on CT: Value of a vessel removal algorithm during software segmentation of subsolid nodules

Lorenzo Garzelli[a,b], Jin Mo Goo[a,c,*], Su Yeon Ahn[a], Kum Ju Chae[a], Chang Min Park[a,c], Julip Jung[d], Helen Hong[d]

[a] Department of Radiology, Seoul National University College of Medicine, and Institute of Radiation Medicine, Seoul National University Medical Research Center, Seoul, Republic of Korea
[b] Pitié-Salpêtrière Hospital, Pierre-and-Marie Curie University, Paris, France
[c] Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea
[d] Department of Software Convergence, Seoul Women's University, Seoul, Republic of Korea

ARTICLE INFO

Keywords:
Lung nodule
Lung cancer
Subsolid nodule
Adenocarcinoma
Segmentation

ABSTRACT

Purpose: To evaluate the value of a vessel removal algorithm in segmentation of subsolid nodules by comparing the software solid component measurement on CT, before and after vessel removal, with the measurement of the invasive component on pathology in lung adenocarcinomas manifesting as subsolid nodules.
Materials and methods: Between January 2014 and June 2015, 73 subsolid nodules with an invasive component of ≤10 mm on pathology were selected for analyses. For each nodule, semi-automated segmentation was performed by 2 radiologists and 3-dimensional (D) longest, axial longest and effective diameters of solid component were obtained from software, before and after using a vessel removal tool. These measurements were compared with the invasive component diameter on pathology using the paired *t*-test and Pearson's correlation test.
Results: Sixty-eight successfully segmented subsolid nodules were included. The mean maximal diameter of the invasive component on pathology was 4.6 mm (range, 0–10 mm). The correlation between software and pathology measurements was significant ($p < 0.01$) and the correlation after vessel removal ($r = 0.49–0.54$) was better than before vessel removal ($r = 0.27–0.41$). The mean measurement difference between solid component on CT and invasive tumor on pathology was significantly larger before vessel removal than after vessel removal in all measurements. The smallest mean measurement difference was obtained with 3D longest diameter of solid component after vessel removal in both readers (−0.26 mm to 0.10 mm), with no significant difference from pathology ($p = 0.53–0.83$).
Conclusion: By adding a vessel removal algorithm in software segmentation of subsolid nodules, the prediction of invasive component in lung adenocarcinomas can be improved.

1. Introduction

Lung adenocarcinoma incidence has been increasing and is now the most common type of lung cancer accounting for almost 40% of all lung cancers [1]. The 2011 IASLC/ATS/ERS classification defines 4 main categories in lung adenocarcinomas [2]: atypical adenomatous hyperplasia (AAH), adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA) and invasive adenocarcinoma (IVA). Those 4 categories can be separated in two groups: Pre-invasive tumors (AAH and AIS) and invasive tumors (MIA and IVA). In the 8th edition of the TNM lung cancer staging, it is now the size of the invasive component rather than the whole tumor size that should be reported for the T stage [3]. The differentiation of MIA from IVA is clinically important because MIA is reported to have nearly a 100% 5-year survival rate after complete resection [2,4]. Therefore, recent data suggested that it can be a good candidate for sub-lobar resection whereas lobectomy stays advised for IVA [5].

CT plays an important role in the management of lung cancer. There

Abbreviations: AAH, atypical adenomatous hyperplasia; AIS, adenocarcinoma in situ; MIA, minimally invasive adenocarcinoma; IVA, invasive adenocarcinoma; GGN, ground-glass nodule; GGO, ground-glass opacity

* Corresponding author at: Department of Radiology, Seoul National University College of Medicine, and Institute of Radiation Medicine, Seoul National University Medical Research Center, 101 Daehak-ro, Jongno-gu, Seoul 110-744, Republic of Korea.
E-mail address: jmgoo@plaza.snu.ac.kr (J.M. Goo).

https://doi.org/10.1016/j.ejrad.2018.01.016
Received 27 April 2017; Received in revised form 15 November 2017; Accepted 15 January 2018

has been a growing concern about persistent ground-glass nodules (GGNs) on CT because many of them turned out to be lung adenocarcinomas or their precursors [6,7]. Pre-invasive lesions of AAH and AIS usually present on CT as pure GGN [8–10]. On the other hand, invasive lesions, MIA and IVA with respectively ≤5 mm and > 5 mm invasion, usually present on CT as part solid nodules [7]. Lee et al. [11] reported that there is a significant correlation between the size of the solid component on thin-section CT and the invasive component on pathology and Hwang et al. demonstrated that the diameter of the solid component was a better prognostic predictor than the largest diameter of the whole nodule in adenocarcinomas appearing as part-solid GGNs on CT [12]. Recently, there were proposals for coding T categories for subsolid nodules by measuring the longest dimension of solid component in part-solid GGNs [13]. However, as there can be considerable measurement variability with manual measurements [14–16], computer-aided volumetry can be employed to reduce interobserver variability [17–19]. Several articles have explored the topic of semi-automated segmentation in GGNs [20–24], but still there are only a few studies that evaluated software performance that can segment areas of ground-glass opacity (GGO) and solid component separately [25,26]. One of the tricky issues in segmenting the solid component in subsolid nodules is that the attenuation value of solid component is similar to that of pulmonary vessels, and therefore, another scheme in addition to attenuation value should be employed to reduce the overestimation of solid component measurements.

The aim of the present study was to evaluate the value of vessel removal algorithm in semi-automatic segmentation of subsolid nodule by comparing the software measurements of the solid component on CT with and without vessel removal, with the measurement of invasive tumor on pathology in lung adenocarcinomas manifesting as subsolid nodules.

2. Material and methods

This study was approved by the Institutional Review Board of our institution and written informed consent was waived in this retrospective study.

2.1. Selection of cases

We retrospectively reviewed the medical records of all patients who had undergone surgical resection for lung adenocarcinomas and pre-invasive lesions that manifested as subsolid nodules on thin- section CT (section thickness < 1.3 mm) at our hospital between January 2014 and June 2015. There were a total of 283 eligible patients for whom pathology slides were available. Among them, we excluded 210 patients based on our exclusion criteria defined as follows: (1) time between CT and surgery of more than 4 weeks (13 patients), (2) presence of 2 or more resected nodules in one lobe (17 nodules in 15 patients) and (3) unavailability of the exact size of the tumor invasive component on pathology because only the invasive component ≤10 mm was reported during that period (204 nodules in 194 patients). Some patients had two or more exclusion criteria. Finally, a total of 73 patients (27 men and 46 women) (median age, 58 years; range, 20–79 years) were included in our study. Surgical procedures included lobar resection in 21 patients and limited resection (segmentectomy or wedge) in 52 patients. The mean time ± standard deviation between CT and surgery was 5.6 ± 8.6 days. All patients had a single subsolid nodule with pathologic proof except 1 patient who had 2 subsolid nodules in different lobes. Finally, a total of 74 subsolid nodules were selected in 73 patients for image analysis.

2.2. CT technique

CT images were obtained using one of the following CT scanners: Sensation 16 (Siemens Medical Solutions, Forchheim, Germany), Somatom Definition (Siemens Medical Solutions), Brilliance 64 (Philips Medical Systems, Best, The Netherlands), or Discovery CT750 HD (GE Medical Systems, Waukesha, WI, USA). Given the retrospective design of this study, different CT protocols were used, including CT with (n = 50) or without (n = 23) intravenous contrast material, and CT with standard (100–150 reference mAs, n = 50) or low-dose technique (30–60 mAs, n = 23). In all patients, CT images were reconstructed using a high-frequency algorithm with a section thickness of < 1.3 mm.

2.3. Software segmentation

Semi-automated segmentation was performed with AVIEW Lung Screen (Coreline Soft, Seoul, Korea). The segmentation method on CT images consists of extraction of initial solid component and areas of ground-glass opacity (GGO), refinement of the extracted solid component and GGO regions, and vessel removal steps. In the initial solid component and GGO extraction step, the solid component region is defined using an intensity thresholding with a −200 HU threshold value and the GGO region is defined using a histogram modeling-based adaptive thresholding. In the solid component and GGO refinement step, the solid component and GGO are simultaneously segmented using an asymmetric multi-phase deformable model with modified energy functional and intensity constrained averaging function. In the vessel removal step, pulmonary vessels with a diameter of 1–3 mm were excluded from the solid component using a multi-scale vessel analysis (Fig. 1). The software provides an option to turn on and off the vessel removal function. In total, segmenting a nodule, takes around 30 s. It took less than 1 s in segmenting the solid component and GGO region, and it took additional 2–3 s when vessel removal is applied.

2.4. Image analysis

For each nodule, two radiologists (LG, JMG) with 3 and 26 year of experience independently measured various dimensions of nodules using the software including 3D longest, axial longest and effective diameters of the whole nodule and its solid component. The 3D longest diameter indicates the longest diameter of a segmented nodule on any plane in 3 dimensions while the axial longest diameter means the longest diameter of a segmented nodule on transverse plane. The effective diameter is the diameter calculated from a sphere whose volume is the same as that of the segmented nodule volume. In all cases, those measures were reported before vessels removal for whole nodule and solid component and after vessels removal for solid component. To assess intra-reader variability, one radiologist (LG) repeated all measurements at a 3 week interval.

2.5. Segmentation accuracy

Similar to the previous study, which has dealt with solid nodule [27] or subsolid [25] nodules, the segmentation accuracy for each nodule was evaluated by the radiologist who processed the nodules with the following visual scale: (1) excellent segmentation of both GGN and solid components; (2) good segmentation in which the proportion of correct segmentation was 80% or greater; (3) insufficient segmentation in which the proportion was less than 80% for ground glass component and (4) failure in which a nodule could not be segmented or failure in applying the vessel removal tool. A manual editing tool for GGO, which was developed to facilitate the editing by applying different thresholds and roundness with simple clicking plus or minus buttons, was allowed to readers. This manual editing process took less than 10 s and was applied in approximately 30% of cases (27% and 32% by two readers, respectively). However, no editing was applied to the solid component of a subsolid nodule.