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Pulmonary adenocarcinomas with ground-glass attenuation on thin-section CT: Quantification by three-dimensional image analyzing method

Hiromitsu Sumikawa [a,*], Takeshi Johkoh [a,b], Tomofumi Nagareda [c], Junko Sekiguchi [d], Kumiko Matsuo [b], Yuka Fujita [a], Javzandulam Natsag [a], Atsuo Inoue [a], Naoki Mihara [a], Osamu Honda [a], Noriyuki Tomiyama [a], Masato Minami [e], Meinoshin Okumura [e], Hironobu Nakamura [a]

[a] *Department of Diagnostic and Interventional Radiology, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0825, Japan*
[b] *Department of Medical Physics, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0825, Japan*
[c] *Department of Clinical Laboratory, Takaraduka City Hospital, 4-5-1 Kohama, Takaraduka, Hyogo 665-0827, Japan*
[d] *FCT Advanced Applications, GE Healthcare Technologies, 4-7-127 Asahigaoka, Hino City, Tokyo 191-8503, Japan*
[e] *Department of Surgery, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0825, Japan*

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Abstract

Purpose: The purpose of this study was to evaluate software designed to calculate whole tumor volumes and the ratio of the solid component to whole volume (%solid) in pulmonary nodules with ground-glass opacity in three dimensions.
Methods: The study included 49 patients with histologically diagnosed adenocarcinomas smaller than 2 cm in diameter. The %solid was calculated both automatically using new software, and by manual measurement of the following four parameters by two observers: the ratio of the largest diameter (a) and the area (b) at the mediastinal window to those at the lung window, and the ratio of the largest diameter (c) and the area (d) of the solid component to those of the ground-glass component at the lung window. Agreement of intra- and inter-observer data by both Spearman's rank correlation test and Bland–Altman's method, and a comparison by Spearman's rank correlation test of the %solid in both Noguchi sub-classifications and vessel invasion in histologic specimens, between the software and manual methods, were assessed.
Results: Of the 49 nodules, 48 were successfully measured and assessed. The agreement of the observers with the software was better (Bland–Altman's method; mean difference, −0.3%; 95% limits of agreement, −3.1 to 2.5%) than with the manual measurements (a: 5.3%, −17.6 to 28.3%; b: 8.3%, −10.6 to 26.9%; c: 10.7%, −17.6 to 39%; d: 6.4%, −22 to 34.8%). The correlation between %solid and the histological group was worse with the software (Spearman's rank correlation test; $r = 0.487$, $p < 0.001$) than with the manual method (a, $r = 0.534$; b, $r = 0.557$; c, $r = 0.552$; d, $r = 0.545$).
Conclusion: Although the software requires improvement in the calculation of %solid with volumetric analysis, this is a reproducible and promising quantitative method for determining the grades of malignancy of small lung cancers.

Keywords: Pulmonary nodules; CT; Volume assessment; Automatic measurement; Volume measurement; Adenocarcinoma; Ground-glass attenuation

1. Introduction

The grade of central fibrosis is one of the most important prognostic factors for localized early-stage adenocarcinomas of the peripheral lungs [1,2]. When tumors with bronchioloalveolar carcinoma components have more central fibrous focus, the prognosis of patients is poorer than that with no or slight fibrosis [1–4]. On the basis of this, Noguchi et al. grouped small pulmonary adenocarcinomas into six distinctive structural patterns based on histological examination [5]. This sub-classification has good correlation with prognosis and thin-section CT findings [6,7]. The bronchioloalveolar carcinoma component, which means replacement cancer cells to alveolar epitherial cells, shows ground-glass attenuation and central fibrosis shows solid attenuation on thin-section CT. Therefore, a greater extent of ground-glass opacity in a tumor

* Corresponding author. Tel.: +81 6 6879 3434; fax: +81 6 6879 3439.
E-mail address: h-sumikawa@radiol.med.osaka-u.ac.jp (H. Sumikawa).

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correlates with a less malignant component in histology and favorable prognosis clinically [6,8–10].

Finer CT collimation on advanced multidetector-row CT is now being used in daily clinical practice, and thus the relative detection rate of pulmonary nodules with ground-glass attenuation will become much higher. In CT screening for lung cancer, nodules with ground-glass opacity are common, and the rate of malignant nodules with ground-glass attenuation has been reported to be high [11]. Consequently, many nodules with ground-glass attenuation are followed-up by CT. However, nodules with ground-glass attenuation grow slowly and the change in size is slight [8,12,13]. In addition, not only volume but also the proportion of the solid component of the nodules needs to be estimated because some nodules with ground-glass attenuation show increase in the solid component while having unchanged size of whole nodules [14]. However, the reproducibility of manual measurements is poor for small nodules [13,15], necessitating the development of a method allowing reproducible estimation of nodules. A previous report stated that volume assessment is a reproducible method for estimation of tumor growth [16]. However, even though using contemporary methods, only solid components can be analyzed [15–18]. The purpose of the present study was to evaluate the reproducibility of software designed to measure whole volumes of pulmonary nodules including ground-glass attenuation component and the ratio of the solid component to whole volume (or the volume with areas with ground-glass attenuation) in three dimensions in comparison with that of manual measurement and to compare the results with the histological data.

2. Materials and methods

2.1. Patients

The study population consisted of consecutive patients with primary pulmonary adenocarcinomas smaller than 2 cm in diameter that had undergone surgery at our institution between January 1998 and December 2003, and total 79 patients were included in this study. In all patients, the pulmonary nodule was 2 cm or less in the longest diameter on CT, and was completely surrounded by the lung or visceral pleura at surgery. The nodules had areas with ground-glass attenuation and/or solid components. Fifteen patients who had previously had adenocarcinomas in the lungs or other organs were excluded because they were difficult to be ruled out metastasis. Three patients who had undergone chemotherapy prior to surgery were also excluded because CT, an histological findings of them were possibly changed by influence of chemotherapy. Moreover, 12 patients whose thin-section CT data was unavailable were excluded. The remaining 49 nodules of 49 patients (26 men and 23 women; age, 43–78 years; mean, 63 years) were included in this study. The duration from CT scan to surgery ranged from 1 to 118 days (mean 25 days).

According to our institutional guidelines, our institutional review board does not require its approval for retrospective analyses and informed consent is also not required.

2.2. CT imaging

Chest CT scans were performed using a LightSpeed QXi Scanner (General Electric Medical Systems, Milwaukee, WI) equipped with a four-detector row or a LightSpeed Ultra Scanner (GE Healthcare Technologies, Milwaukee, WI) with an eight-detector row or an Aquilion V-detector Scanner (Toshiba Medical Systems, Tokyo, Japan) with a four-detector row. Scanning parameters were as follows: collimation was 0.5 or 1.25 mm, pitch was 0.625–1.5, the rotation time was 0.5–0.8 s per rotation, exposure parameters were 120 kV and 200 mA, and the field of view was 200 mm. All image data was reconstructed using a high spatial frequency algorithm at 0.5 or 1.25 mm intervals.

2.3. Assessment of nodules

The ratio of solid component to area with ground-glass attenuation in nodules (%solid) was calculated at a commercially available workstation (Advantage Workstation 4.2; GE Healthcare Technologies, Milwaukee, WI) with CT lung analysis software (Lung VCAR; GE Healthcare Technologies, Milwaukee, WI). This software can segment pulmonary nodules with ground-glass attenuation. Solid nodules are segmented using watershed-based segmentation. For nodules classified as part solid, the segmentation algorithm initially works for the solid component using the algorithm for solid nodule segmentation. In a parallel process, the non-solid portion of the region is segmented using an adaptive threshold based method. For nodules classified as non-solid, the application performs adaptive threshold based segmentation followed by morphological pruning. Segmentation, volume and the ratio of solid area to ground-glass area (%solid) are computed automatically after the operator has placed a marker on the nodule (Fig. 1). To evaluate the reproducibility and correlation with histological classification of the automatic measurements by the software, several manual measurements were also performed. The largest diameter and area of the nodules were measured using a window level of −700 Hounsfield units (HU) with a window width of 1200 HU (lung window setting) and a window level of 30 HU with a window width of 350 HU (mediastinal window setting) on the workstation (Advantage Workstation 4.2; GE Healthcare Technologies, Milwaukee, WI) by each operator for each measurement. At the lung window setting, the diameters and area of the solid component were also measured. Using the result of the manual measurements, the following four ratios were calculated: a, the ratio of the diameter at the mediastinal window to the diameter at the lung window; b, the ratio of the area at the mediastinal window to the area with ground-glass opacity at the lung window; c, the ratio of the diameter without ground-glass opacity to the diameter with ground-glass opacity at the lung window; d, the ratio of the area without ground-glass opacity to the area with ground-glass opacity at the lung window.

To assess the intra-observer variability and inter-observer agreement of volume and %solid measurements, all methods including automatic measurement by the lung analysis software were performed by two independent operators. reader 1 was a