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Parietal pleural invasion/adhesion of subpleural lung cancer: Quantitative 4-dimensional CT analysis using dynamic-ventilatory scanning

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ABSTRACT

Purpose: Using 4-dimensional dynamic-ventilatory scanning by a 320-row computed tomography (CT) scanner, we performed a quantitative assessment of parietal pleural invasion and adhesion by peripheral (subpleural) lung cancers.
Methods: Sixteen patients with subpleural lung cancer underwent dynamic-ventilation CT during free breathing. Neither parietal pleural invasion nor adhesion was subsequently confirmed by surgery in 10 patients, whereas the other 6 patients were judged to have parietal pleural invasion or adhesion. Using research software, we tracked the movements of the cancer and of an adjacent structure such as the rib or aorta, and converted the data to 3-dimensional loci. The following quantitative indices were compared by the Mann-Whitney test: cross-correlation coefficient between time curves for the distances moved from the inspiratory frame by the cancer and the adjacent structure, the ratio of the total movement distances (cancer/adjacent structure), and the cosine similarities between the inspiratory and expiratory vectors (from the cancer to the adjacent structure) and between vectors of the cancer and of the adjacent structure (from inspiratory to expiratory frames).
Results: Generally, the movements of the loci of the lung cancer and the adjacent structure were similar in patients with parietal pleural invasion/adhesion, while they were independent in patients without. There were significant differences in all the parameters between the two patient groups (cross-correlation coefficient and the movement distance ratio, $P < 0.01$; cosine similarities, $P < 0.05$).
Conclusion: These observations suggest that quantitative indices by dynamic-ventilation CT can be utilized as a novel imaging approach for the preoperative assessment of parietal pleural invasion/adhesion.

1. Introduction

Dynamic-ventilation computed tomography (CT) is a novel fluoroscopic imaging method for the thorax, which continuously scans the thorax under free breathing conditions (maximum 160 mm in length). Currently, this scanning method can be provided by commercially available CT scanners that have a very long scanning length in the cranio-caudal axis (z-axis), which are the 320-row multidetector CT (MDCT) scanner ('Aquilion *ONE*' by Toshiba Medical Systems) and 256-row MDCT scanner ('Revolution CT' by GE Healthcare). With the use of powerful iterative reconstruction techniques, current dynamic-ventilation CT covers longer respiratory cycles with limited radiation exposure. The advantages of 4-dimensional dynamic-ventilation CT for observing airway or pulmonary disorders have gradually been revealed in reports on such disorders as central airway stenosis in children and chronic obstructive pulmonary disease [1–4].

Although a limited number of publications are available, dynamic-ventilation CT has been applied to the preoperative analysis of lung cancer and mediastinal liposarcoma [5–7]. The main purpose of preoperative dynamic-ventilation CT in these publications was to determine tumor resectability based on invasion

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to the parietal pleura or surrounding structures such as the aorta or diaphragm. Imaging evidence of the movement of a peripheral (subpleural) lung cancer independent of the movement of the parietal or mediastinal pleura indicates that the cancer does not invade or strongly adhere to the pleura, and therefore is usually resectable [7]. Even when radical surgery is selected for advanced lung cancer with invasion to the parietal pleura or mediastinum, an accurate preoperative assessment of tumor invasion or adhesion can lead to appropriate informed consent before the procedure, and allow the physician to prepare for longer operating time or greater blood loss. Currently, only qualitative (visual) assessment is used to evaluate tumor invasion of the parietal pleura or surrounding structures [5–7], and, to the best of our knowledge, there are no available published reports on investigations of quantitative indices of the movements of tumor and adjacent structures, as determined by dynamic-ventilation CT. Qualitative analysis performed by experienced physicians can be replaced by quantitative assessment, and may be further developed to include automatic assessment by specialized software or workstations.

Although lung cancer invasion of the chest wall or aorta has been investigated by studies using cine-magnetic resonance (MR) imaging or combined inspiratory and expiratory chest CT [8–12], these methods do not yet appear to be mainstream diagnostic approaches and are still considered to be experimental. Considering that preoperative MR is an unusual imaging procedure for lung cancer, and expiratory chest CT requires very careful interpretation by experienced chest radiologists, there remains the need for a new, convenient imaging technique such as dynamic-ventilation CT, for the preoperative assessment of tumor invasion.

Based on previous publications reporting that visual assessment performed on dynamic-ventilation CT scans was able to obtain correct diagnoses of tumor invasion [5–7], it can be hypothesized that these qualitative assessments could be converted to quantitative evaluations by application of selected motion parameters. In this preliminary study, as the first investigators to examine the use of quantitative analysis of dynamic-ventilation CT, we aimed (i) to identify the quantitative CT parameters that can be used to assess parietal pleural invasion/adhesion caused by peripheral (subpleural) lung cancer, and (ii) to examine whether these quantitative parameters can be used to distinguish patients with and without parietal pleural invasion/adhesion.

2. Materials and methods

This retrospective study was approved by the Institutional Review Board of Ohara General Hospital, and written informed consent from enrolled patients was waived. This study was designed as a component of the ACTIve Study, an ongoing multicenter research project in Japan. Based on agreement with the research committee of the ACTIve Study Group, this study was planned as a preliminary investigation of the potential of dynamic-ventilation CT using 320-row MDCT scanners.

2.1. Subjects

From October 2013 to November 2015, 16 patients with a peripheral lung cancer that was found to be located in the subpleural area of the lung (within 10 mm from the pleura) underwent dynamic-ventilation CT at Ohara Medical Center, which is attached to Ohara General Hospital. There were 6 females and 10 males (median age 75 years, range 43–80 years). The dynamic-ventilation scans were originally planned to assess the resectability of the cancer, based on cancer invasion or adhesion to the parietal pleura and adjacent (surrounding) structures such as the aorta, diaphragm, and chest wall. The dynamic scans were requested by pulmonologists or thoracic surgeons and arranged by radiologists. Pleural invasion or adhesion was not subsequently confirmed by surgery in 10 patients. The remaining 6 patients were judged to have pleural invasion or adhesion by the subsequent surgical procedure (n = 2) or by observations on the dynamic-ventilation CT (n = 4).

The lung cancer was located in the right upper lobe (n = 4), right middle lobe (n = 1), right lower lobe (n = 4), left upper lobe (n = 4), and left lower lobe (n = 3). The maximum tumor diameter ranged from 13 to 60 mm (mean 28 mm) on axial CT imaging. Histopathological examinations revealed adenocarcinoma (n = 10), squamous cell carcinoma (n = 3), large cell neuroendocrine carcinoma (n = 1), and metastatic lung cancer from resected rectal cancer (n = 1). One patient who did not receive radical surgery underwent bronchoscopic biopsy, but his lung tumor was diagnosed as indeterminate malignancy due to a small specimen size.

2.2. Dynamic-ventilation CT

All patients were scanned on a 320-row MDCT scanner (Aquilion *ONE*, Toshiba Medical Systems, Otawara, Tochigi, Japan). Using the wide volume mode (non-helical mode), dynamic scanning was performed at a fixed point without bed movement, resulting in a CT fluoroscopy of 160 mm in length. The scanning field of view (FOV) was selected from two settings, based on the patient's body habitus: 320 mm (medium, n = 8) or 400 mm (large, n = 8). Other scanning and reconstruction parameters for the dynamic-ventilatory scan were as follows: tube current = 40 mA, tube voltage = 120 kVp, rotation time = 0.35 s, total scanning time = 4.5–6.5 s, imaging FOV: 320–366 mm, collimation and slice thickness = 0.5 mm, reconstruction kernel = FC52 (for lung), reconstruction interval = 0.5 s/frame (total 9–13 frames), reconstruction method = half reconstruction. Scan data were converted to CT images using an iterative reconstruction method (adaptive iterative dose reduction using three-dimensional processing [AIDR3D], 'mild' setting). Before the dynamic-ventilation scan, patients were coached to perform repeated deep breathing. Radiologic technologists monitored the patient's respiratory movements and started the scan just before peak inspiration. At least one cycle from the inspiratory to the expiratory phase was included in the scan.

2.3. Image analysis

All scan data were anonymized and stored in a research computer. Special in-house software that was based on commercially available software (4D Airways Analysis, Toshiba Medical Systems) synthesized the data of continuous images (320 images/frame × total 9 − 13 frames) for the cine-CT series. Detailed information on the basic software was described in a previous technical note [13]. The software was originally developed to track a single designated airway point throughout the dynamic-ventilation CT scan. This process is facilitated by locating all anatomical positions in a single frame and automatically transferring the same position to all the other frames. In this study, we expanded the software function that registered all spatial information and tracked designated anatomical points, in order to follow designated points in the lung cancer and adjacent structures and to record their foci throughout the dynamic CT scan.

A radiologist (K.S., 8 years of experience in thoracic radiology) set two points for measurements on the inspiratory frame of the dynamic-ventilation CT. One point was placed in the center of the targeted lung cancer. The other point was placed in the extrapulmonary structure adjacent to the cancer; in most patients (n = 13), the extrapulmonary measuring point was placed in the rib nearest the lung cancer, since these cancers had been observed to be located immediately interior to the chest wall. In two patients with lung cancers adjacent to the mediastinum, the extrapulmonary mea-