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Non-small cell lung cancer: Spectral computed tomography quantitative parameters for preoperative diagnosis of metastatic lymph nodes

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ABSTRACT

Objective: To investigate the application value of spectral computed tomography (CT)quantitative parameters for preoperative diagnosis of metastatic lymph nodes in patients with non-small cell lung cancer (NSLC).
Methods: 84 patients with suspected lung cancer who underwent chest dual-phase enhanced scan with gemstone spectral CT imaging (GSI) mode were selected. GSI quantitative parameters including normalized iodine concentrations (NIC), water concentration, slope of the spectral Hounsfield unit curve (λHU) were measured. The two-sample *t* test was used to statistically compare these quantitative parameters. Receiver operating characteristic (ROC) curves were drawn to establish the optimal threshold values.
Results: A total of 144 lymph nodes were included, with 48 metastatic lymph nodes and 96 non-metastatic lymph nodes. The slope of the spectral Hounsfield unit curve (λHU) measured during both arterial and venous phases were signifcantly higher in metastatic than in benign lymph nodes ($P < 0.05$). The area under the ROC curve (AUC = 0.951) of λHU of the arterial phase (AP) was the largest. When the optimal threshold values of λHU was 2.75, the sensitivity, specificity, and overall accuracy in the diagnosis of metastatic lymph nodes were 88.2%, 88.4%, 87.0%, respectively.
Conclusion: Conventional CT diagnostic criteria established in accordance with size (lymph node maximal short axis diameter ≥10 mm) as the basis for judging metastatic lymph node. In quantitative assessment using spectral CT imaging, quantitative parameters showed higher accuracy than qualitative assessment of conventional CT based on the size for preoperative diagnosis of metastatic lymph nodes.

1. Introduction

Despite progress in treatment, lung cancer is the leading cause of cancer-related deaths [1]; however, its prognosis is still relatively poor [1,2], likely because accurate staging, especially that of mediastinal lymph nodes [3], which is closely related to treatment and prognosis is still lacking. The accuracy of traditional computed tomography (CT) in the diagnosis of metastatic lymph nodes of lung cancer is about 60% [4–6]. Current spatial resolution of positron emission tomography/CT (PET/CT) also prevents the detection of small metastatic lymph nodes [6].

Video-assisted thoracoscopic surgery is considered the diagnostic standard (NPV, 89%; PPV, 100%), and the bronchial ultrasound (sensitivity, about 81%; NPV, about91%) can be used for clear diagnosis, but these approaches are invasive [7–10]. Therefore, a non-invasive method that can more accurately characterize mediastinal lymph nodes is desirable, as it would assist in determining the need for and the most appropriate invasive staging procedure.

Gemstone spectral CT imaging (GSI) mode is in one rotation by completing 80 KVp and 140 KVp instantaneous switching to collect data. Compared with the conventional multirow CT, spectral CT provides not only virtual monochromatic spectral images at 40–140 keV but also material decomposition images, effective atomic number images, and spectrum curve, thereby amplifying the slight difference in different tissue sources [11–13]. Quantitative parameters of spectrum CT is clinically used in the diagnosis of pulmonary embolism [14] and differentiating benign masses from malignant tumors [15–18]. However, to our knowledge, the value of GSI for the preoperative diagnosis of nodal metastasis in patients with non-small cell lung cancer (NSLC) has not been well evaluated.

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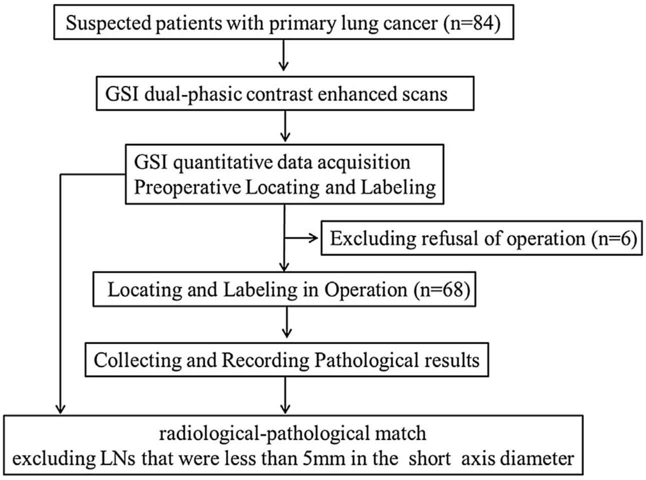

Fig. 1. Strategy for lymph node analysis and data processing in this study.

The purpose of our study is to investigate the application value of spectral CT quantitative parameters for preoperative diagnosis of metastatic lymph nodes in patients with NSLC.

2. Materials and methods

2.1. Patients

This prospective study was approved by our institution's review board, and we obtained written informed consent from all patients. From December 2014 to June 2016, 84 consecutive patients in our hospital with suspected lung cancer who underwent chest dual-phase enhanced scan with GSI mode were selected. All patients who received surgical treatment within 7 days after the CT scan and met the following criteria were eligible for inclusion in the study.

Inclusion criteria: (1) no treatment for chest tumors (such as radiotherapy or chemotherapy); (2) short axis diameter of the lymph node >5 mm in axial image; (3) pathologically confirmed benign and metastatic lymph nodes; (4) confirmed diagnosis of NSLC for all metastatic lymph nodes; and (5) clear images obtained with GSI mode, with no significant motion artifacts, and those that could be easily further analyzed. Sixteen people were excluded because of the lack of concrete pathological results. Fig. 1 shows a detailed time line of the study protocol.

2.2. Acquisition of GSI image

All examinations used the second generation GSI CT (Discovery CT 750 HD, GE Healthcare, USA) with the chest GSI model. An in-dwelling 18-G trocar was placed in the antecubital vein, and non-ionic iodine contrast medium (Ioversol, 350 mgI/L) was injected at a volume of 70 mL and a speed of 3.5 mL/s using a two-chamber high pressure injector (Mallinckrodt, USA). After the injection of iodine contrast medium, the chest dual-phase–enhanced scan delay times were 35 s at the arterial phase (AP) and 90 s at the venous phase (VP). The other parameters of the GSI model are as follows: tube rotation time, 0.6 s; pitch, 1.375; tube current, 600 mA; CT dose index volume for each phase with chest GSI model was 14.28 mGy. For reconstruction of the GSI data images, slice thickness and interval were 1.25 mm and 1.25 mm, respectively; images were then transferred to GE Advantage Workstation AW4.5 with GSI viewer software for further analysis.

2.3. GSI quantitative parameters acquisition and analysis

Two radiologists, with more than 10 years' experience, who were blinded to the pathological results, performed the quantitative analysis of parameters on the GE AW 4.5 (GE Healthcare, USA) post-processing workstation independent of each other. Their disagreement on measurement was resolved by consensus. In the reconstruction of the 70 keV image, the maximal short axis diameter of the target lymph node in axial image was selected, and the region of interest (ROI) was drawn. The area of ROI should be as large as possible to include the entire lymph node; further, care should be taken to avoid the peripheral fat tissue, any necrotic tissue, and calcifications. All measurements were performed in twice on 2 consecutive slices, and the average values were calculated.

The size of the target lymph node was determined by using the maximal short axis diameter in the 70-KeV image. The mean CT value of lesions in the 70-keV image was selected because 120-kVp scanning in conventional polychromatic images has an average energy of about 70 keV with GSI mode in AP and VP. Material density was measured on material decomposition images by the GSI viewer with iodine and water as the base material pair to measure the mean iodine concentrations (ICs) and water concentrations (WCs). In order to minimize the possible variations caused by the circulation status of patients and scanning times, the IC of lymph nodes was normalized to the IC of the thoracic aorta in the same slice to calculate a normalized iodine concentrations (NIC): $NIC = IC/IC_{aorta}$. The GSI viewer also automatically generated a spectral attenuation curve from 40 to 140 keV (1-keV interval). The spectral curve slope (λHU) of each lesion was calculated as the CT attenuation difference at two energy levels (40 and 100 keV) divided by the energy difference (60 keV) from the Hounsfield units (HU) curve, according to the formula, $\lambda HU = (CT_{40\,keV} - CT_{100keV})/(100\ 40)$.

2.4. One-to-one matching of lymph nodes

A total of lymph nodes were confirmed by pathology in patients with NSLC. To facilitate radiological-pathological one-to-one matching of lymph nodes, according to the N staging standard of the seventh edition amended by the International Association for the Study of Lung Cancer (IASLC) [19], regional lymph nodes were categorized into groups. A detailed description of the excised lymph nodes in the operation (e.g. location, size, and distance from the tumor) was recorded, labeled, and sent for pathologic examination. If all the excised lymph nodes were diagnosed as being metastatic in each group, then all of the corresponding lymph nodes on the CT images were considered as metastatic lymph nodes. The same method was also applied to the non-metastatic lymph nodes. If the excised lymph nodes included metastatic and non-metastatic lymph nodes, we tried our best to track the regional lymph nodes according to the lymph node size, location, and the distance from the tumor, during the operation [20].

2.5. Statistical analysis

SPSS17.0 (SPSS, Inc., Chicago, IL, USA) and MedCalc15.6 (MedCalc Software, Mariakerke, Belgium) were used for all the statistical analyses, and continuous variables were expressed as mean ± standard deviation (SD). The two-sample *t*-test was used to statistically compare these quantitative parameters between metastatic lymph nodes and non-metastatic lymph nodes. Receiver operating characteristic (ROC) curves were drawn to establish the optimal threshold values to distinguish metastatic lymph nodes from non-metastatic lymph nodes. The diagnostic capability was determined by calculating the area under the ROC curve (AUC). DeLong method was used for the comparison of AUC. The optimal