First-Pass CT Perfusion in Small Peripheral Lung Cancers:

Effect of the Temporal Interval between Scan Acquisitions on the Radiation Dose and Quantitative Vascular Parameters

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Rationale and Objectives: To evaluate the effect of the temporal interval (TI) between scan acquisitions on the radiation dose and vascular parameters of computed tomography perfusion (CTP) in small peripheral lung cancers.

Materials and Methods: With 7 excluded, 40 patients with peripheral lung cancer (diameter ≤4 cm) prospectively underwent a 30-second CTP study. Vascular parameters were calculated for TI datasets of 0, 1, 1.5, 2, 2.5, and 3.5 seconds. With the TI and tumor diameter as fixed effects, univariate general linear model analysis was used to compare the vascular parameters at interval datasets with the reference CTP of 0 seconds.

Results: The TI had an impact on the blood flow and transit time ($P < .001$ for both) but not on the blood volume and permeability surface area. The diameter influenced four vascular parameters ($P < .001$ for all). Compared to the reference, no statistical differences were found in the four parameters at intervals of 0.5, 1, and 1.5 seconds ($P > .05$ for all). In addition, blood flow was overestimated and transit was underestimated with increasing intervals of 2, 2.5, and 3.5 seconds ($P < .05$ for all), but not the remaining parameters. An increased TI of 0.5–1.5 seconds resulted in an estimated radiation dose reduction of 50–73%.

Conclusion: The TI of 1.5 seconds between scan acquisitions in first-pass phase of CTP could be used to optimally balance the radiation dose and quantitative estimation in small peripheral lung cancers.

Key words: Lung neoplasms; tomography; X-ray computed; blood supply; diagnostic imaging; radiation dosage.

The assessment of tumoral neovascularization can be approximated by computed tomography perfusion (CTP) (1), dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) (2), and DCE ultrasound (DCE-US) (3). Based on the highly linear and predictable contrast pharmacodynamics of CT (4), the high temporal resolution of the scan acquisitions, the benefits of wide availability, and the relatively low cost, the significance of CTP had been explored and verified in clinical oncology studies (1). In the chest, CTP has also been increasingly promoted for use in the differential diagnosis or neovascularization of local pulmonary lesions, especially after the introduction of the volume or whole tumor mode (5–11).

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When CTP is used, the temporal interval (TI) in the scan protocol should be set to a dedicated level for the accurate estimation of vascular parameters and radiation dose. Several authors evaluated the TI in the CTP use of flow phantom (12) for tumors in sites with less respiratory-motion artifacts, such as the retroperitoneal and pelvic cavities (13,14). Recently, Miles et al (1) proposed that the temporal sampling interval should not be less frequent than one image every 2 seconds for the measurement of tumoral blood flow (BF). However, to our knowledge, an appropriate TI in the first-pass phase of CTP in lung cancer, which involves intrinsic respiratory motion, that could be used to estimate the vascular parameters and to substantially reduce the radiation dose has not been studied in a major academic journal. The purpose of our study was to determine this verified TI in a perfusion scan protocol in first-pass CTP used to characterize small peripheral lung cancers.

MATERIALS AND METHODS

Patients

This study was part of our institutional review board–approved clinical study of CT perfusion in patients with lung cancer. All patients included in the study gave written informed consent before participating in the study. Our inclusion criteria of patients with small peripheral lung cancer were as follows: (a) patients with the ability to cooperate with the CTP examination and (b) the longest diameter of the tumor in the axial CT images is 1–4 cm. Our exclusion criteria were as follows: (a) presence of any common contraindication for iodinated contrast media; (b) contrast media injection failure; (c) patients who could not hold their breath during the CT scan, leading to errors in the vascular values and artifacts on the parametric maps; and (d) the location of tumors being too close to the cardiac border with too much image motion artifact to analyze. According to our inclusion criteria, 47 consecutive patients with small peripheral lung cancer that was found on chest radiography or unenhanced CT underwent dynamic scans with the CTP protocol between September 2009 and October 2011 prospectively. Seven patients were excluded according to the exclusion criteria (one patient for [a], one patient for [b], four patients for [c], and one patient for [d]). The remaining 40 patients ranged in age from 34 to 85 years old (median age, 62 years); 22 were men, and 18 were women.

Dynamic and Routine CT Studies

All examinations were performed with a 64-slice row CT scanner (LightSpeed 64; GE Medical Systems, Milwaukee, WI, USA). First, a breath-hold helical unenhanced CT scan was obtained using the following parameters: 120 kV, the smartmA technique (max 440 mA, noise index 9.00) (15), 0.6-second gantry rotation time, pitch 0.984, detector 40 mm, 5-mm slice thickness and 5-mm interval, 512×512 matrix, chest reconformation type, and inspiration breath hold. This sequence helped to locate the tumor and to determine the following section of the perfusion scan. The mean safety scan range of Z-axial coverage was 5.74 cm (range 3–7 cm) based on the visible tumor volume.

In the CTP study, a pump injector (Stellant; Medrad, Pittsburgh, PA, USA) was used to inject a 50-mL bolus of iodinated contrast (Vispague 320; GE Healthcare) via an antecubital vein at a flow rate of 5 mL/sec, followed by a 30-mL saline flush. After a scan delay of 6–9 seconds, eight adjacent 5-mm slices were acquired in a cine mode for 30 seconds without table movement. The slice thickness of 5 mm was determined both to balance the spatial resolution and image nose and to reduce the time required for processing the datasets (1). The following parameters were used: 100 kV, 120 mA, 0.5-second gantry rotation time, cine time between images of 0.5 second (TI of 0 second) (16), total exposure 60 times, detector coverage 40 mm, 5-mm reconstruction width, large body field of view, display field of view of 20 cm, 512×512 matrix, and inspiration breath hold. This sequence provided a total of 480 images (60 images $\times$ 8 slice levels) reconstructed for the perfusion measurements. For eight nodules with a diameter <2 cm, image reconformation with a 2.5-mm slice thickness and 0-mm interval was performed to limit the partial volume effect, yielding a total of 960 slices. The standard reconstruction algorithm at a window wide/window level of 350/40 Hounsfield units (HU) was used for all dynamic images.

After the dynamic CT scan, another wholly thoracic helical scan with enhancement (40 mL iodinated contrast at a flow rate of 2.0 mL/sec and delay time of 30 seconds) was acquired using the same parameters as the earlier mentioned unenhanced scan. This scan was used for routine diagnosis.

CTP Data Processing and Analysis

Dynamic CTP images were analyzed with use of the commercial CT perfusion software Perfusion 3 at the ADW 4.3 work station (GE Medical Systems) by an observer (F.S.). This software uses the distributed parameter analysis, allowing the calculation of parametric maps for BF, blood volume (BV), mean transit time (MTT), and capillary permeability–surface area product (PS). Air and bone pixels were excluded by using HU value thresholds, resulting in a selection range of 0–120 HU. The arterial input region of interest (ROI) was set within the aorta automatically. If the automatic process was judged to be incorrect, the input ROI was drawn with size of 10–15 mm^2 manually in the aorta or in the left subclavian artery if the aorta was not included in the section. A time–density curve (TDC) was automatically generated for the arterial input. Automatic determination was used, detecting the last preenhancement image and the last enhancement image after restricting the search area to the input ROI, while the last second-phase image was set as the last image of the dynamic scan. Perfusion maps within the scanning plane in the selected threshold were generated along with the arterial input setting. Those maps with a slice thickness of 5 mm for BF, BV, MTT, and PS were calculated using standard settings (medium value of 3 for algorithm resolution and of 5 for spatial smoothing, normal of 1000 mL/100 g/min for the maximum BF) and were displayed by the rainbow color method with the BF value scaled from 0 to 1000 mL/100 g/min, BV value scaled from 0 to 10 mL/100 g, MTT value scaled from 0 to 15 seconds, and PS value scaled from 0 to 20 mL/100 g/min.

For each patient, a central slice was chosen, and perfusion datasets were generated, representing different TIs of 0, 0.5, 1, 1.5, 2, 2.5, and 3.5 seconds. The reference TI of 0 second corresponded to the perfusion series acquired with the cine mode technique, with raw data reconstruction for this sampling interval. For the TI of 0.5 second, every second image in the series was deleted. An analogous method was employed for the other interval datasets. Due to the removal effects of different cine acquisition times, the last image (acquired at the cine time of 30 seconds) was added into the sampling series from TIs of 1 second to 3.5 seconds. Thus, the series representing different TIs included a total of 60, 30, 21, 16, 13, 11, and 9 images per slice, respectively, for a 30-second dynamic scan. For the quantitative perfusion assessment at a window wide/window level 350/40 HU, ROIs were drawn freehand around the wholly solid part of the tumor by an observer (F.S.) and care was taken to exclude the surrounding