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Intraobserver and interobserver agreement of volume perfusion CT (VPCT) measurements in patients with lung lesions

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ABSTRACT

Objectives: To evaluate intraobserver and interobserver agreement of manually encompassed lung lesions for perfusion measurements using volume-perfusion computed tomography (VPCT).
Materials and methods: Institutional review board approval and informed consent were obtained. HIPAA guidelines were followed. A 65-s dynamic study was acquired with scan parameters 80 kV, 60 mA s (80 mA s for patients ≥70 kg), 128 × 0.6 mm collimation. Blood flow (BF), blood volume (BV) and K^{trans} parameters were determined by syngo volume perfusion CT body with 88 lesions analyzed retrospectively.
Results: Within-subject coefficients of variation for intraobserver agreement (range 6.59–12.82%) were superior to those for interobserver agreement (range 21.75–38.30%). Size-dependent analysis revealed lower agreements for lesions <4 cm as compared to larger lesions. Additionally, agreements of the upper, middle and lower lung zones were different.
Conclusions: Intraobserver agreement was substantial for VPCT lung cancer perfusion measurements encouraging the use for tumor characterization and therapy response monitoring. Interobserver agreement is limited and unexperienced readers should be trained before using this new method.

1. Introduction

As new biological response modifiers and targeted therapies do not necessarily cause an initial tumor size reduction, more elaborated disease response assessments and biomarkers than linear measurements recommended by the Response Evaluation Criteria in Solid Tumors (RECIST) are required [1]. Recently, Meyer et al. proclaimed that such a biomarker should be a validated disease characteristic which can be reliably measured in a cost-effective, repeatable and generalizable manner, and which acts as a meaningful surrogate for disease presence, absence, activity, or outcome in individuals or groups with the disease process [2].

As tumor angiogenesis plays a decisive role in tumor growth and metastasis, current scientific projects focus on the development of non-invasive imaging techniques to characterize and quantify tumor blood vessels. Several techniques including positron emission tomography (PET), magnetic resonance imaging (MRI) and intravenous contrast-enhanced computed tomography (CT) exist [3]. Tumor perfusion measurements with ^{15}O-labeled water and PET are highly reproducible, however dependent on the vicinity of a cyclotron [4]. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) as an alternate approach requires complex postprocessing and lacks a standardized acquisition protocol [1]. Additionally, its application (e.g., in lung cancer) is limited due to a low spatial resolution [5]. Functional CT is based on the exchange of iodinated contrast material between the intravascular space and the extravascular interstitial space constituting a promising approach that can easily be integrated in day-to-day clinical routine [3]. In 1997, Zhang et al. have proposed the application of CT perfusion imaging for pulmonary nodules and studied the blood flow patterns of a single CT scan section [6]. Early studies were influenced by partial volume effect, image artifacts and variations in breath hold [7]. Acquisition times, time resolution, coverage and image resolution along the *z*-axis improved with the introduction of 16-row spiral CT enabling the characterization of lung nodules via assessment of first pass dynamics [8]. Ng et al. could show that a greater *z*-axis coverage improved the reproducibility and enabled whole-tumor perfusion measurements [9]. The

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64-detector row CT generation further refined these whole-tumor perfusion techniques [10]. Recently, Lind et al. demonstrated a successful therapy monitoring in patients treated with sorafenib and erlotinib for non-small cell lung cancer [5]. To further increase the perfusion coverage without enlarging the physical detector width, repeated spiral scanning and continuous table movements can be combined. Haberland et al. proved that this technique is able to reliably quantify tissue flow [11,12]. Goetti et al. applied this 4D spiral-mode for CT liver perfusion with a 128-row CT and coverage of up to 14.8 cm [13]. A good intraobserver and interobserver agreement for the assessment of lung tumors was demonstrated for the 8-row and 16-row CT generations [14]. The lack of these data for 4D spiral-mode CT perfusion encouraged us to analyze our lung cancer collective. With regard to the limitations of automated lung segmentation and manual encompassment of the volume of interest (VOI) for thoracic CT, this issue is still gaining importance [15,16]. To our knowledge, this is the first study to address intraobserver and interobserver agreement for lung cancer measurements using volume perfusion CT (VPCT).

2. Materials and methods

2.1. Study population

The local Ethics Committee approved our study, and all patients provided written informed consent including information about the radiation exposure. All patients were referred to our institute for tumor staging and therapy monitoring. To be eligible, patients needed to be aged 18 years or older and to suffer from a primary lung tumor. Exclusion criteria for contrast-enhanced CT were nephropathy (defined as a serum creatinine level more than 150 μmol/l), known hypersensitivity to iodine-containing contrast media, pregnancy, and untreated hyperthyroidism. Between September 2009 and July 2010, 61 patients (18 women, 43 men; mean age 68 ± 9.6 years [mean ± SD]; age range 49–87 years) were enrolled. All patients of our cohort had a baseline examination, 21 patients had additional follow-up studies (15 patients with one follow-up; 6 patients with two follow-ups). Therefore a total of 88 scans were analyzed retrospectively. Histological subtypes included: 53 non-small cell lung carcinoma (46 adenocarcinoma, 7 squamous cell lung carcinoma), 5 small cell lung carcinoma, 1 sarcoma, 2 non-malignant tumors.

2.2. CT data acquisition

The CT protocol consisted of a non-enhanced (NECT) low-dose chest-CT, followed by a 6.9 cm *z*-axis coverage chest volume perfusion CT using adaptive spiral scanning technique. All examinations were performed on a 128-row CT scanner (Somatom Definition AS+, Siemens Healthcare, Forchheim, Germany). Acquisition parameters for NECT included 60 mA s, 100 kV, SL = 5.0 mm, 128 × 0.6 mm collimation, 0.5 s tube rotation time, pitch 0.6, and a dose length product (DLP) of 47 mGy cm. An experienced radiologist analyzed the NECT and the scan range was planned for coverage of the most prominent lesion. Dynamic sequential perfusion scanning was performed with 80 kV, 60 mA s (for patients <70 kg) and 80 mA s (for patients ≥70 kg), 128 × 0.6 mm collimation, 3 scans every 3 s, followed by 12 scans every 2 s (inflow phase), another 3 scans every 3 s and further 2 scans 15 and 20 s later (outflow phase), respectively. The total VPCT scanning time was 65.9 s. The mean radiation exposure for perfusion measurements was 3.5 mSv for a male and 6.5 mSv for a female patient [17]. A volume of 50 ml Ultravist 370 (Bayer Vital Leverkusen, Germany) at a flow rate of 5 ml/s was injected in an antecubital vein through an 18-G needle (Vasofix, B. Braun Melsungen AG, Germany) followed by a saline flush of

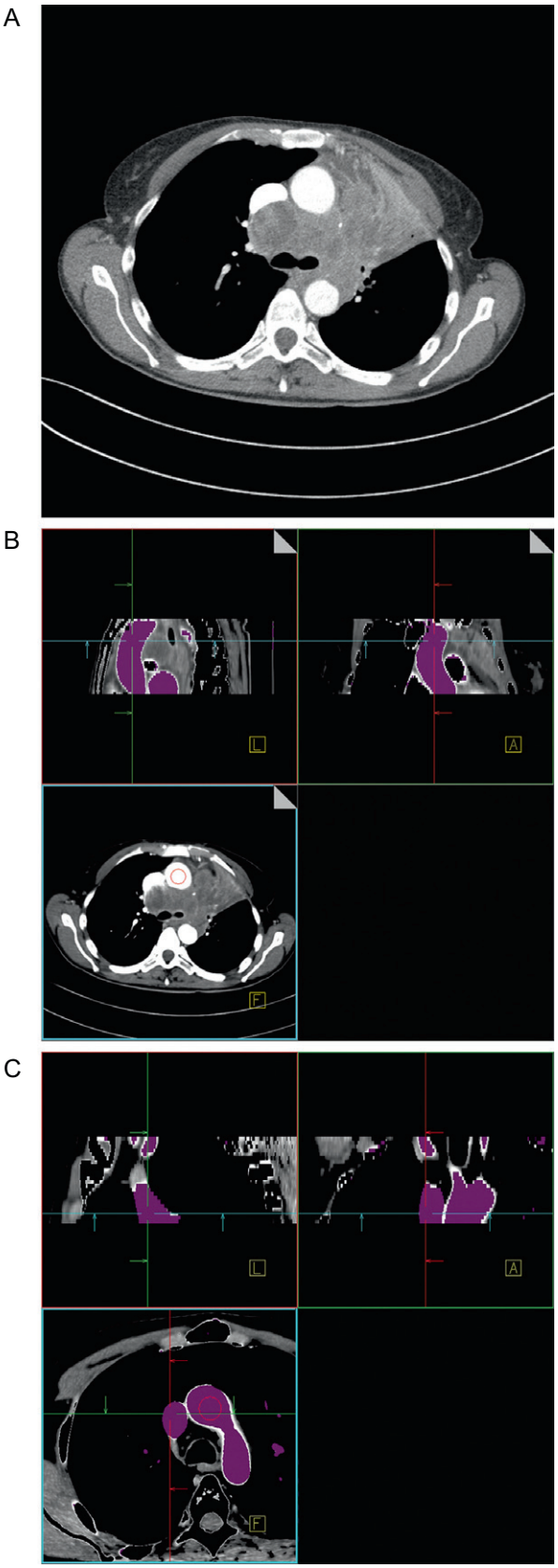

Fig. 1. (A) Bronchial carcinoma of the left upper lobe with extensive mediastinal infiltration. (B) ROI placement inside the ascending aorta to obtain arterial input function. (C) Corresponding MIP, BF, BV and K^{trans} maps with whole-tumor VOI: Calcifications and air-inflated structures cause dark spots (corresponding to excluded values) in the map.