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Diffusion weighted MRI and 18F-FDG PET/CT in non-small cell lung cancer (NSCLC): Does the apparent diffusion coefficient (ADC) correlate with tracer uptake (SUV)?

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ABSTRACT

Introduction: To investigate the potential correlation of the apparent diffusion coefficient assessed by diffusion-weighted MRI (DWI) and glucose metabolism determined by the standardized uptake value (SUV) at 18F-FDG PET/CT in non-small cell lung cancer (NSCLC).
Materials and methods: 18F-FDG PET/CT and DWI (TR/TE, 2000/66 ms; *b*-values, 0 and 500 s/mm^2) were performed in 41 consecutive patients with histologically verified NSCLC. Analysing the PET-CT data calculation of the mean (SUV_{mean}) and maximum (SUV_{max}) SUV was performed. By placing a region-of-interest (ROI) encovering the entire tumor mean (ADC_{mean}) and minimum ADC (ADC_{min}) were determined by two independent radiologists. Results of 18F-FDG PET-CT and DWI were compared on a per-patient basis. For statistical analysis Pearson's correlation coefficient, Bland–Altman and regression analysis were assessed.
Results: Data analysis revealed a significant inverse correlation of the ADC_{min} and SUV_{max} ($r = -0.46$; $p = 0.032$). Testing the correlation of the ADC_{min} and SUV_{max} for each histological subtype separately revealed that the inverse correlation was good for both adenocarcinomas ($r = -0.47$; $p = 0.03$) and squamouscell carcinomas ($r = -0.71$; $p = 0.002$), respectively. No significant correlation was found for the comparison of ADC_{min} and SUV_{mean} ($r = -0.29$; $p = 0.27$), ADC_{mean} vs. SUV_{mean} ($r = -0.28$; $p = 0.31$) or ADC_{mean} vs. SUV_{max} ($r = -0.33$; $p = 0.23$). The κ-value of 0.88 indicated a good agreement between both observers.
Conclusion: This preliminary study is the first to verify the relation between the SUV and the ADC in NSCLC. The significant inverse correlation of these two quantitative imaging approaches points out the association of metabolic activity and tumor cellularity. Therefore, DWI with ADC measurement might represent a new prognostic marker in NSCLC.

1. Introduction

Lung cancer is the leading cause of cancer related death worldwide and is responsible for more deaths annually than breast, prostate and colon cancers combined [1]. More than 80% of primary lung cancers are non-small cell lung cancers (NSCLCs) affecting approximately 1.35 million people throughout the world every year.

The image-guided diagnostic workup relies on multidetector computed tomography (MDCT), positron emission tomography (PET) with 2-(fluorine-18) fluoro-2-deoxy-D-glucose (18F-FDG PET) and skeletal scintigraphy which are routineously performed for accurate imaging and staging of NSCLC. Within the last decade coregistered whole-body 18F-FDG PET/CT has established multiparametric imaging in lung cancer as it allows the investigator to raise information about tumor morphology and extent and also provides information about the tumor glucose metabolism by the calculation of the standardized uptake value (SUV) [2]. Due to the superiority of 18F-FDG PET/CT compared to a stand-alone approach, this technique has become the standard of care in NSCLC patients [3]. Interestingly, there is a strong correlation between the maximum SUV and the clinical course in NSCLC. In this regard, a high SUV of the primary tumor determined at 18F-FDG PET prior to treatment is associated with a shorter time-to-progression, higher recurrence and lower overall survival rates [4]. Furthermore, it has been demonstrated that there is a low likelihood of a substantial

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response to therapy resulting in limited time of survival if there is no decrease in maximum SUV early after the initiation of anti-cancer treatment [5]. Therefore, the standardized FDG uptake is often reported to be a significant prognostic factor in non-small cell lung cancer [6].

Meanwhile, the availability of multichannel MRI with high-performance gradient systems and parallel imaging techniques has opened the door for new interesting approaches to MR-based pulmonary imaging. High-resolution MR imaging can be performed to reliably detect lung malignancies and raise information about tumor morphology [7]. Dynamic contrast-enhanced MRI with high temporal resolution allows for functional imaging in chronic obstructive lung disease and lung cancer [8] and has furthermore been demonstrated to serve as a sensitive discriminator between benign and malignant consolidation [9].

Recently, diffusion-weighted imaging (DWI), an established quantitative technique in neuroimaging, has successfully been transferred into chest imaging and has shown great potential in the detection and interpretation of solid lung lesions [10]. DWI can visualize the random thermal motion of molecules known as Brownian motion, causing incoherent phase shifts resulting in signal attenuation. Thus, this technique allows for quantification of diffusion by calculating the apparent diffusion coefficient (ADC). In malignant tumors the increased cellular density restricts water diffusion in the interstitial space, resulting in lower ADC values. Hence, in NSCLC DWI has been reported to reveal information about tumor cellularity and aggressiveness helping to predict tumor invasiveness even at early stage [10].

Since SUV and ADC values both reflect information about tumor aggressiveness with the SUV displaying tumor activity and the ADC quantifying tumor cellularity, a certain correlation between these two quantitative imaging markers can be expected. The purpose of the presented study was to investigate any potential correlation between SUV determined at 18F-FDG PET/CT and ADC calculated on the basis of diffusion weighted MRI in non-small cell lung cancer.

2. Materials and methods

2.1. Patient population

Within this prospective study 41 consecutive patients (22 men; 19 women; mean age, 66 years; adenocarcinoma, $n = 21$; squamouscell carcinoma, $n = 15$; large cell carcinoma, $n = 5$) with newly diagnosed non-small cell lung cancer were investigated. The inclusion criteria were as follows: (1) current histological prove of NSCLC present, either by endobronchial ultrasound with fine needle aspiration or by CT-guided core biopsy; (2) no prior history of malignant disease, anti-cancer drugs or radiotherapy and (3) an 18F-FDG PET/CT had been performed within 30 days prior to MR imaging. Patients with contraindications to MRI such as pacemakers, metallic implants, severe claustrophobia or pregnancy were excluded.

The study protocol was approved by the local ethical committee and written informed consent was obtained from all patients prior to the examinations.

2.2. 18F-FDG PET/CT image acquisition and reconstruction

PET and CT imaging were performed using the Gemini GXL 10 hybrid PET/CT system (Philips, Best, The Netherlands) [11]. This system combines a full-ring, whole-body, 3D-only PET equipped with gadolinium orthosilicate (GSO) crystal detectors covering an axial field-of-view (FOV) of 18 cm with a 10-slice high-resolution spiral CT. Patients were instructed to fast for a minimum of 6 h before the injection of 18F-fluorodeoxyglucose (FDG). The dose of intravenously administered 18F-FDG was 5 MBq/kg. During the uptake period of 60 min, patients were orally hydrated with water. Imaging started with a single non-enhanced, low-dose CT of the whole body (120 kV, 80 mA, transaxial FOV of 600 mm, slice thickness 5 mm, no gap, collimation 10 mm × 1.5 mm, pitch 1.1, rotation time 0.5 s, matrix 512 × 512). An intravenous contrast agent was administered if requested by the referring physician. Following CT, whole-body PET static emission images were acquired from thigh to head with 90 s per bed position at head and thorax, and 60 s at the legs. Overlap between consecutive bed positions was 50%. Thus, total PET acquisition time was about 20 min. Transversal PET slices were reconstructed into a 144 × 144 matrix using the iterative 3D line-of-response (LOR) reconstruction algorithm of the system software with standard parameter settings. The low-dose CT extrapolated to 511 keV was used for PET attenuation correction. Voxel size was 4 mm × 4 mm × 4 mm. Spatial resolution in the reconstructed PET images was about 8 mm in full-width-at-half-maximum.

Table 1
The details of the imaging parameters used for both diffusion weighted and contrast enhanced T1 weighted MRI.

	DWI	T1w 3D-GRE
TR/TE (ms)	2000/66	4.9/2.4
Voxel size (mm)	4.4 × 5.5 × 5	1.95 × 2.2 × 2
NSA	2	1
Matrix	256	192
FOV (MM)	425	375
Acquisition time (s)	≈240	<20
b-Values (s/mm^2)	0 and 500	

DWI, diffusion weighted imaging; T1w 3D-GRE, T1 weighted three-dimensional gradient recalled echo sequence.

2.3. MR image acquisition

For MR imaging a 1.5 T scanner system (Achieva, Philips Medical Systems, Best, The Netherlands) was used, which was equipped with a gradient system with a slew rate of 160 mT/m/ms and an amplitude of 33 mT/m/ms. A standard phased-array torso surface coil (4-channel SENSE body coil) was used for signal reception. First, a diffusion-weighted single-shot spin-echo (SE) echo-planar imaging (EPI) sequence was performed in axial orientation covering the entire chest in 5 mm sections. For sufficient fat suppression a STIR impulse was implemented into the sequence parameters. Respiratory triggering was used to compensate for motion artifacts. Electrocardiographic (ECG) triggering was not performed. The scan time for the DWI was approximately 4 min. Furthermore, a contrast enhanced (0.1 mmol kg bodyweight^{-1}; Magnevist, Schering, Berlin, Germany) T1-weighted three-dimensional gradient recalled echo (3D-GRE) sequence was performed within a single breathhold of less than 20 s. An automated injector system (Stellant MR Injection System, Medrad, Germany) was used to apply the contrast agent through an 18- to 20-gauge venous catheter, which was placed in an antecubital vein. The time delay between contrast injection and image acquisition was set to 60 s. Table 1 displays the imaging parameters applied for MR image acquisition.

2.4. Image analysis

Evaluation of the 18F-FDG PET/CT data was conjointly performed by two radiologists in collaboration with a board certified nuclear medicine physician.

For SUV measurements, both coregistered PET and CT images as well as fused PET/CT images were reformatted into axial, coronal, and sagittal views, and were analyzed on a dedicated workstation (Extended Brilliance Workstation, Philips Medical Systems, Best, The Netherlands). First, tumor borders of the primary lung cancer were identified on axial slices of the CT scan and a