Original Investigation

A Study of the Feasibility of FDG-PET/CT to Systematically Detect and Quantify Differential Metabolic Effects of Chronic Tobacco Use in Organs of the Whole Body—A Prospective Pilot Study

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Rationale and Objectives: The aim of this study was to assess the feasibility of ^{18}F-fluorodeoxyglucose (FDG)-positron emission tomography/computed tomography (PET/CT) to systematically detect and quantify differential effects of chronic tobacco use in organs of the whole body.

Materials and Methods: Twenty healthy male subjects (10 nonsmokers and 10 chronic heavy smokers) were enrolled. Subjects underwent whole-body FDG-PET/CT, diagnostic unenhanced chest CT, mini-mental state examination, urine testing for oxidative stress, and serum testing. The organs of interest (thyroid, skin, skeletal muscle, aorta, heart, lung, adipose tissue, liver, spleen, brain, lumbar spinal bone marrow, and testis) were analyzed on FDG-PET/CT images to determine their metabolic activities using standardized uptake value (SUV) or metabolic volumetric product (MVP). Measurements were compared between subject groups using two-sample *t* tests or Wilcoxon rank-sum tests as determined by tests for normality. Correlational analyses were also performed.

Results: FDG-PET/CT revealed significantly decreased metabolic activity of lumbar spinal bone marrow (MVPmean: 29.8 ± 9.7 cc vs 40.8 ± 11.6 cc, $P = 0.03$) and liver (SUVmean: 1.8 ± 0.2 vs 2.0 ± 0.2, $P = 0.049$) and increased metabolic activity of visceral adipose tissue (SUVmean: 0.35 ± 0.10 vs 0.26 ± 0.06, $P = 0.02$) in chronic smokers compared to nonsmokers. Normalized visceral adipose tissue volume was also significantly decreased ($P = 0.04$) in chronic smokers. There were no statistically significant differences in the metabolic activity of other assessed organs.

Conclusions: Subclinical organ effects of chronic tobacco use are detectable and quantifiable on FDG-PET/CT. FDG-PET/CT may, therefore, play a major role in the study of systemic toxic effects of tobacco use in organs of the whole body for clinical or research purposes.

Key Words: Fluorodeoxyglucose (FDG); positron emission tomography/computed tomography (PET/CT); CT; tobacco use; smoking; metabolism; inflammation.

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INTRODUCTION

Smoking is one of the most important sources of toxic exposure in humans, and is a major cause of morbidity and mortality worldwide. It is associated with a wide variety of disease conditions that affect multiple organ systems of the body secondary to increased levels of cellular oxidative stress, receptor binding, genetic mutations, and release of proinflammatory chemical substances. However, the subclinical metabolic and proinflammatory effects of chronic tobacco use have not been systematically assessed body wide at the organ level in humans, largely due to the lack of available robust quantitative diagnostic techniques for this purpose. The ability to detect and to quantify the severity of the subclinical organ effects of chronic tobacco use may be important to determine individualized risk for development of various disease conditions, to foster smoking cessation, and to monitor the effects of interventions utilized to mitigate the adverse effects of smoking.

^{18}F-2-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT) is a molecular imaging technique that is available for accurate quantitative assessment of cellular metabolism in the whole body. Although FDG-PET/CT is predominantly used to assess patients with cancer in clinical practice, it is also useful to noninvasively detect and quantify inflammation, infection, and other etiologies of altered tissue metabolism in organs of the body (1–3). As such, it is reasonable to hypothesize that FDG-PET/CT can be used to assess the subclinical metabolic and proinflammatory effects of smoking. Yet, to our knowledge, no human studies with FDG-PET/CT have been performed to systematically study the effects of chronic tobacco use upon organs of the whole body. Therefore, in this pilot study, we assessed the feasibility of FDG-PET/CT to quantitatively assess the differential metabolic and inflammatory changes in organs of the whole body in relation to chronic tobacco use.

MATERIALS AND METHODS

This prospective pilot study was conducted following approval from the Institutional Review Board at the Hospital of the University of Pennsylvania, and following approval for an investigational new drug exemption from the Radioactive Drug Research Committee at the University of Pennsylvania.

Study Sample

Twenty healthy volunteer male subjects were enrolled in this prospective pilot study between January 2010 and August 2011. Ten were nonsmokers (ie, never smokers) and 10 were chronic heavy cigarette smokers. Informed consent was obtained for experimentation with human subjects.

The inclusion criteria were as follows: (1) male sex; (2) age 30–50 years inclusive; and (3) no significant health problems as per subject report and available medical records (although chronic obstructive pulmonary disease [COPD] was allowable in smokers). Additionally, the inclusion criteria for smokers required a ≥15 pack-year smoking history and no recent tobacco quit attempt. We arbitrarily selected only male subjects for participation in this study to eliminate confounding of the results by the potential differential effects of sex (male, female) upon organ metabolism. A relatively older subject sample was selected for participation in this study in order to maximize the likelihood of detecting differences in organ metabolism on FDG-PET/CT secondary to chronic tobacco use.

Nicotine dependence was assessed in chronic heavy smokers using the Fagerström Test of Nicotine Dependence (FTND) (4). The FTND is a six-item self-report measure of nicotine dependence (with a score range of 0–10, where >4 is considered to indicate moderate nicotine dependence) with satisfactory internal consistency and high test-retest reliability (5).

The exclusion criteria were as follows: (1) chronic disease requiring ongoing medical treatment (with exception of COPD in smokers); (2) acute illness within the last 3 months; (3) heavy alcohol use defined as more than two drinks per day on average; (4) known diabetes mellitus or fasting blood glucose level >130 mg/dL; (5) obesity defined by a body mass index (BMI) >30 kg/m^2; (6) a history of hypertension or blood pressure >140/90; (7) a history of any neuropsychiatric disorder; (8) inability to withhold cigarette usage for a minimum of 3 hours (in smokers); and (9) inability to tolerate all imaging and nonimaging test procedures.

Whole-body FDG-PET/CT and Thoracic Diagnostic CT Image Acquisition

Subjects fasted for a minimum of 6 hours and were confirmed to have fingerstick blood glucose levels of ≤130 mg/dL prior to FDG administration. A 16 multidetector row LYSO whole-body PET/CT scanner with time-of-flight capabilities (Gemini TF, Philips Healthcare, Bothell, WA) was used to acquire whole-body FDG-PET/CT images. Approximately 15 mCi MBq (range: 14.41–16.49 mCi) of FDG was administered intravenously to subjects while they were quietly resting on a chair. Subsequently, three-dimensional (3D) PET emission data were acquired from the skull vertex to the toes in supine position beginning 60 ± 15 minutes later for 3 minutes per bed position. The subject's arms were down by the torso during image acquisition from the skull vertex to the base of the neck, and raised above the torso during image acquisition from the base of the neck to the toes. A list-mode maximum-likelihood expectation-maximization algorithm was utilized to perform image reconstruction. The system model included time-of-flight, normalization, randoms, attenuation, and scatter corrections. Attenuation correction of PET images was done utilizing rescaled low-dose CT. PET and CT images were reconstructed at 5-mm slice thickness.

Diagnostic quality unenhanced thin-section high-resolution CT of the chest during full inspiratory breath-hold was subsequently performed on the PET/CT scanner in the same