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Particle doses in the pulmonary lobes of electronic and conventional cigarette users

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ABSTRACT

The main aim of the present study was to estimate size segregated doses from e-cigarette aerosols as a function of the airway generation number in lung lobes. After a 2-second puff, 7.7×10^{10} particles (D_{Tot}) with a surface area of 3.6×10^{3} mm^2 (S_{Tot}), and 3.3×10^{10} particles with a surface area of 4.2×10^{3} mm^2 were deposited in the respiratory system for the electronic and conventional cigarettes, respectively. Alveolar and tracheobronchial deposited doses were compared to the ones received by non-smoking individuals in Western countries, showing a similar order of magnitude. Total regional doses (D^R), in head and lobar tracheobronchial and alveolar regions, ranged from 2.7×10^{9} to 1.3×10^{10} particles and 1.1×10^{9} to 5.3×10^{10} particles, for the electronic and conventional cigarettes, respectively. D^R in the right-upper lung lobe was about twice that found in left-upper lobe and 20% greater in right-lower lobe than the left-lower lobe.

1. Introduction

1.1. Background

Scientific studies have clearly shown that cigarette smoke is a major cause of premature death, and a range of adverse health effects, primarily cancer (e.g., lung, oral cavity, esophagus, larynx, pancreas, bladder, kidney), cardiovascular and chronic obstructive pulmonary diseases (COPD), myocardial infarction and stroke (Caponnetto et al., 2012; Crawford et al., 2012; Doll et al., 2004; Fiore et al., 2008; Moolgavkar et al., 2012; WHO, 2008) in human populations. During the cigarette combustion processes, hundreds of toxins and carcinogens are generated (Baker, 2006; Geiss and Kotzias, 2007). In fact, 9 of the 44 chemical agents classified as "Group 1 carcinogens" by the International Agency for Research on Cancer (IARC) have been reported to be present in both the vapor and particulate phases of mainstream (MS) cigarette smoke (the exhaled smoke released after taking a puff on a lit cigarette) (Smith et al., 2003). Recently, electronic nicotine delivery systems (ENDS), also known as electronic cigarettes (e-cigarettes), have grown in popularity because they are considered to be a less harmful and less toxic alternative to tobacco cigarettes, or as a transitory way to quit smoking (Bullen et al., 2010; Etter, 2010; Etter et al., 2011; Foulds et al., 2011; McQueen et al., 2011; Polosa et al., 2011; Siegel et al., 2011) and they are also allowed to be consumed in smoke-free environments. However, to date, their toxicity has not been scientifically proven compared to tobacco cigarettes (Etter and Bullen, 2011).

E-cigarettes are battery-powered devices made up of an electric atomizer and a replaceable cartridge containing a water-based liquid ("e-liquid"), composed of propylene glycol, glycerin, water, flavors and a variable amount of nicotine (Pellegrino et al., 2012; Flouris et al., 2013; Manigrasso et al., 2015). This e-liquid is heated and vaporized in an atomizer and then inhaled by the user (vaper). Thus, in e-cigarettes, tobacco combustion is replaced by the vaporization of e-liquids and it is for this reason that they are claimed to pose a lower risk for vapers (Cobb et al., 2010; Caponnetto et al., 2013).

1.2. E-cigarette aerosol emission characterization

A limited number of scientific studies have aimed to characterize the mainstream aerosol from e-cigarettes. Schripp et al.

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(2013) analyzed the emission of fine and ultrafine particles (UFPs, particle smaller than 100 nm), as well as volatile organic compounds (VOCs) from e-cigarettes, by testing them in a chamber. An increase in both particle and VOC concentrations was detected. In particular, the e-cigarette-generated aerosol showed a bimodal size distribution peaking at 60 and 100 nm. Zhang et al. (2013) studied the particle size distributions of electronic and conventional cigarette aerosols *in vitro*. The particle number distribution for e-cigarettes was comparable to that of conventional tobacco in the 100–600 nm range. By applying a lung deposition model to estimate deposition in different respiratory tracts, they predicted a 7–18 % alveolar delivery, a 9–19 % venous delivery (mostly in the head) and a 73–80 % loss by exhalation. Fuoco et al. (2014) carried out an experimental campaign to investigate the effect of different operating parameters, such as type of e-cigarette, flavor, nicotine content and puffing time on particle number concentration and size distribution in the mainstream aerosol of e-cigarettes. They found e-liquid nicotine content and puffing time to be the most important parameters influencing particle emission.

1.3. Aims of the work

Data concerning the health effects of e-cigarette vaping are still scarce and far from being definitive (Flouris and Oikonomou, 2010; Borland and Gray, 2011; Gennimata et al., 2012). Studies have been published on: their short term effects (McCauley et al., 2012; Vakaòi et al., 2012; Vardavas et al., 2012; Hua et al., 2013; Marini et al., 2014); the effects exerted by some components of the e-liquid, but not nicotine (Renne, 1992; Moline et al., 2000; Wieslander et al., 2001; Choi et al., 2010; Bahl et al., 2012); and the potential health effects of their aerosols (German Cancer Research Center, 2013; Goniewicz et al., 2013). However, in order to correlate aerosol measurements with their health effects, the particle doses delivered into the respiratory system need to be known. Furthermore, knowledge of their distribution in the respiratory tree is important because the airway pathologies caused by deposition of particulate matter have often been reported to occur at specific sites in the lung, particularly within specific lobes (Winkler-Heil and Hofmann, 2009). From this perspective, Parkash (1977) observed that the right lung is more often the seat of carcinoma than the left lung, and the upper lobes more often than the lower lobes. The author speculated that since the right bronchus is wider, shorter and runs almost as a continuation of the trachea, there is a greater chance of more particles depositing in the right lung than in the left lung as a whole, which is likely to cause a higher frequency of malignancies. For this reason, it is important to assess particle deposition in the respiratory tree, considering the differences between and within the lung lobes. To date, such knowledge is lacking in relation to e-cigarettes, and therefore, the main aim of this study was to obtain and compare data for e-cigarettes with the aerosol doses deposited in the respiratory system of conventional cigarette smokers. For the first time, size segregated dosimetry data for the aerosol from e-cigarettes have been reported as function of the airway generation number in lung lobes. The other aim of this work was to make a comparison between the doses received by vapers and those received by non-smoking individuals frequenting the microenvironments encountered in typical daily life, where aerosols are originated from a variety of sources.

2. Material and methods

2.1. Electronic and conventional cigarettes

A rechargeable, commercial model e-cigarette, comprising of a tank system and a nicotine concentration of 14 mg mL^{-1}, was used in the experimental campaign (the flavor is not important because it was found to have a negligible influence on e-cigarette particle emission (Fuoco et al., 2014)). With regard to the conventional tobacco cigarettes, cigarettes with a nicotine concentration equal to 0.8 mg per cigarette were tested, since this represents the typical nicotine content of commercial cigarettes.

2.2. Instrumentation and aerosol sampling

Cigarette-generated mainstream aerosol measurements were performed in the European Accredited (EA) Laboratory of Industrial Measurements (LAMI) at the University of Cassino and Southern Lazio, Italy, where thermo-hygrometric conditions were continuously monitored, in order to guarantee temperature and relative humidity values equal to 20 ± 1 °C and 50 ± 10%, respectively. Measurements of total particle number concentration and particle size distribution were carried out by a Condensation Particle Counter (CPC 3775, TSI Inc.) and a Fast Mobility Particle Sizer spectrometer (FMPS 3091, TSI Inc.). The CPC 3775 measures total particle number concentration down to 4 nm in diameter with a 1-s resolution, and up to a maximum concentration of 10^7 part. cm^{-3}. It was calibrated before the experimental campaign by comparison with a TSI 3068B Aerosol Electrometer using NaCl particles generated by a Submicrometer Aerosol Generator (TSI 3940) (Venditti et al., 2010; Stabile et al., 2013). The FMPS 3091 measures particle size distribution in the range 5.6–560 nm using the electrical mobility technique, with a 1-s time resolution (Johnson et al., 2004). Because of the high particle number concentration in electronic and conventional cigarette mainstream aerosols, the aerosol was diluted before entering the measurement section of the instrumental setup. To this end, a thermodilution system (two-step dilution), made up of a rotating disk thermodiluter, RDTD (model 379,020, Matter Engineering AG; Hueglin et al., 1997) and a thermal conditioner (model 379,030, Matter Engineering AG; Burtscher, 2005) were used.

Mainstream aerosol measurements were performed for puffs of 2-s duration. In particular, three puff profiles made up of four consecutive puffs with a 30-s inter puff interval were performed for each test using a time-controlled switch valve. The first puff was considered a “warm up” puff as it could lead to possible measurement errors when e-cigarettes were tested, as reported by Ingebrethsen et al. (2012). Before entering the measurement section, the aerosol passed through the thermodilution system, in order to prevent measurement artifacts that may have occurred during the sampling process. A scheme of the experimental setup adopted for mainstream aerosol measurements is reported in Fig. 1 of supplemental material. The thermodilution was performed at a temperature of 37 °C, in order to simulate the temperature of the human respiratory apparatus. Despite the 5.6–560 nm FMPS measurement range, only particle distribution data in the range from 14 nm to 523 nm were considered. This is because (Fuoco et al., 2014) and Ingebrethsen et al. (2012) demonstrated an artifact when measuring particle distributions of mainstream e-cigarette aerosols in the 5.6–14 nm diameter range.

2.3. Particle dose evaluation

Particle deposition in the human respiratory system was evaluated using the Multiple-Path Particle Dosimetry model (MPPD v2.1, ARA 2009), which calculates the deposition and clearance of mono and polydisperse aerosols, from ultrafine to coarse particles in the respiratory system of humans and rats (Anjilvel and Asgharian, 1995; Price et al., 2002). The model includes single and multiple path methods to calculate air flow and aerosol deposition. Dosimetry estimates were made by means of the