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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,  $7.7 \times 10^{10}$  particles ( $D_{Tot}$ ) with a surface area of  $3.6 \times 10^3 \text{ mm}^2$  ( $S_{Tot}$ ), and  $3.3 \times 10^{10}$  particles with a surface area of  $4.2 \times 10^3 \text{ mm}^2$  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  $2.7 \times 10^9$  to  $1.3 \times 10^{10}$  particles and  $1.1 \times 10^9$  to  $5.3 \times 10^{10}$  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.

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## 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; Vakaoui 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<sup>-1</sup>, 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<sup>7</sup> part. cm<sup>-3</sup>. 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

stochastic lung model, because it provides a more realistic lung geometry than the symmetric one considered in the ICRP model (ICRP, 1994; Manigrasso and Avino, 2012; Manigrasso et al., 2013; Avino et al., 2013). In the MPPD model, the ten stochastic lungs proposed by Asgharian et al. (2001) are ordered in size (total number of airways) from the smallest to the largest and the approximate size percentile of each lung is provided. The 60<sup>th</sup> percentile human stochastic lung was considered in this study. The following settings were considered in the application of the MPPD model: i) a uniformly expanding flow; ii) an upright body orientation; and iii) oral breathing with a 0.5 inspiratory fraction and no pause fraction. Moreover, the following parameters were used for a Caucasian adult male who is sitting and awake, based on the ICRP report (ICRP, 1994): i) a Functional Residual Capacity (FRC) of 3300 mL; ii) an Upper Respiratory Tract (URT) volume equal to 50 mL; iii) a 12 min<sup>-1</sup> breathing frequency; and iv) an air volume inhaled during a single breath (tidal volume) of 0.75 L.

In regard to the chemical and morphological properties of the e-cigarette-generated aerosols, the main e-liquid components are propylene glycol and water, and therefore it was assumed that the particles were spherical and of unitary density.

In order to calculate the overall dose for the particle diameter range measured by the FMPS, the MPPD model was run separately for the 26 FMPS size channels (from 14 to 523 nm) considered to be composed of a monodisperse aerosol.

Particle number regional deposition doses in the head (H), tracheobronchial (TB) and alveolar (Al) left-upper (LU), left lower (LL), right-upper (RU), right-middle (RM) and right-lower (RL) lung lobes were calculated as follows:

i) number dose size distributions

$$D_i^R = F_i^R \times C_i \times V_p \quad (1)$$

where  $R$  represents the H, TB–LU, TB–LL, TB–RU, TB–RM, TB–RL, Al–LU, Al–LL, Al–RU, Al–RM, Al–RL regions,  $F_i^R$  is the deposition fraction at a given  $R$  region of particles classified in the  $i$ th size class (calculated by the MPPD model),  $C_i$  is the 2-s puff average concentration of particles in the  $i$ th size class and  $V_p$  is the puff volume. A 50 cm<sup>3</sup> puff volume was used in this study, as an average of the puff volumes, ranging from 31 to 86 cm<sup>3</sup>, based on values reported in the literature for conventional cigarette smoke (Kane et al., 2010; van Dijk et al., 2011; Sahu et al., 2013);

ii) total regional doses:

$$D^R = \sum_{i=1}^{26} D_i^R \quad (2)$$

where 26 is the number of size classes;

iii) functions of particle diameter and of the airway generation number, for each of the five lung lobes:

$$D_i^G = F_i^G \times C_i \times V_p \quad (3)$$

where, for each lung lobe,  $F_i^G$  is the deposition fraction at the  $G^{\text{th}}$  airway generation of particles classified in the  $i$ th size class (calculated by the MPPD model);

iv) total lobar doses per airway generation for each of the five lung lobes:

$$D_G^R = \sum_{i=1}^{26} D_i^G \quad (4)$$

where the summation is performed over the 26 size classes. Total lobar deposition densities per airway generation ( $\tau^R_G$ ) were also calculated using the deposition fraction per unit surface area, instead of  $F_i^G$ , in eq. (3);

v) total number dose of particles deposited in the respiratory system was calculated as the sum of total regional doses:

$$D_{\text{Tot}} = \sum_R D^R \quad (5)$$

where the summation is calculated over the H, TB–LU, TB–LL, TB–RU, TB–RM, TB–RL, Al–LU, Al–LL, Al–RU, Al–RM and Al–RL regions. Total surface area of deposited particles ( $S_{\text{Tot}}$ ) was calculated based on the assumption that all particles were spherical in shape.

### 3. Results and discussion

#### 3.1. Mainstream particle number characterization

Average particle number concentration in the mainstream aerosol of the e-cigarettes under investigation (with a nicotine concentration level of 14 mg mL<sup>-1</sup>) was found to be equal to  $5.3 \pm 0.58 \times 10^9$  part. cm<sup>-3</sup>. This value is comparable to the ones measured by Fuoco et al. (2014) for nicotine-containing e-cigarettes of different flavors. By comparison, the average particle number concentration in the mainstream aerosol produced by the conventional tobacco cigarette (with a nicotine concentration of 0.8 mg) was  $3.1 \pm 0.61 \times 10^9$  part. cm<sup>-3</sup>.

The differences in total particle number concentration values between the two types of cigarettes were tested using the Student's t test, and a  $p$  value <0.01 was regarded as statistically significant. All the tested data were previously checked for normality using the Shapiro–Wilk test, in order to fulfill the conditions of the Student's t test. Statistical analysis showed that the emissions from conventional cigarettes were statistically lower ( $p < 0.01$ ) than from the e-cigarette.

Particle number distributions measured by the FMPS 3091 for both electronic and conventional cigarettes are reported in Fig. 1. Their modes were at about 130 nm and 165 nm, respectively.

#### 3.2. Tracheobronchial and alveolar deposited particle number and surface area doses

Table 1 shows the tracheobronchial and alveolar doses received

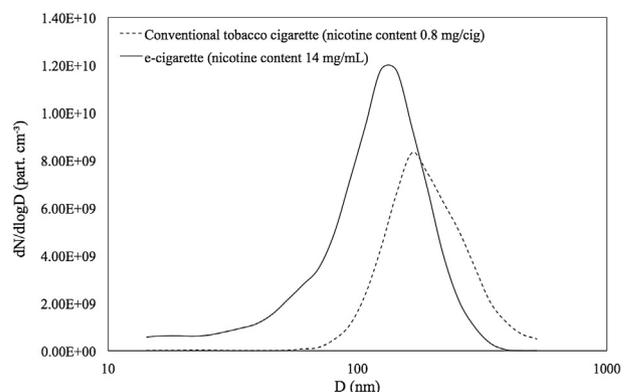


Fig. 1. Comparison between particle number size-distributions of the mainstream aerosol generated by e-cigarettes and conventional tobacco cigarettes measured through the FMPS 3091.

**Table 1**

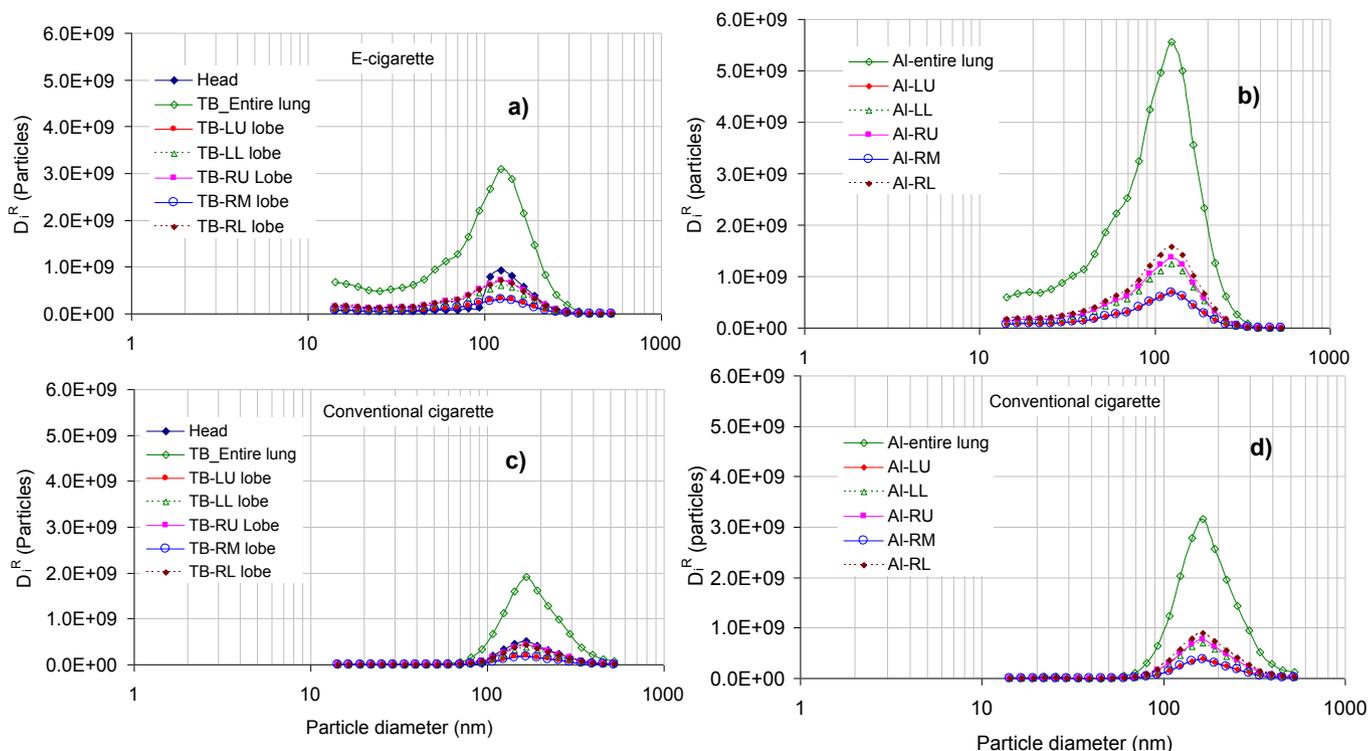
Alveolar (Al) and Tracheobronchial (TB) particle doses in terms of number (N) and surface area (S) received by e-cigarettes vapers and conventional cigarette smokers: comparison with doses experienced by Italian and Australian subjects on a daily-basis and in the most commonly frequented microenvironments. The ratios (TB–N Ratio, TB–S Ratio, Al–N Ratio, Al–S Ratio) between the doses received by vapers after 2-s puff and the ones of Italian and Australian subjects are also reported.

Cigarette	TB–N (particles)		TB–S (mm <sup>2</sup> )		Al–N (particles)		Al–S (mm <sup>2</sup> )	
E-cig. (2-s)	2.6 × 10 <sup>10</sup>		1.2 × 10 <sup>3</sup>		4.6 × 10 <sup>10</sup>		2.1 × 10 <sup>3</sup>	
Conv. cig. (2-s)	1.1 × 10 <sup>10</sup>		1.5 × 10 <sup>3</sup>		1.9 × 10 <sup>10</sup>		2.3 × 10 <sup>3</sup>	
Italian case	TB–N (particles)	TB–N ratio	TB–S (mm <sup>2</sup> )	TB–S ratio	Al–N (particles)	Al–N ratio	Al–S (mm <sup>2</sup> )	Al–S ratio
Daily	6.5 × 10 <sup>10</sup>	0.4	1.0 × 10 <sup>3</sup>	1.2	1.5 × 10 <sup>11</sup>	0.3	2.5 × 10 <sup>3</sup>	0.8
Sleeping	3.6 × 10 <sup>9</sup>	7.2	2.3 × 10 <sup>1</sup>	52.0	5.8 × 10 <sup>9</sup>	7.9	7.3 × 10 <sup>1</sup>	28.7
Cooking and eating	1.9 × 10 <sup>10</sup>	1.4	4.0 × 10 <sup>2</sup>	3.0	4.5 × 10 <sup>10</sup>	1.0	7.7 × 10 <sup>2</sup>	2.7
Working	2.3 × 10 <sup>10</sup>	1.1	2.8 × 10 <sup>2</sup>	4.4	5.8 × 10 <sup>10</sup>	0.8	4.3 × 10 <sup>2</sup>	4.9
Commuting	5.0 × 10 <sup>9</sup>	5.2	2.4 × 10 <sup>1</sup>	50.9	8.4 × 10 <sup>9</sup>	5.5	8.8 × 10 <sup>1</sup>	24.0
Australian case	TB–N (particles)	TB–N Ratio	TB–S (mm <sup>2</sup> )	TB–S Ratio	Al–N (particles)	Al–N Ratio	Al–S (mm <sup>2</sup> )	Al–S Ratio
Daily	1.5 × 10 <sup>10</sup>	1.7	2.1 × 10 <sup>2</sup>	5.6	3.2 × 10 <sup>10</sup>	1.4	4.7 × 10 <sup>2</sup>	4.5
Sleeping	1.8 × 10 <sup>9</sup>	14.7	3.2 × 10 <sup>1</sup>	37.9	3.3 × 10 <sup>9</sup>	14.1	5.6 × 10 <sup>1</sup>	37.2
Cooking and eating	3.4 × 10 <sup>9</sup>	7.6	8.8 × 10 <sup>1</sup>	13.6	7.1 × 10 <sup>9</sup>	6.5	1.9 × 10 <sup>2</sup>	10.8
Working	2.4 × 10 <sup>9</sup>	11.0	2.1 × 10 <sup>1</sup>	58.7	5.9 × 10 <sup>9</sup>	7.9	5.4 × 10 <sup>1</sup>	38.7
Commuting	8.3 × 10 <sup>8</sup>	31.5	7.6 × 10 <sup>0</sup>	158.6	1.7 × 10 <sup>9</sup>	27.3	1.7 × 10 <sup>1</sup>	125.5

by a vaper from a 2-s puff, in terms of deposited particle number and surface area. Alveolar doses of 4.6 × 10<sup>10</sup> particles and 2.1 × 10<sup>3</sup> mm<sup>2</sup>, as well as tracheobronchial doses of 2.6 × 10<sup>10</sup> particles and 1.2 × 10<sup>3</sup> mm<sup>2</sup> were estimated for particle number and surface area, respectively.

To put this into perspective, we compared the daily aerosol deposition doses from a single puff with the daily doses of non-smoking individuals, as well as the doses received while performing activities that made the most significant contribution to daily doses (sleeping, cooking and eating, working and commuting). Two different countries were considered: Italy, in a town (Cassino) characterized by high exposure due to thermal inversion, as well as indoor cooking activities (Buonanno et al., 2011) and Australia

(Brisbane), where lower values were found (Buonanno et al., 2012; Buonanno et al., 2013). As reported in Table 1, the particle number deposited doses received by a vaper from a 2-s puff were equivalent to 40% and 31% of the daily dose received by a non-smoking citizen living in Cassino, for the tracheobronchial and the alveolar regions, respectively. Such doses were higher than the daily dose received by a non-smoking citizen living in Brisbane (1.7-fold and 1.4-fold for tracheobronchial and alveolar regions, respectively). The corresponding particle surface area doses received by vapers during a 2-s puff were similar to the daily dose received in Cassino (1.2-fold and 0.8-fold for tracheobronchial and alveolar regions, respectively) and much higher than those received in Brisbane (5.6-fold and 4.5-fold for tracheobronchial and alveolar regions,



**Fig. 2.** Particle dose number size-distribution in different lung regions: a) head (H) and tracheobronchial (TB) regions for e-cigarette; b) alveolar (Al) region for e-cigarette; c) head (H) and tracheobronchial (TB) regions for conventional cigarette; and d) alveolar (Al) region for e conventional cigarette.

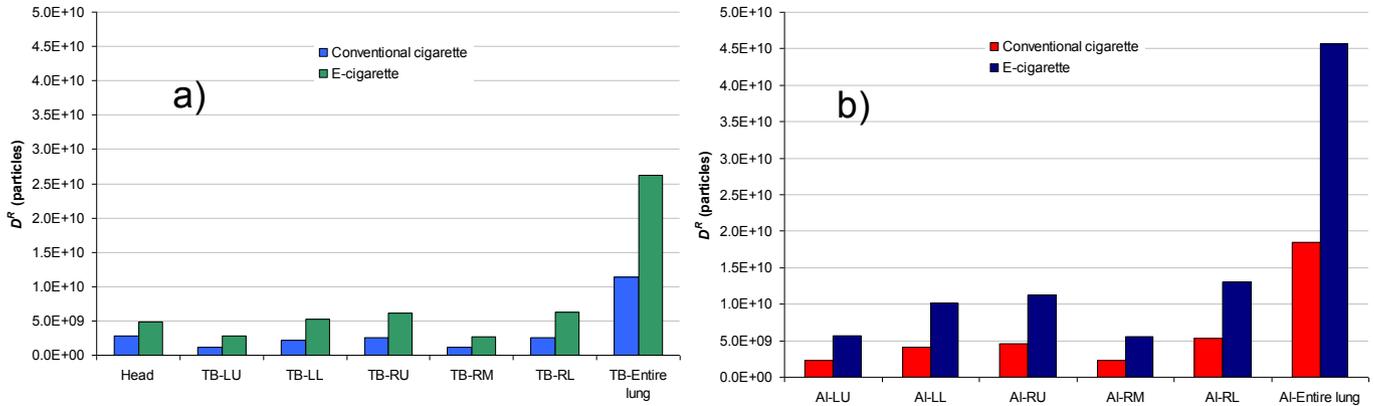


Fig. 3. Total regional lobar doses ( $D^R$ ) in the: (a) head (H) and tracheobronchial (TB); and (b) alveolar (Al) regions.

respectively). Once again, this comparison clearly shows the high doses received by vapers. In Table 1 doses received by conventional cigarette users were also reported. Tracheobronchial and alveolar doses received during a 2-s puff, in terms of deposited particle number and surface area, respectively, were estimated equal to  $1.1 \times 10^{10}$  particles/ $1.5 \times 10^3$  mm<sup>2</sup> (TB) and  $1.9 \times 10^{10}$  particles/ $2.3 \times 10^3$  mm<sup>2</sup> (Al). Therefore, particle number doses were significantly lower than those due to e-cigarette use, whereas particle surface area doses were slightly higher: this was due to the emission of i) lower number of particles and ii) larger particles' mode when conventional cigarettes are used (Fig. 1).

### 3.3. Size resolved lobar doses

After a 2-s e-cigarette puff,  $7.7 \times 10^{10}$  particles ( $D_{Tot}$ ) with a surface area of  $3.6 \times 10^3$  mm<sup>2</sup> ( $S_{Tot}$ ) and  $3.3 \times 10^{10}$  particles with a surface area of  $4.2 \times 10^9$  mm<sup>2</sup> were deposited in the respiratory system, for electronic and conventional cigarettes, respectively. The number dose size distributions,  $D^R_i$ , (Fig. 2) were unimodal for head TB and Al lobar regions, with a mode at 124 nm (e-cigarette)

and 165 nm (conventional cigarette), as exhibited by the relevant aerosol number size distributions. For the tracheobronchial region, at the modal diameter,  $D^R_i$  ranged from  $3.1 \times 10^8$  (TB–RM) to  $7.2 \times 10^8$  (TB–RL) particles and from  $1.8 \times 10^8$  (TB–RM) to  $4.4 \times 10^8$  (TB–RU), for e-cigarettes and conventional cigarettes, respectively. For the alveolar region,  $D^R_i$  ranged from  $6.8 \times 10^8$  (Al–RM) to  $1.6 \times 10^9$  (Al–RL) particles and from  $3.8 \times 10^8$  (Al–RM) to  $9.0 \times 10^8$  (Al–RL) particles, for e-cigarettes and conventional cigarettes, respectively.

Fig. 3 shows the total regional doses,  $D^R$ , deposited in the head, TB and Al lung lobes.  $D^R$  in the head was  $4.9 \times 10^9$  particles for the e-cigarette and  $2.8 \times 10^9$  particles for the conventional one. In the lung lobes, the lowest  $D^R$  was deposited in the RM–TB region ( $2.7 \times 10^9$  particles, for the e-cigarette and  $1.1 \times 10^9$  particles for the conventional cigarette) and the highest was in Al–RL region ( $1.3 \times 10^{10}$  particles for the e-cigarette and  $5.3 \times 10^9$  particles for the conventional cigarette). Total regional doses were higher for right lobes than for the left ones. In the TB region of the RU lobe, 116% (e-cigarette) and 123% (conventional cigarette) more particles were deposited than in the LU, and about 20% (e-cigarette) and 17%,

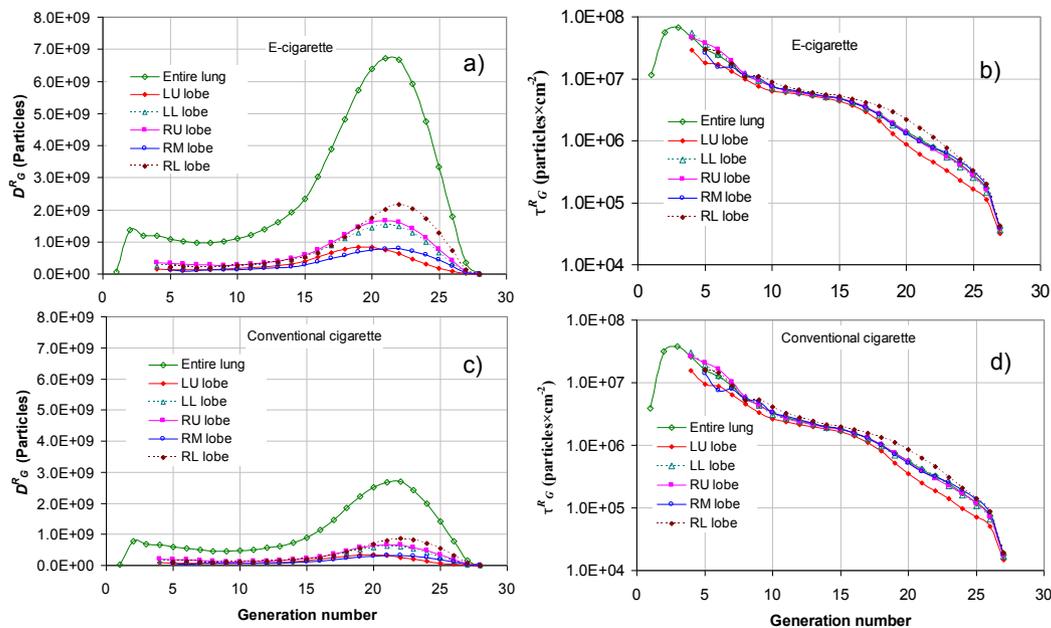
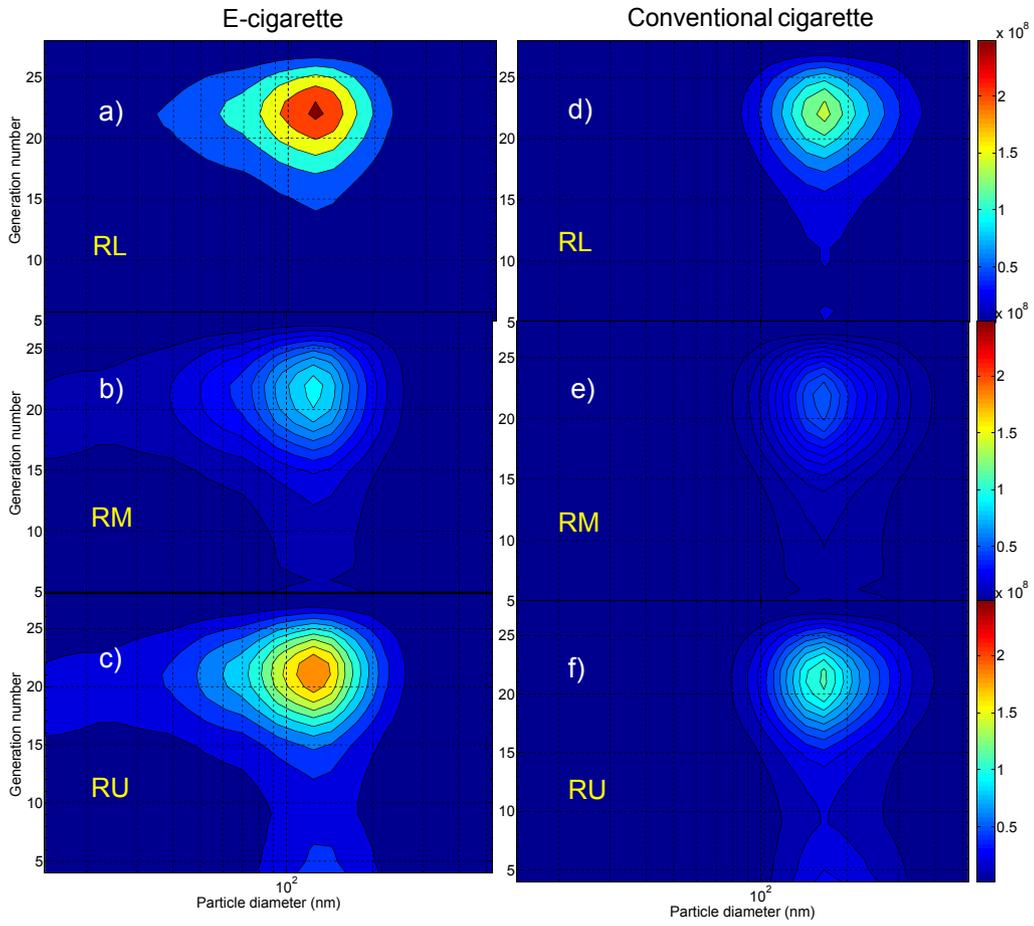
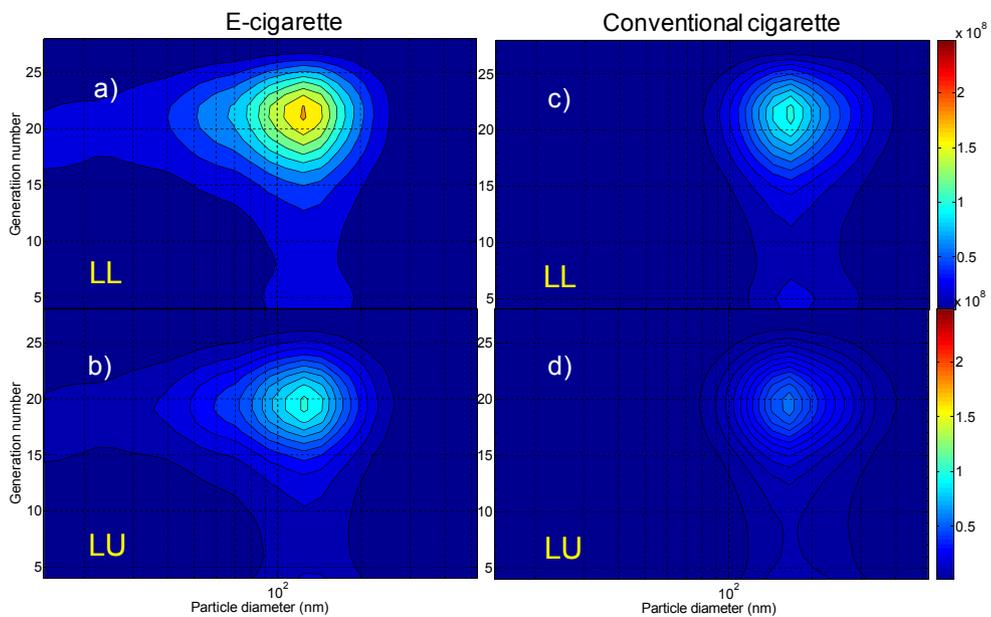


Fig. 4. Total lobar doses per airway generation ( $D_C^R$ ) and total lobar deposition densities per airway generation ( $\tau_C^R$ ) for electronic and conventional cigarettes: a)  $D_C^R$  for e-cigarette; b)  $\tau_C^R$  for electronic cigarettes; c)  $D_C^R$  for conventional cigarettes; and d)  $\tau_C^R$  for conventional cigarettes.



**Fig. 5.** Dose number size distributions as functions of airway generation number in RL (a, d), RM (b, e) and RU (c, f) lung lobes for an electronic (left) and a conventional (right) cigarette smoker.



**Fig. 6.** Dose number size distributions as functions of airway generation number in LL (a, c) and LU (b, d) lung lobes for an electronic (left) and a conventional (right) cigarette smoker.

(conventional cigarette) more were deposited in the RL than in the LL lobe.

In the alveolar region, about 99% (e-cigarette) and 98% (conventional cigarette) more particles were deposited in the RU than in the LU lobe, and about 28% (both kinds of cigarettes) more were deposited in the RL than in the LL lobe.  $D^R$  was higher in lower than in the upper lobes. In the TB region, about 85% (e-cigarette) and 87% (conventional cigarette) more particles were deposited in the LL than in the LU lobe. The dose received by the RL and RU lobe were similar: 3% higher and 1% lower for the RL lobe, for the electronic and conventional cigarettes respectively. In the alveolar region,  $D^R$  was about 79% (both kinds of cigarettes) higher for the LL than for the LU lobe, and about 16% (e-cigarette) and 15% (conventional cigarette) higher for the RL than for the RU lobe.

Fig. 4 shows the total lobar doses per airway generation,  $D^R_G$ , (a, c) and the total deposition densities,  $\tau^R_G$ , (b, d) per airway generation as functions of airway generation number, for each of the five lung lobes. Maximum  $D^R_G$  ranged from  $7.9 \times 10^8$  (e-cigarette) and  $3.2 \times 10^8$  particles (conventional cigarette) for the RM lobe, to  $2.2 \times 10^9$  (e-cigarette) and  $8.7 \times 10^8$  particles (conventional cigarette) for the RL lobe. Maximum  $D^R_G$  were deposited in the 19th (e-cigarette) and 20th (conventional cigarette) airway generations in the LU lobe and in the 21st generation in the LL and RU lobes and the 22nd generation in RM and RL lobes, for both kinds of cigarettes. Total lobar deposition densities per airway generation ( $\tau^R_G$ ) were also estimated (Fig. 4 b, d), since the number of deposited particles per unit airway surface area (deposition density) for inhaled particles, such as irritants which affect tissues on contact, represents a more relevant parameter, rather than particle number (McClellan and Henderson, 1995).  $\tau^R_G$  was highest in the upper bronchial generations, with maximum values of  $6.7 \times 10^7$  and  $3.8 \times 10^7$  particles  $\text{cm}^{-2}$  at the third airway generation (i.e. at lobar bronchi), for e-cigarettes and conventional cigarettes, respectively.  $\tau^R_G$  decreased further down the peripheral bronchiolar airways, due to the increasing airway surface area.

The contour plots in Figs. 5 and 6 show the dose number size distributions ( $D^R_i$ ) as a function of airway generation number and particle diameter in each of the five lung lobes, for both kinds of cigarettes, after a single 2-s puff. The position of peak values were determined by the modes of the size number distribution of the cigarette aerosols and by airway generation numbers at which particle with modal diameter most efficiently deposit. It can be seen that the  $D^R_i$  peaks were located at 124 nm (e-cigarette) and 165 (conventional cigarette) size class particles (the mode of the aerosol size-number distributions) at the 20th airway generation for the LU lobe, at the 21st for the LL and RU lobes, and at the 22nd for the RM and RL lobes, for both kinds of cigarettes.  $D^R_i$  peaks ranged from  $9.5 \times 10^7$  (e-cigarette) and  $5.4 \times 10^7$  (conventional cigarette) in the RM lobe, to  $2.6 \times 10^8$  (e-cigarette) and  $1.5 \times 10^8$  particles in the RL lobe.

#### 4. Conclusions

After a single 2-s puff,  $7.7 \times 10^{10}$  particles ( $D_{Tot}$ ) are deposited, which is more than double the dose compared to conventional cigarettes. In the tracheobronchial and alveolar regions, a single puff delivers total regional doses ( $D^R$ ) that represent 40% and 30% of the daily dose of a no-smoking Italian individual and 170% and 140% of the daily dose of a no-smoking Australian subject, respectively.

Higher total lobar doses per airway generation ( $D^R_G$ ) were deposited in the alveolar region, whereas higher total lobar deposition densities per airway generation ( $\tau^R_G$ ) occurred at the lobar bronchi. Total regional doses,  $D^R$ , were not uniformly distributed in the lung lobes, with twice as many particles deposited in the RU than in the LU lobes and about 20% more in the RL than in the LL

lobes, both for the tracheobronchial and the alveolar regions. Thus, the lobar bronchi and right lung lobes represent sites where effects of the aerosol from e-cigarette smoke may be more likely to occur. Further studies are needed on the chemical composition of e-cigarette aerosols, in order to ascertain the doses of noxious substances delivered by the aerosol doses estimated in this study.

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.envpol.2015.03.008>.

#### References

- Anjilvel, S., Asgharian, B., 1995. A multiple-path model of particle deposition in the rat lung. *Fund. Appl. Toxicol.* 28, 41–50.
- Asgharian, B., Hofmann, W., Bergmann, R., 2001. Particle deposition in a multiple-path model of the human lung. *Aerosol Sci. Tech.* 34, 332–339.
- Avino, P., Lopez, F., Manigrasso, M., 2013. Regional deposition of submicrometer aerosol in the human respiratory system determined at 1-s time resolution of particle size distribution measurements. *Aerosol Air Qual. Res.* 13, 1702–1711.
- Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y.-H., Talbot, P., 2012. Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reprod. Toxicol.* 34, 529–537.
- Baker, R., 2006. Smoke generation inside a burning cigarette: modifying combustion to develop cigarettes that may be less hazardous to health. *Prog. Energy Combust. Sci.* 32, 373–385.
- Borland, R., Gray, N., 2011. Electronic cigarettes as a method of tobacco control. *BMJ* 343, d6269.
- Bullen, C., McRobbie, H., Thornley, S., Glover, M., Lin, R., Laugesen, M., 2010. Effect of an electronic nicotine delivery device (e cigarette) on desire to smoke and withdrawal, user preferences and nicotine delivery: randomised cross-over trial. *Tob. Control* 19, 98–103.
- Buonanno, G., Giovinco, G., Morawska, L., Stabile, L., 2011. Tracheobronchial and alveolar dose of submicrometer particles for different population age groups in Italy. *Atmos. Environ.* 45, 6216–6224.
- Buonanno, G., Morawska, L., Stabile, L., Wang, L., Giovinco, G., 2012. A comparison of submicrometer particle dose between Australian and Italian people. *Environ. Poll.* 169, 183–189.
- Buonanno, G., Stabile, L., Morawska, L., Russi, A., 2013. Children exposure assessment to ultrafine particles and black carbon: the role of transport and cooking activities. *Atmos. Environ.* 79, 53–58.
- Burtscher, H., 2005. Physical characterization of particulate emissions from diesel engines: a review. *J. Aerosol Sci.* 36, 896–932.
- Caponnetto, P., Russo, C., Polosa, R., 2012. Smoking cessation: present status and future perspectives. *Curr. Opin. Pharmacol.* 12, 229–237.
- Caponnetto, P., Russo, C., Bruno, C.M., Alamo, A., Amaradio, M.D., Polosa, R., 2013. Electronic cigarette: a possible substitute for cigarette dependence. *Monaldi Arch. Chest Dis.* 79, 12–19.
- Choi, H., Schmidbauer, N., Sundell, J., Hasselgren, M., Spengler, J., Bornehag, C.-G., 2010. Common household chemicals and the allergy risks in pre-school age children. *PLoS One* 5, 13423.
- Cobb, N.K., Byron, M.J., Abrams, D.B., Shields, P.G., 2010. Novel nicotine delivery systems and public health: the rise of the “e-cigarette”. *Am. J. Public Health* 100, 2340–2342.
- Crawford, T.V., McGrowder, D.A., Barnett, J.D., McGaw, B.A., McKenzie, I.F., James, L.G., 2012. Tobacco-related chronic illnesses: a public health concern for Jamaica. *Asian Pac. J. Cancer Prev.* 13, 4733–4738.
- Doll, R., Peto, R., Boreham, J., Sutherland, I., 2004. Mortality in relation to smoking: 50 years' observations on male British doctors. *Br. Med. J.* 328, 1519–1528.
- Etter, J.F., 2010. Electronic cigarettes: a survey of users. *BMC Public Health* 10.
- Etter, J.F., Bullen, C., 2011. Electronic cigarette: users profile, utilization, satisfaction and perceived efficacy. *Addiction* 106, 2017–2028.
- Etter, J.F., Bullen, C., Flouris, A.D., Laugesen, M., Eissenberg, T., 2011. Electronic nicotine delivery systems: a research agenda. *Tob. Control* 20, 243–248.
- Fiore, M.C., Jaén, C.R., Baker, T.B., Bailey, W.C., Benowitz, N., Curry, S.I., 2008. Treating Tobacco Use and Dependence: 2008 Update. Clinical practice guideline. U.S. Department of Health and Human Services, Public Health Service, Rockville (MD).

- Flouris, A.D., Oikonomou, D.N., 2010. Electronic cigarettes: miracle or menace? *BMJ* 340, c311.
- Flouris, A.D., Chorti, M.S., Poulianiti, K.P., Jamurtas, A.Z., Kostikas, K., Tzatzarakis, M.N., Hayes, A.W., Tsatsaki, A.M., Koutedakis, Y., 2013. Acute impact of active and passive electronic cigarette smoking on serum cotinine and lung function. *Inhal. Toxicol.* 25, 91–101.
- Foulds, J., Veldheer, S., Berg, A., 2011. Electronic cigarettes (e-cigs): views of aficionados and clinical/public health perspectives. *Int. J. Clin. Pract.* 65, 1037–1042.
- Fuoco, F.C., Buonanno, G., Stabile, L., Vigo, P., 2014. Influential parameters on particle concentration and size distribution in the mainstream of e-cigarettes. *Environ. Poll.* 184, 523–529.
- Geiss, O., Kotzias, D., 2007. Institute for Health and Consumer Protection, EUR 22783 EN.
- Gennimata, S.A., Palamidis, A., Kaltsakas, G., Tsikrika, S., Vakali, S., Gratziou, C., Koulouris, N., 2012. Acute Effect of e-cigarette on Pulmonary Function in Healthy Subjects and Smokers. *European Respiratory Society. Abstract, P1053.*
- German Cancer Research Center, 2013. *Electronic Cigarettes – an Overview Heidelberg* available at: <http://www.dkfz.de/en/presse/download/RS-Vol19-E-Cigarettes-EN.pdf>.
- Goniewicz, M.L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., Prokopowicz, A., Jablonska-Czapla, M., Rosik-Dulewska, C., Havel, C., Jacob, P., Benowitz, N., 2013. Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tob. Control.* 23, 133–139.
- Hua, M., Alfi, M., Talbot, P., 2013. Health-related effects reported by electronic cigarette users in online forums. *J. Med. Internet Res.* 15, e59.
- Hueglin, C., Scherrer, L., Burtscher, H., 1997. An accurate, continuously adjustable dilution system (1:10 to 1:10 4) for submicron aerosols. *J. Aerosol Sci.* 28, 1049–1055.
- Ingebrethsen, B.J., Cole, S.K., Alderman, S.L., 2012. Electronic cigarette aerosol particle size distribution measurements. *Inhal. Toxicol.* 24, 976–984.
- International Commission on Radiological Protection, 1994. Human respiratory tract model for radiological protection. A report of a task group of the International Commission on Radiological Protection. *Ann. ICRP* 24, 1–482.
- Johnson, T., Caldwell, R., Pöcher, A., Mirme, A., Kittelson, D., 2004. A New Electrical Mobility Particle Sizer Spectrometer for Engine Exhaust Particle Measurements. SAE Technical Papers.
- Kane, D.B., Asgharian, B., Price, O.T., Rostami, A., Oldham, M.J., 2010. Effect of smoking parameters on the particle size distribution and predicted airway deposition of mainstream cigarette smoke. *Inhal. Toxicol.* 22, 199–209.
- Manigrasso, M., Avino, P., 2012. Fast evolution of urban ultrafine particles: implications for deposition doses in the human respiratory system. *Atmos. Environ.* 51, 116–123.
- Manigrasso, M., Stabile, L., Avino, P., Buonanno, G., 2013. Influence of measurement frequency on the evaluation of short-term dose of sub-micrometric particles during indoor and outdoor generation events. *Atmos. Environ.* 67, 130–142.
- Manigrasso, M., Buonanno, G., Fuoco, F.C., Stabile, L., Avino, P., 2015. Aerosol deposition doses in the human respiratory tree of electronic cigarette smokers. *Environ. Poll.* 196, 257–267.
- Marini, S., Buonanno, G., Stabile, L., Ficco, G., 2014. Short term effects of electronic and tobacco cigarettes on exhaled nitric oxide. *Toxicol. Appl. Pharmacol.* 278, 9–15.
- McCauley, L., Markin, C., Hosmer, D., 2012. An unexpected consequence of electronic cigarette use. *Chest* 141, 1110–1113.
- McClellan, R.O., Henderson, R.F., 1995. *Concepts in Inhalation Toxicology*. CRC Press, Taylor & Francis, ISBN 1-56032-368-X.
- McQueen, A., Tower, S., Sumner, W., 2011. Interviews with 'vapers': implications for future research with electronic cigarettes. *Nicot. Tob. Res.* 13, 860–867.
- Moline, J.M., Golden, A.L., Highland, J.H., Wilmarth, K.R., Kao, A.S., 2000. Health Effects Evaluation of Theatrical Smoke, Haze and Pyrotechnics. Prepared for Actor's Equity Pension and Health Trust Funds.
- Moolgavkar, S.H., Holford, T.R., Levy, D.T., Kong, C.Y., Foy, M., Clarke, L., Jeon, J., Hazelton, W.D., Meza, R., Schultz, F., McCarthy, W., Boer, R., Gorlova, O., Gazelle, G.S., Kimmel, M., McMahon, P.M., de Koning, H.J., Feuer, E.J., 2012. Impact of reduced tobacco smoking on lung cancer mortality in the United States during 1975–2000. *J. Natl. Cancer Inst.* 104, 541–548.
- Parkash, O., 1977. Lung cancer. A statistical study based on autopsy data from 1928 to 1972. *Respiration* 34, 295–304.
- Pellegrino, R.M., Tinghino, B., Mangiaracina, G., Marani, A., Vitali, M., Protano, C., Osborn, J.F., Cattaruzza, M.S., 2012. Electronic cigarettes: an evaluation of exposure to chemicals and fine particulate matter (PM). *Ann. Ig.* 24, 279–288.
- Polosa, R., Caponnetto, P., Morjaria, J.B., Papale, G., Campagna, D., Russo, C., 2011. Effect of an electronic nicotine delivery device (e-cigarette) on smoking reduction and cessation: a prospective 6-month pilot study. *BMC Public Health* 11.
- Price, O.T., Asgharian, B., Miller, F.J., Cassee, F.R., de Winter-Sorkina, R., 2002. Multiple Path Particle Dosimetry Model (MPPD v. 1.0): a Model for Human and Rat Airway Particle Dosimetry, v 1.0. National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands.
- Renne, R.A., 1992. 2-Week and 13-week inhalation studies of aerosolized glycerol in rats. *Inhal. Toxicol.* 4, 95–111.
- Sahu, S.K., Tiwari, M., Bhangare, R.C., Pandit, G.G., 2013. Particle size distribution of mainstream and exhaled cigarette smoke and predictive deposition in human respiratory tract. *Aerosol Air Qual. Res.* 13, 324–332.
- Schripp, T., Markewitz, D., Uhde, E., Salthammer, T., 2013. Does e-cigarette consumption cause passive vaping? *Indoor Air* 23, 25–31.
- Siegel, M.B., Tanwar, K.L., Wood, K.S., 2011. Electronic cigarettes as a smoking-cessation tool results from an online survey. *Am. J. Prev. Med.* 40, 472–475.
- Smith, C.J., Perfetti, T.A., Garg, R., Hansch, C., 2003. IARC carcinogens reported in cigarette mainstream smoke and their calculated log P values. *Food Chem. Toxicol.* 41, 807–817.
- Stabile, L., Vargas Trassierra, C., Dell'Agli, G., Buonanno, G., 2013. Ultrafine particle generation through atomization technique: the influence of the solution. *Aerosol Air Qual. Res.* 13, 1667–1677.
- Vakaöi, S., Tsikrika, S., Gennimata, A., Kaltsakas, G., Palamidis, A., Koulouris, N., Gratziou, C., 2012. Acute Impact of a Single E-cigarette Smoking on Symptoms, Vital Signs and Air Way Inflammatory Response. *European Respiratory Society. Abstract, P4050.*
- van Dijk, W.D., Gopal, S., Scheepers, P.T.J., 2011. Nanoparticles in cigarette smoke: real-time undiluted measurements by a scanning mobility particle sizer. *Anal. Bioanal. Chem.* 399, 3573–3578.
- Vardavas, C.I., Anagnostopoulos, N., Kougias, M., Evangelopoulou, V., Connolly, G.N., Behrakis, P.K., 2012. Short-term pulmonary effects of using an e-cigarette: impact on respiratory flow resistance, impedance and exhaled nitric oxide. *Chest* 141, 1400–1406.
- Venditti, F., Cuomo, F., Ceglie, A., Ambrosone, L., Lopez, F., 2010. Effects of sulfate ions and slightly acid pH conditions on Cr(VI) adsorption onto silica gelatin composite. *J. Hazard. Mat.* 173, 552–557.
- WHO, 2008. *World Health Organization (WHO): Report on the Global Tobacco Epidemic, 2008.* [www.who.int/tobacco/mpower/2008/en/index.html](http://www.who.int/tobacco/mpower/2008/en/index.html).
- Wieslander, G., Norback, D., Lindgren, T., 2001. Experimental exposure to propylene glycol mist in aviation emergency training: acute ocular and respiratory effects. *Occup. Environ. Med.* 58, 649–655.
- Winkler-Heil, R., Hofmann, W., 2009. Inter- and Intra-lobar Deposition of Inhaled Particles. *European Aerosol Conference 2009, Karlsruhe, Abstract T101A01.*
- Zhang, Y., Sumner, W., Chen, D.R., 2013. In vitro particle size distributions in electronic and conventional cigarette aerosols suggest comparable deposition patterns. *Nicot. Tob. Res.* 15, 501–508.