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Tracheobronchial and Alveolar Particle Surface Area Doses in Smokers

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Abstract: Cigarette smoke is the main cause of lung cancer events. Mainstream cigarette smoke (MSS) is a direct concern for smokers, but also the secondhand smoke (SHS) contributes to the smoker exposure. In addition, smoker exposure is affected by the "free-smoke" particle exposure (B), related to the micro-environments where smokers spend time. The aim of this paper is to evaluate the daily alveolar and tracheobronchial deposited fractions of airborne particles for smokers as the sum of these three contributions: MSS, SHS, and B. Measurements of particle surface area distributions in the MSS were performed through a Scanning Mobility Particle Sizer, an Aerodynamic Particle Sizer, and a Thermo-dilution system on five types of conventional cigarettes. A Monte Carlo method was then applied to evaluate the most probable value of dose received during the inhalation of MSS by smokers. Measurements of particle concentrations in SHS and at the "free-smoke" particle background (B) were performed through 24-h monitoring at a personal scale of adult smoker through hand-held devices. This paper found that the total daily deposited dose for typical smokers was 1.03×10^5 $mm^2 \cdot day^{-1}$. The main contribution of such a huge daily dose was addressable to the MSS (98%) while SHS contributed 1.1%, increasing up to 2% for people smoking only while traveling in a car.

Keywords: cigarette smoking; active smokers; particle dose; personal exposure; deposited surface area

1. Introduction

Aerosol exposure is a major environmental health concern due to the ability of particles to penetrate deeply into the respiratory system and cell membranes [1] and translocate from the airways into the blood circulation [2,3]. Particles are also able to deposit in secondary organs [4], including brain tissue [5] and to carry condensed toxic compounds [6–8].

The deposited particle surface area in the lung, defined in this paper as dose, has been identified as a relevant metric for particle exposure quantifications [9].

In assessing human exposure to airborne particles, cigarette smoking is of particular interest as it is the main cause of lung cancer events [10–23]. In fact, about 60% and 90% of lung cancer events for women and men, respectively, are related to cigarette smoking [14,15,19]. Such a high lung cancer risk is due to the physical-chemical characteristics of the mainstream cigarette smoke (MSS). In fact, the cigarette-generated particles contain more than 3500 semi-volatile and non-volatile compounds, some of them classified as carcinogenic such as hydrocarbons (PAHs; [24–27]), dioxins and furans [28], heavy metals [25,29–34], and tobacco-specific nitrosamines [25,31,35–37]. Moreover, in fresh unaged tobacco cigarette mainstream smoke particle concentrations of about 4×10^9 part cm^{-3} were measured, with an arithmetic mean diameter of about 0.2 μm [38–41].

Cigarette smoking affects not only active smokers (through the mainstream cigarette smoke) but also passive smokers are exposed to conventional cigarette second-hand smoke.

In particular, cigarette mainstream smoke (MSS) is the smoke emerging from the mouth end of a cigarette during puffing [36]. Mainstream smoke consists of an aerosol containing liquid droplets (particulate phase) suspended in the gas vapor phase, which is generated by overlapping burning, pyrolysis, pyrosynthesis, distillation, sublimation, and condensation processes [37]. Second-hand smoke (SHS) is the sidestream smoke emitted from the burning of the tip of a cigarette [42,43] plus the smoke exhaled by active smokers. There are more than 3000 chemicals in SHS and more than 60 of them have been identified as toxicants or carcinogens [15,40,44,45].

In assessing personal exposure of smokers to airborne particles, and in understanding smoking-related diseases, the different types of cigarette smokes (MSS and SHS) have to be considered since MSS and SHS aerosols require different experimental set-ups to be measured. The mainstream smoke is usually measured by a smoking machine able to simulate the human puff smoking behavior. Particle concentrations and size distributions of MSS have been investigated by numerous different researchers [46]. In general, fresh MSS has been found to have an average mode of the number size distribution that ranged between 184 and 212 nm particle concentrations on the order of 10^9 part cm^{-3} [41].

In order to evaluate the effect of cigarette smoke on non-smokers, it is common to measure the SHS. The SHS is usually detected by portable real-time airborne particle monitoring instruments which measure the air ambient particles (both indoors and outdoors).

Airborne particles comprise a significant portion of the sidestream and mainstream mass emissions from burning cigarettes and other tobacco products, and indoor particle concentrations associated with SHS are also substantial. The size range of SHS particles is approximately 0.02–2 μm, so that all of the SHS particles fall within the category of fine particulate matter ($PM_{2.5}$).

Based on the aforementioned evidence, SHS results are poorly estimated since it has been only evaluated as an environmental measurement and as a contribution to non-smokers' particle exposure. In fact, while data on the exposure of individuals living with people who smoke are available in literature [47], no data on the contribution of secondhand smoke on the smoker himself are available.

In addition, smoker exposure is also affected by the level of particle background related to the specific environment visited by smokers during the day, defined in this paper as "free-smoke" particle background (B). In fact, it is well known how particle exposure of humans can be affected by the type of environment or activities performed during the day (such as cooking, burning candles, traveling by car, etc. [48,49]).

In the light of the abovementioned aspects, the SHS and B could affect the active smokers' exposure, and as such, it needs to be considered in the assessment of the total daily particle exposure of smokers.

The main objectives of this work are: (i) to evaluate the daily particle (alveolar and tracheobronchial) deposited doses of active smokers due to the contribution of MSS and SHS; (ii) to determine the contributions of MSS, SHS, and B on the daily dose. To this purpose the dose received by typical male and female Italian smokers was evaluated on the basis of particle surface area measured in the cigarette mainstream and secondhand smoke aerosol, taking into account typical smoker lifestyle. A Monte Carlo method was applied to calculate dose values.

2. Material and Methods

The daily (tracheobronchial and alveolar) deposited surface area doses (expressed as sum of alveolar and tracheobronchial contributions) received by a smoker during a day ($\Delta S_{Alv,TB}$) were evaluated as the sum of three contributions: mainstream smoke (MSS), secondhand smoke (SHS), and "free-smoke" particle background (B).

$$\Delta S_{Alv,TB_{Male/Female}} = \Delta S_{Alv,TB_{(MSS)}} + \Delta S_{Alv,TB_{(SHS)}} + \Delta S_{Alv,TB_{(B)}} \quad (1)$$

2.1. Contribution of Mainstream Smoke Aerosol to the Daily Dose

2.1.1. Experimental Campaign

Different types of tobacco cigarettes, as detailed in Table 1 were continuously tested. Measurements were performed in the European Accredited (EA) Laboratory of Industrial Measurements (LAMI) at the University of Cassino and Southern Lazio, Italy, during February–December 2015 in a 150-m^3 room, where thermo-hygrometric conditions were continuously controlled and monitored in order to guarantee temperature and relative humidity values equal to 20 ± 1 °C and 50% ± 10%, respectively.

Table 1. Characteristics of the selected tobacco cigarettes.

Sample	Nicotine Content (mg)
Cigarette A	0.6
Cigarette B	0.6
Cigarette C	0.8
Cigarette D	0.5
Cigarette E	0.6

2.1.2. Instrumentation and Particle Surface area Distributions Measurement

In order to measure particle size distribution in the MSS of the cigarettes, several instruments were used:

- a Scanning Mobility Particle Sizer spectrometer, SMPS 3936 (TSI Inc., Shoreview, MN, USA), made up of an Electrostatic Classifier EC 3080 (TSI Inc.), used to classify the sampled particles in different channels according to their size, and a CPC 3775 (TSI Inc.) to count the particles of the selected size. The SMPS 3936 is able to measure particle surface area distribution in the range of 6–800 nm with a minimum time resolution of 120 s;
- a TSI model 3321 Aerodynamic Particle Sizer (APS) spectrometer which is able to measure the surface area distribution of particles in the range 0.5–20 μm through a time-of-flight technique with a one-second time resolution;
- a thermo-dilution system (two-step dilution) made up of a Rotating Disk Thermodiluter, RDTD (model 379020; Matter Engineering AG) [50] and a Thermal Conditioner Air Supply (model 379030; Matter Engineering AG) [51] which is able to ensure proper sample conditioning during cigarette-generated particle number distribution and total concentration measurements. Temperature control is also allowed in the thermodilution section by a built-in heater with selectable temperatures;
- a TSI model 4410 flow meter to check flow rates in the tubing connecting the cigarette to the measuring devices.

Particle size distributions were measured through the SMPS 3936-APS 3321 system. Sub-micron particle surface area distributions (through the SMPS) and super-micron particle surface area distributions (through the APS) were tested separately. In particular, 30 samplings for each instrument

(SMPS, APS) were performed using the abovementioned cigarettes. A 135-s long sampling time was adopted for SMPS and APS. In particular, an aerosol/sheath flow ratio of 0.3 $L \cdot min^{-1}$/3 $L \cdot min^{-1}$ was selected for the SMPS, which then provided particle surface area distributions in the 14–700 nm mobility diameter range.

In order to test the mainstream aerosol, cigarettes were connected to the aerosol sampling line. In particular, before entering the instruments (SMPS or APS), the aerosol was passed through the thermo-dilution system to prevent measurement artifacts from potentially occurring during the sampling process [50,51]. In fact, cigarette-generated mainstream aerosols are highly concentrated and made up of volatile gaseous compounds that may condense, leading to either the possible formation of stable nuclei (nucleation) or the growth of existing particles (condensation). Therefore, it was necessary to properly dilute the aerosol through the thermo-dilution system to prevent particle size distributions quickly undergoing significant changes in the few seconds lasting between the aerosol sampling and its measurement [50–52]. The thermo-dilution system drew the mainstream aerosol from each cigarette's mouthpiece at a fixed flow rate of 1 $L \cdot min^{-1}$. Flow rates were checked through the Flow meter TSI 4410. The thermo-dilution system temperature was set at 37 °C in order to simulate the respiratory apparatus. After the thermo-dilution process, the aerosol was passed through the SMPS (aerosol flow rate of 0.3 $L \cdot min^{-1}$), or the APS (aerosol flow rate of 1 $L \cdot min^{-1}$) depending on whether sub-micron or super-micron particle size distributions were measured. A dilution ratio equal to 1:1700 was chosen for all the instruments in order to avoid over-range measurements. Moreover, because of the long path experienced by the aerosol before entering the measurement devices, a diffusion loss correction was applied to estimate the particle losses onto the inner surface of the tubing. These corrections were calculated by applying the method proposed in Buonanno et al. (2012) [48]; further details about diffusion loss correction evaluation are reported in Buonanno et al. (2012) [52].

Particle surface area distributions over the entire measurement range (14 nm–20 μm) were obtained by merging and fitting SMPS and APS values through the DataMerge® Software (TSI Inc.) through the approach reported by Shen et al. (2002) [53]. A particle density of 1.1 g cm^{-3} and a unit shape factor were applied for SMPS-APS distribution merging on the basis of the findings reported by Johnson et al. (2014) [54].

2.1.3. Particle (Alveolar and Tracheobronchial) Deposited Doses in the MSS

The daily deposited doses received by a smoker in the mainstream cigarette aerosol ($\Delta S_{Alv,TB}$), were evaluated in terms of particle deposited surface area concentration for males and females as follows [55,56]:

$$\Delta S_{Alv,TB_{Male/Female(MSS)}} = \left(\int_{D=14\ nm}^{10\ \mu m} DF_{Alv,TB_{Male/Female}}(D) \cdot \frac{dS}{dlogD} dD \right) \cdot V_{puff} \cdot N_{puff} \cdot N_{cig_{Male/Female}} \quad (2)$$

where V_{puff} (cm^3) is the puff volume, dS/dlogD ($\mu m^2 \cdot cm^{-3}$) refers the particle surface area concentrations of a certain particle diameter (D) received for each puff of mainstream cigarette aerosol, N_{puff} (puffs/cigarette) is the puffs number per cigarette, N_{cig} (cigarette/day) represents the cigarette consumption per day, and $DF_{Alv,TB}$ represents the deposition fraction in the alveolar and tracheobronchial regions of the lungs, as a function of the particle diameter (D), as adapted from the International Commission on Radiological Protection [57]. DF values were considered for adult males and females performing a sitting activity. Available average data of cigarette consumption among Italian adults, obtained from Istituto Superiore di Sanità [58], reported 14.1 and 11.8 as the number of cigarettes smoked per day for males and females, respectively. A summary of the average data of human smoking patterns, obtained on the basis of a detailed scientific literature analysis performed by Zacny and Stitzer [59], is provided in Table 2. Data were reported as mean value ± standard deviation since they were checked for normality applying a Shapiro-Wilk test.

Table 2. Average data of human smoking patterns summarized by Zacny and Stitzer [59].

Puff Volume, V_{puff} (cm^3)	Puffs per Cigarette, N_{puff}	Puff Time, t_{puff} (s)
42.5 ± 9.3	11.5 ± 2.2	1.8 ± 0.4

Dose values were calculated through the abovementioned Equation (2) by applying a Monte Carlo method [60]. In particular, deposited particle surface area concentrations were expressed as most probable values and 5th–95th intervals.

2.2. Contribution of Secondhand Smoke Aerosol and "Free-Smoke" Particle Background to the Daily Dose

2.2.1. Experimental Campaign

In order to detect particle concentrations in the secondhand smoke aerosol and at "free-smoke" particle background, personal monitoring campaigns were performed. A 24-h monitoring in terms of (alveolar and tracheobronchial) deposited surface area concentration was performed by smoker adults, mainly students, aged between 25–35 years. A total of 20 adults were involved in the campaign. The experimental campaign was carried out in Cassino, Central Italy (41°30′0″ N–13°50′0″ E) during February–December 2015. Adults were asked to lead their normal life.

2.2.2. Instrumentation and Particle Surface Area Distributions Measurement

The mobile experimental apparatus was composed of two hand-held UFP counters (NanoTracer, Philips, Amsterdam, The Netherlands). This device works by diffusion charging: an electrometer measures the number particle concentration by means of the current induced by previously charged particles collected on a filter inside a Faraday cage. The NanoTracer is able to evaluate the different fractions (alveolar and tracheobronchial) of the lung deposited surface area through a semi-empiric algorithm implemented by Marra et al. (2010) [61]. These personal monitors are equipped with an internal rechargeable lithium-ion battery, which allows them to be used during outdoor trips. The total run time (single battery charge) is about 7 h. The counters were calibrated at the beginning of the experimental campaign in order to allow data quality assurance by comparison with a Nanoparticle Surface Area Monitor (NSAM, TSI Model 3550) to assess the human lung deposited surface area of particles corresponding to tracheobronchial (TB) and alveolar (Alv) regions of the lung. The temporal resolution of the NanoTracers was set to 16 s (advance mode).

Each adult kept the NanoTracer device for 24-h, carrying it with them in all of the microenvironments where they usually go during their normal life. Adults were asked to take notes about places visited, and start and end times of each activity. In particular, they were asked to record a note during each smoking event, indicating the start/end of smoking, and the relative environment/activity associated with the smoking event.

In order to detect the level of "free-smoke" particle background, the second Nanotracer was used. In particular, during smoking events, the second device was put on in separate (free-smoke) environments in close vicinity of the smoker.

Based on the time duration of each activity performed by smokers, the average particle deposited alveolar and tracheobronchial surface area concentrations were calculated and were representative of smoker adults' exposure to SHS, whilst the average particle deposited alveolar and tracheobronchial surface area concentrations were calculated based on data from the second Nanotracer device and were representative of "free-smoke" particle background.

From data of 24-h exposure of smoker adults, and data of "free-smoke" background, we calculated the extra-dose due to the smoking activity as the increase of the particle dose received by smokers with respect to the background. Therefore, the extra dose result was not affected by the ambient concentration which, conversely, was included in the "free-smoke" background contribution (B).

2.2.3. Particle (Alveolar and Tracheobronchial) Deposited Doses in the SHS and B

The partial dose (in terms of particle alveolar and tracheobronchial deposited surface area concentration) received by adults in each microenvironment/activity was determined by multiplying the alveolar and tracheobronchial surface area ($S_{Alv,TB}$) for the time spent (T) in the *j*-th microenvironment and the inhalation rate ($IR_{activity}$) corresponding to the activity carried out [62]. Then, we added the partial doses to estimate the daily total deposited alveolar and tracheobronchial surface area, $\Delta S_{Alv,TB_{(SHS)}}$ and $\Delta S_{Alv,TB_{(B)}}$, as reported in Equations (3) and (4); data from smoker adults are representative of daily particle dose obtained as the sum of the dose related to the secondhand smoke aerosol generated by cigarettes and that related to the "free smoke" particle background of the specific environment. Therefore, data from the "free smoke" particle background are representative of particle dose received by non-smoker adults in the same environment.

$$\Delta S'_{Alv,TB_{(SHS)}} = \sum_{j=1}^{n} S_{Alv,TB} \cdot T \cdot IR_{activity} \tag{3}$$

$$\Delta S_{Alv,TB_{(B)}} = \sum_{j=1}^{n} S_{Alv,TB} \cdot T \cdot IR_{activity} \tag{4}$$

In the above reported equations $S_{Alv,TB}$ is the alveolar and tracheobronchial particle deposited surface area concentration ($\mu m^2 \cdot cm^{-3}$), T is the time spent in the three environments (h), and $IR_{activity}$ is the inhalation rate ($m^3 \cdot h^{-1}$). Inhalation rates for the different activities were adopted on the basis of the United States Environmental Protection Agency, (US EPA) approach [63], ranging from 0.3 $m^3 \cdot h^{-1}$ during sleeping and resting to 1.4 $m^3 \cdot h^{-1}$ during sporting activities.

In order to isolate the effect of the secondhand smoke aerosol generated by cigarettes, we calculated the normalized increase of the particle dose, per single cigarette received by smokers, with respect to the "free smoke" particle background. Then, multiplying the normalized increase of particle dose per the average number of cigarettes per day (13 cigarette/day), we calculated the daily extra dose. Therefore, the extra dose ($\Delta S_{Alv,TB_{(SHS)}}$) is involved in the calculation of SHS aerosol on smokers and this resulting value was not affected by the ambient concentration which, conversely, was included in the "free-smoke" background contribution (B).

3. Results and Discussion

3.1. Alveolar and Tracheobronchial Deposited Particle Surface Area Concentrations in the MSS

The average (and standard deviation) values of deposited particle surface area concentrations (alveolar and tracheobronchial fractions) found in the mainstream aerosol of the investigated cigarettes were: 1.48×10^{13} $\mu m^2 \cdot cm^{-3}$ and 4.56×10^{12} $\mu m^2 \cdot cm^{-3}$ for male and 1.20×10^{13} $\mu m^2 \cdot cm^{-3}$ and 5.18×10^{12} $\mu m^2 \cdot cm^{-3}$ for female, respectively.

Alveolar deposited particle surface area concentrations were higher than tracheobronchial deposited ones for males and females. This is due to the lung deposition efficiency, which is known to be higher in the alveolar (Alv) than the tracheobronchial (TB) region [57,64,65].

The lung deposited particle surface area concentrations at the mainstream, regardless of the deposition in the lung tract, are extremely higher than particle concentration levels which people are exposed to in typical indoor, outdoor, and occupational environments [49,56,66–72], thereby resulting in extremely high doses received by smokers as hereinafter reported.

The deposited particle surface area distributions found in the mainstream aerosol of the investigated cigarettes were reported in Figure 1 distinguishing between alveolar (Alv) and tracheobronchial (TB) deposition for males (Figure 1a) and females (Figure 1b). Alveolar and tracheobronchial deposited particle surface area distributions were similar for males and females. Unimodal distributions were found with a mode at 328 nm. Such high values of deposited particle surface area concentrations in the MS of cigarettes are due to the great emission of sub-micron particles [41,73]. Sub-micron particles lead to this outstanding contribution of particles smaller than 1 µm to the overall surface area distributions/concentrations.

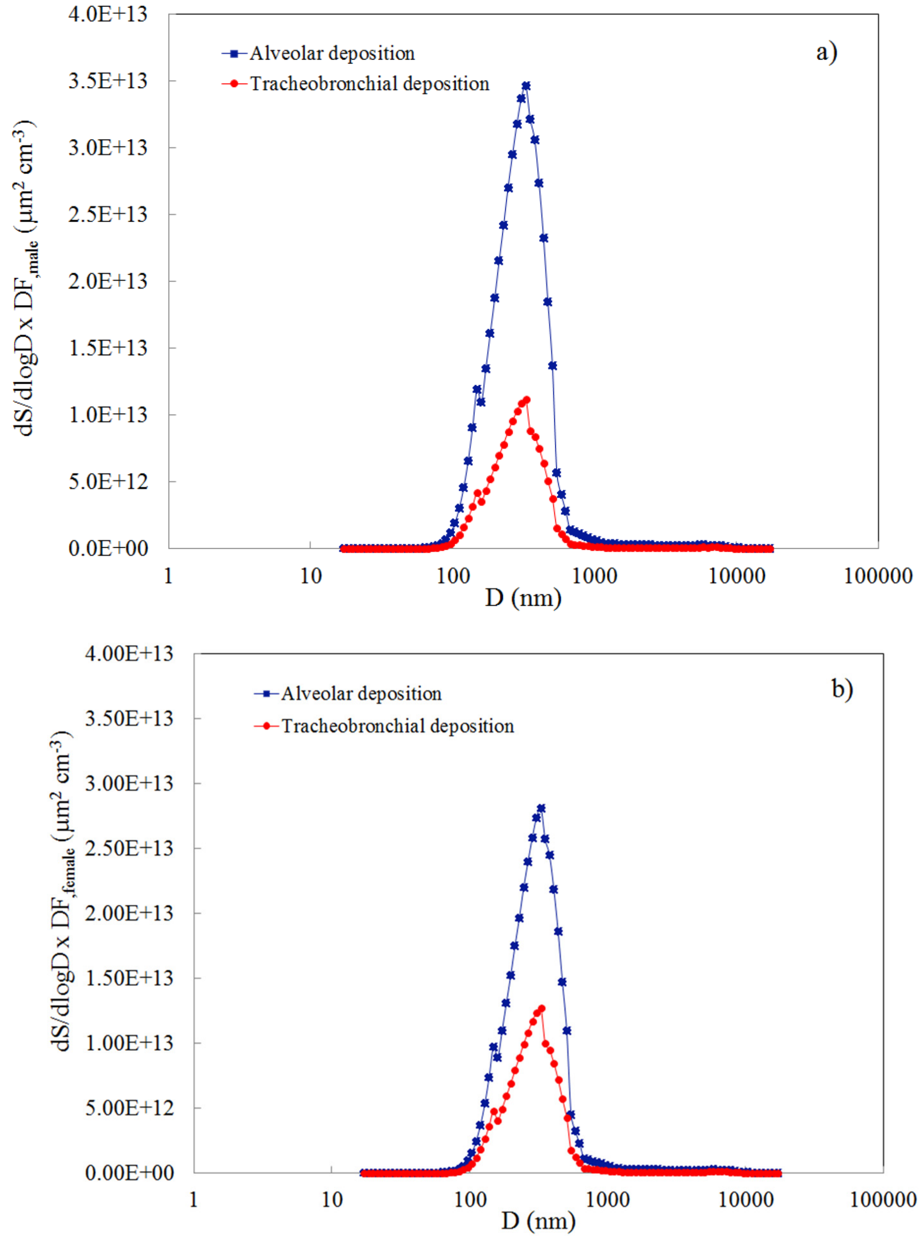

Figure 1. Deposited particle surface area distributions in the mainstream aerosol of the investigated cigarettes in terms of alveolar (Alv) and tracheobronchial (TB) deposition, for males (**a**) and females (**b**).

3.2. Alveolar and Tracheobronchial Particle Dose in the MSS

The daily doses calculated for typical adult Italian smokers (males and females), in terms of deposited particle surface area in the MSS, resulting from the Monte Carlo simulation and expressed as most probable values and 5th–95th intervals, are reported in Table 3. As expected, huge doses from the mainstream particle concentrations were measured, for both males and females, in terms of deposited surface area. Particle surface area doses (expressed as sum of alveolar and tracheobronchial fractions) were 1.13×10^5 mm^2·day^{-1} and 8.85×10^4 mm^2·day^{-1} for male and female smokers, respectively. These huge dose values are larger than the overall daily dose in terms of surface area received by the non-smoking Italian population [56,70], and even larger than those received by people in highly polluted indoor environments, such as kitchens [49].

Table 3. Particle surface area doses per day received by smokers in the MSS ("MPV" represents the most probable value of the dose, and 5th and 95th represent the 5th and 95th percentiles, respectively, of the dose values).

	$\Delta S_{Alv,(MSS)}F$ ($mm^2 \cdot Day^{-1}$)	$\Delta S_{TB,(MSS)}F$ ($mm^2 \cdot Day^{-1}$)	$\Delta S_{Alv,(MSS)}M$ ($mm^2 \cdot Day^{-1}$)	$\Delta S_{TB,(MSS)}M$ ($mm^2 \cdot Day^{-1}$)	$\Delta S_{Alv+TB,(MSS)}F$ ($mm^2 \cdot Day^{-1}$)	$\Delta S_{Alv+TB,(MSS)}M$ ($mm^2 \cdot Day^{-1}$)
MPV	**6.17×10^4**	**2.87×10^4**	**7.96×10^4**	**2.70×10^4**	**8.85×10^4**	**1.13×10^5**
5th	2.69×10^4	1.29×10^4	2.01×10^4	1.19×10^4	4.68×10^4	4.46×10^4
95th	1.22×10^5	5.56×10^4	2.04×10^5	5.60×10^4	1.68×10^5	2.46×10^5

3.3. Alveolar and Tracheobronchial Particle Dose in the SHS and B

The daily doses calculated for typical adult Italian smokers and non-smokers, in terms of deposited particle surface area, related to the extra dose due to the secondhand smoke aerosol (SHS) and the level of "free smoke" particle background (B), are reported in Table 4 as average value ± standard deviation.

Table 4. Particle surface area doses per day received related to the extra dose due to secondhand smoke aerosol (SHS) and the level of "free smoke" particle background (B).

Sampler	Type of Measurement	Micro-Environment	$\Delta S_{Alv(SHS,B)}$ ($mm^2 \cdot Day^{-1}$)	$\Delta S_{TB(SHS,B)}$ ($mm^2 \cdot Day^{-1}$)
(As non-smoker)	"Free smoke" background		$3.72 \pm 1.08 \times 10^2$	$7.51 \pm 2.16 \times 10^1$
Smoker	Secondhand smoke aerosol	Outdoor/urban city	$4.70 \pm 3.85 \times 10^2$	$9.47 \pm 7.84 \times 10^1$
		Indoor/home	$6.80 \pm 1.81 \times 10^2$	$1.38 \pm 0.36 \times 10^2$
		Transportation/car	$1.61 \pm 0.51 \times 10^3$	$3.26 \pm 1.04 \times 10^2$

The average daily particle doses received in the secondhand smoke aerosol by smokers ($9.21 \pm 3.57 \times 10^2$ $mm^2 \cdot day^{-1}$ and $1.86 \pm 0.73 \times 10^2$ $mm^2 \cdot day^{-1}$, for alveolar and tracheobronchial fraction, respectively) were one order of magnitude larger than those found at the "free-smoke" particle background level ($3.72 \pm 1.08 \times 10^2$ $mm^2 \cdot day^{-1}$ and $7.51 \pm 2.16 \times 10^1$ $mm^2 \cdot day^{-1}$, for alveolar and tracheobronchial fractions, respectively).

Values of daily dose received by smokers due to SHS aerosol are comparable to the overall daily dose received by Italian children (1.92–0.60 × 10^3 $mm^2 \cdot day^{-1}$) [74] while daily dose found at the "free-smoke" particle background level could be comparable to the overall daily dose received by Australian children [75,76].

The dose contribution of the "free-smoke" particle background showed the overexposure due to smoking activities. Such doses depended on the time activity pattern of the population under investigation.

Daily particle doses detected from the secondhand smoke aerosol were found to be affected by the specific micro-environments visited by smokers, ranging between $4.70 \pm 3.85 \times 10^2$ for outdoor environments and $1.61 \pm 0.51 \times 10^3$ $mm^2 \cdot day^{-1}$ during transportation. Smoking outdoors was found to be slightly less impactful on daily SHS dose compared to smoking indoors.

However, these values seemed to be lower than typical daily dose values found in previous studies as, for example, values higher than 2×10^3 $mm^2 \cdot day^{-1}$ were found by Buonanno et al. (2012) [70]. This could be attributed to the selected population of this study, since students are typically less exposed to cooking- generated particles, which are known to highly affect daily particle exposure. Moreover, data from this paper could be affected by the seasonal period in which the experimental campaign was carried out (i.e., during spring). In fact, during summer time, particle exposure levels are lower than those that occur during winter time due to higher ventilation conditions [67,71].

3.4. Daily Alveolar and Tracheobronchial Deposited Dose for a Typical Smoker

In order to calculate the total daily deposited (total of alveolar and tracheobronchial fractions) particle surface area dose for a typical smoker, the authors evaluated and considered the contribution of MSS, SHS, and "free-smoke" particle background. Considering that: (i) the average value between the most probable values of dose found in the MSS for male and female was 1.01×10^5 $mm^2 \cdot day^{-1}$; (ii) the sum of average values of the tracheobronchial and alveolar dose found from SHS was 1.11×10^3 $mm^2 \cdot day^{-1}$, and (iii) the sum of the tracheobronchial and alveolar dose found from B was 4.47×10^2 $mm^2 \cdot day^{-1}$, the total daily deposited dose in terms of particle surface area for typical Italian smokers was 1.03×10^5 $mm^2 \cdot day^{-1}$.

The highest contribution to the daily dose was from the MSS with 98.5%, SHS was observed to contribute 1.1%, with contributions increasing up to 2% if the smoker was smoking while travelling by car.

4. Conclusions

This paper provides an evaluation of the overall dose received by smokers which is the sum of three contributions: i.e., mainstream aerosol directly inhaled by the smoker, secondhand smoke produced by the smoker himself and then inhaled, and the background dose typical of a non-smoker.

The dose due to the mainstream aerosol was evaluated by measuring the particle concentration at the mainstream smoke while the dose contribution of the secondhand smoke and of the background level was evaluated through particle concentration exposure at a personal scale. For this analysis, the dose contribution of the background level was important in order to show the overexposure due to smoking activities.

High values of lung deposited particle surface area concentrations were found in the mainstream aerosol of the investigated cigarettes due to the great emission of sub-micron particles generated by cigarettes. In particular, alveolar fractions ranged between 1.48×10^{13} $\mu m^2 \cdot cm^{-3}$ for males and 1.20×10^{13} $\mu m^2 \cdot cm^{-3}$ for females, while tracheobronchial fractions ranged between 4.56×10^{12} $\mu m^2 \cdot cm^{-3}$ for males and 5.18×10^{12} $\mu m^2 \cdot cm^{-3}$ for females. Unimodal distributions were found in terms of the deposited particle surface area for males and females with a mode at 328 nm.

In terms of particle surface area doses, due to the mainstream smoke aerosol, huge values were found: 1.13×10^5 $mm^2 \cdot day^{-1}$ for males and 8.85×10^4 $mm^2 \cdot day^{-1}$ for females.

Particle doses received by smokers due to the secondhand smoke aerosol were 1.11×10^3 $mm^2 \cdot day^{-1}$, while lower values were attributed to the "free-smoke" particle background (4.47×10^2 $mm^2 \cdot day^{-1}$).

This paper found that the total daily deposited dose in terms of particle surface area for typical Italian smokers was 1.03×10^5 $mm^2 \cdot day^{-1}$.

The greater contribution to this huge value of daily dose was addressable to the mainstream smoke-particles generated (98%) while SHS contributed to 1.1%, increasing up to 2% if the smoker was smoking while travelling in a car.

The authors point out that for the very first time a complete analysis of the overall dose received by smokers was carried out, as the sum of three contributions: i.e., mainstream aerosol directly inhaled by the smoker, secondhand smoke produced by the smoker himself and then inhaled, and the background dose typical of a non-smoker. Results of this paper could be useful for lung cancer risk model analysis on the Italian smoking population.

Author Contributions: Fernanda Carmen Fuoco: experimental campaign, analysis of the data, and manuscript writing; Luca Stabile: experimental campaign, analysis of the data, and manuscript writing; Giorgio Buonanno: scientific supervisor of the experimental campaign and data interpretation; Mauro Scungio: data treatment and manuscript writing; Maurizio Manigrasso: data treatment and manuscript writing; Andrea Frattolillo: data interpretation and manuscript writing.

Conflicts of Interest: The authors declare no conflict of interest.

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