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Lung cancer risk of airborne particles for Italian population

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ABSTRACT

Airborne particles, including both ultrafine and supermicrometric particles, contain various carcinogens. Exposure and risk-assessment studies regularly use particle mass concentration as dosimetry parameter, therefore neglecting the potential impact of ultrafine particles due to their negligible mass compared to supermicrometric particles. The main purpose of this study was the characterization of lung cancer risk due to exposure to polycyclic aromatic hydrocarbons and some heavy metals associated with particle inhalation by Italian non-smoking people. A risk-assessment scheme, modified from an existing risk model, was applied to estimate the cancer risk contribution from both ultrafine and supermicrometric particles. Exposure assessment was carried out on the basis of particle number distributions measured in 25 smoke-free microenvironments in Italy. The predicted lung cancer risk was then compared to the cancer incidence rate in Italy to assess the number of lung cancer cases attributed to airborne particle inhalation, which represents one of the main causes of lung cancer, apart from smoking. Ultrafine particles are associated with a much higher risk than supermicrometric particles, and the modified risk-assessment scheme provided a more accurate estimate than the conventional scheme. Great attention has to be paid to indoor microenvironments and, in particular, to cooking and eating times, which represent the major contributors to lung cancer incidence in the Italian population. The modified risk assessment scheme can serve as a tool for assessing environmental quality, as well as setting up exposure standards for particulate matter.

1. Introduction

The International Agency for Research on Cancer (IARC), which is part of the World Health Organization (WHO), has recently classified particulate matter, a major component of air pollution, as carcinogenic to humans (Group 1), based on sufficient evidence that exposure is associated with an increased risk of lung cancer (International Agency for Research on Cancer, 2013; Loomis et al., 2013). The potential of particles to cause adverse health effects is linked to their capacity to enter the lungs, potentially carrying a number of toxic compounds with them. At present, it is not fully known which particle size, morphology or chemical components are most strongly related to the negative effects on human health and further research in this field is required. In terms of particle size, the attention of scientific studies has shifted from mass (PM_{10} or $PM_{2.5}$), to surface area (Buonanno et al., 2013a; Giechaskiel et al., 2009) and particle number concentrations (Franck et al., 2011), to the latter of which is largely comprised of ultrafine particles (UFPs), with a diameter less than 100 nm. Nevertheless, there is strong toxicity-based evidence that surface-area is an appropriate exposure metric for ultrafine particles (Cauda et al., 2012; Oberdörster et al., 2005; Tran et al., 2000) and that the biological response depends more on the surface-area of particles deposited in the lungs (Brown et al., 2001; Hamoir et al., 2003; Stoeger et al., 2006; Tran et al., 2000) than on other metrics of exposure.

Particle's toxicity is clearly related to the compounds which are attached to it, several of which have been classified by the IARC in the Group 1 carcinogens (i.e. there is sufficient evidence of carcinogenicity in humans, such that a causal relationship has been established between exposure to these agents and human cancer). Among these, polycyclic aromatic hydrocarbons (PAHs) and some heavy metals could be considered major contributors to human exposure through the respiratory tract. PAHs are organic compounds with two or more fused aromatic rings, formed during incomplete combustion. In general, the carcinogenic properties of PAHs increase with the number of aromatic rings (Ramirez et al., 2011), as does their complexity and lipophilic characteristics (Bostrom et al., 2002). The PAHs emitted by combustion sources

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are present in the gaseous phase (semi-volatile), as well as being associated with particles (particle-bound). Baek et al. (1991) found that two- and three-ring PAHs were mainly in the gas phase, while four-ringed PAHs were in both the gas phase and particle phase, and five- and six-ringed PAHs were mainly attached to particles. Benzo[a]pyrene (B[a]p) is the most extensively studied PAH and it is the usual marker for carcinogenic levels of PAHs in epidemiology and environmental studies. The World Health Organization International Program on Chemical Safety (World Health Organization, 1999) represents a source of information on the relative carcinogenic potency of PAHs and the European Union developed an extensive body of legislation establishing health-based standards for PAHs and heavy metals in the air. In particular, the annual mean concentration of benzo[a]pyrene, as a representative for PAHs (1 ng m^{-3}), As (6 ng m^{-3}), Cd (5 ng m^{-3}), and Ni (20 ng m^{-3}) were established by Directive 2004/107/EC (European Parliament and Council of the European Union, 2004). The corresponding estimated lifetime lung cancer risk due to PAHs is 8.7 cases per 100,000 people with chronic inhalational exposure to 1 ng m^{-3} of B[a]p over a lifetime of 70 years. Based on this information, the UK Government's Expert Panel on Air Quality Standards (EPAQS) recommended a UK standard for B[a]p of 0.25 ng m^{-3} (Expert Panel on Air Quality Standards, 1999) and when proposing an action plan to reduce environmental health risks in Sweden, the Swedish Governmental Commission on Environmental Health (Commission on Environmental Health, 1996) proposed a value of 0.1 ng m^{-3} as the long-term average limit for B[a]p. This level corresponds to a theoretical lifetime cancer risk of 1×10^{-5} (Bostrom et al., 2002).

The occurrence of PAHs and heavy metals in ambient air is of particular concern due to the continuous nature of exposure and the size of at-risk populations. In fact, the major difficulty facing epidemiological studies is mostly related to the estimation of individual exposure levels. An additional limitation of epidemiological studies is that most of them are focused on an exposure-response, and not a dose–response relationship, which is the main focus of toxicological studies (Sayes et al., 2007) and should be considered for risk characterization studies. This can be achieved through the personal sampling of particle concentrations (for all particle metrics: number, surface area and mass) received by people in every resided microenvironment during a typical day (Buonanno et al., 2014; Buonanno et al., 2013b), as well as the corresponding pollutants attached to the particles. Until now, from a regulatory point of view, the only methodology for estimating human exposure to airborne particles in Western countries is based on the measure of a daily average mass-based concentration (PM_{10}, $PM_{2.5}$) at an outdoor fixed sampling point (FSP) (Buonanno et al., 2010a). The number and position of such FSPs is generally determined as a function of the number of people, without any link to geographic and microclimatic characteristic, which means that measurement data from an FSP is not necessarily representative for the entire population (European Parliament and Council of the European Union, 2008; National Environmental Protection Council, 1998; U.S. Environmental Protection Agency, 2006). However, the evaluation of risk associated with real exposure is particularly complex because: (a) FSP data are not representative of real outdoor exposure, because of the high particle concentration decay with respect to distance from the source; (b) outdoor exposure represents only a fraction of personal integrated exposure, since individuals also move through multiple indoor microenvironments (Buonanno et al., 2012; Morawska et al., 2013); (c) no air quality standards considering other particle metrics (number and, above all, surface area) are defined (Buonanno et al., 2010b; Reche et al., 2015); and (d) existing risk models for chemicals use mass as the dosimetry to assess the health effect. Consequently, health effects induced by ultrafine particles are not considered and/or they are strongly underestimated when assessing exposure to particulate matter. In conclusion, air quality monitoring data and time activity patterns are not sufficient for policymakers to undertake accurate risk analysis, identify the major contributors, recognize high-risk sub-groups, and develop appropriate risk reduction measures.

The primary objective of this study was to characterize the major contributors to lung cancer risk for the Italian population on the basis of a risk assessment scheme modified from an existing risk model, which was designed to consider the lung cancer risk associated with both ultrafine and supermicrometric particles (Sze-To et al., 2012). To this end, we estimated the daily exposure of people of different age groups to PAHs and regulated heavy metals (As, Cd, Ni) on the basis of time activity patterns reported in the Italian Human Activity Pattern Survey. We also examined the exposure profiles of people with respect to different commuting and behavior patterns, in particular comparing the lifestyle of people living in Northern and Central-Southern Italy. Hence, this work represents a population-based study and it should be noted that the results would differ between individuals, especially when on and off road environments are considered.

2. Methodology

Performing a risk assessment (i.e. estimating the risk related to an existing situation (exposure to particles) and a recognized hazard (particles containing PAHs and heavy metals)), involves several major steps (United States National Research Council, 1983): (i) hazard identification, (ii) dose–response assessment, (iii) exposure assessment and (iv) risk characterization.

2.1. Hazard identification

The carcinogenicity of PAHs and heavy metals is generally described in terms of their mass and this dosimetry is then adopted in health risk assessments for many chemicals (U.S. Environmental Protection Agency, 2005). For example, the unit risk (UR) for benzo[a]pyrene is 8.7×10^{-5}, meaning that no more than 8.7 excess cancer cases are estimated for a population of 100,000 people, if exposed to a concentration of 1 ng m^{-3} of benzo[a]pyrene per cubic meter of air for a lifetime. Cancer potency factors may also be referred to as cancer slope factors (*SF*), defined as $SF = UR \times BW/IR$, where *BW* represents the average body weight of an adult (70 kg) and *IR* the average inhalation rate of an adult (20 m^3 day^{-1}). *SF* gives the percent increase in the risk of getting cancer associated with exposure to a given dose of a chemical (expressed as mg of chemical per kg of body weight) every day for a lifetime. Therefore, since *SF* is a plausible upper bound estimate of the probability that an individual will develop cancer, it represents a toxicity value that quantitatively defines the relationship between dose and response.

The *SF*/*UR* of a number of carcinogenic chemicals was obtained from the Office of Environmental Health Hazard Assessment (Office of Environmental Health Hazard Assessment, 2009). Table 1 reports the inhalation unit risks (*URs*) and slope factors (*SFs*) for PAHs, as well as As, Cd and Ni (i.e. the heavy metals classified in Group 1).

Although particle mass cannot be considered exhaustive when describing the dose–response relationship for hazardous substances, UFPs and their corresponding particle surface area are not used as dosimetry parameters in current risk assessments. Because of their small diameters, UFPs make a negligible contribution to particle mass, but are dominant in terms of number and particle surface area concentrations. Even though studies evaluating ultrafine particle health effects are scarce and current findings are