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Exposure assessments for a cross-sectional epidemiologic study of US carbon nanotube and nanofiber workers

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A B S T R A C T

Background: Recent animal studies have suggested the potential for wide-ranging health effects resulting from exposure to carbon nanotubes and nanofibers (CNT/F). To date, no studies in the US have directly examined the relationship between occupational exposure and potential human health effects.
Objectives: Our goal was to measure CNT/F exposures among US workers with representative job types, from non-exposed to highly exposed, for an epidemiologic study relating exposure to early biologic effects.
Methods: 108 participants were enrolled from 12 facilities across the US. Personal, full-shift exposures were assessed based on the mass of elemental carbon (EC) at the respirable and inhalable aerosol particle size fractions, along with quantitatively characterizing CNT/F and estimating particle size via transmission electron microscopy (TEM). Additionally, sputum and dermal samples were collected and analyzed to determine internal exposures and exposures to the hands/wrists.
Results: The mean exposure to EC was 1.00 $\mu g/m^3$ at the respirable size fraction and 6.22 $\mu g/m^3$ at the inhalable fraction. Analysis by TEM found a mean exposure of 0.1275 CNT/F structures/cm^3, generally to agglomerated materials between 2 and 10 µm. Internal exposures to CNT/F via sputum analysis were confirmed in 18% of participants while ~70% had positive dermal exposures.
Conclusions: We demonstrated the occurrence of a broad range of exposures to CNT/F within 12 facilities across the US. Analysis of collected sputum indicated internal exposures are currently occurring within the workplace. This is an important first step in determining if exposures in the workforce have any acute or lasting health effects.

1. Introduction

The unique strength and conductive properties of carbon nanotubes (CNT) and carbon nanofibers (CNF) have made them attractive for a variety of applications, including composite materials, conductive coatings and films, microelectronics, energy storage devices, and biotechnologies (De Volder et al., 2013). Carbon nanotube and nanofiber (CNT/F) materials and products offer enormous potential to meet growing technological and medical needs, but exposures to CNT/F have also raised early concerns for human and environmental health. Although health hazards caused by occupational exposures to CNT/F have not been confirmed in humans, accumulating evidence from animal toxicity studies suggests that exposures may cause harm. Studies have indicated that inhalation of certain types of CNT/F may induce localized and systemic inflammation, cytotoxicity, interstitial fibrosis, mutagenesis, and the potential for CNT to promote lung tumorigenesis after inhalation (Lam et al., 2004; Shvedova et al., 2008; Erdely et al., 2009; Ma-Hock et al., 2009; Pauluhn 2010; Porter et al., 2012; Sargent et al., 2014; Kasai et al., 2016).

In a similar fashion, there has been mounting evidence of

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occupational exposures to CNT/F over the past decade. Two recent review articles by Canu et al. (2016) and Debia et al. (2016) identified > 20 published peer-reviewed journal articles or reports that assessed exposures to SWCNT, MWCNT, or CNF. Generally, these reviews reported high-quality evidence of worker exposures. Coalescing the hazard potential assessed from animal toxicity data and the mounting evidence of workplace exposures has naturally led to the initiation and completion of several epidemiologic studies aiming to establish if an association exists between exposures to CNT/F and potential health effects or markers of early effect. However, many of the previous epidemiologic studies either have collected limited exposure data or were conducted within a single facility and enrolled few participants, ultimately limiting their overall generalizability (Liou et al., 2015).

The purpose of this paper is to present the results of an extensive exposure assessment monitoring study of workers with heterogeneous levels of exposure to CNT/F for an epidemiologic exposure-response analysis. Participants were recruited from across the US as part of a cross-sectional epidemiologic investigation of early effect markers. Occupational exposures were assessed using a multi-metric approach to characterize personal, full-shift exposures for each participant to a variety of CNT/F materials.

2. Methods

2.1. Facilities and participants

A total of 12 site visits were conducted between December 2012 and September 2014 to facilities across the US that produce or use CNT/F. In total, 108 workers were enrolled into the cross-sectional epidemiologic and exposure assessment study, which included workers exposed to CNT/F from various departments and job titles. Each facility had been previously assessed by researchers of the National Institute for Occupational Safety and Health (NIOSH) prior to this study (Evans et al., 2010; Methner et al., 2010; Birch et al., 2011; Dahm et al., 2015; Dahm et al., 2012).

General information was collected for each of the 12 facilities and tabulated in Table 1. This information includes types of CNT/F material handled, material characteristics, observed daily quantities, company size, job tasks performed, as well as engineering controls and personal protective equipment (PPE) used. Additionally, each site was categorized into one of three distinct industries (Dahm et al., 2015), which include:

1. *Primary Manufacturers* – produced SWCNT or MWCNT and subsequently sold their products for research/industrial uses.
2. *Hybrid Producers/Users* – produced MWCNT or CNF and subsequently incorporated them into a product within the same facility.
3. *Secondar y Manufacturers* – manufactured various composites which utilized SWCNT, MWCNT, or CNF within the composites/thermoplastics industries. A single secondary manufacturer in the electronics industry was included in this group as well.

2.2. Personal sampling and data collection

The sampling strategy focused on determining personal exposure to CNT/F for each participant over two full work-shifts. As this was a cross-sectional study, two days of personal sampling data were collected and averaged for each participant to limit daily exposure variations and provide more precise exposure estimates. Personal exposures were assessed based on the mass of airborne elemental carbon (EC) at both the respirable and inhalable aerosol particle size fractions, as well as characterizing airborne CNT/F exposure by transmission electron microscopy (TEM) (Dahm et al., 2015). All three collected personal samples were co-located, with sample inlets positioned together in order to sample the same air space.

Additionally, dermal hand and wrist exposures were assessed by scanning electron microscopy (SEM) and sputum samples were analyzed by enhanced darkfield microscopy to confirm internal exposures to CNT/F. Direct-reading instruments were also used to collect data for the potential confounders of ultrafine and fine particle number as well as particle mass (PM 2.5) for the epidemiologic analysis.

Furthermore, information on current and past work histories obtained via in-person interviews with each participant included information such as: current and past job titles, tasks, and workplace co-exposures (Schubauer-Berigan et al. (in preparation). Worker observation forms regarding daily performed tasks were completed through a combination of workplace observations and a short in-person interview by each participant at the end of each sampled work-shift (see Supplemental Material Appendix I & II). Job titles provided by each participant were grouped, by industry, into one of six general titles which included: Administrator, Chemist, Engineer, Maintenance, Research and Development (R & D), and Technician. The job title groupings were based upon reported and observed daily tasks performed as well as reported job titles. Also, a company-specific information form regarding company policy on PPE and engineering control uses was completed for each site after an interview with the facility or production manager.

2.3. Elemental carbon analyses of air samples

Personal respirable aerosol collection for EC was performed using 25-mm cassettes with quartz fiber filters (QFF) attached to GK 2.69 BGI cyclones (BGI Inc., Waltham, MA, USA) and Airchek XR5000 sampling pumps (SKC Inc., Eighty Four, PA, USA) operating at the cyclone specified flow rate of 4.2 liters per minute (lpm). Customized adapters for the GK 2.69 cyclone (BGI Inc.; catalog number 3503) were used to fit 25-mm cassettes. Personal samples were also collected using open-faced 25-mm cassettes and QFFs (SKC Inc.) to provide an estimate of the inhalable size fraction, as noted in Dahm et al. (2012), using Leland Legacy ™ pumps (SKC Inc.) operating at 5.5–6 l pm.

Daily outdoor and/or indoor background measurements for the airborne mass of EC at the respirable and inhalable fractions were collected at each facility to assess the potential for interference by anthropogenic sources. These sources could include diesel exhaust, emissions from coal or oil-fired power plants, and the seasonal burning of biomass (Schauer, 2003). Locations for background sampling were selected based on professional judgment and knowledge of each facility.

The airborne mass concentration of EC was measured using the NIOSH Manual of Analytical Methods (NMAM) Method 5040 (NIOSH, 2006a), based on a thermal-optical analysis technique for organic and elemental carbon (OC and EC). As described previously (Birch et al., 2011; NIOSH, 2013; Dahm et al., 2015; Fatkhutdinova et al., 2016; Shvedova et al., 2016), for application to CNT/F, a manual assignment of the OC-EC 'split' was made. Bulk samples of the CNT/F materials, where available, were analyzed to obtain their thermal profiles. Manual splits were then assigned based on results for the bulk and background samples (NIOSH, 2013; Dahm et al., 2015; Birch, 2016). The reported limit of detection (LOD) for NMAM 5040 ranged from 0.1 to 0.9 µg EC per cm^2 of filter deposit, with an average of 0.39 µg/cm^2. Based on the total mass of respirable/inhalable EC collected on the filter, and the collected air volume, the respirable/inhalable EC concentration (µg/m^3) was calculated.

2.4. Electron microscopy analyses of air samples

Personal samples were collected to approximate the inhalable size fraction using open-faced 25-mm cassettes with mixed cellulose ester filters (0.8 µm pore size; SKC Inc.) and Airchek XR5000 pumps (SKC Inc.) operating at 3.5–4 l pm. The samples were subsequently analyzed on a JEOL2100F transmission electron microscope (JEOL USA, Inc., Peabody, MA, USA) using a modified NMAM 7402, asbestos by TEM (NIOSH, 2006b; Birch et al., 2017). Modifications relate to counting CNT/F particles, which were observed mainly as agglomerated