Pulmonary Toxicity of Carbon Nanotubes: Ethical Implications and Human Risk Assessment

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Outline

- Potential energy applications of nanotubes
- Ethical Framework
- Framing the risk assessment problem
- Background on single wall nanotube toxicity
- Methods of this study
- Findings of this study
- Conclusions
- Research, Ethics, and Justice

Potential Energy Applications of Carbon Nanotubes

- Hydrogen storage in fuel cells
- Lithium storage in Li-ion batteries
- Supercapacitors
- Solar Cells
- Thermo-electric Devices

Ethical Framework

- Who benefits and who is placed at risk by the new technology and its application? Does who = any life?
- How much of the risk is real and how much is imagined?
- Is there synergy with other uncontrolled risk factors?
- If the risk is real, then how soon will we know its magnitude?
- Can we replace known risks with lesser risks, or are we just adding risk?
- Can risk be transferred to others, and is that ethical?
- What authority has responsibility and control over risks?
- Are those in control knowledgeable, ethical, and accountable?
- To whom are they accountable and when?

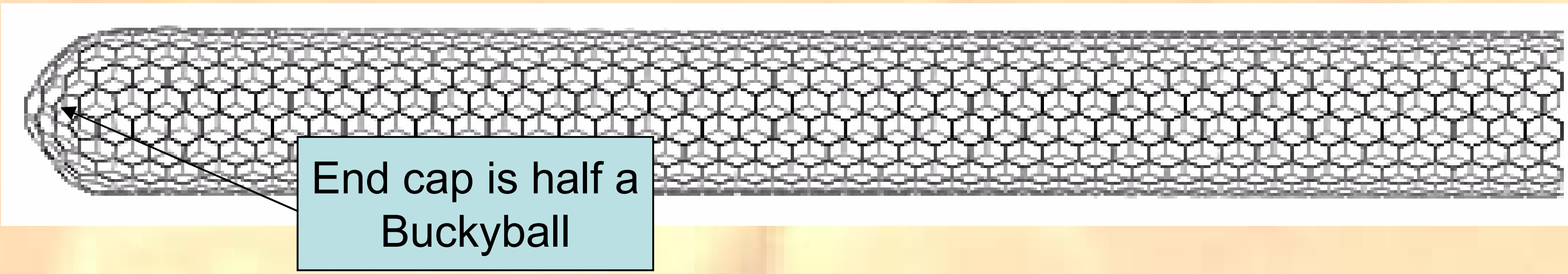
Framing the Nanotube Risk Assessment Problem

- Potential for Human Exposures
  - Manufacturing facilities
  - Research Facilities
  - Shipping and use points
  - Military: Obscurants
  - Exposures by respiratory and dermal routes
  - Medical applications
  - Environmental (multi-walled nanotubes)

Framing the Risk Assessment Problem (continued)

- Inherent Toxicity of Single-walled nanotubes
  - Physical form
    - Shape
    - Surface area
    - Self adhesion
  - Chemistry
    - Impurities
    - Surface chemistry
  - Particle size distribution
  - Translocation within the organism
  - Persistency within the organism
  - Response of the organism to persistent exposure

Properties of SWNT



- Rolled up graphite sheets composed of “benzene” rings
- Diameter of the order of 1 nm
- Length in excess of 1 μm
- Tubes agglomerate into “tattered ropes” of >10nm diameter
- Metal Impurities present from manufacturing process

Preparation of SWNT

- Graphite Vaporization
  - Electric Arc Discharge onto metal particles
  - Laser Vaporization onto metal particles
- Chemical Vapor Deposition from CO under high pressure
- All products contain residual metal catalysts
- Purification can reduce metal content

SWNT PRODUCTS WE STUDIED

Raw HiPco NT

Purified HiPco NT

Carbolex Electric-arc NT

Experimental Protocol

- Determination of metal content of SWNT samples
- Preparation of dust suspensions
  - Suspended in heat inactivated mouse serum
  - 3 types of SWNTs, carbon black, quartz were tested
- Intratracheal instillation of suspended dust
  - Anesthetized male B6C3F1 mice (4-5 per group, 30 g/mouse)
  - 0.1 or 0.5 mg SWNT suspension delivered through small incision into trachea in 50 μl volume of heat-inactivated mouse serum
- Lung collection and histopathology
  - Lungs harvested after 7 and 90 days
  - Treatment group in 90-day study was unknown to the pathologist

Metal content of SWNT and Carbon Black (% of total weight)

Test Material	Fe	Ni	Y
Raw SWNT	26.9	0.8	<0.01
Purified SWNT	2.1	<0.01	<0.01
CarboLex SWNT	0.5	26.0	5.0
Carbon Black	<0.01	<0.01	<0.01

Advantages of Intratracheal Instillation Compared to Inhalation

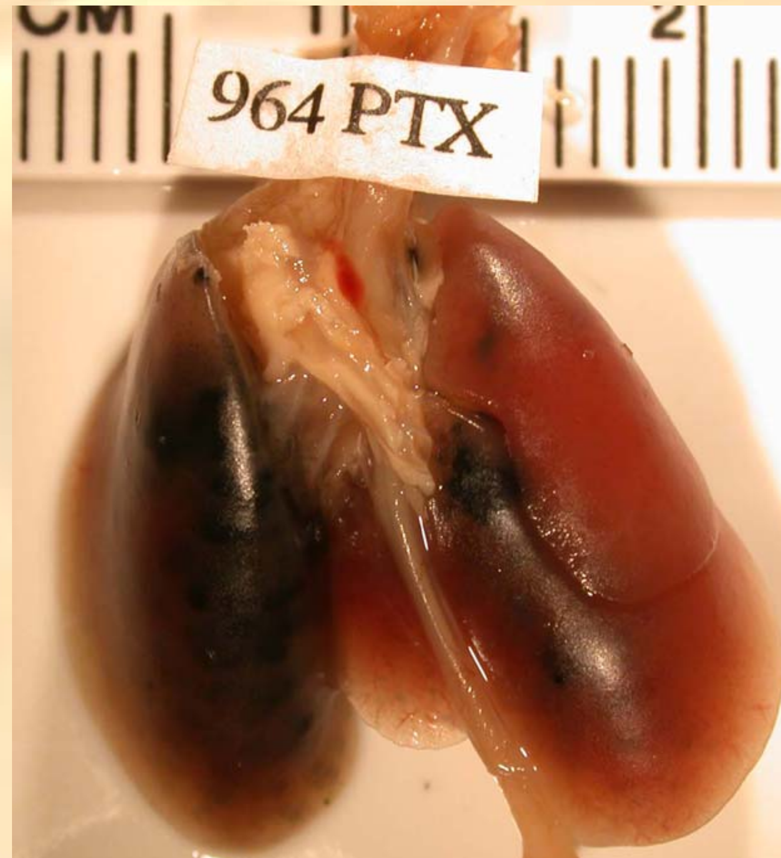
- Less test material required
- Less expensive than inhalation exposures
- Dose delivered is known more precisely
- No concomitant exposures via non-inhalation routes-oral & dermal
- Easier to control risks to those conducting the exposure if agent is highly toxic
- Bypass the filtering capabilities of rodent upper airways
- Can include comparison compounds of known toxicity

Disadvantages of Intratracheal Instillation Compared to Inhalation

- Unnatural delivery to site of effect
  - Slower clearance of instilled particles
  - Deeper penetration into lung
  - Increased bioavailability of soluble components
  - Effects on lung may be exaggerated
- Cannot discover effects on upper respiratory system
- Uneven distribution of material within lung-locally high
- Vehicle influence: delivery and properties of test material
- Animals must be anesthesized and mildly invasive procedure (transtracheal) often used
- Many of the disadvantages can be addressed by parallel testing using compounds of known inhalation toxicity

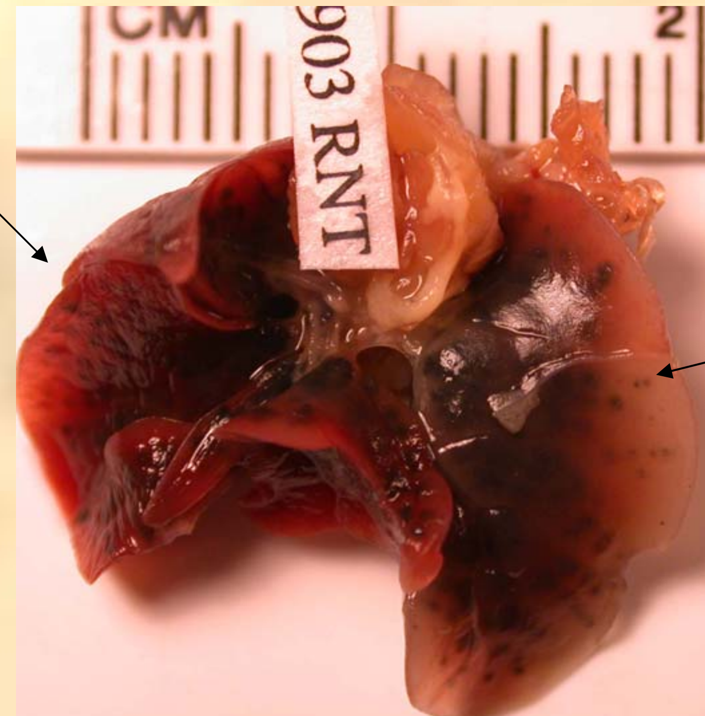
SALINE CONTROL

CARBON BLACK
90 DAYS/HIGH DOSE



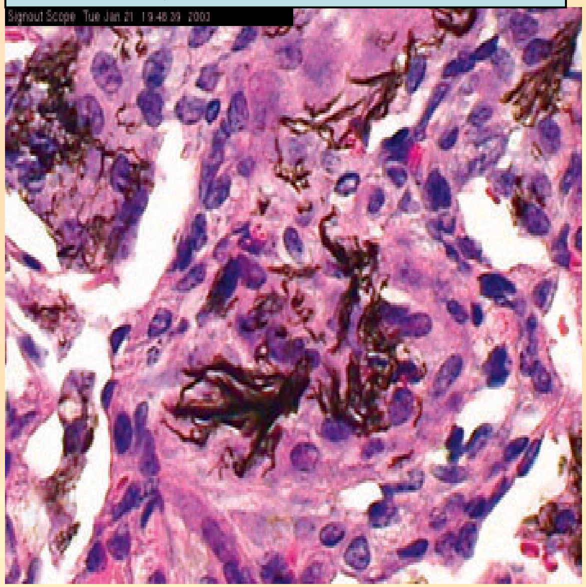
CARBOLEX NANOTUBES
90 DAYS/HIGH DOSE

RAW NANOTUBES
90 DAYS/HIGH DOSE

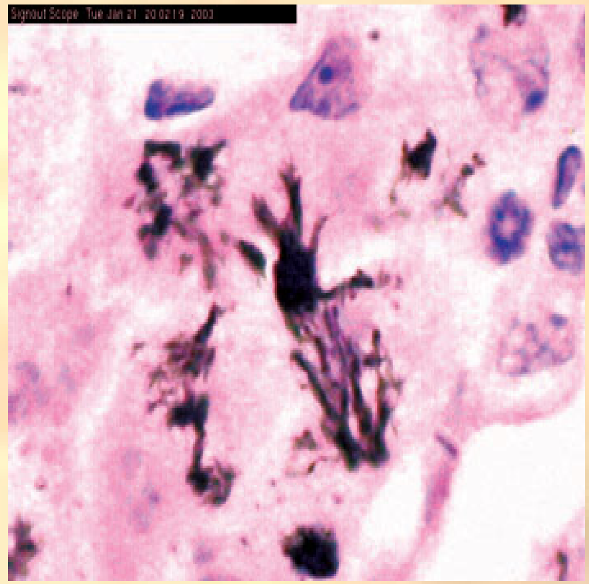


Granulomas from SWNTs, but not Carbon Black-Why?

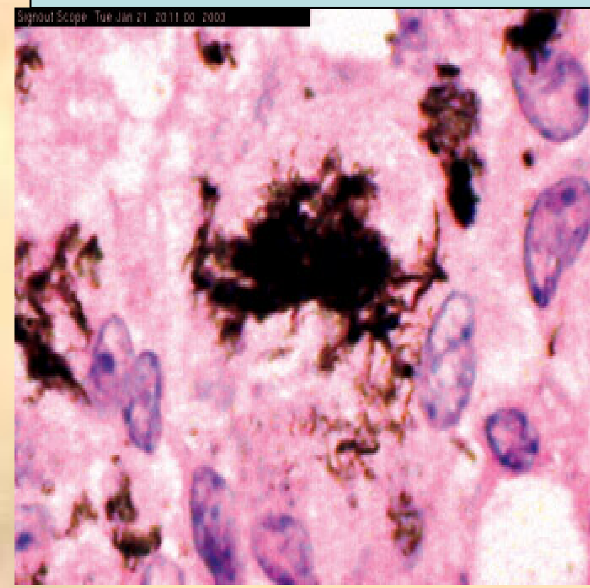
Raw NTs in granuloma 90 days after treatment



Purified NTs in granuloma 90 days after treatment



Purified NTs in granuloma 90 days after treatment

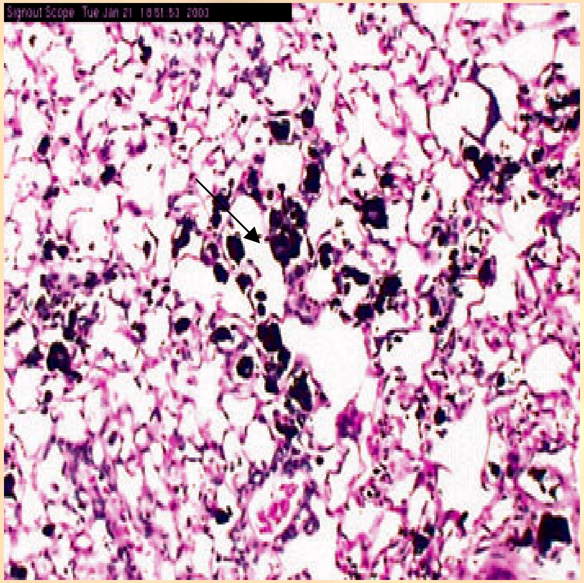


Bundles: NTs pack tightly and in parallel to form ropes or clumps.

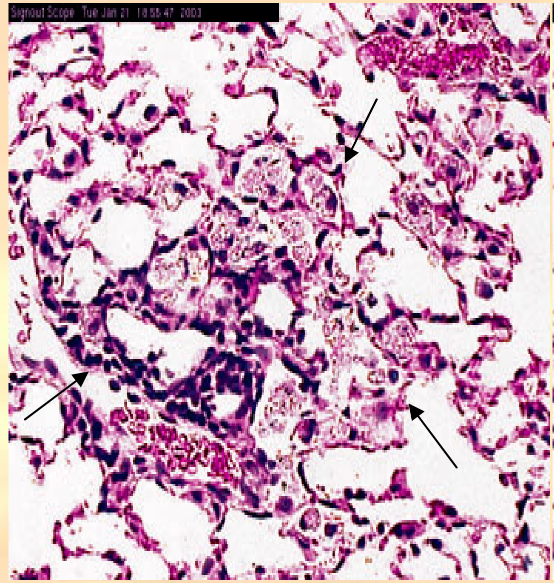
Structurally: Individual tubes or bundles are fibers, CB is amorphous

Histopathologic Micrographs of Lungs from Mice of the HD-90d Groups

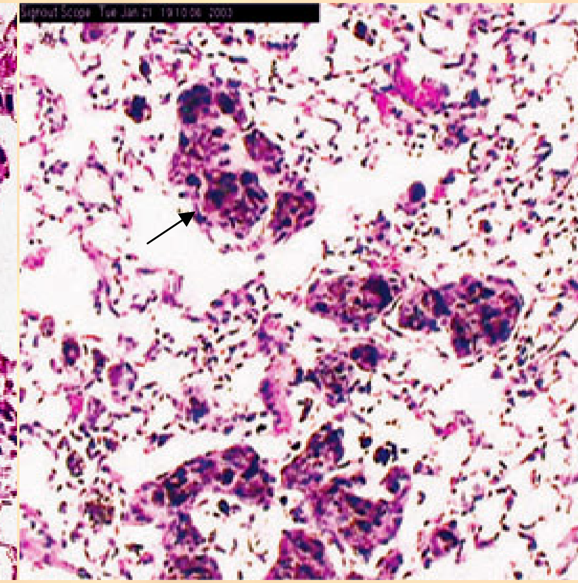
Carbon Black

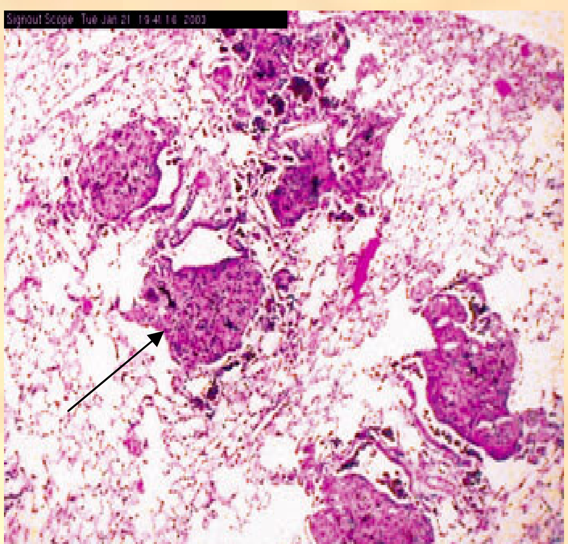


Quartz

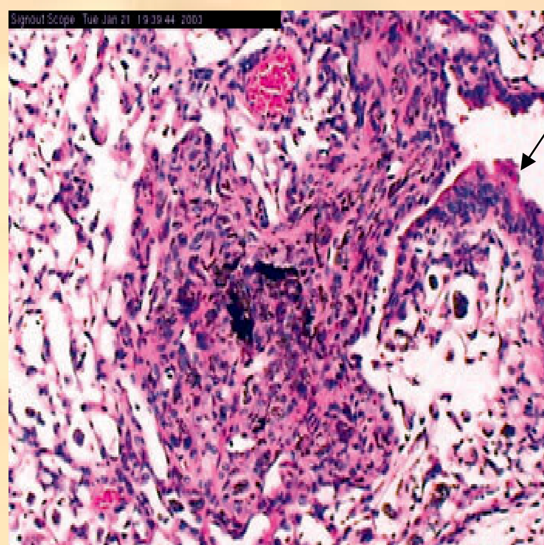


Carbolex NT

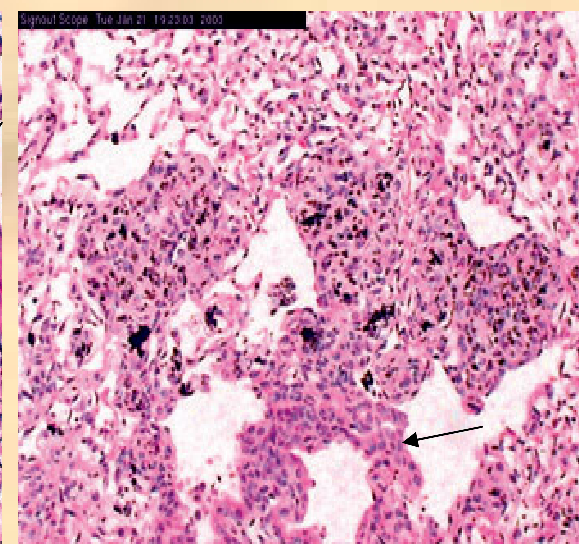




Raw NT (low m.)



Raw NT (high m.)



Purified NT

Incidence of Lesions after 90 Days (n= 5)

Dose of Material (mg)	Lesion	Carbon Black	Quartz	Raw NT	Purified NT	CarboLex NT
0.1	Inflammation	0	1	3	2	0
0.1	Granuloma	0	0	5	2	0
0.5	Inflammation	0	4	3	5	0
0.5	Granuloma	0	0	5	5	5

Relationship to Inhalation Exposures

- Assume: 40% of respirable dust deposits in pulmonary region of the lung
- Assume 30g mouse inhales 30 ml of air/minute
- Assume a concentration of 5 mg/m^3 for 8 hours/day (current PEL for respirable graphite dust)
- Accumulation would be 0.03 mg/day
- Total dose of 0.1 mg (our low dose) would be reached in <4 days and total dose of 0.5 mg (our high dose) would be reached in < 17 days

Conclusions

- On an equal weight basis, and if they reach the pulmonary regions of the lung, single-walled carbon nanotubes can be more toxic than quartz, which is a known occupational health hazard.
- Until more is known about the potential for nanotubes to reach deep into the lung, industrial hygiene practices should minimize any worker exposures.

Researching the Ethical Issues of Nanotube Use

- Discover the properties that make nanotubes toxic to reduce need to test every formulation created
- Monitor the workplace and use locations for respirable nanotubes in the air
- Monitor workers for health effects
- Determine environmental fate of nanotubes

Distribution of Nanotube Economic Value with Justice

- How much ($) and how long do the pioneers and risk takers benefit?
- Are military applications just?
- Whose livelihood will be destroyed?
- Whose environment will be altered?
- Are we passing difficult problems to subsequent generations?
- Who is denied the advantages of the technology because it is too expensive?