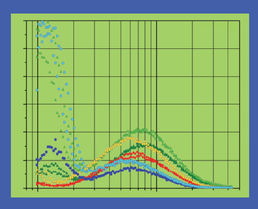
Mass transfer of Inhaled Nanoparticles to other organs



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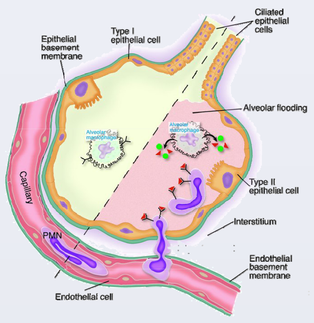
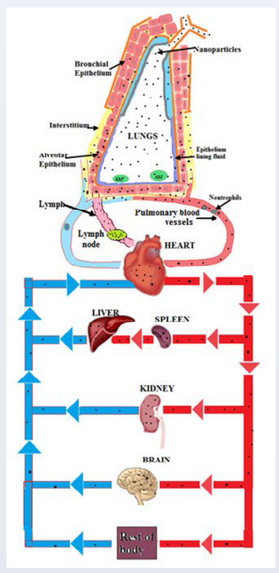
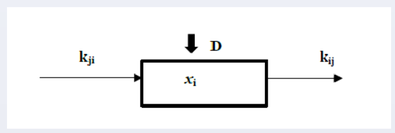
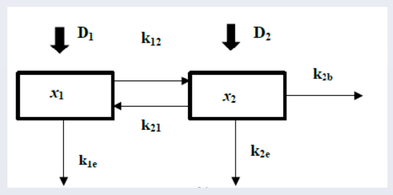
Introduction

Inhaled nanoparticles can have both toxic and therapeutic effects for human. CNTs, asbestos fibers and other industrial nanomaterials could cause pulmonary diseases. On the other hand inhaled nanomedicines have been developed for treating pulmonary or systemic diseases. Thus, many researches in the area of inhaled nanoparticle retention and clearance has been developed. In this research a multi compartmental model has been developed that can predict the bio-kinetics of insoluble nanoparticles translocation from lungs to systematic circulation, lymphatic systems, gastrointestinal tract and organs.









Materials and Methods

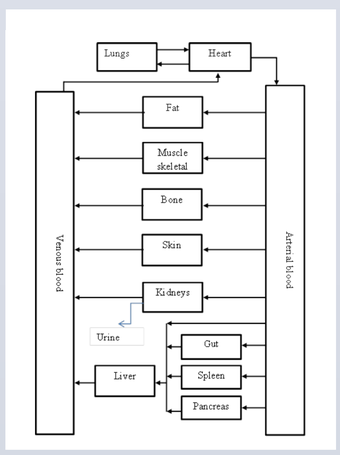
In order to calculate the amount of nanoparticles in each compartment, a system of differential equations quantifying the transport of particles from one compartment to another were solved. Experimental retention of nanoparticles in rat lung was used to find transport rates in the model equations. The model transport rates were found by minimizing the mean square error existed between the model and experimental retention data. Calculated transport rate for the rat has been converted to the human ones using a valid allometric scaling method.

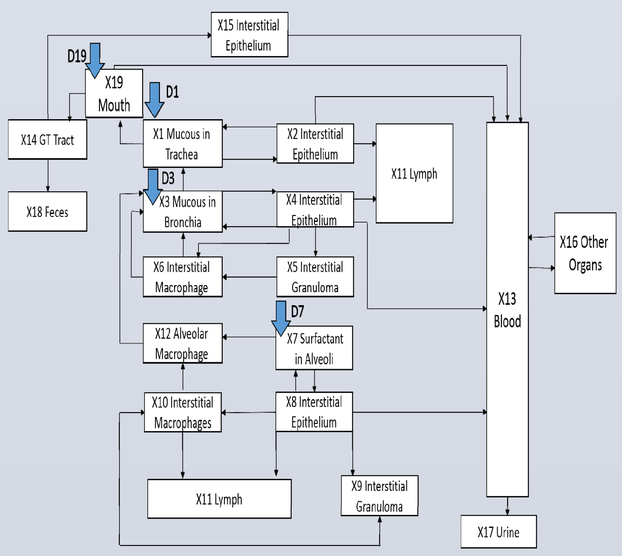
$$Time_{human} / BW^{0.25}_{human} = Time_{animal} / BW^{0.25}_{animal}$$

This model provides a complete specification of the residence time in lungs, blood circulation and other key organs of the body and can be used in diverse fields such as toxicology for exposure-risk analysis and respiratory nano-drug development and targeting.

Assumptions:

- nanoparticles are insoluble
- physico-chemical properties of nanoparticles will not affect the bio-kinetics
- no agglomeration of nanoparticles
- no nanoparticle-overload effects in the lung when compared to micron particles
- all compartments are well mixed, i.e., no spatial gradients

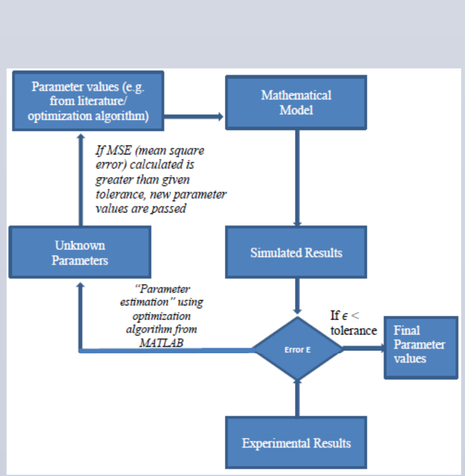




•Experimental exposure conditions:

Particle type	Iridium (^{192}Ir)
Particle diameter	15 - 20 nm (CMD)
Aerosol concentration	0.2 mg / m^3
Duration of exposure	1.25 hours
Breathing scenario	Endotracheal
Length of follow up	6 months
Breathing frequency	45 / min
Inspiratory fraction	75-80 %

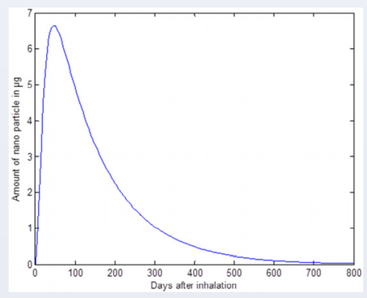
•A function was used to calculate the mean square error between the simulated results produced from the differential equation representing the model and the experimental results



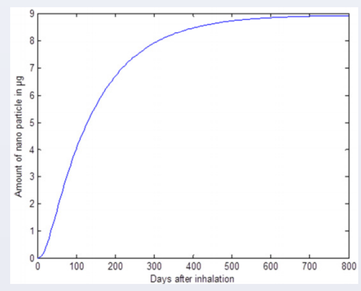
Results

Nanoparticle deposition in mouth, trachea, bronchia and alveoli during inhlation was obtained by the program multiple-path particle dosimetry and was used as an initial condition of the corresponding equation.

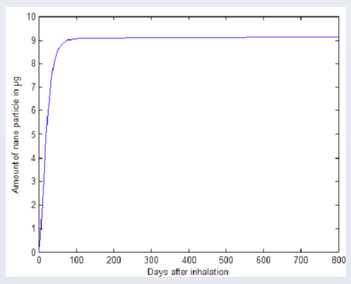
Our results showed taht the amount of 4.2% of the initial nanoparticle deposition will translocate from the lung to the lymphatic system. The human lung alveolar retention after one day is 95% which is in accordance with the experimental results of Moller et al and verifies our modelling. This indicates that clearance mechanism in the lung is very slow and repeated inhalation of nanoparticles from combustion process or environmental atmosphere will cause pulmonary diseases.



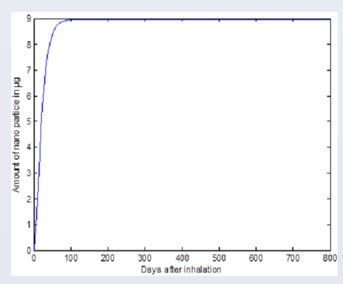
nanoparticle translocated to blood



nanoparticle translocated to other organs



nanoparticle translocated to lymphatic system



nanoparticle translocated to heart

The nanoparticle translocation to systemic circulation is about 0.1% of the initial deposition after one day. The amount of nanoparticles which could reach the other organs including heart, kidney and liver from blood circulation is about 4.2% of the initial deposition. Although a small amount of deposited nanoparticles could transfer to these organs, the accumulation of the nanoparticles could cause nonreversible side effects.

Tissue	Blood flow rate (fraction of cardiac output)
Fat	0.07
Muscle skeletal	0.278
Bone	0.122
Skin	0.058
Kidneys	0.141
Gut	0.131
Spleen	0.02
Pancreas	0.01
Liver	Arterial-0.065; Total-0.226

Conclusion

- **Nanoparticles are found to have increased toxicity than larger particles**
- **The multi-compartment model was calibrated using experimental nanoparticle clearance study on rats, as suitable human lung data are not available**
- **Half-life period of 40 days for the slow particle clearance from lung**
- **Nearly 4.2% of the initial deposition reached extra pulmonary organs through blood**
- **As per the model prediction, nearly 4.2% of the initial nanoparticle deposition was cleared from lungs to the lymphatic system**
- **Nanoparticles that enter the local tissues from the airways plus the alveolar region can easily migrate to the lymphatic system, resulting in local accumulation.**

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