Environment. Technology. Resources. Rezekne, Latvia
Proceedings of the 14th International Scientific and Practical Conference. Volume 2, 23-27

Multiple Path Particle Dosimetry Model Concept and its Application to Determine Respiratory Tract Hazards in the 3D Printing

Anna Borisova
Rīga Stradiņš University
Faculty of Medicine
Riga, Latvia
annaborisova1997@gmail.com

Karīna Rudus
Rīga Stradiņš University
Faculty of Medicine
Riga, Latvia
kariina.rudus@gmail.com

Ilona Pavlovska
Rīga Stradiņš University Laboratory of Hygiene and Occupational Diseases
Institute of Occupational Safety and Environmental Helath
Riga, Latvia
Ilona.Pavlovska@rsu.

Žanna Martinsone
Rīga Stradiņš University, Laboratory of Hygiene and Occupational Diseases
Institute of Occupational Safety and Environmental Helath
Department of Occupational and Enviromental Medicine
Riga, Latvia
Zanna.Martinsone@rsu.lv

Inese Mārtiņsone
Rīga Stradiņš University, Laboratory of Higiene and Occupational Diseases
Institute of Occupational Safety and Environmental Helath
Riga, Latvia
Inese.Martinsone@rsu.lv

Abstract. **The Multiple Path Particle Dosimetry (MPPD) model is computer software that estimates and visualizes the deposition, clearance, and retention of particles in the respiratory tract systems of humans, rats, and other species. The mathematical model provides a broad spectrum of settings and input options. This research aims to explore the MPPD model concept and determine the deposition fraction (DF), clearance, and retained mass in the human respiratory tract (HRT) based on the geometric mean diameter (GMD) and mass concentration (MC) of particulate matter (PM) emitted during the 3D printing process. We used the real-time air sample data collected during the 8-hour working shift in the 3D printing office. Ultrafine PM deposits mainly in lungs (56%), fine PM mostly deposits in the upper respiratory tract (URT) (41%) and lungs (39%), but coarse PM mostly deposits in the URT (81%). The biggest DF in lower respiratory tract is ultrafine PM (487 µg), the smaller DF is coarse PM (185 µg) and the smallest DF is fine PM (123 µg). The biggest DF in lung for all PM - lower lobes (fine PM - 60%, ultrafine PM, coarse PM - 61%). In a model, where exposure was 5 hours a day, five days a week, during one month, followed by one year of post-exposure period, it was shown that retained mass in the tracheobronchial (TB) region was 1% for ultrafine and coarse PM each, 2% for fine PM, and 55% for all PM in the pulmonary region.**
The MPPD software is an easily accessible and valuable tool for assessing the impact of PM on the HRT. Particulate matter decreasing in diameter, tend to deposit mostly in the deeper levels of HRT. Tracheobronchial region clearance is more rapid than pulmonary region clearance.
Potentially for persons using the 3D-printer regularly the worst health impact could be associated with smaller size of PM, due to tendency deposit mostly in pulmonary region where the clearance rate is slower.

Keywords: MPPD model, particulate matter, deposition, clearance.

I. Introduction

In recent years, 3D printing technology has increased rapidly in various industries, such as medicine, military,

Print ISSN 1691-5402
Online ISSN 2256-070X
https://doi.org/10.17770/etr2023vol2.7276

sports, food industries, and spacecraft [1] – [4]. Medicine is no exception – 3D printing is incorporated into the production of patient-specific surgical implants and prosthetics, bio-printed tissues, organ transplants, dental implants and orthodontic aligners, surgical instruments, tools, personalized drug delivery devices [5], [6]. With all the potential developments and trends, the future of 3D printing looks promising and thrilling. We can expect advancements in materials, improved speed, automation of the process, increased use in mass production, customization, personalization, and sustainability [7 – 10].

Nevertheless, using 3D printers has also raised concerns about the potential respiratory health hazards of releasing airborne particles during printing. Multiple studies revealed the increased concentration of different diameter PM and volatile organic compounds in the air samples taken during the printing [11] – [13].

The open - access multiple path particle dosimetry (MPPD v3.04) was used to better understand how 3D printer emissions impact the human respiratory system [14], [15]. It is a mathematical dosimetry model that aids in calculating and visualizing total, regional, lobar, and generation–specific deposition and clearance of particulate matter. MPPD is free of charge and has a user-friendly interface that allows the input of various variables and scenarios. It is successfully used in research, education, and other industries. Since the first time, it was introduced in 1995 by the Hamner Institute for Health Science (USA), the MPPD model has been evolving – applied to the human lung, the rat lung, and particle deposition [16], [17], [18], [19]. The latest model software update included improvements and additions in aerosol distributions, clearance parameters, species geometry models, and visualization of the output files [20]. The dosimetry model is a valuable mathematical tool that can contribute to environmental toxicology research [21].

II. Materials and Methods

Originally, the literature review was conducted to explore the concept of the MPPD model. The MPPD model is one of the most advanced and broadly tested dosimetry models. It considers different aerosol deposition mechanisms such as inertial impaction, gravitational sedimentation, and Brownian diffusion. The input data includes such parameters as airway morphometry, inhalant properties, exposure conditions, deposition, and clearance. In the air morphometry section, the user can choose to model the dose metrics of different species – human, mouse, rhesus, pig and rabbit. Therefore, the model allows intrahuman and interspecies variability. As well as provides multiple choices for the lung models – Yeh/ Schum, Stochastic, Age – specific, Weibel. It is possible to adjust to different scenarios, gender, and age (only for children population, three months – eighteen years) by changing the functional residual capacity (FRC, ml) and upper respiratory tract volume (ml) values. However, there is always a possibility to choose the model's default values. In the next section – inhalant properties, the program provides multiple preferences for the PM characteristics, such as density (g/cm$^{3)}$, diameter (μm), geometric standard deviation (GSD), and mass median aerodynamic diameter (MMAD). Two scenarios - constant and variable exposures - are provided for the exposure conditions by the model. In that section, aerosol concentration (mg/m^3), breathing frequency (x/min), tidal volume (ml), pause, and inspiratory fractions can be modified. Also, it is possible to select preferred orientation and the breathing route – nasal, oral, or combined. MPPD retention and clearance modelling is done in a separate section and contains such parameters as tracheal mucous velocity (mm/min) and lymph node clearance rate (1/days). Additionally, exposure time settings: number of days with exposure to the specific pollutant and number of posts – exposure days. After the calculations, the MPPD output data is presented in textual and graphical form. The model predicts deposition in the entire respiratory tract, as well as based on regions (upper respiratory tract - URT, tracheobronchial - TB, alveolar), lung lobes (RU – right upper, RM – right middle, RL – right lower, LU – left upper, LL – left lower), and by the level of lung generations (from the trachea to the deeper lung tissue - alveoli). The retention, and clearance values are predicted in the tracheobronchial and alveolar regions [14], [16] – [24]. Clearance is the process by which deposited particles are removed from the respiratory tract. Retention - refers to the number of deposited particles present at specific respiratory tract sites that remain after the clearance processes [27].

In this study, the main aspects of the MPPD software were investigated, and three different diameters of particulate matter – ultrafine ($PM_{0.1}$), fine ($PM_{2.5}$), and coarse (PM_{10}) deposition, retention and clearance were modelled in the HRT to explore the possible consequences of working with 3D printers. Real-time air measurement in the 3D printing premises were used during one working shift (8h, including breaks). For the counting of particles was used a low-pressure electrical impactor (ELPI+, Dekati Ltd). All measurements were done at 1.1 meters and as close as possible to the employees' breathing zone. The average value of the geometric mean diameter and mass concentration were calculated for all three groups of PM. We incorporated these two main variables into the model for deposition and clearance. For the PM deposition predictions, all of the available MPPD output was calculated and visualised in the Yeh/Schum lung model. For clearance calculations, the default values were used - for tracheal mucous velocity 5.5 mm/min, clearance rates for the alveolar-interstitial region to the TB region, denoted as slow, medium and fast were 0.0001, 0.001, and 0.02 per day. The lymph nodes clearance rate was 0.00002/per day. Two scenarios were used for the prediction of clearance and retention. The first scenario was 5-hour isolated exposure, the average time 3D office workers would spend in the 3D printing room, followed by a 30-day post-exposure period. The second scenario was

when exposure would be five hours a day, five days a week for one month, followed by a 1-year post-exposure period. The study was approved by the Ethics Committee of Rīga Stradiņš University (Nr. 2-PĒK-4/570/2022).

III. Results

The biggest deposition fraction of PM in the human respiratory tract based on the MPPD model is PM_{10} - 957 µg, the smaller is $PM_{0.1}$ - 569 µg, and the smallest is $PM_{2.5}$ - 209 µg. Furthermore, if we are looking at the particulate matter deposition based on the HRT regions, then $PM_{0.1}$ deposits mainly in the pulmonary region (PU) - 56.2%, $PM_{2.5}$ deposits primarily in the URT - 41.0% and PU region - 39.0 %, but PM_{10} mainly deposits in the URT region - 80.6% (Fig. 1).

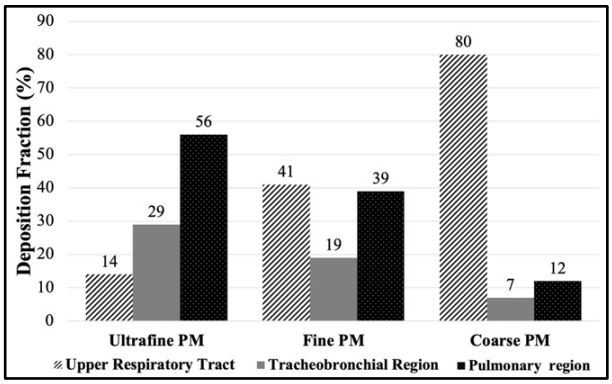

Fig. 1. Ultrafine, fine and coarse PM deposition distribution in HRT.

The biggest deposition fraction in the lower human respiratory tract (LHRT) is $PM_{0.1}$ - 487 µg, the smaller DF is PM_{10} - 185 µg, and the smallest DF is $PM_{2.5}$ - 123 µ (Fig. 2). However, in the URT, the biggest DF is PM_{10} - 771 µg, the smaller DF is $PM_{2.5}$ - 86 µg, and the smaller $PM_{0.1}$ - 82 µg. The biggest DF based on the lung lobe distribution – for all three PM diameters is in the lower lobes: $PM_{0.1}$ - 60.6%, $PM_{2.5}$ - 60.4 %, and PM_{10} - 61.1 %. On the other hand, the smallest DF for all of the PM is in the right middle lobe: $PM_{0.1}$ - 8.0 %, $PM_{2.5}$ - 8.0 %, and PM_{10} - 7.7 %. The peripheral lung region has a higher deposition fraction: $PM_{0.1}$ - 71.3 %, $PM_{2.5}$ - 70.5 %, and PM_{10} - 61.1 %, than the central lung region. For all particulate matter diameters, deposition fraction starts progressing on the level of respiratory bronchioles – 17-19th airway generation and reaches its maximum at the level of alveolar sacs – 23rd airway generation.

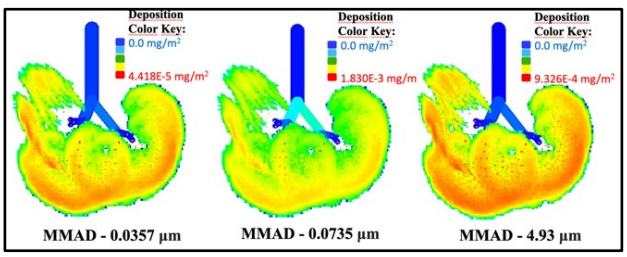

Fig. 2. Deposition Fraction and Mass Deposition rate per area visualization of a – $PM_{0.1}$; b – $PM_{2.5}$; c – PM_{10}. Species and Model Info (Species/Geometry: Human; Breathing route: Nasal; FRC Volume: 3300.0 ml; Head Volume: 50.0 ml. Breathing Parameters (Tidal Volume: 625.0 ml; Breathing Frequency: 12x/min; Inspiratory fraction: 0.5; Pause Fraction: 0. Particle Properties (GSD: 1.0; Aerosol concentration: 0.000025 mg/m^3).

For the clearance of PM, the first scenario was 5-hour isolated exposure, the average time 3D office workers would spend in the 3D printing room, followed by a 30-day post-exposure period. The second scenario is when exposure would be 5 hours a day, five days a week, during one month, followed by one year of post-exposure period.

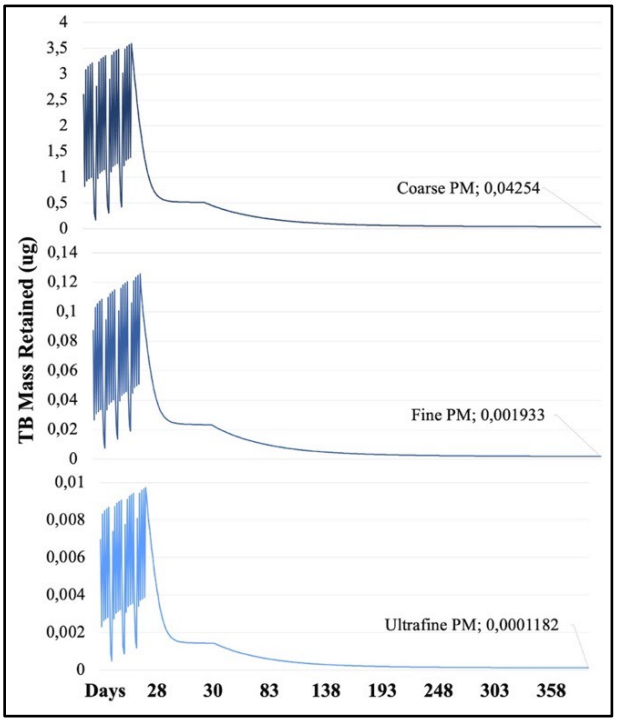

Fig. 3. Ultrafine, fine, and coarse PM retention in the TB region.

In the first scenario, the MPPD model predicted that particulate matter retained mass in the TB region would be: $PM_{0.1}$ - 0.7%, $PM_{2.5}$ - 1.0%, and PM_{10} - 0.8% and in the PU region it would be: $PM_{0.1}$ - 85%, $PM_{2.5}$ - 84.7% and PM_{10} - 84.8%. In the second scenario, the MPPD model predicted that retained mass in the TB region would be $PM_{0.1}$- 1.2%, $PM_{2.5}$ - 1.5%, and PM_{10} - 1.2% (Fig. 3), and in the PU region retained mass would be the same for all three diameters of particulate matter – 54.5% (Fig. 4). The clearance rate of the retained particulate matter for all PM sizes in the TB region was initially high and then decreased. In contrast, the clearance rate in the PU region was consistently low.

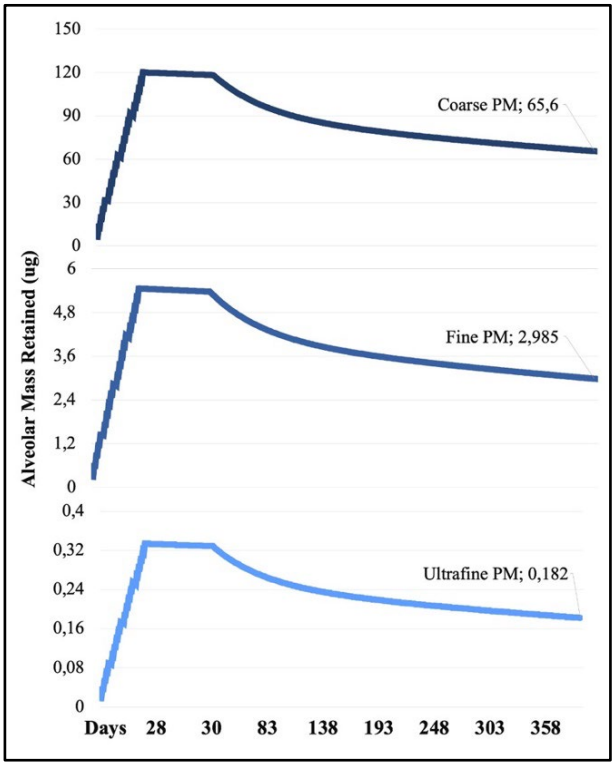

Fig. 4. Ultrafine, fine, and coarse PM retention in the alveolar region.

III. Discussion

The MPPD program is widely used among researchers [16] – [19], [21].

Our results are consistent with previous studies done on this matter. They also suggest similar PM deposition, clearance, and retention patterns in HRT due to 3D printer emissions [20], [23], [26].

Deposition of the inhaled particulate matter can cause inflammation in the different levels and regions of the HRT, especially at the sites with maximum deposit [16]. Multiple studies showed that long – lasting usage of 3D printing could lead to health problems like chronic bronchial asthma (COPD) and bronchial asthma (BA) exacerbation. As well as non – respiratory symptoms such as irritation of eyes and mucus membranes, increased blood pressure, and cardiovascular diseases [23] – [25].

Based on our results, $PM_{0.1}$ has the highest deposition in the pulmonary region. It has a higher probability of reaching the alveoli level of the PU and getting absorbed through the alveolar epithelium, causing systemic inflammation and other organ system and tissue damage. It can also trigger the alveolar macrophages migration, causing the local inflammation [26]. The MPPD model revealed that increased activity level corelates with the increase in the total DF [26].

Study limitations: airway morphometry data entered the program are relevant to the adult person population, so the results cannot be applied to all individuals. It was impossible to include other pertinent parameters in the MPPD model, such as the individual age, medical history, and physical activity. Also, it was challenging to determine the exact amount of time workers spend in a particular with PM polluted 3D printing room during the working day. Still, we predicted that workers spend around 5-hours working in a PM-polluted room.

IV. Conclusions

The MPPD software is an easily accessible, valuable, and widely used tool for assessing the impact of PM on the HRT. It is an excellent addition to inhalation and *in vitro* studies. In some cases, it can be faster and cheaper and give a broader understanding of the deposition, retention, and clearance physiology. It is also a great aid in designing inhalation exposure and human toxicological studies to protect against ambient and occupational biological, chemical, and radiological threats. As well as facilitate dose metrics for the drugs delivered by the inhalation route.

The smaller size of PM tends to deposit in the deeper levels of the human respiratory tract, where the clearance rate is poor. Therefore, people working with 3D – printers for a more extended period and being exposed to the printing emission could have a higher chance of developing chronic inflammation in the respiratory tract and other organ systems or tissue.

V. Acknowledgements

The research was carried out within a project of National Programme Grants (RSU Grants) “Occupational health and safety risks during 3D printing” 6-ZD-22/22/2022.

References

[1] R.A. Buswell, W.R. Leal de Silva, S.Z. Jones, J. Dirrenberger, “3D printing using concrete extrusion : A roadmap for research”, Cement and Concrete Research, vol. 112, pages 37- 49, 2018. https://doi.org/10.1016/j.cemconres.2018.05.006

[2] S. Murphy, A. Atala, “3D bioprinting of tissues and organs”, Nature Biotechnology, vol. 32, pages 773 – 785, 2014. http://dx.doi.org/10.1038/nbt.2958

[3] B. Blakey – miller, P. Gradl, G. Snedden, M. Brooks, J. Pitot, E. Lopez, M. Leary, F. Berto, A. du Plessis, “Metal additive manufacturing in aerospace: A review”, Materials & Design, vol. 209, page 110008, 2021. https://doi.org/10.1016/j.matdes.2021.110008.

[4] Food Printing: 3D Printing in Food Industry. Book. 2022. https://link.springer.com/book/10.1007/978-981-16-8121-9 [Accessed on February 23 2023].

[5] J. Visser, B. Peters , T.J. Burger, J. Boomstra, W.J. Dhert, F.P. Melchels, J. Malda, “Biofabrication of multi – material anatomically shaped tissue constructs”, Biofabrication, vol. 5, no. 3, 2013. https://doi.org/10.1088/1758-5082/5/3/035007

[6] D.D. Wang, Z. Qian, Z. Vukicevic, S. Engelhardt, A. Kheradvar, C. Zhang, S. H. Little, J. Verjans, D. Comaniciu, W. W. O'Neill, M.A. Vannan, “3D Printing, Computational Modeling, and Artificial Intelligence for Structural Heart Disease”, JACC Cardiovasc Imaging, vol. 14, pages 41 – 60, 2021. https://doi.org/10.1016/j.jcmg.2019.12.022

[7] X. Wei, M.L. Jin, H. Yang, X. X. Wang, Y. Z. Long, Z. Chen, "Advances in 3D printing of magnetic materials: Fabrication, properties and their applications", Journal od Advanced Ceramics, vol. 11, pages 665 – 701, 2022.
https://doi.org/10.1007/s40145-022-0567-5

[8] Z. Wang, Z. Guo, Z. Li, K. Zeng, "Design, manufacture, and characterisation of hierarchical metamaterials for simultaneous ultra-broadband sound-absorbing and superior mechanical performance", Virtual ans Physical Prototyping, vol. 18, 2022.
https://doi.org/10.1080/17452759.2022.2111585

[9] F. Bos, R. Wolfs, Z. Ahmed, T. Salet, "Additive manufacturing of concrete in construction: potentials and challenges of 3D concrete printing", Virtual and Physical Prototyping, vol. 11, pages 209–225, 2016.
https://doi.org/10.1080/17452759.2016.1209867

[10] X. Lin, D. Qu, X. Chen, Z. Wang, J. Luo, D. Meng, G. Liu, K. Zhang, F. Li, X. Yu, "Three-dimensional printed metal-nested composite fuel grains with superior mechanical and combustion properties, Virtual and Physical Prototyping, vol. 17, pages 437 – 450, 2022.
https://doi.org/10.1080/17452759.2022.2035934

[11] P. Azimi, D. Zhao, C. Pouzet, N. E. Crain, B. Stephens, "Emissions of Ultrafine Particles and Volatile Organic Compounds from Commercially Available Desktop Three-Dimensional Printers with Multiple Filaments", Environmental Science & Technology, vol. 50, pages 1260 – 1268, 2016.
https://doi.org/10.1021/acs.est.5b04983

[12] E. L. Floyd, J. Wang, J. L. Regens, "Fume emissions from a low-cost 3-D printer with various filaments", Journal of Occupational and Environmental Hygiene, vol. *14*, pages 523–533, 2017.
https://doi.org/10.1080/15459624.2017.1302587

[13] I. Pavlovska , Ž. Martinsone, A. Kļaviņa, L. Akūlova, L. Paegle, "Emissions from 3D Printers as Occupational Environmental pollutants", Sciendo, vol. 25, pages 1018 – 1031, 2021.
https://doi.org/10.2478/rtuect-2021-0077

[14] Applied Research Associates, MPPD: Multiple – Path Particle Dosimetry Model (MPPD V 3.04) [Online]. Available: https://www.ara.com/mppd/ [Accessed: March 10, 2023].

[15] P. Byrley, W. K. Boyes, K. Rogers, A. M. Jarabek, "3D printer particle emissions: Translation to internal dose in adults and children", Journal of Aerosol Science, vol. 154, page 105765, 2021.
https://doi.org/10.1016/j.jaerosci.2021.105765

[16] A. Satish, B. Ashgarian, "A Multiple – path Model of particle Deposition in the Rat Lung", Fundamental and Applied Toxicology, vol. 28, pages 41 – 50, 1995.
https://doi.org/10.1006/faat.1995.1144

[17] B. Asgharian, W. Hofmann, R. Bergmann. "Particle Deposition in a Multiple-Path Model of the HumanLung", Aerosol Science and Technology, vol. 34, pages 332 – 339, 2001.
https://doi.org/10.1080/02786820119122

[18] B. Asgharian, "Respiratory Deposition and Inhalability of Monodisperse Aerosols in Long-Evans Rats", Toxicological Sciences, vol. 71, pages 104 – 111, 2003.
https://doi.org/10.1093/toxsci/71.1.104

[19] B. Asgharian, F. J. Miller, O. Price, J. D. Schroeter, D. R. Einstein, R. A. Corley, T. Bentley, "Modeling particle deposition in the pig respiratory tract", Journal of Aerosol Science, vol. 99, pages 107 – 124, 2016.
https://doi.org/10.1016/j.jaerosci.2016.01.016

[20] F. J. Miller, B. Asgharian, J. D. Schroeter, O. Price, "Improvements and additions to the Multiple Path Particle Dosimetry model", Journal of Aerosol Science, vol. 99, pages 14–26, 2016.
https://doi.org/10.1016/j.jaerosci.2016.01.018

[21] B. Asgharian, O. Price, A. A. T. Borojeni, A. P. Kuprat, S. Colby, R. K. Singh, W. Gu, R. A. Corley, C. Darquenne, "Influence of alveolar mixing and multiple breaths of aerosol intake on particle deposition in the human lungs", Journal of Aerosol Science, vol. 166 , page 106050, 2022.
https://doi.org/10.1016/j.jaerosci.2022.106050

[22] C. Darquenne, "Deposition Mechanisms", Journal of Aerosol Medicine and Pulmonary Drug Delivery, vol. 33, pages 181–185, 2020.
https://doi.org/10.1089/jamp.2020.29029.cd

[23] S. Ragopalan, S. G. Al-Kindi, R. D. Brook, "Air Pollution and Cardiovascular Disease", Journal of the American College of Cardiology, vol. 72, pages 2054 – 2070, 2018.
https://doi.org/10.1016/j.jacc.2018.07.099

[24] A. Karwasz, F. Osiński, "Analysis of Emission Solid Particles from the 3D Printing Process" Lecture Notes in Mechanical Engineering, pages 216–226, 2022.
https://doi.org/10.1007/978-3-031-00805-4_18

[25] Y. Mohammadian, N. Nasirzadeh, "Toxicity risk of occupational exposure in 3D printing and bioprinting industries: A systemic review", vol. 37, pages 415 – 430, 2021.
https://doi.org/10.1177/07482337211031691

[26] A. Goel, S. Izhar, T. Gupta, "Study of Environmental Particle Levels, Its Effects on Lung Deposition and Relationship with Human Behaviour", Environmental Contaminants, pages 77–91, 2017.
https://doi.org/10.1007/978-981-10-7332-8_4.

[27] A. I. Gipsman, N. C. Lapinel, O. H. Mayer, "Airway Clearance in Patients with Neuromuscular Disease", Paediatric Respiratory Reviews, vol. 11, pages 120 – 130, 2023.
https://doi.org/10.1016/j.prrv.2023.02.002