CAMBRIDGE DESIGN PARTNERSHIP

# WAITING FOR THE OUTBREATH – WHAT MIGHT COVID-19 BIOAEROSOL RESEARCH HAVE TO TELL US ABOUT INHALABLE DRUG DELIVERY?

Here, Deborah Norris, Senior Consultant – Healthcare Devices Engineer, Mark Allen, PhD, Associate Mechanical Engineer, Karl Hewson, Senior Consultant – Design and Usability Engineer, and Karla Sanchez, PhD, Senior Consultant – Biomedical Engineer, all at Cambridge Design Partnership, discuss how the covid-19 pandemic has spurred research in the pulmonary space, which suggests that a patient-tailored approach based on their individual lung characteristics, facilitated by advanced technology, could improve patient health outcomes and quality of life.

Over the past year-and-a-half living through the covid-19 pandemic, research into the generation and emission of bioaerosols has increased significantly. Studies have looked into the mechanics of how viruses are communicated through respirable droplet production, not just for droplets generated during coughing and sneezing but also during normal breathing and talking.[1] Examining these mechanisms has reinforced the existence of "super emitters" – people who produce aerosol particles at an order of magnitude greater than the baseline.[2] This research has led to compelling findings.

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There is particular interest in the generation of the small aerosol particles that are believed to be generated primarily in the deep lung, at the level of the bronchioles leading to the alveolar sacs – a phenomenon known as "bronchiolar fluid film burst".[3] These tiny passages close at the end of a forceful exhalation and re-open as the person inhales, but are covered over by a thin mucosal film – similar to a bubble-wand. This film bursts as inhalation completes, generating microscopic droplets of fluid in the alveolus. Then, during the ensuing exhalation, these tiny particles are ejected from the lung and expelled as an extremely fine bioaerosol.

This is instructive in terms of disease transmission and therefore a hot topic for understanding the communication of bioaerosol-borne viruses. However, it also provokes an interesting discussion around inhaled drug delivery mechanisms. Typically, patients are told to breathe out

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strongly immediately before administering an inhaler dose. This encourages the patient to achieve the "empty lung" residual volume point and allows for deep inhalation by pulling inhaled medication deeper into the lung. Or does it? Does it, at least, achieve this most effectively? The strong exhalation cycle may, in fact, be *inhibiting* optimal deposition of drug product by encouraging the closure of areas of the lung for targeted medication. Should we perhaps be looking more closely at understanding and characterising the mechanics of the outbreath to help us improve the efficacy of drug delivery and treatment outcomes?

Studies show that whilst bronchiole closure happens mainly during the deep exhalation stage, age, disease or excess weight can cause this closure point to come at an earlier stage of exhalation, thereby altering bioaerosol emission.[4] Could there be room for a patient-specific protocol based on an individual's lung performance during typical and conscious breathing? This could help healthcare practitioners prescribe patients with inhalers best suited to their physiology – for example, a dry powder, soft mist or pressurised metered dose inhaler, or even a nebuliser – and, in so doing, improve treatment efficacy and possibly adherence too, if the patient feels that they are receiving an enhanced medicinal benefit by using an inhaler that has optimal performance for their breathing patterns.

Devices exist that monitor and analyse patient behaviour in real time during clinical studies and training, such as Cambridge Design Partnership's Quantii.[5] By combining traditional diagnostic technologies with cutting-edge techniques to monitor the condition of the lung during the breath cycle, it is possible to open up further potentially exciting developments. An example is Wheezo (Respiri, Melbourne, Australia), a monitoring tool aimed at helping asthmatics better measure and manage their condition using a connected acoustic device that characterises wheezing episodes.

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This highlights the fact that artificial intelligence-based diagnosis devices are no longer the sole preserve of science fiction but a tangible reality. Therefore, the question is how best to use these new insights into outbreath mechanics to develop diagnostics as technology advances. The possibilities include a smart spirometer that can identify the early warning signs of lung conditions; a handheld device that can identify the current health risk for those with lung conditions posed by the environment they are in; and smart-inhaler technology that gathers long-term patterns of a patient's respiratory profile that, over time, could enable healthcare providers to fine-tune prescriptions and treatment regimens, or even produce on-the-fly adjustments to the applied dose, depending on real-time diagnostic readings at point of care.

Building a picture of an individual's "lung characteristics" could improve the quality of life and health outcomes for patients with respiratory conditions. Combining advances in artificial intelligence with a deeper understanding of lung mechanics could lead to earlier diagnoses for diseases

that are not currently identified before significant structural damage has already occurred. Such a diagnosis could enable healthcare practitioners to offer earlier intervention strategies and a tailored inhaler profile to best match an individual patient's needs.

Some of these ideas still belong in the field of sci-fi – but there are clearly exciting developments for the respiratory field to pursue, courtesy of research catalysed by the covid-19 pandemic.

## ABOUT THE COMPANY

Cambridge Design Partnership is an end-to-end innovation partner, propelling global brands and ambitious start-ups to success. The company builds breakthrough products and services – from insight to ideas, prototypes to production – bringing innovation to life. Its teams are multi-disciplinary, uniting scientific rigour, design ingenuity and engineering excellence for consumer, healthcare and industrial clients.

People-centred, deeply collaborative and, above all, expert, Cambridge Design Partnership is uniquely positioned to shape the future for consumers, patients and industry. Even the company's ownership model is innovative – the company is 100% owned by employees, ensuring an open culture and a total commitment to each project's success.

## REFERENCES


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# ABOUT THE AUTHORS

**Deborah Norris** is Senior Consultant – Healthcare Devices Engineer at Cambridge Design Partnership, and has over 20 years' experience as a development engineer, with the last 15 years focused solely within the medical devices sector, including drug delivery, critical care, medical diagnostics and surgical robotics. Ms Norris has led various R&D programmes in the medical device industry, including design and development of parenteral autoinjectors for highly viscous formulations; concept to clinical development of a critical care dose and monitoring system for neonatal intensive care units; development of a novel gastric breath-gas diagnostic system; and research into novel glucose monitoring technologies with a focus on non-invasive methods.

**Mark Allen**, PhD, is an Associate Mechanical Engineer at Cambridge Design Partnership. He has a PhD and MEng in Mechanical Engineering from Loughborough University (UK) where he specialised in the prediction and measurement of liquid and gas flows and sprays, working on internal flow imaging and analysis of internal combustion engine technologies to reduce harmful emissions and improve performance. After leaving academia, Dr Allen moved to the medical device sector, working on the design and development of a range of devices from early-to-late stage, including the design and development of multiple autoinjectors for highly viscous formulations and a novel nasal spray device. His specialisms include simulation, mathematical modelling and data analysis.

**Karl Hewson** is Senior Consultant – Design and Usability Engineer at Cambridge Design Partnership. Mr Hewson has over 25 years' experience, specialising in usability engineering and user-centred design. He has been involved in product development across the industrial, consumer and medical sectors, within industry-specific safety and regulatory requirements including US FDA guidance on applying human factors and usability engineering to medical devices (AAMI HE75 and IEC62366), and including working with dry powder inhalers, insulin injection devices and critical care products for improving patient recovery from mechanical ventilation and minimisation of hypotension events during elective surgery. Mr Hewson's experience includes ethnography, unmet needs identification and translation to product architectures, user interface and user experience design, product usability evaluation and design for manufacture.

**Karla Sanchez**, PhD, is Senior Consultant – Biomedical Engineer at Cambridge Design Partnership, working as a mathematical modeller, researcher and bioengineer with several years of experience in product development. She obtained her PhD from Imperial College London (UK) at the Physiological Fluids Group, where she focused on blood flow of the cerebral vasculature and distribution of cerebrospinal fluid. She has also worked alongside clinicians and academics to study blood flow in the kidney and complications of chronic kidney disease. Dr Sanchez has managed several successful commercial projects, launching a large range of infusion sets, orthopaedic and surgical devices. She is an enthusiastic STEM ambassador and holds an honorary visiting researcher position at Imperial College London.