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Translational biomedical engineering: Intelligent inhalation system Gentle treatment for premature babies with lung diseases

Premature babies who are born before their lungs have finished maturing often suffer from a lack of surfactant – a substance necessary for lung development. They are also particularly susceptible to illnesses of the respiratory organ, which have to be treated by means of inhalation. However, the inhalation systems available are not geared to the needs of preterm infants and newborns. Researchers at the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM are working with partners to develop a system that would allow drugs to be administered as aerosols in an efficient and breath-triggered manner. This would shorten therapy duration, thereby easing the strain on little bodies.

Worldwide, around 15 million babies are born prematurely every year – and the trend is growing. Industrialized countries are no exception to this development. According to World Health Organization (WHO) figures, the rate in Germany is 9.2 per 100 newborns. One of the most common complications in premature babies is bronchopulmonary dysplasia, a chronic lung disease caused by the artificial ventilation that the infants often need. Also, because the preterm infants' immune systems are not fully developed, they have an increased risk of infection. Lung infections are best treated with inhaled drugs. However, there are no inhalation systems that are specially adapted to the needs of premature babies and other newborns, as developing the corresponding technologies is very complicated due to the specific breathing characteristics of the tiny patients. Preterm infants typically have a high respiratory rate of 40 to over 60 breaths per minute and short inhalation periods of 0.25 to 0.4 seconds. On top of this, neonatal lungs have only a small tidal volume, posing extra difficulties for inhalation treatment. For this reason, scientists at the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM in Hannover are working together with partners from industry and research to develop a new inhalation system allowing premature babies to receive an efficient inhalation therapy that is gentle on their lungs.

"Administering drugs to premature babies by means of inhalation is difficult. The current method of continuously delivering aerosols – that is, drugs in the form of particles – into the airflow is inefficient. For one thing, a large portion of the expensive drug gets lost on account of the inhalation/exhalation ratio and thus provides no medical benefit. Moreover, the aerosol is immediately diluted by the airflow traveling through the respirator," says Dr. Gerhard Pohlmann, head of the Fraunhofer ITEM Division of Translational Biomedical Engineering. The project partners are developing a

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new breath-triggered method whereby the aerosol is administered directly to the nose only when the premature baby inhales. "For the first time, this opens the door to the highly efficient administration of drugs to preterm infants. This means that the amount of active ingredients can be reduced and therapy durations can be shortened. In addition, precise time control with very short inhalation boli permits the focused treatment of specific lung regions," says Pohlmann. A similar system would also be fundamentally suitable for adult patients who require daily inhalation therapy. Shortening the administration time can substantially improve their quality of life.

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Sensor film for monitoring the respiration of premature babies

The innovative inhalation system combines two technologies: A nasal prong with a miniature aerosol valve that is directly applied to the nose of the preterm infant. With a response time of just a few milliseconds, the aerosol valve allows the active ingredient to be released in a rapid, targeted manner. Opening of the valve is controlled by a sensor film. Laid on the abdominal wall of the premature baby, this flexible matrix uses sensors to detect the movement of the upper abdomen, thereby measuring the exact moment the baby breathes in. For the precise release of the aerosol, the measurement signal controls the micro valve via an intelligent algorithm. "The timing of the inhalation must be caught with an accuracy of about 20 milliseconds. Placing normal sensors in the exhalation region of a respirator does not permit this level of precision," explains the researcher. The breath-triggered inhalation systems currently available are either reliant on measuring the breath signal in the breathing hose or else coupled to the ventilation system via an electrical connection. "Our ventilator-independent respiration recording system removes the need to interfere with an already approved device and thus reduces approval obstacles."

Both the sensor film with ultra-thin ICs and the breath-triggered technology are being developed by a consortium in the FLEXMAX project (see box). The German Federal Ministry of Education and Research (BMBF) is funding the project, which addresses key aspects of the New Electronic Systems for Intelligent Medical Engineering (Smart Health) tender.

In tests with adults and in trials using devices that simulate the breathing of premature babies, there was an increase in efficiency of 60 percent compared to conventional inhalation technology. To be able to test the sensor film at an early stage in realistic conditions, the project partners are also developing an artificial abdominal wall that moves like that of a premature baby.

The complete inhalation system is currently available as a demonstrator, and it will take about three to five years before it is production-ready, says Pohlmann.

Breath-triggered administration of dry-powder drugs

The team of experts at Fraunhofer ITEM are also carrying out research into application systems for the administration of dry-powder formulas by means of inhalation, which could be used, for example, to treat premature babies with infant respiratory distress syndrome. This syndrome arises when the not fully developed lung either does not produce enough surfactant or does not produce any at all. Without surfactant, which reduces surface tension in the pulmonary alveoli, the lung is unable to expand. The baby suffers from oxygen deprivation and breathing distress and needs artificial respiration. Usually, surfactant obtained from animal lungs is flushed into the lung in the form of a suspension. The problem is that this so-called instillation is traumatic and the surfactant administered in a suspension does not spread as evenly through the lungs as aerosols do. In contrast, if the surfactant is administered as a moistened dry aerosol to be inhaled, it is distributed more homogeneously and works more effectively.

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Profile: FLEXMAX

Project duration: 4/2018 to 3/2021

Project funded by: German Federal Ministry of Education and Research (BMBF)

Funding: 3.1 million euros

Project partners

- Activoris Medizintechnik GmbH, Gemünden
- AC Aircontrols GmbH, Kempen
- eck*cellent IT GmbH, Braunschweig
- Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover
- Institut für Mikroelektronik Stuttgart
- Reinhardt Microtech GmbH, Ulm
- Technische Universität Carolo-Wilhelmina, Braunschweig

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Demonstrator: Sensor film and nasal prong with integrated miniature aerosol valve on a preterm infant training dummy. © Fraunhofer ITEM | Picture in color and printing quality: www.fraunhofer.de/en/press

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