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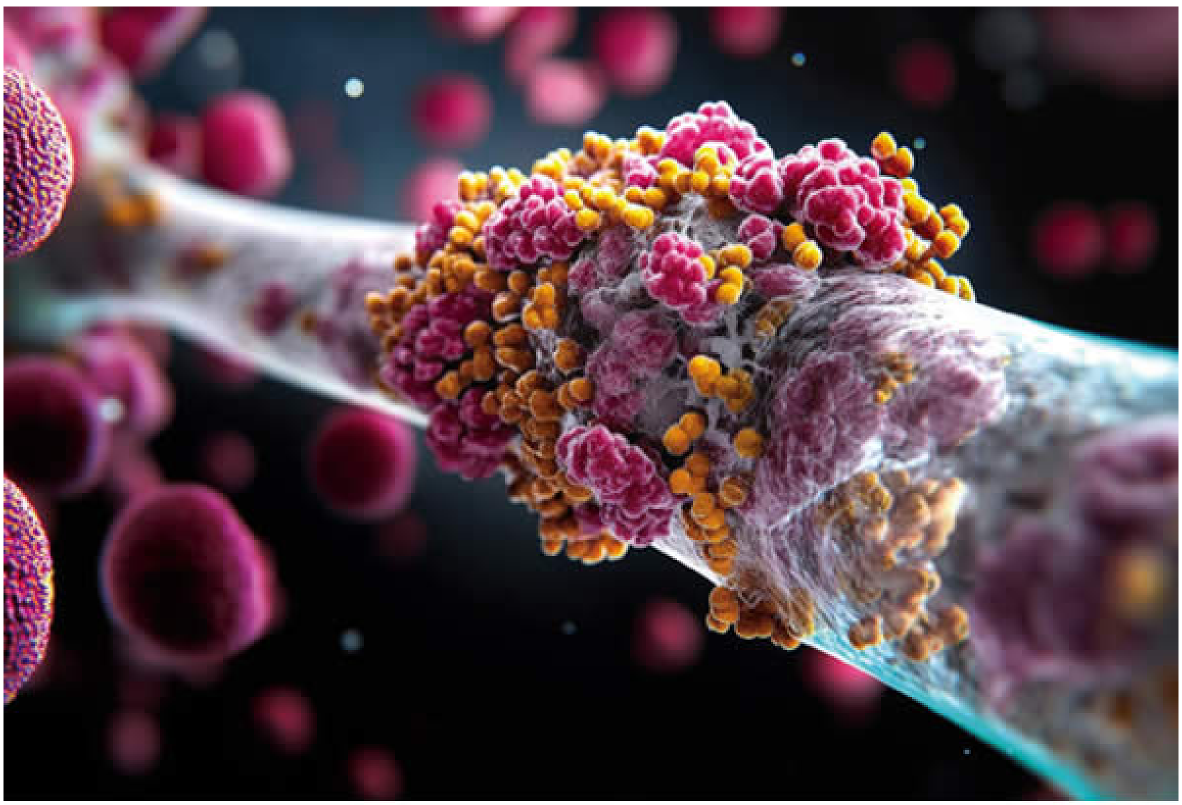
Transforming Respiratory Imaging: Mapping Airway Cilia in Real Time



Cilia in action on the epithelial lining, constantly moving to keep the airway clear. (Credit: Sanchai/AdobeStock)

Cilia, small, slender, hair-like structures present on the surface of all mammalian cells, play a major role in locomotion and are involved in mechanoreception. Ciliary motion in the upper airway is the primary mechanism by which the body transports foreign particulates out of the respiratory system to maintain proper respiratory function.

Ciliary motion plays a critical role in the overall respiratory health of the upper airway. Cilia beat at a native frequency, and in a synchronized pattern, to continuously transport foreign particulate trapped in a layer of mucous out of the upper airway.

The ciliary beating frequency (CBF) is often disrupted with the onset of disease as well as other conditions, such as changes in temperature or in response to drug administration. Disruption of ciliary motion can lead to severe respiratory diseases and compromised respiratory function.

Measuring CBF is a technical challenge and difficult to perform in vivo. Current imaging of cilia motion relies on microscopy and high-speed cameras that cannot be easily adapted to in vivo imaging.

Phase-contrast microscopy (PCM) is the standard for measuring CBF but has limitations. PCM does not permit appreciation of how CBF varies across the complex landscape of the nasal vault and sinus tissues. Additionally, optical coherence tomography (OCT) has proven to be a powerful imaging modality capable of visualization of ciliary activity, but its field of view is limited.

Spectrally Encoded Interferometric Microscopy

A team of scientists and engineers at the Chen F-OCT Group, part of the Beckman Laser Institute of the department of biomedical engineering at the University of California, Irvine (UCI), have designed a system capable of overcoming these limitations. The group's current research focus is on investigating light/tissue interactions; developing medical diagnostic and therapeutic devices and instruments using advanced optical, microfabrication, and biomedical technologies; and applications of these technologies for the early diagnosis of disease.

Previously, the group developed a phase resolved Doppler optical coherence tomography (PR-D-OCT) system that was able to obtain lateral cross-sectional images of cilia and cilia movement in real-time. The inventors realized the need to observe the surface dynamics of cilia over time and spatially, so they developed a spectrally encoded interferometric microscopy (SEIM) system with PR-D technology. As a result, fast, high-resolution en face images of human CBF can be captured and processed in real-time. Additionally, the integration of PR-D-OCT with PR-D-SEIM provides a multidimensional view of cilia.

"SEIM has emerged as a high-speed, high-resolution methodology, allowing for visualization of both temporal and spatial ciliary motion patterns across the surface of upper airway tissues, as well as propagation of metachronal wave," says Zhikai Zhu, PhD candidate with the Chen F-OCT Group. "SEIM can detect displacement on the nanometer scale at a kilohertz frame rate."

"When coupled with a wavelength-swept laser and a spectral disperser, SEIM can image tissue en face," explains Zhu. "SEIM uses a phase-resolved Doppler (PR-D) algorithm to measure and map the CBF within an en face region, providing insight into the changes in CBF across tissue surfaces."

Need for Vibration Isolation

"Since we are imaging cilia tissue that is in motion, we need a stable environment to produce reliable images," continues Zhu. "Without vibration isolation, reliable imaging from our SEIM system is sporadic."

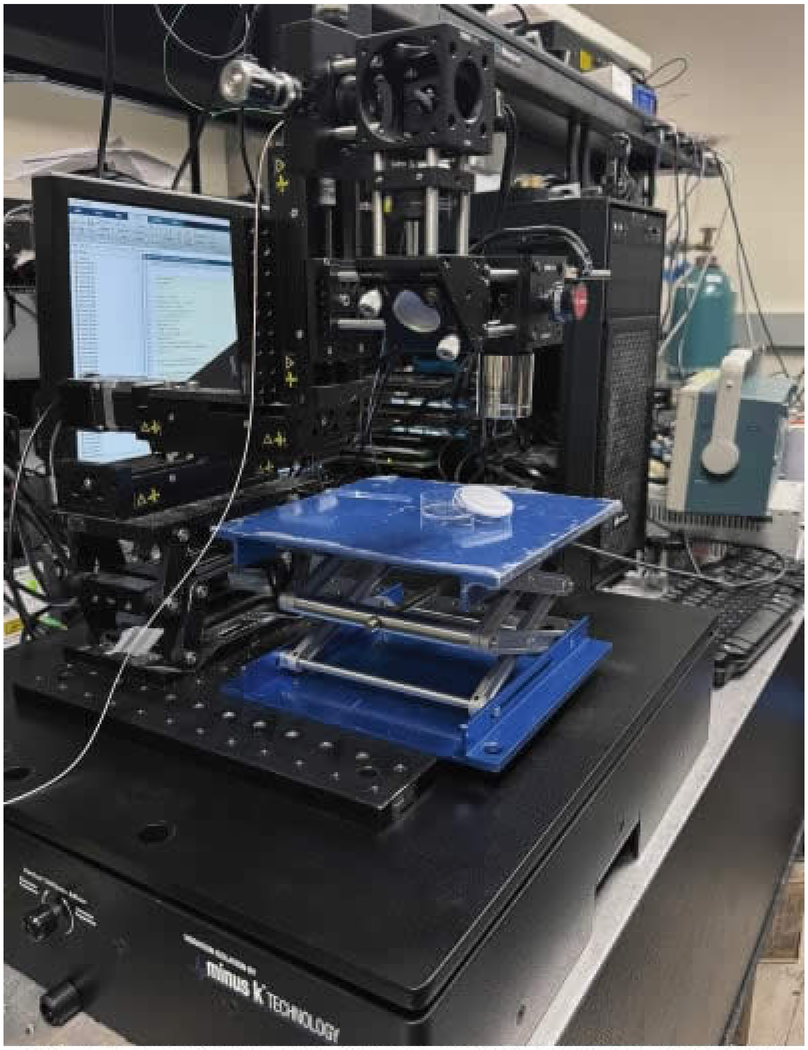
"Our lab is adjacent to a heavy foot traffic area, creating vibrations that affect our signals," adds Zhu. "Our need to isolate these ambient vibrations is critical."

The F-OCT Laboratory selected negative-stiffness vibration isolation for its SEIM system. Introduced in the mid-1990s by Minus K Technology, negative-stiffness vibration isolation has been widely accepted for vibration-critical applications, largely because of its ability to effectively isolate lower frequencies, both vertically and horizontally.

Negative-stiffness isolators are unique in that they operate purely in a passive mechanical mode. They do not require electricity or compressed air. There are no motors, pumps, or chambers, and no maintenance because there is nothing to wear out.

"Vertical-motion isolation is provided by a stiff spring that supports a weight load, combined with a negative-stiffness mechanism," says Erik Runge, vice president of engineering at Minus K. "The net vertical stiffness is made very low without affecting the static load-supporting capability of the spring.

Beam-columns connected in series with the vertical-motion isolator provide horizontal-motion isolation. A beam-column behaves as a spring combined with a negative-stiffness mechanism. The result is a compact passive isolator capable of very low vertical and horizontal natural frequencies and high internal structural frequencies."



Beckman Laser Institute's spectrally encoded interferometric microscopy (SEIM) system with PR-D technology. (Credit: Beckman Laser Institute, UC Irvine)

Negative-stiffness isolators achieve a high level of isolation in multiple directions, with the flexibility of custom-tailoring resonant frequencies to 0.5 Hz vertically and horizontally (with some versions at 1.5 Hz horizontally). When adjusted to 0.5 Hz, the isolators achieve approximately 93 percent isolation efficiency at 2 Hz, 99 percent at 5 Hz, and 99.7 percent at 10 Hz. (Note that for an isolation system with a 0.5 Hz natural frequency, isolation begins at 0.7 Hz and improves with increase in the vibration frequency. The natural frequency is more commonly used to describe the system performance.)

"The negative-stiffness isolator has made a big difference in the quality of our imaging," says Zhu. "It has eliminated all motion artifacts from our SEIM system imaging."

Conclusion

Researchers at the F-OCT Group have developed an imaging technique that can monitor and measure small, mobile cilia structures in human airways. This SEIM system, supported by negative-stiffness vibration isolation, has been validated as a means of finding CBF in human upper airway mucosa, which can provide a quantifiable and standardizable means of evaluating mucosal pathophysiology, potentially having application across a diversity of clinical settings.

This article was written by Jim McMahon, who writes on industrial, manufacturing, and technology issues. For more information on the F-OCT Group, contact Zhikai Zhu at zhikaz1@uci.edu. For more information on negative-stiffness isolators, contact Steve Varma, Minus K Technology, Inglewood, CA, at sales@minusk.com