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Mouse study: Real-time imaging device may improve surgery for congenital colon disease

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Researchers at Cedars-Sinai Medical Center are developing a spectral imaging system that could result in shorter operating times for infants undergoing surgery for Hirschsprung's disease, according to a mouse study reported in the *Journal of Biophotonics*.

The study documents that in addition to its diagnostic potential, spectral imaging may provide an "optical biopsy," allowing precise localization of a needed intervention.

Spectral imaging is based on the fact that light reflected from a target can be captured and measured by highly sensitive equipment to develop a characteristic "signature" based on wavelength. In this study, the colon tissue of six mice with the equivalent of Hirschsprung's disease was analyzed and compared to that of controls. With repeated measurements and calculations, unique signatures for normal tissue and for diseased tissue emerged.

Spectral imaging does not detect the presence or absence of ganglion cells themselves. Instead, the spectral signature reflects differences in the composition of normal and diseased tissue.

As a result of this study in laboratory mice, human clinical trials will be planned, providing spectral imaging for intraoperative decision-making in Hirschsprung's disease, a congenital condition affecting nerve cells of the large intestine. The technology, developed at Cedars-Sinai's Minimally Invasive Surgical Technologies Institute (MISTI) is adaptable

to other types of surgery.

Hirschsprung's usually affects specialized nerve (ganglion) cells in the lower portion of the large intestine, although the entire colon can be involved. Ganglion cells normally stimulate smooth muscle of the intestinal wall to push stool through the colon, but in sections where ganglia are missing (aganglionosis) the process comes to a halt, causing severe constipation that can lead to obstruction, massive infection and even death.

Estimated to affect one in 5,000 babies, the disease can be treated in a minimally invasive surgical procedure that removes the diseased portion of the colon and attaches the healthy colon to the anus. One of the critical portions of the operation is the accurate and precise determination of the point at which normal colon ends and disease begins. If too little colon is removed, the patient is likely to continue to develop significant constipation, but if too much is removed, chronic diarrhea may result, which can lead to other major health problems.

"The location and length of the transition zone between healthy and abnormal tissue varies considerably in Hirschsprung's disease patients and must be precisely identified to properly perform the operation," said Philip K. Frykman, M.D., Ph.D., Associate Director of Pediatric Surgery at Cedars Sinai and first author of the article. "The determination is routinely done by taking a number of small samples from the colon wall and sending them to the lab where a pathologist looks for the presence or absence of ganglion cells and other features. But this process may take 45 to 60 minutes, during which the operation is essentially on hold and the patient remains under general anesthesia.

"Spectral imaging, on the other hand, could provide immediate results, increasing patient safety and operating room efficiency," added Frykman, who specializes in minimally invasive surgery for infants and

children and holds a research grant from Cedars-Sinai to study Hirschsprung's disease.

There is a financial factor, too. Reducing time in the operating room could make a difference of several thousand dollars.

"The images showed a clear distinction, and this was confirmed by pathological analysis. Based on our results, it appears that spectral imaging methods could be used during operations, in real time, to help surgeons distinguish normal from abnormal tissue, without requiring traditional biopsy," said Daniel L. Farkas, Ph.D., vice-chairman for research in the Department of Surgery, director of the Minimally Invasive Surgical Technologies Institute, and senior author of the journal article.

Biophotonics – the interdisciplinary field dealing with interactions between biological entities and photons, basic units of light – is an emerging research area, with translational potential. Although spectral imaging and other photonic technologies have been used in advanced applications such as satellite reconnaissance for many years, only very recently have scientists begun translating these approaches into biological and medical uses.

At Cedars-Sinai and a few biophotonic research centers in the United States and Europe, spectral imaging is being studied for possible use in a variety of surgical situations. For each potential application, newly developed devices, software and criteria are evaluated in animal studies to show "proof of concept" before human clinical trials are launched.

Source: Cedars-Sinai Medical Center