Imaging: a case study

Pushing the boundaries of research into Dysphagia.

The University of Missouri School of Medicine research laboratory has acquired a unique and patented x-ray system employing a high-resolution micro-fluoroscopy technology that enables researchers to view the swallowing functions in mice while eating and drinking. This is the first time such real-time images have been viewed with x-ray technology.

The Department of Otolaryngology, Missouri University School of Medicine at Columbia, Missouri has been engaged in a unique research program for some time to better understand the causes and development of presbyphagia, also known as dysphagia. Persons with dysphagia generally experience slow, delayed, and uncoordinated swallowing that compromises airway function. The condition is associated with a number of diseases, such as Parkinson's disease, amyotrophic lateral sclerosis (ALS) known as Lou Gehrig's disease, Muscular Dystrophy (MD), and literally dozens of different medical conditions. Millions of Americans are chronically afflicted with dysphagia.

The standard technique for diagnosing swallowing disorders is a technique known as videofluoroscopy. A videofluoroscopic swallow study is a radiologic examination of an individual's swallowing function that uses an x-ray device called a fluoroscope. The patient is observed swallowing various foods and liquids mixed with a contrast agent that can be seen by fluoroscopy in order to evaluate his or her ability to swallow safely and effectively.

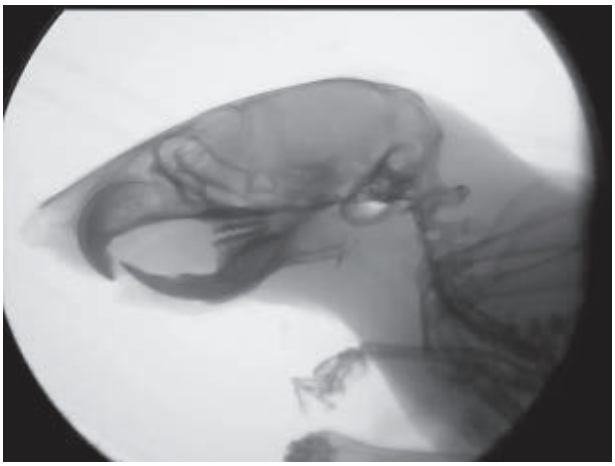

Image 1: Mouse gullet

RESEARCHING MICE WITH DYSPHAGIA

But a long-term study of the swallowing ability of an individual is not feasible. Instead, the research team at the University of Missouri studies the swallowing function of healthy C57 Black Mice throughout their approximate two-year lifespan. C57 Black Mice—the most widely-used mouse model in research—have very long lifespans and low susceptibility to cancer tumors, making them a good model for understanding the aging process relative to swallowing functions, as translates to humans.

By studying the swallowing function of healthy mice over their lifespan, the University's laboratory has found that the mice exhibit many of the same symptoms of dysphagia as healthy aging adults.

"We have established 15 metrics in C57 Mice that could be compared to human swallowing function," said Dr. Teresa Lever, Ph.D., Assistant Professor, and Head Researcher at the Department of Otolaryngology, at the Missouri University School of Medicine. "These include swallow rate, pharyngeal transit time—the time it takes liquid to be swallowed through the pharynx and into the esophagus—and the number of ineffective swallows through the esophagus. We have found that healthy aging mice develop symptoms of swallowing impairment that closely resemble the impairments seen in human older adults, such as slowed swallowing function, impaired tongue function, larger size of the amount swallowed, and an increase in the time it takes liquid to travel through the throat to the stomach."

Until recently, however, these results were unknown. The University's laboratory researchers could only study mice from outside of their bodies, relative to their swallow functions. Existing medical diagnostic fluoroscopes had not had the resolution to see the internal organs of a mouse.

"We could only view the mice from the outside, we could see them licking and chewing, but we had no idea what was happening on the inside," continued Dr. Lever. "One of the biggest challenges

Image 2: Micro-fluoroscope

for us was dealing with the tiny movements in mice that happen about 10 times faster than in humans."

MICRO-FLUOROSCOPY

Dr. Lever became aware that a technology had been developed which allowed minute components to be viewed via micro-fluoroscopy. She speculated that this technology might be adapted for use on a live, moving animal, such as the dynamic structural and functional movements of a mouse during swallowing.

Through a cooperative effort between the University of Missouri and the manufacturer, the micro-fluoroscopy system was customized to adapt to the University's dynamic x-ray imaging requirements, providing real-time imaging capability. It is this unique micro-fluoroscopy technology that has enabled the laboratory's swallow-test protocol to determine if a mouse has dysphagia and to produce the high-resolution, real-time images characterizing the condition.

"Using this system we are able to see swallowing functions in mice while eating and drinking that have never been viewed with x-ray equipment before," added Dr. Lever. "And the quality of the imaging is extremely high resolution."

"The system operates with an anode voltage of 25 to 30 kilovolts (kV), compared to x-ray machines in human medical and veterinary applications which operate at approximately 75 kV," explained Dr. Lever. "The much smaller radiation dosage allows us to fine tune on small features in the mice that have a low volume of tissue mass. It also permits us to more frequently test the mice, allowing for longer-term test protocols."

The lower radiation dose requires less shielding, which is conveniently built into the machine, eliminating the need for a separate x-ray room.

"It has a very small footprint compared to the x-ray systems used on humans," said Dr. Lever. "This allows it to be located directly inside of our laboratory, while being adequately shielded during use. This permits other lab workers to continue performing their activities within the lab space. And we do not need to rely on a radiologist or technician. One researcher within our lab can safely operate the machine."

PUSHING THE BOUNDARIES OF RESEARCH INTO DYSPHAGIA

The addition of the micro-fluoroscopy capability into Dr. Lever's lab is just one of the latest advanced techniques employed for its groundbreaking research into better understanding dysphagia.

"Our lab is outfitted with state-of-the-art equipment for research into dysphagia," added Dr. Lever. "In addition to micro-fluoroscopy, we are set up to conduct electro-physiology experiments, genotyping, behavioral phenotyping, general histology, immunohistochemistry, and a stereology system for bright field and fluorescence microscopy. We are continuing to push the limits of our research."

***Jim McMahon**, Zebra Communications, writes on advances in instrumentation technology.*