Researchers develop novel method using MRI to study diseases modeled in zebrafish

September 20 2023

Credit: Pixabay/CC0 Public Domain

Zebrafish have revolutionized research into a wide variety of rare and complex genetic diseases. In early development stages, their transparent bodies allow researchers to more easily study tissues and organs.

However, studying organ-level defects in adult zebrafish presents a variety of challenges that prevent researchers from studying them at a microscopic level.

In a new study, researchers from Children's Hospital of Philadelphia (CHOP) have developed a noninvasive method for conducting magnetic resonance imaging (MRI) in adult zebrafish. Using this technique, the study team examined the effects of certain genetic mutations associated with mitochondrial disease.

The findings were recently published online in *Zebrafish*.

Zebrafish transition from a single cell to fully formed animal in just one day, with continued larval development over the first week of life. This rapid development and ability to remove their body wall pigment during this early period enables scientists to microscopically image whole organs and perform accurate time-lapse analyses of disease progression. They can also screen drug candidates that may be used to treat various illnesses, since the zebrafish can absorb the drug through their gut, skin, or thin gills. In addition, zebrafish are often used to create models to study diseases because they share about 70% of genes found in humans.

However, as zebrafish get older, their tissue becomes denser and their organs become more difficult to study through usual microscopic imaging techniques. While MRI has been used to study zebrafish, prior studies have been very limited and did not provide systematic organ-level analyses. This is particularly important for diseases like mitochondrial disease, which often impacts multiple organs by disrupting energy levels in cells throughout the body. No prior study has studied adult zebrafish across different times in their adulthood, which has prevented researchers from looking into the progression of disease.

"MRI technology is widely used for a variety of clinical and research

applications, and as zebrafish become a more preferred model for translational research, we wanted to explore how this technology could improve the research we are doing in these animal models," said first study author Sonal Sharma, MD, a pediatric neurologist within the Division of Neurology and the Mitochondrial Medicine Frontier Program in the Division of Human Genetics at CHOP. "This work demonstrated that MRI allows us to rapidly and comprehensively study organ-level growth defects in mutant adult zebrafish in a low-cost, minimally invasive, and unbiased manner."

The researchers developed a new protocol for utilizing MRI in zebrafish research. As a result, they were able to successfully capture high-resolution MRI of eight different organs in adult zebrafish. This allowed the researchers to establish a reference MRI atlas based on images of zebrafish from five to 31 months after fertilization.

Using three different mitochondrial disease mutant models of zebrafish, the researchers were able to discover that significantly increased brain growth occurs in zebrafish with deficiency in the SURF1 gene, which encode mitochondrial complex IV activity and is one of the genes associated with Leigh syndrome. They also noticed heart and spinal cord volumes were smaller in these mutant zebrafish as compared to healthy wild-type controls. These findings reflect some of the clinical observations seen in human patients with SURF1 deficiency, since they may suffer from serious neurological issues as well as cardiomyopathy.

"We plan on exploring the organ-level discoveries we made by using this novel MRI method to screen organ growth in adult zebrafish," said senior study author Marni Falk, MD, senior author on this study and executive director of the Mitochondrial Medicine Frontier Program at CHOP. "We are also working to develop additional biochemical imaging methods to further refine our understanding of the biochemical changes that occur in specific organs of living animals with primary

mitochondrial disease."

More information: Sonal Sharma et al, Novel Development of Magnetic Resonance Imaging to Quantify the Structural Anatomic Growth of Diverse Organs in Adult and Mutant Zebrafish, *Zebrafish* (2023). DOI: 10.1089/zeb.2023.0018

Provided by Children's Hospital of Philadelphia