What the eye may reveal about Alzheimer’s

ASU researchers will use AI to enhance retinal images, combine them with blood biomarkers for early screening

By Kelly deVos, ASU News
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Last month, Yalin Wang went to the eye doctor and left with the usual aftereffects: dilated pupils and hours of light sensitivity. For most patients, it is a minor inconvenience. For Wang, an Arizona State University professor developing AI tools for medical imaging, it was a reminder of the problem he is trying to solve.

Wang is a professor of computer science and engineering in the School of Computing and Augmented Intelligence, part of the Ira A. Fulton Schools of Engineering at ASU.

He wants to know whether a quick, inexpensive, nondilated photograph of the retina could help reveal the earliest biological signs of Alzheimer’s disease, years before memory begins to fail.

In collaboration with Dr. Oana M. Dumitrascu, a neuro-ophthalmologist at Mayo Clinic, Wang will lead a new five-year, $3.2 million project funded by the National Institutes of Health that uses deep learning to enhance low-quality retinal images and combine the information they contain with blood-based biomarkers to screen for preclinical Alzheimer’s risk.

The project brings together collaborators from Mayo Clinic, Banner Alzheimer’s Institute, Banner Sun Health Research Institute and the Translational Genomics Research Institute. The team’s goal is not to replace brain scans, spinal taps or blood tests; it is to build an AI-assisted system that can use retinal images, alone or in combination with blood-based biomarkers, to flag people at risk years before symptoms appear.

"Our vision is that patients’ annual eye scans with an optometrist could be coupled with an AI model that generates a clear and individualized risk profile for neurodegeneration and cerebrovascular disease," Dumitrascu said. "The eye can be a powerful window to the brain health."

Why this research matters

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A new view of Alzheimer’s disease

The eye, Wang says, is not just near the brain. Developmentally and biologically, it is part of the same story.

“The brain is sealed away behind bone,” Wang says. “The retina, by contrast, is accessible, imageable and biologically linked to the central nervous system, giving researchers a unique noninvasive glimpse of brain health.”

That idea sits inside an emerging field called oculomics, which treats the eye as a data-rich window into the rest of the body. Researchers already use retinal imaging with AI for conditions such as diabetic retinopathy and myopic maculopathy. They are now asking whether the same inexpensive, repeatable image could reveal patterns tied to the brain, heart, lungs and vascular system.

For Alzheimer’s, the timing matters. By the time memory loss becomes obvious, the disease process may have been unfolding for years. The need for screening is even greater in Arizona’s rural communities, where access to specialty memory care is limited and long travel distances can delay evaluation.

Researchers increasingly want to find people in the preclinical stage, when they are still cognitively unimpaired. That is essential for prevention studies and for recruiting people into clinical trials earlier, when treatments may have a better chance of working.

But the current tools for identifying those people can be expensive, invasive or impractical at scale. PET scans are powerful but costly. Cerebrospinal fluid testing requires a lumbar puncture. Blood-based biomarkers are promising and rapidly advancing, but Wang says they can still leave an uncertain middle category: people who are neither clearly high-risk nor clearly low-risk.

> **The eye can be a powerful window to the brain health.**
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> **Dr. Oana M. Dumitrascu**
> Mayo Clinic neuro-ophthalmologist

Making the signals stronger

That gray zone is where the new project becomes especially interesting. Wang’s team is not simply asking whether the retina can compete with blood tests. They are asking whether the two can make each other better.

What others are saying ...

"The collaboration between Dr. Wang and Dr. Dumitrascu is a superb example of the type of relationship that ASU and Mayo Clinic have sought to foster over the years. This is exactly the kind of outcome they intended to achieve, though in this particular case, it arose purely organically. I think if I had to take any credit for contributing to this result, it would simply have been helping to introduce the two of them. I am a big fan of an accurate, noninvasive, inexpensive method for diagnosing Alzheimer's disease and related disorders, and I believe the retinal imaging approach they are pioneering could prove to be extremely valuable."

— **Dr. Richard J. Caselli,** neurologist, Mayo Clinic

"We are very interested in the potential of retinal imaging to provide an early, relatively non-invasive window into vascular health. This collaboration gives us an exciting opportunity to pair that potential with high-quality retinal images collected through the MindCrowd Mobile Laboratory from our uniquely diverse, Arizona-wide cohort of research participants."

— **Matt Huentelman**, professor and co-director of TGen's Early Detection and Prevention Division

"I'm excited about the chance to assist Dr. Wang and his colleagues in this effort. If ongoing prevention trials are successful, blood tests will be used to screen cognitively unimpaired people for the presence of amyloid plaques, inform their prognosis, and help them consider medical and non-medical options to substantially prevent the clinical onset of Alzheimer's disease. It may be possible to capitalize on the automated analysis of widely available eye tests to complement the emerging role of blood tests in this critically important endeavor."

— **Dr. Eric Reiman**, founding CEO of the Banner Alzheimer's Institute

"The idea is to combine the retinal image with information such as age, sex and blood-based biomarkers," Wang says. "Blood-based biomarkers are already strong, but we think retinal features may add useful information, especially when the results are less clear."

The project's key innovation is that it uses AI twice, for two different problems. First, the researchers plan to use generative AI to improve the quality of retinal images collected in real-world settings. Nondilated scans are convenient, but they can be messy, blurry or unevenly lit. In mobile clinics and routine care settings, Wang said, a large share of retinal images may not be useable.

The team wants to recover some of those discardable scans. The project will include retinal images collected by TGen's mobile brain health lab in communities across Arizona, helping researchers evaluate the approach with images gathered in community settings.

They plan to develop AI tools that improve image quality while preserving details that may contain disease-relevant clues. If an enhancement tool smooths away tiny vascular details, or invents new ones, it could distort the very signal the researchers are trying to study.

Once the images are usable, the team will train a deep-learning model to search for retinal patterns associated with Alzheimer's risk.

The model will also incorporate demographic and blood-based biomarkers — clues in a person's blood that can suggest Alzheimer's-related changes are happening in the brain. Some of the most important are tied to amyloid and tau, two proteins associated with the disease. Wang's team wants to know whether adding retinal data can make those blood-based signals more useful, especially when the results are not clearly high or low risk.

Wang is careful about the timeline. This is still a research project, not a diagnostic test arriving next week at the optometrist. Clinical use would require more validation, trials and regulatory review. But the logic is compelling: rescue imperfect eye images, read the retinal signals inside them and combine those clues with blood data to look for Alzheimer's before symptoms begin.

For Wang, who began his Alzheimer's work studying brain atrophy and medical imaging, the retina offers a new route into an old problem. The brain is protected, hidden and difficult to image at scale. The eye is exposed to the world.

If it is a window, the question now is what else we can learn by looking through it?

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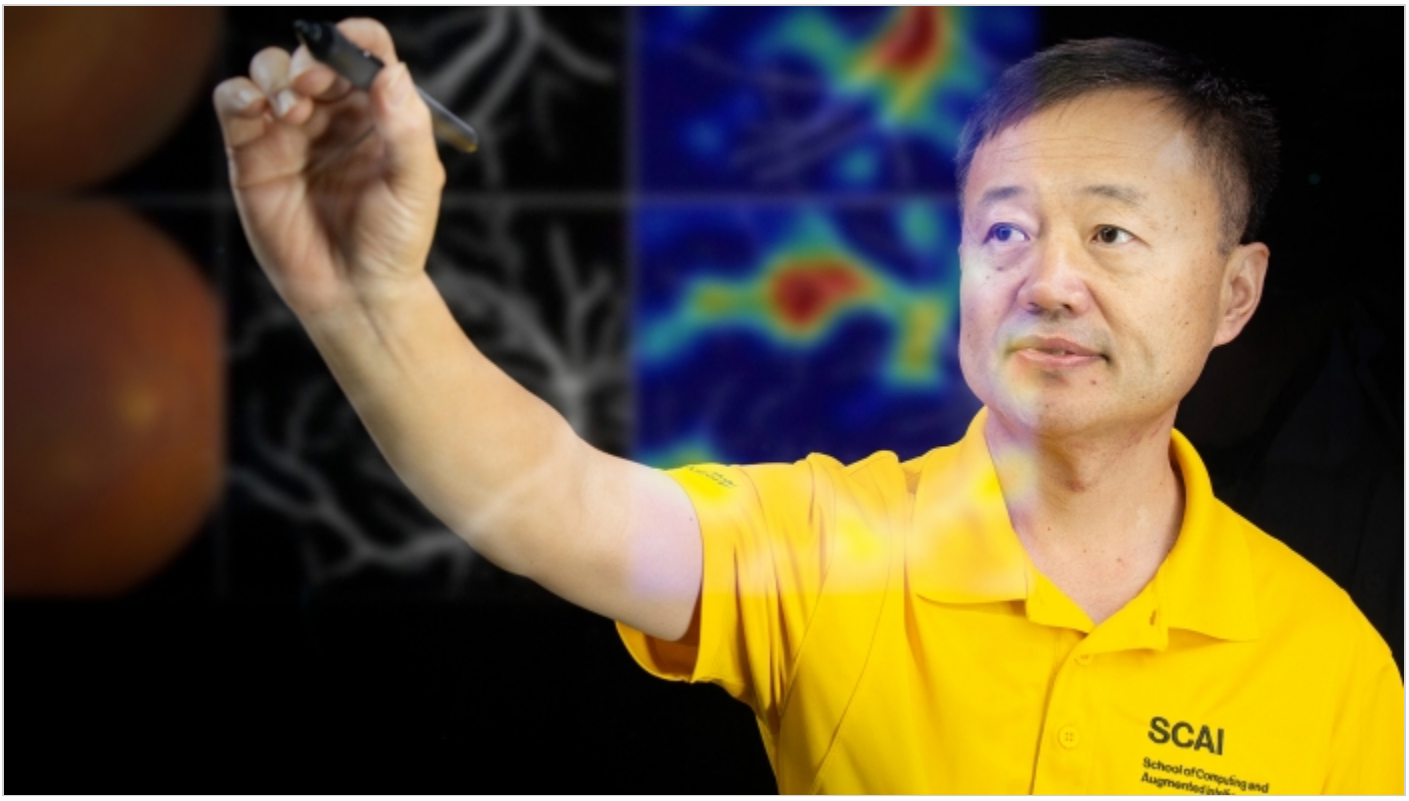
Breakthroughs in Alzheimer’s prevention

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This story originally appeared on ASU News.

Main image



Yalin Wang, a professor of computer science and engineering in the School of Computing and Augmented Intelligence, is collaborating with key Arizona health experts on new artificial intelligence tools that use retinal scans to diagnose Alzheimer’s disease before symptoms appear. Photo by Erika Gronek/ASU