

In diabetic eye disease, peripheral lesions in the retina point to risks of progression

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For decades, clinicians have detected and monitored diabetic eye disease with standard retinal photographs that cover about a third of the retina. In recent years, an emerging class of ultrawide field (UWF) cameras has given a substantially larger view of the retina, providing new insight on the presentation and natural history of retinal disease. Investigators at the Joslin Diabetes Center now have shown that eves with diabetic retinal lesions predominantly in peripheral areas of the retina that are seen in UWF images but not in traditional retinal photographs show surprisingly higher risks of progressing to advanced stages of vision-threatening diabetic retinopathy.

If these results are confirmed in a larger trial, they will help to change how diabetic eye disease is evaluated and treated, says Paolo Silva, M.D., staff ophthalmologist and assistant chief of telemedicine at Joslin's Beetham Eye Institute.

"The importance of the retinal periphery has been recognized for a long time, but we didn't have the technology to image it until recently," says Silva, lead author on a recent paper in Ophthalmology that presents the findings. The traditional Early Treatment Diabetic Retinopathy Study (ETDRS) photography is composed of seven standard 30? retinal photographs to represent about 30 percent of the retina, he explains. "With UWF, we're able to see 82 percent of the retina in a single 200? retinal image, with high resolution."

The Joslin study began with 100 people with diabetes who had participated in an earlier trial to validate the agreement between UWF images and ETDRS photography in determining the presence and severity of diabetic retinopathy. Observations in this initial study showed that peripheral diabetic retinal lesions are present in over a third of patients exams in many eye centers and eye clinics, their and increased the severity of retinopathy in 10 percent of eyes. Based on these initial observations, a follow-up prospective study was

conducted in which the initial validation study participants were asked to return for retinal imaging after four years.

This follow-up study demonstrated that eyes with predominantly peripheral diabetic retinopathy lesions during the initial study had more than a three-fold increased risk of retinopathy progression. These eves also had almost a five-fold increased risk of progression to proliferative diabetic retinopathy, the most advanced form of the disease. The findings held true even after the researchers adjusted for a patient's diabetes type. diabetes duration, average blood glucose levels and other measures.

The Joslin team was not surprised that lesions in the retinal periphery might affect the likelihood of disease progression. "What was a big surprise is how much of a risk this added and how much of the disease was found outside of the area we've traditionally evaluated," says Lloyd Paul Aiello, M.D., Ph.D., Director of the Beetham Institute, Professor of Ophthalmology at Harvard Medical School and senior author on the paper.

A related trial run by the Diabetic Retinopathy Clinical Research Network, which will follow more than 350 diabetes patients across the United States with UWF imaging for at least four years, is now underway.

If the results of the Joslin study are confirmed by this larger study, they will bring major changes for clinical care and research—likely changing the system for rating disease progression in diabetic retinopathy, which is a leading cause of blindness in working-age people.

While UWF devices are in use for regular patient adoption has been slowed by relatively large size and high cost, with prices in the ballpark of \$100,000. Aiello notes, however, that a tabletop



UWF system is now available, and he hopes that equipment pricing will drop over time.

Wider adoption of UWF imaging also might have major implications for the telemedicine programs run by Joslin and many other institutions around the world, which aid treatment for underserved populations with diabetes. Many of these efforts already use UWF systems to generate images that are then interpreted by doctors at a remote center. The systems can acquire high-resolution images very rapidly. These high-quality images are more readily evaluated and analyzed more efficiently by experts than conventional ETDRS photos, Silva says.

In addition to studying peripheral retinal lesions in the clinic, Joslin scientists are looking for the causes of the lesions, with one likely suspect being a failure of blood flow in the affected regions. Better understanding of the underlying mechanisms could help improve the ability to judge each patient's risks and eventually lead to interventions "that help prevent vision loss in a more effective or more easily delivered manner than we have today," Aiello says.

Provided by Joslin Diabetes Center

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