



1768 EAST 25<sup>TH</sup> ST., SUITE 209, CLEVELAND OHIO 44114  
10455 PACIFIC CENTER COURT, SAN DIEGO, CA 92121  
619.846.6666 (CA) 216.881.8360 (OH)

## **SCIENTIFIC RATIONAL FOR SCREENING PATIENTS USING AUTOFLUORESCENCE TO IDENTIFY PATIENTS WHO MAY HAVE DIABETES**

Glucose in the body reacts with the lysine groups in proteins to produce glycated proteins. Over time, these glycated proteins react further to produce Advanced Glycated Endproducts (AGE). Proteins in the lens of the eye do not turnover and therefore give an indication of the average glucose levels over a very long period of time. These AGEs have a unique fluorescence. Many studies have documented that the AGEs in the lens rise steadily over time. These studies have also shown that people with diabetes have much higher levels of AGE in their lens compared to age-matched patients without diabetes.

Freedom Meditech has patented and tested a device that can be used to measure the AGEs in patients as part of a routine optical exam. If a patient's AGEs are elevated compared to age-matched controls, then they are candidates for a further work-up to determine if they have diabetes. Incorporation of this testing into routine eye exams or in health screening events could potentially identify people with diabetes much earlier than they would have otherwise been diagnosed. Data indicates that people with Type 2 diabetes go undiagnosed for 7 years or more before they are diagnosed with their disease (13). This could have a very great savings for this patient and the healthcare system, since an earlier diagnosis leading to an earlier treatment has the potential to decrease the costs of diabetes complications which worsen the longer a patient goes un-diagnosed.

A large number of authors have demonstrated that lens fluorescence is greater in diabetic patients compared to patients without diabetes (1, 2, 3, 4, 5, 6, 7, 8, 9). Many of these authors proposed that this increased lens autofluorescence was due to the accumulation of AGEs and served as an index of long-term glycemic control. This hypothesis was substantiated in studies by Monnier and Cerami (10), Abiko et. al. (11), and Yu et. al. (12).

1. Bleeker, J.C., van Best, J.A., van der Velde, E. A. And Oosterhuis, J.A. (1986). Autofluorescence of the lens in diabetic and healthy subjects by fluorophotometry. Invest. Ophthalmol. Vis. Sci. 27, 791-4.
2. Helve, J. and Nieminen, H. (1976). Autofluorescence of the human diabetic lens in vivo. Am. J. Ophthalmol. 81, 493-3.
3. Larsen, M., Kjer, B., Bendston, I., Dalgaard, P. And Lund-Anderson, H. (1989). Lens fluorescence in relation to metabolic control of insulin-dependent diabetes mellitus. Arch. Ophthalmol. 107, 59-62.
4. Mori, F., Ishiko, S., Abiko, T., Kitaya, N., Kato, Y., Kanno, H. and Yoshida, A. (1997). Changes in corneal and lens autofluorescence and blood glucose levels in diabetics: parameters of blood glucose control. Curr. Eye Res. 16, 534-8.
5. Koefoed Theil, P., Hansen, T., Larsen, M., Pederson, O. and Lund-Anderson, H. (1996). Lens autofluorescence is increased in newly diagnosed patients with NIDDM. Diabetologia 39, 1524-7.
6. Sparrow, J. M., Neil, H. A. and Bron, A. J. (1992). Biometry and auto-fluorescence of the anterior ocular segment in diabetics with and without autonomic neuropathy; a case control study. Eye 6, 50-4.
7. van Wirdum, E., van Best, J., Bruining, G. L., de Beaufort, C. and Oosterhuis, J. (1989). Blood-retinal blood-aqueous barrier permeability lens autofluorescence and transmission in insulin-dependent diabetic youngsters. Grafe's Arch. Clin. Exp. Ophthalmol. 227, 26-9.
8. Zeimer, R. C. and Noth, J. M. (1984). A new method of measuring in vivo the lens transmittance, and study of lens scatter, fluorescence and transmittance. Ophthalmic Res. 16, 246-55.
9. Kjer, B., Larsen, M., Bendtson, I., Binder, C., Dalgaard, P. And Lund-Andersen, H. (1987). Lens autofluorescence in diabetes compared with the levels of glycosylated hemoglobin A1c. Acta Ophthalmol. 65, 100-2.
10. Monnier, V. M. and Cerami, A. (1981). Nonenzymatic browning in vivo: Possible process for aging of long-lived proteins. Science 211, 491-3.
11. Abiko, T., Abiko, A., Ishiko, S., Takeda, M., Horiuchi, S. and Yoshida, A. (1999). Relationship between autofluorescence and advanced glycation Endproducts in diabetic lenses. Exp. Eye Res. 68, 361-6.
12. Yu, N-T., Krantz, B. S., Eppstein, J., A., Ignatz, K. D., Samuels, M., A., Long, J. R. And Price, J. F. (1996). Development of a noninvasive diabetes screening device using the ratio of fluorescence to Rayleigh scattered light. J. Biomed. Optics 1, 280-8.
13. Saudek, C. D., Herman, W., H., Sacks, D., B., Bergenstal, R., M., Edelman, D. and Mayer, B. (2008). A new look at screening and diagnosing diabetes mellitus. J. Clin. Endocrinol. Metab. 93, 2447-53.