Changes in the Internal Structure of the Human Crystalline Lens with Diabetes Mellitus Type 1 and Type 2

Nanouk G. M. Wiemer, MD,[1,2] Michiel Dubbelman, PhD,[2,3] Erik A. Hermans, MSc,[2,3] Peter J. Ringens, MD, PhD,[1,2] Bettine C. P. Polak, MD, PhD[1,2]

Purpose: To investigate the effect of diabetes mellitus (DM) type 1 and type 2 on the internal structure of the lens.

Design: Observational cross-sectional study.

Participants and Controls: One hundred seven patients with DM type 1, 106 patients with DM type 2, and 75 healthy control subjects.

Methods: Scheimpflug photography was used to image the lens of the right eye of 213 patients with DM and 75 healthy control subjects. The densitogram of the Scheimpflug image was used to indicate the nucleus and the different layers of the cortex of the lens. Lenses with cataract were excluded.

Main Outcome Measures: The size of the nucleus and the different layers of the cortex of the lens.

Results: The nucleus and the different cortical layers of the DM type 1 lenses were significantly thicker compared with those of the control group ($P<0.001$). A significant association was found between the duration of DM type 1 and both the anterior and posterior cortex, its different layers, and the nucleus ($P<0.001$). The increase in the anterior and posterior cortex with the duration of DM was comparable with that of the nucleus. No important differences in the internal structure of the lens were found between the patients with DM type 2 and the control group.

Conclusions: Diabetes mellitus type 1 has a significant effect on the internal structure of the lens. The difference in effect of DM type 1 and type 2 on internal lens structure suggests an essential difference in pathogenesis. Furthermore, the results of the present study may indicate that the increase in the size of the lens with DM type 1 is the result of a generalized swelling of the lens, affecting all its different parts.

Financial Disclosure(s): The authors have no proprietary or commercial interest in any materials discussed in this article. *Ophthalmology 2008;115:2017–2023 © 2008 by the American Academy of Ophthalmology.*

It is well known that the human lens continues to grow throughout life and that it becomes more convex and thicker with age.[1–3] In patients with diabetes mellitus (DM), the lens has been reported to become even thicker and more convex with age, compared with that in healthy subjects.[4–12] After adjustment for the effect of age, the independent effect of the duration of DM per year on lens thickness was more than 70% of the effect of age per year.[6,7]

The physiologic thickening of the normal lens with age has been reported to be primarily because of an increase in the anterior and posterior cortex of the lens.[13–16] This was investigated by means of Scheimpflug photography, which provides a detailed image of the various anatomic regions of the lens (i.e., the cortex and the nucleus, as well as alternating light and dark areas within the anterior and posterior cortex).[17] These different light and dark areas can be categorized according to the Oxford Clinical Cataract Classification and Grading System.[13,18] In this system, the cortical areas are divided into 4 zones: C1 to C4. Zones C1 and C3 are zones of high light scatter, whereas zones C2 and C4 are zones of low light scatter (Fig 1). It appeared that the increase in the cortex of the normal lens with age was entirely the result of an increase in 1 particular zone (C2) of the anterior and posterior cortex.[13,14,16]

The origin of the profound increase in the dimensions of the lens in DM has not yet been explained. Sparrow et al[6] found that the increase in lens biometry in patients with DM type 1 was the result of an increase in both the cortex and the nucleus of the lens, and they observed that the cortex of the diabetic lens was affected more than the nucleus. This effect was markedly less apparent in patients with DM type 2.[7] However, these studies did not investigate the influence of DM on the different cortical zones of the lens. Knowledge about changes in the internal structure of the lens with DM could provide insight into the cause of the increase in the size of the diabetic lens. For example, an increase in the C2 zone of the cortex of the lens, as observed in the physiologically ageing lens, could imply an enhanced rate of lens fiber production. However, an increase in all different zones of the lens could be the result of cellular or extracellular swelling of the lens. Furthermore, to examine the thickness of the different layers within the lens, an accurate measurement of the lens is necessary. This can be

ISSN 0161-6420/08/$–see front matter
doi:10.1016/j.ophtha.2008.06.032

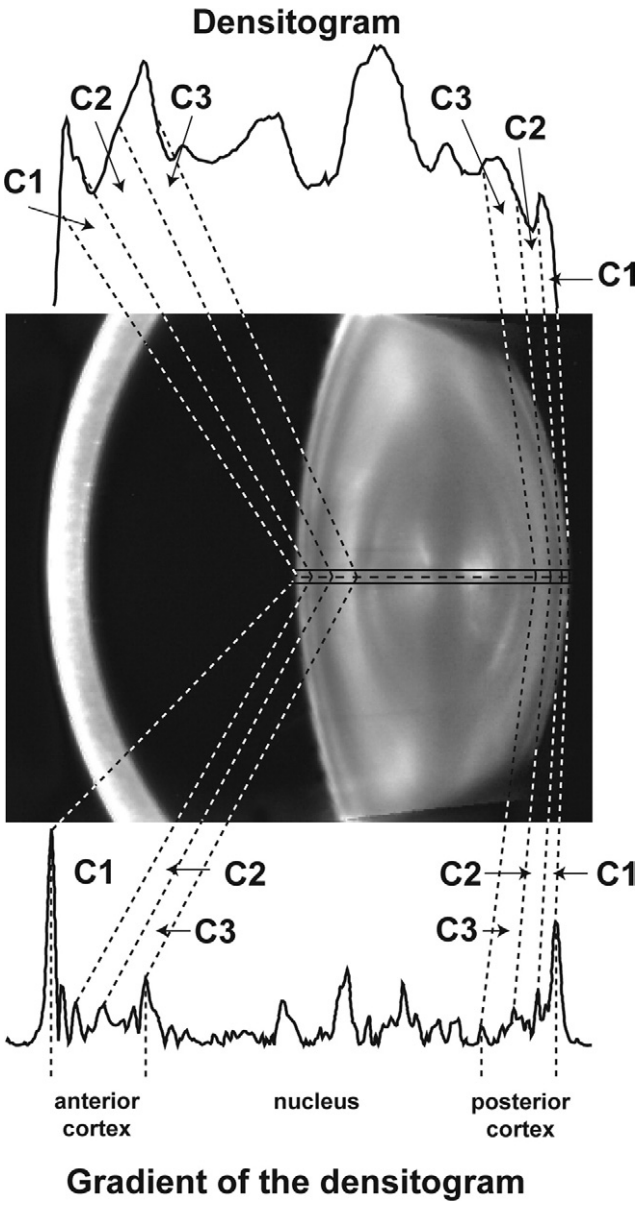

Figure 1. Scheimpflug image of a 32-year-old healthy male. According to the Oxford Classification System, the different anterior and posterior cortical zones (C1–C3) and the nucleus can be defined from the local maximums of the gradient of the densitogram. In the present study, the anterior cortex is represented by a summation of zones C1, C2, and C3. The same holds true for the posterior cortex. The nucleus is defined as the region between the anterior and posterior C3 zones.

obtained with corrected Scheimpflug imaging, which takes into account the distortion caused by the geometry of the Scheimpflug camera and the refraction of the cornea and the lens itself.[2,3,19]

The aim of the present study was to investigate the various cortical zones and the nucleus of the crystalline lens in patients with DM type 1 and 2 and in healthy control subjects by means of corrected Scheimpflug imaging.[2,3] In the 2 diabetic groups, the influence on the internal structure of the lens of several systemic factors, such as the duration of DM, glycated hemoglobin (HbA1c), capillary blood glucose, the level of diabetic retinopathy (DR), and the use of insulin was investigated.

Patients and Methods

In the present study, the right eye of 288 subjects (75 healthy control subjects, 107 patients with DM type 1, and 106 patients with DM type 2) was examined at the Department of Ophthalmology of the VU University Medical Center in Amsterdam, The Netherlands. The diagnosis of DM type 1 or type 2 was determined according to the guidelines published by the World Health Organization.[20] The baseline characteristics of the 3 groups are presented in Table 1. Subjects with cataract, glaucoma, a history of intraocular surgery, or ocular pathologic features other than DR were excluded from the study. Capillary blood glucose levels were measured with a blood glucose analyzer (HemoCue Diagnostics BV, Oisterwijk, The Netherlands). The Medical Ethics Committee of the VU University Medical Center, Amsterdam, approved the protocol of this study, and all participants have given their written informed consent, in accordance with the tenets of the Declaration of Helsinki.

Ocular Measurements

To obtain maximal pupillary dilation and paralysis of accommodation, 1.0% cyclopentolate and 5% phenylephrine eyedrops were administered. Images of the lens were obtained with a Topcon SL-45 Scheimpflug camera, equipped with a charge-coupled device camera (St-9XE; SBIG Astronomical Instruments, Santa Barbara, CA) with a range of 16 bits of grey values (512×512 pixels; pixel size, 20×20 μm; magnification, ×1). One series of 3 Scheimpflug images was made in the vertical (90°) meridian along the optical axis. The initial stage in the analysis of the Scheimpflug images was to identify the different zones within the lens. It was not possible to measure each zone in the lens accurately for all 288 subjects, and therefore the number of measurements differed for each zone. This mainly was because the posterior region of the lens was difficult to visualize in some older participants and in patients who had had DM for a long time. The Oxford Clinical Cataract Classification and Grading System was used to distinguish the different layers in the anterior and posterior cortex of the lens (Fig 1).[13] This system makes use of the gradient of a densitogram, indicated in the lower part of Figure 1. The densitogram itself (upper part of Figure 1) consists of the grey values of the Scheimpflug image along a sagittal strip of 8 pixels (1 pixel = ±0.025 mm) on either side of a line through the vertex of the anterior lens surface. The gradient of the densitogram represents the rate of change of the densitogram, and from the maxima of this gradient the different layers in the anterior and posterior cortex can be determined. Zone C1 consists of a narrow dark (C1α, or anterior clear zone) and light (C1β, or line of disjunction) zone behind the lens capsule. For the sake of convenience, no distinction was made between these 2 subzones within the C1 zone in the present study. Zone C2 is a zone of low light scatter, and the subsequent C3 zone is a zone of high light scatter. In the present study, the nucleus was defined as the area between the anterior and posterior C3 zone, because the C4 low light scatter zone was difficult to distinguish. Furthermore, the anterior cortex is a summation of the anterior C1 to C3 zones, and the same holds true for the posterior cortex. After the different cortical zones had been determined, the Scheimpflug image was corrected for distortion because of the geometry of the Scheimpflug camera and because of the refraction of the different ocular surfaces by means of ray-tracing.[2,3]