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Increased Scleral Stiffness in Diabetes with Retinopathy greater than in Diabetes without Retinopathy

Abstract #4010594

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Purpose

Hyperglycemia in diabetes leads to accumulation of Advanced Glycation Endproducts (AGEs) with formation of non-enzymatic crosslinks within and between collagen fibrils, (Fig 1) including those in the cornea and sclera, leading to increased stiffness greater than that of normal aging. (Fig 2) The current clinical study investigates corneal and scleral stiffness from air puff induced deformation in diabetic subjects without retinopathy (DIA), diabetic subjects with retinopathy (DR), and normal controls (NRL).

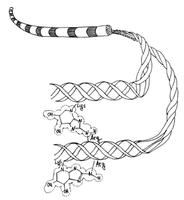


Figure 1: Schematic showing crosslinks from AGEs in collagen fibrils.[1]

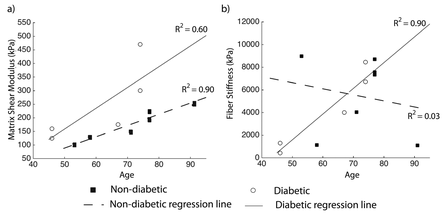


Figure 2: Data from human donors showing greater matrix and fiber stiffness in diabetic sclera than non-diabetic sclera.[2]

Methods & Materials

Prospectively Enrolled Subjects:

- 80 right eyes of 80 DIA, of which 77 passed image quality assessment.
- 86 right eyes of 86 DR, of which 79 passed image quality assessment.
- 107 right eyes of 107 age-matched normal control subjects: All 107 passed image quality assessment.

For diabetic subjects, most recent HbA1c, average HbA1c over time (HbA1c-mean), maximum HbA1c (HbA1c-max), and length of diabetes diagnosis (LoD) without retinopathy were taken from the medical records.

Corvis ST (Oculus, Wetzlar, Germany) Biomechanical parameters included two stiffness parameters (SP) calculated as load over displacement, from undeformed state to first applanation (SP-A1) for cornea stiffness, and from applanation to highest concavity (SP-HC) for sclera stiffness,[3] as well as stress-strain index (SSI) developed from finite element modeling.[4]

Statistical analysis with SAS; Significance threshold was set to $p<0.05$.

- ANOVA was performed to compare groups by age, IOP from Dynamic Contour Tonometry (DCT) and central corneal thickness (CCT).
- ANCOVA was performed on SP-HC, SP-A1, and SSI using significant result(s) of ANOVA as covariate(s).
- HbA1C parameters, LoD compared between DIA and DR using t-tests.

Results

ANOVA Results:

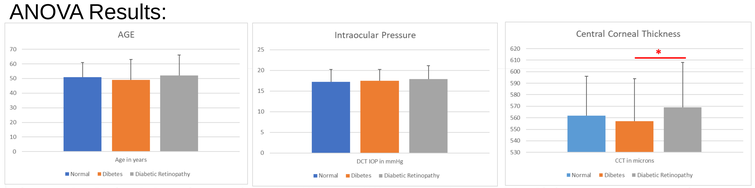


Figure 3: Only CCT showed a significant difference ($p = 0.0356$) between two cohorts.

ANCOVA Results:

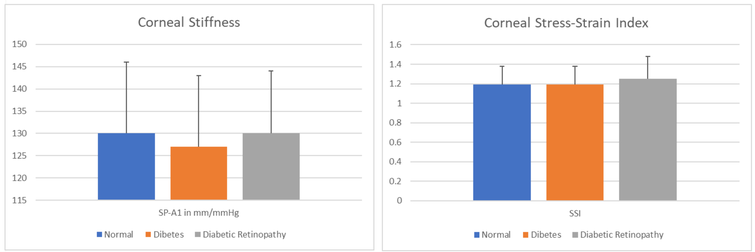


Figure 4: No differences in SP-A1 or SSI ($p > 0.05$) with CCT as sole co-variate.

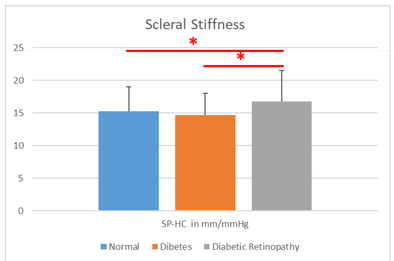


Figure 5: With CCT as a co-variate, SP-HC was significantly greater in DR than both DIA ($p = 0.0081$) and NRL ($p = 0.0215$). DIA and NRL were not different ($p = 0.5650$).

Table 1 shows similar Type I and Type II diabetes distribution in DR and DIA. Table 2 shows greater HbA1c parameters in DR than DIA.

Table 1: Diabetes Type

	Type I	Type II
DIA	18%	82%
DR	26%	74%

Table 2: HbA1c and Length of Diabetes Diagnosis

	HbA1c (%)	HbA1c-mean (%)	HbA1c-max (%)	LoD (yrs)
DIA	7.4 ± 1.8	7.0 ± 1.3	9.1 ± 2.7	8 ± 8
DR	8.5 ± 2.0	8.8 ± 1.9	11.0 ± 2.6	19 ± 10
	p = 0.0004	p < 0.0001	p < 0.0001	p < 0.0001

Disclosures

Cynthia J Roberts: Ziemer (C), Oculus (C)

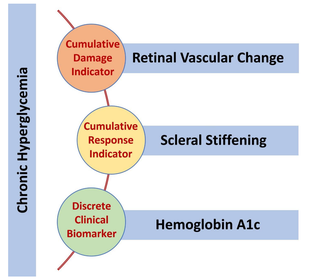
Matthew P Ohr: Alimera, Vitranu (I), Vitranu (P), Apellis, Genentech/Hoffman-LaRoche (F)

All other Co-Authors: None

Conclusions

Diabetic subjects with retinopathy at enrollment had **significantly stiffer scleral response and greater HbA1c parameters** than diabetic subjects without retinopathy at enrollment, which had similar scleral stiffness to age-matched subjects without diabetes. **Scleral stiffness may be a new biomarker as a cumulative indicator of chronic hyperglycemia which could be used at annual diabetic eye exams to identify those at greater risk for developing retinopathy**.

Figure 6: Proposed parallel, independent processes, all driven by chronic hyperglycemia:



Long-term, poorly controlled hyperglycemia leads to retinal vascular deterioration.

Scleral stiffness is the result of non-enzymatic crosslinking and is cumulative.

HbA1c is a discrete biomarker to indicate hyperglycemia, within a 3-month window.

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