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The Relationship between OCT-measured Central Retinal Thickness and Visual Acuity in Diabetic Macular Edema

Diabetic Retinopathy Clinical Research Network^{*}

Abstract

Objective—To compare optical coherence tomography (OCT)-measured retinal thickness and visual acuity in eyes with diabetic macular edema (DME) both before and after macular laser photocoagulation.

Design—Cross-sectional and longitudinal study.

Participants—210 subjects (251 eyes) with DME enrolled in a randomized clinical trial of laser techniques.

Methods—Retinal thickness was measured with OCT and visual acuity was measured with the electronic-ETDRS procedure.

Main Outcome Measures—OCT-measured center point thickness and visual acuity

Results—The correlation coefficients for visual acuity versus OCT center point thickness were 0.52 at baseline and 0.49, 0.36, and 0.38 at 3.5, 8, and 12 months post-laser photocoagulation. The slope of the best fit line to the baseline data was approximately 4.4 letters (95% C.I.: 3.5, 5.3) better visual acuity for every 100 microns decrease in center point thickness at baseline with no important difference at follow-up visits. Approximately one-third of the variation in visual acuity could be predicted by a linear regression model that incorporated OCT center point thickness, age, hemoglobin A1C, and severity of fluorescein leakage in the center and inner subfields. The correlation between change in visual acuity and change in OCT center point thickening 3.5 months after laser treatment was 0.44 with no important difference at the other follow-up times. A subset of eyes showed paradoxical improvements in visual acuity with increased center point thickening (7–17% at the three time points) or paradoxical worsening of visual acuity with a decrease in center point thickening (18%–26% at the three time points).

Conclusions—There is modest correlation between OCT-measured center point thickness and visual acuity, and modest correlation of changes in retinal thickening and visual acuity following focal laser treatment for DME. However, a wide range of visual acuity may be observed for a given degree of retinal edema and paradoxical increases in center point thickening with increases in visual acuity as well as paradoxical decreases in center point thickening with decreases in visual acuity were not uncommon. Thus, although OCT measurements of retinal thickness represent an important

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tool in clinical evaluation, they cannot reliably substitute as a surrogate for visual acuity at a given point in time. This study does not address whether short-term changes on OCT are predictive of long-term effects on visual acuity.

Introduction

Ophthalmologists have associated diabetic macular edema (DME) and a reduction in visual acuity for decades.^{1–4} It is well established that treatments that reduce DME can improve or stabilize visual acuity.^{3, 5, 6} Using optical coherence tomography (OCT), it is now possible to measure objectively macular thickness and investigate quantitatively the relationship of DME and visual acuity.^{7–9} Previous studies have reported different degrees of correlation between OCT-measured retinal thickness and visual acuity ranging from 0.28 to 0.73.^{7–8, 10–16} If the correlation between OCT-measured macular thickness and vision were particularly strong, one might be able to consider the OCT measurement as a surrogate measure of visual function in clinical trials of DME. A surrogate outcome in a clinical trial is used because it predates or predicts the actual measure of interest. In this case, changes in retinal thickening would be a surrogate for changes in visual acuity. For this surrogate outcome to be meaningful and appropriate, it must be well correlated with the measure of primary interest. A surrogate outcome can be valuable if it is easier or less expensive to measure than the variable of primary interest or shows earlier changes that predict longer term changes in the variable of primary interest. From a clinical trial design perspective, use of a surrogate outcome could result in the need for shorter follow up or a smaller sample size or both.

Standardized OCT measurements and best corrected visual acuity were obtained during a multicenter clinical trial of two laser techniques for treatment of DME. In this report, we evaluate those eyes without other concurrent macular disease and describe the relationships between macular thickness and visual acuity, both at baseline and following laser photocoagulation.

Methods

This study analyzes data collected from a multi-center randomized clinical trial comparing modified-ETDRS laser photocoagulation with a modified macular grid approach for the treatment of DME (protocol available at <http://public.drcr.net>, accession date May 13, 2006). The study, funded by the National Eye Institute of the National Institutes of Health, U.S. Department of Health and Human Services, was conducted by the Diabetic Retinopathy Clinical Research Network (DRCR.net) at 79 clinical sites across 30 U.S. states. The protocol and informed consent forms were approved by the respective institutional review boards. Each subject gave written informed consent to participate in the study. Study oversight was provided by an independent data and safety monitoring committee.

Study Population

Participants were at least 18 years old with type 1 or type 2 diabetes, had no history of renal failure requiring dialysis or renal transplant, and had one or both eyes meeting the following criteria: (1) best corrected electronic-ETDRS visual acuity¹⁷ letter score ≥ 19 (approximately 20/400 or better), (2) definite excess retinal thickness due to previously untreated DME (and not primarily due to vitreo-retinal interface disease) within 500 microns of the macular center on clinical examination, and (3) OCT retinal thickness ≥ 250 microns in the central subfield and/or ≥ 300 microns in at least one of the four inner subfields. Eyes were not eligible if they needed or had received panretinal scatter photocoagulation within the prior 4 months, YAG capsulotomy within the prior 2 months, or major ocular surgery including cataract extraction within the prior 6 months. For purposes of this paper, eyes were not included if, at enrollment, there was an ocular abnormality other than DME that in the investigator's judgment was

decreasing acuity by three or more lines or if the red reflex photographs graded by the Reading Center showed a moderate or greater lens or posterior capsule opacity.

Study Procedures

Visual acuity was measured by a certified tester using the electronic-ETDRS (E-ETDRS) procedure¹⁷ following a standardized refraction. E-ETDRS testing was conducted using the electronic visual acuity tester (EVA), which uses a programmed Palm (Palm, Inc., Santa Clara, California, USA) hand-held device communicating with a personal computer and 17-inch monitor at a test distance of 3 meters. A visual acuity score is obtained that is comparable to a standard ETDRS chart score.

OCT images were obtained from each eye following pupil dilation by a certified operator using the OCT2 (9 eyes) or OCT3 (242 eyes) system. For the 9 eyes using OCT2 at baseline, 8 switched to OCT3 during the study. For all other eyes, the same OCT version was used for the duration of the study. Scans were sent to the DRCR.net Reading Center at the University of Wisconsin-Madison where the scans were visually inspected. Scans in which the Reading Center considered the measurement of central retinal thickness to be unreliable [172/1195 (14%) OCT images] were not included in this study. Retinal morphology was assessed using a five-level grading scale for cystic spaces, and a three-level grading scale for the presence or absence of central subretinal fluid.

Fluorescein angiograms were obtained at baseline and 12 months. They were graded by the Reading Center for capillary loss, fluorescein leakage and cystoid abnormalities. Ninety-three percent of eyes at baseline had gradable fluorescein images for fluorescein leakage, but only 68% of eyes at baseline could be graded on capillary loss, a technical consequence of the fact that early frames in the angiogram can be obtained from only one eye.

Treatment and Follow-up

Each study eye received either modified-ETDRS or mild macular grid laser photocoagulation for DME. Follow-up visits occurred at 3.5, 8, and 12 months. Evaluation at each visit included measurement of best corrected E-ETDRS acuity and OCT measurement of retinal thickness. Macular laser photocoagulation was repeated if DME persisted. Of the 176 eyes in this report with 12-month follow-up data, 38% had only initial laser treatment, while 34% received one additional treatment, and 28% received two additional treatments.

Statistical Methods

Center point thickness was used as the OCT measurement of foveal thickness. Results were virtually identical using central subfield mean thickness since the two variables are highly correlated. At baseline, the correlation of central subfield mean thickness and center point thickness was 0.98 (N=251). At 12 months follow-up, the correlation of absolute change in central subfield mean thickness and absolute change in center point thickness was also 0.98 (N=176). We present only the analysis based on center point thickness under the assumption that center point thickness, a foveal measure, may be associated more closely with visual acuity than central subfield which includes contributions from the parafoveal region.

Analyses were based on parametric approaches utilizing least squares regression. Correlations and the coefficient of determination (r^2) were calculated in repeated measures models (to account for the correlation within subjects with two study eyes) based on the likelihood ratio as defined by Magee.¹⁸ Distributions of center point thickness and visual acuity were slightly skewed; however, truncating outliers at ± 3 standard deviations from the mean gave similar results (data not shown). Subgroup analysis on OCT quality (good versus fair) as determined

by the Reading Center was performed by adding an interaction term to the model with center point thickness.

Repeated measures least squares models were fit using visual acuity letter score as the dependent variable. Multivariate models using clinical and demographic factors as the independent variables were constructed using backward elimination ($P < 0.05$ to stay in the model). Median values were imputed for missing predictor variables ($< 10\%$ of eyes for each variable). To reduce potential collinearity, highly correlated variables ($r \geq 0.90$) were not included in the same model.

For the primary predictive factor, center point thickness, residuals were slightly skewed and there was suggestive evidence of larger variance with increasing thickness (assessed by regressing the squared residual on the center point thickness; $p = 0.07$). A transformation, taking the square root of the difference of the maximum letter score and the observed letter score, corrected both of these problems and gave results similar to those of the untransformed visual acuity letter score (data not shown). Linearity was examined by testing for higher order polynomial terms for each continuous variable in the final multivariate model. For center point thickness there was some suggestion of a convex quadratic effect ($p = 0.05$), but this was primarily due to one influential point ($p = 0.18$ when this point is removed). Subgroup analyses at follow-up were done based on method of laser treatment and no differences were found; thus the data from both treatment groups were pooled for analysis in this report.

Eyes were included in the analyses of change from baseline when there was no ocular cause for decreased acuity identified at the follow-up exam and there was a gradable OCT scan (referred to as *eligible eyes*). Change analyses on OCT variables were performed on absolute and relative changes in retinal thickening (excess thickness). Retinal thickening was defined as observed thickness minus mean normal thickness (defined as 171 microns for center point based on unpublished data provided by Carl Zeiss Meditec from a study of 260 nondiabetic eyes with a normal macula). Therefore, relative change in thickening following laser was calculated as (post-treatment thickness – pre-treatment thickness)/(pre-treatment thickness – mean normal thickness). Statistical analyses were performed using SAS software version 9.1.

Results

The study included 210 subjects, of whom 41 (20%) had two study eyes and 169 (80%) had one study eye for a total of 251 eyes. Baseline characteristics of the subjects and of the study eyes are provided in Table 1.

Relationship of OCT Center Point Thickness to Visual Acuity

Figure 1 shows baseline (pre-laser) visual acuity plotted against baseline OCT center point thickness. The correlation coefficient was 0.52. The slope of the best fit line to the data was approximately 4.4 letters (95% C.I.: 3.5, 5.3) better visual acuity for every 100 microns decrease in center point thickness. There was a trend for stronger association for eyes with good quality OCT (slope = 4.6 letters better for every 100 microns decrease in center point thickness, $n = 182$) than for those with fair quality OCT (slope = 3.5 letters, $n = 69$, $P = 0.28$). For any OCT center point thickness, a wide range of visual acuities was observed. In Figure 2, OCT center point thickness has been divided into 4 subgroups and frequency distributions of observed visual acuities for each subgroup are shown. For smaller center point thicknesses, a greater percentage of eyes have better visual acuity than observed with larger center point thicknesses, although a wide range of acuities are evident at all thicknesses.

Table 2 lists the factors examined in multiple regression models for their effect on baseline visual acuity. OCT center point thickness was the most predictive factor, accounting for 27%

of the total variation in visual acuity. Factors of lesser importance included age, baseline fluorescein angiographic leakage at the macular center and inner subfields combined, and baseline HbA1c, which together increased the model r^2 to 36%. Capillary loss at the center was present in 16% of the 170 eyes with capillary loss gradable at baseline, but adding this variable to the model did not significantly improve the prediction of visual acuity.

Of the 251 eyes analyzed at baseline, 185, 181, and 176 eyes were eligible for analysis at the 3.5, 8, and 12 month follow-up visits, respectively. The relationship of visual acuity to OCT center point thickness at 3.5, 8, and 12 months following laser treatment was similar to the relationship observed at baseline (correlation coefficients of 0.49, 0.36, and 0.38 with slopes of approximately 3.8 (95% C.I.: 2.8, 4.9), 3.5 (2.1, 4.9), and 3.5 (2.1, 4.9) letters better visual acuity for every 100 microns decrease in center point thickness, respectively (Figure 3).

Relationship of Center Point Thickness Change to Visual Acuity Change

At 3.5, 8, and 12 months following the initial laser treatment, the mean $\pm$ SD changes in OCT center point thickening were -17 ± 103 , -35 ± 115 , and -49 ± 134 microns, respectively and mean $\pm$ SD visual acuity letter score changes were 1.4 ± 7.7 , 0.3 ± 9.4 , and 0.4 ± 9.3 letters, respectively. The correlation coefficients of change in visual acuity versus absolute change in OCT center point thickening for these time intervals were 0.44, 0.30, and 0.43, respectively (Figure 4). An analysis based on relative OCT center point change in retinal thickening rather than absolute OCT center point change yielded similar results (data not shown).

The slopes of the best fit lines for all plots ranged from 3.3 letters (95% C.I.: 2.3, 4.4) at 3.5 months to 2.5 letters (95% C.I.: 1.3, 3.8) at 8 months better visual acuity for every 100 microns decrease in center point thickness. A subset of eyes showed paradoxical improvement in visual acuity with increased OCT center point thickening (17%, 7%, 7% at the three time points, respectively) or paradoxical worsening of visual acuity with a decrease in OCT center point thickening (18%, 24%, 26%, respectively, Figure 4).

It is possible that visual acuity may not improve with the same time course as thinning of the macula. That is, macular function improvement could possibly lag behind anatomic improvement.¹⁹ The correlation coefficient assessing OCT change at 3.5 months versus visual acuity change at 8 months (assessing this possibility of lag of visual acuity change) was 0.30 suggesting that such a lag, if present, is small and probably clinically unimportant.

Discussion

Although it has long been appreciated that central macular thickening can be associated with a decrease in visual acuity, and that treatments which reduce such retinal thickening can improve vision, quantitative evaluation of these relationships and the effect of laser photocoagulation are scarce. In this study, we document a modest correlation between best corrected visual acuity and OCT center point thickness prior to focal laser photocoagulation, as well as a modest correlation between change in visual acuity and change in OCT center point thickening through the first year following laser treatment. Despite this modest correlation, there was substantial variation in visual acuities at any given retina thickness. Many eyes with thickened maculas had excellent visual acuity, and many eyes with maculas of normal thickness had decreased visual acuity (Figure 2). These results suggest that OCT measurement alone may not be a good surrogate for visual acuity as a primary outcome in studies of diabetic macular edema. Assessment of macular thickness using OCT is certainly clinically useful, but macular thickness is just one of several variables affecting visual acuity in a complex and as yet not fully understood relationship.

The subjects included in this study were seen in diverse settings and are probably representative of subjects with DME seen throughout the United States. The demographics of this study population are similar to those of other large studies of diabetic macular edema both in the United States and Great Britain.^{20–23} However, unlike the ETDRS, which excluded subjects older than 70 years of age,²⁴ the present study did not. With 15% of the subjects over 70 years of age, the findings reported here also apply to this older age group. The current results should not necessarily be extrapolated to subjects with renal failure or other processes that affect visual acuity in addition to macular edema, because such subjects were specifically excluded from this study. In addition, post-baseline analysis was only among eyes receiving laser photocoagulation for DME. These results may or may not be similar when assessing other treatments for DME. Likewise, the results may or may not be similar for other macular disorders such as age-related macular degeneration. The relationship of visual acuity and OCT-measured central retinal thickness before intervention is roughly linear. Other studies have found similar results; however, the strengths of correlation have varied widely (Table 3).^{7–8, 10–16} Some of these studies have used the central subfield mean thickness instead of center point thickness. However, since correlation of the two measures is 0.98, results of these studies can be compared. The coefficient of determination (r^2) of 0.27 in the current study is in the middle of the previously reported range of 0.08–0.54, and may represent the current best estimate given the size of this study and the prospective, tightly regulated fashion in which the data were gathered. On average, visual acuity at baseline was better by 4.4 (95% C.I.: 3.5, 5.3) letters for every 100 microns decrease in center point thickness. This finding is consistent with previous reports of better visual acuity by 2.9–11.7 letters per 100 microns less thickness.

The current report, and those of other studies, demonstrates a nearly linear relationship between center point thickness and visual acuity without evidence for a plateau effect whereby the change in visual acuity per unit of retinal thickness decreases with a thicker macula. In contrast, some other diseases associated with macular edema such as retinal vein occlusion and retinitis pigmentosa fit a nonlinear model (Michael S. Ip, M.D., personal communication).²⁵

The variance of ETDRS letters read at any given observed center point thickness is large, and there may be a tendency for a greater spread in letters read in thicker maculas. Most eyes with DME have center point thicknesses less than 400 microns (74%). In this group, the standard deviation in letters read for any given center point value is 9.7 (approximately two ETDRS lines), illustrating how crude OCT center point thickness is as a surrogate index for visual acuity. For the very edematous eyes, the spread is even greater.

Although center point thickness was the most predictive factor for both baseline and follow-up visual acuity, it only explained 27% of the variation in baseline and similar amounts at subsequent visual acuity measurements. Addition of baseline HbA1c, age, and fluorescein angiographic leakage at the macular center and inner subfields combined accounted for 36% of the variation in baseline visual acuity. These data suggest that additional factors other than those evaluated here also contribute to visual acuity.

The correlation between retinal thickness and visual acuity held relatively stable across all follow-up periods. However, a subset of eyes showed paradoxical improvement in visual acuity with increased center point thickening (7–17%) or paradoxical worsening of visual acuity with reduced center point thickening (18–26%). Thus the predictive value of change in retinal thickening for change in visual acuity in a particular eye is low. Over the follow-up intervals we examined, we did not observe any increase in the slope of the visual acuity change versus foveal thickness change which would have suggested a lag in acuity response.

This study has substantial design strengths including its prospective nature, large number of subjects, use of rigorous ETDRS visual acuity measurement, centralized reading center

interpretation of OCT and fundus photography, and multicenter recruitment from both community and university based sites. A weakness is the lack of information on duration of existing edema at baseline and incompleteness of the data set regarding degree of macular ischemia, both of which may affect edema and vision. Although OCT measured macular thickness is the best clinically available estimate for true macular thickness, it may underestimate true macular thickness by a tendency to exclude outer photoreceptor segments. 26

In summary, there is a modest correlation of OCT-measured center point thickness with visual acuity, and modest correlation of changes in retinal thickening and visual acuity following focal laser treatment for DME. However, confidence intervals are large and a wide range of visual acuity may be observed for a given degree of retinal edema. In addition, paradoxical changes in visual acuity and retinal thickening may be observed in up to 26% of eyes. Indeed, retinal thickness only accounts for up to 27% of variability in concurrently measured visual acuity suggesting that other factors are important determinants of visual acuity in the presence of diabetic macular edema. Thus, although OCT measurements of retinal thickness represent an important tool in clinical evaluation, they cannot reliably substitute as a surrogate for visual acuity at a given point in time. However, this study does not address whether short-term changes on OCT are predictive of long-term effects on visual acuity.

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Figure 1. Comparison of OCT Center Point Thickness and Visual Acuity at Baseline
 The solid line represents the regression line and the dotted lines represent the 95% confidence interval for the mean.

Figure 2. Distribution of Visual Acuity Measurements in Categories Based on OCT Center Point Thickness at Baseline

Box-whisker plot demonstrating mean (dashed horizontal line), median (solid horizontal line), 25 – 75th percentiles (extremes of the box), 10–90th percentiles (whiskers), and 5–95th percentiles (solid circles) of visual acuity at baseline.

Figure 3. Comparison of OCT Center Point Thickness and Visual Acuity at 3.5 Months
 The solid line represents the regression line and the dotted lines represent the 95% confidence interval for the mean. Graphs at 8 months and 12 months appeared similar.

Figure 4. Comparison of Change in OCT Center Point Thickening and Change in Visual Acuity from Baseline to 3.5 Months

The solid line represents the regression line and the dotted lines represent the 95% confidence interval for the mean. Graphs at 8 months and 12 months appeared similar.

Table 1**Baseline Demographics and Clinical Characteristics**

Subject-level Factors	N = 210 subjects
Age (yrs) - <i>Mean ± SD</i>	58 ± 11
Gender: Women - N (%)	86 (41%)
Race/Ethnicity - N (%)	
White - Non Hispanic	138 (66%)
Black/African-American	37 (18%)
Hispanic or Latino	19 (9%)
Other	16 (8%)
Diabetes Type - N (%) [*]	
Type 1	16 (8%)
Type 2	194 (92%)
Duration of Diabetes (yrs) - <i>Mean ± SD</i>	14 ± 9
HbA1c% - <i>Mean ± SD</i> [†]	8.2 ± 1.9
Eye-level Factors	N = 251 eyes
Visual Acuity (approximate Snellen equivalent from letter score) - N (%)	
20/20 or better	67 (27%)
20/25 to 20/40	131 (52%)
20/50 to 20/100	45 (18%)
Worse than 20/100	8 (3%)
<i>Mean ± SD</i> – Letters	75 ± 12
<i>Mean ± SD</i> - Snellen Equivalent	20/32 ± 2.4 lines
Lens Status - N (%)	
Phakic	223 (89%)
Pseudophakic	28 (11%)
Aphakic	0 (0%)
OCT Center Point Thickness - N (%)	
< 225 microns	72 (29%)
225–299 microns	65 (26%)
300–399 microns	48 (19%)
400–499 microns	40 (16%)
≥ 500 microns	26 (10%)
<i>Mean ± SD</i> – microns	317 ± 136
Cystoid Spaces Present on OCT-N (%)	99 (39%)
Subretinal Fluid Present on OCT-N (%)	16 (6%)

^{*} Type 1 diabetes is defined as insulin dependency prior to age 30.

[†] N = 203 baseline HbA1c results.

Table 2
Factors with Significant Effect on Visual Acuity in a Multiple Regression Linear Model

Factor	Univariate Model of Baseline Visual Acuity and Predictive Factor			Multivariate Model of Baseline Visual Acuity [†]		
	r ²	Estimate[Decrease in letter score] (95% C.I.)	P-value *	Cumulative *, ‡ r ²	Estimate[Decrease in letter score] (95% C.I.)	P-value * Final Model(r ² = 36%)
OCT Center point Thickness(per 100 micron increase)	27%	4.4 (3.5, 5.3)	<0.001	27%	3.6 (2.6, 4.6)	<0.001
Age(per decade increase)	4%	2.3 (1.0, 3.6)	<0.001	29%	2.7 (1.5, 3.9)	<0.001
Fluorescein Leakage in the Center and Inner Subfields // (per one-tenth Disc Area increase)	12%	3.2 (2.1, 4.4)	<0.001	33%	1.9 (0.8, 3.0)	<0.001
HbA1c(per 1% increase)	1%	0.7 (-0.1, 1.5)	0.08	36%	1.1 (0.5, 1.8)	0.001

* Adjusted for the correlation within subjects with two study eyes.

[†] Additional factors explored not significantly associated with visual acuity in a multivariate model included: Inner zone thickness, retinal volume, cystoid spaces on OCT and fluorescein angiography, SSR detachment on OCT, number of involved subfields, macular slope, race, gender, diabetes type, duration of diabetes, treatment for hypertension, hard exudates measured on fundus photos, lens status, level of retinopathy measured on fundus photos, hemorrhage and microaneurysms within the grid measured on fundus photos.

[‡] Cumulative r² obtained from backwards elimination regression, calculating the r² after removing factors from the final four variable model. The numbers in this column represent the r² from four models in which the factor in the row has been cumulatively added to the model (e.g., r² = 27% represent the model with center point thickness alone, and r² = 29% represents model with center point and age).

// In the central subfield (within 1/3 DD of center).

Table 3

Visual Acuity versus OCT Macular Thickness Studies

Study	Dependent Variable	N	r ² *	Slope†	P-value
Present Study	Visual Acuity	251	0.27	-.044	<0.001
Bandello [‡] , 2005 ¹⁰	Visual Acuity	28	0.33	-.045	.001
Otani [‡] , 2001 ¹¹	Visual Acuity	11	0.34	-.058	0.06
Martidis [‡] , 2002 ¹²	Visual Acuity	16	0.15	-.062	.14
Laursen [‡] , 2004 ¹³	Visual Acuity	23	0.08	-.038	.20
Catier // 2005 ¹⁴	Visual Acuity	27	0.30	-.07	.003
Ozdemir [‡] , 2005 ¹⁵	Visual Acuity	20	0.54	-.117	<.001
Massini [‡] , 2003 ¹⁶	Visual Acuity	15	0.13	-.029	.19
Goebel // 2002 ⁸	OCT	136	0.15	-.30	<.001
Hee, 1995 ⁷	OCT	75	0.45	DNS	DNS

* r² is the coefficient of determination for the linear regression of the Dependent variable (either VA or OCT macular thickness) versus the Independent variable (either OCT macular thickness or VA).

† Change in the independent variable (either OCT or VA) per one unit change in the dependent variable (either microns or letter score)

‡ R², slope, and p-value calculated based on data provided.

// Slope interpolated from graph provided.

DNS = data not shown.