B-scan Ultrasonography for the Detection of Macular Thickening

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• PURPOSE: **To report the sensitivity and specificity of B-scan ultrasonography to detect macular thickening.**
• DESIGN: **Observational case series.**
• METHODS: **Seventy-seven eyes of 40 consecutive patients (age range, 7–80 years) in a retinal specialty practice were examined. A single masked ultrasound operator performed B-scan ultrasonography on all eyes and graded macular thickening. The final assessment of macular thickening was based on biomicroscopy findings combined with fluorescein angiography (FA) and optical coherence tomography (OCT). The presence or absence of macular thickening as determined by B-scan ultrasonography was compared with the final clinical assessment, FA findings, and OCT measurements.**
• RESULTS: **B-scan ultrasonography detected macular thickening with a high degree of sensitivity (91%) and specificity (96%). There was a high degree of agreement between findings on ultrasonography and FA (kappa = 0.80). Ultrasonographic diagnosis correlated with OCT measurements for both central macular thickness (r = .65, P < .001) and volume (r = .56, P < .001).**
• CONCLUSIONS: **Ultrasonographic detection of macular thickening correlates with findings on slit-lamp biomicroscopy, FA, and OCT. B-scan ultrasonography is a potentially useful technique for assessing macular thickness when biomicroscopy is impossible or when patients cannot tolerate FA or OCT. (Am J Ophthalmol 2003; 136:55–61. © 2003 by Elsevier Inc. All rights reserved.)**

RETINAL THICKENING MAY BE PRESENT IN A NUMBER of ocular conditions and often results in decreased visual acuity.[1,2] Accurate diagnosis of macular thickening is critical to formulating a management plan, instituting treatment, and subsequently monitoring this condition. The detection of macular thickening may be made by careful biomicroscopic examination. However, additional tests are often needed to confirm its presence.

Fluorescein angiography (FA) and optical coherence tomography (OCT) can be useful tests in helping to detect macular thickening. Angiographic macular edema can often be detected even in cases of subtle or no biomicroscopic changes. Optical coherence tomography is a noninvasive, noncontact imaging modality that utilizes optical reflectivity to produce cross-sectional tomographs of ocular tissue.[3] It is a reliable tool for the measurement of retinal thickness in a variety of ocular diseases.[3–7] Correlations between findings on FA and OCT have been documented in a several conditions.[4,5,8]

Fluorescein angiography and OCT have limitations. Both tests require the ocular media to be of sufficient clarity to image the retina. Yet in certain patients, opacities in the ocular media limit biomicroscopy, FA, and OCT. Furthermore, a high degree of patient cooperation is required to ensure reliable and accurate testing. However, certain patients, such as children, often cannot tolerate a FA or follow the specific fixation instructions for OCT testing.

Ophthalmic ultrasonography is a well-accepted noninvasive diagnostic tool. Ultrasonography has the advantage of reliably imaging the posterior segment regardless of the ocular media status.[9,10] Furthermore, ultrasonography is less dependent on patient cooperation for reliable testing than either FA or OCT. Although both B- and A-scan ultrasonograms have been used to detect macular thickening,[10,11] no study has examined the relationships of ultrasonography to FA and OCT.

METHODS

FORTY CONSECUTIVE NEW PATIENTS SEEN IN THE CLINIC of one of the authors (G.J.J.) were enrolled in this study. Duke Institutional Review Board approval was obtained for this study. Patients underwent B-scan ultrasonography by the same masked operator (G.J.J.). Ultrasonography was performed before the history or examination had been revealed to the masked operator in an attempt to minimize

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TABLE 1. Eyes With Final Clinical Determination of Macular Thickening

Eye No.	Age	Sex	Eye	Final Diagnosis	Leakage on FA	OCT Central Thickness (μm)	OCT Central Volume (mm^3)	U/S Grade of Thickening
1	47	F	OD	Idiopathic uveitis	Yes	255	2.57	1
2	71	M	OD	Stage 3 FTMH	Not done	256	2.44	1
3	62	F	OD	DME	Yes	307	2.23	1
4	74	M	OD	DME	Yes	531	4.88	1
5	74	M	OS	DME	Yes	322	2.63	0
6	69	M	OD	Acute retinal necrosis	Yes	322	2.63	1
7	7	M	OD	Pars planitis	Yes	168	2.96	1
8	49	F	OS	Superotemporal BVO sparing fovea	Yes	178	2.88	1
9	73	M	OD	DME	Yes	413	3.13	1
10	73	M	OS	DME	Yes	351	2.65	1
11	77	F	OD	DME	Yes	264	2.33	2
12	77	F	OS	DME	Yes	398	3.48	1
13	43	F	OS	Central serous retinopathy	Yes	194	2.47	1
14	74	M	OD	Stage 3 FTMH	Not done	425	3.16	2
15	34	F	OS	Juvenile rheumatoid arthritis	Yes	867	6.28	2
16	63	M	OD	BVO	Yes	444	3.66	2
17	33	F	OD	Sarcoid uveitis	Yes	426	3.2	2
18	33	F	OS	Sarcoid uveitis	Yes	593	3.61	2
19	52	M	OD	CME from panuveitis	Yes	685	4.92	2
20	76	F	OD	CME from ACIOL	Yes	559	3.58	2
21	69	F	OD	CME from retinitis pigmentosa	Yes	153	1.8	0

ACIOL = anterior chamber intraocular lens; BVO = branch retinal vein occlusion; CME = cystoid macular edema; DME = diabetic macular edema; F = female; FA = fluorescein angiogram; FTMH = full-thickness macular hole; M = male; OCT = optical coherence tomography; U/S = ultrasound.

TABLE 2. Comparison of Echographic Findings of Retinal Thickening With Final Clinical Determination and Fluorescein Angiography

	Ultrasonography		Total No. Eyes
	No Thickening	Thickening	
Final clinical determination			
no thickening	43	2	45
thickening	2	20	22
Total number of eyes	45	22	
FA: no leakage	29	2	31
FA: leakage	3	18	21
Total number of eyes	32	20	

FA = fluorescein angiogram.

any bias. B-scan ultrasonography using a 10-MHz probe on an I^3 System-ABD Diagnostic Ophthalmic Ultrasound (Innovative Imaging, Sacramento, California, USA) was performed using standard ultrasonographic techniques. Proparacaine 0.5% drops were first administered. The ultrasound probe was positioned on the eye through closed lids. Aquasonic 100 Ultrasound Transmission Gel (Parker Laboratories, Fairfield, New Jersey, USA) was used as a coupling agent. Evaluation of the vitreous and macula was performed using various probe positions: horizontal axial, vertical macula, and transverse directed temporally.[12] In certain instances, longitudinal scans and oblique views through the macula were also used to assess thickening. Gain settings were adjusted accordingly to maximize detection of macular pathology. Macular thickening was graded as 0 (none), 1 (subtle), or 2 (pronounced). This qualitative grading system was arbitrarily established after reviewing numerous ultrasounds that were obtained on eyes with macular thickening before the start of our study.

Patients then underwent a complete ophthalmic examination, including best-corrected Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing, intraocular (IOP) measurement, and dilated ophthalmoscopic and slit-lamp biomicroscopic examination.

Eyes in which the media were of sufficient clarity were also tested with optical coherence tomography using the OCT I instrument (Zeiss-Humphrey Instruments Systems, Dublin, California, USA). As described elsewhere,[5] the commercially available mapping program of the A6.1 software was used to measure macular thickness. Briefly, the radial scan function was used to capture six scans (scan length, 5.92 mm), centered on the patient's fixation point, which commenced at the 12, 1, 2, 3, 4, and 5 o'clock positions. A two-dimensional color-coded map of the macula was generated that divided the macula into nine

TABLE 3. Eyes With Discrepancies Between Echographic Findings and Final Clinical Diagnosis

Eye No.	Age	Sex	Eye	Final Diagnosis	Hyperfluorescence on FA	OCT Central Thickness (μm)	OCT Central Volume (mm^3)	U/S Grade of Thickening
1	74	M	OS	Diabetic macular edema	Yes	322	2.63	0
2	69	F	OD	CME from retinitis pigmentosa	Yes	153	1.8	0
3	71	F	OS	Occult CNV with no subretinal fluid	Yes	99	1.8	1
4	60	F	OS	Pseudo-operculum, normal macula	No	310	3.77	1
5	70	M	OS	Subretinal hemorrhage	No	271	2.47	1
6	40	F	OS	Pars planitis without macular edema	Yes	175	2.52	0

CME = cystoid macular edema; CNV = choroidal neovascularization; F = female; FA = fluorescein angiogram; M = male; OCT = optical coherence tomography; U/S = ultrasound.

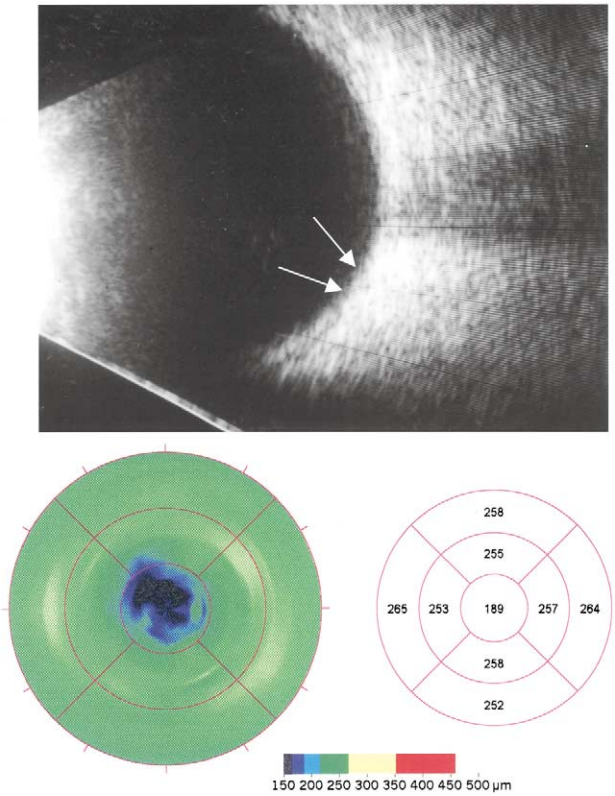

FIGURE 1. Eye with grade 0 thickening. B-scan echogram (top) with probe slightly oblique to the fundus reveals a normal macula (arrows). Optical coherence tomography (bottom) reveals no macular thickening. Brighter colors (red to white) correspond to areas of increased retinal thickness (μm); dimmer colors (blue to black) correspond to areas of decreased retinal thickness.

regions, including a central disk with a diameter of 1,000 μm and an inner and outer ring, each divided into four quadrants, with diameters of 2,220 and 3,450 μm, respectively. The OCT software calculated the average retinal thickness of the nine different macular regions and the central macular volume.

Fluorescein angiograms were obtained when there was a suspicion of either retinal or choroidal pathology.

A final determination of macular thickening, independent of ultrasound findings, was made based on a combination of ophthalmoscopy and slit-lamp biomicroscopy, OCT, and if obtained, fluorescein angiography. Eyes that underwent ultrasonography, but could not otherwise be assessed with biomicroscopy, FA, or OCT, were excluded from the final data analysis.

Baseline characteristics and study outcomes were summarized by means and standard deviations for continuous variables and by frequencies and percentages for categorical variables. To assess the relationships between assessments of macular thickening based on different techniques of examination, pairwise cross-tabulations were obtained. First, echographic findings were compared with final clinical diagnosis. Second, fluorescein findings were compared with ultrasound. Finally, fluorescein findings were compared with final clinical determination of macular thickening. For each pairwise comparison of diagnoses, sensitivity, specificity, and positive predictive value were computed. The "gold standard," which varied for each comparison, is displayed as the column variables in the tables. In addition, the kappa statistic, a measure of agreement, was computed. (Kappa values range from 0–1. The closer the value is to 1, the better the agreement. Values of 0.4 to 0.8 indicate moderate agreement; values greater than 0.8 indicate excellent agreement). The relationship between ultrasound detection and OCT central macular thickness and macular volume were assessed by the Spearman correlation coefficient. (The Spearman correlation coefficient ranges from −1–+1. A value of −1 indicates a strong negative relationship, whereas a value of +1 indicates a strong positive relationship). The relationships between ultrasound detection and OCT central macular thickness and volume were also examined by plotting the values and fitting a regression line to the data. Statistical data analyses were carried out using the SAS system (SAS Institute, Cary, North Carolina, USA).

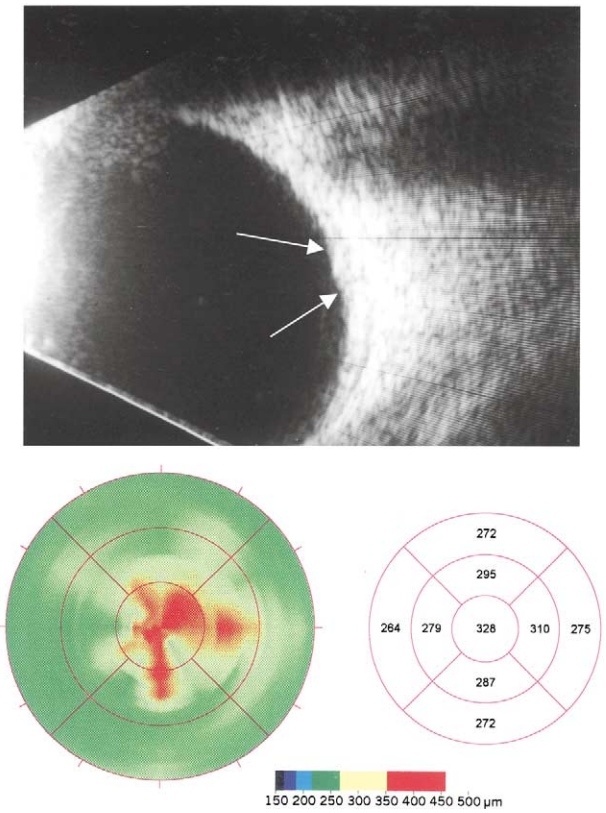

FIGURE 2. Eye with grade 1 thickening. B-scan echogram (top) with probe slightly oblique to the fundus demonstrates subtle macular thickening (arrows). Optical coherence tomography reveals macular thickening (bottom).

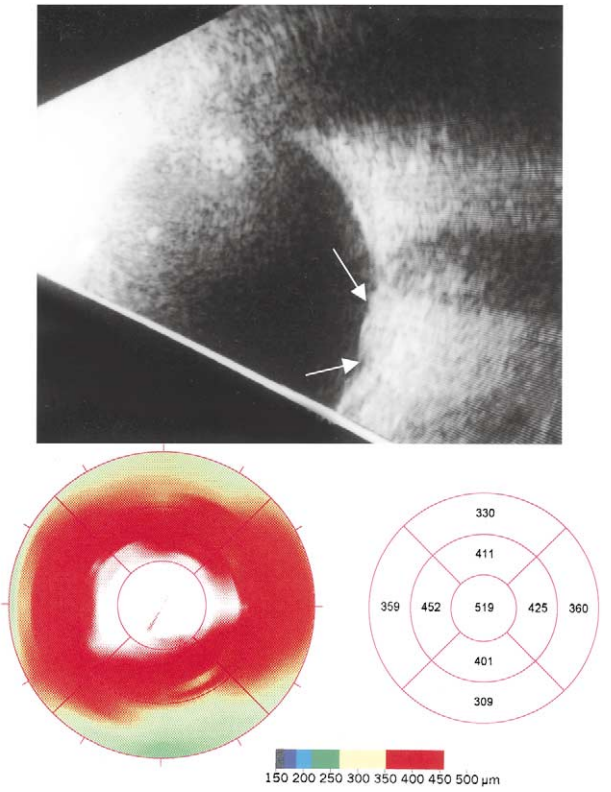

FIGURE 3. Eye with grade 2 thickening. Prominent macular thickening (arrows) is present on B-scan echogram (top) and corresponding optical coherence tomography (bottom).

RESULTS

A TOTAL OF 73 EYES OF 40 PATIENTS (AGE RANGE, 7–80 years) with various ocular conditions underwent B-scan ultrasonography. Six eyes of six patients were excluded from the data analysis because media opacity precluded biomicroscopy (n = 5) or because of a chronic retinal detachment (n = 1). Forty-six eyes had no macular thickening on clinical examination. The final diagnoses for these eyes included: normal examination (n = 12), dry age-related macular degeneration (n = 6), iridocyclitis (n = 5), sarcoid-associated uveitis (n = 4), HLA-B27 associated iridocyclitis (n = 4), pars planitis (n = 4), diabetic retinopathy (n = 2), and others (n = 9). The demographics and characteristics of the 21 eyes with macular thickening detected through a combination of biomicroscopy, OCT, and FA are presented in Table 1. The most common causes of macular thickening were diabetes and uveitis.

The relationship between clinical and echographic findings is summarized in Table 2. There was a high degree of agreement between clinical diagnosis and echographic findings of macular thickening (kappa = 0.86). The sensitivity and positive predictive values of B-scan ultrasonography to detect macular thickening were 91% (20/22 eyes) and 91% (20/22), respectively. Ultrasound did not detect macular thickening in two eyes diagnosed with thickening by clinical examination (Table 3). One eye (Eye 1) had diabetic macular edema that was confirmed on FA and OCT. The other eye (Eye 2) was felt to have trace macular thickening on biomicroscopy and very mild macular leakage on FA. However, OCT did not detect any macular thickening (central thickness, 153 µm). The specificity of B-scan ultrasonography to diagnose macular thickening was 96% (43/45; Table 2). Macular thickening was incorrectly diagnosed with B-scan ultrasonography in two eyes (Table 3). One of these eyes (Eye 3) had occult choroidal neovascularization with some late hyperfluorescence but no subretinal fluid on examination. Another eye (Eye 4) had a pseudo-operculum overlying a normal macula.

The relationship between fluorescein angiographic and echographic findings is summarized in Table 2. Fluorescein angiograms were obtained on 52 eyes of 31 subjects. Thirty-one eyes had a normal fluorescein angiogram. Twenty-one eyes had macular hyperfluorescence. There was a high degree of agreement between FA and ultrasound findings (kappa = 0.80). Of the 20 eyes with ultrasound evidence of macular thickening, 18 eyes also had macular leakage on fluorescein angiography. Of the 2 eyes with no fluorescein leakage but ultrasound thickening,

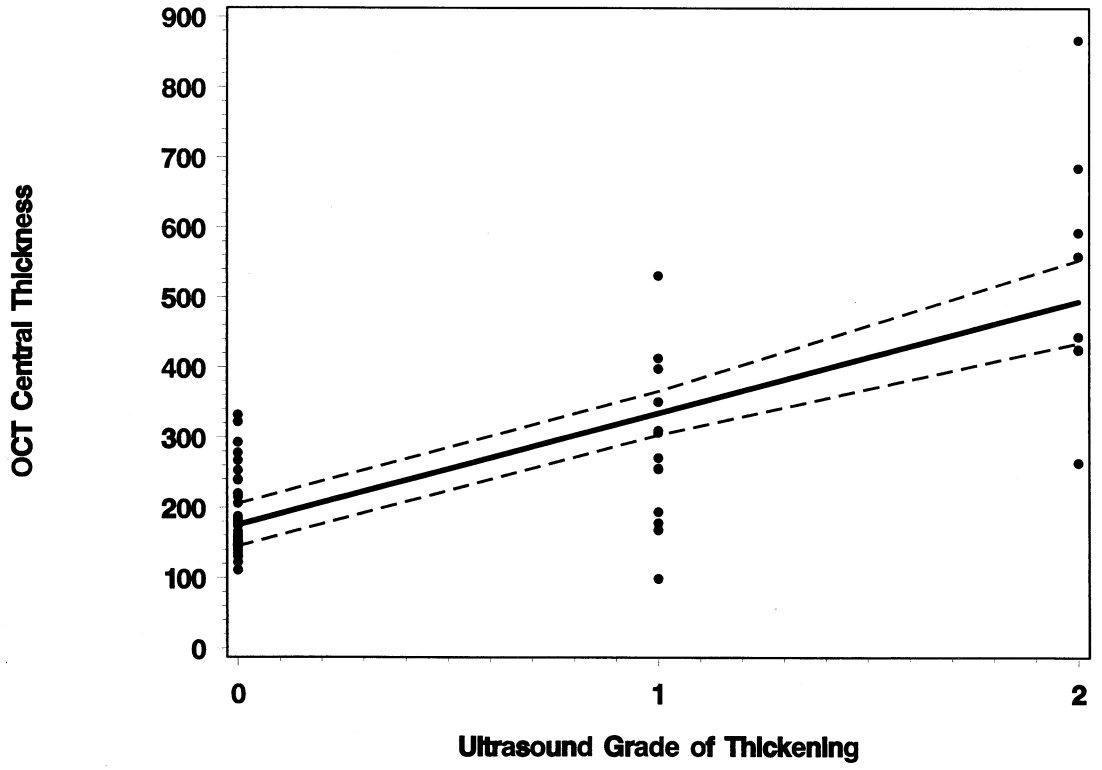

FIGURE 4. Ultrasound grade of macular thickening correlates with optical coherence tomography (OCT) measurements of central macular thickness ([μm] $r = .65$, $P < .001$). Solid line represents fitted regression line. Dotted lines represent 95% confidence limits.

1 had a pseudo-operculum (Eye 4); the other had a subretinal hemorrhage (Eye 5; Table 3). Three eyes with leakage on FA did not have macular thickening on ultrasound examination (Table 3). One eye had mild diabetic macula edema (Eye 1). Another eye had very mild CME from retinitis pigmentosa. The last eye (Eye 6) was diagnosed with pars planitis without macular edema. The FA demonstrated some mild late hyperfluorescence, but no macular thickening was detected on clinical examination, OCT, or ultrasonography.

The relationships between the ultrasound diagnosis and OCT measurements of central macular thickness and volume were examined. Using B-scan ultrasonography, 45 patients were classified with grade 0 thickening, 14 with grade 1 thickening, and 8 with grade 2 thickening. For the group of patients with grade 0 macular thickening, 40 patients were tested with OCT (Figure 1). The mean central OCT thickness (± SD) and volume (± SD) were 183 ± 55 μm and 2.34 ± 0.28 mm^3, respectively. Thirteen of the 14 patients with grade 1 thickening were tested with OCT (Figure 2). The average OCT thickness and volume for those with grade 1 edema were 287 ± 117 μm and 2.9 ± 0.79 mm^3, respectively. The mean OCT thickness and volume for those with grade 2 macular thickening were 533 ± 186 μm and 3.84 ± 1.22 mm^3, respectively (Figure 3). The relationships between echographic and OCT findings are shown in Figures 4 and 5. Ultrasound diagnosis correlated with OCT measurements for both central macular thickness ($r = .65$, $P < .001$) and volume ($r = .56$, $P < .001$).

DISCUSSION

THERE ARE MANY CLINICAL SCENARIOS IN WHICH OPHthalmoscopy, FA, and OCT are difficult, if not impossible. In these instances, B-scan ultrasonography may represent the only way of detecting macular thickening. This study demonstrates that B-scan ultrasonography can accurately detect macular thickening. Findings of macular thickening on ultrasound examination correlate highly with those on clinical, FA, and OCT testing.

A test that can reliably detect macular thickening in cases where the retina is difficult to visualize could have an important impact on patient care. For example, ultrasonography may be the only method to diagnose macular edema in patients with uveitis and dense cataracts or with severe posterior synechiae. Management decisions in these situations might be altered with the additional knowledge that a patient has macular edema. For example, the ophthalmologist may choose to administer a periocular corticosteroid injection before cataract extraction. Con-

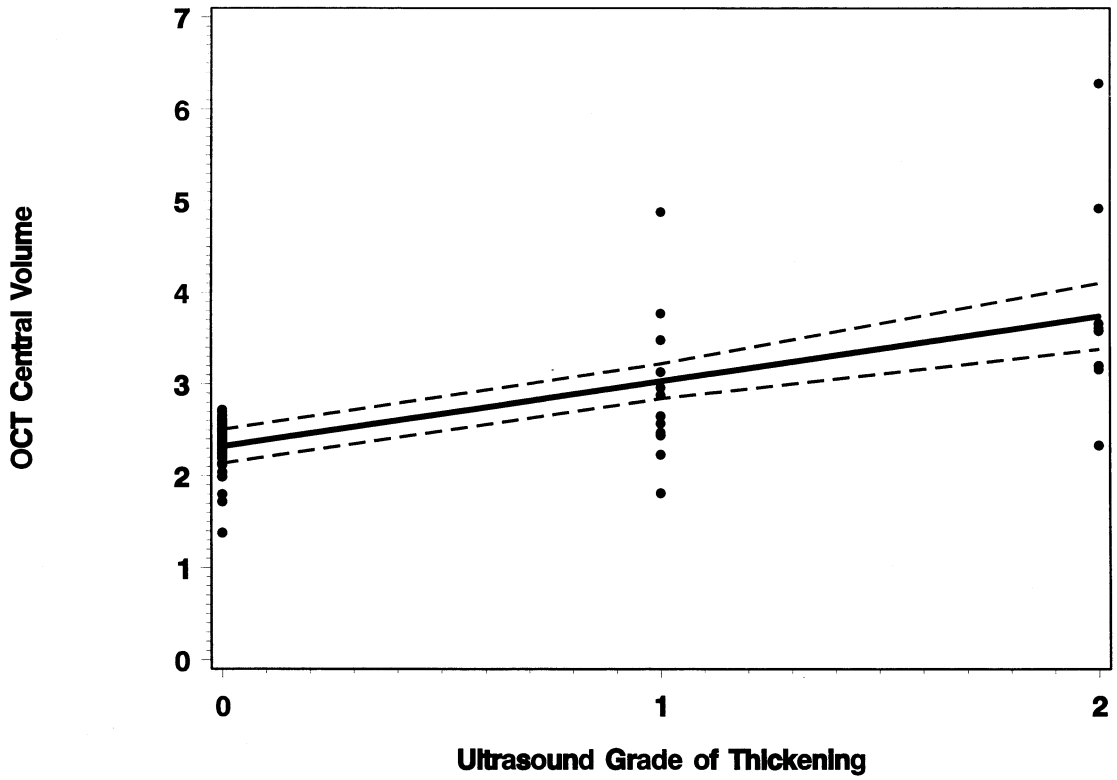

FIGURE 5. Ultrasound grade of macular thickening correlates with optical coherence tomography (OCT) measurements of central macular volume ([mm]^3 $r = .56$, $P < .001$). Solid line represents fitted regression line. Dotted lines represent 95% confidence limits.

versely, the decision may be made to proceed directly with a combined cataract extraction and pars plana vitrectomy with or without periocular or intravitreal corticosteroid injection. Young children represent another population in which ophthalmic examination and ancillary testing with FA and OCT can be extremely difficult. Yet detecting the presence of macular edema in children with uveitis can greatly change the ophthalmologist's management plan. In these cases, ultrasonography may offer the best chance of detecting macular thickening.

B-scan ultrasonography as a modality to detect macular thickness does have limitations, however. The few cases in which ultrasound findings did not match those of the clinical examination occurred in eyes with very subtle retinal thickening. B-scan ultrasonography is neither as accurate nor as sensitive as OCT in detecting and quantitating retinal thickness. Therefore, whenever possible, an OCT or a retinal thickness analyzer[13] would be the preferable option to measure retinal thickening.

The accuracy of B-scan ultrasonography in detecting macular thickening is ultimately dependent on the operator's ability, technique, and experience. Interestingly, one false positive reading during B-scan ultrasonography occurred when a suspended pseudo-operculum was mistakenly interpreted as macular thickening. Others, however, have demonstrated that B-scan ultrasonography can reliably detect macular operculum and pseudo-operculum.[14–16] The ultrasound probe in those reports, unlike our study, was placed directly on the open eye allowing for close monitoring of patient fixation. Patient fixation is less reliably assessed through closed eyelids and may have contributed to our inability to differentiate pseudo-operculum from macular thickening.

This study does have the limitations of a relatively small sample size. Furthermore, the reported sensitivity and specificity of B-scan ultrasonography to detect macular thickening reflect the experience of one single operator with over a decade of ultrasonography experience. Lastly, our results were obtained using a single instrument, the I^3 System-ABD Diagnostic Ophthalmic Ultrasound (Innovative Imaging, Sacramento, California, USA). Extrapolating our results to other B-scan machines should be done cautiously because of likely differences between instruments.

Detection of macular thickening with B-scan ultrasonography correlates highly with findings on slit-lamp biomicroscopy, FA, and OCT. In cases where retinal visualization is impossible, or when inadequate patient cooperation precludes FA or OCT, ultrasonography provides a reliable method to detect macular thickening.

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