

High-resolution Stereoscopic Digital Fundus Photography versus Contact Lens Biomicroscopy for the Detection of Clinically Significant Macular Edema

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Purpose: The purpose of this study was to compare high-resolution stereoscopic digital photography to contact lens biomicroscopy (CLBM) for the diagnosis of clinically significant macular edema.

Study Design: Comparative, prospective, observational case series.

Participants: One hundred twenty diabetic patients.

Methods: Patients underwent clinical retinal examination with CLBM by a retinal specialist. On the same day as clinical grading, patients received high-resolution stereoscopic digital imaging of the macula. The stereoscopic digital images were viewed using liquid crystal shutter goggles at least 2 months after clinical examination by a single masked grader for the presence or absence of diabetic retinopathy.

Main Outcome Measures: Presence or absence of the Early Treatment of Diabetic Retinopathy Study criteria for clinically significant macular edema (CSME) overall, CSME 1, CSME 2, CSME 3, macular edema, microaneurysms, intraretinal hemorrhage, and hard exudate.

Results: Two hundred seven eyes of 105 patients had complete data sets from both diagnostic modalities. Exact agreement was high for all identified pathologic conditions: CSME overall, 83.6%; CSME 1, 83.6%; CSME 2, 96.1%; CSME 3, 88.5%; macular edema, 75.0%; microaneurysms, 77.9%; intraretinal hemorrhage, 83.7%; and hard exudate, 73.1%. Sensitivity ranged from 50.0% (CSME 2) to 90.6% (CSME overall). Specificity ranged from 90.0% (macular edema) to 99.0% (CSME 2).

Conclusions: High-resolution stereoscopic digital photography is both sensitive and specific when identifying CSME and correlates well with the accepted standard of CLBM for the diagnosis of CSME. *Ophthalmology* 2002;109:267-274 © 2002 by the American Academy of Ophthalmology.

One of the first recorded examples of telemedicine was in 1642 when Theophraste Renaudot created a booklet¹ that would allow the sick and suffering to obtain a diagnosis through the mail. Teleophthalmology is a much more recent phenomenon that began with slide film photography² but has now progressed to transmission of digital images from remote locations. Digital imaging of the fundus has been in development for more than two decades for use in a variety of ophthalmologic applications such as glaucomatous cup

assessment,^{3,4} macular pigment analysis,⁵ fluorescein angiography,⁶ and, more recently, for teleophthalmology.⁷⁻¹²

Although several groups have looked at the use of digital imaging for diabetic retinopathy,^{7-9,13} most have evaluated the technology for use as a screening tool. Because stereoscopic film photography has been the standard method to determine the severity of diabetic retinopathy in a number of clinical trials,¹⁴⁻¹⁷ digital photography may also be able to accurately assess patients for treatable diabetic retinopathy. If so, patients could be assessed via teleophthalmology with high-resolution stereoscopic digital imaging and followed at a distance until they require transfer to a tertiary care center for treatment. However, the accepted standard for the diagnosis of clinically significant macular edema (CSME) has been contact lens biomicroscopy (CLBM). The purpose of this study was to evaluate whether diabetic retinopathy and CSME can be identified with high-resolution stereoscopic digital imaging and whether this identification correlates with the accepted standard of CLBM.

For our study, we used the Early Treatment of Diabetic Retinopathy Study definition¹⁸ of CSME. CSME type 1 is thickening of the retina at or within 500 μm of the center of the macula. CSME type 2 is hard exudates at or within 500

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None of the authors hold any commercial interest relating to the Stereoviewer software (MacDonald Dettwiler and Associates), digital camera (Kodak DCS 560), or Zeiss fundus camera (FF 450).

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μm of the center of the macula, if associated with thickening of adjacent retina (not residual hard exudates remaining after disappearance of retinal thickening). CSME type 3 is a zone or zones of retinal thickening 1 disc area or larger, any part of which is within 1 disc diameter of the center of the macula. We defined macular edema as any retinal thickening not fulfilling the criteria for clinical significance but falling within 2 disc diameters of the center of the macula. Because macular edema is often associated with other diabetic retinal diseases, we also identified microaneurysms, intraretinal hemorrhage, and hard exudate.

Materials and Methods

All new diabetic patients referred to a comprehensive retina practice were eligible for inclusion in the study irrespective of the reason for the referral. Exclusion criteria included: (1) cataract or media opacity obscuring adequate clinical evaluation, (2) inability to have fundus photographs taken because of physical or mental impairment, (3) inability to have photographs taken on the same day as clinical evaluation. The study was approved by the University of Alberta, Faculty of Medicine, Ethics Committee, and all participants gave informed consent. Based on the average number of new diabetic referrals seen monthly, a total of 4 months was allotted to prospectively enroll approximately 100 patients. Study enrollment took place between February 1 and June 1, 2000. Two retinal specialists (BJH and MDJG) enrolled all study patients.

Patients underwent clinical examination of the retina after pupillary dilatation using 1 drop of diophrinyl T in each eye (1% tropicamide and 2.5% phenylephrine, Dioptric Laboratories, Markham, Ontario). A hand-held contact lens (Volk Centralis Direct, Volk Optical Incorporated, Mentor, OH) was used with a slit lamp (Haag Streit BM900, Haag-Streit AG, Gartenstadtstrasse, Switzerland) to evaluate each macula. At this time, the presence or absence of macular edema, CSME 1, CSME 2, CSME 3, microaneurysms, intraretinal hemorrhage, hard exudate, and other disease of note were recorded as present or absent.

Patients then underwent mydriatic, stereoscopic digital fundus photography by a trained ophthalmic photographer using a high-resolution digital camera (Kodak/Canon DCS560, Rochester, NY) attached to a 30-degree fundus camera (Zeiss FF450, Carl Zeiss, Jena, Germany). Digital photographs were taken on the same day as the clinical examination. The digital camera provided 6 megapixel digital photographs (3040×2008 pixels) and was attached by means of a firewire to a Windows NT (Microsoft, Redmond, WA) based Intel Pentium (Intel, Santa Clara, CA) workstation. Nonsimultaneous stereoscopic pairs were captured of the macula (standard field 2)¹⁵ through corneal-induced parallax.¹⁹ Image focus, composition, and exposure were evaluated at the time of capture using the Kodak DCS host software for Windows (Kodak, DCS Twain Data Source v5.9.3). One stereo image pair of the macula was required, but additional photographs of the same field could be captured to ensure at least one stereo photograph of maximal quality. Exposure could be adjusted using the Kodak DCS host software at the discretion of the photographer. Images were saved uncompressed as left and right image files in tagged image file format (TIFF) with a file size of 17.4 megabytes.

A minimum of 2 months between clinical examination and photographic grading was allowed to minimize reader recall. The reader (BJH) was masked to the clinical grading of each eye. Digital photographs of the left eye were reviewed in random order, with a minimum of 2 months before review of right eyes. Images were viewed on a computer monitor (Viewsonic P817 Professional series, Viewsonic Corporation, Walnut, CA) through liquid crystal

diode shutter goggles (Stereographics CrystalEyes Wired, Stereographics Corporation, San Rafael, CA) using three-dimensional viewing software (Stereoviewer, MacDonald Dettwiler and Associates, Vancouver, Canada) (Fig 1). The screen resolution was set to 1024×768 pixels, and the minimum threshold for refresh rate required by the liquid crystal display goggles was set (120 Hz). Monitor brightness and contrast were set to the factory default. Ambient light levels in the room were similar to those used for clinical funduscopic examination. The number of stereo images viewed per eye was at the discretion of the reader, with the sharpest photo being used for the final grading. The reader had the option of zooming in to view the image at the maximum pixel resolution. Image quality was assessed as poor, good, or excellent. The reader recorded the presence or absence of macular edema, CSME 1, CSME 2, CSME 3, microaneurysms, intraretinal hemorrhage, hard exudate, and other diseases of note.

During the enrollment period, there were 139 new patients with diabetes mellitus. Twenty patients (35 eyes) were not eligible for enrollment: Six patients (12 eyes) were physically unable to sit at the fundus camera because of fatigue, prior stroke, incontinence, illness, or physical size. Ten patients (16 eyes) had media opacities preventing adequate clinical evaluation. Six patients (3 eyes) were unwilling to be photographed on the same day as the clinical examination, and 1 patient (1 eye) had retinal disease preventing differentiation of diabetic retinopathy. A total of 232 eyes of 120 patients were examined clinically and received same-day high-resolution stereoscopic digital fundus photography. Eleven patients (19 eyes) were excluded after enrollment because the digital image files were lost, and the photos could therefore not be graded. Five patients who had data on only one eye (three right eyes and two left eyes) were dropped from the analysis. Two hundred eight eyes of 104 patients were included in the final analysis. Power calculations were performed²⁰ to verify that a sample size of 104 patients was adequate to evaluate the extent of agreement between the two diagnostic methods.

Exact agreement between the two diagnostic methods was then calculated. To determine the extent of agreement between the two diagnostic methods, a weighted version of the intraclass correlation coefficient κ^{21} was calculated for the 104 complete pairs of right and left eyes examined by both methods. Instead of carrying out separate analyses for the right and left eyes, or pooling them and ignoring the possible correlation between the eyes, a more efficient approach was adopted that takes into account the binocular or paired nature of the data²² (Table 1). With this approach, there is no need to adjust the standard errors,²³ because well-known existing formulae for the standard errors²⁴ still apply. A full weight of 1 was given to those pairs of eyes when both clinical and digital assessment yielded the same diagnoses, and a weight of 0.5 was given to those when there was agreement in only one eye. The guidelines used for evaluating the κ^{25} were as follows: $0 < \kappa \leq 0.4$ indicated marginal reproducibility, $0.4 < \kappa \leq 0.75$ indicated good reproducibility, and $\kappa > 0.75$ indicated excellent reproducibility. Approximate 95% confidence intervals (CIs) were constructed for the κ values calculated for each of the eight diseases. In addition, tests of the hypothesis $\kappa = 0$ were carried out at a 5% level of significance.

Sensitivity and specificity values were calculated for CSME and macular edema using the accepted standard of CLBM for the diagnosis of CSME. Sensitivity and specificity were not calculated for microaneurysms, intraretinal hemorrhage, or hard exudate because the standard for the detection of these changes (traditional film seven field fundus photography) was not available for comparison. Because the conventional way of calculating sensitivities and specificities does not directly apply to binocular data, sensitivities and specificities were computed in two ways. The first approach, referred to as conventional sensitivity or specificity,

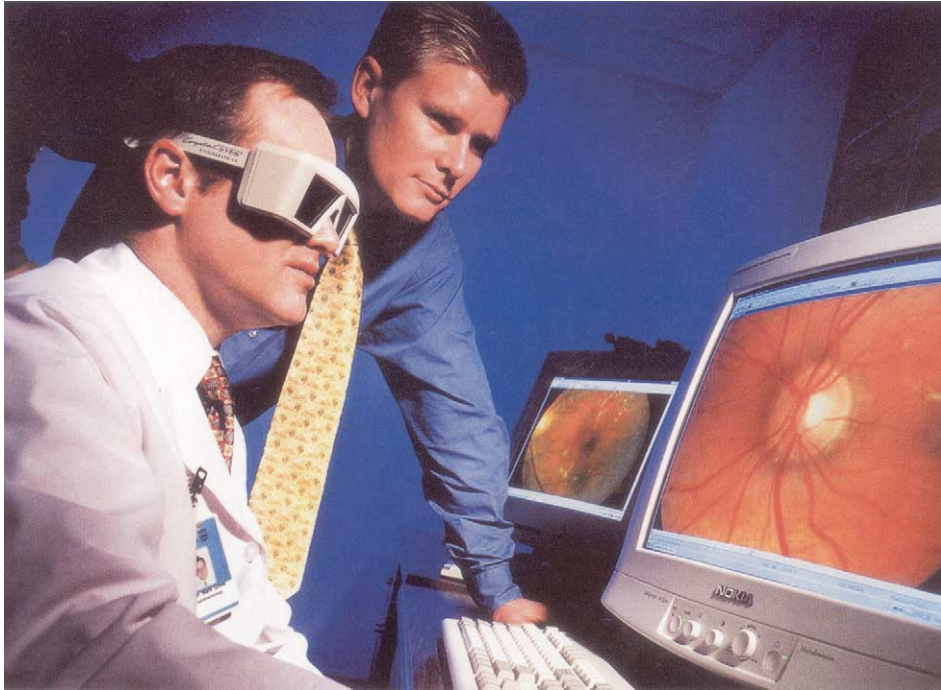


Figure 1. Photograph showing the University of Alberta Tele-Ophthalmology Reading Center. Dr. M. D. J. Greve, wearing the liquid crystal diode shutter goggles, and Dr. M. T. S. Tennant are shown evaluating a high-resolution stereoscopic digital photograph (photograph by Richard Siemens with permission from the *University of Alberta Folio*, 28 April 2000; Vol. 37, Number 16).

ignores the pairing in the data and calculates them the usual way from a total of 208 right and left eyes. The second approach entails looking only at those pairs of eyes where there is perfect agreement between the two diagnostic methods. The latter approach is clearly conservative, because it fails to account for those pairs where there is only partial agreement (that is, there is agreement in only one eye), whereas the former yields possibly inflated values, because it ignores the correlation between the eyes. A more realistic estimate would lie between these two extremes.

Results

Patients ranged in ages from 34 to 87 years, with a median age of 60.2 years; 39.4% of patients were female and 60.6% were male; 83.5% of patients had type 2 diabetes versus 16.5% of patients with type 1 diabetes. Duration of diabetes ranged from 1 month to 38 years, with a median duration of 11.4 years.

For 71 eyes, two stereo images were graded, with the data recorded from the better image. For three eyes, three sets of stereo photographs were graded. For the remaining 134 eyes, only 1 stereo photograph was graded. Thirty-five stereo images were considered of poor quality, 134 were considered good quality, and 39 were considered to be of excellent quality. Fifty-nine eyes had mildly underexposed digital photographs that were adjusted to optimal exposure using the Kodak DCS Twain software.

Gradings were in exact agreement (both examination techniques saying present or both techniques saying absent) between 73.1% (hard exudate) and 96.1% (CSME 2) (Table 2). The κ statistic ranged from 0.310 (95% CI, 0.048, 0.572) for CSME 3 to 0.817 (95% CI, 0.734, 0.900) for intraretinal hemorrhage. The κ statistic indicated excellent reproducibility for CSME overall, CSME 1, and intraretinal hemorrhage. There was good reproducibility for CSME 2, macular edema, microaneurysms, and hard exudate. κ indicated marginal reproducibility for CSME 3.

When examining for CSME overall, the exact agreement between methods was 83.6%, κ 0.812 (95% CI, 0.732, 0.893). CLBM detected this change in at least one eye in 40.4% (42 of 104) of patients. This compared with 45.2% (47 of 104) detection of at least one eye with CSME using stereoscopic, digital photography. Digital photography identified more patients with at least one eye of retinal thickening than did CLBM (Table 3).

When looking at specific eyes, there were 17 eyes of 15 patients in which a disagreement existed between CLBM and digital photography over the diagnosis of CSME (Table 4). Seven of these eyes (41.2%) had poor-quality digital photographs because of media opacity. Four eyes (23.5%) were identified as having macular edema by both diagnostic methods, but digital photography judged the macular edema to fit the definition for CSME 3.

Conventional sensitivity ranged from 50.0% (CSME 2) to 90.6% (CSME overall). Specific sensitivity results were 90.6% for CSME overall, 81.8% for CSME 1, 50.0% for CSME 2, 60.0% for CSME 3, and 82.0% for macular edema (Table 5). Sensitivities calculated based only on perfect agreement between binocular data ranged from 40.0% (CSME 3) to 76.2% (CSME overall).

Conventional specificity ranged from 90.0% for macular edema to 99.0% for CSME 2 (Table 5). Specific specificity results were 92.4% for CSME overall, 94.1% for CSME 1, 99.0% for CSME 2, 95.1% for CSME 3, and 90.0% for macular edema (Table 5). Sensitivities calculated based only on perfect agreement between binocular data ranged from 75.0% (macular edema) to 95.2% (CSME 2).

Discussion

In Canada, it is recommended that all type 2 diabetics be evaluated on an annual basis after diagnosis.²⁶ Canada is a country of enormous geographic boundaries, with the population separated by vast distances. Aboriginal Canadians,

Table 1. Comparison of Digital Photography with Contact Lens Biomicroscopy for the Detection of Diabetic Retinal Pathologies in 104 Pairs of Right (R) and Left (L) Eyes (+ for Presence, - for Absence)

	Digital				Total
	R+L+	R+L-	R-L+	R-L-	
Clinical	18 ¹	3	1	0	22
	13 ²	4	1	1	19
R+L+	0 ³	0	0	0	0
	0 ⁴	0	0	0	0
	21 ⁵	4	2	1	28
	42 ⁶	3	7	3	55
	42 ⁷	7	2	1	52
	26 ⁸	5	1	0	32
R+L-	1	7	0	2	10
	2	6	0	2	10
	0	0	0	1	1
	0	2	0	0	2
	1	7	0	3	11
	3	4	0	3	10
	1	3	0	1	5
	0	3	0	4	7
R-L+	3	0	7	0	10
	1	0	5	1	7
	0	0	2	1	3
	1	0	0	2	3
	4	0	4	3	11
	1	1	1	1	4
	0	1	2	1	4
	3	3	3	2	11
R-L-	0	5	2	55	62
	1	3	1	63	68
	0	0	2	98	100
	0	4	5	90	99
	0	4	4	46	54
	0	0	1	34	35
	0	0	3	40	43
	2	5	3	44	54
Total	22	15	10	57	104
	17	13	7	67	
	0	0	4	100	
	1	6	5	92	
	26	15	10	53	
	46	8	9	41	
	43	11	7	43	
	31	16	7	50	

¹CSME overall, ²CSME 1, ³CSME 2, ⁴CSME 3, ⁵macular edema, ⁶microaneurysm, ⁷intraretinal hemorrhage, ⁸hard exudate.

who have a prevalence of diabetes mellitus type 2 up to 6.7 times that of whites,²⁷ are in large part concentrated in rural areas far from the retina specialists in tertiary care centers. Traditional methods, whereby a general ophthalmologist or retina specialist travels to a remote location to evaluate patients with diabetes mellitus, are inefficient, given the high volume of patients within urban centers. Screening strategies for diabetic retinopathy have been under investigation for many years. We propose an alternative to the notion of "screening" and offer instead the opportunity to perform distance evaluation using stereoscopic digital fundus photography.

The accepted standard for the diagnosis of CSME has been CLBM. The Early Treatment of Diabetic Retinopathy Study²⁸ reported an agreement of 81%, κ 0.61 between

CLBM and traditional stereoscopic film photography for the detection of treatable macular edema. In their study, retinal specialists detected more eyes with CSME using CLBM than graders did with stereoscopic film photography. Our study has higher correlation, with an exact agreement of 83.6%, κ of 0.812 (95% CI, 0.732, 0.893) for the detection of any form of CSME. Although our study compared two different formats, the readers were retina specialists for both formats. There may be several explanations for why they detected more CSME with digital photography than with clinical examination.

With a high-resolution video display, a reader is able to examine a macula at much greater magnification than is possible clinically or with film photographs. Although magnification does not increase the overall resolution of a digital image, it does allow the reader to examine small details that may not be apparent at a macroscopic view. In addition, when grading diabetic retinopathy, the reader is allowed an unlimited and unobstructed examination of retinal detail. Patient movement, discomfort with a contact lens, or outside distraction does not affect examination. Finally, with the three-dimensional viewing software, the reader can measure retinal distances calibrated to optic disc size and accurately determine whether retinal thickening has clinical significance.

Retinal thickening of any type was identified in at least one eye of almost the same number of patients (50 eyes by CLBM, 51 eyes by digital photography) with both diagnostic formats, with the difference being the assessment of whether macular edema was clinically significant. Digital photography judged more macular edema as clinically significant (47 patients) than did CLBM (42 patients). Although one explanation for this discrepancy is that stereoscopic digital photography is actually more sensitive than CLBM, it is equally likely that there were false-positive results with digital imaging. If the latter explanation is correct, we would prefer false-positive results when using the digital system in a teleophthalmology application, because these positives result in a patient being referred to a tertiary care center for reevaluation. Patients would then be assessed clinically, and the decision to treat would be based on that examination.

CSME 3 in particular was diagnosed more often with stereoscopic digital photography than with CLBM. Four eyes of four patients were diagnosed with macular edema by clinical examination, but, when measured with the digital software, the retinal thickening was found to lie within 1 disc diameter (Fig 1). The three-dimensional viewing software includes a measurement tool calibrated to optic nerve size and allows very accurate measurement of retinal thickening from the macular center. This tool may allow an examiner to be more precise about the diagnosis of CSME, particularly for types 2 and 3, in which exact retinal distance is required for accurate diagnosis.

Other discrepancies arose when the clinical examiner using CLBM judged the retinal thickening to be within 500 μ m (CSME 1), when by digital imaging the retinal thickening seemed to be outside that margin (four eyes of four patients). One eye had digital photographs of excellent quality in which retinal thickening 500 μ m from the center

Table 2. Comparison of Stereoscopic High-resolution Digital Imaging with Clinical Examination with Contact Lens Biomicroscopy for Detection of Some Features of Diabetic Retinopathy

Pathology	Exact Agreement (%)	Kappa	Standard Error	95% Confidence Interval	Two-tailed P Value
CSME overall	83.6	0.812	0.041	(0.732, 0.893)	<0.001
CSME 1	83.6	0.763	0.053	(0.659, 0.867)	<0.001
CSME 2	96.1	0.485	0.219	(0.057, 0.914)	<0.001
CSME 3	88.5	0.310	0.134	(0.048, 0.572)	<0.001
Macular edema	75.0	0.722	0.048	(0.628, 0.816)	<0.001
Microaneurysms	77.9	0.738	0.051	(0.638, 0.838)	<0.001
Intraretinal hemorrhage	83.7	0.817	0.042	(0.734, 0.900)	<0.001
Hard exudate	73.1	0.671	0.057	(0.560, 0.782)	<0.001

of the macula, and therefore CSME 1, was identified. Clinical examination of this same eye graded it as CSME 3. Chart review of a 6-week follow-up visit showed that at that time, clinical reexamination with CLBM identified CSME 1. Fluorescein angiography demonstrated focal leakage from a site within 500 μm from the center of the macula. These differences account for the poor sensitivity of diagnosing CSME types 2 and 3 with stereoscopic digital imaging.

To our knowledge, only one previous reported study has evaluated whether digital photography can be used to diagnose CSME. Lim et al¹³ looked at the identification of diabetic retinopathy using a low-resolution, nonmydriatic, nonstereo, digital camera. Their camera had a 640 × 480 pixel, or 0.31 megapixel, resolution. They took three digital images: one shot of the disc and macula, and one each of nasal and temporal retina. Their results showed an exact agreement between standard stereoscopic film photography and digital imaging of 89.7%, κ 0.38 ± 0.15, indicating marginal reproducibility. Our digital camera, with almost 20 times the resolution and a stereoscopic viewing system likely accounts for the improved performance compared with their study.

There is some controversy as to whether such a high-resolution digital camera is even necessary, given that most computer monitors cannot display an entire image at its source resolution. In our study, we displayed 6 megapixel images on a monitor set to a resolution of 1024 × 768 pixels, or 0.786 megapixels (the reader was able to view the image at full resolution, although only a small portion of the image could fit on the screen). Because all 6 million pixels cannot fit onto this screen size at the same time, the computer has to decide, based on complex display algorithms, what color of pixel to display. Color averaging is one of the

ways a computer does this. Each pixel the Kodak DCS 560 digital camera acquired has 12 bits of information attached to it to determine its color. Because there are 7.6 pixels in the original digital image file per displayable pixel, one of the ways a computer handles this excess data is to average the colors of those 7.6 pixels to produce a new color for the displayed pixel. This averaging results in less pixelation artifact. Contributing further is that color averaging occurs at 32-bit true color in the video card that produces smoother transitions and thus better resolution. An image captured by a 0.786 megapixel charged coupled device (CCD) array is not only inherently grainier than the 6-megapixel image, but is displayed only in 12-bit color because color averaging never comes into effect.

Numerous studies have compared clinical examination to traditional stereoscopic film fundus photography. The major thrust behind these studies was to validate a camera or protocol for screening of diabetic patients and not to evaluate specifically CSME.²⁹⁻³² Correlation between clinical examination and graded photographs for the diagnosis of any form of diabetic retinopathy was good, provided broad categories were used to measure agreement. Our goal for high-resolution stereoscopic digital photography was to be able to precisely diagnose CSME rather than simply sort patients into a present or absent dichotomy.

Kiri et al³³ reported on the use of a camera designed to take simultaneous stereo photographs on traditional film. They found a 67% agreement (κ 0.52; 95% CI, 0.41-0.64) between the Nidek camera (Nidek Technologies Inc., Pasadena, California) and CLBM. An explanation for this low exact agreement may be found in a figure of a single split-frame 35-mm Nidek 3Dx stereo photograph that seems to cover only a small area of the macula. From that particular photo, it would be difficult to estimate retinal distances. In addition, it would be difficult to diagnose CSME 3 without being able to judge the area of retinal thickening that lies outside the frame of the photograph.

Lee et al³⁴ compared clinical examination using a non-contact 90-D lens and nonmydriatic, nonstereo, fundus photography. Although they did not attempt to differentiate CSME, they did report an exact agreement of 91.9% (κ 0.440; 95% CI, 0.324-0.557) for macular edema. Our study achieved a much lower exact agreement for macular edema, although a more reproducible one. Lee et al, because they were using nonstereo photography, defined macular edema

Table 3. Number of Patients (n = 104) Identified with at Least One Eye of Retinal Thickening by Subtype with each Diagnostic Modality

Modality	CSME				Macular Edema
	overall	CSME 1	CSME 2	CSME 3	
CLBM	42	36	4	5	50
Digital	47	37	4	12	51

CLBM = contact lens biomicroscopy; CSME = clinically significant macular edema.

Table 4. Specific Eyes in Which Contact Lens Biomicroscopy and Digital Photography Differ in Their Diagnosis of Clinically Significant Macular Edema Overall

Eye	Clinically Significant Macular Edema Overall (Present/Absent)		Macular Edema (Present/Absent)		Clinically Significant Macular Edema Type	Digital Image Quality	Grading Notes
	Contact Lens Biomicroscopy	Digital	Contact Lens Biomicroscopy	Digital			
8	Absent	Present	Absent	Present	1	Good	—
25	Present	Absent	Present	Absent	1	Poor	Questioned the possibility of thickening around the hard exudate
29	Absent	Present	Present	Present	1	Excellent	Very clear image
35	Absent	Present	Present	Present	3	Poor	Borderline retinal distance measurement: 1750 μm
36	Absent	Present	Present	Present	3	Good	Thickening within 640 μm of macular center
46	Present	Absent	Present	Absent	1	Poor	—
47	Present	Absent	Present	Absent	1	Poor	Cataract; very hazy view
53	Present	Absent	Present	Absent	1	Poor	Cataract; very hazy view
54	Present	Absent	Present	Absent	2	Poor	Cataract; very hazy view
63	Absent	Present	Absent	Present	1	Good	Retinal thickening around foveal microaneurysms
68	Absent	Present	Absent	Present	1	Good	Very faint retinal thickening 500 μm from the fovea
83	Absent	Present	Absent	Present	1	Excellent	
94	Present	Absent	Present	Absent	1	Good	Cotton-wool spot present
119	Absent	Present	Absent	Present	1	Good	
155	Present	Absent	Present	Absent	1	Poor	Very hazy; difficult to grade
183	Absent	Present	Present	Present	3	Good	Retinal thickening 1041 μm from macular center
186	Absent	Present	Present	Present	3	Good	Retinal thickening 1192 μm from macular center

as the “presence of hard exudate in a configuration to suggest edema in the center of the macula,” and had a positive identification of this in 10.2% of patients evaluated ophthalmoscopically. In contrast, macular edema was identified using CLBM in 48% of patients (49% by means of digital photography). Thus, the number of eyes identified as not having macular edema bolstered their significantly higher agreement for macular edema.

One limitation of our study is the exclusion of 19 eyes of 11 patients from the final analysis. These eyes were excluded because the digital photograph files were erased

accidentally by a technician and could therefore not be graded. This is perhaps a criticism of the digital format, as well as the robustness of a research computer system.

Despite the use of digital photography and evaluation of the image at the time of capture, 59 photographs (59 eyes) were underexposed and required an adjustment using software. Kodak’s DCS Twain host software uses a slider bar for exposure compensation. This adjusts both brightness and contrast together simulating ± 2 f-stops of exposure. Adjustment of the images was at the discretion of the photographer and accomplished within seconds of selecting a new setting. Adjustments were completely reversible and did not alter the source image. From our experience with more than hundreds of patients, changing the exposure to within ± 1 f-stop digitally has the same effect as adjusting the f-stop on the Zeiss camera itself. Given that standard film characteristics like International Standards Organization (ISO) rating, which reflects the light sensitivity of film to light, are user-determined, digital settings on the camera, the likelihood of creating an artifact that could have an impact on the stereoscopic effect, or the accuracy of diagnosis, is extremely low.

Several questions remain about teleophthalmology and diabetic retinopathy. Should patients with diabetes mellitus be screened for the presence of diabetic retinopathy? Rather, should we attempt to identify those that require treatment and then clinically examine only those few? In countries such as Canada and Australia, where distances are great, the cost of travel necessitates diagnosis and grading at a dis-

Table 5. Sensitivity and Specificity of High-resolution Stereoscopic Digital Photography to Detect Retinal Thickening Compared with Contact Lens Biomicroscopy

Pathology	Sensitivity	Specificity
CSME overall	90.6 (76.2)*	92.4 (84.1)*
CSME 1	81.8 (66.7)*	94.1 (87.0)*
CSME 2	50.0 (50.0)*	99.0 (96.2)*
CSME 3	60.0 (40.0)*	95.1 (88.5)*
Macular edema	82.0 (64.0)*	90.0 (75.0)*

*Values obtained when calculations are performed only on pairs of eyes where there is perfect agreement between the two diagnostic methods.
CSME = clinically significant macular edema.

tance, thereby allowing only those patients in need of treatment to travel to the retina specialist.

Do we need to incorporate stereopsis into a teleophthalmology platform, or are two-dimensional photographs adequate? Screening does not require stereopsis, but distance evaluation does. Typical systems that forego stereopsis are those that use a nonmydriatic camera. The time required to take a stereo photograph is minimally more than for non-stereo. If the capability exists and its implementation is efficient, what reason remains not to incorporate stereo into a teleophthalmology platform? If a patient is inadequately examined for the presence of macular edema, potentially treatable diabetic retinopathy may be missed, and irreversible visual loss may result.

What resolution of digital image is necessary? Do we require high-resolution photographs or are low-resolution photographs adequate? Our experience with digital photography is that to resolve the fine detail of retinal disease there must be a minimum acceptable resolution. This practical finding is supported when the results of this study are compared with other studies that used cameras of lower resolution. However, the minimum resolution has not yet been determined.

High-resolution stereoscopic digital imaging does provide a viable alternative to CLBM in the identification of CSME. In addition, the ability to view a stereoscopic digital image until satisfied of the diagnosis, to consult other ophthalmologists without delay in treatment or additional patient discomfort, to educate patients using their own fundus as a tool, and to examine a patient at a distance are significant advantages over clinical examination. Although digital imaging may not be better than CLBM for the diagnosis of CSME, it is at least as effective and therefore suitable for use within a teleophthalmology system for distance evaluation of diabetic retinopathy by ophthalmologists. Further research is needed to assess whether high-resolution stereoscopic digital imaging is comparable to seven-field slide film photography in the identification of nonproliferative and proliferative diabetic retinopathy.

References

1. Renaudot T. La presence des absens. 1642.
2. Karagiannis A, Newland J. Mobile retinal photography. A means of screening for diabetic retinopathy in aboriginal communities. *Aust N Z J Ophthalmol* 1996;24:333-7.
3. Caprioli J, Klingbeil U, Sears M, Pope B. Reproducibility of optic disc measurement with computerized analysis of stereoscopic video images. *Arch Ophthalmol* 1986;104:1035-9.
4. Algazi VR, Keltner JL, Johnson CA. Computer analysis of the optic cup in glaucoma. *Invest Ophthalmol Vis Sci* 1985;26:1759-70.
5. Abadi RV, Cox MJ. The distribution of macular pigment in human albinos. *Invest Ophthalmol Vis Sci* 1992;33:494-7.
6. Rapkin JS, Rapkin KM, Wilson GW. Digital fundus imaging: a comparison with photographic techniques. *Ann Ophthalmol* 1991;23:46-53.
7. Lin DY, Blumenkranz MS, Brothers R, et al. The role of digital fundus photography in diabetic retinopathy screening. Digital Diabetic Screening Group (DDSG). *Diabetes Technol Ther* 1999;1:477-87.
8. Tennant MTS, Rudnisky CJ, Hinz BJ, et al. Tele-ophthalmology via stereoscopic digital imaging. a pilot project. *Diabetes Technol Ther* 2000; 2:583-7.
9. Tennant MTS, Greve MDJ, Rudnisky CJ, et al. Identification of diabetic retinopathy by stereoscopic digital imaging via teleophthalmology: a comparison to slide film. *Can J Ophthalmol* 2001;36:187-96.
10. Rosengren D, Blackwell N, Kelly G, et al. The use of telemedicine to treat ophthalmological emergencies in rural Australia. *J Telemed Telecare* 1998;(Suppl):97-9.
11. Blackwell NAM, Kelly GJ, Lenton LM. Telemedicine ophthalmology consultation in remote Queensland. *Med J Aust* 1997;167:583-6.
12. Camara JG, Rodriguez RE. Real-time telementoring in ophthalmology. *Telemed J* 1998;4:375-7.
13. Lim JI, LaBree L, Nichols T, Cardenas I. A comparison of digital nonmydriatic fundus imaging with standard 35-millimeter slides for diabetic retinopathy. *Ophthalmology* 2000; 107:866-70.
14. The Diabetic Retinopathy Study. Report 7. A modification of the Airlie House classification of diabetic retinopathy. *Invest Ophthalmol Vis Sci* 1981;21:210-26.
15. Klein R, Klein BEK, Moss SE, et al. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol* 1984;102:520-6.
16. Klein R, Klein BEK, Moss SE, et al. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmol* 1984;102:527-32.
17. Grading diabetic retinopathy from stereoscopic color fundus photographs—an extension of the modified Airlie House classification. ETDRS report no. 10. Early Treatment of Diabetic Retinopathy Study Research Group. *Ophthalmology* 1991;98:786-806.
18. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Early Treatment Diabetic Retinopathy Study Research Group. *Arch Ophthalmol* 1985;103:1796-806.
19. Wong D. Textbook of Ophthalmic Photography. Birmingham, AL: Inter-Optics, 1982;76.
20. Cantor AB. Sample-size calculations for Cohen's kappa. *Psychol Methods* 1996;1:150-3.
21. Agresti, A. Categorical Data Analysis. New York: Wiley, 1990;365-70.
22. Schouten HJA. Estimating kappa from binocular data and comparing marginal probabilities. *Stat Med* 1993;12:2207-17.
23. Oden, NL. Estimating kappa from binocular data. *Stat Med* 1991;10:1303-11.
24. Fleiss JL, Cohen J, Everitt BS. Large sample standard errors of kappa and weighted kappa. *Psychol Bull* 1969;72:323-7.
25. Rosner B. Fundamentals of Biostatistics, 4th ed. Belmont, CA: Wadsworth, 1995;423-8.
26. Meltzer S, Leiter L, Daneman D, et al. 1998 clinical practice guidelines for the management of diabetes in Canada. Canadian Diabetes Association. *CMAJ* 1998;199:159(Suppl): S1-29.
27. Evers S, McCracken E, Antone T, Deagle G. Prevalence of diabetes in Indians and Caucasians living in southwestern Ontario. *Can J Public Health* 1987;78:240-3.
28. Kinyoun J, Barton F, Fisher M, et al. Detection of diabetic macular edema. Ophthalmoscopy versus photography. Early Treatment of Diabetic Retinopathy Study report number 5. *Ophthalmology* 1989;96:746-51.
29. Pugh JA, Jacobsen JM, Van Heuven WAJ, et al. Screening for

- diabetic retinopathy. The wide-angle retinal camera. *Diabetes Care* 1993;16:889–95.
30. Schachat AP, Hyman L, Leske MC, et al. Comparison of diabetic retinopathy detection by clinical examinations and photograph gradings. *Arch Ophthalmol* 1993;111:1064–70.
 31. Moss SE, Klein R, Kessler SD, Richie KA. Comparison between ophthalmoscopy and fundus photography in determining severity of diabetic retinopathy. *Ophthalmology* 1985;92:62–7.
 32. Klein R, Klein BEK, Neider MW, et al. Diabetic retinopathy as detected using ophthalmoscopy, a nonmydriatic camera and a standard fundus camera. *Ophthalmology* 1985;92:485–91.
 33. Kiri A, Dyer DS, Bressler NM, et al. Detection of diabetic macular edema: Nidek 3Dx stereophotography compared with fundus biomicroscopy. *Am J Ophthalmol* 1996;122:654–62.
 34. Lee VS, Kinglsey RM, Lee ET, et al. The diagnosis of diabetic retinopathy. Ophthalmoscopy versus fundus photography. *Ophthalmology* 1993;100:1504–12.