THE ACCURACY OF DIGITAL-VIDEO RETINAL IMAGING TO SCREEN FOR DIABETIC RETINOPATHY: AN ANALYSIS OF TWO DIGITAL-VIDEO RETINAL IMAGING SYSTEMS USING STANDARD STEREOSCOPIC SEVEN-FIELD PHOTOGRAPHY AND DILATED CLINICAL EXAMINATION AS REFERENCE STANDARDS

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ABSTRACT

Purpose: To evaluate the accuracy of two digital-video retinal imaging (DVRI) systems to detect diabetic retinopathy.

Methods: A prospective, masked, technology assessment was conducted for two DVRI systems at a tertiary care Veterans Affairs Medical Center. Group A (n = 151 patients) was imaged with a 640×480 resolution system and group B (n = 103 patients) with an 800×600 resolution system. Four retinal evaluations were performed on each patient: DVRI with undilated pupils using one imaging field (U-DVRI), DVRI with dilated pupils using three imaging fields (D-DVRI), dilated clinical examination, and Early Treatment Diabetic Retinopathy Study stereoscopic seven-field photography (ETDRS-P). Two analyses of accuracy were conducted, one using ETDRS-P as a "gold standard" (ETDRS-GS) and one using dilated clinical examination as a "gold standard" (C-GS).

Results: For group A, using the ETDRS-GS, sensitivities of U-DVRI and D-DVRI were 0.66 and 0.66; specificities of U-DVRI and D-DVRI were 0.66 and 0.86. Using the C-GS, sensitivities of U-DVRI and D-DVRI were 0.79 and 0.80; specificities of U-DVRI and D-DVRI were 0.68 and 0.85. For group B, using the ETDRS-GS, sensitivities of U-DVRI and D-DVRI were 0.76 and 0.85; specificities of U-DVRI and D-DVRI were 0.45 and 0.80. Using the C-GS, sensitivities of U-DVRI and D-DVRI were 0.81 and 0.87; specificities of U-DVRI and D-DVRI were 0.45 and 0.69. For both groups, dilation significantly improved specificities.

Conclusions: The 800×600 resolution DVRI system offers an accurate method of detecting diabetic retinopathy, provided there is adequate pupillary dilation and three retinal images are taken. DVRI technology may help facilitate retinal screenings of growing diabetic populations.

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INTRODUCTION

Diabetes mellitus is now one of our nation's top health concerns. In 1999, Eli Lilly and Company built the largest factory dedicated to the production of a single drug in pharmaceutical history. The drug, with 24% year-on-year sales growth, is insulin.[1] In 2002, 1.3 million new cases of diabetes mellitus were diagnosed in Americans aged 20 years or older.[2] Currently, 18.3% of Americans 60 years and older are diabetic, and 6.3% of the entire US population has the disease.[2] Diabetes strikes individuals of all ages and socioeconomic groups. Each year, over 200,000 people die as a result of diabetes and diabetic retinopathy causes 12,000 to 24,000 new cases of blindness.[2] The annual cost of diabetes in the United States has been reported to be $132 billion.[2] Diabetes mellitus ranks as one of the most deadly, most visually threatening, and most costly diseases known to mankind.

Diabetic retinopathy, a microvascular disease characterized by retinal microaneurysms, hemorrhages, exudates, and vascular proliferation, is a common complication of diabetes mellitus. Twenty years after the onset of diabetes, over 90% of people with type 1 diabetes and over 60% of individuals with type 2 diabetes will have diabetic retinopathy.[3,4]

The scientific basis for current management of diabetes retinopathy is provided by five large multicenter

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clinical trials: the Diabetic Retinopathy Study,[5-10] the Early Treatment Diabetic Retinopathy Study (ETDRS),[11-35] the Diabetic Retinopathy Vitrectomy Study,[36-40] the Diabetes Control and Complications Trial,[41-51] and the United Kingdom Prospective Diabetes Study.[52-57] Laser photocoagulation has been the mainstay of treatment for diabetic retinopathy for the past quarter century. In 1976, the Diabetic Retinopathy Study Research Group published its preliminary report demonstrating the overwhelming benefit of scatter (panretinal) laser photocoagulation for proliferative retinopathy.[58] Nine years later, the ETDRS showed that focal retinal photocoagulation could reduce moderate visual loss from clinically significant macular edema.[59] Good glycemic control[60] and tight blood pressure control[61] have also been shown to retard the progression of retinopathy. Current standards of care can reduce the risk of severe vision loss from diabetic retinopathy to less than 2%.[62]

Despite treatments of proven efficacy, however, diabetic retinopathy continues to be a major cause of blindness[63] and is, in fact, the leading cause of blindness in people under the age of 60 years in industrialized countries, including the United States.[64] Delay in treatment is the main reason for the visual loss and is largely preventable with proper screening.[65] To detect diabetic retinopathy at an optimal stage for intervention, many professional societies in the United States, including the American College of Physicians, the American Diabetes Association, and the American Academy of Ophthalmology, recommend that patients with diabetes receive an annual dilated fundus examination from a qualified eye care provider.[66] The Department of Veterans Affairs has also established performance standards for regular dilated fundus examinations of diabetic patients.[67] Annual eye examination of diabetics has been incorporated into the Health Plan Employer Data and Information Set quality guidelines, adopted throughout the managed care industry. Despite these recommendations, reports indicate that only 35% to 50% of managed care patients actually receive the recommended eye examination in a given year.[68] Similar low rates of retinal evaluations are reported in Medicare beneficiaries[69,70] and the National Health Interview Survey.[71] The current challenge is to access and identify all diabetic patients for regular periodic retinal evaluations. Computer modeling studies have suggested that if appropriate screening and optimally timed photocoagulation treatments for diabetic retinopathy were employed, annual health care expenditures could be reduced by $250 to $500 million per year.[72-74] In addition, over 1,000,000 person-years of sight could be saved if all diabetics had appropriately timed ophthalmic screening and treatment.[75] With such a prevalent and costly disease, and one for which proven treatments exist, there is a critical need for a sensitive and cost-effective screening method.

Background

The optimal strategy for detecting diabetic retinopathy in the large diabetic population is unclear. In addition to clinical evaluations by qualified eye care providers, the mainstay of diabetic eye screening in the United States, other modalities including film-based photography programs are in widespread use, especially in Europe. Several new digital imaging systems for detecting diabetic retinopathy also have been recently reported.

In the United States, there is currently no central agency to oversee, regulate, advise, or perform health technology assessment, so research to address issues raised by new health technology is highly variable in quality.[76] Indeed, Mason and coworkers[77] reviewed the published literature regarding systems for diabetic retinopathy detection and concluded that programs are very difficult to compare on account of inconsistencies and inconclusive evidence. In the United Kingdom, the British Diabetic Association Working Group proposed in 1997 that screening programs should demonstrate a sensitivity of 0.80 when compared to established reference (gold) standards.[78] In the United States, however, standards for sensitivities of systems to detect diabetic retinopathy have not been set.

Detection of Diabetic Retinopathy in the Research Setting: The ETDRS Retinopathy Severity Scale

The ETDRS Final Retinopathy Severity Scale[79] was developed using ETDRS control data to define severity levels of increasing risk of developing neovascularization. In addition to diabetic retinopathy levels, the ETDRS defined stages for diabetic macular edema, which included a subgroup with "clinically significant macular edema." Patients in this subgroup showed the greatest benefit from macular (focal) photocoagulation.[80]

The ETDRS Final Retinopathy Severity Scale involves photographing seven specifically defined fields of each retina with a stereoscopic pair of images (for a total of 14 images of each retina), which are later graded according to strict protocol. ETDRS levels of retinopathy severity were used in the Diabetes Control and Complications Trial.[81] Although this protocol is the most accurate at detecting diabetic retinopathy and is widely used in well-funded large trials, the cost of performing this level of diagnostic evaluation for the large diabetic populations of developed countries makes this method impractical for widespread use.

The ETDRS Final Retinopathy Severity Scale is the only validated reference standard for the detection and staging of diabetic retinopathy. For this reason, the ETDRS grading protocol has recently been referred to by Lee[82] as the "criterion standard" and several years ago by Singer and coworkers[83] as the "gold standard" for the

accurate detection of diabetic retinopathy.

Detection of Diabetic Retinopathy in the Clinical Setting

Dilated Clinical Examination. A dilated clinical examination using ophthalmoscopy, performed by a qualified eye care provider, is currently the most widely accepted and readily available method of detecting diabetic retinopathy in the United States today. Clinical examination may involve direct or indirect ophthalmoscopy as well as slit-lamp biomicroscopy, and most studies report this being done after pupillary dilation. In a recent systematic review of English language literature published between 1983 and 1999, Hutchinson and coworkers[84] showed that the reported sensitivity of ophthalmoscopy by health professionals in detecting diabetic retinopathy ranged from 0.13 (by junior hospital physicians detecting proliferative retinopathy) to 0.84 (by an ophthalmologist detecting any retinopathy). Of the six reported studies using ophthalmologists to perform ophthalmoscopy, the mean of the reported sensitivities was only 0.61, well below the British Diabetic Association Working Group proposed sensitivity cut-off of 0.80.

Dilated Film-Based Fundus Photography. Outside the United States, dilated fundus photography is a widely accepted method of detecting diabetic retinopathy in developed countries, mainly in European countries. Most reported studies included in the review of Hutchinson and coworkers[84] used wide-angle (45 degree) retinal photography, with sensitivities exceeding 0.80. Single-field, wide-angle fundus film-based photography, although less costly than standard stereoscopic seven-field ETDRS photography, nonetheless, requires expensive camera equipment, highly trained photography personnel, and pupillary dilation.

Digital Imaging Systems. Several newly introduced digital imaging systems for the retina have been evaluated in the recent literature and may offer advantages over film-based photographic programs. The new digital systems differ widely in technological parameters such as pixel resolution and the ability to perform stereoscopic analysis. They also have wide variation in cost and in the need for pupillary dilation. Several of the recently published evaluations have compared new digital imaging systems to the "gold standard" ETDRS Scale using stereoscopic seven-field photography.

Bursell and coworkers[85] from the Joslin Vision Network Research Team reported moderate agreement ($\kappa = 0.65$) between the clinical level of diabetic retinopathy assessed from undilated stereoscopic digital images and the dilated "gold standard" 35-mm ETDRS photographs. The sensitivity of their system for detecting mild or moderate nonproliferative retinopathy was 0.86, but for detecting severe or very severe nonproliferative retinopathy was only 0.57. The Joslin Vision Network system includes a nonmydriatic fundus camera interfaced to a standard color video camera. Stereo image viewing is achieved using liquid crystal display shuttered goggles.

Fransen and coworkers[86] from the Inoveon Health Research Group recently showed that the DR-3DT digital imaging system had a sensitivity of 0.98 compared to the film-based ETDRS "gold standard." The system requires pupillary dilation and has a spatial resolution of 1,152×1,152. Liquid crystal shutter glasses were used for the stereo viewing of the DR-3DT system. The authors have a financial interest in the Inoveon Corporation.

Lin and associates[87] of the Digital Diabetic Screening Group conducted a study to evaluate a single-field digital monochromatic nonmydriatic system using Ophthalmic Imaging Systems technology compared to ETDRS "gold standard" photographs and to dilated ophthalmoscopy by an ophthalmologist. They showed a sensitivity of 0.78 of the digital imaging system compared to ETDRS standard photography. (Sensitivity of ophthalmoscopy by ophthalmologists was 0.34.) They did not test the imaging system with pupillary dilation. Two of the authors had a financial relationship with Ophthalmic Imaging Systems.

Massin and coworkers[88] recently reported an evaluation of the Topcon TRC-NW6S digital imaging camera with an 800×600 resolution. Using five overlapping fields imaged through an undilated pupil, they reported sensitivities ranging from 0.92 to 1.00 for moderately severe to severe retinopathy, using ETDRS photographs as the reference standard.

Numerous other reports have been published recently describing comparisons of digital imaging technology to reference standards that have not been validated, including the clinical examination of various eye care providers.[89-95] These will not be discussed further because the methodology was inadequate to assess the efficacy of the technology.

Purpose of Study

This study was undertaken to rigorously assess two commercially available "nonmydriatic" digital-video retinal imaging (DVRI) systems for their ability to accurately screen for diabetic retinopathy.

Hypothesis

Based on assessments of clinical accuracy, one or both digital-video retinal imaging (DVRI) systems is an acceptable method of screening for diabetic retinopathy.

METHODS

A prospective, masked, clinical technology assessment was conducted at a tertiary care Veterans Affairs Medical

Center. The primary outcome measure was accuracy (sensitivity, specificity, and predictive values) of each DVRI system compared to standard ETDRS stereoscopic photographs, the "gold standard." The secondary outcome measure was accuracy compared to dilated clinical examination, the "clinical gold standard."

Subjects

Approval of the Minneapolis Veterans Affairs Medical Center Institutional Review Board was obtained before initiation of the study. Patients with a diagnosis of diabetes mellitus were recruited from the Eye Clinic at the Minneapolis Veterans Affairs Medical Center. The diagnosis of diabetes mellitus was verified in the patient's medical record. To meet the eligibility requirements for the study, the patient must have had at least one eye without previous retinal laser treatment for diabetic retinopathy (panretinal photocoagulation or focal macular photocoagulation). If the fellow eye had previous laser treatment, only the previously untreated eye was entered into the study. The sampling of patients was nonrandom to ensure a distribution of retinopathy levels broad enough to encompass the full range of retinopathy severities. Demographic and historical data was collected from each patient and/or the patient's medical record. A unique nonsequential patient identifier number was assigned to each enrolled patient. The patient identification number was the only identifier used on all digital and photographic images. The patient's date of birth, sex, race, year of diagnosis of diabetes, current diabetic treatment, most recent hemoglobin A_{1C} level, and comorbid ocular conditions were included in the data collection.

Clinical Protocol

On the day of the study evaluation, all patients signed a consent form in accordance with Institutional Review Board guidelines. Distance visual acuity with spectacle correction, undilated pupillary measurements, and DVRI through an undilated pupil were performed. After intraocular pressures were measured, the pupils were dilated with 2.5% neosynephrine and 1% tropicamide. A study ophthalmologist then performed an eligibility determination by assessing that the ocular media was clear and that the patient had no prior retinal photocoagulation. The patient then returned to the photographer for digital imaging using the same DVRI camera as was used in the predilation state. Seven-field stereoscopic ETDRS photographs were taken using the conventional film-based Topcon fundus camera (model TRC-50VT). The patient was then given a complete ophthalmic examination by an ophthalmologist, including the clinical assessment of retinopathy severity for the study.

Digital Imaging Protocol

Two DVRI systems were used in the study, the Topcon TRC-NW5SF with a 640×480-pixel resolution and the Topcon TRC-NW6S with an 800×600-pixel resolution. Patients imaged with the low-resolution system were assigned to group A, and patients imaged with the high-resolution system were assigned to group B. The same system was used to take photographs prior to and following pupillary dilation for each patient. All DVRI images were taken at a 45-degree field size, in the color mode, with nonstereoscopic images. The infrared viewing light was set at maximum, and the exposure light was set at minimum, but both could be adjusted as required.

The undilated images were taken in a room where the ambient lighting was reduced to a minimum, and the computer monitor was turned away from the patient's line of sight. A minimum of 2 minutes was allowed for pupillary dark adaptation, but a longer adaptation period was used if the patient's pupils were still dilating under observation with the camera's infrared observing light. After recording the size of the undilated dark-adapted pupils, nonstereoscopic images were obtained in each eligible eye. One photographic field (field B), centered on the fovea as depicted in Figure 1, was taken of each eye. Multiple images could be taken in each eye until the photographer judged that the best-quality image was obtained. Care was taken after each image captured to give the pupil time to maximally dilate before taking another image (usually 2 to 3 minutes). The best-quality image for each eye was chosen for grading at a later time, and the inferior images were deleted.

After dilation, the size of the pupil was recorded. Three nonstereoscopic images were then obtained in each eligible eye (fields A, B, and C), as depicted in Figure 1. As above, multiple images were allowed to be taken of each field in each eye until the photographer judged that the best-quality image had been obtained. The best-quality image for each field was chosen for grading at a later time, and the other images were deleted.

The stereoscopic photographs of the seven standard ETDRS photographic fields were then taken using a conventional film-based Topcon fundus camera (model TRC-50VT). Photographs were taken according to the University of Wisconsin–Madison Fundus Photograph Reading Center's Fundus Photography Protocol (adapted from the ETDRS Manual of Operations).

Assessment of Retinopathy Severity by Grading ETDRS Stereoscopic Photographs

The grading of the stereoscopic seven-field ETDRS photographs was performed by an experienced nonphysician grader, certified by the University of Wisconsin–Madison Fundus Photograph Reading Center.

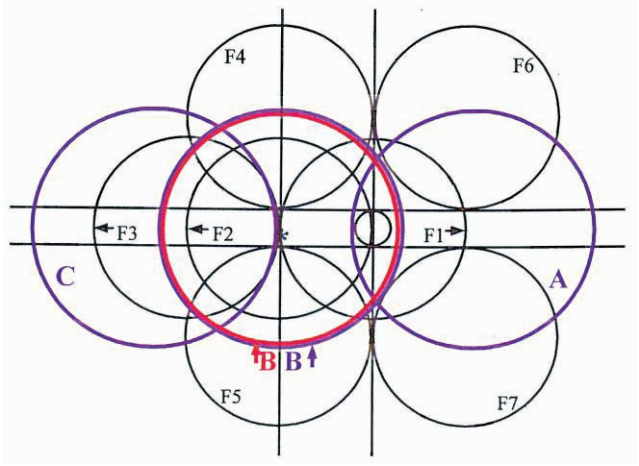

FIGURE 1

Comparison of 45-degree imaging fields to standard Early Treatment Diabetic Retinopathy Study (ETDRS) fields. Designations of the fields taken for the digital-video retinal imaging (DVRI) in relation to the ETDRS seven standard 30-degree fields. One 45-degree field (field B) was imaged through undilated pupils. Three fields (A, B, and C) were imaged through dilated pupils. ETDRS seven standard 30-degree fields: field 1 (F1) - optic disk centered in the field; field 2 (F2) - macula centered in the field; field 3 (F3) - temporal to the macula; field 4 (F4) - superior temporal; field 5 (F5) - inferior temporal; field 6 (F6) - superior nasal; field 7 (F7), inferior nasal. DVRI 45-degree fields: field A - nasal to optic disk: optic disk is placed at temporal edge of the field; field B - macula centered in the field; field C - temporal to macula: macula is placed at nasal edge of the field.

All photographs were assessed by the same grader, who was masked as to patient identity. Of patients with both eyes included in the study, each eye was graded independently. The eyes from the same patient were sent to the grader in different batches separated in time.

Assessment of Retinopathy Severity by Dilated Clinical Examination

The examining ophthalmologists were given a seven-choice scale to document retinopathy severity in each eye, ranging from level 1 (no apparent retinopathy) to level 6 (proliferative diabetic retinopathy). The definitions of the different levels of retinopathy are defined on the Fundus Examination Form in the Appendix and are very similar to the recently proposed International Clinical Diabetic Retinopathy Severity Scale.[96] A severity level of 7 was given if the level of diabetic retinopathy could not be determined. The examiner was also asked to note the presence of hard exudate within one disk diameter of the center of the macula and/or the presence of macular edema, defined as any retinal thickening within one disk diameter of the center of the macula. The ophthalmologist was able to utilize slit-lamp biomicroscopy or direct or indirect ophthalmoscopy at his or her discretion. A simplified grading scale was used because this is how most clinicians categorize diabetic retinopathy in a clinical setting. ETDRS grading requires counting lesions in each field, which is difficult and arguably impossible to accomplish in a face-to-face setting.

Assessment of Retinopathy Severity by Grading DVRI Images

The images taken using the two DVRI cameras were graded by ophthalmologists in a fashion analogous to the dilated clinical examination, using the seven-choice scale of retinopathy severity, as well as determination of the presence of hard exudates or macular edema. The digital images were evaluated directly on the computer screen. The grader was allowed to use software tools (image contrast enhancement and imaging sharpening) to enhance the images for grading purposes. It was left to the grader's judgment for each individual image to choose the best combination of enhancements for that particular image grading. For undilated DVRI (U-DVRI), only one image was analyzed per eye (Figure 2). Three images were analyzed per eye for dilated DVRI (D-DVRI). The three images were analyzed together to determine the overall grade for the particular eye (Figure 3). The ophthalmologists performing the DVRI evaluations were masked to any previous grading of that same eye. A reading queue was established so that no ophthalmologist performed the clinical ophthalmoscopic examination in the same week as a digital image set from the same patient was evaluated. Different identification numbers were given for the dilated and the undilated image sets, which were reviewed independently.

Criteria for Presence or Absence of Diabetic Retinopathy

As new pharmacologic treatments for diabetic retinopathy are being developed, including antioxidants,[97] protein kinase C inhibitors,[98,99] and advanced glycation end products[100] that are designed to block the development of retinopathy, there will be a growing need for earlier diagnosis. Methods that detect only the more severe levels of diabetic retinopathy will become obsolete. For this reason, we established criteria for the distinction between "disease" and "no disease" at low levels for all methods of evaluation. For the "gold standard" ETDRS photographic levels, "disease" was defined as an ETDRS level ≥20 *or* the presence of clinically significant macular edema. "No disease" was defined as an ETDRS level <20 *and* no clinically significant macular edema.

For the dilated clinical retinal examination, "disease" was defined as retinopathy severity levels 2 through 7 *or* the presence of retinal thickening or hard exudates within one disk diameter of the center of the macula. "No disease" was defined as retinopathy severity level 1 (no retinopathy) *and* no hard exudates.

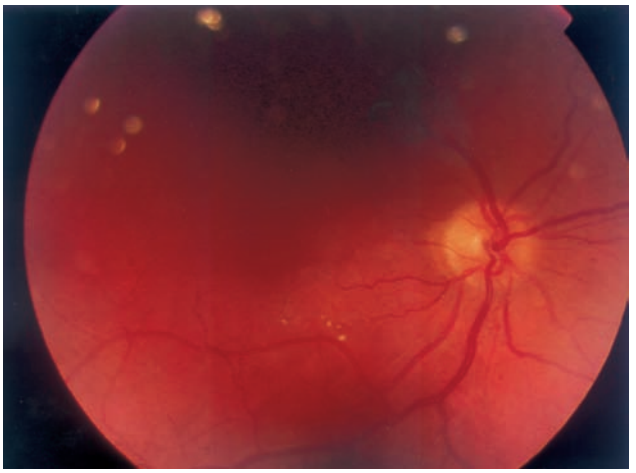

FIGURE 2
Single 45-degree field in an undilated pupil. Field B of the right eye of a 52-year-old man with a 3-mm pupil (undilated) from group B (high-resolution digital-video retinal imaging). Note the superior shadow artifact that obscures a portion of the retina.

The definitions for "referral" and "no referral" for DVRI were analogous to the clinical examination "disease" and "no disease." An eye that was above the threshold for "referral" was defined as retinopathy severity levels 2 through 7 *or* the presence of hard exudates. "No referral" was defined as retinopathy severity level 1 (no retinopathy) *and* no hard exudates.

Statistical Analysis

The study was planned with adequate number of patients to yield expected 95% confidence intervals of 10% or less around the observed measures of accuracy. The variable, "referral" versus "no referral," was dichotomous. The photographic ETDRS severity levels were used to identify *true* "disease" and *true* "nondisease" and served as the reference or "gold standard." Dilated clinical examination is the "clinical standard" for the detection of diabetic retinopathy in the United States. Although there have been no validation studies to confirm its use, the assessment of diabetic retinopathy severity via dilated clinical examination was used as a "clinical gold standard" for calculating measures of accuracy.

Accuracy was assessed using several measures: sensitivity, specificity, false-positive rate, and false-negative rate. In addition, positive predictive value, negative predictive value, and efficiency were calculated for each method. The primary statistical focus was on sensitivity, because of the desire to minimize the number of false negatives. Effective screening programs should have high sensitivity (low false-negative rates), especially at the more severe levels of disease. Another measure of accuracy, given considerable attention, was specificity, because of its ability to describe the false-positive rate. Screening programs with low specificity (high false-positive rates)

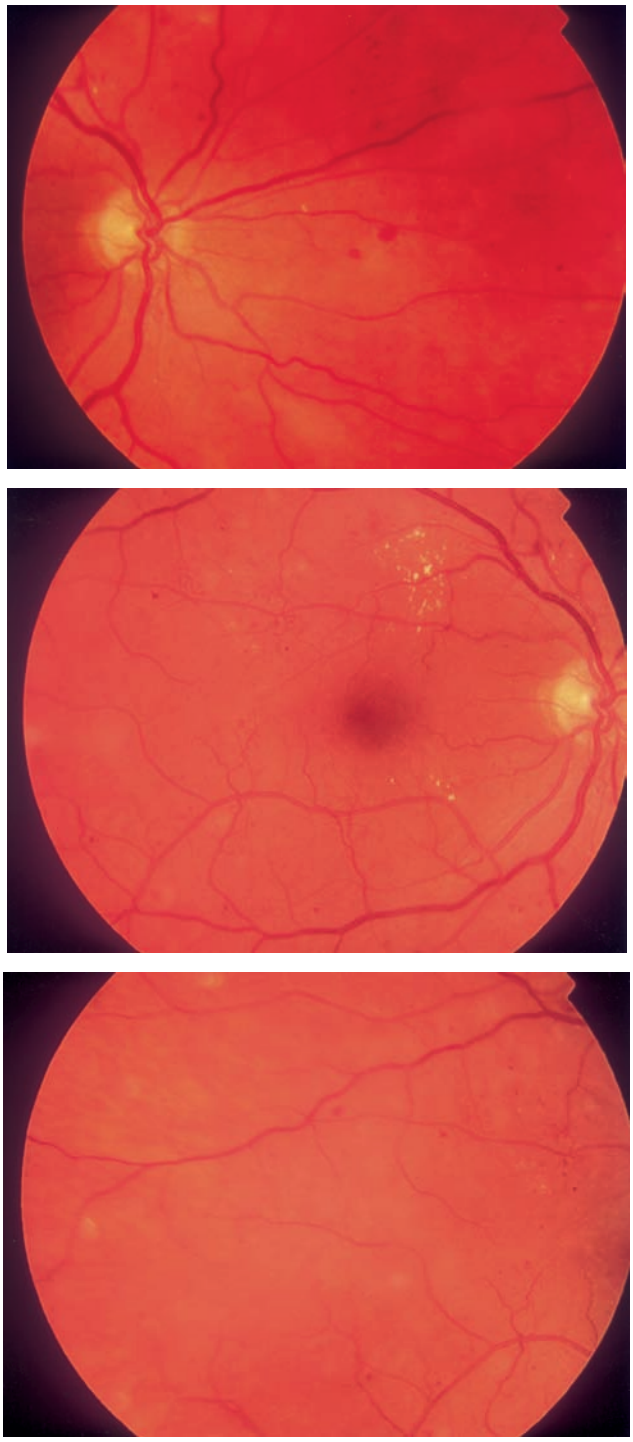

FIGURE 3
Three 45-degree fields in the same eye as in Figure 2 after pupillary dilation. Neovascularization is seen superotemporal to the fovea, which was obscured by shadow artifact in Figure 2.

have low economic utility, because they lead to more, often expensive, testing.

Patients were divided into two groups, depending on the DVRI camera with which they were imaged. Group A was imaged with the 640×480 resolution DVRI camera, and group B was imaged with the 800×600 resolution camera. Accuracy measures were calculated for each of the three methods of retinal evaluation: DVRI through an undilated pupil using one imaging field (U-DVRI), DVRI through a dilated pupil using three imaging fields (D-DVRI), and dilated clinical examination.

Because a large proportion (400/489) of total eyes used in the statistical analysis were paired (in the same patient), it was determined that there may be some dependency in the data. That is, each eye was not truly independent. If dependent data exist, then the use of linear models (eg, standard linear regression) may lead to biased estimates of variance, which could lead to misleading comparisons. Generalized estimating equations, which account for any dependency between paired eyes, were used to obtain the standard errors in order to compute the confidence intervals for all measures of accuracy. Generalized estimating equations were also used to determine the statistical significance of the difference between two measures (via odds ratios).

RESULTS

Between August 4, 1999, and February 23, 2001, 254 diabetic patients with at least one eligible eye were enrolled into the study. Table 1 summarizes the demographic data for all enrolled study participants as well as the demographics for both DVRI camera resolution groups A (151 patients) and B (103 patients). The overall mean age of this predominantly male population was 67.5 years. Caucasian Americans accounted for 93.7% of the study patients, African Americans 3.5%, Hispanic Americans 2%, and Native Americans 0.8%. Other ethnic groups were not represented. This demographic profile is typical of the population served by the Minneapolis Veterans Affairs Medical Center. The demographic data for groups A and B were similar.

The mean duration of diabetes in the study population was 12.4 years (range, 0 to 58). Table 2, summarizing the pertinent diabetic history of study patients, shows the distribution of diabetes duration by intervals. Oral hypoglycemic medication alone was used by 47.4%, insulin alone by 28.9%, oral agents combined with insulin by 20.9%, and diet by only 2.8%. The mean level of the most recent glycosylated hemoglobin was 9.76 (range, 5.8 to 18.5). The diabetic histories of groups A and B were similar.

Table 3 describes the ocular characteristics of the study patients. Spectacle correction was worn by 80.6% of patients. Using the patient's spectacle correction if present, a visual acuity of 20/30 or better was measured in 67.6% of all eyes. A visual acuity of 20/40 or worse was measured in 32.4% of study eyes. The mean intraocular pressure was 15.4 mm Hg. The mean undilated pupil size was 3.9 mm; after dilation it was 7.3 mm. The ocular characteristics of groups A and B were similar.

Of the 508 eligible study eyes, 489 (96.3%) were able to be graded using the standard stereoscopic seven-field ETDRS photographs. The distribution of eyes by disease severity, as determined by the grading of the ETDRS photographs, is shown in Table 4. An ETDRS level of 10 or 14/15, indicating absent or questionable diabetic retinopathy, was detected in 43.1% of eyes. An ETDRS level of 20 or greater, indicating definite diabetic retinopathy, was detected in 53.1%. Nineteen eyes (3.7%) were unable to be graded.

Tables 5A and 5B show the distribution of disease severity for groups A and B, respectively, by individual patient. The disease severity recorded for a patient equals the maximum severity present in either eye. For group A, 41.0% of patients had absent or questionable diabetic retinopathy and 58.3% had an ETDRS level of 20 or greater in their most severe eye. For group B, 28.1% had absent or questionable retinopathy and 71.8% had an ETDRS level of 20 or greater in their worse eye. There is some evidence that the group B patients presented, on average, with greater severity of diabetic retinopathy than the group A patients. Therefore, the differences in each of the accuracy measures between the two groups were adjusted for disease severity, and these adjusted differences were tested for significance. The increase in sensitivity from the low- to the high-resolution group was borderline significant (P = .09); however, none of the other measures exhibit a significant change.

Table 6 shows the participation data of all enrolled patients. Because the ETDRS photographs served as the primary "gold standard," the DVRI images taken in the 19 patients with ungradable ETDRS photographs (even if the quality was adequate) were not used in the accuracy or comparison analyses. One patient's pupils were dilated prior to undilated DVRI, so 488 eyes were included in the undilated DVRI analyses. Approximately 60% of eyes were imaged with the lower-pixel-resolution (640×480) DVRI camera (group A), the remaining 40% with the higher-pixel-resolution (800×600) camera (group B).

To compare the "clinical gold standard" to the previously validated ETDRS "gold standard," estimates of accuracy of the dilated clinical examination were calculated as shown in Table 7. For all eyes studied, including both groups A and B, the dilated clinical examination had a sensitivity of 0.73 and a specificity of 0.91. The positive

TABLE 1. DEMOGRAPHIC DATA FOR STUDY PATIENTS

DEMOGRAPHICS	OVERALL STUDY (n = 254)	GROUP A (LOW-RESOLUTION DVRI) (n = 151)	GROUP B (LOW-RESOLUTION DVRI) (n = 103)
Age (yr)	No. (%)	No. (%)	No. (%)
<50	17 (6.7)	11 (7.3)	6 (5.8)
50-59	50 (19.7)	25 (16.6)	25 (24.3)
60-69	78 (30.7)	46 (30.4)	32 (31.1)
70-79	82 (32.3)	49 (32.4)	33 (32.0)
80-89	27 (10.6)	20 (13.3)	7 (6.8)
Mean age (yr)	67.5	67.9	66.6
Sex			
Male	250 (98.4)	149 (98.7)	101 (98.1)
Female	4 (1.6)	2 (1.3)	2 (1.9)
Ethnicity			
African American	9 (3.5)	6 (4.0)	3 (2.9)
Native American	2 (0.8)	1 (0.7)	1 (1.0)
Asian American	0 (0.0)	0 (0.0)	0 (0.0)
Caucasian American	238 (93.7)	141 (93.4)	97 (94.2)
Hispanic American	5 (2.0)	3 (2.0)	2 (1.9)
Other	0 (0.0)	0 (0.0)	0 (0.0)

DVRI, digital-video retinal imaging.

TABLE 2. DIABETIC MEDICAL HISTORY OF STUDY PATIENTS

HISTORY ITEM	OVERALL STUDY (n = 241)*	GROUP A (LOW-RESOLUTION DVRI) (n = 141)	GROUP B (HIGH-RESOLUTION DVRI) (n = 100)
Duration of diabetes (yr)	No. (%)	No. (%)	No. (%)
<5	70 (29.0)	51 (36.2)	19 (19.0)
5-10	56 (23.2)	35 (24.8)	21 (21.0)
10-15	46 (19.1)	19 (13.5)	27 (27.0)
15-20	31 (12.9)	19 (13.5)	12 (12.0)
20-25	18 (7.5)	9 (6.4)	9 (9.0)
25-30	8 (3.3)	3 (2.1)	5 (5.0)
>30	12 (5.0)	5 (3.6)	7 (7.0)
Mean duration (yr)	12.4	11.2	14.0
Range duration (yr)	(0 - 58)	(0 - 58)	(1 - 51)
Type of diabetes treatment	(n = 249)†	(n = 146)	(n = 103)
Diet controlled	7 (2.8)	3 (2.1)	4 (3.9)
Oral agents	118 (47.4)	79 (54.1)	39 (37.9)
Insulin	72 (28.9)	31 (21.2)	41 (39.8)
Oral agents and insulin	52 (20.9)	33 (22.6)	19 (18.4)
Most recent glycosylated hemoglobin	(n = 235)‡	(n = 142)	(n = 93)
Mean	9.76	9.6	10.0
Range	(5.8 - 18.5)	(5.8 - 18.5)	(6.1 - 17.8)

DVRI, digital-video retinal imaging.
*Data unavailable for 13 patients.
†Data unavailable for 5 patients.
‡Data unavailable for 10 patients.

TABLE 3. OCULAR CHARACTERISTICS OF STUDY PATIENTS (BY EYE)

CHARACTERISTIC	OVERALL STUDY	GROUP A (LOW-RESOLUTION DVRI)	GROUP B (HIGH-RESOLUTION DVRI)
Spectacle correction* (by patient)	No. (%)	No. (%)	No. (%)
Yes	200 (80.6)	121 (83.4)	79 (76.7)
No	48 (19.4)	24 (16.6)	24 (23.3)
Visual acuity†			
OD: 20/30 or better	168 (67.5)	103 (68.7)	65 (65.7)
20/40 or worse	81 (32.5)	47 (31.3)	34 (34.3)
OS: 20/30 or better	168 (67.7)	101 (67.3)	67 (68.4)
20/40 or worse	80 (32.3)	49 (32.7)	31 (31.6)
Intraocular pressure‡			
Mean (mm Hg)	15.4 mm Hg	15.4 mm Hg	15.2 mm Hg
Range	(0 - 27)	(0 - 27)	(3 - 25)
Pupil size (scotopic)§			
Mean (mm)	3.9 mm	3.9 mm	3.85 mm
Range	(2.0 - 6.0)	(2.0 - 6.0)	(2.0 - 6.0)
Pupil size (dilated)¶			
Mean	7.3 mm	7.8 mm	6.6 mm
Range	(4.0 - 9.0)	(4.0 - 9.0)	(4.0 - 8.0)

DVRI, digital-video retinal imaging.
*Data unavailable for 6 patients.
†Data unavailable for 5 patients.
‡Data unavailable for 9 eyes.
§Data unavailable for 38 eyes.
¶Data unavailable for 42 eyes.

TABLE 4. ETDRS RETINOPATHY SEVERITY SCALE FOR OVERALL STUDY (INDIVIDUAL EYES)

LEVEL	SEVERITY	NO.	PERCENT	NO.	PERCENT
10	DR absent	190	37.4	219	43.1
14/15	DR questionable	29	5.7		
20	Microaneurysms only	56	11.0	270	53.1
35	Mild NPDR	119	23.4		
43	Moderate NPDR	53	10.4		
47	Moderately severe NPDR	17	3.3		
53	Severe NPDR	6	1.2		
60	Mild PDR	5	1.0		
66	Moderate PDR	9	1.8		
70	High-risk PDR	5	1.0		
90	Cannot determine	19	3.7	19	3.7
Total		508	100	508	100

ETDRS, Early Treatment Diabetic Retinopathy Study; DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

TABLE 5A. ETDRS RETINOPATHY SEVERITY SCALE FOR GROUP A (INDIVIDUAL PATIENTS*)

LEVEL	SEVERITY	NO.	PERCENT	NO.	PERCENT
10	DR absent	47	31.1	62	41.0
14/15	DR questionable	15	9.9		
20	Microaneurysms only	21	13.9	88	58.3
35	Mild NPDR	32	21.2		
43	Moderate NPDR	18	11.9		
47	Moderately severe NPDR	8	5.3		
53	Severe NPDR	1	0.7		
60	Mild PDR	2	1.3		
66	Moderate PDR	4	2.6		
70	High-risk PDR	2	1.3		
90	Cannot determine	1	0.7	1	0.7
Total		151	100	151	100

ETDRS, Early Treatment Diabetic Retinopathy Study; DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

*The disease severity recorded for a patient equals the maximum severity present in either eye.

TABLE 5B. ETDRS RETINOPATHY SEVERITY SCALE FOR GROUP B (INDIVIDUAL PATIENTS*)

LEVEL	SEVERITY	NO.	PERCENT	NO.	PERCENT
10	DR absent	26	25.2	29	28.1
14/15	DR questionable	3	2.9		
20	Microaneurysms only	9	8.7	74	71.8
35	Mild NPDR	37	35.9		
43	Moderate NPDR	16	15.5		
47	Moderately severe NPDR	3	2.9		
53	Severe NPDR	3	2.9		
60	Mild PDR	2	1.9		
66	Moderate PDR	2	1.9		
70	High-risk PDR	2	1.9		
90	Cannot determine	0	0.0	0	0.0
Total		103	100	103	100

ETDRS, Early Treatment Diabetic Retinopathy Study; DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

*The disease severity recorded for a patient equals the maximum severity present in either eye.

predictive value, the proportion of positive test results that were correct (true positives), was 0.91.

The estimates of the accuracy of DVRI, including sensitivity, false-negative rate, specificity, false-positive rate, positive predictive value, negative predictive value, and overall efficiency using the ETDRS photography as the "gold standard" are presented in Table 8. A comparison of accuracy by dilation status shows that for most measures, including specificity, dilation significantly improved the accuracy for both groups A and B. The sensitivities of group A (low-resolution) and group B (high-resolution) DVRI, for both undilated and dilated eyes, are shown graphically in Figure 4. Using the ETDRS "gold standard," the only method of retinopathy evaluation with a sensitivity above 0.8 (the recommended minimum sensitivity level by the British Diabetic Association Working Group) was the high-resolution DVRI through a dilated pupil. This method also demon-

TABLE 6. PARTICIPATION DATA OF ENROLLED PATIENTS

STEPS IN STUDY DESIGN	NO. OF PATIENTS	% OF POPULATION	NO. OF EYES	% OF EYES	% OF EYES WITH GRADABLE ETDRS PHOTOS
Eligible participants with completed informed consent	254	100	508	100	
Participants with gradable stereoscopic 7-field ETDRS color photography	253	99.6	489	96.3	100
Participants with completed dilated clinical examination and gradable ETDRS photos	253	99.6	489	96.3	100
Participants with undilated DVRI and gradable ETDRS photos	253	99.6	488	96.1	99
Participants with dilated DVRI and gradable ETDRS photos	253	99.6	489	96.3	100
Participants with low-resolution DVRI and gradable ETDRS photos (group A)	157	61.8	292	57.5	59.7
Participants with high-resolution DVRI and gradable ETDRS photos (group B)	96	37.8	197	38.8	40.3

ETDRS, Early Treatment Diabetic Retinopathy Study; DVRI, digital-video retinal imaging.

TABLE 7. ESTIMATES OF ACCURACY OF DCE USING ETDRS-P AS "GOLD STANDARD"

METHOD	SENS	FALSE-	SPEC	FALSE+	PPV	NPV	EFF
Dilated clinical examination	0.73	0.27	0.91	0.09	0.91	0.73	0.81

DCE, dilated clinical examination; ETDRS-P, Early Treatment Diabetic Retinopathy Study Photography; Sens, sensitivity; False-, false-negative rate; Spec, specificity; False+, false-positive rate; PPV, positive predictive value; NPV, negative predictive value; EFF, efficiency.

TABLE 8. ESTIMATES OF ACCURACY OF DVRI SCREENING USING ETDRS-P AS "GOLD STANDARD" AND COMPARISON OF ACCURACY BY PUPILLARY DILATION STATUS

METHOD	SENS	FALSE-	SPEC	FALSE+	PPV	NPV	EFF
Group A (low-resolution DVRI)							
Undilated	0.66	0.34	0.66	0.34	0.66	0.66	0.66
Dilated	0.66	0.34	0.86	0.14	0.82	0.71	0.76
P value	NS	NS	<.01	<.01	<.01	<.01	<.01
Group B (high-resolution DVRI)							
Undilated	0.76	0.24	0.45	0.55	0.72	0.51	0.65
Dilated	0.85	0.15	0.81	0.20	0.89	0.75	0.83
P value	.04	.04	<.01	<.01	<.01	<.01	<.01

DVRI, digital-video retinal imaging; ETDRS-P, Early Treatment Diabetic Retinopathy Study Photography; Sens, sensitivity; False-, false-negative rate; Spec, specificity; False+, false-positive rate; PPV, positive predictive value; NPV, negative predictive value; EFF, efficiency.

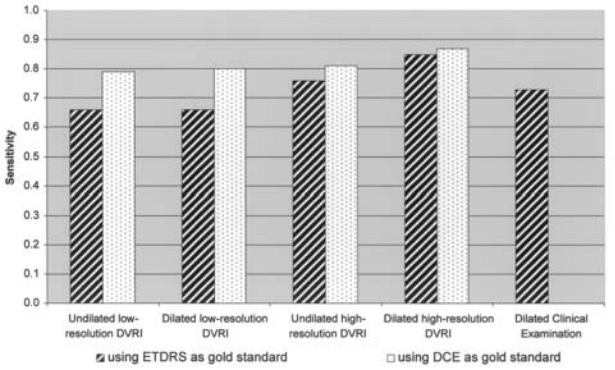

FIGURE 4

Sensitivity of digital-video retinal imaging (DVRI) methods and dilated clinical examination (DCE) using two "gold standards": Early Treatment Diabetic Retinopathy Study (ETDRS) photography and DCE. For every group, the sensitivity of DVRI to accurately detect diabetic retinopathy is higher using the dilated clinical examination as the "gold standard" than using standard ETDRS photography as the "gold standard."

strated the highest efficiency (0.83), a general measure of overall accuracy.

Table 9 shows the estimates of the accuracy, using the dilated clinical examination as the "clinical gold standard." A comparison of accuracy by dilation status also shows that for most measures, including specificity, positive predictive value, and efficiency, dilation significantly improved the accuracy for both groups A and B. Using the "clinical gold standard," only high-resolution DVRI (group B), through both dilated and undilated pupils, demonstrated a sensitivity level above 0.8. Group A, however, approached this level (0.79 and 0.80 for undilated and dilated eyes, respectively).

Generalized estimating equations linear regression models to compare sensitivities and efficiencies of DRVI groups A and B, to the dilated clinical examination, using the ETDRS photography as the "gold standard," are summarized in Table 10. Images from the undilated pupils for both groups A and B performed significantly worse than a clinical examination by an ophthalmologist with respect to efficiency ($P < .01$). In other words, a dilated clinical examination was more accurate at detecting diabetic retinopathy than nonmydriatic DVRI of high or low resolution. The accuracy of evaluation of dilated images of group B (dilated, low-resolution DVRI) was similar to (or perhaps slightly worse than) that of a clinical examination (P values = NS) with respect to sensitivity and efficiency. Group B (high-resolution DVRI) through dilated pupils showed an absolute sensitivity score greater than the clinical examination, but the difference did not reach significance. These comparisons show that *dilated* DVRI performs as well as, or slightly better than, a clinical examination at detecting patients with diabetic retinopathy.

Table 11 and Figure 5 show the sensitivity estimates by increasing levels of disease severity. As the diabetic retinopathy severity increases, the sensitivities of both DVRI systems as well as the dilated clinical examination improve. All screening methods had excellent levels of sensitivity (sens > 0.9) for the more severe (sight-threatening) levels of retinopathy. Dilated group B (high-resolution imaging) performed best at all levels of severity and, in fact, reached a sensitivity of 1.0 for all ETDRS levels ≥43.

Pupillary size also contributed to the ability to grade the undilated DVRI images. Table 12 shows that in all images taken through an undilated pupil, there was a statistically significant difference between the size of the

TABLE 9. ESTIMATES OF ACCURACY OF DVRI SCREENING USING DCE AS "GOLD STANDARD" AND COMPARISON OF ACCURACY BY PUPILLARY DILATION STATUS

METHOD	SENS	FALSE-	SPEC	FALSE+	PPV	NPV	EFF
Group A (low-resolution DVRI)							
Undilated	0.79	0.21	0.68	0.32	0.61	0.84	0.72
Dilated	0.80	0.20	0.85	0.15	0.78	0.87	0.83
P value	NS	NS	.001	.001	.001	NS	.001
Group B (high-resolution DVRI)							
Undilated	0.81	0.19	0.45	0.55	0.66	0.66	0.65
Dilated	0.87	0.13	0.69	0.31	0.78	0.81	0.79
P value	NS	NS	.001	.001	.005	.012	.001

DVRI, digital-video retinal imaging; DCE, dilated clinical examination; Sens, sensitivity; False-, false-negative rate; Spec, specificity; False+, false-positive rate; PPV, positive predictive value; NPV, negative predictive value; EFF, efficiency.

TABLE 10. COMPARISON OF SENSITIVITY AND EFFICIENCY OF DVRI METHODS VERSUS DILATED CLINICAL EXAMINATION USING ETDRS-P AS "GOLD STANDARD"

DVRI GROUP	DILATION STATUS	PERFORMANCE COMPARED TO DCE	SENSITIVITY *P* VALUE	EFFICIENCY *P* VALUE
A	Undilated	Worse	.66	<.01
A	Dilated	Similar	.59	.09
B	Undilated	Worse	.64	<.01
B	Dilated	Better (NS)	.12	.78

DVRI, digital-video retinal imaging; Group A, Low-resolution DVRI; Group B, High-resolution DVRI; NS, not statistically significant; ETDRS-P, Early Treatment Diabetic Retinopathy Study stereoscopic 7-field photography.

TABLE 11. SENSITIVITY OF SCREENING METHODS BY DIABETIC RETINOPATHY SEVERITY

EYE GROUPS	n*	SCREENING METHOD	SENSITIVITY	
			GROUP A LOW RESOLUTION	GROUP B HIGH RESOLUTION
ETDRS ≥10	271	Undilated	0.662	0.762
		Dilated	0.662	0.848
		Clinical exam	0.683	0.794
ETDRS ≥35	214	Undilated	0.773	0.827
		Dilated	0.782	0.903
		Clinical exam	0.846	0.856
ETDRS ≥ 43	95	Undilated	0.887	0.952
		Dilated	0.906	1.000
		Clinical exam	0.981	0.976
ETDRS ≥47	42	Undilated	0.920	1.000
		Dilated	0.920	1.000
		Clinical exam	1.000	0.941
ETDRS ≥53	25	Undilated	0.923	1.000
		Dilated	0.923	1.000
		Clinical exam	1.000	0.917
ETDRS ≥61	14	Undilated	1.000	1.000
		Dilated	1.000	1.000
		Clinical exam	1.000	1.000

EDTRS, Early Treatment Diabetic Retinopathy Study.
*n = number of positives using ETDRS-P as "gold standard."

pupil in gradable versus ungradable DVRI images. The mean pupil size was 4.14 mm in diameter for gradable images, and 3.28 mm for ungradable images ($P < .0001$). As expected, this effect was not seen in the images taken through dilated pupils, because the pupil was of adequate size.

Comparisons of accuracy by low- versus high-resolution DVRI systems (group A versus group B) showed that for dilated eyes, high-resolution DVRI (group B) was significantly more sensitive than the low-resolution DVRI (group A). All other estimates of accuracy, as shown in Table 13, did not show a statistically significant difference.

Table 14 shows the results of an analysis to ascertain whether there was a difference over time in the sensitivity estimates. As time, and the number of patients, progressed (each successive tertile), there was a concomitant increase in the sensitivity of DVRI to detect retinopathy. This is likely due to a "learning effect" experienced by the photographer as well as the ophthalmologist readers.

Thirteen ophthalmologists participated in the DVRI

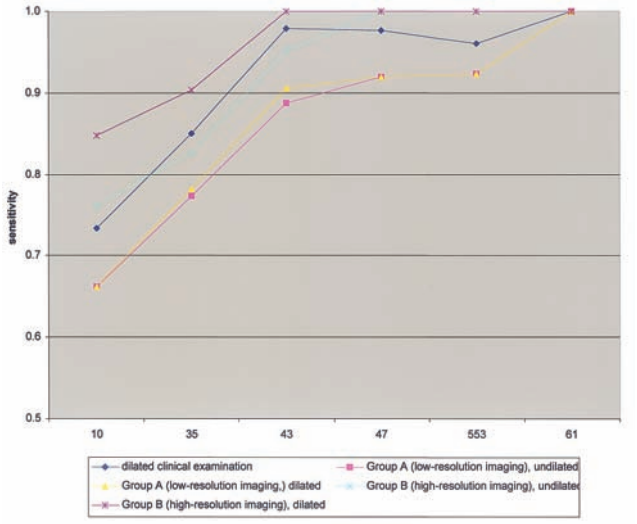

FIGURE 5

Sensitivity of digital-video retinal imaging (DVRI) methods and dilated clinical examination plotted by increasing Early Treatment Diabetic Retinopathy Study (ETDRS) retinopathy severity levels. As the severity levels of diabetic retinopathy increase, the sensitivity of DVRI increases, showing that the rate of false-negatives diminishes with more severe disease.

evaluations using the computer reading station, including two retina specialists, six board certified staff ophthalmologists, and five PGY-4 resident physicians in ophthalmology. Estimates of accuracy, including sensitivity, specificity, positive predictive value, negative predictive value, and efficiency, were calculated for each of the three groups of physicians. Bonferroni 95% confidence intervals were computed for each of the measures. None of the measures differed significantly by physician status. Color contrast enhancement was used by the ophthalmologist to aid in the on-screen evaluation for 83.5% of the eyes.

DISCUSSION

The ETDRS Final Retinopathy Severity Scale is the only validated reference standard for the detection and staging of diabetic retinopathy. For this reason, the ETDRS grading protocol has been referred to by several investigators[101,102] as the "gold standard" for the accurate detection of diabetic retinopathy. The clinical application of ETDRS photographs for periodic retinal evaluations of the diabetic population, however, is impractical, and clinical examination of the retina through a dilated pupil is the mainstay of screening in the United States.

It is important to compare new imaging technology to a validated "gold standard," but it is also of value to compare it to "standard clinical practice," hence the use of the "clinical gold standard" in this analysis. Furthermore, the dichotomous grading system used herein ("disease" versus "no disease") does not require the level of analysis required for the full ETDRS Final Retinopathy Severity Scale. For the determination of presence or absence of disease, it seems justified to use an ophthalmologist's examination, which can evaluate the entire retina, as a reasonable "clinical gold standard." (ETDRS photographic protocol misses some retina nasal to the optic disk.)

Because ETDRS photography has been validated in many studies, the comparative analyses performed for this data used the accuracy estimates derived using ETDRS photographic evaluation as the "gold standard." Sensitivities and negative predictive values were slightly higher for all methods using the "clinical gold standard" instead of the ETDRS "gold standard," but all estimates of accuracy were similar, suggesting that the "clinical gold standard" is an appropriate comparison.

The results of this study suggest that in the presence of an adequately sized pupil, DVRI is an accurate method for detecting diabetic retinopathy. Most, if not all, commercially available DVRI systems, however, are marketed as "nonmydriatic." An exhaustive review of the published literature revealed no peer-reviewed report of a "nonmydriatic" DVRI system that achieved a sensitivity of >0.80, compared to the accepted ETDRS photography "gold standard," across all levels of diabetic retinopathy.

The inverse relationship between age and pupil diameter[103] is also a consideration because almost 29% of the population 60 years and older in the United States has diabetes. The mean age in this study was 67.5 years, significantly older than patients reported in other studies of nonmydriatic systems (48 years in the Bursell study[104]; 50 to 59 years in the Lin study[105]). This study suggests that, given current technology, it may be necessary to routinely dilate patients when using a "nonmydriatic" DVRI system, especially in older populations.

The data herein also suggest that the higher-resolution imaging system may increase the accuracy of screening, especially the sensitivity estimates. It should be noted that the "higher resolution" system used in the reported study is still relatively low in resolution, compared to some systems. Fransen and colleagues[106] report an 1,152×1,152-pixel resolution imaging system. "More" may not be "better," however, when it is applied to digital screening techniques. Transmitting, storing, and archiving large amounts of digital data have associated costs. It will be important for future studies to determine the optimal pixel resolution to maximize accuracy in the detection of disease and minimize data management issues.

Stereoscopic digital imaging technology has been evaluated by Bursell and coworkers[107] and Fransen and coworkers.[108] It is unclear whether the additional stereoscopic capabilities are helpful in increasing the accuracy of the systems. Bursell and coworkers reported that the sensitivity of the Joslin Vision Network (JVN) system in

TABLE 12. GRADABILITY OF DVRI BY PUPIL SIZE

IMAGES	MEAN PUPIL SIZE (MM) OF GRADABLE DVRI	MEAN PUPIL SIZE (MM) OF UNGRADABLE DVRI	*P* VALUE OF DIFFERENCE
Undilated images	4.14	3.28	<.0001
Dilated images	7.31	6.92	.2329

DVRI, digital-video retinal imaging.

TABLE 13. COMPARISON OF ACCURACY MEASURES BETWEEN GROUPS A AND B IN DILATED EYES USING ETDRS-P AS "GOLD STANDARD"

MEASURE	GROUP A LOW-RESOLUTION DVRI (640×480)	GROUP B HIGH-RESOLUTION DVRI (800×600)	*P* VALUE
Sens	0.66	0.85	<.01
Spec	0.86	0.80	.43
PPV	0.82	0.89	.19
NPV	0.71	0.75	.74
EFF	0.76	0.83	.07

EFF, efficiency; DVRI, digital-video retinal imaging; NPV, negative predictive value; PPV, positive predictive value; Sens, sensitivity; Spec, specificity.

TABLE 14. CHANGE IN SENSITIVITY TO DETECT RETINOPATHY BY FIRST, SECOND, AND THIRD TERTILE (DILATED IMAGES ONLY)

	NO. (EYES)	SENSITIVITY
Group A (low-resolution DVRI)		
First third of patient visits	94	0.59
Second third of patient visits	93	0.52
Third third of patient visits	105	0.74
Group B (high-resolution DVRI)		
First third of patient visits	65	0.81
Second third of patient visits	63	0.91
Third third of patient visits	69	0.82

DVRI, digital-video retinal imaging.

detecting any macular edema (using stereoscopic image pairs) was 0.62 and in detecting clinically significant macular edema was only 0.27. Sensitivities in detecting diabetic retinopathy ranged from 0.40 for severe nonproliferative retinopathy to 0.89 for proliferative retinopathy. Fransen and coworkers (also using stereoscopic image pairs) reported a 0.88 sensitivity of the Inoveon DR-3DT system in the detection of macular edema and an overall sensitivity of 0.98 in detecting any retinopathy, including macular edema.

The DVRI systems studied here did not use stereoscopic image pairs. Any suspected macular edema (ie, presence of hard exudate, its surrogate marker) was accounted for because it qualified the eye as being in the "disease detected" category. With the use of the higher-resolution system through a dilated pupil, the sensitivity of detecting disease in our study (0.85 using the ETDRS-P "gold standard," 0.87 using the dilated clinical examination "clinical gold standard") favors comparably with sensitivities reported by Bursell and coworkers,[109] but was less than those reported by Fransen and coworkers.[110]

Only two imaging systems were evaluated in this study, both manufactured by the same vendor. The systems were chosen based on cost, ease of use, pixel resolution, Dicom compliance, potential digital interface compatibility with Veterans Affairs computerized medical record system, and vendor approvals with the Department of Veterans Affairs. Clinical accuracy using

instruments manufactured by other vendors with equivalent pixel resolution may vary due to optical parameters of each system and software characteristics. Variations that might impact clinical accuracy include differences in optical capture performance with respect to pupillary diameter and ambient lighting.

The literature documents that there are many flaws in methodology, as well as inconsistencies in the use of reference (gold) standards and in the reporting of statistical tests of accuracy. All of this calls into question the usefulness of the existing literature in guiding clinical practice. The study described herein indicates that DVRI is clinically effective, but the data are still too sparse to reliably answer questions about pupil size, optimal resolution, and stereoscopic imaging.

An even greater concern is whether DVRI systems are *cost*-effective. DVRI has great potential advantages over traditional clinical examination and traditional film-based photographic techniques. These include lower cost, ease of use of the equipment, ability for providers to share data, greater efficiency of physician time, ease of integration into computerized medical records, and maybe most importantly, the potential to access patients remotely. These potential advantages are alluring but should not deter rigorous assessment of new technology.

CONCLUSIONS

Based on assessments of clinical accuracy, the Topcon TRC-NW6S, 800×600-pixel-resolution digital-video retinal imaging system offers an accurate method of screening for diabetic retinopathy, provided there is adequate pupillary dilation and three imaging fields are analyzed. For an elderly population, the Topcon TRC-NW5SF, 640×480-pixel-resolution digital-video imaging system may be inadequate for accurate diabetic retinopathy screening. Digital-video retinal imaging, because of its ability to utilize telemedicine technology, may help facilitate the implementation of widespread programs, which will result in improved retinal screening and less visual impairment in diabetic populations.

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