# Tele-Screening for Diabetic Retinopathy With the Retinal Thickness Analyzer

ALJOSCHA S. NEUBAUER, MD
ULRICH C. WELGE-LÜßEN, MD
MARTIN J. THIEL, MD
CLAUDIA ALGE, MD
SIEGFRIED G. PRIGLINGER, MD
CHRISTOPH HIRNEIß, MD
MICHAEL W. ULBIG, MD
ANSELM KAMPIK, MD

**OBJECTIVE** — To compare the effectiveness of tele-screening using a novel enhanced retinal thickness analyzer (RTA) with onsite routine ophthalmologic examination for diabetic retinopathy.

**RESEARCH DESIGN AND METHODS** — A consecutive series of 31 eyes from diabetic patients were included. All underwent ophthalmologic examination, including stereoscopic dilated funduscopy and scanning with the RTA. The RTA reports consisted of a wide-angle, red-free fundus photograph and a macular-region retinal thickness map. Reports were graded by three independent graders in a masked manner. The diagnoses of proliferative retinopathy, macular edema, and treatment decisions made by the RTA graders and the clinical examiner were compared.

**RESULTS** — On clinical examination 5 of 31 eyes were diagnosed with proliferative diabetic retinopathy (PDR). All five were referred for treatment by two graders and four eyes by one grader. All eyes with PDR and 12 of the 26 eyes with nonproliferative diabetic retinopathy showed severe macular edema. Seven of the 12 eyes with macular edema were clinically eligible for focal laser treatment, and all of them were detected by all RTA graders. Macular thickening was detected in eight eyes by RTA where no treatment was necessary, as judged by clinical examination. Thus, sensitivity was 93% (mean) for detecting PDR and 100% for detecting macular edema, with a specificity of 58–96% depending on the grader. The RTA did not allow valid assessment due to poor image quality in only one case.

**CONCLUSIONS** — Screening for diabetic retinopathy with a combination of wide-angle fundus photography and macular thickness mapping by an objective method, such as optical coherence tomography or the RTA, offers the prerequisites for establishing a successful tele-screening program.

*Diabetes Care* 26:2890–2897, 2003

Diabetic retinopathy is a leading cause of visual impairment and blindness in developed countries. Macular edema is the major cause of vision loss in diabetic patients, while proliferative retinopathy is another common cause (1). An annual clinical examination of dilated pupils by an ophthalmologist is the current gold standard of care for reducing diabetes-related ocular complications in patients with no or mild diabetic retinopathy (2). In the Early Treatment Diabetic Retinopathy Study (ETDRS), this led to a reduction of moderate visual loss by 50% (3).

In many countries, an effective population-based screening cannot be offered by ophthalmologists and is performed by optometrists or general practitioners (4). One possible way to increase the number of ophthalmologically monitored diabetic patients is teleophthalmologic examination by a specialist (5–9). The gold standard of photographic documentation consists of seven stereoscopic fundus photographs, as defined by the ETDRS, requiring expensive equipment and a skilled photographer (10). Consequently, a number of alternative photographic methods have been evaluated for this purpose and are potentially able to identify patients requiring laser treatment (11). Recently, methods such as digital photography utilizing nonmydriatic stereo color fundus cameras (12) or mydriatic, monochromatic fundus cameras (13) were investigated. Nonstereo photography facilitated photography. Monochromatic photography with adequate red-free illumination is less expensive and may be superior to color photography (13–15).

However, with nonstereo photographic methods, retinal proliferations are detected well but diabetic macular thickening cannot be detected. Therefore, all nonstereo methods require additional information about retinal thickness for accurate assessment of macular edema, as visual acuity provides only limited information (16). The retinal thickness analyzer (RTA; Talia Technology, Neve-Ilan, Israel) is an optical imaging instrument that allows objective, accurate, and quantitative measurement of retinal thickness. It has been shown to be more sensitive than slit-lamp biomicroscopy and photography in detecting localized areas of retinal thickness and may even demonstrate retinal thickening before retinopathy is diagnosed in diabetic patients (17–19). For this purpose, the RTA has been reported to be at least equivalent to another optical imaging instrument allowing macular thickness measurements, the Optical Coherence Tomograph (Zeiss-Humphrey Instruments, San Leandro, CA) (20). The newest generation of the RTA is equipped with an improved monochromatic fundus camera and new software that generates a report intended

From the Department of Ophthalmology, Ludwig-Maximilians-Universität, Munich, Germany.
Address correspondence and reprint requests to Aljoscha S. Neubauer, MD, Department of Ophthalmology, Ludwig-Maximilians-University, Mathildenstr. 8, 80336 Munich, Germany. E-mail: aneubaue@aki.med.uni-muenchen.de.
Received for publication 22 April 2003 and accepted in revised form 12 July 2003.
**Abbreviations:** DRS, Diabetic Retinopathy Study; ETDRS, Early Treatment Diabetic Retinopathy Study; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PPV, pars plana vitrectomy; RTA, retinal thickness analyzer.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

for teleophthalmologic screening in diabetic retinopathy, combining the information from fundus photography and retinal thickness measurement. In this study, we investigated the diagnostic accuracy of diabetic retinopathy by ophthalmologists, based solely on this report, and compared it with onsite examination by retina specialists.

## RESEARCH DESIGN AND METHODS

— Consecutive patients were recruited from the outpatient clinic of the Department of Ophthalmology, Ludwig-Maximilians-Universität, Munich. Patients were included if they had diabetes (based on World Health Organization criteria) for at least 3 years. Eyes were excluded if there were eye diseases other than diabetic retinopathy or media opacities preventing adequate funduscopy.

### Performance of eye examination

All patients underwent complete ophthalmological examination, including a dilated (1% tropicamide) stereoscopic fundus exam with slit-lamp biomicroscopy by one of three experienced retinal specialists (M.J.T., U.C.W.-L. and M.W.U.). The level of diabetic retinopathy and macular edema was assessed using the International Clinical Diabetic Retinopathy Severity Scale (21). Additional tests, such as fluorescein angiography, were performed if needed. Based on this information, the specialist decided whether treatment was necessary based on the Diabetic Retinopathy Study (DRS) (22) and ETDRS criteria (3). The decision was recorded in the chart and served as a reference. Pars plana vitrectomy (PPV) was performed if long-standing macular edema refractory to conventional treatment and an attached taut posterior hyaloid existed (23–25).

### RTA diabetic retinopathy screening

After informed consent was obtained, scanning with the RTA was performed with software version 4.11B on all patients. The RTA is a quantitative and reproducible method to evaluate retinal thickness that can sensitively detect localized areas of macular thickening (20,26). The principles of measurement have been described in detail elsewhere (27,28). Briefly, a helium green neon laser beam (543 nm) is projected onto the retina at an angle, similar to a slit-lamp biomicroscope, and a charge-coupled device (CCD) camera records the backscattered light from the vitreoretinal and chorioretinal interfaces. The digitized fundus picture is used to calculate retinal thickness. The RTA simultaneously projects 16 slits covering a 3 × 3–mm area on the retina. In five overlapping scans, the posterior pole is imaged and a retinal thickness map composed. An improved red-free monochromatic fundus camera allows a new screening mode for diabetes consisting of the usual five scans to generate the thickness map of the posterior pole and six additional, more peripheral fundus photographs. The duration of each scan is 300 ms, and total scanning time is ~3–5 min per eye. The fundus photographs are automatically mounted to create a wide-angle, red-free fundus picture (Fig. 1*A*) covering an area of ~80° horizontally and 60° vertically. If some scans are decentered or do not pass internal quality control due to insufficient fixation or media opacities, the composed wide-angle photograph covers a smaller area. Therefore, any significant change in the covered area of the composed photograph (>15%) is separately listed in this study.

The final report of the RTA's diabetic retinopathy screening mode combines the wide-angle fundus picture described above and a retinal thickness map of the posterior pole (Fig. 1*B*). Areas with retinal thickness beyond the normal population range are color coded toward red and marked dotted in the thickness map. A dashed circle (radius 750 μm) centered at the foveal fixation is printed on the thickness map and the fundus picture to mark the central foveal avascular zone.

### Image interpretation by trained graders

All reports generated by the RTA consisting of the monochromatic wide-angle photograph, the retinal thickness map, and posterior pole thickness indexes were printed in color with an ink-jet printer on regular paper. These reports were independently graded by three retina specialists (A.S.N., S.G.P., and C.H.). The graders had not previously participated in examination of the patients. Additional information, such as visual acuity, duration of diabetes, or clinical symptoms, were not used for grading. The grader, however, could decide not to grade a report due to insufficient picture quality. In an attempt to simulate a teleophthalmologic setting, the graders had to decide on retinopathy, maculopathy, and further treatment. Cases that were found to need further action or that could not be graded were considered for referral to an ophthalmologist in the simulated telescreening setting. The presence of proliferations requiring panretinal laser photocoagulation and presence of a significant grade of diabetic macular edema requiring focal laser coagulation had to be assessed by all graders (21). The decisions of the graders were based on the same criteria as the clinical decisions, mainly based on the DRS (22) and ETDRS criteria (3).

### Statistics

Data were collected in a Microsoft Excel 2000 spreadsheet (Microsoft, Unterschleissheim, Germany) and analyzed using SPSS 11.0 for Windows (SPSS, Chicago, IL). On all tests, $P < 0.05$ was considered significant.

## RESULTS

— A total of 36 eyes from 18 patients were included in the study. Five eyes from five patients were excluded, one with intraocular melanoma, two with dense vitreous hemorrhages making funduscopy impossible, and two with signs of age related maculopathy. Thus, a total of 31 eyes, with a mean patient age of 64 ± 10 years (means ± SD; range 48–81), was included.

### Clinical grading of diabetic retinopathy

Fluorescein angiography was done in addition to funduscopy in five eyes. On clinical examination, five eyes were diagnosed with proliferative diabetic retinopathy (PDR) and 26 eyes with nonproliferative diabetic retinopathy (NPDR) (Table 1). Macular edema was diagnosed according to international clinical diabetic retinopathy criteria as none in 3 eyes, mild in 3, moderate in 8, and severe in 17 (Table 1). All five eyes diagnosed with PDR showed severe macula edema. Of the 12 eyes with NPDR and severe macular edema, 6 received either focal or grid laser treatment. PPV was performed in one eye, and no action was taken for macular edema in five eyes. The decision for taking no action in spite of severe macular edema was based on ischemia in fluorescein angiography (two eyes) or long-standing unchanged macular edema despite multiple treatment sessions and visual acuity <0.1 Snellen (three eyes).

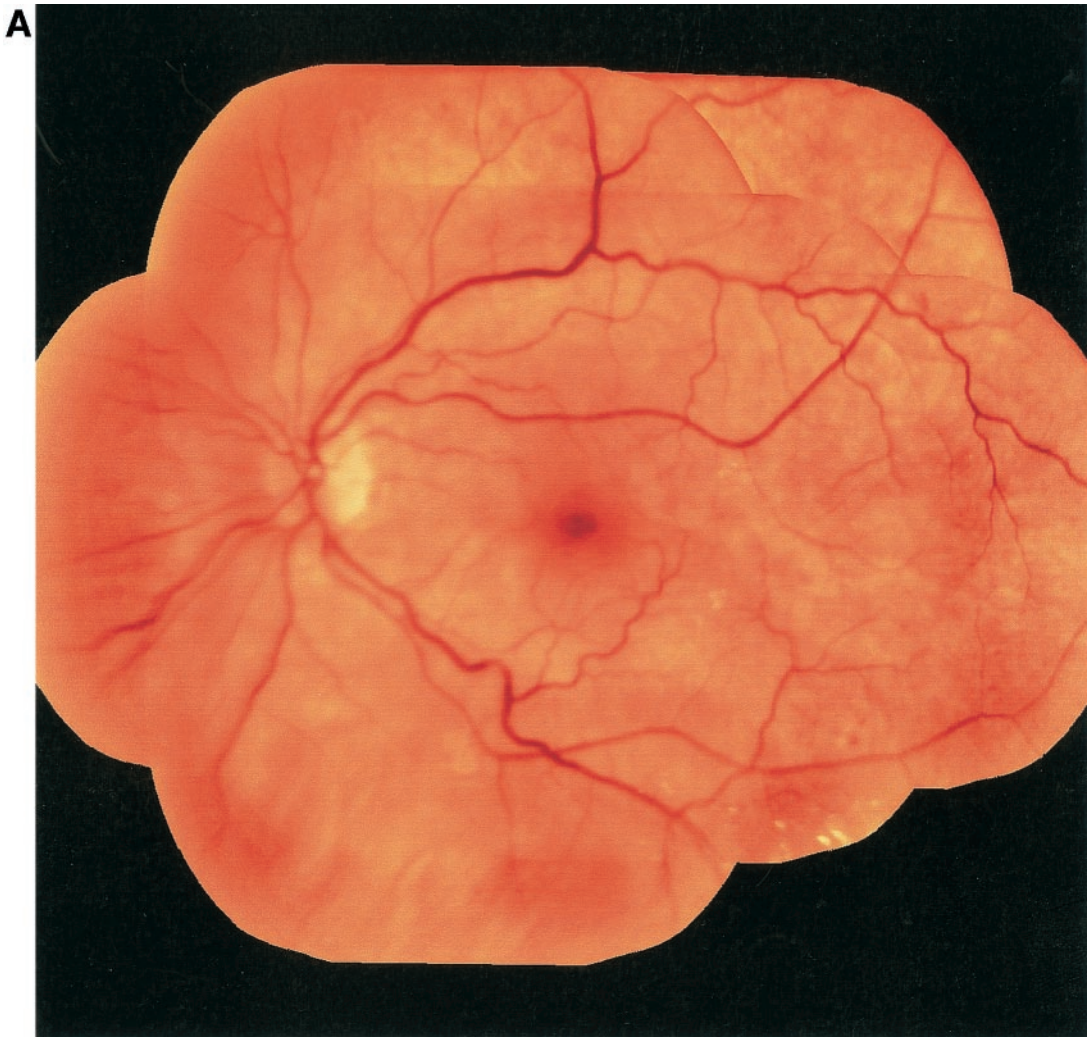


**Figure 1—**A: *Typical monochromatic, red-free fundus picture obtained in the diabetic retinopathy screening mode of the RTA, displayed in false colors. The fundus picture consists of a total of 11 single pictures automatically mounted to a wide-angle view. This fundus picture was obtained from eye no. 19 (Tables 1 and 2).* B: *Corresponding posterior pole retinal thickness map. Measurements of retinal thickness are color coded, and the scale (in microns) is given to the left of the figures. This thickness map is shown superimposed to the fundus image. To the right and below the figure, a cross-section thickness profile through the macula center is printed, including normal reference intervals in gray. The dashed circle gives the central 1,500-μm diameter of the macula. It can be seen that although the center of the macula is only slightly thickened to 187 μm, a somewhat thickened area is measured by the RTA temporal to the fovea. This thickened area is marked by dots. On clinical assessment, focal laser treatment was not yet indicated (see no. 19, Table 1).*

Of the five eyes diagnosed with PDR, three underwent panretinal photocoagulation and, in two, PPV was performed due to the severity of traction and media opacities (nos. 9 and 10 in Table 1). Overall, in 19 of 31 eyes (61%), no action at all was recommended (Table 1).

### Technical quality of RTAs

The full wide-field fundus photograph was available in 15 of 31 (48%) eyes. In eight (26%) eyes, some degree of reduction was observed, with more than 15% but no more than 30% of the total area missing, and at least two disc areas covered nasally. In eight eyes, a larger reduction of the photographic field was observed. In three of those eight eyes, this marked reduction was caused by vitreous hemorrhage due to PDR and, in the remaining five, by a reduced ability to fixate the target point during image acquisition. Scanning patients by RTA was possible in all cases in which funduscopy was possible. However, the composed fundus picture differed in quality according to media opacities and the ability of the patient to cooperate. Sufficient focus of the image was achieved in all but one case (no. 23 in Tables 1 and 2), in which only a blurred or restricted image was obtained. As it was also difficult to grade this eye on biomicroscopy, additional fluorescein angiography was carried out but revealed no maculopathy that required treatment. In summary, in 23 of 31 (74%) eyes, a well-focused, wide-field photograph could be obtained.

In all cases, a retinal thickness map covering the posterior pole could be obtained. Mean foveal thickness was 246 ± 99 μm (range 130–466). Mean foveal thickness was 142 ± 12 μm in the three eyes with no macular edema on clinical investigation, 185 ± 27 μm in the three

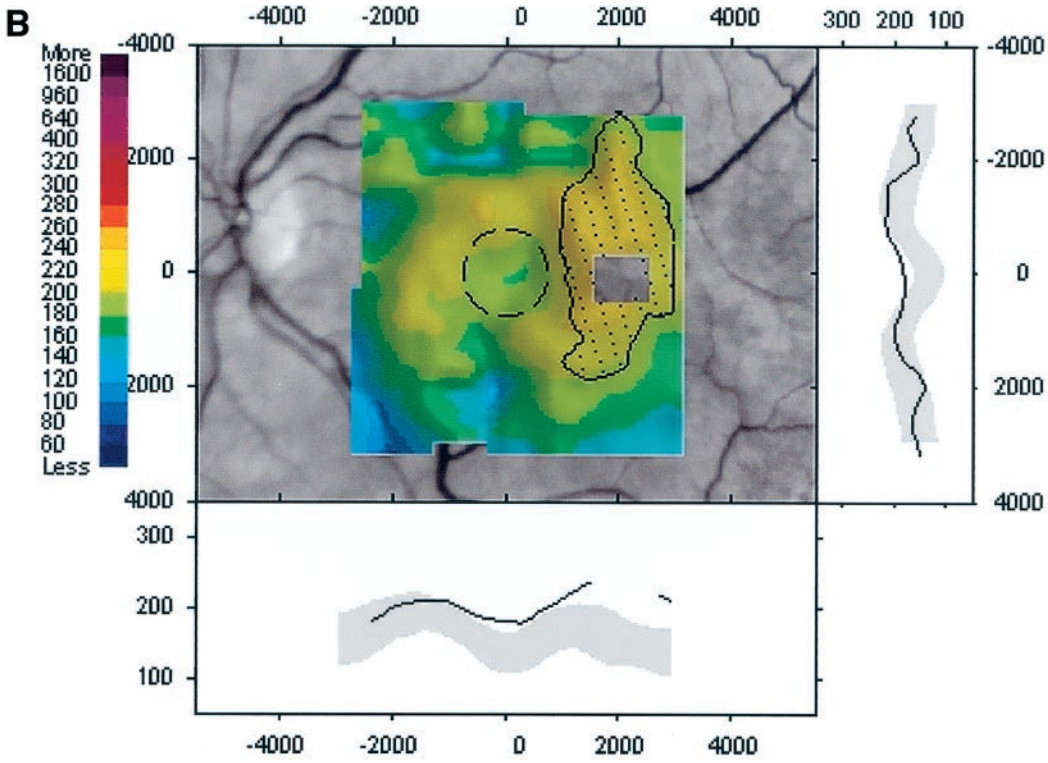


**Figure 1—***Continued.*

eyes with mild edema, and 174 ± 27 μm in the eight eyes with moderate edema. A significantly increased thickness of 309 ± 91 μm was found in the 17 eyes diagnosed with severe macular edema ($P < 0.001$ Mann-Whitney $U$ test). Visual acuity showed a significant correlation with the measured foveal thickness ($r = -0.41$, $P = 0.02$). Eyes with severe edema also showed a significantly ($P < 0.001$) reduced visual acuity compared with the other groups.

### Detection of retinopathy by RTA

All three graders graded all reports for both level of diabetic retinopathy and macular edema. Overall, a good correlation between the three graders regarding PDR was achieved (Spearman's $\rho = 0.4–0.6$, all $P < 0.05$). PDR was diagnosed by grader A in two cases, grader B in eight cases, and grader C in six cases (Table 2). Eyes that were not gradable (grader A one eye, grader B two eyes, and grader C one eye) were considered as referrals for PDR. All five eyes with clinically diagnosed PDR were detected by graders B and C, while grader A detected four of the five eyes as requiring further treatment (Table 3). With the clinical diagnosis of PDR as a reference, a sensitivity of 100% for graders B and C and 80% for grader A is derived. It should be noted, however, that only some of the patients were referred because of the diagnosis of PDR (for panretinal photocoagulation): two by grader A, three by grader B, and four by grader C. The others were referred because of coexisting macular edema (Table 3). This indicates that neovascularization was not correctly realized by the graders in one of five (20%; grader C) to three of five (60%) of the cases. Specificity for PDR diagnosis was 73% (19 of 26; grader B), 88% (23 of 26; grader C), and 96% (25 of 26; grader A).

### Detection of macular edema

Better results were achieved for the diagnosis of macular edema. Correlation between the three graders was very high (Spearman's $\rho = 0.5–0.8$, all $P < 0.01$). All seven cases with macular edema treated according to clinical decision (six focal laser coagulations and one PPV) were also referred for treatment by all three graders (sensitivity 100%). Of 17 eyes with clinically severe macular edema, none (grader C), one (grader B), and three (grader A) eyes were not referred for treatment. Among eyes in which no treatment was found necessary on clinical assessment, depending on the grader, between six and eight eyes, i.e., 19–26%, were referred for treatment of macular edema (Table 3). Among these eyes, additional diagnostics were needed by the clinician in only zero to two cases. With the clinical diagnosis as reference, the RTA-based referral for treatment of macular edema yields a relatively low specificity of between 58% (11 of 19; grader C) and 68% (13 of 19; grader A).

**CONCLUSIONS** — In this study, we have shown that the new tele-screening algorithm of the RTA is a sensitive means of detecting diabetic retinopathy in need of referral for specialist treatment. The combination of a wide-field composite fundus photograph and precise thickness measurement of the macula allows effective screening in the setting used for the study. When applied in a primary care unit, even better results may be expected because, in our patient series, 5 of 31 (16%) eyes had PDR and only 3 of 31 (10%) had no evident diabetic fundus changes. In contrast, in a common screening setting, >60% normal eyes and only 7% sight-threatening changes are expected (4), thereby greatly reducing the amount of patients who are difficult to

**Table 1—*Characteristics of included patients***

| No. | Patient no. | Patient age (years) | Visual acuity (Snellen) | Clinical grading retinopathy | Clinical grading macular edema | Clinical treatment |
|---|---|---|---|---|---|---|
| 1 | 1 | 72 | 0.8 | NPDR | None | FA, no further action |
| 2 | 2 | 72 | 0.1 | NPDR | Severe | Grid laser treatment |
| 3 | 2 | | 0.2 | NPDR | Severe, previous grid laser treatment unsuccessful | None |
| 4 | 3 | 60 | 0.05 | NPDR | Severe | Focal laser treatment |
| 5 | 4 | 54 | 0.25 | NPDR | None | None |
| 6 | 4 | | 0.4 | NPDR | None | None |
| 7 | 5 | 58 | 0.05 | NPDR | Severe edema not resolved after PPV | None |
| 8 | 5 | | 0.029 | NPDR | Severe, foveal scar | None |
| 9 | 6 | 48 | 0.1 | PDR | Severe | PPV |
| 10 | 6 | | Hand motion | PDR | Severe | PPV |
| 11 | 7 | 69 | 0.05 | NPDR | Moderate | FA, no further action |
| 12 | 7 | | 0.5 | NPDR | Mild | FA, no further action |
| 13 | 8 | 81 | 0.3 | NPDR | Moderate | None |
| 14 | 9 | 52 | 0.3 | NPDR | Severe | None |
| 15 | 9 | | 0.2 | PDR | Severe | Panretinal laser treatment |
| 16 | 10 | 79 | 0.1 | NPDR | Severe | PPV |
| 17 | 10 | | 0.5 | NPDR | Moderate | None |
| 18 | 11 | 65 | 0.4 | NPDR | Severe | Focal laser treatment |
| 19 | 11 | | 0.5 | NPDR | Moderate | None |
| 20 | 12 | 60 | 0.4 | NPDR | Moderate | None |
| 21 | 12 | | 0.3 | NPDR | Moderate | None |
| 22 | 13 | 69 | 0.1 | NPDR | Moderate | FA, no further action |
| 23 | 13 | | 0.5 | NPDR | Severe | FA, no further action |
| 24 | 14 | 71 | 0.5 | NPDR | Moderate | None |
| 25 | 14 | | 0.1 | NPDR | Severe | Grid laser treatment |
| 26 | 15 | 68 | 0.1 | NPDR | Severe | Grid laser treatment |
| 27 | 15 | | 0.2 | NPDR | Severe | Grid laser treatment |
| 28 | 16 | 74 | 0.7 | NPDR | Mild | None |
| 29 | 17 | 50 | 0.5 | NPDR | Mild | None |
| 30 | 18 | 56 | 0.1 | PDR | Severe | Panretinal laser treatment |
| 31 | 18 | | 0.029 | PDR | Severe | Panretinal laser treatment |

Clinical grading of diabetic retinopathy and macular edema was based on the International Clinical Diabetic Retinopathy Severity Scale (21). The listed classification and treatment initiated after ophthalmologic examination served as a reference for comparison with the RTA results. FA, fluorescein angiography.

image due to advanced retinal changes impairing fixation. Nevertheless, the screening characteristics obtained for the RTA are comparable to those obtained by ophthalmologists (29) or by trained optometrists in a primary setting, where 87% sensitivity and 91% specificity for sight-threatening eye disease is yielded (4).

## Photography

Numerous protocols have been evaluated for tele-screening based on photographs alone. The seven stereo-photographs required by the EDTRS offer excellent test characteristics for both PDR (10) and macular edema (30). However, such photographs require high skills from the photographer, are costly and time-consuming, and are therefore not ideal for primary screening. The EDTRS photographs cover 75–65° of the central retina. A single 60° nonstereoscopic fundus picture covering 60% of this area was found not to be sensitive enough for screening purposes (31). Two 60° fundus photographs, one macula and the other optic disc centered, cover 80% of the area imaged by EDTRS photographs and even add some areas, making it unlikely to miss areas of neovascularization (32). In a primary care setting, two 45° fundus photographs, one centered on macula and one centered on the optic disc, offer good screening characteristics (16). It has also been shown that 80% of the neovascularizations identified within two 60° photographs were also detected on two 45° photographs (33). The area covered by the mounted photographs of the RTA cover approximately the area of a fovea-centered 60° and disc-centered 45° photograph. This is sufficient for detecting most areas of neovascularization. In our study, all patients with PDR had neovascularization apparent on the fundus photographs. On the two-dimensional photographs of the RTA report, however, some of the neovascularizations were falsely graded as hemorrhages or old membranes in eyes having undergone previous panretinal photocoagulation. Still, only one of three graders missed only one eye with sight-threatening changes.

In a primary care screening, it is very important to sensitively detect early diabetic changes such as microaneurysms.

**Table 2—*Results of RTA measurements and grading of reports by grader A, B, and C in a simulated tele-screening setting***

| No. | RTA photo: significant size reduction | RTA map: foveal average thickness (μm) | Grader A retinopathy | Grader A treatment | Grader B retinopathy | Grader B treatment | Grader C retinopathy | Grader C treatment |
|---|---|---|---|---|---|---|---|---|
| 1 | | 133 | NPDR | None | NPDR | None | NPDR | None |
| 2 | | 337 | NPDR | fALK | PDR | fALK + pALK | Advanced NPDR | fALK |
| 3 | Some | 280 | NPDR | fALK | PDR | fALK + pALK | Advanced NPDR | fALK |
| 4 | Some | 349 | NPDR | fALK | NPDR | fALK | NPDR | fALK |
| 5 | | 156 | NPDR | None | NPDR | None | NPDR | None |
| 6 | | 137 | NPDR | None | NPDR | None | NPDR | None |
| 7 | | 206 | NPDR | fALK | NPDR | None | NPDR | fALK |
| 8 | Some | 321 | Advanced NPDR | None | PDR | fALK + pALK | NPDR | fALK |
| 9 | Marked | 340 | NPDR | fALK | PDR | fALK + pALK | PRD | fALK + pALK |
| 10 | Marked | 150 | Advanced NPDR | None | Advanced NPDR | pALK | PRD | pALK |
| 11 | Some | 162 | NPDR | None | NPDR | None | NPDR | None |
| 12 | Some | 178 | NPDR | None | NPDR | None | NPDR | None |
| 13 | | 163 | NPDR | None | NPDR | None | NPDR | None |
| 14 | | 431 | NPDR | fALK | PDR | fALK + pALK | NPDR | fALK |
| 15 | | 466 | NPDR | fALK | NPDR | fALK | NPDR | fALK |
| 16 | | 365 | NPDR | fALK | NPDR | fALK | NPDR | fALK |
| 17 | Marked | 167 | Cannot grade | refer | Cannot grade | refer | Cannot grade | refer |
| 18 | | 277 | NPDR | fALK | NPDR | fALK | NPDR | fALK |
| 19 | | 187 | NPDR | None | NPDR | None | NPDR | None |
| 20 | Some | 193 | NPDR | None | NPDR | fALK | NPDR | None |
| 21 | Some | 166 | NPDR | None | NPDR | None | NPDR | None |
| 22 | | 130 | NPDR | None | NPDR | fALK | NPDR | None |
| 23 | Marked | 183 | NPDR | None | Cannot grade | refer | PDR? | fALK |
| 24 | Marked | 221 | NPDR | fALK | Advanced NPDR | None | NPDR | fALK |
| 25 | Marked | 341 | NPDR | fALK | PDR | fALK, pALK | PRD | pALK |
| 26 | Marked | 404 | NPDR | fALK | NPDR | fALK | NPDR | fALK |
| 27 | Some | 380 | NPDR | fALK | NPDR | fALK | NPDR | fALK |
| 28 | | 162 | NPDR | fALK | NPDR | None | NPDR | fALK |
| 29 | | 214 | NPDR | None | NPDR | fALK | NPDR | None |
| 30 | | 217 | PDR | pALK | PDR | fALK + pALK | PRD | pALK |
| 31 | Marked | 210 | PDR | pALK + fALK | PDR? | refer | PRD | pALK |

The numbers in the first column refer to the eye number listed in Table 1. The amount of covered retinal area by the composed RTA monochromatic photograph is given in column 2, with "some" restriction corresponding to 15–30% of the area missing. The foveal thickness is listed in column 3, whereas in the other columns, the results of the graders regarding retinopathy and recommended action are listed. fALK, focal or grid photocoagulation; pALK, panretinal photocoagulation; refer, refer to ophthalmologist.

Those early changes are more easily detected by red-free black-on-white photography than on color photographs (34). As the RTA operates with a green helium–neon laser and a black-on-white fundus camera, it meets those requirements. Additionally, by automatically composing several high-resolution images, it is possible to combine high resolution and a wide-angle view. The RTA easily meets the required 50 pixel per angle of view (13), with a resolution of 1,200 × 1,200 pixels in an ~80° image. In our series, however, we observed several patients in whom the RTA's composed fundus image showed not the full wide-angle but a constricted image. This can be explained by reduced patient compliance and difficulties with fixation that would also complicate conventional photography. Another factor may be the operator's learning curve with the new screening algorithm. Interestingly, low image quality with a reduction of the area covered on the fundus photograph is frequently found with advanced NPDR and PDR reflecting media opacities and poor fixation. Consequently, if no adequate picture is produced, high suspicion of the grader is indicated. In a primary care setting, those patients should be referred to an ophthalmologist.

## Retinal thickness maps

In contrast to detecting PDR, where applying only fundus photographs is sufficient for detecting macular edema nonstereoscopic, photographic screening schemes alone are not well suited (35). The RTA was designed to detect macular thickness and offers excellent imaging characteristics (17,18,36). It is similar to another instrument, the optical coherence tomograph, and allows an even more sensitive detection of macular edema than stereoscopic fundus examination by a retina specialist (20,26).

A cutoff of 180 μm has been proposed for foveal thickness to define diabetic macular thickening (19). Given this, 20 of 31 (65%) eyes included in this study had abnormal foveal thickening. The RTA's high sensitivity for retinal thickening at the posterior pole may explain the

**Table 3—*Correlation between clinical reference (see Table 1) and graders assessment (see Table 2)***

| Assessment | Any therapy initiated by clinical criteria | No therapy necessary by clinical criteria | Sum |
|---|---|---|---|
| RTA grader A | | | |
| Any therapy | 11 | 5, 1 referred | 17 |
| No therapy | 1 | 13 | 14 |
| Sum | 12 | 19 | 31 |
| RTA grader B | | | |
| Any therapy | 11, 1 referred | 6, 2 referred | 20 |
| No therapy | 0 | 11 | 11 |
| Sum | 12 | 19 | 31 |
| RTA grader C | | | |
| Any therapy | 12 | 7, 1 referred | 20 |
| No therapy | 0 | 11 | 11 |
| Sum | 12 | 19 | 31 |
| Action for existing PDR ($n = 5$) | | | |
| RTA grader A | 2 panretinal, 2 focal laser indications, 1 missed | 0 | |
| RTA grader B | 3 panretinal, 1 focal laser indication, 1 referral | 0 | |
| RTA grader C | 4 panretinal, 1 focal laser indication | 0 | |
| Action for NPDR ($n = 26$) | | | |
| RTA grader A | 6 laser treatments | 5 focal laser treatments, 1 referred | 6/31 (19%)* |
| RTA grader B | 6 laser treatments | 1 focal, 5 combined laser treatments, 2 referred | 8/31 (26%)* |
| RTA grader C | 6 laser treatments | 7 focal laser treatments, 1 referred | 8/31 (26%)* |

The upper part of the table gives the correlation regarding any therapy taken versus no intervention as judged by graders A, B, and C in a simulated tele-screening setting. In the lower part of the table, the correlation grouped for PDR and NPDR is listed. While grader A missed one PDR, all others would have been referred, but some for significant macular edema and not PDR. No cases of clinically significant macular edema were missed, but some others detected by RTA screening did not receive intervention based on clinical examination: *"unnecessary referrals".

high number of proposed focal laser photocoagulations by the graders and that no macular edemas were missed. On clinical assessment, some of the proposed focal laser treatments were not performed due to ischemia on fluorescein angiography and some because of a history of several prior unsuccessful treatments. Neither of these factors were known to the graders. On the other hand, there may even be some cases in which a retinal thickening clearly shown on the RTA did not reach clinical significance but the patient might still benefit from focal laser treatment. In this regard, it should be emphasized that the low specificity we observed for detection of macular edema in need of treatment, when compared with clinical diagnosis, may actually reflect the very high sensitivity of the RTA. Indeed, we expect that novel imaging techniques such as the RTA or optical coherence tomography will redefine the term "clinically significant macular edema" and the indications for treatment.

The new screening mode of the RTA combines two imaging modalities: a wide-angle, red-free black-on-white fundus photograph and a detailed map of retinal thickness at the posterior pole. The composed fundus photograph covers a sufficient area to detect neovascularizations at good resolution. Using this combination, we achieved mean 93% sensitivity for diagnosis of PDR and 100% for macular edema when compared with clinical examination. Specificities ranged between 58 and 96% in a simulated tele-screening setting in the retina outpatient clinic of a university hospital. In summary, screening for diabetic retinopathy, with the combination of a digital wide-angle fundus photograph and additional thickness information (such as given by optical coherence tomography or the RTA maps), meets the prerequisites for establishing a tele-screening program.

**Acknowledgments**— The authors thank Nayereh Ehsani for expert technical assistance with the RTA.

**References**

1. Klein R, Klein BE, Moss SE: Visual impairment in diabetes. *Ophthalmology* 91:1–9, 1984
2. White JR Jr: Economic considerations in treating patients with type 2 diabetes mellitus. *Am J Health Syst Pharm* 59 (Suppl. 9):S14–S17, 2002
3. Early Treatment Diabetic Retinopathy Study Research Group: Photocoagulation for diabetic macular edema: Early Treatment Diabetic Retinopathy Study report number 1. *Arch Ophthalmol* 103:1796–1806, 1985
4. Hulme SA, Tin-U A, Hardy KJ, Joyce PW: Evaluation of a district-wide screening programme for diabetic retinopathy utilizing trained optometrists using slit-lamp and Volk lenses. *Diabet Med* 19:741–745, 2002
5. Evans PM, Purewal TS, Hopper A, Slater H, Jones DR, O'Hare JP: Screening for diabetic retinopathy in primary care: retinal photography alone can be used efficiently and effectively to exclude those with sight threatening lesions. *J Med Screen* 4:174–176, 1997
6. Lee P: Telemedicine: opportunities and challenges for the remote care of diabetic retinopathy. *Arch Ophthalmol* 117:1639–1640, 1999
7. Greenwood RH: Population-based screening for diabetic retinopathy: a promising start (Editorial). *Diabet Med* 13:925–926, 1996
8. Li HK: Telemedicine and ophthalmology. *Surv Ophthalmol* 44:61–72, 1999
9. Klein R: Barriers to prevention of vision loss caused by diabetic retinopathy. *Arch Ophthalmol* 115:1073–1075, 1997
10. Early Treatment Diabetic Retinopathy Study Research Group: Grading diabetic retinopathy from stereoscopic color fundus photographs: an extension of the modified Airlie House classification: ETDRS report number 10. *Ophthalmology* 98:786–806, 1991
11. Bresnick GH, Mukamel DB, Dickinson JC, Cole DR: A screening approach to the sur-

veillance of patients with diabetes for the presence of vision-threatening retinopathy. *Ophthalmology* 107:19–24, 2000
12. Bursell SE, Cavallerano JD, Cavallerano AA, Clermont AC, Birkmire-Peters D, Aiello LP, Aiello LM, the Joslin Vision Network Research Team: Stereo nonmydriatic digital-video color retinal imaging compared with Early Treatment Diabetic Retinopathy Study seven standard field 35-mm stereo color photos for determining level of diabetic retinopathy. *Ophthalmology* 108:572–585, 2001
13. Zeimer R, Zou S, Meeder T, Quinn K, Vitale S: A fundus camera dedicated to the screening of diabetic retinopathy in the primary-care physician's office. *Invest Ophthalmol Vis Sci* 43:1581–1587, 2002
14. Lin DY, Blumenkranz MS, Brothers RJ, Grosvenor DM: The sensitivity and specificity of single-field nonmydriatic monochromatic digital fundus photography with remote image interpretation for diabetic retinopathy screening: a comparison with ophthalmoscopy and standardized mydriatic color photography. *Am J Ophthalmol* 134:204–213, 2002
15. Lin DY, Blumenkranz MS, Brothers R: The role of digital fundus photography in diabetic retinopathy screening: Digital Diabetic Screening Group (DDSG). *Diabetes Technol Ther* 1:477–487, 1999
16. Stellingwerf C, Hardus PL, Hooymans JM: Two-field photography can identify patients with vision-threatening diabetic retinopathy: a screening approach in the primary care setting. *Diabetes Care* 24:2086–2090, 2001
17. Shahidi M, Ogura Y, Blair NP, Rusin MM, Zeimer R: Retinal thickness analysis for quantitative assessment of diabetic macular edema. *Arch Ophthalmol* 109:1115–1119, 1991
18. Oshima Y, Emi K, Yamanishi S, Motokura M: Quantitative assessment of macular thickness in normal subjects and patients with diabetic retinopathy by scanning retinal thickness analyser. *Br J Ophthalmol* 83:54–61, 1999
19. Sanchez-Tocino H, Alvarez-Vidal A, Maldonado MJ, Moreno-Montanes J, Garcia-Layana A: Retinal thickness study with optical coherence tomography in patients with diabetes. *Invest Ophthalmol Vis Sci* 43:1588–1594, 2002
20. Pires I, Bernardes RC, Lobo CL, Soares MA, Cunha-Vaz JG: Retinal thickness in eyes with mild nonproliferative retinopathy in patients with type 2 diabetes mellitus: comparison of measurements obtained by retinal thickness analysis and optical coherence tomography. *Arch Ophthalmol* 120:1301–1306, 2002
21. Ophthalmology AAO: International clinical diabetic retinopathy severity scale [article online], 2002. Available from http://www.aao.org/aao/education/library. Accessed 20 August 2003
22. The Diabetic Retinopathy Study Research Group: Photocoagulation treatment of proliferative diabetic retinopathy: clinical application of Diabetic Retinopathy Study (DRS) findings, DRS report number 8. *Ophthalmology* 88:583–600, 1981
23. Ho T, Smiddy WE, Flynn HW Jr: Vitrectomy in the management of diabetic eye disease. *Surv Ophthalmol* 37:190–202, 1992
24. Otani T, Kishi S: A controlled study of vitrectomy for diabetic macular edema. *Am J Ophthalmol* 134:214–219, 2002
25. Gandorfer A, Messmer EM, Ulbig MW, Kampik A: Resolution of diabetic macular edema after surgical removal of the posterior hyaloid and the inner limiting membrane. *Retina* 20:126–133, 2000
26. Neubauer AS, Priglinger S, Ullrich S, Bechmann M, Thiel MJ, Ulbig MW, Kampik A: Comparison of foveal thickness measured with the retinal thickness analyzer and optical coherence tomography. *Retina* 21:596–601, 2001
27. Zeimer RC, Mori MT, Khoobehi B: Feasibility test of a new method to measure retinal thickness noninvasively. *Invest Ophthalmol Vis Sci* 30:2099–2105, 1989
28. Zeimer R, Shahidi M, Mori M, Zou S, Asrani S: A new method for rapid mapping of the retinal thickness at the posterior pole. *Invest Ophthalmol Vis Sci* 37:1994–2001, 1996
29. Owens DR, Dolben J, Young S, Ryder RE, Jones IR, Vora J, Jones D, Morsman D, Hayes TM: Screening for diabetic retinopathy (Review Article). *Diabet Med* 8 (Spec. no.):S4–S10, 1991
30. Kinyoun J, Barton F, Fisher M, Hubbard L, Aiello L, Ferris F 3rd: Detection of diabetic macular edema: ophthalmoscopy versus photography: Early Treatment Diabetic Retinopathy Study report number 5: the ETDRS Research Group. *Ophthalmology* 96:746–750, 1989 [discussion 750-751]
31. Moller F, Hansen M, Sjolie AK: Is one 60° fundus photograph sufficient for screening of proliferative diabetic retinopathy? *Diabetes Care* 24:2083–2085, 2001
32. von Wendt G, Ronnholm P, Heikkila K, Summanen P: A comparison between one- and two-field 60 degree fundus photography when screening for diabetic retinopathy. *Acta Ophthalmol Scand* 78:14–20, 2000
33. von Wendt G, Heikkila K, Summanen P: Detection of retinal neovascularizations using 45 degrees and 60 degrees photographic fields with varying 45 degrees fields simulated on a 60 degrees photograph. *Acta Ophthalmol Scand* 80:372–378, 2002
34. von Wendt G, Heikkila K, Summanen P: Assessment of diabetic retinopathy using two-field 60 degrees fundus photography: a comparison between red-free, black-and-white prints and colour transparencies. *Acta Ophthalmol Scand* 77:638–647, 1999
35. Harding SP, Broadbent DM, Neoh C, White MC, Vora J: Sensitivity and specificity of photography and direct ophthalmoscopy in screening for sight threatening eye disease: the Liverpool Diabetic Eye Study. *BMJ* 311:1131–1135, 1995
36. Shahidi M, Ogura Y, Blair NP, Zeimer R: Retinal thickness change after focal laser treatment of diabetic macular oedema. *Br J Ophthalmol* 78:827–830, 1994