The Feasibility of Using Ultra-Widefield Retinal Imaging to Identify Ocular Pathologies amongst Those with Systemic Medical Disease Attending a Tertiary Healthcare Facility at a University Hospital

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Ultra-widefield imaging · Screening · Retina · Feasibility

Abstract
Aims: The aim of the study was to evaluate the feasibility of ultra-widefield (UWF) imaging to identify ocular pathologies amongst in- and out-patients in a tertiary university hospital.

Methods: We followed a prospective double-blinded multicenter clinical study. In total, 634 patients from a university hospital with pulmonary, cardiovascular, and endocrine diseases were examined by two teams by conventional slit-lamp biomicroscopy (CBM). UWF images with Optos Tx200 were taken and subsequently graded independently by two retina specialists and graders from two reading centers for the presence of predefined pathologies. Interrater reliability was calculated using Fleiss statistical software. An independent, trained and certified ophthalmologist with retinal subspecialty (BL) classified all UWF images with retinal hemorrhages by severity and interrater agreement. Results: Complete data were available for 502 patients. The Moorfields Eye Hospital Reading Center, London, UK (RM), reported the highest number of cases with retinal pathologies (378), and the Reading Center GRADE Bonn, Germany (RB), did so for cases with optic disc cupping (466). Two retinal consultants (R1 and R2) from the Department of Ophthalmology, University Hospital Giessen and Marburg GmbH, Campus Giessen, Germany, noted optic disc pathologies. R1 reported 151 cases with optic disc pallor, while R2 reported only 39 disc pathologies. Both for clinical and for image readers, the early changes had equally low interrater reliability. The presence of at least 3 retinal hemorrhages had the highest interrater reliability (0.59). Conclusions: UWF imaging is convenient to identify overt retinal pathologies in patients at risk of ocular complications of their systemic disease who are attending hospital clinics. Imaging the eye allows for remote retinal assessment and for placing the patient into the appropriate clinical pathway for ophthalmology.

Precis: UWF-imaging in a population of in- and out-patients at a university hospital who are at risk of retinal complications is effective to detect overt retinal pathologies and allows for tele-ophthalmology approaches to be enabled for placing the patients into the appropriate clinical pathways.

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Introduction

Chronic systemic diseases may have characteristic ophthalmic signs, such as microvascular retinal changes, that might be seen by regular eye examinations prior to the occurrence of clinical symptoms. Many patients with chronic systemic diseases are elderly and frequently attend hospital services for their systemic disease. This represents an opportunity to check for common eye diseases in that age group, including diabetic eye disease, age-related macular degeneration, and glaucoma [1–3]. Funduscopy by conventional slit-lamp biomicroscopy (CBM) in mydriasis carried out by medically qualified examiners is regarded as the gold standard. This has been complemented by ophthalmic imaging, lately using ultra-widefield (UWF) retinal imaging, in response to the increasing demand for ophthalmic examination and the need for establishing lasting records for comparison [4–10]. The Optos Tx200 camera (Optos, Dunfermline, Scotland, UK) and its newer counterparts allow the imaging and subsequent assessment of up to 200° of the retina without pupil dilatation.

UWF imaging (UWFI) is useful in imaging posterior segment diseases, such as diabetic retinopathy (DR) [11–15] and other retinal pathologies [16–19]. Patients with pulmonary, endocrine, autoimmune, and other systemic diseases often have retinal pathologies such as hemorrhages, inflammatory alterations, and vascular conditions. Relevant retinal changes can be imaged on UWF, then subsequently analyzed and referred for appropriate clinical opinion where required. In addition, UWFI has been shown to be useful for routine fundus examination after cataract surgery [20] and for annual health check-up examinations [21] in detecting silent retinal detachment and retinal holes.

There is no clarity where UWFI-guided referral might fit in for the care of patients with systemic diseases [5, 22–24]. Superiority of UWFI was reported when combined with OCT compared to CBM only in the classification of DR [25]. As a component of the medical retina virtual clinic, UWFI is considered to represent an effective triaging tool in order to detect pathologies that require treatment [26]. With the COVID-19 pandemic, the interest in remote examination has increased further [27].

In this prospective double-blinded study, we analyzed the feasibility of using UWFI compared to CBM to detect pathologies in patients with systemic diseases in- and outpatient clinics of a tertiary referral center. Our aim was to establish what specific retinal pathologies can be detected in such a high-risk cohort and where UWFI might fit into the clinical and referral pathway for such patients.

Methods

Patients

In this prospective double-blinded study conducted over 6 months between July and December 2012, 634 in- and outpatients with endocrine, cardiovascular, and/or pulmonary diseases from the Departments of Internal Medicine of the University Hospital Giessen and Marburg GmbH, Campus Giessen, Germany, were included. These departments were selected as they had the highest number of bedside ophthalmic consultation requests in previous years. The study was approved by the Ethics Committee of the University of Giessen (No. 64/12) and conform to the tenets of the Declaration of Helsinki. All patients signed an informed consent to be included in the study. Exclusion criteria were inability to comply with either CMB or UWFI or contraindication for pupil dilatation due to angle closure or allergy to eye drops (see Fig. 1).

Data Acquisition by UWFI and CBM

UWF images were collected by a trained and certified study nurse. Images were taken without pupil dilatation in the primary position, raising the eyelid to better visualize the peripheral fundus with Optos Tx200. In each patient, for both eyes, images with 3,900 × 3,072 pixels were taken and subsequently analyzed using Optomap Vantage 2 software (OPTOS Plc, Dunfermline, Scotland, UK).

For CBM, tropicamide 1% eye drops (Mydriatikum Stulln®, Pharma Stulln, Stulln, Germany) were instilled twice at a 5-min interval in order to achieve good pupil dilatation. CBM was performed 30 min after pupil dilatation using a 90 diopter lens (Volk Optical Inc., Mentor, OH, USA) on a slit lamp (Haag-Streit Type 900, Haag Streit AG, Koeniz, Switzerland). Each patient was examined by 2 independent teams of certified ophthalmologists, denoted as CBM1 and CBM2. They were masked to each other’s findings and had no access to UWFI.

Assessment Protocol and Statistical Analysis

Predefined pathologies of the optic disc, macula, retinal vessels, and tumors were noted on a specially developed score-sheet as (1) present or (0) absent (see online suppl. Table 2; for all online suppl. material, see www.karger.com/doi/10.1159/000526573).

UWF images were analyzed by 3 different sets of graders:

1. Two independent retinal consultants (R1 and R2) from the Department of Ophthalmology, University Hospital Giessen and Marburg GmbH, Campus Giessen, Germany, in order to understand the variability between retinal specialists.

2. Images were graded by senior image graders both at the Moorfields Reading Centre, Moorfields Eye Hospital NHS Foundation Trust, London, UK (RM), and by the GRADE Reading Centre of the University Eye Hospital Bonn, Germany (RB). All graders were masked to each other’s grades and to the clinical findings reported by R1/R2 and CBM1/CBM2.

3. In order to clarify the inter-rater agreement outcomes, the feature “retinal hemorrhages” was selected for confirmatory grading by an independent, trained, and certified ophthalmologist with retinal subspeciality, BL, who was masked to all results other than knowing that at least one grader had noted retinal hemorrhage on these images. BL had no access to R1/R2 and CBM1/CBM2 grades. The feature “retinal hemorrhage” was selected as it was deemed to be the least ambiguous retinal abnormality.

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Statistical Methods

Statistical analysis was performed with SPSS Statistics 26 (SPSS Inc., Chicago, IL, USA) and Microsoft Excel 2019 (Microsoft Corporation, Redmond, WA, USA). The interrater reliability was calculated using Fleiss’ Kappa.

Interrater reliability was determined for every abnormality by using Fleiss’ Kappa coefficient: <0.00 poor, 0.00–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, 0.81–1.00 almost perfect agreement [28]. Statistical analysis was performed with SPSS Statistics 26 (SPSS Inc.) and Microsoft Excel 2019 (Microsoft Corporation).

Results

Altogether, 634 patients were enrolled. All medical history and relevant data were collected and pseudonymized (see online suppl. Table 1). Incomplete data from 45 patients with poor health condition who were unable to participate in the examination and images with insufficient quality from further 87 patients were excluded. Most of them were over 60 years old (91
Table 1. Pathologies assessed

| Examination method | slit-lamp | retina specialists | reading centers | slit-lamp | retina specialists | reading centers | CBM1 | CBM2 | R1 | R2 | RM | RB | CBM1/ CBM2 | R1/R2 | RM/RB | R1/R2/ RM/RB | all |
|--------------------|-----------|--------------------|----------------|-----------|--------------------|----------------|------|------|-----|-----|----|----|----------|--------|--------|----------------|-----|
| Examiner:          |           |                    |                |           |                    |                |      |      |     |     |     |     |          |        |        |                 |     |
| CBM1               | 68        | 37                 | 151            | 16        | 3                  | 6              | 18   | 7    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| CBM2               | 49        | 38                 | 153            | 31        | 74                 | 466            | 22   | 18   | 49  | 3   | 1   |    |          |        |        |                 |     |
| R1                 | 0         | 1                  | 8              | 0         | 4                  | 1              | 0    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| R2                 | 50        | 53                 | 12             | 83        | 97                 | 11             | 25   | 7    | 8   | 1   | 1   | 1  | 1        |        |        |                 |     |
| RM                 | 4         | 4                  | 2              | 12        | 19                 | 2              | 2    | 1    | 1   | 1   | 1   | 1  | 1        |        |        |                 |     |
| RB                 | 4         | 5                  | 3              | 10        | 1                 | 1              | 1    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| CBM1/ CBM2         | 50        | 53                 | 12             | 83        | 97                 | 11             | 25   | 7    | 8   | 1   | 1   | 1  | 1        |        |        |                 |     |
| R1/R2              | 4         | 5                  | 3              | 10        | 1                 | 1              | 1    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| RM/RB              | 4         | 5                  | 3              | 10        | 1                 | 1              | 1    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| R1/R2/ RM/RB       | 4         | 5                  | 3              | 10        | 1                 | 1              | 1    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Optic disc pallor  | 68        | 37                 | 151            | 16        | 3                  | 6              | 18   | 7    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Optic disc CDR >0.5| 49        | 38                 | 153            | 31        | 74                 | 466            | 22   | 18   | 49  | 3   | 1   |    |          |        |        |                 |     |
| Macula hemorrhage  | 7         | 6                  | 5              | 11        | 46                 | 5              | 1    | 2    | 4   | 1   | 0   | 0  | 0        |        |        |                 |     |
| Macula edema       | 3         | 6                  | 0              | 3         | 5                  | 2              | 2    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Macula NVD         | 4         | 4                  | 2              | 12        | 19                 | 2              | 2    | 1    | 1   | 1   | 1   | 1  | 1        |        |        |                 |     |
| Macula atrophy     | 4         | 5                  | 3              | 10        | 1                 | 1              | 1    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Macula fibrosis    | 11        | 15                 | 8              | 1         | 0                  | 0              | 4    | 1    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Macular epiretinal gliosis| 14 | 25 | 8 | 9 | 40 | 1 | 11 | 1 | 6 | 0 | 0 |          |        |        |                 |     |     |
| Vessel microaneurysms| 1     | 0                  | 4              | 0         | 2                  | 0              | 0    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Vessel macroaneurysms| 2     | 2                  | 2              | 0         | 2                  | 1              | 1    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Vessel IRMA        | 8         | 8                  | 7              | 0         | 5                  | 1              | 3    | 0    | 1   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Retina preretinal hemorrhage| 24 | 25 | 22 | 31 | 64 | 10 | 14 | 22 | 12 | 8 | 4 |          |        |        |                 |     |     |
| Retina intra-/subretinal hemorrhage| 2 | 9 | 7 | 5 | 10 | 4 | 0 | 1 | 0 | 1 | 0 |          |        |        |                 |     |     |
| Retina edema       | 0         | 0                  | 0              | 0         | 1                  | 0              | 0    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Retina detachment  | 2         | 0                  | 14             | 1         | 0                  | 0              | 0    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Retina cotton wools| 5         | 7                  | 7              | 1         | 14                 | 3              | 3    | 1    | 2   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Retina degeneration| 115       | 101                | 51             | 43        | 131                | 22             | 50   | 19   | 26  | 2   | 1   |    |          |        |        |                 |     |
| Retina tear        | 7         | 3                  | 17             | 0         | 1                  | 0              | 0    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Tumor pigmented   | 17        | 19                 | 15             | 7         | 13                 | 14             | 7    | 3    | 4   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Tumor non pigmented| 0 | 1                  | 6              | 0         | 1                  | 1              | 0    | 0    | 0   | 0   | 0   | 0  | 0        |        |        |                 |     |
| Total pathologies  | 402       | 375                | 503            | 266       | 536                | 557            | 23   | 16   |      |      |      |    |                      |        |        |                 |     |

Pathologies detected by the different examiners with different examination methods. CBM1, conventional slit-lamp biomicroscopy Grader 1; CBM2, conventional slit-lamp biomicroscopy Grader 2; R1, OPTOS Reader 1; R2, OPTOS Reader 2; RM, Reader Moorfields; RB, Reader Bonn.
patients) and had lung diseases (47 patients). This resulted in a cohort of 502 patients who had complete data and image-set for analysis. Of these, 167 patients (33.3%) had endocrine disorders, 125 patients (24.9%) had cardiovascular disease, and 183 patients (36.5%) had pulmonary disease. The remaining 27 patients (5.3%) could not be assigned unambiguously to one of the 3 categories.

The average age of the 502 subjects in the final cohort was 61.0 years; 48.9% were male. There was no significant difference between the full cohort of 634 and that of 502 with full dataset in terms of age, gender, and distribution of the disease (p values over 0.1 for all categories).

**Grading Results**

Pathologies detected by the different graders are shown in Table 1. Interrater reliability (Fleiss’ kappa coefficient) is shown in Table 2.

| Table 2. Interrater variability |
|--------------------------------|
| Examiner                  | CBM1, CBM2, R1 | CBM1, CBM2, R2 |
|-----------------------------|----------------|----------------|
| Optic disc total            | 0.151          | 0.167          | 0.259          |
| Macula total                | 0.197          | 0.282          | 0.231          |
| Vessel total                | 0.284          | 0.413          | 0.351          |
| Retina total                | 0.311          | 0.290          | 0.317          |
| Tumor total                 | 0.274          | 0.283          | 0.298          |
| Optic disc palor            | 0.05           | 0.059          | 0.164          |
| Optic disc CDR >0.5         | 0.177          | 0.167          | 0.366          |
| Macula drusen               | 0.130          | 0.209          | 0.172          |
| Vessel microaneurysms       | 0.265          | 0.385          | 0.290          |
| Retina intra-/subretinal hemorrhage | 0.594 | 0.571          | 0.564          |
| Retina degeneration         | 0.209          | 0.208          | 0.221          |

CBM Grading

CBM 1 versus CBM 2 identified 68 and 37 cases of optic disc pallor, macular hemorrhages in 7 and 6 cases, macular drusen in 50 and 53 cases, and epiretinal membrane in 11 and 15 cases, respectively.

Retinal Consultants’ UWF Grading

R1 identified the highest number of optic disc pallor in 151 cases while R2 noted 16 cases; possible peripheral retinal detachment was noted in 14 cases by R1 and in one case by R2. In comparison, R1 detected more optic disc pathologies (161) as opposed to 31 in R2. For macular pathologies, the pattern was reversed (122 cases for R2 as opposed to 30 for R1).

Reading Centers

The two grading centers, RM and RB, identified the highest number of pathologies overall (RM: 536, RB: 557 compared to CBM1: 402, CBM2: 375, R1: 503, and
R2: 266). Data show that RM noted more retinal pathologies, whereas RB preferentially noted optic disc pathologies. RM graded the highest numbers of cases with macular, vascular, and retinal pathologies (144, 44, and 190 cases respectively), whereas RB did so for the optic disc pathologies (470). Macular drusen and macular hemorrhage, microaneurysms, retinal hemorrhage, retinal degenerations were the most frequently seen pathologies by RM (97, 46, 40, 64, and 131, respectively). RB identified the highest number of enlarged optic disc cupping (466) but the lowest number of cases with macular, vascular, and retinal pathologies (19, 2, and 36 cases).

**Overall Comparison between CBM and UWFI Based Grading**

When comparing all UWFI OPTOS image grading (R1, R2, RB, and RM) to the conventional slit-lamp biomicroscopy findings (CBM1 and CBM2), interrater reliability was as follows:

1. Slight for optic disc pathologies for R1 and fair for R2, RB, and RM.
2. Slight for macular pathologies for RM and fair for R1, R2, and RB.
3. Fair for vascular pathologies for R2 and RB.
4. Fair for retinal pathologies and for tumors for all.

Looking at the most prevalent lesions (optic disc pallor, optic disc cupping, macular drusen, microaneurysms, intra-/subretinal retinal hemorrhage, and retinal degeneration) in-

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**Table 3. Initial diagnosis of retinal hemorrhages compared to classification in the posthoc subanalysis**

| Initially diagnosed by n examiners | Retrospectively n lesions found |
|-----------------------------------|-------------------------------|
|                                   | 0    | 1–2 | 3–10 | >10 |
| 1                                  | 45   | 38  | 6    | 1   | 0   |
| 2                                  | 14   | 5   | 5    | 2   | 2   |
| 3                                  | 2    | 0   | 2    | 0   | 0   |
| 4                                  | 7    | 1   | 2    | 2   | 2   |
| 5                                  | 9    | 0   | 2    | 6   | 1   |
| 6                                  | 4    | 0   | 1    | 2   | 1   |

Data were re-evaluated by BL who was masked to the previous results except the fact that at least one of the OPTOS graders had noted retinal hemorrhage. Consensus among examiners was high for clear pathologies i.e., at least 3 hemorrhages. However, only few patients had that many hemorrhages.

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![Fig. 2. Examples of increasing number of retinal hemorrhages. High inter-rater agreement when at least 3 hemorrhages were present. See Table 3.](image-url)

- **a** Optos Optomap Panoramic Tx200 image. Only RM diagnosed retinal hemorrhage. BL did not diagnose retinal hemorrhage in the retrospective grading (right eye, Patient AE0003).
- **b** Optos Optomap Panoramic Tx200 image. Only RM and R2 diagnosed retinal hemorrhage. BL marked the retinal hemorrhage in the retrospective grading (right eye, Patient BM0001).
- **c** Optos Optomap Panoramic Tx200 image. All image readers diagnosed retinal hemorrhage. BL marked the retinal hemorrhage in the retrospective analysis (right eye, Patient SW0002).
- **d** Optos Optomap Panoramic Tx200 image. All image readers diagnosed retinal hemorrhage. BL diagnosed >10 hemorrhages in the retrospective analysis (right eye, Patient HW0004).
The Feasibility of Ultra-Widefield Retinal Imaging

The Feasibility of Ultra-Widefield Retinal Imaging was assessed with a focus on interrater reliability for UWF readers. All four graders of the Optos images (R2, R3, RB, and RM) agreed in identifying pathological cases in 23 patients (4.6%), whereas all graders agreed only in 16 (3.2%). Data were re-evaluated by BL who was masked to the previous results except for the fact that at least one of the OPTOS graders had noted retinal hemorrhage. The results of the subanalysis are shown in Figure 2a–d and Table 3. Examples for optic disc evaluation by image graders are given in Figure 3a–d.

The feature retinal hemorrhage was re-evaluated by BL for all images where at least one grader had seen a retinal hemorrhage. BL was masked to the previous results and classified by severity of changes and interrater agreement. BL found that interrater reliability was lower in uncertain results, i.e., for retinal hemorrhages, interrater reliability was lower if only one or two lesions were present (see Table 3), but high when ≥3 hemorrhages were present (see Fig. 2a–d). Most patients in our cohort had fewer than 3 retinal hemorrhages, which can explain low interrater reliability.

Discussion

We analyzed the potential of using UWF imaging to place patients with systemic diseases at risk of ocular involvement into appropriate clinical pathways when attending their non-eye-related appointment. Enabling such a pathway will minimize additional hospital attendance and will detect retinal and optic disc pathologies in this high-risk patient cohort in a timely manner.

Our results show that UWF imaging has the potential for detecting ocular pathologies that might require referral for assessment and treatment in ophthalmology services. This approach has an impact on reducing burden and planning care for the most vulnerable in our society which has never been more important than during the current pandemic.

For all groups, reliability was fair to moderate when singular pathological changes were considered but increased where obvious pathologies were noted. Our study also showed that slit-lamp examination by multiple ophthalmologists can also produce divergent grading results, a finding that can have far-reaching consequences when establishing ground truth for future studies comparing image grading results and clinical examination.

Recent reports demonstrated a moderate to high interrater reliability for diabetic retinopathy assessment between two Optos UWF graders [11, 12]. Similarly, a high level of agreement was found detecting retinal changes after cataract surgery between Optos UWF, slit-lamp biomicroscopy and Goldmann three-mirror contact lens [20]. However, literature is inconsistent [16–18].

In our study, we attempted to identify pathologies of the optic disc, macula, retinal vessels, retina and tumors using different grading methods as opposed to aiming to detect one disease, such as diabetic retinopathy [11, 12, 29]. In agreement with the literature, retinal hemorrhages showed the highest interrater reliability in our study, especially for UWF, and this might be linked as to why diabetic retinopathy studies show such high interrater reliability [11, 12].

In agreement with studies reporting on image-assisted examination [24], we also found a variation between graders by lesion types. This was true not only for the im-

Fig. 3. Examples of agreement and non-agreement among graders of optic disc pathology. a, b Optos Optomap Panoramic Tx200 image. All image readers consented in grading the excavation of the optic disc >0.5 cup-to-disc ratio (right eye, Patient HF0002). c, d Optos Optomap Panoramic Tx200 image. The image readers did not consent in grading the optic disc as glaucomatous or not.
age analysis but also for clinical examination. Our results suggest that not only those analyzing the images but also clinicians themselves have a predilection for recording and reporting on certain abnormalities. This finding strengthens the argument for good quality training before a new clinical pathway is set up so all healthcare professionals are appropriately trained for analyzing and recording clinical findings.

The Optos device has false color rendering and this can make image analysis difficult for those not familiar with such an image. This was brought out by grading from RB, where graders had limited experience in false rendering images but a vast experience in other UWFI. This might have also contributed to the difficulties in optic disc grading. This learning point might be of interest for establishing automated image analysis software and we are waiting to see if this might eliminate such discrepancies in the interpretation of images.

The strength of the study is the large number of at-risk patients with systemic disease who were systematically examined and imaged by trained staff. The unexpected finding was that our patients had only a lower than anticipated number of sight-threatening disease, therefore limiting our ability to see how a new clinical pathway including Optos UWFI would perform for such patients. The limitation of our study is that we used an older version of the Optos device. We appreciate that with newer devices like the Optos California a higher contrast of the peripheral retinal imaging can be achieved. However, it was shown that with the Optos Tx200 device equal angular UWFI images can be recorded at same visible retinal area [30, 31].

Conclusions

Our analysis demonstrates that Optos UWFI has the potential for being included in a clinical pathway for imaging patients with systemic disease at the time of attending their medical clinic appointments. Such an inclusion would minimize travel burden for the patients and their carers and would lower the number of hospital appointments required for those without treatment-requiring eye diseases noted on their images. Our results also show that training of clinicians and graders must be undertaken so consistent and useful results are generated. Further benefit of imaging repository is that use of artificial intelligence in the future can enable immediate feedback on relevant eye pathologies and will allow for better documentation, prognostication, and new biomarker discovery. Having immediate image analysis results will allow the attending physicians to discuss eye findings with the patients, and only those requiring further assessment and treatment will be seen by the ophthalmology department [32–34].

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Statement of Ethics

The study was approved by the Ethics Committee of the University of Giessen (No. 64/12) and conformed to the tenets of the Declaration of Helsinki. A written informed consent was obtained from participants to participate in the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Matthias Fritz Uhrmann, Tunde Peto, Timo Bullmann, Monika Andressi-Darida, Mathis Schumann, Steffen Schmitz-Valckenberg, Frank Holz, and Birgit Lorenz meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article. They made substantial contributions to the conception and design of the work and interpretation of data and participated in drafting and revising it critical for important intellectual content. They have approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.
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